

PRE-CONGRESS COURSE 9

Organised by the Special Interest Group Reproductive Surgery

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PRE-CONGRESS COURSE 9 - PROGRAM

Diagnostic and operative hysteroscopy in reproductive medicine

Organised by the Special Interest Group Reproductive Surgery

Course co-ordinators: Marco Gergolet (Italy) and Stephan Gordts (Belgium)

Course description: The course concentrates upon the importance and possibilities of diagnostic and operative hysteroscopy in reproductive medicine and the impact of a careful exploration of the uterine cavity on implantation and pregnancy outcome. Instrumentation, technique, indications and complications of the different procedures will be discussed in detail

Target audience: All gynaecologists involved with reproductive medicine 09:00 - 09:30 Hysteroscopy: instrumentation, technique, complications and their management - Stefano Bettocchi (Italy) 09:30 - 09:45 Discussion 09:45 - 10:15 Office hysteroscopy: prospective randomized controlled trial - *Rudi* Campo (Belgium) 10:15 - 10:30 Discussion 10:30 - 11:00 Coffee break Hysteroscopy in the infertile patient - Stephan Gordts (Belgium) 11:00 - 11:30 11:30 - 11:45 Discussion 11:45 - 12:15 Embryoscopy: anatomy and diagnostic value - *Vasilios Tanos* (Cyprus) 12:15 - 12:30 Discussion

12:30 - 13:30	Lunch
13:30 - 14:00	Lysis of intrauterine adhesions: failures, fertility outcome and obstetric risks - <i>Vasilios Tanos (Cyprus)</i>
14:00 - 14:15	Discussion
14:15 - 14:45	Hysteroscopic treatment of uterine congenital malformations and fertility outcome - <i>Marco Gergolet (Italy)</i>
14:45 - 15:00	Discussion
15:00 - 15:30	Coffee break
15:30 - 15:30 15:30 - 16:00	Coffee break Hysteroscopic myomectomy: indications, technique and reproductive outcome - Stefano Bettocchi (Italy)
	Hysteroscopic myomectomy: indications, technique and reproductive
15:30 - 16:00	Hysteroscopic myomectomy: indications, technique and reproductive outcome - <i>Stefano Bettocchi (Italy)</i>

ESHRE, 25th annual meeting Amsterdam, June 28–July 1, 2009

Office hysteroscopy: prospective randomized controlled trial

Rudi Campo, MD
Leuven Institute for Fertility and
Embryology
LIFE
Leuven - Belgium

Diagnostic Hysteroscopy

Prospective multi-centre randomised clinical trial

- 1. Technique and Feasibility of diagnostic Hysteroscopy ?
- 2. Hysteroscopic findings?
 - " Abnormal uterine bleeding versus the infertile patient "



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Conventional hysteroscopy vs. Mini-hysteroscopy

Parameter	Conventional hysteroscopy	Mini- hysteroscopy 2.4/3.5 mm	
Total diameter	5.0 mm		
Speculum	+	-	
Cervical clamping	+	-	
Cervical dilatation	+	-	
Distention medium	CO ₂ /Saline	Saline	
medium	CO ₂ /Saline	Saline	

Prospective, Multicentre, Randomised Controlled Trial Campo R, Molinas CR et al, Hum Reprod 2005 To score objectively Pain Visualisation quality

Stratified for

Total instrument diameter Vaginal delivery (0 versus >=1) Surgeons skills



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Patients randomization Patient with indications for hysteroscopy (n=490) Group II: Group I: nventional hysteroscopy 5.0 mm instruments Mini-hysteroscopy 3.5/2.4 mm instruments (n=244) Group I-B Group II-B Group I-A Group II-A Patients without vaginal deliveries Patients with aginal deliveries Patients without vaginal deliveries inal deliveri (n=107)

Feasibility of Diagnostic Hysteroscopy 4 important study requirements Ambulatory or office endoscopic unit Watery distension medium (Saline) 30 ° Rigid optic with high optical quality Atraumatic technique Prospective multi-centre randomised clinical trial Leuven Institute for Fertilty and Embryology

Mini-hysteroscopy Technique

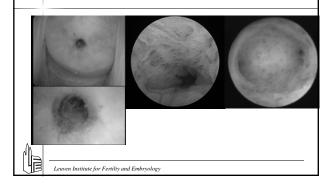
- > No speculum
- > No tenaculum
- > No cervical dilatation
- > No anaesthesia, no analgesia
- Atraumatic and sight controlled insertion of the hysteroscope





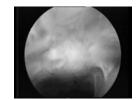
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Atraumatic insertion technique



Atraumatic insertion technique





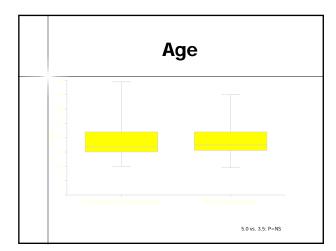


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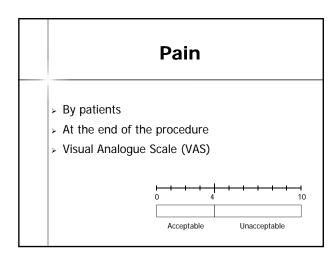
Outcome variables

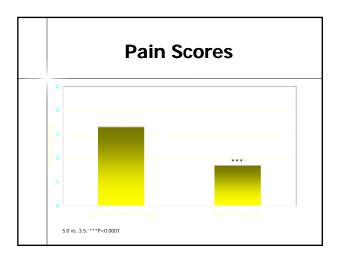
Acceptability and feasibility were evaluated by scoring

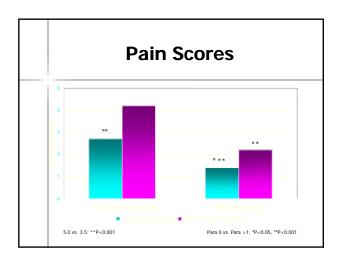
- > Pain
- > Quality of visualization
- > Complication rate
- > Success rate

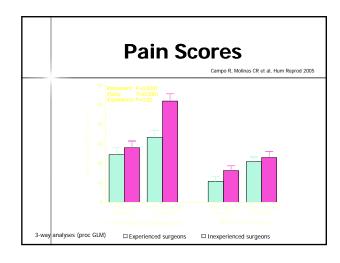


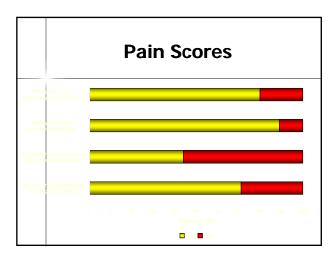




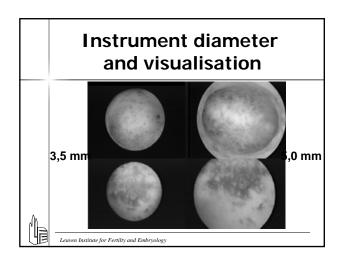


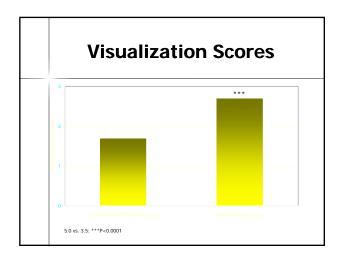


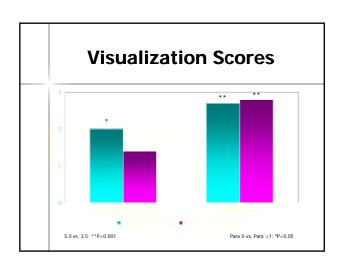


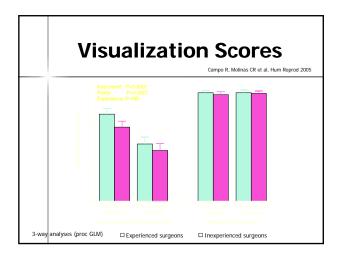


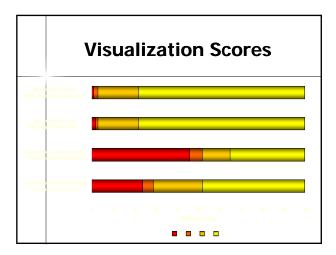
Visualization of uterine cavity > By surgeons > During the procedure Score > 0: No > 1: Insufficient > 2: Sufficient > 3: Excellent



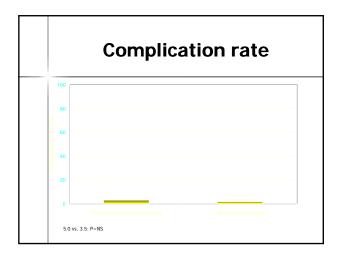


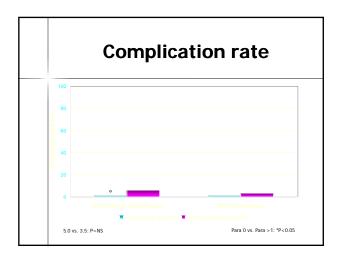


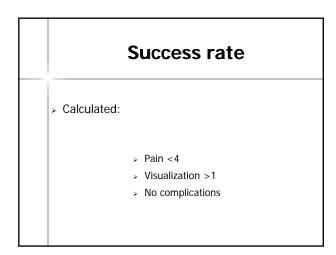


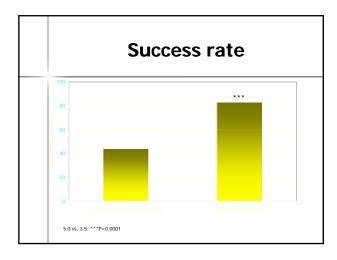


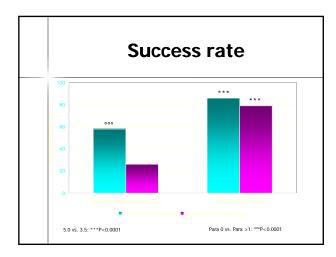
Complications rate > By surgeons > During the procedure > Vasovagal reaction > Uterine perforation > Haemorrhage > Cervical laceration











