

Behandeling van leiomyomen: nieuwe mogelijkheden

Wouter Froyman

Introductie

Myoomtypes
Echografische kenmerken
Differentiële diagnose

Wat is een myoom?

- Frequentste benigne uteriene tumor
- Monoclonale proliferatie van GSC, expressie ER en PR
- 50-60% vd ♀
- ~ toename leeftijd voor de menopauze, etnische afkomst
- ~ reproductieve en omgevingsfactoren
- 30% vd ♀ symptomatisch (AUB, druk, pijn, subfertiliteit), afhankelijk van leeftijd, aantal, grootte en positie



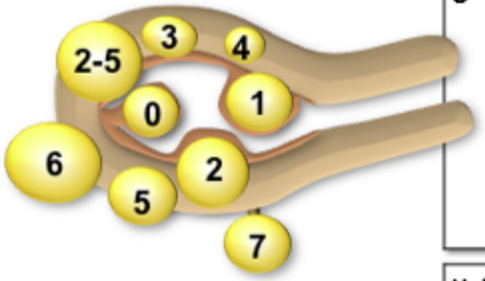
Donnez et al, Hum Reprod Update 2016

Types myomen

Polyp	
Adenomyosis	
Leiomyoma	→ **Sub**mucosal
Malignancy & hyperplasia	→ **O**ther

Coagulopathy
Ovulatory dysfunction
Endometrial
Iatrogenic
Not yet classified

Leiomyoma Subclassification System

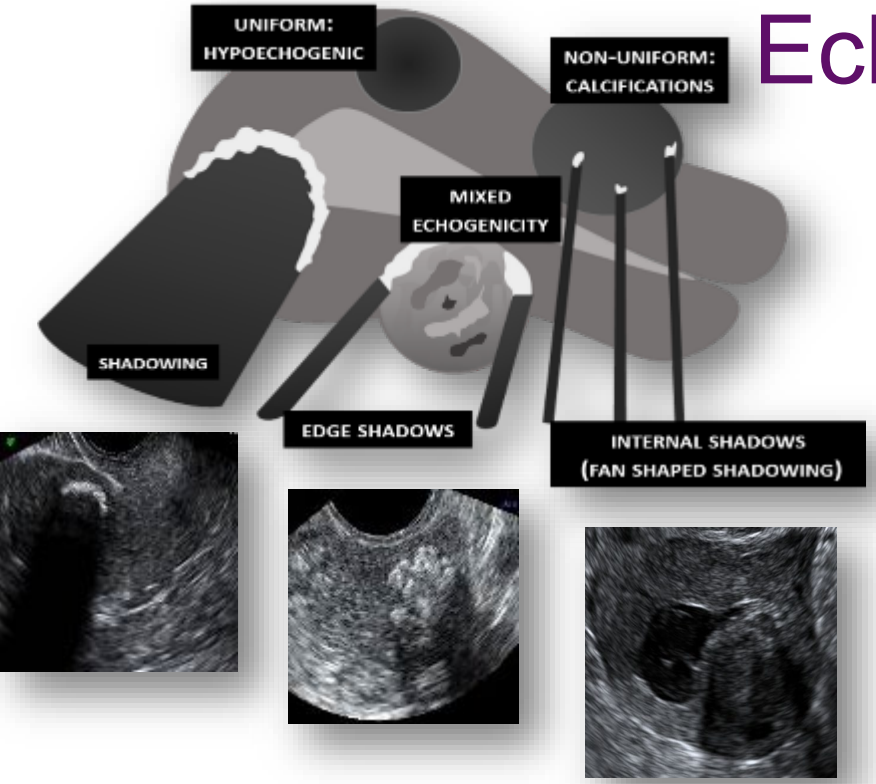


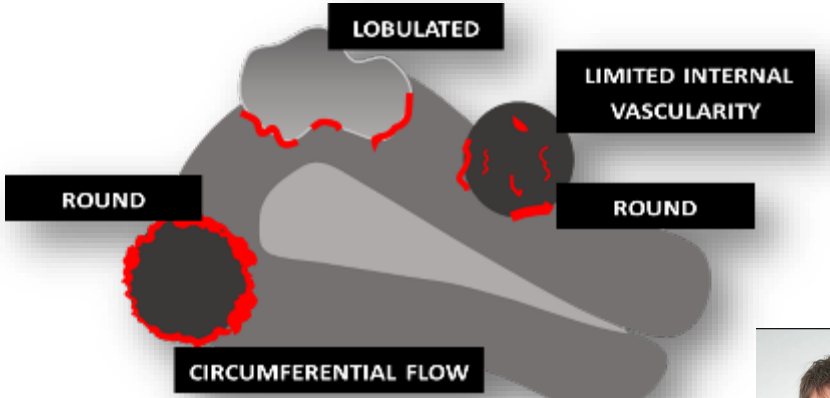
SM- Submucosal	0	Pedunculated Intracavitary
	1	<50% Intramural
	2	≥50% Intramural
O - Other	3	Contacts endometrium; 100% Intramural
	4	Intramural
	5	Subserosal ≥50% Intramural
	6	Subserosal <50% Intramural
	7	Subserosal Pedunculated
	8	Other (specify e.g. cervical, parasitic)

Hybrid Leiomyomas (impact both endometrium and serosa)	Two numbers are listed separated by a hyphen. By convention, the first refers to the relationship with the endometrium while the second refers to the relationship to the serosa. One example is below	
	2-5	Submucosal and subserosal, each with less than half the diameter in the endometrial and peritoneal cavities, respectively.

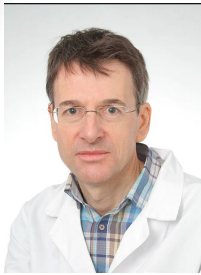
Munro et al, Fertil Steril 2011

Echografische kenmerken







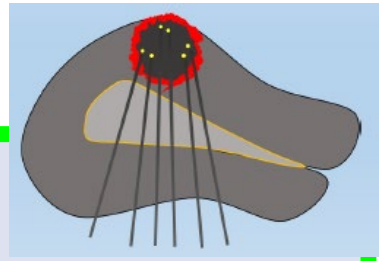


MUSA, Van den Bosch et al, UOG 2015

Differentiële diagnose

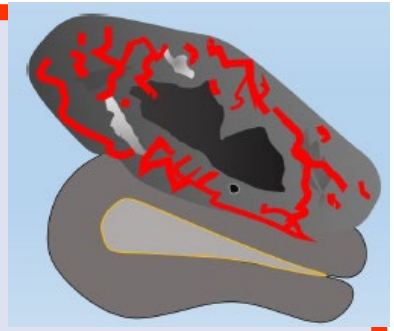


- Sarcoma



Benign features

Round lesion
Several lesions
Wide range of small and large lesions
Absence of central necrosis
Regular outline
Absence or limited growth (over a 3 month interval)
Low blood flow
Calcifications with shadowing

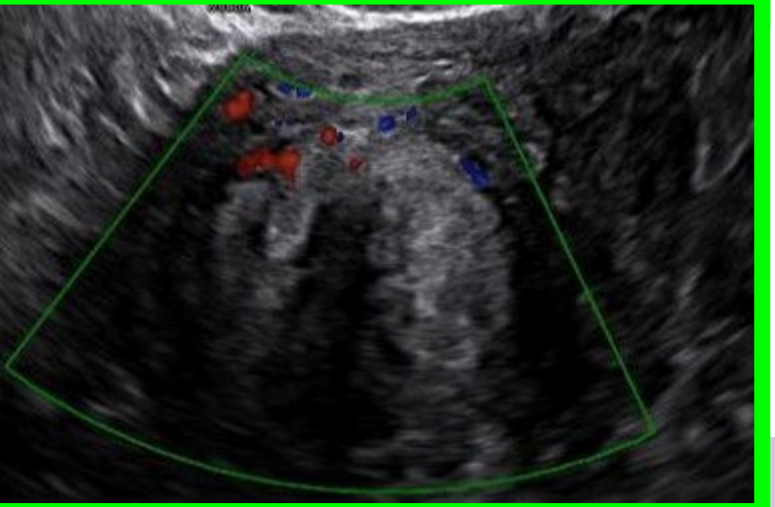


Suspicious features

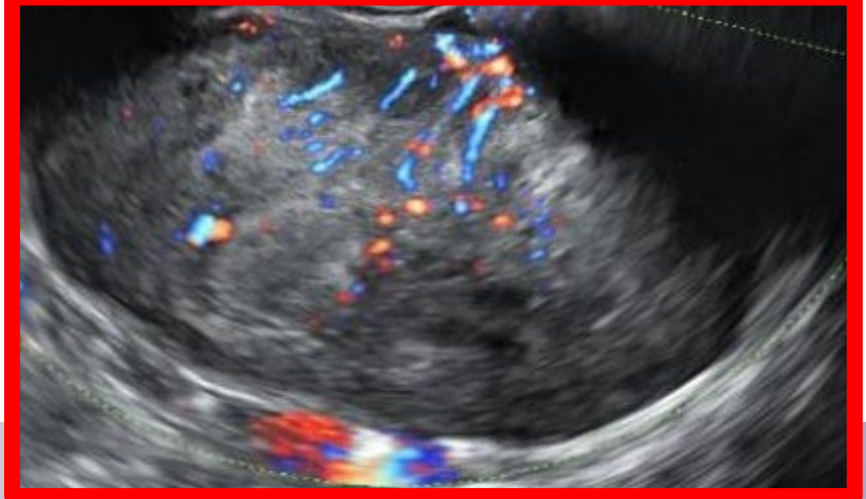
Oval lesion
One lesion
Large lesion
Central necrosis
Irregular or lobulated outline
Fast growth (over 3 months interval)
High blood flow
Absence of calcification and absence of shadowing
Atypical growth (postmenopausal, post-embolisation, and under gonadotropin-releasing hormone analogues)
Ovarian fibroma

Amant et al, Lancet Oncology 2015









Heeft het klinisch belang?

