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Peripheral nerve blocks for postoperative analgesia: From traditional unencapsulated local anesthetic to liposomes, cryoneurolysis and peripheral nerve stimulation

Rodney A. Gabriel, MD, MAS, Associate Professor of Anesthesiology [1],
Brian M. Ilfeld, MD, MS, Professor of Anesthesiology [*, 1]

Department of Anesthesiology, University of California, 200 West Arbor Dr, MC 8770, San Diego, CA 92103, USA

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Peripheral nerve blocks (PNBs) using local anesthetics either via single injection or continuous perineural catheter have been the mainstay for regional anesthesia and are a vital component of postoperative multimodal opioid-sparing pain management. There are some limitations to PNBs, however, mainly its limited duration of action, but also risk of catheter-associated infection and dislodgements. Furthermore, local anesthetic-based blocks can induce sensory deficits and motor weakness, possibly increasing the risk of falling and/or decreasing the ability to participate in postoperative rehabilitation. In this review, we first discuss various local anesthetic-based PNB techniques for major surgery and then review newer modalities, including liposome bupivacaine, cryoanalgesia, and peripheral nerve stimulation; all of which may offer advantages over single and continuous local anesthetic-based PNBs.

Introduction

Multimodal management of postoperative pain following orthopedic, breast, abdominal, or thoracic surgery may involve regional anesthesia. With the ongoing national opioid crisis [1], it is crucial that

* Corresponding author.
E-mail addresses: ragabriel@ucsd.edu (R.A. Gabriel), bilfeld@ucsd.edu (B.M. Ilfeld).
[1] Outcomes Research consortium (Cleveland Clinic).

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perioperative providers implement effective interventions for surgical patients that reduce opioid requirements and pain-related complications. Local anesthetic-based single-injection or continuous peripheral nerve blocks (PNBs) have traditionally been the mainstay for regional anesthesia and provide hours to days of effective analgesia, respectively. However, there are limitations to PNBs such as shorter duration than the pain from many surgical procedures as well as block-induced muscle weakness possibly increasing the risk of falling and decreasing the ability to participate in physical therapy [2]. Furthermore, continuous nerve blocks have the potential risk for catheter-related infection and dislodgement. In this review we briefly discuss the current PNB techniques used for major surgery, followed by more recently introduced alternatives including liposomal bupivacaine [3], ultrasound-guided percutaneous cryoanalgesia [4–16], and ultrasound-guided percutaneous peripheral nerve stimulation (pPNS) [17–23].

Current trends and limitations in peripheral nerve blockade

Lower extremity surgery

Common PNB techniques used for total knee arthroplasty (TKA) include adductor canal, femoral, and iPACK (interspace between the popliteal artery and the capsule of the posterior knee) blocks. Adductor canal blocks have increasingly become the preferred block for the anterior knee (compared with femoral block) due to lesser motor involvement of the quadriceps muscle [2]. Furthermore, iPACK has been recently introduced into practice, in which sensory-only nerves from the sciatic nerve are blocked to provide analgesia to the posterior aspect of the knee [24–27]. Adductor canal and femoral nerve blocks are amenable to continuous perineural catheters and thus patients may receive multiple days-worth of analgesia; however, nerve blocks of the lower extremity may limit participation with physical therapy and increase risk of falls [28].

Patients undergoing hip arthroplasty may also benefit from regional nerve blocks, including lumbar plexus blocks [29,30], quadratus lumborum block [31], femoral nerve blocks, and fascia iliaca blocks. One retrospective study demonstrated that lumbar plexus blocks were associated with reduced opioid use, earlier and farther ambulation, and earlier discharge orders compared to lumbar epidurals [29]. A recent study demonstrated improved analgesia (reduced opioid consumption) when local anesthetic was delivered via lumbar plexus catheters as intermittent boluses versus continuous infusion [30]. Various reports have demonstrated the use of quadratus lumborum blocks for hip arthroplasty [31–33], although high quality prospective trials are still needed to prove its efficacy. Furthermore, high-dose longitudinal supra-inguinal fascia iliaca blocks reduce postoperative opioid use in patients undergoing total hip arthroplasty [34].

Other lower extremity orthopedic surgeries that may benefit from longer-term analgesia include anterior cruciate ligament repair and major foot/ankle surgery (e.g. ankle arthroplasty, hallux valgus repair). The utilization of regional anesthesia in major foot/ankle surgery have been associated with improved outcomes, including reduced opioid consumption and time to discharge [35,36]. Other regional anesthetic modalities that may prolong analgesia while minimizing motor weakness in patients undergoing lower extremity surgery would be ideal for this very large surgical population.

