

Instrumental requirements for minimal invasive fetal surgery

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Minimal invasive intrauterine interventions have gained their place in fetal medicine. Interventions on the placenta, umbilical cord, fetal membranes or on the fetus require special endoscopes with their respective sheaths, cannulas and additional instruments. Instruments for fetal therapy are purpose designed for the procedure of interest and most gynaecologists are therefore not familiar with them. We review the currently available

instrumentation used during operations for complicated monochorionic multiple pregnancies, congenital diaphragmatic hernia, amniotic band syndrome, urinary tract obstruction and hydrothorax.

Keywords Congenital diaphragmatic hernia (CDH), fetal therapy, fetocide, fetoscopy, twin-to-twin transfusion syndrome (TTTS).

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Introduction

At the time of its introduction in the 1970s, fetoscopy was performed for diagnostic as well as therapeutic purposes, for example to obtain fetal blood in the diagnosis of haemoglobinopathies or to administer blood under direct visual control, to demonstrate pathognomic malformations or to biopsy the fetal skin. The technique did not become widely implemented because of its required skills, invasiveness and the lack of appropriate instruments. Later, it became nearly completely abandoned as ultrasound guidance could be used for the same purposes.

Video endoscopy boosted operative endoscopy in the 1980s mainly by miniaturisation of telescopes as well as the use of lightweight cameras.^{1,2} The creation of 'Eurofoetus', a research and development project supported by the European Commission, formalised a collaboration between European fetal medicine specialists and a manufacturer of endoscopic instruments (Karl Storz, Tuttlingen, Germany). European public funds made it possible to manufacture purpose-designed fetoscopes and instruments that would commercially never have been viable because indications are rare and as the perceived medicolegal risks of fetal intervention are high. The first clinical applications were complicated monochorionic twin pregnancies, and a second European research and development project 'Eurotwin2twin' centred on this topic, with as

main deliverable a successful clinical randomised trial comparing fetoscopic laser coagulation and amniodrainage to treat twin-to-twin transfusion syndrome (TTTS).³ Since then, fetoscopy has gained an established place in fetal medicine and is now used to operate on the placenta, the umbilical cord, the fetal membranes as well as the fetus.^{4,5}

Although operative fetoscopy shares some hardware generic to endoscopic surgery, it also requires special endoscopes with a variety of sheaths, cannulas and instruments adapted to the procedure of interest. The purpose of this review was to introduce the obstetricians who are not familiar with these and other devices used in fetal therapy, with the exception of those used for fetal cardiovascular interventions, which is practised only in very few centres at this moment.

Generic instruments

Fetoscopes and embryoscopes

The endoscopes that are used today in gynaecology are between 2.0 and 10.0 mm in diameter, 20–40 cm in length, have typically a rod lens system and an eye cap at the end to which the camera connects. The current spectrum of fetoscopes in contrast has a working length of 20–30 cm to enable working anywhere in a (polyhydramniotic) uterine cavity, and diameters of 1.0–3.8 mm. Their length may occasionally

fall short in the case of obesity. In some, the eyepiece has been moved away (deported) from the working part of the endoscope, reducing weight and allowing manipulation in a similar manner to using needles under ultrasound guidance. In an effort to reduce the scope diameter, and hence the invasiveness of the procedure, a technical compromise between image quality and minimal diameter has been made. This introduced the need of fibre endoscopes that allow more light instillation and higher resolution at a smaller (<2.0 mm) diameter. To permit different angles of view, scopes with angled lenses as well as curved sheaths for the fibre endoscopes were developed (Table 1).

Clinically two types are frequently used. *Rod lens endoscopes* (Figure 1A, insert) contain fibres for light transmission, but the image itself is focused by a Hopkins® rod lens system. This technology is present in most laparoscopes and hysteroscopes. It offers high resolution and a panoramic (opening angle 70° to 95°) either straightforward view (0°; Figure 1D) or forward oblique views (e.g. 12°, 30° and 70°; Figure 1E). Rod lens scopes are by definition straight, stiff and, at small diameter, frail. The length allowing optimal light and image transmission is dependent on the diameter of the endoscope. For a (empirically) defined working length of 26 cm, scopes of 2.0 mm ended up to be the lower limit of light instillation and image transmission that is technically feasible today. The introduction of *fibre endoscopes* (Figure 1A) made smaller diameter telescopes for a similar length possible. Here, light and image transmission occurs through optical fibres. Resolution is determined by the number of individual imaging fibres used (up to 50 000 pixels today and still increasing). Adding

fibres avoids a honeycomb picture, increases light instillation and image conductance, but cuts on the flexibility of the fetoscope. Fibrescopes theoretically give a straightforward view, unless a lens system that enables angled view up to 12° (e.g. 3.8 mm Mini-Laparoscope 8746.401, Richard Wolf, Vernon Hills, IL, USA) is glued to the tip. Alternatively 0° scopes may be inserted in a sheath that is slightly bent. Theoretically *steerable endoscopes* would be helpful as they can be angled acutely and come in variable lengths. However, the mechanical elements require space within the endoscope, so that the endoscope would become unacceptably large in diameter for a reasonable resolution. Conversely, currently available steerable endoscopes do not offer enough light transmission and resolution.

Telescopes used beyond 12 weeks are usually referred to as *fetoscopes*, while those used before are *embryoscopes*. The latter are shorter (20 cm) and smaller in diameter (1.0 mm; 10 000 pixels) but light requirements early in pregnancy are less.⁶

Sheaths, cannulas and uterine access

Fetoscopic sheaths

Endoscopes are used within a sheath that has different functions. It is a protection for the scope and also a guide. At times, it will be curved to force the fibre endoscope into an appropriate angle to the target (Figure 1B). In addition, the sheath can be enlarged to allow irrigation fluids or instruments through 'Luer'-lock connections, side ports or operative canals of variable diameters. Operative canals keep instruments in a fixed position to the scope, but this is at the expense of an increase in diameter. Sheaths can be round

Table 1. Frequently used endoscopes for minimal invasive fetal surgery

Outer diameter (mm)	Working length (cm)	Angle of view	Type	Flexibility	Opening angle	Additional details	Company	Reference Nr
1.0	20.0	0°	Fibre	Semi-rigid	70°	Deported eyepiece	Storz	11510 A
1.2	30.6	0°	Fibre	Semi-rigid	70°	–	Storz	11505 AA
1.3	30.6	0°	Fibre	Semi-rigid	90°	Deported eyepiece	Storz	11540 AA
2.0	27.0	0°	Fibre	Semi-rigid	–	–	Wolf	8754.401
2.0	30.0	0°	Fibre	Semi-rigid	95°	Deported eyepiece	Storz	11630 AA
3.5	30.0	30°	Fibre	Semi-rigid	–	–	Wolf	8930.422S01
3.8	30.0	12°	Fibre	Semi-rigid	–	1.67mm working canal	Wolf	8746.401
2.0	26.0	0°	Rod lens	Rigid	–	–	Storz	26008 AA
2.0	26.0	12°	Rod lens	Rigid	–	–	Storz	26008 FUA
2.0	26.0	30°	Rod lens	Rigid	–	–	Storz	26008 BUA
3.0	60.0	0°	Fibre	Flexible, steerable	–	1.0mm working canal	Wolf	7331.001