Conclusions

- > Mini-hysteroscopy:
 - > Easy to perform
 - > Excellent patient compliance
 - > Excellent quality of visualisation
 - » Real mini-invasive diagnostic procedure
- Mini-hysteroscopy, rather than conventional hysteroscopy, should be systematically used, especially when difficult access to the uterine cavity can be anticipated

Findings

Prospective multi-centre randomized clinical trial

Different pathology in infertile versus AUB patients



Molinas CR, Campo R et al Best Pract Res Clin Obstet Gynaecol. 2006 Mar 2

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Findings

Normal

Abnormal

Congenital malformations Polyp – Myoma Adhesions

Subtle lesions Lesions of unknown pathological significance



No Diagnosis

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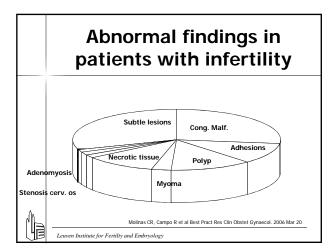
Demographics, indications & findings

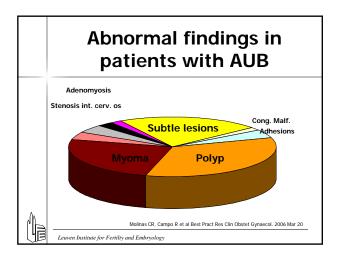
Parameter	Group I	Group II	
Age	34 (20-79)	35 (19-70)	
Indications (%)			
Infertility	45	44	
Bleeding	44	46	
Others	11	10	
Findings (%)			
Normal	54	55	
Abnormal	39	43	
No diagnosis	7	2	

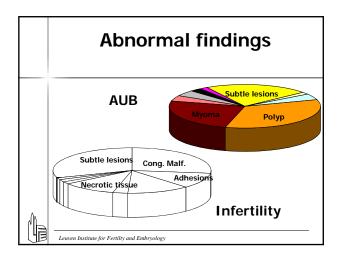
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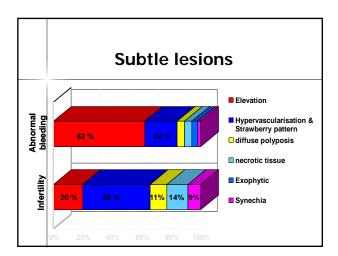
Demographics, indications & findings

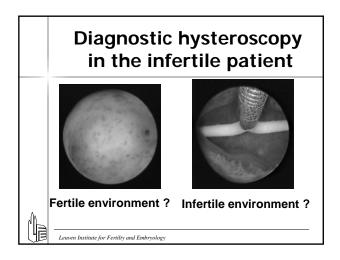
Parameter	Group I		Group II	
Parameter	Para >1	Para 0	Para >1	Para 0
Age	39 (23-79)	31 (20-78)	38 (27-70)	31 (19-67)
Indications (%)				
Infertility	28	69	26	67
Bleeding	59	23	63	25
Others	13	8	11	8
Findings (%)				
Normal	51	57	51	62
Abnormal	42	35	48	36
No diagnosis	7	9	1	2











Subtle lesions Lesions of unknown pathological significance Diffuse polyposis Strawberry pattern Hypervascularization Mucosal elevation

> Endometrial defects

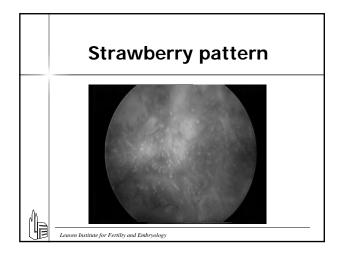


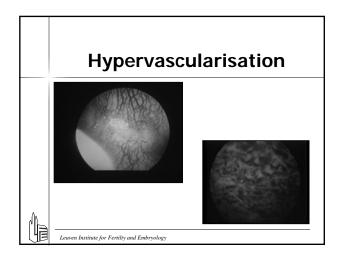
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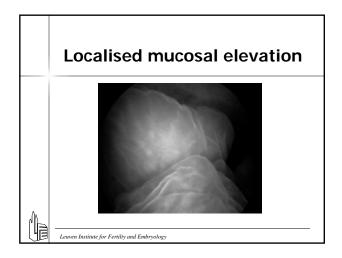
> Others

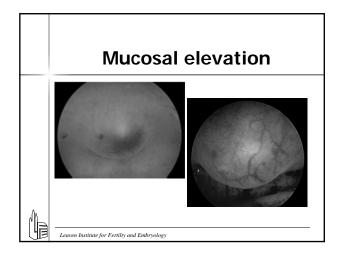
effect of magnifying and hydroflotation These subtle or incipient lesions: significance unclear but could be associated with infertility. Leuven Institute for Fertilly and Embryology

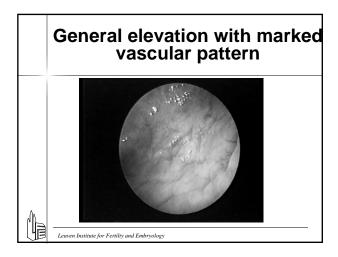
Diffuse polyposis Leuven Institute for Fertilty and Embryology

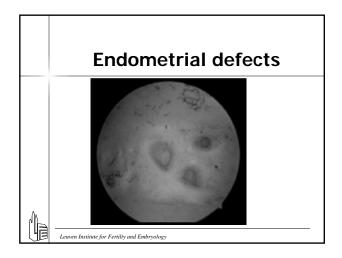












Subtle lesions Effect of magnifying and hydroflotation

Conclusions 1

GRADE A EVIDENCE

By reducing the diameter of the hysteroscope the effects of patient parity and also surgeon's experience are no longer important !!!

Diagnostic mini Hysteroscopy is Simple and Safe with high patient compliance only when a mini-hysteroscope, watery distension medium and an atraumatic insertion technique is used.



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Conclusions 2

Fluid mini hysteroscopy is mandatory in the first line exploration of every infertile patient with significant higher incidence of uterine congenital malformations adhaesions and presence of necrotic tissue.

Diagnostic mini - hysteroscopy has a high visualisation capacity for subtle lesions, there is lack of evidence to identify the importance of those changes for implantation disorders but further exploration of those lesions in the infertile patient seems advisable.



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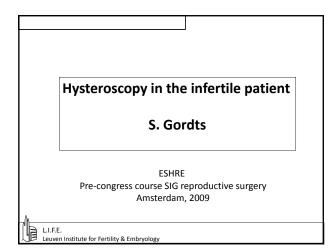
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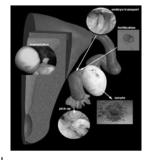
Rudi Campo Stephan Gordts Patrick Puttemans Roger Molinas Sylvie Gordts Marion Valkenburg Ivo Brosens



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Transvaginal Endoscopy



Complete endoscopic investigation of the female reproductive tract.

Hysteroscopy

Transvaginal Laparoscopy (TvL)

Salpingoscopy

Patency test

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Investigation

uterine pathology congenital

acquired

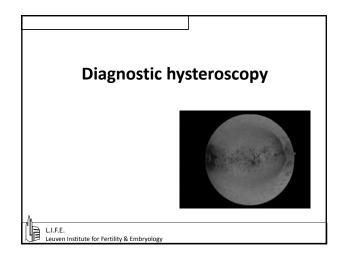
tubal pathology

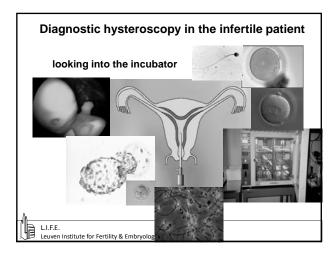
endometriosis

Optimalization offers the potential for spontaneous conception



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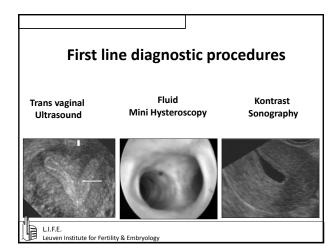


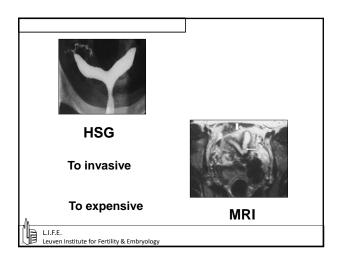
Hysteroscopy in Infertility

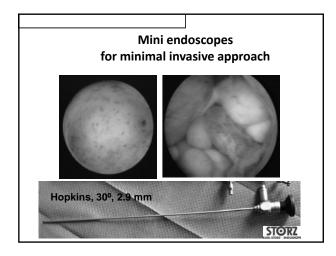
Questions

- Feasibility of office Hysteroscopy in the infertile patient ?
- Importance of Findings for reproductive performance ?









