



# Diffuse and Focal Adenomyosis: Two different entities ?



SEUD 2015



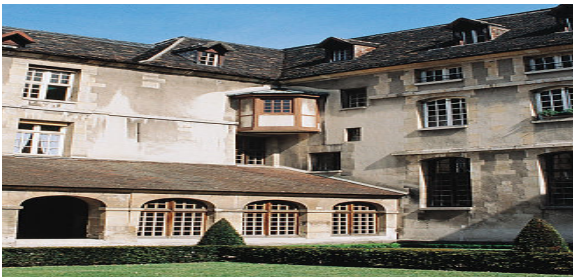
Society Of Endometriosis  
and Uterine Disorders

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## Gynecology

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H Foulot, MC Lafay-Pillet, A Bourret,  
G Pierre, M Even, MC Lamau,  
L Marcellin, P Marzouk

### *Medical unit:*

A Gompel, G Plu-Bureau, L Maitrot

### *Reproductive Endocrinology unit:*

D de Ziegler, P Santulli, V Gayet,  
P Pierteau, FX Aubriot

## Intestinal surgery

B Dousset, S Gaujoux, M Leconte

## Radiology

AE Millischer, L Maitrot

## Laboratory: *Genetic*

D Vaiman

## Laboratory: *Immunology*

F Batteux, S Chouzenoux  
C Nicco, C Chéreau, B Weill

## Laboratory: *Reproductive biology*

JP Wolf, V Lange, K Pocate,  
JM Kuntzman, C Chalas

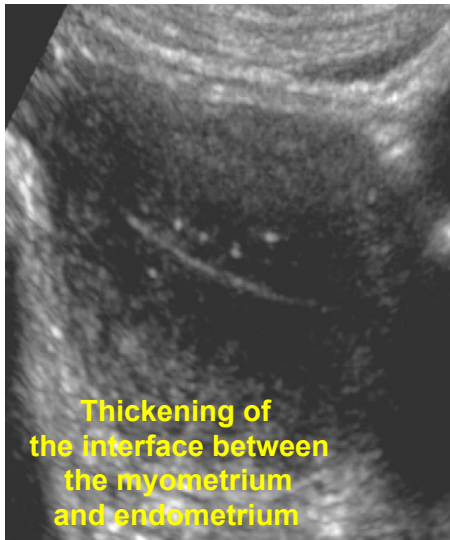
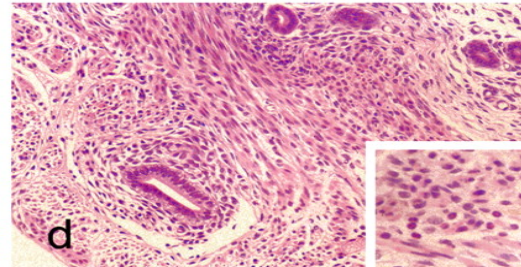
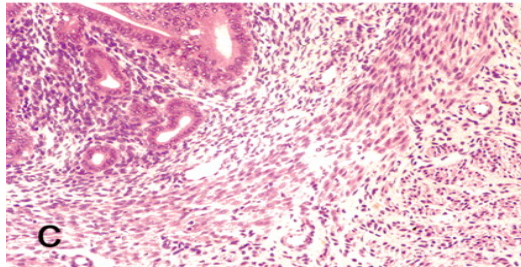
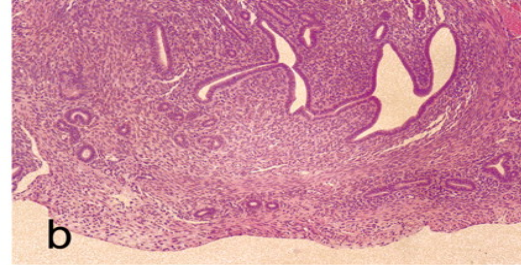
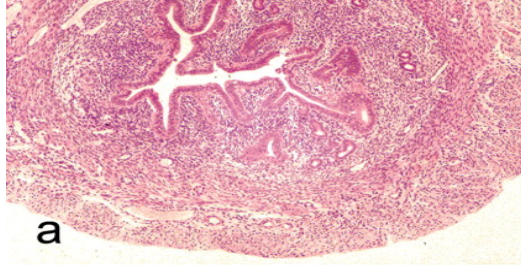
## Statistical unit

F Goffinet, PY Ancel

**Charles Chapron,**  
**Professor and Chair,**

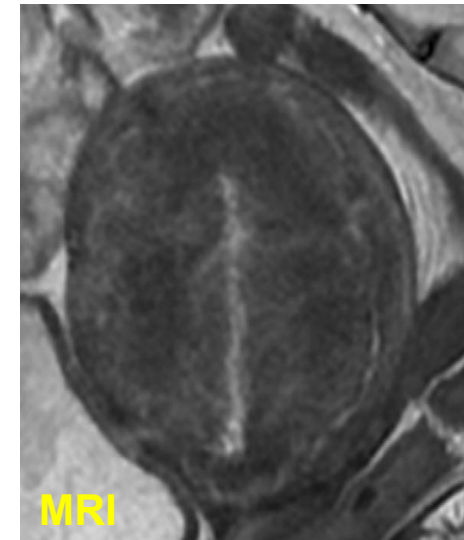
**Department of Obstetrics and Gynecology II and Reproductive Medicine**

# Adenomyosis: Definition



## Histological definition:

Presence of endometrial glands and/or stroma outside the uterine cavity



# Adenomyosis: How is common the disease ?



## Asymetrical myometrial thickening:

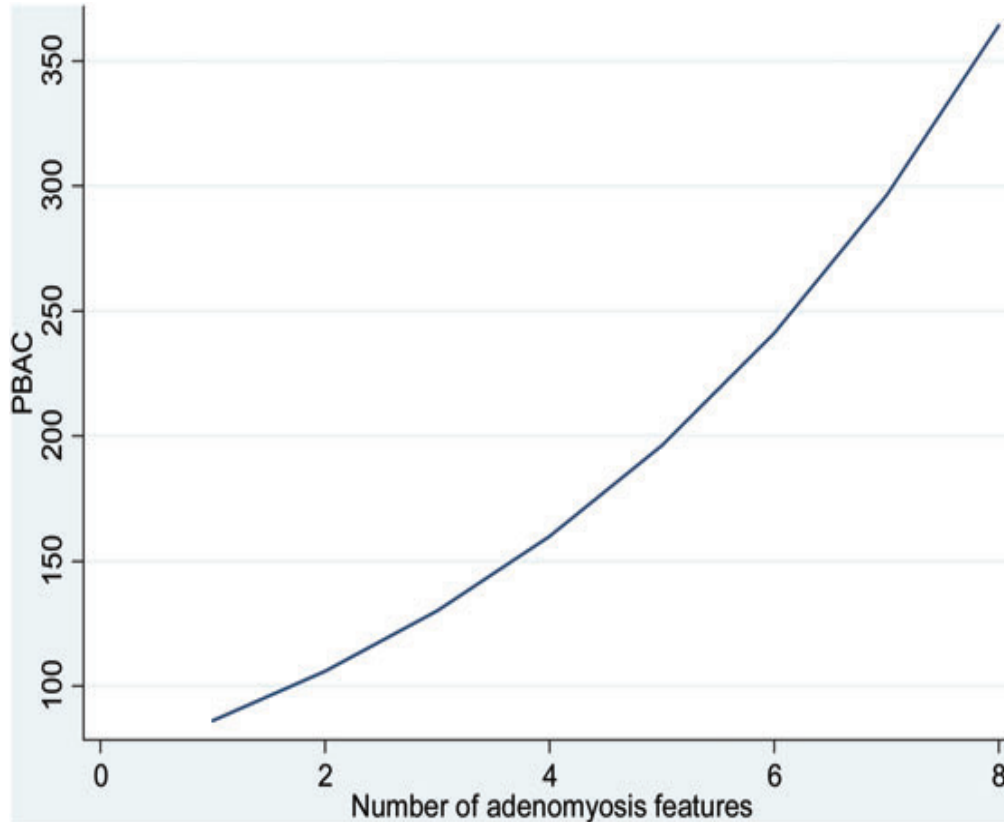
*A longitudinal view of an anteverted uterus in which the distance from the endometrium to anterior serosal surface is much greater than the distance from the endometrium to the posterior serosal surface*

| TVUS<br>N = 985 patients | Adenomyosis        |
|--------------------------|--------------------|
|                          |                    |
|                          | 206 patients       |
|                          | 20.9%              |
|                          | 95% CI: 18.5 23.6% |

