



ERN ITHACA Webinar #8 "In-depth"

Fetal surgery for omen dysraphisms

Tuesday oct 19 - 2023

from 5pm to 6.30 pm French time

Chaired Pr Jean-Marie Jouannic

Co Chair – ITHACA -WG SBoD

**Department of Fetal Medicine, Trousseau Hospital, APHP.
Sorbonne University Medicine, Paris, France**



Co-funded by
the Health Programme
of the European Union



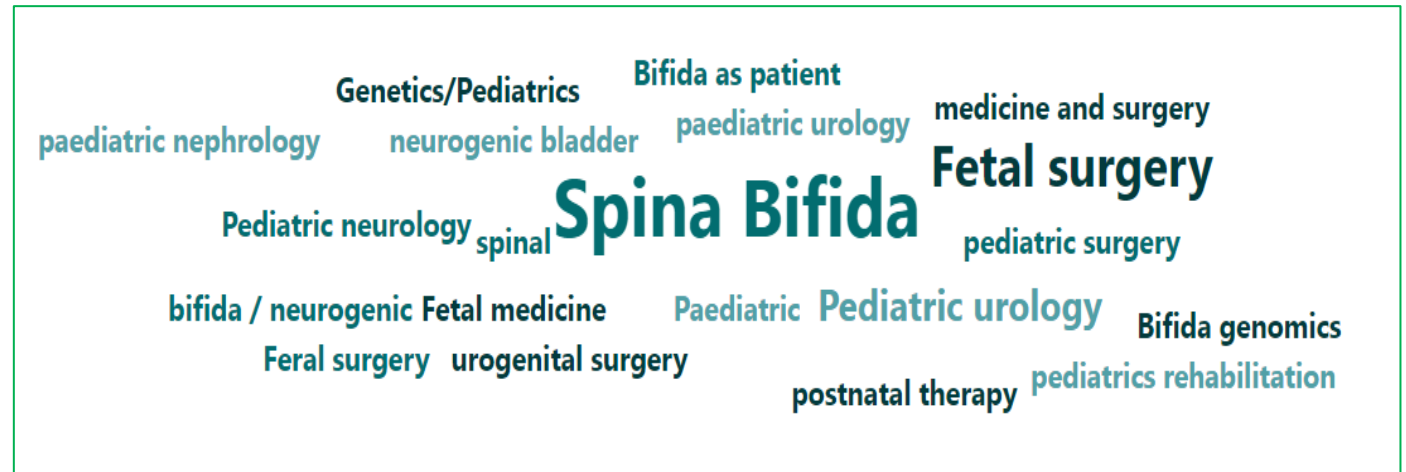
Welcome – Technical points

- *We are pleased to be numerous 58*
- *Webinar is being recorded*
- *Thank you for*
 - *Turn off your microphone and disconnect your camera*
 - *Raise your hand at the time of the questions and discussions*
 - *We will answer the questions sent in the registration form*
 - *A satisfaction survey will be sent to you*
- *Webinars # will be available on ITHACA's Website*
<https://ern-ithaca.eu/documentation/educational-resources/>

Anne Hugon Project Manager ERN ITHACA - anne.hugon@aphp.fr

Survey registration feed back

- 58 Registrations
- 31 ITHACA's members
- 27 others
- 1 Question : How do you see fetal surgery evolving over the next 10 years?



WP T&E - Welcome and Introduction

- Pr Jean-Marie Jouannic

Department of Foetal Medicine, ORIGYNE Medical and University Department, Trousseau Hospital, APHP. Sorbonne University Medicine, Paris, France

- *The perinatal management of myelomeningocele has been modified following the demonstration of the benefits of fetal surgery, which reduces postnatal handicaps. The SBoD group, which is a trans-ERN group involving colleagues from ERN ITHACA and eUROGEN, is dedicated to the lifelong management of patients with SB or other dysraphisms. In this Webinar, recent aspects of fetal surgery for myelomeningocele will be presented by European specialists from the WG SBoD group.*

Agenda

■ Welcome and Introduction

- Pr Jean-Marie Jouannic, Trousseau Hospital, APHP. Sorbonne University Medicine, Paris, France

■ Fetoscopic repair: results from the Val d'Hebron center

- Pr Elena Carreras, Val d'Hebron Hospital, Barcelona

■ Open surgery: technical improvements to limit obstetrical complications

- Pr Jan Deprest, Leuven, Belgium

■ Are intermediate forms of dysraphism eligible for fetal surgery?

- Pr Jean-Marie Jouannic, Dr Timothée de Saint Denis, Trousseau Hospital, Paris, France

■ A role for stem cell therapy to improve the motor prognosis?

- Dr Lucie Guilbaud, Trousseau Hospital, Paris, France

■ Discussion time 20'

■ Conclusion with speakers and moderator

ERN ITHACA Webinar #8 "In-depth" Fetal surgery for open dysraphisms

Fetoscopic repair: results from the Vall d'Hebron center

Elena Carreras,

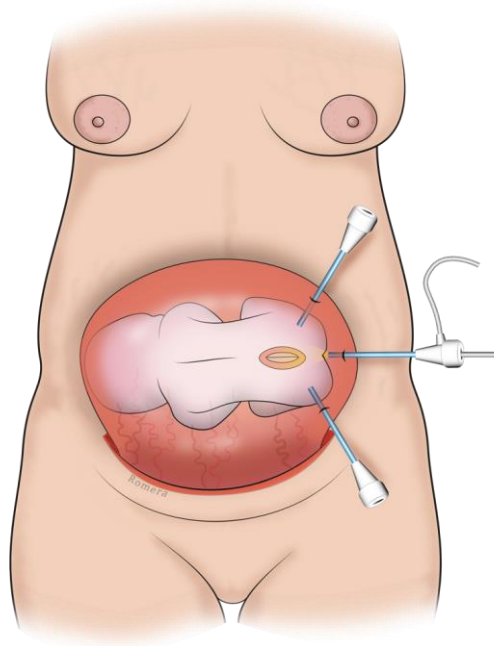
Nerea Maiz, Silvia Arévalo, Manuel López, Carles Giné

Hospital Universitari Vall d'Hebron de Barcelona



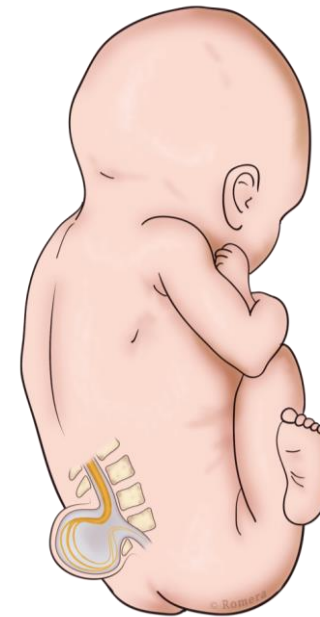
Fetoscopy for Neural Tube Defects

Approach



✓ Obstetrical Outcomes

Surgical technique



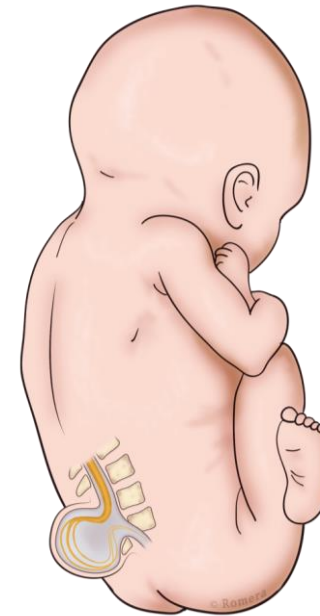
✓ NTD and baby outcomes

Fetoscopy for Neural Tube Defects

Approach

- ✓ Completely Percutaneous
- ✓ Hybrid – exteriorized uterus
 - ✓ Two ports
 - ✓ Three ports
- ✓ Percutaneous with mini-incisions to place the ports

Surgical technique



A study to assess global availability of fetal surgery for myelomeningocele

Adalina Sacco¹, Lynn Simpson², Jan Deprest^{1,3}, Anna L. David^{1,3,4}

Prenat Diagn. 2018 December 01; 38(13): 1020–1027. doi:10.1002/pd.5383.

2018

APPROACH

 Percutaneous


 Hybrid – Exteriorized Uterus

NEUROSURGICAL TECHNIQUE


 Single Patch

 3 port → 1 Layer

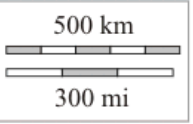
 3 port → 2 layers (dural patch)

