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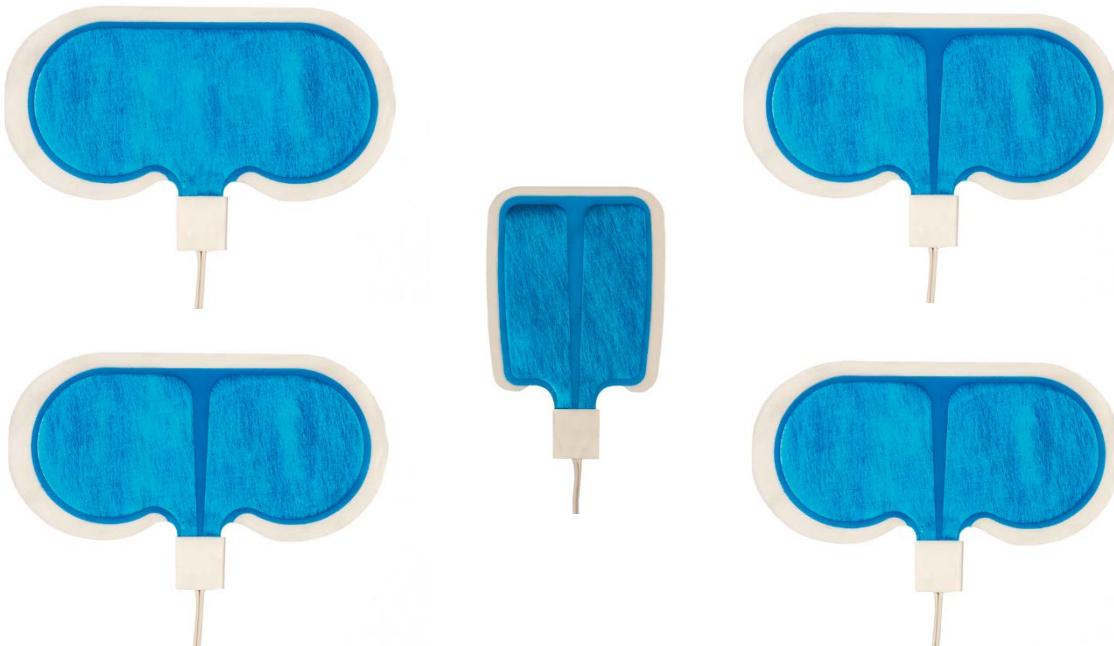
**Megadyne, Inc.**

## **Clinical Evaluation Report**

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### **Disposable Patient Return Electrodes** **SCN070739**

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## 1. EXECUTIVE SUMMARY

This clinical evaluation conducts a comprehensive analysis of all available clinical and non-clinical data for the currently CE marked devices in scope relevant to their intended purpose. The Megadyne Family of Disposable Patient Return Electrodes is intended for use during surgical procedures to conduct monopolar electrosurgical energy from target tissue of a patient back to an electrosurgical unit (ESU), or generator. Electrosurgery is a specialized process and is performed only by trained surgical professionals and is restricted to use by or on the order of a physician. The product family in scope of this update CER includes the following devices:

Product Code	Device Description
0850C	Adult Patient Return Electrode, single plate, with 9-foot (2.7m) pre-attached cord >33 lbs.
0855	Adult Patient Return Electrode, dual plate, no cord >33lbs.
0855CL	Adult Patient Return Electrode, dual plate, with 15-foot (4.6m) pre-attached cord >33 lbs.
0855CN	Adult Patient Return Electrode, dual plate, with 9-foot (2.7m) pre-attached cord >33 lbs.
0865C	Pediatric Patient Return Electrode, dual plate, with 9-foot (2.7m) pre-attached cord 6-33 lbs.

Monopolar electrosurgery represents the oldest and most mature state of the art type of electrosurgical energy used in the majority of surgical procedures globally. This monopolar configuration utilizes three components: 1.) a generator that produces the RF energy for the active electrode; 2.) a dispersive electrode (patient return electrode), which is placed on the patient at a location remote from the surgical site and returns energy back to the generator; and 3.) an active electrode (a pencil and an electrode tip) which conducts radio frequency (RF) energy to the surgical site. Only the patient return electrodes are in scope of this CER.

The subject devices are to conform to the European Council Directive 93/42/EEC (Medical Device Directive (MDD) as amended by 2007/47/EC. The Disposable Patient Return Electrode subject devices in-scope of this CER are defined as Class IIb medical devices by Annex IX Rule 9. The subject device family has been available globally for 13 years, having received CE Mark certification in 2006. Moreover, the adult electrodes (0850C, 0855, 0855CL, 0855CN) received FDA 510(k) clearance in March 2006 and the pediatric electrode (0865C) received FDA 510(k) clearance in August 2007. There have been no serious adverse events or recalls during the past 13 years, demonstrating the safety of these clinically well-established devices.

The body of evidence in support of this CER includes non-clinical bench-top studies (refer to Section 6.2) and clinical data on the Megadyne Disposable Patient Return Electrodes (Sections 6.7, 6.9 and 7) following the clinical route of conformity. The clinical data sources on the subject devices includes post-market surveillance (PMS) data and real-world epidemiology data (Epi Data). In addition, a systematic literature review was conducted for the subject devices, covering the period between 01 January 1986 and 03 September 2019. This period was inclusive of the launch dates for all the subject devices and was undertaken in the core bibliographic databases of Medline and Embase via Ovid, and PubMed. Even with such an exhaustive search, however, zero articles were identified that had published data related to the subject devices. The Megadyne Disposable Patient Return Electrodes are widely used and clinically well-

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established with a low risk profile, and the lack of data in the clinical literature is attributable to the ancillary nature of these devices and that they are generally not the focus of clinical study.

The PMS analysis covers data on the Megadyne Disposable Patient Return Electrodes for the 5-year period from February 2014 through January 2019. The analysis includes: 1) Overall complaint rates (per procedure), 2) Individual Product Experience Code (PEC) complaints types and rates, 3) Patient consequences (adverse events) by Patient Codes (PC) and rates, 4) Medical Device reporting (MDR) and Medical Device Vigilance (MDV) reportable events, and 5) External vigilance data including CAPAS, Escalations, Alerts, and Field Actions. The overall complaint rate for the family of Megadyne Disposable Patient Return Electrodes was very low at 0.0027% for a total of 4,980,999 units sold during the 5-year analysis period. Refer to Section 7.1 for a complete summary of the world-wide sales and complaint data for the subject device family. There were no new patient harms reported for these complaints and no patient safety related issues were identified.

An observational, retrospective cohort study was conducted to collect and analyze real-world Epi data on the subject devices. The observational aspect of this study allowed for understanding the use of Megadyne® Disposable Patient Return Electrodes, and the potential risks associated with the device in the real-world setting. The primary study endpoint was incidence of thermal injury as the only complication of interest. Inclusion criteria consisted of patients who underwent an inpatient or outpatient procedure with utilization of Megadyne Disposable Patient Return Electrodes (n = 22,151). The incidence of thermal injury following use of Megadyne Disposable Patient Return Electrodes across multiple types of surgical procedures and hospital settings was exceedingly low over a 20-year time period. Further, the relative risk of thermal injury from Megadyne Disposable Patient Return Electrodes was comparable to similar devices on the market during the same time period demonstrating that subject devices are within the State of the Art for disposable patient return electrodes.

The clinical route of conformity for the Megadyne Disposable Patient Return Electrodes critically reviews the body of clinical data from the sources described above, and assesses specific predefined safety and performance endpoints such as: 1.) successful use of monopolar electrosurgery in surgical procedures, 2.) successful attachment of the electrode pad, 3.) successful return electrode grounding, 4.) rates of electromagnetic interference (EMI) caused by electro-surgery for various surgical locations, and 5) adverse event reporting as related to monopolar electrosurgery (acute thermal injury, etc.). As demonstrated in this CER, these data individually and collectively consistently and favorably demonstrate safety and performance of the Megadyne Disposable Patient Return Electrodes in accordance with a high degree of protection and health for both the patient and the User (ER1 and ER3).

This CER will objectively analyze all data collected in the post-market phase. This includes consideration of published literature on the subject devices as well as traditional forms of post-market surveillance (complaints and vigilance). These data will be used to closely monitor and further confirm the current favorable benefit-to risk ratio in the post-market phase.

Collectively, sufficient clinical data exists to support the safety and performance of the Megadyne Disposable Patient Return Electrode subject devices in accordance with the intended purpose from the IFUs (Adult IFU NR74330 Rev. G 2016-03, Pediatric IFU NR74380 Rev. F 2016-03). Both PMS and Epi data consistently demonstrate an exceedingly low complaint rate and safe performance (completion of the electrical circuit without burns or thermal injury to the patient). There are no unanswered questions for these clinically well-established legacy device, therefore, no post-market clinical follow-up (PMCF) studies are required at this time. Proactive clinical data in the form of Epi data will continue to be collected on the subject devices.

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Based on the clinical data appraisal and analysis in this report as informed by the Risk Management and PMS documentation, all residual risks are deemed acceptable when weighed against the benefits to the patient based on current knowledge / the state of the art regarding these clinically well-established electrosurgical disposable patient return electrodes. Therefore, the clinical evaluation conforms with the relevant Essential Requirements (Annex 1) of the European Council Directive 93/42/EEC. Given the risk evaluation of the Megadyne Disposable Patient Return Electrodes family, the frequency of updates for the clinical evaluation is determined to be at least every 4 years for these Class IIb legacy devices in scope of this CER.

Refer to Appendix 10.1 for supporting documents referenced in the CER.

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## 2. SCOPE

### 2.1. Objective

The objective of this clinical evaluation process is to establish conformity with the relevant Essential Requirements of the European Medical Device Directive (MDD) 93/42/EEC (amended by Directive 2007/47/EC). The planning and execution of the clinical evaluation is conducted in accordance with the principles of MEDDEV 2.7/1(Revision 4), Guidance for “Clinical Evaluation: A Guide for Manufacturers and Notified Bodies”, and internal processes for planning and executing a CER (Franchise Procedure for Evaluation of Clinical Data for CE-Marking, PR-0000277, Rev. 20) and Literature Review (Megadyne Systematic Literature Review Protocol, Doc #100503711 Rev 1).

This clinical evaluation report (CER) is an output of the process to document the collection, appraisal, and analysis of the available clinical data relevant to the subject devices and to determine whether there is sufficient clinical evidence on the safety and performance in accordance to the intended purpose. In addition, the report documents the benefit-risk profile including side-effects in the intended target patient populations and medical indications by assessing the clinical evidence against the hazards and patient harms as informed by the Risk Management and PMS documentation. The report also demonstrates the acceptability of that profile with basis from the current knowledge/state of the art in the field of energy-based electrosurgery.

### 2.2. Subject Device Overview and Regulatory History

This clinical evaluation of the Megadyne Disposable Patient Return Electrodes product family includes five subject devices as presented in Table 1, below. The legal manufacturer for the Megadyne Disposable Patient Return Electrodes is:

Megadyne Medical Products, Inc.

11506 South State Street

Draper, Utah 84020 USA

Megadyne Medical Products, Inc. is an External Manufacturer of Ethicon, a Johnson & Johnson Company.

The Megadyne Disposable Patient Return Electrode subject devices are single-use, non-sterile electrosurgical accessories used to adhere to the patient over the entire pad surface to complete the electrosurgical circuit between the generator, the active electrode and the patient. The return electrodes are comprised of a power cord (if attached) and a disposable pad. The return pad is made of a biocompatible, adhesive, conductive gel arranged on a flexible foam backing.

The subject devices are single-use non-implantable, surgical devices which involve limited contact with tissue (<24 hour cumulative, limited to contact with the skin surface (refer to Section 4)), and have been designated as a Class IIb medical device in accordance with Annex IX Rule 9 of the European Council Directive 93/42/EEC (MDD). These legacy CE-marked devices have been available for 13 years globally, receiving CE mark certification and launched in the EU in 2006 (*Source: Clinical Evaluation Report, New Deantronics Disposable Grounding Pad, CER-06, Version 06 (05/15/2018)*). The adult return electrodes (0850C, 0855, 0855CL, 0855CN) were FDA cleared on 31 March 2006 (K060255) and the pediatric return electrodes (0865C) received FDA clearance on 31 August 2007 (K071080), so therefore have been

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marketed in the US for over 12 years. A complete list of product codes and descriptions of the devices is also provided in Appendix 10.2.

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**Table 1: Overview of the Megadyne Family of Disposable Patient Return Electrodes**

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Product Code	Description	EU MDD Device Class	Regulatory Status	GMDN TERM	Technical Document Number	Intended Purpose	Device Image
0850C	Patient Return Electrode, Adult, single plate, with 9-foot (2.7m) pre-attached cord >33 lbs	EU Class IIb (Rule 9 Annex IX)	<b>Initial CE Mark:</b> 2006 (CE 96520)  <b>Initial US FDA 510(k):</b> K060255 March 31, 2006	44776: Electrosurgical System, 11490: Electrosurgical System Generator	RA-TECH-0001 Rev. 001  RA-TECH-0001 Rev. 002  Adult IFU NR74330 Rev. G 2016-03	A single use, non-sterile return electrode with a pre-attached cord used to adhere to the patient over the entire return electrode surface to complete the electrosurgical circuit between the generator, the active electrode, and the patient.  The adult pad is only intended for use on patient weighing >15.0 kg (33 lbs).	
0855	Patient Return Electrode, Adult, dual plate, no cord >33 lbs	EU Class IIb (Rule 9 Annex IX)	<b>Initial CE Mark:</b> 2006 (CE 96520)  <b>Initial US FDA 510(k):</b> K060255 March 31, 2006	44776: Electrosurgical System, 11490: Electrosurgical System Generator	RA-TECH-0001 Rev. 001  RA-TECH-0001 Rev. 002  Adult IFU NR74330 Rev. G 2016-03		
0855CL	Patient Return Electrode, Adult, dual plate, with 15-foot (4.6m) pre-attached cord >33 lbs	EU Class IIb (Rule 9 Annex IX)	<b>Initial CE Mark:</b> 2006 (CE 96520)  <b>Initial US FDA 510(k):</b> K060255 March 31, 2006	44776: Electrosurgical System, 11490: Electrosurgical System Generator	RA-TECH-0001 Rev. 001  RA-TECH-0001 Rev. 002  Adult IFU NR74330 Rev. G 2016-03		
0855CN	Patient Return Electrode, Adult, dual plate, with 9-foot (2.7m) pre-attached cord >33 lbs	EU Class IIb (Rule 9 Annex IX)	<b>Initial CE Mark:</b> 2006 (CE 96520)  <b>Initial US FDA 510(k):</b> K060255 March 31, 2006	44776: Electrosurgical System, 11490: Electrosurgical System Generator	RA-TECH-0001 Rev. 001  RA-TECH-0001 Rev. 002  Adult IFU NR74330 Rev. G 2016-03		

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0865C	Patient Return Electrode, Pediatric, dual plate, with 9-foot (2.7m) pre-attached cord 6_33 lbs	EU Class IIb (Rule 9 Annex IX)	<b>Initial CE Mark:</b> 2006 (CE 96520)  <b>Initial US FDA 510(k):</b> K071080 (Pediatric Electrode): August 31, 2007	44776: Electrosurgical System, 11490: Electrosurgical System Generator	RA-TECH-0001 Rev. 001  RA-TECH-0001 Rev. 002  Adult IFU NR74330 Rev. G 2016-03	A single use, non-sterile return electrode with a pre-attached cord used to adhere to the patient over the entire return electrode surface to complete the electrosurgical circuit between the generator, the active electrode, and the patient.  The pediatrics pad is only intended for use on infants weighing 2.7 kg to 15 kg (6 to 33 lbs).	
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## 2.3. Current Clinical Evaluation Route of Conformity

The Megadyne Disposable Patient Return Electrodes have been in clinical use for 13 years globally, receiving CE mark certification and product launch in 2006. The adult return electrodes (0850C, 0855, 0855CL, 0855CN) were FDA cleared on 31 March 2006 (K060255) and the pediatric return electrodes (0865C) received FDA clearance on 31 August 2007 (K071080), so therefore have been marketed in the US for over 12 years.

The clinical evaluation route of conformity (ROC) was initially determined during the planning stage (Stage 0) through the Clinical Evaluation Plan (CEP) and continuously evaluated through the execution stage (Stage 1-3). The ROC is by the clinical route and is based on post-market surveillance (PMS) data and real-world epidemiology data (Epi Data). In addition, a systematic literature review was conducted for the subject devices (refer to section 6.9), covering the period between 01 January 1986 and 03 September 2019. This period was inclusive of the launch dates for all the subject devices and was undertaken in the core bibliographic databases of Medline and Embase via Ovid, and PubMed. Even with such an exhaustive search, however, zero articles were identified that had published data related to the subject devices. The Megadyne Disposable Patient Return Electrodes are widely used and clinically established with a low risk profile, and the lack of data in the clinical literature is attributable to the ancillary nature of these devices and that they are generally not the focus of clinical study. Therefore, the literature route was not used.

Collectively, a combination of the clinical and non-clinical data were confirmed sufficient for demonstrating conformity to the applicable Essential Requirements for clinical safety and performance of the Megadyne family of Disposable Patient Return Electrodes according to their intended purpose as specified in the IFUs (Adult IFU NR74330 Rev. G 2016-03, Pediatric IFU NR74380 Rev. F 2016-03). Details on the relevance and validity of the data sources are provided in Section 6.1.

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### 3. STATE OF THE ART

#### 3.1. State of the Art Methods and Results

The purpose of the systematic literature review is to evaluate the State of the Art (SOA) surrounding the Target Therapy of energy-based surgical cutting, dissection, and sealing (coagulation), which includes the Subject Devices for the clinical evaluation, the Megadyne Electrodes, Electrosurgical Pencils, and Suction Coagulators. The review will provide a comprehensive search of the available published literature to evaluate the clinical safety and effectiveness outcomes of the Target Therapy (monopolar electrosurgical devices) in comparison to Alternative Therapies (bipolar electrosurgical devices, advanced bipolar electrosurgical devices [also known as electrosurgical vessel sealing systems], ultrasonic surgical devices, laser surgical devices or argon beam devices) for the Target Medical Condition/Surgical Job of Tissue Cutting, Dissection, and Sealing.

The literature search for the SOA was designed to focus on higher-level evidence study designs (e.g. systematic reviews, meta-analyses) when possible where the target therapy is compared to the alternative therapies. These more well-designed studies, OCEBM (Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence) Level 1 and 2, provide the proper evidence to support the benefit-risk acceptability of the target therapy in comparison to the alternatives and thus are deemed for inclusion into the SOA section. When such study designs are not available, the search focuses on lower level comparative study design types as available. The detailed search strategy including key search terms, dates, and databases searched is provided in Appendix 10.3.1 of the CER.

In brief, a total number of 527 references resulting from the search were screened for inclusion/exclusion. References were included if they contained data regarding the target condition etiology or epidemiology, clinical performance or safety information relevant to the target and alternative therapies, information pertaining to relevant clinical practice guidelines, or information pertaining to the maturity of the target therapy. References were excluded if they did not contain such data or if the data were superseded by a more recent source of high level of evidence. Ultimately, 40 references overall from the search were included for synthesis of the SOA resulting in 487 references excluded for reasons provided in the screening log. An additional 37 references book chapters/clinical guidelines/high level articles were identified ad hoc for inclusion from either the bibliographies of included references or from the Medical Director's knowledge and guidance; resulting in a total of 77 references unique data sources for State of the Art information. The screening log is available upon request and the bibliography of included references are listed in Appendix 10.4.1.

#### 3.2. Clinical Problem

##### 3.2.1. Target Surgical Job (Tissue Cutting, Dissection and Coagulation)

Surgery is a technology that involves manual and instrumental interventions for investigating or treating a pathological condition such as a disease, injury, deformity, or defect. Surgical interventions result in physical changes to body tissues and organs, including exposure of anatomical structures beneath the skin, as well as bleeding or release of other bodily fluids from tissues or growths that have been penetrated using surgical instruments (Francis, 2006).

The tasks of cutting, dissection, and control of bleeding are performed in both traditional open operations and laparoscopic, or minimally invasive surgery (MIS) surgical procedures. Prior to the advent

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of robotic surgery, the term “minimally invasive surgery” was interchangeable with endoscopic surgery. In the current medical climate, however, endoscopic surgery refers to non-robotic minimally invasive surgery, including laparoscopic surgery, and thoracoscopic surgery. The defining feature of minimally invasive surgery is the use of an endoscope to access internal organs through very small and sometimes fewer incisions. Endoscopy involves insertion of a microchip video camera with a fiber optic telescope containing a light source and specially designed long-handled surgical instruments into the target cavity via the gastrointestinal, respiratory or urinary tract. The surgeon performs the procedure by manipulating the endoscope while viewing the anatomical area of interest a video screen or peering downward into the eyepiece of the instrument (Francis, 2006). While surgery encompasses a variety of techniques, the core interventions needed for any operation in which tissues are altered include cutting, dissection, and control of bleeding.

### **3.2.1.1. Tissue Cutting, Dissection, and Sealing**

#### **3.2.1.1.1. Surgical Cutting (Incision)**

Cutting is a fundamental technique in both open and laparoscopic surgical procedures that is indispensable to accessing the tissues of interest below the skin. A surgical operation is initiated with an incision, defined as a deliberate cut in the skin that is usually made by a scalpel or similar instrument with a sharp edge. Sharps, also known as cutting, incising, or dissecting instruments, refer to scalpels, knife handles, and blades of various lengths, and include scissors, as well as needles and glass. Surgical incisions allow adequate exposure of the anatomical region or structure of interest, so that the operation can be performed safely and quickly (Francis, 2006).

The number, length, and type of incision(s) used may vary, depending on the specific surgical procedure performed and on whether it is open or laparoscopic. For example, in removal of a gallbladder, a minimum 20 cm incision is required in traditional cholecystectomy, whereas four incisions of 0.5–1.0 cm, and more recently a single incision of 1.5–2.0 cm is adequate for a laparoscopic procedure.

Critical outcomes used to evaluate the safety and effectiveness of surgical skin incisions include wound infection rates, scar cosmesis, incision time, incisional blood loss, and postoperative wound pain (Aird and Brown, 2012). The published literature reports differences in some of these outcomes between non-energized and energized forms of surgical cutting instruments (Aird and Brown, 2012) (see Comparative Studies section).

#### **3.2.1.1.2. Surgical Dissection**

Surgical dissection refers to the process of cutting apart or separating tissue to isolate the structure(s) of interest from surrounding connective tissue and other structures with a minimal amount of trauma and bleeding. Ideally, this technique should be performed along tissue planes that are relatively avascular (Francis, 2006). The surgical separation of tissues can be achieved with blunt dissection (using fingers, gauze pledge, hand or other blunt instruments), sharp dissection (using a scalpel or scissors), or diathermy (using high-frequency electric current to stimulate heat generation within body tissues) (Francis, 2006).

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### 3.2.1.1.3. Hemostasis and Coagulation

Surgical hemostasis is defined as the termination of bleeding that occurs when blood vessels are transected during surgical cutting and dissection. It is a broad concept that encompasses related processes such as coagulation, physical hemostatic techniques, and chemical hemostatic agents. Hemostasis is critical for preventing blood loss during surgery and hematoma formation postoperatively, and its importance has increased exponentially with the growth of laparoscopic surgeries over the last two decades. Hemostasis must be achieved at the end of a surgical procedure as well as intraoperatively to maintain visibility of the surgical field, particularly during laparoscopic procedures.

A variety of primary and adjunctive hemostatic interventions are available for surgical use (see Table 2). Traditional methods of surgical hemostasis include application of a hemostatic clamp to a blood vessel and then ligation with a surgical ligature; suture ligation of a vessel (i.e., under-running a bleeding vessel with a figure-of-8 suture which is tied firmly); diathermy coagulation; and localized pressure for several minutes to allow coagulation to occur naturally (Francis, 2006). However, since the conventional means of tying, suture ligating, and pressure used to control bleeding in open operations are less practical and effective in minimally invasive procedures, surgeons must rely on various other techniques of tissue and vessel coagulation (Lantis et al., 1998). Nearly 20 years ago, it was demonstrated that while energy surgical devices in general can achieve some degree of hemostasis during surgery, certain types of instruments are relatively more effective than others (Lantis et al., 1998). Clinical comparisons have focused on bipolar electrosurgical instruments as well as ultrasonic surgical tools and surgical lasers.

**Table 2: Pertinent Characteristics of Various Hemostatic Devices and Agents**

(Klingler et al., 2006)

Device	Hemostatic Background	Ease of Use	Collecting System Sealing	Major Disadvantage
Sutures, loops	Mechanical	-	Yes	Difficult to learn
Titanium clips	Mechanical	+++	No	May slip off
Polymer clips	Mechanical	++	No	Hook-like tip
Vascular endostapler	Mechanical	+	No	Bulky to use, costs
Electrocautery monopolar	Thermal coagulation & cutting	+++	No	Current leakage,
Electrocautery bipolar	Thermal coagulation	++	No	No cutting
Argon beam	Thermal coagulation	+	No	No dissection, capillary bleeding only
Harmonic scalpel	Tissue vaporization & ultrasonic coagulation	++	No	Vessel < 4mm
Bipolar vessels sealer	Thermal coagulation & sealing	++	No	Very slow, vessels ≤ 6mm
Lasers	Tissue vaporization & thermal coagulation	++	No	Expensive, cell spillage
Fibrin glues	Clotting cascade	++	Yes	Dry surface needed
Oxidized methylcellulose	Clotting cascade & hemostyptic bolster	-	Yes	Suturing skills required

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Device	Hemostatic Background	Ease of Use	Collecting System Sealing	Major Disadvantage
Fibrin coated collagen fleece	Clotting cascade & surface covering	+	Yes	Tricky to apply
Gelatin matrix	Clotting cascade	++	Unknown (no)	Bloody surface needed
Polyethylene glycol	Artificial sealants	++	Yes	Experimental

*Ease of use: [+++] = very simple/easy to use, [-] = very difficult/elaborate*

Coagulation, or blood clotting (i.e., the transformation of blood to a gel in the solid or semi-solid state) potentially produces hemostasis, or the termination of blood loss from a damaged vessel, followed by vessel repair. Surgical coagulation is defined as “disruption of tissue by physical means to form an amorphous residuum.” Two forms of electrosurgical coagulation can be achieved in blood vessels: (1) obliterative coagulation, which involves direct contact with or electrical arcing to tissue; and (2) coaptive coagulation, which is produced by mechanical apposition of the edges of the vessel with the hemostat or forceps. Obliterative coagulation, which shrinks the vessel wall and occludes the lumen, is appropriate for vessels < 1mm in diameter. In coaptive coagulation, the adventitia of vessel is destroyed, the muscular layer shrinks, and the intima fuses. This technique is preferred for vessels larger than 1mm and up to 2mm diameter.

Key concepts related to hemostasis include cautery, or the coagulating of blood and destruction of tissue with hot iron, by freezing, or with caustic agent; and electrocautery, or cauterization (cutting or hemostasis) achieved by bringing electrically heated metal instrument into contact with target tissue. Diathermy refers to the generation of heat in tissue by means of electrical current, a process that is distinct from the electron flow which occurs in electrosurgery. Desiccation, or coagulation that produces dehydrated cells, is synonymous with fulguration; and is one of the main types of effects that can be produced with electrosurgery.

### 3.3. Treatment Options and Interventions

#### 3.3.1. Therapeutic Alternatives/Treatment Options

Certain gastrointestinal, gynecologic, thoracic, urologic, spinal, and other conditions may require a nonsurgical rather than a surgical approach, in which case surgical devices are not utilized. The absence of any intervention in a “watch and see approach” constitutes a conservative treatment. However, this approach is not an alternative to electrosurgery or to other energy-based surgical systems. There are no non-surgical or pharmaceutical options for dissection and coagulation of tissue, since these tasks by definition require physical manipulation of tissues with sharp instruments and/or heat. Therefore, all of the alternative therapies included in this State of the Art assessment involved use of either traditional surgical dissection (i.e., cold /blunt dissection) or an energy-based system such as monopolar electrosurgery, bipolar electrosurgery, advanced bipolar electrosurgery, or ultrasonic surgery.

##### 3.3.1.1. Surgical

###### 3.3.1.1.1. Surgical - Non-energy based options

Dissection, one of the core tasks required for surgery, refers to the separation of various parts of the body in order to expose or study its anatomical structures. Surgical dissection encompasses both blunt

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dissection, or the meticulous separation of tissues by the fingers or blunt instruments, and sharp dissection, or the separation of tissue with the sharp edge of a knife, scissors, or scalpel. Non-energy based surgical devices for dissection have been used for millennia, but these instruments are usually too bulky and inappropriately designed to be leveraged in modern laparoscopic procedures. However, they may be used in some minimally invasive procedures, depending on the surgeon's preference and on the availability of manual versus energy-based cutting and hemostatic devices. Additional manual tools such as cautery, forceps, and scissors may be utilized in conjunction with scalpels during surgical dissection.

The "clamp-and-tie" technique for hemostasis was initially standardized in the 19th century, but with several modifications it is still used in current surgical techniques where ligatures, titanium vessel clips or staples are applied. While new tools based on the transmission of electricity and ultrasonic energy have been introduced as hemostatic aids in a variety of surgeries, the traditional "clamp-and-tie" technique remains a state of the art approach for controlling intraoperative and postoperative bleeding (Binsaleh, 2011; Garas et al., 2013). In addition, cautery can be used manually to remove a part of the body or to seal a blood vessel using heat. Topical hemostatic agents provide another medicinal technique for promoting coagulation during surgery. Topicals encompass physical agents that facilitate hemostasis through a passive process as well as biologically active agents that increase coagulation at the bleeding site (Galanakis et al., 2011). The alternative therapies included in this report did not include topical hemostatic agents.

### **3.3.1.1.2. Surgical - Energy based options**

In contemporary clinical settings energy-based surgical systems are used to facilitate the application of energy in the surgical or endoscopic field where they produce clinical effects such as cutting, coagulation, or desiccation of tissue, or fulguration for the destruction or manipulation of the tissue (Sankaranarayanan et al., 2013; Schwitzberg, 2012). These systems encompass devices that utilize technologically sophisticated energy sources such as high frequency (radiofrequency) electrical energy and ultrasonic energy for a wide range of procedures, including minimally invasive surgery (MIS). Energy-based modalities used in laparoscopic procedures and other forms of MIS include monopolar electrosurgery, bipolar electrosurgery, advanced bipolar electrosurgery, ultrasonic energy, laser devices, argon beam devices and hybrid devices that combine electrosurgical and ultrasonic energies. These devices sometimes incorporate additional functions such as tissue sealing, temperature feedback regulation, and simultaneous tissue cutting and hemostasis (Grochola and Vonlanthen, 2016). Some general benefits and risks of these energy based modalities are detailed in Table 3.

Energy systems such as electrosurgery are used in clinical practice in compliance with Clinical Practice Guidelines such as the Dutch Health Care's multidisciplinary evidence-based guideline for minimally invasive surgery and electrosurgical techniques (la Chapelle et al., 2012), AORN's Recommended Practices for Electrosurgery (AORN, 2012; Spruce and Braswell, 2012), AST Standards of Practice for Use of Electrosurgery (AST, 2012), and Guideline Implementation: Surgical Smoke Safety (Fencl, 2017).

**Table 3: Benefits/Advantages and Disadvantages/Risks of Energy-based Systems**

(Law et al., 2014; Sankaranarayanan et al., 2013; Vilos and Rajakumar, 2013)

Energy System	Benefits/Advantages	Disadvantages	Risks
Monopolar Electrosurgery	Varied tissue effects – e.g., desiccation, vaporization, fulguration, coaptation	Higher voltage requirement to achieve desired tissue effect	More pronounced lateral thermal spread than vaporization or fulguration

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Energy System	Benefits/Advantages	Disadvantages	Risks
	Parameters are under surgeon's control Minimal smoke production or carbonization Superior dissecting capabilities according to some surgeons Relatively low cost	Risk for thermal injury Smoke plume Technique requires extensive knowledge, understanding, and vigilance to avoid inducing unintentional thermal injury	Potential stray current injuries due to capacitive coupling, insulation coupling, and direct coupling Laparoscopic electrosurgical injuries: reported rate of 1 to 5 per 1000 operations
<b>Bipolar Electrosurgery</b>	Decreased risk of stray current injury than with monopolar electrosurgery Ability to seal larger vessels Lower voltage requirement than monopolar electrosurgery to achieve desired tissue effect More even distribution of thermal effect that might reduce risk of lateral thermal spread Reduced risk of stray current injury from capacitive coupling Shorter dissection time High success rates Better sealing quality Less blood loss Fewer conversion rates More cost effective than monopolar electrosurgery	Decreased ability to modify operational parameters compared with monopolar electrosurgery Lack of versatility of tissue effects (e.g., no vaporization or fulguration) Requires mechanical cutting blade because bipolar electrodes cannot cut tissue Smoke plume Risk for thermal injury	Lateral thermal spread Electrode adherence to tissues Disengagement of instrument tips may cause tissue trauma or tearing of blood vessels
<b>Advanced Bipolar Electrosurgery</b>	Thermal effects may be minimized with advanced bipolar Seal vessels up to 7 mm in diameter Lowest possible power setting can be used utilized to achieve desired tissue effect Advanced Bipolar electrosurgery systems alert the operator via an audio signal when desired tissue effect has been achieved, minimizing Optimal thermal and mechanical properties to seal the tissues	Instruments need to be changed to transect the desiccated tissue Smoke plume Risk for thermal injury Requires mechanical cutting blade because bipolar electrodes cannot cut tissue	Lateral thermal spread risk still exists (potentially associated with prolonged device activation) Electrode adherence to tissues Disengagement of instrument tips may cause tissue trauma or tearing of blood vessels
<b>Ultrasonic Surgery</b>	No need for electric current to pass through the tissues  Provides hemostasis and cuts tissues  Vessel-sealing tissue effects are comparable to those of advanced bipolar electrosurgery	More expensive than conventional electrosurgical devices  Instrument tip temperatures higher than with advanced bipolar devices Risk for thermal injury Dissection capability of some ultrasonic devices is more limited compared to monopolar	Lateral thermal spread risk still exists  Plume aerosol produced consisting of tissue, blood, and blood products can adversely affect patients and OR personnel.  Heat generated from use can cause tissue burning.

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Energy System	Benefits/Advantages	Disadvantages	Risks
	<p>Can perform desiccation and coagulation with resultant coaptation at temperatures lower than 100°C</p> <p>Harmonic ACE+7 seals vessels up to 7-mm diameter (beyond 5-mm limit associated with all the other ultrasonic devices)</p> <p>Overall dissection time may be shorter after initial learning curve</p> <p>Less instrument traffic due to the combined vessel-sealing and tissue cutting functionality, less tissue and charring, reduced lateral thermal spread</p> <p>Less smoke plume (Harmonic Scalpel)</p>	<p>scissors or conventional bipolar forceps</p> <p>Slower coagulation compared to electrosurgery; can coagulate only while cutting</p> <p>Changing frequency or impedance of surgical system may be due to blade fatigue, temperature elevation, excessive applied pressure, or improper use</p> <p>Some ultrasonic devices are less efficient than other advanced energy devices in sealing medium to large sized blood vessels</p> <p>Higher average temperatures that are not reliable in sealing vessels larger than 3mm</p> <p>Sealing efficiency is more technique dependent than advanced bipolar instrumentation</p>	
Argon Beam Coagulation	<p>Enhances vessel sealing capabilities of monopolar electrosurgery</p> <p>Argon jet blows away blood and debris from the surgical field.</p> <p>Suitable for minor capillary bleeding after dissection</p> <p>Beneficial for procedures involving major blood loss</p> <p>Oncological indications (e.g., advanced tumor resection)</p> <p>Non-oncological indications (endoscopic bleeding control in the gastrointestinal tract and general surgery)</p>	<p>Cannot be used for tissue dissection</p> <p>Inappropriate for control of significant bleeding or larger vessels</p> <p>Risk for thermal injury</p>	<p>Insolubility of argon gas results in risk for serious complications (e.g., potentially fatal argon gas embolism, pneumothorax)</p> <p>Risks for complications of pseudoaneurysm formation and hemobilia in laparoscopic cholecystectomy</p> <p>May interference with surgical equipment</p> <p>Higher risk for death from complications than other energized surgical methods (except for laser surgery coagulation)</p>
Laser Energy Surgery	<p>Used largely in surgical procedures to treat benign prostatic hyperplasia (BPH) and gynecological, eye, and dermatological condition</p> <p>Reduces the risk of infection, promoting healing</p>	<p>Expensive</p> <p>Requires specialized training and skill</p> <p>Poor sealing capability</p> <p>Higher risk for causing damage away from the operative site</p>	<p>Risks for pregnancy</p> <p>Contra-indications for the use of photosensitizing drug</p> <p>Higher risk for death from complications than other energized surgical methods (except for argon beam coagulation)</p>

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Energy System	Benefits/Advantages	Disadvantages	Risks
		Risk for thermal injury	Laparoscopic cholecystectomy pseudoaneurysm formation and hemobilia in laparoscopic cholecystectomy  Risk for hemorrhage

### 3.3.1.2. Electrosurgery

#### Overview

Electrosurgery is an umbrella term encompassing multiple surgical modalities that use a high-frequency (radiofrequency) electric current of alternating polarity. More than 80% of surgical procedures performed in the current clinical environment utilize advanced devices such as electrosurgical instruments (Meeuwsen et al., 2017).

Electrosurgical instruments are precisely crafted to allow skilled surgeons to perform a variety of techniques during surgical procedures that involve tissue grasping, tissue cutting (incision, dissection, resection) and coagulation to achieve hemostasis (sealing of blood vessels). Electrosurgical devices play a pivotal role in MIS such as laparoscopic procedures, including appendectomy, cholecystectomy, colorectal procedures, and various other gastrointestinal operations, as well as hepatic, gynecologic, thoracic, urologic, and spinal procedures. MIS is performed with the use of various instruments, often custom designed, that have been scaled down in size or in some cases miniaturized for ease of insertion into the surgical field. Electrosurgical instruments are also increasingly used in traditional or open, operations as an alternative to the conventional dissection and hemostatic techniques. The core equipment in electrosurgery, as performed in clinical practice, is an electrosurgical unit (ESU) consisting of a generator and hand piece with one or multiple electrodes. The operator controls the unit with the use of a hand- or foot-controlled pencil or switch (Cordero, 2015). High-frequency electrical current, generated from the flow of electrons, is applied to living tissue in order to perform surgical cutting or to control bleeding (Law et al., 2014).

Of note, electrocautery is technically not a form of electrosurgery, but instead refers to direct current in which electrons flow in one direction without passing through the patient's body (Cordero, 2015). By contrast, electrosurgery uses alternating current that enters the patient's body (see Table 4). An overview of key terms used in discussion of electrosurgery are noted in Table 5.

**Table 4 : Comparison of Electrosurgery vs Electrocautery**

From: (Taheri et al., 2014)

Electrosurgery	Electrocautery
High frequency alternating current through living tissue	Direct current through a high resistance metallic (alloy) conductor
Manipulation of electrons to generate heat within cells that destroys the tissue	Heated alloy is then applied to the tissue

From: (AORN, 2012)

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**Table 5: Definitions of Key Terminology in Electrosurgery**

Terminology	Definition
<i>Active electrode</i>	The electrosurgical unit (ESU) accessory that directs current flow to the surgical site (e.g., pencils, various pencil tips).
<i>Alternate site injury</i>	Patient injury caused by an electrosurgical device that occurs away from the dispersive electrode site.
<i>Bipolar electrosurgery</i>	Electrosurgery in which current flows between two tips of a bipolar forceps that are positioned around tissue to create a surgical effect. Current passes from the active electrode of one tip of the forceps through the patient's desired tissue to the other dispersive electrode tip of the forceps—thus completing the circuit without entering another part of the patient's body.
<i>Capacitance</i>	Ability of an electrical circuit to transfer an electrical charge from one conductor to another, even when separated by an insulator.
<i>Capacitive coupling</i>	Transfer of electrical current from the active electrode through intact insulation to adjacent conductive items (e.g., tissue, trocars).
<i>Direct coupling</i>	The contact of an energized active electrode tip with another metal instrument or object within the surgical field.
<i>Dispersive electrode</i>	The accessory that directs electrical current flow from the patient back to the electrosurgical generator—often called the patient plate, return electrode, inactive electrode, or grounding pad.
<i>Electrosurgical accessories</i>	The active electrode with tip(s), dispersive electrode, adapters, and connectors to attach these devices to the electrosurgery generator.
<i>Electrosurgery</i>	The cutting and coagulation of body tissue with a high-frequency (i.e., radio frequency) current.
<i>Generator</i>	The machine that produces radio frequency waves (e.g., ESU, power unit).
<i>Insulation failure</i>	Damage to the insulation of the active electrode that provides an alternate pathway for the current to leave that electrode as it completes the circuit to the dispersive electrode.
<i>Monopolar electrosurgery</i>	Electrosurgery in which only the active electrode is in the surgical wound, and the electrical current is directed through the patient's body, received by the dispersive pad, and transferred back to the generator, completing the monopolar circuit.
<i>Ultrasonic scalpel</i>	A cutting/coagulation device that converts electrical energy into mechanical energy, providing a rapid ultrasonic motion.
<i>Vessel sealing device</i>	Bipolar technology that fuses collagen and elastin in the vessel walls and permanently obliterates the lumen of the vessel.

Radiofrequency electrosurgery requires the creation of an electrical circuit that includes two electrodes, the patient, the ESU, and the connecting wire (Munro, 2012). There are two configurations of electrosurgery: monopolar and bipolar. Both modes of electrosurgery revolve around the production of electrical energy followed by the transfer of the electrical currents and voltages from an active (i.e., operative) electrode to a return (i.e., dispersive) electrode (Law et al., 2014; Sarkisian et al., 2015). The electrical energy traveling between two electrodes completes a circuit while heating the tissues. Regardless of their exact placement in relation to the patient, two electrodes are essential for both types of electrosurgery. All forms of radiofrequency electrosurgery are therefore technically bipolar because both electrosurgical modes require two poles, or essentially two electrodes, to complete the electrical circuit through which the electrical current passes (Law et al., 2014).

The two modes of electrosurgery are distinguished by the location and function of the second electrode (Munro, 2012) (see Figure 1). Monopolar electrosurgery involves a focused electric current entering the patient at the point of contact of the active electrode. With monopolar devices, only one electrode, called the “active electrode,” is mounted on the device. The patient’s full body is then placed between this

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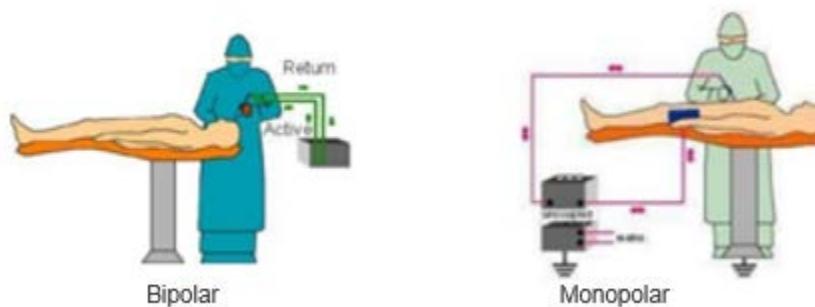
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“active electrode” and the large dispersive electrode which is also connected to the ESU, though situated relatively distant from the target tissue, such as on the thigh or back. The narrow active electrode focuses the current (and therefore the power) at the targeted site, which increases the intracellular temperature. The dispersive electrode serves as the other pole by “processing” the same amount of current (and power), but dispersing it over the totality of the large surface area. The wide dispersion prevents the temperature in the underlying skin from rising, thereby preventing tissue injury (Munro, 2012). In monopolar electrosurgery, therefore, the circuit is completed via the dispersive or return electrode which is located distally from the surgical site (Law et al., 2014).

Earlier monopolar electrosurgical systems were ground referenced, meaning that that the “ground” became an intrinsic part of the circuit. However, contemporary electrosurgical systems use isolated circuits, such that the “ground” is excluded. The term “ground pad” which sometimes appears in the older literature is no longer applicable (Munro, 2012). Bipolar electrosurgery utilizes the electrical current flowing between an active electrode and a return electrode in close proximity within the device (e.g., bipolar forceps), with the circuit completed as the current passes from one electrode to the other (Law et al., 2014). Bipolar instruments have both electrodes mounted on the device, usually located on or near the distal end so that only the tissue located between the two electrodes is included in the circuit (Munro, 2012).

**Figure 1: Electrode Positions in Monopolar and Bipolar Electrosurgical Circuits**



Whereas the entire patient is affected in systems that use monopolar devices, with bipolar instruments only the tissue interposed between the two electrodes is involved in the circuit. These differences underlie the safety and performance features that distinguish the two systems (Munro, 2012). Despite these differences, however, the fundamental principles of electrosurgery apply to the circuit systems used with both the monopolar and bipolar modes. Depending upon its strength and resistance, the electrical current yields variable effects of vaporization, charring, coagulation, desiccation (drying), and fulguration of the target tissue. (Fulguration is a superficial form of coagulation involving destruction and removal of quickly desiccated and coagulated tissue.) The intended effect on the tissue is determined by a number of electrical properties and by factors such as tissue exposure time as well as the size and shape of the surface of the electrode near to or in contact with the target tissue (Munro, 2012). These key factors are discussed in the next section.

### **Impact of Alternating Current on Intracellular Activity and Tissues**

Cells contain electrically charged particles/ions in the form of atoms and molecules. Cations are positively charged particles whereas anions are negatively charged particles. When direct current (DC) is applied to the cell, the ions move towards oppositely charged electrode, a phenomenon known as the galvanic

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effect. When an alternating current (AC) is applied to the cell, the ions migrate to the opposite poles, but instead of maintaining a single orientation within the cell they oscillate in conjunction with the different polarity of the output. When the frequency of the AC is low (20-30KHz), the radiofrequency (RF) current depolarizes the muscles and nerves due to an action potential, resulting in muscle fasciculation and pain. This action is called the faradic effect (Munro, 2012).

The depolarization process is initiated via the voltage gated sodium and potassium channels in the neural and muscular cell membranes. However, neural and muscular stimulations do not occur if the current switches rapidly (100KHz-3MHz). When high frequency current is applied across a cell membrane, the pulse duration is so short that the sodium and potassium ionic channel gates do not open, preventing depolarization from occurring. In this case, the electromagnetic energy is converted to mechanical energy since the cations and anions rapidly oscillate within the cellular structure. The frictional forces subsequently convert mechanical energy into thermal, or heat, energy, which then facilitates the rise in temperature of cellular/ tissue structures, producing the desired tissue effects. When either AC or DC flows through a resistor, the resulting effect is the production of heat because the resistance/impedance to the flow of current generates thermal (heat) energy. This effect is explained by Joule's law ( $Q=I^2\times R\times t$ ) (Munro, 2012).

The three interacting properties of electricity that affect the temperature rise in tissue are current (I), voltage (V), and impedance or resistance (R). (see Table 6) .Voltage refers the electrical differential created between two points in a circuit that determines the pressure with which electrons are "pushed" within the circuit, including the parts of the circuit comprising tissue. Voltage is measured in volts. Resistance is measured in ohms, and is an indicator of the difficulty a particular substance (e.g., tissue or the composition of the electrical wires) presents to the passage of electrons. The term resistance is typically used for DC whereas the term impedance is generally employed for AC (Munro, 2012).

From: (Munro, 2012)

**Table 6: Variables in Electrosurgery Associated with Cellular and Tissue Effects**

Variable	Definition	Units
Current (I)	Flow of electrons past a point in the circuit/unit time	Amperes (coulombs/second)
Voltage (V)	Difference in electrical potential between two points in the circuit; force required to push a charge along the circuit	Volts (joules/coulomb)
Impedance (resistance) (R)	Degree to which the circuit or a portion of the circuit impedes the flow of electrons	Ohms
Power (P)	Work; amount of energy per unit time; Product of V and I	Watts (Joules/second)
Energy	Capacity of a force to do work; cannot be created or destroyed	Joules (watts/second)

The ability of the radiofrequency current to increase cellular and tissue temperature is responsible for the varied tissue effects of electrosurgery. As noted previously, these effects are due to two basic mechanisms: (1) the conversion of electromagnetic energy to mechanical (kinetic) energy, which is subsequently is converted to thermal energy by frictional forces; and (2) resistive heating, which though less significant, signals the flow of current across a resistor to elevate the temperature of that resistor. RF electrosurgical devices achieve hemostasis by the first mechanism.(Munro, 2012; Park and Portenier, 2012). In addition, an indirect mechanism of tissue heating is conductive heat transfer in which the tissue adjacent to the area being touched is affected by the RF current

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The temperature of the human body is normally 37°C, occasionally reaching as high as 40°C during infection, but a cellular temperature of 50°C results in cell death in about 6 minutes. At a local temperature of 60°C cellular death is instantaneous. Heightened temperatures produce two distinct cellular effects -- coagulation and desiccation -- that bear directly on the efficacy and performance of electrosurgical procedures. Between approximately 60°C and 95°C protein denaturation occurs, causing bonds between protein molecules to break and then quickly reform as the local temperature cools. The reformed molecules produce homogenous coagulum through a process called "coagulation" (Munro, 2012). This elevated temperature range is also associated with cellular loss of water that exits through the thermally injured cellular wall, resulting in dehydration or desiccation. The process is akin to boiling the white of an egg until it is dehydrated enough to form a homogenous, coagulum or gelatinous structure, known as "white coagulation". This tissue effect is well-suited for occluding blood vessels in order to achieve hemostasis. If the intracellular temperature rises to 100°C or higher, intracellular water boils and becomes steam. The intracellular contents then expand, causing the cell to vaporize with a cloud of steam, ions, and organic matter. At still higher local temperatures of 200°C or more, the organic molecules are degraded through carbonization, a process that gives the tissue a black and/or brown appearance.

From: (Sinha, 2014)

**Table 7: Tissue Effect and Electrosurgical Generator Output**

	Electrosurgical Cutting	Electrosurgical Coagulation	Electrosurgical Fulguration
Tissue temperature	100 C	60 – 95 C	>200 C
Tissue effect	Vaporization	White coagulation	Black coagulation
Best achieved with	Cut output	Cut output	Coag output
Electrode position	Near contact	Contact	None or near contact
Electrode shape	Needle	Wider	Needle

### 3.3.1.2.1. Categories of Electrosurgical Devices

Electrosurgical instruments utilized in both MIS and traditional open operations fall into three main categories: monopolar, traditional bipolar, and advanced bipolar. In addition, a small number of hybrid devices are currently commercially available that combine two or more distinct types of RF energy, integrate RF energy with ultrasonic energy, offer multifunctional clinical applications, or provide both multiple energy platforms and multifunctional features within the same instrument (Law et al., 2014; Obonna and Mishra, 2014).

RF electrosurgery is now widely used as an effective method of cutting and, to some extent, of achieving hemostasis, at least in smaller blood vessels, during a broad array of surgical procedures (Munro, 2012). In contrast to other modes of electrosurgery, monopolar electrosurgical devices are typically used in clinical settings for achieving hemostasis in vessels smaller than 2mm in diameter (Ferreira, 2015). Bipolar electrosurgical instruments offer some safety advantages when used for the processes of coagulation and desiccation, but in general these devices provide limited benefit for cutting or vaporization (Munro, 2012).

ESUs utilize three different waveforms known as Cut, Coag, and Blend output settings to achieve different tissue effects (Alkatout et al., 2012). The "cut" setting delivers an unmodulated, continuous current,

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whereas the “coag” setting delivers a modulated, interrupted current. Per Ohm’s law, at the same power settings, an interrupted waveform has a higher voltage but a lower current than a continuous waveform. Continuous waveform current uses lower-energy electrons than those used in interrupted waveform current, thereby making continuous waveform a safer waveform option for most laparoscopic applications. Various “blend” settings can be adjusted on most ESUs to alter the proportion of time in which the current flow is interrupted (Law et al., 2014). All modern ESUs are designed to provide power in either monopolar or bipolar configurations (Vilos and Rajakumar, 2013).

### 3.3.1.2.1.1 Monopolar Electrosurgery

#### Background

Monopolar electrosurgery represents the oldest of the modern energy-based systems and is used for cutting and coagulation (i.e., sealing vessels < 2mm) in a wide range of laparoscopic and open surgical procedures. The monopolar configuration utilizes both an active (i.e., high power density pole) electrode, or probe, and a second dispersive (i.e., low-power density pole) electrode (return pad), which is placed on the patient at a location remote from the surgical site. The relatively large surface area of the dispersive electrode is designed to defocus or disperse the current in order to prevent tissue injury (Munro, 2012).

Active electrodes have multiple designs, depending on their intended uses. Those with a point, hook, narrow tip, or bladed edge are typically utilized to concentrate current and power in order to facilitate tissue vaporization and cutting. When the active electrode has a slightly larger surface area, such as the side of a blade or when it is shaped like a ball or takes the form of a grasper, the same output used for cutting will produce only local coagulation and desiccation, thereby making it suitable for hemostasis (Munro, 2012).

Dispersive electrodes are usually designed with an adhesive that allows continued contact with the patient while also helping to prevent a clinically significant local thermal effect. However, if there is partial detachment, the current or power density will increase, causing the dispersive electrode to become “active”, potentially triggering a thermal injury, or “burn”. Most ESUs sold in the past 20 years can measure the impedance at the level of the dispersive electrode. This “upgraded ability” also necessitates a specialized dispersive electrode design, which generally takes the form of a “split pad” with two dispersive electrodes in one. Any difference between the measured impedance in the two dispersive electrodes usually signals a partial attachment or detachment, thereby preventing the machine from starting, or, if it already “on”, forces the ESU to shut off automatically (Munro, 2012).

Monopolar electrosurgery can perform diverse functions such as desiccation, vaporization, fulguration (for ablation), and coaptive coagulation. These different tissue effects are achieved by selecting specific parameters such as current power settings, contact versus noncontact mode, current waveform, duration of current activation, electrode size/configuration, and tissue conductivity (Law et al., 2014). Vaporization is employed for cutting, while fulguration and desiccation are utilized for hemostasis of small vessels (<1mm), and coaptive coagulation or sealing is used for small-medium vessels (<2mm) (Law et al., 2014).

In monopolar electrosurgery tissue cutting is achieved through activation of the continuous waveform without tissue contact, which results in a flow of low-energy electrons that causes vaporization of the cells (Law et al., 2014). This technique is associated with minimal smoke production or carbonization. By contrast, activation of the interrupted waveform without tissue contact results in a spray of high-energy electrons to the tissue and fulguration, an effect suitable for hemostasis of small blood vessels (Law et

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al., 2014). However, in cases involving adipose tissue transection, interrupted waveform is more appropriate due to the high fat content of the tissues (Law et al., 2014). The medium through which the current passes influences the tissue effect. Activation of either continuous or interrupted waveform with tissue contact yields tissue desiccation and protein coagulation, whereas contact with small-medium vessels results in vessel sealing or coaptation (Law et al., 2014).

### **Advantages and Benefits of Monopolar Electrosurgery**

The advantages of monopolar electrosurgery configuration include its wide availability, relatively low cost, and ease in leveraging both the active electrode and return electrode at the surgical site (Cordero, 2015). Monopolar electrosurgery is valued by some surgeons for the continuous and “mix/blend” current used to perform dissection with ease while simultaneously enabling sufficient fulguration in the interrupted mode to achieve hemostasis, as well as a wide range of tissue effects (Jaiswal and Huang, 2017). Furthermore, monopolar grasping forceps can be used for coaptive coagulation (i.e., compression and cauterization) of grasped tissue in desiccated areas with denatured proteins to achieve hemostatic sealing (i.e., a “collagen weld”) (Munro, 2012; Vilos and Rajakumar, 2013).

### **Disadvantages and Risks of Monopolar Electrosurgical Devices**

The use of monopolar electrosurgery carries well-documented risks, particularly electrothermal injury due to accidental direct application of the device (Vilos and Rajakumar, 2013). Although tissue desiccation is associated with lower tissue temperatures, it is also linked with a larger amount of lateral thermal spread compared to both vaporization or fulguration. On the other hand, contact monopolar electrosurgery overall results in a tissue effect comparable to that produced using bipolar electrosurgery (Law et al., 2014).

In the monopolar configuration, the electrical current completes a full circuit via an active cable. As noted previously, the current passes from the probe electrode to the target tissue and through the patient’s body to the dispersive electrode placed at a different location on the patient’s body. Resistance to the electrical current in the target tissue results in a localized rise in temperature to produce either coagulation or cutting, depending upon the parameters of the device set by the operator. The dispersive electrode has a relatively large surface area designed to reduce the current intensity of the high frequency current as it flows back to the patient, thus preventing burns. However, if the current is not safely dissipated by the dispersive electrode, the patient will likely suffer a return electrode burn (Cordero, 2015).

In monopolar electrosurgery, particularly when used as laparoscopically, the risk of stray current injuries is specifically linked with insulation failure, direct coupling, and capacitive coupling (Law et al., 2014). The use of older grounded electrosurgical generators reportedly could trigger “alternate site” burns if the current flow through the patient failed to return to ground via the operating table, but instead was directed through other sites such as the adhesive pads of electrocardiogram leads. This problem has been eliminated with the widespread use of isolated electrosurgical generators, which allow the circuit to be completed via the patient return electrode pad back to the generator (Law et al., 2014). However, the patient return electrode introduced a new risk of burns at the return electrode if the current flow to the pad were directed through a small area of the patient’s skin due to poor pad attachment. This problem was largely resolved by utilizing a return electrode monitoring system via an interrogation circuit that traveled back to the electrosurgical generator, using a split electrode return pad (Law et al., 2014).

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In laparoscopic procedures, the overall reported incidence of electrosurgical injuries is 1 to 5 per 1000 operations (0.010%-0.05%). Some of these injuries are linked with a lack of surgical proficiency, but others arise from inadvertent current leakage from the active electrode device via capacitive coupling, insulation failure, and direct coupling (Law et al., 2014). Many of the electrosurgical injuries associated with MIS are not immediately evident since only about 10% of laparoscopic instruments are within the laparoscope field of vision (Law et al., 2014). Additionally, patients may present with nonspecific symptoms rather than an unequivocal cause of the injury, thereby postponing an accurate diagnosis by 4 to 11 days (Law et al., 2014). For instance, a region of thermal coagulation necrosis may be difficult to diagnose histologically when accompanied by prolonged inflammation and secondary infection. In such a case, a thermal injury may be erroneously categorized as a mechanical laceration or trocar-related injury (Law et al., 2014). Accordingly, some authors have suggested that the incidence of electrosurgical injuries may be higher than currently reported (Law et al., 2014).

