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Minimally Traumatic Techniques for In Utero Access and Fetal Surgery

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ABSTRACT

Background and Objectives: Prenatal interventions may prevent some sequelae of congenital anomalies, yet open fetal surgery is limited by pre-term labor. We are developing amnioscopic strategies to reduce risks for in utero surgery.

Methods: Seven fetal sheep were accessed percutaneously under ultrasound guidance, via maternal laparoscopy/transuterine trocars, or via laparoscopically assisted partial uterine exteriorization (mini-hysterotomy). Three fetal immobilization methods were investigated: 2 mm grasping forceps, 2-0 absorbable Roeder loop lasso, and detachable metal T-fasteners.

Results: Percutaneous access with 2 mm trocars required accessible amniotic fluid pockets. The laparoscopically assisted method enabled 5 mm trocar placement under direct fetal visualization. Mini-hysterotomy avoided trocars and was leak-proof. 2 mm graspers enabled fetal manipulation with repeatable applications. Roeder loop sutures were not readily repositioned, and required two 3 mm or larger trocars. T-fasteners were easily deployed into fetal skin via the self-contained needle applicator with minimal hemorrhage. Cutaneous marks were present immediately from the grasper and T-fastener, but not at postoperative day 10. The Roeder loop produced no observable effects. All devices demonstrated adequate intrauterine performance.

Conclusions: Minimally invasive fetal surgery promises to lower maternal-fetal risks. All strategies permitted prolonged amnioscopy and fetal manipulation. The 2 mm grasper was easiest to use, producing no observable lasting trauma.

Key Words: Fetus, Surgery, Urinary obstruction, Endoscopy.

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INTRODUCTION

The ideal method of accessing the fetal surgical patient remains undefined. It is well established that prenatal intervention via open hysterotomy is limited by preterm labor despite recent advances in tocolysis. Several investigators have achieved minimally invasive fetal access in various animal models.[1-6] Endoscopic surgical techniques are now enabling the repair of select complex congenital anomalies such as diaphragmatic hernia.[7] Despite the target organ system for repair, all disciplines concerned with fetal intervention will likely benefit from minimally invasive techniques. We are currently developing a minimally invasive vesicostomy model for the in utero treatment of obstructive uropathies.

Prenatally diagnosed fetal obstructive uropathies have unpredictable outcomes possibly due to stage-specific compensatory abilities of the developing kidney.[8] Absolute criteria for selecting fetuses appropriate for prenatal treatment of lower urinary tract obstruction remain controversial as direct correlations between prenatal findings and postnatal outcome are inconclusive. For example, fetal urine electrolyte and osmolality determination fails to accurately predict either normal function or renal dysplasia.[9,10] There remains a percentage of fetuses diagnosed via screening ultrasonography and urine electrolyte analysis with obstructive uropathy who might benefit from in utero urinary diversion.

The development of small caliber flexible endoscopes has rapidly advanced our ability to exploit percutaneous access for the performance of procedures more complex than amniocentesis. This study reports a means of accessing the gravid uterus in experimental animals for the treatment of obstructive uropathies without the insertion of needles or trocars and compares this technique to previous methods. Additionally, several strategies for the operative positioning of the fetus for genitourinary procedures are evaluated.

MATERIALS AND METHODS

Pregnant ewes of 70-75 or 95-100 days gestational age were selected with twins such that one fetus could serve as a control for surgical manipulations completed in the

