

Black Box of the Endometrium: Fibroids and Reproductive Failure

By Dr Stavros Karampelas



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The Clinical Paradox

The Question

- Intramural myoma
- No cavity distortion
- Normal hysteroscopy
- Good embryos
- Repeated implantation failure

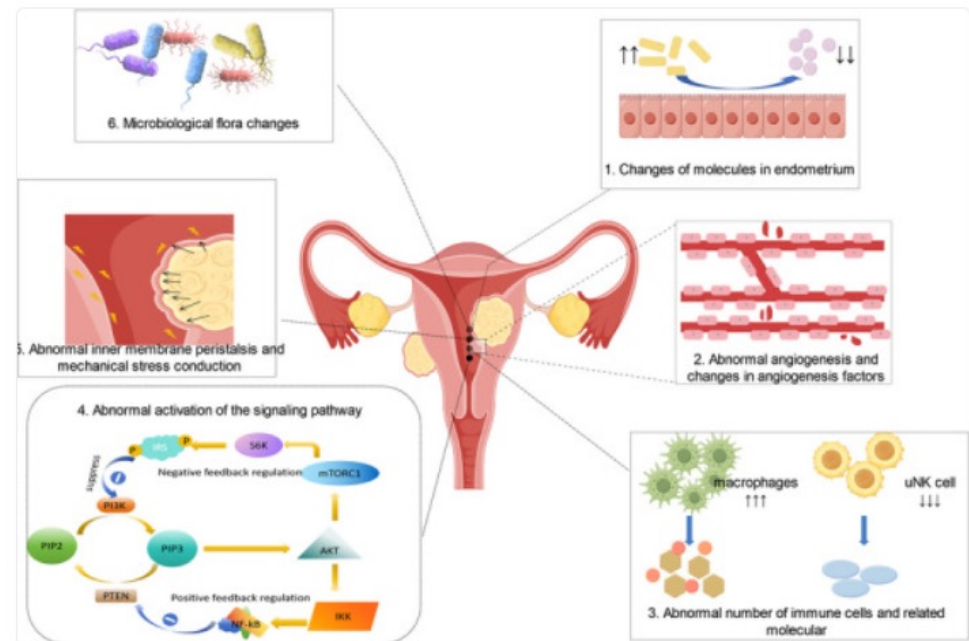
So... what are we missing?

The “Black Box” Concept

- Myoma → (unknown mechanisms) → Endometrial dysfunction → Implantation failure

“We correct anatomy. But do we correct function?”

- The endometrium is not just structurally affected
- There is a hidden functional impairment