In addition to potential harms that may result from leakage of electrical current, electrosurgery generates smoke that is hazardous to both patients and OR personnel. Surgical plume is also formed during procedures that utilize lasers and ultrasonic equipment such as the Harmonic Scalpel, but until recently, little attention was paid to the “diathermy emissions,” or smoke, linked with specifically electrosurgery. Surgical smoke is produced when mechanical tools or heat-producing devices commonly used in dissection and hemostasis interact with tissue, disrupting and vaporizing tissue protein and fat (ULMER 2008). The resulting diathermy plumes are filled with visible and odorous gaseous by-products. Surgical smoke is composed of 95% water or steam and 5% cellular debris in the form of particulate material containing chemicals, blood and tissue particles, viruses, and bacteria (ULMER 2008).

While the limited amount of high quality published data on the potential health hazards of surgical smoke reflect gaps in this area, there is no expert consensus on the precise risks of ill health caused by exposure to surgical smoke (Beswick 2012). Nonetheless, empirical data reveal that electrosurgical smoke contains volatile toxic, carcinogenic and mutagenic compound, which, if inhaled, pose a potential chemical risk that can affect the health of personnel in surgical spaces (ULMER 2008). (Tramontini). Accordingly, clinical practice guidelines for management of electrosurgical smoke call for compliance with safety measures, including proper air exchange, surgical masks, wall suction, and portable smoke evacuation systems in theaters where electrosurgical equipment is used. ULMER 2008. In addition, some of the newly developed electrosurgical instruments on the market have innovative design features that facilitate smoke evacuation during procedures, thereby reducing possible health risks linked with the use of both monopolar and bipolar electrosurgical devices (see Maturity of Technology ).

To mitigate the risk of any potential adverse events and hazards, the surgeon must gain adequate knowledge, understanding, skill, and vigilance to avoid unintentional thermal injury by accidental contact of active or heated electrodes with the patient's viscera. Moreover, surgeons who perform monopolar electrosurgical procedures need to be aware of potential direct or capacitive coupling, insulation defects in the instruments or connecting wires, problems with the functionality or positioning of the return electrode, and potential combustion of volatile substances (Law et al., 2014; Vilos and Rajakumar, 2013).

### **3.3.1.2.1.2 Traditional Bipolar Electrosurgery**

#### **Background**

Despite the ability of monopolar electrosurgical instruments to desiccate, coagulate, vaporize, cut, and fulgurate tissues, these devices have limitations. In addition to the risk for collateral injury associated with the remote placement of the dispersive electrode, many monopolar RF electrosurgical devices lack

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precision and control. This limitation hampers the surgical effectiveness of using monopolar RF electrosurgical devices in electricity-sensitive tissues, complex surgical procedures, and “wet” surgical fields contaminated by blood and other fluids (Park and Porteenier, 2012). Bipolar RF electrosurgical instruments were first developed in the early twentieth century specifically to overcome these shortcomings of the monopolar mode (Park and Porteenier, 2012). As the bipolar modality evolved, the focus turned to designing devices that could reduce the risk of stray current injury associated with monopolar electrosurgery while simultaneously occluding and sealing larger vessels (Law et al., 2014).

In contemporary medicine, traditional bipolar electrosurgery refers to an energy-based surgical technology indicated especially for hemostasis and coagulation, including larger vessel sealing, that is designed to decrease complications from stray current risk of stray current in various operations. In contrast to the monopolar mode with one wire connecting the ESU and the dispersive electrode and another linking the ESU to the “active” electrode, in the bipolar configuration both electrodes are contained in one cable that joins the generator to the bipolar instrument. In the bipolar mode, the only part of the patient involved in the circuit is the tissue interposed between the two electrodes. The bipolar configuration prevents complications associated with current diversion and provides more accurate measurements of local tissue parameters such as temperature and impedance (Munro, 2012).

### **Advantages and Benefits of Traditional Bipolar Electrosurgical Devices**

Bipolar devices are designed primarily in configurations of forceps and clamps. In both cases, the circuit allows electrons to travel from the ESU to the active electrode, through the grasped tissues to the return electrode, and then back to the ESU (Vilos and Rajakumar, 2013). A grasper provides an appropriate design for bipolar electrosurgical devices since one electrode can be positioned in each jaw. Electrical current travels from one jaw of a grasper (the equivalent of the active electrode) to the other jaw (the equivalent of the return pad electrode). This design is well-suited for facilitating the flow of electrical current through only the targeted (i.e., “grasped”) tissue area, thereby eliminating the potential of unintended stray current circuits through the patient if a return pad electrode were attached to the patient (Law et al., 2014) (Park and Porteenier, 2012). Consequently, only the target tissues and tissues in the immediate surrounding area are affected by the heat produced from the flow of electrons (Vilos and Rajakumar, 2013) (Law et al., 2014). The risks of burns are reduced because the leakage currents are smaller and produce a more evenly distributed area of thermal spread (Law et al., 2014). An additional advantage of this design is that the desired tissue effect can be achieved with a decreased amount of voltage (Law et al., 2014) (Park and Porteenier, 2012). The two electrodes embedded in the grasper have high density power and are positioned across from one another (Law et al., 2014; Vilos and Rajakumar, 2013). Current traveling through tissue between the instrument jaws will therefore be desiccated in a manner similar to that occurring in “closed circuit” (i.e., with the active electrode in direct contact with the tissues) (Law et al., 2014).

Bipolar electrosurgical devices facilitate tissue sealing and hemostasis by two main mechanisms: (1) compression of tissue and (2) local delivery of RF energy to produce cellular and tissue heating. The direct compression of a bleeding vessel obstructs the continued flow of blood, resulting in the development of a proximal thrombus and eliminating “heat sink” (e.g. where the ongoing flow of blood cools the tissues and interferes with coagulation) (Park and Porteenier, 2012). If compression of the tissue is excessive or inadequate, electrical bypass may occur, leading to ineffective sealing of the target tissue. Once compression has been achieved, the delivery of RF energy to a target vessel generates heat and rearranges the protein matrix of the vascular wall. These changes result in the formation of a hemostatic seal. The presence of water and ions within the tissue creates ionic oscillation which in turn triggers the

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conversion of RF energy into intracellular heat. Depending upon the degree to which the temperature of the tissue is increased, different surgical effects such as coagulation, desiccation, and vaporization may be achieved (Park and Porteenier, 2012).

However, bipolar electrosurgical devices can affect only a relatively small amount of tissue at a time, limiting its performance and effectiveness in rapid cutting and dissection of tissue. Bipolar instruments were designed specifically to disperse energy over a larger electrode surface area than can be achieved using monopolar instruments. These devices were initially intended to produce coagulation and provide vessel sealing in intricate surgical fields. As such, they were not intended to produce substantial tissue vaporization, which is needed for effective tissue cutting (Park and Porteenier, 2012). Electrosurgical cutting requires sufficient energy delivery to increase the intracellular temperature to 100°C or more to rapidly allow thermal energy to impact the cell wall, resulting in cellular vaporization. Vaporization is achieved with focused delivery of RF energy using electrodes such as a blade or needle tip that have a very small surface area (Park and Porteenier, 2012).

Total destruction of tissue is undesirable when attempting to achieve electrosurgical coagulation or vessel sealing while simultaneously providing at least basic cutting abilities. Most currently available, proprietary bipolar ESUs are designed to deliver only enough energy to elevate the target tissue temperature above the threshold for protein bond to degradation (around 60°C). The electrosurgical energy is delivered in an interrupted fashion (with the ESU rapidly cycling on and off) to promote tissue cooling and to decrease lateral thermal spread (Park and Porteenier, 2012).

Compared with the monopolar mode, bipolar technology uses a lower voltage and less current to achieve the desired effect (Law et al., 2014). Since the electrodes on bipolar devices are placed in close proximity to each other, tissue impedance is relatively low. This essentially eliminates the possibility of alternate site burns as well as the likelihood of direct and capacitive coupling (Vilos and Rajakumar, 2013). There is no risk of stray current injury from capacitive coupling in bipolar electrosurgery because the bidirectional flow of current in the instrument does not induce capacitive current (Law et al., 2014). Furthermore, since no dispersive electrode is used, the electrical interference from pacemakers or other devices (e.g., ECG, EEG) connected to the patient is less than occurs when using monopolar electrosurgical instruments (Law et al., 2014). Since electrosurgery utilizes alternating current, the active and return electrodes rapidly alternate, yielding a more even distribution of a thermal effect (Law et al., 2014). Also, there is no threat of hyponatremia during resectoscopic surgery because bipolar technology is used with a conductive irrigant solution such as saline (Vilos and Rajakumar, 2013).

### **Disadvantages and Risks of Standard Bipolar Electrosurgical Devices**

Despite the overall advances of bipolar electrosurgery, this mode is associated with several disadvantages. Chief among them is the surgeon's decreased ability to change operational parameters, which he can do when using monopolar electrosurgery (Law et al., 2014). Although bipolar electrosurgical devices allow the electrical current to be delivered only in a "closed circuit," the tissue effects are limited due to the continuous electrical waveform, which is combined with relatively large electrodes that permit optimal contact with the tissues (Law et al., 2014). As a result, standard bipolar electrosurgery is unable to achieve tissue vaporization and fulguration (Law et al., 2014).

Bipolar electrosurgical devices do not totally eliminate the risk of stray current injury from insulation failure (with or without direct coupling to other instruments) (Law et al., 2014). The use of reusable bipolar instruments is associated with a risk of adverse events due to stray current injury from insulation failure (Alkatout et al., 2012). In addition, prolonged activation of the electrode can generate substantial

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heat, which is absorbed by the metal electrode head, potentially causing injury to other tissues upon contact (Vilos and Rajakumar, 2013).

In monopolar electrosurgery the heat energy in the pure cut mode, which is commonly used, is so intense that it causes cells to vaporize. But in conventional bipolar electrosurgery, the blended cut rather than “pure cut” function is applied, which allows simultaneous cutting and coagulation. The term “blended” refers to a blend of surgical effects on the target tissue rather than to a mixing of electrical currents. However, traditional bipolar devices are inefficient for cutting tissue because only a small quantity of tissue can be cut at a time.

The blended cut waveform is characterized by the slow dehydration of cellular fluid and protein, with cooling periods slowing down the action to a dehydrating crawl. This action stops the bleeding precisely when the cuts are being made. The surgeon must adjust the blend to produce different degrees of hemostasis. This waveform is acceptable for sealing off small bleeding vessels when cutting through soft tissue. It is also suitable for resecting tissue masses and decreasing and recontouring redundant tissue using continuous cutting. Additionally, it allows the surgeon to minimize bleeding and work in a clear operating field.

Unlike monopolar electrosurgery, traditional bipolar electrosurgery performs poorly in achieving tissue coaptation. The instrument tips of bipolar electrosurgical devices may disengage, resulting in tissue trauma or tearing of blood vessels that can lead to charring and subsequent poor performance in achieving tissue coaptation (Law et al., 2014). Disconnection of the instrument tips can be prevented by a pulsatile activation of energy and by releasing the tissue right before current flow is terminated (Law et al., 2014). (These thermal effects are minimized with the use of advanced bipolar electrosurgical devices.)

As noted previously, the main disadvantage of bipolar electrosurgery compared to monopolar electrosurgery is that bipolar electrodes cannot efficiently cut tissue (Vilos and Rajakumar, 2013). The main goal of bipolar electrosurgery is not to achieve cutting or dissection, even though this modality can be utilized for this purpose. Bipolar electrosurgical devices are capable of using a continuous waveform associated with the “cut” feature, but cutting is relatively inefficient because only a small amount of tissue can be targeted at a time. Older models of bipolar devices may require changing instruments to cut the desiccated tissue, which in turn extends the time of the procedure. Furthermore, vaporization produced by bipolar electrosurgical devices is cumbersome and unproductive. Nonetheless, bipolar electrosurgical devices signal an important advancement because of their main benefit: vessel sealing ability. Advanced bipolar devices, discussed in the next section, were designed to overcome the obstacle of limited cutting capacity in an efficient vessel sealing device (Vilos and Rajakumar, 2013).

### **3.3.1.2.1.3 Advanced Energy Surgical Devices**

#### **Overview**

“Advanced Energy Surgical Devices” comprise a relatively new class of energized surgical instruments that utilize different forms of energy, such as advanced bipolar (e.g. LigaSure™ Small Jaw, Medtronic, Covidien; Enseal, Ethicon) and ultrasound (e.g. Harmonic Focus; Ethicon, Johnson and Johnson), as well as hybrid devices that integrate these two technologies (e.g. Thunderbeat by Olympus, Japan) (Materazzi et al., 2017).

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Traditional ESUs were not designed to deliver pulsed outputs to decrease lateral thermal spread during electrosurgery and therefore did not require feedback control systems for impedance or temperature. This limitation prevented operators from controlling the delivery of RF energy to target tissues (Park and Porteenier, 2012). Instead, RF energy delivery was ineffective, forcing the surgeon to use manual operations based on visual cues (such as tissue color changes, smoke production, etc.). Inadequacies in the design of the bipolar hand piece with both jaws active worsened problems with this type of device. In some cases, energy was transmitted from both jaws to a target vessel from the outside in, which desiccated the superficial tissues and visibly changed their color before the core tissues were sufficiently denatured to produce hemostasis. Furthermore, the intense application of energy to a target vessel increased the impedance (electrical resistance) due to desiccation, allowing the electrical current to preferentially follow the path of least resistance. The movement of current through less resistive, surrounding tissues produces the “mushroom effect” where the risk of collateral damage extends beyond the lateral thermal spread. To compensate for this potential problem, operators were forced to rely on estimation rather than quantitative assessments of the correct timing for terminating energy delivery (Park and Porteenier, 2012).

### **Advantages and Benefits of Advanced Bipolar Electrosurgical Devices**

The last few years have seen the development of a new generation of bipolar devices, known in the industry as “advanced bipolar electrosurgical devices” that are designed primarily to improve homeostasis by providing enhanced coagulation for vessel sealing. Accordingly, modern ESUs and proprietary advanced bipolar electrosurgical devices are sometimes referred to as vessel sealing systems (VSS) or electrothermal bipolar vessel sealers (EBVS) in the published literature. Some of these devices have received FDA approval to seal blood vessels up to 7 mm in diameter (Law et al., 2014).

Advanced electrosurgical systems feature innovative electrosurgical generators paired with various ligating-cutting instruments. These devices have overcome limitations surrounding the proper amount of energy delivery by incorporating sophisticated microprocessors and feedback systems to monitor and provide continuous feedback about tissue impedance (resistance) and/or temperature at the treatment site. The computer-controlled tissue feedback response system installed in proprietary electrosurgery generator units allows delivery of either pulsed or continuous electrical output with constant voltage by moderating the output current. Because of the nearly instantaneous response to incremental changes in tissue resistance, the total energy delivery using these newer devices is substantially less than with traditional bipolar systems (Brill, 2011; Law et al., 2014; Obonna and Mishra, 2014).

The feedback mechanisms of these “smart generators” automatically adjust the delivery of RF electrical energy in real time, thereby ensuring adequate tissue sealing while minimizing collateral tissue damage (Park and Porteenier, 2012). The electrosurgical energy is delivered in an interrupted fashion (with the ESU rapidly cycling “on and off”) to promote tissue cooling and decrease lateral thermal spread (Park and Porteenier, 2012). Audible signals are relayed to the operator to indicate when adequate coagulation has been achieved, thereby facilitating consistent vessel sealing (Law et al., 2014). Additionally, the potential for collateral tissue injury is reduced, and relatively less smoke and carbonization develop during the procedure. These features combined help to ensure that most currently available proprietary bipolar ESUs deliver only enough energy to elevate the target tissue temperature above the threshold for protein bond degradation (around 60°C).

With the growing demand for multi-functional surgical devices in MIS, newer versions of bipolar devices on the market typically incorporate proprietary modifications to deliver sufficient energy to safely seal bleeding vessels and also cut target tissues without compromising patient safety and effective

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hemostasis (Park and Porteenier, 2012). Some advanced bipolar devices are equipped with innovative components such as a mechanical cutting blade (built into the center of the jaw). Other instruments have specialized jaw designs to maximize ESU energy delivery for bipolar vessel sealing and electrosurgical cutting simultaneously and/or sequentially (Park and Porteenier, 2012; Vilos and Rajakumar, 2013). The addition of a blade into certain contemporary bipolar devices at the electrode site allows nearly virtually bloodless dissection after excellent tissue desiccation without changing instruments. This feature saves time by decreasing “instrument traffic” (Law et al., 2014; Vilos and Rajakumar, 2013). Other novel designs and additions that minimize instrument exchanges to reduce surgery time include a dual action jaw that supports mechanical tissue dissection, bipolar instruments with built-in monopolar electrosurgical dissection tips, and laparoscopic bipolar devices capable of grasping and manipulating intra-abdominal organs with more stability and less tissue trauma (Park and Porteenier, 2012).

Advanced bipolar instruments can achieve consistent vessel sealing within seconds at seal bursting pressures significantly above physiologic blood pressure levels (Park and Porteenier, 2012). By alerting the surgeon when the desired tissue effect has been achieved, the audio signaling system helps to mitigate against potential device-related injuries. The alert systems have been credited with minimizing charring (and grasper sticking during release) and lateral thermal spread that may be associated with prolonged device activation (Law et al., 2014). One of the defining features of state-of-the-art advanced bipolar electrosurgical devices is impedance monitoring with grasper designs that optimize mechanical pressure delivery to the vascular pedicle. This configuration optimizes the vessel-sealing capabilities of advanced bipolar electrosurgical devices.

In summary, the major advantages of advanced bipolar electrosurgical devices, or EBVS, include diminished thermal injuries, decreased thermal spread, reduced tissue necrosis, visual control of sealing (translucent seal of the vessel walls), and sealing of vessels up to 7 mm in diameter (FDA cleared), diminished charring, and an absence of foreign material left behind post-procedure (Entezari et al., 2007). Though controversial, some evidence suggests that the burst strength of EBVS is comparable to that of the clip (Entezari et al., 2007).

There are three innovative bipolar platforms currently on the market that utilize low constant voltage and impedance feedback in conjunction with paired ligating– cutting devices: LigaSure Vessel Sealing Device (Covidien, Boulder, CO, USA); EnSeal Laparoscopic Vessel Fusion System (Ethicon Endo-Surgery, Inc, Cincinnati, OH, USA); and Plasmakinetics Cutting Forceps (Gyrus ACMI, a division of Olympus Corporation, Southborough, MA, USA) (Brill, 2011). While LigaSure remains the premier advanced bipolar electrosurgical device used in clinical practice, all of these devices integrate optimal thermal and mechanical capabilities that improve tissue sealing for hemostasis relative to conventional monopolar and bipolar electrosurgical instruments.

#### **Disadvantages and Risks of Advanced Bipolar Electrosurgical Devices**

The major disadvantages of EBVS include the high cost as well as the firing time 3 to 6 seconds per cycle which is reportedly less effective than clips and which results in more thermal spreading than clips (Entezari et al., 2007). In addition, EBVS is associated with poor grasping, in contrast to Harmonic forceps, and requires more time to achieve vessel occlusion (Entezari et al., 2007).

#### **3.3.1.2.1.4 Ultrasonic Energy Devices**

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Ultrasonic shears or scissors utilize sound waves characterized by vibrations with a high frequency greater than 20,000 Hz, falling beyond the audible spectrum of the human ear. These devices are often referred to by the generic name (i.e., proprietary eponym) of Harmonic Scalpel, the leading trademarked product among ultrasonic energy shears and scissors. The Harmonic Scalpel delivers a form of energy that simultaneously divides and coagulates tissue using a titanium blade vibrating at 55,000 Hz while preventing bleeding. The resulting temperature (ranging from 50 to 100°C) creates denatured protein coagulum (Binsaleh, 2011). This device differs from electrosurgical tools by not requiring conduction through tissues, but it does demand contact with tissues (Baggish, 2012). In MIS, ultrasonic energy is used in the operation of surgical devices designed mainly to provide vessel sealing. Ultrasonic devices are based only on mechanical action without passage of any current affecting the patient, thereby decreasing the risk of nerve damage.

### **Advantages and Benefits of Ultrasonic Shears**

Modern ultrasonic technology reportedly allows for more uniform hemostasis as well as increased functionality and improved efficiency when compared to other energized surgical instruments during procedures (see Table 8). Ultrasonic surgical devices generate physiologic burst pressure for sealing blood vessels that is comparable to the burst pressure used in earlier versions of surgical clips or ligatures. Ultrasonic energy systems are associated with minimal lateral thermal damage and minimal smoke (mist or vapor) (Broughton et al., 2013). The Ethicon Harmonic Scalpel and related devices in this product family are multifunctional ultrasonic devices used to perform coagulation and transection of tissue, vessel sealing, and fluid evacuation.

Clinical evidence shows that the Harmonic Scalpel seals vessels ≤ 5mm with decreased operating time and intraoperative blood loss than observed with other energy surgical devices. The Harmonic ACE+7, another product in this line, has received FDA clearance for sealing of vessels up to 7mm. The benefits of Harmonic Scalpel instruments include minimal heat production, less charring and plume, and less thermal injury to surrounding tissues compared with bipolar energy devices (Alkatout et al., 2012; Entezari et al., 2007). Additional reported advantages of these devices include less tissue necrosis, less instrument traffic (required to perform coagulating and cutting), absence of electrical current and therefore no electrical current passage to the patient, and no foreign material left behind after the procedure (Entezari et al., 2007). Harmonic Scalpel shearing instruments allow for a tension free application and in some studies have demonstrated better healing compared with electrosurgery and lasers for certain applications, as well as improved visualization (Alkatout et al., 2012).

Some evidence demonstrates that ultrasonic shears, particularly Harmonic Scalpel devices, are more effective than other advanced energized surgical tools for cutting through thicker tissue, generating safer as well as less smoke, and potentially offering greater precision. Furthermore, lower rates of tissue damage and wound complications have been reported for ultrasonic surgical energy when compared with electrocautery (standard electrosurgery) (Sinha, 2014). In kidney surgical procedures, ultrasonic shears are advantageous for tumor excision without vascular occlusion, thereby reducing the possibility of renal ischemic damage (Binsaleh, 2011).

From: (Bittner et al., 2012)

**Table 8: Differences Between Electrosurgical Devices and Ultrasonic Shears**

Category	Electrosurgery	Ultrasonic Shears
Grounding electrode	Yes	No

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Category	Electrosurgery	Ultrasonic Shears
Smoke generation	Yes	No
Electrocardiogram, pacemaker interference	Yes	No
Current travels through patient	Yes	No
Heat generation	Constant	Time dependent
Thermal spread	Moderate	Minimal
Cost	Low/intermediate	Intermediate/High
Complications	Current concentration Direct coupling Capacitive coupling Tissue sticking	Thermal injury

### Disadvantages and Risks of Ultrasonic Shears

The main disadvantages of the Harmonic Scalpel include the high cost, the FDA cleared maximum vessel diameter 3 mm, a temperature of 80–100°C required to achieve sealing in vessels with a 2–3 mm diameter (Entezari et al., 2007), and operational limitations when performing coagulation (Sinha, 2014). The Harmonic Scalpel is associated with more thermal spreading than clips (Entezari et al., 2007). The friction produced by ultrasonic energy devices generates heat, rendering these instruments hot enough to cause unintended tissue burning. The burns can be caused by tissue inadvertently touching the hot tip or by heat delivered from the surgical site via thermal conduction (Baggish, 2012). Although the Harmonic Scalpel can achieve effective coagulation, it cannot be maneuvered as easily as conventional electrosurgical devices, such that it takes longer to cut and coagulate tissue (Sinha, 2014). Unlike electrosurgical devices that can be used to coagulate bleeding tissue at any time during the procedure, the Harmonic Scalpel can coagulate only as it cuts (Sinha, 2014).

Surgical risks associated with use of the Harmonic Scalpel include the formation of aerosolized fatty droplets from target tissue, which can interfere with visualization through a laparoscope (Alkatout et al., 2012). According to some published reports, ultrasonic dissectors produce less surgical plume than do other energized surgical technologies during laparoscopic procedures. However, ultrasonic shears still release particles from the friction of the blades and tissue attached to the laparoscope, thus generating a significant amount of vapor or spray during use (Messenger et al., 2017).

Risks associated with this surgical vaporized plume include compromised visualization of the operative field, which may require the surgeon to remove obstructing particles, including aerosolized fatty droplets, from target tissue (Alkatout et al., 2012; Devassy et al., 2015). Plume aerosol produced by ultrasonic shears typically consists of tissue, blood, and blood products and can be identified up to 40 cm from the point of production (Devassy et al., 2015). In one study, compared with surgical plume produced from electrocautery, the aerosolized plume associated with an ultrasonic scalpel contained large quantities of cellular debris ( $> 1 \times 10^7$  particles/mL), but about 25% of the amount of particle concentration (Devassy et al., 2015).

In kidney surgical procedures, the risks of ultrasonic shears include tissue charring, which causes tissue to adhere to the device, creating an inexact line of parenchymal incision with poor visualization of the tumor bed. Additionally, some, though not necessarily all, ultrasonic energy surgical devices are inadequate when used as the exclusive hemostatic agent for controlling major renal parenchymal bleeding (Binsaleh, 2011).

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### 3.3.1.2.1.5 Argon Beam Tissue Coagulators

#### Background

Argon beam tissue coagulators, also known as argon gas coagulation units, argon beam coagulation systems, and argon-enhanced coagulation electrosurgical units, are monopolar electrocautery instruments designed to enhance coagulation for vessel sealing. Argon-enhanced monopolar ESU's contain a system for delivery of monopolar current through a flow of ionized argon gas. The argon beam coagulator conducts a RF current to the tissue along a jet of inert, noncombustible argon gas. Argon gas has a lower ionization potential than air and therefore directs the flow of the current. It may also blow away blood and other liquids on the tissue surface or the surgical field, enhancing visualization of operative area.

The electrosurgical current delivered via a monopolar device forms an ionized channel, or arc, within an argon gas stream that flows between the active electrode and the tissue surface. In argon coagulation, there is no contact of the active electrode with the tissue, and the distance between the surgical instrument and the tissue in open surgery is up to about 5 mm, and in endoscopic surgery up to about 3 mm. The thermal effect occurs at the time when a spark jumps from the active electrode tip to the tissue. The length of the plasma arc between the probe tip and the tissue depends on the selected power, resistance of the target tissue, and argon flow rate. The distance between the active electrode and the tissue is usually 3 to 5 mm, depending on the selected coagulation parameters. When using argon coagulation, precautions for standard monopolar coagulation should be observed (Emed, 2015).

#### Advantages and Benefits of Argon Beam Tissue Coagulators

Control of capillary bleeding in renal parenchyma was initially achieved using the argon beam coagulator. Since the argon beam tissue coagulator leaves a more uniform coagulated surface after blowing away blood and debris from the surgical field, it is considered adequate for minor capillary bleeding after dissection. It is a highly effective form of hemostasis and therefore is still sometimes used in procedures involving major blood loss (Klingler et al., 2006). Because the beam concentrates the electrosurgical current, the resulting eschar produced during the procedure is smoother and more pliable than that resulting from other electrosurgical techniques. Blood is dispersed by the gas, reportedly improving visualization of the operative field. Also, less smoke is produced due to the heavier argon displacing some of the oxygen at the operative site (Brill, 2011).

Argon beam coagulation has broad application in local treatment of cancer, both in the case of advanced tumor resection and in the treatment of benign or pre-cancerous lesions (Emed, 2015). Argon coagulation is often used during procedures performed for oncological indications and various non-oncological indications, such as endoscopic bleeding control and destruction of vascular lesions in the gastrointestinal tract, and general surgery (Emed, 2015).

#### Disadvantages and Risks of Argon Beam Tissue Coagulators

The argon beam coagulator by itself cannot be used for tissue dissection and is unsuitable for control of significant bleeding or larger vessels. The insolubility of argon gas in blood puts patients at risk for significant complications such as argon gas embolism, both non-fatal and fatal, as well as pneumothorax even when the device is used correctly, particularly in the presence of unfavorable anatomical conditions (Klingler et al., 2006; Sankaranarayanan et al., 2013). The selected flow rate for argon should be as low as possible to decrease the risk of argon gas embolism. Direct contact of the tool tip on the target

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anatomical region should be avoided, and the electrode tip should be held at an oblique angle. Furthermore, since this device uses electricity, there is a risk of interference with surgical equipment.

### 3.3.1.2.1.6 Laser Surgery

#### Background

Several lasers have been developed specifically for surgical applications of cutting or vaporizing tissue while leaving a coagulated field. The efficacy of these devices to coagulate or excise tissue is regulated by a specific wavelength, energy, or power setting and mode of operation (i.e. continuous or pulsed) (Binsaleh, 2011). The first use of lasers in laparoscopic surgery was recorded in 1979, with regular use of laparoscopic laser surgery underway as early as 1982. In a short span of time, lasers became very widespread in the medical field, ranging from cosmetic treatments to highly complicated surgeries such as atrial fibrillation treatment. Their utilization has faded, however, and currently lasers are relegated primarily to gynecological procedures (Sankaranarayanan et al., 2013) and urologic applications (Lerner and Rajender, 2015).

Lasers generate heat by applying a concentrated beam of light. In a laser system, electromagnetic or light waves are amplified multiple fold in an optical resonator (which contains mirrors and a gain medium) and passed out in the form of high intensity light waves. The amount of amplification in the resonator determines the amount of energy transmitted by the light waves which are then absorbed by the tissue. This energy absorbed by the tissue then manifests itself into heat which cuts and coagulates the tissue. The frequency of the laser determines the width of the beam generated (the higher the frequency of the wave, the lower the diameter of the beam). Most commercial lasers use infra-red to ultraviolet frequencies for medical applications (Sankaranarayanan et al., 2013).

The energy delivered by the laser, whose intensity can be modulated, can cut, destroy, or alter the cellular or extracellular structure of biological tissue. Laser treatment of benign prostatic hyperplasia (BPH) using enucleation techniques has grown in the field of urology (Lerner and Rajender, 2015). Laser enucleation of the prostate (LEP) is a transurethral procedure that utilizes several different types of lasers to dissect the adenoma from the surgical capsule in a retrograde fashion. Contemporary laser prostate enucleation techniques include Holmium-LEP (HoLEP), Thulium-LEP (ThuLEP), Greenlight-LEP (GreenLEP) and Diode-LEP (DiLEP) applications. Each laser device used for prostate enucleation is intended to remove the adenoma from the surgical capsule, but each laser has unique characteristics (i.e. wavelength, absorption rates) that must be understood by the practicing surgeon (Lerner and Rajender, 2015).

#### Advantages and Benefits of Laser Surgery

Laser applications have the advantage of reducing the risk of infection and promoting healing. Various LEP techniques have demonstrated similar, if not superior, postoperative results to transurethral resection of the prostate (TURP), the current gold standard in the treatment of BPH (Lerner and Rajender, 2015). Lasers utilized in laparoscopic surgery include the Nd:YAG KTP 532 and carbon dioxide lasers, most commonly employed in gynecologic procedures. The carbon dioxide laser is considered the safest device for intra-abdominal use due to its wavelength and ability for precision and control (Baggish, 2012). Energy from the carbon dioxide laser is effectively absorbed by water. This allows for efficient hydro dissection that can backstop the carbon dioxide laser beam in strategic locations, helping to prevent injury to surrounding structures. Since, lasers are not conducted in tissue they are advantageous for vaporizing endometrial implants and cutting adhesions (Baggish, 2012)

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### Disadvantages and Risks of Laser Surgery

Although laser surgery was once widely used in many laparoscopic procedures such as cholecystectomy, the high cost of these devices has limited their use in contemporary medicine primarily to gynecologic, urologic, and dermatologic applications. Laser surgery is currently integrated into certain surgical procedures for improved focus and precise cutting, but it holds risks for pregnant women and has contraindications when used in patients receiving photosensitizing drugs (Legres et al., 2014). Lasers and argon beam coagulation are linked with more reported cases of mortality-related complications than are any other forms of energized surgery. Other drawbacks to using laser surgery is the need for advanced training in laser and laparoscopic surgery (Sankaranarayanan et al., 2013).

Additional risks associated with laser surgery include fire from flammable materials ignited by lasers and increased operative time. The extended sedation period resulting from prolonged surgical time also means a lengthened recovery time. Cellular damage may occur around the area of laser impingement, depending upon the size of the laser tip. Other complications associated with the use of laser surgical energy source are potentially fatal air embolism, injury to the hepatic artery with pseudoaneurysm formation and hemobilia during laparoscopic cholecystectomy, and hemorrhage (Sankaranarayanan et al., 2013).

### 3.4. Comparative Studies

The purpose of the literature review was to assess the performance and safety of the subject devices in relation to these parameters in alternative therapies and devices used to achieve the same surgical goals. In order to leverage the highest level of available evidence on comparisons between surgical energy instruments, the SOA literature evaluation focused on systematic reviews/meta-analyses that compared outcomes of various pairs of energy devices. The goal was to use published data on each of the four categories of energy devices compared with non-energy devices, with each other or with argon beam or laser devices. There were multiple possible combinations of head-to-head to comparisons. Not all the possible combinations of comparative studies were available in the included literature. Due to the limited amount of data available on certain comparisons of paired energy devices, the SOA literature evaluation included two RCTs and two comparative studies that compared monopolar electrosurgical devices either with conventional, non-energized techniques of cutting and/or hemostasis (i.e., cold dissection/blunt dissection) or with standard bipolar electrosurgical devices.

While the investigations pertained to a wide array of surgical procedures, including both laparoscopic and open approaches, the data analysis has been organized by head-to-head paired comparisons of energy devices, whenever possible, rather than by procedure type or anatomical region. A few studies presented data for three-way comparisons between energy instruments, the results of which were teased apart for analysis of direct two-way comparisons, where possible. The four types of energy devices evaluated in the comparative literature spanned the four categories of target therapies to which potential ETHICON subject devices belong: (1) monopolar electrosurgical devices, (2) bipolar electrosurgical devices, (3) advanced bipolar electrosurgical devices, and (4) ultrasonic energy surgical devices.

A conventional electrosurgical device, also known as a radiofrequency dissecting sealer (RFDS), can be used in either monopolar electrosurgery or standard bipolar electrosurgery. Some studies in this literature review that examined conventional electrosurgery did not differentiate between monopolar and bipolar electrosurgical devices, and therefore the results of these studies were grouped together as

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RFDS or conventional (ES) electrosurgical devices rather than as separate monopolar or bipolar instruments.

The majority of studies assessed in this document reported on multiple comparisons of various energy devices used in surgical cutting and/or hemostasis, largely, but not exclusively, between advanced bipolar instruments and ultrasonic energy devices. Relatively fewer studies focused on monopolar or bipolar electrosurgical devices, particularly compared to each other. A small number of studies explored head-to-head comparisons of various energized devices with a variety of traditional non-energized techniques, such as clamp-and-tie or suturing, used to achieve hemostasis or, in some cases, cutting or dissection.

Although argon beam therapy and laser therapy fall under the rubric of energy devices employed in surgical coagulation and cutting, respectively, none of the studies included in the SOA Report evaluated the use of these devices in surgical procedures. Laparoscopic laser cholecystectomy was a popular procedure nearly two decades ago, but it is rarely used for this indication in the current medical climate (Sankaranarayanan et al., 2013). While lasers are still widely utilized in various gynecological treatments such as endometriosis (Sankaranarayanan et al., 2013), this indication was not addressed in any study that presented “higher level evidence” (i.e., systematic review and/or meta-analysis). Despite its association with complications, argon beam coagulation is sometimes coupled with electrosurgery to improve coagulation. However, no studies with “higher level evidence” that were identified through the literature screening utilized argon beam coagulation as an ancillary strategy to promote hemostasis.

#### **Abbreviations for Literature Data Analysis Tables 8 – 17.**

- Cold Dissection/Blunt Dissection: CD
- Monopolar electrosurgery: MES
- Bipolar electrosurgery, conventional / standard: BES
- Conventional electrosurgery (ES) / Radiofrequency Dissecting Sealer (RFDS) (monopolar and/or bipolar): ES/RFDS
- Advanced bipolar electrosurgery (Electrothermal/electrosurgical bipolar vessel sealer): EBVS \*
- Ultrasonic energy surgery: UES
- Primary Outcomes: OT (operating time/surgical duration), BL (blood loss), AEs (adverse events), PP (postoperative pain), LOS (length of hospital stay)
- TURP: Transurethral resection of the prostate
- M-TURP: Monopolar electrosurgical TURP
- B-TURP: Bipolar electrosurgical TURP

*\*EBVS is used in this SOA report because it is a more common clinical term than advanced bipolar electrosurgical device.*

#### **Monopolar Electrosurgery versus Conventional Dissection or Hemostasis**

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Bukhari 2007 et al. compared the outcomes of monopolar electrodissection with cold dissection (blunt dissection) in 100 pediatric patients who underwent tonsillectomy using a different surgical procedure on each tonsil (Bukhari and Al-Ammar, 2007). As noted previously, some confusion exists in the literature regarding the terminology of electrosurgery versus diathermy. Bukhari et al. labeled the technique they evaluated as monopolar diathermy, but the terms electrodiathermy (including electrocautery) and electrosurgery are sometimes used interchangeably, particularly in some of the older literature.

The NICE Guidance document on tonsil conditions published in December 2005 titled “Electrosurgery (diathermy and coblation) for tonsillectomy: Interventional procedures guidance [IPG150],” (<https://www.nice.org.uk/guidance/ipg150>) illustrates that diathermy is categorized by at least some professional societies as a form of electrosurgery (NICE, 2005). Based on this rationale, Bukhari et al.’s article has been included in the SOA literature analysis (seeTable 9). This study demonstrated that compared with traditional blunt dissection performed with a scalpel, electrodissection was associated with performance and safety outcomes that were not inferior and furthermore that showed significant benefit. These findings are consistent with the reported advantages of RF energy-based systems, the first of which consisted of monopolar electrosurgical devices, as compared with traditional manual surgical dissection instruments and methods.

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**Table 9: Monopolar Electrosurgery (MES) (Diathermy) vs Cold Dissection (CD) (Blunt Dissection)**

	No statistically significant difference in outcome between MES and CD
	MES had a statistically significant better outcome than CD
	CD had a statistically significant better outcome than MES
	Outcome not measured or not a primary outcome

Author/Yr Study Type # Patients	Surgical Type Primary Outcome(s) Sample Size (XX/YY)	OT	BL	AEs	PP	LOS	Conclusion / Summary
(Bukhari and Al-Ammar, 2007)  Comparative clinical study (100 pediatric patients; 200 tonsils)	Tonsillectomy  Operative time (<3 mins >3), intraoperative bleeding, post-operative bleeding, pain  Monopolar electrosurgery: Right side (n=81 patients), Left side (n=19 patients)  Cold technique: right side (n=19 patients), Left side (n=81 patients)	p=0.0011	No p value provided				Monopolar dissection tonsillectomy was found to be a safe technique that significantly reduced operative time and intra-operative blood loss. It caused more pain on 1st postoperative day, but no significant difference in pain was observed on remaining days until 10th postoperative day.

### Monopolar Electrosurgery vs Bipolar Electrosurgery

Four studies on monopolar electrosurgery vs bipolar electrosurgery compared outcomes of monopolar transurethral resection of the prostate (TURP), a common monopolar electrosurgical procedure, with those of bipolar TURP, a standard bipolar electrosurgical modality. These studies included a systematic review and meta-analysis of randomized controlled trials (RCTs) (Mamoulakis et al., 2009), two RCTs (Lin et al., 2006; Singh et al., 2005), and a retrospective comparative clinical study (Srivastava et al., 2016). One study concluded that the two techniques achieved comparable effectiveness, but the other three investigations demonstrated relatively more advantageous outcomes for the bipolar technique (SeeTable 10).

In both a systematic review and an RCT, the International Prostate Symptom Score (IPSS), QoL, postvoid residual urine volume (PVR), and Q-max showed similar improvement in B-TURP and M-TURP (Lin et al., 2006; Mamoulakis et al., 2009). However, the between-group differences in these outcomes were not significant in the retrospective comparative study (Srivastava et al., 2016). The difference in the postoperative serum sodium level and the mean sodium change were significantly greater with bipolar electrosurgery, which was associated with a lower risk of TUR syndrome (Srivastava et al., 2016), shorter catheterization duration, shorter hospital stay, and fewer complications (Lin et al., 2006). Although the rates of complications, including blood clot retention, were lower in the B-TURP groups than in the M-TURP groups, the differences were neither significant (Lin et al., 2006) nor highly significant (Singh et al., 2005). However, the duration of irrigation and catheterization was significantly longer with M-TURP than with B-TURP (Mamoulakis et al., 2009; Srivastava et al., 2016). Based on these results, the authors of these studies concluded that the use of B-TURP was preferable in TURP procedures. Yet, comparable

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efficacy was achieved in one study (Singh et al., 2005) and no significant differences in adverse events overall occurred in most studies.

**Table 10: Monopolar Electrosurgery (M-TURP) vs Bipolar Electrosurgery (B-TURP) in Transurethral Resection of the Prostate (TURP)**

No statistically significant difference in outcome between M-TURP and B-TURP
B-TURP had a statistically significant better outcome than M-TURP
M-TURP had a statistically significant better outcome than B-TURP
Outcome not measured or not a primary outcome

Author/Yr Study Type # Patients	Surgical Type Primary Outcome(s) Sample Size (XX/YY)	OT	BL	AEs	PP	LOS	Conclusion / Summary
(Lin et al., 2006)  Prospective RCT of transurethral resection of the prostate (TURP)	Transurethral resection of the prostate (TURP)  International Prostate Symptom Score (IPSS), urinalysis, serum creatinine, serum PSA, peak flow rate (Qmax), serum sodium, hemoglobin, resection time, blood loss,  Monopolar TURP (M-TURP (n=18) vs Bipolar TURP (B-TURP) (n=22)  AE: postoperative serum sodium level			p< 0.001			The devices described in the study appear to be electrosurgical instruments that function with an ESU. The bipolar electrocautery device was safer than the traditional monopolar device for the TURP procedure. The bipolar device decreased the risk of TUR syndrome and produces results similar to those obtained with the monopolar device at 6-month and 1 year follow-ups.
(Singh et al., 2005)  RCT	Transurethral resection of the prostate (TURP)  Resection time, amount of tissue resected, irrigant amount, blood loss, fluid absorption, and change in serum sodium and hemoglobin  Bipolar TURP (n=30) vs Monopolar TURP (n=30) AE: Fall/change in serum Na (mEq/L); Postoperative dysuria was less common with bipolar resection (no p value) Pain: Based on analgesic requirement			P < 0.001		p= 0.019	Operative time was divided into resection and coagulation times. Coagulation time was higher (p = 0.019) in the bipolar group (5.6 v 4.6 minutes). Data presented in this table are for resection time and total operative time (no difference between the groups). Improvement in symptom and QoL scores and Qmax were similar in the two groups  Bipolar resection of the prostate is as effective as monopolar TURP. It does not lead to any change in serum Na and causes less postoperative dysuria compared with monopolar resection.
(Srivastava et al., 2016)  Retrospective comparative clinical study	Transurethral resection of prostate (TURP)  International Prostate Symptom Score (IPSS), quality of life (QoL) scores, PVR, serum creatinine and Q-max at baseline, 1, 3, 6 and 12 months Group 1: Monopolar TURP (M-TURP) (n=72 patients) vs Group 2: Bipolar TURP (BP-TURP) (n=81 patients) Group 3: Open prostatectomy (OP): Data not the focus of this analysis. n=52 patients	G1 > G2 > G3; p<0.001		G1 > G2 = G3 B-TURP (p=0.04)			Operative time was shorter for bipolar TURP than for monopolar TURP. Statistical values for outcomes were for Group 1 vs Group 2 vs Group 3.

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Author/Yr Study Type # Patients	Surgical Type Primary Outcome(s) Sample Size (XX/YY)	OT	BL	AEs	PP	LOS	Conclusion / Summary
(Mamoulakis et al., 2009) Systematic Review and Meta-analysis of 16 RCTs 1406 patients	Transurethral resection of prostate (TURP)  Efficacy (maximum flow rate [Qmax], International Prostate Symptom Score [IPSS])  Bipolar TURP (B-TURP) vs Monopolar TURP (M-TURP)  # patients varied across outcomes assessed. Bipolar technique involved PlasmaKinetic TURP, an advanced bipolar electrosurgical technology.						No clinically relevant differences in short-term (12-mo) efficacy were detected (Qmax: weighted mean difference [WMD]: 0.72 ml/s; 95% confidence interval [CI], 0.08–1.35; p = 0.03). However, B-TURP is preferable due to a more favorable safety profile (lower TUR syndrome (post-TURP hyponatremia) and clot retention rates) and shorter irrigation and catheterization duration.

**Monopolar Electrosurgery vs Advanced Bipolar Electrosurgery (aka Electrosurgical Bipolar Vessel Sealer) (EBVS)**

Monopolar electrosurgical devices were compared with LigaSure, an advanced bipolar tissue sealing and cutting device, in a systematic review (Janssen et al., 2012) and in two RCTs (Martucci et al., 2015; Parlakgumus et al., 2011). Although Janssen et al.'s systematic review included 7 studies, the data for monopolar instruments pertained to only two laparoscopic RCTs. The operative time was significantly shorter for LigaSure than for the monopolar instrument in all three systematic reviews. No statistically significant differences between monopolar techniques and Ligasure were reported for the volume of blood loss, rate of complications, or length of hospital stay (Table 11).

**Table 11: Monopolar Electrosurgical (MES) Device vs. Advanced Bipolar Device (Electrosurgical Bipolar Vessel Sealer) (EBVS)**

	No statistically significant difference in outcome between EBVS and MES
Green	EBVS had a statistically significant better outcome than MES
Yellow	MES had a statistically significant better outcome than EBVS
Blue	Mixed or inconsistent results across studies
White	Outcome not measured or not a primary outcome

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Author/Yr Study Type # Studies # Patients per Study	Surgical Type Primary Outcome(s) Sample Size (XX/YY)	OT	BL	AEs	PP	LOS	Conclusion / Summary
(Janssen et al., 2012)  Systematic review  7 RCTs with 554 patients	Colectomy  Dissection time, blood loss, postoperative complications, Data for monopolar electrosurgery were based on 2 laparoscopic colectomy RCTs: Hubner et al., 2008 and Targarona et al. 2005. (Use of monopolar device as conventional electrosurgery was not verified in Targarona et al.'s study. Full article was unavailable). Hubner et al: MES (n=20 patients) vs EBVS (n=21 patients)	P < 0.001					Considering the relatively low number of complications, all hemostatic devices used may be considered relatively safe. Vessel-sealing devices may be considered safe and their use may reduce costs due to reduced blood loss and shorter operating time in some abdominal surgical procedures compared to mono- or bipolar electrothermal devices. In 2 laparoscopic colectomy RCTs, operating time was significantly shorter with LigaSure device compared to monopolar electroscissor and bipolar electrothermal devices.
(Martucci et al., 2015)  Pilot RCT with 119 patients	Open Pulmonary Lobectomy  Postoperative atrial fibrillation  LigaSure™ tissue fusion (n=57 patients) vs electrosurgical pencil (standard hemostatic procedure) (n=62 patients)	P = 0.017					There was no statistically significant difference between LigaSure and electrosurgical pencil in terms of postoperative atrial fibrillation (P = 0.31).
(Parlakgumus et al., 2011)  Prospective RCT with 128 patients	Pilonidal Sinus Surgery  Surgical site infection, early wound failure (dehiscence), and unhealed wound rate  Monopolar electrosurgical device (Aesculap GN 300) (group ME) n=64) vs advanced bipolar tissue sealing-cutting device (LigaSure V 20 cm Instrument [LS1520]) (group TSD) (n=64)	MES (P<.01)	Mixed results wound dehiscence (P=.02)	EBVS / LS			The efficacious use of devices with low thermal energy spread reduces seroma and infection rates. Despite the long operation time, TSDs may be a method of choice in surgery for pilonidal sinus because of their positive effects on patient outcomes, especially in the early postoperative period.

### Monopolar Electrosurgery vs Ultrasonic Energy

Head to head comparisons of monopolar electrosurgical devices vs ultrasonic energy devices were reported in two meta-analyses (Jiang et al., 2017; Xiong et al., 2012) and one retrospective comparative cohort study of laparoscopic cholecystectomy (Zanghi et al., 2014). These three studies had a total of 3175 patients. Compared to the monopolar instruments, the ultrasonic surgical devices were advantageous in terms of a statistically significant shorter operating time, less blood loss, and fewer complications (Jiang et al., 2017; Xiong et al., 2012; Zanghi et al., 2014). Jiang et al.'s performed a meta-analysis and trial sequential analyses of 19 studies with 1955 patients on outcomes of monopolar electrosurgery versus ultrasonic dissection in laparoscopic cholecystectomy (Jiang et al., 2017). These authors concluded that compared to the electrosurgery device, the ultrasonic device could be superior

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because it showed greater clinical effectiveness. The specific ultrasonic instruments were not identified by manufacturer in each study, but the Harmonic ultrasonic shears resulted in shorter operative time ( $P < 0.00001$ ), less blood loss  $P = 0.004$ , fewer gallbladder perforations  $0.00001$ , shorter hospital stay ( $P = 0.002$ ), and fewer abdominal pains (Table 12). However, the relative risk (RR) or mean differences (MDs) for these outcomes was based on a small number of trials, many of which included only 2 to 3 studies (Jiang et al., 2017).

The length of hospital stay was significantly shorter for ultrasonic surgical devices compared with monopolar electrosurgery ( $P = 0.002 - 0.01$ ) in the two meta-analyses (Jiang et al., 2017; Xiong et al., 2012). No significant difference between the groups was reported for pain or for length of hospitalization in the retrospective comparative cohort study (Zanghi et al., 2014).

**Table 12: Monopolar Electrosurgical Device (MES) vs Ultrasonic Energy Device (UES)**

No statistically significant difference in outcome between MES and UES
UES had a statistically significant better outcome than MES
MES had a statistically significant better outcome than UES
Outcome not measured or not a primary outcome

Author/Yr Study Type # Studies # Patients per Study	Surgical Type Primary Outcome(s) Sample Size (XX/YY)	OT	BL	AES	PP	LOS	Conclusion / Summary
(Jiang et al., 2017). Meta-analysis and trial sequential analyses; 19 studies with 1955 patients	Laparoscopic Cholecystectomy  Operative time  (1006 in ultrasonic device group and 949 in electrosurgical [ES] device group)	P < 0.00001	P = 0.004	P < 0.00001	P < 0.0001	P = 0.002	Compared with the electrosurgery device, the ultrasonic device could be superior with more clinical effectiveness. The trial sequential analysis demonstrated that further studies to confirm the superior operative time associated with the ultrasonic device were not needed.
(Xiong et al., 2012)  Meta-analysis 8 high-quality RCTs with 1056 patients	Laparoscopic Cholecystectomy  Mean operation time, mean blood loss, mean hospital stay  Number of patients varied across outcomes measured; ranged from 413-1280 in all studies and from 2113-925 in high quality studies	P < .00001	P < .00001	P < .00001		P = .01	Ultrasonic energy is as safe and effective as electrosurgical energy and potentially might be safer in laparoscopic cholecystectomy. However, the financial implications of this technical modality need to be established in cost-effectiveness analysis.  In 6 studies, no statistically significant difference was found between the two groups (OR, 0.75; 95% CI, 0.33–1.67; $P = .48$ ).  AES refer to pooled results for gallbladder perforation: In 6 studies, the pooled result favored the ultrasonic dissection (OR, 0.31; 95% CI, 0.22–0.44; $P < .00001$ ).

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Author/Yr Study Type # Studies # Patients per Study	Surgical Type Primary Outcome(s) Sample Size (XX/YY)	OT	BL	AES	PP	LOS	Conclusion / Summary
(Zanghi et al., 2014)  Retrospective comparative cohort study with 164 patients	Laparoscopic Cholecystectomy  Mean operative time, rate of gallbladder perforation, intraoperative volume blood loss  Monopolar coagulation (n=121 patients) vs Harmonic ACE (n=43 patients)	UES $p < 0.0001$	UES $p < 0.0001$	UES $p < 0.05$			The Harmonic Scalpel shows some statistically significant advantages (i.e., duration of the operation, rate of gallbladder perforation, intraoperative bile leaks or escapes, volume of blood loss), but no statistical differences were observed in remaining intraoperative (i.e., amount of drainage, visceral injuries conversion rates) or postoperative (i.e., hospital stay and morbidity), complications. These factors, combined with the US cost, show that harmonic scalpel does not offer sufficient advantages to make it the reference technique.

### Conventional (Mono- or Bipolar) Electrosurgery (ES/RFDS) vs Conventional Clamp-crushing (CC) Technique

In a systematic review and meta-analysis of various energy devices used in liver resection, Alexiou et al. reported on outcomes of a radiofrequency dissecting sealer (RFDS) compared with other energy surgical instruments (Alexiou et al., 2013) (Table 13). The study included 8 RCTs and 7 nonrandomized studies that evaluated 1539 patients. The RFDSs referred to either monopolar or bipolar electrosurgical devices, but the exact type of instruments used in the studies was not revealed. There were no statistically significant differences between the patients treated with a RFDS device and those who underwent conventional clamping to achieve hemostasis in the outcomes of blood loss, rate of adverse events, and length of hospital stay. The data showed that RFDS did not exhibit any significant advantage over conventional clamp-crushing (Alexiou et al., 2013).

**Table 13: Monopolar/Conventional Bipolar Electrosurgical (ES/RFDS) Device vs Conventional Clamp-crushing (CC) Technique**

	No statistically significant difference in outcome between ES/RFDS and CC
	ES/RFDS had a statistically significant better outcome than CC
	CC had a statistically significant better outcome than ES/RFDS
	Outcome not measured or not a primary outcome

Author/Yr Study Type # Studies # Patients per Study	Surgical Type Primary Outcome(s) Sample Size (XX/YY)	OT	BL	AES	PP	LOS	Conclusion / Summary
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(Alexiou et al., 2013)  Systematic Review and Meta-analysis;  15 trials [8 RCTs and 7 non-randomized studies] with 1539 patients	Liver Resection  Blood loss  Sample sizes varied across 2-way and 3-way comparisons; and across outcome analyses  RFDS: Monopolar or bipolar electrosurgical devices (not differentiated)  RFDS (ES) vs Conventional Clamp-crushing Technique (CC)				RFDS did not exhibit any significant advantage over the Conventional Clamp-crushing Technique (CC)
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### **Conventional (Mono- or Bipolar) Electrosurgical Devices (ES/RFDS) vs Advanced Bipolar (Electrosurgical Bipolar Vessel Sealer) (EBVS) or Ultrasonic Surgical (UES) Devices**

There were no direct head-to-head comparisons of outcomes between a standard bipolar electrosurgical device and either an advanced bipolar electrosurgical vessel sealer or an ultrasonic energy device in the included SOA literature. However, Allaix et al.'s systematic review of laparoscopic colorectal resection compared outcomes of unspecified conventional electrosurgical devices (either monopolar or bipolar) with advanced bipolar electrosurgical devices (such as Ligasure or Enseal vessel sealing systems) as well as a multifunctional ultrasonic surgical dissector-sealer, the Cavitron Ultrasonic Surgical Aspirator (CUSA) (Allaix et al., 2016). Since no meta-analysis was performed, the findings were summarized for individual studies (Allaix et al., 2016). Both types of advanced vessel sealing systems were found to be advantageous in terms of less blood loss compared with conventional electrosurgical devices. The operative time for the vessel sealing systems was significantly shorter in one study (Hubner et al., 2007), but not in the other. There were no statistically significant differences between the conventional electrosurgical devices and Cavitron Ultrasonic Surgical Aspirator (CUSA) in operative time and intraoperative blood loss in three studies. The authors concluded that ultrasonic surgical devices and advanced bipolar vessel systems are advantageous in terms of less blood loss and/or a shorter operative time compared with conventional electrosurgical devices. However, they noted that the current evidence does not demonstrate which multifunctional instrument is the most effective in laparoscopic colorectal resection (Allaix et al., 2016).

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**Table 14: Monopolar/Conventional Bipolar Electrosurgical Device ES/RFDS vs Advanced Bipolar Electrosurgical (Electrosurgical Bipolar Vessel Sealer) (EBVS) Device**

No statistically significant difference in outcome between ES/RFDS and EBVS
EBVS had a statistically significant better outcome than ES/RFDS
ES/RFDS had a statistically significant better outcome than EBVS
Outcome not measured or not a primary outcome

Author/Yr Study Type # Studies # Patients per Study	Surgical Type Primary Outcome(s) Sample Size (XX/YY)	OT	BL	AEs	PP	LOS	Conclusion / Summary
(Janssen et al., 2012)  Systematic review (no meta-analysis)  7 RCTs with 554 patients	Abdominal Surgery  Dissection time, blood loss, postoperative complications, (Hubner et al., 2007)  In 2 laparoscopic colectomy RCTs: Ligasure (36 patients) vs 31 patients received MES or BES (n=31 patients) in laparoscopic colectomy	EBVS	EBVS	10/20 vs 6/20			In 2 laparoscopic colectomy RCTs, operating time was significantly shorter with LigaSure vs monopolar electroscissor and bipolar electrothermal devices.  Outcomes analyzed in this table are for Hubner, et al., 2008.  Considering the relatively low number of complications, all hemostatic devices used may be considered relatively safe. Vessel-sealing devices may be considered safe and their use may reduce costs due to reduced blood loss and shorter operating time in some abdominal surgical procedures compared to mono- or bipolar electrothermal devices.
(Allaix et al., 2016)  Systematic Review (no meta-analysis)	Laparoscopic Colorectal Resection  Operative time  7 studies; 6 comparative studies with 615 patients. Cohort sizes varied across paired comparisons.	P < .001, P < .05					No meta-analysis was performed. Data reported in these tables are based on overviews of individual study assessments. In 2 studies, operative time was shorter with EBVS compared with ES; blood loss was lower with EBVS compared with ES Although US and EBVS have the advantages of less blood loss and/or a shorter operative time compared with ES, the current evidence does not demonstrate which multifunctional instrument is the most effective in laparoscopic colorectal resection.