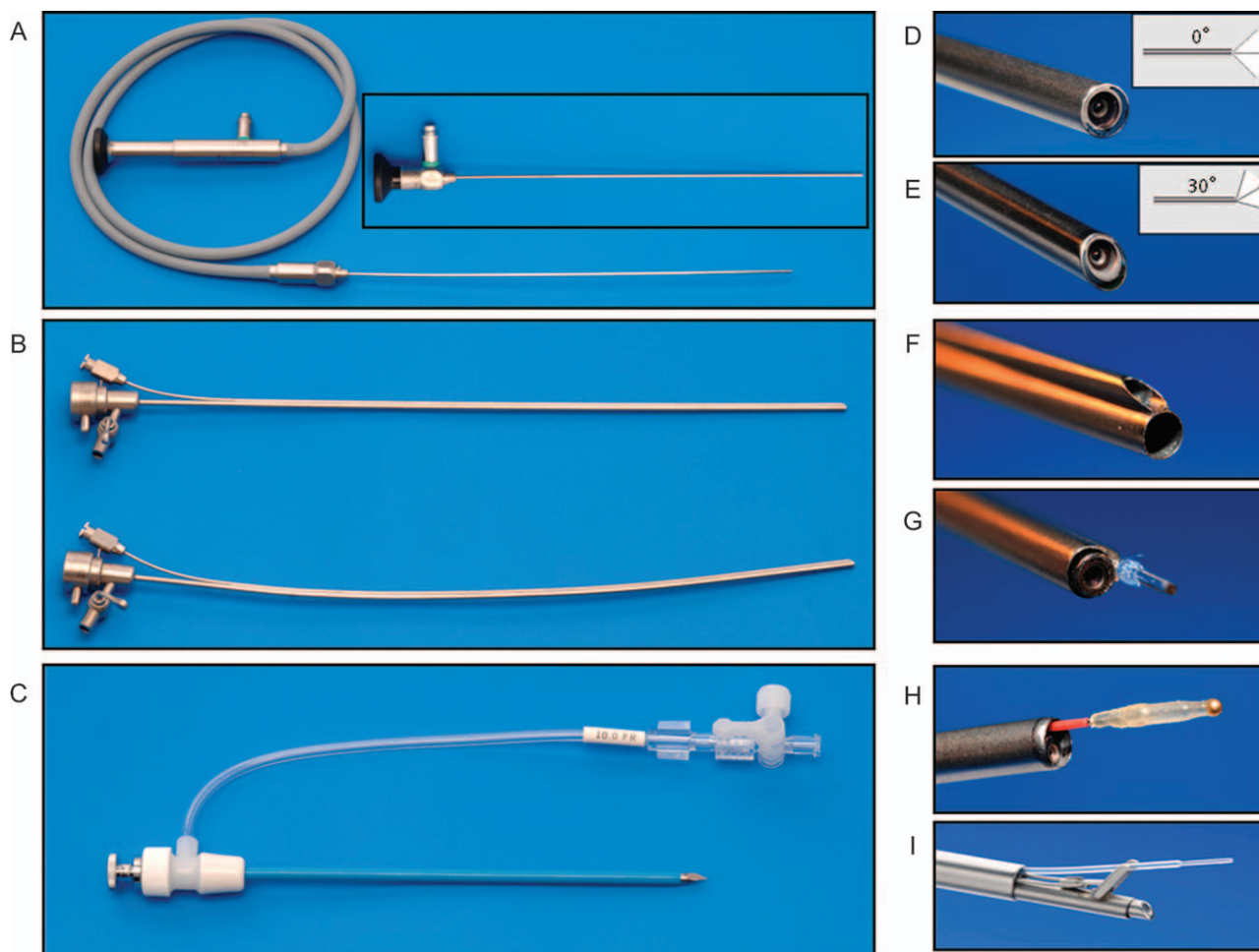


Figure 1. (A) 2.0-mm fibre fetoscope with deported eyepiece; insert: 2.0-mm rod lens fetoscope with standard eyecap. (B) 3.0-mm straight and curved double lumen sheath for use with a 2.0 mm fetoscope. (C) 10 Fr flexible cannula loaded with sharp trocar for direct insertion into the amniotic cavity. (D) Tip of a 2.0-mm rod lens fetoscope with straightforward 0° view. (E) Tip of a 2.0-mm rod lens fetoscope with forward oblique 30° view. (F) Tip of empty double lumen sheath; (G) same sheath when loaded with fetoscope and laser fibre; (H) sheath when loaded with scope and a deflated balloon at the tip of loading catheter. (I) Tip of 3.8 mm sheath, loaded with a 2.0 mm rod lens fetoscope with forward oblique 30° view and a deflecting mechanism working insert – steering lever deflected. Fig 1G has been reprinted with permission of John Wiley & Sons Ltd. on behalf of the International Society of Ultrasound in Obstetrics & Gynaecology (ISUOG). Huber A, Baschat AA, Bregenzer T, Diemert A, Tchirikov M, Hackelöer BJ, Hecher K. Laser coagulation of placental anastomoses with a 30 degrees fetoscope in severe mid-trimester twin-twin transfusion syndrome with anterior placenta. *Ultrasound Obstet Gynecol* 2008;31:412–16.

or oval, or irregular when they are composed of two parallel tube elements (Figure 1F).

Cannulas

In analogy to laparoscopy, one can use a cannula (or port) to enter the amniotic cavity. This allows multiple instrument changes, and *theoretically* may reduce friction and therefore membrane dehiscence. The cannula can also be used for irrigation, drainage or exchange of fluid. However, the additional use of a cannula inherently increases the total outer diameter. The range of reusable cannulas that come in different lengths and sizes is wide. Metal cannulas are not flexible and overall have a relatively thick wall. To reduce this,

we use thin-walled plastic cannulas which were originally designed for vascular access (Check-Flo Performer® Introducer Set, Cook Medical Inc., Bloomington, IN, USA, Figure 1C). These are also flexible, have a leak proof port house, a length of 13 cm and come in any diameter between 4 and 15 Fr (1.33 and 5.0 mm), so that one can choose the diameter according to the planned surgery.

Uterine access

Fetoscopic sheaths can be introduced *directly*, that is, without a cannula. For that purpose, they are loaded with sharp obturators allowing stabbing the instrument into the uterus under ultrasound guidance.

Cannulas can be inserted either by the 'Seldinger' technique (as for vascular access) or directly using purpose-designed reusable trocars with pyramidal tip (2.5–4.7 mm, length 16–17 cm; Karl Storz) (Figure 1C). The primary port (secondary ports are rarely used) is inserted percutaneously under ultrasound guidance, preferentially in an area devoid of placenta, and taking into account the location of the region of interest. This requires at least local anaesthesia of the insertion point, but locoregional anaesthesia may be used as well.⁷ Mini-laparotomy, laparoscopic assisted or open insertion of endoscopic ports is carried out in a limited number of conditions.^{8–10}

Camera system and double image display

The fetoscope is connected to a high-quality cold light source (e.g. Xenon light) via an adapted small diameter (e.g. 2.5 mm) light cable that matches the light transmission bundle. It is useful to choose the longer cables (e.g. 230 cm) to allow different positions of the equipment to the patient. Cameras are no different from those used in laparoscopy, but the generated image is not the only one that is relevant to the operative team. Manipulations are also guided by ultrasound and therefore the operator must be able to see both images during the entire operation. Images can be displayed separately or as a 'Picture in Picture' generated by software within modern screens or a video mixer. Some modern ultrasound machines generate a video graphics array rather than a typical composite signal, which may cause connection mismatches to some screens or documentation hardware. As the surgeon and the ultrasound operator are usually not situated at the same side of the patient, two screens may be useful. Modern advanced operating theatres have such facilities integrated, at times, as part of an entire hardware package providing simplified work processes by intuitive device control and optimal image reproduction by various camera systems and other signal sources.