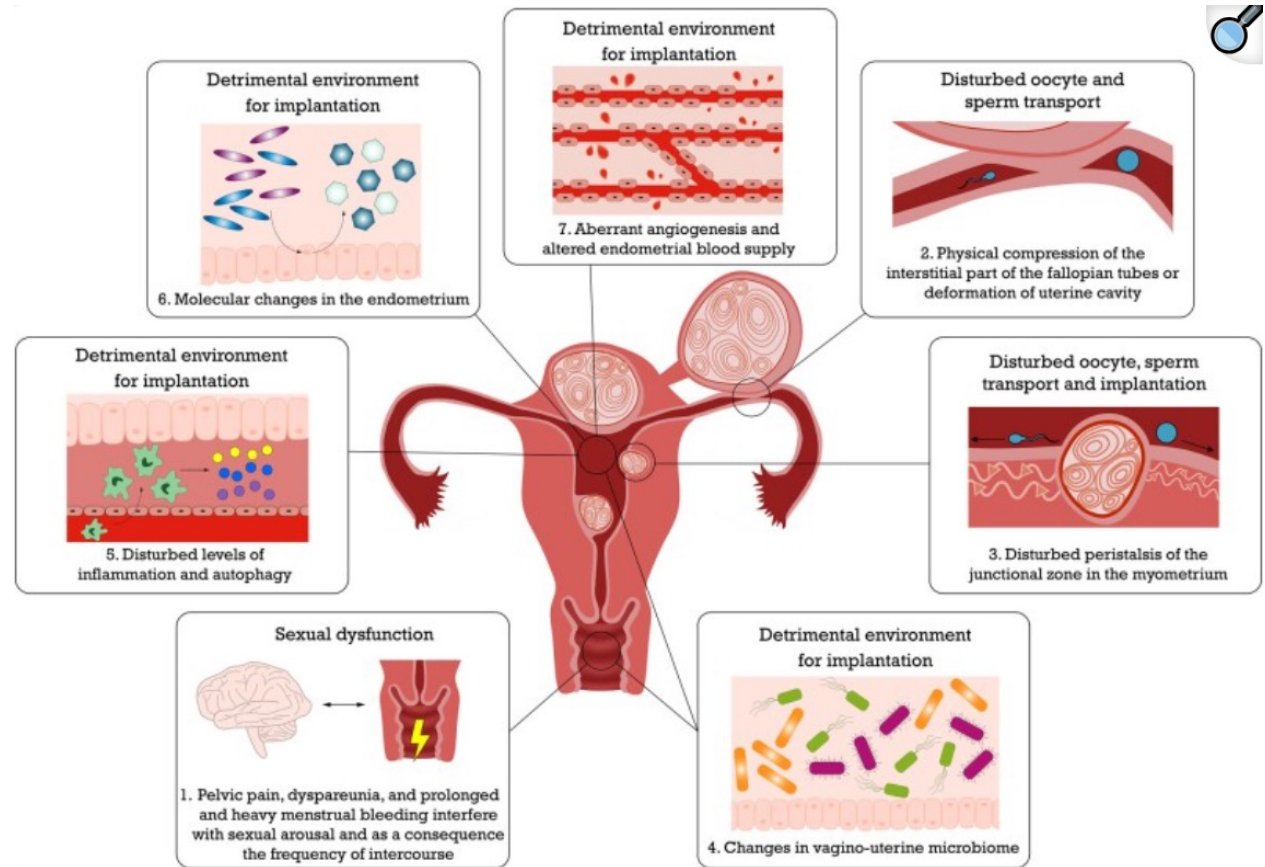


Hypothesis?

• Hum Reprod. 2023 Sep 28;38(11):2045–2054. doi: [10.1093/humrep/dead194](https://doi.org/10.1093/humrep/dead194)

Infertility in patients with uterine fibroids: a debate about the hypothetical mechanisms

Emma E Don^{1,2,6}, Velja Mijatovic^{3,4}, Judith A F Huirne^{5,6}



Junctional Zone Disruption

- Impact on frequency, direction, amplitude, and coordination of junctional zone peristalsis
- Disrupted uterine architecture
- Impaired sperm transport & embryo implantation

Review > [Am J Reprod Immunol. 2024 Dec;92\(6\):e70022. doi: 10.1111/aji.70022.](#)

Mechanism of Endometrial Receptivity Affected by Fibroids

[Ping Sun](#)¹, [Chunyan Zhang](#)², [Weisha Wang](#)², [Huagang Ma](#)¹

Vagino-uterine microbiome

- Only two studies have investigated the microbiome in women with fibroids
- Different bacterial profiles in vagina and endometrium samples of patients with fibroids
- Endometrium samples were generally collected transcervically or after hysterectomy

Endometrial Blood Flow and Angiogenic Factors

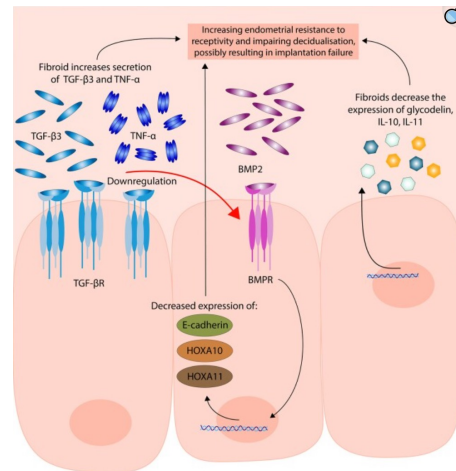
- Fibroids may lead to abnormal intimal blood flow by causing abnormal endometrial angiogenesis and vascular maturation.
- VEGF dysregulation
- Impaired endometrial vascular maturity, and increased vascular fragility and permeability
- Local hypoxia
- Intramural fibroids > 4 cm significantly increase endometrial vascularity.