 Thomas Kohl - Bonn

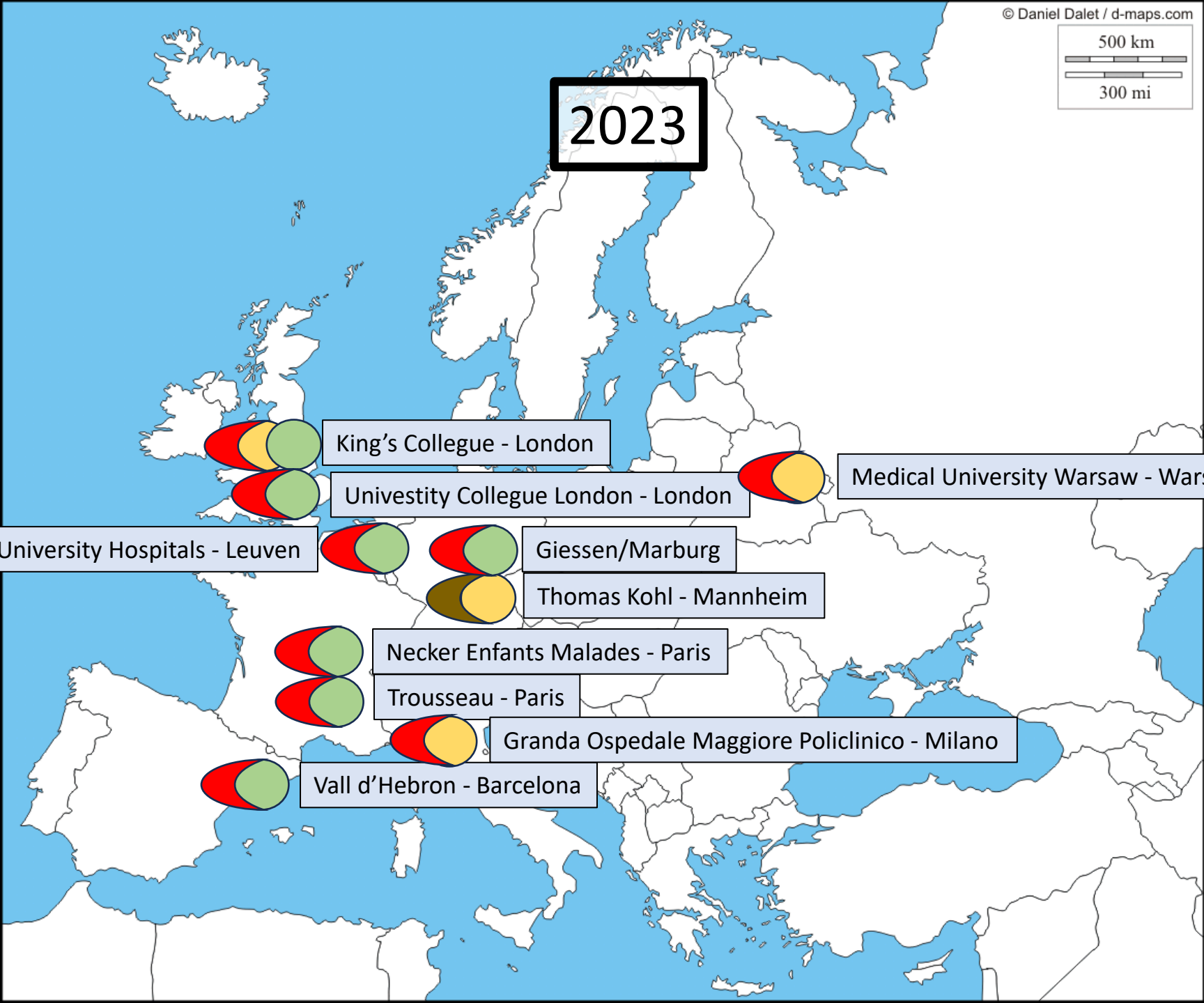
 Necker Enfants Malades - Paris

 Vall d'Hebron - Barcelona





2023



APPROACH

 Percutaneous

 Hybrid – Exteriorized Uterus

NEUROSURGICAL TECHNIQUE

 Single Patch

 3 port → 1 Layer

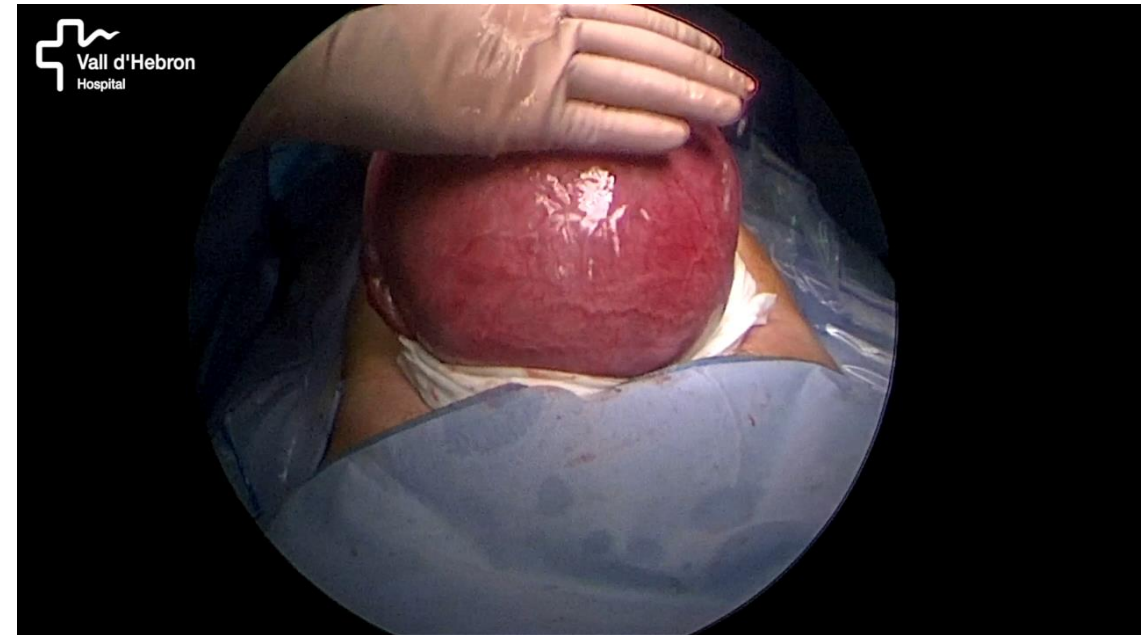
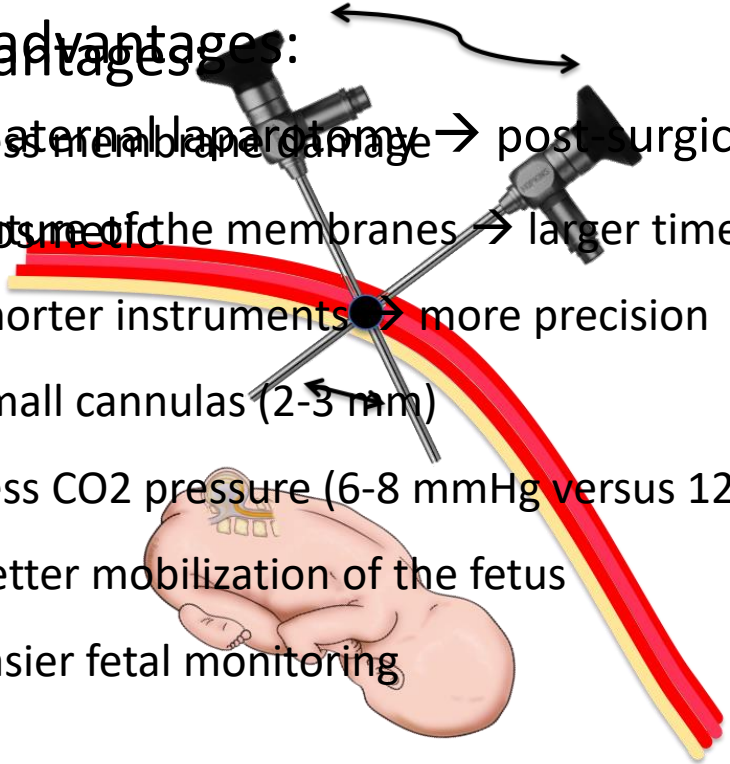
 3 port → 2 layers (dural patch)

Approach

Exteriorized uterus

Disadvantages:

- ✓ Less maternal laparotomy → post-surgical pain control
- ✓ Less membrane damage → post-surgical pain control
- ✓ Sutured membranes → larger time to delivery
- ✓ Shorter instruments → more precision
- ✓ Small cannulas (2-3 mm)
- ✓ Less CO2 pressure (6-8 mmHg versus 12-15 or more)
- ✓ Better mobilization of the fetus
- ✓ Easier fetal monitoring



Ultrasound Obstet Gynecol 2019; 53: 855–863
 Published online in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/uog.20308



Proceedings of the First Annual Meeting of the International Fetoscopic Myelomeningocele Repair Consortium

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 N. MAIZ⁵, J. L. PEIRO⁶, F. Y. LIM⁶, J. MILLER⁷, A. BASCHAT⁷, G. SEPULVEDA⁸,
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 M. YAMAMOTO¹³, H. FIGUEROA¹³, L. SIMPSON¹⁴ and K. H. NICOLAIDES¹⁵

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OBSTETRICS

Experience of 300 cases of prenatal fetoscopic open spina bifida repair: report of the International Fetoscopic Neural Tube Defect Repair Consortium



Magdalena Sanz Cortes, MD; Ramen H. Chmait, MD; Denise A. Lapa, MD; Michael A. Belfort, MD; Elena Carreras, MD; Jena L. Miller, MD; Robert Brawura Biskupski Samaha, MD; Gerardo Sepulveda Gonzalez, MD; Yuval Gielchinsky, MD; Masami Yamamoto, MD; Nicola Persico, MD; Marta Santorum, MD; Lucas Otaño, MD; Ermos Nicolaou, MD; Yoav Yinon, MD; Fernanda Faig-Leite, MD; Reynaldo Brandt, MD; William Whitehead, MD; Nerea Maiz, MD; Ahmet Baschat, MD; Przemyslaw Kosinski, MD; Adriana Nieto-Sanjuanero, MD; Jason Chu, MD; Amir Kershenovich, MD; Kypros H. Nicolaides, MD



- Experience of 300 cases of prenatal fetoscopic open spina bifida repair:
 - Report of the International Fetoscopic Neural Tube Defect Repair Consortium
 - Report of Vall d'Hebron University Hospital

Variable	Consortium N=300	Post-MOMS N=100	P value	Vall d'Hebron N=46
Gestational age at surgery	25.9 (22.7-31.6)	23.3 (20.2- 25.6)	-	24.7 (23.9-25.4)
Placental abruption	25/280 (8.9%)	2/96 (2.1 %)	0.022	0
Chorioamniotic membrane separation	72/190 (37.9%)	22/96 (22.9%)	0.012	11/40 (27.5%)
Oligohydramnios	53/267 (19.9%)	6/96 (6.3%)	0.001	1/40 (2.5%)
Preterm prelabor rupture of membranes	153/280 (54.6%)	31/96 (32.3%)	0.0002	20/40 (50%)

Vall d'Hebron technique

Approach:

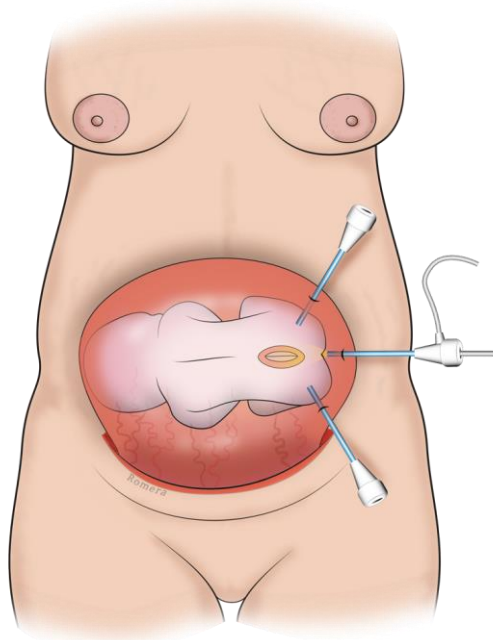
- Hybrid: exteriorized uterus

Surgical Technique: always 3-port

- **Plan A: Two Layer closure**
- **Plan B: Myofascial patch and skin closure**
- **Plan C: Myofascial patch and Skin patch**

Fetoscopy for Neural Tube Defects

Approach



Surgical technique

- ✓ Cover with a patch (stitched)
- ✓ Patch & Glue
- ✓ Single layer closure
- ✓ Two-layer closure (myofascial and skin)
- ✓ Three-layer closure (duramater, myofascial, skin)
- ✓ Hybrid techniques (myofascial patch and skin, myofascial and patch in skin...)

Surgical Technique

Dissection

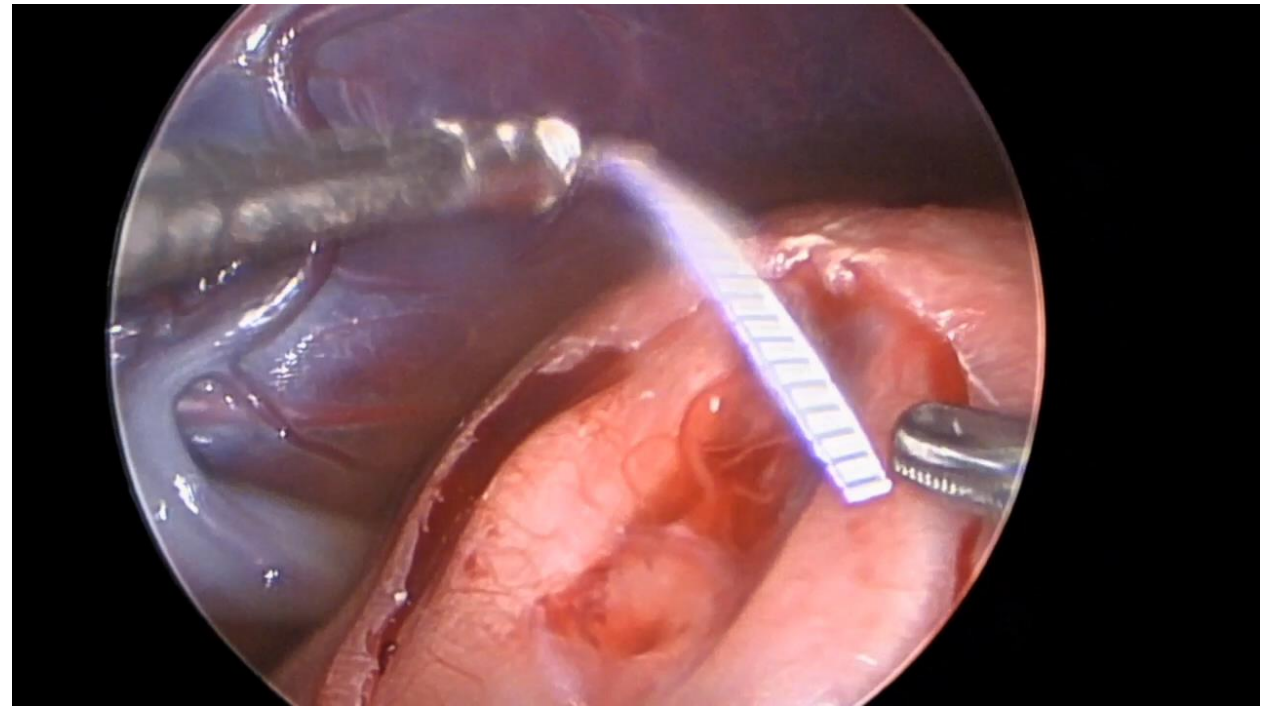
- ✓ NOT TOUCH neural tissue
- ✓ Identify neural roots
- ✓ Resect dysplastic tissue as much as possible
- ✓ Placode must remain free in the vertebral canal