Upper extremity surgery

Surgical populations that may benefit from regional anesthesia include, but not limited to, those patients undergoing forearm/hand surgery (e.g. open reduction and internal fixation of radial fracture), rotator cuff repair, and total shoulder arthroplasty. Nerve blocks for the brachial plexus include interscalene blocks (covers the trunks and roots of the brachial plexus), supraclavicular block (covers the divisions), infraclavicular block (covers the cords of the brachial plexus), and axillary block (covers the terminal branches) [37]. Furthermore, individual nerves may be blocked more distally in the forearm, including the median, ulnar, radial, lateral antebrachial cutaneous nerve, and medial antebrachial cutaneous nerve. Unique concerns related to interscalene block include risk of phrenic nerve block causing respiratory distress, risk of epidural/intrathecal spread, and pneumothorax. For supraclavicular blocks, providers and patients should be aware of the risk for pneumothorax and phrenic

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nerve block. Infraclavicular nerve blocks have lesser risk of pneumothorax given that the block can be performed lateral to the apex of the lung, however it is a deeper block and risk of vascular puncture should be understood.

Alternatives to traditional local anesthetic peripheral nerve blocks

In this next section, we discuss PNB alternatives to traditional local anesthetics – each with its own potential unique advantage: 1) liposome bupivacaine providing up to 72 h of analgesia with a single injection; 2) ultrasound-guided percutaneous cryoanalgesia providing weeks to months of analgesia with a single application; and 3) ultrasound-guided pPNS providing up to 8 weeks of analgesia free of motor or sensory blockade.

Liposomal bupivacaine

By encasing bupivacaine in liposomes, the duration at which the local anesthetic is released with natural break down of the liposomal reservoir is prolonged to approximately 72 h. Liposomal bupivacaine was approved by the United States Food and Drug Administration (EXPAREL®, Pacira Pharmaceuticals, Inc., San Diego, California) in 2011 exclusively for infiltration at the surgical site, and has since gained approval for TAP blocks and interscalene blocks for major shoulder surgery. While a discussion of surgical infiltration as well as neuraxial administration [38] lays outside the PNB topic area of the present article, information is readily available from other sources [3]. Regarding PNBs, a medication that could be introduced as a single injection and provide 72 h of analgesia would be an advantage over a catheter-based regional anesthetic technique both from technical (obviating the need for catheter placement and management) and safety standpoints (decreasing the infection risk).

Early reports of using liposome bupivacaine as part of a PNB suggested effects for greater than 72 h [39,40]. When used clinically as part of a femoral nerve block, a single bolus of liposome bupivacaine appeared to provide analgesia for at least 48 h following TKA when compared to a placebo injection [41]. When compared with traditional bupivacaine HCl, three clinical trials suggest benefits of liposomal bupivacaine [42–44]. Vandepitte and colleagues reported improved pain scores in patients undergoing major shoulder surgery who received liposome bupivacaine as part of their interscalene nerve block compared to standard bupivacaine alone [44]. In this study, 52 patients undergoing major shoulder surgery were randomized to either 15 mL of unencapsulated bupivacaine 0.25% or 5 mL of unencapsulated bupivacaine 0.25% combined with 10 mL of liposome bupivacaine (133 mg) for an interscalene nerve block. Liposome bupivacaine decreased worst pain scores and improved patient satisfaction scores. Unfortunately, no pain scores other than the worst for each day were included in the report, and therefore full interpretation of the differences between treatment groups is somewhat compromised. A potential concern for using liposome bupivacaine for interscalene blocks is having a prolonged phrenic nerve block causing respiratory depression. When using unencapsulated bupivacaine, blockade of the phrenic nerve may be tolerable for the ~12–24 h of local anesthetic activity; however, 72 h of phrenic nerve blockade with liposome bupivacaine has serious concerns.

Two studies reported decreased pain scores and opioid requirements for robot-assisted hysterectomy and laparoscopic hand-assisted donor nephrectomy when liposome bupivacaine was used in TAP blocks compared with bupivacaine HCl [42,43]. Ultrasound-guided bilateral subcostal TAP blocks were performed in patients undergoing laparoscopic hand-assisted donor nephrectomy and were randomized to either liposome bupivacaine or unencapsulated bupivacaine. Liposome bupivacaine provided superior analgesia up to 72 h after injection compared with the unencapsulated version. Unfortunately, public registration of these trials occurred only following enrollment concluded and no primary outcome was reported *a priori*, thus decreasing confidence in the results.

In summary, there is still much needed evidence comparing liposomal bupivacaine used as part of PNBs compared to single-injection unencapsulated bupivacaine and/or continuous PNBs. Cost-benefit analyses should be included within any future trials. If future studies can demonstrate superiority or even non-inferiority relative to CPNB, the days of inserting and managing perineural catheters will probably come to a close.