> Arch Gynecol Obstet. 2018 Feb;297(2):539-545. doi: 10.1007/s00404-017-4607-2. Epub 2017 Dec 14.

Effect of intramural fibroid on uterine and endometrial vascularity in infertile women scheduled for in-vitro fertilization

Ahmed Kamel ¹, Akmal El-Mazny ², Wafaa Ramadan ², Suzy Abdelaziz ², Sherine Gad-Allah ², Hany Saad ², Ahmed M Hussein ², Emad Salah ²

Molecular Receptivity



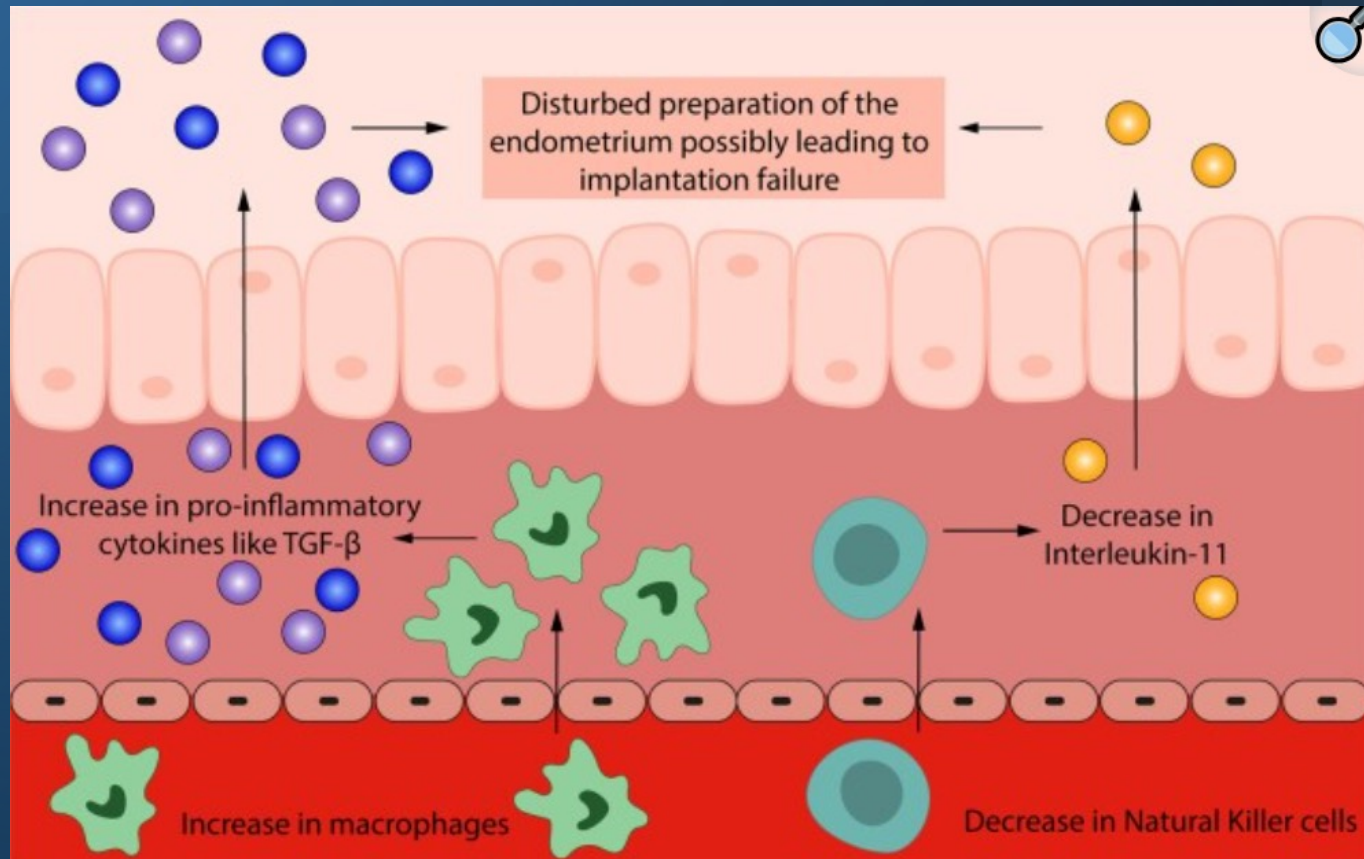
> *Fertil Steril.* 2010 Apr;93(6):2027-34. doi: 10.1016/j.fertnstert.2008.03.029. Epub 2008 Jun 13.