Distension medium

Although fetoscopy can be performed in the amniotic fluid environment, distension media may be used to create additional working space or improve visualisation. We use warmed Hartmann solution (lactated Ringer's solution), which has been shown to be safe in experimental and clinical working conditions and within normal pressure limits.¹¹ It is infused by an infusion fluid warmer (e.g. Hotline® Smiths Medical, Watford, UK), although purpose-designed pumps have been described.¹² Gas distension theoretically allows a clearer view and less interference by occasional bleeding but precludes the use of ultrasound. CO₂ is soluble and therefore theoretically at lower risk to cause gas embolus. Its safety is, however, a matter of debate because some argue CO₂ induces fetal acidosis,^{13–15} and therefore the use of nitrous oxide has been proposed.¹⁶ However, centres that have performed very complex interventions using CO₂ for placental surgery did not report fetal adverse effects.^{17–19}

Specific instruments used in particular indications

Laser coagulation for TTTS

Laser coagulation of chorionic vessels is the most effective therapy for TTTS.^{3,20} The surgical goal of the intervention is to ablate all intertwin anastomoses, on the assumption that these can be identified and run at the surface of the chorionic plate. This requires appropriate visualisation as well as a reasonable angle of the laser fibre to the vessels. The above are a function of placental location, fetal position and the composition of the amniotic fluid, all factors that are typically beyond control of the surgeon. The diameter of the endoscope is chosen according to the gestational age. For cases beyond 20 weeks, most use a 2.0-mm fibrescope or a 2.0- to 3.8-mm rod lens endoscope, with adapted sheaths (Figure 1G). At lower gestational ages, smaller scopes (e.g. 1.2 mm) may do as well. Laser sources most often used are either neodymium:yttrium–aluminium–garnet (Nd:YAG; wavelength 1064 nm, reported power requirements 50–100 W, e.g. Medilas Fibertom 8100; Dornier MedTech, Wessling, Germany), diode (940 nm, 20–60 W, e.g. Medilas D Multibeam; Dornier MedTech) or potassium–titanyl–phosphate (KTP, 532 nm, e.g. 800 Series; Laserscope, San Jose, CA, USA). These have an optimal energy absorbance in the spectrum of haemoglobin (Figure 2A). Fibres are typically 400–600 µm in core diameter and have a bare tip, but the outer diameter is determined by the plastic isolation that surrounds it (total ≤1.0 mm; Figure 2B). Lateral light emission (side-firing) is possible through special tips (e.g. 600 µm core; however, with a tip diameter of 1.9 mm; Sidefocus, Dornier MedTech, Figure 2C). When purchasing hardware, the colour of the pilot light needs to be chosen in advance. We prefer green light. The laser is fired at a distance of about 1 cm over a 1- to 2-cm section of the vessel until visual cessation of flow.

Optimal energy impact is obtained at an angle as close as possible to 90°. This becomes difficult through anterior abdominal wall access when the placenta is anterior. A variety of techniques to overcome this problem has been proposed, including the use of curved scopes,⁸ a deflecting mechanism (Figure 1I),²¹ side-firing fibres through an additional port,²² and even posterior uterine access under laparoscopic assistance⁹ or through laparotomy.²³ Alternatively, one can tumble the placenta to a certain extent by external pressure or, internally and more functionally, by using the cannula. The latter also prevents direct contact between the fibre and placenta (and fetus) and contributes to local vessel compression facilitating coagulation (see Video S1).²⁴ When the cannula is in complete contact with the placenta, it is wise to lower the laser energy. At that moment, the amount of water wherein the energy can spread is limited to that entrapped in the cannula, increasing the risk for vessel perforation.²⁵ At present, it is uncertain what the best technique for cases with anterior

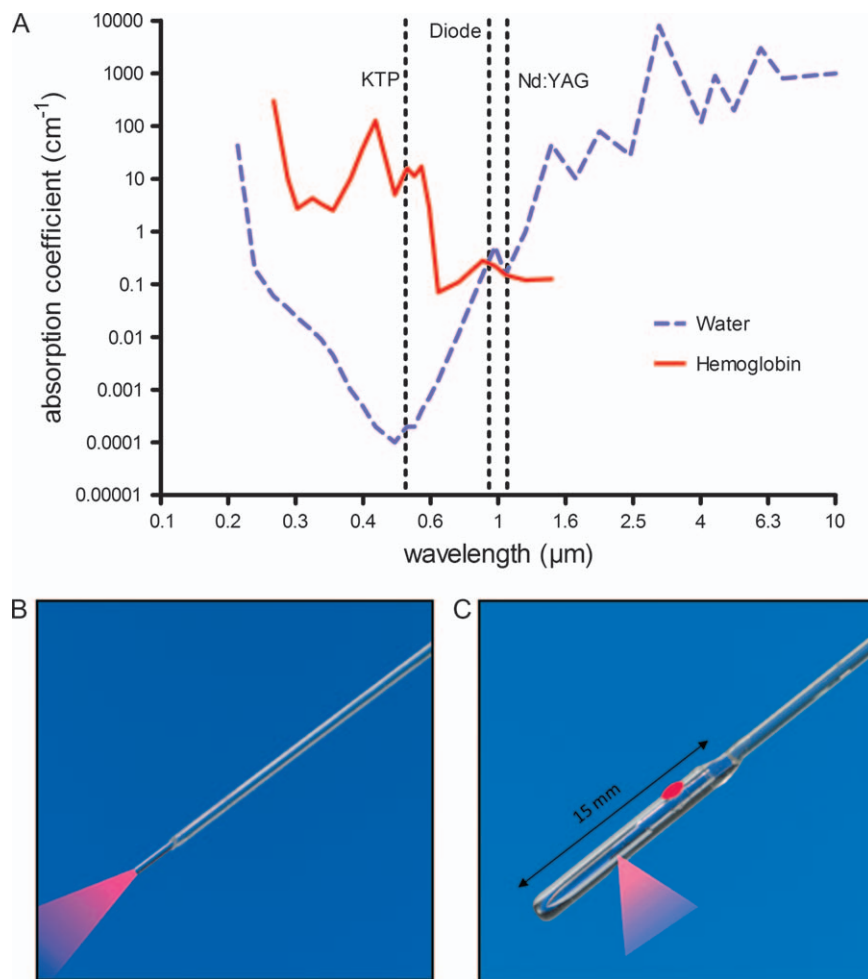


Figure 2. (A) Absorption coefficients of haemoglobin and water with wavelengths of KTP (wavelength 532 nm), Nd:YAG (wavelength 1064 nm) and diode laser (wavelength 940 nm). (B) Standard light guide (Dornier MedTech), diameter 1.0 mm. (C) Light guide with directed lateral (side firing) emission (Dornier MedTech), tip diameter 1.9 mm.