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Ultrasound-guided percutaneous cryoneurolysis

Cryoneurolysis, also termed "cryoablation" or "cryoanalgesia", is a U.S. Food and Drug Administration-cleared modality used to reversibly ablate peripheral nerves with extremely cold temperatures, subsequently providing analgesia until the nerve regenerates which is measured in weeks to months. The modern cryoprobe consists of a hollow tube with a smaller inner tube (Fig. 1). Highly pressurized gas (e.g., nitrous oxide or carbon dioxide) travels from the proximal aspect of the tube to the distal portion where it is passes through a narrow annulus, allowing the gas to rapidly expand within the closed tip [41]. Due to the Joule-Thomson effect, a drop of temperature to approximately −70 °C accompanies the drop in pressure, creating an ice ball at the tip of the probe. The cold gas is vented back proximally through the outer tube, therefore ensuring that no gas enters or remains in the patient's tissues.

At the location of application along the nerve, Wallerian degeneration (breakdown of the axon) occurs which results in partial-to-complete sensory and/or motor blockade. The endo-, peri-, and epineurium remain intact so that regeneration of the axon may occur over the next few weeks to months along these structures [45].

Initially, cryoanalgesia had been popularized in treating chronic pain over the past several decades [45]. Its use for management of acute postoperative pain originally was limited to intraoperative application via surgical exposure of target nerves [4–16]. Many of these studies targeted post-thoracotomy pain in which cryoanalgesia was applied to intercostal nerves intraoperatively by the surgeon under direct vision [5–8,10,11,13,14]. Percutaneous administration under ultrasound guidance is now an option which opens the door for anesthesiologist and other providers to administer cryoneurolysis blocks pre- and post-operatively (Fig. 2) [22,46–48]. Accessibility is furthered with the recent advent of portable cryoneurolysis devices [49].

Dasa and colleagues performed a blind-approach using landmarks to block the anterior femoral cutaneous nerve and the infrapatellar branch of the saphenous nerve for management of post-TKA pain [9]. These two nerves provide sensory innervation to the anterior aspect of the knee. Because of their superficial and predictable locations, applying cryoanalgesia with landmark techniques is technically feasible. This retrospective study consisting of 100 patients reported a reduced rate of prolonged hospitalization and opioid consumption up to 12 weeks following TKA. Similarly, in a separate study this same technique was also applied to the infrapatellar branch of the saphenous nerve to treat non-surgical pain associated with knee osteoarthritis, which demonstrated improved pain scores and a health-related functional index compared to the control group [50].

The use of ultrasound-guided percutaneous approaches for cryoanalgesia has been recently described in case series [46–48]. In one series [46], ultrasound-guided percutaneous cryoanalgesia was performed on the infrapatellar branch of the saphenous nerve preoperatively in patients undergoing TKA and to the suprascapular nerve just superior to the suprascapular notch in patients who underwent rotator cuff repair. All individuals in this series experienced excellent postoperative analgesia and had decreased opioid consumption compared to historic controls. No adverse events were reported. In

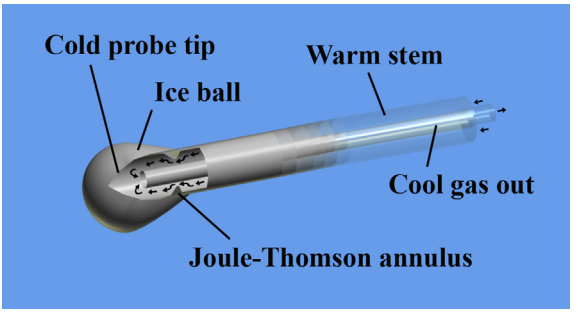

Fig. 1. Schematic of how gas travels within the cryoanalgesia probe (used with permission, Brian M. Ilfeld, MD, MS).

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Fig. 2. Movable console for cryoanalgesia. Used with permission (Brian M. Ilfeld, MD, MS).

another case series [47], ultrasound-guided percutaneous cryoanalgesia was used to treat (1) intercostal nerves for refractory pain following a nephrolithotomy procedure; (2) subcostal and intercostal nerves in a patient with hip pain following iliac crest bone grafting; and (3) the saphenous, sural, posterior tibial, and superficial peroneal nerves to help manage pain in a patient with burn injuries to the foot. In all cases, patients reported adequate analgesia for at least 2 weeks following treatment with no subsequent nerve injury or neuropathic pain. No other adverse events occurred in relation to cryoanalgesia. In the third case series [48], cryoanalgesia of the involved major nerves was performed in 3 patients who underwent major limb amputation. All reported profound analgesia postoperatively for weeks to months and did not develop phantom limb pain up to 6 months follow-up.

Cryoanalgesia has relatively few risks and contraindications. The relative contraindications include Reynaud's syndrome, cryoglobulinemia, and cold urticarial. Potential complications include those also associated with traditional needle-based percutaneous regional anesthesia techniques – including bleeding, infection, and nerve injury for direct trauma. Furthermore, the duration of nerve blockade is variable – weeks to months – with a prolonged sensory and motor blockade may not be appropriate in various clinical scenarios. As with any modality that involves a peripheral nerve, there is a theoretical risk of nerve injury; however, cryoneurolysis has been in clinical use for well-over five decades without a single published case of permanent nerve injury or neuroma.