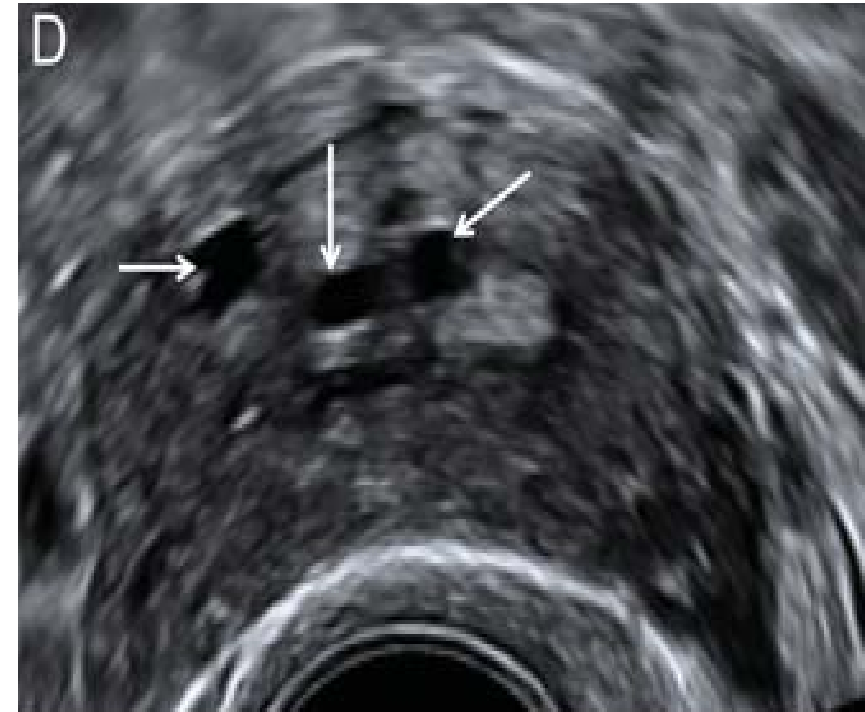
# Adenomyosis: Associations between demographic and clinical variables

| Variable         | Category/term | Odds ratio (95% CI) | P-value |
|------------------|---------------|---------------------|---------|
| Age <sup>a</sup> | Linear term   | 34.3 (9.9, 118)     | <0.001  |
|                  | Squared term  | 0.70 (0.62, 0.80)   |         |
| Gravidity        | 0             | 1                   | <0.001  |
|                  | 1             | 1.83 (1.09, 3.06)   |         |
|                  | 2             | 2.46 (1.44, 4.30)   |         |
|                  | 3–5           | 2.66 (1.62, 4.28)   |         |
|                  | 6+            | 4.90 (2.57, 9.35)   |         |
| Endometriosis    | No            | 1                   | <0.001  |
|                  | Yes           | 4.06 (2.25, 7.33)   |         |

# Adenomyosis: Association with menorrhagia



Significant positive correlation between the Nb of features of AdOsis at TVUS and the objectively assessed menstrual loss by pictorial blood loss analysis chart (PBAC)

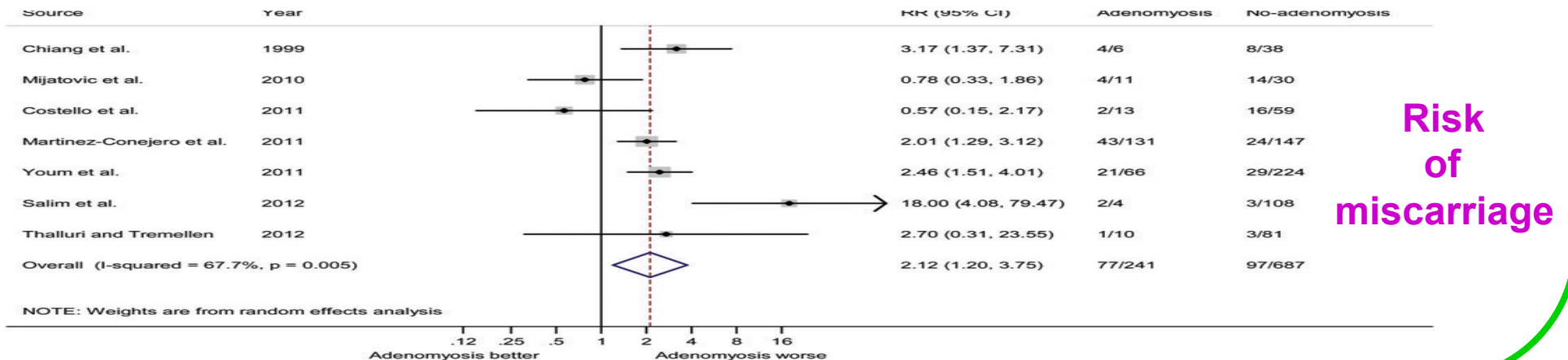
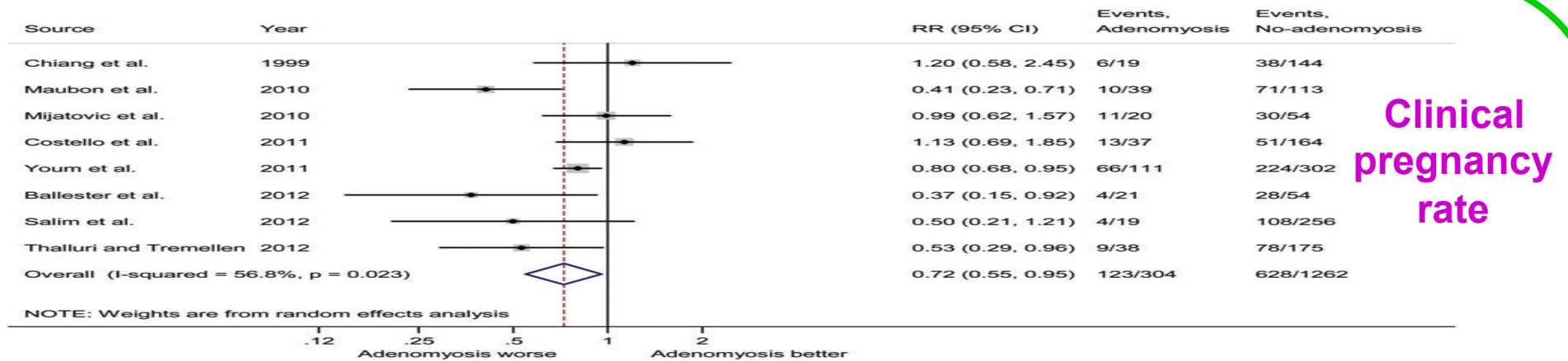


Several myometrial cysts seen as anechoic lesion within the myometrium

Naftalin *et al.*, Hum Reprod (2014)

