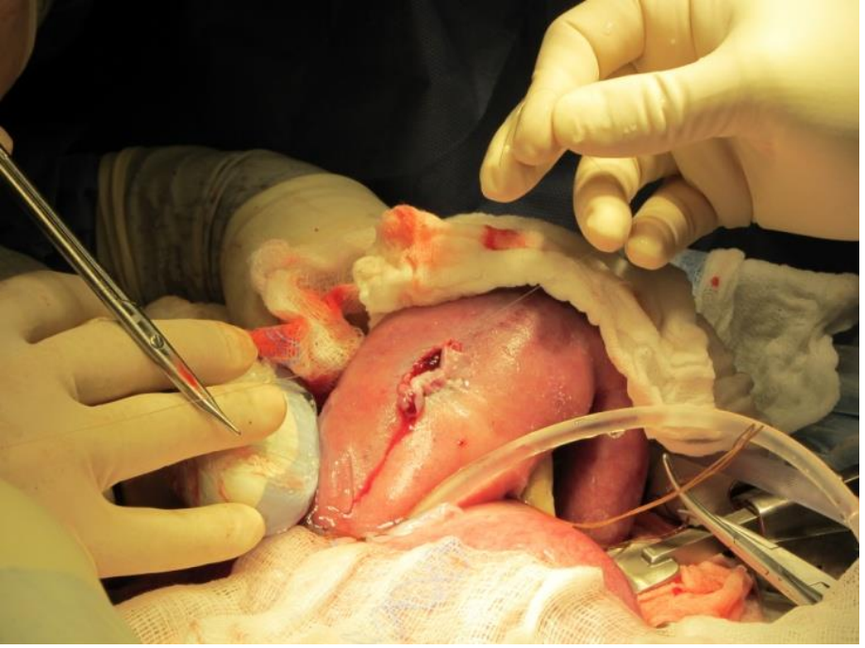
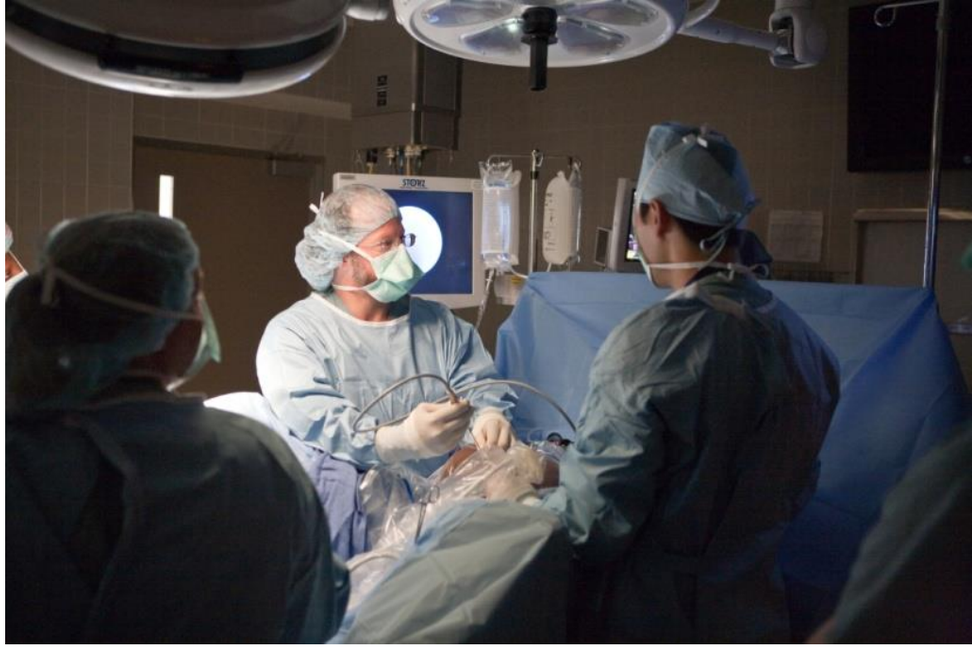


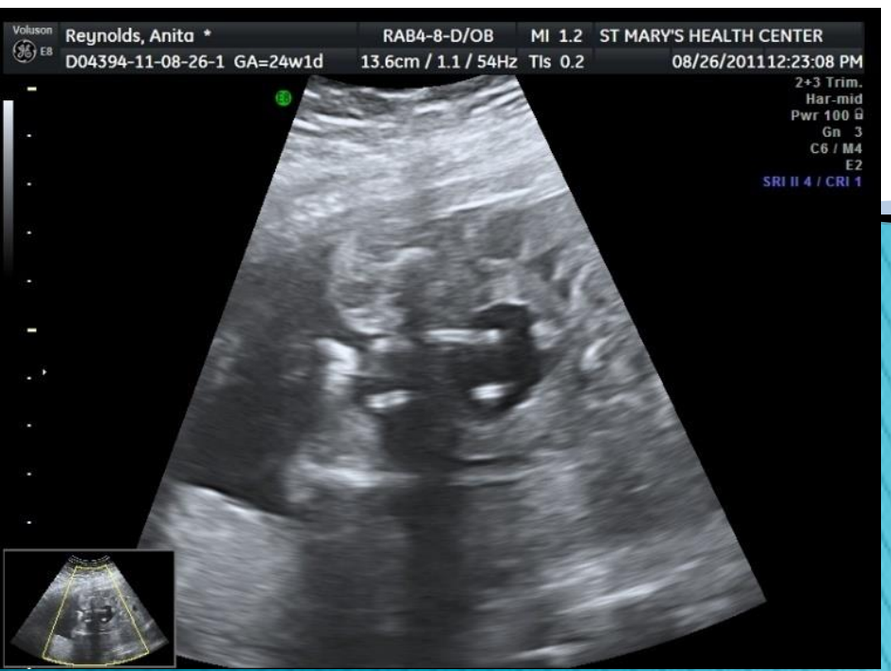


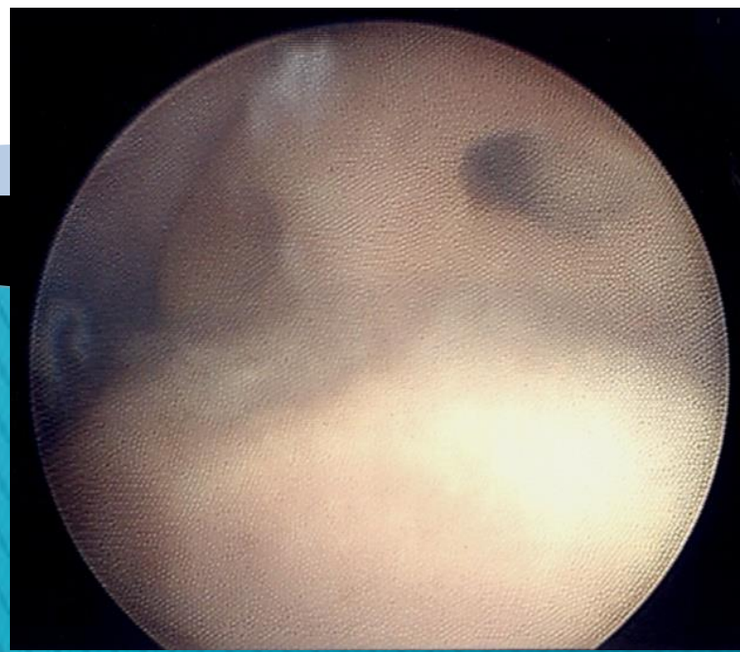
Fetal Intervention in the 21st Century

Emanuel “Mike” Vlastos, MD FACOG

ACOG District V &VII

2018 Annual Meeting September 21 – 23





Objectives

- Enumerate the common fetal interventions
- Differentiate the inclusion and exclusion criteria for consideration of fetal myelomeningocele repair
- State the stages of Twin Twin Transfusion Syndrome (TTTS)

Disclosure/Conflicts

- None*

**Open to securing*

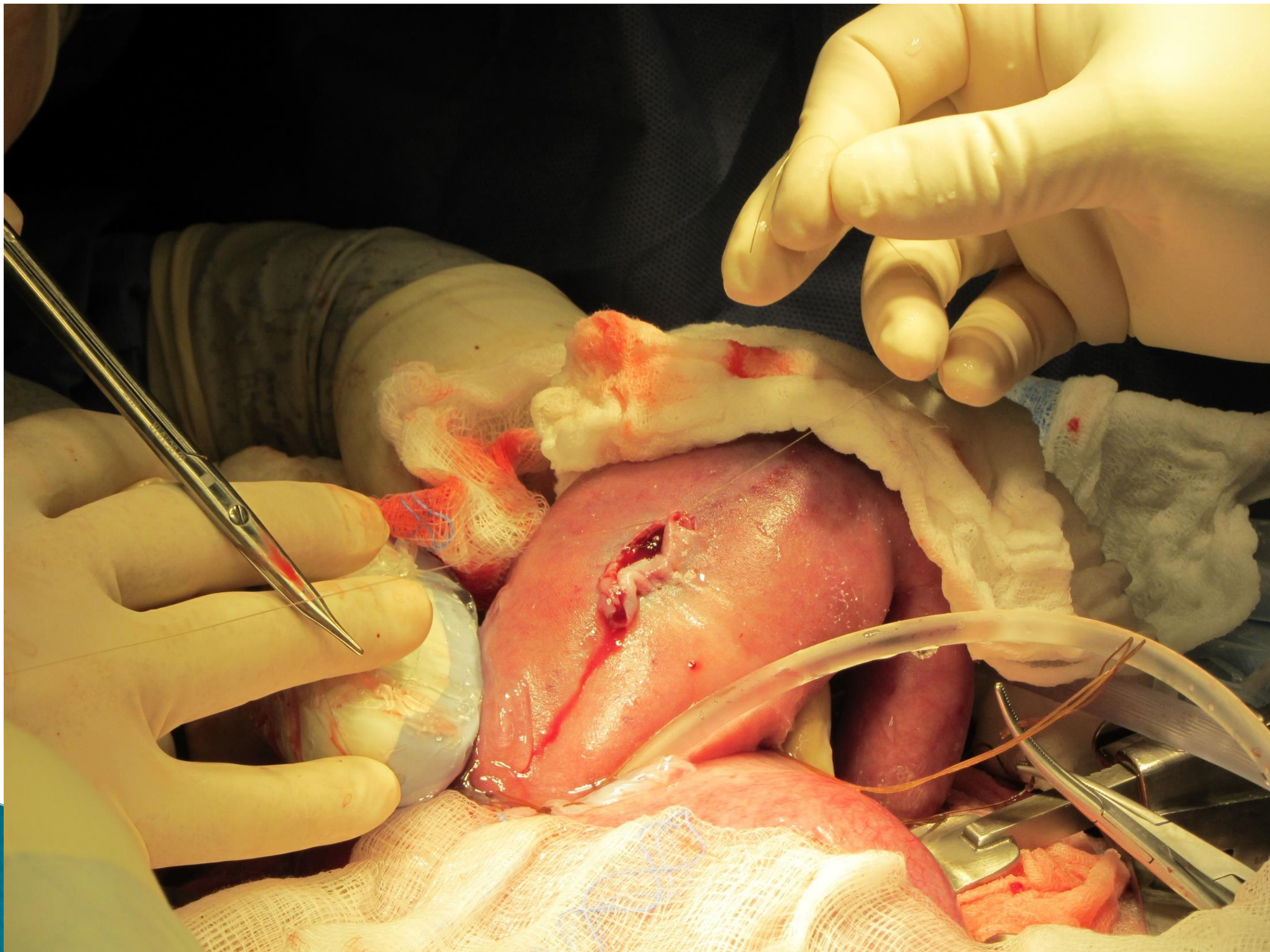
Preterm Birth in America

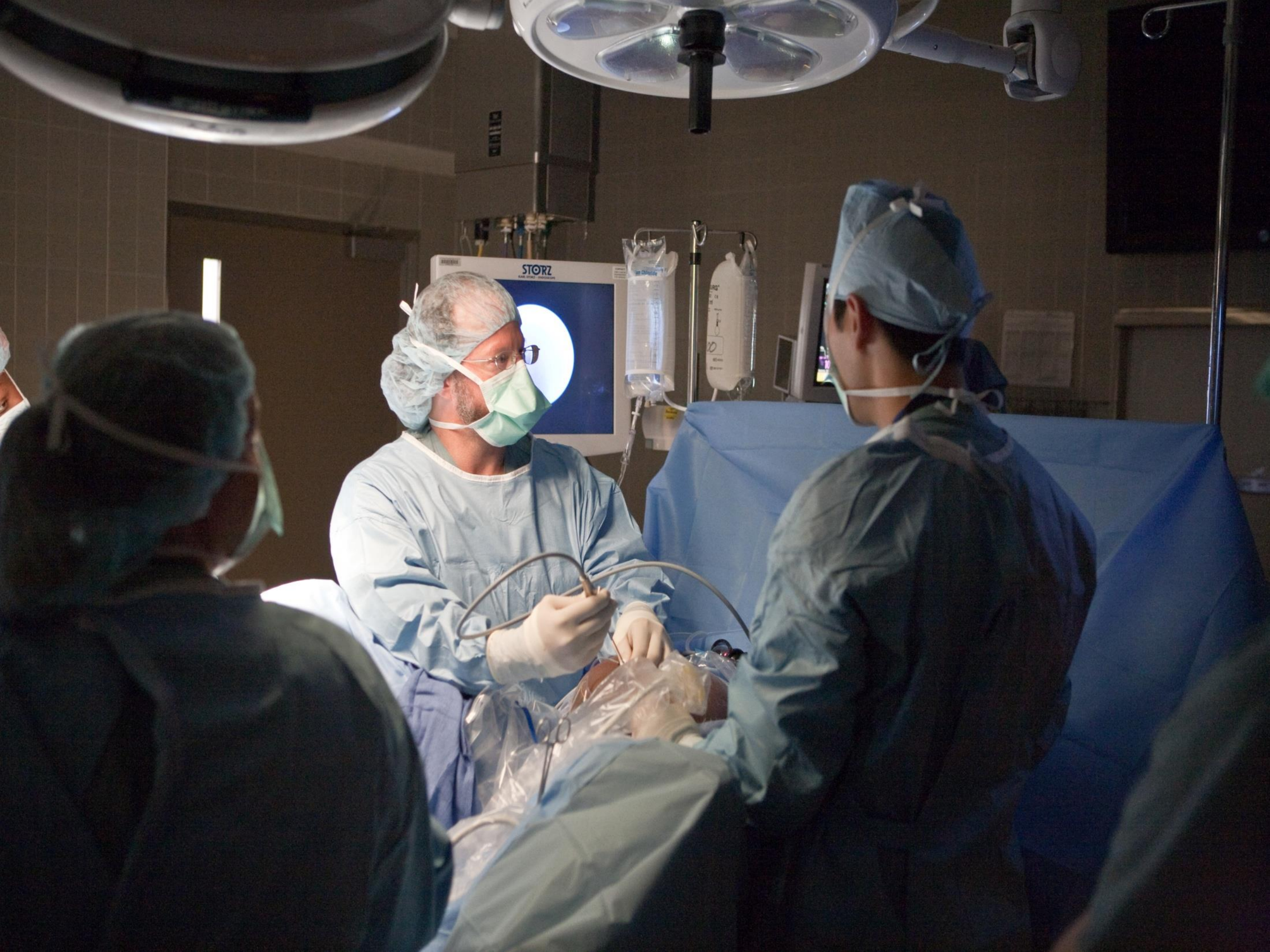
- 2016[1]
- ~ 4,000,000 births
- ~450,000* prior to 37 weeks
- 1/10 (9.6%*) are born PRETERM
- Some babies, however, are going to be born preterm

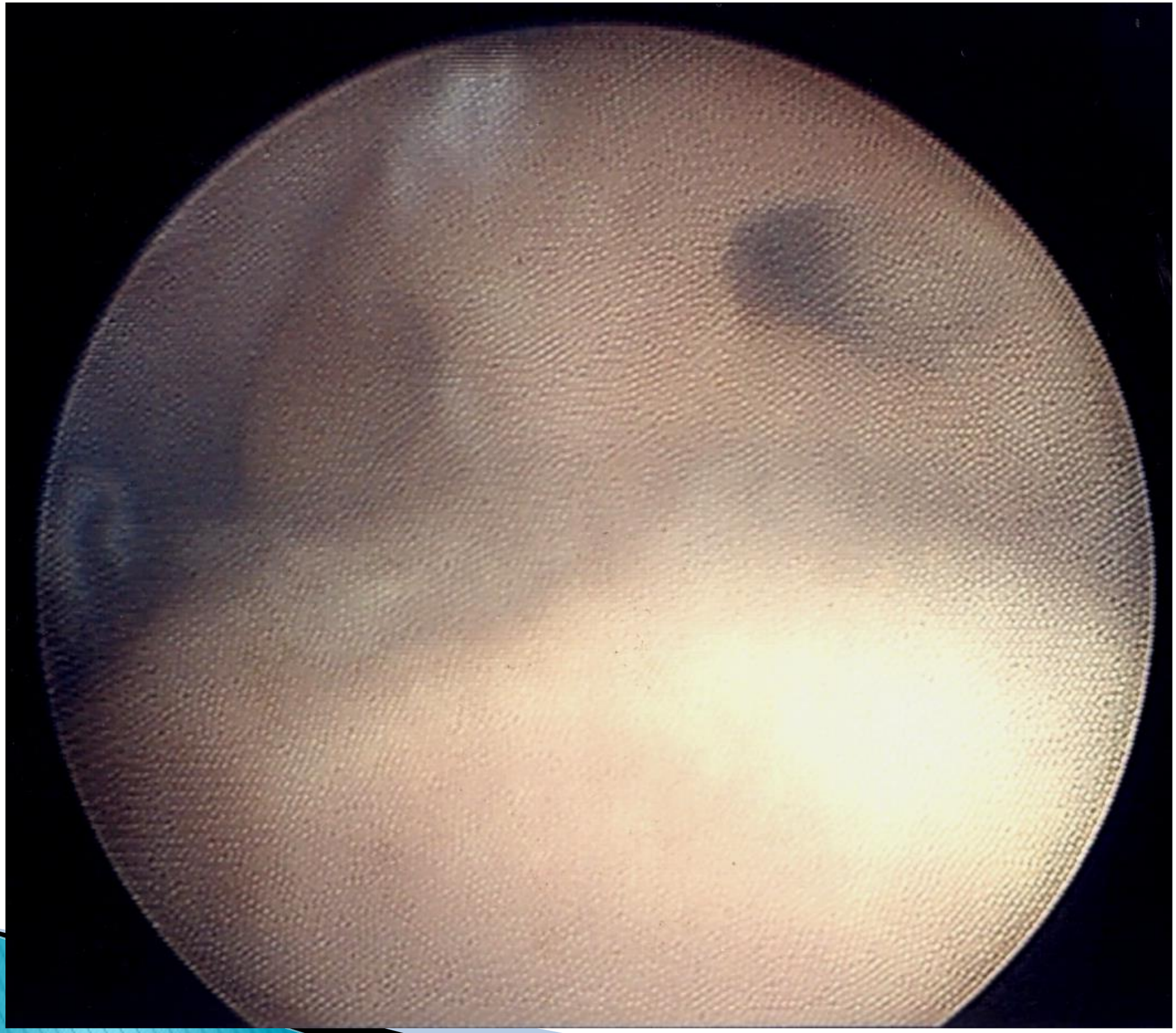
[1] *March of Dimes Data, 2017*

Fetuses with Anomalies

- Most fetal anomalies represent changes in development which are “fixed”
  - Aneuploidy, syndromes, infections
- A few fetal anomalies present with pathophysiologies with potentials for interruption
  - tumors, obstructions, shared circulations, bands, anemias
- Of these few fetuses, approximately 1 out of 10 are candidates for prenatal intervention




STORZ



D04394-11-08-26-1 GA=24w1d 13.6cm / 1.1 / 54Hz TIs 0.2 08/26/201112:23:08

2+3

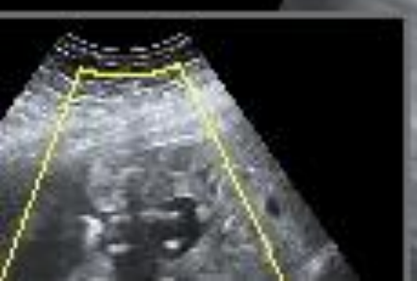
Har

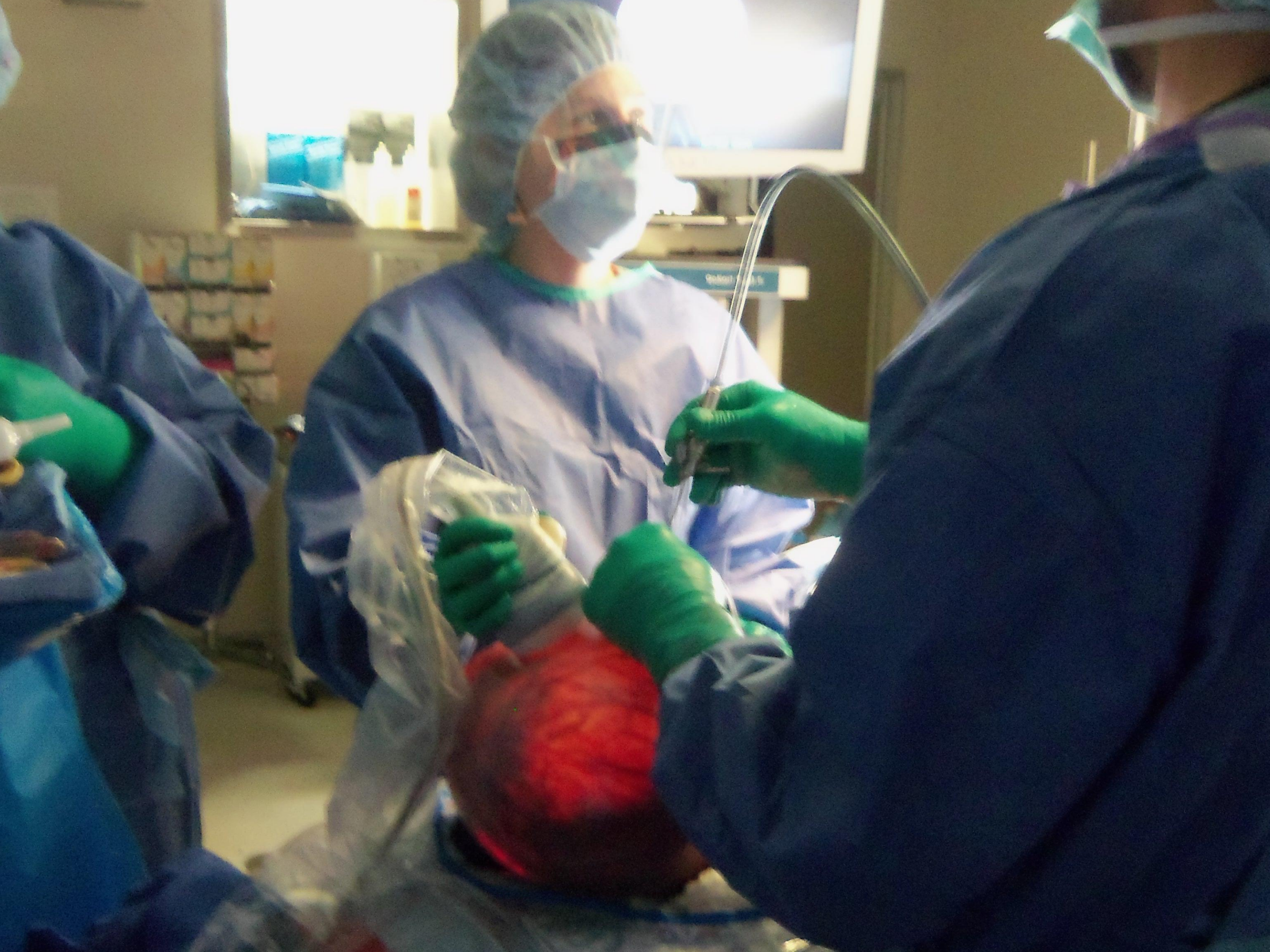
Pwr 1

G

C6

SRI II 4 / C



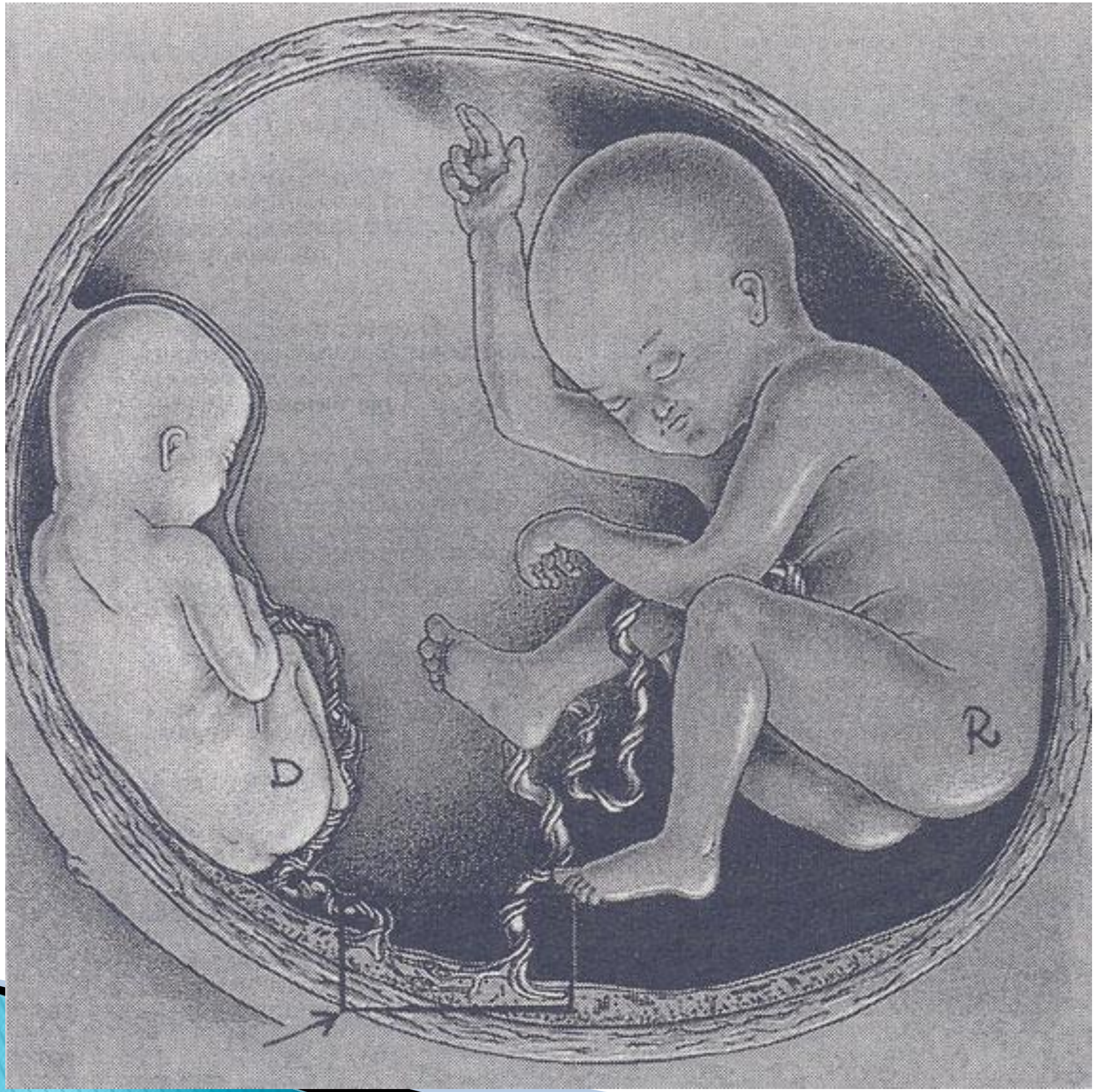


The Path Back to the Womb

- Initial fetal assessment
- Confirmation of assessment: Diagnosis
- Criteria: potential intervention
- When to hold ‘em (keep them at home)
- When to fold ‘em (referral to quaternary center)
- Home Coming: Surveillance at Home

Fetus: How Did I Get Here?

- Twin Twin Transfusion Syndrome
- Amniotic Band Syndrome
- Bladder Outlet Obstruction
- Myelomeningocele
- Thoracic Masses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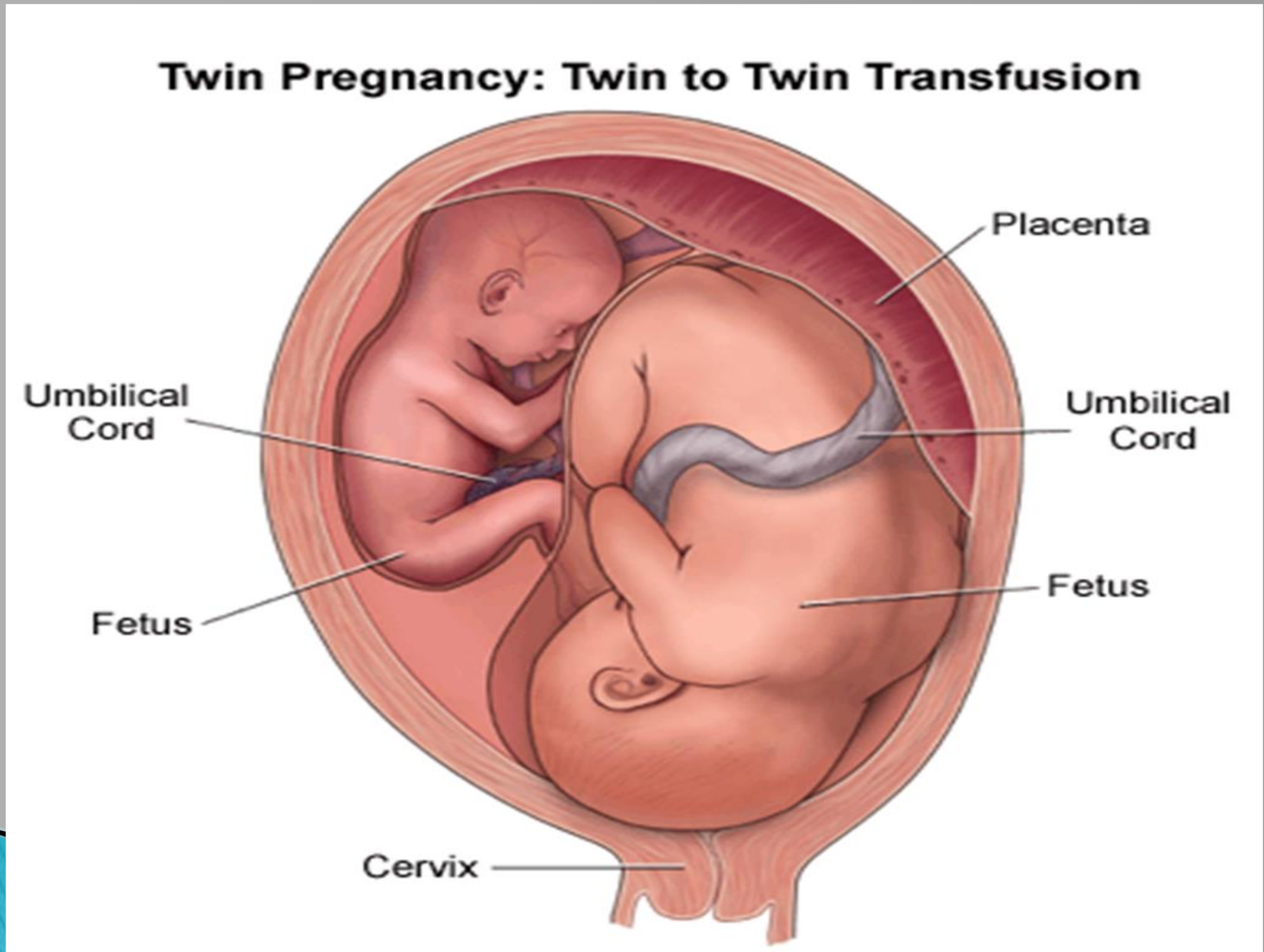
Twin Twin Transfusion Syndrome



Fetus: How Did I Get Here?

- Twins
  - Identical: Monozygotic (1 egg and 1 sperm)
  - Fraternal: Dizygotic (2 eggs and 2 sperm)

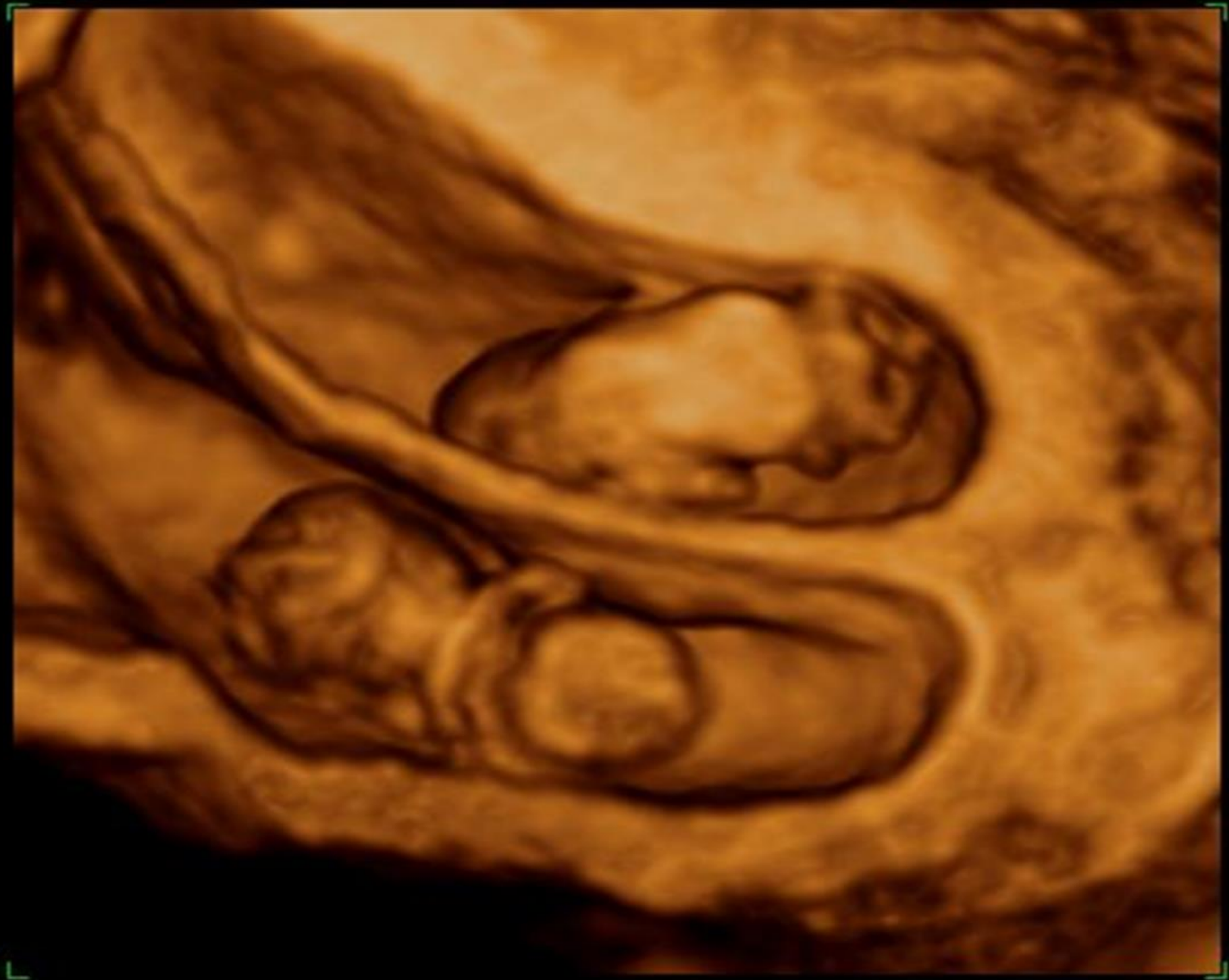
- Monochorionic: 1 placenta
  - Diamniotic: dividing membrane
  - Monoamniotic: no diving membrane
  - Conjoined: joined to some degree

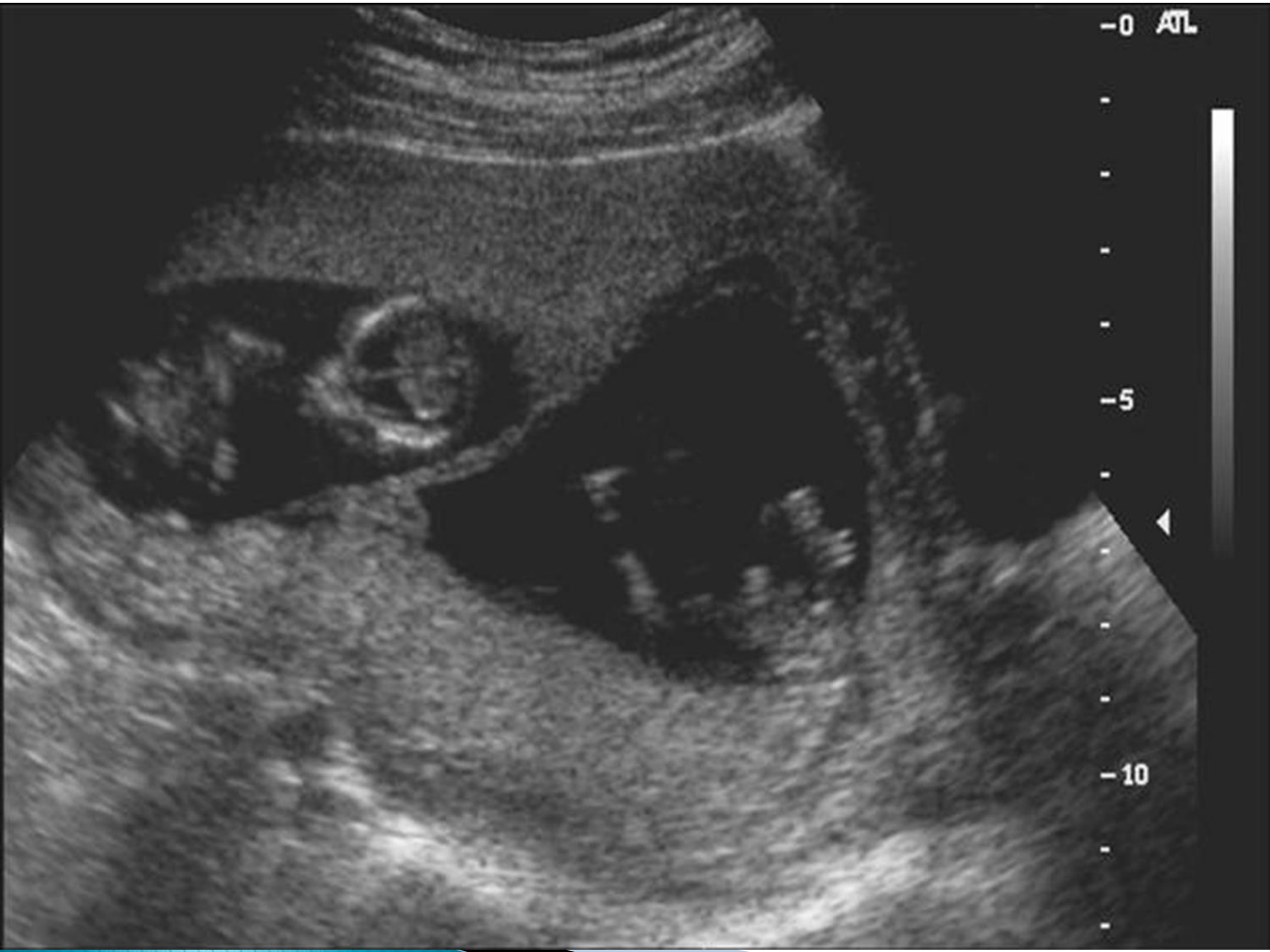
- Monochorionic, diamniotic twins
  - 1 placenta and two sacs/membranes
  - ie, one sac/membrane for each twin

Dichorionic, Diamniotic: DiDi

- Two Eggs – polyovulation
- Two Sperm – of millions!
- Two placentas – two different individuals
  - Two types of cells within the placentas
  - Two genetically unique fetuses
    - Gals, guys or one of each!

