Fetal Surgery at Brown: The First 25 Years

FRANCOIS I. LUKS, MD, PhD; JULIE MONTEAGUDO, MD; DEBRA WATSON-SMITH, RN; STEPHEN R. CARR, MD

Nowadays, fetal surgery is a niche specialty that, for some, evokes the "final frontier": operating on patients before they're even born. It has captured the imagination of many, thanks to regular coverage in the media[1] and countless appearances in television's medical shows. Operations *in utero* are now offered in a growing number of tertiary and quaternary medical centers, albeit for a still-limited number of indications. Three decades ago, however, it was considered experimental. There were only two comprehensive fetal surgery centers in North America—at the University of California San Francisco, where fetal surgery was "born," and a relatively new program at the Children's Hospital of Philadelphia (CHOP). Two other specialists, in Milwaukee, Wisconsin and Tampa, Florida, offered fetal endoscopic treatment for a single indication, twin-to-twin transfusion syndrome (TTTS).

Fetal surgery is only the tip of the iceberg called fetal medicine. For every pregnant woman who undergoes an operation on her fetus, there are innumerable patients who need close prenatal monitoring, advanced fetal diagnosis, modified birthing plans, and even non-invasive maternal-fetal treatment. At Brown, all these aspects of maternal-fetal care had been present for a long time, and countless neonatal and pediatric specialists were expert in the management of congenital conditions. When, in the late 1990s, fetal surgery was being considered, the first priority was to create a coherent, unified approach to the diagnosis and management of fetal conditions: the concept of Multidisciplinary Antenatal Diagnosis and Management (MADAM) was born in 1997. Its twice-a-month conferences were mirrored after the model of a tumor board, and its many goals included multispecialty discussions of complex cases, mutual evidence-based education on the rapid advances in fetal care, establishment of perinatal treatment protocols, and an ethics/sounding board for new forms of fetal therapy—including fetal surgery.

The expertise required for the technical aspects of fetal surgery was already present at Brown and its affiliated institutions, Women & Infants, Hasbro Children's and Rhode Island hospitals. There already existed robust research in fetal physiology and fetal surgery[2-4]; Hasbro Children's was at the forefront of minimally invasive surgery (laparoscopy) in infants and neonates[5,6]; the Neonatal Intensive Care Unit was the second-largest in New England and its neonatologists nationally renowned[7,8]; and the Divisions of Maternal-Fetal Medicine and Pediatric Cardiology were known for their expertise in ultrasound diagnosis, fetal echocardiography and ultrasound-guided invasive therapy.[9,10] Following consultation with the very few existing fetal surgery centers worldwide, a protocol was drafted and critiqued by the MADAM board, which ultimately approved it; and clearance was obtained from the Institutional Review Board (IRB) at both hospitals and the chiefs of surgery and obstetrics & gynecology. In the spring of 2000, the first two patients with severe TTTS underwent endoscopic fetal surgery—a single-port technique aimed at laser ablation of all communicating placental vessels responsible for the unbalanced transfusion of blood from one fetus to its identical twin.[11]

This was a first in New England, and it made the local and regional news. (That same year, the International Fetal Medicine and Surgery Society (IFMSS) met in Nantucket, hosted by the CHOP team. Guests from around the globe who checked into their hotel room were treated to the local news, on a loop—including Rhode Island's first fetal operations.)

Endoscopic laser treatment is the only therapy that addresses the root problem of TTTS—to interrupt the unbalanced transfusion from donor to the recipient twin. Unfortunately, the intervention does not make the fetuses better, it just prevents them from getting worse, and poses risks to fetus and mother. Survival of at least one twin was only 70%, due to a combination of preterm (pre-viability) labor and postoperative intrauterine demise of already very compromised fetuses—still far better than the near-100% mortality of both twins in advanced cases that did not undergo intervention. As this was a new field, there was plenty of opportunity to discover hitherto unknown aspects of the condition,[12-15] develop new diagnostic modalities,[16] and perfect surgical techniques.[17-19] For the first few years, the number of patients we had operated on was dwarfed by the number of abstracts, papers and scientific presentations from our Fetal Treatment Program. Since its inception, our program has published more than 100 peer-reviewed articles and produced more than 250 abstracts, presentations, and book chapters, on topics ranging from the epigenetic changes in TTTS[20] and the *in vivo* determination of hemoglobin concentrations in donor and recipient vessels,[21] to short- and long-term outcome of TTTS.[22] Among the novel techniques

established by our program, the description of placental vascular anastomoses after laser surgery has resonated the most.[23] In a 2025 study on the 25 most paradigm-shifting articles in fetal surgery in the world literature, our 2004 study was ranked number 1, with a higher disruption factor than the next five studies combined.[24]

In 2004, the results of the first randomized controlled study were published, showing a significant survival advantage of endoscopic laser ablation of placental vessels over serial amnioreduction.[25] This international study comprised more than 30 fetal centers in six countries, although patients randomized to surgery were treated at one of only three centers: Leuven (Belgium), Paris (France) and Providence, RI (the only North American center in the study).