Watery distension medium For minimal invasive approach



Hydro floatation shows subtle lesions,

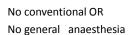
Rinsing effect in case of bleeding

Less discomfort than CO2 gas.

Scientific evidence that ringer lactate Is to be preferred

Only for unipolar surgery Purisole is indicated

Ambulatory Endoscopic Unit For minimal invasive approach





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Specific characteristics for minimal invasive approach

Ambulatory endoscopic unit

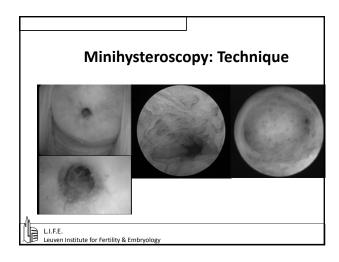
Watery distension medium

Small diameter instrumentation with high optical quality

Atraumatic technique



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Minihysteroscopy: Technique

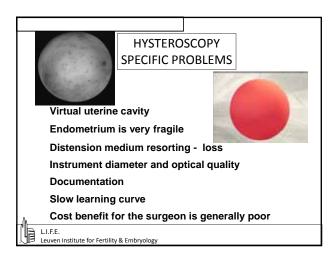
Minihysteroscopy Atraumatic technique No speculum No tenaculum No cervical dilatation No anaesthesia, no analgesia Atraumatic and sight controlled

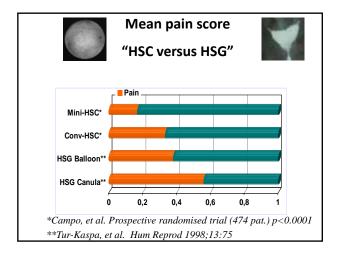
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insertion of the hysteroscope.

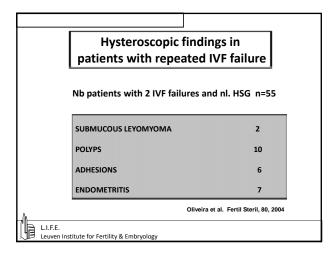
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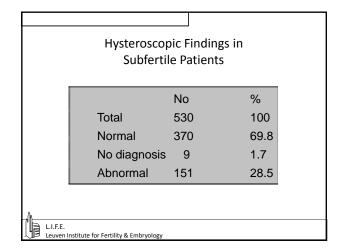


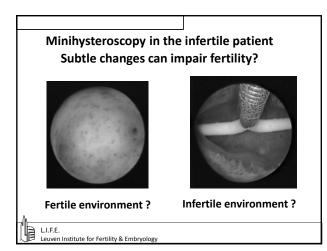


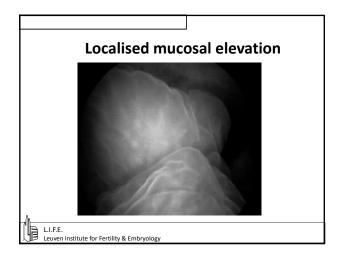


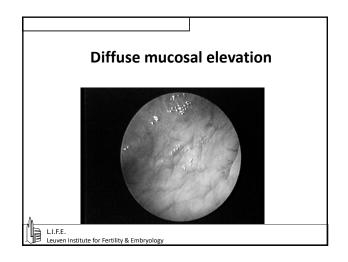
Minihysteroscopy: Findings Congenital pathologies Acquired pathologies: Large lesions: Myoma, polyp, adhesions Subtle lesions: Mucosal elevation, hypervascularisation, strawberry pattern, diffuse polyposis, exofitic or necrotic lesions,

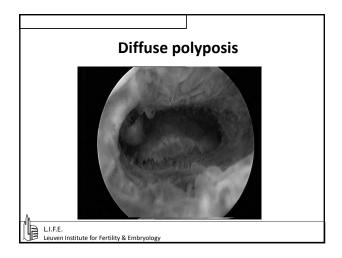


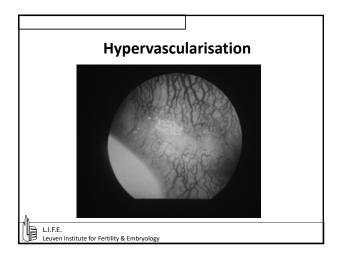












Subtle lesions Lesions of unknown pathological significance Diffuse polyposis Strawberry pattern Hypervascularization Mucosal elevation Endometrial defects Others LI.F.E. Leuven institute for Fertility & Embryology

Subtle lesions Increased vascular pattern DD Endometritis Prolonged Hypo oestrogenic environment adenomyosis Intramural myoma Others? L.I.F.E. Leuven Institute for Fertility & Embryology

Increased vascular pattern

Current LIFE strategy

Microbiology

Histology

Sequential hormone therapy

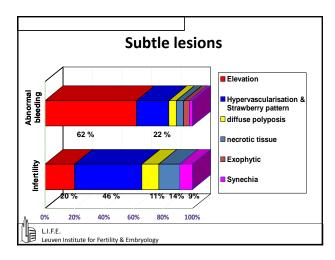
Doxycycline 200 mg/ day 10 days

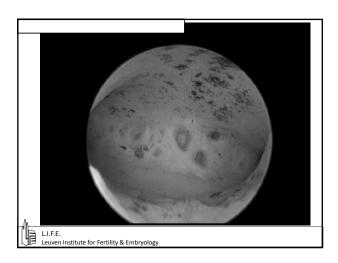
Control HSC after 2 months

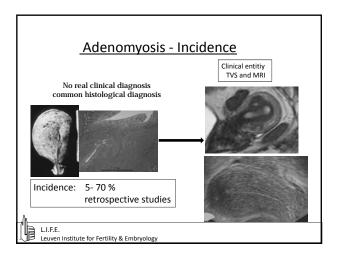
In case of remaining problem MRI

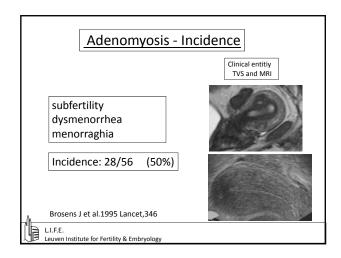
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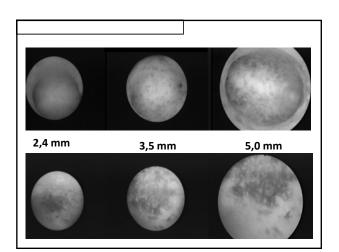
Strawberry pattern L.I.F.E. Leuven Institute for Fertility & Embryology

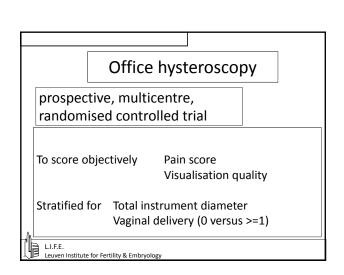


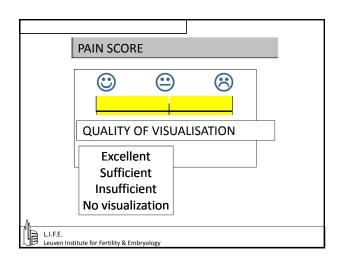


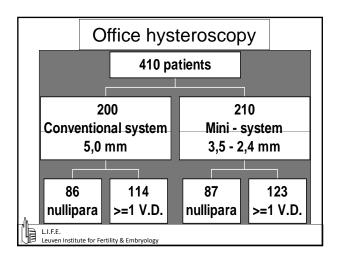


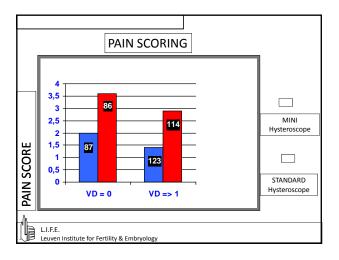


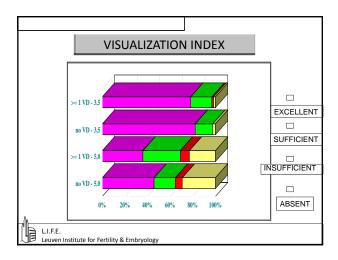












CONCLUSIONS

Diagnostic hysteroscopy is a first line ambulatory office procedure.

Our data shows that the best results are obtained with the mini-hysteroscopes of 3.4 \mbox{mm}



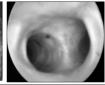
Diagnostic Procedure congenital malformation THE SEPTUM T-SHAPED UTERUS

Diagnostic Procedure congenital malformation Kontrast Trans vaginal Mini Hysteroscopy Sonography



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Ultrasound





Hysteroscon	ic m	otron	lactv	in	infor	+ili+v

Indication for hysteroscopic ambulatory repair

No GRADE A evidence for surgical intervention.

High compliance and low complication rate of hysteroscopic metroplasty

Current classifications are insufficient for scientific appraoch.

Strategy?