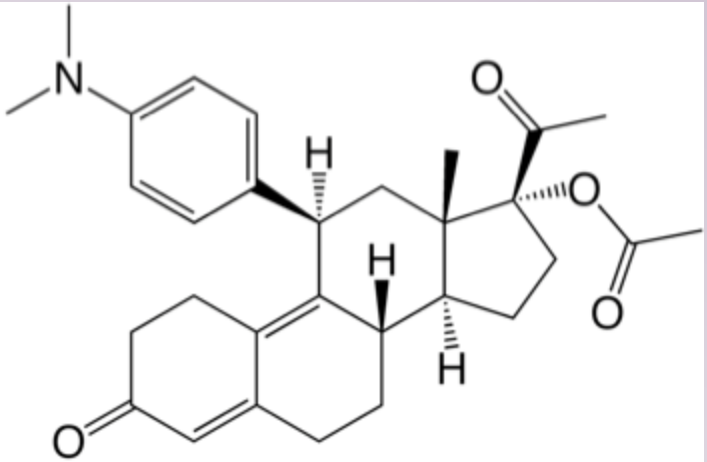
- Neen? (asymptomatisch, pte met actieve zs wens, peri-postmenopauzaal…)

→ **Conservatieve opvolging:** indien afwezigheid van klinische - echografisch alarmteken(s), stabiele ø

- **JA?**

→ **Behandeling afhankelijk van:** leeftijd, kinderwens, aard vd klachten, positie-grootte-aantal myomen, wens vd pte, comorbiditeit, etc…

Medicamenteuze therapie



- Niet-hormonaal
- Hormonale contraceptiva
- GnRH analogen
- PRMs

Niet-hormonale opties

- Tranexaminezuur: oraal antifibrinolyticum, 2 à 4,5 g pd[1]



- NSAID: ↓ menstruele pijn en bloeding[2]

[1]Bryant-Smith et al, Cochrane 2018; [2]Rodriguez et al, Cochrane 2019

Hormonale contraceptiva

- Eerste lijn, indien voornaamste symptoom menorragie - geen actieve kinderwens
- Uitz type 0-1 myomen
- Types:
  - LNG-spiraal (cave bij distorsie van de caviteit)[1]
  - Oestroprogestagenen[2]
  - Orale progestagenen[3]

NICE National Institute for Health and Care Excellence

[1]Lethaby et al, Cochrane 2015; [2]Lethaby et al, Cochrane 2019; [3]Rodriguez et al, Cochrane 2019

GnRH analogen

- Agonisten: triptoreline (Decapeptyl 3,75 mg [115€], Gonapeptyl 3,75 mg [3 inj 283€), gosereline (Zoladex 3,6 mg [132€]):
  - 3 (6) maanden, preoperatief of late perimenopauze
  - Inductie amenorree (Hb↑, +Fe), volumereductie (myoom-uterus → MIGS), perop outcomes ↑
  - Nevenwerkingen: hypo-oestrogene status R/ add-back therapie
  - Kosten: terugbetaling preop transhysteroscopische myomectomie

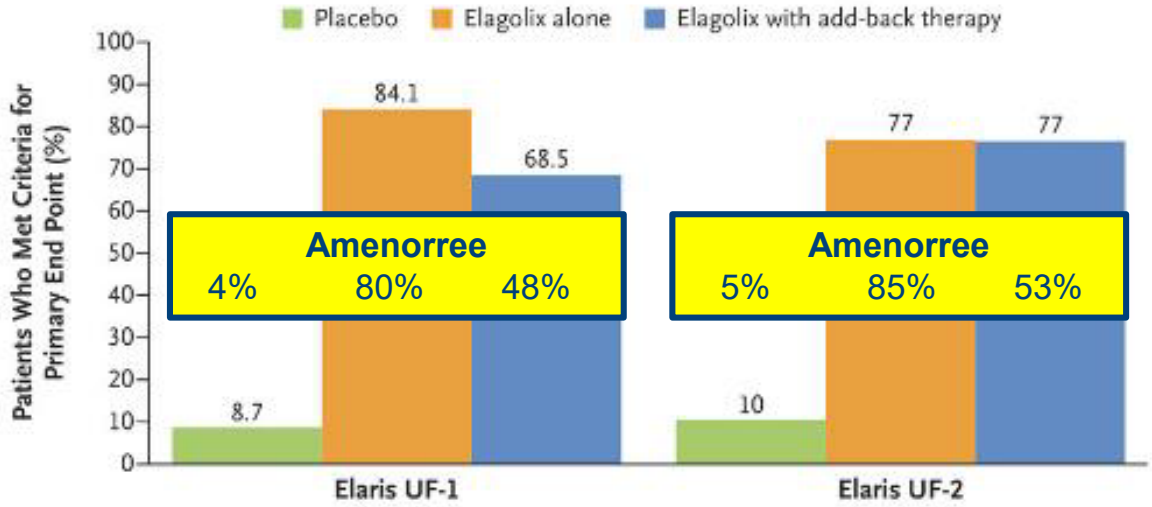


www.bcfi.be; Lethaby et al. Cochrane 2017

GnRH analogen

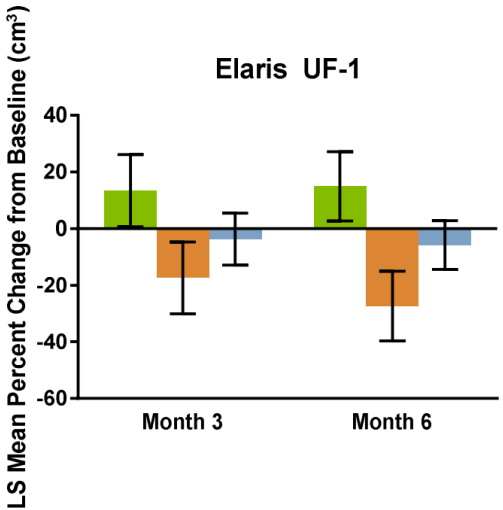
- Antagonisten:
  - *Elagolix 300 mg 2x/d PO 6m*





N=102 N=104 N=206
Totaal N=412

N=94 N=95 N=189
Totaal N=378



Schlaff et al. NEJM 2020

GnRH analogen



- Antagonisten:
  - *Elagolix 300 mg 2x/d PO 6m*

Veiligheid:

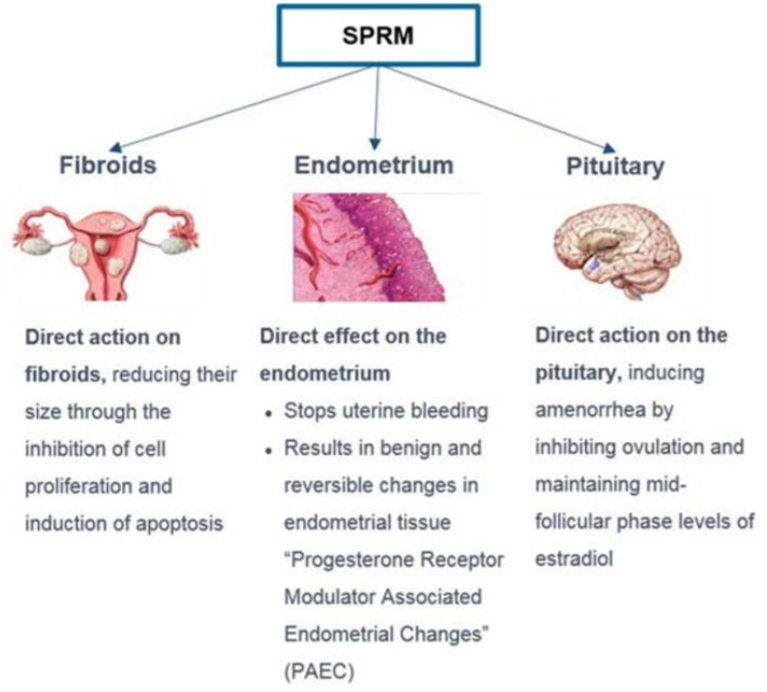
- Hot flushes: elagolix 64-43% vs elagolix/add-back 20%-20% vs placebo 9-4%
- Botdensiteit:
  - placebo vs elagolix/add-back geen verschil in gem % verandering
  - placebo vs elagolix alleen: significante vermindering
- Lipiden: stijging bij beide elagolix groepen, eerste drie maanden waarna stabilisatie
- Leverfunctie: 10 pten bij elagolix groepen met stijging transaminasen, zelflimiterend
- Endometrium-ovarium: geen hyperplasie of maligniteiten, geen nieuwe ovariële cysten

Schlaff et al. NEJM 2020

Progesteron receptor modulatoren (PRMs)

- Ulipristal acetaat (UPA):