placentas is. Moreover, published data do not show that results are clinically different.^{3,26,27}

There is continuing debate on the selection and order which way the chorionic plate vessels should be coagulated, but is widely accepted that selective laser coagulation along the vascular equator should be attempted when feasible.^{28–31}

Selective feticide in complicated monochorionic pregnancies

Selective feticide in monochorionic multiples cannot be performed by injection of potassium chloride or xylocain because the substance may embolise to the healthy fetus or the surviving fetus may exsanguinate via the ever-present anastomoses into the fetoplacental unit. Vascular embolising agents were abandoned because of high failure rates,³² probably because of incomplete vascular obliteration or product migration. Ligation of the umbilical cord achieves an immediate and complete cord occlusion but is a cumbersome and lengthy procedure.³³

It has become replaced by cord or intrafetal thermocoagulation. Different thermal energy sources can be used, such as laser that can be applied by embryo fetoscopy or interstitially.^{34,35} Laser coagulation of the cord may be less effective than ultrasound-guided bipolar coagulation at later gestational ages because of increasing size of the cord vessels.^{36–38} For the latter, a 2.4- and 3.0-mm reusable forceps with length of 26 and 30 cm (Bipolar Grasping Forceps; Karl Storz) have been developed (Figure 3D, top). There are also 3.0-mm disposable forceps on the market (e.g. Everest MoLly Forceps; Gyrus ACMI, Maple Grove, MN, USA; Figure 3E). Some clinicians requested the development of a so-called optical forceps (2.4 and 3.0 mm, length 24.5 cm, Optical Bipolar Grasping Forceps; Karl Storz; Figure 3D, bottom). The forceps is loaded with a 1.2- or 1.3-mm fetoscope to directly visualise the cord at the expense of a larger diameter (13.5 Fr). All these require the use of a cannula, which preferentially is inserted such that septostomy is avoided, as this would cause an iatrogenic monoamniotic

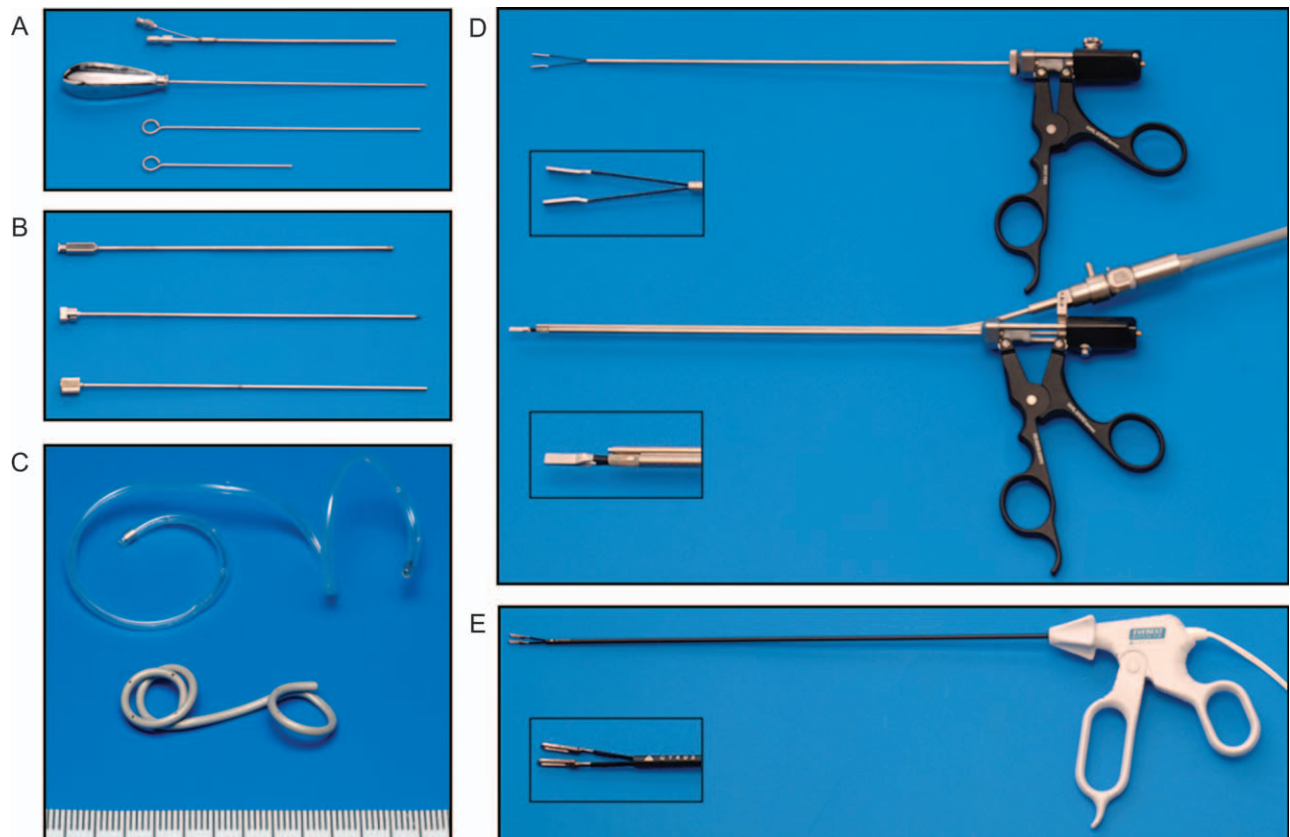


Figure 3. (A) Introduction set for the Rocket shunting system by Rocket and (B) by Storz. (C) Rocket shunt (top) and Harrison shunt (bottom). (D) 2.4-mm bipolar grasping forceps (top) and insert with details of forceps blades; 3.0-mm optical bipolar forceps (bottom) loaded with a 1.3 mm fibre fetoscope and insert with detail of the forceps tip with the inserted scope. (E) 3.0-mm disposable bipolar forceps (bottom) and insert details of forceps blades.

status. In those circumstances, section of the cord is recommended to prevent cord entanglement. The overall success rate of cord coagulation is around 80%.^{39,40}

Intrafetal vessels can be ablated by interstitial laser,⁴¹ monopolar⁴² or radiofrequency electrodes^{43,44} (e.g. RF 3000 with LeVein Needle Electrode; Boston Scientific, Natick, MA, USA or Starburst; RITA Medical Systems, Manchester, GA, USA or Cool-tip RF; Valleylab, Tyco Healthcare Group LP, Boulder, CO, USA), with reported survival rates of 76–94%.^{45–47} As this is carried out through needles that are smaller than the above cannulas, it is an attractive alternative particularly early in gestation. Whether it is as effective later in gestation (especially in the presence of two normal pumping hearts) remains to be demonstrated.