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Hysteroscopic metroplasty in infertility

Indication for hysteroscopic ambulatory repair

Women with long-standing (unexplained) infertility

Recurrent miscarriage

Women > 35 years of age

Women in whom assisted conception is being contemplated or before starting any invasive fertility treatment



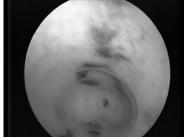
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Incidence of congenital anomalies in the infertile patient

	N	%
Uterus septus	44	63
T-Shaped	23	33
Uterus unicornis	3	4

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One Stop Therapeutic Potential Dissection of uterine septum





Septated Uterus and Implantation after IVF

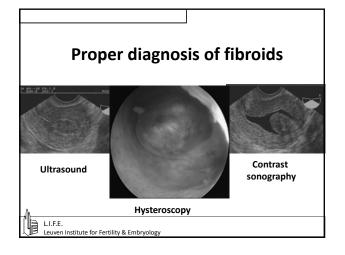
	uteroplasty	control
Pregn.rate	20%	12.5%
Impl. Rate	10.5%	4.6%

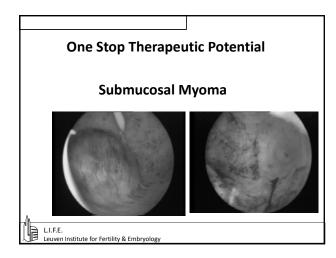
Lavergne et al.Eur.J.Obstet.Gynec. 68,1996

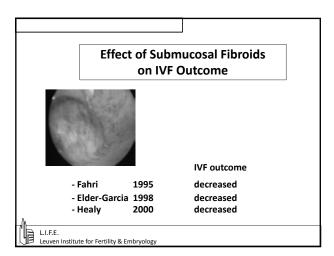
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UTERINE SEPTUM <u>Pre - and Post-operative Pregnancy Outcome</u> Pre-operative Post-operative Patients 43 31 117 37 Pregnancies • abortions *104 (88.9%) *5 (13.5%) 6 (5.1%) 5 (13.5%) • premature 27 (73%) • at term 7 (6.0%) • children *12 (10.2%) *32 (86.5%) alive L.I.F.E. Leuven Institute for Fertility & Embryology

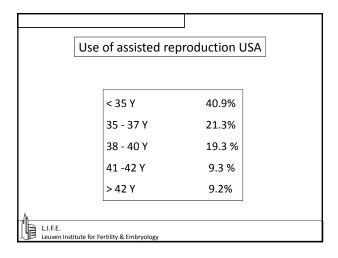
		Septated u	terus		
			Gergolet et al	, subm. Fertil Steril	
	Sm	all	Larg	ge	
	n=	125	n= 5	54	
	before	after	before	after	
Time	22.44	6.6	20.88	4.98	
Pregn	109	97	38	42	
Deliv	16.5%	90.7%	18.4%	88.1%	
Abort.	78%	8.2%	71.1%	11.9%	
Ectop.	5.5%	1.1%	10.5%		
L.I.F.E. Leuven Institute for Fertility & Embryology					







Delayed childbearing USA Women having their first baby ≥ 35 y increased 50 % between 1981 and 1999 40 – 45 y increased 75% between 1981 and 1995 LI.F.E. Leuven Institute for Fertility & Embryology



Conclusions

- + easy to perform
- + visualization quality is excellent
- + excellent patient compliance
- + safe procedure
- cost benefit for the surgeon is generally poor
- = first-line diagnostic procedure



L.I.F.E.

Leuven Institute for Fertility & Embryology

Conclusions

Although frequently detected at hysteroscopy in infertile patients, the impact of subtle lesionson implantation is still unclear.

Operative hysteroscopic procedures can be performed in a day hospital setting.



L.I.F.E. Leuven Institute for Fertility & Embryology

Embryoscopy Anatomy & Diagnostic Value

Presentation Objectives Terminology

The development of embryoscopy Technique failure rate

Early Embryo anatomy Diagnostic value

Possibilities for embryo treatment Review of the literature ESHRE 2009

Amsterdam, The Netheralands 28 June to 1st July 2009

Pre-congress course 9

Diagnostic and operative hysteroscopy in reproductive medicine

Vasilios Tanos, MD, PhD.
Prof in Obstetrics & Gynaecology



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Terminology

- ☑ Embryoscopy direct visualization of an embryo usually 5-10 weeks previous to fusion of the chorion and amnion
- ☑ Fetoscopy usually 14-25 weeks. Phenotypic evaluation added to the karyotype analysis
- ☑ Should be restricted to families at high risk for recurrence of genetic conditions associated with external fetal anomalies not detectable by ultrasound



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Entry and Inspection

Embryoscopy can be performed

- ▼ Trans abdominally
- Trans cervically
- ☑ Usually before 11 weeks the telescope reaches the extracoelomic space
- ☑ The amniotic cavity is formed after 11 weeks of gestation



The Development of Embryoscopy O Dr Bjorn Westin in 1954, performed hysteroembryoscopy in 3 embryos before TOP during early 2nd trimester • He used the McCarthy's 10 mm telescope • Two cases were performed under GA and one with local anaesthesia He reported active embryo extremities movements and he counted over 30 swallowing movements per minute The development of Embryoscopy Scrimgeour JB and Valenti C, 1970's Direct endocopic examinations of embryos by laparotomy and a small opening of the myometrium The development of Embryoscopy and the first direct fetal biopsies ☑Rodeck 1980 and Elias 1983 ☑Perform the first "Fetoscopies"

☑Transabdominal insertion of the

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endoscope under real-time US guidance for direct fetal observation, fetal blood sampling and fetal skin biopsies

The Development of Embryoscopy

- Embryoscopy was considered as an obsolete option during 1980 while the abortion rate was 4 8%
- The US was then well developed and helped a lot in early fetal anomaly diagnosis
- Daffos F performs an US guided direct fetal blood sampling



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Technological advances...

The recent optic and instrument technological advances offer better visualization with smaller diameter telescopes enabling better and more accurate diagnostic capabilities

Also enable minimal operative procedures to the fetus with less complications for the fetus and the mother



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Embryoscopy and recent molecular achievements

- First trials presented minor benefits and limited diagnostic potentials due to poor technical facilities
- Recent molecular biology achievements and technical advances as well as social needs and demands will accelerate the clinical application of embryoscopy for early diagnosis and probably embryo treatment...



The value of Embryoscopy ■ Diagnostic ✓ Etiology of missed and recurrent abortions √ Reevaluate normal embryo status / anatomy, physiology ✓ Phenotype of embryos with suspected US abnormalities □Therapeutic √ Cervical ectopic pregnancy √ Stem cell therapy √ Gene therapy In Vivo Evaluation of early embryo development and its surrounding environment The following can be clearly visualized Cervical canal Intrauterine cavity Pregnancy sac Chorion and amnion Embryo Umbilical cord Alantois **Cervical Ectopic Pregnancy** Output US evaluation at 5+4 weeks. Mild bleeding Pregnancy G4 after 3 TOPs Embryoscopy in order to inject methotrexate. Successful hysteroscopic clearance of the cervical ectopic pregnancy (video) University of Cyprus, Medical Informatics Laboratory

Embryoscopy: Searching for the Etiology of Recurrent Spontaneous Abortions

Vasilios Tanos MD, PhD Aretaeion Medical Center

Demetra Georgiou BSc, Dipl.Gen, PhD MakIII. Hospital, Dpt Cytogenetics

Eleftherios Meridis, MD Minas Paschopoulos MD Ioannina University Hospital, Dpt Obstetrics and Gynaecology, Ioannina, Greece



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Definition and Abortion Risk Rate

- ✓ Recurrent spontaneous abortions (RSA) refer to three or more consecutive spontaneous abortions (Hannes 1992)
- ✓ Risk for SA after 1st Abortion 20-25%
- ✓ Risk for SA after 2nd Abortion 40-50%
- ✓ Risk for SA after ≥ 3rd Abortion 60% and levels of
- Most couples have at least a 60% chance of delivering a live-borne infant with three or more spontál୩୯୯୪ ଶର୍ଚମଧିତା



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The frequency of factors affecting RSA

(Dhont M. 2003, Kuttech WH 1999)

- 1. Genetic abnormalities 3-5%
- 2. Uterine anatom. abnor. (hereditary & acquired 15-20%)
- 3. Immunologic (Antiphosphol.& Anticardiolipin 15-25%)
- 4. Endocrine / metabolic disorders 5-8% (DM, PCOD etc)
- 5. Environmental factors 5-10% (occupation, smoking etc)
- 6. Unexplained 40% can not identify the etiology





Patients and Methods

- ≥38 patients with history of RSA
- All patients underwent history, general body and gynecological examinations and laboratory investigations and hysteroscopy during their last abortion



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Patients

Our study - RSA patients with

- O unexplained etiology
 O uterine cavity abnormalities corrected
 O anticardiolipin syndrome
 O endocrinological factor
 O suspected thrombophilia, treated w LMH
 O treated with husband WBC
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The technique of Embryoscopy

- ⇒Visualization of dead human embryos up to the age of 12 weeks
- ⇒ TransCervical
- ⇒ Instruments: Telescope 3.5mm, 5mm, 30°, single flow
- ⇒ Metal Halide light source 270 Watts
- ⇒ Distention medium: Normal saline
- ⇒ No use of anesthesia or sedation

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Targets of the Study

- ✓ Standardization of the technique.
- ✓ Evaluation of the potentials of the technique.
- ✓ Evaluation of the characteristics of the pregnancy sac and its contents.
- ✓ Correlation of the embryo external characteristics and its genetic analysis