Th30




0
ATL
5
10


Triangular peak of villi
extending into the
intertwin membrane
"Twin peak" sign

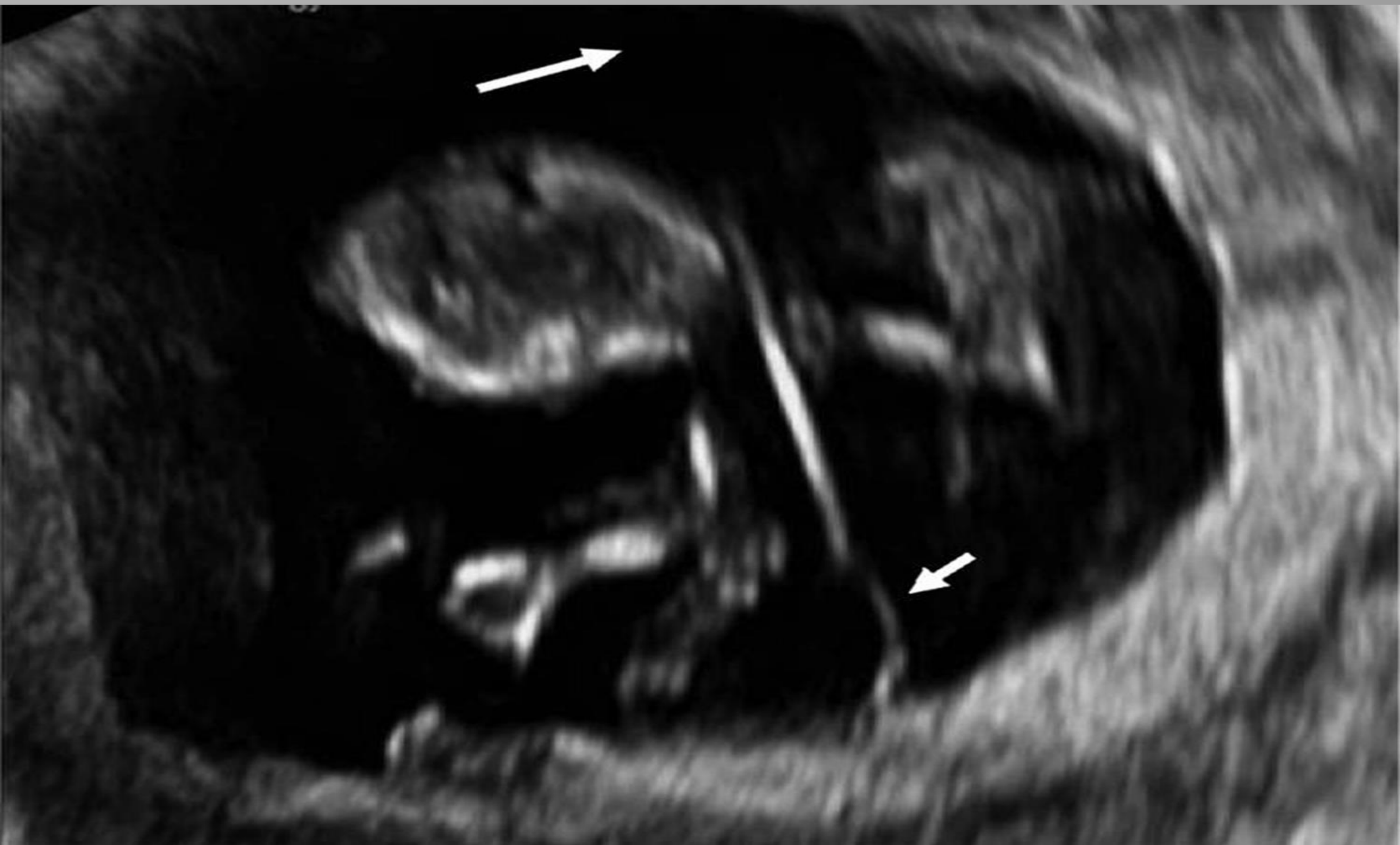
Monochorionic Twins

- One egg and one sperm
- Early split – dichorionic, diamniotic (DiDi)
  - Can be confused with dizygotic twins!
  - Hence, 20% of DiDi twins are monozygotic!
- Medium split – monchorionic, diamniotic
- Late split – monochorionic, monoamniotic
- Last minute split – conjoined twins

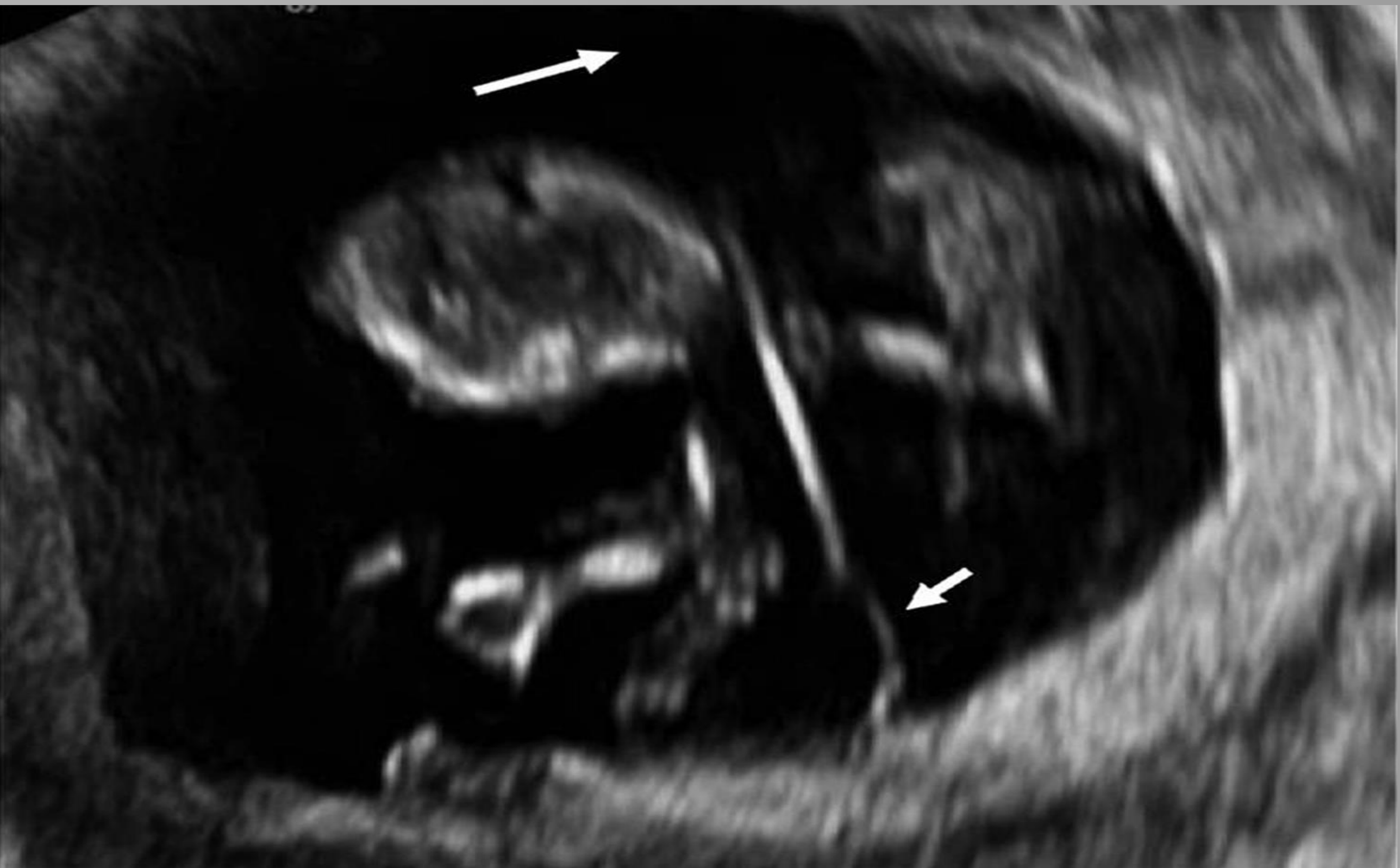
Monochorionic, Diamniotic Twins

- Once placenta
- “Twin Peak” sign – MISSING!!
- Thin dividing membrane
- Same Sex

One Placenta

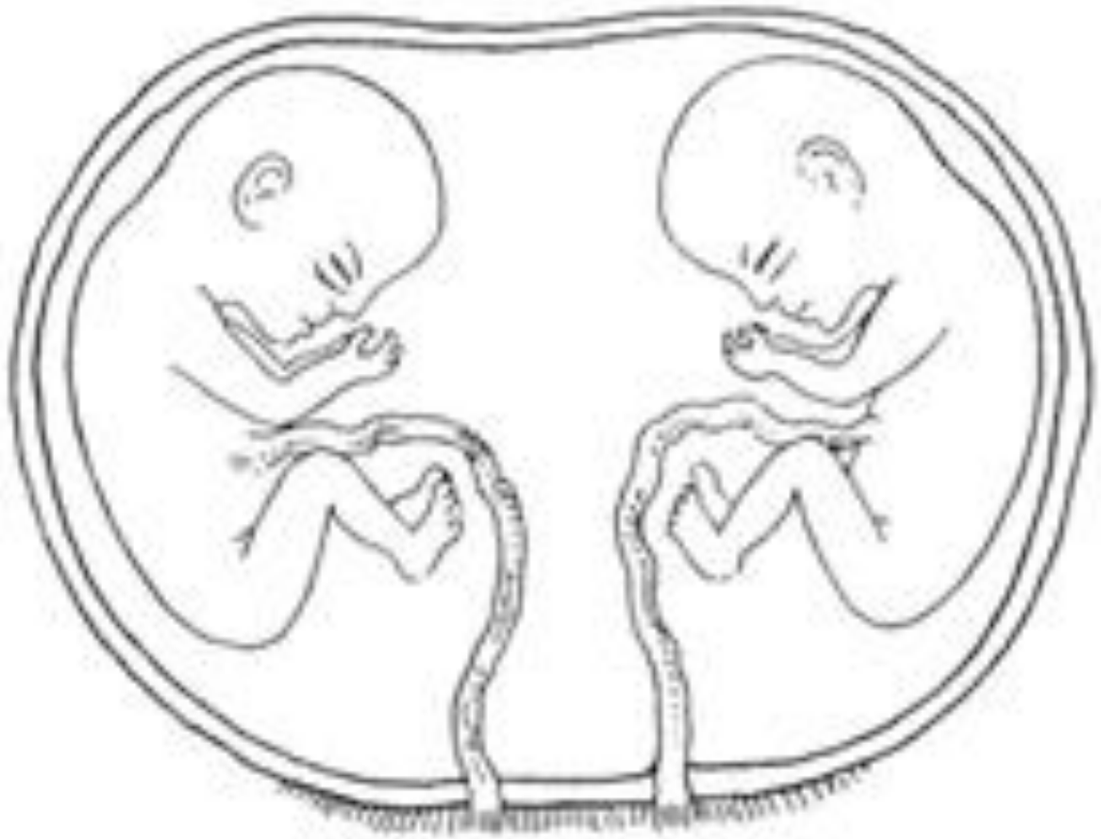


Thin Dividing Membrane: < 2mm

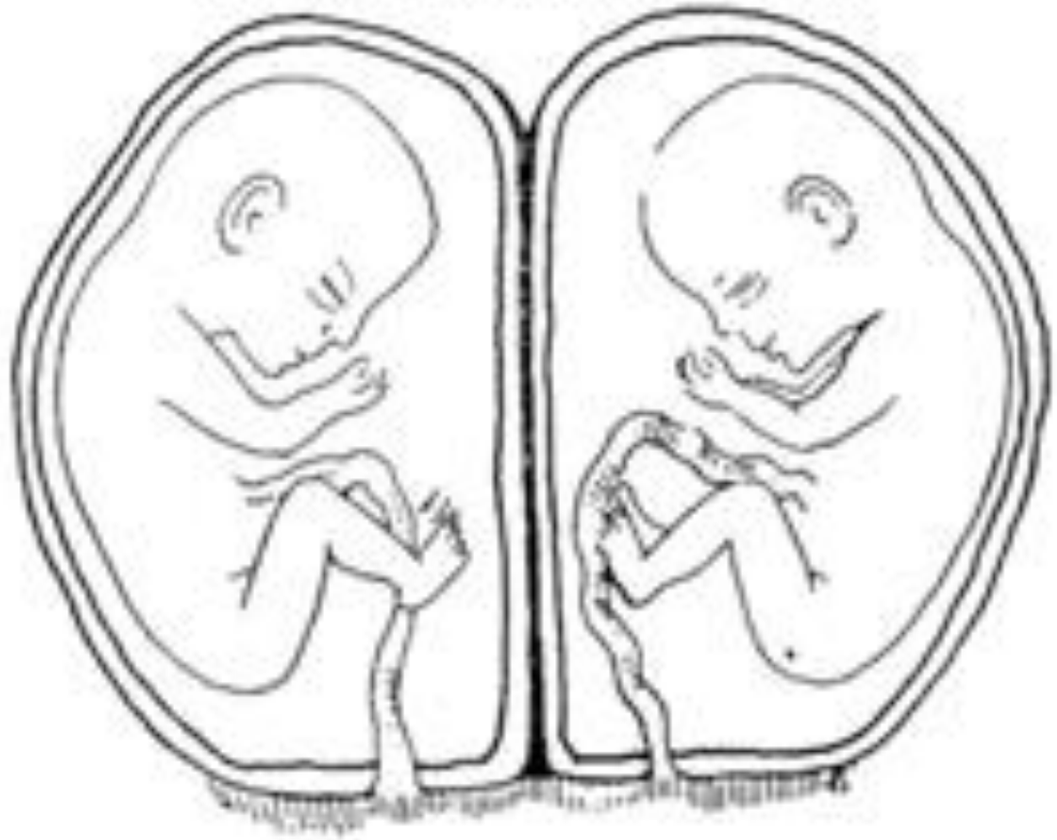


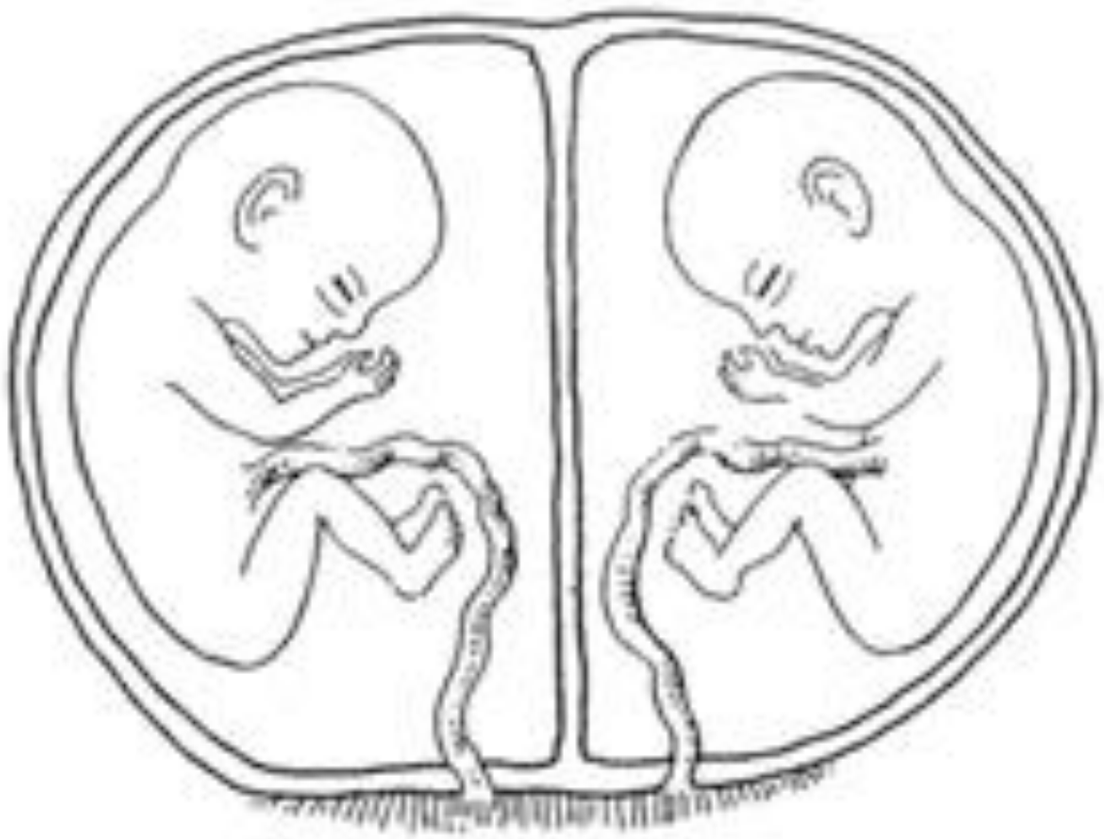
Same Sex

Monoamniotic monochorionic

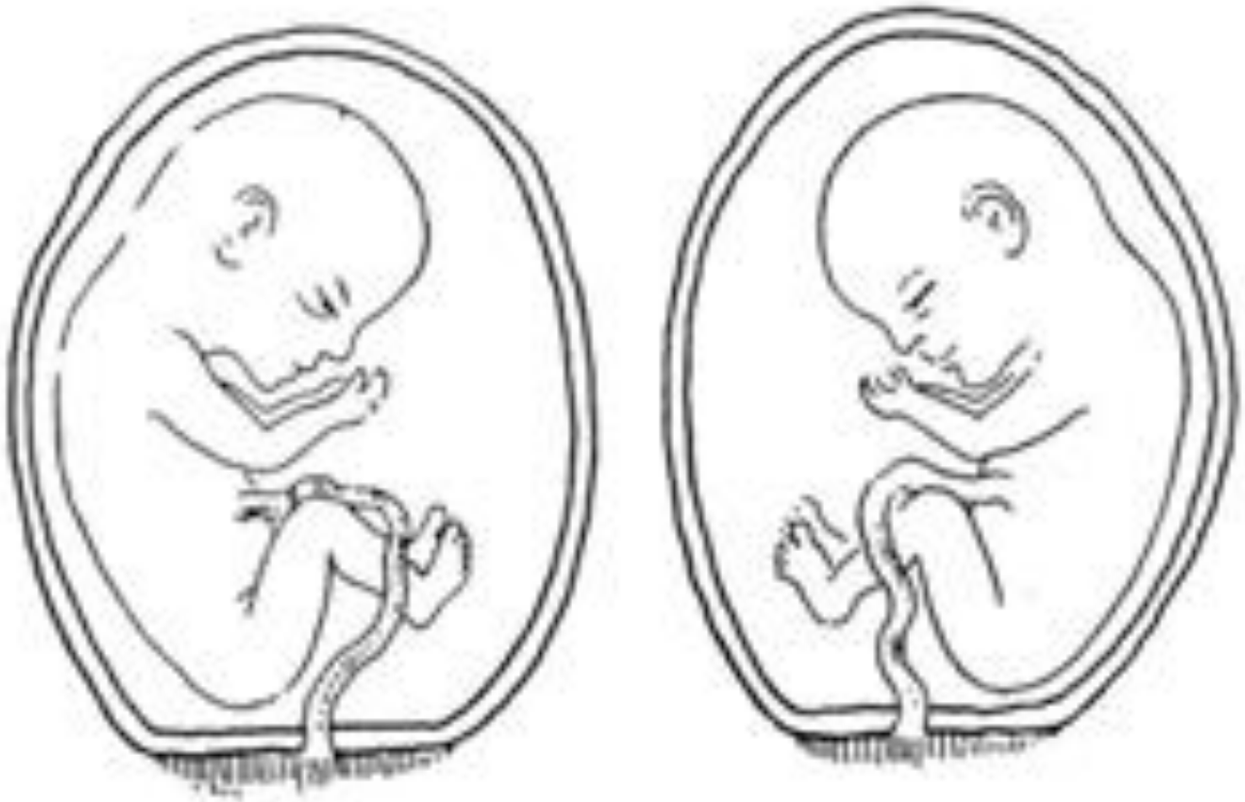


Diamniotic dichorionic (fused)





Diamniotic monochorionic



Diamniotic dichorionic (separated)

Monochorionic, Diamniotic Twins

- 80-85% will move through gestation without complications of monochorionicity
- 10%-15% will manifest Twin Twin Transfusion Syndrome (TTTS)*
- All will share blood: genetically identical
- The sharing is through vascular anatamoses
- The majority of anastamoses are superficial

**Variations: sIUGR and TAPS*

Twin Twin Transfusion Syndrome

- Known for many centuries
- Placental description
- Uncertain of “true” diagnosis
- Argued therapies
- Laser’s Advent and criteria

De Wikkellkinderen 1617[2]

[2]*Lancet* 2000;356:847-848

Twin Twin Transfusion Syndrome:

STAGING[3]

- Stage 1: Oligohydramnios and Polyhydramnios
  - Usually this is concomitant with growth discordance: > 20%
- Stage 2: The small twin has no bladder
- Stage 3: Doppler changes manifest
  - Usually the smaller twin has AEDF of the umbilical artery
  - Often the smaller twin manifests anemia: PSV MCA > 1.5MoM
  - Often the larger twin manifests plethora: PSV MCA < 0.8MoM
- Stage 4: Hydrops of one or both twins
- Stage 5: Death of one or both twins

[3]Quintero 1999

GA(EDD)=30W6D 16cm 4348c
BT OB-2/3
CINE 0024
51G
69DR
E4 MA* A2

TWIN A

77

cm/s

A

B

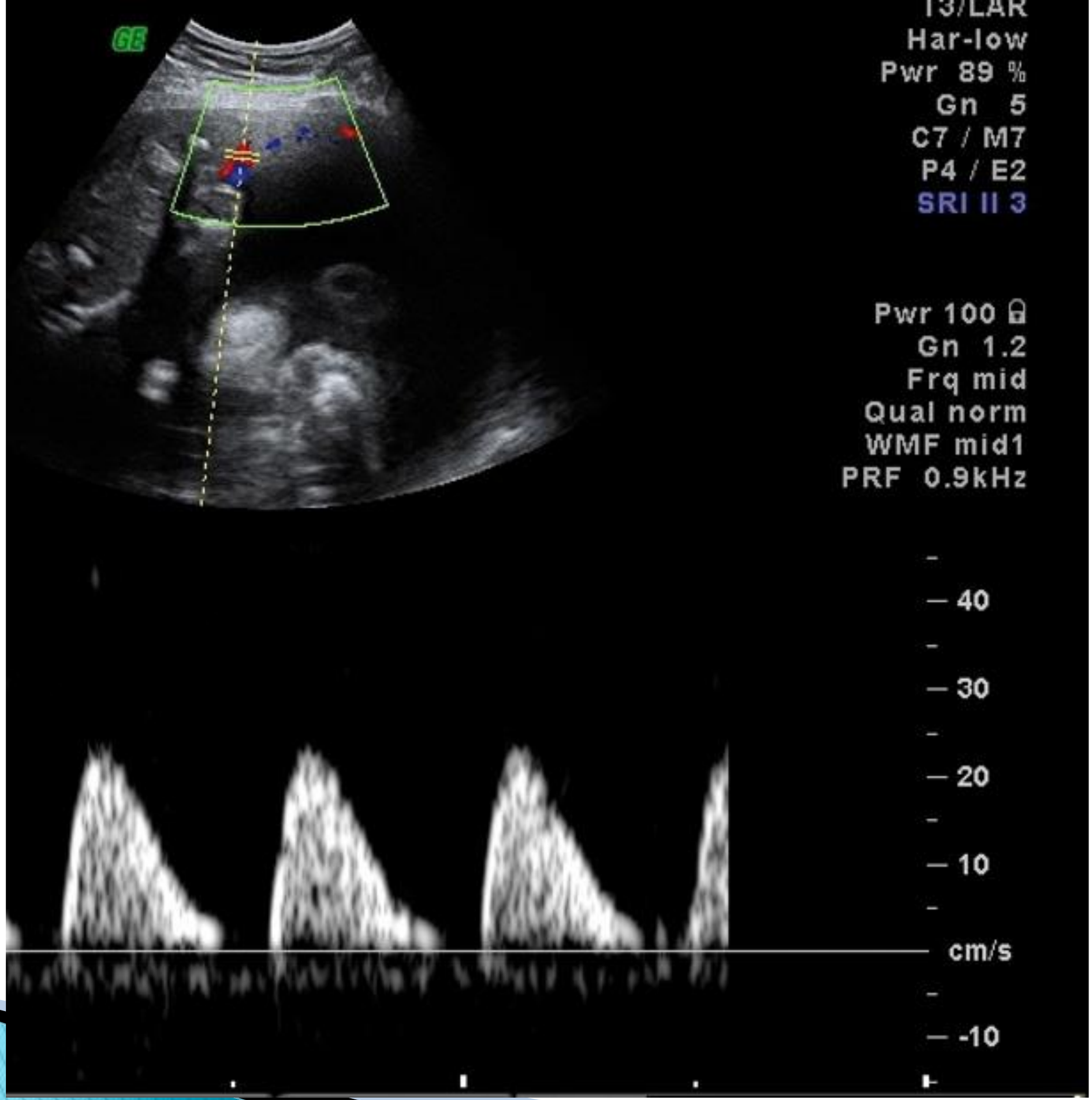
4010P
81F
37DG
0.4CM
0°

A= 56.3CM/S
B= 25.6CM/S

Crd-S/D(a)=2.20

-46

TIS<0.4 MI<0.4 AO=69%


GE
T3/LAR
Har-low
Pwr 89 %
Gn 5
C7 / M7
P4 / E2
SRI II 3
Pwr 100
Gn 1.2
Frq mid
Qual norm
WMF mid1
PRF 0.9kHz
40
30
20
10
cm/s
-10

Hz 20°

P

PW
40%
WF 40Hz
SV2.0mm
M3
2.5MHz
4.8cm

6.8

TTTS: Fetal Center Evaluation

- Diagnosis confirmation
- Staging at time of evaluation
  - Has progression occurred?
- Echocardiography - Key
  - This is a vascular disease!! Anemia and plethora!
- Placentation - where is it?
- Cord insertions: close versus far
- Cervix - 5% of patients will manifest cervical insufficiency requiring cerclage
- Counseling

TTTS

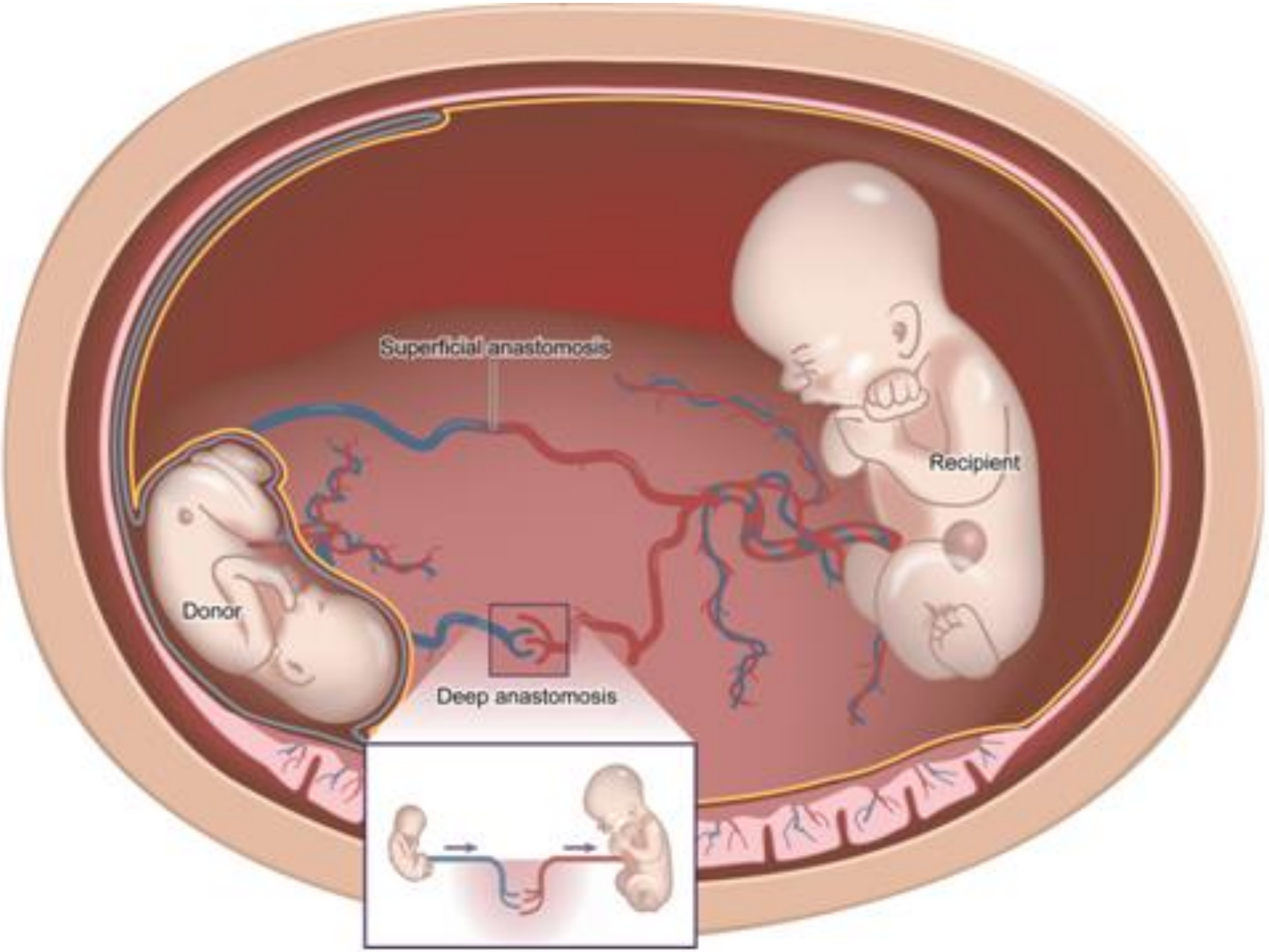
- The survival of the twins is poorer when there is progression to a higher stage over time. It has been estimated that half of patients will progress to a higher stage, 30% will remain at the same stage if stage 2 or less and 20% will improve to a lower stage if stage 2 or less.

  - Taylor MJ, Govender L, Jolly M, Wee L, Fisk NM. Validation of the Quintero staging system for twin-twin transfusion syndrome. Obstet Gynecol 2002; 100:1257-65.
  - Dickinson JE, Evans SF. The progression of disease stage in twin-twin transfusion syndrome. J Matern Fetal Neonatal Med 2004; 16:95-101.