Congenital diaphragmatic hernia

Fetuses with isolated congenital diaphragmatic hernia (CDH) have variable degrees of lung hypoplasia, which still is lethal in around 30%. Triggering of prenatal lung growth may increase their survival chances and can be achieved through fetal tracheal occlusion. We refer to the experimental surgical literature for further pathophysiological details.⁴⁸ Today, percutaneous fetal endoscopic tracheal occlusion (FETO) is offered clinically for

severe cases of isolated left-sided CDH, defined as those with liver herniation and observed over expected (O/E) lung area to head circumference ratio (LHR) <25%. The procedure involves insertion of an endoluminal balloon during the late canalicular phase of lung development (26–28 weeks) and prenatal removal during the transition of the saccular to alveolar phase (34 weeks; plug–unplug sequence).⁴⁹ The largest experience at this stage is that gathered by the ‘FETO-Task Group’,⁵⁰ but it has also been carried out by others. Currently, the instruments used include a 1.3-mm 17 000 pixel straightforward fibrescope housed within a 3.0-mm sheath (Karl Storz), allowing the detachable balloon occlusion delivery system (e.g. GVB16; Nfocus Neuro-medical Inc., Palo Alto, CA, USA; Figure 1H). For retrieval, a forceps or puncture needle is used. There is also a purpose-designed blunt tip, double-flow rod lens tracheoscope with forceps (Karl Storz) for postnatal balloon retrieval. This instrumentation is being improved as part of the EuroSTEC project, which also hosts a recently approved study evaluating the potential of FETO in moderate cases of pulmonary hypoplasia (<http://www.totaltrial.eu>). Fetal tracheoscopy for balloon removal is also possible when the patient ruptures membranes subsequently and develops oligohydramnios. As a consequence,

one could also consider applying FETO in case of persistent oligohydramnios as a consequence of *spontaneous* preterm prelabour rupture of membranes (PPROM), as described by Kohl et al.⁵¹ The main limitation, however, to this investigational indication is the absence of validated criteria for lethal lung hypoplasia because of PPRM.

Amniotic band syndrome

The aetiology of amniotic bands remains a matter of controversy, but in exceptional cases progressive constriction and vascular changes can be documented *in utero*.⁵² The first clinical attempts for *in utero* release of amniotic bands were described by Quintero et al.,⁵³ and since then several reports have been published.^{54,55} It may be quite difficult to identify and release the membrane constriction deep within edematous tissue. The instruments required are, next to a fetoscope, adapted sheaths and laser energy, but that may cause collateral damage.⁵⁶ For that reason 'optical' scissors were developed, that is, a pair of parrot-beaked scissors with an endoscope within (Karl Storz), allowing direct visualisation of the operating field.

Shunting and fetal cystoscopy

Intrauterine shunting has been proposed to treat obstructive uropathy,⁵⁷ to drain cystic lesions of the thorax on very specific indications^{58,59} and historically also hydrocephalus.⁶⁰ Shunts are placed under ultrasound guidance⁶¹ and typically have a double-pigtail shape, reducing the risk of dislodgment. The most widely used shunt is that made by Rocket, also known as the 'Rodeck shunt', named after its designer (KCH; Rocket Medical, Watford, UK, Figure 3C, top). It has a diameter of 2.1 mm, features a radiopaque and echogenic tip, and comes with a purpose-designed introducer set consisting of a 3.0-mm cannula, trocar with echogenic tip and pusher rods of 12 and 22 cm (Figure 3A). More recently, an alternative set with a 3.0-mm-diameter cannula, loaded with a 20-cm-sharp obturator and pusher was developed within the 'Eurofoetus' project (Shunting Set; Karl Storz; Figure 3B). The Harrison shunt (Fetal Bladder Stent Set®; Cook Medical Inc.; Figure 3C, bottom) is smaller in diameter (5 Fr = 1.67 mm) and can be introduced through a 13-Gauge needle. We are also aware of another Japanese shunting system (Inner-stoma Forming Catheter Set; Hakko Shoji Co. Ltd, Tokyo, Japan). Which shunt is better is unknown, and the choice is likely to be dictated by the precise clinical situation, diameters and operator preferences. Smaller shunts, however, may be more prone to obstruction or dislodgement that may occur in up to 20% of cases.⁶²

The use of fetoscopy has also been proposed for exploring the lower urinary tract. This is, however, still in its early stages and more appropriate instrumentation is certainly required.⁶³ The instrument size is still too large and it is often difficult to direct the endoscope percutaneously to the bladder neck (which is the area of interest). This limits even pioneers to distinguish between urethral valves and atresia.⁶⁴ Neverthe-

less, the potential to extend fetal cystoscopy to a therapeutic procedure is an important prospect, and both fetoscopic antegrade catheterisation and hydro- or laser ablation of urethral valves have been described.^{65,66}

Other considerations

In general, all the above instruments are relatively unique and it is unlikely that hospital sterilisation services or tabulating nurses will be familiar with these. They are also very frail and expensive. For these reasons, we trust their care into the hands of specialised nursing staff who are familiar with their use as they assist in the operations in our unit. European regulations require instrumentation to be autoclavable, which initially has been a challenge for the endoscopes but today this problem seems solved. Of note is that many of these instruments cannot be marketed without restrictions in the USA. Whereas in Europe Conformité Européenne (CE) marking can be issued to fetoscopic instrumentation, in the USA they are referred to as mini-laparoscopes (e.g. 'Mini-Operating Laparoscope and Instrument Set'; Richard Wolf Medical Instruments). This avoids pointing to its actual use or indication, for which they are not officially approved. When instruments are registered formally for fetoscopy, they may obtain *ad hoc* clearance or an exempt status for 'single-patient' or 'compassionate' use by the Food and Drug Administration (Humanitarian Device Exemption).^{67,68} This seems mainly a local problem and the rationale for these restrictions is not always well understood.

Future trends and perspectives

Development in this field is continuing, boosted by the increasing number of applications, centres performing fetoscopy, private and public investment (<http://www.eurostec.eu>) as well as technical innovation. For instance, manufacturers are still increasing the resolution of fibrescopes. The increase in numbers of optical fibres improves light transmission and resolution, however, at the same time it limits flexibility of the scope. This may be disadvantageous for a number of applications. Also, it is technically possible to glue lenses, allowing views at different angles similar to rod lens scopes. If small diameter, high-resolution steerable scopes, which are also resistant to the legally imposed sterilisation methods, could be made, this may be a true step forward.