Surgical Technique

Myofascial

- ✓ Patch over the placode
- ✓ Direct closure of myofascial layer
- ✓ Defects at least up to 16 mm wide
- ✓ Avoid muscular flaps

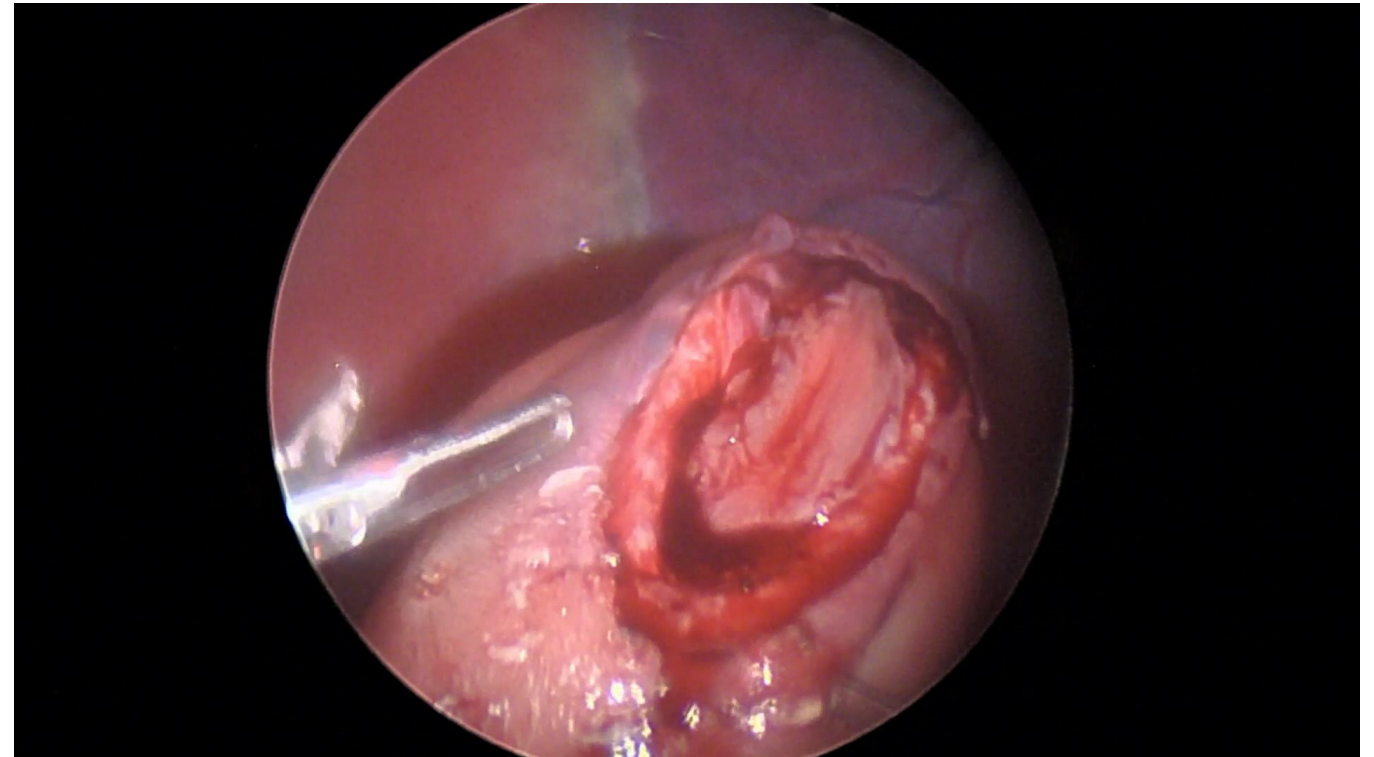


Surgical Technique

Myofascial patch

✓ In cases of:

- Wide defect

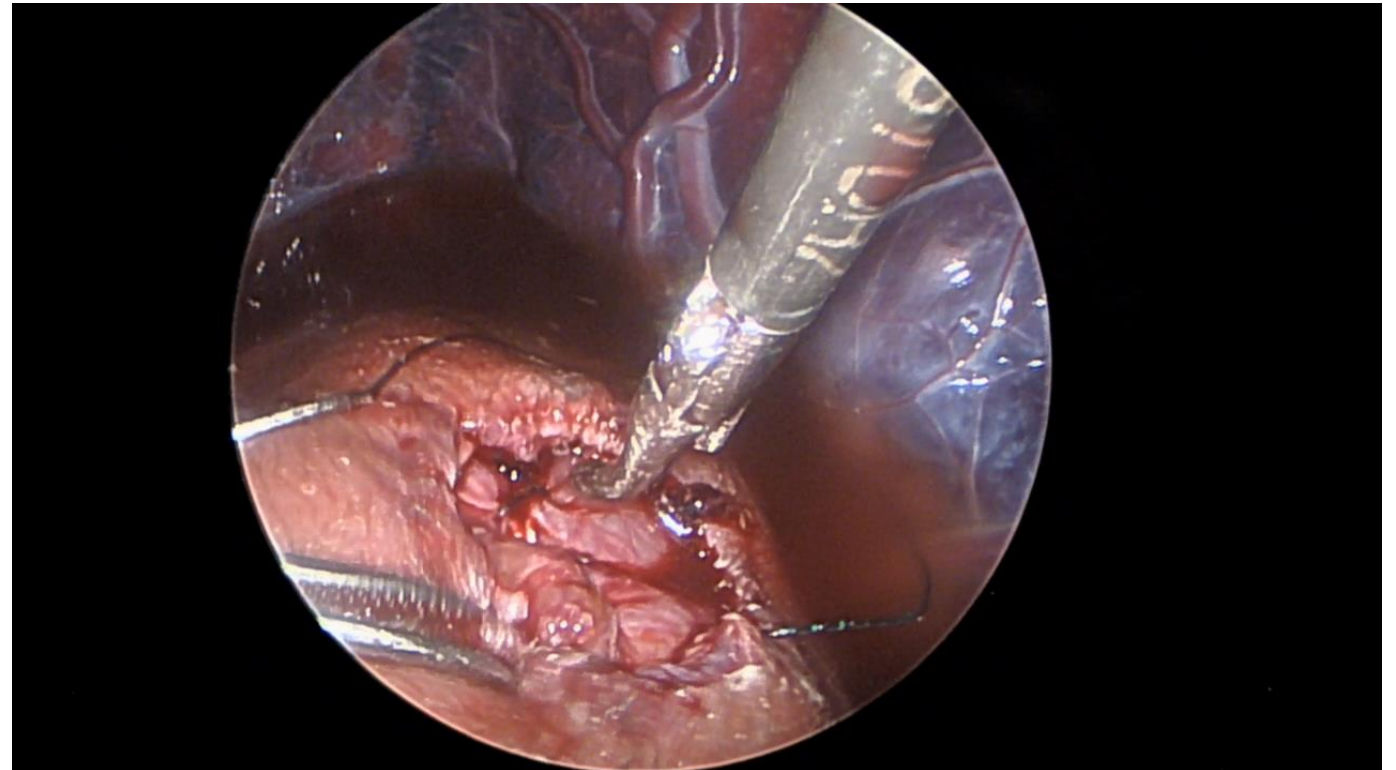


Surgical Technique

Myofascial patch

✓ In cases of:

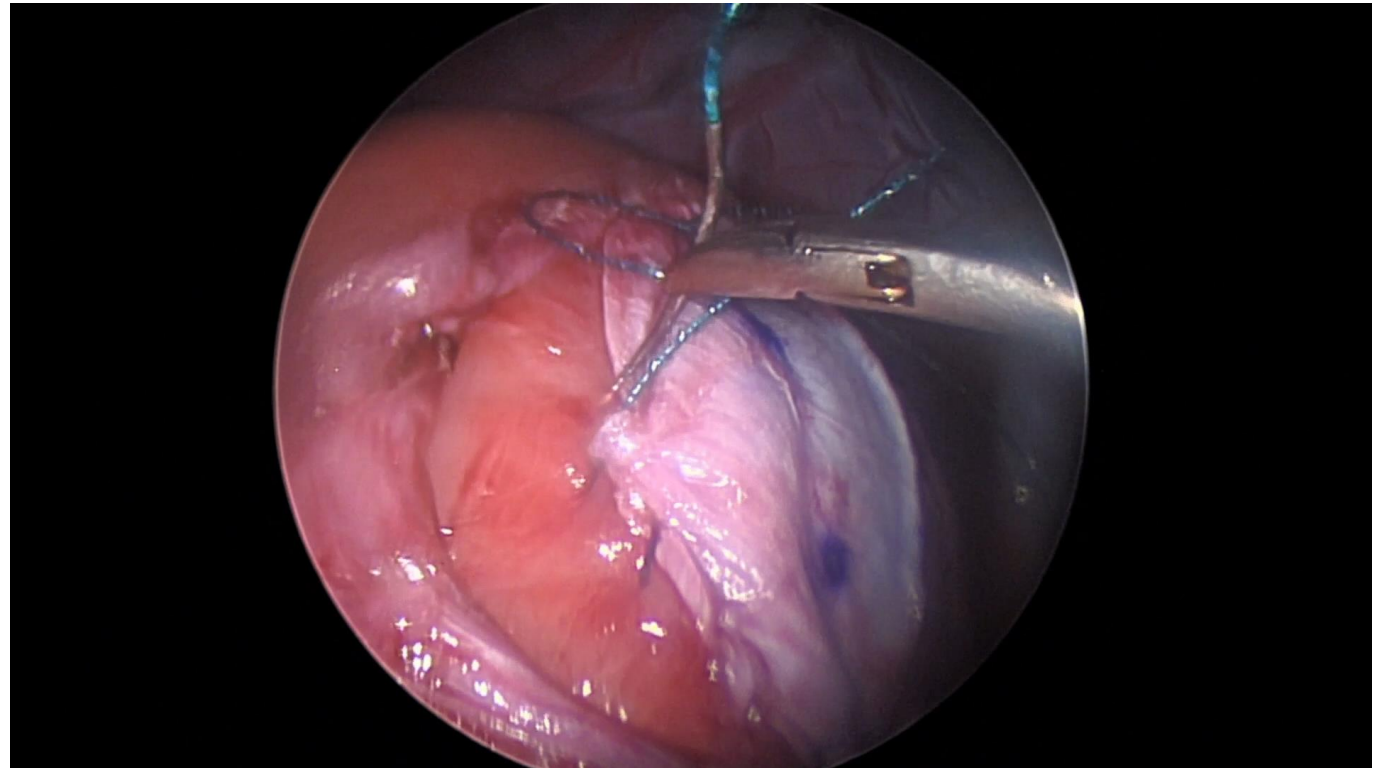
- Wide defect
- Narrow defect



Surgical Technique

Myofascial patch

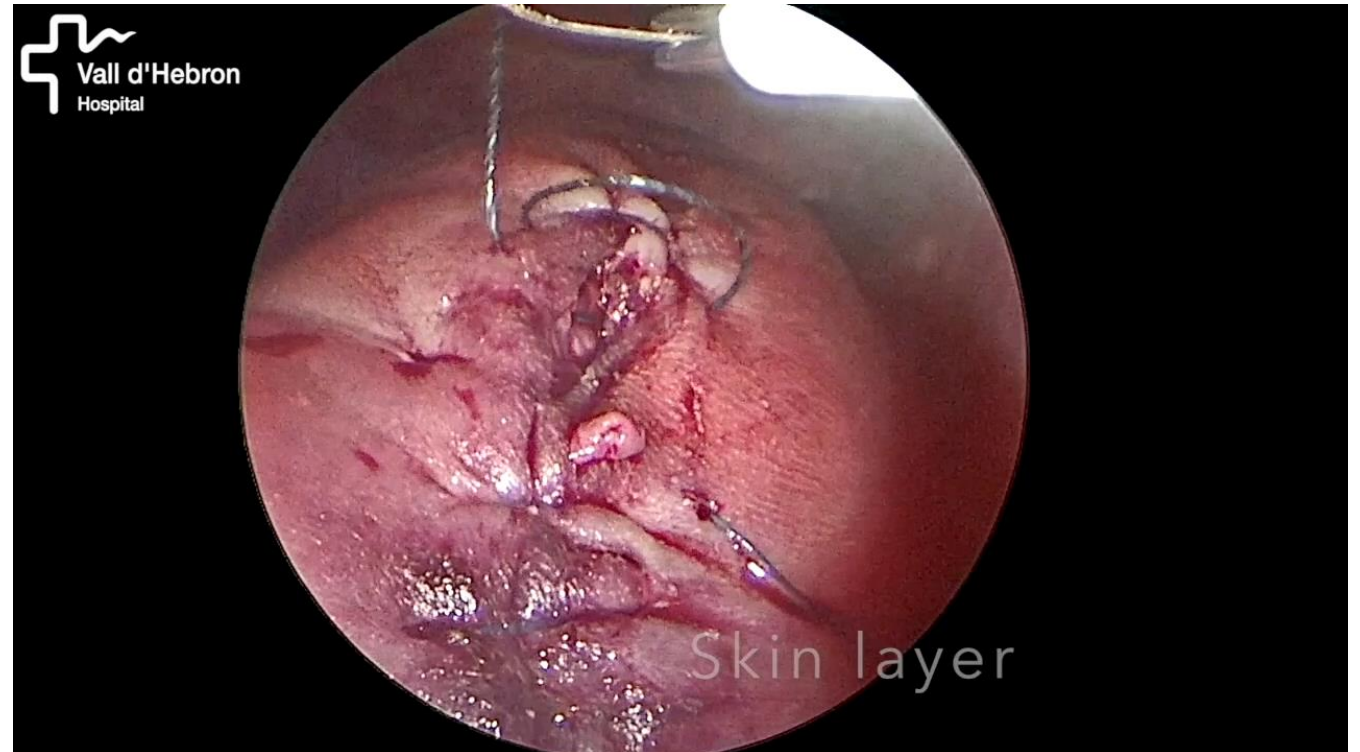
- ✓ In cases of:
 - Wide defect
 - Narrow defect
- ✓ Bovine pericardium



Surgical Technique

Skin

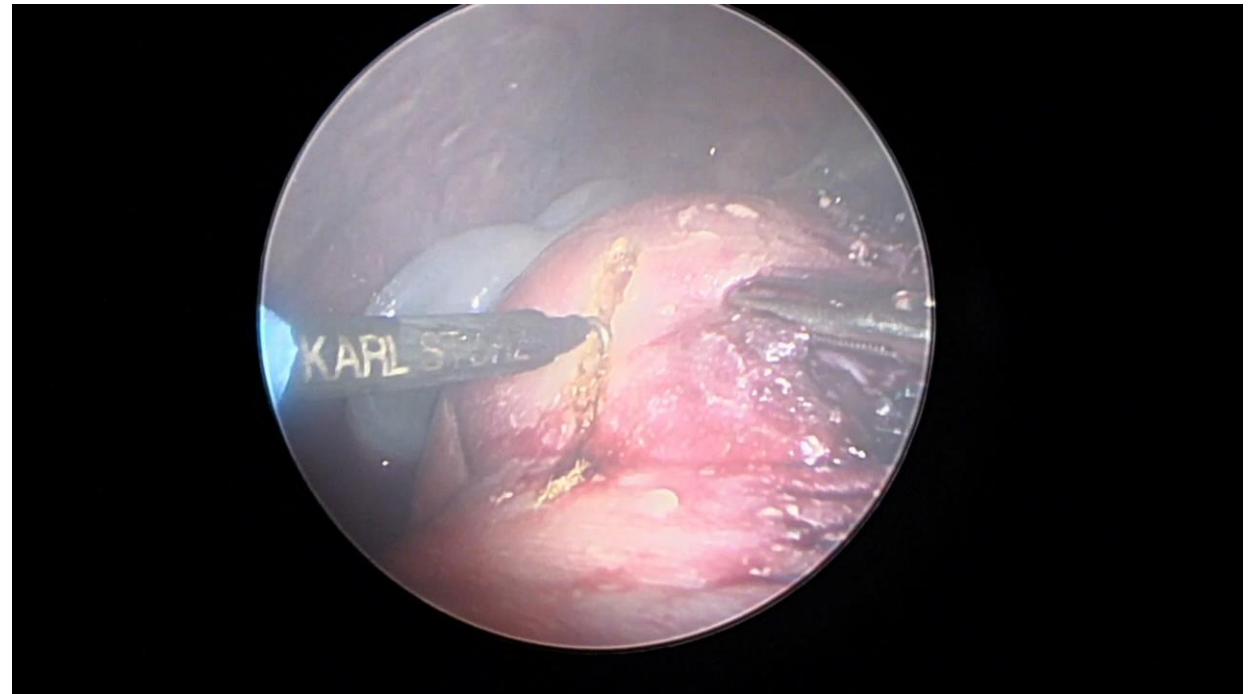
- ✓ Direct closure
- ✓ Release flank incisions
- ✓ Skin flaps
- ✓ Acellular dermal patch



Surgical Technique

Skin

- ✓ Direct closure
- ✓ Release flank incisions
- ✓ Skin flaps
- ✓ Acellular dermal patch



Case series

75 cases

- ✓ 2011-2013 → Open Patch & Glue → 7 cases
- ✓ 2013 – 2015 → Fetoscopic Patch & Glue → 12 cases
- ✓ 2015 – 2017 → Fetoscopic Skin Closure → 10 cases
- ✓ 2017 – today → Fetoscopic Two Layer closure → 46 cases

Ultrasound Obstet Gynecol 2018; 52: 452–457
Published online 10 September 2018 in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/uog.19104

Fetoscopic two-layer closure of open neural tube defects

C. GINÉ^{1,2}, S. ARÉVALO^{2,3}, N. MAÍZ^{2,3}, C. RODÓ^{2,3}, S. MANRIQUE^{2,4}, A. POCA^{2,5,6},
J. A. MOLINO¹, E. CARRERAS³ and M. LÓPEZ^{1,2}

¹Pediatric Surgery Department, Hospital Universitari Vall d'Hebron, Barcelona, Spain; ²Universitat Autònoma de Barcelona, Barcelona, Spain; ³Maternal-Fetal Medicine Department, Hospital Universitari Vall d'Hebron, Barcelona, Spain; ⁴Anesthesiology and Reanimation Department, Hospital Universitari Vall d'Hebron, Barcelona, Spain; ⁵Pediatric Neurosurgery Department, Hospital Universitari Vall d'Hebron, Barcelona, Spain; ⁶Neurotraumatology and Neurosurgery Research Unit (UNINN), Barcelona, Spain



Case series

2017 – today → Fetoscopic Two Layer closure → 46 cases

- ✓ Three-layer reconstruction (dural suture + myofascial suture + skin suture) 1/46 → 2,2%
- ✓ Two-layer reconstruction (dural patch + myofascial suture + skin suture) 38/46 → **82,6%**
- ✓ Dural patch + myofascial patch + skin suture 5/46 → 10,9%
 - Muscular defect too wide → 1 patient (22 mm)
 - Vertebral canal too narrow → 4 patients
- ✓ Dural patch + myofascial patch + dermal patch 2/46 → 4,3%
 - Very severe defects

- Experience of 300 cases of prenatal fetoscopic open spina bifida repair:
- Report of the International Fetoscopic Neural Tube Defect Repair Consortium
- Report of Vall d'Hebron University Hospital

Variable	Consortium N=300	Post-MOMS N=100	P value	Vall d'Hebron N=46
Gestational age at delivery (weeks)	34.3 (SD 3.6)	34.3 (22.2-37.49)	-	35.8 (33.6-37.0) 34.9 (SD 3.33)
Cesarean section delivery	192/280 (68.6%)	96/96 (100%)	<0.0001	21/41 (51.2%)

Hydrocephalus treated by shunt or ETV	88/201 (43.8%)	MOMS 31/76 (40.8%)	0,591	13/29 (44.8%)
Motor function compared with upper anatomic level of the lesion				
≥ 2 levels better	98/257 (38.1%)	24/80 (30,0%)	0,231	18/31 (41.9%)
≥ 2 levels worse	12/257 (4.7%)	1/80 (1,3%)	0,315	0

Comments

- ✓ Hybrid technique offers critical surgical advantages compared to percutaneous
- ✓ Regardless the approach that may impact the obstetrical outcome, surgical technique must be the key factor in order to compare neurosurgical outcomes
- ✓ Every defect is different and may require a particular surgical solution
- ✓ The surgical team must be prepared to modify its initial technique accordingly

Thank you

TOPIC 2

- Open surgery: technical improvements to limit obstetrical complications
 - Pr Jan Deprest, Leuven, Belgium

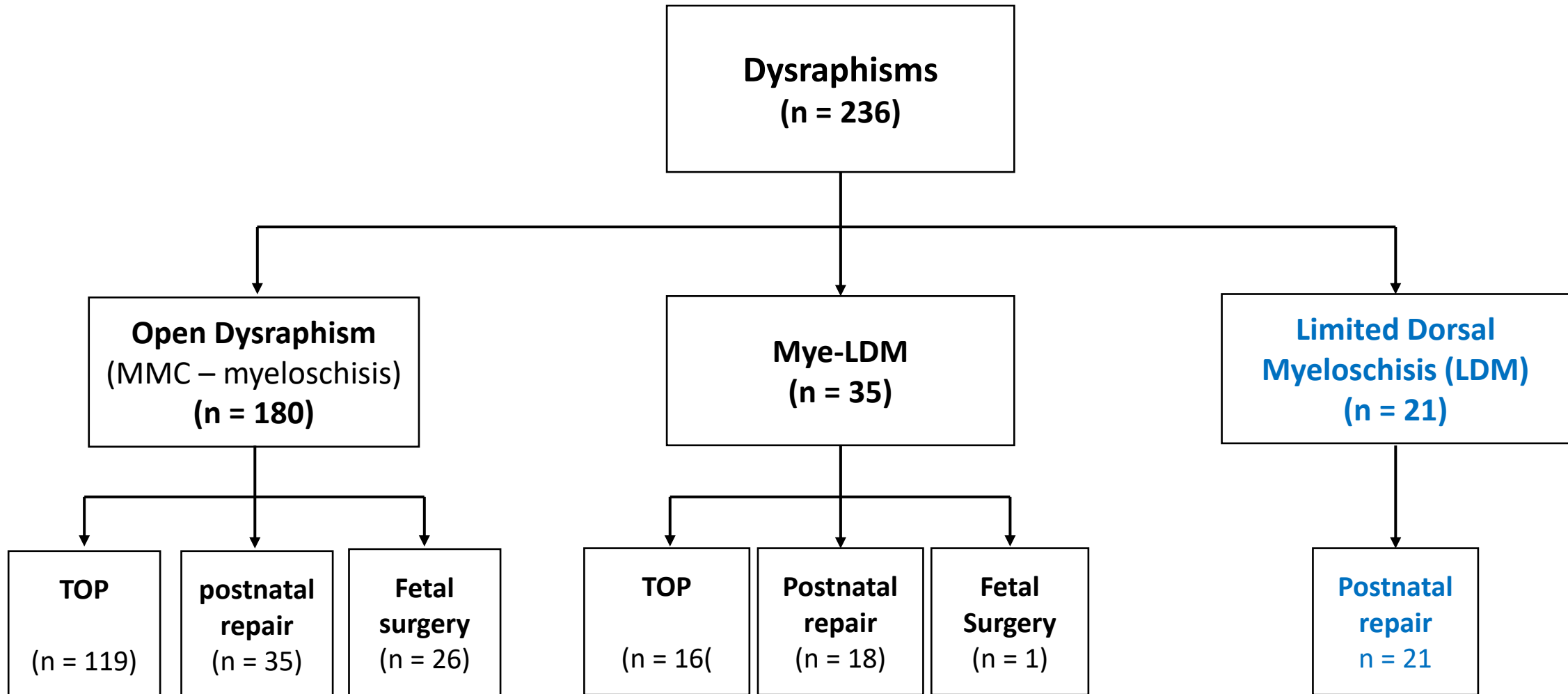
Are intermediate forms of dysraphisms eligible for fetal surgery?