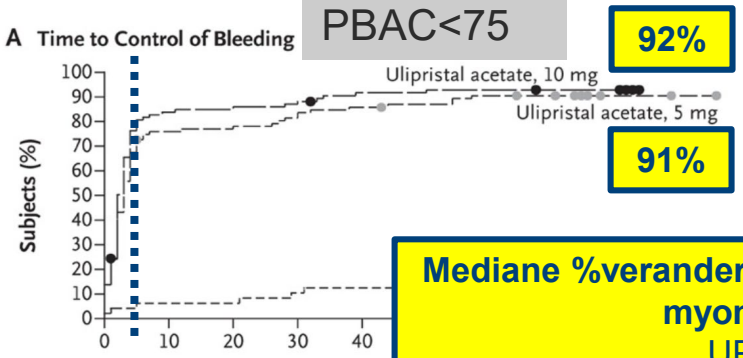






Donnez et al, Hum Reprod Update 2016

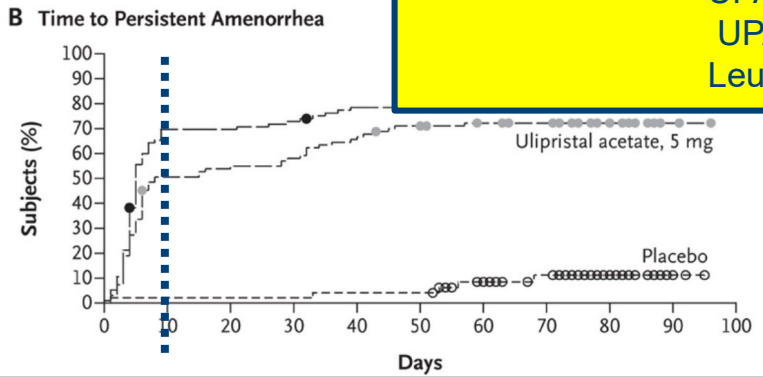
Progesteron receptor modulatoren (PRMs)



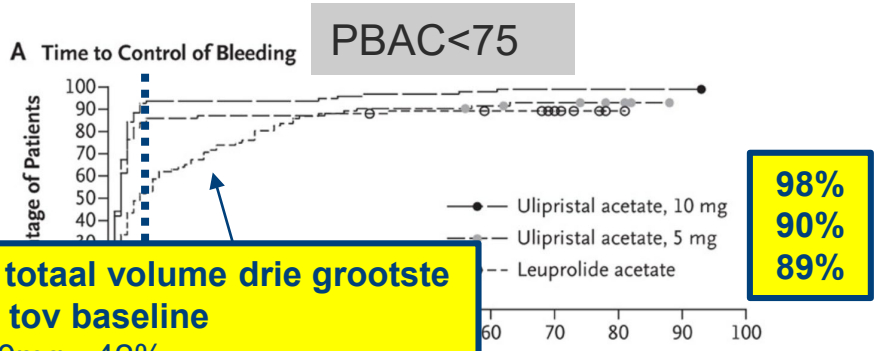
PBAC<75

92%

91%

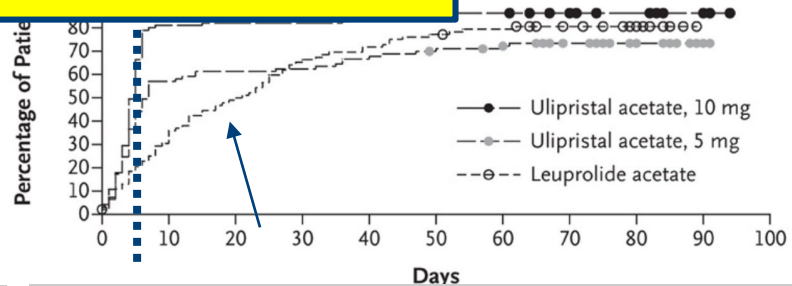


UPA 10mg N=98, UPA 5mg N=96, placebo N=48



PBAC<75

98%
90%
89%



UPA 10mg N=103, UPA 5mg N=97, leuprolide N=101

Mediane %verandering totaal volume drie grootste myomen tov baseline

UPA 10mg: -42%

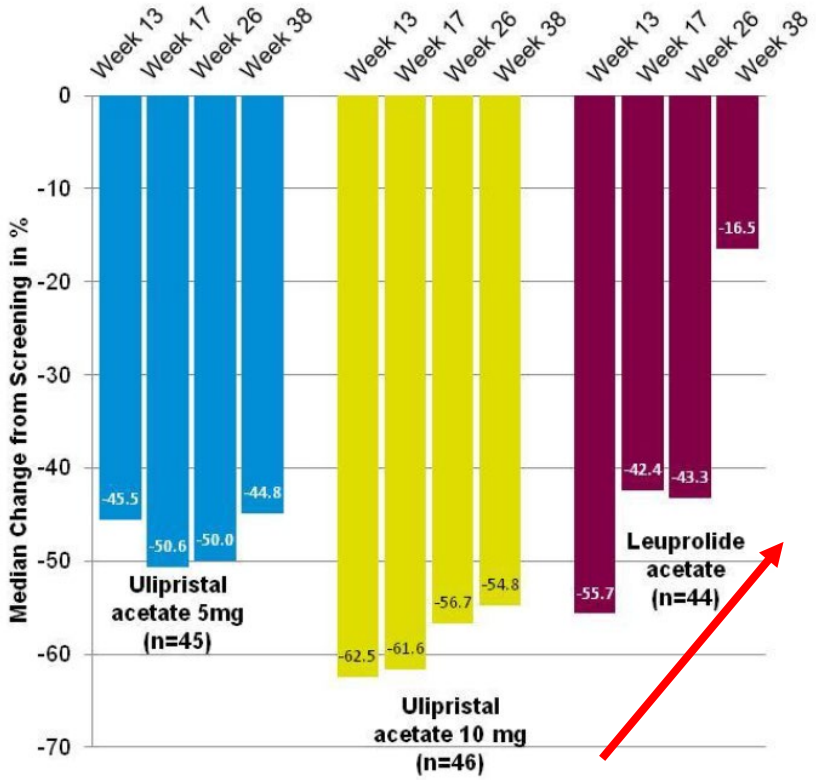
UPA 5mg: -36%

Leuprolide: -53%

PEARL I Donnez et al. NEJM 2012; PEARL II Donnez et al. NEJM 2012

Progesteron receptor modulatoren (PRMs)

Reductie myoomvolume 6m na stop behandeling (N=135, waarbij geen hysterectomie of myomectomie werd uitgevoerd)



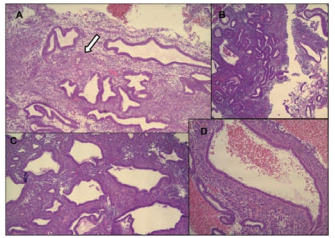
PEARL II Donnez et al. NEJM 2012

Progesteron receptor modulatoren (PRMs)

- Ulipristal acetaat (UPA):

Table 2. Key Efficacy End Points and Safety Outcomes at 13 Weeks for Ulipristal Acetate, as Compared with Leuprolide Acetate.*

Variable	Ulipristal Acetate		Leuprolide Acetate
	5-mg Dose	10-mg Dose	
Safety population			
No. of patients	97	103	101
Serum estradiol — pg/ml			
Median	64.0	60.5	25.0
Interquartile range	45.0 to 110.0	35.0 to 121.0	10.0 to 36.0
Geometric mean	78.8	69.7	24.0
Moderate-to-severe hot flashes — no. (%)	11 (11)	10 (10)	40 (40)
Endometrial thickness — mm	9.4±5.7	10.7±5.9	5.1±3.5



PAEC: +/- 60%
Niet premaligne
Reversibel

Hoofdpijn, mastalgie: geen verschil tussen UPA en leuprolide

PEARL II Donnez et al. NEJM 2012

Progesteron receptor modulatoren (PRMs)

Table 1 Benefits and side effects of long-term treatment with 5 mg ulipristal acetate for large fibroids associated with heavy menstrual bleeding

Population: A total of 228 premenopausal women aged 18–50 with moderate-to-severe symptoms of uterine fibroids (at least 1 fibroid >3 cm) treated with courses of ulipristal acetate (UPA) 5 mg/day (PEARL IV study), the only dose approved by the European Medicines Agency

	UPA 5 mg
Benefits	
• Amenorrhea	
≤1 day of spotting within 5 weeks	
After 2 courses combined	62%
After 4 courses combined	49%
• Controlled bleeding	
No heavy bleeding AND ≤8 days bleeding during the last 2 months of treatment	
After 2 courses combined	81%
After 4 courses combined	67%
• Change in 3 largest fibroids	
Median change in volume from baseline	
After course 2	54% smaller
After course 4	67% smaller
Side effects	
• Hot flushes	
After course 2	4%
After course 4	3%
• Breast pain/discomfort	
After course 2	1%
After course 4	1%
• Headache	
After course 2	6%
After course 4	2%

PEARL IV Donnez et al. Fertil Steril 2016

Progesteron receptor modulatoren (PRMs)

- Ulipristal acetaat (UPA): terugbetalingscriteria
  - 1 cyclus **preop** hysterectomie bij ferriprieve anemie of myomectomie bij FIGO type 3-6; indien 3-10 cm, PBAC >150
  - 2 cycli (4 cycli) **onvruchtbaarheid** tgv myomen; indien één myoom min 3 cm, of som min 5 cm
  - 4 cycli (8 cycli) **vruchtbaarheid behouden**; indien indien één myoom min 3 cm, of som min 5 cm; PBAC >150
  - 4 cycli (8 cycli) **perimenopauze**; indien indien één myoom min 3 cm, of som min 5 cm; PBAC >150 en/of dysfunctionele pijn en/of dysfunctionele druk in bekken

Progesteron receptor modulatoren (PRMs)

- Ulipristal acetaat (UPA):

Results: Two hundred and twenty-two women were recruited for the trial. The requirement for surgery decreased with the use of UPA, with 54% of women undergoing surgery after treatment. The reduction in surgery performed was lower for women willing to conceive (40%) compared to women who were not (49%). The volume of the fibroids decreased significantly, with the largest measured fibroid decreasing by 50%. Bleeding and pain were significantly decreased with the use of UPA. No major complications were recorded, and no liver function abnormalities were reported during the treatment and in follow-up.



Conclusion: By administering UPA, the required rate of surgery was significantly decreased. Also, the resulting reduction in size of the fibroids could have the potential benefit of reducing surgery-related complications, and long-term use may be warranted to avoid surgery completely.