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Results

- ♦ The total of 35 embryos were evaluated
- In 35/38 cases embryoscopy was successful and complete evaluation of the embryo and pregnancy sac was performed.
- ☼ The beta-hCG serum level was zero in three weeks after the D&C



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Correlation of the embryo morphology and embryo karyotype

	Variety of possibilities	Cases	%
Α	Normal phenotype and normal karyotype	5/35	14
В	Normal phenotype and abnormal karyotype	2/35	6
С	Abnormal phenotype and normal karyotype	5/35	14
D	Abnormal phenotype and abnormal karyotype	23/35	66



14				
56				
ory 1				

ZT

⊠29 y old, M+1

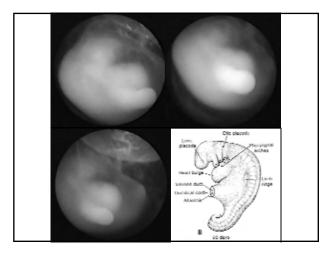
⊠G1-G3 Recurrent Abortions

⊠Complete Workup for RA – normal results

☑G4 – Crystal Heparine (CH) and LMH – term pregnancy healthy baby

☑G5 – CH + LMH at 6 weeks missed abortion - Embryoscopy revealed anencephaly and abdominal malformations





HAA

⊠40y old, 2yM+0,

■Subserous & Intramural fibroids

☑Uterus enlarged 17w,

⊠G5, Ab(2)3

■Recurent Abortions

■Embryo missing right Eye



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Embryoscopy of Missed Abortion ≥233 cases by Philipp T et al in 2003 found ≥75% with abnormal karyotype, ≥ 18% - abnormal phenotype and normal karyotype compared to [14% our results SRA] ≥ 7% - normal phenotype and karyotype compared to [14% our results SRA] Investigation of RSA etiology

- ➤ Rubio Carmen et al. 2004 (MSRM)
- >RSA couples undergoing PGD compared to those cases that did not have RSA
- > Numerical chromosomal abnormalities in human preimplantation embryos of women with RSA was 66% as compared to 33% found in non RSA patients.



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Conclusions

- ☑ Embryoscopy seems to be a valuable method for accurate diagnosis of the cause of spontaneous recurrent and missed abortions. This can be especially useful for future treatment purposes.
- ☑ The embryo external characteristics differ in cases of the same genetic abnormalities.
- $\ensuremath{\boxtimes}$ Both Alantois and Chorion seem to be also affected from the genetic abnormality expressed in the embryo
- ☑ Cervical ectopic pregnancy can be treated by embryoscopy



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Lysis of Intrauterine adhesions Failures, Fertility outcome and Obstetric Risks

Presentation Objectives Etiology – Causes - Mechanism Frequency Clinical Symptoms Diagnosis Treatment options

Treatment success rate
Treatment complications, failure rate
Pregnancy complications
Review of the literature

ESHRE 2009 Amsterdam, The Netheralands 28 June to 1st July 2009

Pre-congress course 9

Diagnostic and operative hysteroscopy in reproductive medicine

Tanos Vasilios, MD, PhD. Prof in Obstetrics & Gynaecology



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Intrauterine adhesions Asherman's Syndrome

Joseph Asherman first described IUA in 1948

- destruction of the endometrium
- formation of adhesions / synechiae
- anterior and posterior uterine walls are adhered



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Intrauterine adhesions (IUA)

may be thin, filmy, dense, calcified and Obliterate

- the endometrial cavity partially or completely
- internal cervical os and /or
- cervical canal



Ε Λ	۰ŧ	05
50	OI	95

Why hematometra does not occur	
despite stenosis or atresia of the Cx internal OS	
Theory A	
 The endometrium perhaps in response to a build-up of pressure, becomes refractory, and simple cervical dilation cures the problem 	
simple cervical dilation cures the problem	
Theory D	
Theory B • The process of adhesions formation is very	
 The process of adhesions formation is very slow and symptoms pass uneventfully 	
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]
US measurement of Endometrial thickness in	
patients with uterine outlet obstruction	
Lo ST et al 2008 Hum Reprod	
 16/26 pts with only outlet cervical adhesions 	
 Compared with 50 normal menses patients 	
 Endometrium was 3.9mm (+/- 0.4mm) 	
No haematometra	
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-	
Aetiology of Asherman's Sy - IUA	
Generally after overzealous postpartum curettage (March et al 1983 Berman JM 2008 SemRepMed)	
 Very severe adhesions have been noted following severe postpartum haemorrhage / curettage and postpartum hypogonadism (Sheehan's Sy) 	
After abortion / incomplete / repeated abortions – neglected / sharp curettage	
 Following uterine surgery extensive endometrial trauma (cesarean section, myomectomy, metroplasty, hysteroscopic surgery) 	
Post severe endometritis and / or PID	
 As a complication of uterine artery embolization for the treatment of uterine (as an ischemic response following this procedure) 	
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Incidence of IUA after abortion □After 1 abortion the incidence is 16.3% ☐ After 3 or more abortions the incidence rises to 32% (Friedler S et al 1986) ☐ The severity of adhesions also rises increasing the number of abortions (Yu D et al Fertil Steril 2008) Prevalence of IUA after placental remnants or incomplete abortion In 50 patients undergoing · secondary removal of placental remnants or • repeat curettage for incomplete abortions Ambulatory hysteroscopy 3months after intervention Intra uterine adhesions found in 40% - 5 with Asherman's Sy – 6 had grade II - 6 had grade III - 3 had grade IV Westendorp IC 1998 Hum Reprod. 1998 Dec;13(12):3347-50. ARETAEION HOSPITAL University of Cyprus, Medical Informatics Laboratory Rare causes of IUA formation √ Tuberculosis (Dg is made by culture of the menstrual discharge or by endometrial biopsy) ✓ uterine Schistosomiasis (check eggs of the parasite in urine, faeces, rectal scrapings. menstrual discharge or endometrium. (Speroff L 2005)

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Clinical Symptoms	
☐ Hypomenorrhea or amenorrhea or dysmenorrhea☐ Menstruation can be even normal☐ Miscarriages / Recurrent miscarriages☐ Infertility can be present even with mild adhesions	
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Diagnosis of IUA	
☐ Hysteroscopy is the gold standard method accurate detecting even minimal adhesions that are not apparent on a hysterogram	
 □ Typical pattern of multiple adhesions seen in Hysterosalpingogram (filling defect) □ HSG is an insufficient diagnostic method because the filling defects of the endometrial cavity or obliteration of the tubes are not conclusive for the exact condition of the endometrial cavity 	
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	1
Ultrasound diagnosis and correct grading of IUA	
Knopman J & Copperman AB in J Reprod Med 2007 evaluated the 3D US in the management of suspected Asherman's Syndrome	
 54 infertility patients 3Dimensional Sonography sensitivity was 100% HSG sensitivity was 66.7% 	
OARETAEION HOSPITAL University of Cyprus, Medical Informatics Laboratory	

Treatment ☐ In the past IUA were treated with curettage (D&C) to break up the synechiae. Of course this is an obsolete and wrong way of todays standard care of treatment ☐ Hysteroscopy is the best tool for accurate diagnosis and simultaneous treatment / lysis of □Offers direct visualization, evaluation of the severity of the case and excision Diagnostic hysteroscopy for IUA Evaluate the □Degree of adhesion formation ☐ Deformity of the uterine cavity ☐ Pay attention to small adhesion openings and □ possible flow of tiny fragments and tissue debris might lead you to anatomic landmarks (ostia, myometrium) (Van Belle Y et al textbook 2004) University of Cyprus, Medical Informatics Labora Ways to avoid false route and uterine perforation during resection of IUA Hysteroscopic resection of IUA is a very high risk of creating false routes and uterine perforation Concomitant use of US / laparoscopy / X-ray imaging with contrast / fluoroscopically guided approach (Chason RI et al Fertl Ster 2008) > US is of great help especially to identify the distance to the fundus Laparoscopy is of great help especially in the area of the ostia whereas hysteroscopic transillumination can be detected and guided accordingly > Laparoscopically injecting the uterus with methylen blue dye may help to identify the junction at which the anterior and posterior walls are adhered

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Hysteroscopic technique Strategy for cutting IUA adhesions

- > First cut filmy and central adhesions
- > Follow the fluid flow
- ➤ Marginal and dense adhesions cut last
- ➤ Maintain the hysteroscope in mid-channel axis relative to the uterine walls
- ➤ Bleeding usually occurs when you operate between adhesions and myometrium



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Tools to be used for IUA lysis

- $\hfill \square$ Use the smallest diameter operative hysteroscope available
- ☐ Continuous flow
- lacksquare Do not try to break the adhesions with the scope
- ☐ For adhesion lysis can be used

Cold Scissors

HF electrical energy – Bipolar / Versapoint etc Nd:YAG laser



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Most important tips

- > Select the patient / according to your experience and set up
- > Operate with patience
- > Use cold scissors, it is the best option (tanctile feeling, more precise, dissection is possible)
- > except in cases with very hard adhesions/ calcifications
- ➤ Simultaneous use of US / Laparoscopy
- $\operatorname{\hspace{1pt} extstyle Try}$ to identify and reach the endometrium / myometrium cleavage
- > Try to keep the correct orientation identify the ostia if possible