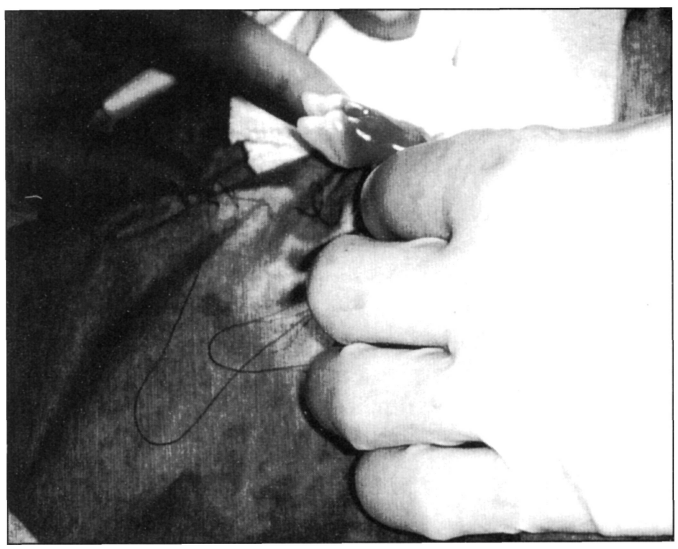

Figure 1a. Hindlimb of a fetal sheep exposed via mini-hysterotomy. Leak-proof uterine access was achieved without the intra-amniotic insertion of needles or trocars and in this case permitted placement of sutures for wound healing studies.

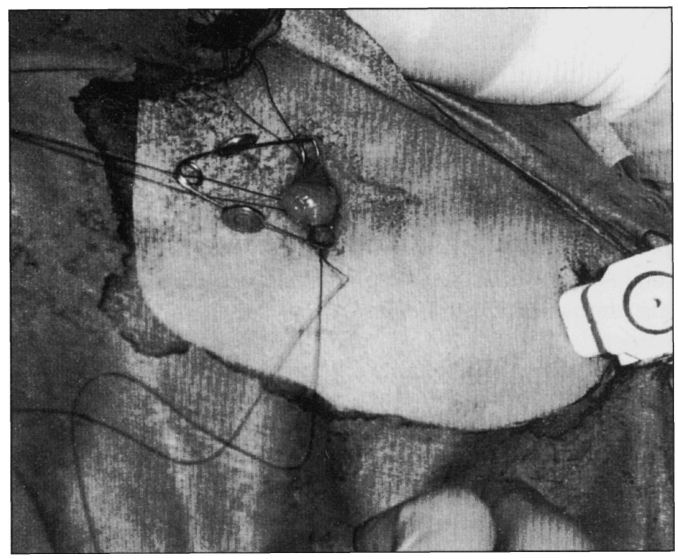

Figure 1b. Closure of mini-hysterotomy. The 3 cm maternal abdominal incision was originally expanded from a 10 mm trocar site. Antibiotic in sterile saline is administered via syringe to the amniotic cavity.

contralateral side. All methods were approved by the Institutional Animal Care and Use Committee at Albany Medical College. Animals were prepped and draped in sterile fashion. General endotracheal anesthesia was administered via Halothane at 1-2%. Seven total fetuses were examined, with one additional macerated fetus discovered upon initial surgical exploration. Ultrasound guided percutaneous access and laparoscopically guided transuterine trocar placement was achieved as previously described.[6]

The mini-hysterotomy was created as follows. After Veress needle placement and insufflation of the maternal peritoneum to 14 mm Hg, a 5 mm trocar passing a 0 degree laparoscope (Olympus, Lake Success, NY) was then introduced. A segment of the gravid uterus overlying the fetal hind-region was then identified by maternal laparoscopy. A second (10 mm) trocar was inserted into the maternal abdomen under endoscopic vision through which a Szabo-Berci laparoscopic grasper (Karl Storz, Culver City, CA) was used to secure a portion of the uterus. The ewe's abdomen was then desufflated, and the uterine segment brought to the inner surface of the abdominal wall where the trocar site incision was then expanded to 2-3 cm using a number 15 blade scalpel. The uterus and chorioamniotic membranes were opened in layers using electrocautery. Each flap was then slightly rotated and sutured to the maternal abdominal wall such that a leak-proof valve was created. Utilizing this careful approach resulted in minimal (<5-10 ml) amniotic fluid loss. However, previous experience with fetal sheep has shown that larger fluid losses may be readily replaced intraoperatively by introducing an appropriate amount of saline at physiologic temperature via the infusion port of the transuterine trocar. The uterus was closed with 4-0 silk at the end of the procedure such that the hysterotomy was buried and so that the developmental membranes remained contiguous to prevent fluid dissection.