TTTS

- North American Fetal Treatment Network: (NAFTNet)[4]
- Multicenter study of stage 1 TTTS
- Revealed 60% of stage 1 will progress to stage 2 and higher
- To be published in 2018

[4]http://www.naftnet.org/


Superficial anastomosis
Recipient
Donor
Deep anastomosis

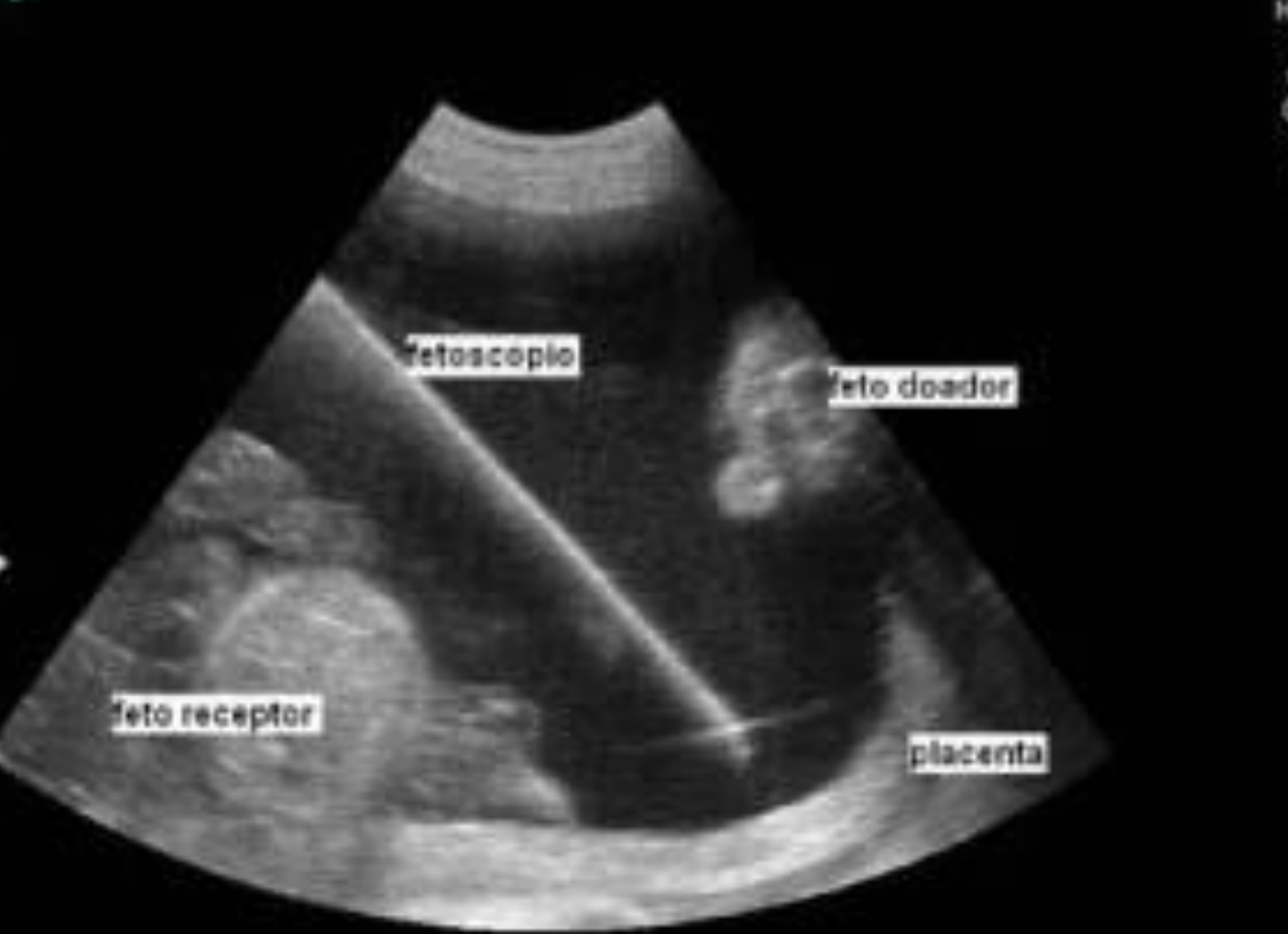
Twin Twin Transfusion Syndrome

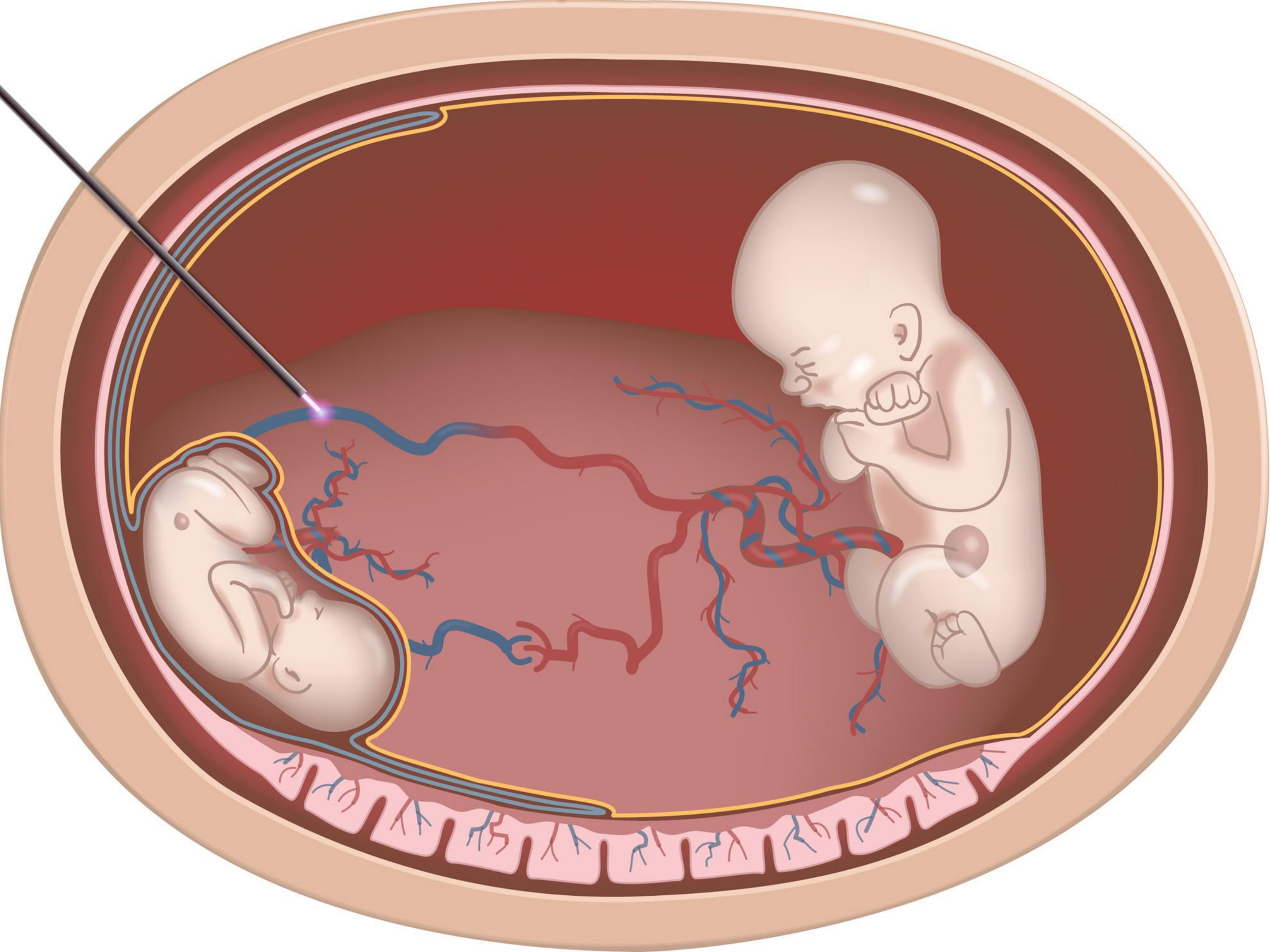
- Treatments:
  - Digoxin – Foxglove plant
    - Ameliorate cardiac function
    - Did NOT work
  - Amnioreduction at amniocentesis
    - 10 – 15% will stop TTTS
  - Septostomy
    - Created MONOAMNIOTIC TWINS
    - Created AMNIOTIC BAND SYNDROME
    - Increased MORTALITY
  - Laser Photocoagulation

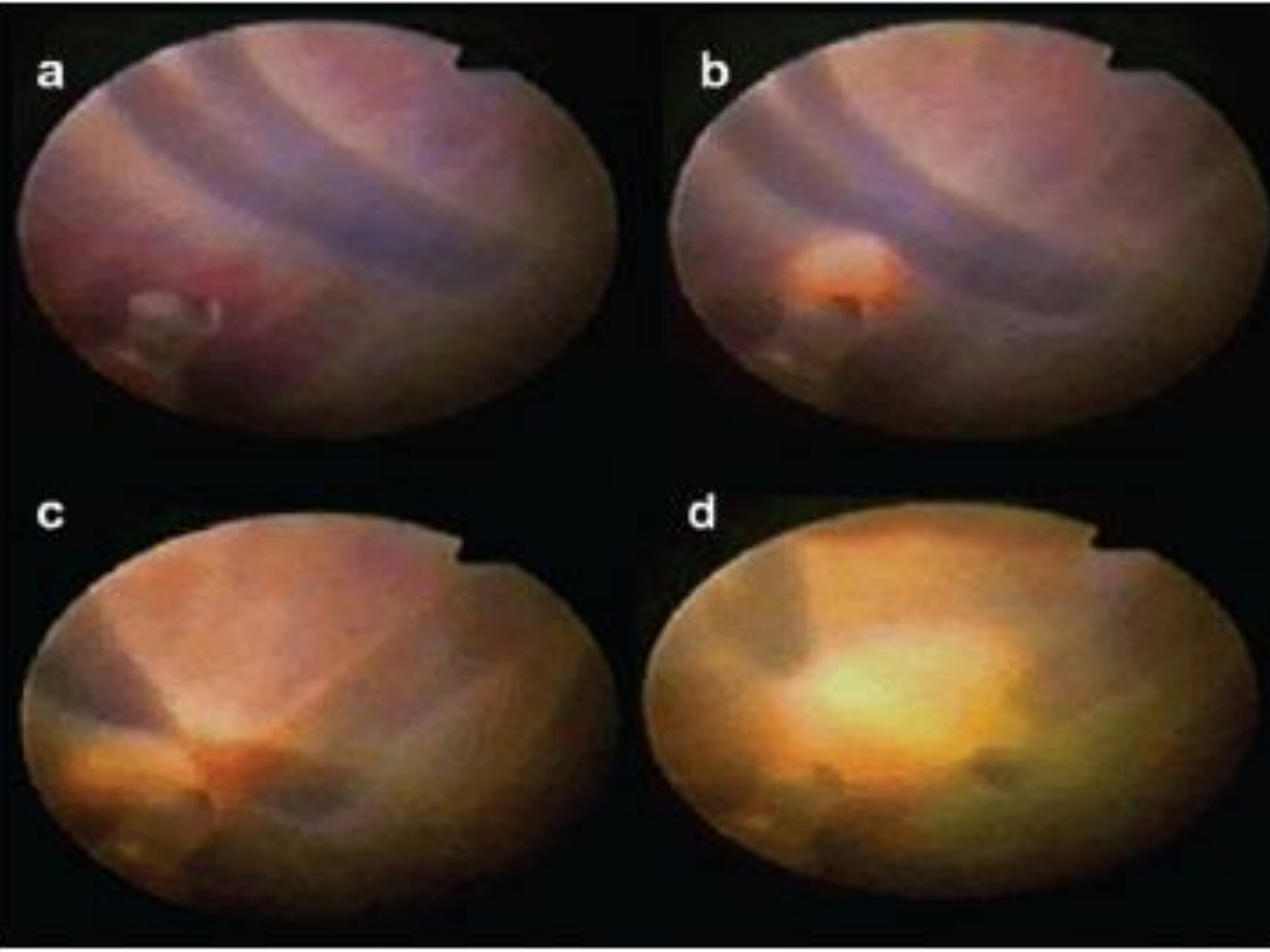
Fetoscopic Laser Photocoagulation[5]

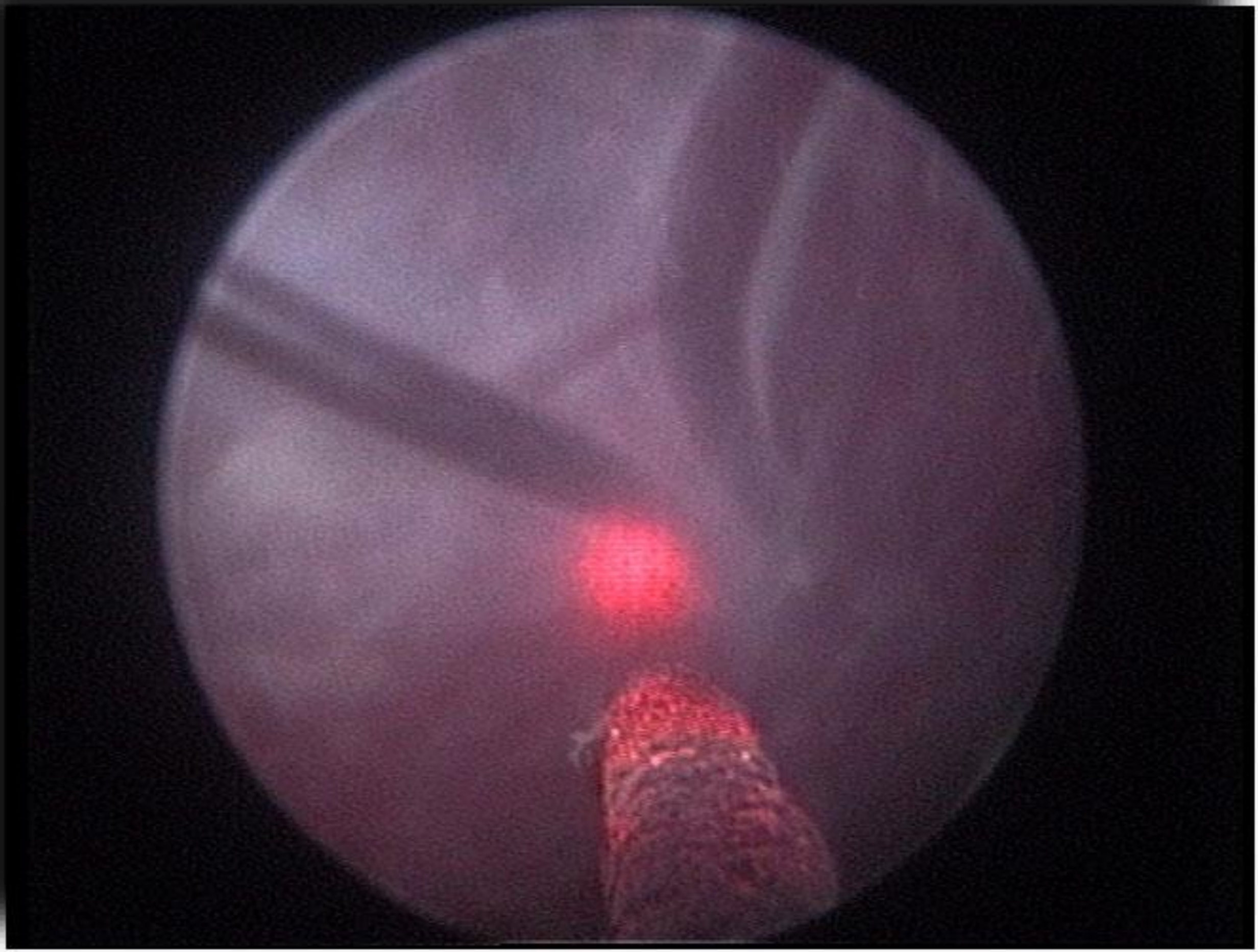
- Julian De Lia: 1988
- Endoscope into the uterus
- Application of Laser Technology
- Photocoagulation of Anastomotic Vessels
- Mortality after Laser: 30 – 40%
  - NB: Stage 3: 80 – 100% Mortality if untreated

[5]De Lia *Obstet Gyncol* 1990


Feto receptor
placenta




a
b
c
d



Twin Surveillance

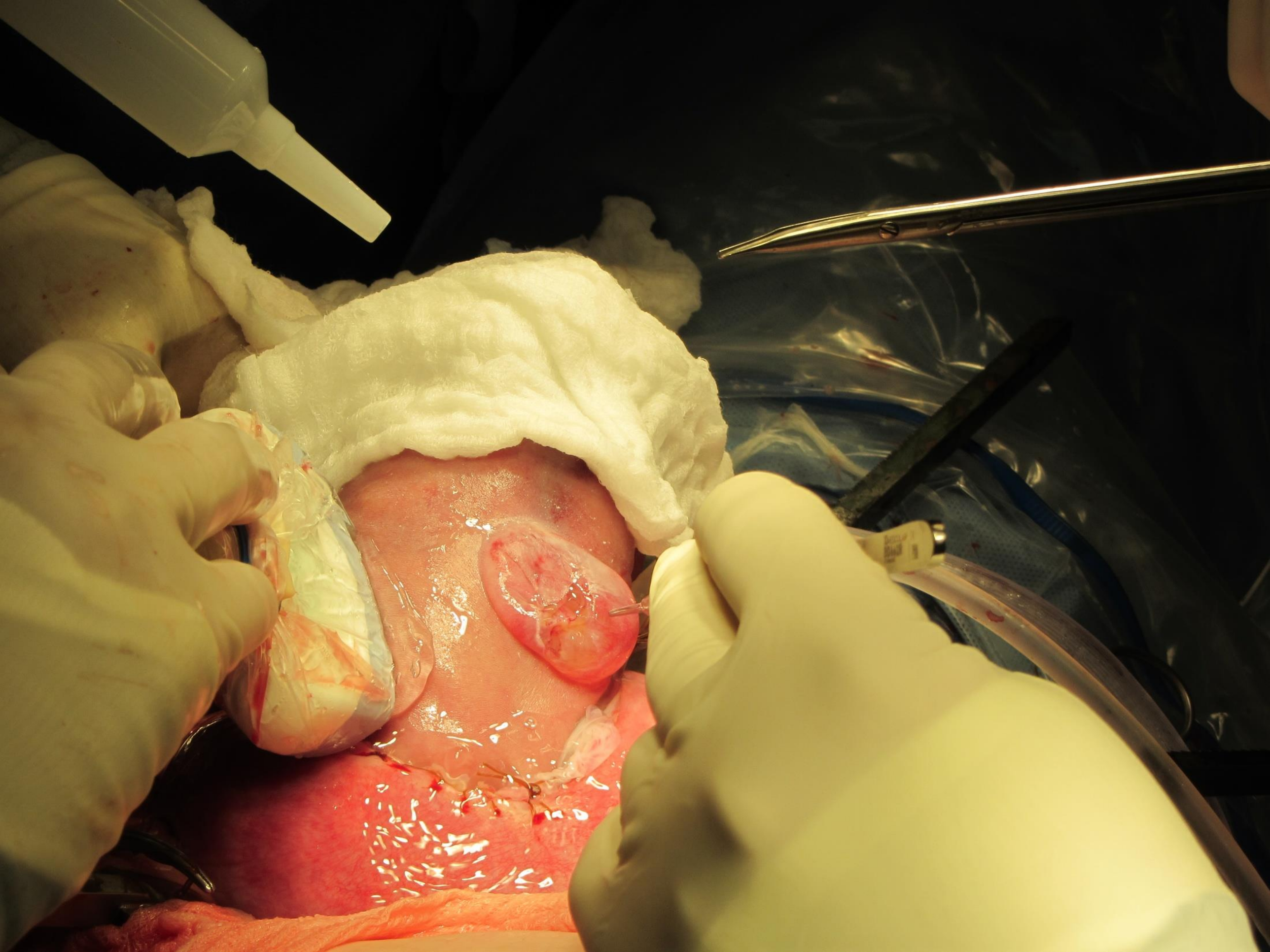
- Most are followed every 4 weeks
- Many centers are following monochorionic, diamniotic twins every 3 weeks
- Yet, TTTS may evolve rapidly

Twin Surveillance

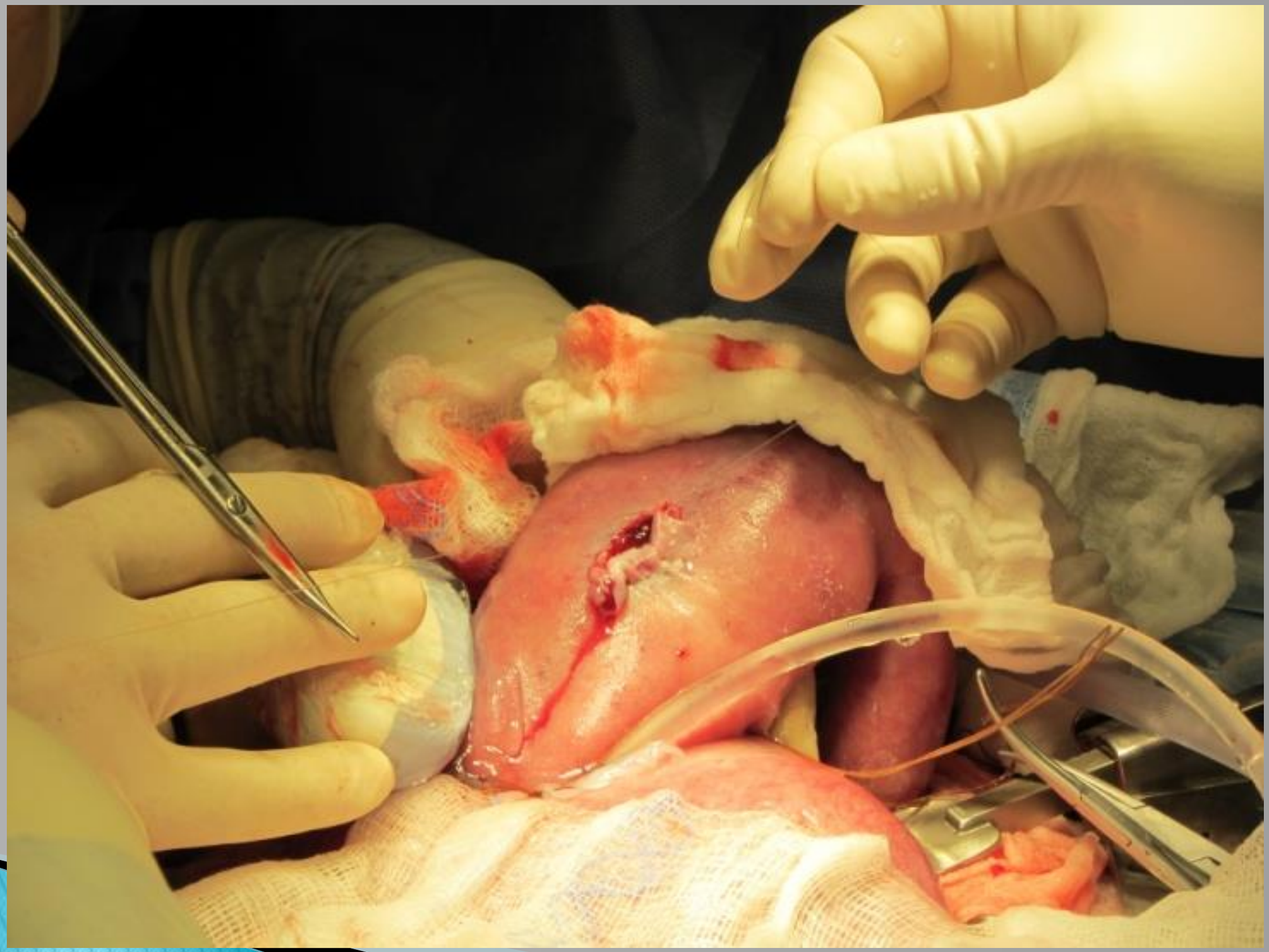
- Screen all twin gestations for CHORIONICITY
- If monochorionic, US evaluation beginning at 14 - 15 weeks gestation: every two weeks
  - Graduation to the second trimester: placental growth
  - If smaller twin is < 10%, add Doppler studies
    - Growth is every 4 weeks if remain normal
- 20 week evaluation includes completion of anatomical survey
- If TTTS is not present, continuation of surveillance at 2 week intervals (Late TTTS)
- If TTTS is present, weekly evaluation

After Birth

- Relief! However, we're not done!
  - Average delivery gestational age is 33-34 weeks
- Hemoglobin levels to start
- Head ultrasounds
- Echocardiographic evaluations
  - Cardiomyopathy of the recipient twin may take up to 2 – 3 years to remodel
- MRI – CNS changes may initially be subtle
  - 32 weeks gestation, and
  - 6 – 12 weeks of life

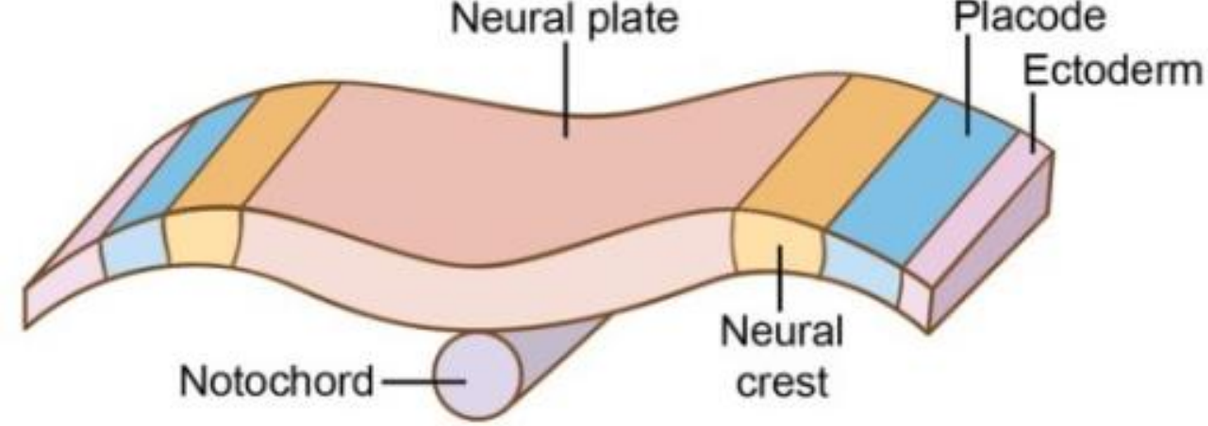


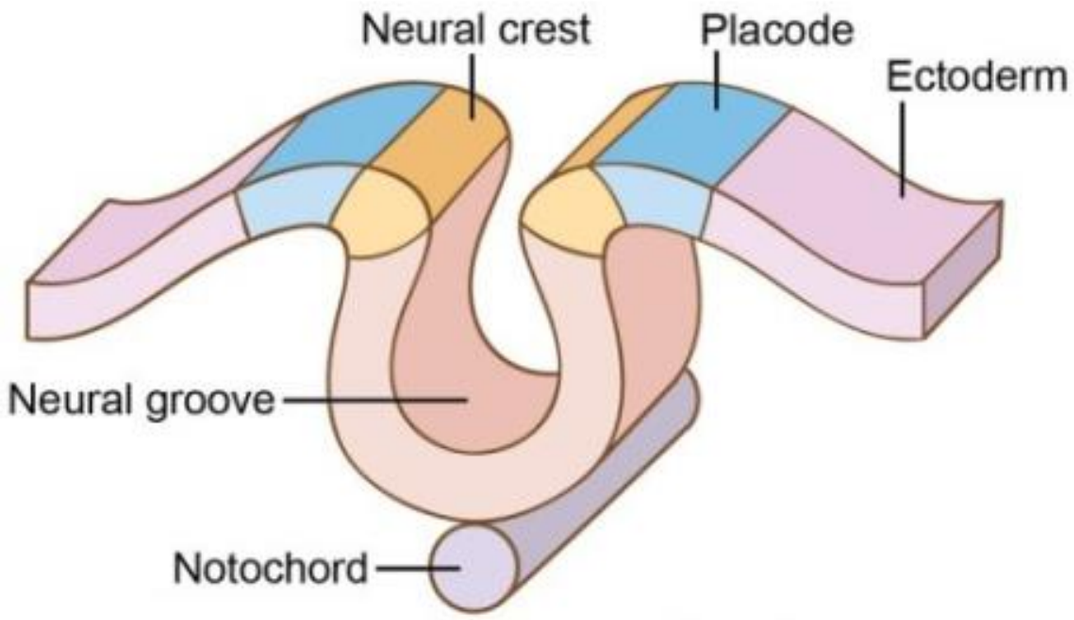
Myelomeningocele

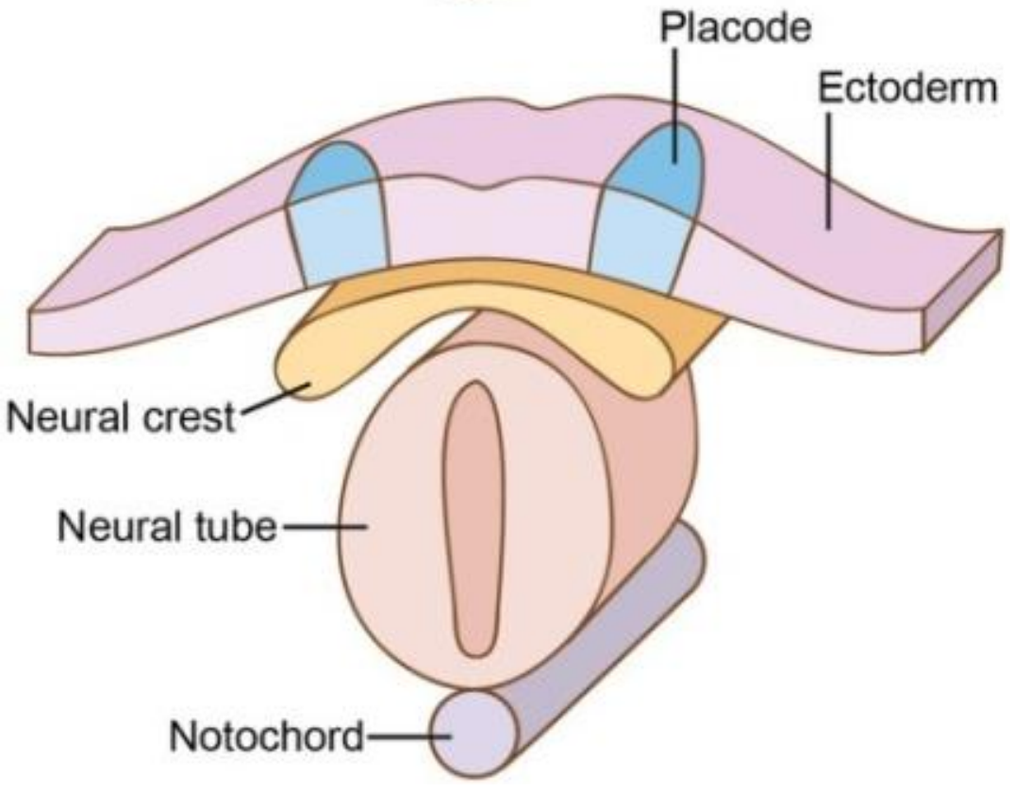


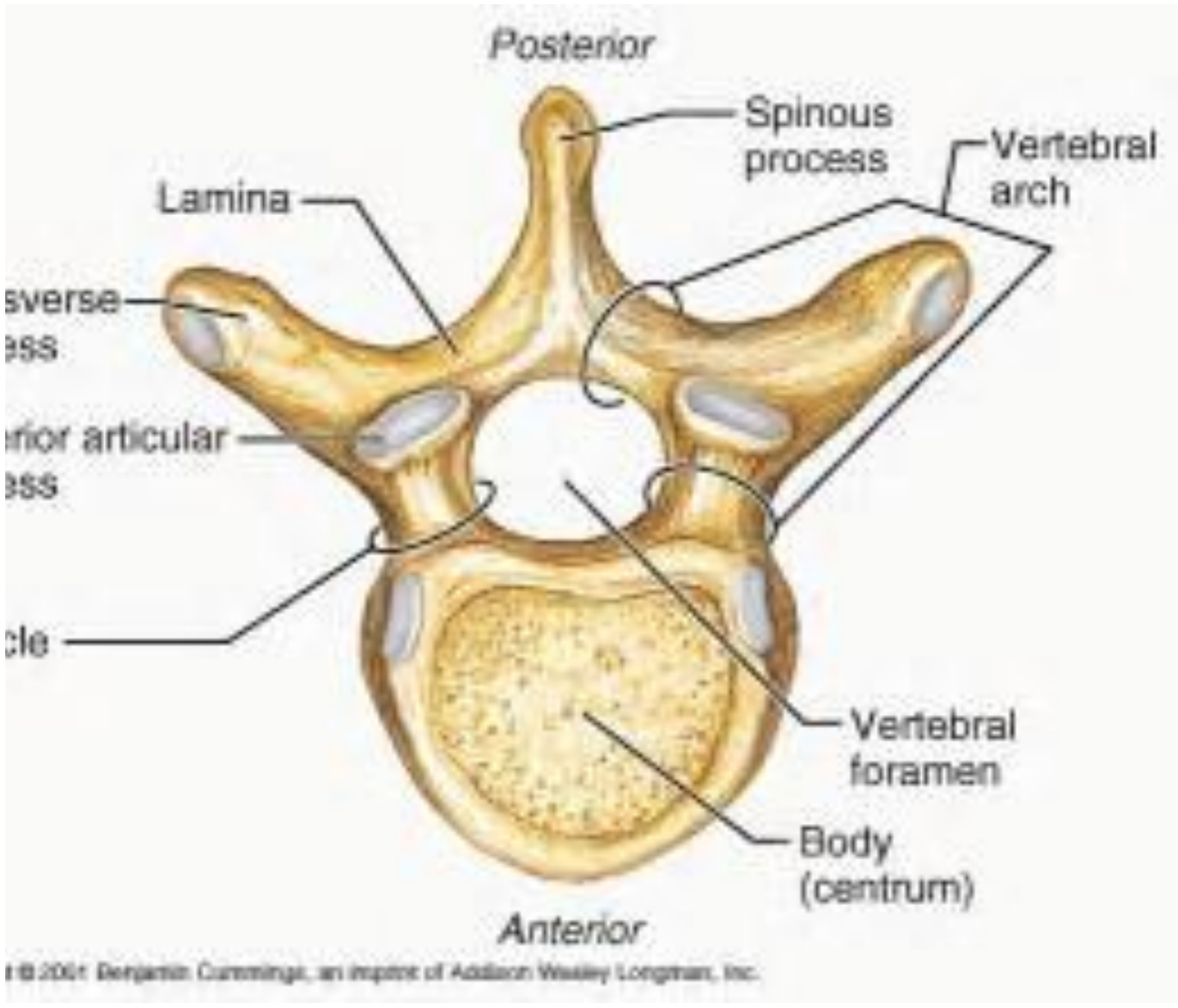
Myelomeningocele

- Spina bifida – non-fusion of the vertebral ossification centers
- Meningocele – a form of spina bifida with the defect containing meninges and cerebrospinal fluid
- Myelomeningocele – similar to a meningocele with the inclusion of neuronal elements, either central nervous system or spinal cord

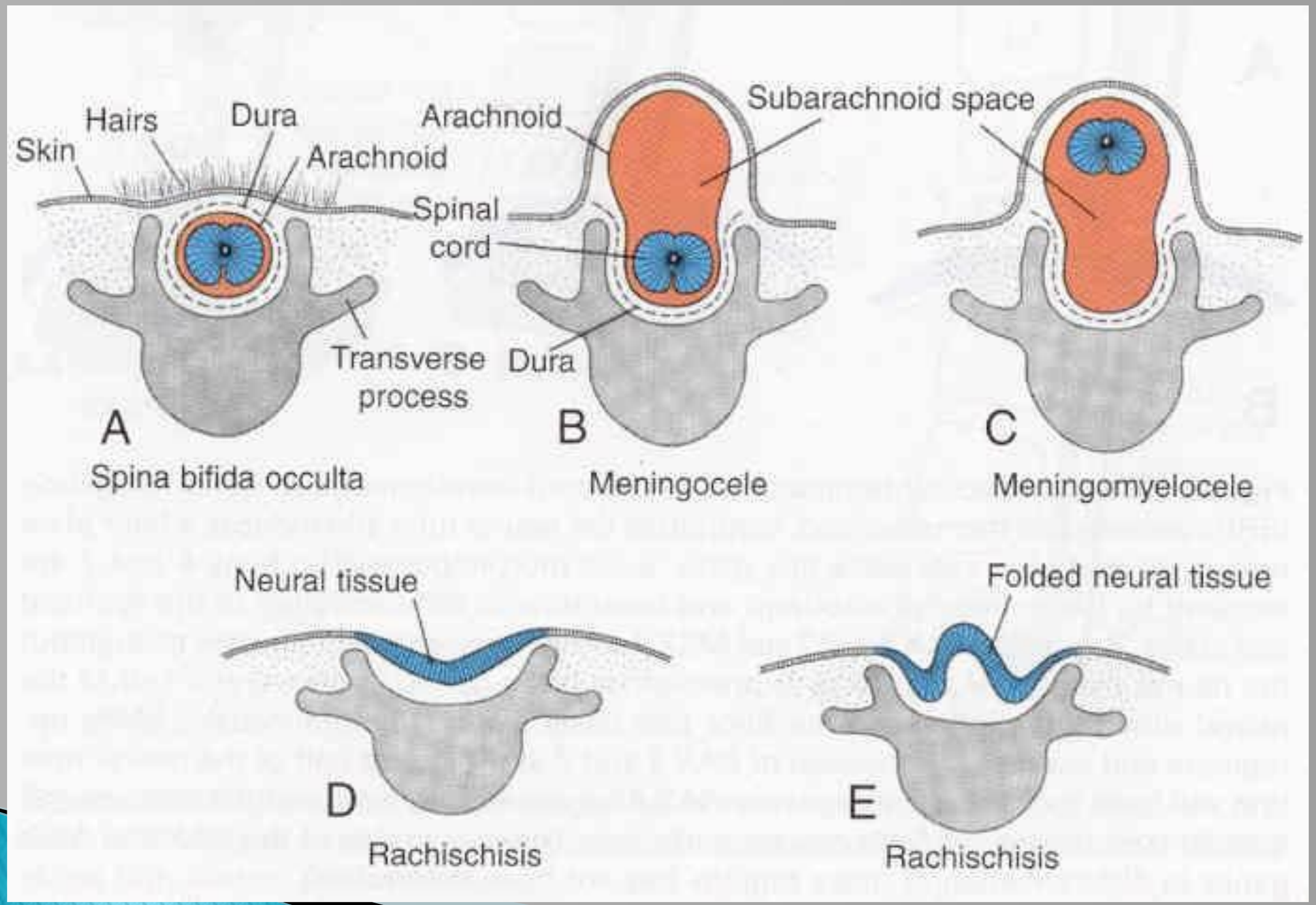

Neural plate
Placode
Ectoderm
Notochord
Neural
crest


Neural crest
Placode
Ectoderm
Neural groove
Notochord

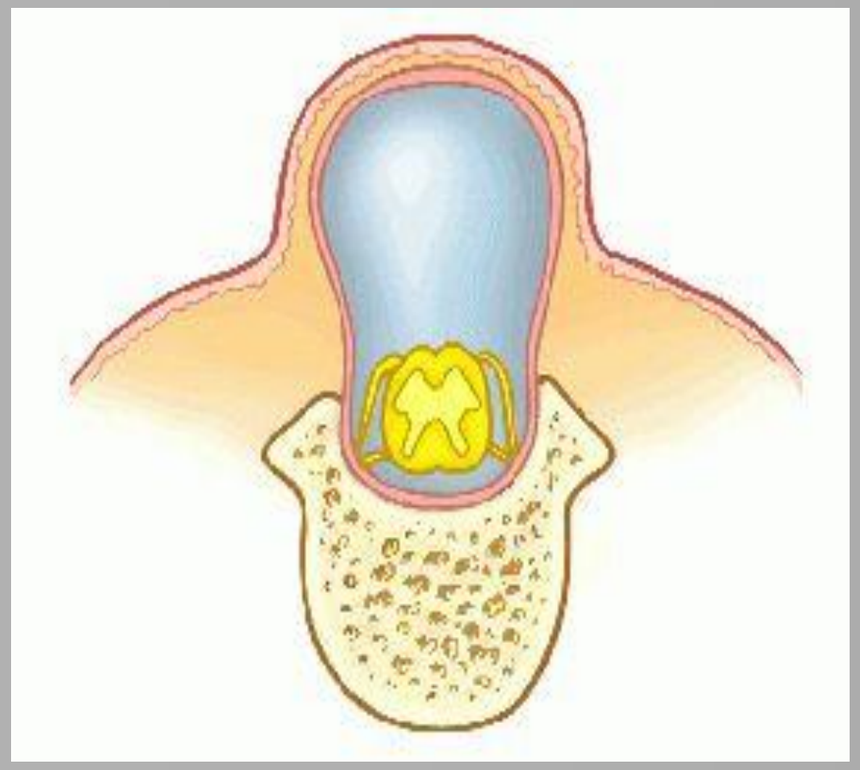

Placode
Ectoderm
Neural crest
Neural tube
Notochord

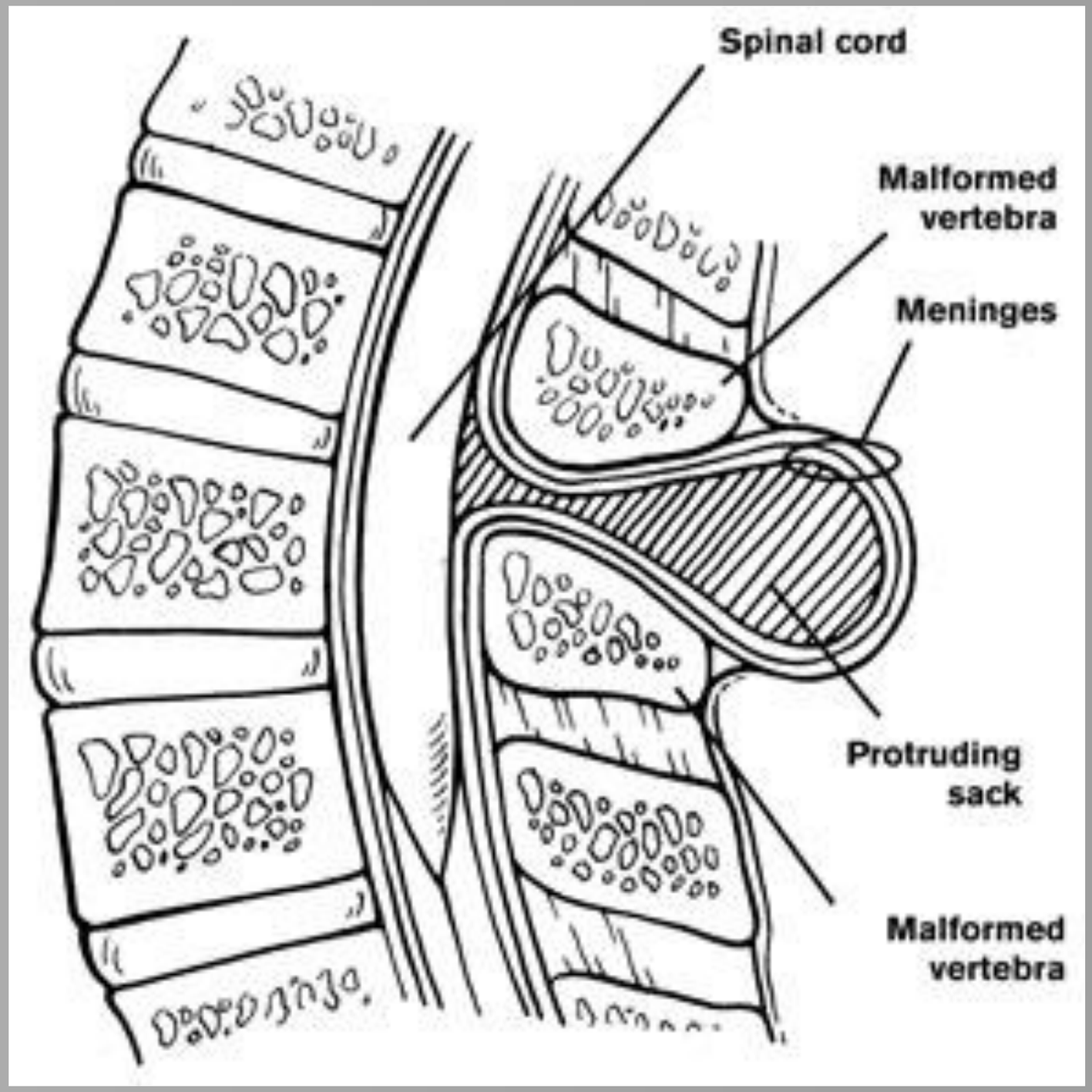

Posterior
Spinous
process
Vertebral
arch
Lamina
sverse
ess
rior articular
ess
cle
Vertebral
foramen
Body
(centrum)
Anterior