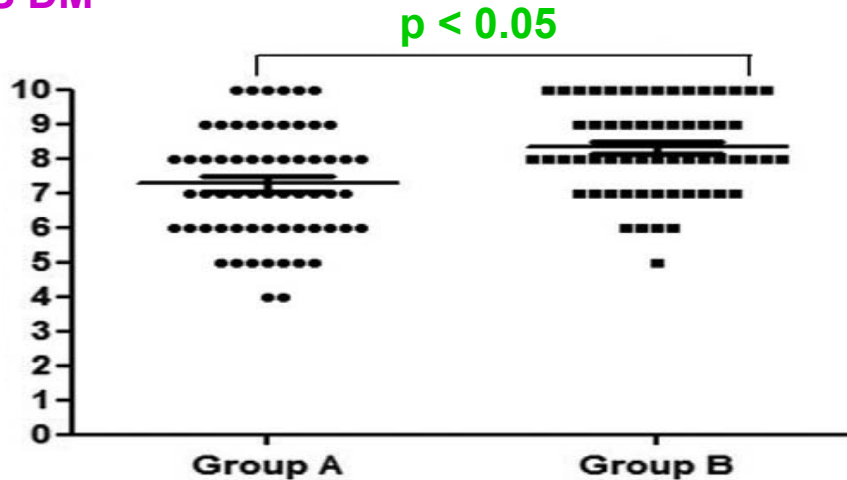
# Adenomyosis and Infertility

## Infertile women undergoing IVF / ICSI

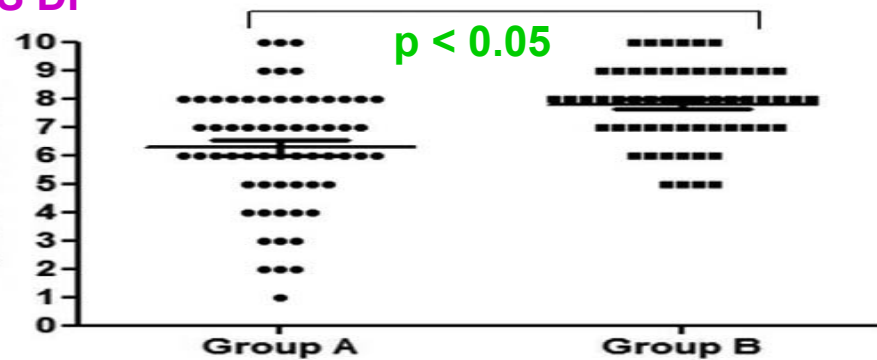


# Adenomyosis and pelvic pain

VAS DM



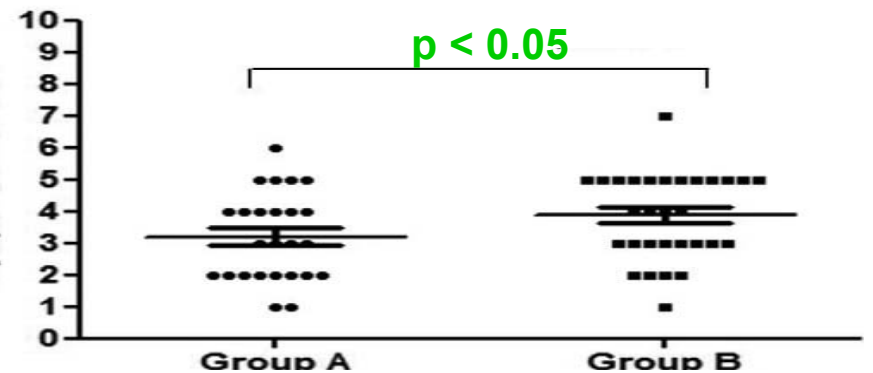
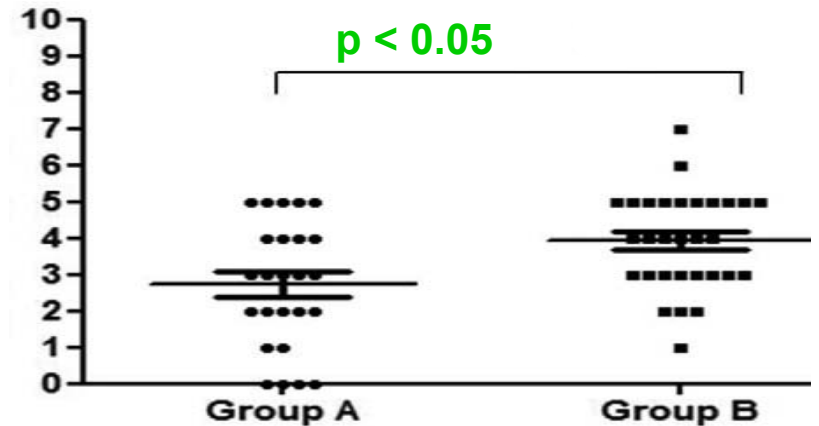
VAS DP