Intraoperative assessment of retraction and fetal positioning within the non-insufflated uterus included the following devices: A 2 mm spring-tensioned endoscopic grasper (Cook Urological, Spencer, IN), a 2-0 absorbable Roeder loop deployed as a lasso (Ethicon Endosurgery, Cincinnati, OH), and T-fasteners (Moss Tubes, NY). The 2 mm grasper is supplied with a 2 mm trocar which is inserted under amnioscopic vision, while the T- fasteners are placed via a self-contained needle system similar to surgical staplers. All three devices were subjectively graded for ease of deployment and for adequacy of retraction and fetal positioning based upon the following scale: 1 = excellent, 2 = fair, and 3 = poor. Half of the animals were

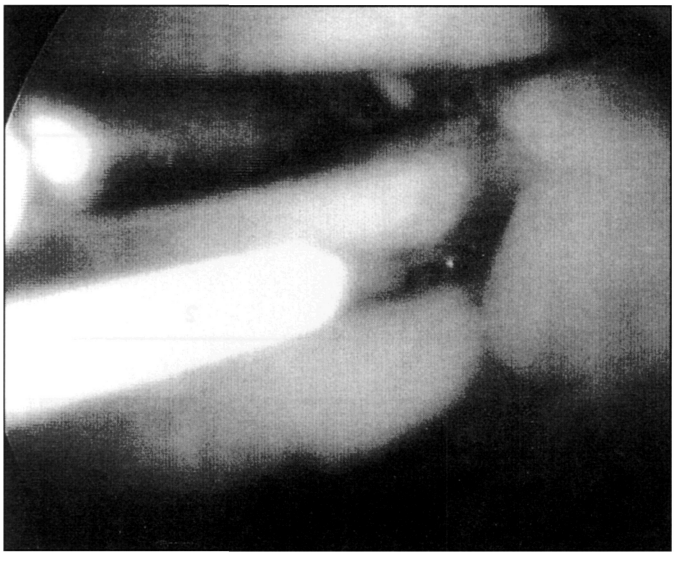

Figure 2a. Spring-tensioned micro-retractors have been inserted into the amniotic cavity via a 2 mm trocar. These devices permitted excellent manipulation of the fetal hindlimbs such that the fetal ventral abdominal wall was easily accessed in preparation for vesicostomy creation.

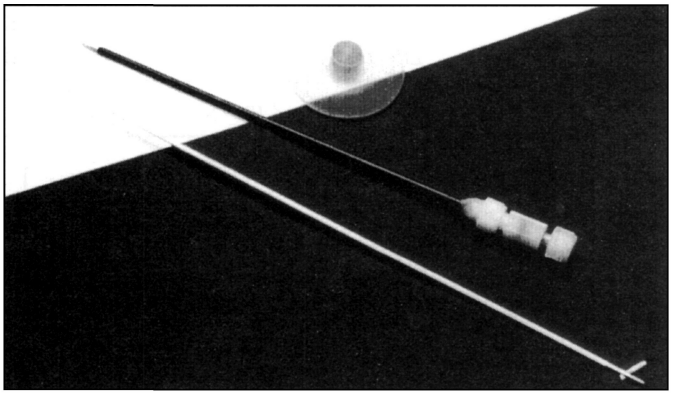

Figure 2b. Micro-retractor set as supplied by Cook Urologic (Spencer, IN). Included is a 2 mm trocar/sheath which easily inserts into the amniotic cavity with minimal tenting of the chorioamniotic membranes, a problem encountered with larger trocars in previous studies. Graspers are available in two tension settings, with neither causing trauma appreciable at delivery.

humanely sacrificed with Beuthanasia (pentobarbital and phenytoin) administered intravenously at 10 mg/kg for immediate examination of acute effects of the various instruments upon the fetus, while the other animals were allowed to recover. On postoperative day 10, remaining animals were also sacrificed to assess the effects of the retraction devices.