Jean-Marie Jouannic

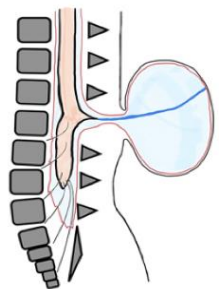
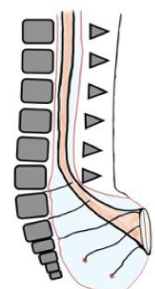
Timothée de Saint Denis

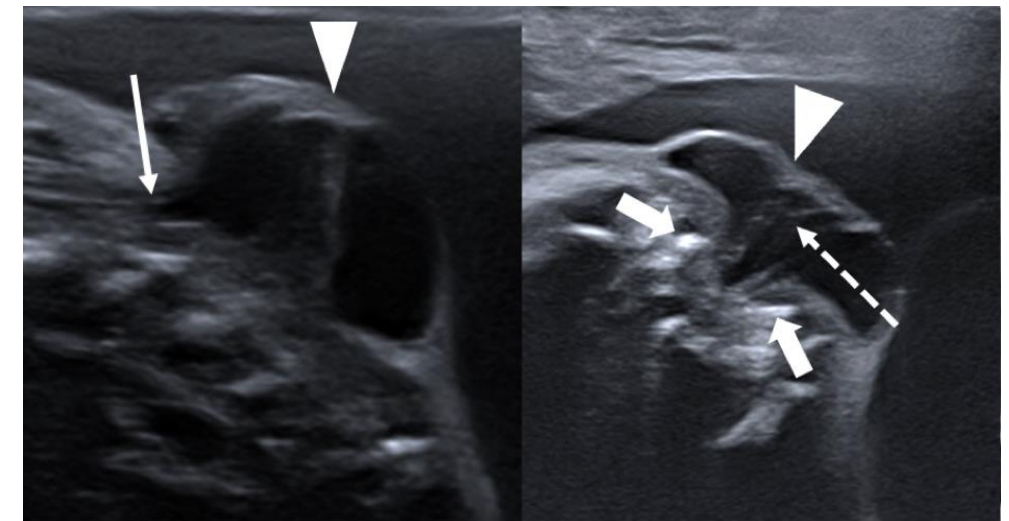
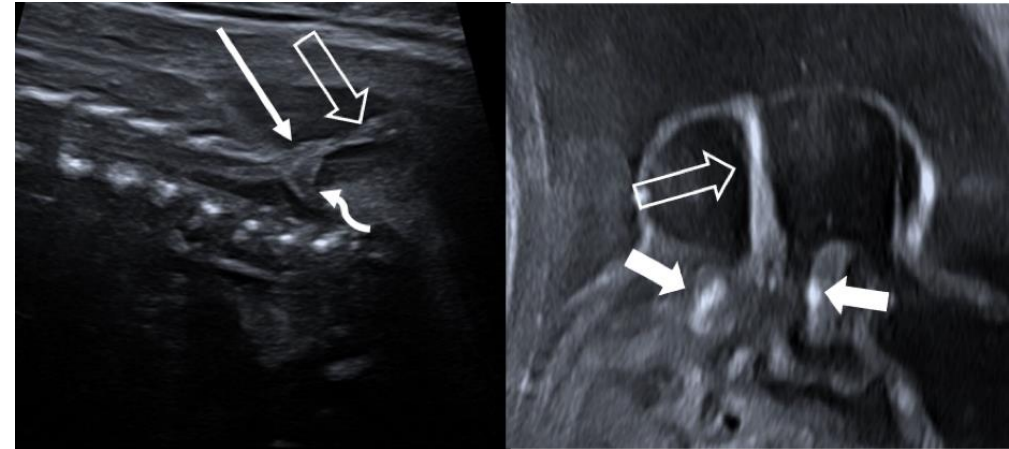


Patients referred to Trousseau Fetal center (Jan 2014 – May 2023)



Limited Dorsal Myeloschisis

Characteristics	Limited dorsal myeloschisis	Myelomeningocele
Dysraphism	Closed	Open
Shape of the conus medullaris	Variable (frequently low lying)	Abnormal, Open
Type of lesion	Saccular *	Saccular
Peripheral lining	Epithelial	Arachnoid membrane
Content of the lesion	Fibroneural stalk + cerebrospinal fluid	Nerve roots + neural placode + cerebrospinal fluid
Cerebral findings	None	Constant (complete Chari II)
		



Vande Perre et al. FDT 2021

LDM outcome (N=9)

Pregnancy and delivery

- GA at diagnosis: 22+1 weeks (+/- 5d)
- Prenatal anatomical levels: L3-S3
- No cerebral signs
- AF: normal CGH and AChE negative
- Delivered at term
 - 4 C section (obstetrical indications)
- Normal birth weight (3140g, range: 2700-4180g)

Surgery

- M Zerah and T de Saint Denis
- Median age: 31 d (2-96 d)

* 1 anomaly at PN exome sequencing

LDM outcome at 36 months

Able to walk		9/9
Autonomous walking		8/9
Walking with orthotics		1/9
Wheelchair		0/9
Urinary catheterization		2/9 (S1 level))
Urinary tract infections		0/9
Anticholinergic treatment		1/9

	Laxative treatment	2/9
	Daily transanal enemas	1/9
	Use of diapers	5/9
	School without special assistance	9/9
	Neurodevelopmental retardation	0/9
	CSF shunt	0/9
	Fully Asymptomatic	5/9

LMD: benefit of a prenatal repair?

- No chiari
- Spinal lesions with the increase in the size of the sac?
- Exception: ruptured of the sac



ULTRASOUND
in Obstetrics & Gynecology

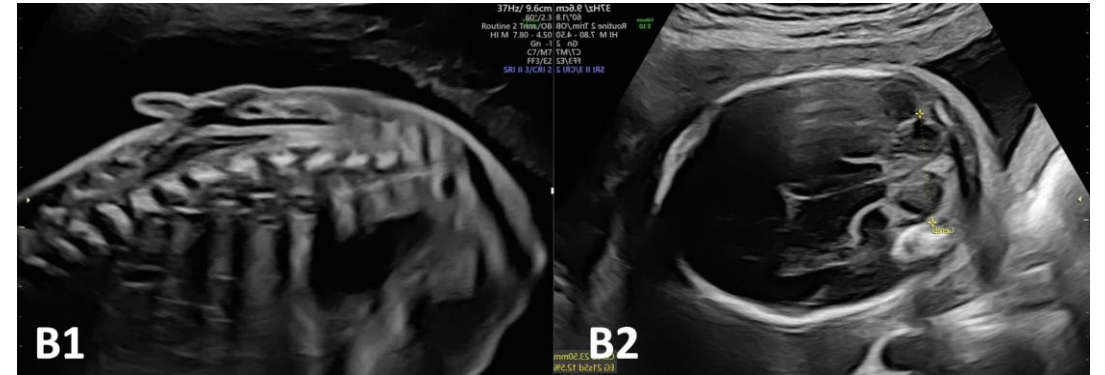
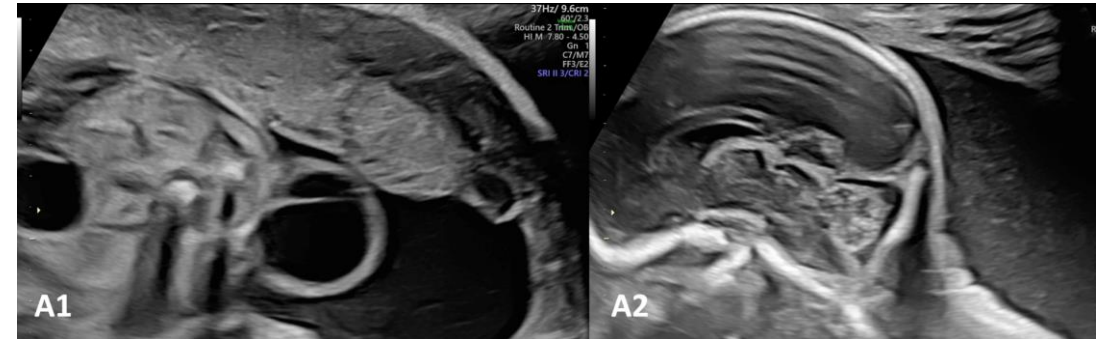


Letter to the Editor | Full Access

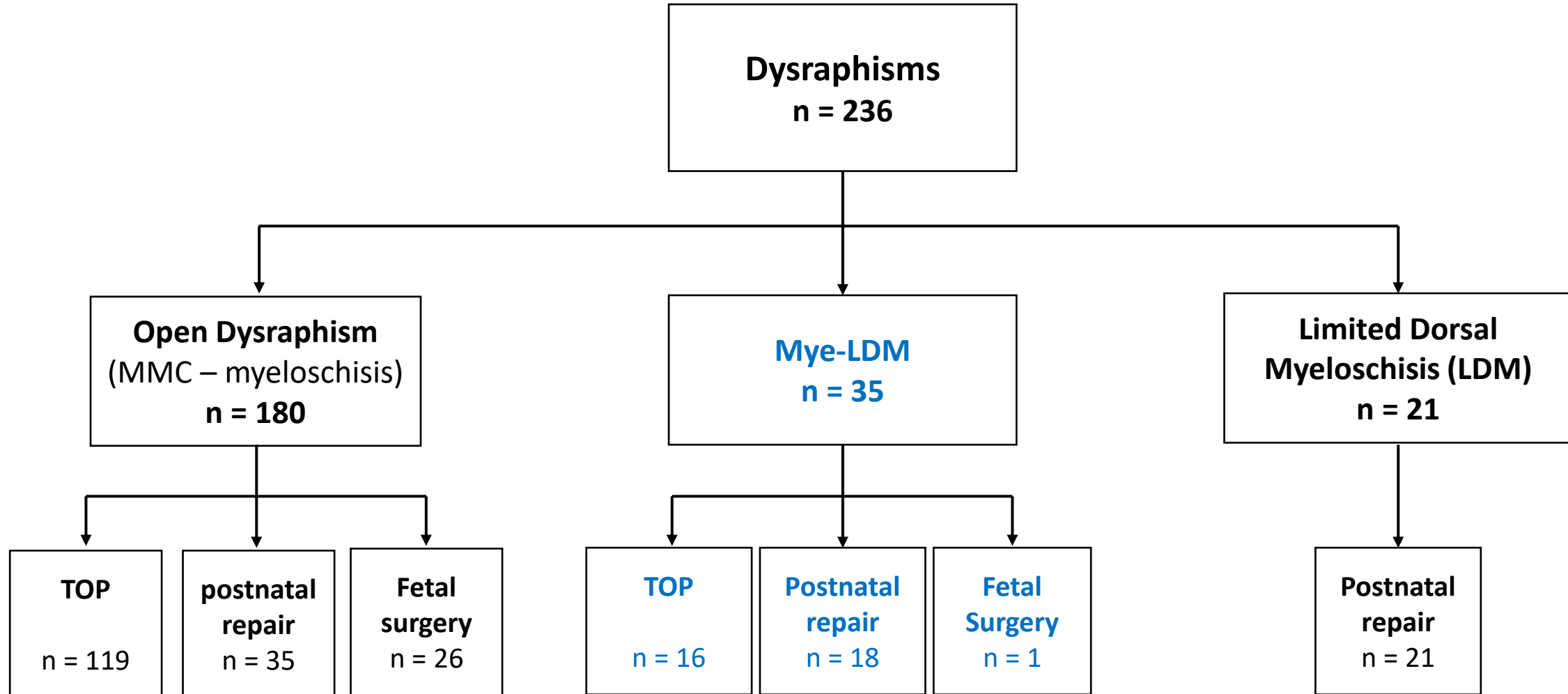
Ruptured saccular limited dorsal myelomeningocele: good indication for fetal repair

