

MYOMAS

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TERMINOLOGY

MYOMA

Terminology SYNONYMS

- leiomyomas
- fibromyomas
- myofibromas
- fibroids
- fibromas
- myomas

EPIDEMIOLOGY

MYOMAS

MOST COMMON:

- Women tumors (in 50 - 70% women of fertile age)
- Gynecological tumors
- The reason for gynecological laparotomy
- 40% women who undergo hysterectomy, due to benign tumors, are diagnosed with myoma

ETIOLOGY

Predisposing factors:

- Race– African-American women 3 x more than caucasian women
- Obesity
- Nutrition
- Hypertension/CVI risk
- Hereditary predisposition
- Tamoxifen
- Estrogen, Growth hormone and Progesterone

Protective factors:

- Smoking
- Parity
- Exercise (Menopause)

ESTROGEN HYPOTHESIS

- Estrogens - the main fibroid growth promoter
- Act locally synergistic via more polypeptide growth factors (EGF, TGF, IGF, FGF, MGF)
- Elevated EGF, EGF receptors (EGF-R) and Proliferating cell nuclear antigen (PCNA) levels, due to estrogen, lead to myoma occurrence

PROGESTERONE HYPOTHESIS

- Progesterone, along with estrogen, elevates EGF and PCNA levels
- Progesterone elevates Bcl-2 protein, which inhibits muscle cells apoptosis, and that enables myoma growth (Estrogen lowers Bcl-2 level)

CHROMOSOMAL ABERRATION HYPOTHESIS

- Myoma occurs when individual muscle cells seclude from myometrium as monoclonal neoplastic transformation process tumors
- Dietary factors can act as initiators and lead to muscular cell chromosomal DNA damage
- Promoter - Steroid hormones and Growth factors induce mitotic activity synergistically

MENARCHE

Age at menarche

Age at menarche	Relative risk (RR) of uterine fibroids
<10 years old	1.2
12 years old	1
>16 years old	0.68

- Earlier menarche increases the risk of myoma development
- Increased mitosis number and bigger odds for gene mutation, which control myometrial proliferation

Flake GP et al, *Environmental Health Perspectives* 2003; 111(8):1037-54

PARITY

Up to 50% reduction in RR vs. nulliparity

Possible explanation:

- Pregnancy reduces estrogen exposure
- Anovulation could be the cause of elevated estrogen levels in women who have not given birth

Flake GP et al, *Environmental Health Perspectives* 2003; 111(8):1037-54
Viswanathan M et al, *Evidence Report/Technology Assessment* 2007, Nr 14

AGE

Incidence of pathologically diagnosed fibroids*

- Prevalence increases with age
- Longer estrogen/progesterone stimulation

Age group	Fibroid incidence per 100 women-years
25-30 years	0.31
40-60 years	6.2

OBESITY


For each 10kg-increase in body weight: 21% risk increase

For each increase in BMI unit: 6% risk increase

* A significant increase occurs in the conversion of circulating adrenal androgens (Precursors that are converted by the liver to testosterone and estrone) to oestrone by excess adipose tissue

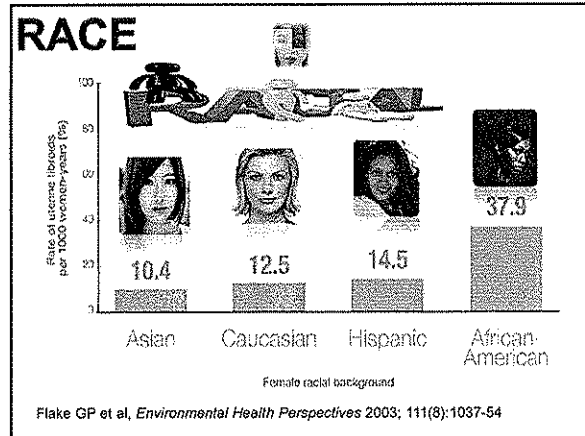
* In obese premenopausal women, metabolic conversion of estradiol to inactive metabolites is reduced, which could result in a relatively hyperestrogenic state

EXERCISE




- Based on self-reporting of physical activity levels for recreation and household chores, the highest levels of activity **reduced the risk of having myomas (fibroids) by 40%**.
- **POSSIBLE CAUSES:** The impact of physical activity on body habitus, energy metabolism, sex steroid levels, and ovulatory function.