RESULTS

The mini-hysterotomy provided a safe means of accessing the gravid uterus without necessitating insufflation with either gas or sterile saline. We were able to pass numerous instruments and endoscopes for intrauterine examination of the fetus without losing significant volumes of amniotic fluid. **Figure 1a** demonstrates the exteriorization of a fetal hindlimb for microscopically assisted suturing studies. This technique avoids either the blind or ultrasound-guided placement of needles and trocars into the uterus, theoretically reducing risks of stab wounds to the fetus and placenta common to other methods. Additionally, the chorioamniotic membranes are always under control, minimizing the occurrence of membrane dissection which may occur with trocar placement. Closure of the mini-hysterotomy is shown in **Figure 1b**.

The 2 mm spring-tension endoscopic graspers were initially utilized to position the fetus. In **Figure 2a** the placement of 2 mm graspers upon the fetal hoof is seen. These instruments **(Figure 2b)** enabled easy manipulation of the fetal hind region. **Figure 3** is a view of the fetal suprapubic region as positioned for vesicostomy. The phallus, umbilical cord, and scrotum with bilateral descended testes are all clearly visible in this image obtained via a 5 mm, 0 degree amnioscope. The Roeder loop lasso could be positioned about the fetal hind limb only once the animal was properly aligned utilizing the 2 mm grasper. T-fasteners were deployed with the self-contained applier and could be inserted from almost any position as long as visual control was possible.

The grasper retraction method fostered excellent fetal extremity manipulation by repeatable applications. The absorbable 2-0 Roeder loop sutures were used as a lasso but required placement of two 3 mm or larger trocars and could not be readily repositioned. The T-fasteners were easily inserted into the fetal skin and had minimal associated hemorrhage which spontaneously resolved. Superficial cutaneous marks were present at immediate necropsy from both the 2 mm grasper and the T-fastener. No effects from the grasper were observed in the day 10 postoperative fetus. The Roeder loop produced no observable effects at either time point investigated. While all devices demonstrated adequate performance for in

Table 1.
Effects of various intrauterine retraction devices for operative positioning of fetal sheep.

	2 mm grasper	T-fastener	Roeder loop
Acute	indentations	minimal hemorrhage	none observed
10 days postop	none observed	none observed*	none observed
Ease of deployment	1	2	3
Ease of manipulation	1	2	2

Scale: 1=excellent, 2=fair, 3=poor. *device must remain in place until delivery.

utero fetal manipulation, the spring-tensioned 2 mm grasper was the easiest and most flexible device to use, producing no observable lasting trauma **(Table 1)**.

DISCUSSION

Preterm labor is a major limitation of open fetal surgical correction of prenatally diagnosed anomalies. The creation of a large hysterotomy has been associated with uterine irritability and abnormal contractions of the myometrium. However, endoscopic access in a primate model resulted in decreased myometrial electrical activity as compared to hysterotomy.[11] While modified laparoscopic access utilizing trocars admittedly permits smaller uterine incisions, the constraints of intrauterine space remain problematic. Addition of fluid or gas to the amniotic cavity has been investigated for the purpose of increasing the working space and also to maximize endoscopic visual clarity. Operating within the amniotic cavity without manipulating or exchanging the fluid offers the least disruptive method of fetal intervention. We have not encountered video resolution difficulties caused by suspended vernix in either the 70-75 day or 95-100 day sheep fetuses. However, the use of a continuous flow, constant pressure/volume irrigation system would obviate these possible complications.