Submucosal uterine leiomyomas have a global effect on molecular determinants of endometrial receptivity

Beth W Rackow ¹, Hugh S Taylor

- ↓ HOXA10 and HOXA11
- ↓ LIF
- ↓ Integrins

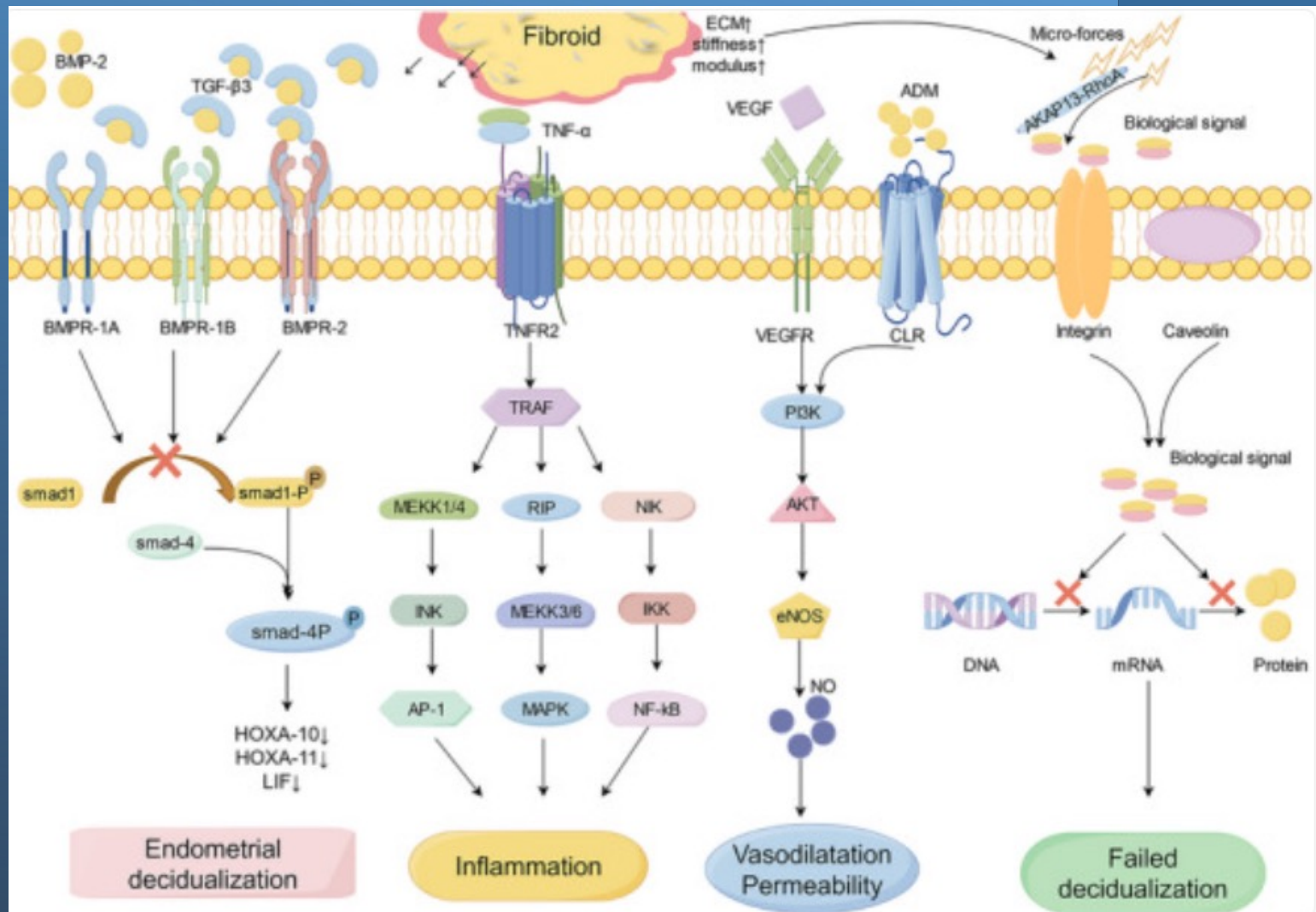
Inflammation & Cytokines



Review > Fertil Steril. 2022 Jun;117(6):1107-1120. doi: 10.1016/j.fertnstert.2022.04.023.

Immune determinants of endometrial receptivity: a biological perspective

Sarah A Robertson¹, Lachlan M Moldenhauer², Ella S Green², Alison S Care², M Louise Hull³



ART Outcomes

- ↓ implantation rates
- ↑ miscarriage rates
- Especially multiple myomas
- The clinical pregnancy rate for women undergoing myomectomy for intramural leiomyomas was no different than those with intramural leiomyomas

[Meta-Analysis](#) > [Obstet Gynecol.](#) 2024 Aug 1;144(2):171-179.

doi: 10.1097/AOG.0000000000005661. Epub 2024 Jun 27.

Intramural Leiomyomas and Fertility: A Systematic Review and Meta-Analysis

[Taina Laurore Pritts](#)¹, [Meghan Ogden](#), [William Parker](#), [Jennifer Ratcliffe](#), [Elizabeth A Pritts](#)

Increased risk of miscarriage?

- The presence of multiple submucosal lesions in infertile women, may increase the risk of pregnancy loss
- Slightly increased risks of placenta previa, placental abruption and fetal malpresentation

Review > [Reprod Sci.](#) 2022 Aug;29(8):2145-2151. doi: 10.1007/s43032-021-00656-6.