Verguts et al. Int J Gynaecol Obstet 2019

Independent liver expert causality assessment of severe liver injury cases

- >765000 women treated with Esmya® worldwide
- 105 cases with liver dysfunction
- 34 severe cases with 8 where Esmya® may have contributed

Case number	Country	Patient age (y)	Results	Panel consensus	Confounding factors
1	Germany	38	Recovered	Unlikely	Confirmed autoimmune hepatitis, not DILI
2	Canada	54	Recovered	Unlikely	Concomitant medication, and inconsistencies in clinical versus chronologically reported symptoms
3	Canada	48	Recovered	Possible	Missing autoimmune data
4	Portugal	55	Liver transplantation	Possible	Concomitant Medications (cefuroxime)
5	France	58	Liver transplantation	Possible	Cirrhosis and potential autoimmune hepatitis in the background
6	Germany	46	Liver transplantation	Possible /probable (50%)	Hepatitis E not completely ruled out PRAC no other reasonable explanation
7	France	45	Liver transplantation	Possible /probable (50%)	Genomic effect of HHV6 (Atrophic liver (? chronic disease)

Consensus on the role of Esmya:
- possible/probable (50%) (n=2)
- possible (n=3)
- unlikely (n=2)

+ 1 case not assessable (8)

0.65/100,000

Esmya: new measures to minimise risk of rare but serious liver injury

EMA concludes review of medicine for uterine fibroids

On 31 May 2018, the European Medicines Agency (EMA) recommended that several measures be put in place to minimise the risk of rare but serious liver injury with Esmya (ulipristal acetate). Certain women may start treatment with Esmya once the new measures are implemented.

The measures include: contraindication in women with known liver problems; liver tests before, during and after stopping treatment; a card for patients to inform them about the need for liver monitoring and to contact their doctor should they develop symptoms of liver injury. In addition, use of the medicine for more than one treatment course has been restricted to women who are not eligible for surgery.

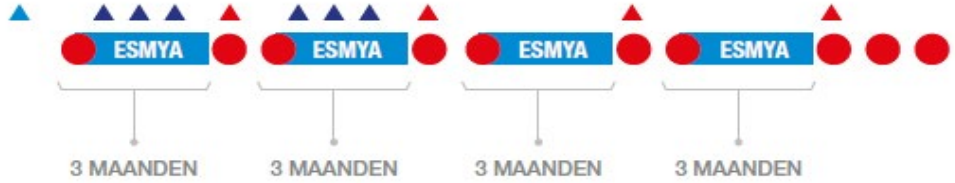
Esmya is used to treat moderate to severe symptoms of uterine fibroids (benign tumours of the womb). The medicine has been shown to be effective at reducing bleeding and anaemia associated with the condition, as well as the size of the fibroids.

ESMYA dosing schedule and liver monitoring

▲ **VOOR AANVANG VAN DE BEHANDELING**
de behandeling mag niet worden opgestart wanneer de transaminasen (ALAT of ASAT)* 2x de BGN overschrijden (alleen of in combinatie met een bilirubinewaarde > 2x BGN)**

▲ **TIJDENS DE BEHANDELING**
gedurende de eerste twee behandelcycli moeten er éénmaal per maand leverfunctietesten worden uitgevoerd. Stopzetting behandeling indien transaminasen (ALAT of ASAT)* > 3x de BGN

▲ **LEVERFUNCTIETESTEN**
- vóór elke behandelcyclus
- bij klinische indicatie
- 2 à 4 weken na het einde van elke behandelcyclus



▲ Leverfunctietest vóór de start van de behandeling
▲ Maandelijkse leverfunctietesten (alleen tijdens de eerste twee cycli)
▲ Leverfunctietest vóór elke nieuwe behandelcyclus en/of 2 à 4 weken na het einde van de behandeling
■ ESMYA éénmaal per dag
● Menstruatie

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Ulipristal acetate 5mg medicinal products

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CURRENT STATUS:
Under evaluation

Procedure started → **Under evaluation** → PRAC recommendation → CHMP opinion → European Commission final decision

Table of contents

- Overview
- Key facts
- All documents

Overview

Suspension of ulipristal acetate for uterine fibroids during ongoing EMA review of liver injury risk

On 12 March 2020, EMA's safety committee (PRAC) recommended women to stop taking 5-mg ulipristal acetate (Esmya and generic medicines) for uterine fibroids while a safety review is ongoing. No new patients should start treatment with the medicines, which will be temporarily suspended throughout the EU during the review.

EMA is starting its review at the request of the European Commission following a recent case of liver injury, which led to liver transplantation in a patient taking the medicine.

1 extra case van leverfalen
>900,000 gebruiksters
Advies van EMA verwacht in september 2020

Chirurgie

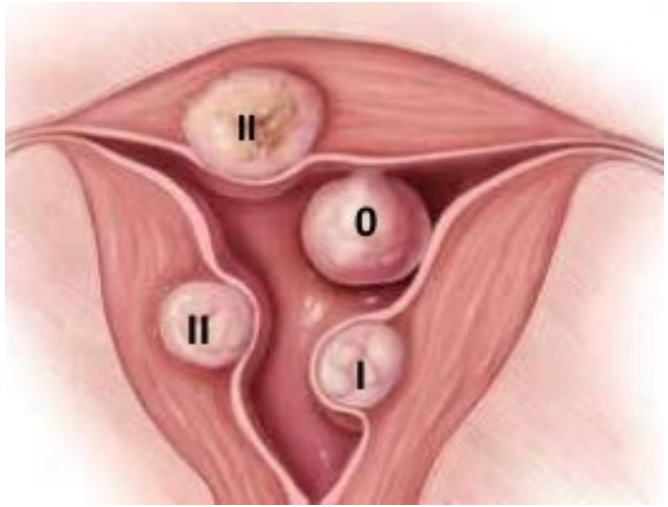


Myomectomie (hysteroscopie – laparoscopie – RALM – laparotomie)
Hysterectomie

Myomectomie

- Hysteroscopisch

+ aantal, myometriale vrije marge (MFM)



Wamsteker - ESGE

	Size (cm)	Topography	Extension of the base	Penetration	Lateral Wall	Total
0	< 2	Low	< 1/3	0	+ 1	
1	> 2 a 5	Middle	>1/3 - 2/3	< 50%		
2	> 5	Upper	> 2/3	> 50%		
Score	+	+	+	+	+	

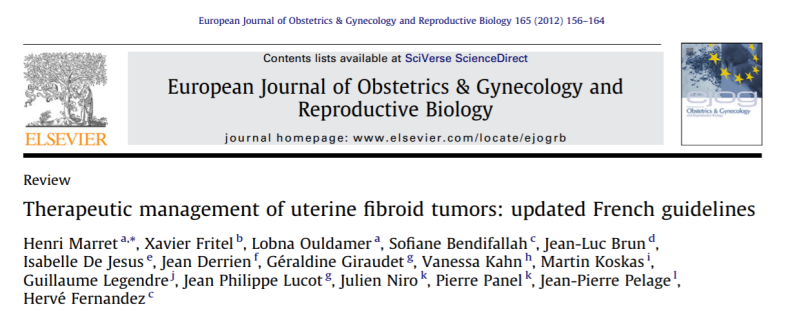
Score	Group	Complexity and therapeutic options
0 to 4	I	Low complexity hysteroscopic myomectomy.
5 to 6	II	High complexity hysteroscopic myomectomy. Consider GnRH use? Consider Two-step hysteroscopic myomectomy.
7 to 9	III	Consider alternatives to the hysteroscopic technique

STEPW Submucous fibroid classification

Wamsteker et al. Obstet Gynecol 1993, Lasmar et al. Fertil Steril 2011

Myomectomie

- Hysteroscopisch
  - AUB: resultaat afhankelijk van oa andere myomen, adenomyose, onvolledige wegname intramurale gedeelte; evt + ablatie[1] of LNG-spiraal
  - Subfertiliteit:



European Journal of Obstetrics & Gynecology and Reproductive Biology 165 (2012) 156–164

Contents lists available at SciVerse ScienceDirect

European Journal of Obstetrics & Gynecology and Reproductive Biology

journal homepage: www.elsevier.com/locate/ejogrb

Review

Therapeutic management of uterine fibroid tumors: updated French guidelines

Henri Marret[a,*], Xavier Fritel[b], Lobna Ouldamer[a], Sofiane Bendifallah[c], Jean-Luc Brun[d], Isabelle De Jesus[e], Jean Derrien[f], Géraldine Giraudet[g], Vanessa Kahn[h], Martin Koskas[i], Guillaume Legendre[j], Jean Philippe Lucot[g], Julien Niro[k], Pierre Panel[k], Jean-Pierre Pelage[l], Hervé Fernandez[c]

Hysteroscopic resection of submucosal fibroids < 4cm symptomatic & asymptomatic

Intramural fibroids: treatment does not improve fertility myomectomy if symptomatic

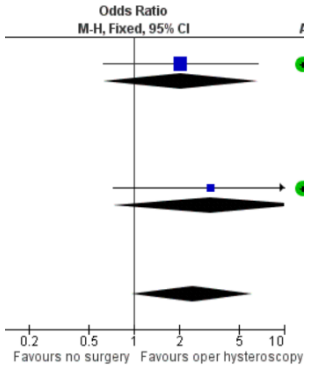
[1]Di Spiezio Sardo et al. Hum Reprod Update 2008; [2]Bosteels et al. Cochrane 2018

Myomectomie

- Hysteroscopisch
  - AUB: resultaat afhankelijk van oa andere myomen, adenomyose, onvolledige wegname intramurale gedeelte; evt + ablatie[1] of LNG-spiraal
  - Subfertiliteit:



Uncertainty remains concerning an important benefit with the hysteroscopic removal of submucous fibroids for improving the clinical pregnancy rates in women with otherwise unexplained subfertility[2]