That same year, we were invited to participate in a National Institutes of Health (NIH)-sponsored workshop on the future of fetal medicine.[26] Of the 20 participants, only four represented fetal surgery centers; we had argued successfully that, while the presence of the largest such programs was essential, representation from smaller, regional centers was important to develop a national policy on access to advanced fetal care. (The contributions from the Brown Fetal Treatment Program may or may not have had lasting effects, but the term "MADAM conference" entered the vernacular.)

One of the consequences of the NIH workshop on fetal medicine was the creation of the North American Fetal Therapy Network (NAFTNet) in 2005, comprising 15 fetal treatment centers in the United States and Canada (not all of them fetal surgery centers).[27,28] The Brown Fetal Treatment Program was one of the founding members of NAFTNet—a network that now, in its 20th year, comprises more than 50 centers worldwide. When, in 2015, the Fetal Therapy Nurse Network (FTNN) was created as an off-shoot of NAFTNet, our fetal nurse coordinator was one of the original members, too. At the time, the Rhode Island program was still the only such initiative in New England; it would take another few years for the Yale program to start, and another decade-and-a-half before Boston began to offer fetal surgery as well. Consequently, more than 85% of our patients were referred in from adjoining states (all of New England), and as far away as New York, New Jersey, Georgia, Louisiana, Florida, Minnesota and North Dakota. Ours was a model of cooperation, not only between specialty services and departments, but between two hospitals and the medical school. To emphasize this combined approach and stress collaboration over rivalry, the hospitals joined forces in a renamed Fetal Treatment Program of New England, and both have continued to proudly promote the program as a joint effort. That example of collaboration was prominently displayed when the program hosted the annual IFMSS meeting in the summer of 2014, in what remains the largest such conference in the society's 43-year history.

Fetal surgery for TTTS was the tip of that proverbial iceberg, but the program has touted many other fetal firsts over the decade, including:

- The first EX-utero/Intrapartum ("EXIT") procedure, in 2005, for a giant cervical tumor that would have made it impossible for the newborn baby to breathe on her own; a team of highly specialized nurses, respiratory therapists and physicians from five different specialties at both hospitals partially delivered the infant, keeping it on placental support while a surgical airway was obtained.
- The first, and so far only case of identical quadruplets treated for feto-fetal transfusion syndrome.[29]
- The first Food and Drug Administration (FDA)-sanctioned Investigational Device Exemption (IDE) for a detachable balloon inserted in the trachea of fetuses with severe congenital diaphragmatic hernia and extreme pulmonary hypoplasia, a technique shown experimentally to cause accelerated lung growth.[30]
- One of the youngest-ever sets of conjoined twins to be separated, mere weeks after a premature delivery—in large part because of the collaborative prenatal planning of our team, including a novel method of early gestation visualization.[31]
- And in 2018, following the results of the Management of Myelomeningocele Study (MOMS),[32] the first open fetal surgery in New England to repair a spina bifida *in utero*.[33]

Research and clinical excellence have been two driving forces of the fetal treatment program at Brown. As the MADAM experience showed us, education was another major consideration. Educating the next generation of fetal medicine specialists was felt to be equally important. Thus, in 2003, we started to offer a unique opportunity: a course in fetal medicine to medical students at what was then the Brown University Medical School, and to undergraduate students in the Program in Liberal Medicine Education (PLME). In a survey of the first four classes (2003–2007), students credited the course with helping them understand embryology and human development (87%), the link between basic science and clinical medicine (70%), the role of ethics in medicine (90%), and the importance of a multidisciplinary approach to medicine (93%).[25] Twenty years later, the course is still being taught.

Fetal surgery as a field of medicine is no longer considered experimental, but it remains a niche specialty that requires the highest degree of expertise, coordination and engagement. The Fetal Treatment Program of New England is no longer the only such initiative in the region, but it is the oldest. Many of our former fetal patients are now old enough to drive; some have voted twice in presidential elections, gone to college and started families of their own. A generation later, our program continues to thrive, and younger fetal specialists have joined the ranks of the "old guard."

Even as the healthcare landscape in Rhode Island and the region undergo major changes, mothers, their fetuses, and their families continue to benefit from a talented and experienced team that exemplifies collaboration across specialties and hospitals. The program itself continues to be at the forefront of innovation—*in utero* repair of fetal spina bifida using robotic surgery is now in a preclinical phase,[35] offering the promise of highly precise interventions on the fetus with minimal pain, discomfort and risk to mothers. Today, the Fetal Treatment Program of New England continues to offer fetal surgery to patients in our community and beyond. It serves as a model for fledgling programs around the country and gladly shares its 25-year experience; and it continues to advance the field of fetal medicine for all.