The complexity of surgery could dramatically increase when the instrumentation required for robotic surgery could be miniaturised, providing three-dimensional views, motion scaling and seven degrees of freedom, enabling extremely precise surgery.⁶⁹ The feasibility of robot-assisted fetoscopy has already been demonstrated for experimental myelomeningocele repair and vesicostomy in a sheep model.^{70,71} However, multiple ports as well as port size remain a limitation. Single access robotic surgery may solve this and is under development. Meanwhile, complex procedures may become possible

under gas distension, if concerns about maternal, fetal and membrane safety can be ruled out. Another limitation of gas amniodistension is that simultaneous ultrasound is not possible. The surgical patient would also benefit from perioperative monitoring. Noninvasive fetal electrocardiography is at present marketed, however does not allow permanent intraoperative registration and requires electrodes in the operative field. Alternatively, telemetric implantable devices can be used but need miniaturisation.⁷²

Next to the technical, another challenge emerges, which is training and credentialing of clinicians. Fetal surgery has become a clinical reality with reasonable caseloads in large referral units. It frequently attracts the attention of the media, and this tempts many hospitals and clinicians to offer such services. The complexity and the overall rare indications are a limitation for wider implementation. There is a need to determine viability of new programmes, both in terms of number of patients as well as true needs. The learning curve as well as lower caseload might affect efficacy and outcomes. It is unclear whether, and who is entitled to regulate this, but in North America, the medical profession has already taken its own initiative.⁷³ Certainly, for investigational procedures, widespread use should be avoided, and for instance myelomeningocele repair is currently only offered at three sites and within a trial. Fetoscopic laser coagulation is much more widely available, and a number of fetal medicine centres voluntarily gathered within the North American Fetal Therapy Network (NAFTNET). This remains unofficial, just as in Europe where consortia like Eurofoetus are voluntary collaborations without official endorsement. In Europe, regulatory or funding authorities in fetal medicine that are empowered at a supranational level do not exist at present, with the exception of an European drug agency (European Medicines Agency, EMEA). This is unfortunate and health care remains so far a responsibility of the individual member states, who usually do not take action in this matter.

All surgery remains an invasive enterprise inherently introducing complications. However, simultaneous development of less invasive therapies, including cellular or gene therapy, noninvasive energy modalities (e.g. high-intensity focused ultrasound) or medical alternatives may eventually render surgery redundant for a number of conditions.^{74–76}

Disclosure of interests

There is no direct or indirect commercial or financial incentive associated with publishing this article. The instruments that were developed with Karl Storz were all developed within two R&D projects funded by the European Commission and none of the clinical partners had any financial interest in its marketing or sales.

Contribution to authorship

P.K. wrote the article. T.V.M., L.G. and E.D. critically revised and substantially contributed to the clinical content of the review. K.A.

and B.B. substantially contributed to technical details, instrument's care and handling. J.D. contributed to the conception, design, writing, revising of the article and approved its final version.

Ethical approval

This technical review of instruments did not include patients or animals and did not require ethical approval.

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Supporting Information

Additional Supporting Information may be found in the online version of this article.

Video S1. Fetoscopic laser coagulation in case of anterior placenta: instrument modifications, tips and tricks.

Figures present in the online video (left side of slide 5 & left side slide 7) are published with permission of John Wiley & Sons Ltd. on behalf of the International Society of Ultrasound in Obstetrics & Gynaecology (ISUOG). Deprest JA, Van Schoubroeck D, Van Ballaer PP, Flageole H, Van Assche FA, Vandenberghe K. Alternative technique for Nd: YAG laser coagulation in twin-to-twin transfusion syndrome with anterior placenta. *Ultrasound Obstet Gynecol* 1998;11:347–52. Huber A, Baschat AA, Bregenzer T, Diemert A, Tchirikov M, Hackelöer BJ, Hecher K. Laser coagulation of placental anastomoses with a 30 degrees fetoscope in severe mid-trimester twin-twin transfusion syndrome with anterior placenta. *Ultrasound Obstet Gynecol* 2008;31:412–16.