Insufflation of the amniotic cavity to augment the operative working volume may also result in chorioamniotic membrane disruption, as well as myometrial irritation possibly leading to preterm labor. Carbon dioxide insufflation of the ovine amniotic cavity produced severe fetal hypercapnia and acidosis without effecting maternal pH or carbon dioxide pressure.[12] Amniotic insufflation with Helium to 15 mm Hg produced no significant fetal or maternal physiologic changes, while water infusion (15 mm Hg) induced mild fetal hyponatremia and hypochloremia without effecting acid-base or oxygen balance.[13] When amnio-insufflation is utilized, preservation of uteroplacental blood flow and oxygen delivery must be maintained for successful fetal surgery. Uterine artery blood flow and uteroplacental oxygen delivery are both preserved during endoscopic fetal access.[14] Insufflation pressures of less than 20 mm Hg do not effect placental blood flow, but pressures above 20 mm Hg result in fetal hypoxia.[15] Presumably, increased intra-amniotic pressure increases placental resistance which decreases blood flow. If insufflation must be utilized, it is recommended that intra-amniotic pressure should be limited to 15 mm Hg.

Each specific prenatal intervention will likely have an ideal access strategy dependent upon the instrumentation required to perform the surgical procedure. A theoretical risk inherent with needle or trocar access is the evolution of amniotic band sequence. Disruption of the chorioamniotic membranes may result in strips of fibrous mesenchymal tissue capable of entrapping the fetus. Amniotic bands have been reported following amniocentesis, and result in serious anomalies including digital and extremity amputations as well as ventral wall disruptions mimicking gastroschisis. However, a fetal sheep model has demonstrated that even amniotic bands can be managed via prenatal surgery.[16] Control of the chorioamniotic membranes is also as important as tocolysis in preventing premature labor. Ruptured membranes lead to ascending infection as well as stimulating premature con-

tractions and labor. Trocar insertion may distend the membranes before puncture, creating a potential space which could fill with amniotic fluid resulting in membrane dissection.[6]

The percutaneous approach to the gravid uterus is the least invasive method and is also technically feasible.[3,4,6] Sheep have numerous placental cotyledons which result in several amniotic fluid pockets readily visualized via ultrasonography as appropriate percutaneous access targets. However, such an approach is not recommended in cases of anterior placentation and would be an unreliable standard methodology in primates. Modified Seldinger and vascular access techniques have been developed for percutaneous approaches to the fetus in both sheep and monkeys.[3,4] If the uterus must be punctured, as it must be with all forms of percutaneous access, it is likely best accomplished with the smallest diameter needle or wire available. Larger caliber devices may then be introduced over the primary guide wire, but little or no data exist describing the occurrence and degree of damage to the chorioamniotic membranes.

In the laboratory setting, ultrasound guided percutaneous access in experimental animals is not necessary for the proctoring of intra-amniotic techniques. Maternal laparoscopy may also be avoided if the laparotomy is large enough to allow exteriorization of the gravid uterine horn. Trocars may then be placed across the uterine wall under direct vision and secured with purse string sutures.[17] Numerous endoscopic procedures may then be performed as if the feto-placental unit were intra-abdominal.[2] There is, however, a risk of uterine injury upon exteriorization. In our sheep model, the laparoscopically assisted mini-hysterotomy provided a safe means of establishing amniotic access without excessive risk to mother or fetus.

Minimally invasive instrumentation is increasingly being sought to overcome the problems of open fetal surgery. One inherent problem of operating in the uterus is the fetus floating within the fluid-filled confines of the amniotic cavity. Even in cases of oligohydramnios resulting from obstructive uropathies, the mobile fetus is not ideally situated for surgical interventions. This study assessed three devices originally designed for non-fetal laparoscopic applications. The Roeder loop may be removed with some difficulty at the end of a procedure, and the T-fasteners remain in place until parturition. The developmental effects of both absorbable and non-absorbable materials remaining in utero are poorly defined, and would need to be fully investigated before recommendation of clinical trials. The 2 mm grasper did provide the most effective means of manipulating the fetal limbs, could be re-applied at will, and was completely removable. Additionally, there was no hemorrhage, trauma, or scarring at the site of deployment as evidenced on post-operative day 10. This device facilitated positioning of the fetus for a supra-pubic surgical approach to the bladder.