Viswanathan M et al, *Evidence Report/Technology Assessment* 2007.




PATHOLOGY


- Smooth muscle and connective tissue, to a lesser extent
- Monoclonal expansion
- Rarely solitary - often multiple

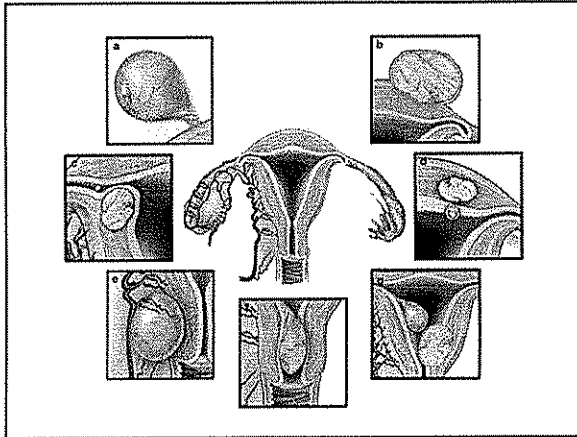


- **Microscopic versions:**
 - Cellular myoma
 - Mitotically active myoma
 - Bizarre myoma
 - Lipoleiomyoma
- **Intravenous leiomyomatosis**
- **LPD – leiomyomatosis peritonealis disseminata**
- **Leiomyosarcoma**



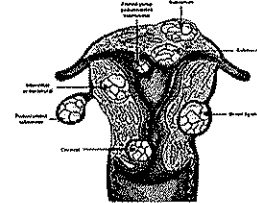
CLASSIFICATION





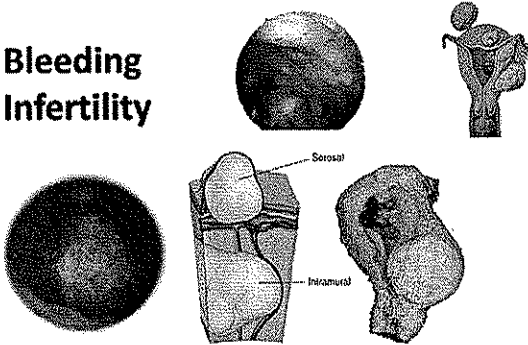
Classification by site:

- Submucous
- Intramural
- Subserosal
- Pedunculated
- Intracavitary
- Cervical
- Fundal
- Uterine cavity front wall/back wall myoma



SUBMUCOUS MYOMA

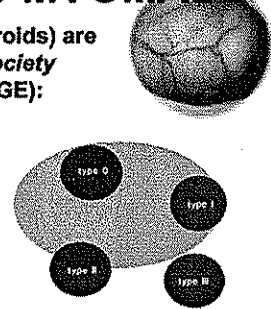
- Bleeding
- Infertility



SUBMUCOUS MYOMAS

Submucous myomas (fibroids) are classified by *European society for gynec endoscopy (ESGE)*:

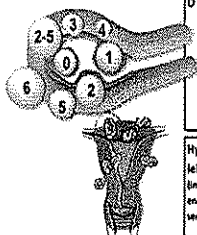
- Type 0 – No intramural extension
- Type I – Intramural extension < 50 %
- Type II – Intramural extension > 50 %



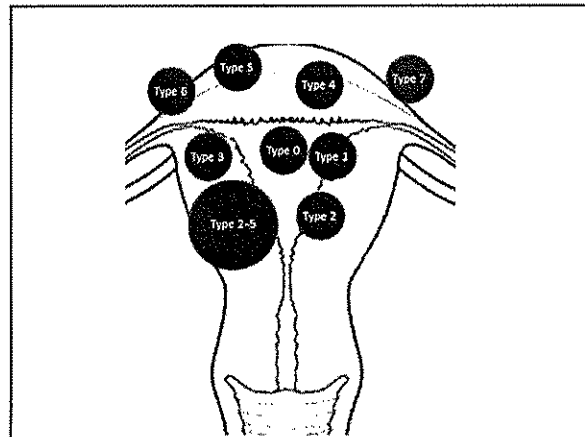
PALM – COEIN MYOMA SUBCLASSIFICATION

M. Munroe 2011.

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)	2-5	Submucosal and subserosal, each with less than half the diameter in the endometrial and peritoneal cavities, respectively.