C. Gine, N. Malz, S. Arévalo, C. Rodó, M. López, E. Carreras

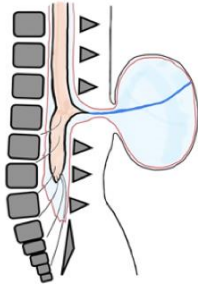
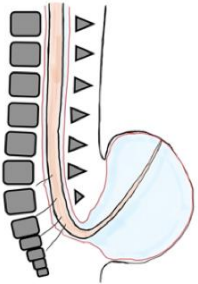
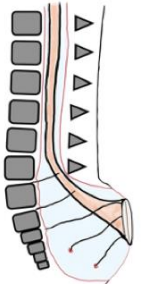
First published: 22 August 2023 | <https://doi.org/10.1002/uog.27457>

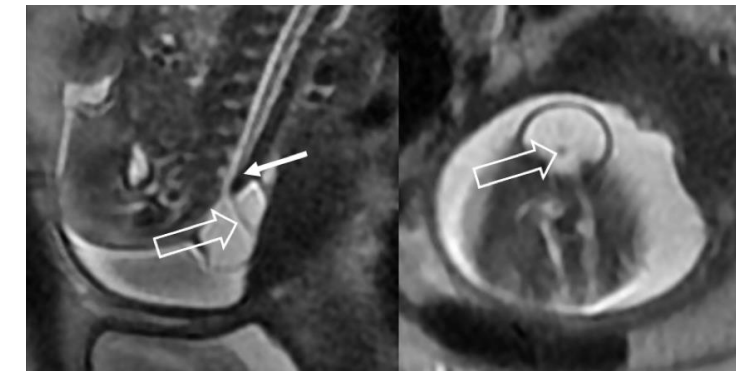
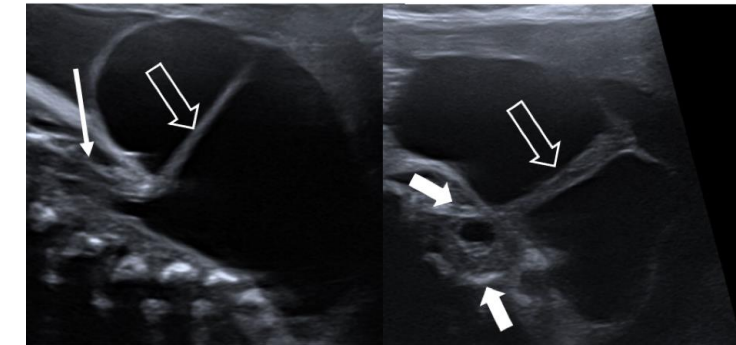


Patients referred to Trousseau Fetal center (Jan 2014 – May 2023)



Myelic Limited Dorsal Malformation: an intermediate form of open dysraphism

Characteristics	Limited dorsal myeloschisis	Myelic limited dorsal malformation	Myelomeningocele
Dysraphism	Closed	Intermediate	Open
Shape of the conus medullaris	Variable (frequently low lying)	Abnormal, attenuated	Abnormal, Open
Type of lesion	Saccular *	Saccular	Saccular
Peripheral lining	Epithelial	Epithelial ± arachnoid membrane	Arachnoid membrane
Content of the lesion	Fibroneural stalk + cerebrospinal fluid	Variable amount of nerve roots + cerebrospinal fluid	Nerve roots + neural placode + cerebrospinal fluid
Cerebral findings	None	Heterogeneous	Constant (complete Chari II)
			

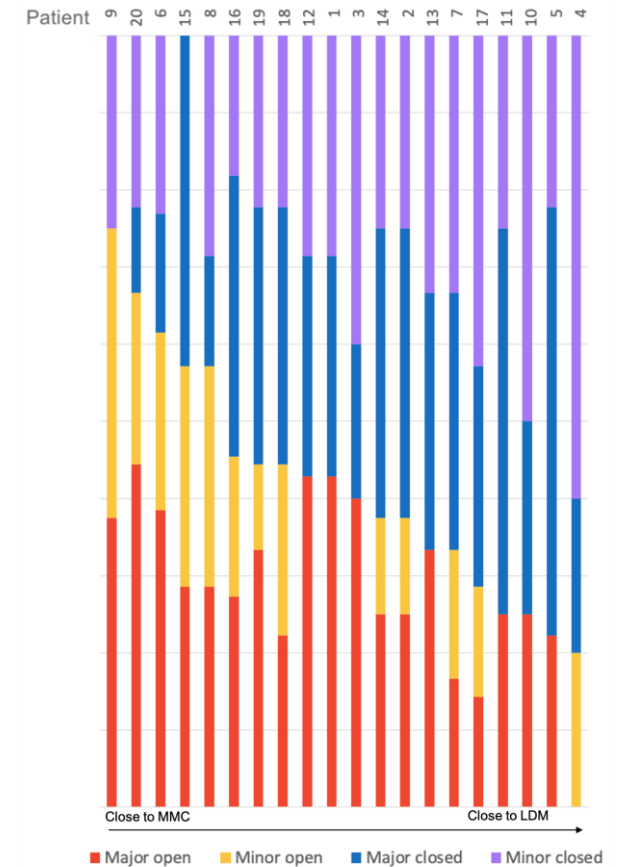


MyeLDM: prenatal imaging

The Myelic Limited Dorsal Malformation: Prenatal Ultrasonographic Characteristics of an Intermediate Form of Dysraphism

Saskia Vande Perre^a Lucie Guilbaud^b Timothée de Saint-Denis^c
 Paul Maurice^b Pauline Lallemand-Dudek^d Emeline Maisonneuve^b
 Ferdinand Dhombres^b Eléonore Blondiaux^a Hubert Ducou le Pointe^a
 Michel Zerah^c Jean-Marie Jouannic^b Catherine Garel^a

Neural tube malformation	Open	Closed
Major criteria	Chiari II malformation Flattening of frontal bones Neural placode Parallel or everted vertebral laminae Present AChE in the amniotic fluid	No chiari II malformation No frontal bones flattening No neural placode Conus medullaris inside the spinal canal Absent AChE in the amniotic fluid
Minor criteria	Muscular atrophy of the lower limbs Abnormal position of the inferior limbs and feet Nerves roots inside the sac Microcephaly (cranial circumference < 3rd percentile) Bilateral ventricular dilatation (>15 mm) Subependymal heterotopia Dysgenesis of the CC (too thick and/or too short)	No muscular atrophy of the lower limbs Normal position of the inferior limbs and feet Slight caudal course of the conus medullaris into the spinal canal



Vande Perre et al. FDT 2021

MyeLDM outcome (n=8)

Pregnancy and delivery (N=8)

- GA at diagnosis: 22 weeks (+/- 6d)
- Prenatal anatomical levels: L2-S3
- Cerebral signs (CII 6/8)
- AF: normal CGH and AChE positive 6/8
- Delivered at term
 - 1 C section (obstetrical indications)
- Normal birth weight (3192g, range: 2720-4330g)

Surgery

- M Zerah and T de Saint Denis
- Median age: 2 d (0-46 d)

MyeLDM: outcome at 36 months

Able to walk		8/8
Autonomous walking		6/8
Walking with orthosis		2/8
Wheelchair		0/8
Urinary catheterization		5/8 (all sacral levels)
Urinary tract infections		2/8
Anticholinergic treatment		4/8

	Laxative treatment	5/8
	Retrograde colonic enemas	0/8
	Use of diapers	8/8
	School without special assistance	6/8
	Neurodevelopmental retardation	2/8*
	CSF shunt	2/8
	Asymptomatic	2/8

* Postnatal exome sequencing gene PAK1

MyeLDM: rationale for a prenatal surgery

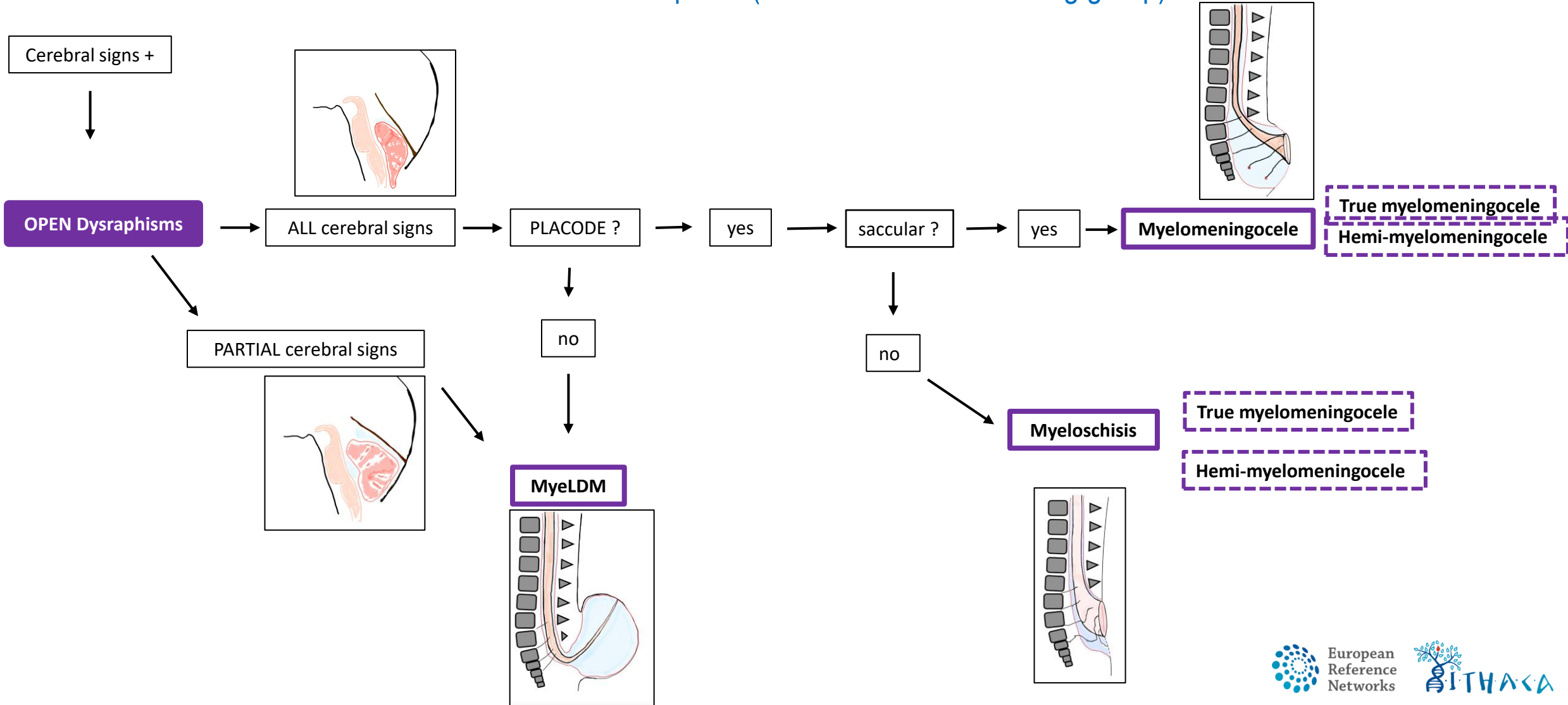
Points that need to be balanced

- Open dysraphism
- The spinal cord is stretched
 - This could be worsened when the sac is closed and increases in volume throughout the pregnancy
- Open dysraphisms are associated with a higher level of spinal cord dysplasia
- MyeLDM may be associated with a better outcome as compared to MMC

- no clear indication
- fetal surgery is probably indicated in the more severe cases
- benefit of a prenatal detethering of the spinal cord?