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References

- Quintero RA, Abuhamad A, Hobbins JC, Mahoney MJ. Transabdominal thin gauge embryofetoscopy: a technique for early prenatal diagnosis and its use in the diagnosis of a case of Meckel Gruber Syndrome. *Am J Obstet Gynecol* 1993;168:1552–7.
- Luks FI, Deprest JA. Endoscopic fetal surgery: a new alternative? *Eur J Obstet Gynecol Reprod Biol* 1993;52:1–3.
- Senat MV, Deprest J, Boulvain M, Paupe A, Winer N, Ville Y. Endoscopic laser surgery versus serial amnioreduction for severe twin-to-twin transfusion syndrome. *N Engl J Med* 2004;351:136–44.
- Deprest J, Jani J, Lewi L, Ochsenbein-Kobler N, Cannie M, Done E, et al. Fetoscopic surgery: encouraged by clinical experience and boosted by instrument innovation. *Semin Fetal Neonatal Med* 2006;11:398–412.
- Gratacós E, Deprest J. Current experience with fetoscopy and the Eurofoetus registry for fetoscopic procedures. *Eur J Obstet Gynecol Reprod Biol* 2000;92:151–9.
- Deprest J, Ville Y. Obstetric endoscopy. In: Harrison M, Evans M, Adzick NS, Holzgreve W, editors. *The Unborn Patient: The Art and Science of Fetal Therapy*. Chapter 15. Philadelphia, PA: W.B. Saunders, 2000;213–32.
- Rossi AC, Kaufman MA, Bornick PW, Quintero RA. General vs local anesthesia for the percutaneous laser treatment of twin-twin transfusion syndrome. *Am J Obstet Gynecol* 2008;199:137.e1–7.
- Deprest JA, Van Schoubroeck D, Van Ballaer PP, Flageole H, Van Assche FA, Vandenberghe K. Alternative technique for Nd: YAG laser coagulation in twin-to-twin transfusion syndrome with anterior placenta. *Ultrasound Obstet Gynecol* 1998;11:347–52.
- Middeldorp JM, Lopriore E, Sueters M, Jansen FW, Ringers J, Klumper FJ, et al. Laparoscopically guided uterine entry for fetoscopy in twin-to-twin transfusion syndrome with completely anterior placenta: a novel technique. *Fetal Diagn Ther* 2007;22:409–15.
- Bruner JP, Tulipan NE, Richards WO. Endoscopic coverage of fetal open myelomeningocele in utero. *Am J Obstet Gynecol* 1997;176:256–7.
- Evrard VA, Verbeke K, Peers KH, Luks FI, Lerut AE, Vandenberghe K, et al. Amnioinfusion with Hartmann's solution: a safe distention medium for endoscopic fetal surgery in the ovine model. *Fetal Diagn Ther* 1997;12:188–92.
- Quintero RA, Romero R, Reich H, Gonçalves L, Johnson MP, Carreño C, et al. In utero percutaneous umbilical cord ligation in the management of complicated monochorionic multiple gestations. *Ultrasound Obstet Gynecol* 1996;8:16–22.
- Luks FI, Deprest J, Marcus M, Vandenberghe K, Vertommen JD, Lerut T, et al. Carbon dioxide pneumoamnios causes acidosis in fetal lamb. *Fetal Diagn Ther* 1994;9:105–9.
- Saiki Y, Litwin DE, Bigras JL, Waddell J, König A, Baik S, et al. Reducing the deleterious effects of intrauterine CO₂ during fetoscopic surgery. *J Surg Res* 1997;69:51–4.
- Gratacós E, Wu J, Devlieger R, Van de Velde M, Deprest JA. Effects of amniodistention with carbon dioxide on fetal acid-base status during fetoscopic surgery in a sheep model. *Surg Endosc* 2001;15:368–72.
- Gratacós E, Wu J, Devlieger R, Bonati F, Lerut T, Vanamo K, et al. Nitrous oxide amniodistention compared with fluid amniodistention reduces operation time while inducing no changes in fetal acid-base status in a sheep model for endoscopic fetal surgery. *Am J Obstet Gynecol* 2002;186:538–43.
- Bruner JP, Richards WO, Tulipan NB, Arney TL. Endoscopic coverage of fetal myelomeningocele in utero. *Am J Obstet Gynecol* 1999;180:153–8.
- Kohl T, Hering R, Van de Vondel P, Tchatcheva K, Berg C, Bartmann P, et al. Analysis of the stepwise clinical introduction of experimental percutaneous fetoscopic surgical techniques for upcoming minimally invasive fetal cardiac interventions. *Surg Endosc* 2006;20:1134–43.
- Kohl T, Tchatcheva K, Berg C, Geipel A, Van de Vondel P, Gembruch U. Partial amniotic carbon dioxide insufflation (PACI) facilitates fetoscopic interventions in complicated monochorionic twin pregnancies. *Surg Endosc* 2007;21:1428–33.
- Roberts D, Neilson JP, Kilby M, Gates S. Interventions for the treatment of twin-twin transfusion syndrome. *Cochrane Database Syst Rev* 2008;23:CD002073.
- Huber A, Baschat AA, Bregenzner T, Diemert A, Tchirikov M, Hackelöer BJ, et al. Laser coagulation of placental anastomoses with a 30 degrees fetoscope in severe mid-trimester twin-twin transfusion syndrome with anterior placenta. *Ultrasound Obstet Gynecol* 2008;31:412–16.
- Quintero RA, Bornick PW, Allen MH, Johnson PK. Selective laser photocoagulation of communicating vessels in severe twin-twin transfusion syndrome in women with an anterior placenta. *Obstet Gynecol* 2001;97:477–81.
- De Lia JE, Kuhlmann RS, Harstad TW, Cruikshank DP. Fetoscopic laser ablation of placental vessels in severe previable twin-twin transfusion syndrome. *Am J Obstet Gynecol* 1995;172:1202–8.
- Deprest J. Some tools in case of an anterior placenta. Eurofoetus Annual Meeting on Monochorionic Twins, 12–14 May 2006, Paris.
- Evrard VA, Deprest JA, Van Ballaer P, Lerut TE, Vandenberghe K, Brosens IA. Underwater Nd:YAG laser coagulation of blood vessels in a rat model. *Fetal Diagn Ther* 1996;11:422–6.
- Ville Y, Hyett J, Hecher K, Nicolaides KH. Preliminary experience with endoscopic laser surgery for severe twin-twin transfusion syndrome. *N Engl J Med* 1995;332:224–7.
- Yamamoto M, El Murr L, Robyr R, Leleu F, Takahashi Y, Ville Y. Incidence and impact of perioperative complications in 175 fetoscopy-guided laser coagulations of chorionic plate anastomoses in fetofetal transfusion syndrome before 26 weeks of gestation. *Am J Obstet Gynecol* 2005;193:1110–16.
- De Lia J, Fisk N, Hecher K, Machin G, Nicolaides K, Hyett J, et al. Twin-to-twin transfusion syndrome—debates on the etiology, natural history and management. *Ultrasound Obstet Gynecol* 2000;16:210–13.
- Quintero RA, Comas C, Bornick PW, Allen MH, Kruger M. Selective versus non-selective laser photocoagulation of placental vessels in twin-to-twin transfusion syndrome. *Ultrasound Obstet Gynecol* 2000;16:230–6.
- Quintero RA, Ishii K, Chmait RH, Bornick PW, Allen MH, Kontopoulos EV. Sequential selective laser photocoagulation of communicating vessels in twin-twin transfusion syndrome. *J Matern Fetal Neonatal Med* 2007;20:763–8.
- Ierullo AM, Papageorgiou AT, Bhida A, Fratelli N, Thilaganathan B. Severe twin-twin transfusion syndrome: outcome after fetoscopic laser ablation of the placental vascular equator. *BJOG* 2007;114:689–93.
- Denbow ML, Overton TG, Duncan KR, Cox PM, Fisk NM. High failure rate of umbilical vessel occlusion by ultrasound-guided injection of absolute alcohol or enbucrilate gel. *Prenat Diagn* 1999;19:527–32.
- Deprest JA, Van Ballaer PP, Evrard VA, Peers KH, Spitz B, Steegers EA, et al. Experience with fetoscopic cord ligation. *Eur J Obstet Gynecol Reprod Biol* 1998;81:157–64.
- Hecher K, Hackelöer BJ, Ville Y. Umbilical cord coagulation by operative microendoscopy at 16 weeks' gestation in an acardiac twin. *Ultrasound Obstet Gynecol* 1997;10:130–2.
- Jolly M, Taylor M, Rose G, Govender L, Fisk NM. Interstitial laser: a new surgical technique for twin reversed arterial perfusion sequence in early pregnancy. *BJOG* 2001;108:1098–102.
- Deprest JA, Audibert F, Van Schoubroeck D, Hecher K, Mahieu-Caputo D. Bipolar coagulation of the umbilical cord in complicated monochorionic twin pregnancy. *Am J Obstet Gynecol* 2000;182:340–5.
- Ville Y, Hyett JA, Vandebussche FP, Nicolaides KH. Endoscopic laser coagulation of umbilical cord vessels in twin reversed arterial perfusion sequence. *Ultrasound Obstet Gynecol* 1994;4:396–8.