DIE only

DIE + AdOsis

Before surgery

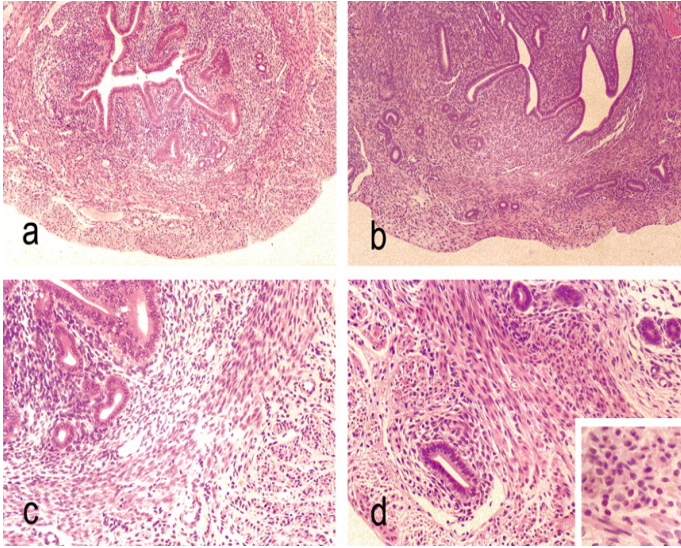


DIE only

DIE + AdOsis

After surgery

# Adenomyosis: Definition



## Histological definition:

**Presence of endometrial glands and/or stroma outside the uterine cavity**

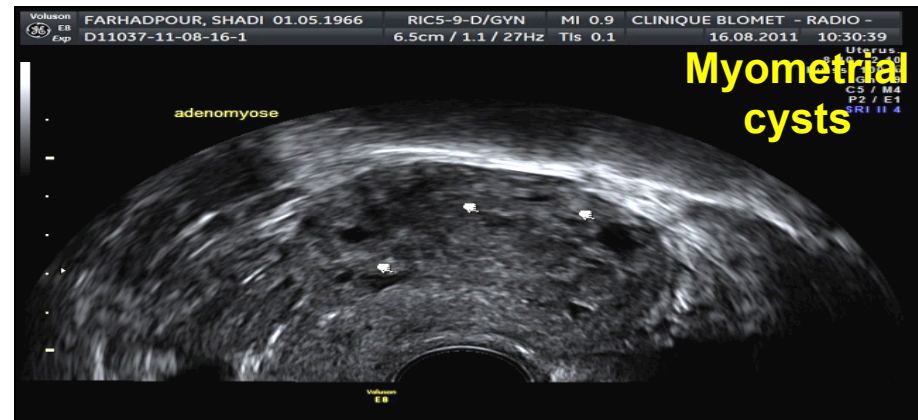
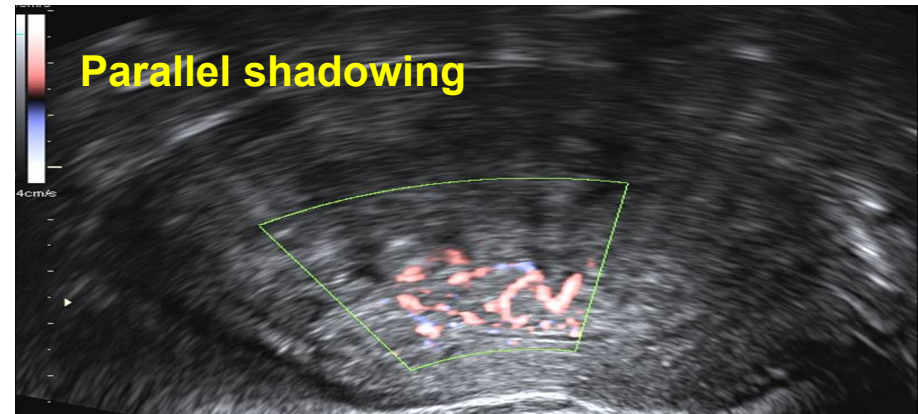
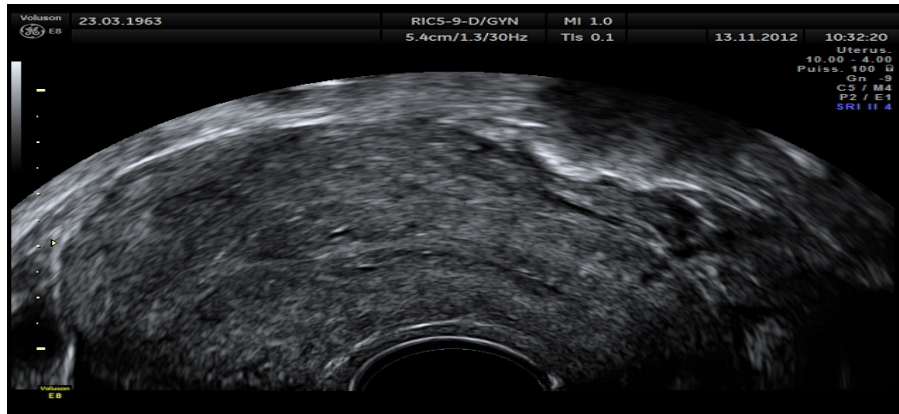


## Two distinct histologic types:

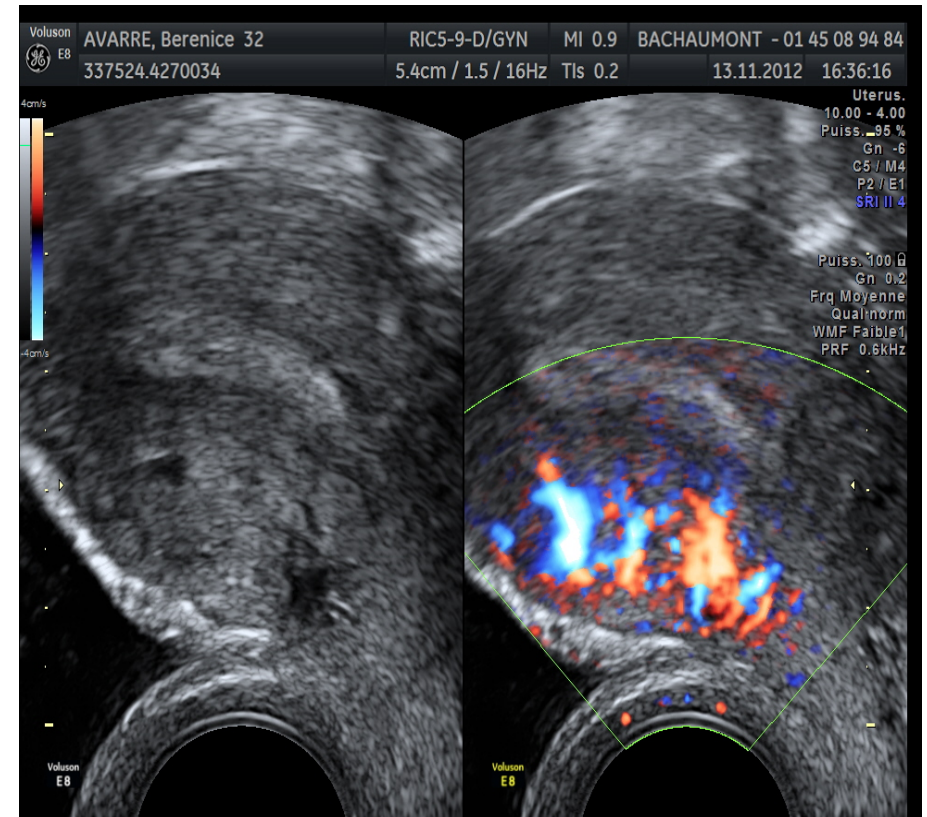
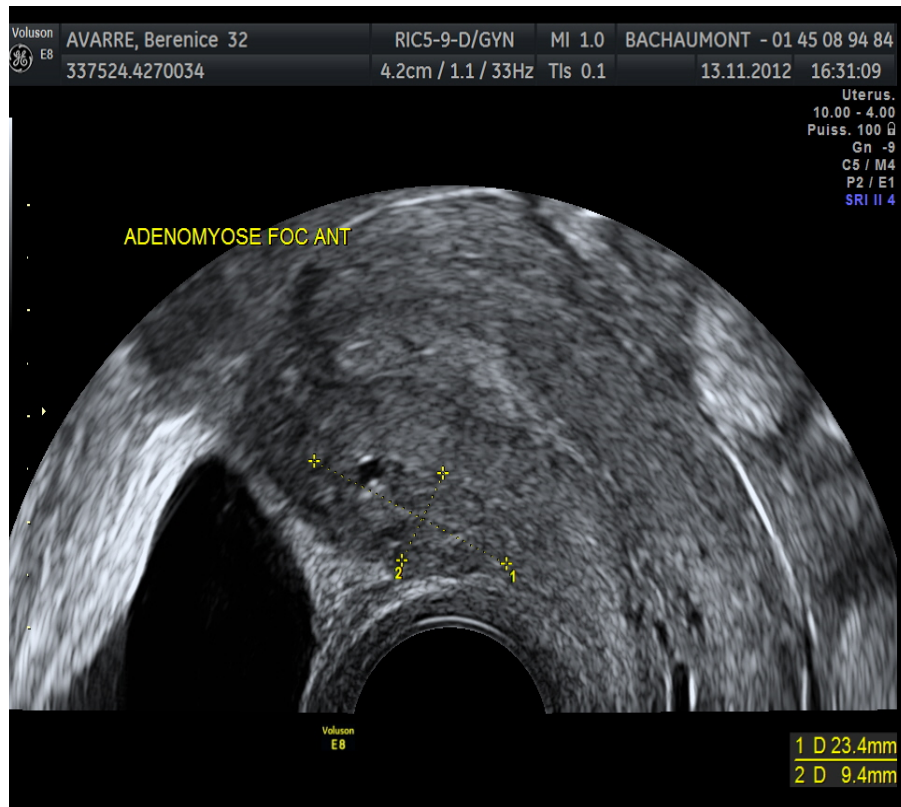
- **Diffuse Adosis +++++** The invasion of endometrial glands and/or stroma within the myometrium
- **Focal Adosis or Adenomyomata:** circumscribed tumors made up of endometrium and muscle tissue