SYMPTOMATOLOGY

Symptomatology depends on:




- Localization
- Size
- Growth rate
- Relation to adjacent organs

75% asymptomatic







SYMPTOMATOLOGY

- Bleeding (extended/ profuse/ irregular menstruation)
- Pelvic pressure
- Pain (Peritoneum dilatation or pressure on the organs)
- Increased urination, urinary retention, hydroureter, hydronephrosis, urolinfection (front wall myoma – pressure on the bladder)
- Cramps, ileus, opstipation (back wall myoma – pressure on intestine)
- Leg varices, phlebothrombosis, leg oedema, hemorrhoids (pressure on blood vessels)

Complications:

- Torsion (loop myoma)
- Rupture
- Necrosis
- Reproductive dysfunction (infertility)
- Malignant transformation <3%

MYOMA AND INFERTILITY

- Myomas are linked with infertility in less than 10% cases
- They are mentioned as single and sole factors in only 2-5% cases
- Women age (over 35) is a significant factor
- Myoma localization/size- larger than 5 cm deform uterine cavity and pose a problem for fertility

MYOMA MECHANISM IMPACT ON INFERTILITY

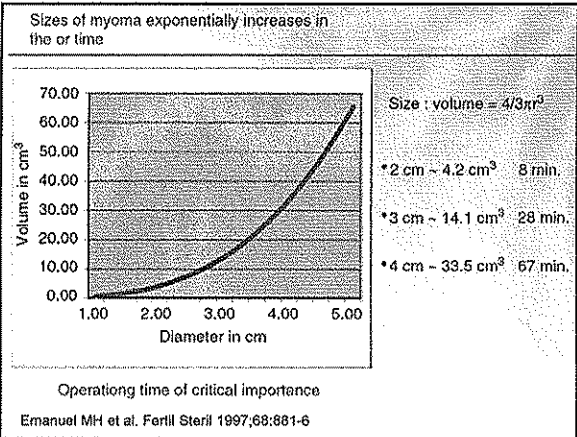
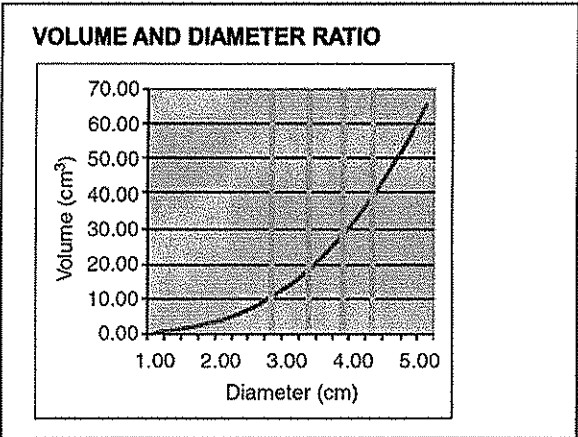
- MECHANICAL
- MYOMETRIAL CONTRACTIONS – IMPLANTATION INTERFERENCE
- CIRCULATORY DISORDERS
- ENDOMETRIAL CHANGES

DIAGNOSTICS

- Bimanual examination
- US (ultrasound), TV US, 3D US(volumen), SHG (Sonohysterography)
- CT scan
- MRI
- HSC (hysteroscopy)

50% volume reduction = 21% diameter decrease

Globe volume:

$$V = \frac{4R^3\pi}{3}$$


DIFFERENTIAL DIAGNOSIS






- Differential diagnosis:**
- Pregnancy
 - Ovarian neoplasms
 - Adenomyosis
 - Malignant tumors of uterus
 - ✓ uterine sarcoma
 - ✓ endometrial carcinoma
 - ✓ cervical cancer

TREATMENT

- ## TREATMENT DEPENDS ON:
- MYOMA SIZE
 - MYOMA LOCALIZATION
 - SYMPTOMS/ HEALTH PROBLEMS
 - AGE
 - REPRODUCTIVE PLAN AND OBSTETRIC ANAMNESIS
 - SUSPICION OF SARCOMA

- ## TYPES OF TREATMENT
- Expectant– follow-up
 - Pharmacological
 - Minimally invasive methods
 - Surgical