- 38 Ville Y. Selective feticide in monochorionic pregnancies: toys for the boys or standard of care? *Ultrasound Obstet Gynecol* 2003;22:448–50.
- 39 Lewi L, Gratacós E, Ortibus E, Van Schoubroeck D, Carreras E, Higuera T, et al. Pregnancy and infant outcome of 80 consecutive cord coagulations in complicated monochorionic multiple pregnancies. *Am J Obstet Gynecol* 2006;194:782–9.
- 40 Robyr R, Yamamoto M, Ville Y. Selective feticide in complicated monochorionic twin pregnancies using ultrasound-guided bipolar cord coagulation. *BJOG* 2005;112:1344–8.
- 41 Soothill P, Sohan K, Carroll S, Kyle P. Ultrasound-guided, intra-abdominal laser to treat acardiac pregnancies. *BJOG* 2002;109:352–4.
- 42 Rodeck C, Deans A, Jauniaux E. Thermocoagulation for the early treatment of pregnancy with an acardiac twin. *N Engl J Med* 1998;339:1293–305.
- 43 Tsao K, Feldstein VA, Albanese CT, Sandberg PL, Lee H, Harrison MR, et al. Selective reduction of acardiac twin by radiofrequency ablation. *Am J Obstet Gynecol* 2002;187:635–40.
- 44 Moise KJ Jr, Johnson A, Moise KY, Nickleleit V. Radiofrequency ablation for selective reduction in the complicated monochorionic gestation. *Am J Obstet Gynecol* 2008;198:198.e1–5.
- 45 Lee H, Wagner AJ, Sy E, Ball R, Feldstein VA, Goldstein RB, et al. Efficacy of radiofrequency ablation for twin-reversed arterial perfusion sequence. *Am J Obstet Gynecol* 2007;196:459.e1–4.
- 46 Livingston JC, Lim FY, Polzin W, Mason J, Crombleholme TM. Intrafetal radiofrequency ablation for twin reversed arterial perfusion (TRAP): a single-center experience. *Am J Obstet Gynecol* 2007;197:399.e1–3.
- 47 O'Donoghue K, Barigye O, Pasquini L, Chappell L, Wimalasundera RC, Fisk NM. Interstitial laser therapy for fetal reduction in monochorionic multiple pregnancy: loss rate and association with aplasia cutis congenita. *Prenat Diagn* 2008;28:535–43.
- 48 Nelson S, Cameron A, Deprest J. Fetoscopic surgery for in utero management of congenital diaphragmatic hernia. *Fetal Matern Med Rev* 2006;17:69–104.
- 49 Deprest J, Jani J, Gratacós E, Vandecruys H, Naulaers G, Delgado J, et al. Fetal intervention for congenital diaphragmatic hernia: the European experience. *Semin Perinatol* 2005;29:94–103.
- 50 Deprest J, Gratacós E, Nicolaides KH, FETO Task Group. Fetoscopic tracheal occlusion (FETO) for severe congenital diaphragmatic hernia: evolution of a technique and preliminary results. *Ultrasound Obstet Gynecol* 2004; 24:121–6.
- 51 Kohl T, Müller A, Franz A, Heep A, Willinek WA, Bartmann P, et al. Temporary fetoscopic tracheal balloon occlusion enhanced by hyperoncotic lung distension: is there a role in the treatment of fetal pulmonary hypoplasia from early preterm premature rupture of membranes? *Fetal Diagn Ther* 2007;22:462–5.
- 52 Tadmor OP, Kreisberg GA, Achiron R, Porat S, Yagel S. Limb amputation in amniotic band syndrome: serial ultrasonographic and Doppler observations. *Ultrasound Obstet Gynecol* 1997;10:312–15.
- 53 Quintero RA, Morales WJ, Phillips J, Kalter CS, Angel JL. In utero lysis of amniotic bands. *Ultrasound Obstet Gynecol* 1997;10:316–20.
- 54 Sentilhes L, Verspyck E, Eurin D, Ickowicz V, Patrier S, Lechevallier J, et al. Favourable outcome of a tight constriction band secondary to amniotic band syndrome. *Prenat Diagn* 2004;24:198–201.
- 55 Ronderos-Dumit D, Briceño F, Navarro H, Sanchez N. Endoscopic release of limb constriction rings in utero. *Fetal Diagn Ther* 2006;21:255–8.
- 56 Keswani SG, Johnson MP, Adzick NS, Hori S, Howell LJ, Wilson RD, et al. In utero limb salvage: fetoscopic release of amniotic bands for threatened limb amputation. *J Pediatr Surg* 2003;38:848–51.
- 57 Morris RK, Khan KS, Kilby MD. Vesicoamniotic shunting for fetal lower urinary tract obstruction: an overview. *Arch Dis Child Fetal Neonatal Ed* 2007;92:F166–8.
- 58 Deurloo KL, Devlieger R, Lopriore E, Klumper FJ, Oepkes D. Isolated fetal hydrothorax with hydrops: a systematic review of prenatal treatment options. *Prenat Diagn* 2007;27:893–9.
- 59 Wilson RD, Hedrick HL, Liechty KW, Flake AW, Johnson MP, Bebbington M, et al. Cystic adenomatoid malformation of the lung: review of genetics, prenatal diagnosis, and in utero treatment. *Am J Med Genet* 2006;140:151–5.
- 60 Clewell WH, Johnson ML, Meier PR, Newkirk JB, Zide SL, Hendee RW, et al. A surgical approach to the treatment of fetal hydrocephalus. *N Engl J Med* 1982;306:1320–5.
- 61 Johnson MP, Freedman AL. Fetal uropathy. *Curr Opin Obstet Gynecol* 1999;11:185–94.
- 62 Sepulveda W, Galindo A, Sosa A, Diaz L, Flores X, de la Fuente P. Intrathoracic dislodgement of pleuro-amniotic shunt. Three case reports with long-term follow-up. *Fetal Diagn Ther* 2005;20:102–5.
- 63 Welsh A, Agarwal S, Kumar S, Smith RP, Fisk NM. Fetal cystoscopy in the management of fetal obstructive uropathy: experience in a single European centre. *Prenat Diagn* 2003;23:1033–41.
- 64 Quintero RA, Johnson MP, Romero R, Smith C, Arias F, Guevara-Zuloaga F, et al. In-utero percutaneous cystoscopy in the management of fetal lower obstructive uropathy. *Lancet* 1995;346:537–40.
- 65 Quintero RA, Hume R, Smith C, Johnson MP, Cotton DB, Romero R, et al. Percutaneous fetal cystoscopy and endoscopic fulguration of posterior urethral valves. *Am J Obstet Gynecol* 1995;172:206–9.
- 66 Clifton MS, Harrison MR, Ball R, Lee H. Fetoscopic transuterine release of posterior urethral valves: a new technique. *Fetal Diagn Ther* 2008; 23:89–94.
- 67 Thompson L. Experimental treatments: unapproved but not always unavailable. *FDA Consumer Magazine* 2000;34:1.
- 68 Rubin BK, Steinberg KP. Respiratory controversies in the critical care setting. When caring for critically ill patients, do clinicians have a responsibility to be innovative and try unproven approaches when accepted approaches are failing? *Respir Care* 2007;52:408–15.
- 69 Fichter MA, Dornseifer U, Henke J, Schneider KT, Kovacs L, Biemer E, et al. Fetal spina bifida repair—current trends and prospects of intra-uterine neurosurgery. *Fetal Diagn Ther* 2008;23:271–86.
- 70 Aaronson OS, Tulipan NB, Cywes R, Sundell HW, Davis GH, Bruner JP, et al. Robot-assisted endoscopic intrauterine myelomeningocele repair: a feasibility study. *Pediatr Neurosurg* 2002;36:85–9.
- 71 Passerotti CC, Barnewolt C, Xuewu J, Passerotti AM, Ward V, Dunning P, et al. In utero treatment for bladder outlet obstruction using robot assisted laparoscopic techniques. *J Urol* 2008;180:1790–4.
- 72 Hermans B, Lewi L, Jani J, De Buck F, Deprest J, Puers R. Feasibility of in utero telemetric fetal ECG monitoring in a lamb model. *Fetal Diagn Ther* 2008;24:81–5.
- 73 Moise KJ Jr. Neurodevelopmental outcome after laser therapy for twin-twin transfusion syndrome. *Am J Obstet Gynecol* 2006;194: 1208–10.
- 74 Merchant AM, Flake AW. Surgeons and stem cells: a pragmatic perspective on shifting paradigms. *Surgery* 2004;136:975–80.
- 75 Toelen J, Deroose CM, Gijsbers R, Reumers V, Sbragia LN, Vets S, et al. Fetal gene transfer with lentiviral vectors: long-term in vivo follow-up evaluation in a rat model. *Am J Obstet Gynecol* 2007;196: 352.e1–6.
- 76 Ichizuka K, Ando S, Ichihara M, Ishikawa T, Uchiyama N, Sasaki K, et al. Application of high-intensity focused ultrasound for umbilical artery occlusion in a rabbit model. *Ultrasound Obstet Gynecol* 2007;30: 47–51.