However, two randomized, controlled trials reported an increase in neuropathic pain associated with cryoneurolysis when administered via surgical incision for thoracotomy relative to controls [7,10].

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Caution is warranted since multiple comparisons was not controlled for in these two investigations; and, 14 other randomized, controlled trials involving thoracotomy failed to detect any increased risk [46]. Furthermore, cryoanalgesia was applied via surgical exposure with possible nerve retraction. This is significant because preclinical evidence suggests that any physical manipulation of the nerve at the time of cryoneurolysis may be a mitigating factor in producing a sustained chronic pain condition [51]. The combination of nerve ablation from the cold temperature and nerve retraction may have contributed to the subsequent neuropathic pain.

In summary, ultrasound-guided percutaneous cryoneurolyosis is a U.S. Food and Drug Administration-cleared promising alternative to CPNB for certain surgical procedures where long-term blockade of sensory and/or motor nerves is desired. This modality provides an option for "very long" analgesia (measured up to months) with a single application. It also avoids other drawbacks associated with perineural catheters such as an increased risk of infection, catheter dislodgement, and patient burden carrying a reservoir bag.

Ultrasound-guided percutaneous peripheral nerve stimulation (PNS)

The technique of administering an electric current to a nerve is termed "neuromodulation." The mechanism which induces analgesia remains hotly debated; but, "gate control theory" is a common hypothesis in which electrical activation of large-diameter myelinated afferent peripheral nerve fibers inhibits the signal from the smaller pain fibers to the central nervous system at the level of the spinal cord [52]. The use of ultrasound-guided pPNS to treat acute postoperative pain is relatively novel and has been recently described for hallux valgus correction [17], total knee arthroplasty [18,20], rotator cuff repair [23], and anterior cruciate ligament repair [21]. Prior to these published reports, its use was mainly in treating chronic pain states. Generally, the process of placement and testing leads are too invasive and time-consuming to be appropriate for use in a fast-paced perioperative environment (i.e. performing preoperatively on the day of surgery). However, extremely small, insulated electrical leads were developed that allow more rapid placement via a percutaneous approach guided by ultrasound (Fig. 3) [53,54]. One device cleared exclusively for the treatment of chronic pain (Stimwave Technologies Incorporated Freedom SCS System, Pompano Beach, FL) uses an implantable lead and an externally worn transmitter to power the device transdermally. Such wireless devices avoid the need to use a fully implanted battery that is hardwired under the skin to the electrodes [55–57]. However, at the time of this writing there is only a single lead/stimulator combination cleared for use in the treatment of acute pain (Endura, insert SPR info).

There has been one small clinical trial published that describes the use of ultrasound-guided pPNS for hallux valgus correction (i.e. bunionectomy) [17]. This study included 7 subjects who had PNS leads percutaneously placed adjacent to the sciatic nerve preoperatively using ultrasound guidance. No subjects demonstrated a weakness in plantar flexion with the application of stimulation. Within the recovery room and in a randomized fashion, subjects received either 5 min of active stimulation followed by 5 min of sham stimulation; or these treatments in the reverse order. A decrease in pain was noted during the activation period in both treatment groups. Following this 10-min period, all subjects received 30 min of active stimulation, which led to a decrease in pain to 50% of baseline. Both cohorts received continuous stimulation thereafter until lead removal about 2–4 weeks postoperatively and reported minimal pain and opioid requirements relative to historic controls. This proof-of-concept feasibility study suggests the promise of pPNS for foot and ankle surgery.

Fig. 3. Illustration of percutaneous needle with electric lead (used with permission, Brian M. Ilfeld, MD, MS).

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Another study investigated utilization of ultrasound-guided pPNS for rotator cuff repairs during the immediate postoperative period [23]. Fourteen patients received preoperative placement of implanted leads to target either the suprascapular nerve or brachial plexus trunks/roots. In the recovery room, they underwent the same randomized treatment as for the study involving hallux valgus correction (5 min stimulation and 5 min sham followed by 2–4 weeks of active stimulation for all) [17]. Clinically significant analgesia was not appreciable for subjects who received pPNS to the suprascapular nerve. However, subjects who received lead placements through the middle scalene muscle posterolateral to the brachial plexus reported meaningful analgesia. During the first two postoperative weeks, the median daily pain score was 1 or less and opioid consumption averaged less than 5 mg of oxycodone daily.

A third pilot study using the same protocol inserted leads adjacent to the femoral nerve for subjects undergoing anterior cruciate ligament reconstruction [21]. Postoperatively, 80% of patients required additional continuous adductor canal nerve block for rescue analgesia during the first 2 days after surgery, suggesting inadequate analgesia relative to the subjects undergoing shoulder and foot surgery. It remains unknown if this is due to increased pain following the knee surgery relative to the other two anatomic locations (doubtful); inferior analgesia with femoral nerve neuromodulation (also doubtful due to other positive clinical trials); or knee pain originating with the obturator and sciatic nerves (probable). Following the initial 2 postoperative days, both pain scores and opioid use were minimal.