TYPES OF TREATMENT

- Expectant/ follow-up 
- Pharmacological...
 - IUD-LNG (Mirena) 
- Surgical (Hysterectomy/ enucleation; HSC / laparotomy/ hysterectomy) 
- Minimally insvasive methods
 - embolization 
 - MR Guided Focused UltraSound - MRgFUS 

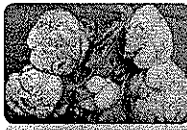



Expectant attitude:

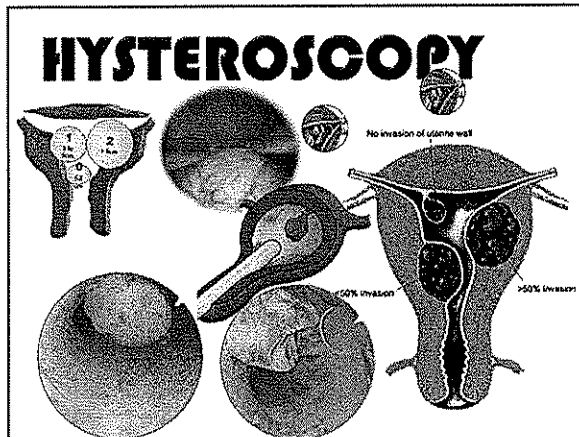
(regular check-up visits 2x a year)

- **Without health problems**
- **Size < 12 weeks of pregnancy**
- **Menopause proximity**



SURGICAL TREATMENT

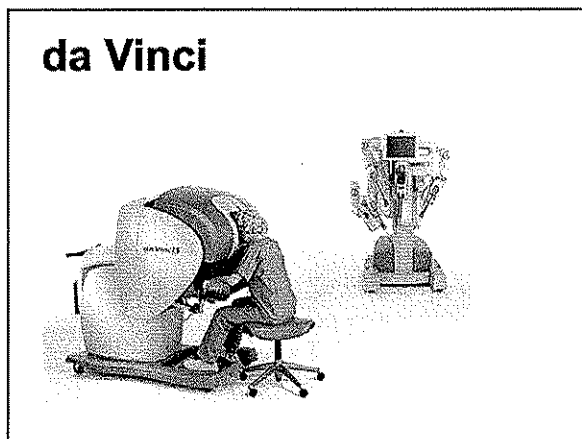
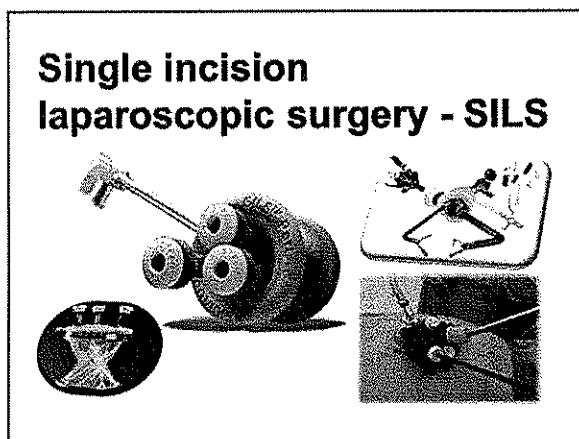
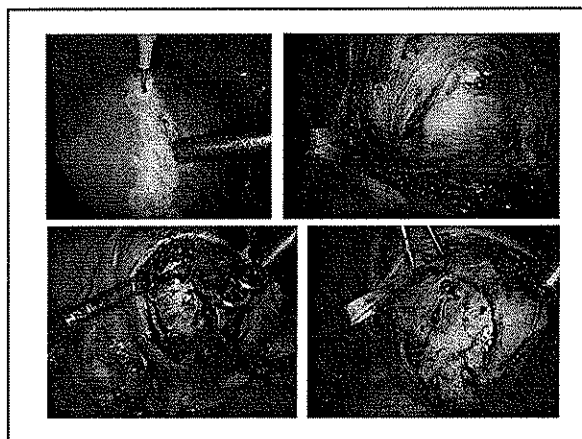
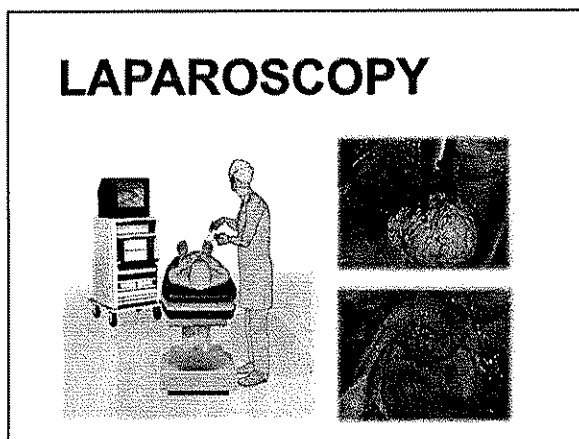
- **Hysterectomy**
 - abdominal 
 - vaginal 
 - laparoscopic
 - LAVH
 - TLH
- **Enucleation**
 - abdominal 
 - vaginal 
 - endoscopic
 - HSC
 - LPSC