[1]Di Spiezio Sardo et al. Hum Reprod Update 2008; [2]Bosteels et al. Cochrane 2018

Myomectomie

- Laparoscopisch – robotisch (RALM) – Laparotomie
  - Cut-off laparoscopie: 7-10 cm voor intramuraal myoma
  - RALM vs laparoscopie: gelijkwaardige perioperatieve uitkomsten ↔ langere duur ingreep, kostprijs
  - RALM vs laparotomie: ↓bloedverlies, ↓postop complicaties, ↓opnameduur
  - Geen evidentie voor verschil in fertiliteitsuitkomsten

  + extra voordeel: moeilijker bereikbare posterior myomen

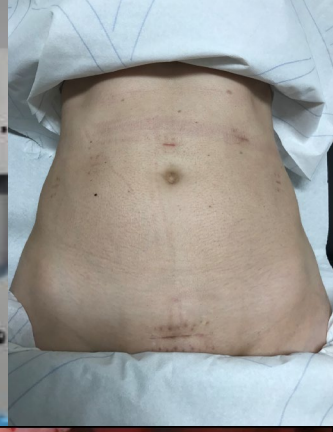
  → **Robot-geassisteerde chirurgie laat toe de grenzen van de minimaal invasieve chirurgie te verleggen**

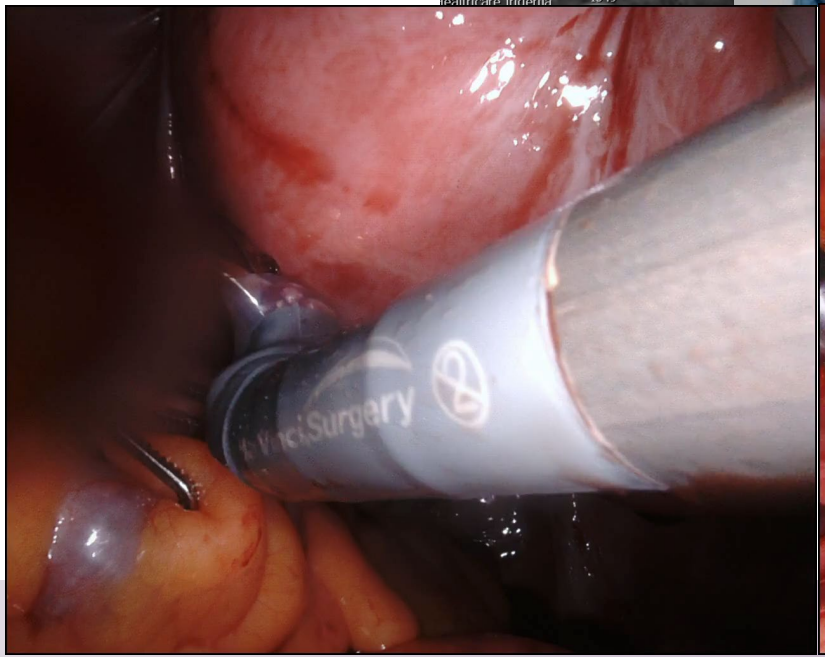
Lonnerfors, Best Pract & Research Clinical Obstet & Gynaecol 2018

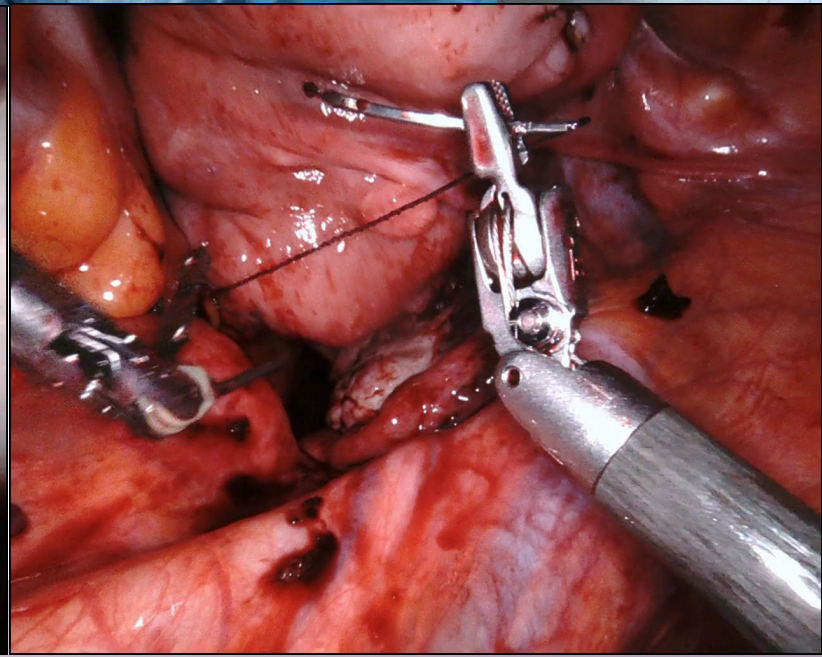
Myomectomie



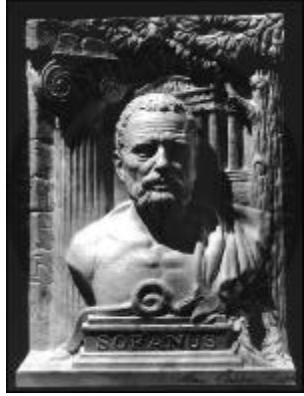






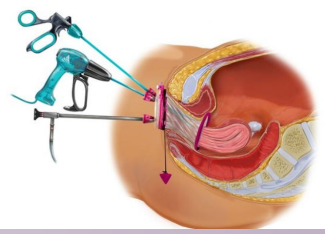


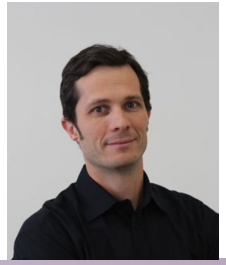
Hysterectomie



- Laatste lijn
- Eerste vaginale hysterectomie: Oude Grieken
  - Soranus van Efeze 120 na Christus, Themison van Athene 20 jaar voor Christus
- Eerste abdominale hysterectomie:
  - Charles Clay, Manchester, UK 1843
- LAVH, TLH, RALH, vNOTES







Embolisatie van de a. uterina



Arterial embolisation to treat uterine myomata

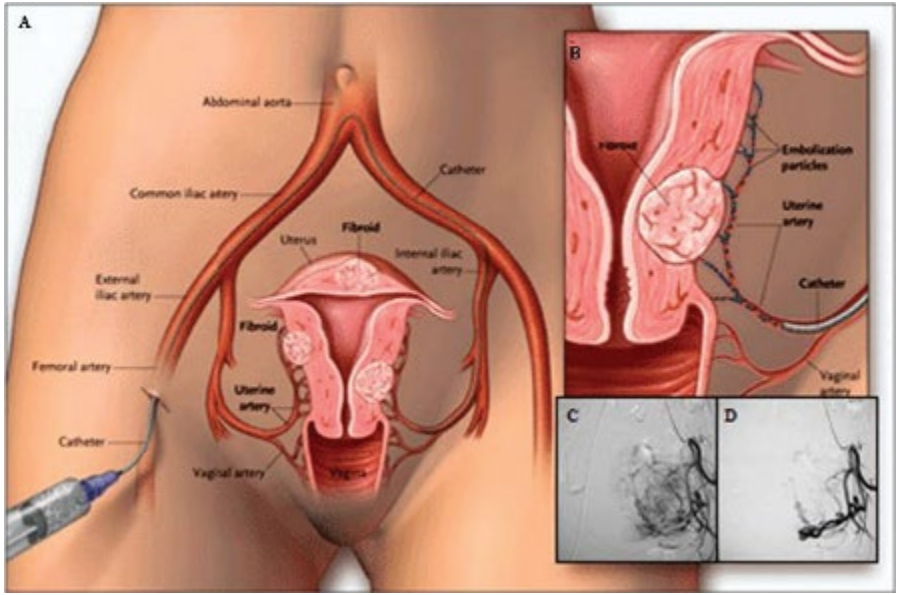
J H Ravina, D Herbreteau, N Ciraru-Vigneron, J M Bouret, E Houdart, A Aymard, J J Merland

Haemorrhage, probably related to hypervascularisation, is the commonest complication of uterine myomata and is difficult to treat. 16 patients, aged 34–48 years, with symptomatic uterine myomata, for which a major surgical procedure was planned after failure of medical treatment, were treated by selective free-flow arterial embolisation of the myomata with Ivalon particles. With a mean follow-up of 20 months (range 11–48) in the responders, symptoms resolved in 11 patients; menstrual cycles returned to normal in ten of these. Three patients had partial improvement. Two failures required surgery. In 14 cases embolisation caused pelvic pain, which required analgesia in all.