Ultrasound-guided pPNS has also been described in providing analgesia in patients undergoing knee arthroplasty [19]. One of the major concerns with continuous femoral nerve blocks for knee surgery is the increased risk of falling due to induced quadriceps femoris weakness [58]. Thus, pPNS has some very important advantages over CPNB, including avoidance of motor and sensory blockade, and leads that may remain *in situ* for up to two months with a dramatically lower risk of infection [59].

Three studies have demonstrated the use of neuromodulation following knee arthroplasty [18,60,61]. In one pilot study, femoral (and in most cases sciatic) lead(s) were placed 8–58 days following surgery in 5 subjects with pain poorly controlled with oral analgesics which subsequently led to immediate analgesia for all subjects [18]. In another study, leads were placed *preoperatively* in 7 patients and remained *in situ* for up to 6 weeks postoperatively [61]. Pain was reported to be well-controlled in 88% of patients for the first two weeks, in which 4 required no opioids. This is a clinically significant improvement when compared to studies reporting median time to opioid cessation was about 2 months [62–65] with a 1-month opioid-independence rate of 11–33% for patients having the same surgical procedure within the United States [66].

Initial, limited experience with pPNS used to treat acute pain following surgery suggests minimal risks associated with the technique [19,59,67]. Infection has been reported for helically coiled leads, but the risk appears extraordinarily small as reported by one meta-analysis (fewer than 1 infection per 32,000 indwelling days), especially when compared with the 1% risk for perineural catheters just within the first few postoperative days [59]. The rare infection risk is likely due to the helical coil design, which allows tissue ingrowth between coils that creates a peri-lead seal that blocks the passage of bacteria. Nerve injury has not been reported, possibly because the lead insertion needle optimally remains 1–2 cm distant from the target nerve, greatly decreasing the risk of direct needle/lead-nerve contact with ultrasound guidance [68]. There is also the non-insignificant risk (8–20%, depending on the anatomic location) of lead dislodgement/fracture, which was noted in some of the mentioned pilot studies [17,20] in addition to intramuscular insertion used for over two decades [54]. In more than 200 patients with a fractured lead, the remnants were uniformly left *in situ* without any subsequent negative sequelae [19].

Conclusions

In this review, we discuss the current practices of regional anesthesia for common major surgical procedures. PNB can significantly decrease postoperative opioid use, particularly for major abdominal, extremity, and chest wall surgery. The duration of analgesia is limited by the duration of action of the local anesthetic used, however, which can range from hours with a single administration to days with prolonged administration using a perineural catheter. If perineural liposome bupivacaine ultimately proves to prolong postoperative analgesia beyond the duration of unencapsulated bupivacaine, multiple days of analgesia may be provided with a single injection without the patient burden carrying an infusion pump and local

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anesthetic reservoir. When postoperative pain is anticipated to last beyond a few days, cryoneurolysis is an option to provide multiple weeks of analgesia. However, due to the potentially dense sensory and motor block along with the unpredictable duration of action, the applications for cryoanalgesia are limited. pPNS is an exciting analgesic possibility in that it avoids the sensory and motor block of local anesthetics and cryoneurolysis, yet may provide up to 60 days of postoperative analgesia. However, validation is required for all of these relatively new postoperative analgesics, along with a determination of their relative benefits and risks. Regardless, there is now at least the opportunity to extend our postoperative PNB armamentarium beyond simply local anesthetics.

Practice points

- PNBs are a vital component of postoperative multimodal opioid-sparing pain management.
- Limitations to PNBs include shorter duration than the pain from many surgical procedures; catheter-related infection and dislodgement; as well as block-induced muscle weakness possibly increasing the risk of falling and decreasing the ability to participate in physical therapy.
- Longer term analgesia may be provided through more novel acute pain modalities including liposome bupivacaine (compared to single injection of unencapsulated bupivacaine), cryoanalgesia, and peripheral nerve stimulation.

Research agenda

- Further research is needed to determine equivalency or superiority of liposome bupivacaine compared to continuous PNBs via perineural catheter.
- Further research is needed to determine the efficacy and safety profile of ultrasound-guided cryoanalgesia for acute pain indications.
- Further research is needed to determine the efficacy and safety profile of ultrasound-guided peripheral nerve stimulation for acute pain indications.

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References

[1] Kharasch ED, Brunt LM. Perioperative opioids and public health. Anesthesiology 2016;124:960–5.
[2] Ilfeld BM. Continuous peripheral nerve blocks: an update of the published evidence and comparison with novel, alternative analgesic modalities. Anesth Analg 2017;124:308–35.
[3] Ilfeld BM, Gabriel RA, Eisenach JC. Liposomal bupivacaine infiltration for knee arthroplasty: significant analgesic benefits or just a bunch of fat? Anesthesiology 2018;129:623–6.
[4] Graves C, Idowu O, Lee S, et al. Intraoperative cryoanalgesia for managing pain after the Nuss procedure. J Pediatr Surg 2017;52:920–4.
[5] Ba YF, Li XD, Zhang X, et al. Comparison of the analgesic effects of cryoanalgesia vs. parecoxib for lung cancer patients after lobectomy. Surg Today 2015;45:1250–4.