MyeLDM: rationale for a prenatal surgery

ORPHANET classification update (SBoD Trans ERN working group)



MyeLDM: rationale for a prenatal surgery

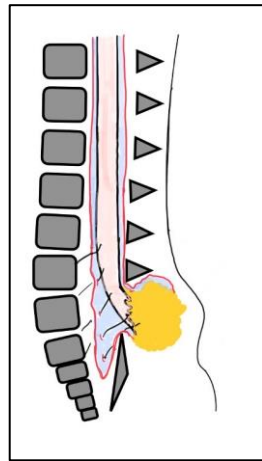
Types of dysraphism leading to a functional threatening

OPEN



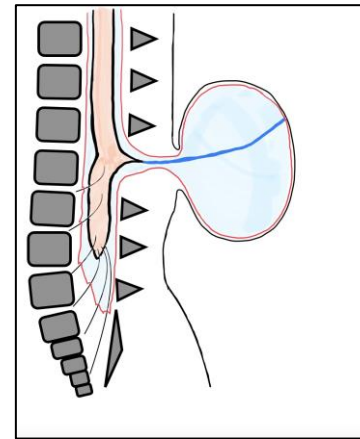
Chiari II

DYSPLASIA



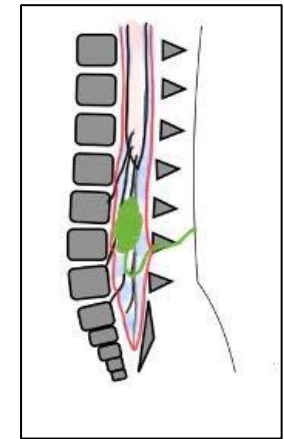
Lipomyéломéningocèle

TETHERING



Saccular LDM

environment



Dermal sinus

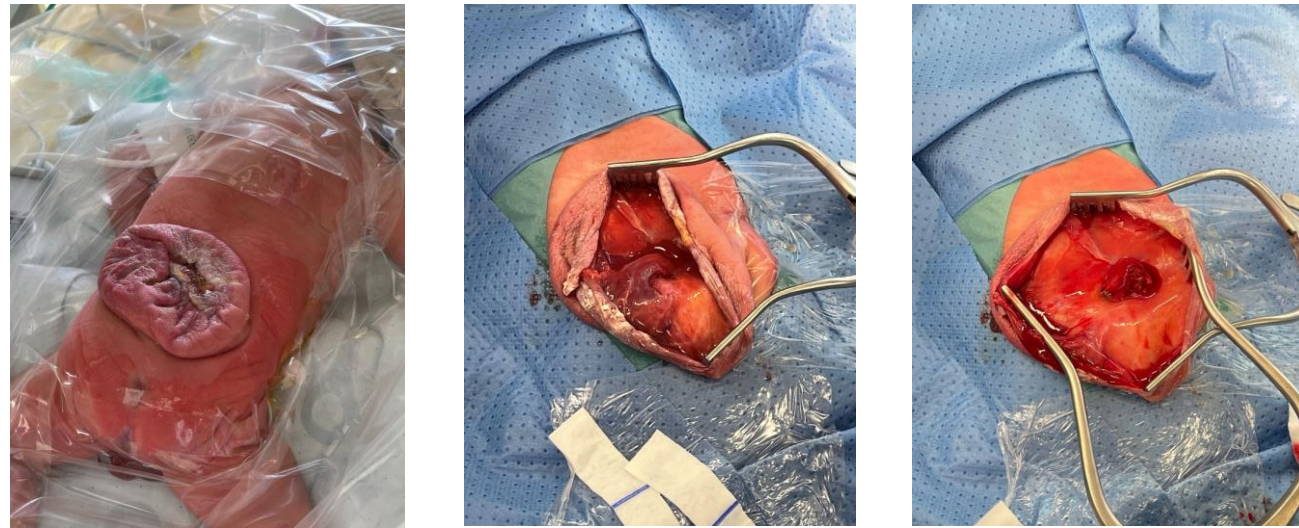
Each dysraphism can lead to a neurological impairment by one of these factors or a combination of these four

MyeLDM: rationale for a prenatal surgery

Closure



Detethering



Dysraphism surgery consists in an optimisation of a dysplasic spinal cord environment.

The dysplasia always remains

Goal of multidisciplinary management (including surgery) is to lead to the best global long-term outcome

Team of Trousseau Hospital for Fetal Surgery

Radiology/US/MRI

Catherine Garel
Eléonore Bondiaux
Toan Nguyen
Saskia Vande Perre

Neurosurgery

Timothée de Saint Denis
M Zerah

Anesthesiology

Agnès Rigouzzo
Marie-Pierre Bonnet

Fetal Medicine and Surgery

Jean-Marie Jouannic
Lucie Guilbaud
Paul Maurice
Loriane Franchinard
Ferdinand Dhombres

Psychologist

Célia du Peuty

RPM

Pauline Lallemand
Hina Simmonet
Rebecca Haddad



Spina Bifida and

SBOD

other **Dysraphisms**



Fetal myelomeningocele surgery

71% unable to walk independently

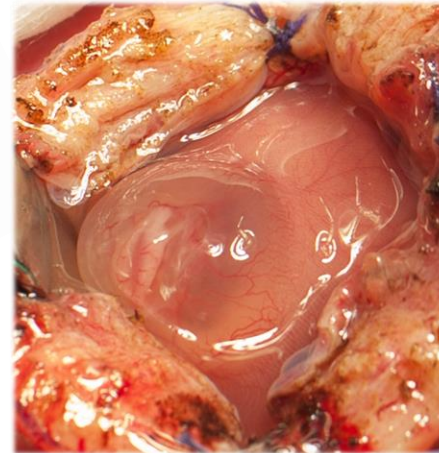
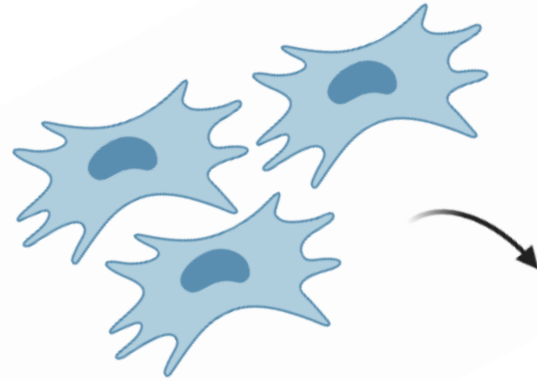
62% clean intermittent catheterizations



**Adjuvant strategies
are needed
to augment spinal
cord repair
and improve prognosis**

Objective

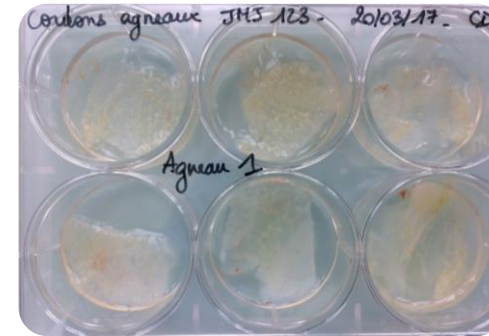
UC-MSCs



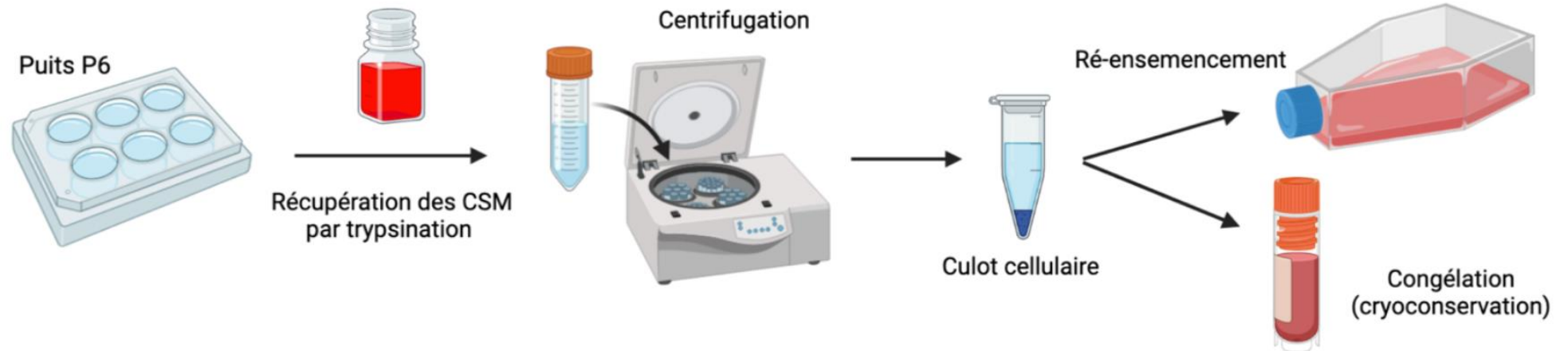
To experiment a **patch of mesenchymal stromal cells (MSC)**
as an **adjuvant treatment for fetal myelomeningocele (MMC) surgery**
in the ovine model of MMC

Umbilical Cord-Mesenchymal Stromal Cells (UC-MSC)

Explants
method

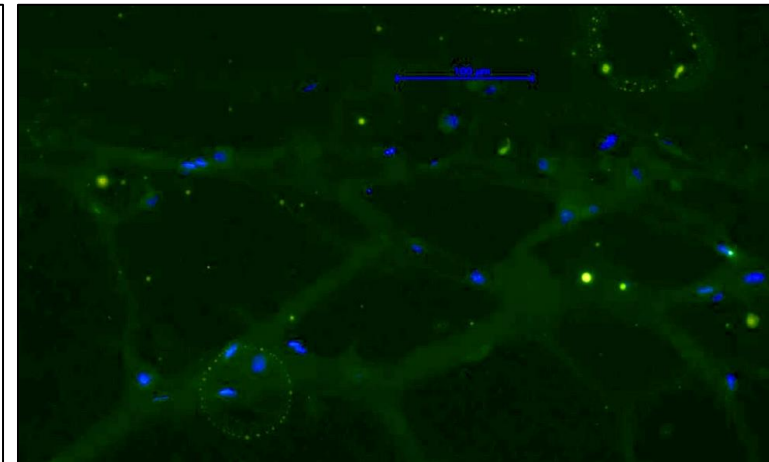
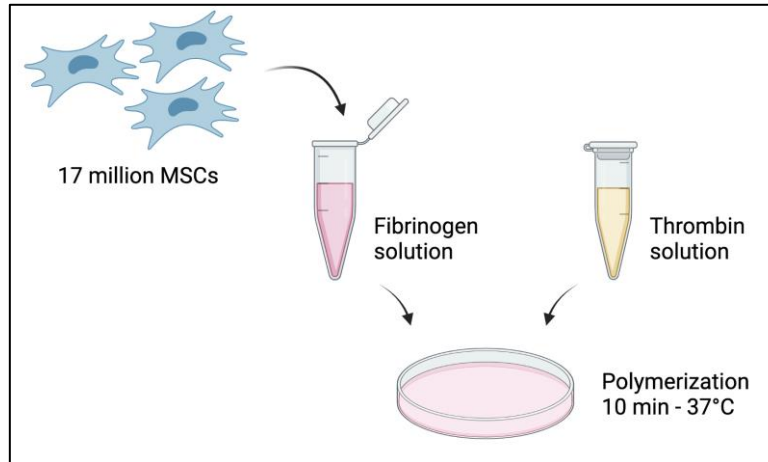


Cells
Culture



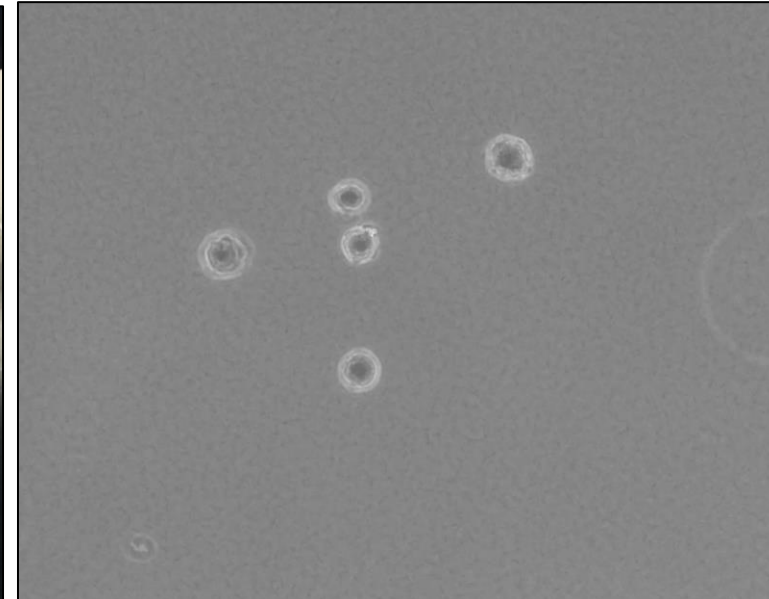
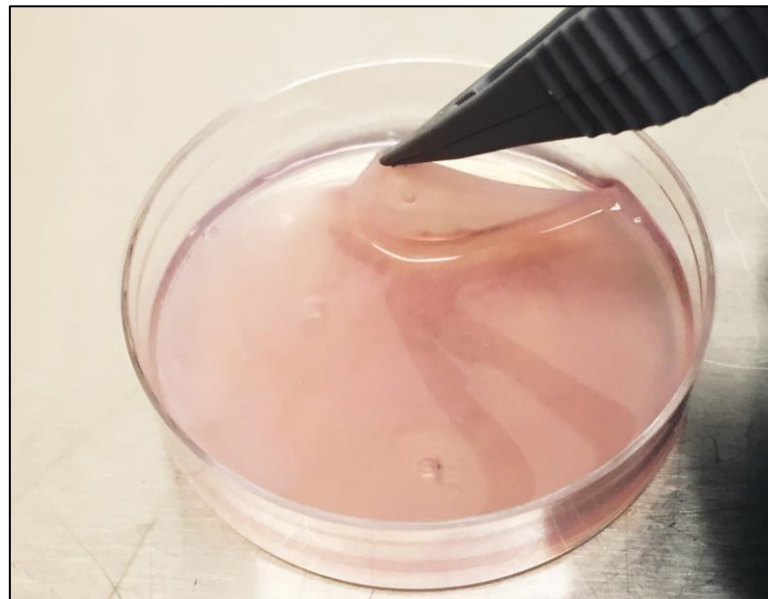
Patch of UC-MSCs