# Adenomyosis: TV Sonographic signs

Globular uterus and asymmetrical myometrial thickening  
not caused by the presence of fibroids

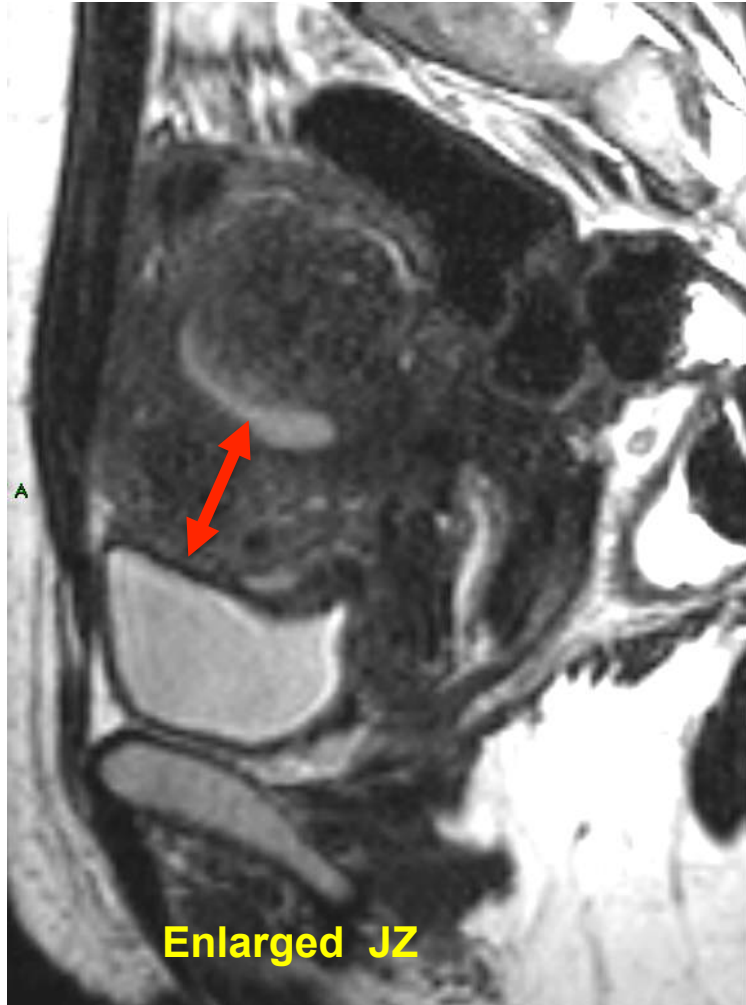


# Adenomyoma: TV Sonographic signs

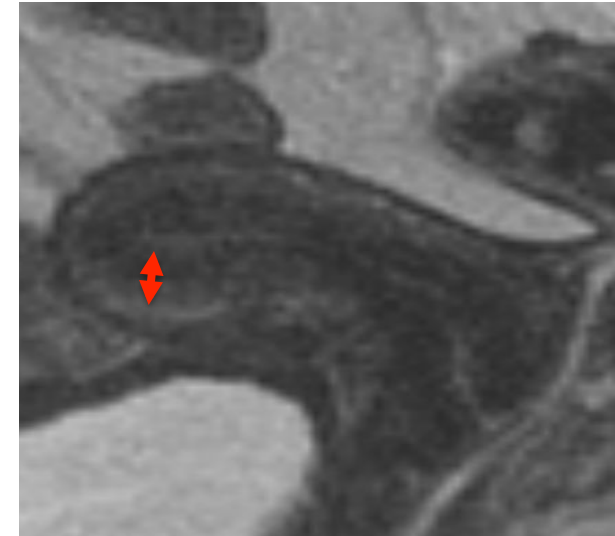




# Adenomyosis: MRI



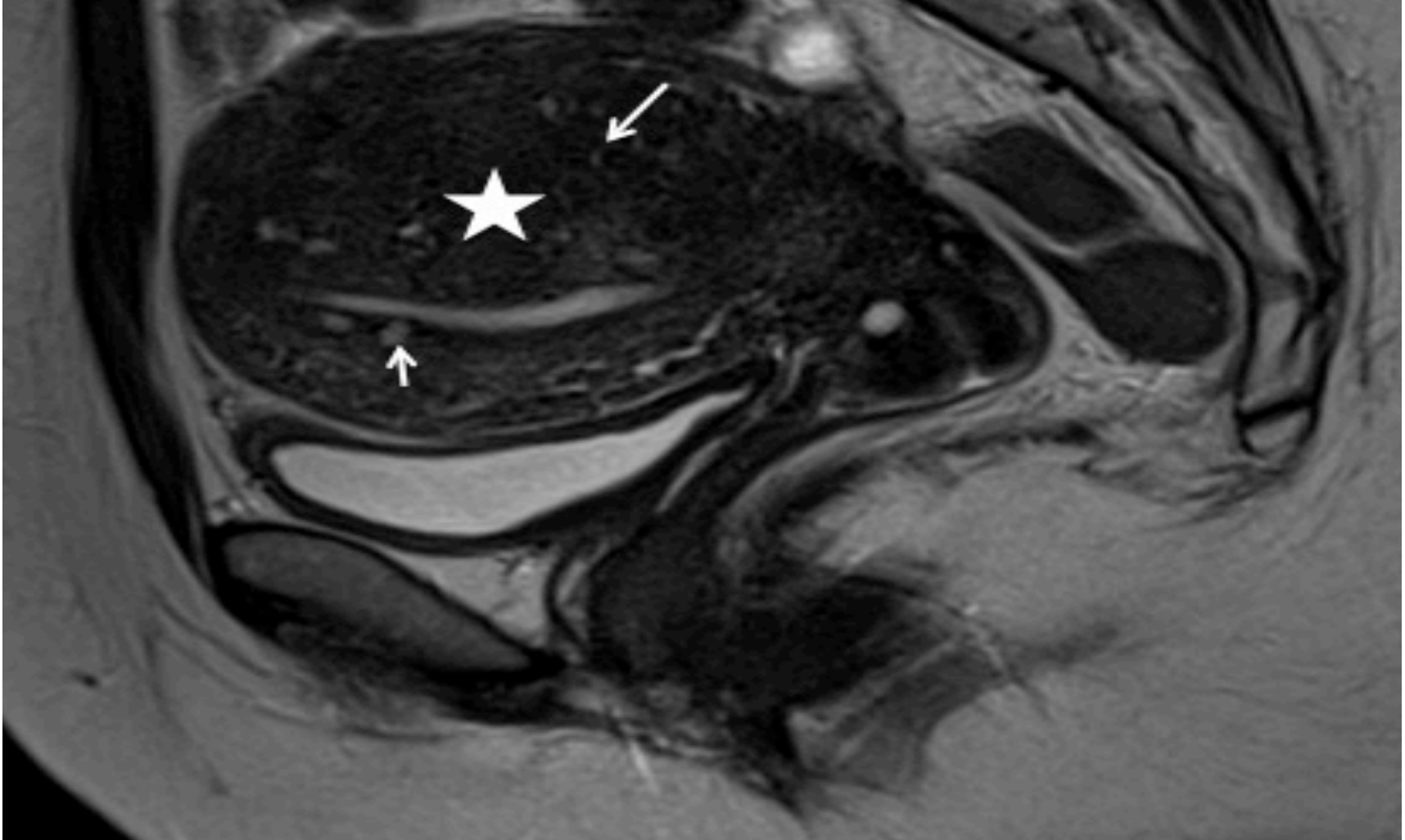
- High signal - intensity myometrial spots
- Visible Junctional Zone with a threshold value  $> 12$  mm
- Presence of an ill-defined-low-signal intensity area of myometrium
- Ratio ZJ/Myometrium  $> 40\%$