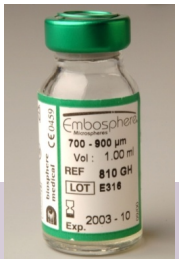
Lancet 1995; **346:** 671–72

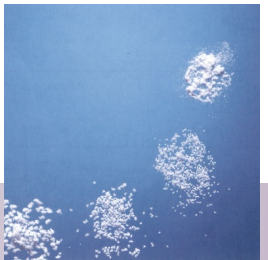


Embolisatie van de a. uterina

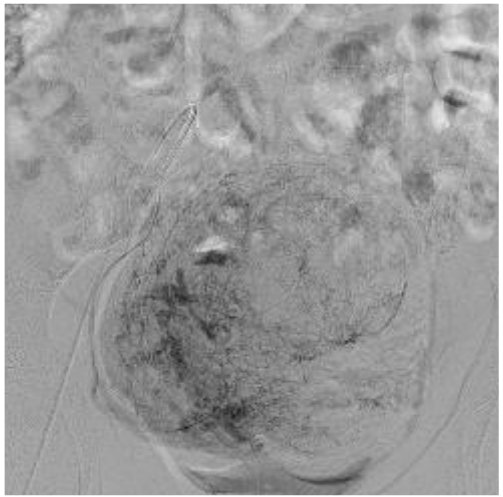


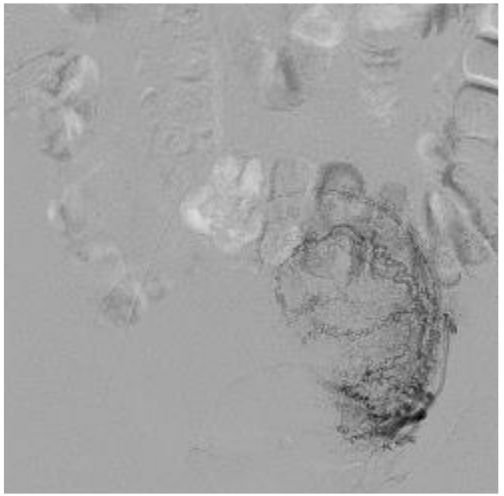


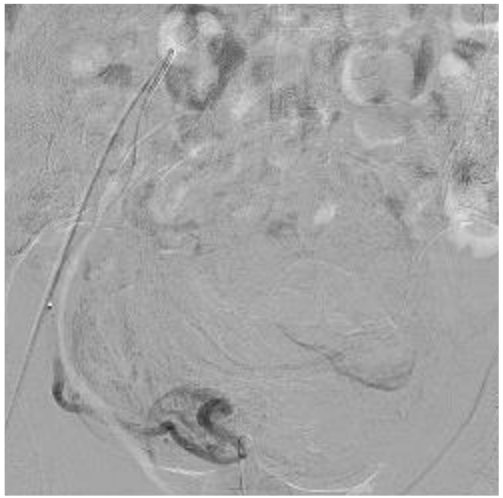


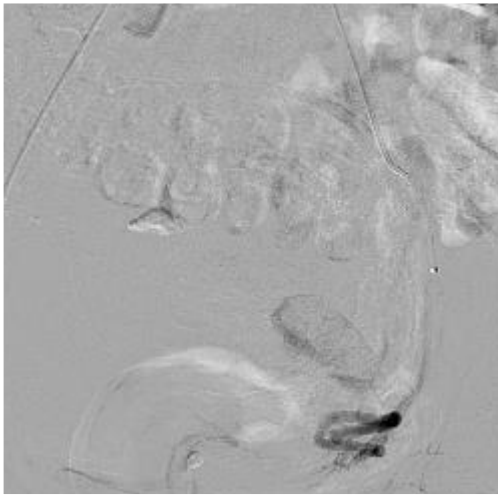


- Toegang via a. femoralis communis
- Polyvinyl alcohol partikels of Tris-acryl gelatine microsferen
- Occlusie/reductie van uteriene bloedflow arteriolair → irreversibele ischemie, necrose ↔ normaal endometrium

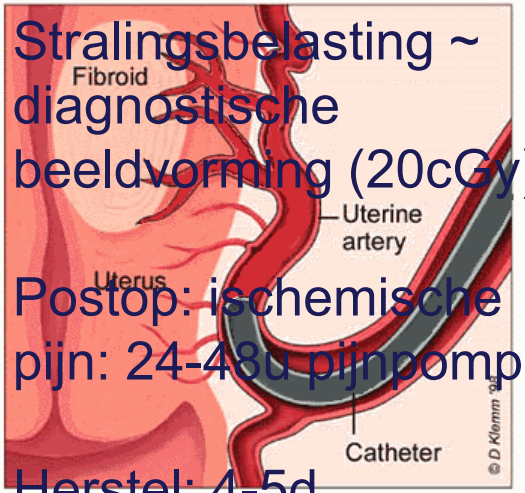








Stralingsbelasting ~ diagnostische beeldvorming (20cGy).



Postop: ischemische pijn: 24-48u pijnpomp.

Herstel: 4-5d baarmoederkrampen en embolisatiesymptomen (malaise, vermoeidheid, nausea en lichte T).

Hernemen normale activiteit na 8-14d.

Embolisatie van de a. uterina

Vrouwen met significante **symptomen** (cyclusstoornissen, pijn en/of druksymptomen) die duidelijk kunnen toegeschreven worden aan **fibromen**, en die anders chirurgische therapie zouden geadviseerd worden.

Contra-indicaties:

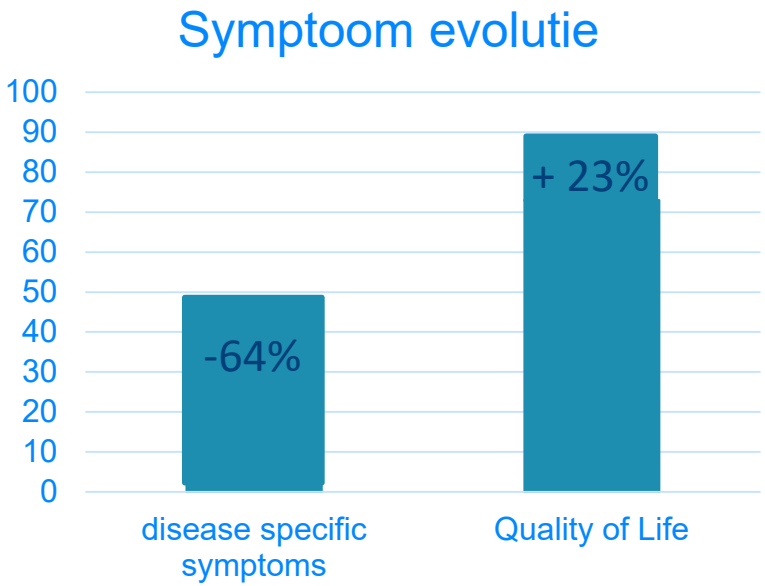
Absoluut: infectieuze pathologie, vermoeden van maligniteit, proceduregebonden (contrastallergie, stollingsaandoeningen, nierinsufficiëntie); indien hysterectomie volledig wordt geweigerd

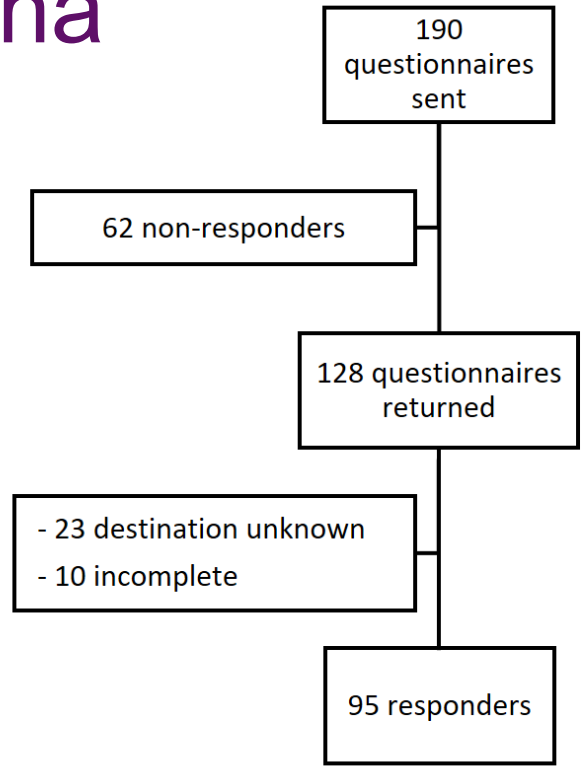
Relatief: recent gebruik van GnRH agonisten, anatomisch (submuceuze myomen, nauwgesteelde subserosale myomen), **fertiliteitswens**

Embolisatie van de a. uterina



Geert Maleux

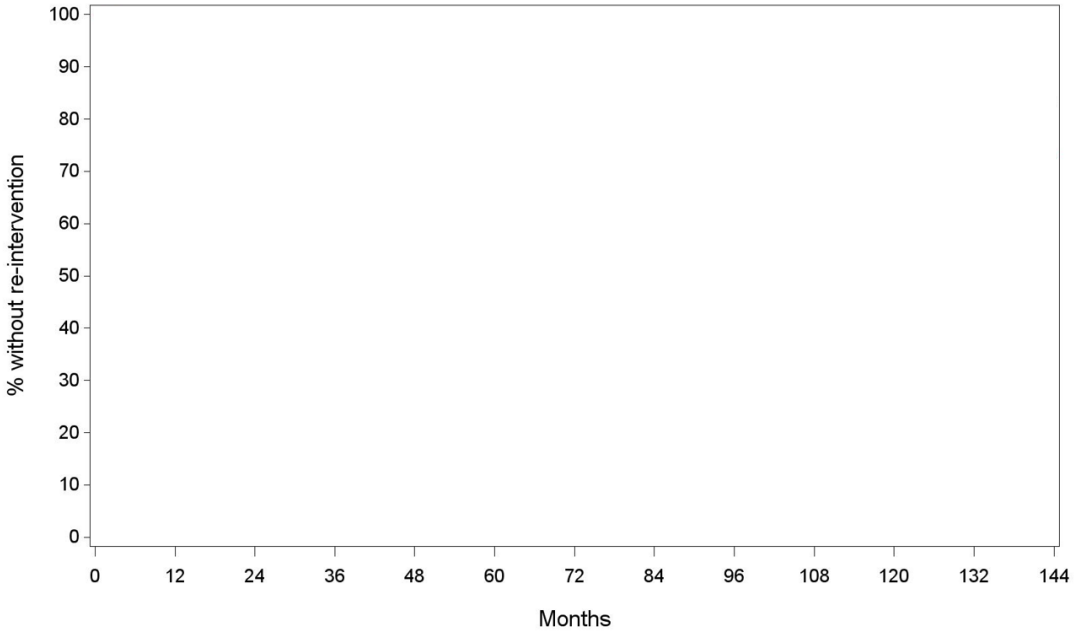




D'hoore et al. Eur J Obstet Gynecol Reprod Biol 2020

Embolisatie van de a. uterina

Geen reinterventie	77/95 (81,05%)
Reinterventie	18/95 (18,95%)