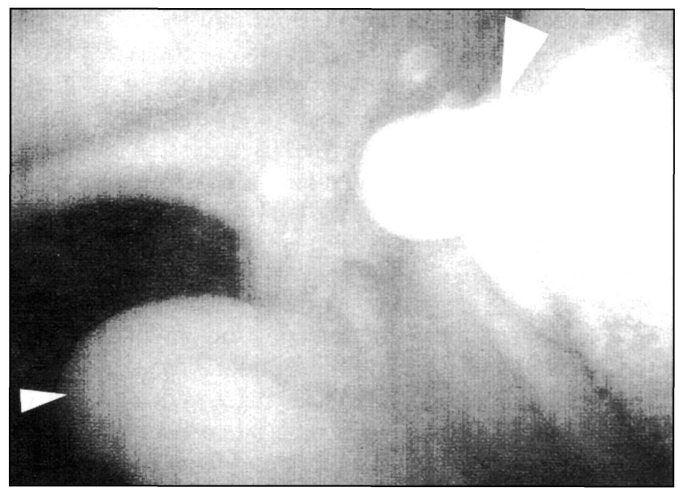

Figure 3. Microamnioscopic image of the external genitalia of a male sheep fetus positioned for vesicostomy (90 days gestational age). The small arrow indicates the scrotum containing descended testes bilaterally, while the phallus is marked by the large arrow. The umbilical cord is clearly seen, as is the ventral abdominal wall overlying the bladder which is our surgical target for vesicostomy (view through 5 mm endoscope).

We are currently applying many of these new techniques and instruments to develop a minimally invasive laser vesicostomy for the prenatal treatment of obstructive uropathies. Our preliminary investigations have utilized the Holmium:YAG laser. The 2100 nm wavelength is highly absorbed by water and provides a means of dissecting urologic soft tissues while maintaining hemostasis in an aqueous environment.[18,19] Commercially available fibers for the Holmium:YAG laser (Versa Pulse 2.1, Coherent, Palo Alto, CA) easily pass through the working channels of several small diameter flexible deflectable endoscopes. Ideally, a single 2 mm trocar would be inserted under ultrasonographic guidance into the amniotic cavity, permitting full endoscopic fetal examination followed by creation of a vesicostomy via laser dissection

without the need for amniotic fluid infusion or replacement. If necessary, a second 2 mm trocar could be placed for deployment of a spring-tension grasper to properly position a mobile fetus. In cases of anterior placentation which severely limits percutaneous access, a mini-hysterotomy as described would provide a safe means of intrauterine instrumentation for fetal repair.

CONCLUSIONS

There are several means of accessing the gravid uterus for experimental fetal surgery. Ultrasonography, if available, permits completely percutaneous placement of small (2 mm) trocars for microamnioscopic procedures. It is likely that the risk of injury to mother and fetus are comparable to amniocentesis. Percutaneous access is limited, however, in clinical cases of anterior placentation. Maternal laparoscopy followed by endoscopically guided placement of transuterine trocars is useful in sheep models in which there are numerous placental cotyledons to be avoided. A laparoscopically assisted mini-hysterotomy allows complete inspection of the uterine contents prior to entry. This technique also ensures that the minimal uterine incision is placed in the ideal location over the fetus. Additionally, no trocars or needles are inserted into the amniotic cavity, reducing the risk of injury.

Three methods of grasping and manipulating the fetus in utero were investigated. The ideal device would be atraumatic to the uterus and fetus. The spring-tensioned 2 mm endoscopic retractor is available with either a tight or loose grip and was ideal for manipulating the lower extremities in the non-insufflated amniotic confines. The Roeder loop was cumbersome while the T-fasteners were more invasive and remained in place until delivery.

Minimally invasive fetal surgery is a clinical reality for selected fetuses. We believe that placement of a spring-tensioned grasper via a 2 mm trocar may be a valuable addition to instrumentation available to the fetal surgeon.

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