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[6] Sepsas E, Misthos P, Anagnostopulu M, et al. The role of intercostal cryoanalgesia in post-thoracotomy analgesia. Interact Cardiovasc Thorac Surg 2013;16:814–8.
[7] Mustola ST, Lempinen J, Saimanen E, et al. Efficacy of thoracic epidural analgesia with or without intercostal nerve cryoanalgesia for postthoracotomy pain. Ann Thorac Surg 2011;91:869–73.
[8] Keller BA, Kabagambe SK, Becker JC, et al. Intercostal nerve cryoablation versus thoracic epidural catheters for postoperative analgesia following pectus excavatum repair: preliminary outcomes in twenty-six cryoablation patients. J Pediatr Surg 2016;51:2033–8.
[9] Dasa V, Lensing G, Parsons M, et al. Percutaneous freezing of sensory nerves prior to total knee arthroplasty. Knee 2016;23:523–8.
[10] Ju H, Feng Y, Yang BX, et al. Comparison of epidural analgesia and intercostal nerve cryoanalgesia for post-thoracotomy pain control. Eur J Pain 2008;12:378–84.
[11] Yang MK, Cho CH, Kim YC. The effects of cryoanalgesia combined with thoracic epidural analgesia in patients undergoing thoracotomy. Anaesthesia 2004;59:1073–7.
[12] Gwak MS, Yang M, Hahm TS, et al. Effect of cryoanalgesia combined with intravenous continuous analgesia in thoracotomy patients. J Korean Med Sci 2004;19:74–8.
[13] Moorjani N, Zhao F, Tian Y, et al. Effects of cryoanalgesia on post-thoracotomy pain and on the structure of intercostal nerves: a human prospective randomized trial and a histological study. Eur J Cardiothorac Surg 2001;20:502–7.
[14] Bucerius J, Metz S, Walther T, et al. Pain is significantly reduced by cryoablation therapy in patients with lateral minithoracotomy. Ann Thorac Surg 2000;70:1100–4.
[15] Robinson SR, Purdie GL. Reducing post-tonsillectomy pain with cryoanalgesia: a randomized controlled trial. Laryngoscope 2000;110:1128–31.
[16] Callesen T, Bech K, Thorup J, et al. Cryoanalgesia: effect on postherniorrhaphy pain. Anesth Analg 1998;87:896–9.
*[17] Ilfeld BM, Gabriel RA, Said ET, et al. Ultrasound-guided percutaneous peripheral nerve stimulation: neuromodulation of the sciatic nerve for postoperative analgesia following ambulatory foot surgery, a proof-of-concept study. Reg Anesth Pain Med 2018;43:580–9.
*[18] Ilfeld BM, Gilmore CA, Grant SA, et al. Ultrasound-guided percutaneous peripheral nerve stimulation for analgesia following total knee arthroplasty: a prospective feasibility study. J Orthop Surg Res 2017;12:4.
*[19] Ilfeld BM, Grant SA. Ultrasound-guided percutaneous peripheral nerve stimulation for postoperative analgesia: could neurostimulation replace continuous peripheral nerve blocks? Reg Anesth Pain Med 2016;41:720–2.
*[20] Ilfeld BM, Grant SA, Gilmore CA, et al. Neurostimulation for postsurgical analgesia: a novel system enabling ultrasound-guided percutaneous peripheral nerve stimulation. Pain Pract 2017;17:892–901.
*[21] Ilfeld BM, Said ET, Finneran JJt, et al. Ultrasound-guided percutaneous peripheral nerve stimulation: neuromodulation of the femoral nerve for postoperative analgesia following ambulatory anterior cruciate ligament reconstruction: a proof of concept study. Neuromodulation 2018 [Epub ahead of print].
[22] Gabriel RA, Ilfeld BM. Novel methodologies in regional anesthesia for knee arthroplasty. Anesthesiol Clin 2018;36:387–401.