Preventive measures for recurrent adhesions Following hysteroscopic adhesiolysis	-
➤ Application of intrauterine device (IUD) * ➤ A pediatric Foley catheter (3ml balloon dilatation	
for 7 days) *	
Usage of anti-adhesive agents as a distending medium (Adept) during hysteroscopic surgery or as a hyalobarrier gel at the end of the operation (under research)	
* Nowadays are abandoned proved to be inefficient	
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Pre & Post operative care	
☑A broad spectrum antibiotic is started preoperatively and maintained for 10 days	
✓ An inhibitor of prostaglandin synthesis can be	
used if uterine cramping is a problem	
☑The patient is treated for 2 months with high	
doses of estrogen (conjugated estrogens 2-6	
mg daily for 3 -4 weeks with progesterone added during the third week	
added daring the tima week	
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	i I
Operation success	
ি Regain of menstruation cycle (43-67%)	
☐ To achieve a pregnancy / delivery of a baby (28-43%)	
When an initial attempt fails to re-establish menstrual flow, repeated attempts ARE WORTHWHILE even upto x 5 (Fernadez н 2008)	
Persistent treatment with repeated procedures may be necessary to regain reproductive potential	
라 Approximately 70-80% of patients with regaining menses can achieve a successful pregnancy (Speroff)	
(ACIX)	
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Review of the literature

	Cases Number	Method Used	Preg Rate %	Live Birth %	Complications
Robinson JK et al 2008	24	blunt	46	46	non
Yu D et al 2008	85	HF energy	46	38	Uterine Perforation 0.9% Adhesion Regenera 28%
Fernadez H et al 2006	64	Monopolar 31 Bipolar 40	44	33	Adhesion Regener 45% Placenta acreta 3 pts
Zikopoulos et al 2004	47	Resectosc 21 Versapoint 26			Adhesion Regenerat 6%

Technological improvements, increasing knowledge and experiences in the last 10 years seems that raised the treatment efficacy of IUA, increasing the chances for menses restoration and pregnancy as well as live birth deliveries



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The efficacy of IUA Resection is corelated to patient's age

- Among 71 patients studied
- 31 patients needed only 1 operation
- 20 needed 2 operations
- 15 needed 3 operations
- 5 needed 4 operations
- Patients with age < 35 Pregnancy rate was 67%
- Patients with age > 35 Pregnancy rate was 24%

Fernadez H et al. J Minim Invasive Gynecol. 2006 Sep-Oct;13(5):398-402



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Pregnancy after IUA treatment is frequently complicated

- ⊕ spontaneous abortion
- **⊕ IUGR**
- ⊕ by premature labor
- placenta accreta
- placenta praevia
- ⊕ uterine rupture (Shiau CS et al CGMJ 2005)
- © postpartum haemorrhage (YuD et al Fertil Steril 2008)



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⊚ Thank U!!!	
Operation Upperstant Community Medical Information Inhomotory	

Hysteroscopic treatment of uterine congenital malformations and fertility outcome

Marco Gergolet, MD, MSc PCC 9 25° ESHRE ANNUAL MEETING AMSTERDAM

Congenital uterine anomalies Prevalence

A critical analysis of studies from 1950 to 2007, done with different diagnostic tools :

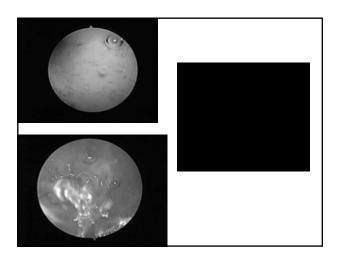
- Most accurate diagnostic procedures: hysteroscopy + laparoscopy sonohysterography (SHG) 3D ultrasound
- Less accurate tools: 2D US, and HSG

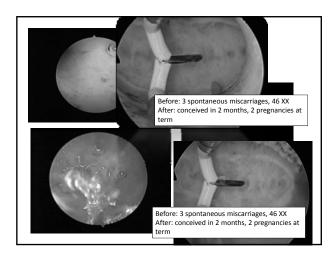
The study found a 6.7% prevalence of congenital uterine anomalies in the general population, 7.3% in the infertile population and 16.7% in the RM population.

The arcuate uterus was the commonest anomaly found in the general and RM population.

Septate uterus was the commonest anomaly found in the infertile population

(Saravelos Hum Rep Update 2008)





Prevalence of congenital uterine malformations General population

Author	Method	Anomalies (%)
Raga 1997	HSG, HSC	3.8
Acién 1997	Vag. US, HSG	4.6*, 7.8**, 16.7***
Jurković 1997	3D US	5.4
Maneschi 1995	HSC	10
Nasri 1990	US	2.7

*:Previous term pregnancies, **: previous pregnancies and some miscarriage, *** nulligravidae

Prevalence of congenital uterine malformations Infertile population

Author	Method	Incidence %
Tulandi 1980	HSG	1.0
Sorensen 1981	HSG	23.9
Raga 1996	HSG, Vag. US, 3D US	26.2
Acién 1997	HSG, Vag. US	16.0

Prevalence of congenital uterine malformations RM population

Author	Method	Incidence %
Clifford 1994	HSG, Vag US	1.8
Jurković 1995	HSG, Vag. US, 3D US	19.7
Raga 1997	HSG, HSC, LAP	6.3
Acién 1997	HSG, Vag, US	25.4

Prevalence of different types of uterine malformations

Author	Method	Arcuate %	Septate %
Exalto 1978	US, Lap	4	40
Acién 1996	Vag US, HSG	27.1	17.1
Raga 1997	HSG, HSC	32.8	33.6
Vercellini 1999	HSC	8.1	54.2

AFS Classification

AFS Classification

Class I segmental agenesis and variable degrees of utervoaginal hypoplasia.

Class It unicornuate uteri (partia or complete unilateral hypoplasia).

Class III: unicornuate uteri (partia or complete unilateral hypoplasia).

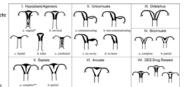
Class III: uterus didelphys (duplication of the uterus results from complete onoffusion of the muellerian ducts.

Class IV: biornuate uteri with incomplete fusion of the superior segments of the uterovaginal canal.

Class IV: Septate uterus, the external shape of the uterus is a single unit. (distinct from the biocrnuate uterus which can be seen branching into two distinct horns when viewed from the outside).

outside).

Class VI: Arcuate uterus. The uterus is essentially normal in shape with a small, midline indentation in the fundus which results from failure to completely dissolve the median septum



The American Fertility Society 1988

TELINDE'S OPERATIVE GYNECOLOGY MODIFIED CLASSIFICATION

(BASED ON EMBRIOLOGIC CONSIDERATION)

This classification consider only complete septum or partial. The term "arcuate uterus" has been abandoned, considered to be a radiologic diagnosis



TeLinde's Operative Gynecology 2003

TELINDE'S OPERATIVE GYNECOLOGY MODIFIED CLASSIFICATION

(BASED ON EMBRIOLOGIC CONSIDERATION)

Class I: Dysgenesis of Muellerian Ducts: includes agenesis of uterus and vagina (Mayer –Rokitansky-Kuester- Hauser syndrome)

Class II: Disorders of the Vertical Fusion of the Muellerian Ducts: transverse vaginal septum, cervical

agenessa of ungenessa Class III: Disorders of the Lateral Fusion of the Muellerian Ducts: can be symmetric – unobstructed or assymmetric - obstructed. Obstructive forms associated with absence of ipsilateral kideny. Bilateral obstruction associated with bilateral kidney agenesia- nonviability of the embryo.

Three asymmetric obstructions

Unicornuate uterus, Unilateral obstruction of a cavity of double uterus, Unilateral vaginal obstruction

Five symmetric unobstructed disorders

Didelphic ut., Septate ut., Bicornuate ut., T shaped and unicornuate with rudimentary horn

Class IV: Unusual Configuration of Vertical - Lateral Fusion Defects: unusual configuration of

TeLinde's Operative Gynecology 2003

WHICH IS THE BEST DIAGNOSTIC TOOL?

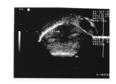
HSG: Characterization of uterine anomalies can be difficult, however, expecially regard to differentiation of a septate from a bicornuate uterus

(Pellerito 1992)

Vaginal US: reported accuracy of approximately 90%–92%

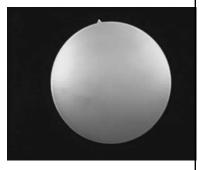
(Pellerito 1992)





Diagnostic "office" hysteroscopy

- Visual confirmation of US findings
- Elective in case of uncertain ulstrasound
- •High compliance of patients. No need of anesthesia or analgesia.



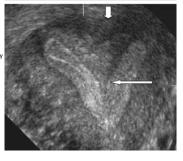
3D US

3D ultrasound is a reproducible method for the diagnosis of congenital uterine anomalies and for the measurement of uterine cavity dimensions.

(Salim et al. 2003)

In experienced hands, a sensitivity of 93% and a specificity of 100% have been achieved

(Kupešić and Kurjak 2000)



MRI

Magnetic resonance (MR) imaging has a reported accuracy of up to 100% in the evaluation of muellerian duct anomalies (Fedele et al. 1989)

Complex anomalies and secondary diagnoses such as endometriosis can often be optimally characterized noninvasively. (Troiano and McCarty 2004)





WHEN	IN	NFCF	SSΔRY	TO	TRFAT?
VVIILIV	114	IAFCE	JJAILI	10	11112

When in necessary to treat?