Indications for myomectomy:

- Uterus larger than 12 weeks pregnant
- Bleeding
- Pain/pressure
- Rapid growth
- Postmenopausal growth
- Infertility
- Habitual miscarriage
- Bladder or ureter compression

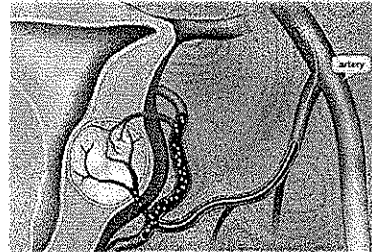
UpToDate



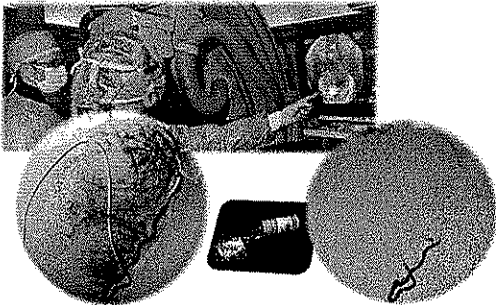
VAGINAL MYOMECTOMY



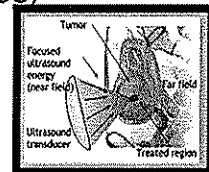
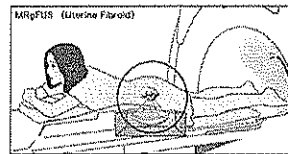
MYOMY EMBOLIZATION




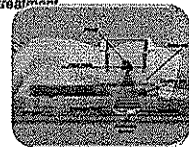
- interventional radiologists
- polyvinyl – plastic granules 0,3 – 0,7 mm in diameter that have been used over 20 years for embolization
- Postembolization syndrome (fever, pain, vomiting...)



Magnetic resonance-guided focused ultrasound surgery (MRgFUS)

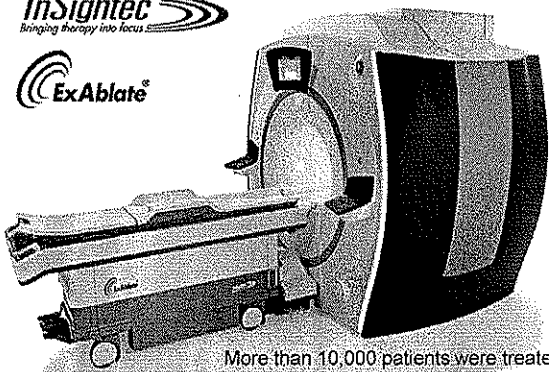


- MRI-GUIDED ULTRASOUND
- Used for the first time in 1993, for prostate cancer treatment
- Approved by FDA in 2004. 
- Neurosurgery, Gynecology - myoma
- Temperature increase for 60°C
- Thermal ablation coagulation necrosis
- tissue destruction accurate to the millimeter



InSightec
Bringing therapy into focus.

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PHARMACOLOGICAL TREATMENT

- ORAL HORMONAL CONTRACEPTIVES (↓ bleeding)
- Progestogen
- IUD (Mirena)
- GnRH analogues (expensive, unpleasant side effects)
- Antigestagens (mifepristone)
- Androgens (*danazol, gestrinone*)
- Aromatase inhibitors (*letrozole*)
- SERM – selective estrogen receptor modulator (*Raloxifen*)
- SPRM – selective progesterone receptor modulator (*Asoprisnil; UPA-ullipristal acetate= Esmya*)



PHARMACOLOGICAL TREATMENT

- Definitive treatment ???
- Symptomatic
- Preoperatively due to size reduction
- Permanently
- Non-invasive