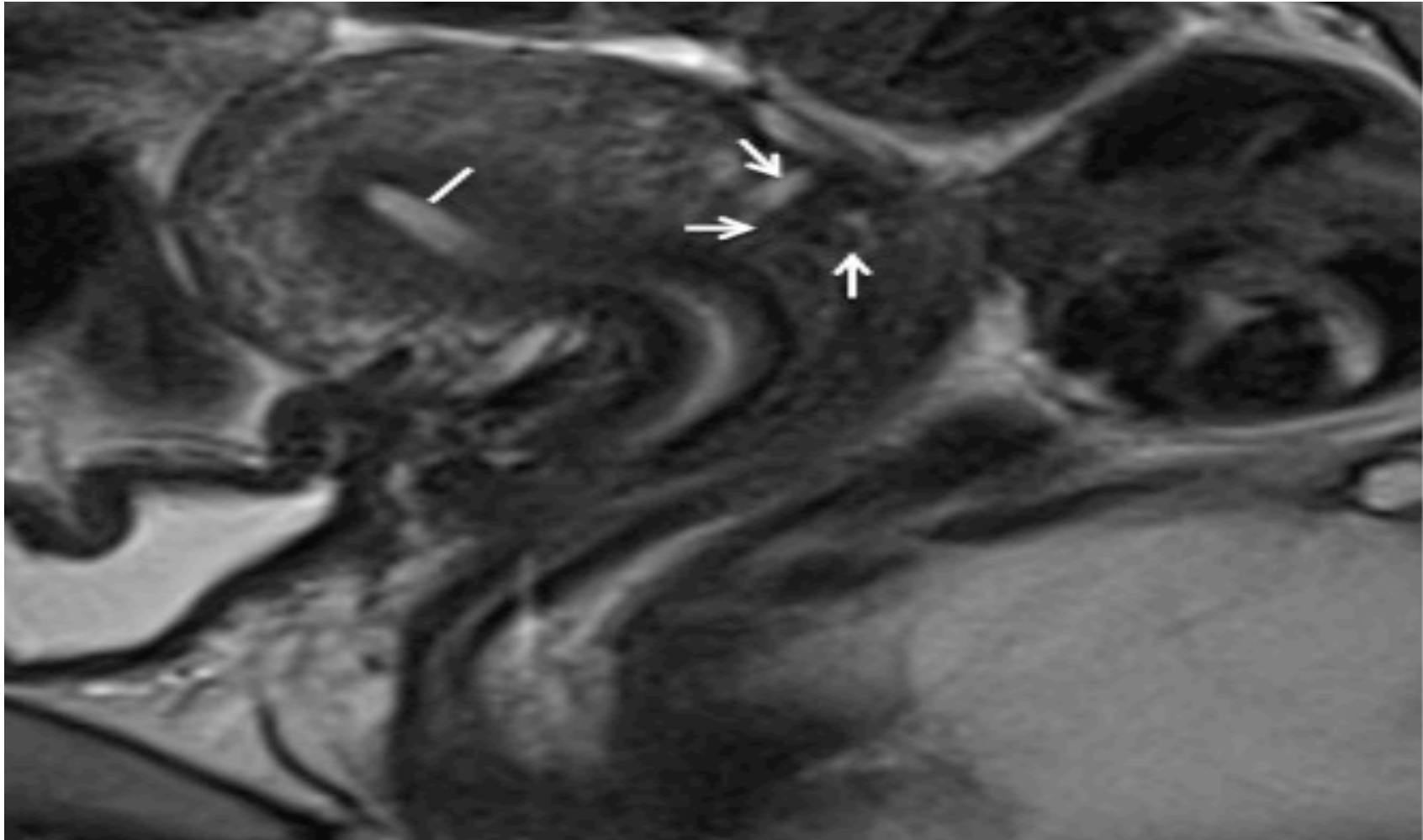
Normal Junctional Zone

Combination of these 3 criteria:  
accuracy of 85.5%

# MRI: Isolated diffuse adenomyosis

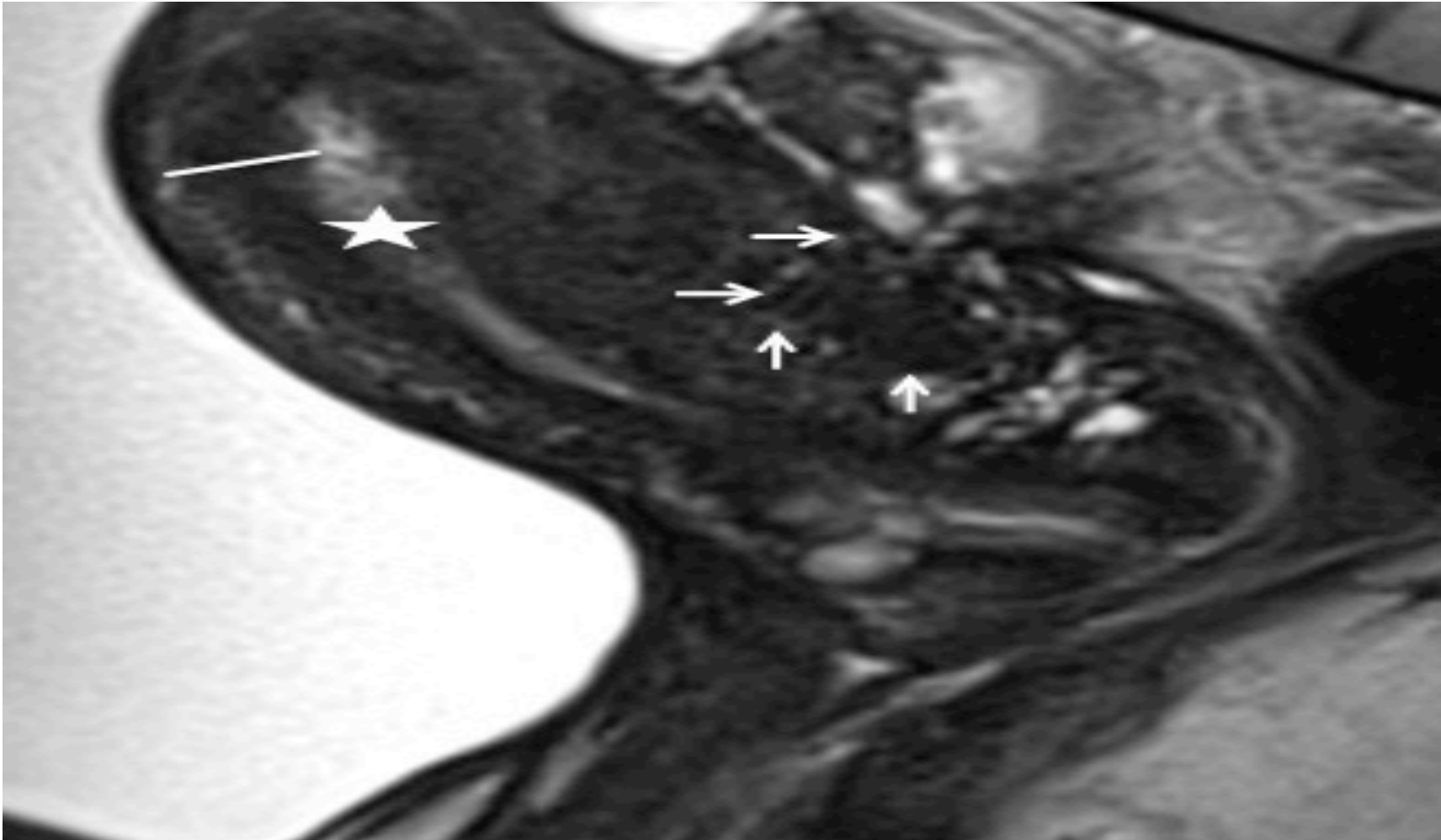


# MRI: Isolated focal adenomyosis



# MRI:

Associated **diffuse** and **focal** adenomyosis



# Endometriosis: *The implantation theory*



Sampson JA AJOG (1927)