Pregnancy outcome in untreated patients

Pregnancy outcome after metroplasty

Author	Miscarriage	Preterm d.
Fayez 1986	90.5 %	9.5 %
Perino 1987	88.9 %	11.1 %
Daly 1989	86.7 %	8.7 %
Grimbizis 1998	31.7 %	14.5 %

Author	Miscarriage	Preterm d.
Perino 1987	9.1 %	0 %
Daly 1989	20.2 %	6.0 %
Fedele 1993	15.2 %	15.2 %
Grimbizis 1998	25.0 %	4.5 %

Author	N. cases	Conclusions
Heinonen et al 2000	17	Women with uterine anomalies who underwent ART had low implantation rates
Pabuçcu et al 2004	61	11% spontaneous misc. after metroplasty (9 cerclage)
Dendrinos et al. 2005	411	Treatment significantly reduced the miscarrage rate
Pace et al.2006	40	75 % spontaneous pregnancy aceived
Kormanyos et al. 2006	94	Removal even of small residual septa > 1 cm after metroplasty
Ban & Tomaževič et al 2007	31	Resection of <i>small</i> uterine septa, improves implantation rate in IVF cycles.

Uterine anomalies rationale for treatment

The distortion of uterine anatomy is more severe in congenital anomalies, which are found in women with a history of recurrent first trimester miscarriage.

The degree of distortion of uterine architecture was quantified by the ratio F/F+C, where F was the length of the uterine septum or depth of the fundal indentation and C was the length of the remaining uterine cavity

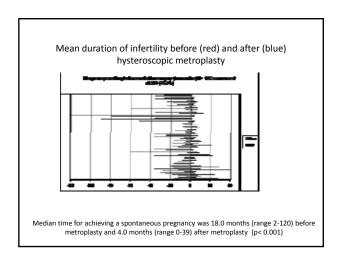
(Salim et al 2003)

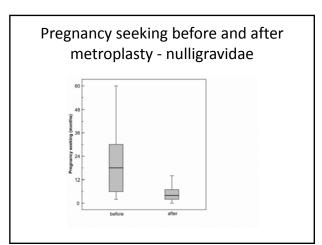


- F: lenght of septum
 C lenght ot remaining cavity

AIM OF THE STUDY

Aim of the study was to verify whether hysteroscopic metroplasty could be advantageous in treatment of primary and secondary infertility in term of shortening of pregnancy seeking time and reduction of spontaneous miscarriage rate.





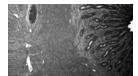
Outcome	Larger septum (Group 1) n.= 204		Smaller septum (Group 2) n.= 84	
	Before metroplasty	After metroplasty	Before metroplasty	After metroplasty
Pregnancy seeking Months (median and range)	18 (2-120)	4.9 (0-40)	18 (3-108)	4.4 (1-25)
Pregnancies	157	150(137 women)	52	59 (55 women)
Deliveries	32 (20.4 %) a	121 (80.7 %) b	6 (11.5 %) c	51 (86.4 %)d
Abortions	118 (75.2%)	25 (16.7 %)	39 (75 %)	8 (13.6 %)
Ectopic	7 (4.5%)	4 (2.7 %)	7 (13.4 %)	0

Statistics

	Group 1, before vs. after metroplasty	Group 2, before vs. after metroplasty	Before metroplasty, Group 1 vs. Group 2	After metroplasty, Group 1 vs. Group 2
Pregnancy seeking duration (Mann Whitney test)	p < 0.001	p < 0.001	n.s.	n.s.
Pregnancy failure rate (χ ² test)	p < 0.001	p < 0.001	n.s.	n.s.

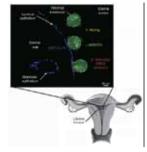
WHY SEEMS TO BE INDIPENDENT FROM THE SIZE? MRI ULTRASTRUCTURE • MRI intensity similar to myometrium(Carrington et al 1990 ENDOMETRIUM COVERING SEPTUM • Fedele described a morphologicalalteration of mucosa covering the septum (Fedele et al. 1996).

VASCULARIZATION



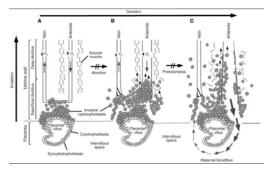
• Increased miscarriage rate could be consequence of a disrupted vascular architecture within septa (Fayez et al 1986)

ROLLING AND TETHERING



The mechanism of the trophoblast invasion has analogies with the rolling and tethering of leucocytes on blood vessels. (Red-Horse et al. 2004). Could be that septum covering endometrium cannot express ligands such MECA 79 recognized antibodies that recognize L selectin expressed on blastocyst surface (Red-Horse et al. 2004

INVASION OF UTERUS



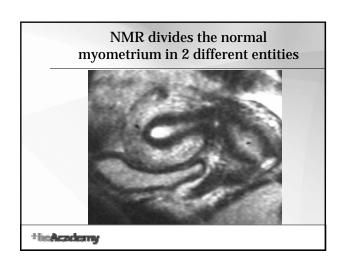
CONCLUSION Uterine congenital anomalies seem to be an important factor of pregnancy failure and metroplasty seems to improve dramatically the outcome of pregnancies. In front of the benefit of favourable pregnancy outcome after metroplasty, at least vaginal ultrasound should be performed in all cases with history of spontaneous abortion. In case of positive US, office diagnostic hysteroscopy should be performed even after first abortion. **CONCLUSION** The long duration of infertility before surgery, absence of other factors to explain their not conceiving, and short time interval subsequent to surgery in which conception occurs, suggests metroplasty has value in treatment of patients with septa and otherwise unexplained infertility **CONCLUSION** No differences have been found between women with large septa and those with arcuate uterus either in the obstetric anamnesis before metroplasty or in the outcome after metroplasty. Further studies are needed to assess why the

mechanisms that lead to miscarriage seem to be independent

from the size of septum.

HOME Hysteroscopic Operative Myometrial Exploration in the infertile patient? Rudi Campo, MD Leuven Institute for Fertility and Embryology LIFE Leuven - Belgium ESHRE, 25th annual meeting Amsterdam, June 28–July 1, 2009

Is the myometrium a homogeneous smooth muscle mass? Normal myometrium is seen as a homogenuous structure in ultrasound



Myometrium 2 structural entities small central zone of increased density Larger outer hypodenser zone

THE JUNCTIONAL ZONE

Different structure and function



high nuclear/cytopl. ratio decreased extracellular matrix low water content

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Junctional Zone Myometrium

Functional important entity in reproduction

- Ontogenetically related to endometrium
- Cyclic changes in SSH receptors
- Role in gamete transport and implantation
- Early changes from time of implantation

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Junctional Zone Myometrium Important role in Reproduction

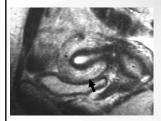
Functional important entity in reproduction

- Early changes from time of implantation
- Decidualisation and trophoblast invasion
- Defective transformation of JZ spiral arteries in spectrum of pregnancy complications

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THE OUTER MYOMETRIUM

Less important role in reproduction

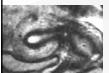


Muscle contractions during delivery

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Junctional Zone Pathology

Myoma







Normal JZ

JZ laesion

Outer myometrium Laesion

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Junctional Zone Pathology Adenomyosis uteri Diffuse enlargement Normal JZ Focal lesion of Junctional zone *ineAcademy First line - ONE STEP - procedure HOME Ultrasound Exploration of Fluid Mini – Hysteroscopy sub endometrial Kontrast sonography myometrium low risk - low cost - high compliance +heAcademy $First\ line\ -\ ONE\ STEP-procedure$ Ultrasound $Fluid\ Mini-Hysteroscopy$ Kontrast sonography low risk - low cost - high compliance

Proper Uterine diagnosis?

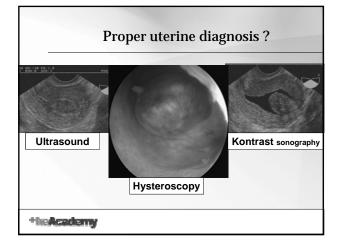
Ultrasound

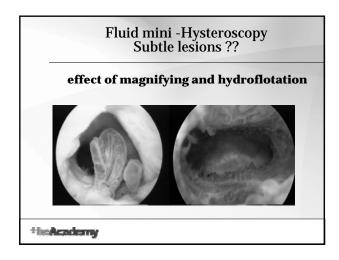
Distortion of homogenous myometrium? Myometrial thickness?

Hysteroscopy Cavity form? Subtle lesions?

Kontrast sonography Cavity form?

Measure Intracavitary laesions.





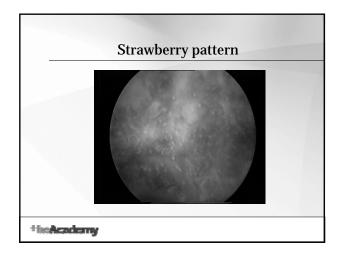
Subtle lesions

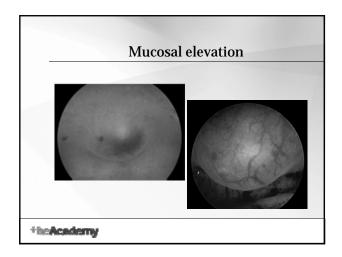
clinical significance unclear but could be associated with infertility.