Fibrin patch



Homogeneous distribution

Polymerization



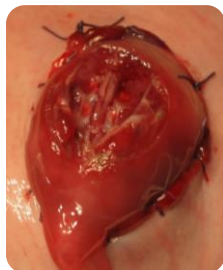
Migration within the mesh

In vivo experiments of ovine UC-MSCs patch

- **Animal model:** surgical ovine model of MMC
- Comparison of **two groups**:
 - UC-MSC patch + skin suture
 - Acellular patch + skin suture
- **Surgical protocole:**

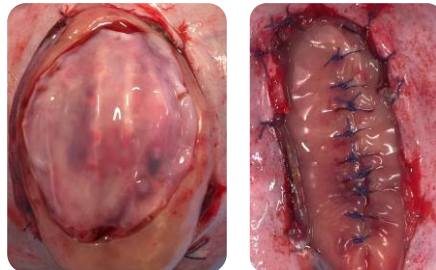
MMC
Creation

D 75



MMC
Repair

D 90



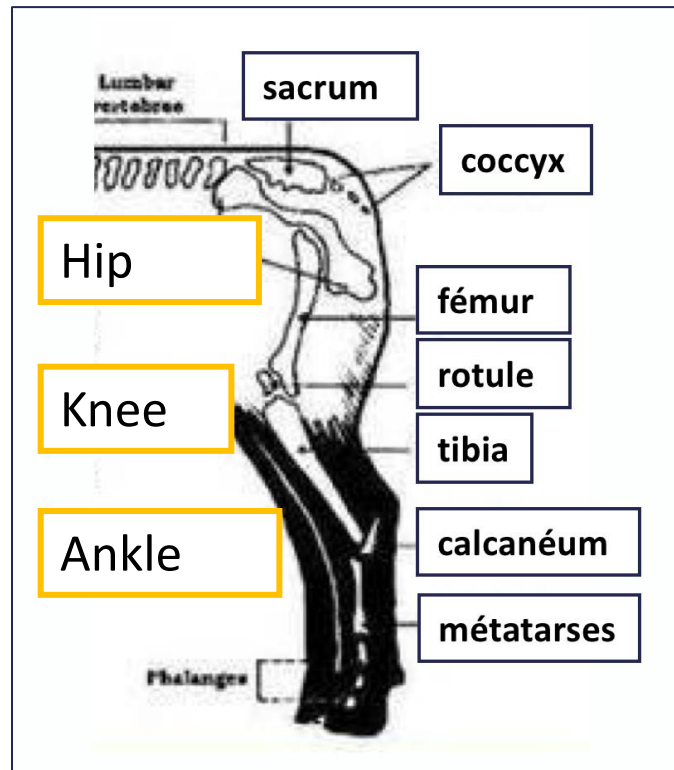
Birth
C section

D 143



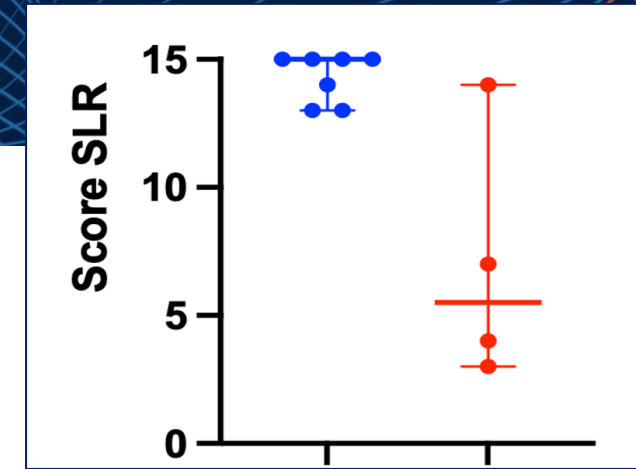
Clinical examination

- Score: **SHEEP LOCOMOTOR RATING**
- validated in the ovine model of MMC



SEVERE	Grade 0: complete paraplegia, no movement of any joints
	Grade 1: total of 1-3 points for joint movement
	Grade 2: total of 4-6 points for joint movement
	Grade 3: total of 7-9 points for joint movement
MODERATE	Grade 4: total of 10-12 points for joint movement
	Grade 5: capable of stance with help, ≥ 4 joints with slight movement
	Grade 6: capable of stance with help, ≥ 4 joints with extensive movement
	Grade 7: capable of spontaneous hindlimb weight support, ≥ 4 joints with slight movement
MILD	Grade 8: capable of spontaneous hindlimb weight support, ≥ 4 joints with extensive movement
	Grade 9: capable of stance with help, capable of 1-4 steps
	Grade 10: capable of stance with help, capable of ≥ 5 steps with no or occasional forelimb-hindlimb coordination
	Grade 11: capable of stance with help, capable of ≥ 5 steps with frequent forelimb-hindlimb coordination
	Grade 12: capable of standing up spontaneously on hindlimbs, capable of 0-4 steps
NORMAL	Grade 13: capable of standing up spontaneously on hindlimbs, capable of ≥ 5 steps with no or occasional forelimb-hindlimb coordination
	Grade 14: capable of standing up spontaneously on hindlimbs, capable of ≥ 5 steps with frequent forelimb-hindlimb coordination, not able to pass hindlimb clearance test
	Grade 15: capable of standing up spontaneously on hindlimbs, capable of ≥ 5 steps with frequent forelimb-hindlimb coordination, able to pass hindlimb clearance test

Clinical examination (ovine UC-MSCs)



	UC-MSCs patch <i>n</i> = 5	acellular patch <i>n</i> = 4	<i>P</i>
SLR at 2 hours of life	2 [1-7]	2 [1-6]	0.8
SLR at 24 hours of life	14 [13-15]	5 [4-14]	0.04
Hind limbs amyotrophy	0 (0%)	3 (75%)	0.02
Incontinence	0 (0%)	4 (100%)	0.002



Histological examination (ovine UC-MSCs)

	UC-MSC patch <i>n</i> = 5	Acellular patch <i>n</i> = 4	<i>P</i>
Fibrosis thickness between spinal cord and dermis (μm)	453 (139 -872)	3921 (1469-52401)	0.03
Fibrosis thickness around spinal cord (μm)	48 (0 – 58)	158 (137 – 176)	10^{-4}
Grey matter area (mm^2)	8.2 (0.5 – 12.5)	7.1 (0.3 – 8.9)	NS
Spinal cord area (mm^2)	21.8 (14.8 – 24.5)	16.7 (13.5 – 21.0)	NS
Neuronal density (number of large neurons/mm^2)	14.5 (10.8-17.7)	5.6 (5.2 - 8.9)	10^{-3}
Tumor	0	0	NS



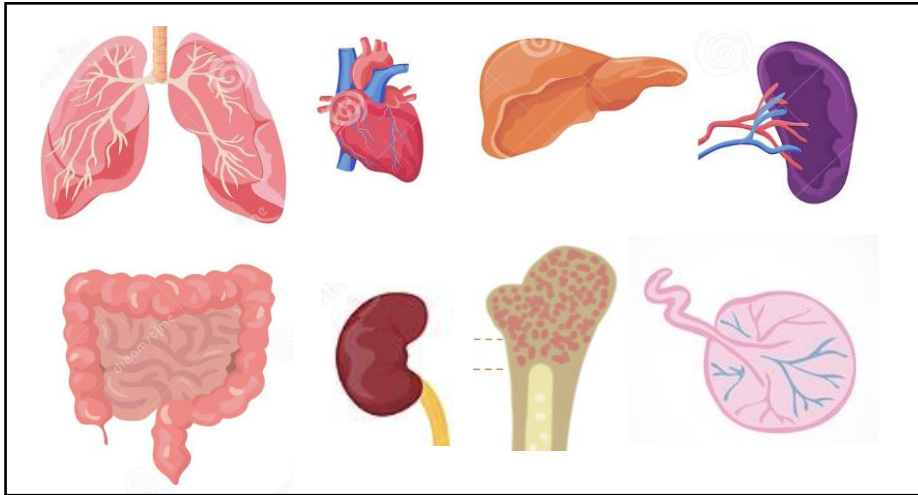
Guilbaud 2021



Athiel 2023

UC-MSCs potential side effects

Organs biopsies
of UC-MSCs
lambs



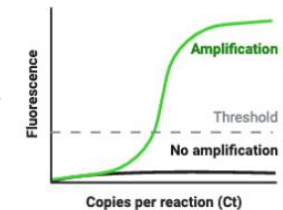
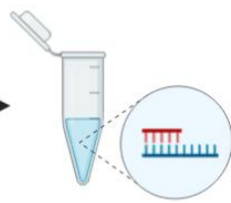
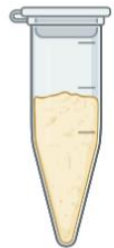
No GFP DNA



Cryo-broyage
tissulaire

DNA extraction

PCR: search for GFP DNA



Athiel 2022

UC-MSCs potential side effects

Follow-up of *h*UC-MSCs lambs

Day 1
graft + 53 days

n = 6
No Tumor

2 Months
graft + 113 days

n = 2
No Tumor

4 Months
graft + 233 days

n = 2
Still alive, no
side effect

Safety of Cell Therapy with Mesenchymal Stromal Cells (SafeCell): A Systematic Review and Meta-Analysis of Clinical Trials

Manoj M. Lalu^{1,5}, Lauralyn McIntyre^{2,5*}, Christina Pugliese⁵, Dean Fergusson⁵, Brent W. Winston⁶, John C. Marshall⁷, John Granton⁸, Duncan J. Stewart^{3,4}, for the Canadian Critical Care Trials Group

2012

The safety of MSC therapy over the past 15 years: a meta-analysis

Yang Wang^{1*†}, Hanxiao Yi^{2†} and Yancheng Song^{1*}

2021

Placental Mesenchymal Stromal Cells: Preclinical Safety Evaluation for Fetal Myelomeningocele Repair

Jordan E Jackson, MD,^{a,b,*} Christopher Pivetti, MS,^b Sarah C Stokes, MD,^{a,b} Christina M Theodorou, MD,^{a,b} Priyadarsini Kumar, PhD,^b Zachary J Paxton, BS,^b Alicia Hyllen, BS,^b Lizette Reynaga, BS,^b Aijun Wang, PhD,^b and Diana L Farmer, MD^{a,b}

2021

Conclusion : UC-MSCs in fetal MMC surgery

Efficiency

Clinical benefits

- motor function
- urinary function ?

Preservation of large neurons

Prevention from fibrosis

No risk

Transplantation of allogenic UC-MSCs does not seem to be associated with any side effect

Perspectives

- Better understand the mechanisms of action
- Clinical trial

Satisfaction survey "your feed back"

- <https://forms.office.com/e/KCcLh2rb71>



■ Thank you !