Spina bifida

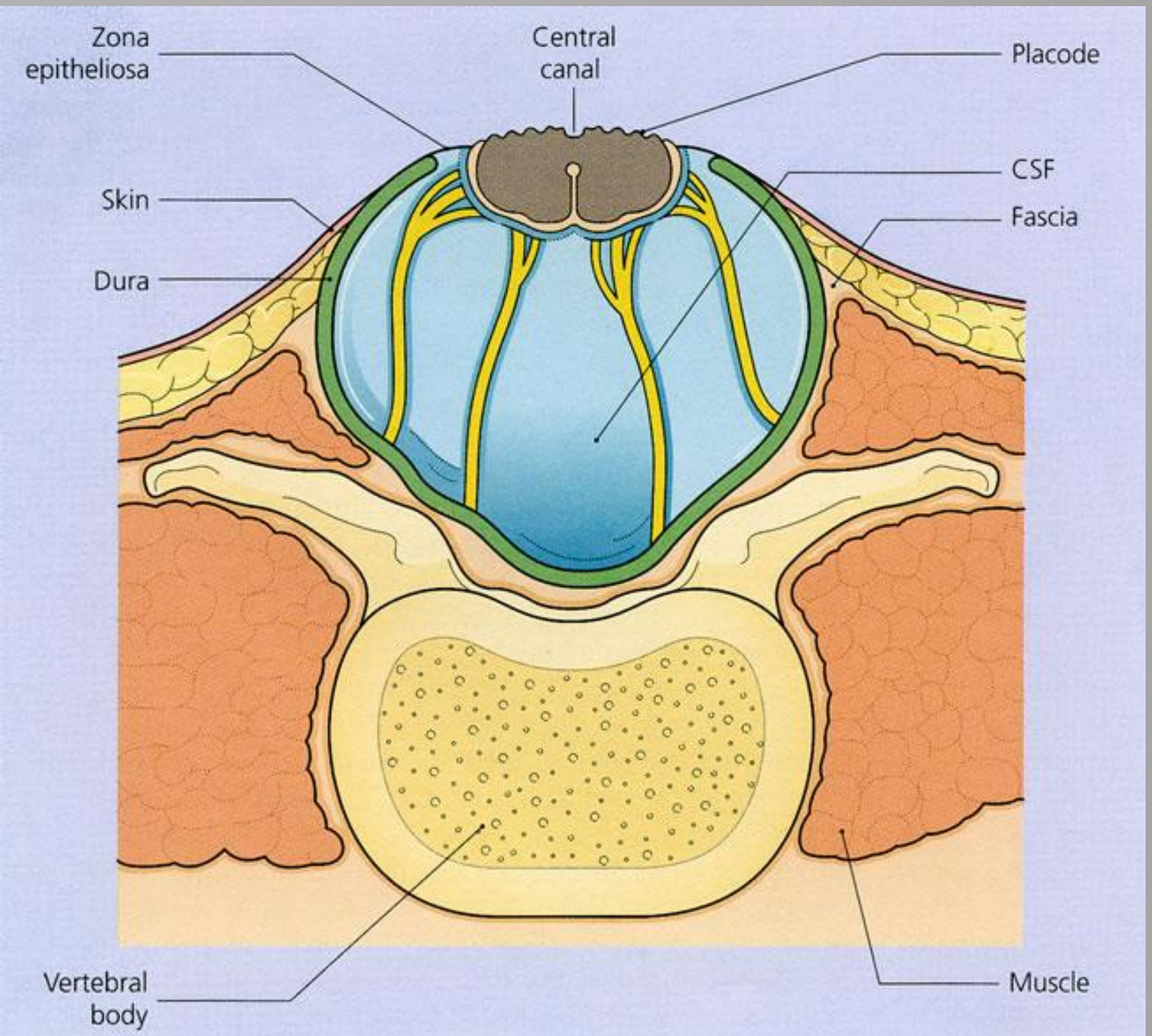


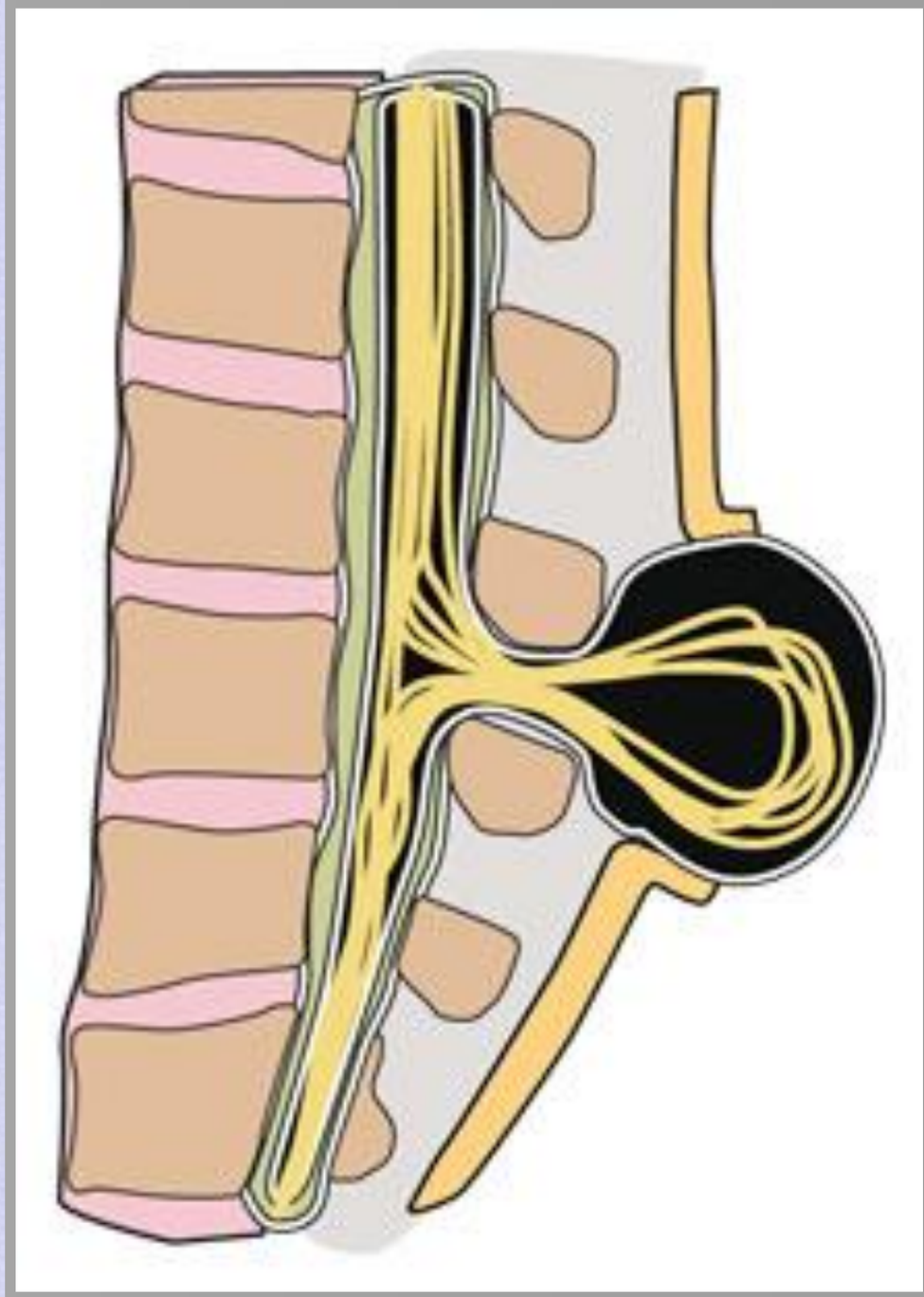
Meningocele





Myelomeningocele





Myelomeningocele

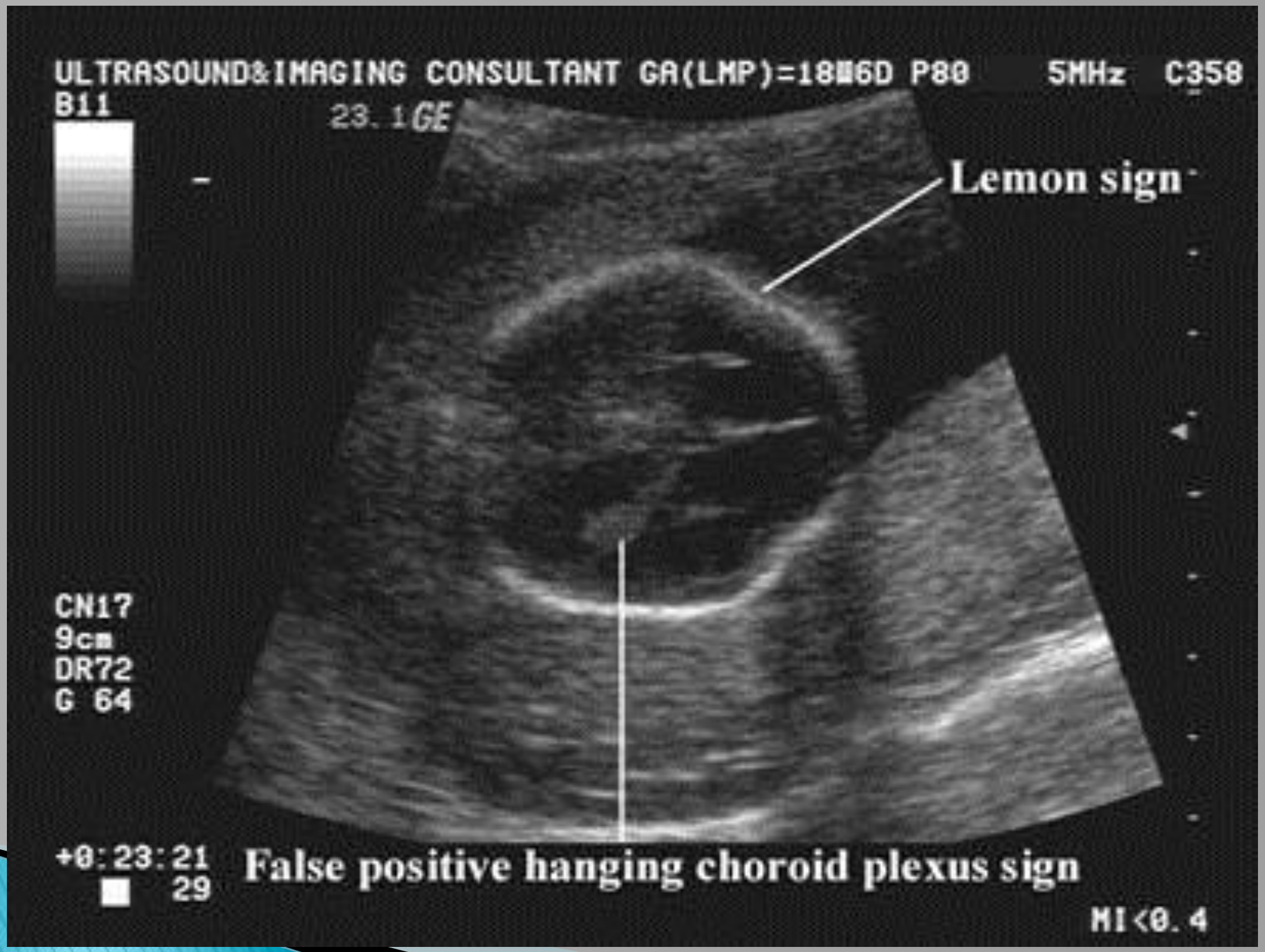
- Initial ultrasound
  - Fetal head is not normal
  - Clubbed foot or feet are often noted
  - Polyhydramnios may be present

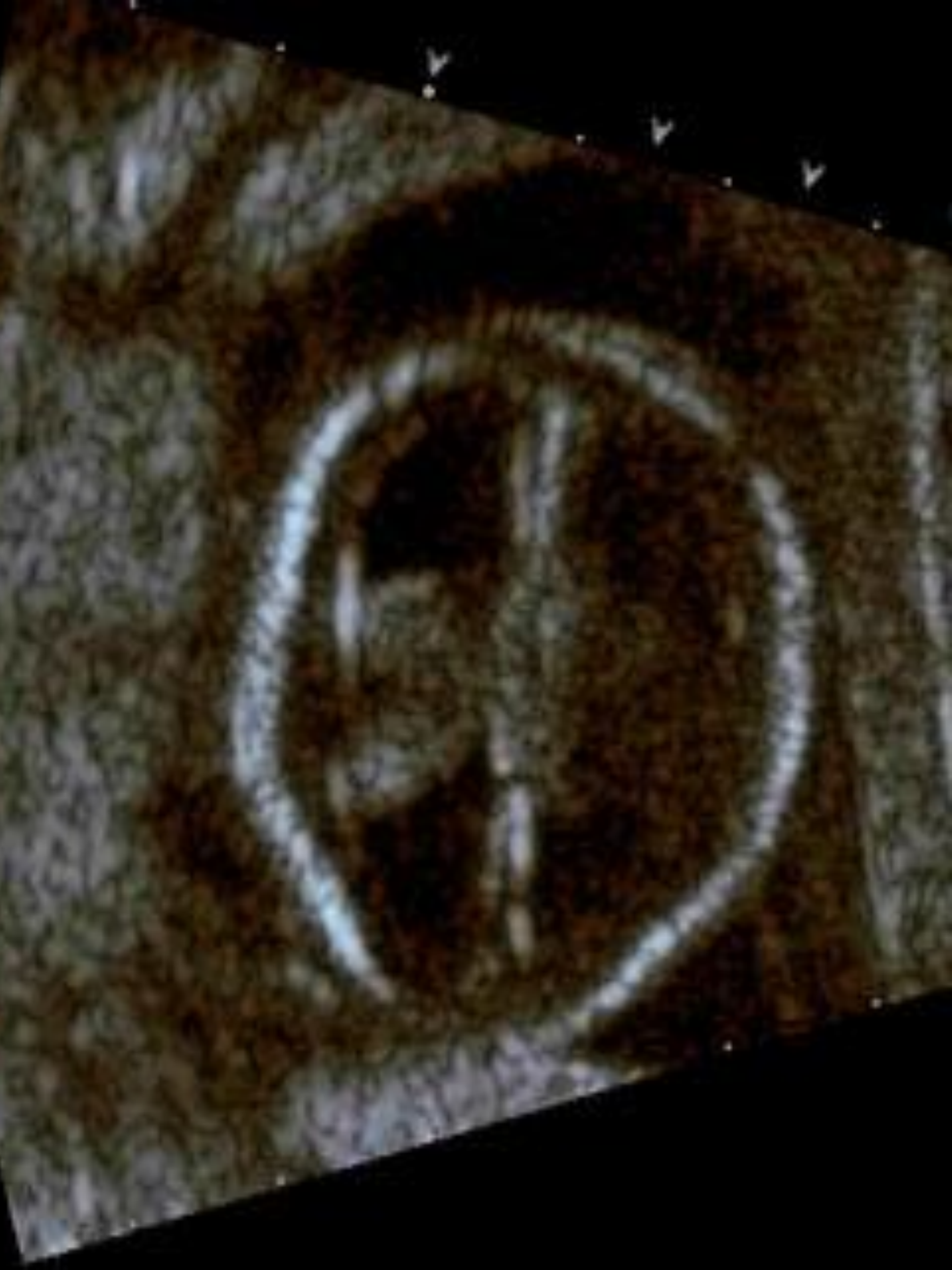
- Confirmation
  - Level 2 ultrasound
  - Maternal-Fetal Medicine consultation

Myelomeningocele

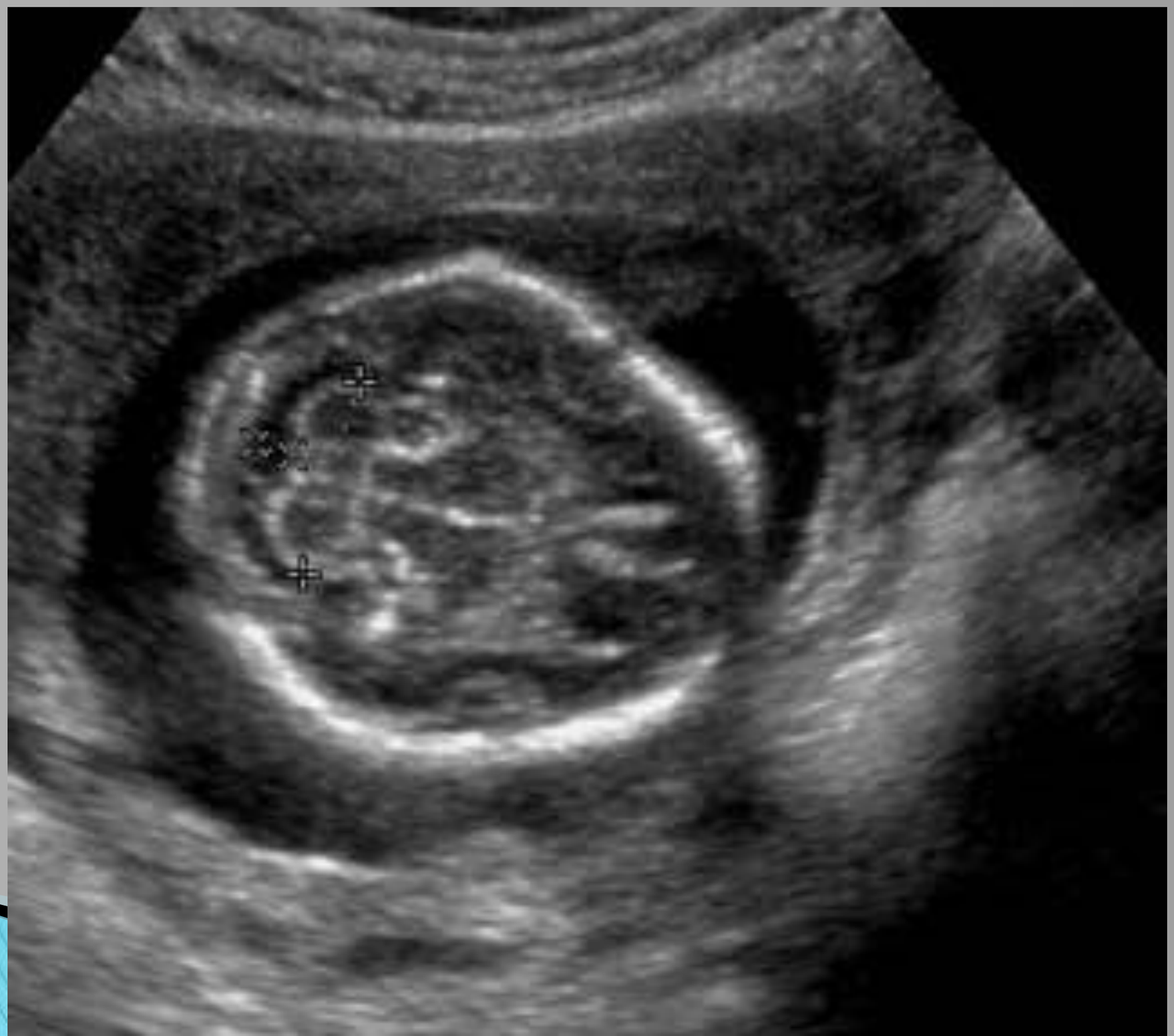
- Lemon sign
  - Flattened or scalloped frontal bones
- Banana sign
  - Flattened or smoothed cerebellum
- Chiari malformation (Arnold-Chiari 2)
  - Obliteration of the cisterna magna
  - Herniation of the cerebellum into the spinal canal through the foramen magna
- Abnormal spinal series
  - Bony and skin abnormalities

Lemon Sign

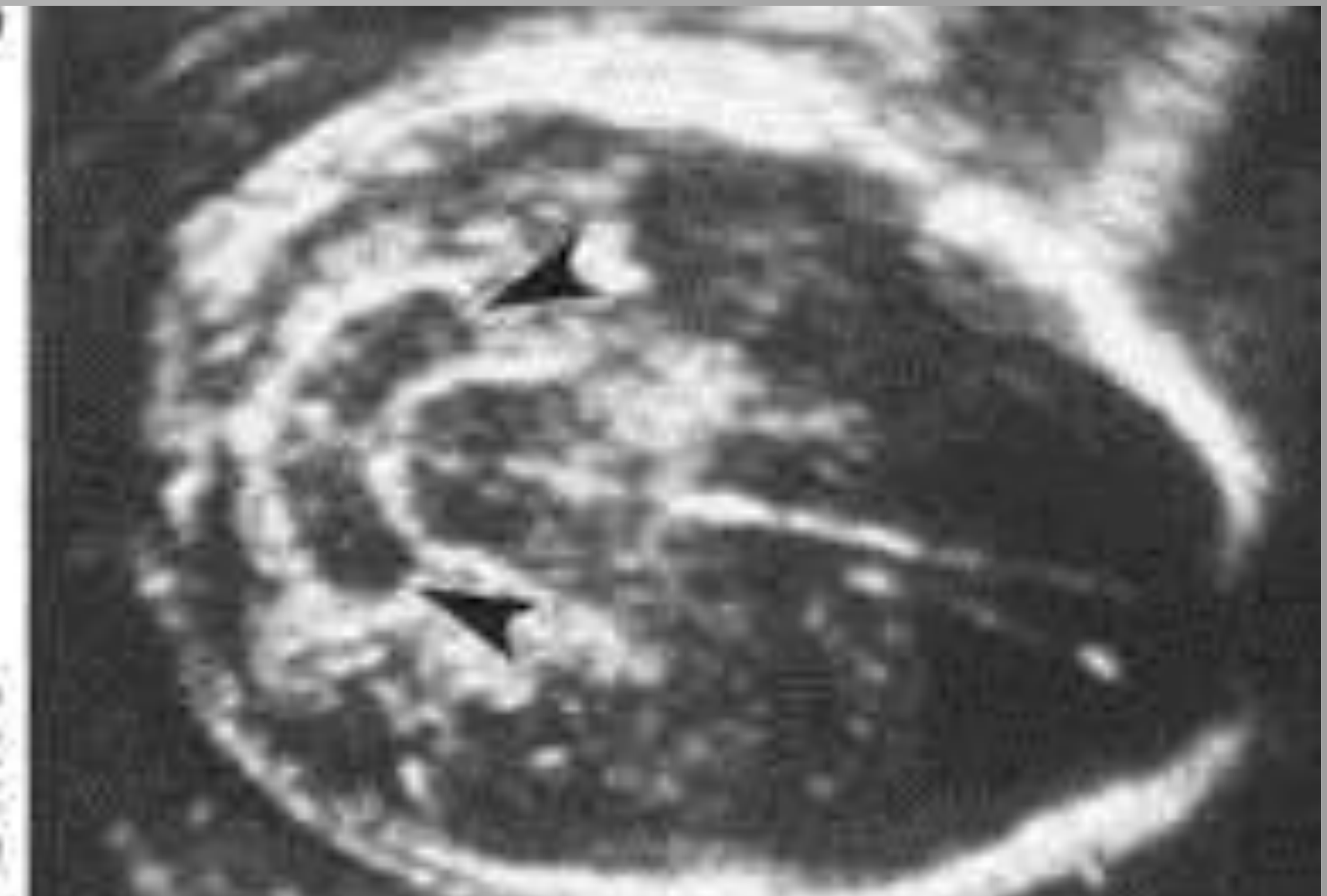

ULTRASOUND&IMAGING CONSULTANT GA(LMP)=18■6D P80 5MHz C358
B11
23.1 GE
Lemon sign
CN17
9cm
DR72
G 64
+0:23:21
■ 29
False positive hanging choroid plexus sign
MI<0.4



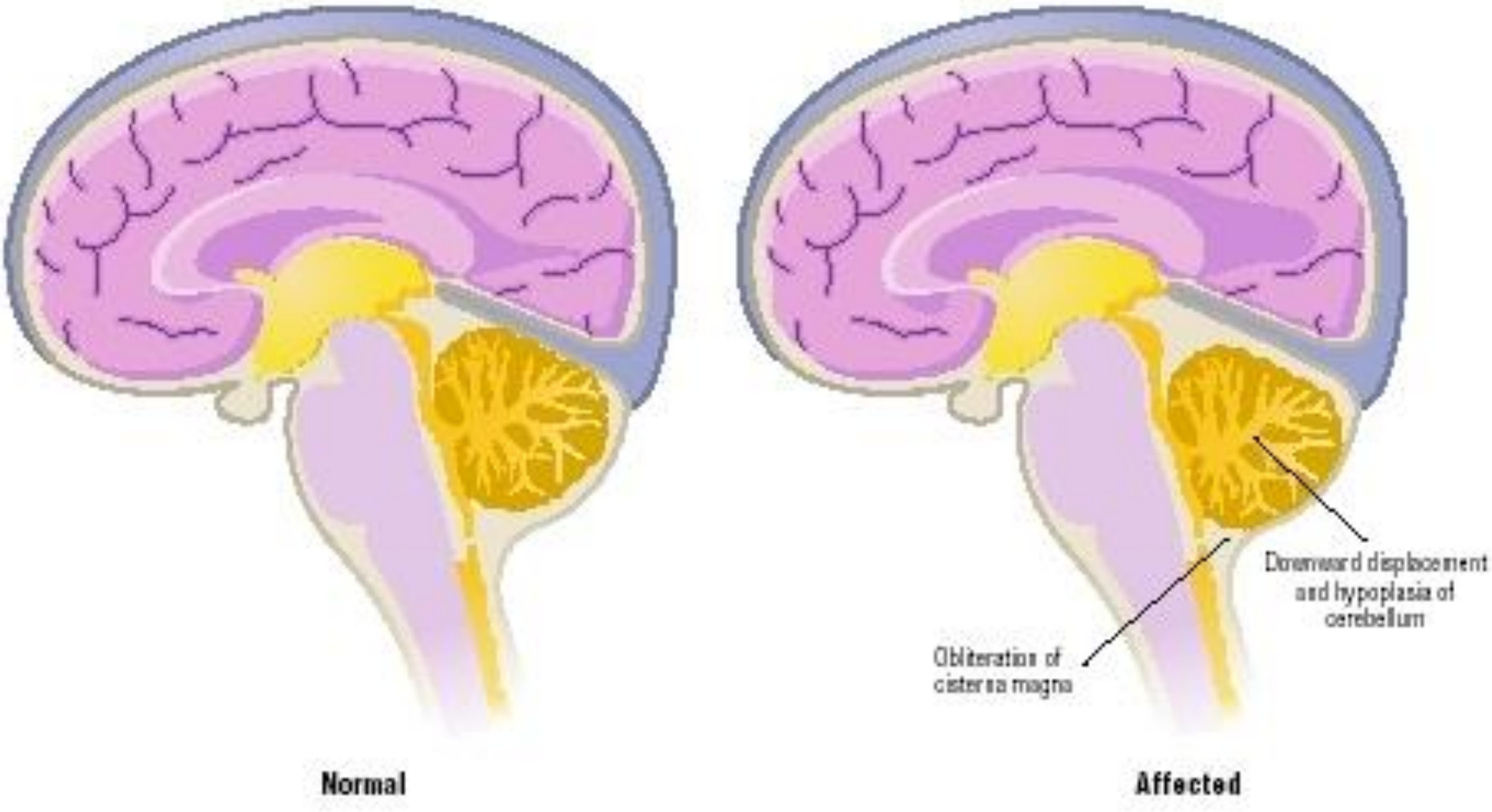
Normal Fetal Cerebellum



Banana Sign

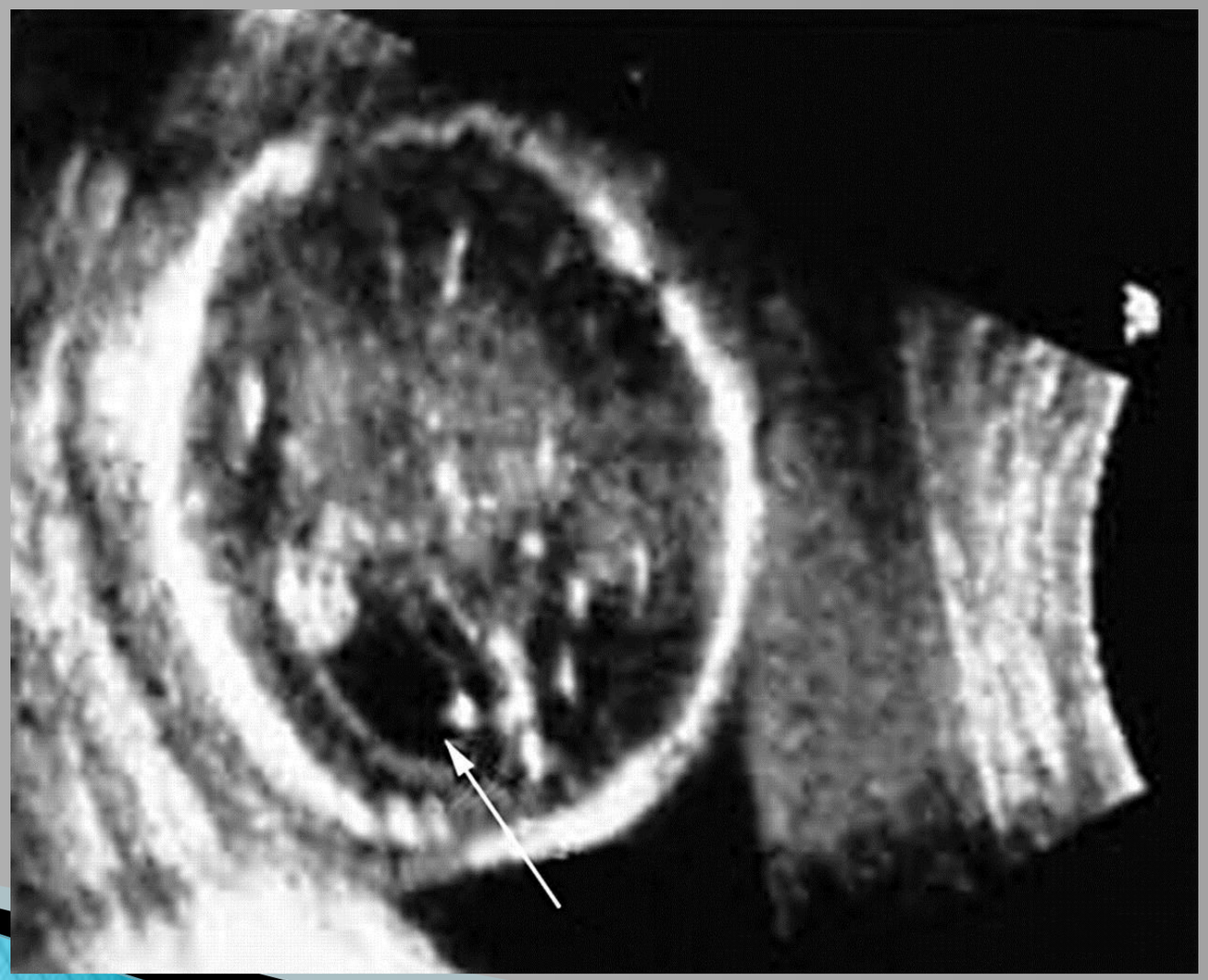


Chiari Malformation

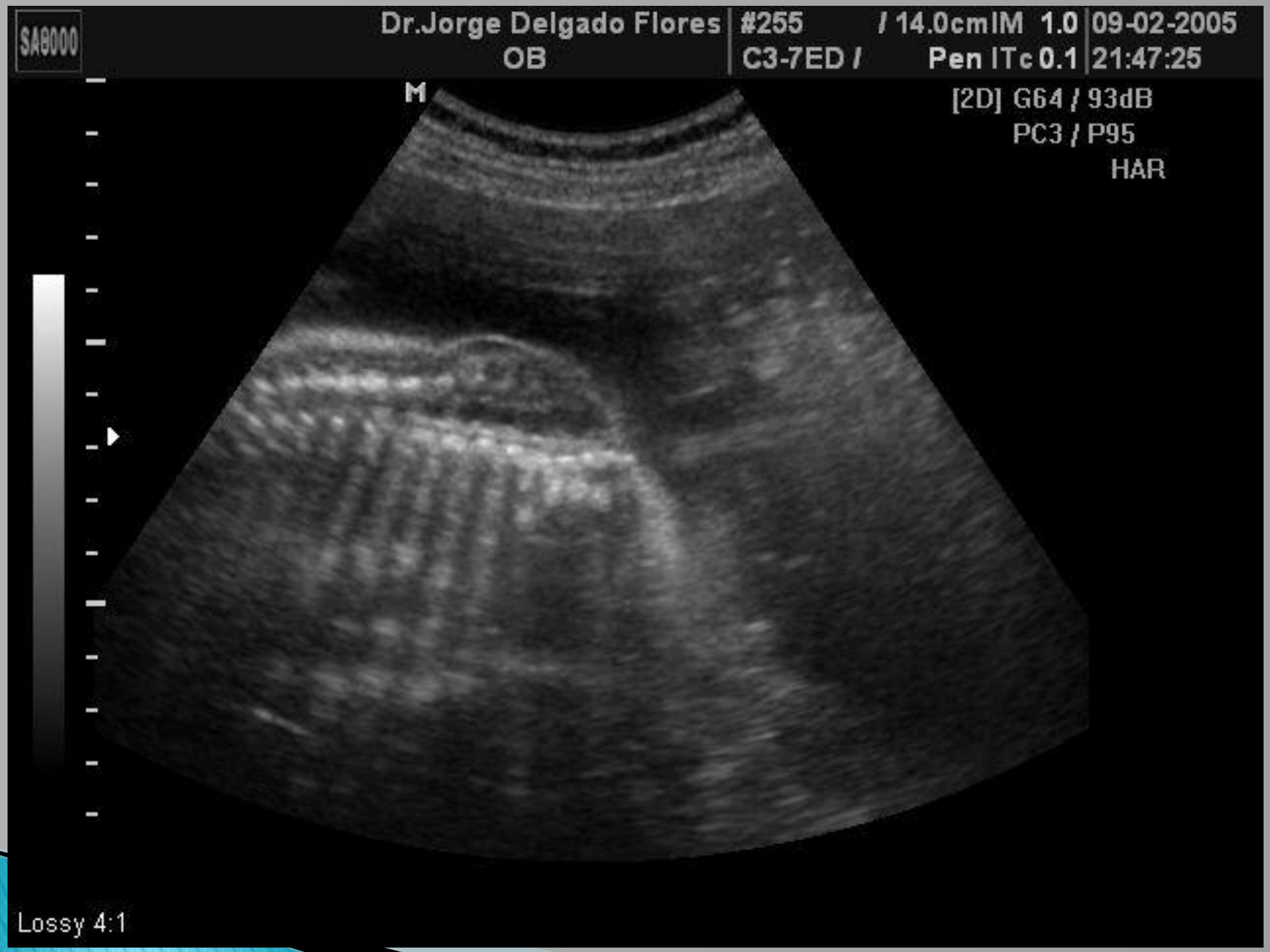


Chiari Malformation

- Often leads to the development of hydrocephalus with advancing pregnancy



Abnormal Spinal Series



Myelomeningocele

- Neonates
  - 85% or more require ventriculoperitoneal shunts
  - 100% surgical repair
- Children
  - Approx 50% will become ambulatory
  - Hence, approx 50% will not
- Teenagers
  - Half of the ambulatory population will become wheelchair-bound
  - Struggle with bladder and bowel issues

[7]Oski's Pediatrics, 5th Edition

Myelomeningocele

- 1997 - First prenatal myelomeningocele repair in the human
- 2003 - over 200 cases had been performed
- Reports of remarkable outcomes
- Cautionary tales of fetal and neonatal losses
- Again, no consensus on technique
- Maternal safety concerns grew