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**Table 15: Monopolar/Conventional Bipolar Electrosurgical ES/RFDS Device vs Ultrasonic Energy (UES) Device**

	No statistically significant difference in outcome between ES/RFDS and UES
	UES had a statistically significant better outcome than ES/RFDS
	ES/RFDS had a statistically significant better outcome than UES
	Outcome not measured or not a primary outcome

Author/Yr Study Type # Studies # Patients per Study	Surgical Type Primary Outcome(s) Sample Size (XX/YY)	OT	BL	AES	PP	LOS	Conclusion / Summary
(Jiang et al., 2017) Meta-analysis and trial sequential analyses; 19 studies with 1955 patients	Laparoscopic Cholecystectomy  Operative time  UES (n=1006 patients) vs ES (n=949 patients)	P < 0.00001	P = 0.004	P < 0.00001	P < 0.0001	P = 0.002	Compared with the electrosurgery device, the ultrasonic device could be superior with more clinical effectiveness. The trial sequential analysis demonstrated that further studies to confirm the superior operative time associated with the ultrasonic device were not needed.
(Allaix et al., 2016)  Systematic Review (no meta-analysis)  7 studies; 6 comparative studies with 615 patients	Laparoscopic Colorectal Resection  Operative time  One RCT: ES (n=7 patients) vs UES (n=74 patients) (Morino et al.)	p < 0.05					No meta-analysis was performed. Data reported in these tables are based on overviews of individual study assessments. Although ultrasonic surgical devices (US) and electrothermal bipolar vessel sealers (EBVS) have the advantages of less blood loss and/or a shorter operative time compared with conventional electrosurgery (ES), the current evidence does not demonstrate which multifunctional instrument is the most effective in laparoscopic colorectal resection.

### Advanced Bipolar Electrosurgical Devices vs Conventional Hemostatic Techniques or Conventional Excisional Techniques

Ten studies, including 7 systematic reviews and 3 RTCs, compared advanced bipolar electrosurgical device (particularly, an advanced bipolar vessel sealer) with conventional methods of hemostasis, such as suturing and clamp-and-tie, or excision (see Table 16). Compared with traditional techniques, advanced bipolar electrosurgical devices resulted in statistically significant better outcomes in surgical time in meta-analyses of thyroidectomy, including an assessment of LigaSure (n=813 patients) vs conventional hemostasis (n=2735) patients (Luo et al., 2017); an evaluation of LigaSure vs “clamp-and-tie” (11 studies) (Garas et al., 2013); and an examination of LigaSure vs conventional hemostasis (7 trials, with 730 patients) (Contin et al., 2013). Statistically significant lower amounts of blood loss were associated with LigaSure in some, though not all, studies on thyroid surgery (Luo et al., 2017)(Chavez et al., 2017).

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Reduced surgical time when compared with traditional techniques was also reported for an advanced bipolar electrosurgical device in an RTC of female patients who underwent thyroidectomy with either an advanced bipolar electrosurgical instrument (the Enseal G2 Curved Tissue Sealer, one of the subject devices) (n=21 patients) or traditional tie and suture (n=20 patients) (Chavez et al., 2017). The use of an advanced bipolar device in thyroid operations decreased operative time by >30 minutes when compared with the traditional tie and suture technique (Chavez et al., 2017).

Pain was decreased with the use of an advanced bipolar vessel sealer in one study and hospital stay was shorter in another study, but the differences associated with the two types of energized surgical devices were not significant for several outcomes. In some cases, the benefit was minimal. For example, the use of a bipolar vessel sealing system in performing axillary node dissection for breast cancer was safe and feasible, but offered marginal advantages when compared to the conventional technique (Nespoli et al., 2012).

Variable outcomes were reported for other studies that compared electrosurgical with conventional excision, resection, or suturing. Pergialiotis et al.'s meta-analysis of 8 RCTs evaluated outcomes of electrosurgical bipolar vessel sealing systems (EBVS) (advanced bipolar devices) versus conventional suture ligation in 772 female patients who underwent vaginal hysterectomy (Pergialiotis et al., 2014). Six studies used Ligasure and two studies used BiClamp as the EBVS. There was no overall significant difference in operative time or rate of complications between patients treated with EBVS (n=386) and traditional suture ligation (n=386). However, EBVS were associated with significantly lower intraoperative blood loss (Pergialiotis et al., 2014).

The findings demonstrated that EBVS seemed to produce less intraoperative blood loss during vascular clamping without significantly lowering intraoperative time or complication rate. However, the authors cautioned against drawing firm conclusions due to factors such as heterogeneous recruitment of participants, inconsistent inclusion of patients with vaginal prolapse, and the lack of a definition of randomization (Pergialiotis et al., 2014). In addition, it is not clear if the different types of EBVS devices, including Ligasure and BiClamp, could have affected the outcomes. Six of the RCTs in Pergialiotis et al.'s meta-analysis utilized LigaSure whereas two studies used BiClamp (Pergialiotis et al., 2014). In Zubke et al.'s multicenter RCT, BiClamp (n= 88 patients) resulted in a significantly shorter operative time and significantly less blood loss than conventional suture ligation (n= 88 patients) (Zubke et al., 2009). Postoperative pain was decreased in the BiClamp group, but not significantly. The authors concluded that BiClamp was easier to use and more cost effective than conventional suture ligation (Zubke et al., 2009).

Milito et al., conducted a meta-analysis with 608 patients that compared the use of advanced bipolar devices (LigaSure) with conventional excisional techniques, circular stapling and Harmonic Scalpel in patients with symptomatic hemorrhoids (Milito et al., 2010). Compared with conventional excisional hemorhoidectomy, Ligasure hemorhoidectomy was found to be a fast procedure characterized by a shorter operation time ( $P < 0.001$ ) limited postoperative pain ( $P < 0.001$ ), short hospitalization, and fast wound healing and convalescence (Milito et al., 2010). However, there was no significant difference between the two groups in blood loss. Anal stenosis and hemorrhoids relapse incidence were significantly lower in the Ligasure group than in other excisional treatments ( $P = 0.024$ ). No case of recurrence was reported in either groups. Also, there was no significant difference in the proportion of patients cured after Ligasure hemorhoidectomy or other excisional techniques ( $P > 0.05$ ) (Milito et al., 2010). Nonetheless, the series was limited and had a short term follow-up of not longer than 12 months (Milito et al., 2010).

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In Alexiou et al.'s meta-analysis, 220 patients in 3 RCTs and 3 nonrandomized studies underwent liver resection using either Ligasure (n=110 patients) or conventional clamping (n=110 patients). While there was no significant difference between the two groups in surgical time, Ligasure seemed to offer significant benefit over standard conventional clamping in terms of total blood loss ( $p=0.01$ ), incidence of postoperative bile leak ( $p=0.010$ ), and shorter total hospital stay ( $p=0.0001$ ). These results provide further support for the advantage of an advanced bipolar electrosurgical device in sealing both biliary and vascular structures. Nonetheless, the generalization of the findings was limited by the scarcity and clinical heterogeneity of the published literature (Alexiou et al., 2013).

Macario et al.'s systematic review of 29 RCTs with 2186 patients evaluated safety and performance outcomes who underwent EBVS-LigaSure) (n=1107 patients) or clamping with suture ligation/electrocautery (n =1079 patients) in various procedures (Macario et al., 2008). The conventional mechanical hemostatic methods included suture, clips, vascular/circular stapler, and/or monopolar diathermy. EBVS decreased surgical time by about 25% for diverse surgeries. Compared with the traditional techniques, EBVS resulted in a significantly shorter operative time ( $P < .0001$ ), less blood loss ( $P =.02$ ), fewer complications ( $P =.02$ ), and lower pain scores ( $P =.02$ ) (Macario et al., 2008).

**Table 16: Advanced Bipolar Electrosurgical (Electrosurgical Bipolar Vessel Sealer) (EBVS) Device vs Conventional Clamp-crushing (CC) Technique or Conventional Hemostats or Excision Techniques**

No statistically significant difference in outcome between EBVS and CC/conventional hemostats/excision
EBVS had a statistically significant better outcome than CC/conventional hemostats/excision
CC/conventional hemostats/excision had a statistically significant better outcome than EBVS
Outcome not measured or not a primary outcome

Author/Yr Study Type # Studies # Patients per Study	Surgical Type Primary Outcome(s) Sample Size (XX/YY)	OT	BL	AES	PP	LOS	Conclusion / Summary
(Alexiou et al., 2013)  Systematic Review and Meta-analysis  EBVS vs CC: 3 RCTs and 3 nonrandomized studies	Liver Resection  Blood loss  Sample sizes varied across 2-way and 3-way comparisons; and across outcomes analyses  Vessel sealing systems (VSSs—LigaSure) (EBVS) vs Conventional Crush-clamping (CC) (Patient counts differed across outcomes)		p=0.01			p=0.0001	Of the 3 modalities used in liver resection (VSS/EBVS, Cavitron Ultrasonic Surgical Aspirator [CUSA], and RFDS), only (VSS/EBVS appeared to offer significant benefit over standard CC in terms of total blood loss, incidence of postoperative bile leak, and shorter total hospital stay. Findings may support LigaSure's advantage in the ability to seal both biliary and vascular structures. However, the generalization of our findings is limited by the scarcity and clinical heterogeneity of the published studies.

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Author/Yr Study Type # Studies # Patients per Study	Surgical Type Primary Outcome(s) Sample Size (XX/YY)	OT	BL	AES	PP	LOS	Conclusion / Summary
(Milito et al., 2010)  Meta-analysis  8 studies with 608 patients	Hemorrhoidectomy (open and closed)  Ligasure vs conventional excisional hemorrhoidectomy  Patient counts per cohort were not reported.	P < 0.001			P < 0.001		<p>Conventional excisional hemorrhoidectomy techniques used in this study consisted of diathermy hemorrhoidectomy, Harmonic Scalpel hemorrhoidectomy and Ferguson procedure.</p> <p>There was no significant difference in the proportion of patients cured after Ligasure hemorrhoidectomy or other excisional techniques (<math>P &gt; 0.05</math>). The meta-analysis showed that Ligasure hemorrhoidectomy is a fast procedure characterized by limited postoperative pain, short hospitalization, fast wound healing and convalescence. (No quantitative data were presented on the number of hours by which LS reduced hospitalization.)</p>
(Pergialiotis et al., 2014)  Meta-analysis 8 RCTs with 772 patients	Vaginal Hysterectomy  Operative duration  EBVS (n=386 patients) vs traditional suture ligation (n=386 patients)		p < 0.001				<p>This meta-analysis showed that application of EBVS systems during vaginal hysterectomies may significantly limit intraoperative blood loss when compared with traditional ligation of vascular pedicles. Neither operative duration nor intraoperative and postoperative complications seem to be affected from usage of such systems.</p> <p>The limitations of the meta-analysis included heterogeneous recruitment of participants, inconsistent inclusion of patients with vaginal prolapse, no definition of randomization, concern over criteria for predetermined</p>
(Zubke et al., 2009)  Multicenter RCT with 175 patients  (Also included in Pergialiotis et al.'s study 2014)	Vaginal Hysterectomy  Postoperative pain  Bipolar vessel sealing (BVS; BiClamp®) (EBVS) (n = 88) vs conventional suture ligation (VSL) (n = 87)	P = 0.00	P < 0.00				<p>Postoperative pain was decreased in the BVS group, but not significantly. The BiClamp® procedure proved superior or similar to conventional ligation, particularly with regard to intraoperative blood loss, operating time and postoperative pain, although statistical significance was not attained for postoperative pain. Moreover, BVS was easier to use and more cost effective.</p>
(Contin et al., 2013)  Meta-analysis  34 RCTs with 3875 patients	Open Thyroidectomy  Operation time  LigaSure (LS) (EBVS) (7 trials, 882 patients total in 2-way and 3-way designs)						<p>This three-way comparison of CH with HS and LS in thyroid surgery showed a significant reduction of operation time of HS and LS compared with CH and a marginal benefit of HS for several safety outcomes. The postoperative morbidity was not affected by employing energized devices.</p>

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Author/Yr Study Type # Studies # Patients per Study	Surgical Type Primary Outcome(s) Sample Size (XX/YY)	OT	BL	AES	PP	LOS	Conclusion / Summary
(Chavez et al., 2017)  RTC with 41 patients	Thyroidectomy  Surgical time  Advanced bipolar device (ABD) (n=21 patients) vs traditional tie and suture n=(20 patients)  All patients were women	P = .006			P = .015		The use of an advanced bipolar device in thyroid operation reduces operative time by >30 minutes, with a similar postoperative outcome profile when compared with the traditional tie and suture technique.
(Nespoli et al., 2012)  RCT with 116 women with breast cancer	Thyroidectomy  Total volume of fluid collected in the axillary drain  Conventional node dissection surgical technique (scalpel and monopolar cautery (n = 58 patients) vs electrothermal BVSS (Ligasure Precise) (EBVS) (n = 58 patients)	P = 0.03					The use of a bipolar vessel sealing system in performing axillary node dissection for breast cancer is safe, feasible, and offers marginal advantages when compared to the conventional technique. There were significant benefits in terms of earlier drain removal and reduction of lymph aspirated percutaneously
(Garas et al., 2013)  Network meta-analysis  35 RCTs with 2,856 Total patients	Thyroid Surgery  Hypoparathyroidism (permanent)  Pair-wise comparisons within RCTs: Ligasure (EBVS) vs "clamp-and-tie" (11 studies)	p=0.03 *  p<0.01 **			p<0.01 *  p=0.01 *		Of the three modalities, ultrasonic coagulation demonstrates the best profile in terms of the majority of clinical outcomes (operative time, hypoparathyroidism, blood loss, drain output and cost) followed by Ligasure and then "clamp-and-tie". Conversely, ultrasonic coagulation demonstrated the highest risk for RLN palsy whereas "clamp-and-tie" offered the lowest cumulative probability of this complication. For LOS and neck collection, ultrasonic coagulation again had the best profile but was followed by "clamp-and-tie" and finally Ligasure. These results can contribute to establishing guidelines for thyroid surgery.  AE refers to Hypoparathyroidism Pair-wise comparisons *  Network meta-analysis ** Jadad score (meta-regression analyses of direct comparisons)
(Luo et al., 2017)  Meta-analysis  47 RCTs with 6219 patients	Thyroidectomy  LigaSure vs Conventional Hemostasis  Operation time  2671 patients received Harmonic Scalpel, 813 patients received LigaSure, 2735 patients were treated with conventional hemostasis	p<0.001	p<0.023				The data were evaluated both by pair-wise meta-analyses and network meta-analysis within a Bayesian framework using Markov chain Monte Carlo methods. Recorded Results in this table were based on pair-wise comparison.  Harmonic scalpel decreased operation time compared with the conventional hemostasis. Harmonic scalpel was also associated with lower intra-operative blood loss, and it had the lowest risk of definitive recurrent laryngeal palsy compared with conventional hemostatic methods.

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Author/Yr Study Type # Studies # Patients per Study	Surgical Type Primary Outcome(s) Sample Size (XX/YY)	OT	BL	AES	PP	LOS	Conclusion / Summary
(Macario et al., 2008)  Systematic review and meta-analysis  29 RCTs with 2186 patients:	Various Procedures/Diverse Anatomical Regions  Operative time  EBVS-LigaSure (n=1107 patients); clamping with suture ligation / electrocautery (n =1079 patients), ultrasonic energy (e.g., Harmonic Scalpel) (patient count not reported)	13 studies: P < .0001	13 studies: P = .02	P = .02	P < .0001		The meta-analysis of 26 studies indicates that when compared with conventional mechanical hemostatic methods (such as suture, clips, vascular/circular stapler, and/or monopolar diathermy), EBVS reduces operative time by about one fourth for a variety of surgeries. This use is not associated with increased blood loss, pain scores, or complications.

### Advanced Bipolar Devices (Electrosurgical Bipolar Vessel Dissector-Vessel Sealers) vs Ultrasonic Surgical Devices

Some studies included in the SOA provided three-way comparisons of various energy surgical devices, with the most revealing data often pertaining to either direct or indirect comparisons between EBVS and ultrasonic instruments. For example, Contin et al.'s three-way comparison of conventional techniques for hemostasis with ultrasonic systems (e.g. UltraCision® or Harmonic Focus® devices) and LigaSure in thyroid surgery showed a significant reduction of operation time of Harmonic Focus and LigaSure compared with conventional hemostasis and a marginal benefit of Harmonic Focus for several safety outcomes (Contin et al., 2013). The postoperative morbidity was not affected by employing energized devices (Contin et al., 2013).

Garas et al.'s network meta-analysis was designed to evaluate the incidence of a postoperative adverse event, permanent hypoparathyroidism, following thyroid surgery (Garas et al., 2013). The meta-analysis overall encompassed 35 RCTs with 2,856 total patients. Outcomes were assessed via various comparisons of paired energy surgical devices, including an evaluation of Ligasure vs "clamp-and-tie" in 11 studies (patient count was not provided) (Garas et al., 2013). Ligasure showed a significantly shorter operative time ( $p<0.01$ ) and shorter length of hospitalization ( $p= 0.01$ ), but there were no significant differences in blood loss and adverse events compared to the traditional hemostatic technique. Although Ligasure exhibited a more favorable profile in terms of outcomes than "clamp-and-tie", the outcomes associated with ultrasonic coagulation were superior to the other two techniques (Garas et al., 2013)

A total of 13 studies, primarily meta-analyses, provided data on head-to-head comparisons of outcomes associated with advanced bipolar vessel sealing devices (mainly LigaSure) vs ultrasound (primarily Harmonic Scalpels) in a variety of procedures, such as liver resection (Scatton et al., 2015), laparoscopic colorectal resection (Allaix et al., 2016; Di Lorenzo et al., 2012), hemorrhoidectomy (Milito et al., 2010), thyroid surgery (Cannizzaro et al., 2016{Contin, 2013 #607; Garas et al., 2013; Lang et al., 2013; Luo et al., 2017; Pastore et al., 2013; Upadhyaya et al., 2016} and other operations in diverse anatomical regions (Macario et al., 2008) (see Table 17). Of the studies that reported data on surgical time, ultrasonic surgical devices showed a significant advantage over EBVS in laparoscopic colorectal surgery (Di Lorenzo) and

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thyroid surgery (Garas et al., 2013; Luo et al., 2017), including open thyroidectomy (Contin et al., 2013; Upadhyaya et al., 2016) and total thyroidectomy (Cannizzaro et al., 2016; Lang et al., 2013). However, in one of the RCTs in Milito et al's meta-analysis, the operative time for hemorrhoidectomy was significantly shorter with LigaSure than with the ultrasonic surgical instrument ( $P < 0.001$ ) (Milito et al., 2010). In regard to volume of blood loss, LigaSure (EBVS) was favored in two studies (Allaix et al., 2016; Scatton et al., 2015), whereas ultrasonic surgical devices were favored in one study (Lang et al., 2013), with the majority of studies reporting no significant differences. Lower levels of pain were recorded for LigaSure compared with ultrasonic surgical devices in a meta-analysis of hemorrhoidectomy (Milito et al., 2010) and a meta-analysis of a variety of procedures (Macario et al., 2008). Some studies demonstrated the advantages of electrothermal bipolar vessel sealing over ultrasonic energy in procedures such as laparoscopic colorectal surgery (Di Lorenzo et al., 2012), hemorrhoidectomy (Milito et al., 2010) and laparoscopic radical prostatectomy (Pastore et al., 2013).

In a systematic review, Janssen et al. performed a direct head-to-head comparison of outcomes between LigaSure (an advanced bipolar electrosurgical device) and ultrasonic energy device in laparoscopic colectomy (Janssen et al., 2012). Although no meta-analysis was performed, outcomes were reported for two of the laparoscopic colectomy RCTs (Janssen et al., 2012). LigaSure device was associated with a significantly shorter operating time and significantly less blood loss compared with the bipolar electrosurgery device. The overall rate of adverse events was 50% for standard bipolar devices and 30% for the advanced bipolar instrument (LigaSure). The authors concluded that vessel-sealing devices such as LigaSure may be considered safe and their use may decrease costs due to their advantages in reduced surgical time and amount of blood loss. (Janssen et al., 2012).

In several studies of thyroid surgery, the Harmonic Scalpel exhibited superiority over advanced bipolar vessel sealing devices such as LigaSure in surgical time (Garas et al., 2013; Lang et al., 2013; Luo et al., 2017; Upadhyaya et al., 2016), but not necessarily in lower volume of blood loss. Janssen et all's. meta-analysis included a direct head-to-head comparison of 673 patients treated with an advanced bipolar electrosurgical device vs ultrasonic energy device in thyroid surgery (Janssen et al., 2012). The meta-analysis provided a reduction in operation time by 9.3 minutes when using Harmonic Scalpel (95% CI, [-17.8, -0.8];  $P = 0.032$ ; 6 studies. When the one study that used the Ligasure instrument (LF121) (which was relatively newer at the time of publication) was removed, both the overall result and the "total thyroidectomy" subgroup results became statistically significant. For total thyroidectomies, the use of the Ligasure was slower by 7.1 min compared with the Harmonic Scalpel (95%CI, [-11.1, -3.0] ( $P < 0.001$ ); and in 2 studies and overall, LigaSure resulted in a decrease in surgical time reduction by 12.3 minutes [-20.4, -4.2];  $P = 0.003$ ; 5 studies (Janssen et al., 2012). According to the authors, the amount of time saved in operative time when using Harmonic Scalpel devices could be beneficial for high volume centers conducting many thyroidectomies a day, but not for institutions with a low surgical volume (Contin et al., 2013; Upadhyaya et al., 2016).

Other evidence suggests that the performance outcomes of these two types of energy surgical instruments may be comparable, particularly in total thyroidectomy (Cannizzaro et al., 2016; Lang et al., 2013). Compared to Ligasure, Harmonic Scalpel when used in total thyroidectomy significantly reduced blood loss and operating time. However, the overall mean difference appeared small, and with the wider availability of a more recent version of LigaSure, this difference may become even smaller such that it is not clinically relevant. There was no significant difference in the rate of complications, overall morbidity, and hospital stay between the two devices in Lang et al.'s meta-analysis of total thyroidectomy (Lang et al., 2013). Cannizzaro et al found no significant differences in complications between the Harmonic Scalpel, such that the choice of the device may be determined by cost (Cannizzaro et al., 2016).

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Recent published evidence, therefore, suggests that there is no appreciable difference in clinical outcomes associated with these two types of "advanced energy surgical devices" (Cannizzaro et al., 2016). As noted previously, Allaix et al. concluded that while ultrasonic surgical instruments and advanced bipolar electrosurgical devices (EBVS) are both advantageous in terms of less blood loss and/or a shorter surgical time compared with conventional surgical devices, the data do not show the superiority of one these multifunctional instruments over the other in laparoscopic colorectal resection (Allaix et al., 2016). The anatomical region and type of procedure, including minimally invasive vs traditional open operations, as well as multiple patient characteristics may affect outcomes.

**Table 17: Advanced Bipolar Device (Electrosurgical Bipolar Vessel Sealer) (EBVS) vs Ultrasonic (UES) Surgical Energy Device**

No statistically significant difference in outcome between EBVS and UES
EBVS had a statistically significant better outcome than UES
UES had a statistically significant better outcome than EBVS
Outcome not measured or not a primary outcome

Author/Yr Study Type # Studies # Patients per Study	Surgical Type Primary Outcome(s) Sample Size (XX/YY)	OT	BL	AEs	PP	LOS	Conclusion / Summary
(Scatton et al., 2015)  Systematic Review  30 heterogeneous studies (1 RCT in data analysis)	Liver Resection  Blood loss  No meta-analysis data reported  Data reported for 1 RCT: (Campagnacci et al., 2007)  LS (100 patients) vs HS (100 pt)		EBVS p < 0.001 - 0.002				No meta-analysis of pooled data was presented. Results were qualitative except for the 1 RCT (Campagnacci et al.). Due to the low quality and heterogeneity of the studies, no firm conclusion can be drawn, but meticulous dissection of vessels does not usually lead to vascular damage.  Campagnacci et al., 2007 (RCT): LigaSure Hepatectomy is safe and effective with less blood loss than occurs with an ultrasound surgical device.
(Allaix et al., 2016)  Systematic Review (no meta-analysis)  7 studies; 6 comparative studies with 615 patients	Laparoscopic Colorectal Resection  Operative time  US (n=102) versus EBVS (n=106): 3 Studies Targarona et al. Hubner et al. Rimonda et al.		EBVS p < 0.001, p = 0.002				No meta-analysis was performed. Data reported in these tables are based on overviews of individual study assessments. Although US and EBVS have the advantages of less blood loss and/or a shorter operative time compared with ES, the current evidence does not demonstrate which multifunctional instrument is the most effective in laparoscopic colorectal resection.

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Author/Yr Study Type # Studies # Patients per Study	Surgical Type Primary Outcome(s) Sample Size (XX/YY)	OT EBVS p<0.05	BL EBVS p>0.05	AES	PP	LOS	Conclusion / Summary
(Di Lorenzo et al., 2012)  Meta-analysis  4 studies (including 2 RCTs) with 397 patients were included in final analysis	Laparoscopic Colorectal Surgery  Operative time, blood loss  EBVS (n=200 patients) vs. UES (n=197 patients)						The meta-analysis indicated that electrothermal bipolar vessel sealing is associated with a shorter operative time and less blood loss than ultrasonic energy in laparoscopic colorectal surgery.
(Macario et al., 2008)  Systematic review and meta-analysis  29 RCTs with 2186 patients	Various Procedures / Diverse Anatomical Regions  Operative time  Electrothermal bipolar vessel sealing system (EBVS-LigaSure) (n=1107 patients); clamping with suture ligation / electrocautery (n =1079 patients), ultrasonic energy (e.g., Harmonic Scalpel) (patient count not reported)						The meta-analysis of 26 studies indicates that when compared with conventional mechanical hemostatic methods (such as suture, clips, vascular/circular stapler, and/or monopolar diathermy), EBVS reduces operative time by about one fourth for a variety of surgeries. This use is not associated with increased blood loss, pain scores, or outcomes associated with the Harmonic Scalpel.
(Milito et al., 2010)  Meta-analysis  8 studies with 608 patients	Hemorrhoidectomy (open and closed)  1 RCT: Ligasure (n=24) vs Ultracision (n=255 (ultrasonic surgical device))				EBVS P < 0.001		Conventional excisional hemorrhoidectomy techniques used in this study consisted of diathermy hemorrhoidectomy, Harmonic Scalpel hemorrhoidectomy and Ferguson procedure.  There was no significant difference in the proportion of patients cured after Ligasure hemorrhoidectomy or other excisional techniques ( $P > 0.05$ ). The meta-analysis showed that Ligasure hemorrhoidectomy is a fast procedure characterized by limited postoperative pain, short hospitalization, fast wound healing and convalescence. (No quantitative data were presented on the number of hours by which LS reduced hospitalization.)
(Cannizzaro et al., 2016)  Systematic review and meta-analysis  14 RCTs with 2293 patients:	Total Thyroidectomy  Operating time  Five studies: Focus Harmonic Scalpel (n=238 patients) vs LigaSure Precise (EBVS) (n=236 patients)	UES p = .000			UES p = .005		In total thyroidectomy, the Focus Harmonic scalpel is a reliable and safe tool.  There was no appreciable difference between the Focus Harmonic scalpel and the LigaSure Precise Vessel Sealing System. No significant differences were found in complications and when compared with the LigaSure Precise, so the choice of the device may be determined by cost.

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Author/Yr Study Type # Studies # Patients per Study	Surgical Type Primary Outcome(s) Sample Size (XX/YY)	OT	BL	AES	PP	LOS	Conclusion / Summary
(Lang et al., 2013)  Systematic Review and Meta-analysis  8 studies (5 RCTs, 3 retrospective studies) with 963 patients	Total Thyroidectomy  Total operating time, volume of blood loss  Harmonic Scalpel (n=433 patients) vs (EBVS/Ligasure (n=530 patients)	UES SMD = -0.28, 95 %CI = -0.42-0.15  UES SMD] = -0.2, 95 % CI =-0.38 to -0.02					Compared with Ligasure, Harmonic Scalpel when used in total thyroidectomy significantly reduced blood loss and operating time. However, the overall mean difference appeared small, and with the availability of the newer version of LS this difference may become even smaller, and therefore may not be clinically relevant There was no significant difference in the rate of complications, overall morbidity, and hospital stay between the two devices.
(Upadhyaya et al., 2016)  Meta-analysis  7 RCTs with 981 patients	Open Thyroidectomy  Surgical time  UES n=492 patients0 vs LS/EBVS N=489 patients)	UES P=0.02					The meta-analysis indicated superiority of Harmonic Scalpel only in terms of surgical time compared with LigaSure hemostasis techniques in open thyroid surgery. The postoperative morbidity was not affected. The results of the present study may be useful for high-volume centers performing numerous thyroidectomies every day.
(Contin et al., 2013)  Meta-analysis  34 RCTs with 3875 patients in final meta-analysis	Open Thyroidectomy  Operation time  RCTs had three-arm or two-arm parallel group design: HS vs. LS (3 trials, 471 patients)	UES P=0.032					This three-way comparison of CH with HS and LS in thyroid surgery showed a significant reduction of operation time of HS and LS compared with CH and a marginal benefit of HS for several safety outcomes. The postoperative morbidity was not affected by employing energized devices. The 23 min saved in operative time associated with HS may be beneficial for high volume centers performing many thyroidectomies a day, but not for institutions with a low operation volume.
(Garas et al., 2013)  Meta-analysis  35 RCTs with 2,856 Total patients	Thyroid Surgery  Hypoparathyroidism (permanent)  Pair-wise comparisons within RCTs: ultrasonic coagulation vs Ligasure (5 studies)	UES p= 0.01 *					Ultrasonic coagulation demonstrates the best profile in terms of the majority of clinical outcomes (operative time, hypoparathyroidism, blood loss, drain output and cost) followed by Ligasure and then "clamp-and-tie". Ultrasonic coagulation demonstrated the highest risk for RLN paralysis whereas "clamp-and-tie" offered the lowest cumulative probability of this complication. For LOS and neck collection, ultrasonic coagulation again had the best profile These results can contribute to establishing guidelines for thyroid surgery.  AE refers to hypoparathyroidism.  Pair-wise comparisons * Network-adjusted score (meta-regression analyses of direct comparisons)

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Author/Yr Study Type # Studies # Patients per Study	Surgical Type Primary Outcome(s) Sample Size (XX/YY)	OT	BL	AES	PP	LOS	Conclusion / Summary
(Luo et al., 2017)  Meta-analysis  47 RCTs with 6219 patients	Thyroidectomy  Operation time  2671 patients received Harmonic Scalpel vs 813 patients received LigaSure, 2735 patients were treated with conventional hemostasis	UES (significant, but no P value)					The data were evaluated both by pair-wise meta-analyses and network meta-analysis within a Bayesian framework using Markov chain Monte Carlo methods. Recorded results were based on pair-wise comparison.  Harmonic Scalpel decreased operation time compared with the conventional hemostasis, Harmonic scalpel was also associated with lower intra-operative blood loss, and it had the lowest risk of definitive recurrent laryngeal paralysis compared with conventional hemostatic methods.  Pair-wise meta-analysis * Subgroup analysis via pair-wise comparison**
(Pastore et al., 2013)  Prospective RCT with 132 men	Laparoscopic Radical Prostatectomy  Recovery of urinary Continence (ICIQ-UI score at 180-day follow-up, recovery of erectile function (IIEF-5 score at 180-day follow-up)  Group A (LigaSure radiofrequency [RF] scalpels) (n = 66) vs group B (ultrasound [UES] scalpels (n = 66)						In RF group vs US group, recovery of urinary continence at 180 days occurred in 53 (80%) vs 41 (62%) patients (P = 0.048); recovery of erectile function at 180 days occurred in 56 (84%) vs 41 (62%) patients (P = 0.009)  At postoperative day 180, better functional outcomes (recovery of continence and erectile function) were found in the RF group (LigaSure) compared with the US group (UltraCision).

### Ultrasonic Energy Device vs Conventional Crush-clamping Technique

In comparisons of ultrasonic energy device and conventional clamping (see **Table 18**), the Harmonic Scalpel generally outperformed traditional hemostatic techniques in the clinical outcome of operative time during thyroid surgery (Contin et al., 2013; Garas et al., 2013; Luo et al., 2017). Meta-analyses of thyroid surgery also showed that Harmonic Scalpel was also associated with lower intra-operative blood loss (Garas et al., 2013; Luo et al., 2017) and had the lowest risk of definitive recurrent laryngeal paralysis when compared with conventional hemostatic methods (Garas et al., 2013).

The liver crush clamp technique is used in hepatic parenchymal transection to crush liver tissue without destroying hepatic vascular or ductal structures of the liver, thereby reducing excessive blood loss (Aragon and Solomon, 2012). The surgeon uses basic surgical clamps to crush the hepatic parenchyma as he grasps the tissue between his fingers, enabling him to expose and isolate small vessels and biliary radicals. The crush-clamp method is viewed as a point of reference for all other hepatic parenchymal transection techniques (Aragon and Solomon, 2012). In a comparison of the Cavitron Ultrasonic Surgical Aspirator (CUSA), a multifunctional instrument, vs the crush-clamp technique, CUSA did not exhibit any significant advantage over crush-clamping. No differences were observed between the two groups of patients who underwent these techniques in operating time, complications, or length of hospital stay (Alexiou et al., 2013).

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**Table 18: Ultrasonic Energy (UES) Device vs Conventional Crush-clamping (CC) or Other Conventional Hemostatic Technique**

	No significant statistical difference in outcome between UES and CC
	UES had a statistically significant better outcome than CC
	CC had a statistically significant better outcome than UES
	Outcome not measured or not a primary outcome

Author/Yr Study Type # Studies # Patients per Study	Surgical Type Primary Outcome(s) Sample Size (XX/YY)	OT	BL	AEs	PP	LOS	Conclusion / Summary
(Alexiou et al., 2013)  Systematic Review and Meta-analysis  (15 trials [8 RCTs and 7 non-randomized studies] with 1539 patients)	Liver Resection  Blood loss during the operation and/or the transection  Clamp-crushing technique (CC) (n=111 patients) vs Cavitron Ultrasonic Surgical Aspirator (CUSA) (n=111 patients)						CUSA did not exhibit any significant advantage over CC
(Cannizzaro et al., 2016)  Systematic review and meta-analysis  Total: 14 RCTs with 2293 patients:	Open thyroidectomy  Operating time Focus Harmonic scalpel (FHS) versus conventional techniques (classic ligation with/without electrocoagulation): 12 studies: 968 patients with FHS (968 patients) vs classic ligation w/o electrocoagulation (n=952 patients)	UES p=.000	UES p = .000		UES p = .000	UES p = .000	Outcomes were recorded for both Focus Harmonic scalpel vs conventional techniques (knot and tie with/without electrocoagulation); and for Focus Harmonic scalpel vs classic ligation with/without electrocoagulation. In total thyroidectomy, the Focus Harmonic scalpel is a reliable and safe tool. This meta-analysis confirmed that its use is more effective than conventional techniques in terms of operative time, blood loss, and length of stay, with a statistically and clinically difference in results.
(Contin et al., 2013)  Meta-analysis  34 RCTs with 3875 patients in final meta-analysis	Open Thyroidectomy  Operation time  RTCs had three-arm or two-arm parallel group design: HS vs. LS (3 trials, 471 patients)	UES P < 0.001					This three-way comparison of CH with HS and LS in thyroid surgery showed a significant reduction of operation time of HS and LS compared with CH and a marginal benefit of HS for several safety outcomes. The postoperative morbidity was not affected by employing energized devices. The 23 min saved in operative time associated with HS may be beneficial for high volume centers performing many thyroidectomies a day, but not for institutions with a low operation volume.

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Author/Yr Study Type # Studies # Patients per Study	Surgical Type Primary Outcome(s) Sample Size (XX/YY)	OT	BL	AES	PP	LOS	Conclusion / Summary
(Garas et al., 2013)  Network meta-analysis  35 RCTs with 2,856 Total patients	Thyroid Surgery  Hypoparathyroidism (permanent)  Pair-wise comparisons within RCTs: ultrasonic coagulation vs "clamp-and-tie" (24 studies)	UES p= p=0.03	UES p<0.01				<p>Of the three modalities, ultrasonic coagulation demonstrates the best profile in terms of the majority of clinical outcomes (operative time, hypoparathyroidism, blood loss, drain output and cost) followed by Ligasure and then "clamp-and-tie". Conversely, ultrasonic coagulation demonstrated the highest risk for RLN paralysis whereas "clamp-and-tie" offered the lowest cumulative probability of this complication. For LOS and neck collection, ultrasonic coagulation again had the best profile but was followed by "clamp-and-tie" and finally Ligasure. These results can contribute to establishing guidelines for thyroid surgery.</p> <p>AE refers to hypoparathyroidism.</p>
(Luo et al., 2017)  Meta-analysis  47 RCTs with 6219 patients	Thyroid Surgery Harmonic Scalpel vs Conventional Hemostasis  Operation time  2671 patients received Harmonic Scalpel, 2735 patients were treated with conventional hemostasis	UES 95 % CI -28.11 to -20.44 min,  UES 95 % CI -56.011 to -16.329 ml,  UES OR 0.275, 95 % CI 0.102 - 0.743,					<p>The data were evaluated both by pair-wise meta-analyses and network meta-analysis within a Bayesian framework using Markov chain Monte Carlo methods. Recorded results were based on pair-wise comparison.</p> <p>Harmonic scalpel decreased operation time compared with the conventional hemostasis, Harmonic scalpel was also associated with lower intra-operative blood loss, and it had the lowest risk of definitive recurrent laryngeal paralysis compared with conventional hemostatic methods.</p>

### Comparative Studies: Conclusions

The critical analysis of the clinical data within this CER (see Benefit/Risk Analysis in Section 8) as well as the analysis provided within this section sufficiently determines and supports each of the four main types of energy-based therapies, which are represented by the subject devices, as state of the art tools for surgical cutting, dissection, and coagulation. All energy-based devices exhibited overall advantages over conventional non-energized techniques of cutting, dissection, and coagulation in terms of surgical time, blood loss, and a majority of complications.

Both advanced bipolar devices and ultrasonic surgical instruments, as the two representatives of advanced energized devices, were generally associated with superior clinical safety and performance outcomes relative to conventional electrosurgical devices. However, there is no consensus over which advanced energy-based device is superior overall in vessel sealing across a wide range of traditional and minimally invasive surgical procedures. The Harmonic Scalpel appeared to result in more favorable outcomes when compared to advanced bipolar vessel sealing devices, particularly LigaSure, in multiple studies of thyroid surgery. However, other evidence supported the superiority of electrothermal advanced bipolar vessel sealing devices over ultrasonic energy surgical devices in laparoscopic colorectal surgery (Di Lorenzo et al., 2012) and laparoscopic radical prostatectomy (Pastore et al., 2013).

The reviewed comparative studies on energy-based systems demonstrated an overall advantage in terms of safety and performance outcomes for bipolar electrosurgery in tonsillectomy and TURP and for ultrasonic energy in cholecystectomy, when these techniques were compared with monopolar

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electrosurgery. Jiang et al.'s meta-analysis of studies on laparoscopic cholecystectomy reported superior outcomes for ultrasonic surgery compared with monopolar electrosurgery, but the merit of these results might be limited because many of the trials included only three or fewer studies. Furthermore, despite the benefits of ultrasonic surgery, the higher cost of ultrasonic instruments compared with standard electrosurgical devices may make their use prohibitive for numerous surgeons and health care centers (Jiang et al., 2017). Additionally, ultrasonic surgical devices generate aerosol plume, which poses a health hazard for both patients and OR staff.

In patients who underwent hepatic resection, there was no difference in clinical outcomes of surgical time, complications and length hospitalization in patients treated with the crush-clamp technique versus the Cavitron Ultrasonic Surgical Aspirator (CUSA) (Alexiou et al., 2013). It is not known if a different ultrasonic surgical dissector would have yielded different outcomes.

The clinical outcomes of the included studies seem to suggest that bipolar and advanced bipolar technologies, as well as ultrasonic surgical devices, are superior to conventional monopolar electrosurgery. However, this conclusion might be misleading because it does not take into account the many evidence-based benefits of standard monopolar technology, including its established longer history of use, preference by numerous clinicians, similar rates of overall efficacy compared with advanced bipolar electrosurgery in some studies, relatively low re-operation rates, and continually decreasing rates of the complication of TUR syndrome in prostate surgery.

TUR syndrome, or dilutional hyponatremia, resulting from irrigation using hypotonic/hypo-osmolar nonconductive fluids, is traditionally one of the most important disadvantages of monopolar electrosurgery. In bipolar electrosurgery, there is minimal if any risk of TUR syndrome because irrigation is performed in a conductive rather than nonconductive medium. Although this difference is often used as a rationale for utilizing bipolar technologies in prostate procedures, the literature reveals that TUR syndrome can still occur in B-TURP, since bipolar electrosurgery does not prevent fluid absorption. Moreover, TUR is statistically not necessarily a high risk for most monopolar electrosurgical procedures, as evidenced in some studies that compared M-TURP with B-TURP (Singh et al., 2005; Srivastava et al., 2016). TURP remains the reference standard, and according to some sources, the gold standard, for the operative treatment of benign prostatic hyperplasia (BPH) due to the longevity of outcomes and overall low occurrence adverse events (Muslimanoglu et al., 2012).

Compared with cold/blunt dissection, electrodiathermy (electrosurgery) was associated with a significantly shorter surgical time and considerably less blood loss in patients who underwent tonsillectomy. The benefits of monopolar electrosurgery underscore the maturity of a technology that has advanced considerably beyond manual cutting that has been used in surgical operations for millennia. One of the primary advantages of monopolar electrosurgery is the ease with which it can be used, its familiarity to many operators, and its relatively low cost, rendering equipment affordable to individual surgeons and to surgical clinics. The current literature review demonstrates that standard electrosurgery is associated with overall acceptable rates of performance, efficacy, and safety in regard to multiple surgical tasks across different anatomical therapeutic areas, including tonsillectomy, TURP, and laparoscopic cholecystectomy.

Advanced energized surgical devices, consisting of EBVS and ultrasonic instruments, utilized in contemporary surgery, are associated with a significantly shorter operating time, lesser perioperative bleeding, and lesser postoperative pain. It bears repeating that the findings reported across studies do not consistently demonstrate the superiority of one form of energized surgery tool over the other. As in the utilization of monopolar and standard bipolar electrosurgical devices, the selection

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of a particular advanced energized surgical devices may ultimately depend on surgeon preference, based on factors such as cost, skill in using the instrument, type of surgical operation, and patient characteristics.

Hemostasis in various surgeries such as thyroidectomy remains a paramount goal after preserving vital structures. Advanced electrothermal bipolar vessel sealing technology and ultrasonic dissectors have been shown to significantly decrease surgical times without increasing costs or complications (Materazzi et al., 2017). While these instruments result in a significant elevation of temperature in the tissues, the temperatures they produce are never as high as those of standard monopolar electrosurgery. In clinical scenarios where small bleeding occurs in close proximity to critical structures, energy devices pose considerable risk. The use of clamp and tie may not always be technically feasible in these anatomical regions, making adjunctive hemostatic agents the preferred method of controlling bleeding in these cases (Materazzi et al., 2017).

Overall, however, energized surgical devices, in general, and advanced bipolar and ultrasonic energized devices, in particular, have dramatically enhanced the surgeon's armamentarium with options for safely and effectively achieving hemostasis in a wide range of both open and laparoscopic surgical procedures. Although conventional electrosurgical devices, including monopolar and standard bipolar instruments, performed less efficiently than advanced energy devices in coagulation for sealing larger vessels (> 3mm), basic electrosurgical instruments were adequate and sometimes the preferred modality for tissue cutting and dissection in some studies. Monopolar electrosurgical devices are therefore an appropriate option for physician and surgeon use in the appropriate therapeutic spaces based on their experience, patient needs, and surgical requirements for tissue dissection, coagulation, and in the case of the Endopath Probe Plus II and Megadyne All-In-One, for surgical irrigation, and fluid evacuation.

When assessing multiple surgical functions across diverse therapeutic areas, the literature supports the safety and performance of the four categories of subject devices in comparison to alternate therapies utilized within the same surgical spaces and intended use.

## **GUIDELINES**

The use of energy-generating equipment, including electrosurgical units (ESUs), lasers, and argon beam coagulators used for tissue dissection and coagulation poses a risk for unintended injury if these items are used incorrectly. Some guidelines, including the Association of periOperative Registered Nurses (AORN) "Guideline for safe use of energy-generating devices" provide guidance on the use and maintenance of devices that deliver energy in the forms of radiofrequency waves, ultrasound waves, or lasers (Eder, 2017). Electrosurgical equipment used in perioperative settings potentially can cause thermal injuries (including burns to surgical and nursing staff), interfere with implanted devices, ignite fires and generate detrimental plume that can adversely affect both patients and perioperative personnel.

Therefore, current evidence-based guidelines on energy-based devices address precautions to mitigate the risk associated with electrosurgical units, particularly during minimally invasive surgery; fire safety practices the safe use of these instruments in patients who have an implanted electronic device; and actions to take following an injury or equipment failure during the use of an energy-generating device (Eder, 2017). Published guidelines for energy-based devices are limited and primarily include publications issued by AORN on the use of energy-generating devices for Perioperative RNs. These guidelines are applicable to a wide range of health care practitioners and surgical technicians who work in the presence

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of a large number of energy generating devices used in the OR. However, only some of the guidelines identified in the current literature are based on systematic literature reviews as described below (see **Table 19**).

**Table 19: Examples of Current Guidelines for Energy-based Surgical Devices**

Tonsillectomy using ultrasonic scalpel Interventional procedures guidance [IPG178] Published date: June 2006	AORN Recommended Practices for Electrosurgery	AST Standards of Practice for Use of Electrosurgery (AST, 2012).
Published in June 2006	Effective July 1, 2009.  Originally published March 1985, <i>AORN Journal</i> .	2012
Makes recommendations on the safety and efficacy of the procedure. It does not cover whether or not the NHS should fund the procedure	These recommended practices provide guidance to perioperative nurses in the use and care of electrosurgical equipment, including high frequency, ultrasound, and argon beam modalities.	To support healthcare facilities (HCF) and reinforce best practices related to electrosurgery safety in the perioperative setting. The purpose of the Standards is to provide an outline that surgical team members can use to develop and implement policies and procedures for electrosurgery safety. The Standards are presented with the understanding that it is the responsibility of the HCF to develop, approve and establish policies and procedures for electrosurgery safety, per established HCF protocols
The medical literature was searched to identify studies and reviews relevant to ultrasonic scalpel for tonsillectomy. Searches were conducted via the following databases, covering the period from their commencement to August 2005 MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and Science Citation Index. Trial registries and the Internet were also searched. No language restriction was applied to the searches.	These recommended practices address all of these technologies and do not endorse any specific product.	Measurable criteria include educational standards as established by the Core Curriculum for Surgical Technology.
Narrative literature review with expert conclusions based on current evidence on the safety and efficacy of tonsillectomy using ultrasonic scalpel appears adequate to support the use of this technique provided that normal arrangements are in place for consent, audit and clinical governance.	These recommended represent what is believed to be an optimal level of practice.	The publication consists of 14 <b>Standards of Practice</b> researched and written by the Association of Surgical technologists (AST) Education and Professional Standards Committee.
The Specialist Advisers did not have any particular concerns about the efficacy of this procedure but noted that the evidence base was still small and that a number of the studies had methodological limitations. The Specialist Advisers stated that the safety is much the same as for any other method of tonsillectomy, however it appeared that there is a slight increase in postoperative	Electrical Surgical Units (ESUs )and accessories should be selected based on safety features that minimize patient and personnel injury. the risk of alternate site injuries. the risk of insulation failure and capacitive coupling injuries, the risk of unintentional activation.	"CSTs are knowledgeable of the risks, patient and surgical personnel hazards and safety principles associated with the use of ESU and accessory items."

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Tonsillectomy using ultrasonic scalpel Interventional procedures guidance [IPG178] Published date: June 2006	AORN Recommended Practices for Electrosurgery	AST Standards of Practice for Use of Electrosurgery (AST, 2012).
hemorrhage compared with cold steel dissection.		
-Nine comparative studies, including three randomized between-patients comparisons and three within-patient comparisons -Six studies assessed pain following tonsillectomy using ultrasonic scalpel, cold steel dissection or diathermy. Return to normal diet or appetite was assessed in four studies.	66 References were cited; no further information provided.	Risk factors identified with the use of electrosurgery included fire, patient burns, surgical personnel injuries, and biological hazards, such as plume, which are addressed by safety standards.

### 3.5. Maturity of Technology

Energy-based systems involving monopolar electrosurgery, bipolar electrosurgery, advanced bipolar electrosurgery, ultrasonics, and hybrid configurations of two or more of these systems have become the standard of care in cutting, dissection, coagulation, and in some cases, additional functions required for MIS in diverse anatomical regions. Energy-based instruments are commonly used to perform various gastrointestinal as well as hepatic, gynecologic, thoracic, urologic, and spinal procedures. These technologies collectively provide state-of-the-art interventions whose safety and efficacy have been demonstrated in multiple studies, as discussed in section 3.4.

Historically, the origins of electrosurgery can be traced to the first use of electrocautery in the early 1800s. The predecessor of the contemporary electrosurgical devices was invented in the 1920s and used therapeutically until a smaller unit was manufactured in the 1960s. In current clinical practice, electrosurgery, including electrosurgical instrumentation, plays a critical role in laparoscopic surgery, utilizing various devices inserted into the surgical field, sometimes through a trocar sleeve. These instruments are used routinely in surgical operations, both traditional open and minimally invasive, to provide essential functions of tissue cutting, dissection, and coagulation (Rozner and Jones, 2012).

Laparoscopic surgery often requires drainage of fluids and irrigation of wound surfaces in order to render them clean and sufficiently visible to the surgeon (Ferreira, 2015). In traditional electrosurgery, an irrigator is used to clear debris or blood from bleeding, whereas a suction pump or central vacuum supply system may be employed to remove irrigation fluid or intraperitoneal air and smoke. Alternatively, a large suction-irrigation probe may be utilized to remove blood clots in cases of abrupt bleeding. Only a limited number of electrosurgical combined suction-irrigation devices are currently on the market that simultaneously perform versatile functions, including blunt dissection, coagulation, irrigation, and fluid suction (e.g., the Endopath Probe Plus II and Megadyne All-in-One, two subject devices of this SOA Report, and the GORDTS/CAMPO coagulating suction and irrigation cannula by Karl Storz).

Monopolar electrosurgical devices such as the Ethicon Endopath Electrosurgery Probe II and Megadyne All-In-One perform multiple functions of tissue dissection, coagulation, irrigation, and fluid evacuation (resulting in desiccation), which are essential for laparoscopic surgical procedures. The Endopath Electrosurgery Probe Plus II operates with electrosurgical generators and has high frequency maximum voltage of 5750 Volts peak. The device leverages two interchangeable shafts of different lengths and four

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types of interchangeable handles that allow for a variety of handle/shaft configuration to meet the surgeon's needs. The shafts are designed for use through a 5 mm, 10 mm, or larger diameter trocar with a 5 mm reducer. Shaft EPS13 permits the introduction of a non-conductive flexible device, such as a laser, through the side port of shaft (IFU P40237P13).

**Table 20: Ethicon & Megadyne Energy-based Surgery Subject Devices**

Ethicon & Megadyne Energy-based Surgical Products as categorized on Website
<b>Monopolar Electrosurgery</b>
Ethicon Endopath Probe Plus II
Megadyne All - In One® Hand Control Device
Megadyne Ace Scalpel
Megadyne E-Z Pen™
Megadyne Mega Soft Patient Return Electrode
Megadyne Suction Coagulators
Megadyne Mega Power Generator with ACE Mode
<b>Bipolar Electrosurgery</b>
Megadyne Reusable Electrosurgical Bipolar Forceps
<b>Advanced Bipolar Electrosurgery</b>
Enseal
<b>Ultrasonic Surgery</b>
Harmonic Scalpel

As a multifunctional monopolar energy-based device, the Endopath Electrosurgery Probe Plus II can be used with irrigation and suction devices that are compatible with monopolar electrosurgery units. Shaft EPS11 allows increased capacity of suction (10 mm) with irrigation and without electrosurgery (IFU P40237P13). Ergonomics for user control includes a pistol or pencil grip as well as options for foot control or hand control. Cutting and coagulation can be achieved with the use of the appropriate configuration of electrodes, including the Hook Electrode, Spatula Electrode, Curved Dissector Electrode, and L-hook Electrode, placed with either a 29 cm length or 34 cm length shaft (IFU P40237P13).

The various capabilities of electrosurgical devices are typically achieved using electrodes of three basic shapes: needle tip, spatula, and L-hook or J-hook. Electrodes with hooks or narrow tips allow concentration of current and power and are therefore generally used in tissue vaporization and cutting (Munro, 2012). Active electrodes characterized by a slightly larger surface area, ball-shape, or grasper-shape are suitable for achieving hemostasis (Munro, 2012). An electrode with a wide surface is advantageous for initiating coagulation, the effect of which can be increased by physical maneuvers to decrease the amount of tissue to coagulate (Dargent and Sergio, 2005). The versatility of electrodes in this subject device provides multiple options for performing crucial surgical tasks.

The Megadyne All - In One® Hand Control Device is designed as a hand controlled monopolar electrosurgical tool that provides irrigation, aspiration and electrosurgery in a single device. This instrument is intended to conduct monopolar electrosurgical energy from an electrosurgical generator to target tissue. It is suitable for use whenever monopolar electrosurgical cutting and coagulation are indicated. The modified tips of this device are totally insulated. The Megadyne All-In-One® Hand Control Device is configured for use with Coated Laparoscopic Electrodes that resist splitting up to 700° and

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minimize risk of damage to surrounding tissue. These features are designed to save surgeons time during a procedure. A damp sponge wipe is sufficient for cleaning the electrode (IFU 3000016-02).

Megadyne Electrosurgical Pencils have an ergonomic and lightweight design that is comfortable and minimizes fatigue. The water-resistant construction minimizes electrical shocks and inadvertent activations. The device is equipped with cords that are flexible and "memory-free" for easier handling of the pencil. With the option of a Push Button or Rocker Switch configuration, Megadyne Electrosurgical Pencils are available with E-Z Clean or stainless steel blade electrodes. The product line includes the Megadyne Reusable E-Z Pen™ with an innovative safety lockout mechanism that prevents usage after 12 applications. The 12-use life span promotes cost efficiency. The E-Z Clean PTFE coating on the Megadyne Reusable E-Z Pen™ lasts longer and requires less cleaning than other coatings (IFU 3000009-02).

Other Megadyne monopolar electrosurgical products include Patient Return Electrodes and Suction Coagulators. The Patient Return Electrodes eliminate the small disposable sticky pad that can damage the patient's skin. The Suction Coagulators provide precise coagulation with controlled fluid evacuation and feature an ergonomic handle combined with a flexible, kink-resistant cannula to maximize suction. The ergonomic configuration allows the surgeon to customize the instrument to the specific procedure at hand. While the ergonomic handle reduces fatigue over time, the bendable shaft facilitates precise application and the integrated guard prevents user shocks (IFU 3000137-01).

The Megadyne portfolio of energized surgical products includes a novel monopolar device, the Megadyne Ace Scalpel, that provides a fourth mode of electrosurgical cutting called the Advanced Cutting Effect (ACE). This device achieves a scalpel like cutting effect that results in little to no thermal necrosis as well as no hemostasis. It utilizes proprietary software to maintain a constant voltage at the tip of the electrode rather than constant power like traditional Cut modes (IFU 3000153-01).

The importance of smoke evacuation during electrosurgery was discussed in section XXXX. To help meet this need, Megadyne manufactures multiple smoke evacuation systems designed to remove smoke from the OR during either open or laparoscopic surgery. These devices include the Mega Vac Smoke Evacuator (2100), Mega Vac PLUS Smk Evac, Laparoscopic Mode (2200), Charcoal Filter Mega Vac Smoke Evacuator (2220), Mini Vac Smoke Evacuators 120v (ECVV120), Fluid Trap Mini Vac Smoke Evacuator 220V (ECVV220), and RF Sensor Mini Vac Smoke Evacuator (MGEZLINK01).

Megadyne also produces Smoke Evacuation Pencils for electrosurgery intended for use with various smoke evacuators. These devices facilitate precise electrosurgery while minimizing the hazards of inhaling surgical smoke. The Zip Pen™ Smoke Evacuation Pencil provides surgeons with three ergonomic use options to maximize XXXX and functionality. The Zip Pen has ergonomic features that promote significantly less torque on the back end of the pencil compared with both standard smoke evacuation pencils and standard non-smoke evacuation pencils. The lightweight design helps to minimize hand fatigue, while allowing surgeons to experience both comfort and precision.

The Zip Pen incorporates the Megadyne patented E-Z Clean® coated electrode technology designed to decrease eschar buildup during surgery, thereby potentially increasing the safety of the OR environment. In addition, Zip Pen is equipped with large activation buttons for ease of use, full 360 degree swivel capabilities for maximum procedural flexibility and a safety grip for comfort and control. The buttons have a tactile "pop" which provides positive and instant feedback for activation and deactivation of electrosurgical energy. An innovative "one-size-fits-most" connector allows the ZIP Pen to easily connect to smoke evacuators.

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The Megadyne Reusable Electrosurgical Bipolar Forceps is a bipolar electrosurgical device intended to provide improved safety and performance compared to traditional bipolar electrosurgical instruments. In addition to state-of-the-art cutting functions, this device has a disposable suction coagulator that allows precise coagulation in conjunction with controlled fluid evacuation. Substantial re-bleeding and scarring are common adverse events triggered by tissue adherence during surgery. To help mitigate this problem, the Megadyne Reusable Electrosurgical Bipolar Forceps are crafted with highly polished tips designed to reduce tissue adherence. The light closing force causes less fatigue for the surgeon over time. This device is manufactured from lightweight, highly durable stainless steel and coated with a nylon material that resists abrasion and provides superb insulation. It has a precision tip alignment to aid fine control and it greatly reduces the risks of user error or equipment malfunction. This capacity for precision potentially may reduce the threat of removing coagulum from sealed vessel (NR7 4001 Rev C 2012-11).

The Megadyne Mega Power Generator is an innovative electrosurgical unit (ESU) that provides a Proprietary Advanced Cutting Effect (ACE) mode. Built to work in tandem with the ACE Blade, it is designed to provide a scalpel-like cutting effect for minimal thermal necrosis and reduced scarring. This device can be used with the Monopolar Footswitch (3-meter cable), Bipolar Footswitch (3-meter cable), and /or Monopolar Adapter that comes with the Generator. The unit is equipped with Constant Control Technology installed to automatically monitor tissue impedance and adjust power output to diminish tissue damage and drag. The Megadyne Mega Power Generator is intended to facilitate smooth, clean, accurate cutting effect at the lowest possible setting for maximum patient safety (IFU 3000105-01).