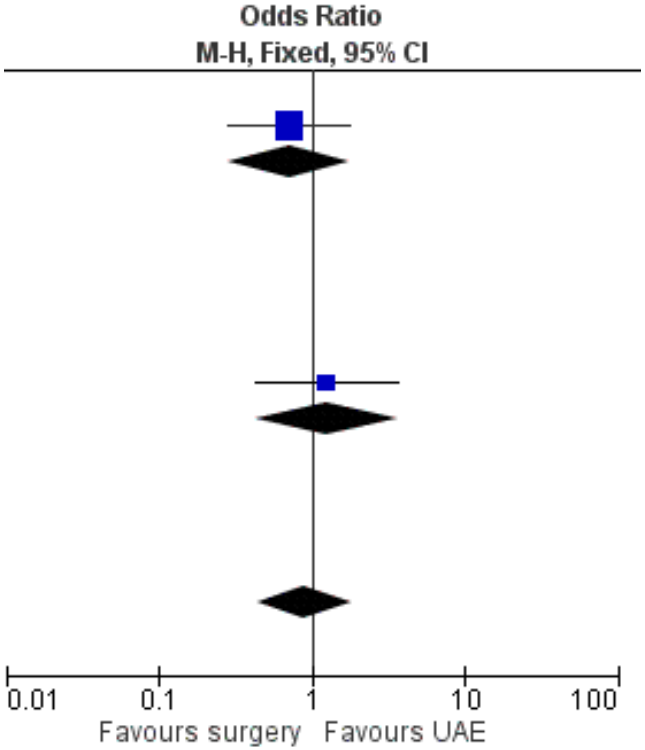


Cumulative rate of freedom of TF
after 60 mo: 82,18%
after 108 mo -144 mo: 72,88%

D'hoore et al. Eur J Obstet Gynecol Reprod Biol 2020

Embolisatie van de a. uterina

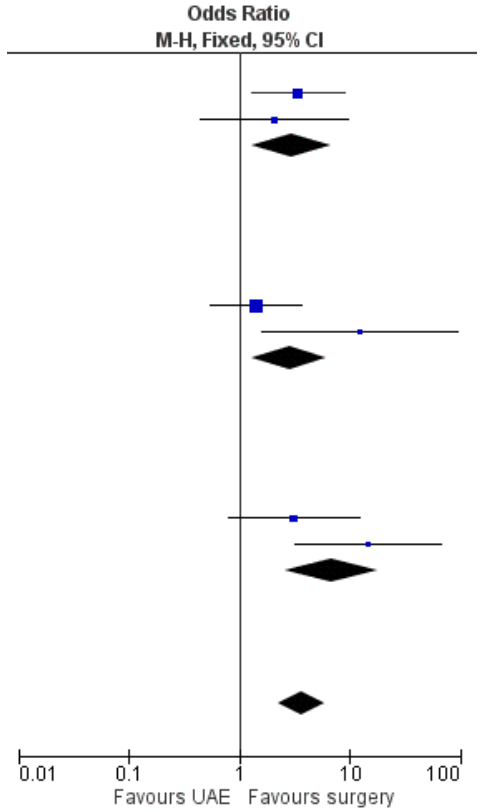
- **Patiënttevredenheid** na 5 jaar:
  - UAE vs hysterectomie (1 studie)
  - UAE vs hysterectomie/myomectomie (1 studie)



Gupta JK et al Cochrane 2014

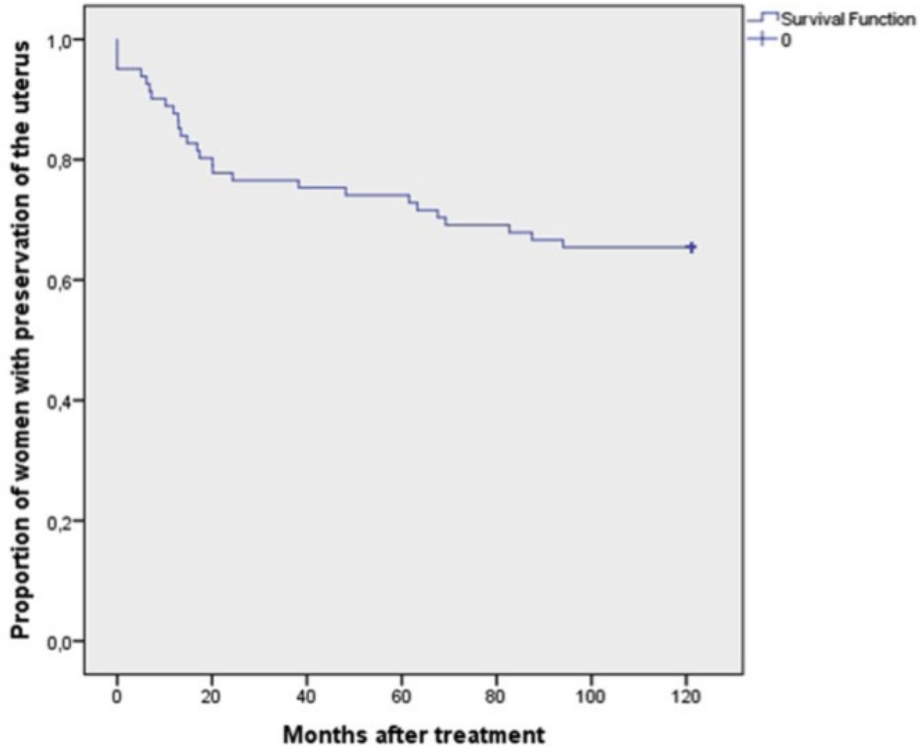
Embolisatie van de a. uterina

- **Reïnterventies** na 2 jaar:
  - UAE vs hysterectomie (2 studies)
  - UAE vs hysterectomie/myomectomie (2 studies)
  - UAE vs myomectomie (2 studies)



Gupta JK et al Cochrane 2014

Embolisatie van de a. uterina



Hysterectomy-free survival for uterine artery embolization patients.

de Bruijn et al AJOG 2016

Embolisatie van de a. uterina

- **Heropnames** binnen 4-6 weken OR 2.74 (95% CI 1.42-5.26).
- **Duur van procedure:** niet gepoold
  - In subgroepen: benefit van UAE (MD +/- 16-50 min)
- **Duur van hospitalisatie:** niet gepoold
  - In subgroepen: benefit van UAE (MD +/- 1-4 dagen)
- **Hervatten van normale activiteit**
  - In subgroepen: benefit van UAE (MD +/- 10-23 dagen)



Gupta JK et al Cochrane 2014

Embolisatie van de a. uterina

Relatieve contra-indicatie: fertiliteitswens?

Royal College of Obstetricians & Gynaecologists

A desire to preserve fertility in women of childbearing age with symptomatic fibroids is a relative contraindication. Decision-making in this situation is complex and is considered more fully below (Section 6).

ACOG
The American College of Obstetricians and Gynecologists

There is insufficient evidence to ensure its safety in women desiring to retain their fertility, and pregnancy-related outcomes remain understudied. The American College of Obstetricians and Gynecologists' Committee on Gynecologic Practice considers the procedure investigational or relatively contra-indicated in women wishing to retain fertility.

Embolisatie van de a. uterina

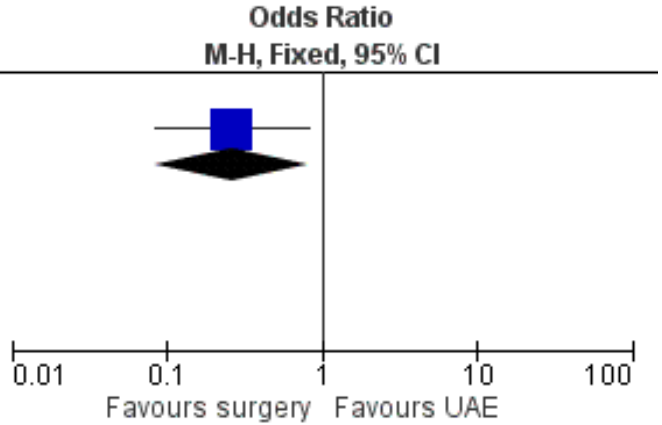
Minder zwangerschappen UAE groep (OR 0.29 CI 0.10-0.85)

Levendgeboorten:

Study or Subgroup	UAE Events	UAE Total	Surgery Events	Surgery Total	Weight	Odds Ratio M-H, Fixed, 95% CI
1.3.1 UAE versus myomectomy						
Mara 2008	5	26	19	40	100.0%	0.26 [0.08, 0.84]
Subtotal (95% CI)		**26**		**40**	**100.0%**	**0.26 [0.08, 0.84]**
Total events	5		19			

Heterogeneity: Not applicable

Test for overall effect: Z = 2.26 (P = 0.02)