MOMS
Management of Myelomeningocele Study

MOMS Trial[8]

- Three United States centers were designated
  - CHOP, UCSF and Vanderbilt
- All other fetal surgery centers complied with a moratorium on performing MMC repair
- 8 years came and went
- 2 interim analyses were done
- 17 March 2011 the NEJM carried the results

[8]Adzick, *NEJM* 2011

MOMS Trial

- Primary outcome: fetal/neonatal death or VP shunt placement
  - 68% in the prenatal repair arm
  - 98% in the postnatal repair arm
  - Actual number of shunts: 40% prenatal/82% postnatal
- Primary outcome: 30 month composite mental development and motor function
  - Prenatal surgery group had improved mental development and motor function at 30 months

MOMS Trial and FCI: Maternal

- No Maternal Deaths
- MOMS Trial
- Blood transfusion 9%
- Chorioamniotic separation 26%
- Pulmonary edema 6%
- Oligohydramnios 21%
- Placental abruption 6%
- Preeclampsia/Gest HTN 4%
- SROM 46%
- Spontaneous labor 38%

MOMS Trial: Maternal

- Status of Hysterotomy site at Delivery
  - Intact, well-healed 49/76 (64%)
  - Very thin 19/76 (25%)
  - Area of dehiscence 7/76 (9%)
  - Complete dehiscence 1/76 (1%)

MMC: Coordination of Care

- Evaluations
  - Multidisciplinary Meeting
  - Delineation of known fetal risks and benefits
  - Delineation of maternal risks
- Offer for prenatal repair
- Patient and Family are required to leave and consider their options
- An acceptance/declination of prenatal repair is not considered on the day of offer

Myelomeningocele Repair: Inclusion Criteria

- Singleton pregnancy
- MMC upper boundary between T1 and S1
- Evidence of hindbrain herniation
- Gestational age: 19w0d and 25w6d
- Normal karyotype
- US residency
- Maternal age of 18 years or greater

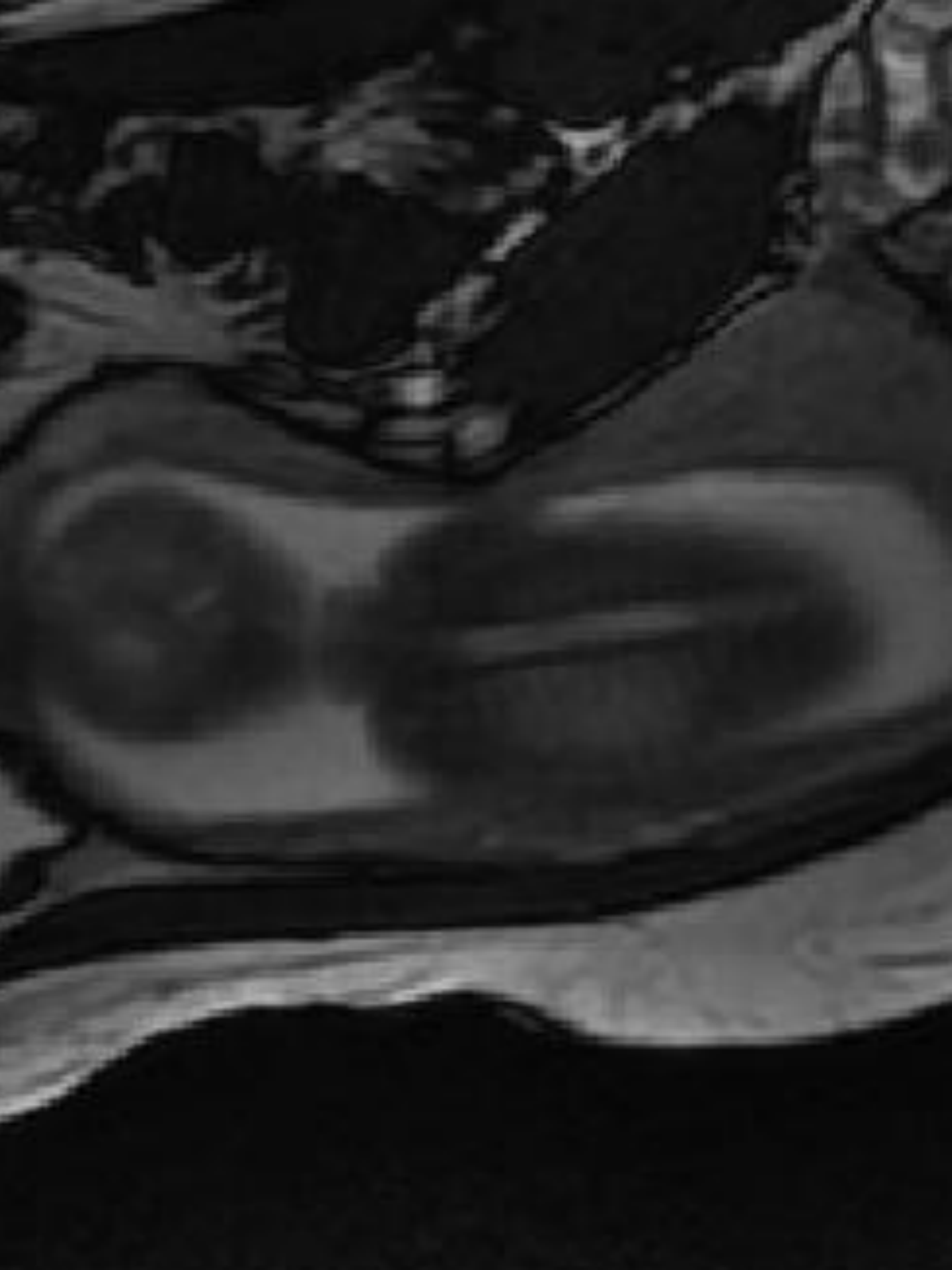
Myelomeningocele Repair: Exclusion Criteria

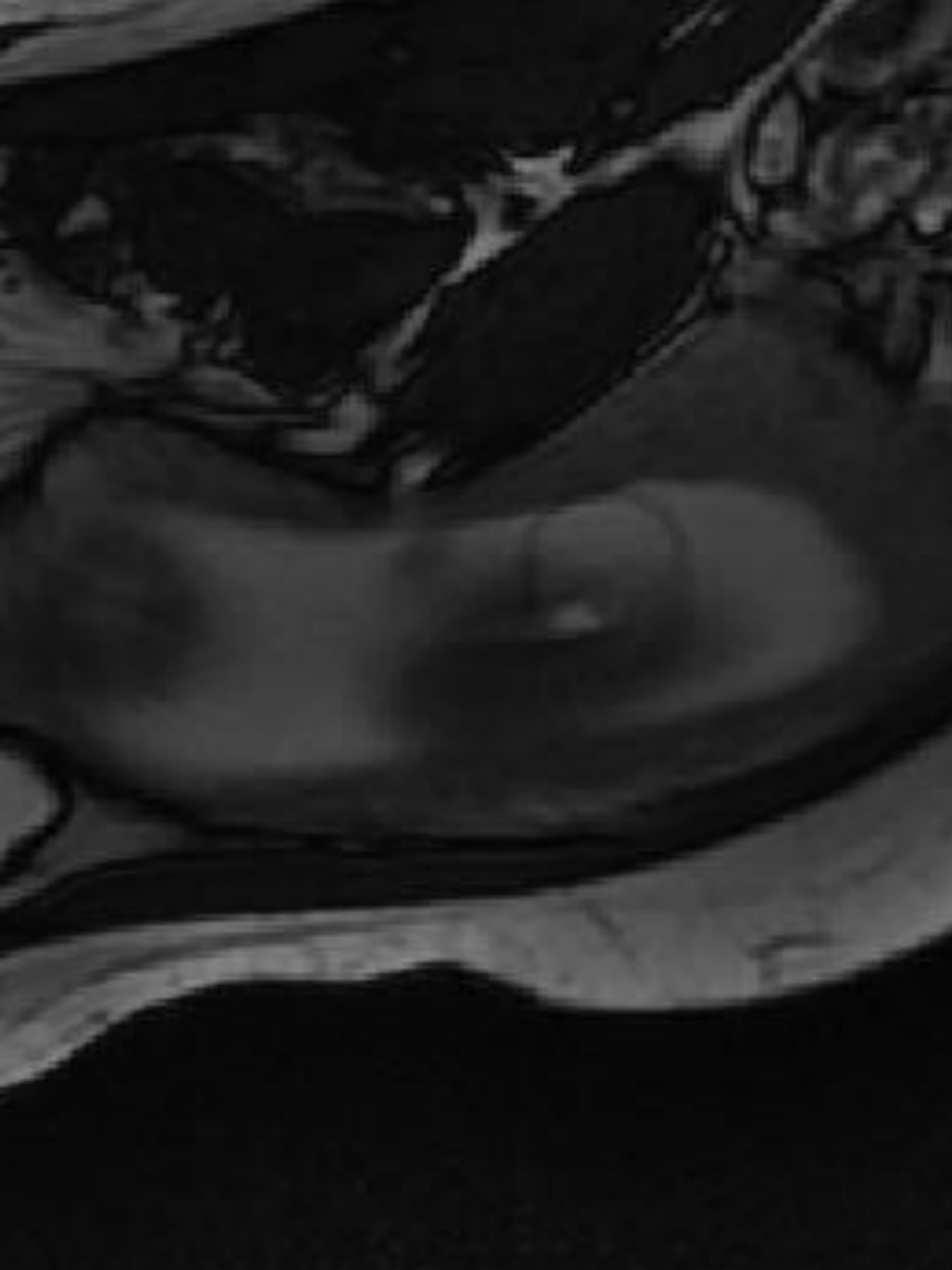
- Fetal anomaly unrelated to MMC
- Severe kyphosis (> 30%)
- Risk of premature birth
  - Short cervix
  - Previous preterm birth
- Placental abruption
- BMI > 35 (Now Trial at SLFCI to BMI of 40)
- Contraindication to surgery
  - Prior hysterotomy in the active phase
  - HIV, HCV

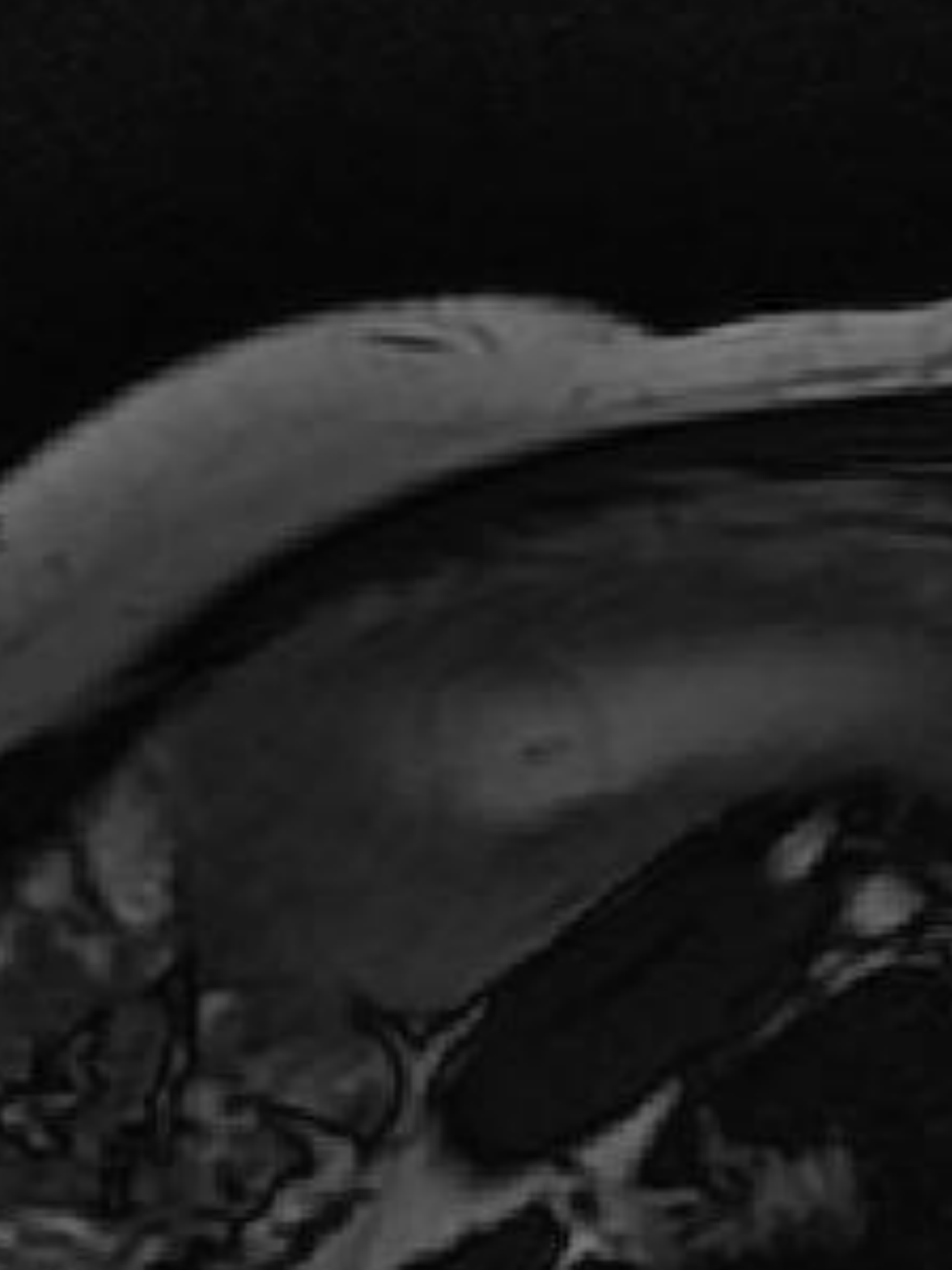
MOMS Trial

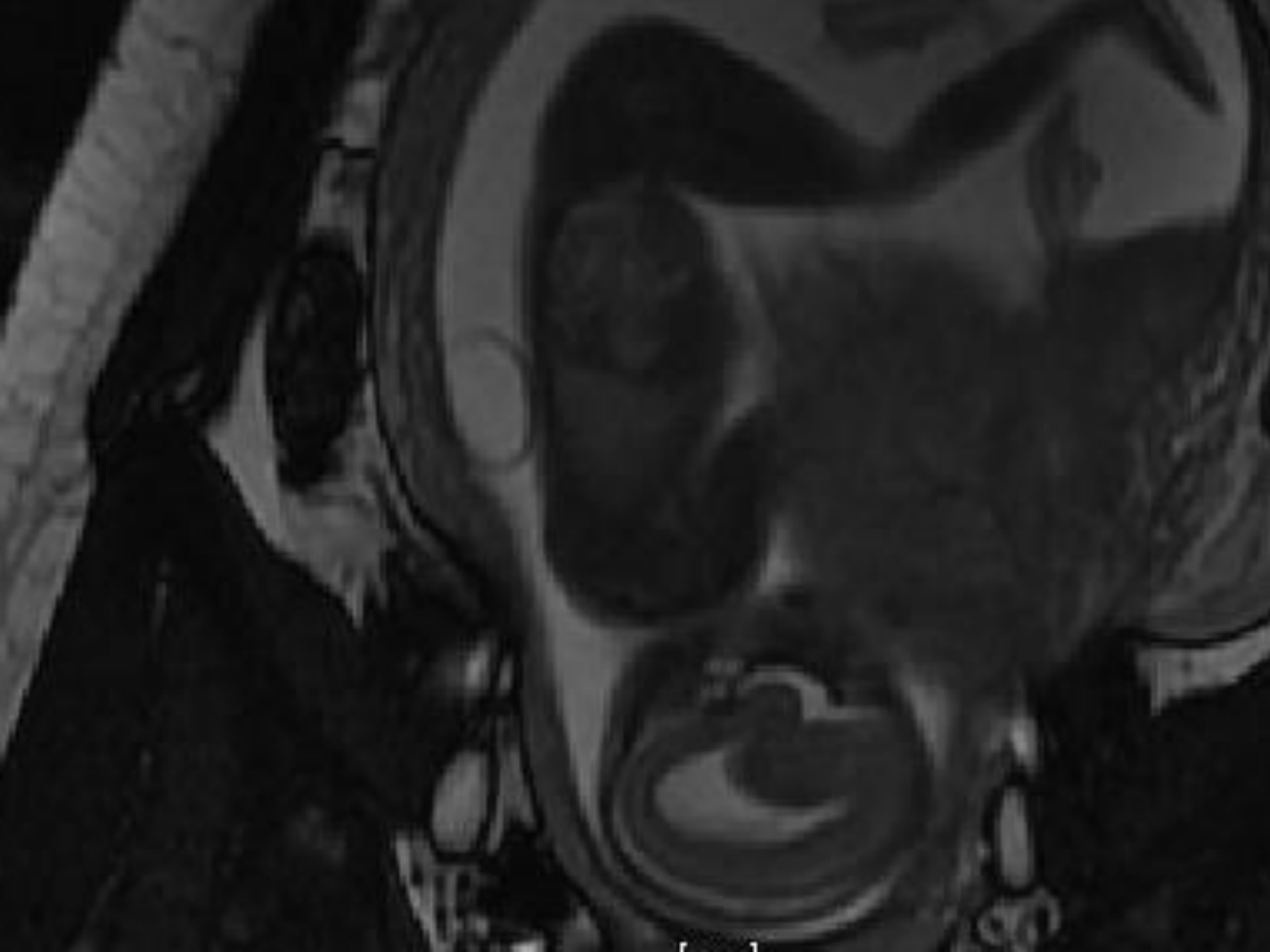
- Analysis provided evidence of neonatal advantage to prenatal repair

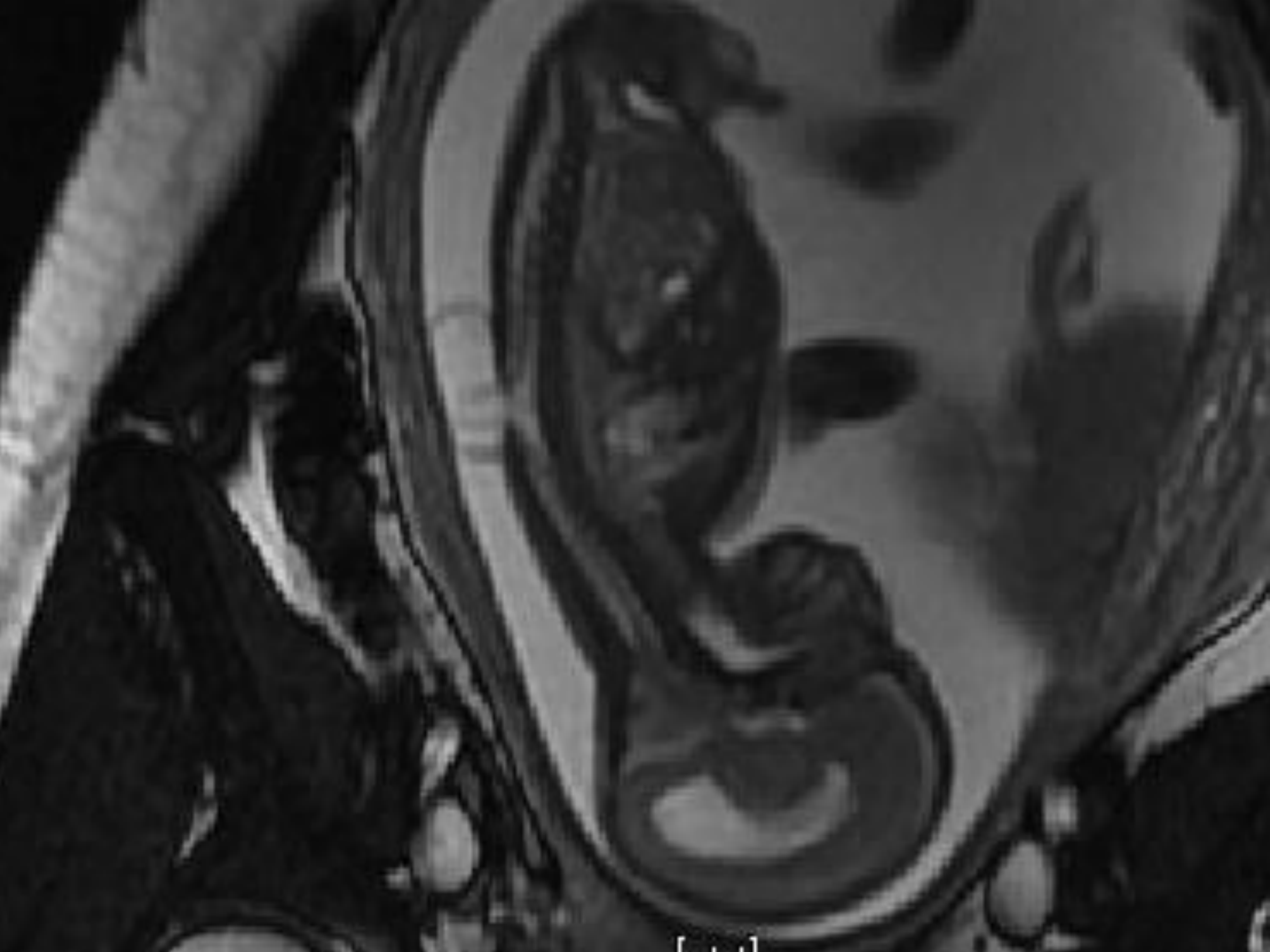
- Significant risks:
  - Prematurity: 33 to 34 weeks for prenatal repair
  - Increased infection risk for the neonate
  - Maternal uterine risks from “classical” incision
  - Maternal necessity for all deliveries by cesarean
  - Increased maternal risks of uterine dehiscence/rupture











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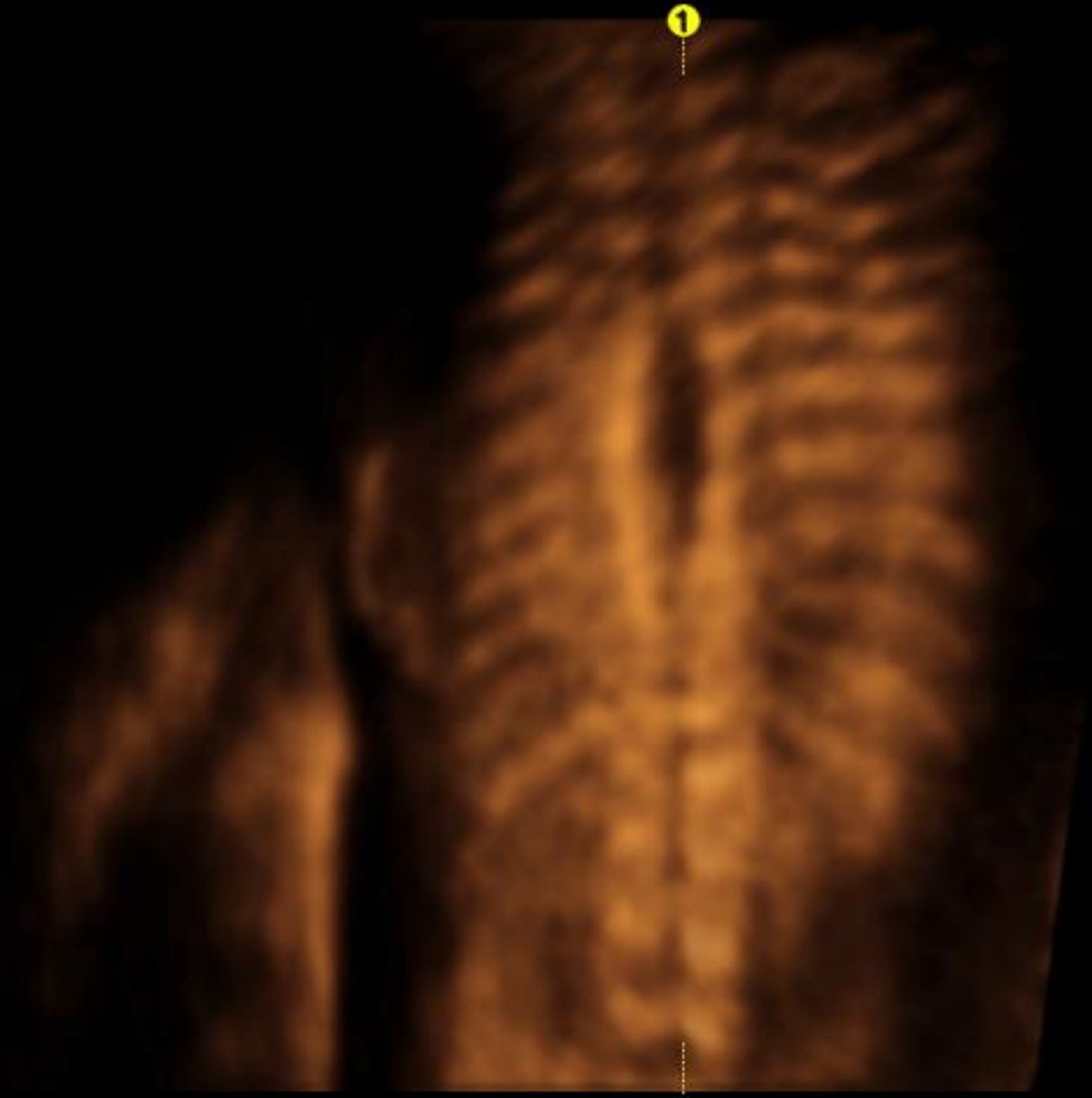
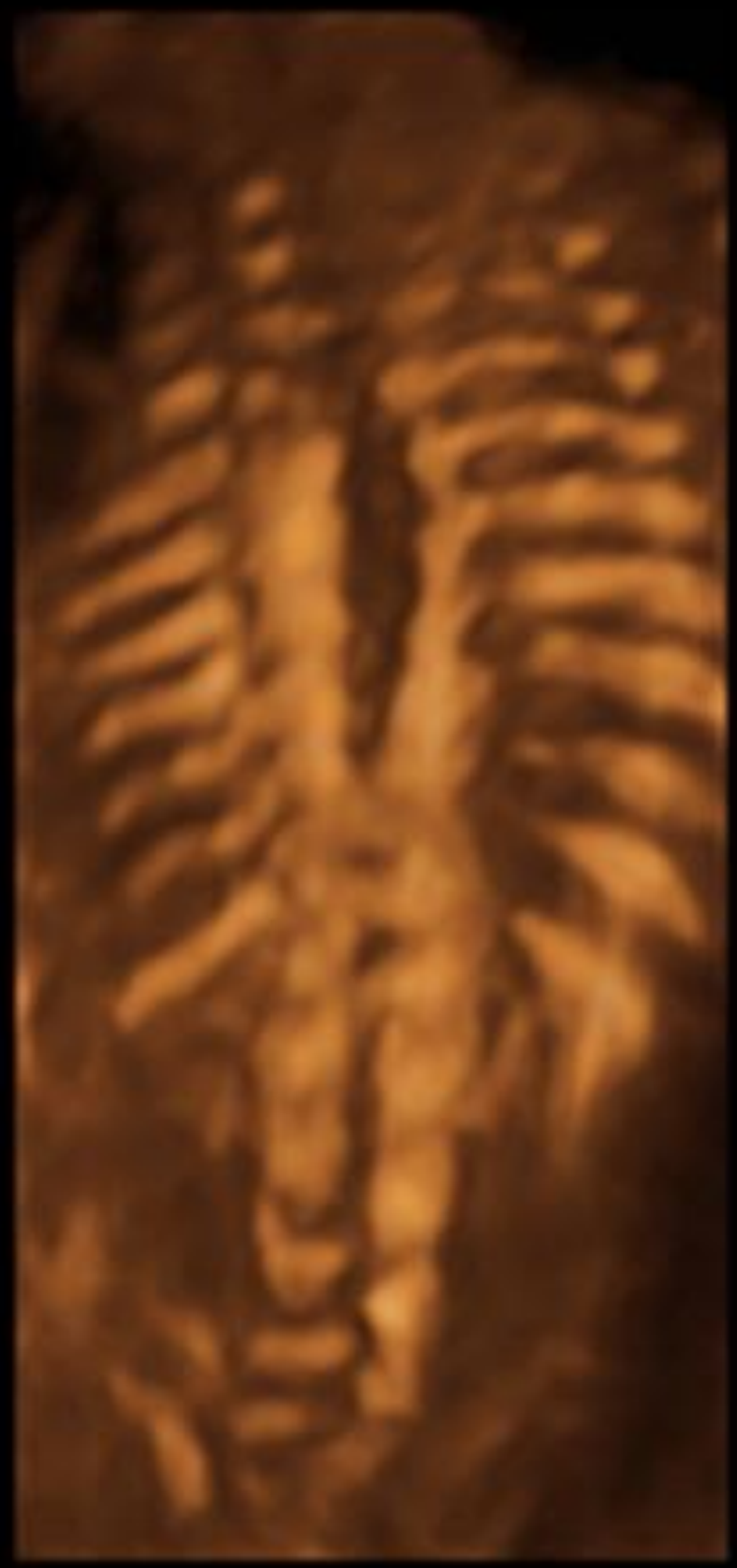
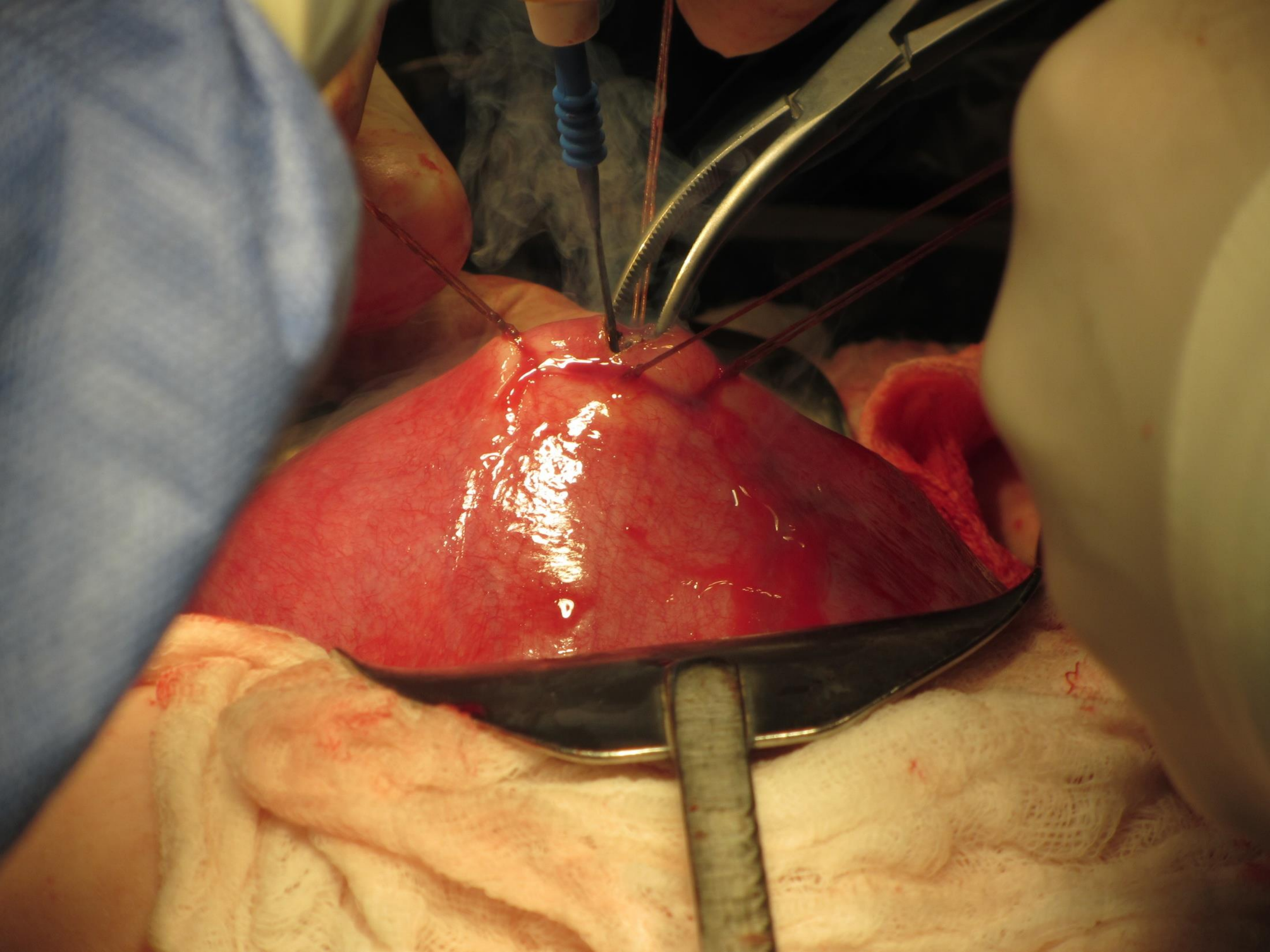
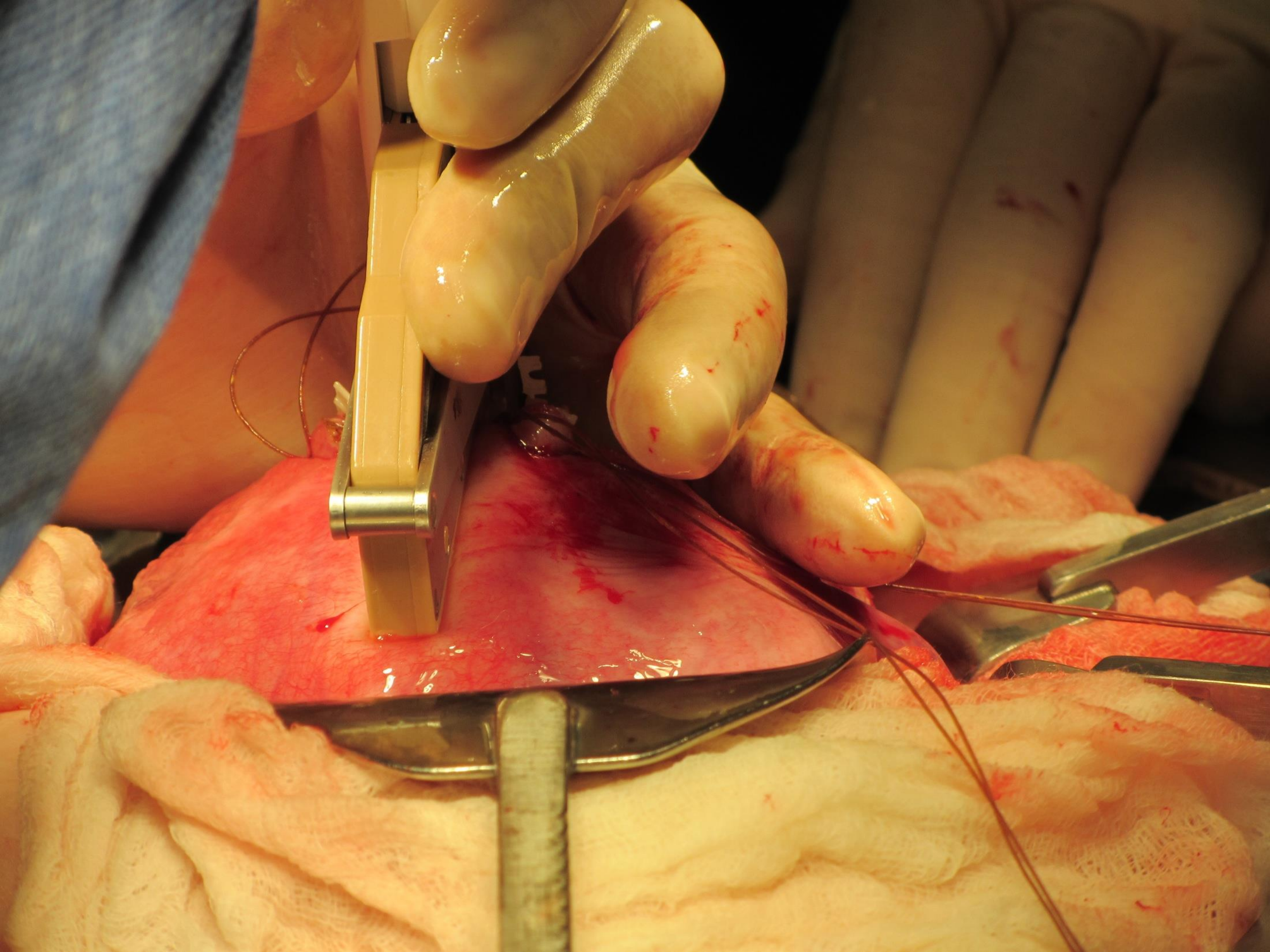
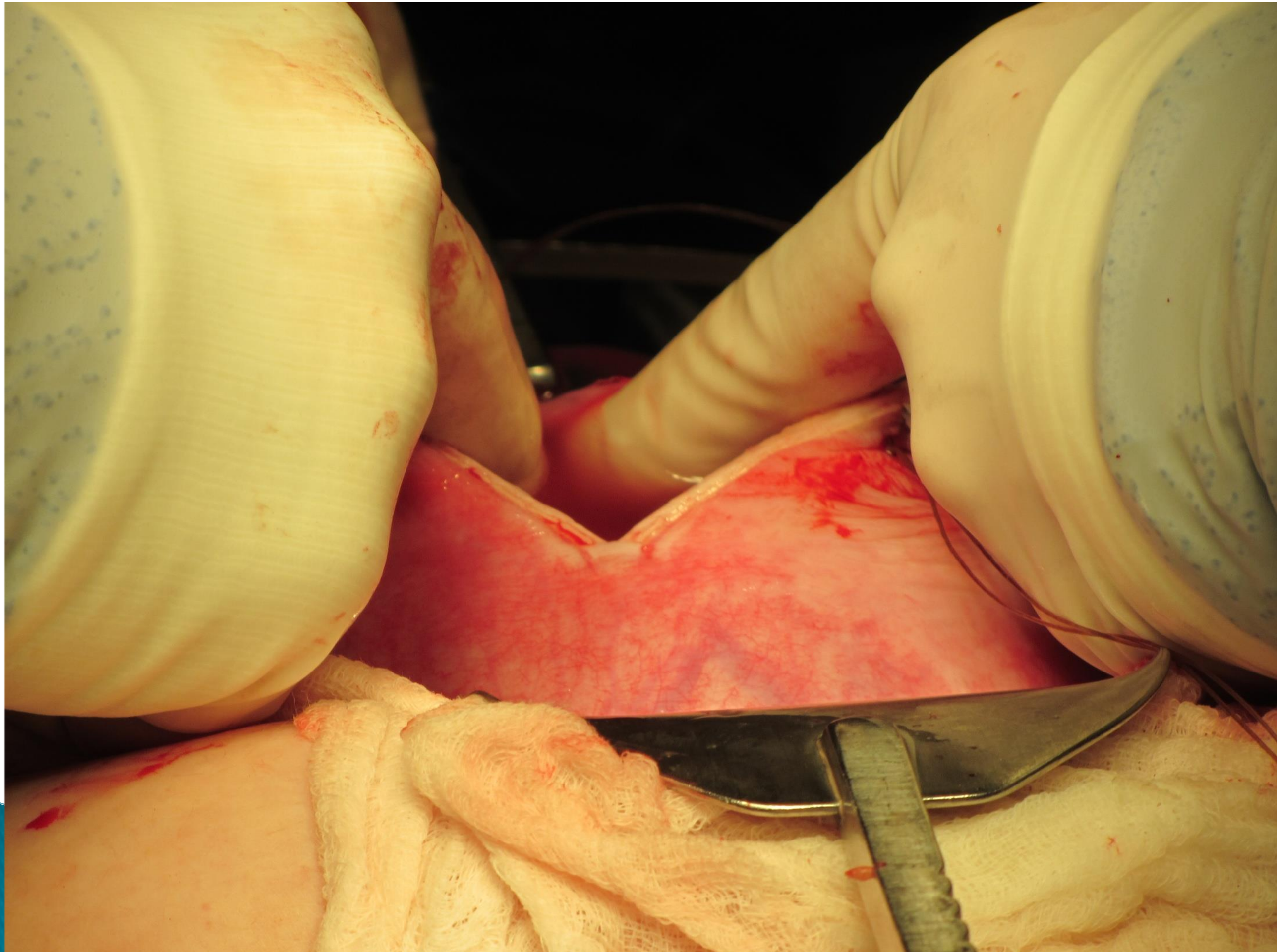