*[23] Ilfeld BM, Finneran JJ, Gabriel RA, et al. Ultrasound-guided percutaneous peripheral nerve stimulation: neuromodulation of the suprascapular nerve and brachial plexus for postoperative analgesia following ambulatory rotator cuff repair, a proof of concept study. Reg Anesth Pain Med 2018 [Epub ahead of print].
[24] Tran J, Giron Arango L, Peng P, et al. Evaluation of the iPACK block injectate spread: a cadaveric study. Reg Anesth Pain Med 2019 [Epub ahead of print].
[25] Kandarian B, Indelli PF, Sinha S, et al. Implementation of the IPACK (Infiltration between the Popliteal Artery and Capsule of the Knee) block into a multimodal analgesic pathway for total knee replacement. Korean J Anesthesiol 2019 [Epub ahead of print].
[26] Kim DH, Beathe JC, Lin Y, et al. Addition of infiltration between the popliteal artery and the capsule of the posterior knee and adductor canal block to periarticular injection enhances postoperative pain control in total knee arthroplasty: a randomized controlled trial. Anesth Analg 2018 [Epub ahead of print].
[27] Sankineani SR, Reddy ARC, Eachempati KK, et al. Comparison of adductor canal block and IPACK block (interspace between the popliteal artery and the capsule of the posterior knee) with adductor canal block alone after total knee arthroplasty: a prospective control trial on pain and knee function in immediate postoperative period. Eur J Orthop Surg Traumatol 2018;28:1391–5.
[28] Elkassabany NM, Antosh S, Ahmed M, et al. The risk of falls after total knee arthroplasty with the use of a femoral nerve block versus an adductor canal block: a double-blinded randomized controlled study. Anesth Analg 2016;122:1696–703.
[29] Wilson SH, Wolf BJ, Algendy AA, et al. Comparison of lumbar epidurals and lumbar plexus nerve blocks for analgesia following primary total hip arthroplasty: a retrospective analysis. J Arthroplasty 2017;32:635–40.
[30] Ueshima H, Tanaka N, Otake H. Greater analgesic effect with intermittent compared with continuous mode of lumbar plexus block for total hip arthroplasty: a randomized controlled trial. Reg Anesth Pain Med 2019;44:632–6.
[31] Ueshima H, Otake H. Ultrasound-guided supra-iliac anterior quadratus lumborum block provides effective perioperative analgesia for total hip arthroplasty. J Clin Anesth 2019;59:2.
[32] Stuart Green M, Ryan Hoffman C, Iqbal U, et al. Transmuscular quadratus lumborum block reduces length of stay in patients receiving total hip arthroplasty. Anesth Pain Med 2018;8:e80233.
[33] Bak H, Bang S, Yoo S, et al. The continuous quadratus lumborum block for multimodal analgesia after total hip arthroplasty. Korean J Anesthesiol 2019 [Epub ahead of print].
[34] Desmet M, Vermeylen K, Van Herreweghe I, et al. A longitudinal supra-inguinal fascia iliaca compartment block reduces morphine consumption after total hip arthroplasty. Reg Anesth Pain Med 2017;42:327–33.
[35] Bjorn S, Wong WY, Baas J, et al. The importance of the saphenous nerve block for analgesia following major ankle surgery: a randomized, controlled, double-blind study. Reg Anesth Pain Med 2018;43:474–9.
[36] White PF, Issioui T, Skrivanek GD, et al. The use of a continuous popliteal sciatic nerve block after surgery involving the foot and ankle: does it improve the quality of recovery? Anesth Analg 2003;97:1303–9.