Advanced bipolar instruments can quickly achieve consistent vessel sealing within seconds at seal bursting pressures significantly above physiologic blood pressure levels (Park and Porteener, 2012). By alerting the surgeon when the desired tissue effect has been achieved, the audio signaling system helps to mitigate against potential device-related injuries. These types of alert systems have been credited with minimizing charring (and grasper sticking during release) and lateral thermal spread that may be associated with prolonged device activation (Law et al., 2014). One of the defining features of state-of-the-art advanced bipolar electrosurgical devices, is impedance monitoring with grasper designs that optimize mechanical pressure delivery to the vascular pedicle. This configuration optimizes the vessel-sealing capabilities of advanced bipolar electrosurgical devices. The Ethicon Enseal Seal Tissue Sealing and Hemostasis System includes multiple advanced bipolar electrosurgical devices that employ nanotechnology to control energy at the electrode–tissue interface. The jaws contain a temperature-sensitive matrix with embedded conductive carbon spherules that “sense” tissue characteristics. These technologically advanced graspers utilize extremely high jaw compression to create uniform tissue effects. Ethicon Enseal Seal Tissue Sealing devices do not require a dedicated electrosurgical unit for use. Instead, the adapter allows it to function with most generators (P40632P01, P40627P04).

Ethicon EndoSurgery Harmonic Scalpel Devices are multifunctional ultrasonic surgical dissector-shears used to perform coagulation and transection of tissue, vessel sealing, and fluid evacuation. These devices employ ultrasound technology (high-frequency ultrasonic transducer - 55,000 cycles/second) to cut tissues while simultaneously sealing the edges of the cut. They are used in open and/or endoscopic procedures, depending upon the specific Harmonic device. Clinical evidence reveals that the Harmonic Scalpel seals vessels ≤5mm with decreased operating time and intraoperative blood loss. The Harmonic ACE+7, another product in this line, has received FDA clearance for sealing of vessels up to 7mm (IFU P000162P01).

The Ethicon Endo-Surgery (EES) Generator for HARMONIC® and ENSEAL® has a universal connector and automatic instrument recognition. It has a universal connector, automatic instrument recognition, a touchscreen for easy setup and operation, and a high-resolution display with wider viewing angles.

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Software updates to ensure that the system is operating optimally are available via USB memory stick. The compact design that takes up less space in the OR, promoting the spatial economy of this device (HARH23).

From: (Sankaranarayanan et al., 2013), Manufacturers' Marketing Literature

**Table 21: Examples of Energy Devices in Open and/or Minimally Invasive Surgery**

Type	Product Name
Monopolar electrosurgery	<ol style="list-style-type: none"> <li>1. Covidien / Valleylab Opti4™</li> <li>2. Encision AEM™</li> <li>3. Ethicon Endopath Probe Plus II</li> <li>4. Megadyne All - In One® Hand Control Device</li> <li>5. Megadyne Ace Scalpel</li> <li>6. Megadyne E-Z Pen™ Electrosurgical Pencils</li> <li>7. Megadyne Suction Coagulators</li> <li>8. Megadyne Mega Power Generator with ACE Mode</li> <li>9. Covidien SURGIWAND™ II,</li> <li>10. Stryker StrykeFlow 2</li> </ol>
Bipolar electrosurgery	<ol style="list-style-type: none"> <li>1. Megadyne Reusable Electrosurgical Bipolar Forceps</li> <li>2. Olympus Gyrus Medical PKS Cutting Forceps</li> </ol>
Advanced bipolar electrosurgery	<ol style="list-style-type: none"> <li>1. Covidien LigaSure™</li> <li>2. Olympus PKS Bipolar System – Laparoscopic Loop (BiLL), HALO PKS Cutting Forceps, PKS™ Cutting Forceps, PKS PlasmaSord, PKS Omni, PKS SEAL Open Forceps</li> <li>3. Ethicon EnSeal™</li> </ol>
Ultrasonic energy	<ol style="list-style-type: none"> <li>1. Ethicon Ultracision Harmonic Scalpel</li> <li>2. Ethicon Harmonic ACE</li> <li>3. Ethicon Harmonic FOCUS</li> <li>4. Olympus SonoSurg</li> <li>5. US Surgical Corp / Covidien AutoSonic</li> <li>6. Covidien Sonicision™ Cordless Ultrasonic Dissection Device</li> </ol>

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Type	Product Name
Laser energy	<p>Most commonly referred to their type than a product name.</p> <ol style="list-style-type: none"> <li>1. Nd: YAG laser (neodymium-doped yttrium aluminum garnet)</li> <li>2. Argon laser</li> <li>3. CO2 laser</li> </ol>
Argon beam coagulator	<ol style="list-style-type: none"> <li>1. System 7550™ ABC®</li> <li>2. Cardioblate®</li> </ol>
Radio Frequency (RF) energy	<ol style="list-style-type: none"> <li>1. RF 3000® Radiofrequency Ablation System</li> <li>2. StarBurst®</li> <li>3. Cardioblate®</li> </ol>

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## 4. SUBJECT DEVICE DESCRIPTION

The subsequent sections provide details on the design and specifications, accessories, materials and biocompatibility, and intended purpose and claims for the devices in scope of this CER. The documents listed in Table 22 below were accessed and used to inform the contents of the sections that follow:

**Table 22: Megadyne Source Documents**

Document Name	Document Number	Revision
MEGADYNE Patient Return Electrode for Adults IFU	IFU NR74330	Rev. G 2016-03
MEGADYNE Patient Return Electrode for Pediatrics IFU	IFU NR74380	Rev. F 2016-03
Disposable Grounding Pad Technical File	RA-TECH-0001	Rev. 001
Disposable Grounding Pad Technical File	RA-TECH-0001	Rev. 002

### 4.1. Design and Specifications

As detailed in the Technical File (RA-TECH-0001), the Megadyne Disposable Patient Return Electrode subject devices are single-use, non-sterile electrosurgical accessories used to adhere to the patient over the entire pad surface to complete the electrosurgical circuit between the generator, the active electrode and the patient. As specified in the Technical File (RA-TECH-0001), the following safety and performance features were designed into the subject devices:

- The device must be able to disperse electric current
- The materials must be biocompatible
- There should be no current leakage and the device must comply with IEC 60601-2-2:2009 standard
- The temperature rise of the electrode and patient contact site shall not exceed 6°C
- The patient return electrode shall adhere to the patient with adequate adherence strength while maintaining comfort
- The device shall pass fluid tolerance testing
- The device shall have a shelf-life >2.5 years
- The device must be RoHS 2.0 compliant
- The IFU must provide warnings and/or precautions as well as compatibility information.

The patient return electrodes are composed of an electrode body and a cable (if attached). The materials used for production of the patient return electrodes contains an adhesive-coated thermoplastic foam border with a hydrogel conductive adhesive layer covering an aluminum metalized on a polyethylene foam backing. There are 5 types of Disposable Patient Return Electrodes that are in-scope of the CER, designed for different patient groups. The adult pads are only intended for use on patients weighing >15 kg (33 lbs). The pediatric pad is only intended for use on pediatric patients weighing 2.7 kg to 15 kg (6 to 33 lbs). The main differences among these pads are the size/surface area and pad shape, in which the

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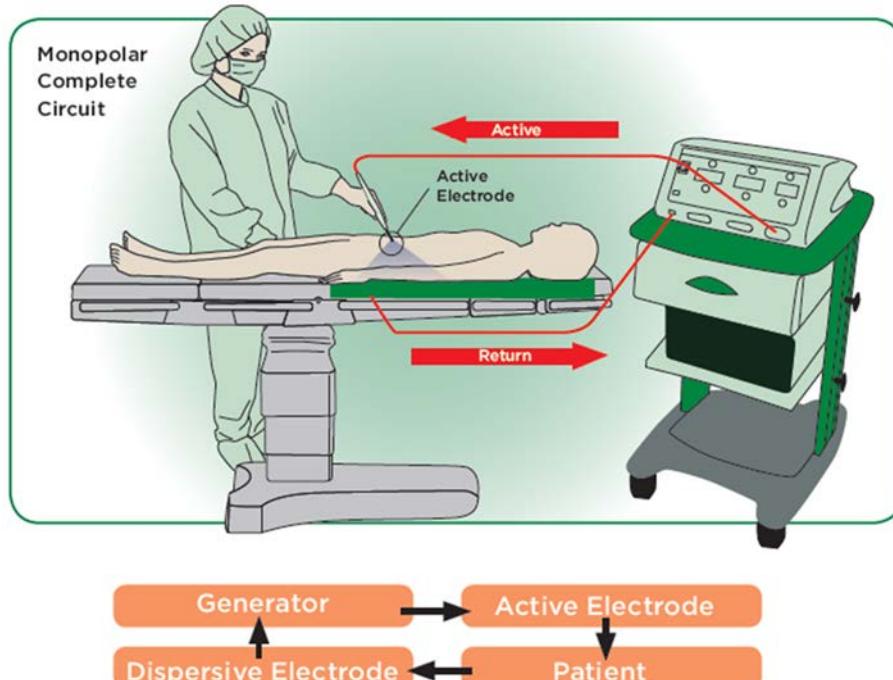
adult pad has the largest size and the pediatric pad has the smallest size. The adult patient return electrodes are also divided into two categories, single element and dual elements. A split dual conductive design of patient return electrode allows the device to be used with Contact Quality Monitoring System (also called Return Electrode Monitor System) that was initially developed by Valleylab, Inc.

The subject devices are non-implantable, surgical devices which involve limited contact with tissue (<24 hour cumulative, limited to contact with the skin surface (refer to Section 4)), and have been designated as a Class IIb medical device in accordance with Annex IX Rule 9 of the European Council Directive 93/42/EEC (MDD). These legacy CE-marked devices have been available for 13 years globally, receiving CE mark certification and launched in 2006. The adult return electrodes (0850C, 0855, 0855CL, 0855CN) were FDA cleared on 31 March 2006 (K060255) and the pediatric return electrodes (0865C) received FDA clearance on 31 August 2007 (K071080), so therefore have been marketed in the US for over 12 years.

The Megadyne Disposable Patient Return Electrodes in scope of this CER and detailed in Section 2.2 comprise one component of an integrated monopolar electrosurgical system used in the majority of surgical procedures. The three major components of the monopolar electrosurgical system include a generator, an active electrode and a dispersive/return electrode. An example of a monopolar circuitry and set up for use during surgery is shown below in Figure 2.

**Figure 2. Monopolar Electrosurgery System Circuitry (adapted from *Principles of Electrosurgery, Megadyne publication, #3000114-01 Rev A 2005-07-01*)**

(Note: image not to scale, for demonstration purposes only)



A summary of the device characteristics, design specifications and materials of construction are detailed in Table 23 below for all devices in scope of this CER.

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**Table 23: Summary of the device characteristics, design specifications and materials of construction for the Megadyne Disposable Patient Return Electrodes**

Subject Device: <b>Megadyne Disposable Patient Return Electrodes</b>
<p><b>Picture (include pictures of all component types)</b></p> <p><b>Megadyne Disposable Patient Return Electrodes.</b> The Patient Return Electrode is a single use, non-sterile return electrode with or without a pre attached cord used to adhere to the patient over the entire return electrode surface to complete the electrosurgical circuit between the generator, the active electrode, and the patient. The following disposable patient return electrode subject devices are in-scope of the CER:</p>  <p><b>Patient Return Electrode 0850C:</b> Adult, single plate, with 9-foot (2.7m) pre-attached cord &gt;33 lbs</p>  <p><b>Patient Return Electrode 0855CL:</b> Adult, dual plate, with 15-foot (4.6m) pre-attached cord &gt;33 lbs</p>  <p><b>Patient Return Electrode 0855CN:</b> Adult, dual plate, with 9' (2.7m) pre-attached cord</p>

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	<b>Subject Device:</b> <b>Megadyne Disposable Patient Return Electrodes</b>
	 <p><b>Patient Return Electrode 0865C:</b> Pediatric, dual plate, with 9-foot (2.7m) pre-attached cord 6-33 lbs</p>  <p><b>Patient Return Electrode 0855:</b> Adult, dual plate, no cord &gt;33 lbs</p>
<b>Intended Purpose</b>	<p>A single use, non-sterile return electrode with a pre-attached cord used to adhere to the patient over the entire return electrode surface to complete the electrosurgical circuit between the generator, the active electrode, and the patient.</p> <p><i>Source: IFU NR74330 Rev. G 2016-03, IFU NR74380 Rev. F 2016-03</i></p> <p>The adult pad is only intended for use on patient weighing &gt;15.0 kg (33 lbs). The pediatrics pad is only intended for use on infants weighing 2.7 kg to 15 kg (6 to 33 lbs).</p> <p><i>Source: Technical File RA-TECH-0001</i></p>
<b>Indication(s) / Clinical Condition</b>	<p>Same as Intended Purpose, above.</p> <p><i>Source: IFU NR74330 Rev. G 2016-03, IFU NR74380 Rev. F 2016-03</i></p>

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	<b>Subject Device:</b> <b>Megadyne Disposable Patient Return Electrodes</b>
<b>Contraindication(s)</b>	No contraindications are specified in the IFUs for the Megadyne Disposable Patient Return Electrodes subject devices in scope of this CER. Refer to the warning section for appropriate cautionary statements.  <i>Source: IFU NR74330 Rev. G 2016-03, IFU NR74380 Rev. F 2016-03</i>
<b>Anatomic Areas of Use</b>	<p><b><u>0850C, 0855, 0855CL, 0855CN (adult electrodes):</u></b></p> <p>Select a smooth, well-vascularized, muscular area as close to the surgical site as possible for electrode placement, but not closer than 15cm. Avoid areas where fluids may pool, scar tissue, bony prominences, and excessive adipose tissue. If the patient has a cardiac pacemaker or other active implant, consult with qualified physician on suitability of HF surgery and placement of the return electrode and cables.</p> <p><i>Source: IFU NR74330 Rev. G 2016-03</i></p> <p><b><u>0865C (pediatric electrode):</u></b></p> <p>Select a smooth, well-vascularized, muscular area as close to the surgical site as possible for electrode placement, but not closer than 15 cm. The recommended application site is on the torso or a thigh. Avoid areas where fluids may pool, scar tissue, bony prominences, and excessive adipose tissue. If the patient has a cardiac pacemaker or other active implant, consult with qualified physician on suitability of HF surgery and placement of the return electrode and cables.</p> <p><i>Source: IFU NR74380 Rev. F 2016-03</i></p>
<b>Patient Population</b>	<p><b><u>0850C, 0855, 0855CL, 0855CN (adult electrodes):</u></b></p> <p>For adult use, &gt; 33 lb (&gt; 15 kg)</p> <p><i>Source: IFU NR74330 Rev. G 2016-03</i></p> <p><b><u>0865C (pediatric electrode):</u></b></p> <p>For pediatric use, 6 - 33 lb (2.7 – 15 kg)</p> <p><i>Source: IFU NR74380 Rev. F 2016-03</i></p>

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	<b>Subject Device:</b> <b>Megadyne Disposable Patient Return Electrodes</b>
<b>Duration of Application</b>	Single use only. Dispose of the used patient return electrode. <i>Source: IFU NR74330 Rev. G 2016-03, IFU NR74380 Rev. F 2016-03</i>  The shelf-life of the assembled pad is 3 years after being manufactured. <i>Source: Technical File RA-TECH-0001 Rev 002</i>

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State: Released

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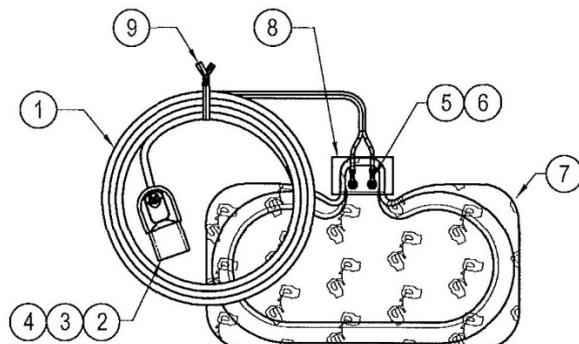
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**Design Parameters**

Single use, non-sterile electrosurgical accessory used to adhere to the patient over the entire pad surface to complete the electrosurgical circuit between the generator, the active electrode and the patient. The subject devices are comprised of a power cord (if attached) and a pad. The return pad is made of a biocompatible, adhesive, conductive gel arranged on a flexible foam backing.

*Source: Technical File RA-TECH-0001 Rev 002*

The following drawings depict the major design elements of the Megadyne Disposable Patient Return Electrodes subject devices:

**Adult, Single Plate Electrode, Model 0850C**

ITEM	DRAWING NO.	DESCRIPTION
9	A200300	TWIST TIE, YELLOW, REEL
8	D001100	PAD COVER, WHITE, ADULT/PEDIATRIC PAD
7	D100700	PAD, SINGLE ELEMENT, ADULT, WHITE FOAM
6	M903200	RIVET, φ2.3 X φ4.5 X 4.0L MM
5	T300103	EYELET CONTACT TERMINAL, φ2.5X6.0MM
4	F501901	PLUG, CLAM SHELL, LOWER, GRAY, RETURN PAD
3	F501801	PLUG, CLAM SHELL, UPPER, GRAY, RETURN PAD
2	T200302	FEMALE CONTACT TERMINAL, ID: 2.35MM
1	C203900	2C CABLE, 26 AWG, GRAY, REEL

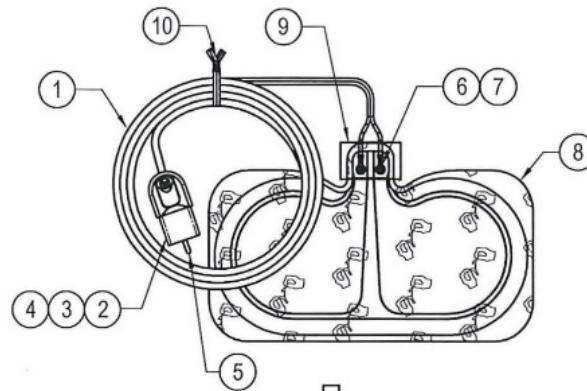
**Adult, Dual Plate Electrodes, Models 0855CL, 0855CN, and 0855**

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ITEM	DRAWING NO.	DESCRIPTION
10	A200101	TWIST TIE, YELLOW, L:110MM
9	D001100	PAD COVER, WHITE, ADULT/ PEDIATRIC PAD
8	D201100	PAD, DUAL ELEMENT, ADULT, WHITE FOAM
7	M903200	RIVET, $\varphi$ 2.3 X $\varphi$ 4.5 X 4.0L MM
6	T300103	EYELET CONTACT TERMINAL, $\varphi$ 2.5X6.0MM
5	F906000	REM PIN
4	F501901	PLUG, CLAM SHELL, LOWER, GRAY, RETURN PAD
3	F501801	PLUG, CLAM SHELL, UPPER, GRAY, RETURN PAD
2	T200302	FEMALE CONTACT TERMINAL, ID: 2.35MM
1	C203900	2C CABLE, 26 AWG, GRAY, REEL

Pediatric, Dual Plate Electrode, Model 0865C

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	<b>Subject Device:</b> <b>Megadyne Disposable Patient Return Electrodes</b>																																	
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1	C203900	2C CABLE, 26 AWG, GRAY, REEL																																
<b>Specifications, Properties (NOTE: Break out key parameters into new rows as warranted)</b>	Refer to Design Parameters, above.																																	
<b>Conditions of Use</b>	<p>Use the lowest power settings for desired surgical effect.</p> <ul style="list-style-type: none"> <li>The adult pad is only intended for use on patient weighing &gt;15.0 kg (&gt;33 lbs).</li> <li>The pediatrics pad is only intended for use on infants weighing 2.7 kg to 15 kg (6 to 33 lbs).</li> </ul> <p>Source: Technical File RA-TECH-0001 Rev. 002, IFU NR74330 Rev. G 2016-03, IFU NR74380 Rev. F 2016-03</p>																																	

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<b>Preparation for Use</b>	<p><b><u>0850C, 0855, 0855CL, 0855CN (adult electrodes):</u></b> Source: IFU NR74330 Rev. G 2016-03</p> <ol style="list-style-type: none"> <li>1. Prepare the patient return electrode application area on patient. Clean and dry the application site as needed. The application site must be free of oils and lotions to ensure secure contact between the patient's skin and the return electrode. Select a smooth, well-vascularized, muscular area as close to the surgical site as possible for electrode placement, but not closer than 15cm. Avoid areas where fluids may pool, scar tissue, bony prominences, and excessive adipose tissue. If the patient has a cardiac pacemaker or other active implant, consult with qualified physician on suitability of HF surgery and placement of the return electrode and cables.</li> <li>2. To minimize the potential for electrosurgical burns, excessive hair at application site must be removed before placement of the patient return electrode. Dry it thoroughly, in particular if alcohol or other skin cleaning fluids are used. DO NOT use lubricating jelly on the return electrode.</li> <li>3. Open the package only prior to use and remove the patient return electrode.</li> <li>4. Remove the liner, and lightly touch the surface of the return electrodes. DO NOT use dry patient return electrodes. Apply the patient return electrode using firm, steady pressure to ensure full, even contact with the patient. Check the patient return electrode, the cord, and the connector for defects.</li> <li>5. Apply the patient return electrode with the long side facing the surgical site.</li> <li>6. Turn on generator to ensure proper operation. Use the lowest power settings that will achieve the desired surgical effect.</li> <li>7. Connect the patient return electrode cord to generator to correct the alarm issue.</li> </ol> <p><b><u>0865C (pediatric electrode):</u></b> Source: IFU NR74380 Rev. F 2016-03</p> <ol style="list-style-type: none"> <li>1. Prepare the patient return electrode application area on patient. Clean and dry the application site as needed. The application site must be free of oils and lotions to ensure secure contact between the patient's skin and the return electrode. Select a smooth, well-vascularized, muscular area as close to the surgical site as possible for electrode placement, but not closer than 15 cm. The recommended application site is on the torso or a thigh. Avoid areas where fluids may pool, scar tissue, bony prominences, and excessive adipose tissue. If the patient has a cardiac pacemaker or other active implant, consult with qualified physician on suitability of HF surgery and placement of the return electrode and cables.</li> <li>2. To minimize the potential for electrosurgical burns, excessive hair must be removed before placement of the return electrode. Dry it thoroughly, in particular if alcohol or other skin cleaning fluids are used. DO NOT use lubricating jelly on the return electrode.</li> <li>3. Open the package only prior to use and remove the patient return electrode.</li> <li>4. Remove the liner, and lightly touch the surface of the return electrodes. DO NOT use dry patient return electrodes. Apply the patient return electrode using firm, steady pressure to ensure full, even contact with the patient. Check the patient return electrode, the cord, and the connector for defects.</li> <li>5. Apply the patient return electrode with the long and non-corded side facing the surgical site.</li> </ol>
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	<b>Subject Device:</b> <b>Megadyne Disposable Patient Return Electrodes</b>
	<p>6. Turn on generator to ensure proper operation. Use the lowest power settings that will achieve the desired surgical effect.</p> <p>7. Connect the patient return electrode cord to generator to correct the alarm issue.</p>
<b>Application (e.g. how the device achieves its intended performance)</b>	See mode of action, below.
<b>Technique / Deployment Method</b>	<p><b><u>0850C, 0855, 0855CL, 0855CN (adult electrodes):</u></b> Source: IFU NR74330 Rev. G 2016-03</p> <p>Select a smooth, well-vascularized, muscular area as close to the surgical site as possible for electrode placement, but not closer than 15cm. Avoid areas where fluids may pool, scar tissue, bony prominences, and excessive adipose tissue. Apply the patient return electrode with the long side facing the surgical site.</p> <p>The un-split electrode is NOT for generators with a Contact Monitoring System, therefore, always check that the return electrode remains in complete contact with the patient and the cord is properly attached.</p> <p><b><u>0865C (pediatric electrode):</u></b> Source: IFU NR74380 Rev. F 2016-03</p> <p>Select a smooth, well-vascularized, muscular area as close to the surgical site as possible for electrode placement, but not closer than 15 cm. The recommended application site is on the torso or a thigh. Avoid areas where fluids may pool, scar tissue, bony prominences, and excessive adipose tissue. Apply the patient return electrode with the long and non-corded side facing the surgical site.</p>
<b>Mode of Action</b>	<p>Single use, non-sterile electrosurgical accessory used to adhere to the patient over the entire pad surface to complete the electrosurgical circuit between the generator, the active electrode and the patient.</p> <p>Source: Technical File RA-TECH-0001 Rev 001</p>
<b>Human Tissue or Body Fluids in Contact with the Device</b>	<p>The subject devices are affixed to the patient's skin by means of a biocompatible adhesive.</p> <p>Source: Technical File RA-TECH-0001 Rev 002</p>

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## 4.2. Required and Adjunctive Devices and Accessories Not Included in CER Scope

The following accessory devices to the Megadyne Disposable Patient Return Electrodes are not in-scope of the CER:

- Megadyne P/N 0875: Reusable Cable, Dual Style, 3m (10")

## 4.3. Materials and Biocompatibility

### 4.3.1. Materials of Construction

The materials used in the construction of the Megadyne Disposable Patient Return Electrode subject devices are listed in Table 24, below. As specified in the Technical File (RA-TECH-0001 Rev 001), all materials are obtained from suppliers with COA, MSDS, and/or certifications. In addition, all incoming materials are inspected for safety and compliance with applicable standards.

**Table 24: Megadyne Disposable Patient Return Electrodes, Materials of Construction**

Component	Material	Function/Performance	Chemical/Physical Characteristics	MSDS General Toxicology Information
Contact Plug	PVC	Connecting to the generator for electric current transfer.	Colorless, odorless, powder. Gamma irradiation can induce degradation of PVC and PVC may appear yellow. Ref: MSDS	Route of exposure: Inhalation, eye, skin contact.
	REM pin (polycarbonate, PC)		Colorless, powder. Heat resistant, impact resistant, and flame retardant. Ref: MSDS	The use of polycarbonate containers for the purpose of food storage is controversial due to the potential for hydrolysis occurring at high temperatures and release of BPA.
	Colorant		Blue color powder	Route of entry: Inhalation, skin, ingestion. Toxicological information is not available in MSDS.
Cable	PVC (outer jacket)	Connecting to the generator for electric current transfer.	Colorless, odorless, powder. Gamma irradiation can induce degradation of PVC and PVC may appear yellow. Ref: MSDS, Sterigenics publication	Route of exposure: Inhalation, eye, skin contact.
	Colorant (outer jacket)		Blue color powder	Route of entry: Inhalation, skin, ingestion. Toxicological information is not available in MSDS.
	PP (inner cable jacket)		Colorless, odorless, solid. Irradiated PP may degrade over time. Validate with real time aging. Ref: MSDS, Sterigenics publication	Route of exposure: Inhalation, ingestion, skin and eye contact. Exposure to this material may cause adverse effects or damage to skin, eyes, and respiratory tract.
Gel	Foil (aluminum)	Adhere to patient to complete the electrosurgical circuit	Oderless, solid, silver-white	Slightly hazardous in case of skin contact (irritant). Non-irritating to the eyes. Non-

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		between the generator, the active electrode and the patient.		hazardous in case of ingestion.
Hydrogel			Glycerol, Water, Polyvinyl Ether Acrylate and Polyquaternium.	NO
Foam			Polyethylene foam single coated with medical grade acrylic adhesive.	NO
Release Liner	PET and Silicone coating film sheet	Prevent a sticky surface from prematurely adhering.	White, solid.	NO

### 4.3.2. Biocompatibility

The subject devices are affixed to the patient's skin by means of a biocompatible adhesive and remain in contact for the duration of the electrosurgical procedure (< 24 hrs.). Table 25 below presents a summary of the patient contact and potential hazards associated for each material (*Source: Technical File RA-TECH-0001 Rev 001*).

**Table 25: Summary of Patient Contacting Components and Materials**

Material	Body Contact	Potential Hazard (ex: additives, leachable, biomaterial, degradable, etc.)
PVC Plug	Rare or no body contact	Non-DEHP PVC material is used.
PVC (outer jacket)	Rare or no body contact	Low Cd, low Pb, non-DEHP material is used. Although the PVC contains plasticizer DIDP, carcinogenicity is lower.
Colorant (outer jacket)	Rare or no body contact	NO
PP (inner cable jacket)	No body contact	NO
Gel	Body contact	NO
Release Liner	Body contact	NO

A systematic biological evaluation, based on criteria including nature of body contact, material characteristics, previous biological/toxicity test reports, and risk analysis, etc., as required in ISO 10993-1:2009 was performed. A summary of the non-clinical biocompatibility studies of the Disposable Patient Return Electrodes is presented in Table 26, below. Refer to the Technical File (RA-TECH-0001, Rev. 001) for the complete set of biocompatibility test reports.

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**Table 26: Summary of Biocompatibility Testing for the Megadyne Disposable Patient Return Electrodes**

Evaluation Item	Criteria	Results	Reference
Nature of Body Contact	Contact Duration	Contact Duration ≤24 hrs Contact Skin	EN ISO 10993-1
Material Characteristics	Materials that may cause biological safety concern, mainly plastics and plasticizers	N/A	MSDS and COA documents
Biocompatibility Test Reports	Cytotoxicity Test	PASS	Refer to reports R130517-E, R150810-E, and R150811-E
	Sensitization Test	PASS	
	Irritation Test	PASS	
History of Safe Use and Market Feedback	Adverse event caused by biocompatibility problem	No adverse events due to biocompatibility safety	Post Market Surveillance analysis and US FDA MAUDE database.

### 4.3.3. Materials and Biocompatibility Conclusion

The materials selected for the construction of these devices, with their intended additives, are fit for purpose with regard to the characteristics and properties of the material (chemical, toxicological, physical, electrical, morphological and mechanical). Laboratory testing (per EN ISO 10993-1) supported by over 12 years of clinical use in which tissue/patient reactions to the materials have not been confirmed, demonstrate a safe history of use in the physical form and intended role, and reveal no significant potential biological hazards. As summarized in sections 4.3.1 and 4.3.2 above, in accordance with EN ISO 10993-1:2009, a complete suite of biocompatibility testing was conducted for each subject device family. Passing results were obtained for all tests performed. The testing reports can be found in the Megadyne Master Control document control system.

As a result of this biocompatibility assessment, all subject devices are considered biocompatible per EN ISO 10993-1 when used as intended.

### 4.4. Intended Purpose

A single use, non-sterile return electrode with a pre-attached cord used to adhere to the patient over the entire return electrode surface to complete the electrosurgical circuit between the generator, the active electrode, and the patient.

*Source: IFU NR74330 Rev. G 2016-03, IFU NR74380 Rev. F 2016-03*

The adult pad is only intended for use on patient weighing >15.0 kg (33 lbs). The pediatrics pad is only intended for use on infants weighing 2.7 kg to 15 kg (6 to 33 lbs).

*Source: Technical File RA-TECH-0001*

The adult pad is only intended for use on patient weighing >15.0 kg (33 lbs). The pediatrics pad is only intended for use on infants weighing 2.7 kg to 15 kg (6 to 33 lbs).

*Source: Technical File RA-TECH-0001*

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## 4.5. Clinical Claims

Same as Intended Purpose, above.

Source: IFU NR74330 Rev. G 2016-03, IFU NR74380 Rev. F 2016-03

As stated in the Technical File (RA-TECH-0001), the device is for general electrosurgical procedures. The device is NOT intended to be used for specific therapeutic or diagnostics indications.

## 4.6. Indications

A single use, non-sterile return electrode with a pre-attached cord used to adhere to the patient over the entire return electrode surface to complete the electrosurgical circuit between the generator, the active electrode, and the patient.

Source: IFU NR74330 Rev. G 2016-03, IFU NR74380 Rev. F 2016-03

## 4.7. Contraindications

No contraindications are specified in the IFUs for the Megadyne Disposable Patient Return Electrodes subject devices in scope of this CER. Refer to the warning section for appropriate statements.

Source: IFU NR74330 Rev. G 2016-03, IFU NR74380 Rev. F 2016-03

## 4.8. Adverse Events / Side Effects

Per IFUs NR74330 Rev. G 2016-03 and NR74380 Rev. F 2016-03: NOT FOLLOWING THESE INSTRUCTIONS MAY LEAD TO BURNS, PRESSURE NECROSES OR OTHER SKIN TRAUMA DURING USE.

## 4.9. Warnings and Precautions

### 4.9.1. Adult Electrodes (0850C, 0855, 0855CL, 0855CN)

- These instructions are for patient safety. NOT FOLLOWING THESE INSTRUCTIONS MAY LEAD TO BURNS, PRESSURE NECROSES OR OTHER SKIN TRAUMA DURING USE.
- PRODUCT LIMITATION: DO NOT use in high-current and/or long-duty cycle procedures. These conditions increase the risk of excessive heating under a fully applied return electrode to the point of seriously injuring the patient. Limit the surgical procedure duty cycle to 25% or less, for example: 10 seconds on followed by 30 seconds off.
- For surgical procedures where the HF current could flow through parts of the body having a relatively small cross-sectional area, the use of bipolar techniques may be desirable in order to avoid unwanted tissue damage.
- Monitoring electrodes or other devices which may provide alternate pathway to ground for HF current must be placed as far away from the operating field as possible. It is recommended to use only monitoring cables and leads incorporating High Frequency current limiting devices, e.g. Radio Frequency (RF) suppressors or RF chokes. If this is not possible, the patient return electrode has to be placed closer to the operating field than the other electrodes or cables.

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- DO NOT reduce size by cutting. Ensure there are no folds in the patient return electrode.
- DO NOT use the patient return electrode if the package seal is broken or if the adhesive is dry or discolored, expired, damaged or modified. Product performance may be compromised. Replace before proceeding.
- DO NOT remove and relocate the patient return electrode after initial application.
- If the patient is repositioned after electrode application, ensure the return electrode remains in complete contact with the patient and the cord is properly attached.
- Always check the patient return electrode site whenever the electrosurgical unit fails to produce the desired effect.
- DO NOT prewarm the patient return electrode. Avoid using warm blankets over the patient return electrode.
- DO NOT reuse the patient return electrode. It is single-use only.
- DO NOT use electrolytic solution in the area of the patient return electrode.
- Position patient return electrode cables to avoid contact with the patient or other leads.
- When applying the patient return electrode, DO NOT allow adjoining edges to touch or overlap.
- Avoid skin-to-skin contact, e.g., between the arms and the body of the patient, by insertion of dry gauze where skin-to-skin contact would occur.
- Refer to the generator's guide for additional cautions and warnings.
- Remove metal jewelry.
- This product is not made with natural rubber latex.

Source: IFU NR74330 Rev. G 2016-03

#### 4.9.2. Pediatric Electrode (0865C)

- These instructions are for patient safety. NOT FOLLOWING THESE INSTRUCTIONS MAY LEAD TO BURNS, PRESSURE NECROSES OR OTHER SKIN TRAUMA DURING USE.
- PRODUCT LIMITATION: The patient return electrode for pediatrics is only intended for use on infants weighing 2.7 – 15.0 kg (6-33 lbs). For infants smaller than the recommended weight, use a neonatal return electrode. DO NOT use the return electrode for pediatrics on patients weighing more than 15 kg (33 lbs).
- PRODUCT LIMITATION: Use the patient return electrode for pediatrics only at power settings up to 120W. Use an adult-sized patient return electrode for procedures requiring power above 120W to reduce the possibility of patient burns.
- PRODUCT LIMITATION: DO NOT use in high-current and/or long-duty cycle procedures. These conditions increase the risk of excessive heating under a fully applied return electrode to the point of seriously injuring the patient. Limit the surgical procedure duty cycle to 25% or less.

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- Surgeons should be familiar with literature on electrosurgical effects on small patients, and may wish to consider bipolar electrosurgery, which does not require a patient return electrode.
- Monitoring electrodes or other devices which may provide an alternate pathway to ground for HF current must be placed as far away from the operating field as possible. It is recommended to use only monitoring cables and leads incorporating High Frequency current limiting devices, e.g. Radio Frequency (RF) suppressors or RF chokes. If this is not possible, the patient return electrode has to be placed closer to the operating field than the other electrodes or cables.
- DO NOT reduce size by cutting. Ensure there are no folds in the patient return electrode.
- DO NOT use the patient return electrode if the package seal is broken or if the adhesive is dry or discolored, expired, damaged or modified. Product performance may be compromised. Replace before proceeding.
- DO NOT remove and relocate the patient return electrode after initial application.
- If the patient is repositioned after electrode application, ensure the return electrode remains in complete contact with the patient and the cord is properly attached.
- Always check the patient return electrode site whenever the electrosurgical unit fails to produce the desired effect.
- DO NOT prewarm the patient return electrode. Avoid using warm blankets over the patient return electrode.
- DO NOT reuse the return electrode. It is single use only.
- DO NOT use electrolytic solution in the area of the patient return electrode.
- Position patient return electrode cables to avoid contact with the patient or the other leads.
- When applying the patient return electrode, DO NOT allow adjoining edges to touch or overlap.
- Avoid skin-to-skin contact, e.g., between the arms and the body of the patient, by insertion of dry gauze where skin-to-skin contact would occur.
- Refer to the generator and electrosurgical pencil user's guides for additional cautions and warnings.
- Remove metal jewelry.
- This product is not manufactured with natural rubber latex.

Source: IFU NR74380 Rev. F 2016-03

#### 4.10. Device Lifetime / Duration of Use

Single use only. Dispose of the used patient return electrode.

Source: IFU NR74330 Rev. G 2016-03, IFU NR74380 Rev. F 2016-03

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The shelf-life of the assembled pad is 3 years after being manufactured.

Source: *Technical File RA-TECH-0001 Rev 002*

## **4.11. Magnetic Resonance Imaging (MRI) Compatibility**

Not applicable. The Megadyne Disposable Patient Return Electrodes are not implantable devices and use within an MRI environment is not anticipated.

## **4.12. Sterility**

A single use, non-sterile return electrode with a pre-attached cord used to adhere to the patient over the entire return electrode surface to complete the electrosurgical circuit between the generator, the active electrode, and the patient.

Source: *IFU NR74330 Rev. G 2016-03, IFU NR74380 Rev. F 2016-03*

## **4.13. Principles of Operation**

Single use, non-sterile electrosurgical accessory used to adhere to the patient over the entire pad surface to complete the electrosurgical circuit between the generator, the active electrode and the patient. The subject devices are comprised of a power cord (if attached) and a pad. The return pad is made of a biocompatible, adhesive, conductive gel arranged on a flexible foam backing.

When performing electrosurgical procedures using monopolar devices, the patient return electrode grounding pad, which is adhered to the patient's skin away from the surgical site, is used and intended to safely return the electrical current from the patient back to the generator through a cord or cable. Because the conductive surface area of the grounding pad is much larger than the active electrode (where cutting, coagulation, or ablation occur), the current is dispersed over a wide area, minimizing the heating of the tissue under the grounding pad.

Source: *Technical File RA-TECH-0001 Rev 002*

### **4.13.1. Installation/Application of the Adult Electrodes (0850C, 0855, 0855CL, 0855CN)**

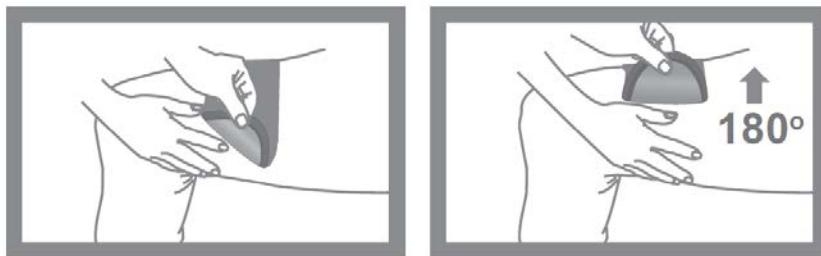
Source: *IFU NR74330 Rev. G 2016-03*

1. Check the patient return electrode's expiration date. If expired, discard the patient return electrode.
2. Prepare the patient return electrode application area on patient. Clean and dry the application site as needed. The application site must be free of oils and lotions to ensure secure contact between the patient's skin and the return electrode. Select a smooth, well-vascularized, muscular area as close to the surgical site as possible for electrode placement, but not closer than 15cm. Avoid areas where fluids may pool, scar tissue, bony prominences, and excessive adipose tissue. If the patient has a cardiac pacemaker or other active implant, consult with qualified physician on suitability of HF surgery and placement of the return electrode and cables.

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3. To minimize the potential for electrosurgical burns, excessive hair at application site must be removed before placement of the patient return electrode. Dry it thoroughly, in particular if alcohol or other skin cleaning fluids are used. DO NOT use lubricating jelly on the return electrode.
4. Open the package only prior to use and remove the patient return electrode.
5. Remove the liner, and lightly touch the surface of the return electrodes. DO NOT use dry patient return electrodes. Apply the patient return electrode using firm, steady pressure to ensure full, even contact with the patient. Check the patient return electrode, the cord, and the connector for defects.
6. Apply the patient return electrode with the long side facing the surgical site.
7. Turn on generator to ensure proper operation. Use the lowest power settings that will achieve the desired surgical effect.
8. Connect the patient return electrode cord to generator to correct the alarm issue.
9. For non-corded patient return electrodes: Check the reusable return electrode cable for defects. DO NOT use if the metal electrode contacts are soiled, or show other defects like damaged insulation. Open the clamp of the return electrode cable by lifting the lever. Insert the electrode's contact tab completely into the clamp. Lock clamps by fully depressing the lever. Make sure the entire tab is inserted in the clamp and does not come in contact with the patient's skin. The clamp must not lie under the patient.
10. After the procedure, disconnect the patient return electrode connector from the electrosurgical generator.
11. DO NOT remove patient return electrode by pulling on cable or cord.
12. Start at corner. Slowly peel back at 180 degree angle with one hand while supporting skin with the other to avoid skin irritation. Tugging, pulling or rapid removal may cause skin trauma.



13. Take extra care when skin is overly delicate, e.g. on elderly patients, diabetics, or because of prolonged specific medication e.g. steroids.
14. Dispose of the used patient return electrode.

#### **4.13.2. Installation/Application of the Pediatric Electrode (0865C)**

*Source: IFU NR74380 Rev. F 2016-03*

1. Whenever patient size permits, use an adult-size patient return electrode to reduce the possibility of patient burns. The patient return electrode must adhere completely to the application site without overlapping.

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2. Check the patient return electrode's expiration date. If expired, discard the patient return electrode.
3. Prepare the patient return electrode application area on patient. Clean and dry the application site as needed. The application site must be free of oils and lotions to ensure secure contact between the patient's skin and the return electrode. Select a smooth, well-vascularized, muscular area as close to the surgical site as possible for electrode placement, but not closer than 15 cm. The recommended application site is on the torso or a thigh. Avoid areas where fluids may pool, scar tissue, bony prominences, and excessive adipose tissue. If the patient has a cardiac pacemaker or other active implant, consult with qualified physician on suitability of HF surgery and placement of the return electrode and cables.
4. To minimize the potential for electrosurgical burns, excessive hair must be removed before placement of the return electrode. Dry it thoroughly, in particular if alcohol or other skin cleaning fluids are used. DO NOT use lubricating jelly on the return electrode.
5. Open the package only prior to use and remove the patient return electrode.
6. Remove the liner, and lightly touch the surface of the return electrodes. DO NOT use dry patient return electrodes. Apply the patient return electrode using firm, steady pressure to ensure full, even contact with the patient. Check the patient return electrode, the cord, and the connector for defects.
7. Apply the patient return electrode with the long and non-corded side facing the surgical site.
8. Turn on generator to ensure proper operation. Use the lowest power settings that will achieve the desired surgical effect.
9. Connect the patient return electrode cord to generator to correct the alarm issue.
10. Never exceed the maximum power settings of 120 Watts while using the patient return electrode for pediatrics.
11. After the procedure, disconnect the patient return electrode connector from the electrosurgical generator.
12. DO NOT remove patient return electrode by pulling on cable or cord.
13. Start at corner. Slowly peel back at 180 degree angle with one hand while supporting skin with the other to avoid skin irritation. Tugging, pulling or rapid removal may cause skin trauma.



14. Take extra care when skin is overly delicate, e.g. on diabetics, or because of prolonged specific medication e.g. steroids. Dispose of the used patient return electrode.

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## 5. EQUIVALENCE

### 5.1. Equivalence Rationale

The ROC is by the clinical route and is based on post-market surveillance (PMS) data and real-world proactive post market clinical data (Epi Data). An observational, retrospective cohort study was conducted to collect and analyze real-world Epi data on the subject devices on 22,151 patients. The observational aspect of this study allowed for understanding the use of Megadyne® Disposable Patient Return Electrodes, and the potential risks associated with the device in the real-world setting. Based on the nature of the device and ample sufficiency, equivalency is not required or utilized.

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## 6. DATA SOURCES - IDENTIFICATION AND APPRAISAL (STAGE 1, 2)

### 6.1. Data Appraisal Plan

Comprehensive methods were utilized to identify and appraise all data sources that are generated and held by Megadyne Medical, Inc. for the Disposable Patient Return Electrode subject devices including evidence from Europe and other countries. The appraisal of each data source is described below, with further details in subsequent sections for each data source.

For all data sources, suitability and contribution were determined by assessing whether the data were generated on the subject device or other devices considered representative. More weight was given to data collected directly on the subject device. Where the data were collected on (an)other device(s), a rationale was included as to why these data were considered representative. Where data were considered off-label, the rationale for this determination was identified and the data stratified. Data were only included if the reports contained sufficient information to be able to undertake a rationale and objective assessment.

For nonclinical testing (Section 0), the test methods/study design were assessed to ensure they were considered representative of the intended use of the subject device and of the treatment population. More weight was given to representative in vivo analyses and testing to international / national standards but all studies were included if the data were of sufficient quality. More weight was given to in vivo and/or in vitro studies where the follow-up time was representative of the functional lifetime of the device.

Proactive clinical data [Section 6.7]) were critically appraised to determine whether the outcome measures reflected the intended performance of the subject device, the study design was adequate, whether the intended treatment population reflected the entire target population, how the follow-up time compared with the lifetime of the device, and whether the quality of the data were sufficient to allow a rationale and objective analysis in order to determine the overall weight of the data (as assessed by the aforementioned characteristics).

While of lower quality (due to the availability of limited information), post-market surveillance data (Section 7), including complaints and sales, vigilance, CAPA, Escalations, Field Actions, and Alerts; still provides valuable information towards the assessment of safety for the subject devices and reflects real world usage. While the follow-up times and clinical use of the devices relative to the intended purpose cannot easily be ascertained, the data obtained are representative of the treated population and are of sufficient quality to allow a rationale and objective assessment.

Risk management data (Section 8), including identified clinical risks, benefits, and information provided to the user on residual risks are evaluated in comparison to the other data sources and the SOA to determine the acceptability of the known side effects and benefit-risk ratio.

The following matrix identifies the data sources being used to support safety and / or performance of the subject devices to substantiate the identified Essential Requirements (ERs).

**Table 27: Data Source Contribution**

Data Source	Performance / Clinical Benefits	Safety/Clinical Risks	Side-Effect Acceptability	Benefit-Risk Profile Acceptability
MDD ERs	3	1	6	1
<b>Nonclinical</b>				
Bench-Top Data	X	X	X	X

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Data Source	Performance / Clinical Benefits	Safety/Clinical Risks	Side-Effect Acceptability	Benefit-Risk Profile Acceptability
<b>Analytical Data</b>	X	X	X	X
<b>Complaints / Sales Data</b>		X	X	X
<b>Vigilance Data (MDVs, FDA-MDRs)</b>		X	X	X
<b>CAPAs, Field Actions, Escalations</b>		X	X	X
<b>Clinical</b>				
<b>Proactive Clinical Data (Epi data)</b> • Epi Data		X	X	X

## 6.2. Non-Clinical Data

The design requirements of the Megadyne Disposable Patient Return Electrodes have been investigated and defined in the specification documents in Technical File RA-TECH-0001. The design verification activities have been confirmed through examination and provision that the design outputs of device design meet the design requirements (design inputs). The design validation activities have ensured that finished device design and manufacturing, including packaging and labeling, conforms to defined customer requirements (user and patient needs) to allow the specific intended purpose to be consistently fulfilled. The design validation further evaluated the performance of initial production units, lots, batches, or devices justified to be representative under actual or simulated use conditions. Megadyne Medical Products, Inc. has undertaken all necessary steps to apply standard techniques in designing and manufacturing the subject devices to ensure they are safe and perform as intended. The available non-clinical dataset further substantiates the Megadyne Disposable Patient Return Electrodes as state of the art medical devices to complete the electrosurgical circuit between the generator, the active electrode, and the patient during electrosurgical procedures, and identifies the residual risks from their design and production as specified in the Data Appraisal Plan Section. The subsequent section summarizes the non-clinical datasets where key design requirements are provided from the Technical Documentation (Table 28). For complete details of the testing, refer to the Technical File (RA-TECH-0001, Rev. 001) for test reports.

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**Table 28: Megadyne Disposable Patient Return Electrodes Non-Clinical Data Summary**

Reference	Device	Test Description	Specification and Acceptance Criteria	Results	Conclusion
Technical File RA-TECH-0001, Rev. 001	0850C, 0855CL, 0855CN (adult electrodes with cords)	Resistance Measurement of Entire Assembly	9 ft. cord: the resistance of the full entire assembly must be less than 800 milliohm.	Max: 0.72 Ω Min: 0.65 Ω	PASS
Technical File RA-TECH-0001, Rev. 001	0850C, 0855CL, 0855CN (adult electrodes with cords)	Plug Extraction from Generator	The maximum extraction force should be within 2 to 15 lbf.	Max: 6.9 lbf Min: 6.2 lbf	PASS
Technical File RA-TECH-0001, Rev. 001	0850C, 0855CL, 0855CN (adult electrodes with cords)	0.26kg Dynamic Strain Relief	The resistance must not exceed 800 milliohm.	Max: 0.74 Ω Min: 0.68 Ω	PASS
Technical File RA-TECH-0001, Rev. 001	0850C, 0855CL, 0855CN (adult electrodes with cords)	10 Pound Static Strain Relief	The resistance must not exceed 800 milliohm.	Max: 0.73 Ω Min: 0.68 Ω	PASS
Technical File RA-TECH-0001, Rev. 001	0850C, 0855CL, 0855CN (adult electrodes with cords)	Thermal Performance Test	The maximum temperature rise of any 1 cm square area current 350 mA hypodermis 10mm must not exceed 6°C immediately after a 60s application of the specified test current.	Max: 3.0°C Min: 2.5°C	PASS
Technical File RA-TECH-0001, Rev. 001	0850C, 0855CL, 0855CN (adult electrodes with cords)	Contact Impedance Test	The contact impedance over the tested frequencies shall not exceed 50 Ω.	Max: 27.3 Ω Min: 26.1 Ω	PASS
Technical File RA-TECH-0001, Rev. 001	0850C, 0855CL, 0855CN (adult electrodes with cords)	Adhesion Test (Pull Test)	No more than 10% of the NE adhesive area shall separate from the skin surface in at least 90% of the test.	No more than 5% separated surface	PASS
Technical File RA-TECH-0001, Rev. 001	0850C, 0855CL, 0855CN (adult electrodes with cords)	Adhesion Test (Conformability Test)	No more than 10% of the adhesive area of the NE shall have separated from the skin surface at 1 h after application.	No more than 10% separated surface	PASS
Technical File RA-TECH-0001, Rev. 001	0850C, 0855CL, 0855CN (adult electrodes with cords)	Adhesion Test (Fluid Tolerance Test)	No more than 10% of the adhesive area of the NE shall have separated from the skin surface within 15 min after the saline is poured..	No more than 10% separated surface	PASS
Technical File RA-TECH-0001, Rev. 001	0850C, 0855CL, 0855CN (adult electrodes with cords)	HF Leakage	The measured HF leakage capacitance shall not exceed the 182.51 mA.	Max: 62.4 mΩ Min: 60.0 mΩ	PASS
Technical File RA-TECH-0001, Rev. 001	0850C, 0855CL, 0855CN (adult electrodes with cords)	HF Dielectric strength Test (Cord)	At 660Vp, no breakdown of the insulation or flashover shall occur.	No breakdown	PASS
Technical File RA-TECH-0001, Rev. 001	0850C, 0855CL, 0855CN (adult electrodes with cords)	Main Frequency Dielectric Strength Test (Cord)	At 2.1 kVp, no breakdown of the insulation or flashover shall occur.	No breakdown	PASS
Technical File RA-TECH-0001, Rev. 001	0865C (pediatric electrode)	Resistance Measurement of Entire Assembly	9 ft. cord: the resistance of the full entire assembly must be less than 800 milliohm.	Max: 0.75 Ω Min: 0.71 Ω	PASS
Technical File RA-TECH-0001, Rev. 001	0865C (pediatric electrode)	Plug Extraction from Generator	The maximum extraction force should be within 4 to 15 lbf.	Max: 7.5 lbf Min: 5.6 lbf	PASS
Technical File RA-TECH-0001, Rev. 001	0865C (pediatric electrode)	0.26kg Dynamic Strain Relief	The resistance must not exceed 800 milliohm.	Max: 0.78 Ω Min: 0.69 Ω	PASS
Technical File RA-TECH-0001, Rev. 001	0865C (pediatric electrode)	10 Pound Static Strain Relief	The resistance must not exceed 800 milliohm.	Max: 0.75 Ω Min: 0.69 Ω	PASS
Technical File RA-TECH-0001, Rev. 001	0865C (pediatric electrode)	Thermal Performance Test	The maximum temperature rise of any 1 cm square area current 500 mA hypodermis 10mm must not exceed 6°C immediately after a 60s application of the specified test current.	Max: 2.6°C Min: 2.2°C	PASS

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Reference	Device	Test Description	Specification and Acceptance Criteria	Results	Conclusion
Technical File RA-TECH-0001, Rev. 001	0865C (pediatric electrode)	Contact Impedance Test	The contact impedance over the tested frequencies shall not exceed 50 Ω.	Max: 20.4 Ω Min: 20.2 Ω	PASS
Technical File RA-TECH-0001, Rev. 001	0865C (pediatric electrode)	HF Leakage	The measured HF leakage capacitance shall not exceed the 182.51 mA.	Max: 55.7 Ω Min: 51.0 Ω	PASS
Technical File RA-TECH-0001, Rev. 001	0865C (pediatric electrode)	HF Dielectric strength Test (Cord)	At 500Vp, no breakdown of the insulation or flashover shall occur.	No breakdown	PASS
Technical File RA-TECH-0001, Rev. 001	0865C (pediatric electrode)	Main Frequency Dielectric Strength Test (Cord)	At 2.1 kVp, no breakdown of the insulation or flashover shall occur.	No breakdown	PASS

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### 6.3. Pre-Market Clinical Investigations

There were no pre-market clinical investigations for the Megadyne Disposable Patient Return Electrodes subject device family.

### 6.4. Review of External Registry Data

There are no external registries for the Megadyne Disposable Patient Return Electrodes to report in this CER.

### 6.5. Review of Internal Registry Data

There are no internal registries for the Megadyne Disposable Patient Return Electrodes to report in this CER.

### 6.6. Post-Market Clinical Follow-Up (PMCF)

There are no post-market clinical follow-up studies for the Megadyne Disposable Patient Return Electrodes to report in this CER.

### 6.7. Post Market Proactive Clinical Data (Epi Data)

The Megadyne Disposable Patient Return Electrode subject devices are single-use, non-sterile electrosurgical accessories used to adhere to the patient over the entire pad surface to complete the electrosurgical circuit between the generator, the active electrode and the patient.

As described in the clinical literature results (Section 6.9), zero articles were identified that had published data related to the subject devices. The Megadyne Disposable Patient Return Electrodes are widely used and clinically well-established with a low risk profile, and the lack of data in the clinical literature is attributable to the ancillary nature of these devices and that they are generally not the focus of clinical study. As such, a Proactive Clinical Data review was undertaken of the use of the Megadyne Disposable Patient Return Electrode subject devices.

As part of the effort in developing proactive clinical evidence for the Megadyne Disposable Patient Return Electrodes Clinical Evaluation Report (CER), a post-market proactive analysis was conducted using real-world data to describe select clinical outcomes. Details of the methods, outcomes of interest and results of the analysis are presented in the following sections below. The following information was taken from Post-market Proactive Analysis Report (Epi Data): Utilization and Comparative Analysis of Megadyne Disposable Patient Return Electrodes.

#### 6.7.1. Summary of Findings

**Purpose:** The purpose of this study was to identify real-world evidence related to the safety of Megadyne® Disposable Patient Return Electrodes. The findings from this study will be used in support of the development of a Clinical Evaluation Report (CER).

**Methods:** This was a two-arm, observational, retrospective cohort study. The observational aspect of this study allowed for understanding the use of Megadyne® Disposable Patient Return Electrodes, and the

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potential risks associated with the device in the real-world setting. The exposure cohort consisted of patients undergoing a surgical procedure where Megadyne® Disposable Patient Return Electrodes were used. Whereas, the reference cohort included patients undergoing surgical procedures where similar products manufactured by Bovie and Valleylab (Medtronic) were used. The timeframe of this study spanned from January 2000 to March 2019, based on the availability of data licensed by Premier Healthcare Data and the time the products were available in the US market.

Inclusion criteria consisted of patients who underwent an inpatient or outpatient procedure with utilization of Megadyne® Disposable Patient Return Electrodes (Megadyne® DPRE) or any of the similar products manufactured by Bovie and Valleylab (BoVL). Exclusion criteria consisted of procedures where both Megadyne® and the Bovie or Valleylab devices were used in the same procedure or if age or sex were missing in the dataset.

The primary endpoint was incidence of thermal injury as the only complication of interest. It was identified with diagnoses captured during the in-patient hospitalization or hospital-based outpatient procedure only. Additional demographic and procedural variables for the study group and the comparator group were researched and reported.

Inverse probability weighting (IPW) for the two study cohorts (Megadyne® DPRE and BoVL) was applied to reduce the effect from the potential confounders by balancing the distribution of baseline characteristics between the two comparison groups. Using IPW, multivariate logistic regression was conducted to estimate the adjusted risk of complications in patients undergoing surgical procedures where the Megadyne® or Other brands of disposable patient return electrodes were used.

**Results:** There were 22,151 patients in the Megadyne® DPRE group, with a mean age of 49.6 years. There were 36,898 patients in the BoVL group, with a mean age of 50.7 years. Sex, race, and Charlson Comorbidity score were similarly distributed between the groups. A total of 13 unique procedure types were identified where devices from both groups were used. The majority of procedures in the Megadyne® DPRE group took place in the years 2007, 2008, 2009, 2018, or 2019 (20,036 procedures, 90.5%). Procedures in the BoVL group were dispersed evenly across the 20-year timeframe.

Procedures were split approximately evenly between the inpatient and outpatient settings in both groups. The majority of surgical approaches utilized in both groups were open (Megadyne® DPRE: 81.4%; BoVL: 81.6%). A majority of procedures were performed in urban locations in both groups. Physician specialty was widely distributed in each group.