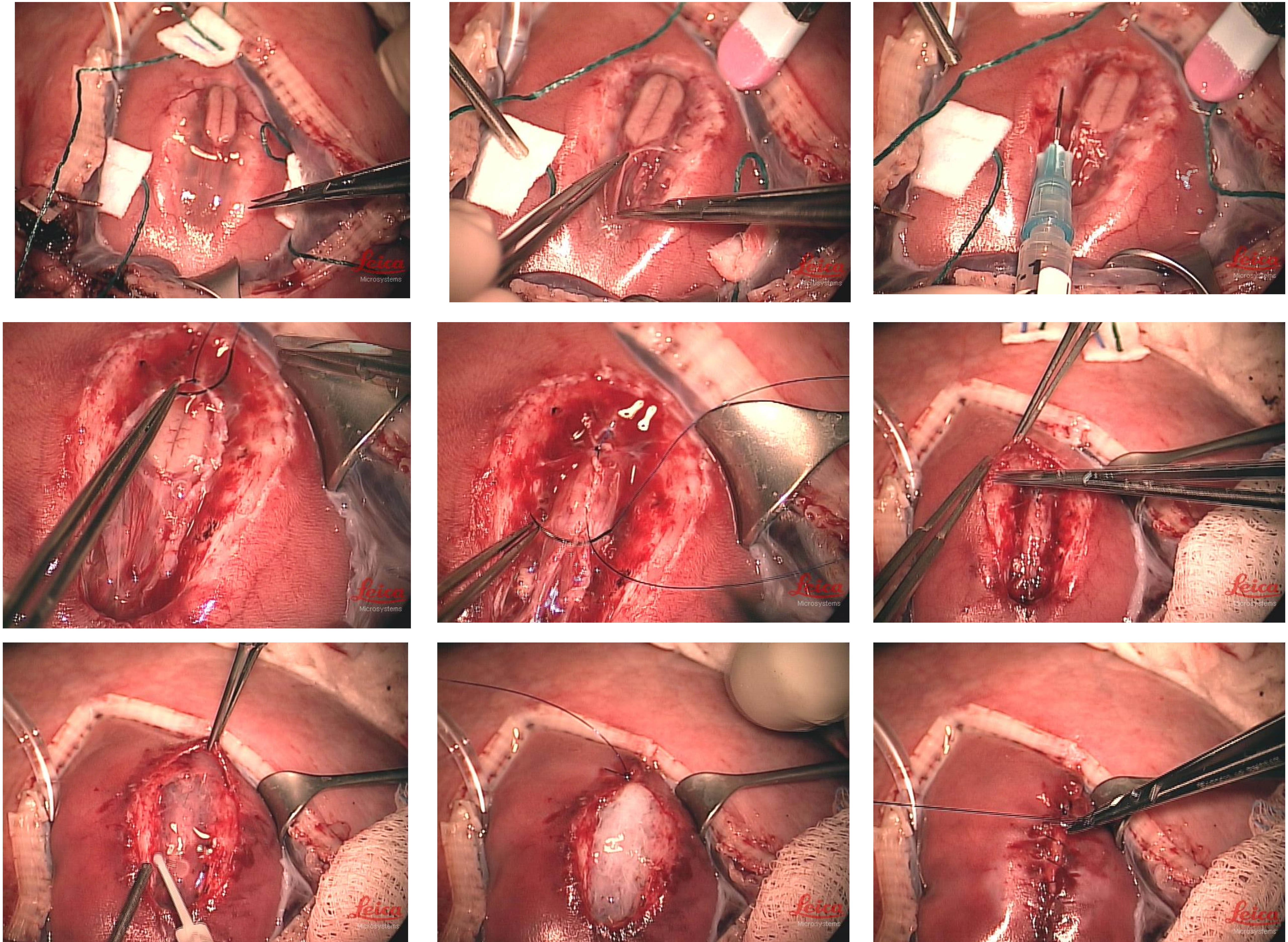


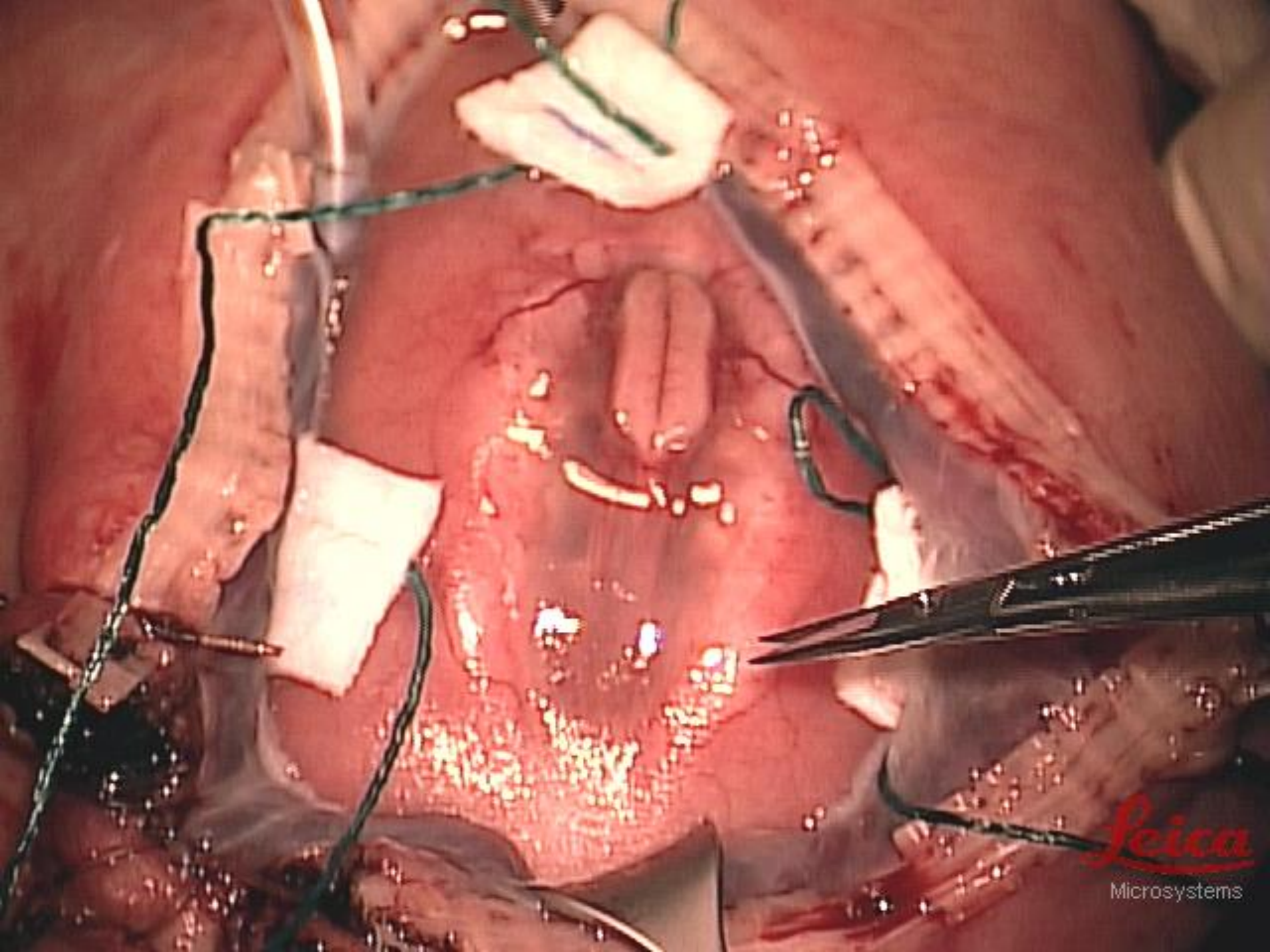




Fetal Myelomeningocele Repair

First: Typical

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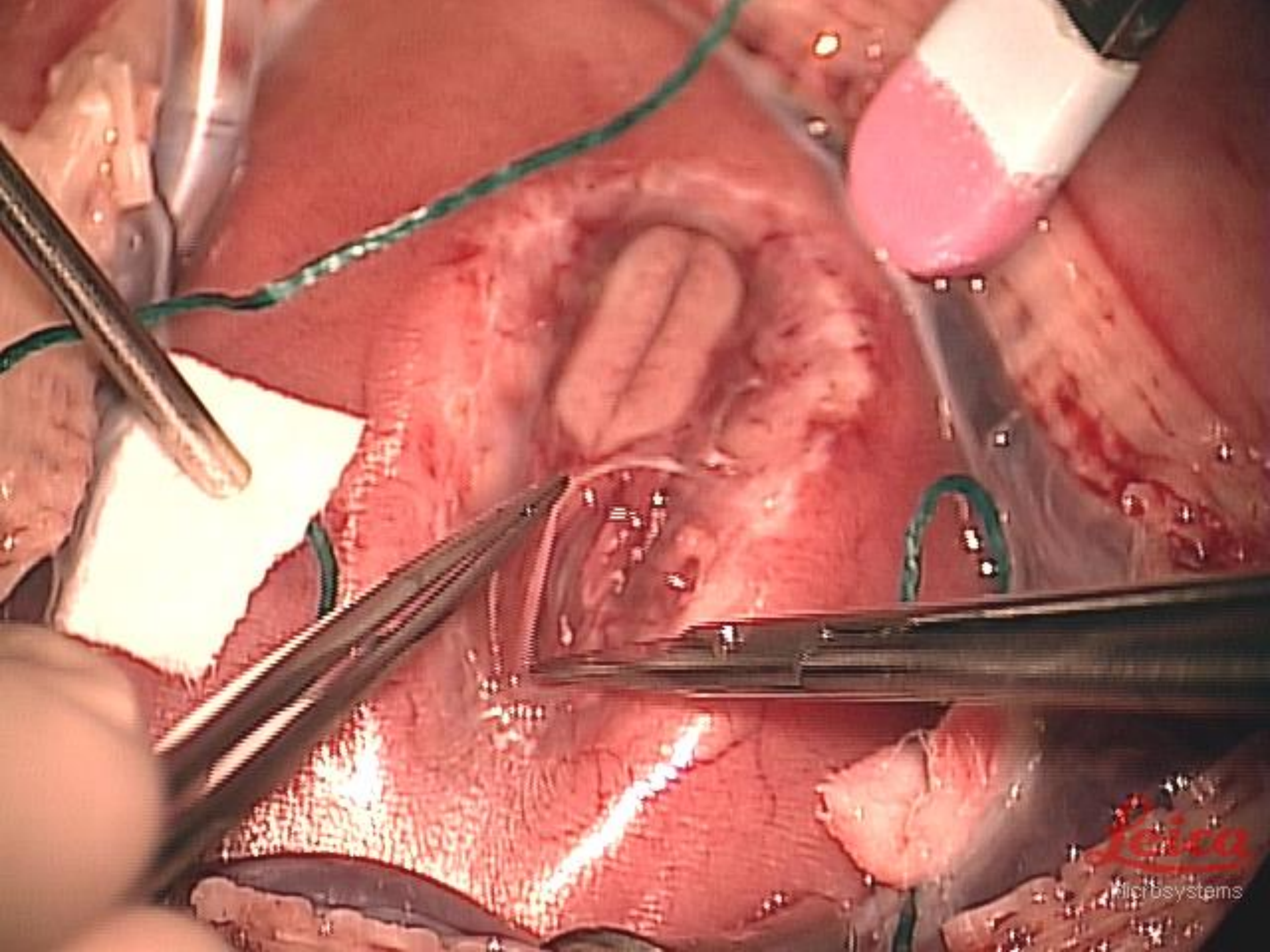

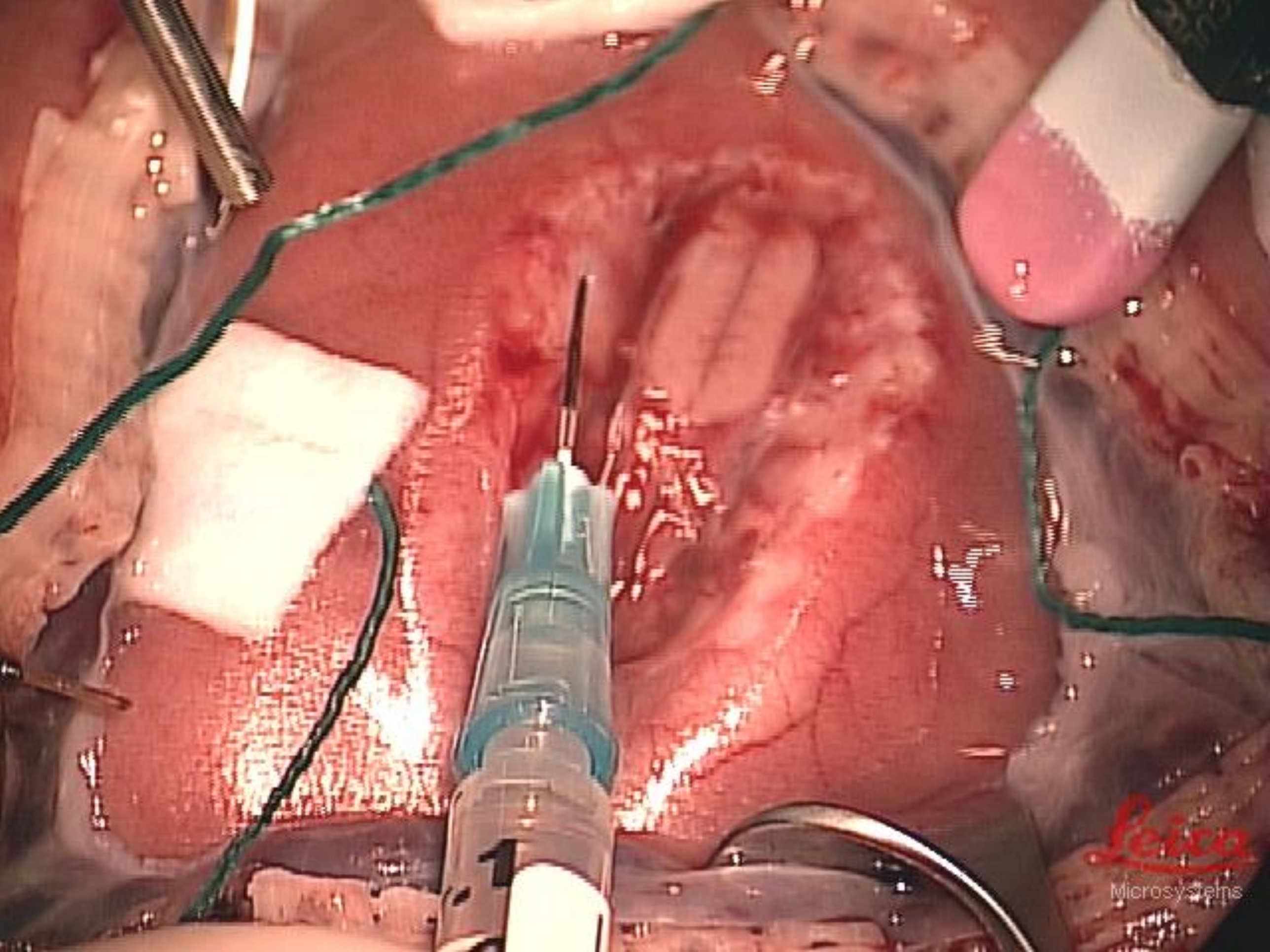
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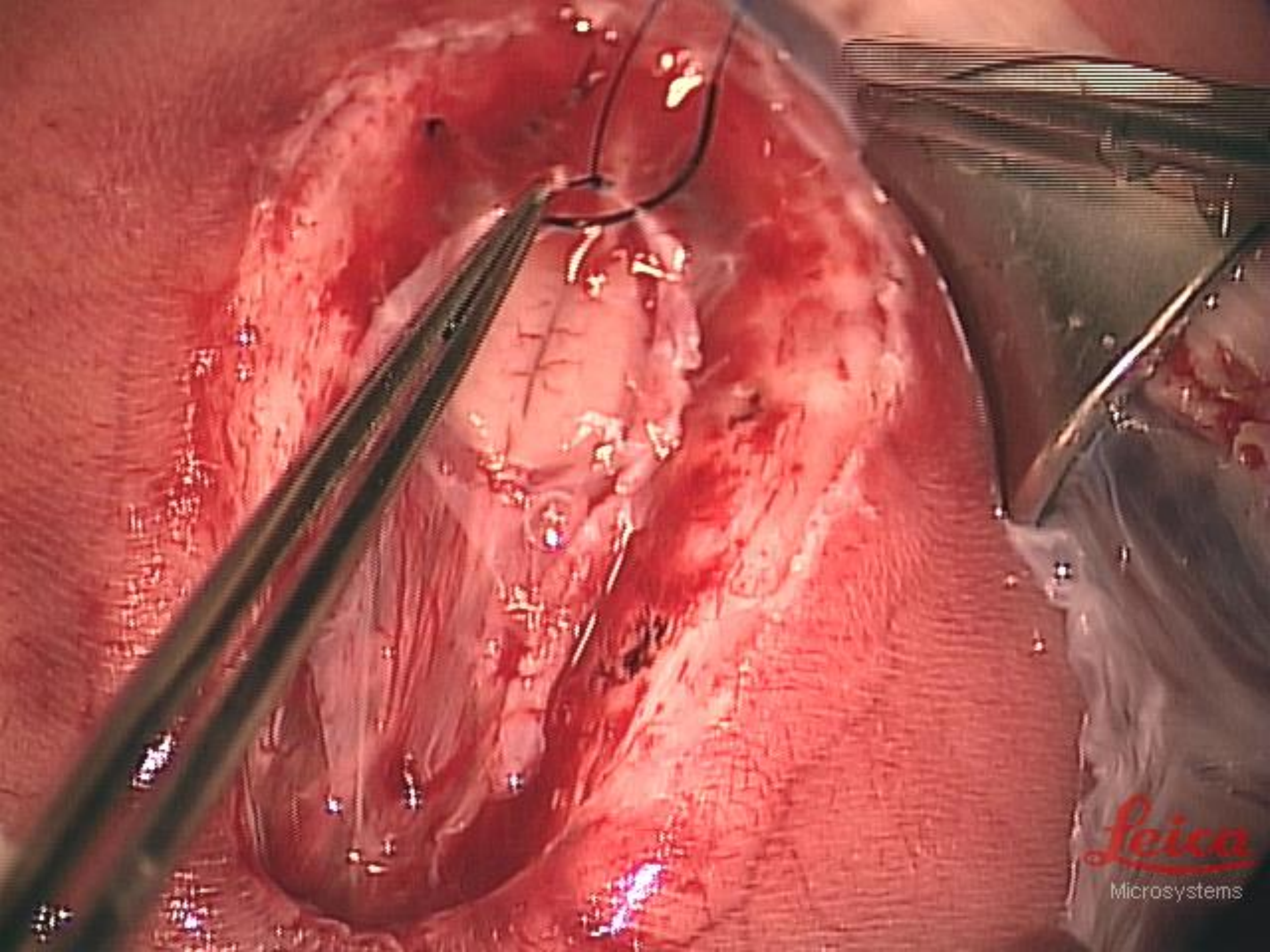
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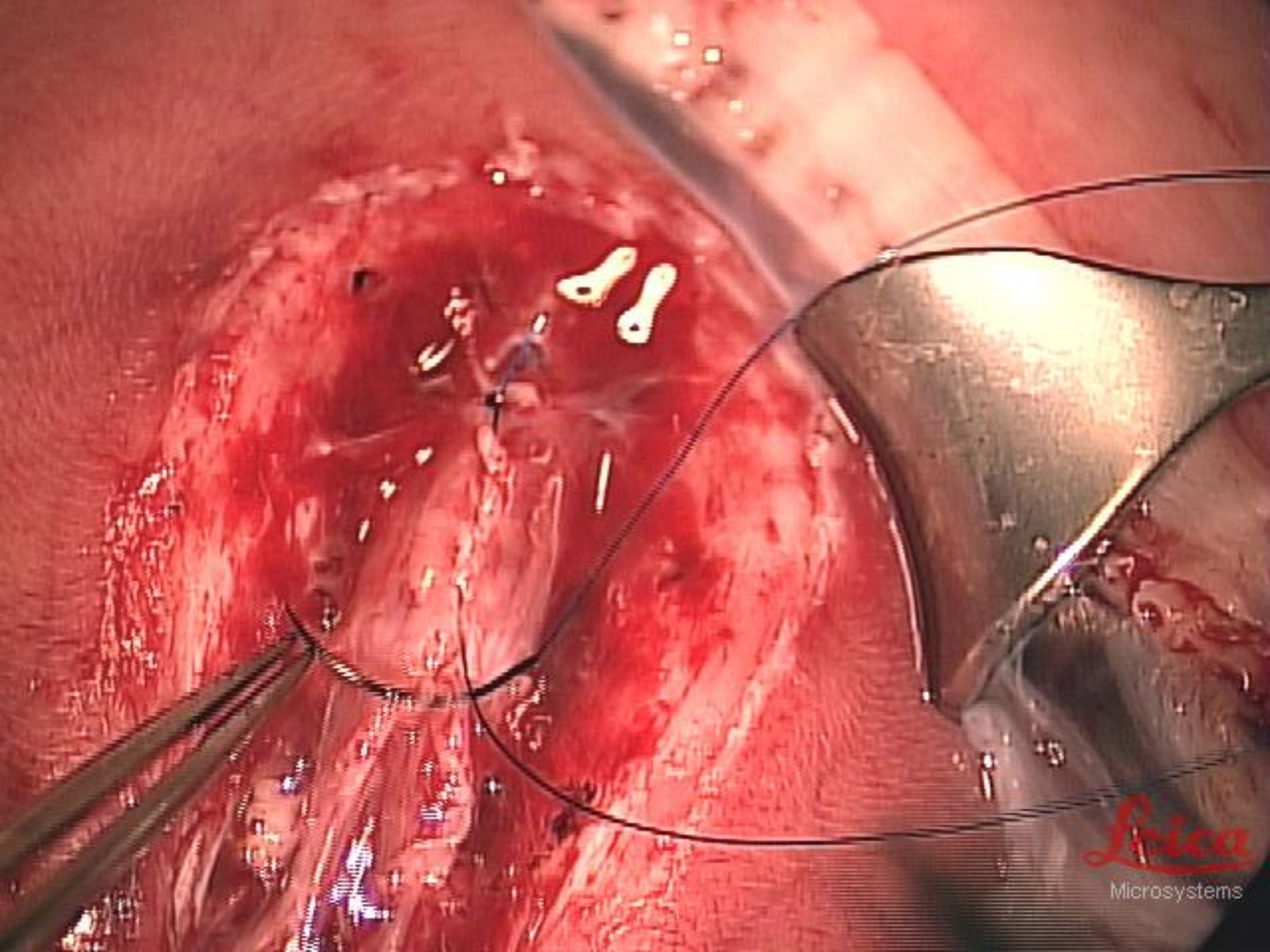
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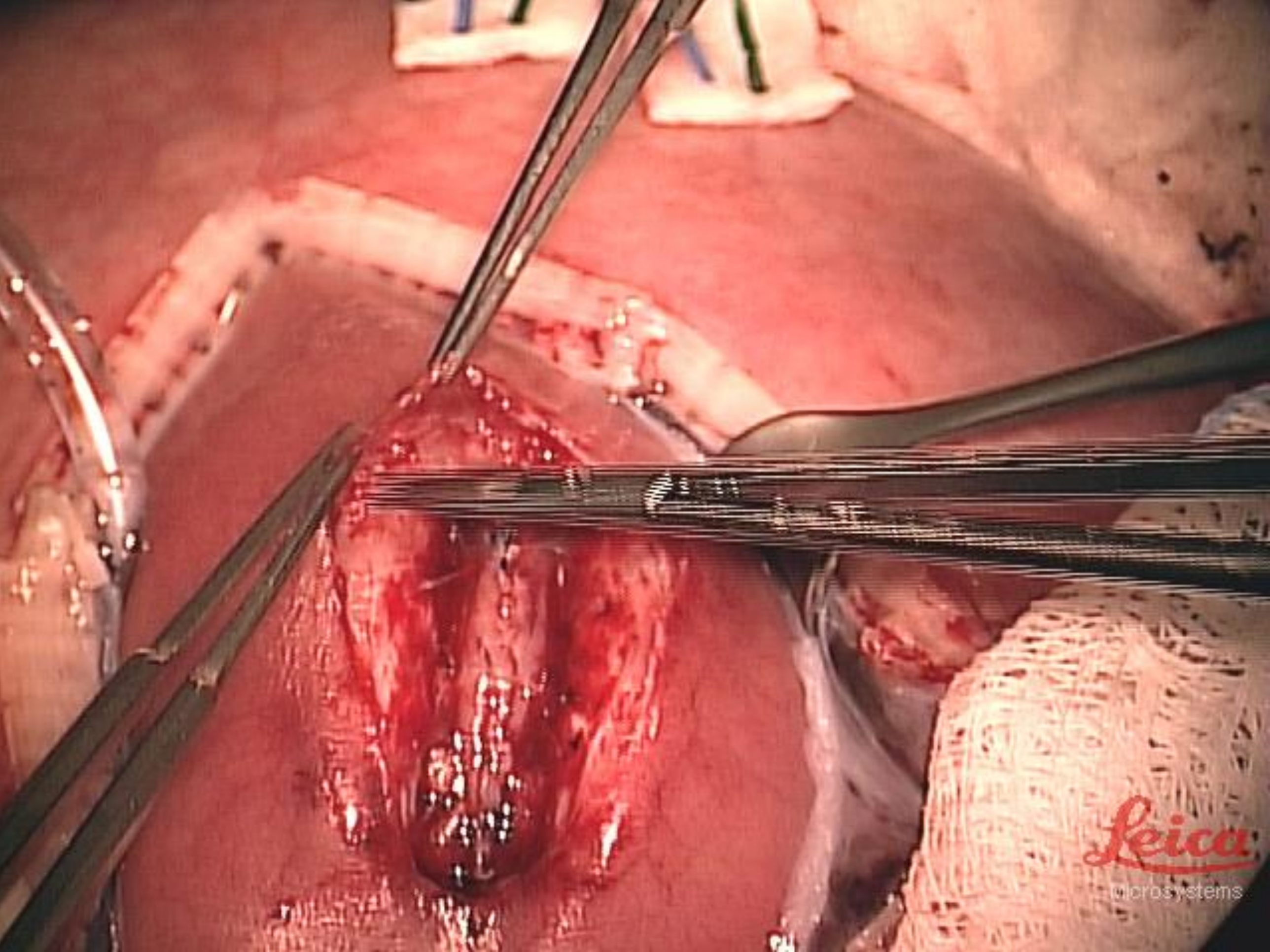
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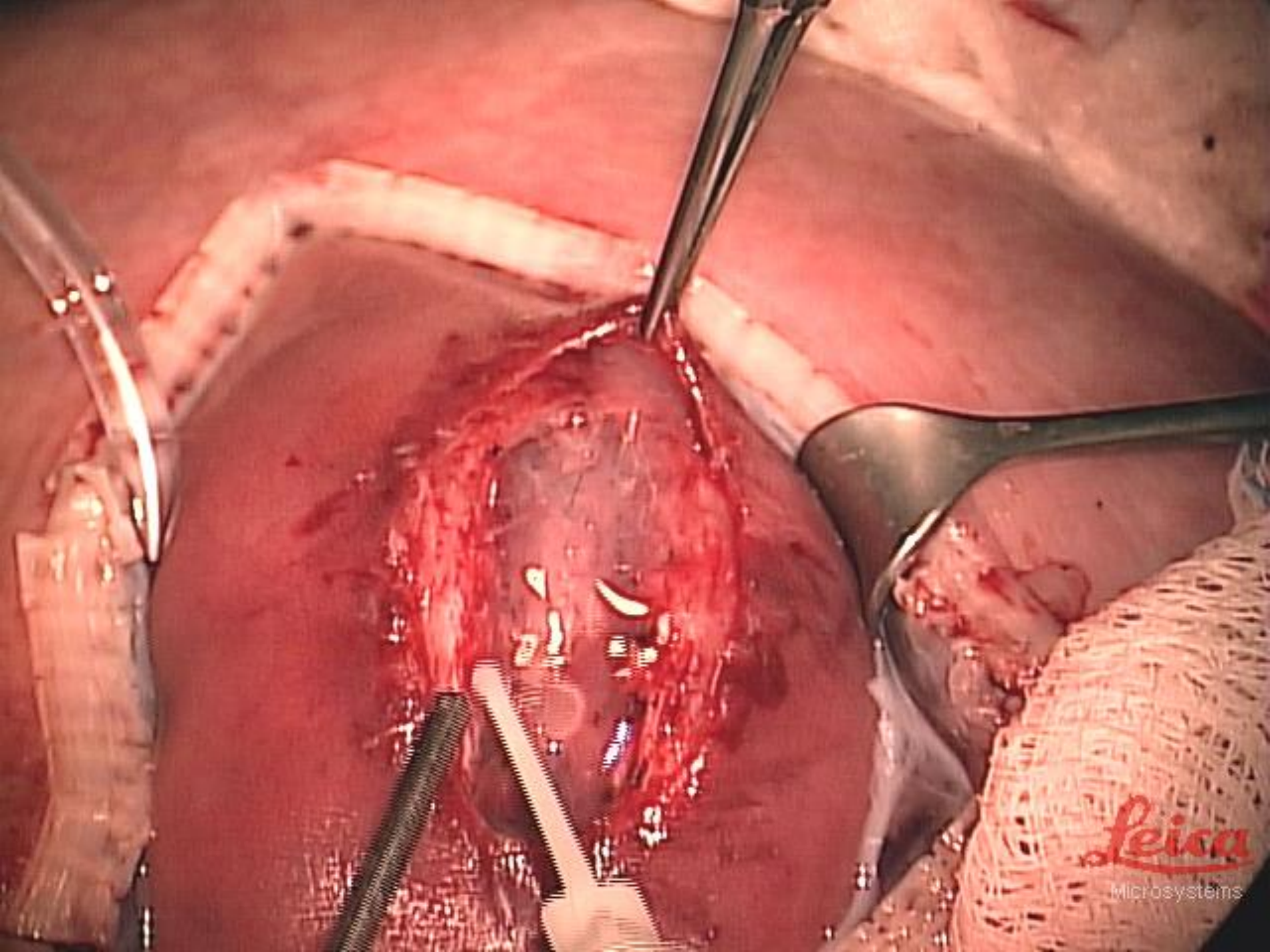
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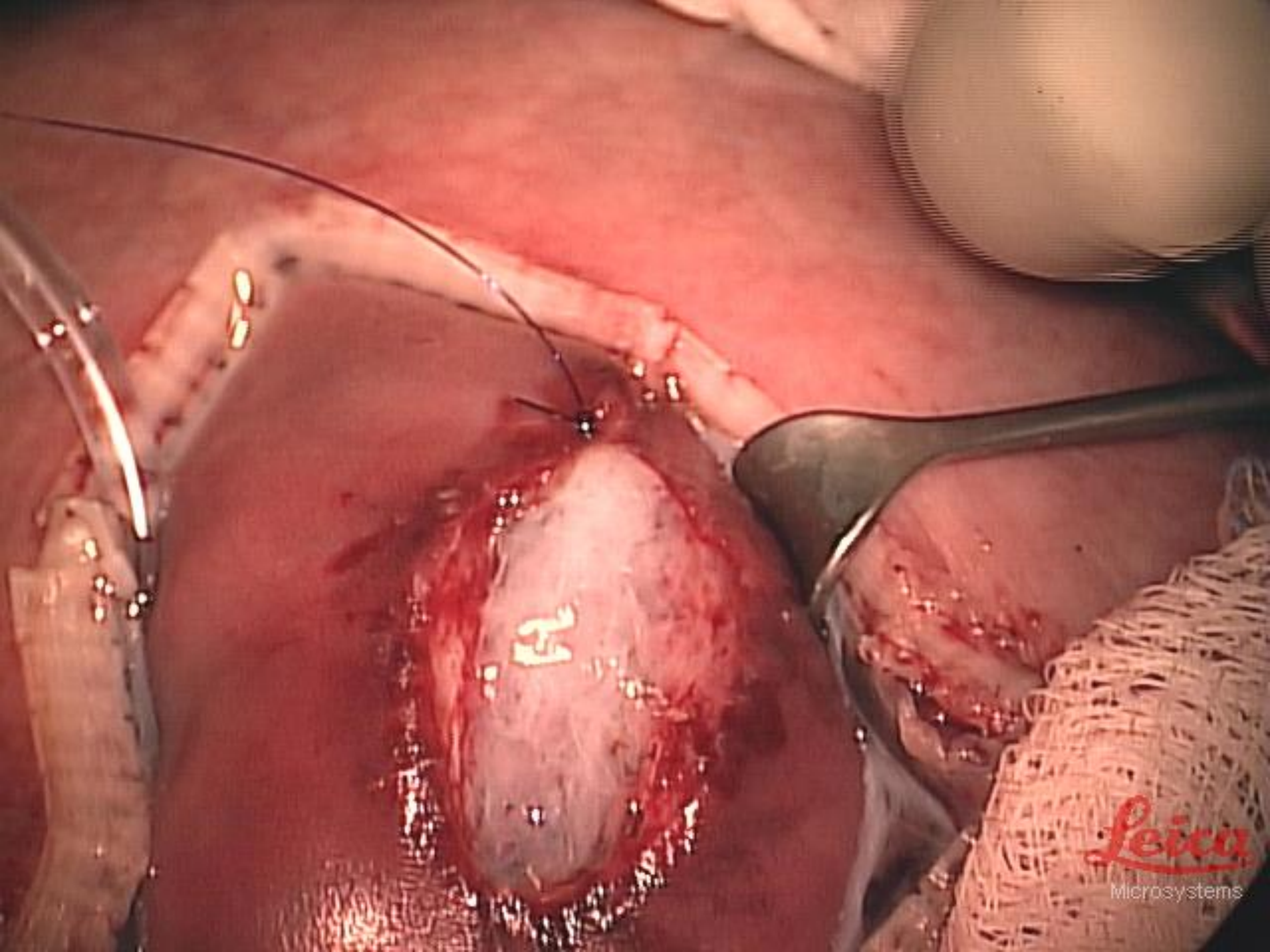
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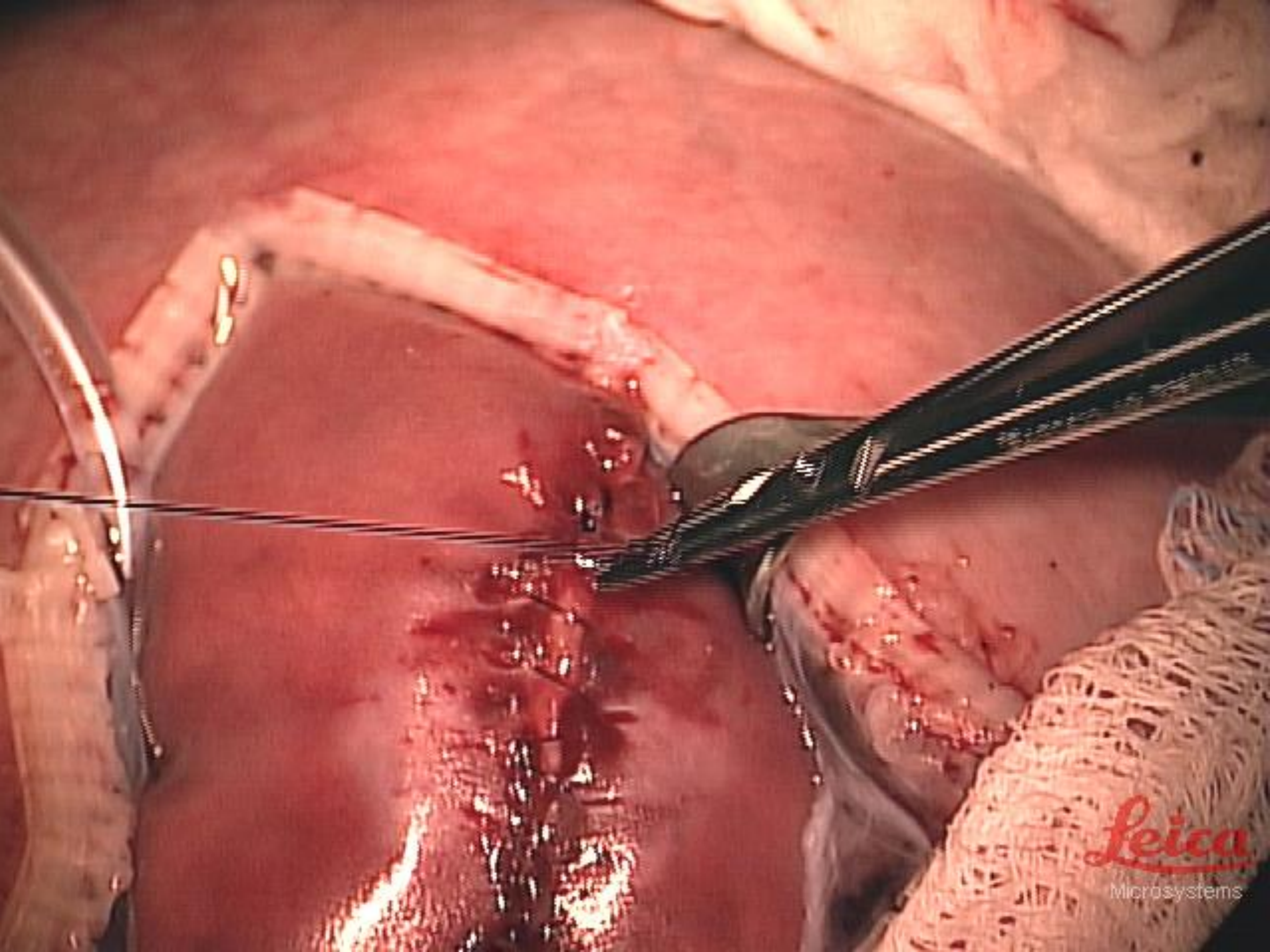
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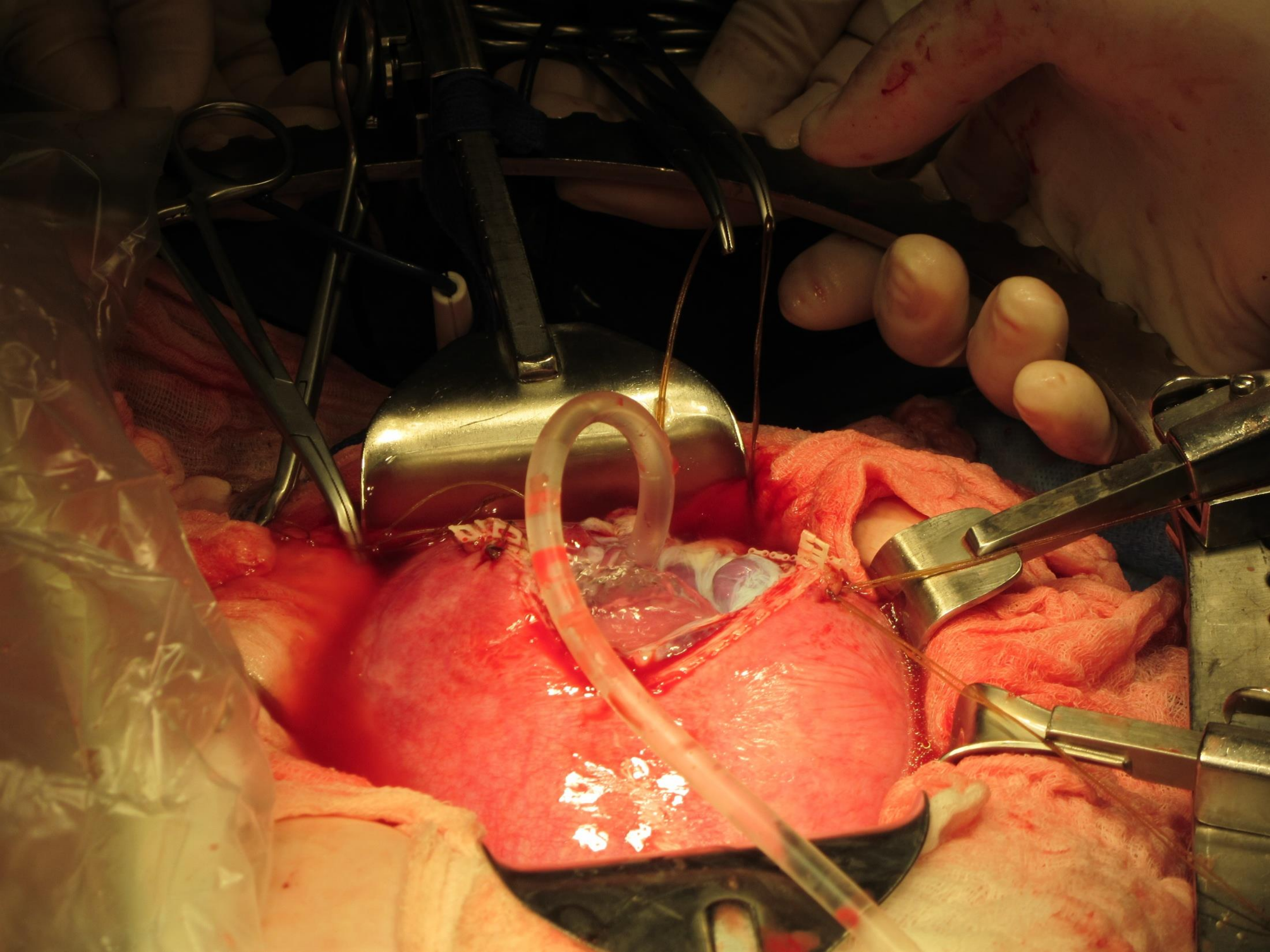
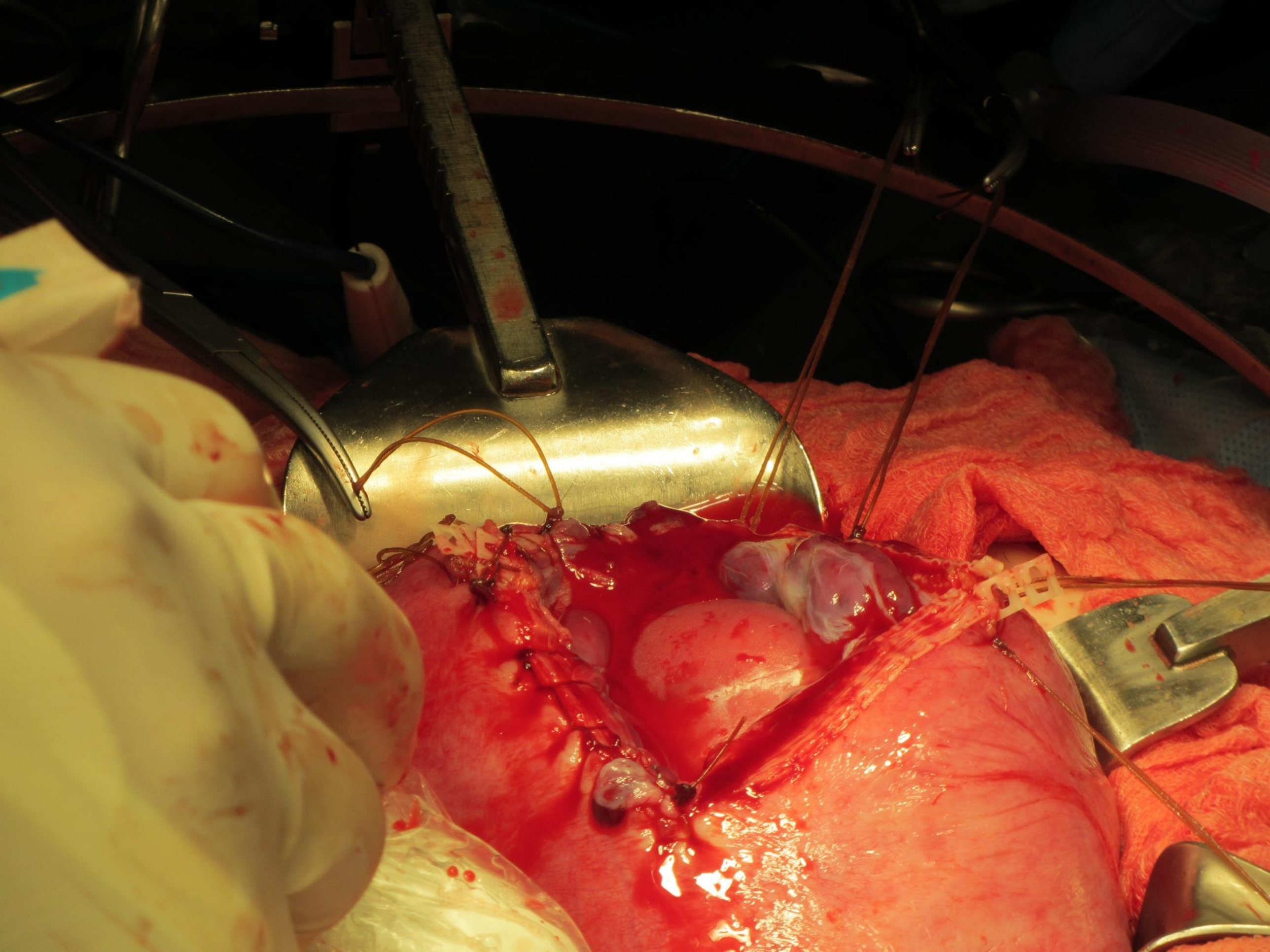
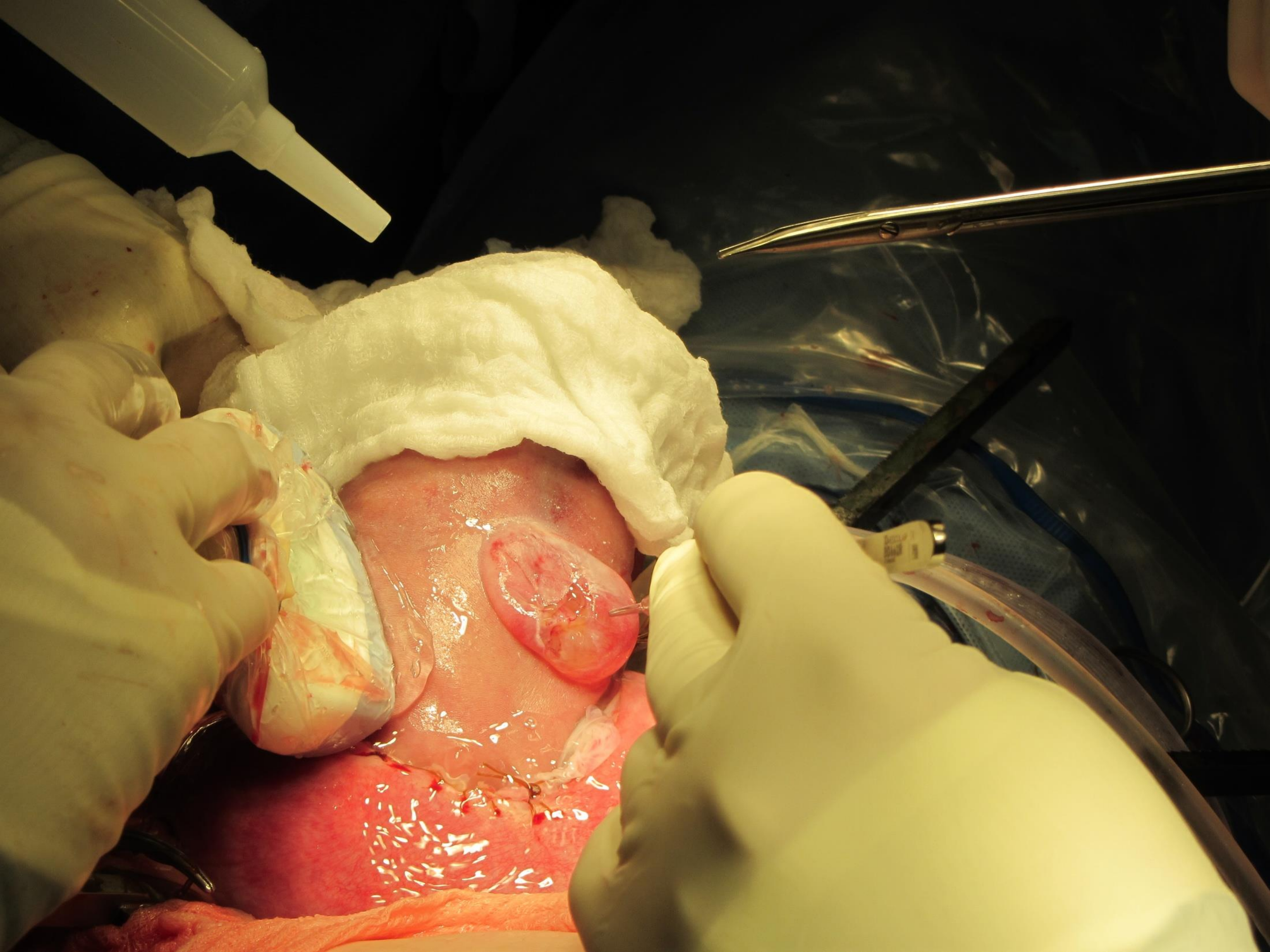
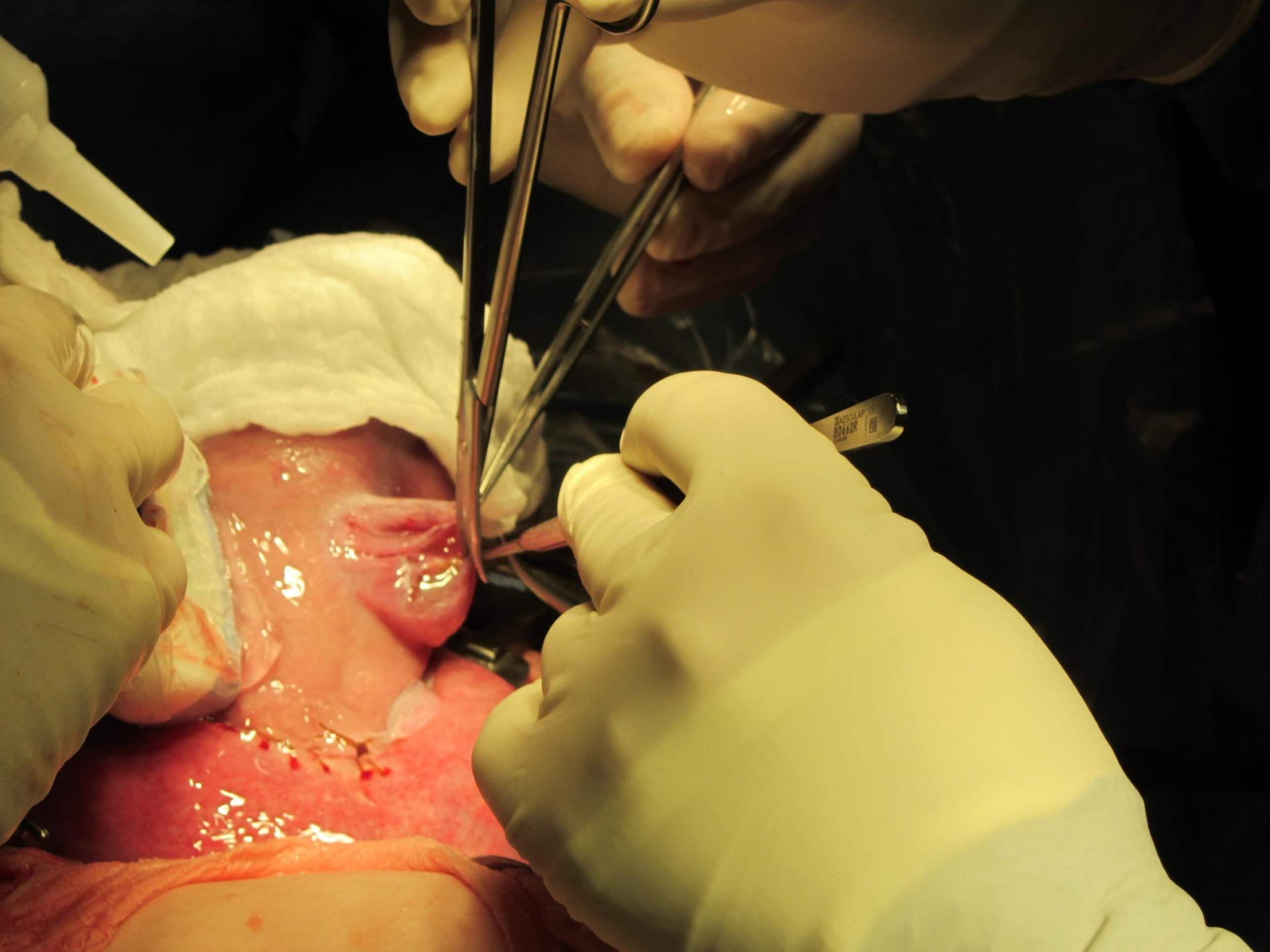
Fetal Myelomeningocele Repair