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[37] Lin E, Choi J, Hadzic A. Peripheral nerve blocks for outpatient surgery: evidence-based indications. Curr Opin Anaesthesiol 2013;26:467–74.
[38] Viscusi ER, Candiotti KA, Onel E, et al. The pharmacokinetics and pharmacodynamics of liposome bupivacaine administered via a single epidural injection to healthy volunteers. Reg Anesth Pain Med 2012;37:616–22.
[39] Kopacz DJ, Lacouture PG, Wu D, et al. The dose response and effects of dexamethasone on bupivacaine microcapsules for intercostal blockade (T9 to T11) in healthy volunteers. Anesth Analg 2003;96:576–82 [table of contents].
[40] Ilfeld BM, Malhotra N, Furnish TJ, et al. Liposomal bupivacaine as a single-injection peripheral nerve block: a dose–response study. Anesth Analg 2013;117:1248–56.
[41] Hadzic A, Minkowitz HS, Melson TI, et al. Liposome bupivacaine femoral nerve block for postsurgical analgesia after total knee arthroplasty. Anesthesiology 2016;124:1372–83.
[42] Hutchins J, Delaney D, Vogel RI, et al. Ultrasound guided subcostal transversus abdominis plane (TAP) infiltration with liposomal bupivacaine for patients undergoing robotic assisted hysterectomy: a prospective randomized controlled study. Gynecol Oncol 2015;138:609–13.
[43] Hutchins JL, Kesha R, Blanco F, et al. Ultrasound-guided subcostal transversus abdominis plane blocks with liposomal bupivacaine vs. non-liposomal bupivacaine for postoperative pain control after laparoscopic hand-assisted donor nephrectomy: a prospective randomised observer-blinded study. Anaesthesia 2016;71:930–7.
[44] Vandepitte C, Kuroda M, Witvrouw R, et al. Addition of liposome bupivacaine to bupivacaine HCl versus bupivacaine HCl alone for interscalene brachial plexus block in patients having major shoulder surgery. Reg Anesth Pain Med 2017;42:334–41.
*[45] Trescot AM. Cryoanalgesia in interventional pain management. Pain Physician 2003;6:345–60.
*[46] Ilfeld BM, Gabriel RA, Trescot AM. Ultrasound-guided percutaneous cryoneurolysis providing postoperative analgesia lasting many weeks following a single administration: a replacement for continuous peripheral nerve blocks?: a case report. Korean J Anesthesiol 2017;70:567–70.
*[47] Gabriel RA, Finneran JJ, Asokan D, et al. Ultrasound-guided percutaneous cryoneurolysis for acute pain management: a case report. A A Case Rep 2017;9:129–32.
*[48] Gabriel RA, Finneran JJt, Trescot AM, et al. Ultrasound-guided percutaneous cryoneurolysis for postoperative analgesia after limb amputation: a case series. A A Pract 2019;12:231–4.
[49] Ilfeld BM, Preciado J, Trescot AM. Novel cryoneurolysis device for the treatment of sensory and motor peripheral nerves. Expert Rev Med Devices 2016;13:713–25.
[50] Radnovich R, Scott D, Patel AT, et al. Cryoneurolysis to treat the pain and symptoms of knee osteoarthritis: a multicenter, randomized, double-blind, sham-controlled trial. Osteoarthritis Cartilage 2017;25:1247–56.
[51] Myers RR, Heckman HM, Powell HC. Axonal viability and the persistence of thermal hyperalgesia after partial freeze lesions of nerve. J Neurol Sci 1996;139:28–38.
[52] Melzack R, Wall PD. Pain mechanisms: a new theory. Science 1965;150:971–9.
[53] Deer TR, Levy RM, Rosenfeld EL. Prospective clinical study of a new implantable peripheral nerve stimulation device to treat chronic pain. Clin J Pain 2010;26:359–72.
[54] Yu DT, Chae J, Walker ME, et al. Percutaneous intramuscular neuromuscular electric stimulation for the treatment of shoulder subluxation and pain in patients with chronic hemiplegia: a pilot study. Arch Phys Med Rehabil 2001;82:20–5.
[55] Shellock FG, Audet-Griffin AJ. Evaluation of magnetic resonance imaging issues for a wirelessly powered lead used for epidural, spinal cord stimulation. Neuromodulation 2014;17:334–9. Discussion 9.
[56] Weiner RL, Yeung A, Montes Garcia C, et al. Treatment of FBSS low back pain with a novel percutaneous DRG wireless stimulator: pilot and feasibility study. Pain Med 2016;17:1911–6.
[57] Herschkowitz D, Kubias J. Wireless peripheral nerve stimulation for complex regional pain syndrome type I of the upper extremity: a case illustration introducing a novel technology. Scand J Pain 2018;18:555–60.
[58] Ilfeld BM, Duke KB, Donohue MC. The association between lower extremity continuous peripheral nerve blocks and patient falls after knee and hip arthroplasty. Anesth Analg 2010;111:1552–4.
[59] Ilfeld BM, Gabriel RA, Saulino MF, et al. Infection rates of electrical leads used for percutaneous neurostimulation of the peripheral nervous system. Pain Pract 2017;17:753–62.
[60] Ilfeld BM, Ball ST, Gabriel RA, et al. Perioperative percutaneous peripheral nerve stimulation utilizing preoperative lead placement for the treatment of postoperative pain [abstract] Reg Anesth Pain Med 2017 [Epub ahead of print].
[61] Ilfeld BM, Gilmore CA, Chae J, et al. Percutaneous peripheranl nerve stimulation for the treatment of postoperative pain following total knee arthroplasty [abstract]. In: North American neuromodulation society conference; 2016 [Epub ahead of print].
[62] Namba RS, Inacio MC, Pratt NL, et al. Postoperative opioid use as an early indication of total hip arthroplasty failure. Acta Orthop 2016;87(Suppl. 1):37–43.
[63] Hah JM, Mackey S, Barelka PL, et al. Self-loathing aspects of depression reduce postoperative opioid cessation rate. Pain Med 2014;15:954–64.
[64] Carroll I, Barelka P, Wang CK, et al. A pilot cohort study of the determinants of longitudinal opioid use after surgery. Anesth Analg 2012;115:694–702.
[65] Rozet I, Nishio I, Robbertze R, et al. Prolonged opioid use after knee arthroscopy in military veterans. Anesth Analg 2014;119:454–9.
[66] Goesling J, Moser SE, Zaidi B, et al. Trends and predictors of opioid use after total knee and total hip arthroplasty. Pain 2016;157:1259–65.
[67] Shellock FG, Zare A, Ilfeld BM, et al. In vitro magnetic resonance imaging evaluation of fragmented, open-coil, percutaneous peripheral nerve stimulation leads. Neuromodulation 2017 [Epub ahead of print].
[68] Mekhail NA, Cheng J, Narouze S, et al. Clinical applications of neurostimulation: forty years later. Pain Pract 2010;10:103–12.

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