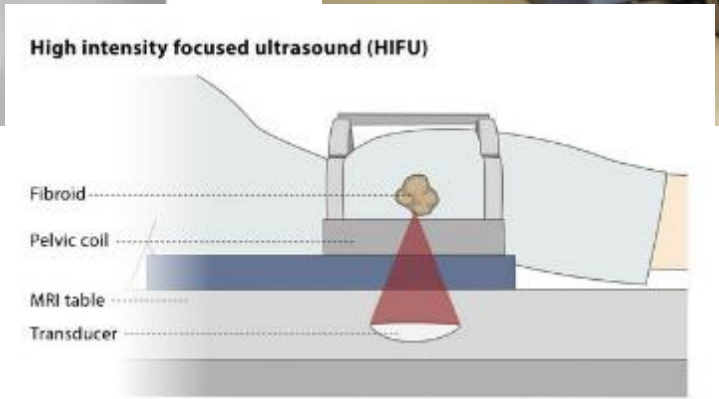
Gupta JK et al Cochrane 2014

Focused Ultrasound Surgery (HIFU - MRgFUS)









Echogeleiding (USgHIFU)

MR-geleiding (MRgFUS)

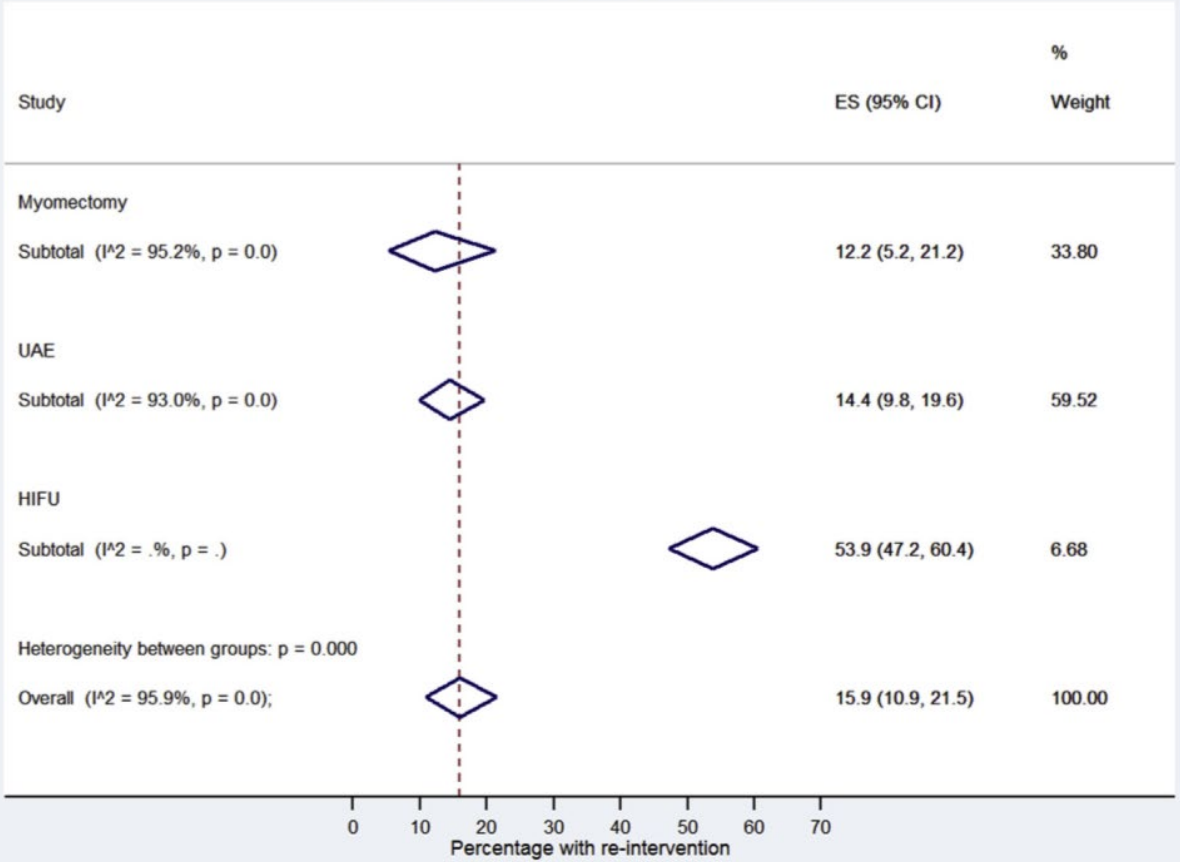
Focused Ultrasound Surgery

- USgHIFU
  - Vs lapsc myomectomie (N=83 vs 39) na 12m: geen verschil in QoL of symptomen, maar kortere hospitalisatieduur, snellere werkhervatting, minder complicaties (postop koorts, transfusie,..)

    ! brandwonden thv huid (13,4%)[1]
- MRgHIFU:
  - 12m gemiddelde sympt↓ 60% fibroomvol↓ 38%[2]
  - N=109 !brandwonden 5%, 1 N. ischiadicus letsel[3]
  - Vs UAE (N=43 vs 40) na 24m: minder verbetering in symptomen, meer kans op herinterventie (30 vs 13%), minder daling AMH[4]

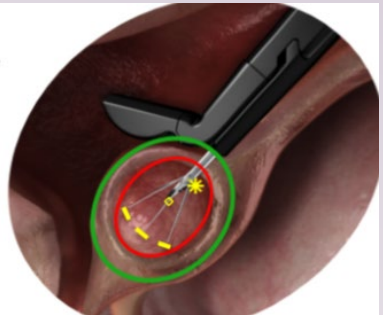
[1]Wang et al. JMIG 2012, [2]Verpalen et al. Eur J Rad 2019, [3]Stewart et al. Fertil Steril 2006, [3]Laughlin-Tommaso et al. AJOG 2019

Reintervention risk 60 months



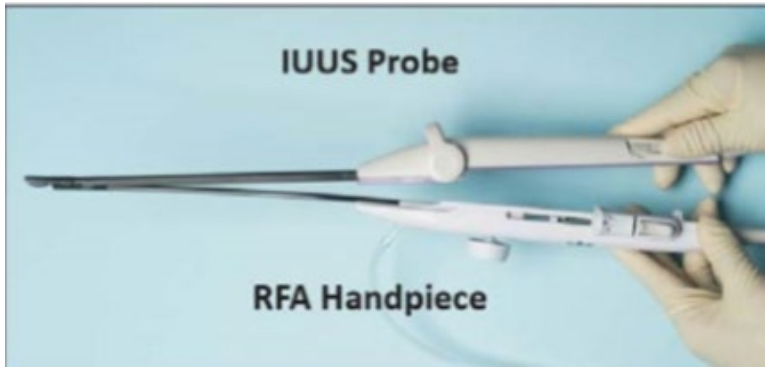
Sandberg et al, Fertil Steril 2018

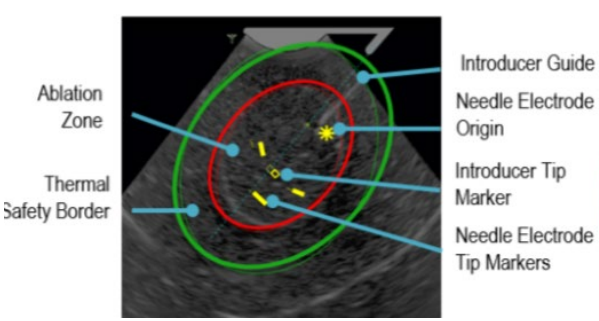
Radio Frequentie Ablatie (RFA)

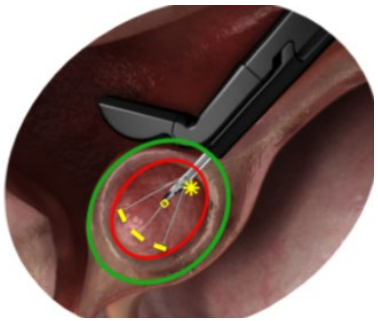


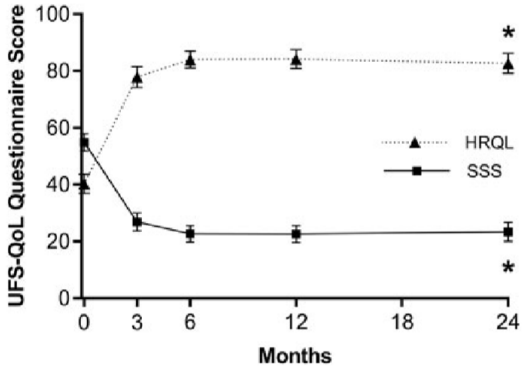
Radio Frequentie Ablatie

- SONATA









Miller et al, J Gynecol Surgery 2019

TAKE HOME MESSAGES (1/2)

- Echografisch diagnose en differentiële diagnose (MUSA)
- Asympt pt en echo geruststellend: FU (uitz submuceus - zs wens)
- Bij klachten, behandeling afh van vele factoren
- Hoofdzakelijk AUB: goede resultaten LNG-spiraal, orale oestoprog, tranexaminezuur (uitz type 0-1 myomen R/hysteroscopie)
- GnRH analogen
  - Ag.: amenorree++, volume↓↓ (tijdel.), cave nevenwerkingen ++ add-backR/, €
  - (Antag. – elagolix: amenorree++, volume↓, cave nevenwerkingen, add-backR/, veiligheid)

TAKE HOME MESSAGES (2/2)

- Ulipristal: amenorree++, volume↓↓ (langer), minder nevenwerkingen (E), PAEC, brede indicatie, onbeschikbaar tgv case levertoxiciteit
- Chirurgie:
  - Hysterosc myomectomie 1e keus bij submuceuze myomen en fertiliteitswens, ook bij AUB en intracavitaire myomen
  - Myomectomie via laparosc-robot-abdominaal, evt na voorbehandeling, indien kinderwens
- Niet eerste keuze bij kinderwens:
  - Embolisatie: bloeding↓ volume ↓↓, vs chir snellere mobilis, doch heropname en 20-30% kans op hysterect
  - HIFU: kosten, brandwonden, veel reïnterventies (50%), (nog) niet in België
  - RFA: meer onderzoek nodig, (nog) niet in België