Epub 2021 Jun 17.

Uterine Fibroids and Pregnancy: How Do They Affect Each Other?

Larissa M Coutinho ^{1, 2}, Wiviane A Assis ², Ananda Spagnuolo-Souza ², Fernando M Reis ^{3, 4}

The effect of type 0,1 and 2 fibroids on fertility

Submucosal LMs negatively affect fertility, when compared to women without fibroids.

[Biomed Res Int](#). 2018; 2018: 2804830.
Published online 2018 Sep 3. doi: [10.1155/2018/2804830](https://doi.org/10.1155/2018/2804830)

PMCID: PMC6140098
PMID: [30250847](https://pubmed.ncbi.nlm.nih.gov/30250847/)

Submucous Fibroids, Fertility, and Possible Correlation to Pseudocapsule Thickness in Reproductive Surgery

[Andrea Tinelli](#),^{1, 2} [Ioannis Kosmas](#),^{2, 3} [Osman A. Mynbaev](#),^{2, 4, 5} [Alessandro Favilli](#),⁶ [Grigoris Gimbrizis](#),⁷ [Radmila Sparic](#),⁸ [Marcello Pellegrino](#),⁹ and [Antonio Malvasi](#)^{2, 10}

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What is the impact on fertility of type 3 fibroids

- FIGO type 3 myomas are significantly associated with a lower implantation rate, cumulative pregnancy rate, and live birth rate
- No firm conclusions could be drawn about the potential benefits of surgery for FIGO type 3 uterine fibroids on IVF outcomes

[Review](#) > [Int J Gynaecol Obstet.](#) 2023 Nov;163(2):528-539. doi: 10.1002/ijgo.14838.
Epub 2023 May 15.