There were 4 (0.018%) instances of thermal injury in the Megadyne® DPRE group and 6 (0.016%) instances of thermal injury in the BoVL group. Results of inverse probability weighting analysis demonstrated an incidence of thermal injury probability of 0.015% (95% CI: 0.005% - 0.047%) in the Megadyne® DPRE group and 0.012% (0.003% - 0.043%) in the VBVL group. In comparing the two groups, the risk ratio was 1.34 (0.24 - 7.56).

**Conclusions:** The incidence of thermal injury following use of Megadyne® Disposable Patient Return Electrodes across multiple types of surgical procedures and hospital settings was exceedingly low over a 20-year time period. Further, the relative risk of thermal injury from Megadyne® Disposable Patient Return Electrodes was comparable to similar devices on the market during the same time period.

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## 6.7.2. Proactive Clinical Data Methods

### 6.7.2.1. Rationale and Background

This study was designed to generate evidence on Megadyne® Disposable Patient Return Electrodes using real-world data (RWD). To establish the state of the art for these devices, comparative analyses were conducted against similar products manufactured by competitors. The findings in this study will be used to evaluate the use of these devices in support of the development of Clinical Evaluation Report (CER).

### 6.7.2.2. Research Question, Objectives and Methods

#### 6.7.2.2.1. Research Question(s)

1. What is the utilization of Megadyne® Disposable Patient Return Electrodes in different surgical procedures?
2. What is the risk of thermal injury in surgical procedures where Megadyne® Disposable Patient Return Electrodes were used intraoperatively?

#### 6.7.2.3. Research Objectives

Among all patients who had Megadyne® Disposable Patient Return Electrodes or other brands of similar products manufactured by competitors used during surgical procedures:

1. To describe and compare the patient demographics, procedural characteristics, and hospital and provider characteristics at the time of index surgery between the two cohorts.
2. To estimate and compare the risk of thermal injury during the index procedure hospitalization between the two cohorts.

#### 6.7.2.4. Methods

##### 6.7.2.4.1. Study Design

This was a two-arm, observational, retrospective cohort study. The observational aspect of this study allowed for understanding the use of Megadyne® Disposable Patient Return Electrodes, and the risks associated with the device in the real-world setting. The exposure cohort consisted of patients undergoing surgical procedures where Megadyne® Disposable Patient Return Electrodes were used. Whereas, the reference cohort included patients undergoing surgical procedures where similar products manufactured by Bovie and Valleylab were used. The timeframe of this study spanned from January 2000 to March 2019, based on the availability of data licensed by Premier Healthcare Data and the time the products were available in the US market.

##### 6.7.2.4.2. Data Sources

This study used hospital billing records contained in the Premier Healthcare Database (PHD). The PHD contains complete clinical coding, hospital cost, and patient billing data from more than 970 hospitals throughout the United States. The Premier Healthcare Database represents 1 in 5 inpatient hospital stays

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in the US, and it includes a wide variety of regions and most healthcare insurances in the United States (US). Premier collects data from participating hospitals in its health care alliance. The Premier Alliance was formed to improve the quality of care. Participation in the Premier Alliance is voluntary. Although the database excludes federally funded hospitals (e.g., Veterans Affairs), the hospitals included are nationally representative. The database contains a date-stamped log of all billed items by cost-accounting department including medications; laboratory, diagnostic, and therapeutic services; and primary and secondary diagnoses for each patient's hospitalization. Identifier-linked enrollment files provide demographic and payor information. Detailed service level information for each hospital day is recorded; this includes details on medication and devices received.[1]

#### **6.7.2.4.3. Device Details**

The Megadyne® Disposable Patient Return Electrode is a single use, non-sterile return electrode with or without a pre-attached cord used to adhere to the patient over the entire return electrode surface to complete the electrosurgical circuit between the generator, the active electrode, and the patient.

The comparative devices manufactured by Bovie and Valleylab (Medtronic) are of similar overall design with similar instructions for use.

#### **6.7.2.4.4. Patient Inclusion and Exclusion Criteria**

##### **6.7.2.4.4.1 Inclusion Criteria**

Patients who met the following criteria were included in this study:

1. Patients underwent an inpatient or outpatient procedure with utilization of Megadyne® Disposable Patient Return Electrodes or any of the similar products manufactured by Bovie and Valleylab.

##### **6.7.2.4.4.2 Exclusion Criteria**

Patients who met at least one of the following criteria were excluded:

1. Patient encounters where both Megadyne® and the Bovie or Valleylab disposable patient return electrodes were used in the same procedure, or
2. Missing age or sex.

#### **6.7.2.4.5. Variables and Outcomes:**

##### **6.7.2.4.5.1 Primary Independent Variable (Exposure)**

- Use of Megadyne® Disposable Patient Return Electrodes or Bovie Disposable ESU Grounding Pad or Valleylab PolyHesive Patient Return Electrodes, which are manufactured by Bovie and Valleylab, respectively.

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In the PHD, there are two data fields that contain device information as unconstructed text: hospital charge master description and standard charge master description. In this analysis, disposable patient return electrodes were captured by querying both text fields with model numbers and/or brand names, and their variants like misspellings and abbreviations. For example: '*PAD GROUNDING MEGADYNE*', and '*PAD BOVIE GROUND E7506*'.

The identification of disposable patient return electrodes were as follows:

- Megadyne® Disposable Patient Return Electrode were identified by searching the hospital charge master description with key words: 'Megadyne', 'Pad', 'Return' and/or model numbers (Appendix 2, Table 1);
- Bovie and Valleylab Disposable Patient Return Electrode were identified by the following standard charge descriptions: 'Electrode', 'Blade', manufacture name (e.g. Bovie, Valley) and/or model numbers (Appendix 2, Table 2).

#### **6.7.2.4.5.2 Dependent Variables (Outcomes)**

- Thermal injury was the only complication of interest in this study. It was identified with diagnoses captured during the in-patient hospitalization or hospital-based outpatient procedure only (Appendix 2, Table 3).

#### **6.7.2.4.5.3 Other Variables**

##### Patient Demographics

- Age (0 to 17; 18-44; 45-64; 65-74; >=75)
- Sex (Male or Female)
- Race (Caucasian; African American; other)
- Co-morbidity Index (Charlson comorbidity score: 0; 1-2; 3-4; >=5)
  - The Charlson Comorbidity Score is a sum of weighted indices for 19 conditions. It represents the comorbid burden and is commonly used for adjustment of comorbidities in observational studies.[2]

##### Procedural Characteristics

- Admission type (inpatient; outpatient)
- Procedure type (Breast procedure, cardiovascular procedure, digestive procedure, Ear/Nose/Head procedure, endocrine procedure, Hepato-Pancreato-Biliary (HPB) procedure, male genital procedure, neurological procedure, orthopedic procedure, respiratory procedure, skin procedure, urologic procedure and other procedure)

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- Year of the procedure
- Type of surgery (elective surgery; urgent/emergency surgery): elective surgery was scheduled in advance, while urgent or emergency surgery was performed due to an urgent medical condition.

#### Hospital and Provider Characteristics

- Hospital location (urban hospital; rural hospital)
- Teaching status (teaching hospital; non-teaching hospital)
- Bed size (0-199 beds; 200-299 beds; 300-399 beds; 400-499 beds; >=500 beds)
- Surgeon specialty (Cardiovascular Surgeon, Gastrointestinal Surgeon, General Surgeon, Neurological Surgeon, OB/GYN Surgeon, Orthopedic Surgeon, Thoracic Surgeon, Other/Unknown)

#### Subgroups/Stratification Variables

- N/A

#### 6.7.2.4.5.4 Sample Size

A pre-study feasibility analysis of the Premier database during the period from January 2000 to December 2018 found that there were 21,415 procedures performed with Megadyne® Disposable Patient Return Electrodes, and 39,897 procedures performed with Bovie or Valleylab Disposable Patient Return Electrodes.

#### 6.7.2.4.6. Data Analysis

- Descriptive summary of baseline characteristics of patients undergoing procedures where the Megadyne® disposable patient return electrodes and other brands of disposable patient return electrodes were used. Continuous data were summarized as mean and standard deviation. Categorical data were summarized as frequency and percent.
- Frequency counts and percentages of complications (thermal injury) by study cohort.

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- Inverse probability weighting (IPW) for the two study cohorts (Megadyne® DPRE group and BoVL group) was performed to reduce the effect from the potential confounders by balancing the distribution of baseline characteristics between the two comparison groups. The following baseline variables were considered in the IPW calculation based on their clinical relevance to the safety and performance of disposable patient return electrodes: patient demographics (age, sex, race, comorbidity score), procedural characteristics (procedure type, inpatient/outpatient setting, elective/urgent admission, surgeon specialty), and hospital type (teaching status, urban/rural, bed size).
- Using the IPW, multivariate logistic regression was conducted to estimate the adjusted risk of complications in patients undergoing surgical procedures where the Megadyne® or Other brands of disposable patient return electrodes were used.

### 6.7.3. Proactive Clinical Data Results

#### 6.7.3.1. Attrition

The use of Megadyne® Disposable Patient Return Electrodes or similar products manufactured by Bovie or Valleylab were observed in 59,051 patients in the Premier Healthcare Database between January 1, 2000 and March 31, 2019 (Table 29). Two (2) patients were excluded following identification that more than one of the study products were used in the same procedure. No patients were excluded due to missing age or sex. Overall, 59,049 patients (99.99%) were retained for analysis.

**Table 29: Study Cohort Attrition**

Study Patient Cohort	N (patients)	Percent Retained
Include patients who underwent an inpatient or outpatient procedure with utilization of Megadyne® Disposable Patient Return Electrodes or any of the similar products manufactured by Bovie and Valleylab.	59,051	100%
Exclude patient encounters where both Megadyne® and the Bovie or Valleylab disposable patient return electrodes were used in the same procedure.	59,049	99.99%
Exclude patients with missing age or sex	59,049	99.99%

#### 6.7.3.2. Patient Demographics

Patient demographics, stratified by comparator group, are presented in Table 30. There were 22,151 patients in the Megadyne® DPRE group, with a mean age of 49.6 years. In a sub-analysis by age of the Megadyne® DPRE group, 10.8% were aged 0-17 years; 26.3% were aged 18-44 years; 35.2% were aged

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45-64 years; 14.8% were aged 65-74 years; and 12.9% were aged >75 years. There were 36,898 patients in the BoVL group, with a mean age of 50.7 years. In a sub-analysis by age of the BoVL group, 6,981 18.9% were aged 0-17 years; 12.6% were aged 18-44 years; 28.9% were aged 45-64 years; 18.2% were aged 65-74 years; and 21.3% were aged >75 years.

With respect to sex, 59.4% of patients in the Megadyne® DPRE group were female, while female patients accounted for 44.9% in the BoVL group.

With respect to race, 74.1% of patients in the Megadyne® DPRE group were Caucasian, 9.5% were African-American, and 16.4% were of other racial identification. In the BoVL group, 57.5% of patients were Caucasian, 9.4% were African-American, and 23.5% were of other racial identification.

A majority of patients had a Charlson Comorbidity score of 0 (Megadyne® DPRE: 62.8%; BoVL: 57.5%).

**Table 30: Baseline Characteristics of Patients Who had Disposable Patient Return Electrodes Used in a Surgical Procedure**

Characteristics	Category	Megadyne Disposable Patient Return Electrodes (n=22,151)	Bovie or Valleylab Disposable Patient Return Electrodes (n=36,898)
Age (years)	mean (SD)	49.6 (21.8)	50.7 (28.0)
Age Category	0 - 17	2,390 (10.8%)	6,981 (18.9%)
	18 - 44	5,817 (26.3%)	4,648 (12.6%)
	45 - 64	7,801 (35.2%)	10,662 (28.9%)
	65 - 74	3,279 (14.8%)	6,731 (18.2%)
	>=75	2,864 (12.9%)	7,876 (21.3%)
Sex	Female	13,148 (59.4%)	16,582 (44.9%)
	Male	9,003 (40.6%)	20,316 (55.1%)
Race	Caucasian	16,412 (74.1%)	24,753 (67.1%)
	African American	2,098 (9.5%)	3,466 (9.4%)
	Other	3,641 (16.4%)	8,679 (23.5%)
Charlson Comorbidity Scores	0	13,903 (62.8%)	21,217 (57.5%)
	1 or 2	5,607 (25.3%)	11,112 (30.1%)
	3 or 4	1,449 (6.5%)	3,153 (8.5%)
	>= 5	1,192 (5.4%)	1,416 (3.8%)

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### 6.7.3.3. Device Utilization

The procedure types and device usage by year for both groups are shown in Table 31. A total of 13 unique procedure types were identified using primary procedure. The three most prevalent identified procedure types in the Megadyne® DRPE group were: Digestive (18.9%); Orthopedic (16.7%); and HPB (9.2%). The three most prevalent identified procedure types in the BoVL group were: Cardiovascular (28.0%); Digestive (26.0%); and Orthopedic (10.0%). In the Megadyne® DPRE group, 18.6% of procedures were either not classified into 12 mentioned procedure types, or not provided with primary procedure code in the data, classified as “Other”. In the BoVL group, 6.1% of procedures met one of the two criteria to be classified as “Other”. The majority of procedures in the Megadyne® DPRE group took place in the years 2007, 2008, 2009, 2018, or 2019 (90.5%). No usage of Megadyne® DPRE was reported in the PHD from 2010 to 2017. Procedures in the BoVL group were dispersed across the 20-year timeframe.

**Table 31: Utilization of Disposable Patient Return Electrodes**

Characteristics	Category	Megadyne Disposable Patient Return Electrodes (n=22,151)	Bovie or Valleylab Disposable Patient Return Electrodes (n=36,898)
Procedure type	Breast procedure	1,142 (5.2%)	300 (0.8%)
	Cardiovascular procedure	1,319 (6.0%)	10,338 (28.0%)
	Digestive procedure	4,193 (18.9%)	9,591 (26.0%)
	ENT procedure	1,161 (5.2%)	1,425 (3.9%)
	Endocrine procedure	333 (1.5%)	115 (0.3%)
	Gynecologic procedure	1,969 (8.9%)	1,375 (3.7%)
	HPB procedure	2,044 (9.2%)	1,522 (4.1%)
	Male genital procedure	404 (1.8%)	1,949 (5.3%)
	Neurological procedure	361 (1.6%)	822 (2.2%)
	Orthopedic procedure	3,692 (16.7%)	3,685 (10.0%)
	Respiratory procedure	302 (1.4%)	839 (2.3%)
	Skin procedure	765 (3.5%)	1,620 (4.4%)
	Urologic procedure	356 (1.6%)	1,079 (2.9%)
	Other	4,110 (18.6%)	2,238 (6.1%)

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Characteristics	Category	Megadyne Disposable Patient Return Electrodes (n=22,151)	Bovie or Valleylab Disposable Patient Return Electrodes (n=36,898)
Year	2000	0	2,255 (6.1%)
	2001	921 (4.2%)	1,094 (3.0%)
	2002	960 (4.3%)	416 (1.1%)
	2003	139 (0.6%)	549 (1.5%)
	2004	27 (0.1%)	499 (1.4%)
	2005	43 (0.2%)	1,304 (3.5%)
	2006	25 (0.1%)	3,116 (8.4%)
	2007	4,472 (20.2%)	2,946 (8.0%)
	2008	4,757 (21.5%)	2,741 (7.4%)
	2009	3,527 (15.9%)	4,432 (12.0%)
	2010	0	2,102 (5.7%)
	2011	0	268 (0.7%)
	2012	0	2,368 (6.4%)
	2013	0	2,288 (6.2%)
	2014	0	2,819 (7.6%)
	2015	0	3,891 (10.5%)
	2016	0	2,614 (7.1%)
	2017	0	809 (2.2%)
	2018	4,553 (20.6%)	372 (1.0%)
	2019*	2,727 (12.3%)	15 (0.0%)

\*first quarter in 2019 only

#### 6.7.3.4. Setting and Surgical Characteristics

Procedure setting, surgical approach type, hospital characteristics, and physician specialty are presented in Table 32. Procedures were split approximately evenly between inpatient (Megadyne® DPRE: 49.1%; BoVL: 48.0%) and outpatient (Megadyne® DPRE: 50.9%; BoVL: 52.0%). In the Megadyne® DPRE group 72.7% of procedures were for elective admissions. A similar proportion occurred in the BoVL group (69.2%). The majority of surgical approaches utilized in both groups were open (Megadyne® DPRE: 81.4%; BoVL: 81.6%).

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A majority of procedures were performed in urban locations in both groups (Megadyne® DPRE: 90.5%; BoVL: 97.6%). In the Megadyne® DPRE group, 99.8% of procedures were performed at teaching institutions compared to 63.9% procedures in the BoVL group. In terms of hospital facility bed size, a majority of procedures (58.1%) in the Megadyne® DPRE group took place at facilities with 200-499 beds. A majority of procedures (55.7%) in the BoVL group took place at facilities with 500+ beds.

The top three identified physician specialties associated with procedures in the Megadyne® DPRE group were: General Surgery (35.0%); Orthopedic Surgery (13.8%); and OB/GYN (9.7%). In the BoVL group, the top three identified physician specialties were: Cardiovascular Surgery (21.5%); Gastrointestinal Surgery (13.2%); and General Surgery (11.6%). Physician specialty was not identified in 25.1% of procedures in the Megadyne® DPRE group and 22.0% of procedures in the BoVL group.

**Table 32: Procedure, Provider and Hospital Characteristics**

Characteristics	Category	Megadyne Disposable Patient Return Electrodes (n=22,151)	Bovie or Valleylab Disposable Patient Return Electrodes (n=36,898)
Hospital setting	Inpatient	10,876 (49.1%)	17,701 (48.0%)
	Outpatient	11,275 (50.9%)	19,197 (52.0%)
Admission type	Elective admission	16,103 (72.7%)	25,524 (69.2%)
	Emergent or urgent admission	6,048 (27.3%)	11,374 (30.8%)
Surgical approach	Laparoscopic or percutaneous	4,037 (18.2%)	6,776 (18.4%)
	Open	18,114 (81.8%)	30,122 (81.6%)
Location	Rural	2,115 (9.5%)	876 (2.4%)
	Urban	20,036 (90.5%)	36,022 (97.6%)
Teaching status	No	22,096 (99.8%)	23,578 (63.9%)
	Yes	55 (0.2%)	13,320 (36.1%)
Bed size	000-199	2,158 (9.7%)	1,459 (4.0%)
	200-499	12,864 (58.1%)	14,875 (40.3%)
	500+	7,129 (32.2%)	20,564 (55.7%)
Physician specialty	Cardiovascular Surgeon	619 (2.8%)	7,929 (21.5%)
	Gastrointestinal Surgeon	52 (0.2%)	4,883 (13.2%)
	General Surgeon	7,763 (35.0%)	4,297 (11.6%)
	Neurologic Surgeon	404 (1.8%)	1,796 (4.9%)

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Characteristics	Category	Megadyne Disposable Patient Return Electrodes (n=22,151)	Bovie or Valleylab Disposable Patient Return Electrodes (n=36,898)
	OB/GYN Surgeon	2,138 (9.7%)	1,432 (3.9%)
	Orthopedic Surgeon	3,057 (13.8%)	2,091 (5.7%)
	Thoracic Surgeon	528 (2.4%)	903 (2.4%)
	Unknown Specialty	5,561 (25.1%)	8,114 (22.0%)
	Urology Surgeon	562 (2.5%)	2,122 (5.8%)

### 6.7.3.5. Inverse probability weighting

Inverse probability weighting method was used to replace propensity score matching (PSM) method in this study, where PSM was infeasible due to extremely large disparity between two study cohorts. Among 45 potential confounding factors selected from baseline characteristics, 33 of them had the absolute standardized mean different at or above 0.1, which is indicative of unbalance between the study cohorts. After IPW, the number of characteristics with SMD  $\geq 0.1$  reduced to 27. More notably, the values of SMD have decreased drastically. The number of characteristics with extreme unbalance (SMD  $\geq 0.05$ ) reduced from 6 to 2 after the implementation of IPW. (Appendix 2, Table 4)

During IPW, weight trimming was applied, and explored at different cut-off values. The weights trimmed at 95th percentile resulted in optimal balance between the two study cohorts.

Propensity score matching (PSM) was also attempted. With the same 45 potential confounding factors, the PSM found that merely 14.1% of study sample was retained. Low matching rate undermined the generalizability despite the large sample size before matching. The extremely rare outcome of this study (see Outcomes section below) disallows the feasibility of using partially matched sample, which can result in inconsistent estimate of relative risk.

### 6.7.3.6. Outcomes

The incidence of thermal injury in both groups is reported in Table 33. Diagnosis codes for Thermal Injury can be found in Appendix 2, Table 3: Diagnosis Code for Complications. There were 4 (0.018%) instances of thermal injury in the Megadyne® DPRE group, and 6 (0.016%) instances of thermal injury in the BoVL group. Results of inverse probability weighting analysis demonstrated an incidence of thermal injury probability of 0.015% (0.005% - 0.047%) in the Megadyne® DPRE group and 0.012% (0.003% - 0.043%) in the BoVL group. In comparing the two groups, the risk ratio was 1.34 (95% CI: 0.24 - 7.56).

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**Table 33: Risk of Complications in Surgical Procedures with Use of Disposable Patient Return Electrodes**

Complication	Original Sample		Inverse Probability Weighting		
	Megadyne Disposable Patient Return Electrodes (n=22,151)	Bovie or ValleyLab Disposable Patient Return Electrodes (n=36,898)	Adjusted Risk in Megadyne Disposable Patient Return Electrodes (n=22,151)	Adjusted Risk in Bovie or ValleyLab Disposable Patient Return Electrodes (n=36,898)	Risk Ratio (95% CI)
Thermal Injury	4 (0.018%)	6 (0.016%)	0.015% (0.005%, 0.047%)	0.012% (0.003%, 0.043%)	1.34 (0.24, 7.56)

#### 6.7.4. Limitations of the Research Methods

In this study, a US population was used to estimate uses of disposable patient return electrodes for an EU population. This study has generalizability to the EU population because the clinical presentation of patients should not differ across the US and EU populations. Furthermore, use of the subject device is expected to be similar across surgeons, hospitals, and regions among US and EU populations.

PHD represents data from hospitals that are part of the Premier healthcare performance improvement alliance of approximately 970 U.S. hospitals from around the U.S., but are not a random selection of U.S. hospitals, and under-represents hospital outpatient procedures. Although the database represents all regions and most payers, this characteristic of the database may affect the generalizability of the study results.

The search strategy designed in this study may underestimate the prevalence of products in the database if the search strategy missed any incorrectly coded entries for target devices such as misspellings leading to misclassification of the exposure. However, there is no evidence that misclassification bias would be differential between the comparison groups.

PHD is an administrative database. The complication (thermal injury) coded in the database cannot be directly related to the use of the targeted devices in this study.

#### 6.7.5. Conclusions

The incidence of thermal injury following use of Megadyne® Disposable Patient Return Electrodes across multiple types of surgical procedures and hospital settings was exceedingly low over a 20-year time period. Further, the relative risk of thermal injury from Megadyne® Disposable Patient Return Electrodes was comparable to similar devices on the market during the same time period. These clinical data collected on 22,151 patients demonstrates safety and performance in accordance with the State of the Art for these disposable patient return electrodes.

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## 6.7.6. References

1. Premier Healthcare Database White paper: Data the informs and performs, July 29, 2018. Premier Applied Sciences, Premier Inc. <https://learn.premierinc.com/white-papers/premier-healthcare-database-whitepaper>.
2. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40(5):373-83.

## 6.7.7. Appendices

### 6.7.7.1. Appendix 1

#### a. Database Description

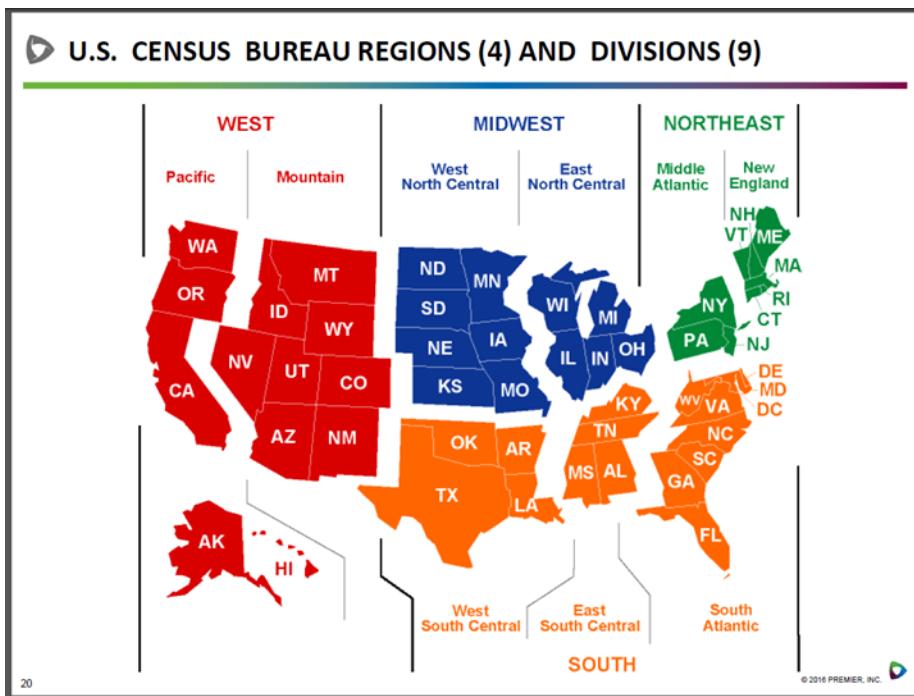
This study used hospital billing records contained in the Premier Healthcare Database (PHD). The PHD contains complete clinical coding, hospital cost, and patient billing data from more than 700 hospitals throughout the United States. Premier collects data from participating hospitals in its health care alliance. The Premier health care alliance was formed for hospitals to share knowledge, improve patient safety, and reduce risks. Participation in the Premier health care alliance is voluntary. Although the database excludes federally funded hospitals (e.g., Veterans Affairs), the hospitals included are nationally representative based on bed size, geographic region, location (urban/rural) and teaching hospital status. The database contains a date-stamped log of all billed items by cost-accounting department including medications; laboratory, diagnostic, and therapeutic services; and primary and secondary diagnoses for each patient's hospitalization. Identifier-linked enrollment files provide demographic and payor information. Detailed service level information for each hospital day is recorded; this includes details on medication and devices received.

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b. US Geographic Regions



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## 6.7.7.2. Appendix 2

**Appendix 2, Table 1: Product Code for Disposable Patient Return Electrode**

Megadyne Product Code	Megadyne Product Description	Bovie Product Code	Valleylab (Medtronic) Product Code
0850	Patient Return Electrode, Single-Use, non Contact Quality Monitoring, Adult, Without Cord, For Patients Weighing over 33lbs. (15kg)		
0850C	Rtn Elec Adult, Single Plate 9ft Cord	ESRSC	E7506, E7607
0855	Rtn Elec Adult, Dual Plate No Cord (for reusable cords)	ESRS, A1202	E7508, E7509, E7509B,
0855CL	Rtn Elec Adult, Dual Plate 15ft (4.6m) Cord	E7507DB	
0855CN	Rtn Elec Adult, Dual Plate 9ft (2.7m) Cord	ESREC	
0860	Patient Return Electrode (disposable)		
0865C	Rtn Elec Pediatric Dual 9ft Cd	E7510-25 (Infant) E7512 (Neonatal)	
0865CL	Patient Return Electrode (disposable)		
0870	Reusable Patient Return Electrode Cable, Single Plate, 3m (10 ft)		

**Appendix 2, Table 2: Product Description in Premier Healthcare Data for Megadyne® Disposable Patient Return Electrode**

Standard Charge Description	Hospital Charge Description
CAUTERY GROUNDING PAD/PLATE	PAD GROUNDING MEGADYNE
SUPPLY MISC	PAD MEGADYNE 2000 (D
CAUTERY GROUNDING PAD/PLATE	ESU GROUNDING PAD 9IN MEGADYNE
CAUTERY GROUNDING PAD/PLATE	GEN, MEGADYNE PAD
SUPPLY MISC	PAD MEGADYNE 2000 RE
CAUTERY GROUNDING PAD/PLATE	PADMEGADYNE2000RE
CAUTERY GROUNDING PAD/PLATE	PAD MEGADYNE 2000 RE
CAUTERY GROUNDING PAD/PLATE	GEN MEGADYNE PAD
CAUTERY ELECTRODE ANY	MEGADYNE ELECTROSURGICAL PATIENT RETURN
CAUTERY GROUNDING PAD/PLATE	MEGADYNE PAD
CAUTERY GROUNDING PAD/PLATE	MEGADYNE CAUTERY PAD
CAUTERY GROUNDING PAD/PLATE	PAD MEGADYNE 2000 REUSABL

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Standard Charge Description	Hospital Charge Description
CAUTERY ELECTRODE ANY	MEGADYNE PATIENT RETURN ELECTRODE
CAUTERY ELECTRODE ANY	MEGADYNE RETURN ELECTRODE

**Appendix 2, Table 3: Diagnosis Code for Complications**

COMPLICATION	CODE TYPE	CODE	CODE DESCRIPTION
Thermal injury	ICD9	942.x	Burn of trunk
Thermal injury	ICD9	943.x	Burn of upper limb except wrist and hand
Thermal injury	ICD9	945.x	Burn of lower limb(s)
Thermal injury	ICD9	946.x	Burns of multiple specified sites
Thermal injury	ICD9	949.0	Burn of unspecified site, unspecified degree
Thermal injury	ICD10	T21.0x	Burn of unspecified degree of trunk
Thermal injury	ICD10	T21.1x	Burn of first degree of trunk
Thermal injury	ICD10	T21.2x	Burn of second degree of trunk
Thermal injury	ICD10	T21.3x	Burn of third degree of trunk
Thermal injury	ICD10	T22.0x	Burn of unspecified degree of shoulder and upper limb, except wrist and hand
Thermal injury	ICD10	T22.1x	Burn of first degree of shoulder and upper limb, except wrist and hand
Thermal injury	ICD10	T22.2x	Burn of second degree of shoulder and upper limb, except wrist and hand
Thermal injury	ICD10	T22.3x	Burn of third degree of shoulder and upper limb, except wrist and hand
Thermal injury	ICD10	T24.0x	Burn of unspecified degree of lower limb, except ankle and foot
Thermal injury	ICD10	T24.1x	Burn of first degree of lower limb, except ankle and foot
Thermal injury	ICD10	T24.2x	Burn of second degree of lower limb, except ankle and foot
Thermal injury	ICD10	T24.3x	Burn of third degree of lower limb, except ankle and foot
Thermal injury	ICD10	T30.0	Burn of unspecified body region, unspecified degree
Thermal injury	ICD10	T31.0	Burns involving less than 10% of body surface

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**Appendix 2, Table 4: Standardized Mean Difference of Baseline Characteristics Before and After Using Inverse Probability Weighting Method**

Characteristics	Category	Megadyne Disposable Patient Return Electrodes (n=22,151)	Bovie/ Valleylab Disposable Patient Return Electrodes (n=36,898)	SMD before IPW	SMD after IPW
Admission type	Inpatient (vs Outpatient)	10,876 (49.1%)	17,701 (48.0%)	0.02	0.07
Surgical approach	Lap (vs Open)	4,037 (18.2%)	6,776 (18.4%)	0.02	0.01
Procedure type	Breast procedure	1,142 (5.2%)	300 (0.8%)	0.20*	0.21*
	Cardiovascular procedure	1,319 (6.0%)	10,338 (28.0%)	0.93**	0.48*
	Digestive procedure	4,193 (18.9%)	9,591 (26.0%)	0.18*	0.16*
	ENT procedure	1,161 (5.2%)	1,425 (3.9%)	0.06	0.05
	Endocrine Procedure	333 (1.5%)	115 (0.3%)	0.10*	0.10*
	Gynecologic procedure	1,969 (8.9%)	1,375 (3.7%)	0.18*	0.17*
	HPB procedure	2,044 (9.2%)	1,522 (4.1%)	0.18*	0.17*
	Male genital procedure	404 (1.8%)	1,949 (5.3%)	0.26*	0.16*
	Neurological procedure	361 (1.6%)	822 (2.2%)	0.05	0.02
	Orthopedic procedure	3,692 (16.7%)	3,685 (10.0%)	0.18*	0.18*
	Respiratory procedure	302 (1.4%)	839 (2.3%)	0.08	0.03
	Skin procedure	765 (3.5%)	1,620 (4.4%)	0.05	0.03
Age Category	Urologic procedure	356 (1.6%)	1,079 (2.9%)	0.11*	0.08
	Other	4,110 (18.6%)	2,238 (6.1%)	0.32*	0.30*
	0 - 17	2,390 (10.8%)	6,981 (18.9%)	0.26*	0.21*
	18 - 44	3,123 (14.1%)	2,096 (5.7%)	0.24*	0.23*
	45 - 64	3,723 (16.8%)	4,675 (12.7%)	0.11*	0.10*
Sex	65 - 74	3,279 (14.8%)	6,731 (18.2%)	0.10*	0.07
	75 Plus	2,864 (12.9%)	7,876 (21.3%)	0.25*	0.17*
	Female (vs Male)	13,148 (59.4%)	16,582 (44.9%)	0.29*	0.24*
Race	Caucasian	16,412 (74.1%)	24,753 (67.1%)	0.16*	0.13*
	African American	2,098 (9.5%)	3,466 (9.4%)	0.00	0.00
	Other	3,641 (16.4%)	8,679 (23.5%)	0.19*	0.16*

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Characteristics	Category	Megadyne Disposable Patient Return Electrodes (n=22,151)	Bovie/ Valleylab Disposable Patient Return Electrodes (n=36,898)	SMD before IPW	SMD after IPW
Hospital location	Rural (vs urban)	2,115 (9.5%)	876 (2.4%)	0.24*	0.24*
Teaching status	Non-teaching (vs teaching)	22,096 (99.8%)	23,578 (63.9%)	7.20**	0.93**
Hospital Bed size	000-199	2,158 (9.7%)	1,459 (4.0%)	0.20*	0.18*
	200-499	108 (0.5%)	11,961 (32.4%)	4.58**	0.84**
	500+	7,129 (32.2%)	20,564 (55.7%)	0.50**	0.34*
Physician Specialty	Cardiovascular Surgeon	619 (2.8%)	7,929 (21.5%)	1.13**	0.45*
	Gastrointestinal Surgeon	52 (0.2%)	4,883 (13.2%)	2.69**	0.48*
	General Surgeon	7,763 (35.0%)	4,297 (11.6%)	0.49*	0.45*
	Neurologic Surgeon	404 (1.8%)	1,796 (4.9%)	0.23*	0.09
	OB/GYN Surgeon	2,138 (9.7%)	1,432 (3.9%)	0.20*	0.19*
	Orthopedic Surgeon	3,057 (13.8%)	2,091 (5.7%)	0.24*	0.24*
	Thoracic Surgeon	528 (2.4%)	903 (2.4%)	0.00	0.01
	Unknown Specialty	5,561 (25.1%)	8,114 (22.0%)	0.07	0.04
	Urology Surgeon	562 (2.5%)	2,122 (5.8%)	0.20*	0.13*
	Other	1,467 (6.6%)	3,331 (9.0%)	0.10*	0.06
Admission type	Elective (vs urgent/emergent)	16,103 (72.7%)	25,524 (69.2%)	0.08	0.04
Charlson Comorbidity Scores	0	13,903 (62.8%)	21,217 (57.5%)	0.11*	0.06
	1 - 2	5,607 (25.3%)	11,112 (30.1%)	0.11*	0.07
	3 - 4	1,449 (6.5%)	3,153 (8.5%)	0.08	0.05
	5 +	1,192 (5.4%)	1,416 (3.8%)	0.07	0.07

\*absolute SMD >=0.1, \*\* absolute SMD >=0.5

## 6.8. Literature Review Methods (Literature Protocol)

The review was conducted in accordance with the prospective Systematic Literature Review Protocol. The protocol documents the explicit plan for the systematic review and details the priori methodological and analytical approaches including the search strategy, selection and eligibility criteria, data collection

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methods, and analysis plan. Refer to attachment, Systematic Literature Review Protocol Megadyne Disposable Patient Return Electrodes.

This systematic literature review will evaluate the safety and performance of the subject devices, the Megadyne Disposable Patient Return Electrodes, based on published literature for the subject devices.

## 6.9. Literature Review Results (Literature Report)

This review was undertaken to support the clinical evaluation of the Megadyne Disposable Patient Return Electrodes. The devices in scope for this review are detailed below, along with the assumptions used throughout the review.

### Subject devices

1. Megadyne Disposable Patient Return Electrodes, are single use, non-sterile return electrodes with a pre-attached cord (or non pre-attached for one device with a reusable cord) used to adhere to the patient over the entire return electrode surface to complete the electrosurgical circuit between the generator, the active electrode, and the patient. This product family includes the following devices:
  - a. Pre-attached cords
    - i. Adult, single plate, with 9' (2.9m) pre-attached cord. >33lbs (>15kg)
    - ii. Adult, dual plate, with 15' (4.6m) pre-attached cord. >33lbs (>15kg)
    - iii. Adult, dual plate, with 9' (2.7m) pre-attached cord. >33lbs (>15kg)
    - iv. Pediatric, dual plate, with 3m (10') pre-attached cord. 6-33lbs (2.7-15kg)
  - b. Reusable Cord
    - i. Adult, dual plate, no cord. >33lbs (>15kg)

The following assumption was used throughout the systematic literature review:

- The Megadyne Disposable Patient Return Electrodes have no unique or trademarked brand name. The manufacturer name in conjunction with model number are both necessary to identify each subject device.

### 6.9.1. Search and Selection Results

Broad literature searches were conducted to identify all published literature on Megadyne devices, including the Megadyne Disposable Patient Return Electrodes. The search was performed for the period of 01 January 1986 to 03 September 2019 (see corresponding literature review protocol for details). The core bibliographic databases were Medline and Embase via Ovid, and PubMed. These databases are reliable and cover the vast majority of medical and scientific journals. In addition to the databases, Google Scholar was also searched.

The search results were imported into an internal literature management system (QUOSA). The full text, abstract, key words and title were then searched by the subject device name and equivalent comparator. The Literature Search Reports, with detailed search queries, are provided in the appendices. Out of the

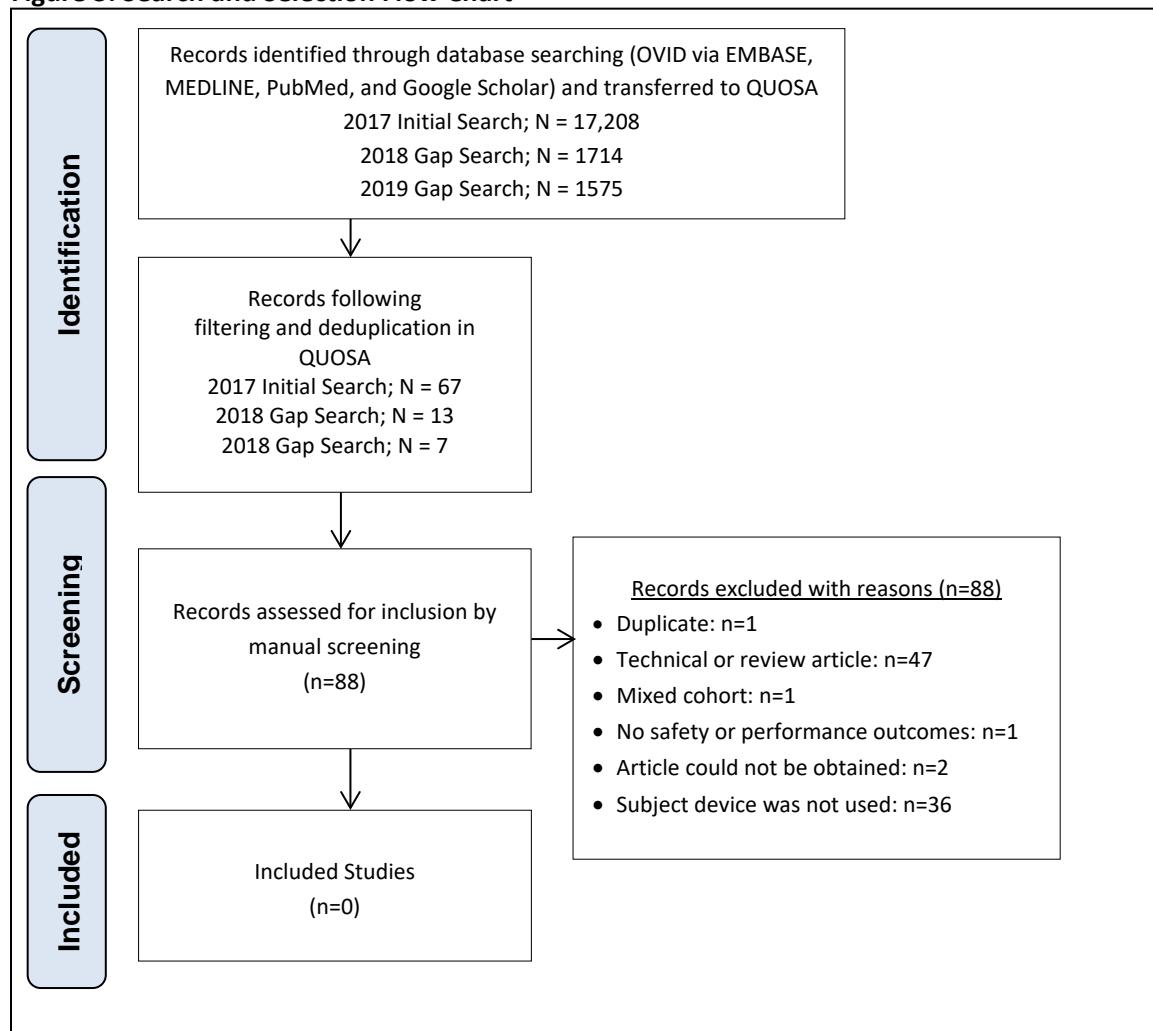
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88 possible results, 0 articles were included and all 88 were excluded due to the reasons presented in Figure 3.

**Figure 3: Search and Selection Flow Chart**



**No relevant studies were identified in the search**, as none met the previously defined criteria noted in the literature review protocol.

### 6.9.2. Literature Review Conclusions

A comprehensive literature search was performed covering the period between 01 January 1986 and 03 September 2019. This period was inclusive of the launch dates for all the subject devices and was undertaken in the core bibliographic databases of Medline and Embase via Ovid, and PubMed. Additionally, a supplementary database, Google Scholar, was also searched in an attempt to identify articles that published data on the subject devices but may not have mentioned them in the title or abstract. Even with such an exhaustive search, however, zero articles were identified that had published data related to the subject devices.

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The Megadyne Disposable Patient Return Electrodes are widely used and clinically established with a low risk profile. Despite their common usage, these devices are generally not the focus of clinical study, which is likely due to their ancillary nature. This may also account for the lack of clinical data in the published literature that was related to the subject devices.

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## 7. POST-MARKET EXPERIENCE AND SURVEILLANCE (PMS)

Post Market Surveillance (PMS) process for the subject device is conducted under PR-0000385, Franchise Procedure for Post Market Surveillance Plans and Reports (Shared). In accordance with this procedure, the methods should obtain relevant and new production and post-production information to evaluate any potential early warning signs of design and quality problems, emerging issues or safety signals, and to assign action items as necessary throughout the lifetime of the medical device. The PMS for the Megadyne Disposable Patient Return Electrodes includes internal, external, and market-based sources of active data analysis as defined in the PMS Plan (Table 34). PMS data has been provided from 01 February 2014 through 31 January 2019 as extracted from the PMS Report (Table 34).

**Table 34: Megadyne Disposable Patient Return Electrodes PMS Plan and Report Overview**

PMS Plan and Report	Report Review Period and Conclusions
Megadyne Disposable Patient Return Electrodes <u>Plan # RA-REC-020, Rev. 001</u> <u>Report # RA-REC-021, Rev. 001</u>	01-Feb-2014 to 31-Jan-2019 (Complaints: 01-Nov-2014 to 31-Jan-2019) <u>Report Conclusion:</u> Overall complaints and rates were low in the reporting period. There were no adverse trends or signals that could contribute to the efficacy of the Disposable Patient Return Electrodes product families. The periodic data review will continue as per the PMS procedures. The current PMS plan RA-REC-020 is deemed acceptable.

### 7.1. Executive Summary

Overall, there were no new harms, unknown adverse trends, signals, or unanticipated risks identified for Disposable Patient Return Electrodes product family during the overall review period of February 1, 2014 - January 2019. The occurrence rates for all harms were below the predicted frequencies. All CAPA's and NC's initiated during the review period are now closed.

No action is recommended at this time. The periodic data review will continue as per the PMS procedures. The current PMS plan (RA-REC-020 Rev 001) is deemed acceptable.

### 7.2. Complaint and Vigilance Data

Reactive PMS monitoring was performed by analyzing complaint data and data from other quality system data sources at a granular level. Data reported from November 2014 – January 2019 was extracted from the applicable complaint database(s) and other various quality system data sources and analyzed using statistical summaries and critical analyses.

Complaint data (including coding) is reflective of the data in the complaint system at a particular point in time. The data captured in this report is current as of April 12, 2019, including open complaints still within investigation. Complaint data is a dynamic attribute that is updated real time per Complaint Handling procedures and this data, including Product Experience and Analysis Codes, may be updated as additional information is received and processed.

**NOTE:** Non-complaints, complaints alleging Shipping or Data Entry Errors, and complaints that deemed to be concomitant are not included in the scope of this analysis.

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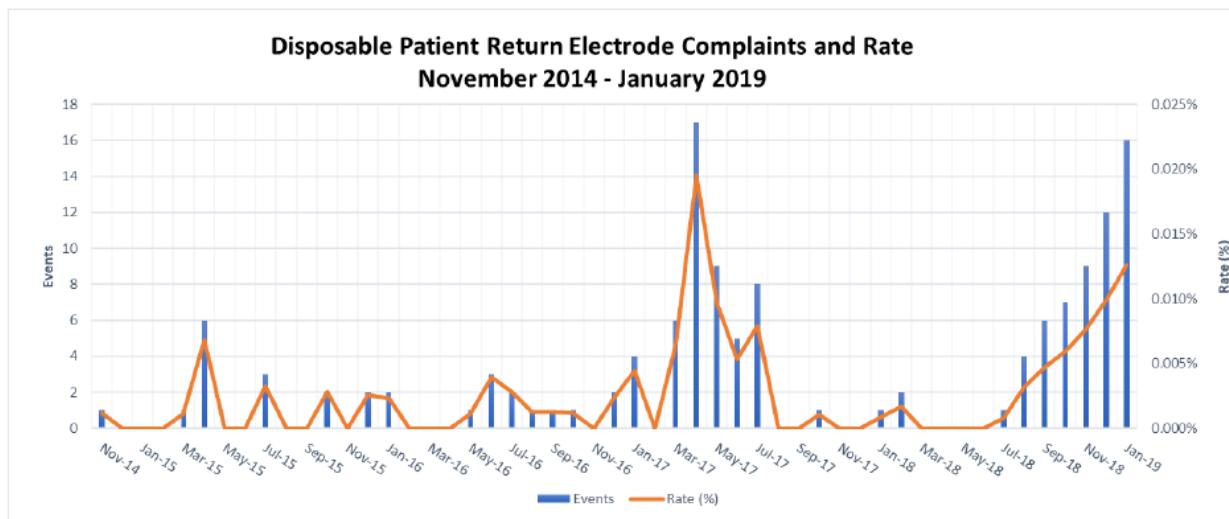
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## 7.2.1. Overall Complaints/ Sales Data

This complaint review is for the Disposable Patient Return Electrode product family. There were 130 complaint events received from November 2014 – January 2019 reporting 136 events with an overall complaint rate of 0.0027%. Figure 4 presents the total number of complaints and the complaint rate for the PMS Review period. The complaint counts captured in this graph reflect the total product quantity involved in the unique reported events.

**Figure 4: Disposable Patient Return Electrode Complaints and Rate**



Below, Table 35 show the total number of events and event rate for Disposable Patient Return Electrode product family. Further details on the top contributing PEC and PC categories can be found under Critical Analysis of Complaints.

The 4 years' worth of data was stratified into multiple time periods, highlighting the current time period, during the review to allow for comparison of complaint rates and identification of trends. The complaint rates per period were calculated by using the total complaints of the period divided by the total sales of the period.

**Table 35: Summary of Overall Disposable Patient Return Electrode Complaints**

Complaint Summary		Nov 2014-Jan 2016	Feb 2016-Jan 2017	Feb 2017-Jan 2018	Feb 2018 - Jan 2019	Grand Total
<b>Complaints (Unique Files)</b>		17	15	47	51	130
<b>Events (Total qtn involved)</b>		17	15	47	57	136
<b>WW Sales</b>		1,247,371	1,015,192	1,214,922	1,503,514	4,980,999
<b>Complaint Rate</b>	%	0.0014%	0.0015%	0.0039%	0.0038%	0.0027%

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## 7.2.2. Complaints Data by Category

### 7.2.2.1. Critical Analysis of Disposable Patient Return Electrode Complaints by Product Experience Codes

There were no veterinary procedures over the current period. The following Product Experience Code (PEC) are to be discussed due to their complaint volume and rates for Disposable Patient Return Electrode: Adhesion Issue, Performance Failure Unknown and Injury. The PECs are discussed in further detail below. The remaining PECs are not discussed due to their low volume and all rates being below the lowest risk management occurrence rate of 1 (<1 in 105 or 0.0010%). Table 36 captures the exhaustive list of all complaints received during the review period.

**Table 36: Summary of Disposable Patient Return Electrode Complaints by Product Experience Code**

Product Experience Code Breakdown	Nov 2014-Jan 2016		Feb 2016-Jan 2017		Feb 2017-Jan 2018		Feb 2018-Jan 2019		Grand Total	
	N	Rate (%)	N	Rate (%)						
Adhesion Issue	4	0.0003%	2	0.0002%	37	0.0030%	32	0.0021%	75	0.0015%
Not Specified	0	0.0000%	0	0.0000%	0	0.0000%	19	0.0013%	19	0.0004%
Performance Failure Unknown	2	0.0002%	8	0.0008%	5	0.0004%	0	0.0000%	15	0.0003%
Injury	9	0.0007%	1	0.0001%	3	0.0002%	0	0.0000%	13	0.0003%
Patient Related Issue	0	0.0000%	0	0.0000%	0	0.0000%	3	0.0002%	3	0.0001%
Skin Lesion That Is Pressure Chemical or Thermal	2	0.0002%	0	0.0000%	0	0.0000%	1	0.0001%	3	0.0001%
Alarming	1	0.0001%	1	0.0001%	1	0.0001%	0	0.0000%	3	0.0001%
Damaged Product	1	0.0001%	0	0.0000%	1	0.0001%	0	0.0000%	2	0.00004%
Fit/Connection	0	0.0000%	0	0.0000%	0	0.0000%	2	0.0001%	2	0.00004%
Tip Cleaning Issue	0	0.0000%	2	0.0002%	0	0.0000%	0	0.0000%	2	0.00004%
Unintended Thermal Injury	0	0.0000%	0	0.0000%	0	0.0000%	2	0.0001%	2	0.00004%
Misassembly	0	0.0000%	1	0.0001%	0	0.0000%	0	0.0000%	1	0.00002%
Grand Total	19	0.0015%	15	0.0015%	47	0.0039%	59	0.0039%	140	0.0028%

*NOTE: Multiple PE Codes can be chosen per complaint. N captures the total product quantity involved for the reported Code.*

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**Table 37: Summary of Disposable Patient Return Electrode Complaints by Analysis Code**

Analysis Code Breakdown	Nov 2014-Jan 2016		Feb 2016-Jan 2017		Feb 2017-Jan 2018		Feb 2018-Jan 2019		Grand Total	
	N	Rate (%)	N	Rate (%)						
Device/Records Meet Specifications	9	0.0007%	11	0.0011%	24	0.0020%	0	0.0000%	44	0.0009%
No Device Returned	0	0.0000%	0	0.0000%	0	0.0000%	35	0.0023%	35	0.0007%
Misassembly (Supplier)	0	0.0000%	0	0.0000%	19	0.0016%	1	0.0001%	20	0.0004%
Performs Within Specifications	6	0.0005%	1	0.0001%	1	0.0001%	2	0.0001%	10	0.0002%
User Error	1	0.0001%	2	0.0002%	0	0.0000%	1	0.0001%	4	0.0001%
User Damage	0	0.0000%	1	0.0001%	0	0.0000%	1	0.0001%	2	0.00004%
Unmet Expectations	0	0.0000%	0	0.0000%	2	0.0002%	0	0.0000%	2	0.00004%
Gen - Skin Lesion - Pressure/Chem/Therm	2	0.0002%	0	0.0000%	0	0.0000%	0	0.0000%	2	0.00004%
Procedure Related Photo Review	0	0.0000%	0	0.0000%	0	0.0000%	2	0.0001%	2	0.00004%
Conforming	0	0.0000%	0	0.0000%	0	0.0000%	1	0.0001%	1	0.00002%
Unable to Duplicate	0	0.0000%	0	0.0000%	1	0.0001%	0	0.0000%	1	0.00002%
Grand Total	18	0.0014%	15	0.0015%	47	0.0039%	43	0.0029%	123	0.0025%

*NOTE: The quantity for the AC is expected to be lower than the PE Code rate because not all devices are returned for analysis. However, multiple AC can be assigned per complaint. N captures the total product quantity involved in complaints where the AC was assigned.*

**PEC1. Adhesion Issue:** A total of 75 Adhesion Issue events with a rate of 0.0015% were reported during the time periods included in this PMS report. These events were reviewed and evaluated. The reported product codes were 0855CN (32), 0865C (20), 0855C (14) and 0855CL (9). The reporting countries for the events were USA (73), and Latin America (2). Of the 75 events, none were MDV reportable and one was MDR reportable for malfunction during the November 2014-January 2016 time period. There greatest number of Adhesion Issues occurred during the review period from February 2017-January 2018 with 37 events reported. There was 1 Patient code (Potential Safety Hazard) associated with the Adhesion Issue PEC. The Analysis Codes associated with the Adhesion Issue events were Device/Records Meet Specifications (24), No Device Returned (21), Misassembly (Supplier) (19) and no other event greater than (3). The PEC, "Adhesion Issue," is included in the Risk Analysis (TCF-06) and is below the predicted Occurrence rate of 7 (<2500 ~5000 in 105 or between 5.0000% and 2.5000%).

**PEC2. Performance Failure Unknown:** A total of 15 Performance Failure Unknown events with a rate of 0.0003% were reported during the time periods included in this PMS report. These events were reviewed and evaluated. The reported product codes were 0855CN (7), 0855 (3) 0855C (3)and 0855CL (2). The reporting countries for the events were USA (14), and Russia (1). Of the 15 events, none were MDV or MDR reportable. There greatest number of Performance Failure Unknown occurred during the review period from February 2016-January 2017 with 8 events reported. There were no Performance Failure Unknown events reported during the February 2018- January 2019 time period. There was 1 Patient code (Injury) associated with the Performance Failure Unknown PEC which occurred during the November 2014- January 2016 time period. The Analysis Codes associated with the Performance Failure Unknown events were Device/Records Meet Specifications (8), Performs Within Specifications (3), and no other code reported greater than 2. The PEC, "Performance Failure: Unknown," is included in the Risk Analysis

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(TCF-06) under various line items and is below the predicted Occurrence rate of 5 (<500 ~1000 in 105) or between 1.0000% and 0.5000%).

**PEC3. Injury:** A total of 13 Injury Issue events with a rate of 0.0003% were reported during the time periods included in this PMS report. These events were reviewed and evaluated. The reported product codes were 0855C (10), 0855CN (2), and 0865C (1). The reporting country for all 13 events was USA. Of the 13 events, none were MDV or MDR reportable. The greatest number of Injury Events occurred during the review period from November 2014- January 2016 with 9 events reported. There were no Injury events reported during the February 2018 - January 2019 time period. The 2 Patient codes reported were Injury (12) and Potential Safety Hazard (1). The Analysis Codes associated with the Injury event were Device/Records Meet Specifications (9), Performs Within Specifications (3), and GEN - Skin Lesion - Pressure/Chem/Therm (1). The PEC, "Injury," is included in the Risk Analysis (TCF-06) under various line items and is below the predicted Occurrence rate of 5 (<500 ~1000 in 105 or between 1.0000% and 0.5000%).

### 7.2.2.2. Critical Analysis of Disposable Patient Return Electrode Patient Codes

"Injury" was the highest rated and reported Patient Code (PC) for the Disposable Patient Return Electrode product family. This PC is discussed in further detail below. The remaining PCs are not discussed due to their low volume and all rates being below the lowest risk management occurrence rate of 1 (<1 in 105 or 0.0010%). Table 38 captures the exhaustive list of all Patient Codes (PCs) received during the review period.

**Table 38: Summary of Complaints by Patient Codes**

<b>Patient Codes Breakdown</b>	<b>Nov 2014-Jan 2016</b>		<b>Feb 2016-Jan 2017</b>		<b>Feb 2017-Jan 2018</b>		<b>Feb 2018-Jan 2019</b>		<b>Grand Total</b>	
	N	Rate (%)	N	Rate (%)						
Injury	10	0.0008%	1	0.0001%	2	0.0002%	0	0.0000%	13	0.0003%
Potential Safety Hazard	1	0.0001%	0	0.0000%	1	0.0001%	0	0.0000%	2	0.00004%
Rash	0	0.0000%	0	0.0000%	0	0.0000%	1	0.0001%	1	0.00002%
Burns Second Degree	0	0.0000%	0	0.0000%	0	0.0000%	1	0.0001%	1	0.00002%
Burn	0	0.0000%	0	0.0000%	0	0.0000%	1	0.0001%	1	0.00002%
<b>Grand Total</b>	<b>11</b>	<b>0.0009%</b>	<b>1</b>	<b>0.0001%</b>	<b>3</b>	<b>0.0002%</b>	<b>3</b>	<b>0.0002%</b>	<b>18</b>	<b>0.0004%</b>

*Note: Multiple Patient Codes can be chosen per complaint. N captures the total product quantity involved for the reported Code.*

**PC1. Injury:** A total of 13 Injury events with a rate of 0.0003% were reported during the time periods included in this PMS report. These events were reviewed and evaluated. The reporting country was USA 13 reported PC's. The reported PEC's for the Injury PC, were Performance Failure Unknown (1). There was no MDR or MDV reportable events during this time period under review. The patient code is addressed in the Risk Analysis TCF-06 under various line items.