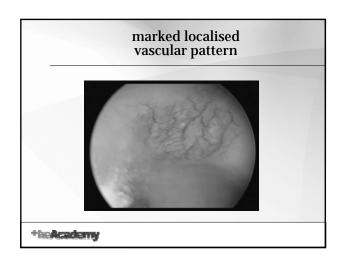
- > Diffuse polyposis
- > Strawberry pattern
- > Hypervascularization
- > Mucosal elevation
- > Endometrial defects
- > Others

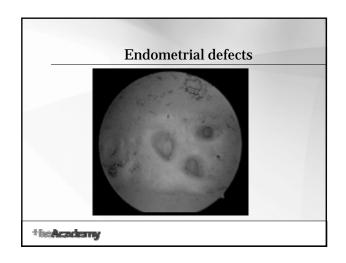
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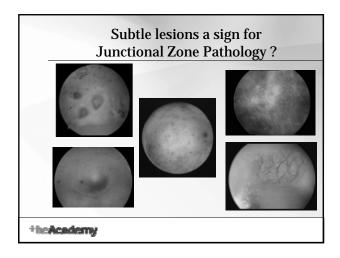
Diffuse polyposis











Proper Uterine diagnosis?

When do we have to enlarge the diagnosis

Ultrasound

Distortion of homogenous myometrium Increased myometrial thickness >15mm

Hysteroscopy

Endometrial defect Reddisch endometrium of unknown origin Subtle cystic lesions Localised vascular pattern

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How to enlarge diagnosis?

NMR

Diffuse enlargement of uterine wall

Subtle endometrial lesions with normal ultrasound

номь

 ${\bf ``Hysteroscopic\ Operative\ myometrium\ exploration''}$

Subtle endometrial lesions.

Focal subendometrial lesion seen in ultrasound or MRI.

LIFE vzw. Leuven Institute for Fertility & Embryology



Hysteroscopic Operative Myometrial Exploration

4 important conditions

Ambulatory or office endoscopic unit

Watery (Saline) distension medium

Small diameter instrumentation with high optical quality

Atraumatic technique

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Ambulatory Endoscopic Unit

See and threat

Separate surgical room, Only sedation





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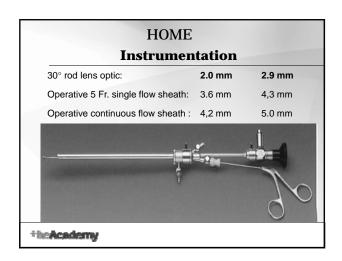
Watery distension medium

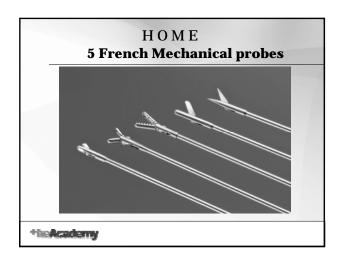


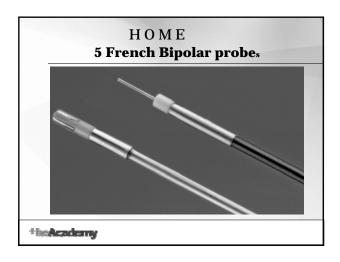
Grade A evidence Less painful!!

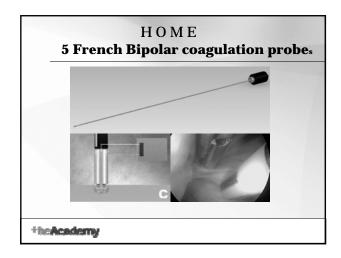
Hydro-flotation subtle lesions!!

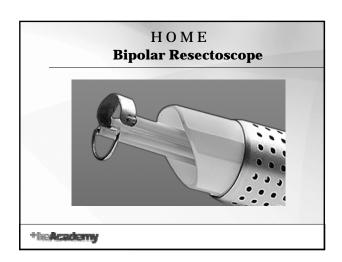
Saline for bipolar surgery

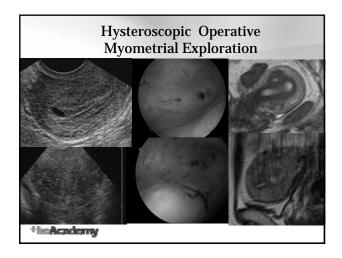






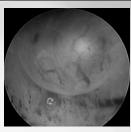






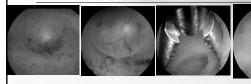
$$H\ O\ M\ E$$ Subtle lesions and adenomyosis ?

23-year-old patient of Indo-African origin with a primary infertility of 20 months . A cystic lesion is seen at HSC



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$H\ O\ M\ E$ Subtle lesions and infertility ?



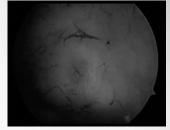
Pathology of subtle lesion seen at HSC revealed adenomyosis

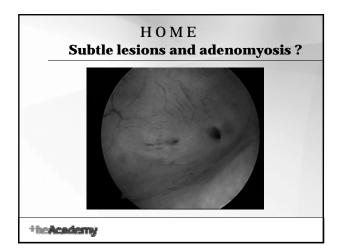
Spontaneous pregnancy occurred within 3 months after hysteroscopic removal of subtle lesion

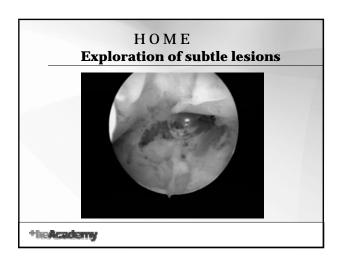
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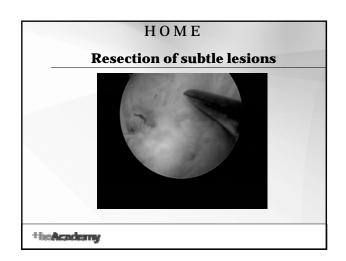
$H\ O\ M\ E$ Subtle lesions and adenomyosis ?

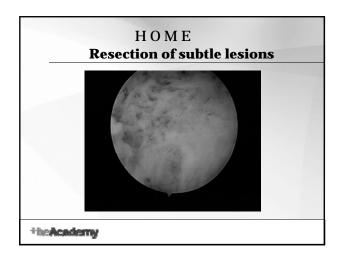


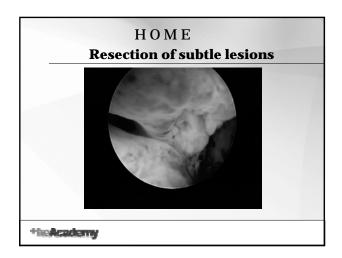


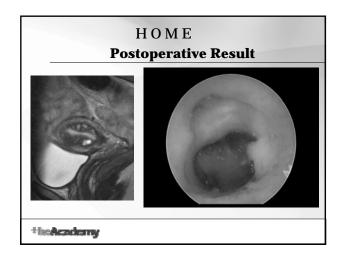


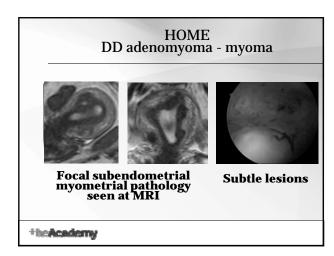


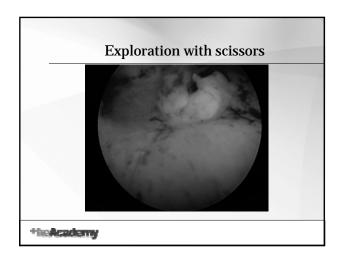


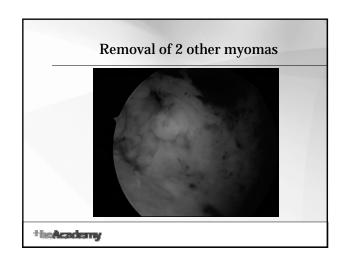




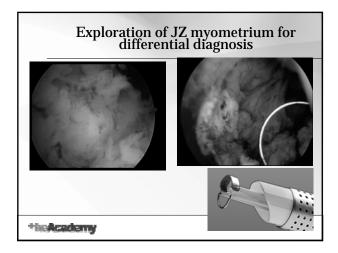








Exploration of JZ myometrium for differential diagnosis



Conclusions 1 Diagnostic fluid mini - hysteroscopy is an accurate tool with high visualisation capacity for subtle lesions. See and threat can be done in an ambulatory environment under conscious sedation.

Conclusions 2	
MRI divides the myometrium in	_
two structural and functional different zones.	
Especially in the field of reproductive medicine the	
exploration of the junctional zone myometrium seems	
an interesting idea.	
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Conclusions 3	
Mini Hysteroscopy in combination with ultrasound	
provides the possibility to enlarge the diagnostic	
procedure with a minimal invasive surgical act aiming	
an endoscopic inspection of the sub endometrial myometrium with resection of suspicious myometrial	
areas for histological examination.	
and the motions ground strainmanner.	
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Leuven Institute for Fertility &	
Embryology	
Rudi Campo	
Stephan Gordts Patrick Puttemans	
Roger Molinas Sylvie Gordts	
Marion Valkenburg Ivo Brosens	

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