# Endometriosis: *The implantation theory*



## Three phenotypes

- SUP: Peritoneal superficial endometriosis
- OMA: Ovarian endometrioma
- DIE: Deep infiltrating endometriosis



SUP



OMA



DIE

# Relationship between endometriosis *and* adenomyosis

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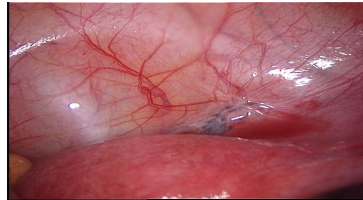
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# Relationship between **endometriosis** *and* **adenomyosis**

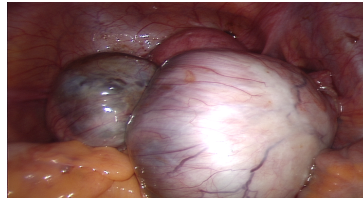
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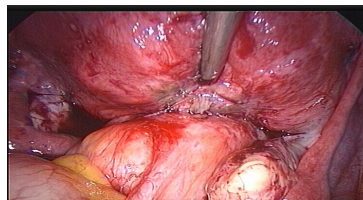
SUP



OMA



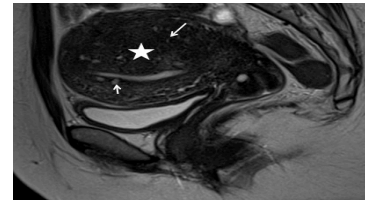
DIE



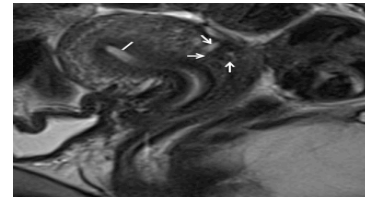
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# Relationship between endometriosis *and* adenomyosis

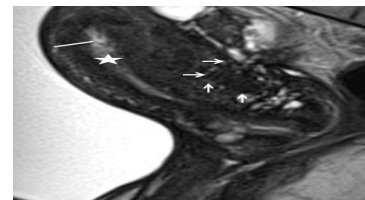
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Diffuse



Focal



Diffuse  
and  
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# Relationship between endometriosis *and* adenomyosis

Adenomyosis: MRI definition

Junctional Zone (JZ)  $\geq 12$  mm

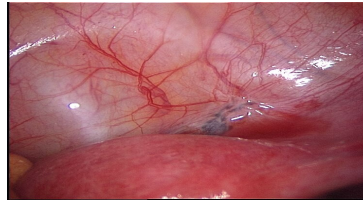
**and**

Ratio JZ / Myometrium  $> 40\%$

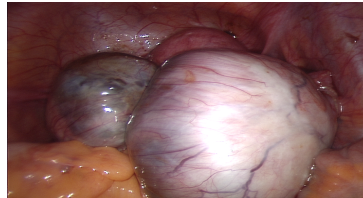
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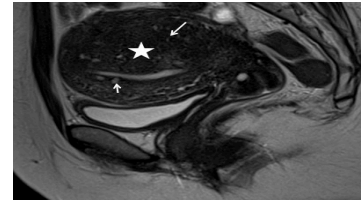
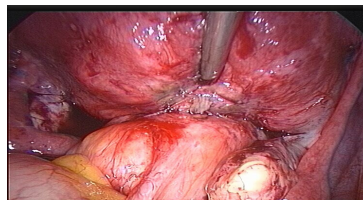
SUP



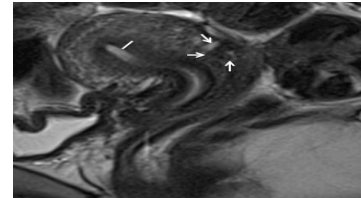
OMA



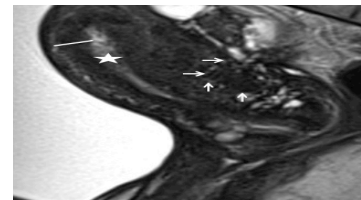
DIE



Diffuse



Focal



Diffuse  
and  
Focal

# Relationship between endometriosis *and* adenomyosis

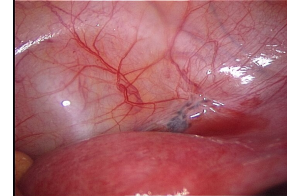
n = 292

**Controls**

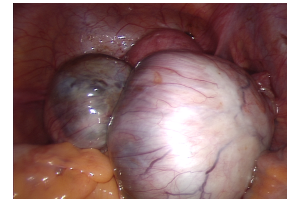
N = 55

**Endometriosis**

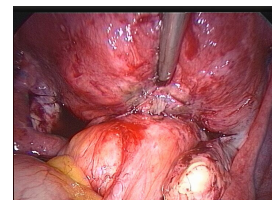
N = 237



**SUP** N = 40



**OMA** N = 31



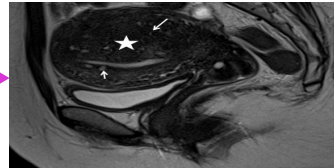
**DIE** N = 166

# Relationship between endometriosis *and* adenomyosis

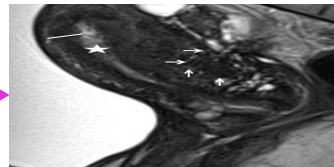
n = 292

**ADM -**  
N = 117

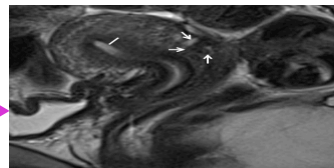
**ADM +**  
N = 175



**Isolated Diffuse** N = 53



**Associated D + F** N = 48



**Isolated Focal** N = 74

# Relationship between endometriosis *and* adenomyosis

| Patients' phenotype | N   | DIFFUSE Adenomyosis |
|---------------------|-----|---------------------|
|                     |     |                     |
| Controls            | 55  | 20 (36.4%)          |
|                     |     |                     |
| Endometriosis       | 237 | 81 (34.2%)          |
|                     |     |                     |
|                     |     | $p = 0.437$         |

# Relationship between endometriosis *and* adenomyosis

| Osis patients'<br>phenotype | N   | DIFFUSE<br>Adenomyosis |
|-----------------------------|-----|------------------------|
|                             |     |                        |
| SUP                         | 40  | 8 (20.0%)              |
| OMA                         | 31  | 14 (45.2%)             |
| DIE                         | 166 | 59 (35.5%)             |
|                             |     |                        |
|                             |     | $p = 0.068$            |

# Relationship between **Osis** and **Diffuse** adenomyosis

| <b>Patients’<br/>phenotype</b> | <b>N</b> | <b>JZ ≥ 12 mm<br/><b>AND</b><br/>Ratio &gt; 40%</b> | <b>JZ ≥ 12 mm<br/><b>OR</b><br/>Ratio &gt; 40%</b> |
|--------------------------------|----------|---|--|
|                                |          |   |  |
| <b>Controls</b>                | 55       | 20 (36.4%)  | 33 (60.0%)   |
|                                |          |   |  |
| <b>SUP</b>                     | 40       | 8 (20.0%)   | 19 (47.5%)   |
| <b>OMA</b>                     | 31       | 14 (45.2%)  | 20 (64.5%)   |
| <b>DIE</b>                     | 166      | 59 (35.5%)  | 108 (65.1%)  |
|                                |          |   |  |
| <b>Total</b>                   | 292      | 101 (34.6%)   | 180 (61.6%)  |