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### 7.2.3. MDR/MDV Data

#### 7.2.3.1. Medical Device Reporting (MDR) Review

A total of 136 events were reported for the Disposable Patient Return Electrode product family over the total review period included in this PMS Report (November 2014 – January 2019). Of the 136 events, 3 were MDR reportable with zero (0) Death, (1) Serious Injury, and (2) Malfunction.

**Table 39: Summary of Disposable Patient Return Electrode MDR Reportable Events by MDR Type**

MDR Breakdown by Type	Nov 2014-Jan 2016		Feb 2016-Jan 2017		Feb 2017-Jan 2018		Feb 2018-Jan 2019		Grand Total	
	N	Rate (%)	N	Rate (%)						
Death	0	0.00000%	0	0.00000%	0	0.00000%	0	0.00000%	0	0.00000%
Malfunction	1	0.0001%	0	0.0000%	0	0.0000%	1	0.0001%	2	0.00004%
Serious Injury	0	0.0000%	0	0.0000%	0	0.0000%	1	0.0001%	1	0.00002%
Grand Total	1	0.0001%	0	0.0000%	0	0.0000%	2	0.0001%	3	0.0001%

#### 7.2.3.2. Medical Device Vigilance (MDV) Review

There were no reportable MDV's for Disposable Patient Return Electrode during this timeframe.

### 7.2.4. Death-Related Events

There were no reportable Death-Related events for Disposable Patient Return Electrode during this timeframe.

### 7.2.5. External Vigilance Data

External Vigilance is not applicable as technical documentation is available for the subject devices.

### 7.2.6. Harm Evaluation Summary Review for Disposable Patient Return Electrodes

A total of 130 complaint events, with 18 identified Patient Codes, were reported on Disposable Patient Return Electrode from the November 2014 – January 2019 time period. All rates were below predicted for the harms analysis results. It should be noted that no new harms were identified within the time period.

### 7.2.7. Overall Complaint Analysis Conclusions

Overall complaints and rates were low. There were 130 complaint events received from November 2014 – January 2019 reporting 136 issues with an overall complaint rate of 0.0027%. Of those 130 complaints

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there were 18 Patient Codes were reported. No trends or signals were identified. The product family complaint review identified no new harms or hazards.

## 7.3. Corrective Actions

### 7.3.1. Corrective and Preventive Actions (CAPAs)

The Corrective and Preventative Action process for the subject device is conducted under PR-0000385. In accordance with the procedure, a risk assessment is conducted to evaluate the significance of the risk of the issue and its associated impact. If the CAPA requires escalation, the appropriate management representatives are required to review and assess the escalation based on their scope of responsibility. For further details pertaining to the CAPAs, refer to applicable CAPA file.

#### 7.3.1.1. Corrective and Preventative Actions (CAPAs) Review

During the period covered by this PMS review, 2 CAPA's were initiated in relation to the Disposable Patient Return Electrodes.

**Table 40: Corrective and Preventative Actions (CAPAs)**

CAPA Number	CAPA Title	CAPA Create Date	CAPA Closed Date	CAPA Status	CAPA Description	CAPA Root Cause(s)
16005	Catalog# 0855C: Adhesive too aggressive.	June 29, 2016	October 25, 2016	Closed	Catalog# 0855C: Adhesive too aggressive.	Material
CAPA-007647	Gel Residue from use of pad - Complaint	December 15, 2017	May 18, 2018	Closed	Between the period of March 2017 and July 2017 Megadyne has received 25 complaints on 0855CN and 0855CL patient return electrode pad for blue gel residue. This is an elevated complaint rate compared to the previous 12 months.	Undetermined

#### 7.3.1.2. CAPAs Conclusion

Both CAPA's are closed in relation to the Disposable Patient Return Electrodes Product family. No further action required.

## 7.3.2. Escalations

During the period covered by this PMS review, 1 Escalation was initiated related to the Disposable Patient Return Electrodes. There were no field actions taken during the review period.

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**Table 41: Escalations**

Escalation Number	Escalation Orig. Date	Escalation Origination Source	Descriptions	Field Action: Yes / No	CAPA #
PIA-0000002	5/28/2017	Complaint	An upward trend in complaints related to sticky gel residue left after removal of Megadyne Return Electrode Gel Pads	No	007647

### 7.3.2.1. Escalations Conclusion

There was 1 escalation in 2017 due to complaint trending related to sticky gel residue after pad removal. Reference CAPA-007647. The escalation did not result in a field action. No further action was required.

### 7.3.3. Alerts

#### 7.3.3.1. MHRA Review

A total of 18 alerts came back in the Medicines and Healthcare Products Regulatory Agency (MHRA) Database maintained by the Department of Health of the United Kingdom. The search was conducted on April 17, 2019 for "Electrode". Of the 18 alerts that came back in the search, none were related to the Disposable Patient Return Electrode for the period of February 2014- January 2019.

### 7.3.4. Field Actions and Recalls

There were no field actions or recalls taken during the review period.

### 7.4. PMS Report Conclusion

Overall complaints and rates were low in the reporting period. There were no adverse trends or signals that could contribute to the efficacy of the Disposable Patient Return Electrodes product families. The periodic data review will continue as per the PMS procedures. The current PMS plan RA-REC-020 is deemed acceptable.

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## 8. BENEFIT / RISK ANALYSIS

The Megadyne Disposable Patient Return Electrodes subject devices have a well-established history of safety and reliable performance. These devices have been in general distribution for 13 years and as explained in Section 3, State of the Art, have improved the safety of electrosurgery. They are intended for use by or on the order of a physician who is well trained in the associated risks. The anticipated clinical benefits of using these high-frequency surgical devices as compared to other surgical techniques outweigh the residual and overall risks. This family of devices presents no risks to patients or users that are unacceptable or unreasonable when weighed against the benefits to the patient. The Megadyne Disposable Patient Return Electrodes subject devices have been objectively shown to be safe and perform effectively as intended to adhere to the patient over the entire return electrode surface to complete the electrosurgical circuit between the generator, the active electrode, and the patient during electrosurgical procedures. The Benefit / Risk Analysis (RBA) presented in the following sections collectively covers all subject devices in-scope of this CER and includes the following:

**0850C:** Adult Patient Return Electrode, single plate, with 9-foot (2.7m) pre-attached cord >33 lbs.

**0855:** Adult Patient Return Electrode, dual plate, no cord >33lbs.

**0855CL:** Adult Patient Return Electrode, dual plate, with 15-foot (4.6m) pre-attached cord >33 lbs.

**0855CN:** Adult Patient Return Electrode, dual plate, with 9-foot (2.7m) pre-attached cord >33 lbs.

**0865C:** Pediatric Patient Return Electrode, dual plate, with 9-foot (2.7m) pre-attached cord 6-33 lbs.

### 8.1. Clinical Benefits / Performance Analysis

A clinical claim is a statement linking the use of a medical device to a clinical safety or clinical performance outcome. Clinical benefits include any claims about clinical safety and performance outcomes of the subject device. Clinical safety and performance outcomes include the ability of the subject device to achieve its intended purpose as claimed. As per MEDDEV 2.7.1 Revision 4, the scope of the clinical evaluation must identify such claims in promotional material (e.g., in the IFU, surgical technique, patient information, website) and must provide objective and balanced evidence to substantiate the claims. Note: Non-clinical claims, those claims which are unrelated to clinical safety and performance (e.g., statements of fact related to device features or geographic sales data) are not included or analyzed in the CER.

The clinical benefits of the Megadyne Disposable Patient Return Electrodes have been substantiated via objective evidence from the appraised data (either clinical, non-clinical, or both) in accordance with the Data Appraisal Plan (Section 6.1) to assess the ability of a medical device to achieve its intended purpose as claimed by the manufacturer including any direct or indirect medical effects on humans as well as the clinical benefit on patients.

As discussed in Section 3, State of the Art, cutting into skin and subcutaneous tissues is a fundamental technique in both open and laparoscopic surgical procedures that is indispensable to accessing the tissues of interest. The surgical separation of tissues can be achieved with blunt dissection, sharp dissection, or diathermy (the introduction of electrical energy for dissection and coagulation of tissue).

In contemporary clinical settings energy-based surgical systems are used to facilitate the application of energy in the surgical or endoscopic field where they produce clinical effects such as cutting, coagulation,

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or desiccation of tissue, or fulguration for the destruction or manipulation of the tissue (Sankaranarayanan et al., 2013; Schwartzberg, 2012)

In the modern surgical suite, energy based systems have become the standard of care in cutting, dissection, coagulation, and in some cases, additional functions required for minimally invasive surgery (MIS) in diverse anatomical regions. Hemostasis must be achieved at the end of a surgical procedure as well as intraoperatively to maintain visibility of the surgical field, particularly during laparoscopic procedures. Monopolar electrosurgery represents the oldest and most mature state of the art type of electrosurgical energy used in the majority of surgical procedures globally. The monopolar configuration utilizes three components including a generator that produces the RF energy for the active electrode an active electrode (a pencil and an electrode tip) which conducts radio frequency (RF) energy to the surgical site, and a dispersive electrode (patient return electrode), which is placed on the patient at a location remote from the surgical site and returns energy back to the generator. The Megadyne Disposable Patient Return Electrodes subject devices represent one such dispersive electrode intended to adhere to the patient over the entire return electrode surface to complete the electrosurgical circuit between the generator, the active electrode, and the patient during electrosurgical procedures. The relatively large surface area of the dispersive electrode is designed to defocus or disperse the current in order to prevent thermal tissue injury. Specific benefits associated with use of the subject device are presented in Table 42, following.

**Table 42: Megadyne Disposable Patient Return Electrodes Clinical Benefits**

Source	Benefits and Claims	Reference
<b>IFU</b>	The device meets the intended purpose to conduct monopolar electrosurgical energy from target tissue of a patient back to one or two electrosurgical units (ESU), or generators.	<p>There is a large body of clinical evidence discussed in Section 3, State of the Art, to support the use of monopolar electrical surgical systems to conduct monopolar electrosurgical energy from target tissue of a patient back to one or two electrosurgical units (ESU), or generators.</p> <p>MEGADYNE Patient Return Electrode for Adults IFU (IFU NR74330, Rev. G 2016-03)</p> <p>MEGADYNE Patient Return Electrode for Pediatrics IFU (IFU NR74380, Rev. F 2016-03)</p>
<b>Literature based claims/benefits for monopolar surgical systems</b>	<ul style="list-style-type: none"> <li>• Established and familiar technology</li> <li>• Low cost</li> <li>• Varied tissue effects – e.g., desiccation, vaporization, fulguration, coaptation</li> <li>• Parameters are under surgeon's control</li> </ul>	<p>State of the Art literature discussion in Section 3 (Law et al., 2014; Munro, 2012; Sankaranarayanan et al., 2013; Vilos and Rajakumar, 2013)</p>

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	<ul style="list-style-type: none"> <li>• Minimal smoke production or carbonization</li> <li>• Superior dissecting capabilities according to some surgeons</li> <li>• Capability for coaptive coagulation (compression and cauterization) of grasped tissue using monopolar forceps</li> </ul>	
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## 8.2. Clinical Risks / Safety Analysis

### 8.2.1. Discussion of Harms Identified Within the Risk Documentation

Megadyne Medical Devices, Inc. takes all necessary steps to ensure that risks are reduced as far as possible by applying the available State of the Art techniques in designing and manufacturing the target devices to ensure safe usage. Potential hazards and harms have been identified via the Megadyne Risk Management Procedures.

The potential risks for the Disposable Patient Return Electrodes Product Family are assessed during the risk management process under the Risk Management Plan TCF-06, which is conducted according to ISO 14971:2012 (Medical Devices - Risk management - Application of risk analysis) and SOP QA-SOP-015. The results of the risk management process are presented in the documents identified in Appendix 10.1, and are summarized below:

- Risk Management Plan (RMP) for the Disposable Grounding Pad, TCF-06
- Risk Management Report (RMR) for the Disposable Grounding Pad, TCF-06, Version 22. The FMEA encompasses all known hazards during use of the devices within the Megadyne Disposable Patient Return Electrodes Family and identifies possible patient and user harms resulting from these hazards. For this reason, the FMEA is used to assess risk in this clinical evaluation. The FMEA assesses risks before and after mitigation activities and categorizes them based on a calculated Risk Priority Number (RPN) as described in Figure 5: Risk Severity and RPN Severity Ranking. Further details of the procedure are described in QA-SOP-015 Rev 005 (Risk Management of Medical Devices).

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**Figure 5: Risk Severity and RPN Severity Ranking**

### Severity Risk Ranking

Description	Impact	Rank
Critical	The potential problem could result in death or serious injury to the patient or user, such as alternate current site injury, patient burn, or infection.	10
Important	The potential problem could result in a non-serious injury to the patient or user that requires medical intervention, such as reduced or no surgical effect, pressure sore, or allergic reaction.	5
Minor	The potential problem could result in a non-serious injury to the patient or user that does not require medical intervention, such as a delay in the procedure.	3
Negligible	There is no risk of injury to the patient or user.	1

### Probability of Occurrence Risk Ranking

Qualitative Description	Quantitative Description	Rank
Continual (expected to occur)	$\geq 10\%$	5
Frequent (likely to occur)	> 1% and < 10%	3
Occasional (can occur)	> 0.1% and $\leq 1\%$	2
Rare (unlikely to occur)	$\leq 0.1\%$	1

### Determination of RPN

Probability of Occurrence Risk Ranking	Ranking	Severity Risk Ranking			
		Negligible	Minor	Important	Critical
		1	3	5	10
Probability of Occurrence Risk Ranking	Continual	5	5	15	50
	Frequent	3	3	9	15
	Occasional	2	2	6	10
	Rare	1	1	3	5

The Risk Management Report (RMR) includes all known hazards during use of the subject device and identifies possible patient and user harms resulting from these hazards. For this reason, the RMR is used to assess risk in this clinical evaluation. The risk assessment in the RMR found that individual risks identified in the applicable risk assessments were mitigated to levels *as low as possible*, and within the acceptable region of the Risk Rating Table included in Risk Management Plan (TCF-06). Based on the residual risk profile, the overall residual risk for the both the Megadyne Disposable Patient Return Electrodes Family was deemed acceptable (TCF-06, Version 22).

Table 44 presents the harms identified in the risk documentation for the Megadyne Disposable Patient Return Electrodes Product Family cross-referenced to harms found in the clinical data, PMS, and the IFUs for the respective devices in scope. Clinical safety signals reported from all the data sources were compared to potential harms identified in the risk management documents and verified that the IFU sufficiently identifies potential adverse events. Refer to Table 43 for a description of the abbreviations and definitions used in these tables.

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**Table 43: Legend for Abbreviations in Table 44**

<b>Abbreviation:</b>	<b>Applies To:</b>	<b>Definition:</b>
A	Clinical Data / PMS	“Analyzed” data set within CER
NO	Clinical Data / PMS	“No Occurrence” as part of data set within CER
C	RM / IFU	“Captured” in the applicable Risk Document and/or IFU
HNR	RM / C	“Harm Not in Risk” documents – identified new or emerging potential harm that is not currently included in the Risk Assessment Summary (RAS)
NC	IFU	“Not Captured” - risk analyzed in the Risk Documents and not required to be declared in the IFU.  Or “Not Captured” - harm not previously identified; i.e. identified new or emerging potential harm that is not currently included in the IFU or Risk Assessment Summary (RAS).
TBD	RM / IFU	“To Be Determined” Analysis Pending”

**Table 44: Harms Summary Table for the Megadyne Disposable Patient Return Electrodes**

<b>Harm Category</b>	<b>Proactive Clinical</b>	<b>PMS</b>	<b>RM</b>	<b>IFU* [a]</b>
Electric Shock	NO	NO	C	NC
Burn	A	A	C	C
Serious Burn	A	A	C	C
EM Interference	NO	NO	C	NC
Cancer Generation	NO	NO	C	NC
Toxic Reaction	NO	NO	C	NC
Short Term Discomfort	NO	A	C	C
Surgery Delay	NO	NO	C	NC

**\*Note:** Harms noted as “C” (captured) in the IFU column of the table above denotes that the harm is listed directly in the IFU. For those harms noted as “BRL” (below risk level), note that many potential harms have an Overall Residual Risk level (ORR) that is below that required to be explicitly included in the IFU. However, even when the specific harm is not captured in the IFU, it is additionally important to note that the harm is often inferred in Contraindications, Warnings, and Precautions and other sections (as applicable) of the IFU as described in the Risk Documentation.

**[a]** No Adverse Events or Side Effects or contraindications are specified in any of the IFUs for the respective devices in scope of this CER. Harms are either addressed directly or inferred in the Warnings and Precautions within the IFU.

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## 8.2.2. Discussion of Harms Not Identified in the Risk Documentation

There were no new harms found in the clinical or PMS data that are not already addressed in the risk documentation.

## 8.3. Side-Effects Acceptability

Acceptability of the subject device side-effects needs to be interpreted considering currently available alternative treatments and acceptability of side-effects from those treatments. As discussed in Section 3.3, there are numerous energy based and non-energy-based options available to the surgeon for dissection and coagulation of tissues, each with their own risk and benefit profiles. The specific benefits for the subject devices, and for monopolar surgical systems with which the subject devices are used, are discussed in Section 8.1. The specific risks and associated potential patient/user harms for devices in scope of this CER, the family of Megadyne Disposable Patient Return Electrodes, are discussed in the risk documentation. A summary of potential patient/user harms crossed-referenced to their occurrence in the clinical literature and their discussion in the subject devices IFUs is provided in Section 8.2.

A review of the individual clinical data sources available for this CER on the Megadyne Family of Disposable Patient Return Electrodes shows that there are no new or emerging risks that are a cause for concern, and no new potential patient harms or emerging risks have been identified through this clinical evaluation. The reviewed clinical data verifies that all adverse events reported in the clinical data specific to the Megadyne Disposable Patient Return Electrodes were appropriately addressed in the IFU and risk documentation and does not suggest any further risk mitigation or required amendments to the product information, IFU, or warnings.

## 8.4. Benefit-Risk Profile Acceptability

The Megadyne Disposable Patient Return Electrodes subject devices are intended for use during electrosurgical procedures to conduct monopolar electrosurgical energy from target tissue of a patient back to an electrosurgical unit (ESU), or generator. Energy-based systems have become the standard of care and as discussed in Section 3 (State of the Art), the patient return electrode is a required component of the integrated energy-based electrosurgical system.

Hemostasis must be achieved at the end of a surgical procedure as well as intraoperatively to maintain visibility of the surgical field, particularly during laparoscopic procedures; however, conventional means of tying, suture ligating, and pressure used to control bleeding in open operations are less practical and effective in minimally invasive procedures, surgeons must rely on various other techniques of tissue and vessel coagulation (Lantis et al., 1998).

The Megadyne Disposable Patient Return Electrodes product family enables surgeons to perform surgical separation and coagulation of tissues in both open and laparoscopic surgical procedures. The patient return electrode, which is placed under the patient at a location remote from the surgical site, serves as a dispersive electrode (return pad) allowing for the safe use of monopolar electrical surgical devices in the surgical suite. The relatively large surface area of the dispersive electrode is designed to defocus or disperse the current in order to prevent tissue injury. Energy-based devices requiring the use of a patient return electrode have exhibited overall advantages over conventional non-energized techniques of cutting, dissection, and coagulation in terms of surgical time, blood loss, and a majority of complications.

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Additionally, evidence-based benefits of standard monopolar technology include its established longer history of use, preference by numerous clinicians, similar rates of overall efficacy compared with advanced bipolar electrosurgery in some studies, relatively low re-operation rates, and continually decreasing rates of the complication (i.e., TUR syndrome in prostate surgery, Section 3.4).

In considering the overall benefit risk analysis for the Megadyne Disposable Patient Return Electrodes product family, it is important to consider the risk of these events to the patient as part of the residual risks of the use of monopolar generators and electrical devices with which the subject device is used. It is also important to consider that the risks of these events are possibly associated with general surgical and hospitalization procedures and are not always directly device related. In addition to the device itself, patient factors related to anatomy, concomitant diseases, concomitant medications, implanted devices, and other confounding factors may also impact the clinical performance and safety and the ability of the patient return electrode to perform as intended.

The primary claimed benefit to the use of the Megadyne Disposable Patient Return Electrodes is that the devices meet their intended purpose to conduct monopolar electrosurgical energy from target tissue of a patient back to one or two electrosurgical units (ESU), or generators. There is a large body of clinical evidence discussed in Section 3, State of the Art, to support the use of monopolar electrosurgical systems to conduct monopolar electrosurgical energy from target tissue of a patient back to one or two electrosurgical units (ESU), or generators.

Non-clinical testing (bench testing, analytical testing, and animal testing) has shown biocompatibility, electrical safety, and support the performance and effectiveness of the Mega Soft Patient Return Electrodes Product Family for their intended use (Section 4.3 and Section 6.2).

The post-market proactive clinical data (Section 6.7) extracted from the Premier Healthcare Database (PHD) substantiates the continued use of the Megadyne Disposable Patient Return Electrodes in a broad array of surgical procedures in a population that is aligned with the intended use of the devices. This two-arm, observational, retrospective cohort study was conducted in order to collect and analyze real-world Epi data on the Megadyne subject devices and similar products manufactured by Bovie and Valleylab. The observational aspect of this study allowed for understanding the use of Megadyne Disposable Patient Return Electrodes, and the potential risks associated with the device in the real-world setting. The primary study endpoint was incidence of thermal injury as the only complication of interest. Inclusion criteria consisted of patients who underwent an inpatient or outpatient procedure with utilization of Megadyne Disposable Patient Return Electrodes ( $n = 22,151$ ) or the competitor devices ( $n = 36,898$ ). The incidence of thermal injury following use of Megadyne Disposable Patient Return Electrodes across multiple types of surgical procedures and hospital settings was exceedingly low over a 20-year time period, as there were only 4 (0.018%) instances of thermal injury. Similar results were obtained from the competitor group, with only 6 (0.016%) instances of thermal injury. Therefore, the relative risk of thermal injury from Megadyne Disposable Patient Return Electrodes was comparable to similar devices on the market during the same time period.

As described in Section 6.8 and 6.9, a systematic literature review was conducted for the subject devices, covering the period between 01 January 1986 and 03 September 2019. This period was inclusive of the launch dates for all the subject devices. The search identified zero articles that had published data related to the subject devices. The Megadyne Disposable Patient Return Electrodes are widely used and clinically established with a low risk profile, and the lack of data in the clinical literature is attributable to the

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ancillary nature of these devices and that they are generally not the focus of clinical study due to their routine use and favorable history of safety and performance.

The harms review during the PMS process did not identify any new harms. The analysis of complaints by PEC and PC for the Megadyne Family of Disposable Patient Return Electrodes shows consistent complaint types being reported for product family overall. No new harms were found in the clinical or PMS data that are not already addressed in the risk documentation. Furthermore, no adverse trends were observed for CAPA, Issue Escalation, or Field Actions during the current reporting period. No additional safety concerns or adverse events were identified in the analysis of MHRA Alerts. There were no deaths reported in the PMS review period for the devices in scope of this CER.

The body of data including the Clinical Evaluation Report, Post Market Surveillance data, Post-Market Proactive Clinical Data and Literature Review was sufficient to assess the benefits and the risks associated with use of the Megadyne Disposable Patient Return Electrodes product family, and to conclude that patient benefits from use of these State of the Art devices in monopolar electrosurgical procedures outweighs possible risks when these return electrodes are used in accordance with the IFU. Megadyne, Inc. has undertaken all necessary steps to ensure that residual risks associated with use of the Disposable Patient Return Electrodes product family are reduced as far as possible through application of existing State of the Art techniques in the design and manufacture of these medical devices to ensure safe usage.

Thus, it is objectively concluded from this clinical evaluation that the benefits of the Megadyne Disposable Patient Return Electrodes outweigh the very low associated residual risks. The low rate of complications from the reviewed PMS and post-market proactive clinical data support the acknowledgment that while risks do exist, they remain at a very low level and there are no emerging trends. This Clinical Evaluation Report documents that there are no new emerging clinical performance or safety issues that would require clinical investigations for the Megadyne Disposable Patient Return Electrodes subject devices given the clinical data which exists on these clinically well-established CE marked legacy devices. Therefore, based on the overall medical benefits and the possible harms identified in the preceding sections above, it has been determined that if the Megadyne Disposable Patient Return Electrodes subject devices are utilized according to the intended use, the occurrence of the risks identified for the system have been reduced as far as possible and the benefits outweigh the possible risks over the procedure based lifetime of the devices.

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## 9. CONCLUSION

The Megadyne Disposable Patient Return Electrodes subject devices have a well-established history of safety and reliable performance. These devices have been in general distribution for 13 years and have improved the safety of electrosurgery. The subject devices have been objectively shown to be safe and perform effectively as intended as defined by: 1) adherence to the patient over the entire return electrode surface and 2) to safely complete the electrosurgical circuit between the generator, the active electrode, and the patient during electrosurgical procedures. Given that electrosurgery is a clinically well-established and accepted technology with very low complaint rates and complications as reported from PMS and real world proactive post-market Epi clinical data, there is sufficient data available from real-world clinical use to confirm safety and performance of the Megadyne Disposable Patient Return Electrodes subject devices as detailed below.

Post-market surveillance (Section 7) did not identify any new harms, unknown adverse trends, signals, or unanticipated risks for the subject devices, and showed that overall complaints and rates were low in the 5-year reporting period.

Real-world post-market proactive clinical data (Epi data) were analyzed on 22,151 patients in real-world clinical settings to evaluate select clinical outcomes of the Megadyne Disposable Patient Return Electrodes subject devices when compared to similar products manufactured by other device companies (Section 6.7). The primary study endpoint was incidence of thermal injury as the only complication of interest. The incidence of thermal injury following use of Megadyne Disposable Patient Return Electrodes across multiple types of surgical procedures and hospital settings was exceedingly low over a 20-year time period, as there were only 4 (0.018%) instances of thermal injury out of a total of 22,151 cases. No unanticipated risks or harms were identified by the Epi data, and the subject devices demonstrated no evidence of increased risk for any complications in the perioperative period of surgery.

Monopolar electrosurgery procedures are well-established and consistent with the State of the Art for this medical field (Section 3). The body of evidence reviewed is representative of the intended population and intended use of the Megadyne Disposable Patient Return Electrodes subject devices. A risk assessment of the subject devices was conducted according to EN ISO 14971:2012 (Medical devices - Application of risk management to medical devices) and QA-SOP-015 Risk Management (Section 8). The detailed Failure Mode and Effect Analysis (FMEA) for each subject device family determined that all identified risks have been deemed acceptable (refer to Disposable Grounding Pad Risk Management Report, TCF-06). None of the risks identified in the FMEAs are unique to Megadyne's electrosurgery devices. All monopolar electrosurgery accessory manufacturers face the same set of risks, and have addressed them in very similar ways. No new, unanticipated, or unacceptable risks were identified in the body of evidence to indicate any new performance or safety issues in the clinical setting that were previously unknown. The risks have been analyzed and assessed individually within the Risk Assessment Summary of the subject device family. Appropriate risk control measures are in place and the overall residual risk is very low and acceptable. The risks associated with these devices are well understood by the market and surgical professionals, and they are intended for use by or on the order of a physician who is well trained in the associated risks. Megadyne Medical Products, Inc. has undertaken all necessary steps to ensure that the residual risk factors associated with Megadyne Family of Patient Return Electrodes are mitigated by applying existing State of the Art techniques for the design, testing, and manufacturing of these medical devices to ensure safe usage and that the devices will perform as intended.

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These devices are intended for use by or on the order of a physician who is well-trained in the techniques and safety of electrosurgery and familiar with the associated risks. The clinical benefits provided by the Megadyne Disposable Patient Return Electrodes subject devices outweighs the residual and overall risks identified in the FMEA. As supported by the PMS (Section 7) and post-market proactive clinical data (Section 6.7), the subject devices present no risks to patients or users that are unacceptable or unreasonable when weighed against the benefits to the patient. The risks associated with electrosurgery are accepted by the patient through informed consent prior to the procedure.

In conclusion, based on the sum-total of existing nonclinical and clinical data, as well as the continual post market surveillance throughout the subject device's procedure based device lifetime, it has been objectively verified that these data support the safety and performance of the Megadyne Disposable Patient Return Electrodes. The subject devices present no risks to patients or users that are unacceptable or unreasonable when weighed against the benefits to the patient. Based on an objective review of the verification and validation testing and the acute clinical safety and performance data, there are no unanswered questions about safety or performance for these devices. Existing bench-top verification and validation testing, post market proactive clinical data, and PMS data of the Megadyne Disposable Patient Return Electrodes confirm the safety and performance of the devices as previously discussed.

Regarding device lifetime, the subject devices are utilized intraoperatively and have a therapeutic lifetime that is limited to the duration of the surgery (<24 hrs.). The clinical evidence, both proactive and reactive, in this CER confirm both safety and performance over the lifetime of the devices. In addition, ongoing PMS will continue and is expected to further confirm safety and performance for these devices.

Therefore, this clinical evaluation has established that the available clinical data are sufficient to establish conformity with all applicable Essential Requirements of the European Council Directive 93/42/EEC (MDD) and confirm the safety and performance of the Megadyne Disposable Patient Return Electrodes subject devices.

## 9.1. Post Market Clinical Follow-up (PMCF)

### Rationale for no PMCF Studies for the Megadyne Disposable Patient Return Electrodes

This CER is actively updated with data from post-market surveillance (PMS) in accordance with the Medical Devices Regulation (EU) 2017/745 (MDR). Megadyne Medical Devices, Inc. uses an established PMS system that monitors clinical safety and performance of the Disposable Patient Return Electrodes as part of its quality management system (QMS). This QMS was audited and found compliant with current EU regulatory requirements. Where applicable, any new clinically significant data detected from complaints, vigilance reports, safety reports, published literature, device registries, or PMCF studies (or any other source) are monitored and trended regularly. The data are critically and objectively analyzed with respect to the device's clinical benefit-risk profile to confirm and maintain a high degree of protection of safety for the patient and user of these devices. These PMS data are incorporated into the CER regularly based on device classification and residual risk presented in the CER Frequency Update Matrix (Table 45).

Collectively, sufficient nonclinical and clinical data exists to support the safety and performance of the Megadyne Disposable Patient Return Electrodes subject devices when used within their intended purpose and instructions. Therefore, no PMCF studies are required. The detailed justification for not conducting PMCF Studies for the Megadyne Disposable Patient Return Electrodes subject devices is based on the following:

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- As discussed in Sections 2.2, 7 and 8, the class IIb Megadyne Disposable Patient Return Electrodes subject devices have a clinically well-established history of safety and reliable performance through use in millions of cases in thousands of operating rooms throughout the world. These devices have been in general distribution for 13 years and have helped to revolutionize and improve the safety of electrosurgery. As evidenced by the first CE-Mark certification date, clinical data, and PMS data collected to date, the Megadyne Disposable Patient Return Electrodes subject devices have been in safe and continuous clinical use for over a decade.
- Following an exhaustive literature search, zero articles were identified that had published data related to the subject devices (Section 6.9). The Megadyne Disposable Patient Return Electrodes are widely used and clinically established with a low risk profile, and the lack of data in the clinical literature is attributable to the ancillary and reliable nature of these devices and that they are consequently not the focus of clinical study.
- As reported in Section 6.7, real-world post-market proactive clinical data (Epi data) were analyzed in order to understand the use of Megadyne Disposable Patient Return Electrodes and the potential risks associated with these devices in the real-world setting. The primary study endpoint was incidence of thermal injury. The incidence of thermal injury following use of Megadyne Disposable Patient Return Electrodes across multiple types of surgical procedures and hospital settings was exceedingly low over a 20-year time period, as there were only 4 instances of thermal injury out of a total of 22,151 cases (0.018%). No unanticipated risks or harms were identified by the Epi data, and the subject devices demonstrated no evidence of increased risk for any complications in the perioperative period of surgery. The findings of this study provide further confirmatory evidence for the safety and performance of the Megadyne Disposable Patient Return Electrodes subject devices
- Notably, these clinically mature, EU Class IIb, non-implant devices represent a well-established technology and have demonstrated an established safety and performance profile since their regulatory approval.

In conclusion, based on the sum total existing nonclinical and clinical data, and continual post market surveillance throughout the device lifecycle, it is objectively verified that these data support continued safety and performance of the Megadyne Disposable Patient Return Electrodes subject devices. An objective review of these data show that there are no unanswered questions of safety or performance. Therefore, it is duly justified that PMCF studies for these clinically well-established EU class IIb electrosurgical return electrode devices are not required and the existing bench-top and Epi clinical data are sufficient to confirm their safety and performance. Table 45, below, summarizes this rationale.

**Table 45: Megadyne Disposable Patient Return Electrodes Post Market Clinical Follow-up Studies Guide**

Circumstances that may justify PMCF studies include, for example:	Yes/No
• Innovation, e.g., where the design of the device, the materials, substances, the principles of operation, the technology or the medical indications are novel	No
• Significant changes to the products or to its intended use for which premarket clinical evaluation and re-certification has been completed	No
• High product related risk e.g. based on design, materials, components, invasiveness, clinical procedures	No
• High risk anatomical locations	No

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Circumstances that may justify PMCF studies include, for example:	Yes/No
• High risk target populations e.g. pediatrics, elderly	No
• Severity of disease/treatment challenges	No
• Questions of ability to generalize clinical investigation results	No
• Unanswered questions of long-term safety and performance	No
• Results from any previous clinical investigation, including adverse events or from post-market surveillance activities	No
• Identification of previously unstudied subpopulations which may show different benefit/risk-ratio e.g. hip implants in different ethnic populations	No
• Continued validation in cases of discrepancy between reasonable premarket follow-up time scales and the expected life of the product	No
• Risks identified from the literature or other data sources for similar marketed devices	No
• Interaction with other medical products or treatments	No
• Verification of safety and performance of device when exposed to a larger and more varied population of clinical users	No
• Emergence of new information on safety or performance	No
• Where CE marking was based on equivalence	No
<b>PMCF Recommended (based on factors above indicating residual risk):</b>	<b>No</b>

## 9.2. CER Frequency

The CER is an output of the clinical evaluation process, which is ongoing to ensure that safety and performance of medical devices are based on sufficient clinical evidence throughout the lifetime that the medical device is on the market (e.g. device lifecycle). For existing devices, the CER should be updated at planned intervals.

For the Megadyne Disposable Patient Return Electrodes, the frequency of periodic updates was determined by completing the CER Frequency Matrix where the justification for the next periodic update is provided at the end of the table. The justification was based on all subject devices in-scope for the clinical evaluation and considered the device risk category across all attributes (very low, low, medium, high as listed in the Matrix) taking into account worse-case scenarios in order to determine whether the device is well-established. The attribute of the “Highest Potential Risk to the Patient as a Result of Device Failure” defined the risk band (very low/low or medium/high).

In conclusion, the overall risk classification for Megadyne Disposable Patient Return Electrodes subject devices was deemed to be LOW, where thus the planned periodic update for the CER will be every 4 years. For further details on the justification and background, refer to the CER Frequency Matrix in the following section (Table 46).

NOTE: CERs may require an off-cycle update in the event that new information (i.e. potential safety signals) are received with the potential to change the current clinical evaluation.

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**Table 46: Megadyne Disposable Patient Return Electrodes CER Frequency Matrix**

CER Update Frequency - Risk Determination Matrix						
What attribute is addressing	Attribute	Very Low	Low	Med	High	
- characterizes patient health consequences associated with device failure	Highest potential risk to patient as a result of device failure*	Limited (transient, minor impairment, or complaints) <b>OR</b> No adverse health consequences	Failure unlikely to cause or contribute to serious injury, or death under circumstances of normal use with results being temporary or reversible without medical intervention	Failure likely to cause or contribute to serious injury, or death under circumstances of normal use that is likely reversible with medical / surgical intervention	Results in permanent impairment of body function or permanent damage to a body structure <b>OR</b> Life-threatening (death has or could occur) regardless of medical / surgical intervention	Device Risk Category
- characterizes # of complaint events per determined volume associated with device to provide evidence if device is not safe or is not performing	Complaint Rate*	Negligible rate per time or volume	Low rate per time or volume	Medium rate per time or volume	High/Very High rate per time or volume	*High rating in any of these attribute categories mandates highest update frequency within risk band
- characterizes how long (theoretically, how often) subject device used for the intended use  - lower risk the longer the device is on market / more devices used  - worst case = devices with highest potential risk to patient as a result of device failure	Subject Device Product Maturity  # Units of worst case variant(s) sold / shipped since launch  Time on Market: Implantable Device: N/A  Time on Market: Non-Implantable Device:					Well-established Device Category
- characterizes how long the equivalent device technology (design, mfg,	Technological Maturity of Equivalent Device (if applicable)	x > 10,000	1000 < x < 10,000	100 < x < 1000	x < 100	
		> 10 years	5 - 10 years	3 - 5 years	< 3 years	
		> 5 years	3 - 5 years	1 - 3 years	< 1 year	

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CER Update Frequency - Risk Determination Matrix						Device Risk Category
materials) has been on the market  - lower risk the longer the device is on market / more devices used  Not Applicable	Time on Market: Implantable Device:	> 10 years	5 - 10 years	3 - 5 years	< 3 years	
	Time on Market: Non-Implantable Device:	> 5 years	3 - 5 years	1 - 3 years	< 1 year	
	Maturity of Clinical Science					
- characterizes how well established the clinical science is (i.e. how long clinicians have been using similar devices for the intended use / technique)	Time of Clinical Use:	> 10 years	5 - 10 years	3 - 5 years	< 3 years	
	MDD Device Classification	I	IIa	IIb	III	
- characterizes degree of device contact	Degree and Duration of Device Invasiveness	Non-Invasive Device No patient contact or exposure to device	Invasive Device (non-implantable, body orifice) Transient / Short-Term patient contact or exposure (seconds / minutes / Hours)	Surgically Invasive Device (non-implantable) Transient / Short-Term patient contact or exposure (seconds / minutes / Hours)	Surgical Implant Extended time frame of contact or exposure to the device (partially implantable devices that are implanted >30 days and/or fully implantable devices)	
- characterizes state of health (i.e. patient motivation/risk), not about the device	Natural course and consequences of medical conditions if left untreated	Limited (transient, minor impairment or pain) OR No adverse health consequences	Natural course unlikely to cause or contribute to serious injury, pain, or death	Natural course could possibly cause or contribute to serious injury, pain, or death	Natural course likely causes or contributes to serious injury, pain, or death	
- characterizes risk by anatomic area / physiological functions	Anatomical location where device used	No body contact	Body orifice, intact skin	All other anatomical locations	CNS, CCS	

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CER Update Frequency - Risk Determination Matrix					Well-established Device Category
Clinical Data (quantity / quality)	Ample level I - III data on subject device across all indications / lifetime <b>OR</b> Clinical data was deemed not necessary (e.g. MDD - Annex X, 1.1d; AIMD - Annex 7, 1.5)	Nominal level I - III data on subject device and ample data on equivalent device across all indications / lifetime	No level I - III data on subject device and ample data on equivalent device across all indications / lifetime	No level I - III data on subject device and nominal data on equivalent device across all indications / lifetime	
Attribute	CER Update Frequency - Risk Determination Matrix				
Highest potential risk to patient as a result of device failure*	Limited (transient, minor impairment, or complaints) <b>OR</b> No adverse health consequences	Failure unlikely to cause or contribute to serious injury, or death under circumstances of normal use with results being temporary or reversible without medical intervention	Failure likely to cause or contribute to serious injury, or death under circumstances of normal use that is likely reversible with medical / surgical intervention	Results in permanent impairment of body function or permanent damage to a body structure <b>OR</b> Life-threatening (death has or could occur) regardless of medical / surgical intervention	*High rating mandates highest update frequency
CER Update Frequency Guide:	<b>5 years</b>		<b>3 years</b>	<b>2 years</b>	<b>1 year</b>
<b>Justification for selection:</b>	<ul style="list-style-type: none"> <li>The CER frequency for the EU Class IIb Megadyne Disposable Patient Return Electrodes is every 3 years. The Megadyne Disposable Patient Return Electrodes are well-established devices that have been in clinical use for more than 10 years, with a history of safety and reliable performance.</li> <li>Based on the degree of technical maturity of the Megadyne Disposable Patient Return Electrodes (&gt;10 years), favorable non-clinical and clinical data, when combined with a low rate of reported adverse events and evaluation per the Risk Determination Matrix, the CER Frequency is designated as every 3 years.</li> </ul>				
<b>Background:</b>	<p>The Megadyne Disposable Patient Return Electrodes are comprised of the following 5 CE Marked subject devices:</p> <ul style="list-style-type: none"> <li>Adult Return Electrodes (0850C, 0855, 0855CL, 0855CN)</li> <li>Pediatric Return Electrode (0865C)</li> </ul>				

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CER Update Frequency - Risk Determination Matrix	
Megadyne Disposable Patient Return Electrodes have been available globally for more than 10 years and are well-established, state of the art devices for their intended purpose to adhere to the patient over the entire return electrode surface to complete the electrosurgical circuit between the generator, the active electrode, and the patient during electrosurgical procedures. This family of Disposable Patient Return Electrode devices have been demonstrated to be safe and performs as intended based on benchtop and non-clinical study data, as well as real world proactive epidemiological data (Epi data) and reactive PMS data. Based on the sum total of evidence presented in this CER, there are no uncertainties or unanswered questions for the subject devices and their intended use. Proactive real world epidemiological data will continue to be collected and analyzed. Based on the technological / clinical maturity of these patient return electrode devices, and data sources cited, there are no uncertainties or unanswered questions for the subject devices and their intended use.	

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## 10.APPENDICES

### 10.1. Supporting Documents Reference

Document Name	Document Number	Revision
MEGADYNE Patient Return Electrode for Adults IFU	IFU NR74330	Rev. G 2016-03
MEGADYNE Patient Return Electrode for Pediatrics IFU	IFU NR74380	Rev. F 2016-03
Franchise Procedure for Evaluation of Clinical Data for CE-Marking	PR-0000277	Rev. 19
Megadyne Systematic Literature Review Protocol	Doc #100503711	Rev. 1
Disposable Grounding Pad Technical File	RA-TECH-0001	Rev. 001
Disposable Grounding Pad Technical File	RA-TECH-0001	Rev. 002
Systematic Literature Review Protocol, Megadyne Disposable Patient Return Electrodes	N/A	Rev. A
Systematic Literature Review Report, Megadyne Disposable Patient Return Electrodes	N/A	Rev. A
Post-market Proactive Analysis Report (Epi Data): Utilization and Comparative Analysis of Megadyne Disposable Patient Return Electrodes	N/A	N/A
PMS Plan, Megadyne Disposable Patient Return Electrodes	RA-REC-020	Rev. 001
PMS Report, Megadyne Disposable Patient Return Electrodes	RA-REC-021	Rev. 001
Disposable Grounding Pad Risk Management Plan	TCF-06	Version 04/24/2018
Disposable Grounding Pad Risk Management Report	TCF-06	Version 22

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## 10.2. Product Codes

Product Code	Description	Device Class (MDD)	GMDN Number	Original CE-Mark Date	Technical File
0850C	Patient Return Electrode, Adult, single plate, with 9-foot (2.7m) pre-attached cord >33 lbs	EU Class IIb (Rule 9 Annex IX)	44776: Electrosurgical System, 11490: Electrosurgical System Generator	2006	RA-TECH-0001 Rev. 001 RA-TECH-0001 Rev. 002
0855	Patient Return Electrode, Adult, dual plate, no cord >33 lbs	EU Class IIb (Rule 9 Annex IX)	44776: Electrosurgical System, 11490: Electrosurgical System Generator	2006	RA-TECH-0001 Rev. 001 RA-TECH-0001 Rev. 002
0855CL	Patient Return Electrode, Adult, dual plate, with 15-foot (4.6m) pre-attached cord >33 lbs	EU Class IIb (Rule 9 Annex IX)	44776: Electrosurgical System, 11490: Electrosurgical System Generator	2006	RA-TECH-0001 Rev. 001 RA-TECH-0001 Rev. 002
0855CN	Patient Return Electrode, Adult, dual plate, with 9-foot (2.7m) pre-attached cord >33 lbs	EU Class IIb (Rule 9 Annex IX)	44776: Electrosurgical System, 11490: Electrosurgical System Generator	2006	RA-TECH-0001 Rev. 001 RA-TECH-0001 Rev. 002
0865C	Patient Return Electrode, Pediatric, dual plate, with 9-foot (2.7m) pre-attached cord 6_33 lbs	EU Class IIb (Rule 9 Annex IX)	44776: Electrosurgical System, 11490: Electrosurgical System Generator	2006	RA-TECH-0001 Rev. 001 RA-TECH-0001 Rev. 002

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## 10.3. Literature Search Results

### 10.3.1. Systematic SOA Search

### 10.3.2. Systematic Literature Review Search

#### 10.3.2.1. Literature Search Results

##### 10.3.2.1.1. Search 1

###### Megadyne CER – Literature Search Results

**Product:** Megadyne Products and Accessories

**Ref:** Megadyne Systematic Literature Review Protocol, Doc #100503711 Rev 1.

**Dates Searches run:** December 28, 2017 and January 4, 2018

**Contains:** 67 documents

**Databases:** Embase/Medline in OVID, PubMed, Google Scholar

**Search Date Limitation:** January 1, 1986 to the present.

**Search Strategies:**

**EMBASE/MEDLINE in OVID:**

Embase 1988 to 2018 Week 01

Ovid MEDLINE(R) 1946 to December Week 4 2017

Ovid MEDLINE(R) Epub Ahead of Print January 03, 2018

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations January 03, 2018

Ovid MEDLINE(R) Daily Update January 03, 2018

**NOTE:** MEDLINE Daily and Ovid MEDLINE were frozen on November 22, 2017 due to the annual MEDLINE reload.

	Search Statement	Results
1	electrosurgery/ or electrocoagulation/ or cautery/ or cauterization/ or diathermy/	44616
2	(electrosurger* or electrocauter* or electrodessicat* or electrosurgical* or electrodiatherm* or diatherm* or cauter* or electrodissect* or fulgurat* or (electro* adj (surger* or cauter* or dessicat* or diatherm* or surgical* or dissect*))).mp.	46875
3	1 or 2	59332
4	Surgical Instruments/ or surgical equipment/	43713
5	exp Electrodes/	232835
6	((adson* or scoville-greenwood* or jeweler* or cushing* or semkin* or gerald*) and (forcep* or bipolar)).mp.	263
7	(pencil* or needle* or electrode* or probe or probes or instrument*).mp.	1971089
8	4 or 5 or 6 or 7	2051481
9	3 and 8	11791
10	electrosurgery/is, mt or electrocoagulation/is, mt or diathermy/is, mt or cautery/is, mt	7661

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11	electrosurgical knife/	222
12	Suction Diathermy/	3
13	(suction adj3 (diatherm* or coagulat* or irrigat*)).mp.	1122
14	((smoke or fluid?) adj3 (evacuat* or remov*).mp.	6533
15	or/10-14	15482
16	megadyne*.mp.	16
17	("EZ clean" or "E-Z clean" or "E Z clean").mp.	4
18	("stainless steel" adj5 (ball? or electrode*).mp.	1505
19	("reusable stainless steel" and "indicator shaft").mp.	0
20	((ssteel or s-steel or rocker or button or stainless or steel) adj3 pencil?).mp.	0
21	"ace blade?".mp.	2
22	LERIS.mp.	39
23	"laparoscopic electrode reusable indicator shaft".mp.	0
24	(Electrosurgical adj pencil?).mp.	25
25	((ez clean" or "e-z clean" or "e z clean") adj3 (pen? or pencil?)).mp.	0
26	((rocker or button) adj3 electrode?).mp.	69
27	(MegaTip* or "Mega Tip*" or (reposable adj mega adj tip*).mp.	3
28	(indicator adj shaft?).mp.	0
29	(LLETZ adj3 (loop? or electrode?)).mp.	65
30	(LLETZ and LEEP).mp.	65
31	(large adj loop adj excision?).mp.	865
32	((All-in-One or "all in one" or AIO) adj5 (handpiece? or electrode*).mp.	10
33	("mega power*" or mega-power* or megapower*).mp.	3
34	((Megasoft or megasoftTM or mega-soft or mega-softTM or "mega soft" or "mega softTM") and electrode*).mp.	0
35	("Mega 2000" or "Mega 2000TM" or Mega-2000 or Mega-2000TM or Mega2000 or Mega2000TM).mp.	7
36	"disposable patient return electrode*".mp.	0
37	(re-CORDABLE* or "re CORDABLE*").mp.	0
38	(MegaVac or Mega-Vac or "Mega Vac" or UltraVac or Ultra-Vac or "Ultra Vac" or Attachavac or Attachavac or "Attachavac").mp.	8
39	("ZIP Pen" or ZIP-pen).mp.	0
40	or/16-39	2596

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41	9 or 15 or 40	27180
42	conference abstract.pt.	2834045
43	41 and 42	2423
44	limit 43 to yr="1986 -Current"	2418
45	41 not 42	24757
46	limit 45 to yr="1986 - 2002"	8678
47	remove duplicates from 46	5757
48	limit 45 to yr="2003 - 2010"	6549
49	remove duplicates from 48	4295
50	limit 45 to yr="2011 -Current"	6802
51	remove duplicates from 50	4291
52	44 or 47 or 49 or 51	16761

**Within the above search sets, results from set 52 were exported to QUOSA.**

## PUBMED

**Search completed: 12/28/17**

#	Searches	Results
1	(electrosurg*[Title/Abstract] OR electrocoagulat*[Title/Abstract] OR cauter*[Title/Abstract] OR diatherm*[Title/Abstract] OR electrodessian*[Title/Abstract] OR electrodiatherm*[Title/Abstract] OR electrodissect*[Title/Abstract] OR fulgurat*[Title/Abstract])	15315
2	(electro surg*[Title/Abstract] OR electro cauter*[Title/Abstract] OR electro dessicat*[Title/Abstract] OR electro diatherm*[Title/Abstract] OR electro dissect*[Title/Abstract] OR electro coagulat*[Title/Abstract])	294
3	1 or 2 Executed by PubMed: (((electrosurg*[Title/Abstract] OR electrocoagulat*[Title/Abstract] OR cauter*[Title/Abstract] OR diatherm*[Title/Abstract] OR electrodessian*[Title/Abstract] OR electrodiatherm*[Title/Abstract] OR electrodissect*[Title/Abstract] OR fulgurat*[Title/Abstract])) OR (((((electro surg*[Title/Abstract]) OR electro cauter*[Title/Abstract]) OR electro dessicat*[Title/Abstract]) OR electro diatherm*[Title/Abstract]) OR electro dissect*[Title/Abstract]) OR electro coagulat*[Title/Abstract])	15501
4	(surgical instrument*[Title/Abstract] OR surgical device*[Title/Abstract])	4066
5	(electrode[Title/Abstract] OR electrodes[Title/Abstract])	128172
6	((adson*[Title/Abstract] OR jeweler*[Title/Abstract] OR cushing*[Title/Abstract] OR gerald*[Title/Abstract])) AND ((forcep*[Title/Abstract] OR bipolar[Title/Abstract]))	80
7	((scoville-greenwood*[Title/Abstract] OR semkin*[Title/Abstract] OR pencil[Title/Abstract] OR pencils[Title/Abstract] OR needle[Title/Abstract] OR needles[Title/Abstract] OR	499505

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	electrode*[Title/Abstract] OR probe[Title/Abstract] OR probes[Title/Abstract] OR forcep*[Title/Abstract]))	
8	4 or 5 or 6 or 7  Executed by PubMed: (((((surgical instrument*[Title/Abstract] OR surgical device*[Title/Abstract])))) OR (((electrode[Title/Abstract] OR electrodes[Title/Abstract])))) OR (((adson*[Title/Abstract] OR jeweler*[Title/Abstract] OR cushing*[Title/Abstract] OR gerald*[Title/Abstract]))) AND (((forcep*[Title/Abstract] OR bipolar[Title/Abstract])))) OR (((scoville-greenwood*[Title/Abstract] OR semkin*[Title/Abstract] OR pencil[Title/Abstract] OR pencils[Title/Abstract] OR needle[Title/Abstract] OR needles[Title/Abstract] OR electrode*[Title/Abstract] OR probe[Title/Abstract] OR probes[Title/Abstract] OR forcep*[Title/Abstract]))))	503173
9	3 and 8  Executed by PubMed: (((((((electrosurg*[Title/Abstract] OR electrocoagulat*[Title/Abstract] OR cauter*[Title/Abstract] OR diatherm*[Title/Abstract] OR electrodessian*[Title/Abstract] OR electrodiatherm*[Title/Abstract] OR electrodisssect*[Title/Abstract] OR fulgurat*[Title/Abstract])))) OR (((electro surg*[Title/Abstract] OR electro cauter*[Title/Abstract] OR electro dessicat*[Title/Abstract] OR electro diatherm*[Title/Abstract] OR electro dissect*[Title/Abstract] OR electro coagulat*[Title/Abstract])))) AND ((((((surgical instrument*[Title/Abstract] OR surgical device*[Title/Abstract])))) OR (((electrode[Title/Abstract] OR electrodes[Title/Abstract])))) OR (((adson*[Title/Abstract] OR jeweler*[Title/Abstract] OR cushing*[Title/Abstract] OR gerald*[Title/Abstract]))) AND (((forcep*[Title/Abstract] OR bipolar[Title/Abstract])))) OR (((scoville-greenwood*[Title/Abstract] OR semkin*[Title/Abstract] OR pencil[Title/Abstract] OR pencils[Title/Abstract] OR needle[Title/Abstract] OR needles[Title/Abstract] OR electrode*[Title/Abstract] OR probe[Title/Abstract] OR probes[Title/Abstract] OR forcep*[Title/Abstract])))))	2050
10	((("electrosurgical knife"[Title/Abstract] OR "electrosurgical knives"[Title/Abstract] OR "electrosurgical loop"[Title/Abstract] OR "electrosurgical needle"[Title/Abstract] OR "electrosurgical needle knife"[Title/Abstract] OR "electrosurgical pencil"[Title/Abstract] OR "electrosurgical pencils"[Title/Abstract] OR "electrosurgical scalpel"[Title/Abstract])))) OR ((("electrosurgical cautery"[Title/Abstract] OR "electrosurgical device"[Title/Abstract] OR "electrosurgical devices"[Title/Abstract] OR "electrosurgical forceps"[Title/Abstract] OR "electrosurgical generator"[Title/Abstract] OR "electrosurgical generators"[Title/Abstract] OR "electrosurgical instrument"[Title/Abstract] OR "electrosurgical instrumentation"[Title/Abstract] OR "electrosurgical instruments"[Title/Abstract])))	393
11	("suction coagulation"[Title/Abstract] OR "suction coagulator"[Title/Abstract] OR "suction coagulators"[Title/Abstract] OR "suction diathermy"[Title/Abstract] OR "suction irrigating"[Title/Abstract] OR "suction irrigation"[Title/Abstract] OR "suction irrigator"[Title/Abstract] OR "suction irrigators"[Title/Abstract])	230
12	smoke evacuat*[Title/Abstract]	99
13	("fluid evacuation"[Title/Abstract]) OR ("fluid removal"[Title/Abstract])	827
14	10 or 11 or 12 or 13  Executed by PubMed: (((((((("electrosurgical knife"[Title/Abstract] OR "electrosurgical knives"[Title/Abstract] OR "electrosurgical loop"[Title/Abstract] OR "electrosurgical needle"[Title/Abstract] OR "electrosurgical needle knife"[Title/Abstract] OR "electrosurgical pencil"[Title/Abstract] OR "electrosurgical pencils"[Title/Abstract]))))	1546

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	scalpel"[Title/Abstract])) OR (("electrosurgical cautery"[Title/Abstract] OR "electrosurgical device"[Title/Abstract] OR "electrosurgical devices"[Title/Abstract] OR "electrosurgical forceps"[Title/Abstract] OR "electrosurgical generator"[Title/Abstract] OR "electrosurgical generators"[Title/Abstract] OR "electrosurgical instrument"[Title/Abstract] OR "electrosurgical instrumentation"[Title/Abstract] OR "electrosurgical instruments"[Title/Abstract]))) OR (((("suction coagulation"[Title/Abstract] OR "suction coagulator"[Title/Abstract] OR "suction coagulators"[Title/Abstract] OR "suction diathermy"[Title/Abstract] OR "suction irrigating"[Title/Abstract] OR "suction irrigation"[Title/Abstract] OR "suction irrigator"[Title/Abstract] OR "suction irrigators"[Title/Abstract]))) OR smoke evacuat*[Title/Abstract]) OR (((("fluid evacuation"[Title/Abstract]) OR "fluid removal"[Title/Abstract]))	
15	megadyne*[Title/Abstract]	5
16	((EZ clean[Title/Abstract]) OR E-Z clean[Title/Abstract]) OR "E Z clean"[Title/Abstract]	10
17	((("stainless steel ball"[Title/Abstract] OR "stainless steel balls"[Title/Abstract]))) OR ("stainless steel electrode"[Title/Abstract] OR "stainless steel electrodes"[Title/Abstract]))	367
18	("reusable stainless steel"[Title/Abstract]) AND indicator shaft[Title/Abstract]	0
19	(((((("ssteel"[Title/Abstract] OR s-steel[Title/Abstract]) OR "rocker"[Title/Abstract]) OR "button"[Title/Abstract] OR "stainless"[Title/Abstract]) OR "steel"[Title/Abstract]) AND ("pencil"[Title/Abstract] OR "pencils"[Title/Abstract]))	23
20	("ace"[Title/Abstract]) AND ("blade"[Title/Abstract] OR "blades"[Title/Abstract])	8
21	"leris"[Title/Abstract]	2
22	laparoscopic electrode reusable indicator[Title/Abstract]	0
23	("electrosurgical pencil"[Title/Abstract] OR "electrosurgical pencils"[Title/Abstract])	10
24	("button electrode"[Title/Abstract] OR "button electrodes"[Title/Abstract] OR rocker electrode*[Title/Abstract])	17
25	((megatip*[Title/Abstract]) OR "mega tip"[Title/Abstract]) OR mega-tip*[Title/Abstract])	1
26	("indicator"[Title/Abstract]) AND ("shaft"[Title/Abstract] OR "shafts"[Title/Abstract])	78
27	("lletz"[Title/Abstract]) AND ("loop"[Title/Abstract] OR "loops"[Title/Abstract] OR "electrode"[Title/Abstract] OR "electrodes"[Title/Abstract])	252
28	("lletz"[Title/Abstract]) AND "leep"[Title/Abstract]	24
29	((("large loop excision"[Title/Abstract] OR "large loop excisions"[Title/Abstract])))	341
30	((("all in one"[Title/Abstract] OR "aio"[Title/Abstract])) AND ((("hand piece"[Title/Abstract] OR "hand pieces"[Title/Abstract] OR "handpiece"[Title/Abstract] OR "handpieces"[Title/Abstract]) OR "electrode"[Title/Abstract] OR "electrodes"[Title/Abstract]))	29
31	(mega-power*[Title/Abstract]) OR megapower*[Title/Abstract])	0
32	((("megasoft"[Title/Abstract]) OR mega soft*[Title/Abstract]) AND ("electrode"[Title/Abstract] OR "electrodes"[Title/Abstract]))	0
33	("mega 2000"[Title/Abstract]) OR mega2000[Title/Abstract]	3