References

1. Miller GW. Fetal surgery gives baby brighter future. The Providence Journal. Providence, RI; 2019.
2. Papadakis K, Luks FI, De Paepe ME, Piasecki GJ, Wesselhoeft CW, Jr. Fetal lung growth after tracheal ligation is not solely a pressure phenomenon. J Pediatr Surg. 1997;32(2):347-351.
3. Papadakis K, De Paepe ME, Tackett LD, Piasecki GJ, Luks FI. Temporary tracheal occlusion causes catch-up lung maturation in a fetal model of diaphragmatic hernia. J Pediatr Surg. 1998;33(7):1030-1037.
4. De Paepe ME, Papadakis K, Johnson BD, Luks FI. Fate of the type II pneumocyte following tracheal occlusion in utero: a time-course study in fetal sheep. Virchows Arch. 1998;432(1):7-16.
5. Lessin MS, Luks FI. Laparoscopic appendectomy and duodeno-colonic dissociation (LADD) procedure for malrotation. Pediatr Surg Int. 1998;13(2-3):184-185.
6. Tomicic JT, Luks FI, Shalon L, Tracy TF. Laparoscopic gastrostomy in infants and children. Eur J Pediatr Surg. 2002;12(2):107-110.
7. Rubin LP, Kifor O, Hua J, Brown EM, Torday JS. Parathyroid hormone (PTH) and PTH-related protein stimulate surfactant phospholipid synthesis in rat fetal lung, apparently by a mesenchymal- epithelial mechanism. Biochim Biophys Acta. 1994;1223(1):91-100.
8. Padbury JF, McGonnigal B, Tseng YT, Nguyen TT, Stabila JP. Cloning and sequence analysis of the rat norepinephrine transporter promoter. Brain Res Mol Brain Res. 2000;83(1-2):128-132.
9. Canick JA, Carr SR. Screening for birth defects: integrating laboratory evaluation, genetic counseling and clinical intervention. Med Health R I. 1998;81(4):122-126.
10. Carr SR, Gilchrist JM, Abuelo DN, Clark D. Treatment of antenatal myasthenia gravis. Obstet Gynecol. 1991;78(3 Pt 2):485-489.
11. Bussey JG, Luks F, Carr SR, Plevyak M, Tracy TF, Jr. Minimal-access fetal surgery for twin-to-twin transfusion syndrome. Surg Endosc. 2004;18(1):83-86.
12. De Paepe ME, Stopa E, Huang C, Hansen K, Luks FI. Renal tubular apoptosis in twin-to-twin transfusion syndrome. Pediatr Dev Pathol. 2003;6(3):215-225.
13. Carr SR, Luks F, Tracy T, Plevyak M. Antenatal Necrotic Injury in Severe Twin-to-Twin Transfusion Syndrome. A Case and Review. Fetal Diagn Ther. 2004;19(4):370-372.
14. Poch M, De Koninck P, Luks FI, Carr SR, De Paepe ME. Net vascular cross-sectional area correlates with twin-to-twin transfusion. International Fetal Medicine and Surgery Society Annual Meeting. 2004.
15. Luks FI, Carr SR, Plevyak M, et al. Limited prognostic value of a staging system for twin-to-twin transfusion syndrome. Fetal Diagn Ther. 2004;19(3):301-304.
16. Luks FI, Carr SR, Ponte B, Rogg JM, Tracy TF, Jr. Preoperative planning with magnetic resonance imaging and computerized volume rendering in twin-to-twin transfusion syndrome. Am J Obstet Gynecol. 2001;185(1):216-219.
17. Lombardo ML, Watson-Smith DJ, Muratore CS, Carr SR, O'Brien BM, Luks FI. Laser ablation of placental vessels in twin-to-twin transfusion syndrome: a paradigm for endoscopic fetal surgery. J Laparoendosc Adv Surg Tech. 2011;21(9):869-872.
18. Ahmed S, Luks FI, O'Brien BM, Muratore CS, Carr SR. Influence of experience, case load, and stage distribution on outcome of endoscopic laser surgery for TTTS–a review. Prenat Diagn. 2009;30(4):314-319.
19. Duron VD, Watson-Smith D, Benzuly SE, et al. Maternal and fetal safety of fluid-restrictive general anesthesia for endoscopic fetal surgery in monochorionic twin gestations. J Clin Anesth. 2014;26(3):184-190.
20. Marsit CJ, Koestler DC, Watson-Smith D, Boney CM, Padbury JF, Luks F. Developmental genes targeted for epigenetic variation between twin-twin transfusion syndrome children. Clin Epigenetics. 2013;5(1):18. doi: 10.1186/1868-7083-5-18.
21. Curran S, McMurdy JW, Carr SR, et al. Reflectance spectrometry for real-time hemoglobin determination of placental vessels during endoscopic laser surgery for twin-to-twin transfusion syndrome. J Pediatr Surg. 2010;45(1):59-64.
22. Kowitt B, Tucker R, Watson-Smith D, et al. Long-term morbidity after fetal endoscopic surgery for severe twin-to-twin transfusion syndrome. J Pediatr Surg. 2012;47(1):51-56.
23. De Paepe ME, Friedman RM, Poch M, Hansen K, Carr SR, Luks FI. Placental findings after laser ablation of communicating vessels in twin-to-twin transfusion syndrome. Pediatr Dev Pathol. 2004;7(2):159-165.
24. Vaughn CR, Han XY, White M, Becerra AZ, Chon AH, Sun RC. Return of the Disruption Score: Fetal Surgery in the Spotlight (1975-2021). J Pediatr Surg. 2025;60(7):162338. doi: 10.1016/j.jpedsurg.2025.162338. Epub 2025 Apr 24.
25. 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(2):136-144.
26. Chescheir NC, Socol M. The National Institutes of Health Workshop on Fetal Treatment: needs assessment and future directions. Obstet Gynecol. 2005;106(4):828-833.
27. Johnson MP. The North American Fetal Therapy Network (NAFTNet): a new approach to collaborative research in fetal diagnosis and therapy. Semin Fetal Neonatal Med. 2010 Feb;15(1):52-7. doi: 10.1016/j.siny.2009.05.006. Epub 2009 Jun 24.
28. Luks FI, Johnson A, Polzin WJ, North American Fetal Therapy N. Innovation in maternal-fetal therapy: a position statement from the North American Fetal Therapy Network. Obstet Gynecol. 2015;125(3):649-652.
29. O'Brien BM, Feltovich HM, Carr SR, Luks FI. Feto-fetal transfusion syndrome in monochorionic quadruplets. Obstet Gynecol. 2010;115(2 Pt 2):470-472.
30. Liao SL, Luks FI, Piasecki GJ, Wild YK, Papadakis K, De Paepe ME. Late-gestation tracheal occlusion in the fetal lamb causes rapid lung growth with type II cell preservation. J Surg Res. 2000;92(1):64-70.
31. Luks FI, Monteagudo J, Collins S, et al. Surface rendering of cross-sectional imaging and medical illustration for perinatal planning in conjoined twins. Fetal Diagn Ther. 2025;52:254-261.
32. Adzick NS, Thom EA, Spong CY, et al; MOMS Investigators. A Randomized Trial of Prenatal versus Postnatal Repair of Myelomeningocele. N Engl J Med. 2011;364(11):993-1004.