Impact of FIGO type 3 uterine fibroids on in vitro fertilization outcomes: A systematic review and meta-analysis

[Alessandro Favilli](#)¹, [Andrea Etrusco](#)², [Vito Chiantera](#)², [Antonio Simone Laganà](#)², [Ettore Cicinelli](#)³, [Sandro Gerli](#)¹, [Amerigo Vitagliano](#)³

[Affiliations](#) + expand

PMID: 37183601 DOI: 10.1002/ijgo.14838

Is there an impact on fertility of small fibroids that don't touch the cavity of the uterus?

- 2-6 cm sized noncavity-distorting intramural fibroids have a deleterious effect on live birth rates in IVF.
- No evidence that myomectomy may have a positive impact prior to IVF

Review > [Fertil Steril](#). 2023 Jun;119(6):996-1007. doi: 10.1016/j.fertnstert.2023.02.018.
Epub 2023 Feb 21.

The effect of ≤ 6 cm sized noncavity-distorting intramural fibroids on in vitro fertilization outcomes: a systematic review and meta-analysis

[Murat Erden](#)¹, [Esra Uyanik](#)¹, [Mehtap Polat](#)², [Irem Yarali Ozbek](#)³, [Hakan Yarali](#)⁴, [Sezcan Mumusoglu](#)⁵

Affiliations + expand

PMID: 36813123 DOI: 10.1016/j.fertnstert.2023.02.018

Free article

Functional Effect of Surgery

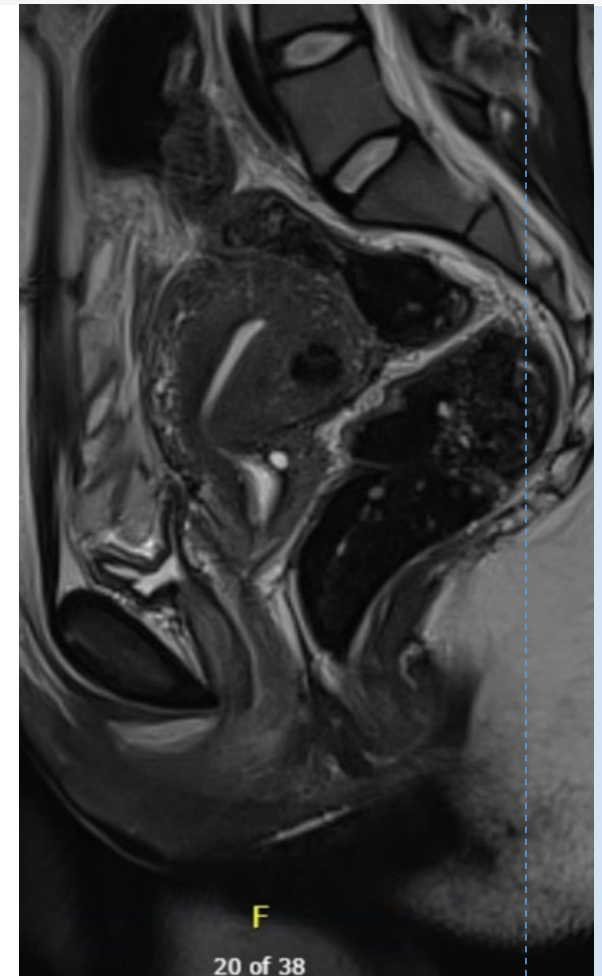
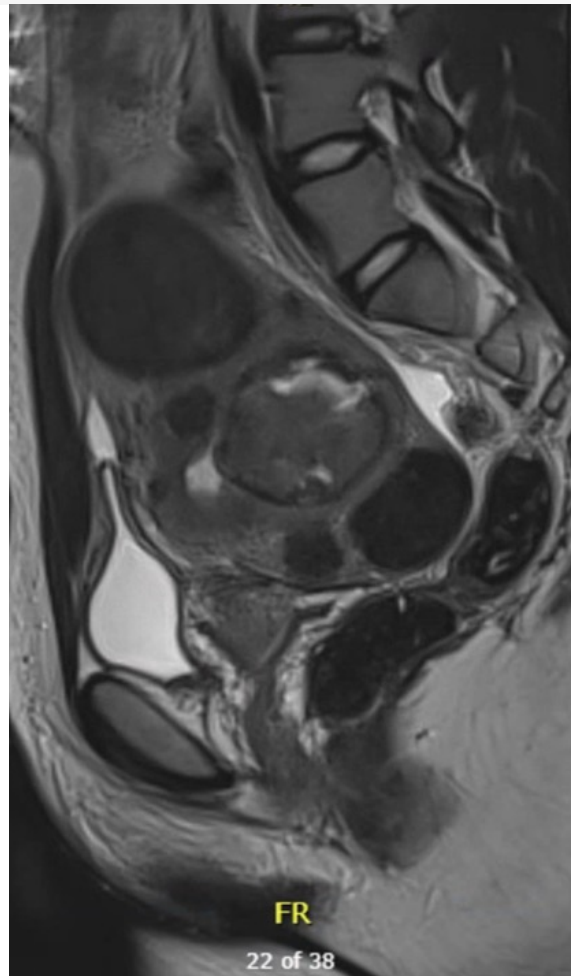
Myomectomy → restore physiology → improve receptivity