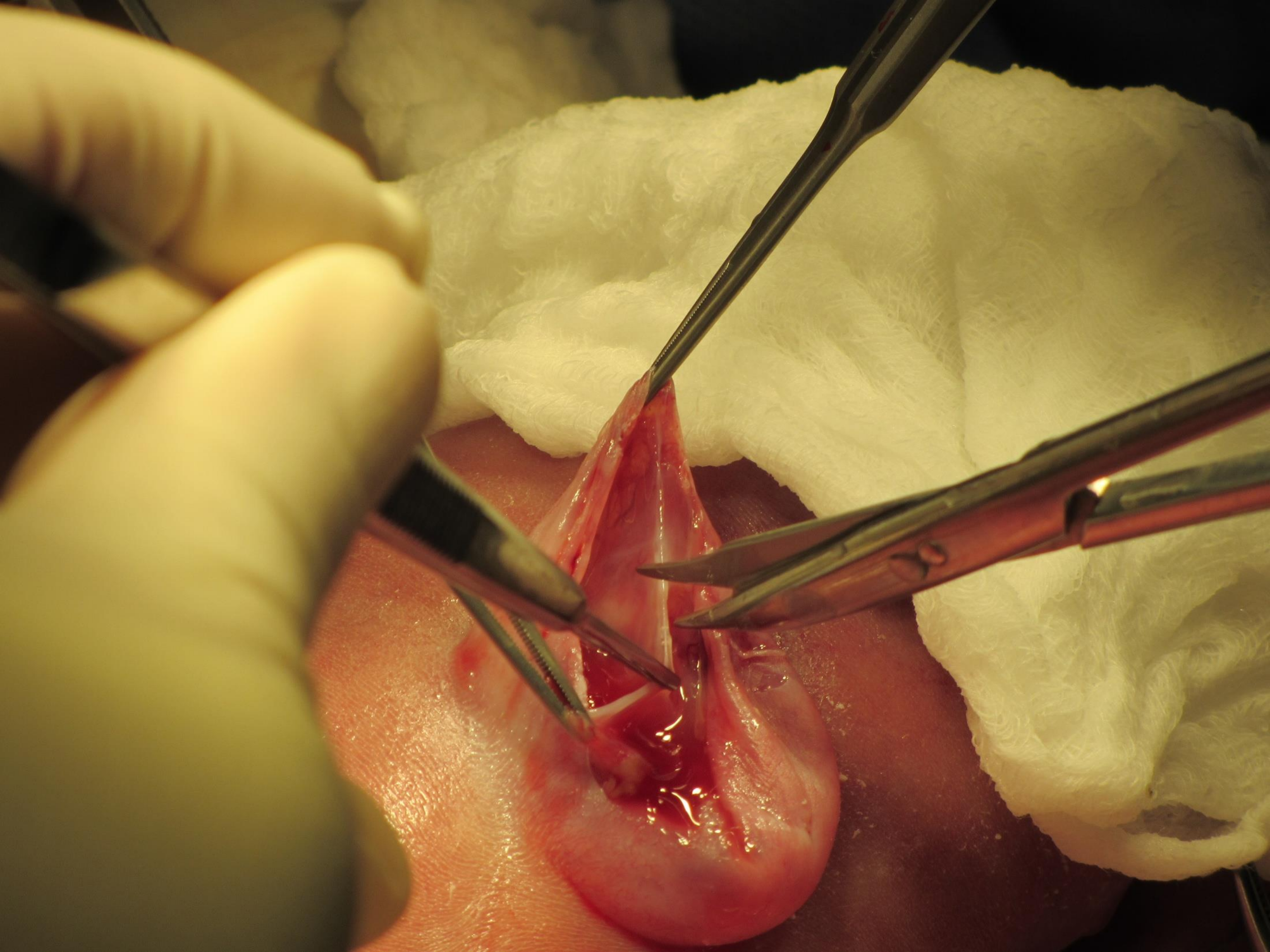
Second: Atypical

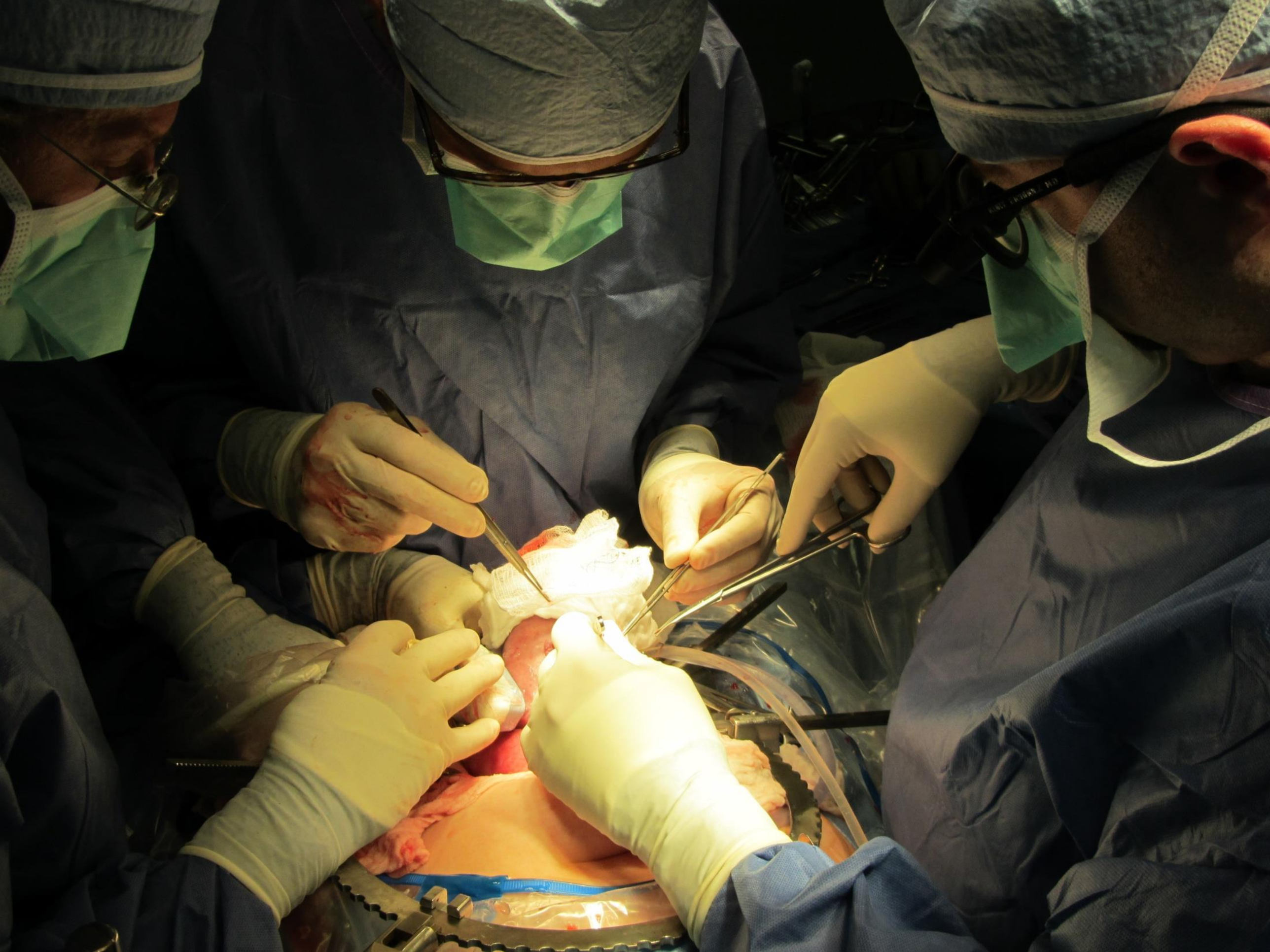


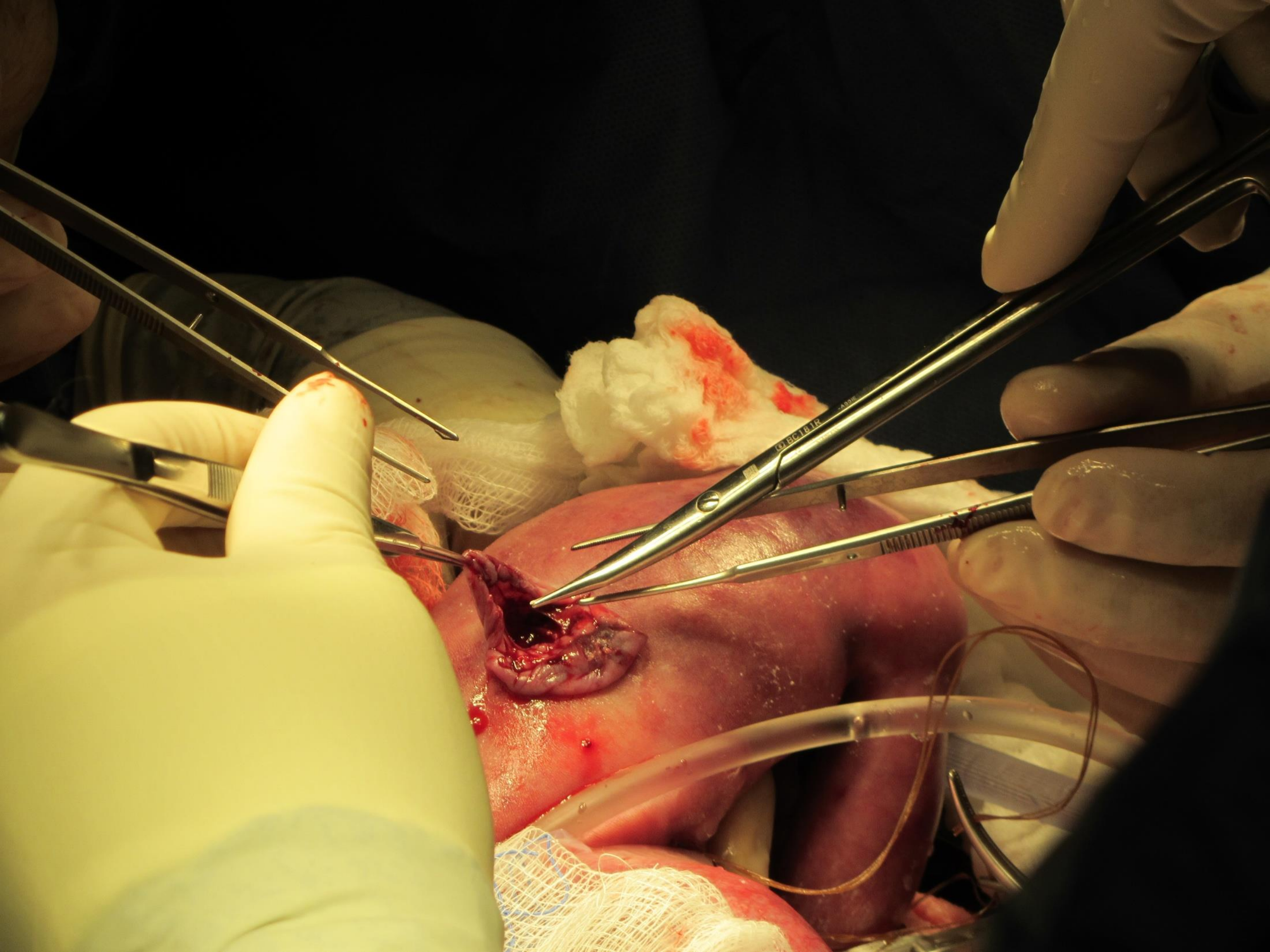


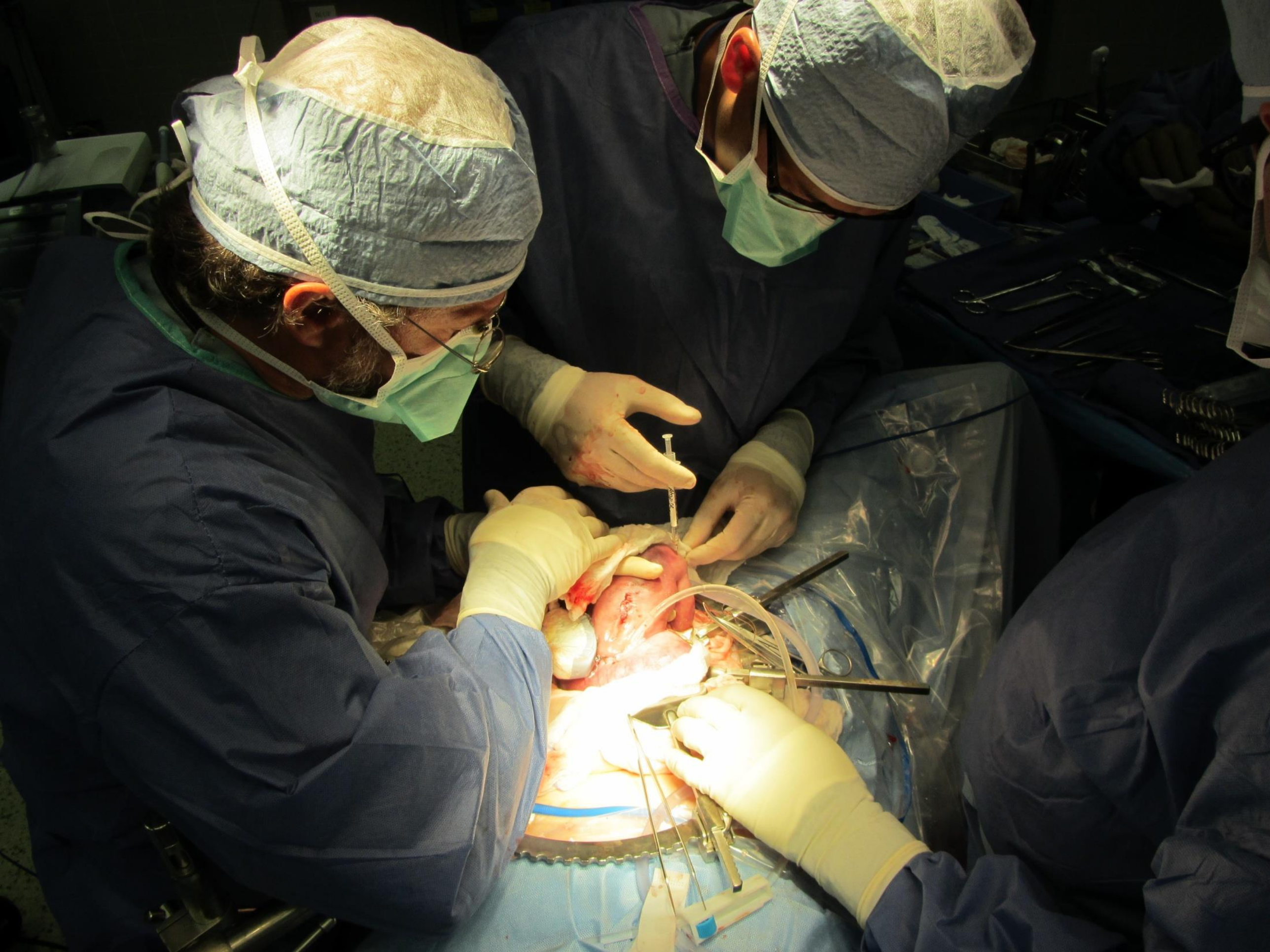


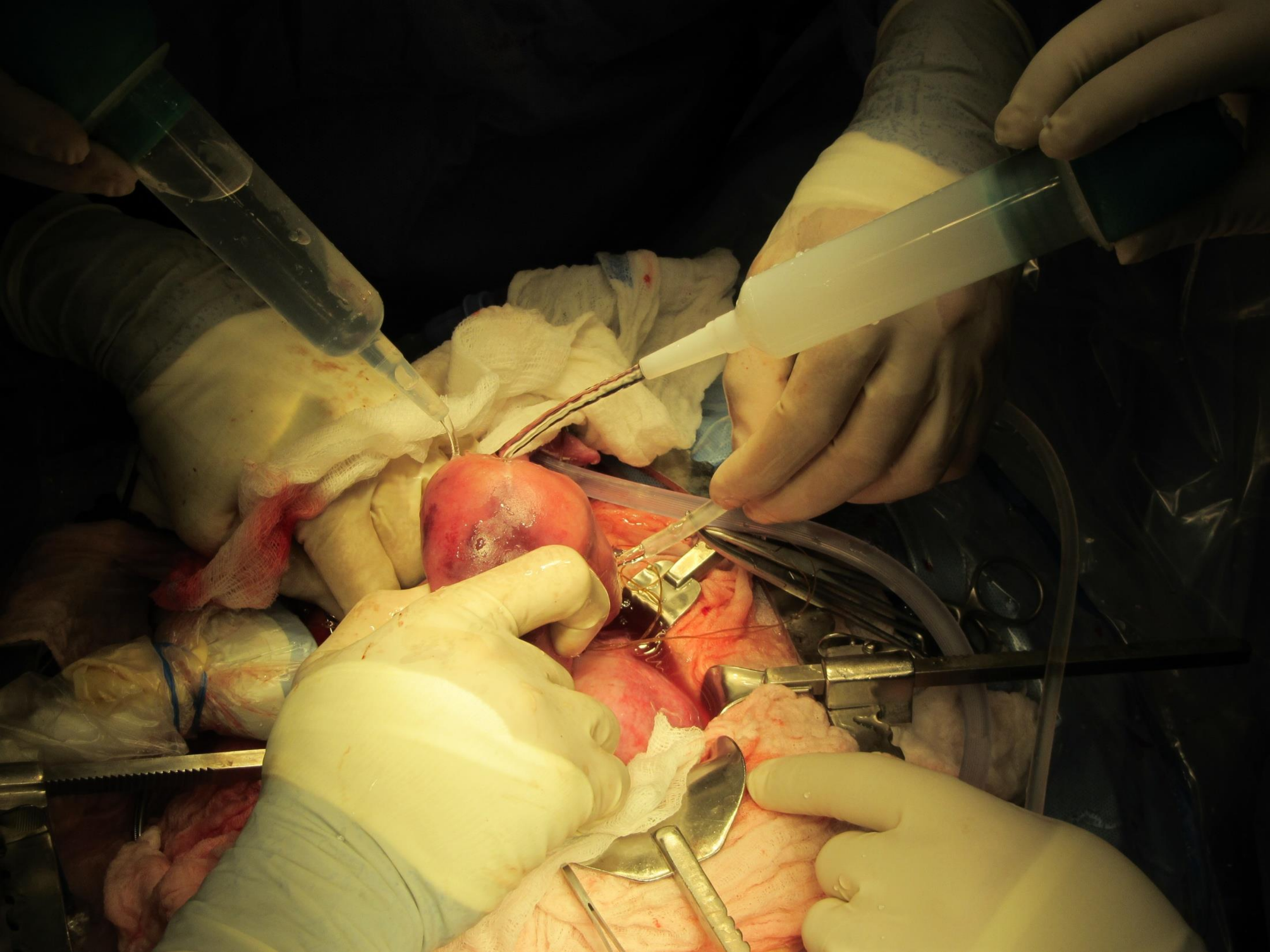


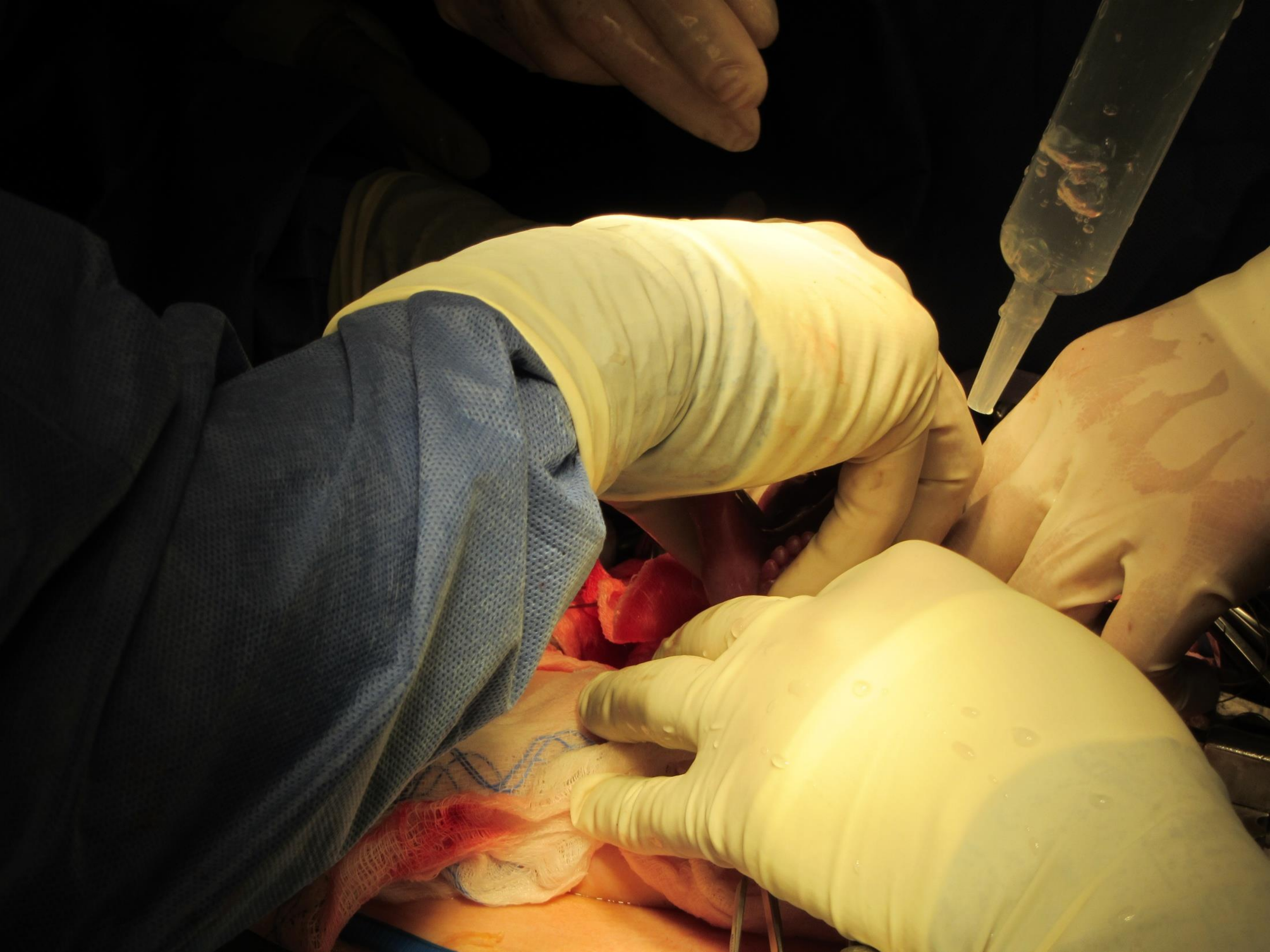


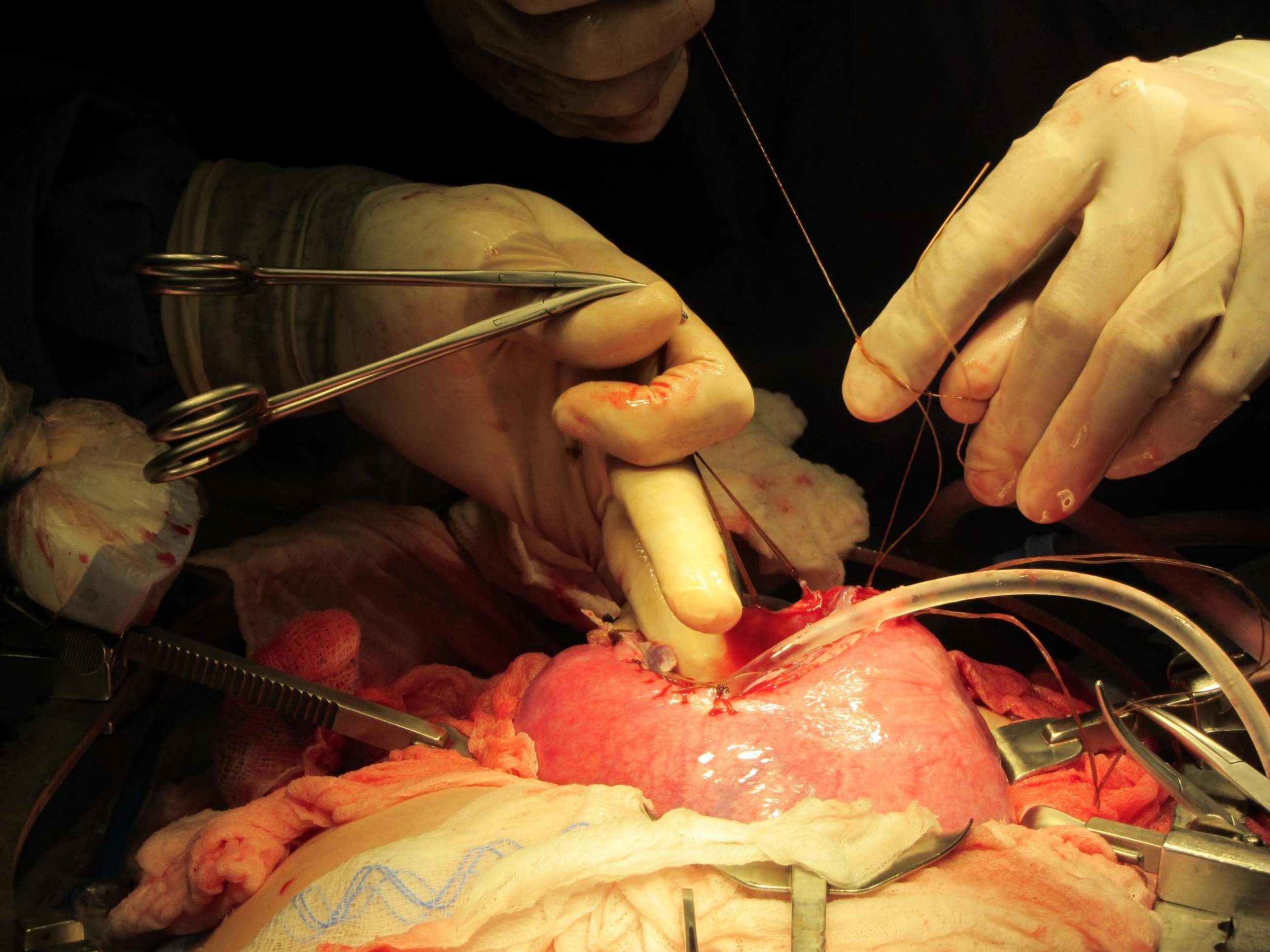


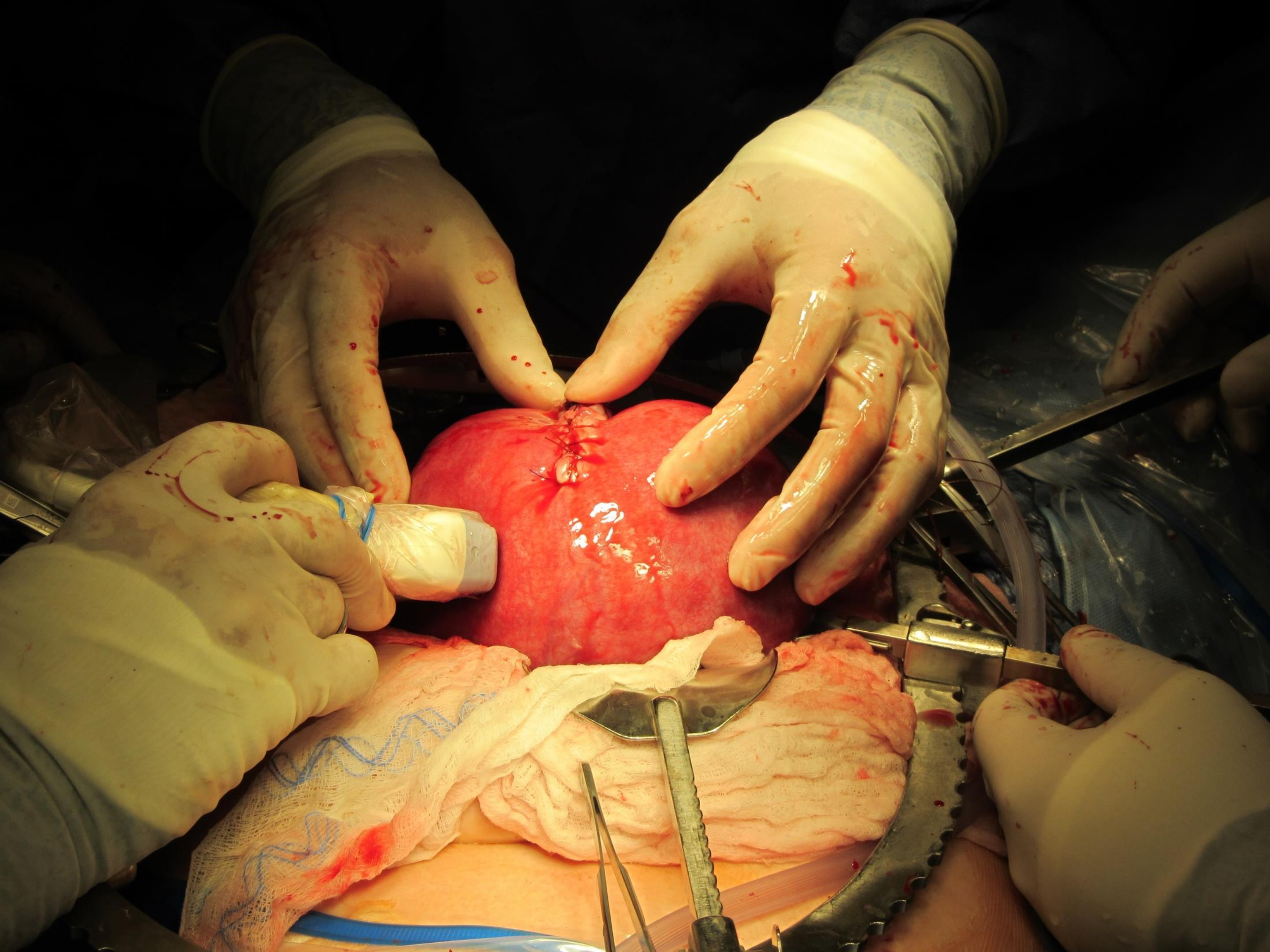










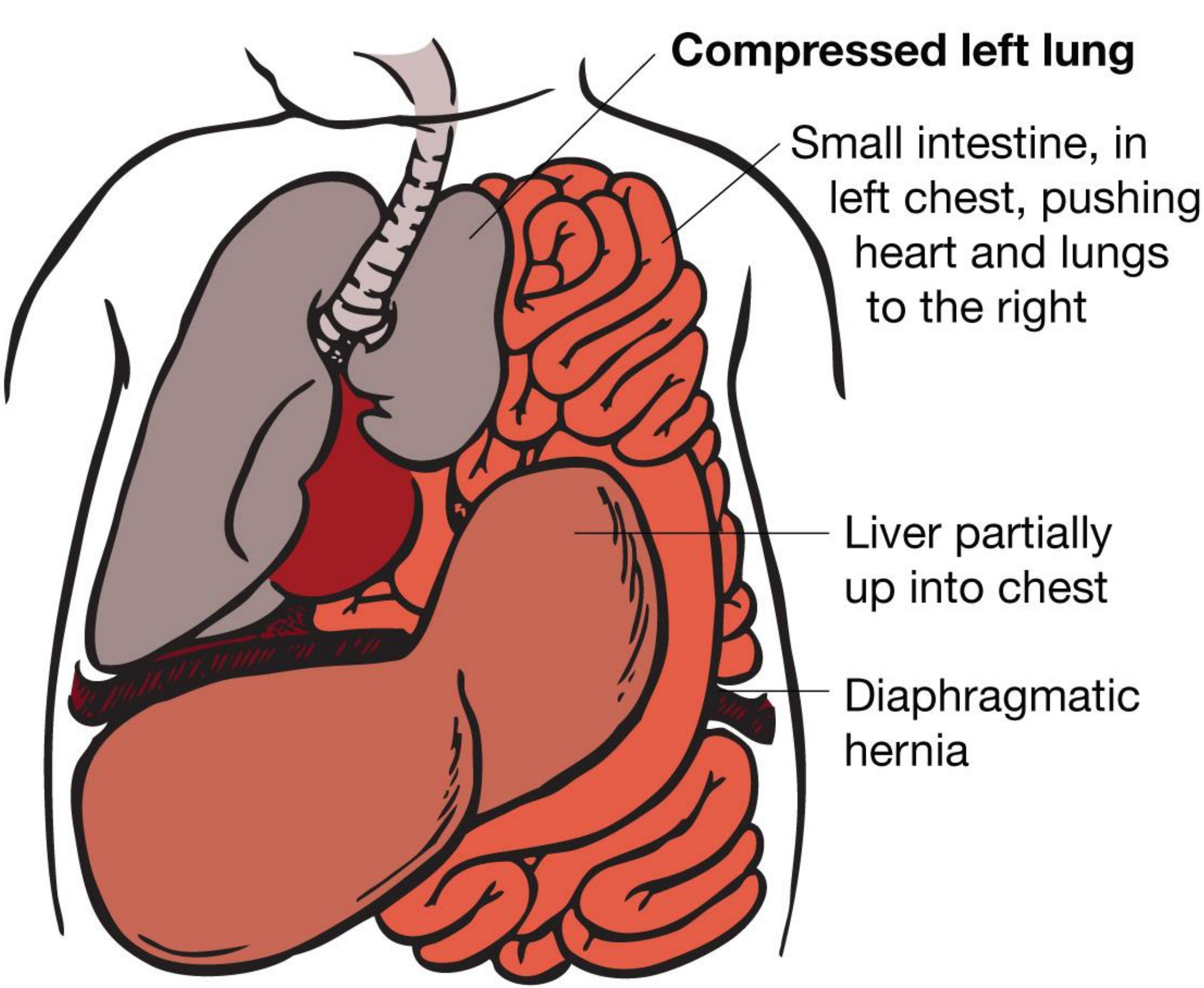


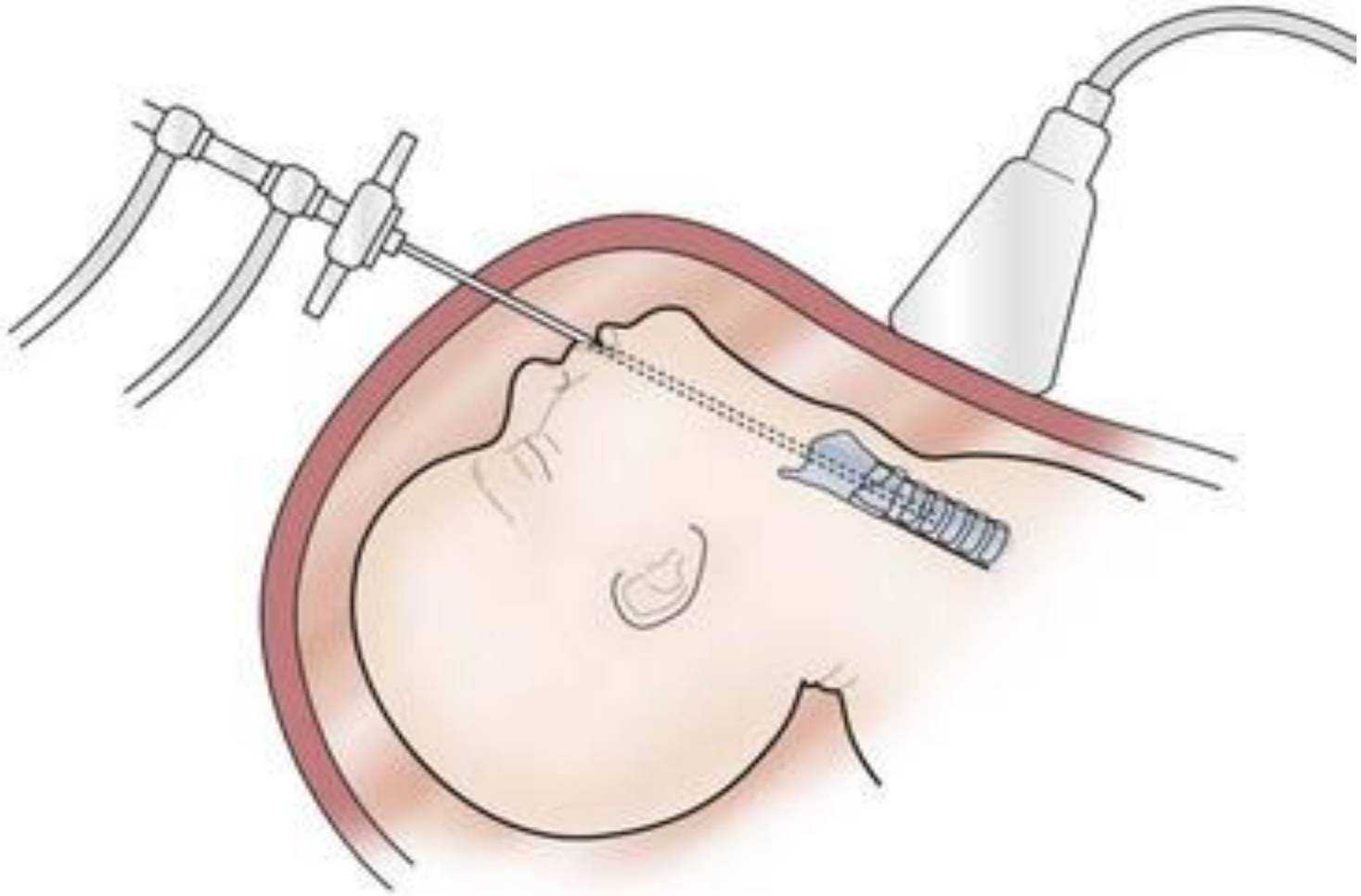
Post MMC Repair

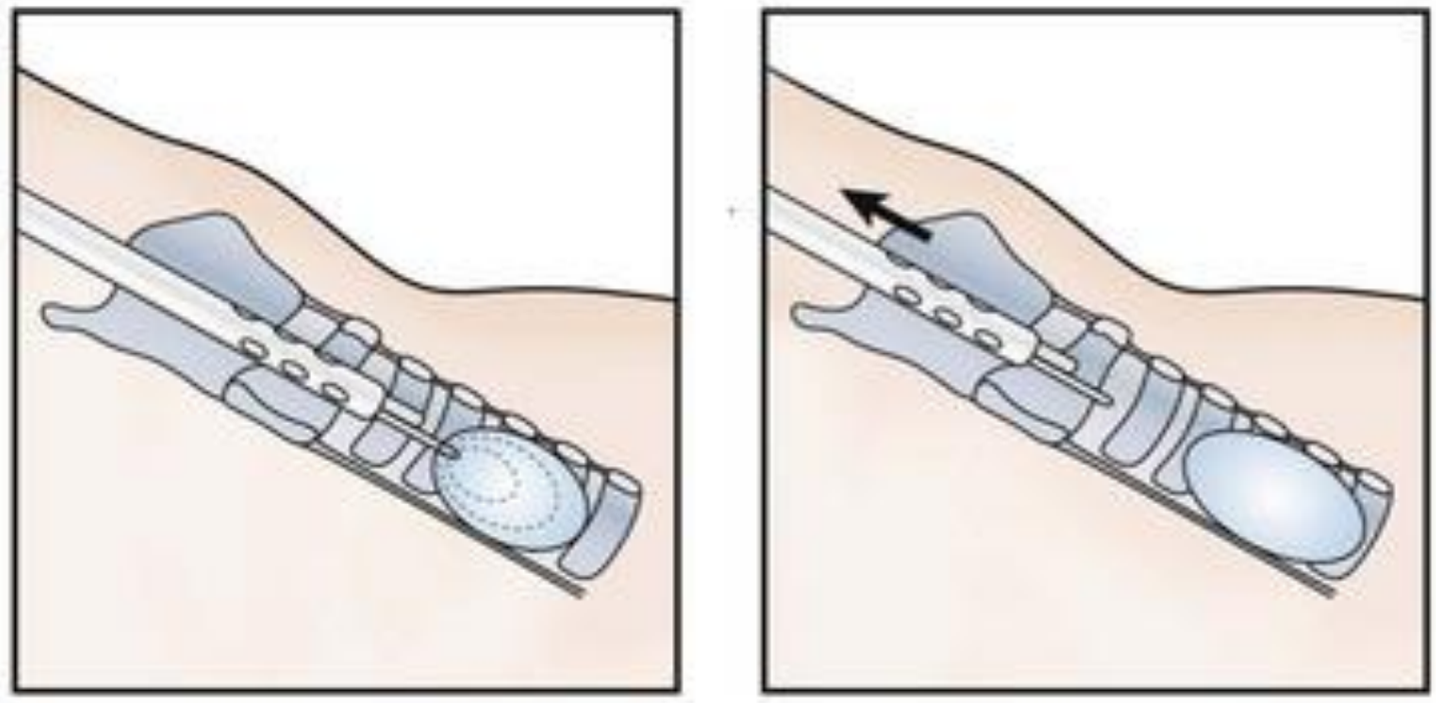
- Patient and driver/caretaker must stay in the Center's city for at least two weeks
- Twice weekly evaluations
- After two weeks, return home
- At home, weekly evaluations
- Hospitalization with PTL or PPROM
- Delivery by cesarean section at 37 weeks at center with pediatric neurosurgery services
  - Classical Hysterotomy on Uterus

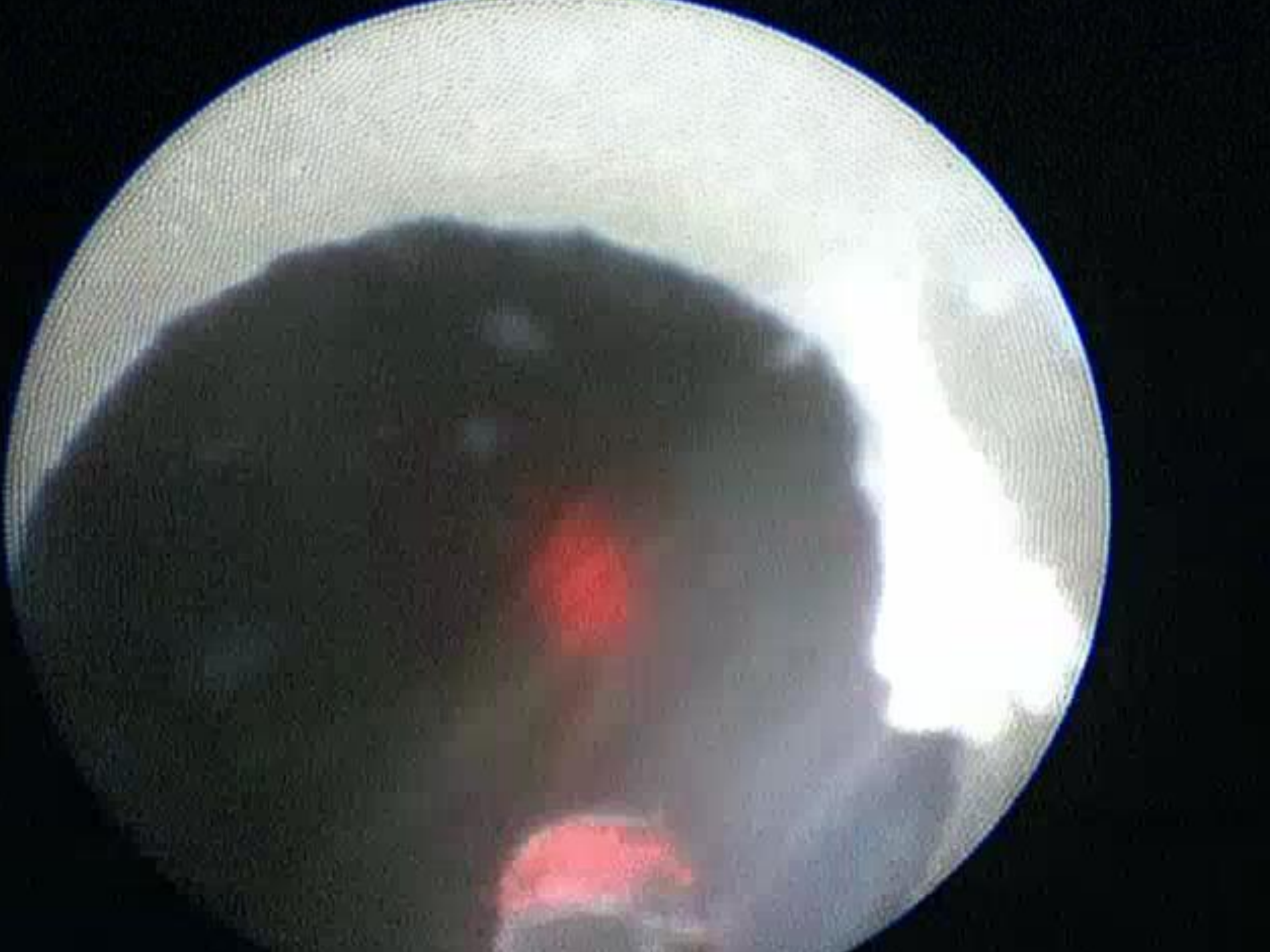
Fetal Cystoscopy For Bladder Outlet Obstruction

ST. LOUIS FETAL CARE INSTITUTE

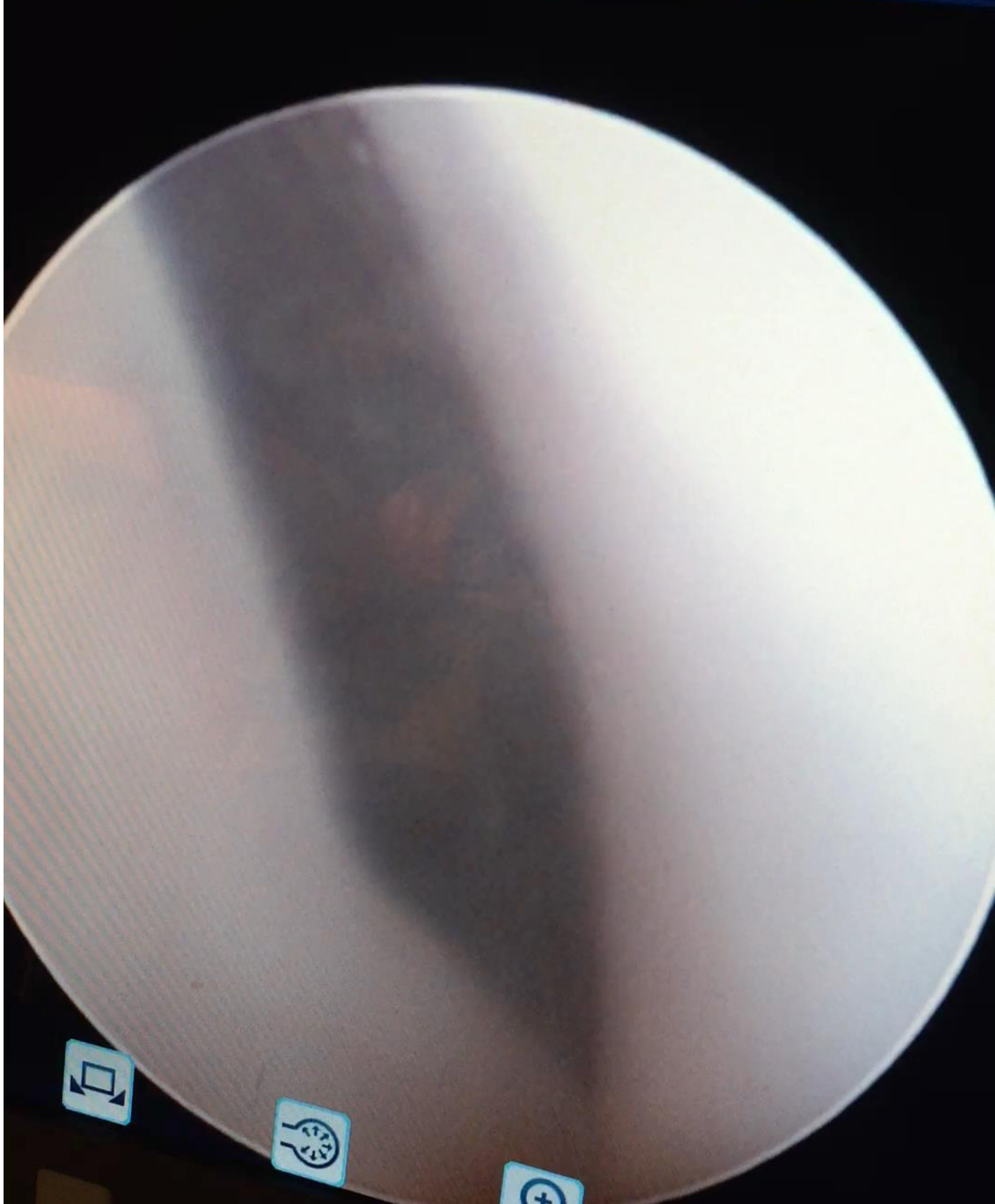

Compressed left lung
Small intestine, in left chest, pushing heart and lungs to the right
Liver partially up into chest