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34	((("disposable electrode"[Title/Abstract] OR "disposable electrodes"[Title/Abstract]))) AND "patient return"[Title/Abstract]	0
35	((("patient return electrode"[Title/Abstract] OR "patient return electrodes"[Title/Abstract]))) AND "disposable"[Title/Abstract]	0
36	(re cordable[Title/Abstract]) OR re-cordable[Title/Abstract]	0
37	("megavac"[Title/Abstract] OR mega vac[Title/Abstract] OR ultravac*[Title/Abstract] OR ultra vac[Title/Abstract] OR attachavac*[Title/Abstract] OR attacha vac[Title/Abstract] OR mega vactm[Title/Abstract] OR ultra vactm[Title/Abstract] OR attacha vactm[Title/Abstract])	7
38	("zip pen"[Title/Abstract] OR "zip-pen"[Title/Abstract] OR "zip pentm"[Title/Abstract] OR "zip-pentm"[Title/Abstract])	0
39	15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38  Executed by PubMed: (((((((((((((EZ clean[Title/Abstract]) OR E-Z clean[Title/Abstract])) OR "E Z clean"[Title/Abstract]))) OR (((("stainless steel ball"[Title/Abstract] OR "stainless steel balls"[Title/Abstract]))) OR ((("stainless steel electrode"[Title/Abstract] OR "stainless steel electrodes"[Title/Abstract])))) OR (((("reusable stainless steel"[Title/Abstract] AND indicator shaft[Title/Abstract]))) OR (((("ssteel"[Title/Abstract]) OR s-steel[Title/Abstract]) OR "rocker"[Title/Abstract]) OR "button"[Title/Abstract]) OR "stainless"[Title/Abstract]) OR "steel"[Title/Abstract]) AND ("pencil"[Title/Abstract] OR "pencils"[Title/Abstract])))) OR (((("ace"[Title/Abstract]) AND ("blade"[Title/Abstract] OR "blades"[Title/Abstract]))) OR "leris"[Title/Abstract]) OR laparoscopic electrode reusable indicator[Title/Abstract]) OR (((("electrosurgical pencil"[Title/Abstract] OR "electrosurgical pencils"[Title/Abstract]))) OR (((("button electrode"[Title/Abstract] OR "button electrodes"[Title/Abstract] OR rocker electrode*[Title/Abstract]))) OR (((("megatip*[Title/Abstract]) OR "mega tip"[Title/Abstract]) OR mega-tip*[Title/Abstract]))) OR (((("indicator"[Title/Abstract]) AND ("shaft"[Title/Abstract] OR "shafts"[Title/Abstract]))) OR (((("Iletz"[Title/Abstract]) AND ("loop"[Title/Abstract] OR "loops"[Title/Abstract] OR "electrode"[Title/Abstract] OR "electrodes"[Title/Abstract]))) OR (((("Iletz"[Title/Abstract]) AND "leap"[Title/Abstract]))) OR (((("large loop excision"[Title/Abstract] OR "large loop excisions"[Title/Abstract]))) OR (((("all in one"[Title/Abstract] OR "aio"[Title/Abstract]) AND ("hand piece"[Title/Abstract] OR "hand pieces"[Title/Abstract] OR "handpiece"[Title/Abstract] OR "handpieces"[Title/Abstract] OR "electrode"[Title/Abstract] OR "electrodes"[Title/Abstract]))) OR (((("mega-power*[Title/Abstract]) OR megapower*[Title/Abstract]))) OR (((("megisoft"[Title/Abstract]) OR mega soft*[Title/Abstract]) AND ("electrode"[Title/Abstract] OR "electrodes"[Title/Abstract]))) OR (((("mega 2000"[Title/Abstract]) OR mega2000[Title/Abstract]))) OR (((("disposable electrode"[Title/Abstract] OR "disposable electrodes"[Title/Abstract]))) AND "patient return"[Title/Abstract])) OR (((("patient return electrode"[Title/Abstract] OR "patient return electrodes"[Title/Abstract]))) AND "disposable"[Title/Abstract])) OR (((("re cordable[Title/Abstract] OR re-cordable[Title/Abstract]))) OR (((("megavac"[Title/Abstract] OR mega vac[Title/Abstract] OR ultravac*[Title/Abstract] OR ultra vac[Title/Abstract] OR attachavac*[Title/Abstract] OR attacha vac[Title/Abstract] OR mega vactm[Title/Abstract] OR ultra vactm[Title/Abstract] OR attacha vactm[Title/Abstract]))) OR (((("zip pen"[Title/Abstract] OR "zip-pen"[Title/Abstract] OR "zip pentm"[Title/Abstract] OR "zip-pentm"[Title/Abstract]))	929
40	9 or 14 or 39	4343

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<p>Executed by PubMed: (((((((((electrosurg*[Title/Abstract] OR electrocoagulat*[Title/Abstract] OR cauter*[Title/Abstract] OR diatherm*[Title/Abstract] OR electrodessian*[Title/Abstract] OR electrodiatherm*[Title/Abstract] OR electrodissect*[Title/Abstract] OR fulgurat*[Title/Abstract])))) OR (((electro surg*[Title/Abstract] OR electro cauter*[Title/Abstract] OR electro dessicat*[Title/Abstract] OR electro diatherm*[Title/Abstract] OR electro dissect*[Title/Abstract] OR electro coagulat*[Title/Abstract])))) AND ((((((surgical instrument*[Title/Abstract] OR surgical device*[Title/Abstract])))) OR (((electrode[Title/Abstract] OR electrodes[Title/Abstract])))) OR (((adson*[Title/Abstract] OR jeweler*[Title/Abstract] OR cushing*[Title/Abstract] OR gerald*[Title/Abstract])))) AND (((forcep*[Title/Abstract] OR bipolar[Title/Abstract])))) OR (((scoville-greenwood*[Title/Abstract] OR semkin*[Title/Abstract] OR pencil[Title/Abstract] OR pencils[Title/Abstract] OR needle[Title/Abstract] OR needles[Title/Abstract] OR electrode*[Title/Abstract] OR probe[Title/Abstract] OR probes[Title/Abstract] OR forcep*[Title/Abstract]))))) OR (((((((("electrosurgical knife"[Title/Abstract] OR "electrosurgical knives"[Title/Abstract] OR "electrosurgical loop"[Title/Abstract] OR "electrosurgical needle"[Title/Abstract] OR "electrosurgical needle knife"[Title/Abstract] OR "electrosurgical pencil"[Title/Abstract] OR "electrosurgical pencils"[Title/Abstract] OR "electrosurgical scalpel"[Title/Abstract]))) OR ("electrosurgical cautery"[Title/Abstract] OR "electrosurgical device"[Title/Abstract] OR "electrosurgical devices"[Title/Abstract] OR "electrosurgical forceps"[Title/Abstract] OR "electrosurgical generator"[Title/Abstract] OR "electrosurgical generators"[Title/Abstract] OR "electrosurgical instrument"[Title/Abstract] OR "electrosurgical instrumentation"[Title/Abstract] OR "electrosurgical instruments"[Title/Abstract])))) OR (((("suction coagulation"[Title/Abstract] OR "suction coagulator"[Title/Abstract] OR "suction coagulators"[Title/Abstract] OR "suction diathermy"[Title/Abstract] OR "suction irrigating"[Title/Abstract] OR "suction irrigation"[Title/Abstract] OR "suction irrigator"[Title/Abstract] OR "suction irrigators"[Title/Abstract])))) OR smoke evacuat*[Title/Abstract]) OR (((("fluid evacuation"[Title/Abstract] OR "fluid removal"[Title/Abstract])))) OR (((((((((((("EZ clean[Title/Abstract] OR E-Z clean[Title/Abstract] OR "E Z clean"[Title/Abstract])))) OR (((("stainless steel ball"[Title/Abstract] OR "stainless steel balls"[Title/Abstract])))) OR (((("stainless steel electrode"[Title/Abstract] OR "stainless steel electrodes"[Title/Abstract])))) OR (((("reusable stainless steel"[Title/Abstract] AND indicator shaft[Title/Abstract])))) OR (((((((("ssteel"[Title/Abstract] OR s-steel[Title/Abstract]) OR "rocker"[Title/Abstract] OR "button"[Title/Abstract] OR "stainless"[Title/Abstract] OR "steel"[Title/Abstract)))) AND ("pencil"[Title/Abstract] OR "pencils"[Title/Abstract])))) OR (((("ace"[Title/Abstract] AND ("blade"[Title/Abstract] OR "blades"[Title/Abstract])))) OR "leris"[Title/Abstract]) OR laparoscopic electrode reusable indicator[Title/Abstract]) OR (((("electrosurgical pencil"[Title/Abstract] OR "electrosurgical pencils"[Title/Abstract])))) OR (((("button electrode"[Title/Abstract] OR "button electrodes"[Title/Abstract] OR rocker electrode*[Title/Abstract])))) OR (((("megatip*[Title/Abstract] OR "mega tip"[Title/Abstract] OR mega-tip*[Title/Abstract])))) OR (((("indicator"[Title/Abstract] AND ("shaft"[Title/Abstract] OR "shafts"[Title/Abstract])))) OR (((("lletz"[Title/Abstract] AND ("loop"[Title/Abstract] OR "loops"[Title/Abstract] OR "electrode"[Title/Abstract] OR "electrodes"[Title/Abstract])))) OR (((("lletz"[Title/Abstract] AND "leep"[Title/Abstract])))) OR (((("large loop excision"[Title/Abstract] OR "large loop excisions"[Title/Abstract])))) OR (((("all in one"[Title/Abstract] OR "aio"[Title/Abstract])) AND ((("hand piece"[Title/Abstract] OR "hand pieces"[Title/Abstract] OR "handpiece"[Title/Abstract] OR "handpieces"[Title/Abstract] OR "electrode"[Title/Abstract] OR "electrodes"[Title/Abstract])))) OR (((("mega-power*[Title/Abstract] OR megapower*[Title/Abstract])))) OR (((("megisoft"[Title/Abstract] OR mega soft*[Title/Abstract] AND ("electrode"[Title/Abstract] OR "electrodes"[Title/Abstract])))) OR (((("mega 2000"[Title/Abstract] OR mega2000[Title/Abstract])))) OR (((("disposable"</p>	
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	electrode"[Title/Abstract] OR "disposable electrodes"[Title/Abstract])))) AND "patient return"[Title/Abstract])))) OR (((("patient return electrode"[Title/Abstract] OR "patient return electrodes"[Title/Abstract]))) AND "disposable"[Title/Abstract])) OR (((re cordable[Title/Abstract] OR re-cordable[Title/Abstract]))) OR (((megavac"[Title/Abstract] OR mega vac[Title/Abstract] OR ultravac*[Title/Abstract] OR ultra vac[Title/Abstract] OR attachavac*[Title/Abstract] OR attacha vac[Title/Abstract] OR mega vactm[Title/Abstract] OR ultra vactm[Title/Abstract] OR attacha vactm[Title/Abstract])))) OR (((zip pen"[Title/Abstract] OR "zip-pen"[Title/Abstract] OR "zip pentm"[Title/Abstract] OR "zip-pentm"[Title/Abstract])))	
41	#40 and ("1986/01/01"[Date - Publication] : "3000"[Date - Publication])) NOT MEDLINE [sb]	447

***Within the above search sets, results from set 41 were exported to QUOSA.***

#### GOOGLE SCHOLAR

#	SEARCH STATEMENTS	RESULTS
1	With <b>all</b> of the word(s): megadyne  With <b>at least one</b> of the words: diathermy or electrosurgery or electrosurgical or electrocautery or electrocauterization or electrocauterisation or medical or electrode or electrodes or cauterization or cauterisation or cautery or monopolar Return articles <b>dated</b> between: 1986-2017	162

Results from the above search were reviewed. Duplicates, books, dissertations and conference abstracts where the only mention of Megadyne is as a sponsor were removed. The remaining 44 results were compared to the results from the Ovid and PubMed searches and 11 duplicates were removed. The 33 items that remained were added to the final search results.

#### QUOSA

17,208 documents from the Ovid and PubMed search results were exported to QUOSA. Citations and available full-text were searched for the following terms with the listed results:

#	Search	Results
1	Megadyne*	17
2	"EZ clean" OR "EZ cleanTM"	1
3	"E-Z clean" OR "E-Z cleanTM" OR "E Z clean" OR "E Z cleanTM"	4
4	"ssteel pencil"~3 OR "ssteel pencils"~3 OR "ssteel pencilTM"~3	0
5	"s steel pencil" OR "s steel pencils" OR "s steel pencilTM"	0
6	"ace blade"~3 OR "ace blades"~3 OR "acetm blade"~2	4
7	Leris OR lerisTM	2
8	"laparoscopic indicator"~3	1
9	megatip* OR "mega tip" OR "mega tipTM" OR mega-tip OR mega-tipTM	2

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10	("all in one" OR "AIO") AND (handpiece* OR "hand piece" OR "hand pieces")	<b>0</b>
11	mega-power* OR megapower* OR "mega power"	<b>4</b>
12	(megasoft* OR "mega soft" OR "mega softTM") AND electrode*	<b>1</b>
13	"mega 2000" OR "mega 2000tm" OR mega2000*	<b>4</b>
14	"re cordable" OR re-cordable* OR "re cordableTM"	<b>0</b>
15	megavac* OR "mega vac" OR "mega vacTM" OR mega-vac*	<b>4</b>
16	ultravac* OR "ultra vac" OR "ultra vacTM" OR ultra-vac*	<b>4</b>
17	attachavac* OR "attacha vac" OR "attacha vacTM" OR attacha-vac*	<b>0</b>
18	"zip pen" OR "zip pens" OR "zip penTM" OR zip-pen*	<b>1</b>

After deduplication, there were 34 results from sets 1-18 above. These items were combined with the 33 Google Scholar results as noted above, resulting in 67 final items. These are listed below for your review.

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### 10.3.2.1.2. Search 2

#### Megadyne CER – Literature Search Results

**Product: Megadyne Products and Accessories**

**Ref:** Megadyne Systematic Literature Review Protocol, Doc #100503711 Rev 1., Megadyne CER December 2017

**Dates Searches run:** October 12, 2018

**Contains:** 13 documents

**Databases:** Embase/Medline in OVID, PubMed, Google Scholar

**Search Date Limitation:** November 1, 2017- Present (October 2018)

**Search Strategies:**

**EMBASE/MEDLINE in OVID:**

Embase 1988 to 2018 October 11

Ovid MEDLINE(R) 1946 to October Week 1 2018

Ovid MEDLINE(R) Epub Ahead of Print October 11, 2018

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations October 11, 2018

Ovid MEDLINE(R) Daily Update October 11, 2018

Embase, Ovid MEDLINE(R)		
#	Search Statement	Results
1	electrosurgery/ or electrocoagulation/ or cautery/ or cauterization/ or diathermy/	41053
2	(electrosurger* or electrocauter* or electrodessicat* or electrosurgical* or electrodiatherm* or diatherm* or cauter* or electrodissect* or fulgurat* or (electro* adj (surger* or cauter* or dessicat* or diatherm* or surgical* or dissect*))).mp.	43540
3	1 or 2	54625
4	Surgical Instruments/ or surgical equipment/	40159
5	exp Electrodes/	222016
6	((adson* or scoville-greenwood* or jeweler* or cushing* or semkin* or gerald*) and (forcep* or bipolar)).mp.	246
7	(pencil* or needle* or electrode* or probe or probes or instrument*).mp.	2332388
8	4 or 5 or 6 or 7	2400137
9	3 and 8	13403
10	electrosurgery/is, mt or electrocoagulation/is, mt or diathermy/is, mt or cautery/is, mt	6963
11	electrosurgical knife/	310
12	Suction Diathermy/	3
13	(suction adj3 (diatherm* or coagulat* or irrigat*)).mp.	1046
14	((smoke or fluid?) adj3 (evacuat* or remov*)).mp.	6126
15	or/10-14	14388
16	megadyne*.mp.	15
17	("EZ clean" or "E-Z clean" or "E Z clean").mp.	4
18	("stainless steel" adj5 (ball? or electrode*)).mp.	1394
19	("reusable stainless steel" and "indicator shaft").mp.	0

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20	((sssteel or s-steel or rocker or button or stainless or steel) adj3 pencil?).mp.	0
21	"ace blade?".mp.	2
22	LERIS.mp.	40
23	"laparoscopic electrode reusable indicator shaft".mp.	0
24	(Electrosurgical adj pencil?).mp.	27
25	(("ez clean" or "e-z clean" or "e z clean") adj3 (pen? or pencil?)).mp.	0
26	((rocker or button) adj3 electrode?).mp.	74
27	(MegaTip* or "Mega Tip*" or (reposable adj mega adj tip*)).mp.	3
28	(indicator adj shaft?).mp.	0
29	(LLETZ adj3 (loop? or electrode?)).mp.	60
30	(LLETZ and LEEP).mp.	64
31	(large adj loop adj excision?).mp.	818
32	((All-in-One or "all in one" or AIO) adj5 (handpiece? or electrode*)).mp.	11
33	("mega power*" or mega-power* or megapower*).mp.	4
34	((Megasoft or megasoftTM or mega-soft or mega-softTM or "mega soft" or "mega softTM") and electrode*).mp.	0
35	("Mega 2000" or "Mega 2000TM" or Mega-2000 or Mega-2000TM or Mega2000 or Mega2000TM).mp.	7
36	"disposable patient return electrode?".mp.	0
37	(re-CORDABLE* or "re CORDABLE*").mp.	0
38	(MegaVac or Mega-Vac or "Mega Vac" or UltraVac or Ultra-Vac or "Ultra Vac" or AttachaVac or Attacha-Vac or "Attacha Vac").mp.	8
39	("ZIP Pen" or ZIP-pen).mp.	0
40	or/16-39	2443
41	9 or 15 or 40	25857
42	limit 41 to yr="2016-Current"	3424
43	limit 42 to ed=20171101-20181012 use ppez [Limit not valid in Embase; records were retained]	421
44	limit 42 to dc=20171101-20181012 use emefd	899
45	limit 42 to dd=20171101-20181012 use emefd [Limit not valid in Ovid MEDLINE(R),Ovid MEDLINE(R) Daily Update,Ovid MEDLINE(R) In-Process,Ovid MEDLINE(R) Publisher; records were retained]	439
46	limit 42 to rd=20171101-20181012 use emefd	560
47	limit 42 to up=20171101-20181012 use medp	48
48	42 and 2017-11-01:2018-10-12.(dt). use prem	174
49	43 or 44 or 45 or 46 or 47 or 48	1631
50	remove duplicates from 49	1338

Within the above search sets, results from set 50 were exported to QUOSA.

**PUBMED** - Search completed on October 12<sup>th</sup>, 2018

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#	<b>Searches</b>	<b>Results</b>
1	(electrosurg*[Title/Abstract] OR electrocoagulat*[Title/Abstract] OR cauter*[Title/Abstract] OR diatherm*[Title/Abstract] OR electrodessicat*[Title/Abstract] OR electrodiatherm*[Title/Abstract] OR electrodissect*[Title/Abstract] OR fulgurat*[Title/Abstract])	15,771
2	(electro surg*[Title/Abstract] OR electro cauter*[Title/Abstract] OR dessicat*[Title/Abstract] OR electro diatherm*[Title/Abstract] OR electro dissect*[Title/Abstract] OR electro coagulat*[Title/Abstract])	310
3	<b>#1 or #2</b>  <b>Executed as:</b>  (((electrosurg*[Title/Abstract] OR electrocoagulat*[Title/Abstract] OR cauter*[Title/Abstract] OR diatherm*[Title/Abstract] OR electrodessicat*[Title/Abstract] OR electrodiatherm*[Title/Abstract] OR electrodissect*[Title/Abstract] OR fulgurat*[Title/Abstract])) OR (((((electro surg*[Title/Abstract]) OR electro cauter*[Title/Abstract]) OR electro dessicat*[Title/Abstract]) OR electro diatherm*[Title/Abstract]) OR electro dissect*[Title/Abstract]) OR electro coagulat*[Title/Abstract])	15,967
4	(surgical instrument*[Title/Abstract] OR surgical device*[Title/Abstract])	4,270
5	(electrode[Title/Abstract] OR electrodes[Title/Abstract])	135,491
6	((adson*[Title/Abstract] OR jeweler*[Title/Abstract] OR cushing*[Title/Abstract] OR gerald*[Title/Abstract])) AND ((forcep*[Title/Abstract] OR bipolar[Title/Abstract]))	80
7	((scoville-greenwood*[Title/Abstract] OR semkin*[Title/Abstract] OR pencil[Title/Abstract] OR pencils[Title/Abstract] OR needle[Title/Abstract] OR needles[Title/Abstract] OR electrode*[Title/Abstract] OR probe[Title/Abstract] OR probes[Title/Abstract] OR forcep*[Title/Abstract]))	521,910
8	<b>#4 or #5 or #6 or #7</b>  <b>Executed as:</b>  ((((((surgical instrument*[Title/Abstract] OR surgical device*[Title/Abstract])))) OR (((electrode[Title/Abstract] OR electrodes[Title/Abstract])))) OR (((((adson*[Title/Abstract] OR jeweler*[Title/Abstract] OR cushing*[Title/Abstract] OR gerald*[Title/Abstract])))) AND ((forcep*[Title/Abstract] OR bipolar[Title/Abstract])))) OR (((scoville-greenwood*[Title/Abstract] OR semkin*[Title/Abstract] OR pencil[Title/Abstract] OR pencils[Title/Abstract] OR needle[Title/Abstract] OR needles[Title/Abstract] OR	525,761

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	electrode*[Title/Abstract] OR probe[Title/Abstract] OR probes[Title/Abstract] OR forcep*[Title/Abstract])))	
9	#3 and #8  Executed as:  (((((((electrosurg*[Title/Abstract] OR electrocoagulat*[Title/Abstract] OR cauter*[Title/Abstract] OR diatherm*[Title/Abstract] OR electrodessicat*[Title/Abstract] OR electrodiatherm*[Title/Abstract] OR electrodissect*[Title/Abstract] OR fulgurat*[Title/Abstract])))) OR (((electro surg*[Title/Abstract] OR electro cauter*[Title/Abstract] OR electro dessicat*[Title/Abstract] OR electro diatherm*[Title/Abstract] OR electro dissect*[Title/Abstract] OR electro coagulat*[Title/Abstract])))) AND (((((surgical instrument*[Title/Abstract] OR surgical device*[Title/Abstract])))) OR (((electrode[Title/Abstract] OR electrodes[Title/Abstract])))) OR (((adson*[Title/Abstract] OR jeweler*[Title/Abstract] OR cushing*[Title/Abstract] OR gerald*[Title/Abstract])))) AND (((forcep*[Title/Abstract] OR bipolar[Title/Abstract])))) OR (((scoville-greenwood*[Title/Abstract] OR semkin*[Title/Abstract] OR pencil[Title/Abstract] OR pencils[Title/Abstract] OR needle[Title/Abstract] OR needles[Title/Abstract] OR electrode*[Title/Abstract] OR probe[Title/Abstract] OR probes[Title/Abstract] OR forcep*[Title/Abstract])))))	2,128
10	((("electrosurgical knife"[Title/Abstract] OR "electrosurgical knives"[Title/Abstract] OR "electrosurgical loop"[Title/Abstract] OR "electrosurgical needle"[Title/Abstract] OR "electrosurgical needle knife"[Title/Abstract] OR "electrosurgical pencil"[Title/Abstract] OR "electrosurgical pencils"[Title/Abstract] OR "electrosurgical scalpel"[Title/Abstract])))) OR ((("electrosurgical cautery"[Title/Abstract] OR "electrosurgical device"[Title/Abstract] OR "electrosurgical devices"[Title/Abstract] OR "electrosurgical forceps"[Title/Abstract] OR "electrosurgical generator"[Title/Abstract] OR "electrosurgical generators"[Title/Abstract] OR "electrosurgical instrument"[Title/Abstract] OR "electrosurgical instrumentation"[Title/Abstract] OR "electrosurgical instruments"[Title/Abstract])))	415
11	("suction coagulation"[Title/Abstract] OR "suction coagulator"[Title/Abstract] OR "suction coagulators"[Title/Abstract] OR "suction diathermy"[Title/Abstract] OR "suction irrigating"[Title/Abstract] OR "suction irrigation"[Title/Abstract] OR "suction irrigator"[Title/Abstract] OR "suction irrigators"[Title/Abstract])	235
12	smoke evacuat*[Title/Abstract]	104
13	("fluid evacuation"[Title/Abstract]) OR ("fluid removal"[Title/Abstract])	851
14	#10 or #11 or #12 or #13  Executed as:	1,601

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	((((((("electrosurgical knife"[Title/Abstract] OR "electrosurgical knives"[Title/Abstract] OR "electrosurgical loop"[Title/Abstract] OR "electrosurgical needle"[Title/Abstract] OR "electrosurgical needle knife"[Title/Abstract] OR "electrosurgical pencil"[Title/Abstract] OR "electrosurgical pencils"[Title/Abstract] OR "electrosurgical scalpel"[Title/Abstract]))) OR ((("electrosurgical cautery"[Title/Abstract] OR "electrosurgical device"[Title/Abstract] OR "electrosurgical devices"[Title/Abstract] OR "electrosurgical forceps"[Title/Abstract] OR "electrosurgical generator"[Title/Abstract] OR "electrosurgical instrument"[Title/Abstract] OR "electrosurgical instrumentation"[Title/Abstract] OR "electrosurgical instruments"[Title/Abstract])))) OR (((("suction coagulation"[Title/Abstract] OR "suction coagulator"[Title/Abstract] OR "suction coagulators"[Title/Abstract] OR "suction diathermy"[Title/Abstract] OR "suction irrigating"[Title/Abstract] OR "suction irrigation"[Title/Abstract] OR "suction irrigator"[Title/Abstract] OR "suction irrigators"[Title/Abstract])))) OR smoke evacuat*[Title/Abstract]) OR (((("fluid evacuation"[Title/Abstract]) OR "fluid removal"[Title/Abstract])))	
15	megadyne*[Text Word]	5
16	((EZ clean[Text Word]) OR E-Z clean[Text Word]) OR "E Z clean"[Text Word]	12
17	((("stainless steel ball"[Text Word] OR "stainless steel balls"[Text Word]))) OR ((("stainless steel electrode"[Text Word] OR "stainless steel electrodes"[Text Word])))	376
18	("reusable stainless steel"[Text Word]) AND indicator shaft[Text Word]	0
19	(((((("ssteel"[Text Word]) OR s-steel[Text Word]) OR "rocker"[Text Word]) OR "button"[Text Word]) OR "stainless"[Text Word]) OR "steel"[Text Word]) AND ("pencil"[Text Word] OR "pencils"[Text Word])	24
20	("ace"[Text Word]) AND ("blade"[Text Word] OR "blades"[Text Word])	8
21	"leris"[Text Word]	2
22	laparoscopic electrode reusable indicator[Text Word]	0
23	("electrosurgical pencil"[Text Word] OR "electrosurgical pencils"[Text Word])	11
24	("button electrode"[Text Word] OR "button electrodes"[Text Word] OR rocker electrode*[Text Word])	19
25	((megatip*[Text Word]) OR "mega tip"[Text Word]) OR mega-tip*[Text Word]	1

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26	("indicator"[Text Word]) AND ("shaft"[Text Word] OR "shafts"[Text Word])	79
27	("lletz"[Text Word]) AND ("loop"[Text Word] OR "loops"[Text Word] OR "electrode"[Text Word] OR "electrodes"[Text Word])	265
28	("lletz"[Text Word]) AND "leep"[Text Word]	26
29	(("large loop excision"[Text Word] OR "large loop excisions"[Text Word]))	356
30	((("all in one"[Text Word] OR "aio"[Text Word])) AND ((("hand piece"[Text Word] OR "hand pieces"[Text Word] OR "handpiece"[Text Word] OR "handpieces"[Text Word] OR "electrode"[Text Word] OR "electrodes"[Text Word])))	37
31	(mega-power*[Text Word]) OR megapower*[Text Word]	0
32	((("megasoft"[Text Word]) OR mega soft*[Text Word])) AND ("electrode"[Text Word] OR "electrodes"[Text Word])	0
33	("mega 2000"[Text Word]) OR mega2000[Text Word]	3
34	((("disposable electrode"[Text Word] OR "disposable electrodes"[Text Word]))) AND "patient return"[Text Word])	0
35	((("patient return electrode"[Text Word] OR "patient return electrodes"[Text Word]))) AND "disposable"[Text Word])	0
36	(re cordable[Text Word]) OR re-cordable[Text Word]	0
37	("megavac"[Text Word] OR mega vac[Text Word] OR ultravac*[Text Word] OR ultra vac[Text Word] OR attachavac*[Text Word] OR attacha vac[Text Word] OR mega vactm[Text Word] OR ultra vactm[Text Word] OR attacha vactm[Text Word])	8
38	("zip pen"[Text Word] OR "zip-pen"[Text Word] OR "zip pentm"[Text Word] OR "zip-pentm"[Text Word])	0
39	#15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38  Executed as:  (((((((((((((EZ clean[Text Word]) OR E-Z clean[Text Word]) OR "E Z clean"[Text Word])))) OR (((("stainless steel ball"[Text Word] OR "stainless steel balls"[Text Word])))) OR ((("stainless steel electrode"[Text Word] OR "stainless steel electrodes"[Text Word])))))	969

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	OR (((("reusable stainless steel"[Text Word]) AND indicator shaft[Text Word]))) OR (((((("ssteel"[Text Word]) OR s-steel[Text Word]) OR "rocker"[Text Word]) OR "button"[Text Word]) OR "stainless"[Text Word]) OR "steel"[Text Word]) AND ("pencil"[Text Word] OR "pencils"[Text Word)))) OR (((("ace"[Text Word]) AND ("blade"[Text Word] OR "blades"[Text Word])))) OR "leris"[Text Word]) OR laparoscopic electrode reusable indicator[Text Word]) OR (((("electrosurgical pencil"[Text Word] OR "electrosurgical pencils"[Text Word])))) OR (((("button electrode"[Text Word] OR "button electrodes"[Text Word] OR rocker electrode*[Text Word])))) OR (((("megatip*[Text Word]) OR "mega tip"[Text Word]) OR mega-tip*[Text Word])))) OR (((("indicator"[Text Word]) AND ("shaft"[Text Word] OR "shafts"[Text Word])))) OR (((("Iletz"[Text Word]) AND ("loop"[Text Word] OR "loops"[Text Word] OR "electrode"[Text Word] OR "electrodes"[Text Word])))) OR (((("Iletz"[Text Word]) AND "leep"[Text Word])))) OR (((("large loop excision"[Text Word] OR "large loop excisions"[Text Word])))) OR (((("all in one"[Text Word] OR "aio"[Text Word]) AND ("hand piece"[Text Word] OR "hand pieces"[Text Word] OR "handpiece"[Text Word] OR "handpieces"[Text Word] OR "electrode"[Text Word] OR "electrodes"[Text Word])))) OR (((("mega-power*[Text Word]) OR megapower*[Text Word])))) OR (((("megasoft"[Text Word]) OR mega soft*[Text Word]) AND ("electrode"[Text Word] OR "electrodes"[Text Word])))) OR (((("mega 2000"[Text Word]) OR mega2000[Text Word])))) OR (((("disposable electrode"[Text Word] OR "disposable electrodes"[Text Word])))) AND "patient return"[Text Word])))) OR (((("patient return electrode"[Text Word] OR "patient return electrodes"[Text Word])))) AND "disposable"[Text Word])))) OR (((("re cordable"[Text Word] OR re-cordable[Text Word])))) OR (((("megavac"[Text Word] OR mega vac[Text Word] OR ultravac*[Text Word] OR ultra vac[Text Word] OR attachavac*[Text Word] OR attacha vac[Title/Abstract] OR mega vactm[Text Word] OR ultra vactm[Text Word] OR attacha vactm[Text Word])))) OR (((("zip pen"[Text Word] OR "zip-pen"[Text Word] OR "zip pentm"[Text Word] OR "zip-pentm"[Text Word]))	
40	#9 or #14 or #39  Executed as:  ((((((((("electrosurg*[Title/Abstract] OR electrocoagulat*[Title/Abstract] OR cauter*[Title/Abstract] OR diatherm*[Title/Abstract] OR electrodессicat*[Title/Abstract] OR electrodiatherm*[Title/Abstract] OR electrodissect*[Title/Abstract] OR fulgurat*[Title/Abstract])))) OR (((("electro surg*[Title/Abstract] OR electro cauter*[Title/Abstract] OR electro dessicat*[Title/Abstract] OR electro diatherm*[Title/Abstract] OR electro dissect*[Title/Abstract] OR electro coagulat*[Title/Abstract]))))) AND (((((((("surgical instrument*[Title/Abstract] OR surgical device*[Title/Abstract])))) OR (((("electrode[Title/Abstract] OR electrodes[Title/Abstract])))) OR (((("adson*[Title/Abstract] OR jeweler*[Title/Abstract] OR cushing*[Title/Abstract] OR gerald*[Title/Abstract])))) AND (((("forcep*[Title/Abstract] OR bipolar[Title/Abstract])))) OR (((("scoville-greenwood*[Title/Abstract] OR semkin*[Title/Abstract] OR pencil[Title/Abstract] OR pencils[Title/Abstract] OR needle[Title/Abstract] OR needles[Title/Abstract] OR electrode*[Title/Abstract] OR probe[Title/Abstract] OR probes[Title/Abstract] OR forcep*[Title/Abstract]))))) OR (((((((("electrosurgical knife*[Title/Abstract] OR "electrosurgical knives"[Title/Abstract] OR "electrosurgical loop"[Title/Abstract] OR "electrosurgical needle"[Title/Abstract] OR "electrosurgical needle knife"[Title/Abstract] OR "electrosurgical pencil"[Title/Abstract] OR "electrosurgical pencils"[Title/Abstract] OR "electrosurgical cautery"[Title/Abstract] OR "electrosurgical device"[Title/Abstract] OR "electrosurgical devices"[Title/Abstract] OR "electrosurgical forceps"[Title/Abstract] OR "electrosurgical generator"[Title/Abstract] OR "electrosurgical	4,505

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	generators"[Title/Abstract] OR "electrosurgical instrument"[Title/Abstract] OR "electrosurgical instrumentation"[Title/Abstract] OR "electrosurgical instruments"[Title/Abstract])))) OR (((("suction coagulation"[Title/Abstract] OR "suction coagulator"[Title/Abstract] OR "suction coagulators"[Title/Abstract] OR "suction diathermy"[Title/Abstract] OR "suction irrigating"[Title/Abstract] OR "suction irrigation"[Title/Abstract] OR "suction irrigator"[Title/Abstract] OR "suction irrigators"[Title/Abstract)))) OR smoke evacuat*[Title/Abstract]) OR (((("fluid evacuation"[Title/Abstract] OR "fluid removal"[Title/Abstract)))))) OR ((((((((((((((((EZ clean[Text Word] OR E-Z clean[Text Word] OR "E Z clean"[Text Word]))) OR (((("stainless steel ball"[Text Word] OR "stainless steel balls"[Text Word]))) OR (((("stainless steel electrode"[Text Word] OR "stainless steel electrodes"[Text Word])))) OR (((("reusable stainless steel"[Text Word]) AND indicator shaft[Text Word]))) OR (((("ssteel"[Text Word]) OR s-steel[Text Word]) OR "rocker"[Text Word]) OR "button"[Text Word]) OR "stainless"[Text Word]) OR "steel"[Text Word]) AND ("pencil"[Text Word] OR "pencils"[Text Word)))) OR (((("ace"[Text Word]) AND ("blade"[Text Word] OR "blades"[Text Word])))) OR "leris"[Text Word]) OR laparoscopic electrode reusable indicator[Text Word]) OR (((("electrosurgical pencil"[Text Word] OR "electrosurgical pencils"[Text Word)))) OR (((("button electrode"[Text Word] OR "button electrodes"[Text Word] OR rocker electrode*[Text Word]))) OR (((("megatip*[Text Word] OR "mega tip"[Text Word] OR mega-tip*[Text Word])))) OR (((("indicator"[Text Word]) AND ("shaft"[Text Word] OR "shafts"[Text Word])))) OR (((("lletz"[Text Word]) AND ("loop"[Text Word] OR "loops"[Text Word] OR "electrode"[Text Word] OR "electrodes"[Text Word])))) OR (((("lletz"[Text Word]) AND "leep"[Text Word])))) OR (((("large loop excision"[Text Word] OR "large loop excisions"[Text Word])))) OR (((("all in one"[Text Word] OR "aio"[Text Word])) AND ("hand piece"[Text Word] OR "hand pieces"[Text Word] OR "handpiece"[Text Word] OR "handpieces"[Text Word] OR "electrode"[Text Word] OR "electrodes"[Text Word])))) OR (((("megapower*[Text Word] OR megapower*[Text Word])))) OR (((("megasoft"[Text Word] OR mega soft*[Text Word] AND ("electrode"[Text Word] OR "electrodes"[Text Word])))) OR (((("mega 2000"[Text Word] OR mega2000[Text Word])))) OR (((("disposable electrode"[Text Word] OR "disposable electrodes"[Text Word])) AND "patient return"[Text Word])))) OR (((("patient return electrode"[Text Word] OR "patient return electrodes"[Text Word])))) AND "disposable"[Text Word])))) OR (((("re cordable[Text Word] OR re-cordable[Text Word])))) OR (((("megavac"[Text Word] OR mega vac[Text Word] OR ultravac*[Text Word] OR ultra vac[Text Word] OR attachavac*[Text Word] OR attacha vac[Title/Abstract] OR mega vactm[Text Word] OR ultra vactm[Text Word] OR attacha vactm[Text Word])))) OR (((("zip pen"[Text Word] OR "zip-pen"[Text Word] OR "zip pentm"[Text Word] OR "zip-pentm"[Text Word])))) and ("2017/11/01"[Date - Publication] : "3000"[Date - Publication]) NOT medline[sb]	
41	#40 and ("2017/11/01"[Date - Publication] : "3000"[Date - Publication]) NOT medline[sb]	376

Within the above search sets, results from set 41 were exported to QUOSA.

GOOGLE SCHOLAR- This search was run on October 12<sup>th</sup>, 2018.

#	SEARCH STATEMENT	RESULTS
1	With <b>all</b> of the word(s): megadyne  With <b>at least one</b> of the words: diathermy or electrosurgery or electrosurgical or electrocautery or electrocauterization or electrocauterisation or medical or electrode or electrodes or cauterization or cauterisation or cautery or monopolar  Return articles <b>dated</b> between: 2017-2019	29

Results from the above search were reviewed. Duplicates, books, dissertations and conference abstracts were removed. The remaining 15 results were added to the final search results.

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**QUOSA-** 1,714 documents from the Ovid and PubMed search results were exported to QUOSA, which automatically de-duplicated resulting in 1,312 documents. Citations and available full-text were searched for the following terms with the listed results:

#	Search	Results
1	Megadyne*	2
2	"EZ clean" OR "EZ cleanTM"	0
3	"E-Z clean" OR "E-Z cleanTM" OR "E Z clean" OR "E Z cleanTM"	0
4	"ssteel pencil"~3 OR "ssteel pencils"~3 OR "ssteel pencilTM"~3	0
5	"s steel pencil" OR "s steel pencils" OR "s steel pencilTM"	0
6	"ace blade"~3 OR "ace blades"~3 OR "acetm blade"~2	0
7	Leris OR lerisTM	0
8	"laparoscopic indicator"~3	0
9	megatip* OR "mega tip" OR "mega tipTM" OR mega-tip OR mega-tipTM	0
10	("all in one" OR "AIO") AND (handpiece* OR "hand piece" OR "hand pieces")	0
11	mega-power* OR megapower* OR "mega power"	1
12	(megasoft* OR "mega soft" OR "mega softTM") AND electrode*	1
13	"mega 2000" OR "mega 2000tm" OR mega2000*	0
14	"re cordable" OR re-cordable* OR "re cordableTM"	0
15	megavac* OR "mega vac" OR "mega vacTM" OR mega-vac*	0
16	ultravac* OR "ultra vac" OR "ultra vacTM" OR ultra-vac*	0
17	attachavac* OR "attacha vac" OR "attacha vacTM" OR attacha-vac*	0
18	"zip pen" OR "zip pens" OR "zip penTM" OR zip-pen*	1

After deduplication, there were 3 results from sets 1-18 above. These items were combined with the 15 Google Scholar results as noted above, resulting in 16 results. These were de-duplicated against the previous search (CER December 2017), resulting in 13 results for review.

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### 10.3.2.1.3. Search 3

#### Megadyne CER – Literature Search Results

**Product:** Megadyne Products and Accessories

**Ref:** Megadyne Systematic Literature Review Protocol, Doc #100503711 Rev 1.

**Date Search run:** September 3, 2019

**Contains:** 7 documents,

**Databases:** Embase/Medline in OVID, PubMed, Google Scholar

**Search Date Limitation:** October 1, 2018 to present (August 30, 2019)

#### Search Strategy:

##### EMBASE/MEDLINE in OVID:

Embase 1980 to 2018 August 30

Ovid MEDLINE(R) 1946 to August Week 5 2018

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations August 30, 2018

Ovid MEDLINE(R) Daily Update August 30, 2018

Ovid MEDLINE(R) Epub Ahead of Print August 30, 2018

Embase, Ovid MEDLINE(R)		
#	Search Statement	Results
1	electrosurgery/ or electrocoagulation/ or cautery/ or cauterization/ or diathermy/	43066
2	(electrosurger* or electrocauter* or electrodessicat* or electrosurgical* or electrodiatherm* or diatherm* or cauter* or electrodissect* or fulgurat* or (electro* adj (surger* or cauter* or dessicat* or diatherm* or surgical* or dissect*))).mp.	46241
3	1 or 2	57645
4	Surgical Instruments/ or surgical equipment/	41430
5	exp Electrodes/	240203
6	((adson* or scoville-greenwood* or jeweler* or cushing* or semkin* or gerald*) and (forcep* or bipolar)).mp.	259
7	(pencil* or needle* or electrode* or probe or probes or instrument*).mp.	2472733
8	4 or 5 or 6 or 7	2543230
9	3 and 8	14029
10	electrosurgery/is, mt or electrocoagulation/is, mt or diathermy/is, mt or cautery/is, mt	7122
11	electrosurgical knife/	436
12	Suction Diathermy/	3
13	(suction adj3 (diatherm* or coagulat* or irrigat*)).mp.	1102

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14	((smoke or fluid?) adj3 (evacuat* or remov*).mp.	6521
15	or/10-14	15122
16	megadyne*.mp.	16
17	("EZ clean*" or "E-Z clean*" or "E Z clean*").mp.	4
18	("stainless steel" adj5 (ball? or electrode*).mp.	1496
19	("reusable stainless steel" and "indicator shaft").mp.	0
20	((ssteel or s-steel or rocker or button or stainless or steel) adj3 pencil?).mp.	1
21	"ace blade?".mp.	2
22	LERIS.mp.	43
23	"laparoscopic electrode reusable indicator shaft".mp.	0
24	(Electrosurgical adj pencil?).mp.	30
25	((ez clean* or "e-z clean*" or "e z clean*") adj3 (pen? or pencil?)).mp.	0
26	((rocker or button) adj3 electrode?).mp.	77
27	(MegaTip* or "Mega Tip*" or (reposable adj mega adj tip*).mp.	4
28	(indicator adj shaft?).mp.	0
29	(LLETZ adj3 (loop? or electrode?)).mp.	60
30	(LLETZ and LEEP).mp.	70
31	(large adj loop adj excision?).mp.	863
32	((All-in-One or "all in one" or AIO) adj5 (handpiece? or electrode*).mp.	21
33	("mega power*" or mega-power* or megapower*).mp.	4
34	((megasoft* or mega-soft* or "mega soft*") and electrode*).mp.	1
35	("Mega 2000*" or Mega-2000* or Mega2000*).mp.	7
36	"disposable patient return electrode*".mp.	0
37	(re-CORDABLE* or "re CORDABLE*").mp.	0
38	(MegaVac* or Mega-Vac* or "Mega Vac*" or UltraVac* or Ultra-Vac* or "Ultra Vac*" or AttachaVac* or Attach-a-Vac* or "Attacha Vac*").mp.	16
39	(ZIP-pen* or "ZIP Pen*").mp.	0
40	or/16-39	2624
41	9 or 15 or 40	27272

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42	limit 41 to yr="2017 -Current"	3498
43	limit 42 to ed=20181001-20190830 use medall [Limit not valid in Embase; records were retained]	396
44	limit 42 to dc=20181001-20190830 use emefd	885
45	limit 42 to dd=20181001-20190830 use emefd [Limit not valid in Ovid MEDLINE(R),Ovid MEDLINE(R) Daily Update,Ovid MEDLINE(R) In-Process,Ovid MEDLINE(R) Publisher; records were retained]	344
46	limit 42 to rd=20181001-20190830 use emefd	784
47	limit 42 to up=20181001-20190830 use medp	53
48	limit 42 to dt=20181001-20190830 use prem [Limit not valid in Embase; records were retained]	160
49	limit 42 to dt=20181001-20190830 use prem1 [Limit not valid in Embase; records were retained]	0
50	limit 42 to dt=20181001-20190830 use prem2 [Limit not valid in Embase; records were retained]	12
51	43 or 44 or 45 or 46 or 47 or 48 or 49 or 50	1745
52	remove duplicates from 51	1379

**Within the above search sets, results from set 52 were exported to QUOSA.**

#### PUBMED Search performed September 3, 2019

#	Searches	Results
1	electrosurg*[Title/Abstract] OR electrocoagulat*[Title/Abstract] OR cauter*[Title/Abstract] OR diatherm*[Title/Abstract] OR electrodessicat*[Title/Abstract] OR electrodiatherm*[Title/Abstract] OR electrodissect*[Title/Abstract] OR fulgurat*[Title/Abstract]	16271
2	electro surg*[Title/Abstract] OR electro cauter*[Title/Abstract] OR electro dessicat*[Title/Abstract] OR electro diatherm*[Title/Abstract] OR electro dissect*[Title/Abstract] OR electro coagulat*[Title/Abstract]	317
3	<b>1 or 2</b>  <b>Executed as:</b> (electrosurg*[Title/Abstract] OR electrocoagulat*[Title/Abstract] OR cauter*[Title/Abstract] OR diatherm*[Title/Abstract] OR electrodessicat*[Title/Abstract] OR electrodiatherm*[Title/Abstract] OR electrodissect*[Title/Abstract] OR	16468

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	fulgurat*[Title/Abstract] OR (electro surg*[Title/Abstract] OR electro cauter*[Title/Abstract] OR electro dessicat*[Title/Abstract] OR electro diatherm*[Title/Abstract] OR electro dissect*[Title/Abstract] OR electro coagulat*[Title/Abstract])	
4	surgical instrument*[Title/Abstract] OR surgical device*[Title/Abstract]	4550
5	electrode[Title/Abstract] OR electrodes[Title/Abstract]	144832
6	((adson*[Title/Abstract] OR jeweler*[Title/Abstract] OR cushing*[Title/Abstract] OR gerald*[Title/Abstract]) AND (forcep*[Title/Abstract] OR bipolar[Title/Abstract]))	84
7	scoville-greenwood*[Title/Abstract] OR semkin*[Title/Abstract] OR pencil[Title/Abstract] OR pencils[Title/Abstract] OR needle[Title/Abstract] OR needles[Title/Abstract] OR electrode*[Title/Abstract] OR probe[Title/Abstract] OR probes[Title/Abstract] OR forcep*[Title/Abstract]	549378
8	<b>4 or 5 or 6 or 7</b>  <b>Executed as:</b> (surgical instrument*[Title/Abstract] OR surgical device*[Title/Abstract]) OR (electrode[Title/Abstract] OR electrodes[Title/Abstract]) OR ((adson*[Title/Abstract] OR jeweler*[Title/Abstract] OR cushing*[Title/Abstract] OR gerald*[Title/Abstract]) AND (forcep*[Title/Abstract] OR bipolar[Title/Abstract])) OR (scoville-greenwood*[Title/Abstract] OR semkin*[Title/Abstract] OR pencil[Title/Abstract] OR pencils[Title/Abstract] OR needle[Title/Abstract] OR needles[Title/Abstract] OR electrode*[Title/Abstract] OR probe[Title/Abstract] OR probes[Title/Abstract] OR forcep*[Title/Abstract])	553481
9	<b>3 and 8</b>  <b>Executed as:</b> (((electrosurg*[Title/Abstract] OR electrocoagulat*[Title/Abstract] OR cauter*[Title/Abstract] OR diatherm*[Title/Abstract] OR electrodessicat*[Title/Abstract] OR electrodiatherm*[Title/Abstract] OR electrodissect*[Title/Abstract] OR fulgurat*[Title/Abstract]) OR (electro surg*[Title/Abstract] OR electro cauter*[Title/Abstract] OR electro dessicat*[Title/Abstract] OR electro diatherm*[Title/Abstract] OR electro dissect*[Title/Abstract] OR electro coagulat*[Title/Abstract])) AND ((surgical instrument*[Title/Abstract] OR surgical device*[Title/Abstract]) OR (electrode[Title/Abstract] OR electrodes[Title/Abstract]) OR ((adson*[Title/Abstract] OR jeweler*[Title/Abstract] OR cushing*[Title/Abstract] OR gerald*[Title/Abstract]) AND (forcep*[Title/Abstract] OR bipolar[Title/Abstract])) OR (scoville-greenwood*[Title/Abstract] OR semkin*[Title/Abstract] OR pencil[Title/Abstract] OR pencils[Title/Abstract] OR needle[Title/Abstract] OR needles[Title/Abstract] OR	2216

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	electrode*[Title/Abstract] OR probe[Title/Abstract] OR probes[Title/Abstract] OR forcep*[Title/Abstract]))	
10	"electrosurgical knife"[Title/Abstract] OR "electrosurgical knives"[Title/Abstract] OR "electrosurgical loop"[Title/Abstract] OR "electrosurgical needle"[Title/Abstract] OR "electrosurgical needle knife"[Title/Abstract] OR "electrosurgical pencil"[Title/Abstract] OR "electrosurgical pencils"[Title/Abstract] OR "electrosurgical scalpel"[Title/Abstract] OR "electrosurgical cautery"[Title/Abstract] OR "electrosurgical device"[Title/Abstract] OR "electrosurgical devices"[Title/Abstract] OR "electrosurgical forceps"[Title/Abstract] OR "electrosurgical generator"[Title/Abstract] OR "electrosurgical generators"[Title/Abstract] OR "electrosurgical instrument"[Title/Abstract] OR "electrosurgical instrumentation"[Title/Abstract] OR "electrosurgical instruments"[Title/Abstract]	442
11	"suction coagulation"[Title/Abstract] OR "suction coagulator"[Title/Abstract] OR "suction coagulators"[Title/Abstract] OR "suction diathermy"[Title/Abstract] OR "suction irrigating"[Title/Abstract] OR "suction irrigation"[Title/Abstract] OR "suction irrigator"[Title/Abstract] OR "suction irrigators"[Title/Abstract]	238
12	smoke evacuat*[Title/Abstract]	112
13	"fluid evacuation"[Title/Abstract] OR "fluid removal"[Title/Abstract]	901
14	<b>10 or 11 or 12 or 13</b>  <b>Executed as:</b> ((((("electrosurgical knife"[Title/Abstract] OR "electrosurgical knives"[Title/Abstract] OR "electrosurgical loop"[Title/Abstract] OR "electrosurgical needle"[Title/Abstract] OR "electrosurgical needle knife"[Title/Abstract] OR "electrosurgical pencil"[Title/Abstract] OR "electrosurgical pencils"[Title/Abstract] OR "electrosurgical scalpel"[Title/Abstract] OR "electrosurgical cautery"[Title/Abstract] OR "electrosurgical device"[Title/Abstract] OR "electrosurgical devices"[Title/Abstract] OR "electrosurgical forceps"[Title/Abstract] OR "electrosurgical generator"[Title/Abstract] OR "electrosurgical generators"[Title/Abstract] OR "electrosurgical instrument"[Title/Abstract] OR "electrosurgical instrumentation"[Title/Abstract] OR "electrosurgical instruments"[Title/Abstract])) OR ("suction coagulation"[Title/Abstract] OR "suction coagulator"[Title/Abstract] OR "suction coagulators"[Title/Abstract] OR "suction diathermy"[Title/Abstract] OR "suction irrigating"[Title/Abstract] OR "suction irrigation"[Title/Abstract] OR "suction irrigator"[Title/Abstract] OR "suction irrigators"[Title/Abstract])) OR smoke evacuat*[Title/Abstract]) OR ("fluid evacuation"[Title/Abstract] OR "fluid removal"[Title/Abstract]))	1687
15	megadyne*[Text Word]	5
16	EZ clean*[Text Word] OR E-Z clean*[Text Word] OR "E Z clean"[Text Word]	26
17	"stainless steel ball"[Title/Abstract] OR "stainless steel balls"[Title/Abstract] OR "stainless steel electrode"[Title/Abstract] OR "stainless steel electrodes"[Title/Abstract]	393

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18	"reusable stainless steel"[Title/Abstract] AND (indicator shaft[Title/Abstract] OR indicator shafts[Title/Abstract])	0
19	("ssteel"[Title/Abstract] OR s-steel[Title/Abstract] OR "rocker"[Title/Abstract] OR "button"[Title/Abstract] OR "stainless"[Title/Abstract] OR "steel"[Title/Abstract]) AND ("pencil"[Title/Abstract] OR "pencils"[Title/Abstract])	25
20	(ace{Title/Abstract} OR aceTRADE[Text Word] OR aceTM[Text Word] OR aceR[Text Word]) AND ("blade"[Title/Abstract] OR "blades"[Title/Abstract])	14
21	leris[Text Word] OR lerisTRADE[Text Word] OR lerisR[Text Word] OR lerisTM[Text Word]	2
22	laparoscopic electrode reusable indicator[Title/Abstract]	0
23	"electrosurgical pencil"[Title/Abstract] OR "electrosurgical pencils"[Title/Abstract]	12
24	"button electrode"[Title/Abstract] OR "button electrodes"[Title/Abstract] OR rocker electrode*[Title/Abstract]	20
25	megatip*[Text Word] OR mega-tip*[Text Word] OR "mega tipTM"[Text Word] OR "mega tipR"[Text Word] OR "mega tipTRADE"[Text Word]	1
26	"indicator"[Title/Abstract] AND ("shaft"[Title/Abstract] OR "shafts"[Title/Abstract])	83
27	"lletz"[Title/Abstract] AND ("loop"[Title/Abstract] OR "loops"[Title/Abstract] OR "electrode"[Title/Abstract] OR "electrodes"[Title/Abstract])	271
28	"lletz"[Title/Abstract] AND "leep"[Title/Abstract]	27
29	"large loop excision"[Title/Abstract] OR "large loop excisions"[Title/Abstract]	363
30	("all in one"[Title/Abstract] OR "aio"[Title/Abstract]) AND ("hand piece"[Title/Abstract] OR "hand pieces"[Title/Abstract] OR "handpiece"[Title/Abstract] OR "handpieces"[Title/Abstract] OR "electrode"[Title/Abstract] OR "electrodes"[Title/Abstract])	50
31	mega-power*[Text Word] OR megapower*[Text Word]	0
32	(megasoft*[Text Word] OR "mega soft"[Text Word]) AND ("electrode"[Title/Abstract] OR "electrodes"[Title/Abstract])	0
33	"mega 2000"[Text Word] OR mega2000*[Text Word]	3
34	("disposable electrode"[Title/Abstract] OR "disposable electrodes"[Title/Abstract]) AND "patient return"[Title/Abstract]	0
35	("patient return electrode"[Title/Abstract] OR "patient return electrodes"[Title/Abstract]) AND "disposable"[Title/Abstract]	0
36	re cordable*[Title/Abstract] OR re-cordable*[Title/Abstract]	0
37	megavac*[Text Word] OR mega vac*[Text Word] OR ultravac*[Text Word] OR ultra vac*[Text Word] OR attachavac*[Text Word] OR attacha vac*[Text Word]	360

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38	zip-pen*[Text Word] OR "zip pen"[Text Word] OR "zip penTM"[Text Word] OR "zip penR"[Text Word] OR "zip penTRADE"[Text Word]	0
	<b>15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38</b>	779
	<p><b>Executed as:</b></p> <p>((((((((((((((((megadyne*[Text Word]) OR (EZ clean*[Text Word] OR E-Z clean*[Text Word] OR "E Z clean"[Text Word])) OR ("stainless steel ball"[Title/Abstract] OR "stainless steel balls"[Title/Abstract] OR "stainless steel electrode"[Title/Abstract] OR "stainless steel electrodes"[Title/Abstract])) OR ("reusable stainless steel"[Title/Abstract] AND (indicator shaft[Title/Abstract] OR indicator shafts[Title/Abstract]))) OR ((ssteel*[Title/Abstract] OR s-steel[Title/Abstract] OR "rocker"[Title/Abstract] OR "button"[Title/Abstract] OR "stainless"[Title/Abstract] OR "steel"[Title/Abstract])) AND ("pencil"[Title/Abstract] OR "pencils"[Title/Abstract]))) OR (ace{Title/Abstract} OR aceTRADE[Text Word] OR aceTM[Text Word] OR aceR[Text Word]) AND ("blade"[Title/Abstract] OR "blades"[Title/Abstract])) OR leris[Text Word] OR lerisTRADE[Text Word] OR lerisR[Text Word] OR lerisTM[Text Word]) OR ("electrosurgical pencil"[Title/Abstract] OR "electrosurgical pencils"[Title/Abstract])) OR ("button electrode"[Title/Abstract] OR "button electrodes"[Title/Abstract] OR rocker electrode*[Title/Abstract])) OR</p> <p>(megatip*[Text Word] OR mega-tip*[Text Word] OR "mega tipTM"[Text Word] OR "mega tipR"[Text Word] OR "mega tipTRADE"[Text Word])) OR ("indicator"[Title/Abstract] AND ("shaft"[Title/Abstract] OR "shafts"[Title/Abstract])) OR ("lletz"[Title/Abstract] AND ("loop"[Title/Abstract] OR "loops"[Title/Abstract] OR "electrode"[Title/Abstract] OR "electrodes"[Title/Abstract])) OR ("lletz"[Title/Abstract] AND "leep"[Title/Abstract]) OR ("large loop excision"[Title/Abstract] OR "large loop excisions"[Title/Abstract])) OR (("all in one"[Title/Abstract] OR "aio"[Title/Abstract]) AND ("hand piece"[Title/Abstract] OR "hand pieces"[Title/Abstract] OR "handpiece"[Title/Abstract] OR "handpieces"[Title/Abstract] OR "electrode"[Title/Abstract] OR "electrodes"[Title/Abstract])) OR (mega-power*[Text Word] OR megapower*[Text Word])) OR (megasoft*[Text Word] OR mega soft*[Text Word]) AND ("electrode"[Title/Abstract] OR "electrodes"[Title/Abstract])) OR ("mega 2000"[Text Word] OR mega2000*[Text Word])) OR ("disposable electrode"[Title/Abstract] OR "disposable electrodes"[Title/Abstract]) AND "patient return"[Title/Abstract])) OR ("patient return electrode"[Title/Abstract] OR "patient return electrodes"[Title/Abstract]) AND "disposable"[Title/Abstract])) OR (re cordable*[Title/Abstract] OR re-cordable*[Title/Abstract])) OR (megavac*[Text Word] OR mega vac*[Text Word] OR ultravac*[Text Word] OR ultra vac*[Text Word] OR attachavac*[Text Word] OR attacha vac*[Text Word])) OR (zip-pen*[Text Word] OR "zip pen"[Text Word] OR "zip penTM"[Text Word] OR "zip penR"[Text Word] OR "zip penTRADE"[Text Word]))</p>	
39	<b>9 or 14 or 39</b>	4496
	<p><b>Executed as:</b></p>	