33. Snegovskikh D, Svokos K, Souza D, et al. An Open Fetal Myelomeningocele Repair With Incorporation of a Skin Allograft. J Obstet Gynaecol Can. 2020;42(2):177-178.
34. Luks FI, Carr SR, Caldamone AA, Feit LR. Teaching fetal medicine to the next generation of physicians. International Fetal Medicine and Surgery Society (IFMSS). Aruba, 2007.
35. Monteagudo J, Giorgi M, Luhrs A, et al. Robotic-assisted fetal myelomeningocele repair: Feasibility and technique refinement using a surgical model. International Fetal Medicine and Surgery Society (IFMSS). Napa, CA, 2025.

Authors

Francois I. Luks, MD, PhD, Professor of Surgery, Pediatrics, and Obstetrics & Gynecology, Alpert Medical School of Brown University; Pediatric Surgeon-in-Chief, Hasbro Children's, Brown University Health, Providence, RI.

Julie Monteagudo, MD, Assistant Professor of Surgery and Pediatrics, Alpert Medical School of Brown University; Pediatric Surgeon, Hasbro Children's, Brown University Health, Providence, RI.

Debra Watson-Smith, RN, Fetal Treatment Program Nurse Manager, Fetal Treatment Program of New England, Brown University Health and Care New England, Providence, RI.

Stephen R. Carr, MD, Professor of Obstetrics & Gynecology, Alpert Medical School of Brown University; Maternal-Fetal Medicine Specialist, Department of Obstetrics & Gynecology, Care New England, Providence, RI.

Disclosures

None.

Disclaimer: The views expressed herein are those of the authors and do not necessarily reflect the views of the Alpert Medical School of Brown University, Brown University Health, or Care New England.

Ethical approval: Not applicable for this article.

Correspondence

Francois I. Luks, MD, PhD
Hasbro Children's
593 Eddy Street, Suite HCH 120
Providence, RI 02903
Francois_Luks@brown.edu