Diaphragmatic hernia



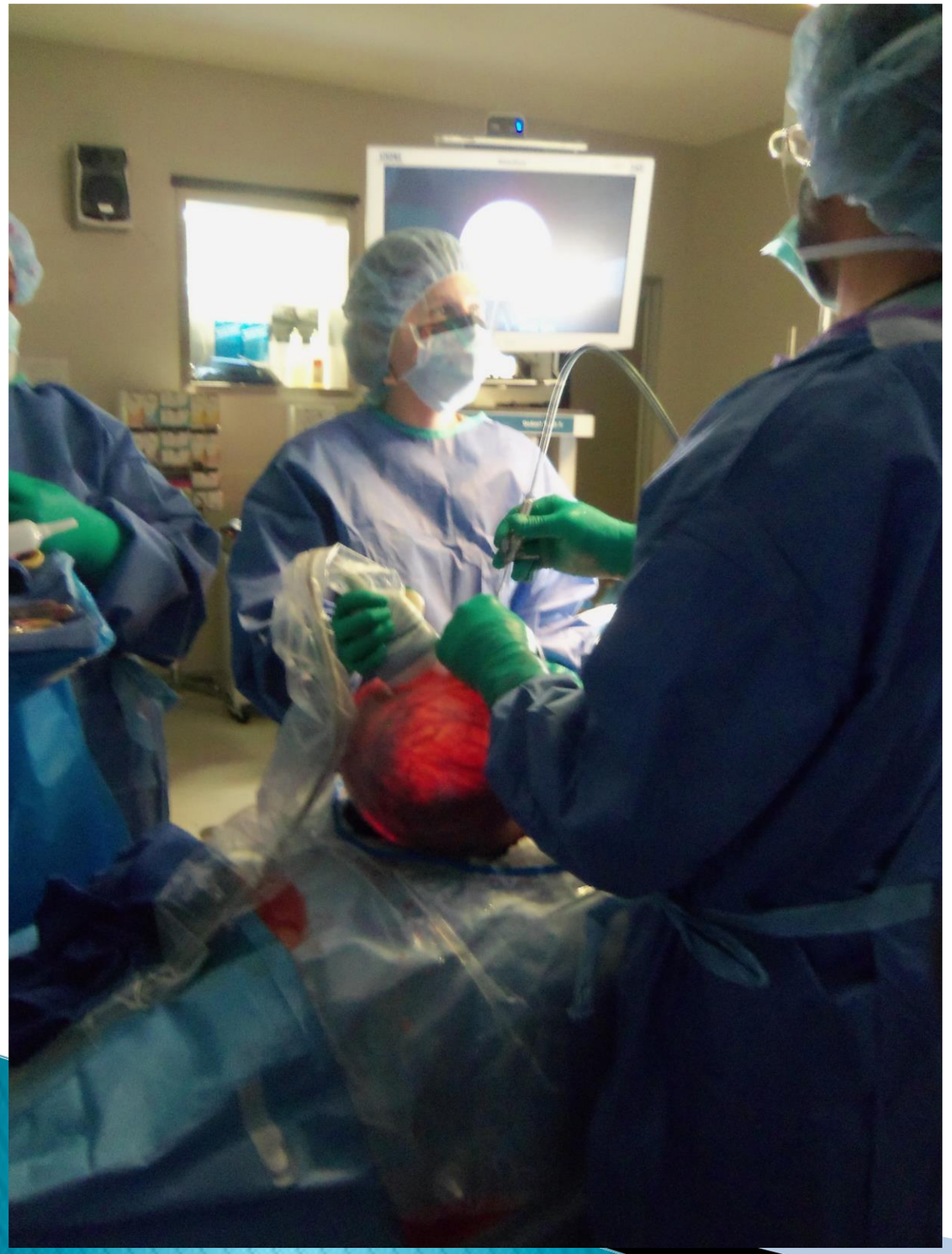


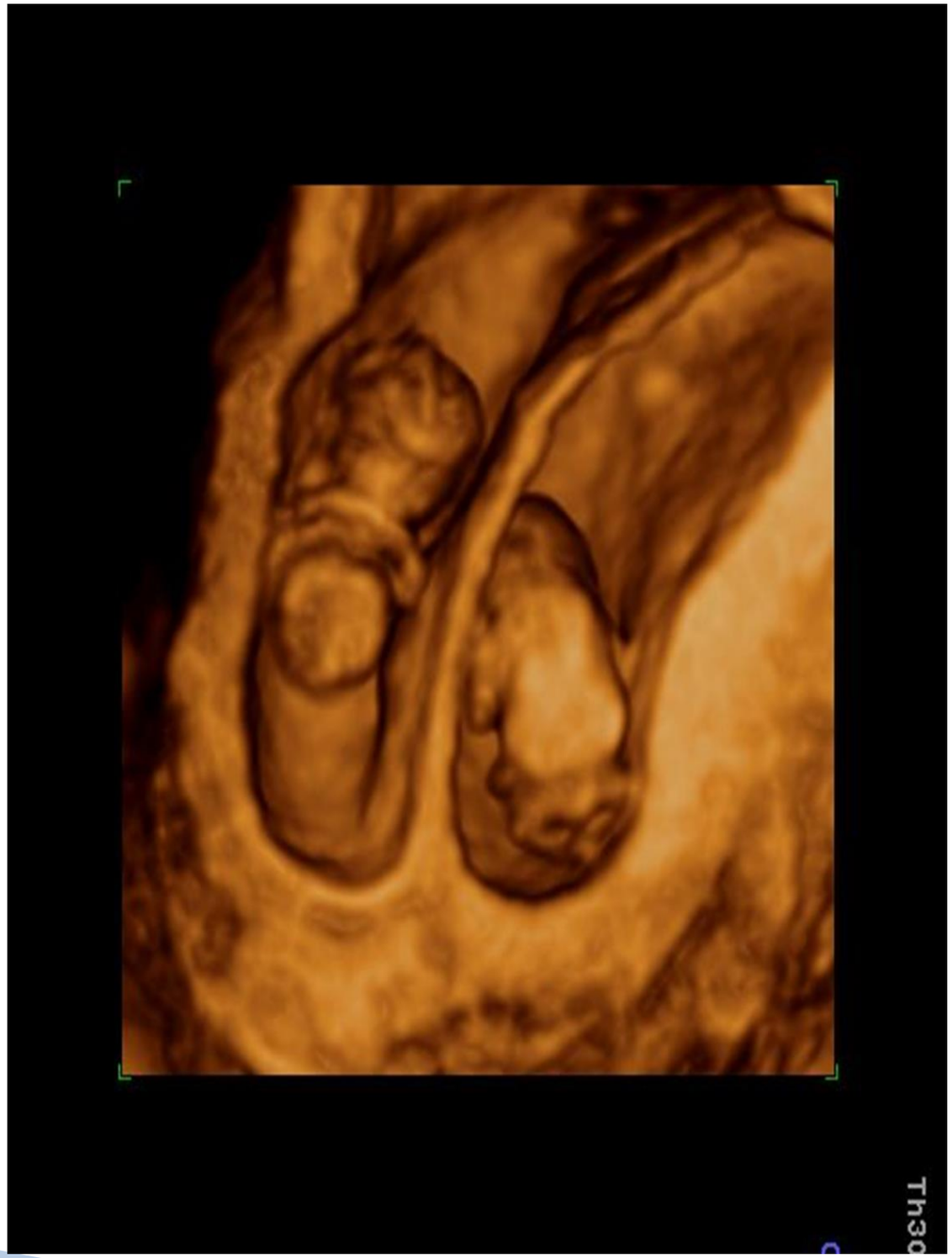


RESEARCH



Fetus: How Did I Get Here?





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1. MarchofDimes.org – Premature Birth Report Card
2. *De Wikkellkindren Lancet* 2000;356:847-848
3. Quintero, R et al. Staging of twin-twin transfusion syndrome *J Perinatol* 1999;19:550-5
4. NFTNet www.naftnet.org
5. De Lia, et al. *Obstet Gynecol* 1990;75:1046-1053
6. ACOG Committee Opinion 560, April 2013/reaffirmed 2017 at www.acog.org
7. Oski's Pediatrics, 5th Edition.
8. MOMS Trial *NEJM* 2011;364:993-1004
9. TOTAL TRIAL at www.totaltrial.eu

???Questions???

Experience

- Fetoscopy: > 250
  - 215 Twin Twin Transfusion Syndrome
  - 22 Selective Intrauterine Growth Restriction
  - 7 Cases of Amniotic Band Sequence
  - 13 Cases of Bladder Outlet Obstruction
- Open fetal Repair of Myelomeningocele
  - 60 cases from 15 States
  - 1 Case in Heidelberg, Germany
  - 2 Cases in Buenos Aires, Argentina
  - 15 Cases in Kansas City, MO
  - 3 Orlando, FL
- Laser ablation of Bronchopulmonary Sequestration – 4 cases