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<pre> ((((((electrosurg*[Title/Abstract] OR electrocoagulat*[Title/Abstract] OR cauter*[Title/Abstract] OR diatherm*[Title/Abstract] OR electrodessicat*[Title/Abstract] OR electrodiatherm*[Title/Abstract] OR electrodissect*[Title/Abstract] OR fulgurat*[Title/Abstract]) OR (electro surg*[Title/Abstract] OR electro cauter*[Title/Abstract] OR electro dessicat*[Title/Abstract] OR electro diatherm*[Title/Abstract] OR electro dissect*[Title/Abstract] OR electro coagulat*[Title/Abstract])))) AND (((surgical instrument*[Title/Abstract] OR surgical device*[Title/Abstract]) OR (electrode[Title/Abstract] OR electrodes[Title/Abstract])) OR ((adson*[Title/Abstract] OR jeweler*[Title/Abstract] OR cushing*[Title/Abstract] OR gerald*[Title/Abstract])) AND ((forcep*[Title/Abstract] OR bipolar[Title/Abstract])) OR (scoville-greenwood*[Title/Abstract] OR semkin*[Title/Abstract] OR pencil[Title/Abstract] OR pencils[Title/Abstract] OR needle[Title/Abstract] OR needles[Title/Abstract] OR electrode*[Title/Abstract] OR probe[Title/Abstract] OR probes[Title/Abstract] OR forcep*[Title/Abstract])))) OR (((("electrosurgical knife"[Title/Abstract] OR "electrosurgical knives"[Title/Abstract] OR "electrosurgical loop"[Title/Abstract] OR "electrosurgical needle"[Title/Abstract] OR "electrosurgical needle knife"[Title/Abstract] OR "electrosurgical pencil"[Title/Abstract] OR "electrosurgical pencils"[Title/Abstract] OR "electrosurgical scalpel"[Title/Abstract] OR "electrosurgical cautery"[Title/Abstract] OR "electrosurgical device"[Title/Abstract] OR "electrosurgical devices"[Title/Abstract] OR "electrosurgical forceps"[Title/Abstract] OR "electrosurgical generator"[Title/Abstract] OR "electrosurgical generators"[Title/Abstract] OR "electrosurgical instrument"[Title/Abstract] OR "electrosurgical instrumentation"[Title/Abstract] OR "electrosurgical instruments"[Title/Abstract])) OR ("suction coagulation"[Title/Abstract] OR "suction coagulator"[Title/Abstract] OR "suction coagulators"[Title/Abstract] OR "suction diathermy"[Title/Abstract] OR "suction irrigating"[Title/Abstract] OR "suction irrigation"[Title/Abstract] OR "suction irrigator"[Title/Abstract] OR "suction irrigators"[Title/Abstract])) OR smoke evacuat*[Title/Abstract]) OR ("fluid evacuation"[Title/Abstract] OR "fluid removal"[Title/Abstract])))) OR ((((((((((((((((((megadyne*[Text Word] OR (EZ clean*[Text Word] OR E-Z clean*[Text Word] OR "E Z clean"[Text Word])) OR ("stainless steel ball"[Title/Abstract] OR "stainless steel balls"[Title/Abstract] OR "stainless steel electrode"[Title/Abstract] OR "stainless steel electrodes"[Title/Abstract])) OR ("reusable stainless steel"[Title/Abstract] AND (indicator shaft[Title/Abstract] OR indicator shafts[Title/Abstract])))) OR (("ssteel"[Title/Abstract] OR s-steel[Title/Abstract] OR "rocker"[Title/Abstract] OR "button"[Title/Abstract] OR "stainless"[Title/Abstract] OR "steel"[Title/Abstract])) AND ("pencil"[Title/Abstract] OR "pencils"[Title/Abstract])))) OR (ace{Title/Abstract} OR aceTRADE[Text Word] OR aceTM[Text Word] OR aceR[Text Word]) AND ("blade"[Title/Abstract] OR "blades"[Title/Abstract)))) OR leris[Text Word] OR lerisTRADE[Text Word] OR lerisR[Text Word] OR lerisTM[Text Word]) OR ("electrosurgical pencil"[Title/Abstract] OR "electrosurgical pencils"[Title/Abstract])) OR ("button electrode"[Title/Abstract] OR "button electrodes"[Title/Abstract] OR rocker electrode*[Title/Abstract])) OR (megatip*[Text Word] OR mega-tip*[Text Word] OR "mega tipTM"[Text Word] OR "mega </pre>	
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	tipR"[Text Word] OR "mega tipTRADE"[Text Word])) OR ("indicator"[Title/Abstract] AND ("shaft"[Title/Abstract] OR "shafts"[Title/Abstract]))) OR ("Iletz"[Title/Abstract] AND ("loop"[Title/Abstract] OR "loops"[Title/Abstract] OR "electrode"[Title/Abstract] OR "electrodes"[Title/Abstract]))) OR ("Iletz"[Title/Abstract] AND "leep"[Title/Abstract])) OR ("large loop excision"[Title/Abstract] OR "large loop excisions"[Title/Abstract])) OR (("all in one"[Title/Abstract] OR "aio"[Title/Abstract]) AND ("hand piece"[Title/Abstract] OR "hand pieces"[Title/Abstract] OR "handpiece"[Title/Abstract] OR "handpieces"[Title/Abstract] OR "electrode"[Title/Abstract] OR "electrodes"[Title/Abstract]))) OR (mega-power*[Text Word] OR megapower*[Text Word])) OR (megasoft*[Text Word] OR mega soft*[Text Word]) AND ("electrode"[Title/Abstract] OR "electrodes"[Title/Abstract])) OR ("mega 2000"[Text Word] OR mega2000*[Text Word])) OR ((("disposable electrode"[Title/Abstract] OR "disposable electrodes"[Title/Abstract]) AND "patient return"[Title/Abstract])) OR ((("patient return electrode"[Title/Abstract] OR "patient return electrodes"[Title/Abstract]) AND "disposable"[Title/Abstract])) OR (re cordable*[Title/Abstract] OR re-cordable*[Title/Abstract])) OR (megavac*[Text Word] OR mega vac*[Text Word] OR ultravac*[Text Word] OR ultra vac*[Text Word] OR attachavac*[Text Word] OR attacha vac*[Text Word])) OR (zip-pen*[Text Word] OR "zip pen"[Text Word] OR "zip penTM"[Text Word] OR "zip penR"[Text Word] OR "zip penTRADE"[Text Word]))	
41	#40 AND ("2018/10/01"[Date - Publication] : "2019/08/30"[Date - Publication])	272
42	#41 NOT medline (sb)	196

*Within the above search sets, results from set 42 were exported to QUOSA.*

#### GOOGLE SCHOLAR: Search performed on September 4, 2019

#	SEARCH STATEMENTS	RESULTS
1	With all of the word(s): megadyne  With at least one of the words: diathermy electrosurgery electrosurgical electrocautery electrocauterization electrocauterisation medical electrode cauterization cauterisation cautery monopolar  Return articles dated between: 2018 - 2020	24

**Results from the above search were reviewed. Duplicates, books, dissertations and conference abstracts were removed. The remaining 8 results were added to the final search results.**

**QUOSA:** 1575 documents from the Ovid and PubMed search results were exported to QUOSA, which automatically de-duplicated resulting in 1433 documents. Citations and available full-text were searched for the following terms with the listed results:

#	Search	Results
1	Megadyne*	3
2	"EZ clean" OR "E-Z clean" OR "E Z clean"	0
3	"EZ cleanTM" OR "E-Z cleanTM" OR "E Z cleanTM"	0

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4	"EZ cleanR" OR "E-Z cleanR" OR "E Z cleanR"	0
5	"ssteel pencil"~3 OR "ssteel pencils"~3	0
6	"ssteel pencilTM"~3 OR "ssteel pencilR"~3	0
7	"s steel pencil" OR "s steel pencils"	0
8	"s steel pencilTM" OR "s steel pencilR"	0
9	"ace blade"~3 OR "ace blades"~3	0
10	"aceTM blade"~2 OR "aceR blade"~2	0
11	"aceTM blades"~2 OR "aceR blades"~2	0
12	Leris*	0
13	"laparoscopic indicator"~3 OR "laparoscopic indicators"~3	0
14	megatip* OR mega-tip* OR "mega tip"	1
15	"mega tipTM" OR "mega tipR"	0
16	("all in one" OR "AIO") AND (handpiece* OR "hand piece" OR "hand pieces")	0
17	mega-power* OR megapower* OR "mega power"	0
18	"mega powerTM" OR "mega powerR"	0
19	(megasoft* OR "mega soft") AND electrode*	1
20	("mega softR" OR "mega softTM") AND electrode*	0
21	mega2000* OR "mega 2000"	0
22	"mega 2000TM" OR "mega 2000R"	0
23	re-cordable* OR "re cordable"	0
24	"re cordableTM" OR "re cordableR"	0
25	megavac* OR mega-vac* OR "mega vac"	0
26	"mega vacTM" OR "mega vacR"	0
27	ultravac* OR ultra-vac* OR "ultra vac"	3
28	"ultra vacTM" OR "ultra vacR"	0
29	attachavac* OR attacha-vac* OR "attacha vac"	0
30	"attacha vacTM" OR "attacha vacR"	0
31	zip-pen* OR "zip pen" OR "zip pens"	0
32	"zip penTM" OR "zip penR"	0

After deduplication, there were 7 results from sets 1-32 above. These items were combined with the 8 Google Scholar results as noted above, resulting in 13 unique results. These were de-duplicated against the previous search (October 2018), resulting in 7 results for review.

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## 10.4. Bibliography

### 10.4.1. SOA and General Articles

Aird, L.N., and Brown, C.J. (2012). Systematic review and meta-analysis of electrocautery versus scalpel for surgical skin incisions. *Am J Surg* 204, 216-221.

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## **10.4.2. Literature and Included Articles**

### **10.4.2.1. General Articles**

N/A

### **10.4.2.2. Included Articles (n=0)**

N/A

## **10.4.3. Literature and Excluded Articles**

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Lee, B. J.. Comparative Damage to Tissue Created By Two Advanced Electrosurgery Devices. Surg Res Pract. 2017.

## 10.5. Abbreviations

Abbreviation	Definition
AC	alternating current
BSE	Biological Safety Evaluation
CAPA	Corrective and Preventative Action
CER	Clinical Evaluation Report
CV	Curriculum Vitae
DOI	Declaration of Interest
DCRM	Design & Clinical Risk Management
dFMEA	Design Failure Modes and Effects Analysis
EBV	Electrothermal Bipolar Vessel Sealer

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Abbreviation	Definition
ECG	Electrocardiogram
EEG	Electroencephalogram
ER	Essential Requirement
ESU	Electrosurgical Unit
EU	European Union
FDA	US Food and Drug Administration
Hrs.	Hours
IFU	Instructions for Use
Kg	Kilograms
KHz	Kilohertz
Lbs.	Pounds
m	Meters
MDD	Medical Device Directive
MDV	Medical Device Vigilance
MHz	Megahertz
MIS	Minimally Invasive Surgery
mm	Millimeters
PC	Patient Codes
PEC	Product Experience Code
PHD	Premier Healthcare Database
PMCF	Post-Market Clinical Follow-up
PMS	Post-Market Experience and Surveillance
P/N	Part Number
RBA	Risk Benefit Analysis
RCT	Randomized Controlled Trial
RF	Radio Frequency Energy
RMR	Risk Management Report
SOA	State of the art
VSS	Vessel Sealing System

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## 10.6. CER Team

Role	Name
Medical Affairs Evaluator	Dr. Raymond Fryrear
Regulatory Affairs Evaluator	Kim Shoemaker
Medical Operations Evaluator	Luis Blanco
Post Market Surveillance	Katharine Seppa
Clinical Research	N/A
Risk Management / Quality	Scot Harris
R&D / Product Development	N/A – Legacy CER Update
Other	N/A

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## 10.7. CV Of Medical Affairs (MA) Evaluator

### CURRICULUM VITAE

**NAME:** Raymond S Fryrear II, M.D.

**ADDRESS:** Ethicon – 4545 Creek Road, Cincinnati, Ohio 45242

**CONTACT:** Cell (803) 391-6702

**EMAIL:** rfryrear@its.jnj.com

### EDUCATION:

B.S. 1997 University of Memphis, Memphis, TN

Major: Dual Biology/Chemistry

B.A. 2003 Trinity College, Dublin Ireland

Major: Life Sciences

M.D. 2003 Trinity College of Medicine, Dublin Ireland

Major: Medicine/Surgery

### CERTIFICATION:

2005-Present

Ohio Medical Licensure - pending

South Carolina Medical Licensure

American Board of Surgery BE

Minnesota Medical Licensure

BLS/ACLS

ATLS

ECFMG Certification

2016 Robotic Thoracic Surgery Certification

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2015 Robotic Colon-Rectal Surgery Certification  
 2014 Robotic Surgery Certification  
 2012. Laparoscopic Hepatopancreaticobiliary Surgery  
 2011. Advanced Laparoscopic General Surgery  
 2009. Fundamentals of Laparoscopic Surgery  
 1997. Investment Banking Licensure – Series 7 & 63  
 1996 Polysomnography Registry Eligible  
 Electroencephalography Registry Eligible

**INDUSTRY:**

2019-Present Vice President and Integrated Platform Lead – Medical, Clinical, and Pre-Clinical Affairs,  
 Ethicon-EndoSurgery - Cincinnati OH

- Leads and inspires an organization of approximately 15-20 Medical, Clinical, Pre-clinical Affairs professionals. Accountable for ensuring that the Medical, Clinical and Pre-Clinical organization works in a harmonized, efficient way to drive customer satisfaction and partnership with cross-functional teams and the regional Regulatory, Medical and Clinical groups.
- Drives global innovation agenda (i.e. the short and long term strategic directions) across Ethicon's EndoMechanical, Energy and Torax Platforms through strategic accountability, alignment, and leadership with the following innovation leaders and business partners: Global Strategic Marketing, New Business Development, R&D, Regulatory, HEMA, Quality and Supply Chain, leveraging deep medical and (pre-) clinical expertise.
- Ensures team is successful in establishing long-term product opportunities, as well as unmet medical needs, designing inputs and evidence needs for development programs and post market products.
  - Delivers on the portfolio's evidence strategies: Able to conduct gap analysis and data generation strategies to support the brand from a commercial, medical and market access perspective.
  - Conceive and deliver clinical and pre-clinical studies of the highest scientific quality, within timelines and budgets. Align strategy, budget and resource allocation in close partnership with the cross-functional and regional partners in Regulatory and Medical and (Pre-) Clinical Affairs Operational Groups, as well as integrate the health

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economic and market access aspects, to allow market leadership while insuring patient safety.

- Develop and implement evidence generation strategies (Pre-and Post-Market approval- studies, Investigator Initiated, Real World Evidence) aligned to the needs of the R&D, Regulatory and Commercial organization.
- Plan and bring timely resources on board (internal and external).
- Explore new trends in data-collection (Real World Data, Predictive Analytics...)
- Lead clinical scientific discussions with regulatory agencies / notified bodies to drive support of the clinical and regulatory strategy, including proposed clinical investigations; review process of clinical evidence generated for marketing authorization, line extensions, etc, including during sponsor regulatory inspections.
- Oversee Life Cycle Medical and Clinical affairs (e.g. copy review, medical information requests, medical/clinical input CERs, etc.)
- Responsible for talent attraction development engagement and management.

#### **HOSPITAL APPOINTMENTS:**

2017-2019	General Surgery, Chief of Surgery, Lexington Medical Center - Columbia, SC
2015-2019	General Surgery, Chief of Robotic Surgery, Lexington Medical Center - Columbia, SC
2011-2019	General Surgery Staff, Lexington Medical Center - Columbia, SC
2006-2011	General Surgery Residency, Mayo Clinic - Rochester MN
2005-2006	Internal Medicine Internship, Mayo Clinic - Rochester MN
2004-2005	General Surgery Sub-Internship: Exempla St Joseph Hospital - Denver CO.
2003-2004	Pathology Research Fellowship: Wake Forest University Baptist Hospital - Winston-Salem, NC
2002	Interventional Radiology Subinternship: Johns Hopkins Medical Institute - Baltimore MD

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- 2001           Neurosurgery Subinternship: Cleveland Clinic Foundation - Cleveland OH
- 2001           Neurosurgery Research Fellowship: Cleveland Clinic Foundation - Cleveland OH
- 2001           Hematology/Oncology Research Elective: St Jude Children's Research Hospital - Memphis TN
- 2000           Neurosurgery Elective: St Jude Children's Research Hospital and Semmes Murphy Neurosurgical Clinic - Memphis TN
- 1997-1998      Investment Banker, Vining Sparks Investment Banking Group - Memphis, TN
- 1993-1997      Neuroscience Center Developer and Neuroscience Specialist, LeBonheur Children's Hospital - Memphis, TN
- 1989-1993      Talent Acquisition Leader, Federal Express Corporation - Memphis, TN
- 1986-1989      Chief Operating Officer, Crystal Industries/Peck Daniels Corporation - Memphis, TN

**SOCIETY MEMBERSHIPS:**

- 2014-Present   International Hernia Collaboration  
                  The Americas Hernia Society Quality Collaborative  
                  Robotic Surgery Collaboration  
                  SAGES Robotic Surgery Masters Program Collaboration  
                  SAGES Colorectal Surgery Masters Program Collaboration  
                  Robotic Colorectal Surgery Group  
                  Society of Robotic Surgery
- 2011-Present   South Carolina Medical Society
- 2007-Present   Society of Vascular Surgery
- 2006-Present   American College of Surgeons
- 2005-Present   American College of Physicians
- 2005-Present   Minnesota Medical Association

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2003-Present The International Society of Dermatopathology  
 2001-2003 Trinity College Student Medical Journal, Editor  
 1998-2003 International Medical Student Association  
 1998-2003 Medical Defense Union  
 1998-2003 Trinity College Medical Association  
 1998-Present American Medical Association  
 1995-1997 Alpha Epsilon Delta Pre-Medical Honor Society, President  
 1995-2000 Golden Key National Honor Society, Vice President

#### PUBLICATIONS/PRESENTATIONS/POSTER SESSIONS:

1. Perspectives in Vascular Surgery, Case Report: Endograft Collapse, Andrew Knott M.D., Manju Kalra M.D., Raymond S. Fryrear II M.D., Submitted 2008.
2. Annals of Plastic Surgery, Clinical Experience with the Anconeus Muscle Flap: Advantages for Coverage of Defects about the Elbow, Raymond S. Fryrear II M.D., Steven L Moran M.D., In-Press 2008.
3. ASSH Pocket Manual, Avascular necrosis in the carpus and phalanges, Steven L. Moran M.D., Raymond S. Fryrear II M.D., Book Chapter: In-Press 2008.
4. World Journal of Surgery, Surgery for Cushing's Syndrome: An Historical Review and Recent Ten-year Experience, Porterfield JR, Thompson GB, Young WF, Chow JT, Fryrear RS, van Heerden JA, Farley DR, Atkinson JR, Meyer FB, Abboud CF, Nippoldt TB, Natt N, Erickson D, Vella A, Carpenter PC, Richards ML, Carney JA, Larson D, Schleck C, Churchward M, Grant CS In Press 2008.
5. AM J Dermatopathology, Early Juvenile Xanthogranuloma Clinically Mimicking Infantile Fibrosarcoma, Raymond S Fryrear, M.D., Omar Sangueza, M.D., 26(2):138, April 2004.
6. J AM Acad Dermatology, Rapid onset of cutaneous squamous cell carcinoma of the penis in a patient with psoriasis on Etanercept, Raymond S Fryrear II, M.D., Anna Kay Wiggins, M.D., Gil Yosipovitch, M.D., Omar Sangueza, M.D., 2005 Aug;53(2):354-5.
7. JVIR, Endovascular treatment of ruptured aneurysms, Kieran J Murphy, M.D., Raymond Fryrear, B.S., Phillip Gailoud, M.D., March 2005.
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9. JVIR, Percutaneous vertebroplasty for compression fracture in an HIV-infected patient. Murphy KJ, Malhotra AD, Parker MW, Fryrear RS, Khandelwal N, Gailloud P, Morgan RH, 2004 Dec;15(12):1487.

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10. JVIR, Spontaneous vertebral arterial venous fistula at the V4 segment treated by a combination of endovascular coiling and stenting, Murphy KJ, Fryrear RS, Gailloud P, March 2005.
11. CNS Philadelphia, Pennsylvania, A standardized biomechanical comparison of interbody fusion cages, Ferrara LA, Secor JL, Fryrear R, September 2002.
12. SRS Seattle Washington, A standardized biomechanical comparison of interbody fusion cages, Ferrara LA, Secor JL, Fryrear R, September 2002.
13. Textbook of Neurological Surgery: Principles and Practices. Invasive Epilepsy Monitoring in Pediatric Patients, Boop F, Fryrear R, Book Chapter: Lippincott Williams & Wilkins Published September 2002.
14. Annual Pediatric Medical Student Research Meeting, The prevalence of childhood obesity in Ireland, Fryrear RS, McKenna F, Bell L, Chong V, Mak G, Peirce J, July 2002.
15. IMAST, Montreux Switzerland. A standardized biomechanical comparison of interbody fusion cages, Ferrara LA, Secor JL, Fryrear R, May 2002.
16. ISSLS, Cleveland Ohio. Subsidence and push-out resistance of interbody fusion cages. Ferrara LA, Secor JL, Fryrear RS, Whitefield M, July 2002.
17. Joint Section. Orlando, Florida, A standardized biomechanical assessment of the push-out strength of threaded interbody fusion cages. Ferrara LA, Secor JL, Fryrear RS, Whitfield M, February 2002.
18. Global Spine: Surgical Principles and the Latest Techniques. Percutaneous pedicle screws; techniques and results, Foley KT, Fryrear RS. Maui, Hawaii July 2002.
19. Sixth Annual Detroit Neurosurgery Symposium. Percutaneous pedicle screw replacement. Detroit, Michigan, Foley KT, Fryrear RS. September 2002.
20. American Association of Neurological Surgery. Atlanta, Georgia. Slit Ventricle Syndrome in children. Sanford RA, Muhlbauer MS, Igarashi M, Thomas E, Fryrear RS. 2001
21. American Association of Neurological Surgery: San Francisco, CA. Division of the transverse sinus and tentorium cerebelli to allow vault expansion and posterior fossa decompression in the treatment of Arnold Chiari Malformation. Burson T, Muhlbauer MS, Sanford RA, Fryrear RS. February 2000.
22. Pharmacology Medical Student Research Meeting. Dublin, Ireland. The role of endothelin in arteriosclerosis. 2000.
23. Annual Physiology Medical Student Research Meeting. Dublin, Ireland. The role of adjuvant haemostatic support with Protein-C replacement therapy in Pupura Fulminans associated Meningococcemia. Fryrear RS, Gallagher J, Wolfe E, Kong B, Jain A, Smith O. 1999.
24. CANCER. Peritoneal metastases in children with cancer. Kaste SC, Mariana N, Fryrear R, Jedlund GL, Jones L, Poe D, Jenkins JJ III, 1998 Jul 15;83(2):385-90.
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26. American Association of Neurological Surgery. San Diego, CA, Placement of On/Off Switches in Post-Tumoral Hydrocephalus, Donahue D, Fryrear RS, Sanford RA, Muhlbauer MS. April 1994.

**RESEARCH IN PROGRESS: AVAILABLE UPON REQUEST.**

**HOBBIES & INTERESTS:**

Triathlons, Martial Arts (Aikido), Competition Field Trials, Snow skiing, Hiking, Golf, Tennis, Music and Theater.

**LANGUAGE:**

Spanish – currently limited due to lack of usage, but previously fluent.  
French – same as above.

**OTHER AWARDS/ACCOMPLISHMENTS:**

*Residency:*

*Society for Vascular Surgery Scholarship, 2007*  
*Silver Retractor Award, 2007*

*Medical School:*

Cofounder of the Trinity Medical Student Journal  
Editor of the Trinity Medical Student Journal  
Distinction in Neuroanatomy, Physiology, and Pharmacology  
Trinity Book Prize for overall honors 3rd Year

*Undergraduate:*

President of AED Premedical Honor Society  
Vice President of Golden Key National Honor Society  
Pre-Medical Student of the Year, 1996  
Dean's List each semester

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## 10.8. CV Of Regulatory Affairs (RA) Evaluator

### Kimberly Shoemaker, RAC

#### Profile

- ◆ 25+ years experience in the health care industry, including In Vitro Diagnostics and Medical Devices serving in diversified roles in Research and Development, Quality and Regulatory Affairs.
- ◆ Business Leader with expertise in Regulatory Affairs demonstrating a solid track record
- ◆ Highly driven to achieve and exceed results and drive growth in developed and emerging markets
- ◆ Strong interpersonal skills with the ability to collaborate with global business partners to align priorities and mitigate risk and business continuity in a dynamic regulatory environment
- ◆ Excellent verbal and written communication skills, resulting in successful interfacing with regulatory authorities
- ◆ Demonstrate expertise and strong people development skills, with the ability to maintain a highly engaged team and high retention rate

#### Leadership Skills Summary

- |   |  |   |
|---|--|---|
| <ul style="list-style-type: none"> <li>◆ Results and Performance Driven</li> <li>◆ Strategic and Influencing</li> </ul> | <ul style="list-style-type: none"> <li>◆ Organization and Talent Development</li> <li>◆ Collaboration and Teaming</li> </ul> | <ul style="list-style-type: none"> <li>◆ Integrity and Credo Based Actions</li> <li>◆ Sense of Urgency</li> </ul> |
|---|--|---|

#### Professional Experience

##### ***Ethicon Endo-Surgery, Inc / ETHICON, LLC (Cincinnati, OH) 2001-Present***

WW Senior Director, Regulatory Affairs – Platform Lead  
 (2014-Present)

- ◆ Member of the Platform Leadership Teams and Project Sponsor (New Product Development) for Ethicon platforms (currently Endomechanical and Energy; prior responsibility included

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Robotics); provide advice, guidance and analysis of critical projects and the global regulatory environment;

- ◆ Identify, prioritize, allocate and manage resources to ensure achievement of strategy objectives;
- ◆ Provide guidance in the preparation and compilation of regulatory submissions consistent with regulatory policies;
- ◆ Interact with regulatory agencies as appropriate to expedite approval or resolve regulatory matters for pending applications;
- ◆ Provide leadership, personnel development, training, coaching and mentoring to staff as well as associates in other functional areas;
- ◆ Successful integration of personnel and regulatory processes of acquired companies (e.g., Megadyne Medical Products, Inc; Torax Medical)
- ◆ Operationalize strategy for the global Ethicon business; includes operating in a new business model, collaborating with a non-J&J company, Verb Surgical Inc., in the development of a Digital Surgery (Robotic) Platform

Director, Regulatory Affairs – Energy (2012-2014)

- ◆ Served on the Global Management Board and Platform Leadership Team, providing advice, guidance and analysis of critical projects and the global regulatory environment
- ◆ Operationalize strategy for the Ethicon Energy business; translate strategic plan to department objectives and goals
- ◆ Identify, prioritize, allocate and manage resources to ensure achievement of strategy objectives; Met and exceeded goals for product clearances and approvals across Energy portfolio (e.g., Harmonic ACE+7, Harmonic Focus+, EnSeal Articulating Tissue Sealers)
- ◆ Provide guidance to direct reports for the preparation and compilation of regulatory submissions consistent with regulatory policies
- ◆ Interact with regulatory agencies as appropriate to expedite approval or resolve regulatory

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matters for pending applications

- ◆ Provide leadership, personnel development, training, coaching and mentoring to staff as well as associates in other functional areas

Group Manager, Regulatory Affairs, 2007-2012

- ◆ Successfully led regulatory affairs team throughout product lifecycle for multiple product portfolios: 510(k), PMA (Supplements and Annual Reports), Technical Files and Design Dossiers (CE mark) filings and change determinations, including GMP requirements.
- ◆ Accountable for the development and execution of robust global regulatory strategies and plans in order to drive growth; proven record of exceeding schedule for delivery of government registrations/approvals (e.g. first to market Powered Endocutter received clearance in 44 days).
- ◆ Successfully promoted five associates within a 2 year timeframe; fostered talent development by presenting stretch assignments as well as other growth opportunities to direct reports; coach/develop direct reports with respect to personal and technical development to support business objectives.
- ◆ Led the US RA team in the implementation of the 2010 Medical Device Directive (EU) revisions, ensuring continued compliance to maintain CE marked product and distribution in the European Market without disruption; streamlined process and documentation requirements.
- ◆ Regulatory lead and key contributor on the Global Logistics Center(GLC) conversion team; developed strategies to obtain global registrations due to the creation of Ethicon-Endo Surgery, LLC, and sustainment of current global supply/product shipments (largest labeling conversion project in company's history)
- ◆ Key contributor to divisional and company Action Teams identifying key areas for improvement; nominated member of the company's Engagement Champion Team to assist teams with low engagement.
- ◆ Served on Risk Management Board, providing regulatory risk assessments related to various field issues and input to escalation process (Health Hazard Evaluation and Quality Review

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Board).

- ◆ EES Group Sponsor (2005-2006) and contributing member of the Women's Leadership Initiative (WLI)
- ◆ Presenter at Advamed's 510(k) Submissions "101" at the associate level (2004)

### **Employment History**

#### ***Stewart Rose and Associates (Cincinnati, OH) 1998-2001***

Senior Research Analyst/Associate

Conducted market feasibility studies for retailers and shopping center developers; responsibilities included demographic analysis and evaluation of economic factors, trade area delineation and market/lifestyle segmentation.

#### ***Abbott Laboratories (Abbott Park, IL) 1989-1998***

Senior Regulatory Specialist

Developed strategies and filed IVD International Product Master Files; ensured compliance to import-export regulations. Drafted operating procedures and work instructions for training purposes; Served as the International Regulatory representative on Global Labeling Task Force and IVD Directive Labeling Team.

Product Coordinator, Quality Assurance

Facilitated product development activities to ensure timely market entry of new products and facilitated management reviews. Reviewed/analyzed supporting data to ensure product met specified design goals and package insert claims; served as department reviewer and approver for diagnostic assay manuals and package inserts.

R&D Technician

Developed assays for new and reformulated assays (FMEA and FPIA technologies); performed design testing, analysis, interpretation, organization and presentation of data; Designed test protocols for specific assay development.

#### ***University Hospital (Cincinnati, OH) 1988-1989***

Medical Technologist

Performed therapeutic drug monitoring, comprehensive drug screening, and pharmacokinetic studies  
Instrumentation knowledge includes: HPLC, TLC, GC, Mass Spectroscopy, TDx, and Hitachi Analyzer

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### **Education / Certifications**

xavier University – Cincinnati, OH  
BSBA Medical Technology

the christ hospital – Cincinnati, OH  
School of Medical Technology, ASCP Certification received (not renewed)

six sigma green belt certification  
Ethicon Endo-Surgery (2002)

Regulatory affairs professional society  
US RAC Certified since 2003

management fundamentals I and II  
LEADERS Developing Leaders  
Johnson & Johnson

kellogg school of management  
Creating and Leading a Culture of Innovation (2011)

smith college executive education  
Smith College/Johnson & Johnson: The Leadership Edge (2011)

SMITH-TUCK WOMENS LEADERSHIP PROGRAM (2014)  
Global Leaders Program for Women

HARVARD BUSINESS SCHOOL (2015)  
Johnson & Johnson: R&D Leadership Program

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## 10.9. CV Of Medical Operations (MO) Evaluator

### CURRUCULUM VITAE

Luis Blanco

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#### SUMMARY OF QUALIFICATIONS

Senior Manager for the Medical Operations – Shared Services Group with over 20 years of experience in Johnson & Johnson and has held various Quality Assurance, Quality Systems, Complaint and MDR/MDV Reporting, Compliance, Medical Operations roles of increasing responsibility during his career. Worked at various J&J sites globally including international assignments in the Netherlands, India and China. BS in Metallurgical Engineering from the University of Texas at El Paso and a Masters in Microelectronic Manufacturing Engineering from Rochester Institute of Technology (RIT). Holds a MBA from the University of Texas at El Paso and is a member of American Society for Quality (ASQ), as well as a Certified Quality Auditor (CQA). Core competencies include: Thorough understanding of medical device regulations and requirements for US, EU, Canadian, China, Japan, and other international standards and regulations.

#### WORK EXPERIENCE

Sr. Manager, Medical Operations

**Ethicon and Ethicon Endo-Surgery: Medical Operations – Shared Services (a Johnson & Johnson Company) –**

July 2017 – Present

**Highlight(s):**

Central Process Owner for Clinical Evaluation Report Process for Global Surgery (at Johnson & Johnson). Ensures respective CERs for both Ethicon and Ethicon Endo-Surgery products (Existing and New Product Introductions) are compliant to the MedDev Rev. 4 requirements, EU MDR and respective standards and regulations, where applicable.

- Central process owner for the Clinical Evaluation Report process across Global Surgery
- Responsible for the effective optimization and harmonization of CER processes within Global Surgery

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- Manages CER processes and linkages within the Quality Systems and Regulatory Processes (e.g. Risk Management, PMS, etc.)
- Manages New Product Development, CFDA and Rest of World CER requirements and documents
- Acts as the CER liaison with respective Notified Bodies and regulatory agencies
- Develops strategies, policies and efficiencies within procedures and processes for current and future regulatory requirements
- Partners with cross-functional business SMEs such as Medical Directors, Post Market Surveillance, Design Quality Engineers, R&D, and
- Regulatory Affairs relating to Performed an Internal Audit on Regulatory Affairs, which included the assessment of Tech File, Design Dossier, Clinical Evaluation Report (CER) Documentation for the Mentor Franchise
- Manages timelines and project deliverables
- Manages the CER staff including project managers, technical and medical writers
- Manages the budget and schedule related to current and projected future CER activities
- Supports CAPA, Audit Observation Failure Investigations, Action Planning and Effectivity Monitoring Activities related to the CER Process

#### Compliance Manager

**Mentor Irving (a Johnson & Johnson Company)** – Implants (Class III), Sizers (Class II) and Expanders (Class II) at **Mentor Irving Facility (Texas, USA)** and **Mentor Leiden Facility (The Netherlands)**

January 2016 – Present

#### **Highlight(s):**

Recently completed an international assignment at the Mentor Leiden Facility (The Netherlands) in order to prepare the site for Un-Announced Inspections and enhance their Internal Audit Program. The goal was to establish a compliance structure that will be able to manage Un-Announced Inspections and enhance site compliance posture. Currently, stationed at the Mentor Irving Facility performing the Compliance Manager role while continuing to provide compliance support/guidance to the Mentor Leiden facility, where required. Served as the Acting Sr. Compliance Manager from November 2016 to March 2017 for the Mentor Sites.

- Provide compliance education and training (QSR-21CFR Part 820, ISO 13485:2003, Canadian MDR, SOR/98-282, MEDDEV 2.12-1 Rev. 8, European MDD (93/42/EEC as amended by 2007/47/EC and respective Standards and Regulations including

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Industry Trends) to the Mentor Organization (at Mentor Leiden and Irving Manufacturing Facilities) in support of overall compliance initiatives.

- Leading the Audit Readiness Program and preparation activities for Un-Announced Inspections at Mentor Irving and supporting Mentor Leiden
- Lead the Audit preparation and successful execution of the 2017 BSI 13485/MDSAP Re-Cert Audits at Mentor Irving
- Led the Audit successful preparation and execution of the OCP (Brazil) and TuV ISO 13485 Re-Cert Audits at Mentor Leiden (2016)
- Participate and assist in Internal and External Quality Audits (which include Criss Cross Audits for the Mentor Sites)
- Responsible to establish an Internal Auditor Training Program for the Mentor Leiden Facility - Completed on August and December 2016
- Responsible for the Compliance Metrics and Statistical Trending (Audit Schedule Adherence, Observation, Action Timeliness, Due Date Adherence) for the Site and escalate to CAPA, as applicable.
- Develop, implement, and support Mentor Organization and Corporate Regulatory and Compliance Strategies at Mentor Irving /Leiden
- Support Escalation, CAPA, Field Action and Risk based assessment activities for the Mentor Sites
- Support the adherence and assessments to the J&J MD and Technical Standards
- Lead a Mentor/Ethicon Cross Functional team to update the respective Standards and Regulations listing for the Mentor Franchise in order to improve Tech File, Design Dossier and Risk Management documentation and linkages
- Support New Product Introductions and Development as part of the 4-Corners Project at Mentor Leiden (2016). Worked with R&D/RA/QA/RM Cross functional teams for the development of FDA Submission documentation related to the Mentor Leiden manufacturing process.
- Supported the closure of 2015 ANSM Audit Observations for the Mentor Leiden in compliance to the MEDDEV 2.12-1 Rev. 8 Guidance on Medical Device Vigilance Systems
- Performed an Internal Audit on Regulatory Affairs, which included the assessment of Tech File, Design Dossier, Clinical Evaluation Report (CER) Documentation for the Mentor Franchise.
- Contributed and Participated in Local and Franchise Management Reviews for the Compliance (Internal / External Audit) Section
- Support CAPA, Audit Observation Failure Investigations, Action Planning and Effectivity Monitoring

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- Provide guidance with regards to ISO standards, Medical Device Directive (MDD) and FDA regulations, to assess, and verify corrective actions effectiveness. Trend, report, and present results/ recommendations to Mentor Management

### Interim ASPAC Regional Compliance Manager

**Ethicon (a Johnson & Johnson Company)** – Sutures (Class II) and Kitting Products at the **Ethicon Aurangabad** and **Baddi Facilities** and the **Minhang (China) Facility**

November 2014 – December 2015

#### **Highlight(s):**

Completed a one (1) year term International assignment as the Regional Compliance Lead for the ASIA Pac area (India and China). The goal was to establish a compliance organization, improve its compliance performance and sustain compliance according to the local, franchise and regulatory requirements. Within the timeframe, the ASIA Pac sites compliance status improved from a RED/RED position to a GREEN/GREEN status based on JJRC reviews and follow-ups. External Inspection performance, Audit metrics and Schedule Adherence were improved. Established an Internal Audit training program to further enhance the skill sets and awareness of the Internal Auditors.

- Provide compliance education and training (QSR-21CFR Part 820/ISO 13485:2003, ISO9001:2008, India D&C Act (Schedule M/Schedule L), WHO/GMP/TRS and respective Standards and Regulations including Industry Trends) to the Ethicon Organization (for the Asia Pac Facilities in India and China) in support of overall compliance initiatives.
- Lead the efforts for the preparation and adherence to Internal and External Quality Audits and Inspections.
- Established the Internal Auditor Training Program for the Ethicon India Facilities
- Responsible for the Audit Readiness Program for the Asia Pac Facilities in India and China (Ethicon).
- Interface with Notified Bodies (BSI and TuV) and Regulatory (Local FDA) representatives during audits (BSI, Local FDA). Sites achieved excellent compliance audit results at the India and China sites (Ethicon).
- Develop, implement, and support AsiaPac (Ethicon India and China) Organization and Corporate Regulatory and Compliance Strategies
- Provide guidance with regards to ISO standards and FDA regulations, to assess, and verify corrective actions effectiveness. Trend, report, and present results/ recommendations to management
- Responsible for managing and improving the Compliance culture and metrics for the AsiaPac facilities

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- Core Member of the MD&D (Multi- Op Cos) Audit Readiness Initiative 2013, 2014 and 2015.
- Leading Sub-Team (MD Op Cos) for the Risk Score Team under the MD&D Audit Readiness Initiative 2013, 2014 and 2015.
- Lead the MD Op Cos Sub-team regarding Internal Auditor Qualifications and Training requirements to be deployed across the MD level.
- Responsible for the Compliance Metrics and Trending (Audit Schedule Adherence, Observation and Action Timeliness, Due Date Adherence) for the Site
- Supported Escalation, CAPA, Field Action and Risk based assessment activities for the Mentor Site
- Support CAPA, Audit Observation Failure Investigations, Action Planning and Effectivity Monitoring
- Contributed and Participated in Local and Franchise Management Reviews for the Compliance (Internal / External Audit) Section
- Support the adherence and assessments to the J&J MD and Technical Standards
- Site Deployment Team Member for the India Sites (Aurangabad and Baddi) for the ADAPTIV project (Document Change, MVI and Change Project)

#### Quality Systems and Compliance Systems Manager

**Mentor Texas (a Johnson & Johnson Company)** – Implants (Class III), Sizers (Class II) and Expanders (Class II) at **Mentor Irving Facility and Distribution Center – Coppell, Texas**

March 2013 – December 2014

#### **Highlight(s):**

As the QS and Compliance Manager for the Mentor Irving site, the goal was to develop the QS and Compliance organization, improve its Quality Systems (by deploying EtQ Audit and ADAPTIV), Compliance performance and sustain compliance according to the local, Franchise and Regulatory requirements in a highly regulated environment. During this period, the Mentor Irving site was able to achieve excellent External Inspection performance (2 FDA, 2 BSI and OCP Audits with Zero Observations). Audit metrics and Schedule Adherence were improved.

Established Internal Audit training program and auditor council to further enhance the skill sets and awareness of the Internal Auditors for the Mentor site.

- Provide compliance education and training (QSR-21CFR Part 820, ISO 13485:2003, Canadian MDR, SOR/98-282, European MDD (93/42/EEC as amended by 2007/47/EC and respective Standards and Regulations including Industry Trends) to the Mentor Organization (at Irving, Texas Manufacturing Facility and Coppell, Texas Distribution facility) in support of overall compliance initiatives.

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- Lead guidance and preparation for the FDA Inspections at Mentor Irving in July 2013 and May 2014 – Zero Non-Conformances
- Lead guidance and preparation for the BSI Re-Cert and Surveillance Audits at Mentor Irving in October 2013 and May 2014 – Zero Non-Conformances
- Lead guidance and preparation for the OCP (Brazilian) Audit at Mentor Irving May 2014 – Zero Non-Conformances
- Lead guidance and preparation for the BSI Tech File Audit for Mentor Santa Barbara Audit – 4 Minor Non-Conformances for Santa Barbara Franchise
- Established and Lead Trainer for the Internal Auditor Training Program for the Ethicon San Lorenzo Facility - Nov 2013 and Mentor Irving Facility - Mar 2014
- Responsible for the Audit Readiness Program for Mentor Irving Facility and Distribution Center at Coppell, Texas
- Interface with Notified Bodies (BSI) and Regulatory (FDA) representatives during audits (BSI, FDA, OCP and PMDA).
- Supported the External Audits for Ethicon San Angelo Facility (Co-Backroom Lead and Front Room Scribe) for PMDA Audit (February 2014) and JJRC Audit (June 2014).
- Leading Sub-Team (Multi-Op Cos) for the Risk Score Team under the MD&D Audit Readiness Initiative 2013 and 2013 YTD
- Management the Document Control and Training groups for the Mentor Irving Site.
- Responsible for the Compliance Metrics and Statistical Trending (Audit Schedule Adherence, Observation, Action Timeliness, Due Date Adherence) for the Site and escalate to CAPA, as applicable.
- Supported Escalation, CAPA and Field Action activities for the Site
- Contributed and Participated in Local Management Reviews for the Compliance (Internal / External Audit) Section
- Support CAPA, Audit Observation Failure Investigations, Action Planning and Effectivity Monitoring
- Supported the Mentor Irving in compliance to the MEDDEV 2.12-1 Rev. 8 Guidance on Medical Device Vigilance Systems
- Business Partner and Site Deployment Core Team Member for the Mentor Irving for the ADAPTIV project (Document Change, MVI and Change Project)

#### Quality Systems and Compliance Systems Manager

**Ethicon (a Johnson & Johnson Company)** – Suture (Cobalt, Split-Flow and Specialties – Class II) and Catheter (Class III)  
Business Units - **Ciudad Juarez, Chihuahua, Mexico at the Torres and Independencia Facilities**

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June 2009 – March 2013

**Highlight(s):**

As the Compliance Manager for the sites, lead the compliance program that resulted in excellent External Inspection performance (BSI and ANVISA Audits with Zero Observations). Co-Lead the Ethicon Franchise Worldwide deployment of Do it Right.

- Provide compliance education (QSR-21CFR Part 820, ISO 13485:2003, Canadian MDR, SOR/98-282, European MDD (93/42/EEC as amended by 2007/47/EC and respective Standards and Regulations including Industry Trends) to the Juarez Organization (at Ethicon Torres and Independencia facilities) in support of overall compliance initiatives, including support of Ethicon LLC BSI/ISO Certification initiative.
- Successfully deployed and obtained ISO 13485:2003 Certification for the Ethicon Juarez facilities (Torres and Independencia)
- Lead guidance and preparation for the ANVISA Regulation and Audit – Zero Non-Conformances
- Lead the Organization in achieving successful external inspection results. Develop, implement, and maintenance of the Inspection Readiness process. Coordinate and report inspection schedules and progress. ISO 13485:2003 Re-Certification – Zero NCs. ANVISA Audit – Zero NCs.
- Participate and assist in Internal and External Quality Audits (which include Corp. Ethicon and Criss Cross Audits for the Juarez Torres and Independencia Facilities and other Ethicon Sites).
- Interface with Notified Bodies (BSI) and Regulatory (FDA) representatives during audits (Juarez – BSI 2009/2010/2011/2012 and San Angelo –FDA January 2010
- Responsible for the Ethicon Juarez FDA Audit Readiness Program.
- Provide guidance with regards to ISO standards and FDA regulations, to assess, and verify corrective actions effectiveness. Trend, report, and present results/ recommendations to facility management
- Responsible for the Internal Audit Program Adherence and activities
- Responsible for the Compliance Metrics and Statistical Trending (Audit Schedule Adherence, Observation, Action Timeliness, Due Date Adherence) for the Site and escalate to CAPA, as applicable.
- Supported Escalation, CAPA and Field Action activities for the Site
- Support CAPA, Audit Observation Failure Investigations, Action Planning and Effectivity Monitoring
- Support Customs Import / Export adherence activities from a Compliance perspective (including Site FDA Customs Reviews at El Paso J&J Warehouse)
- Lead Site Assessments and Training for Combination Products for the Ethicon Juarez.

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- Lead the Local Management Reviews for the Ethicon Juarez Sites (including inputs to Internal and External Audit performance)
- Responsible for the Operator Certification Program for the Ethicon Juarez Operations. Now a benchmark for the J&J Juarez Campus
- Co-Lead for the Deployment of the Do It Right/HER Initiative for the Ethicon Franchise
- Business Partner and Site Deployment Lead for the Ethicon Juarez Operations for the ADAPTIV project
- Acting Quality Systems Compliance Leader for the San Angelo Facility from October 2009 to February 2010. Completed the 2009 Internal Audit Schedule on time and Lead the FDA Readiness Activities for the FDA Audit in San Angelo on January 2010 with Zero NCs.
- Acting Quality Operations Leader for the Ethicon Juarez Operations from September 2011 to September 2012. Supported the Thermachoice, Cobalt, D-Specials and E-Pack processes during this time frame.

#### Worldwide Customer Quality (WCQ) Manager

##### **Ethicon (a Johnson & Johnson Company) – Somerville, New Jersey**

Feb 2006 – June 2009

##### **Highlight(s):**

As the WW Complaint Manager for Ethicon, lead the Complaint Handling and Vigilance Reporting Groups in Somerville, New Jersey and the respective Complaint Handling units across France, Scotland, Brazil, Germany and Switzerland. Successful FDA inspections were achieved with no 483s from February 2006 – June 2009 in the Complaint Handling Process. Deployed eMDR application for the Ethicon Franchise.

- Global Process Owner of the Complaint Management System Application (Remetrex)
- Lead Oversight of Ethicon Complaint Handling Units Worldwide (France, Switzerland, Germany, Brazil, Scotland) and Partnered with JJKK, JJ Canada and Australian Affiliates.
- Reduce regulatory exposure through increase efficacy in management of product complaints by improvement in multiple complaint process metrics Accountable for department compliance with all Food & Drug Administration (FDA) and European Union Medical Device Directives (MDD) regulations governing adverse event reports such as Medical Device Reports (MDR) and Medical Device Vigilance (MDV).
- Provide compliance education (QSR-21CFR Part 820/QSR-21 CFR Part 803/ISO 13485:2003 including Industry Trends) with regards to the Product Complaint Handling Process to the Ethicon Organization (including global facilities and functions) in support of overall compliance and product complaint handling initiatives

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- Participates and assists in Internal and External Quality Audits (which include Corp. Ethicon and Q&CWW)
- Interface with Notified Bodies (BSI) and Regulatory (FDA) representatives during audits at Corporate and Manufacturing Sites (Juarez Plant – May 2008, San Lorenzo Plant – August 2008 and Neuchatel Plant August 2008).
- Responsible for the Complaint Metrics and Statistical Trending (Complaint Timeliness, Complaint Codes, MDR/MDV Reporting) for the Ethicon Franchise and escalate to CAPA, as applicable.
- Supported Escalation, CAPA and Field Action activities for the Site.
- Support CAPA, Audit Observation Failure Investigations and Complaint Investigations for the Ethicon sites.
- Contributed and Participated in Local Site(s) and Franchise Management Reviews for the Complaint Handling and Vigilance Reporting Section
- Coordinates the communication of MDR complaints with FDA and MDV for product complaints with the Competent Authorities (MHRA, Swiss Medic), Authorized Representatives and Regulatory Franchise Managers, as applicable.
- Oversight of the FDA quarterly reports (ASR) and managed requests and responses from Competent Authorities such as MHRA, Swiss Medic related to complaint files and MDR/MDV reporting.
- Supported Device Registries and Clinical Trials that feed into the Complaint Handling process and Medical Device Reporting processes for Ethicon Franchise
- Supported Post Market Surveillance and Risk Management Activities and Initiatives and partnered with IM to deploy a data extraction database for complaint handling and post market surveillance reports and trending.

#### Compliance Systems Leader

**Ethicon (a Johnson & Johnson Company)** – Suture and Gynecare Business Units

**Ciudad Juarez, Chihuahua, Mexico at the Torres and Salvarcar Facilities**

May 2002 – Feb 2006

- Provide compliance education (QSR-21CFR Part 820/ISO 13485:2003 including Industry Trends) to the Juarez Organization (at Ethicon Torres and Salvarcar facilities) in support of overall compliance initiatives
- Lead guidance, preparation and Audit Co-Host for the FDA Inspection at Ethicon Juarez (June 2004) – One (1) Minor Non-Conformance
- Lead the FDA Response Action and Documentation for the June 2004 Audit.

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- Successfully deployed and obtained ISO 13485:2003 Certification for the Ethicon Juarez facilities (Torres and Salvarcar)
- Participate and assist in Internal and External Quality Audits (which include Corp. Ethicon and QCS for the Juarez Torres and Salvarcar facilities
- Interface with Notified Bodies (BSI) and Regulatory (FDA) representatives during audits
- Supported the CAPA activities and assessments for the Site
- Management the Document Control and Quality Systems groups for the Ethicon Juarez Sites.

#### Interim Plant Quality Manager

**Ethicon (a Johnson & Johnson Company)** – Suture and Gynecare Business Units

**Ciudad Juarez, Chihuahua, Mexico at the Torres and Salvarcar Facilities**

Jan 2005 – July 2005

- Ensure compliance to the QSR/ISO requirements for the Juarez Facilities
- Established and operate within an effective budget and manpower plan for the QA Organization.
- Served as a Management Representative for the Juarez Facilities

#### Supply Chain Leader

**Ethicon (a Johnson & Johnson Company)** – Sutures and Gynecare Business Units - **Ciudad Juarez, Chihuahua, Mexico**

May 2001 - May 2002

- Supervised and Coordinate New Hire Training and Development for the Juarez Quality Systems Engineers and Technicians for the Gynecare Product Line
- Responsible for reviewing and approving all Quality Assurance test methods and inspections procedures of raw material, work in progress and finished product.
- Acted as plant management deputy during corporate internal audits and any plant regulatory inspection.

#### Sr. Quality Systems Engineer

**Ethicon Endo-Surgery (a Johnson & Johnson Company)** – Ligation/Hand-Held/Open Manufacturing (Lubrication and Staple Making) and Raw Material Inspection (RMI) - Business Units - **Ciudad Juarez, Chihuahua, Mexico**

May 1999 – May 2001

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- Supervised and Coordinate New Hire Training and Development for the Juarez Quality Systems Engineers
- Co-Lead guidance and preparation for the FDA Inspection at Ethicon Endo-Surgery – One (1) Minor Non-Conformance
- Managed the Communications Room for Corporate, ISO/GMP and FDA audits for the Juarez facility

#### Quality Systems Engineer

**Ethicon Endo-Surgery (a Johnson & Johnson Company)** – Access (Trocars)/Ligation/Endo Stapler and Cutter/Breast Care Business Units - **Ciudad Juarez, Chihuahua, Mexico**  
April 1996 – May 1999

- Supervised Eight Quality Systems Technicians for both 1<sup>st</sup> and 2<sup>nd</sup> Shift Operations
- Coordinated the Internal Audit Program for the Ethicon Endo-Surgery Juarez facility
- Provided technical support for Operational and Performance validations and product transfers (Ligation and Breast Care Business Units)

#### Automated Wet Stations (AWS) Process Engineer

**Intel Corporation** - Components Manufacturing Group - **Rio Rancho, New Mexico**  
July 1994 - April 1996

- Resolved Manufacturing Wet Etch/Clean Process and Technology Issues
- Assisted in the development of the Backend processes at Intel's Development Site (Portland, Oregon) for the Pentium Processor (125-175 MHz) chip set.

#### Surface Mount (SMT) Process Engineer

**Rockwell International** - Telecommunications Division - **El Paso, Texas**  
May 1993 - June 1994

- Responsible for Process Support and Development of Surface Mount Operations for products such as PCMCIA's, GPS units, Automotive Electronics and Modems.
- Implemented Manufacturing Process Improvements and Enhancements

#### Process Development Engineer

**IBM Corporation** - Advanced Semiconductor Technology Center - **East Fishkill, New York**  
February 1991 - March 1993

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- Resolved Manufacturing Wet Etch/Clean and Thin Films Process and Technology Issues
- Assisted in the development of the Backend processes at IBM's Development Site (East Fishkill, New York) for the 64 Meg DRAM chip set.

## EDUCATION

### **Masters in Business Administration (MBA)**

The University of Texas at El Paso (El Paso, Texas)

Date of Graduation: May 2001

### **Masters of Engineering in Microelectronics Manufacturing Engineering**

Rochester Institute of Technology (Rochester, New York)

Date of Graduation: August 1992

### **Bachelor of Science in Metallurgical Engineering**

The University of Texas at El Paso (El Paso, Texas)

Date of Graduation: December 1990

## CERTIFICATIONS/TRAINING/MEMBERSHIPS

- CQA Certified Auditor (ASQ – June 2009 – June 2018)
- Attended JJRC Auditor Training (July 2014)
- MD&D Supply Chain Compliance Education Audit Training (January 2014)
- Management Fundamentals I (Johnson & Johnson 2006)
- Black Belt Trained (EES- Johnson & Johnson Process Excellence - August 1999)
- Certificate in Management (Sponsored by AMA-1998)
- Certificate of Supervision (Sponsored by AMA-1997)

## SKILLS

Knowledge of Medical Device and Quality System Regulation such as 21 CFR Part 820 and 803 Regulations, ISO 13485:2003, ISO 9001:2008, India D&C Act (Schedule M/Schedule L), WHO/GMP/TRS, ANVISA RDC 16/2013, Japan MHLW Ministerial Ordinance No.169, 2004, Australian Therapeutic Goods (Medical Devices) Regulations 2002, China Medical Device Regulation, Canadian MDR SOR/98-282, MEDDEV 2.12.1 Rev. 8, European MDD (93/42/EEC as amended by 2007/47/EC, MEDDEV 2.7.1 Clinical Evaluation: A Guide for Manufacturers and Notified Bodies plus respective Standards and Regulation (Rev. 4) and the New EU MDR. Background in statistical methods and tools (SPC, Minitab). Trained in Six

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Sigma (Process Excellence and Lean Tools). Knowledge of Office Windows (Excel/Word/Visio and Powerpoint).

## REFERENCES

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## 10.10. CER Revision History

Revision history for CER (CER # SCN070739)

Revision Number	Date (DD Month YYYY)	Description of Change
001	17 December 2019	New MEDDEV 2.7/1, R4 CER

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## 10.11. CER Approval Signatures (E-Signatures)

### Medical Affairs Evaluator

Approver Name/Title	Signature
Medical Evaluator  Raymond Fryrear, II, MD VP Integrated Leader, ENERGY, ENDOMECH AND TORAX	

### Regulatory Affairs Evaluator

Approver Name/Title	Signature
Regulatory Evaluator  Kimberly Shoemaker Sr. Director Global Regulatory Affairs	

### Medical Operations Evaluator

Approver Name/Title	Signature
Medical Operations Evaluator  Luis Blanco Senior Manager Medical Operations	

**Declaration of Interest (DOI) Forms will be uploaded as attachments to the CER**

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