- Normalize peristalsis
- Improve vascularization
- Restore molecular signaling

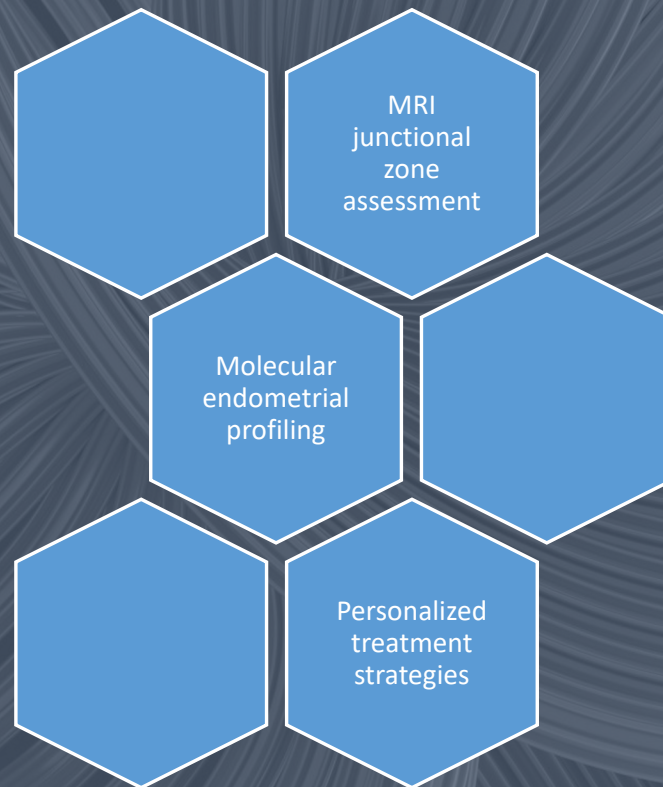


Surgical Perspective

- Prioritize Laparoscopic or Hysteroscopic myomectomy
- Preserve uterine integrity
- Minimize adhesions



Future Directions-Opening the black box!



Take-Home Messages

Myomata affect function, not just anatomy

Intramural fibroids can impair receptivity

Molecular mechanisms are key

Surgery may be functional, not cosmetic

Patient selection is critical

The uterus is
not just a
cavity — it is a
dynamic,
signaling organ



THANK YOU