# Relationship between **Osis** and **Diffuse** adenomyosis

| Patients' phenotype | N   | JZ ≥ 12 mm<br><b>AND</b><br>Ratio > 40% | JZ ≥ 12 mm<br><b>OR</b><br>Ratio > 40% | JZ ≥ <b>15 mm</b><br><b>AND</b><br>Ratio > 40% | JZ ≥ <b>15 mm</b><br><b>OR</b><br>Ratio > 40% |
|---------------------|-----|---|--|--|---|
|                     |     |   |  |  |   |
| <b>Controls</b>     | 55  | 20 (36.4%)                              | 33 (60.0%)                             | 11 (20.0%)                                     | 33 (60.0%)                                    |
|                     |     |   |  |  |   |
| <b>SUP</b>          | 40  | 8 (20.0%)                               | 19 (47.5%)                             | 3 (7.5%)                                       | 19 (47.5%)                                    |
| <b>OMA</b>          | 31  | 14 (45.2%)                              | 20 (64.5%)                             | 4 (12.9%)                                      | 20 (64.5%)                                    |
| <b>DIE</b>          | 166 | 59 (35.5%)                              | 108 (65.1%)                            | 23 (13.9%)                                     | 108 (65.1%)                                   |
|                     |     |   |  |  |   |
| <b>Total</b>        | 292 | 101 (34.6%)                             | 180 (61.6%)                            | 41 (14.0%)                                     | 180 (61.6%)                                   |

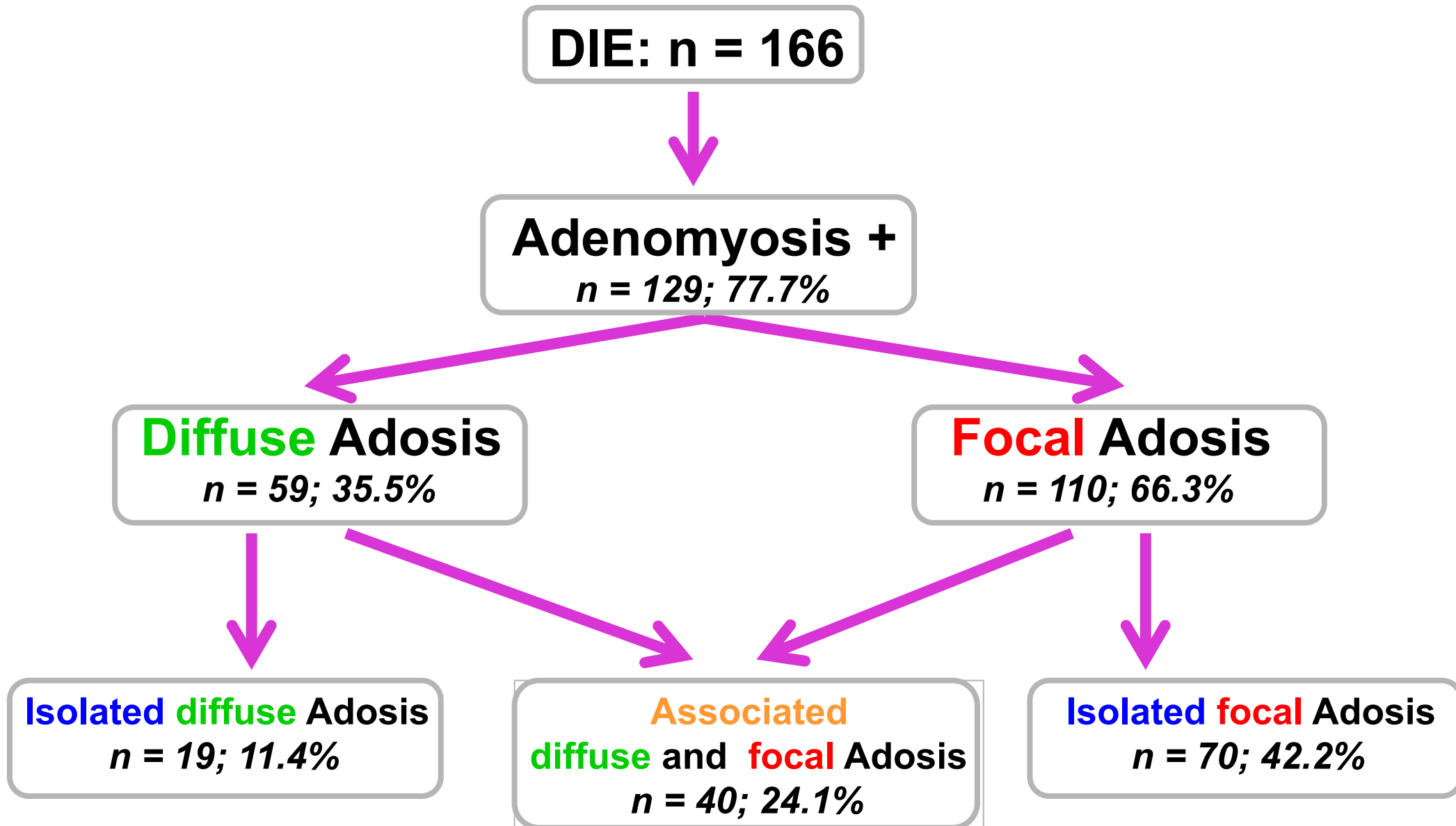
# Relationship between endometriosis *and* adenomyosis

| Patients' phenotype | N   | DIFFUSE Adenomyosis | FOCAL Adenomyosis |
|---------------------|-----|---------------------|-------------------|
| Controls            | 55  | 20 (36.4%)          | 3 (5.4%)          |
| Endometriosis       | 237 | 81 (34.2%)          | 119 (50.2%)       |
|                     |     | $p = 0.437$         | $p < 0.001$       |

# Relationship between endometriosis *and* adenomyosis

| Osis patients' phenotype | N   | DIFFUSE Adenomyosis | FOCAL Adenomyosis |
|--------------------------|-----|---------------------|-------------------|
| SUP                      | 40  | 8 (20.0%)           | 3 (7.5%)          |
| OMA                      | 31  | 14 (45.2%)          | 6 (19.3%)         |
| DIE                      | 166 | 59 (35.5%)          | 110 (66.3%)       |
|                          |     | $p = 0.068$         | $p < 0.001$       |

# Deep endometriosis *and* adenomyosis



# Relationship between Endometriosis, DIE *and* MRI diffuse adenomyosis

|      | Diffuse adenomyosis +<br>(n = 101) |      | Diffuse adenomyosis -<br>(n = 191) |      |      |
|------|------------------------------------|------|------------------------------------|------|------|
|      | N                                  | %    | N                                  | %    | p    |
| Osis | 81                                 | 80.2 | 156                                | 81.7 | 0.44 |

# Relationship between Endometriosis, DIE *and* MRI diffuse adenomyosis

|      | Diffuse adenomyosis +<br>(n = 101) |      | Diffuse adenomyosis -<br>(n = 191) |      |      |
|------|------------------------------------|------|------------------------------------|------|------|
|      | N                                  | %    | N                                  | %    | p    |
| Osis | 81                                 | 80.2 | 156                                | 81.7 | 0.44 |
| DIE  | 59                                 | 58.4 | 107                                | 56.0 | 0.40 |

# Relationship between Endometriosis, DIE *and* MRI focal adenomyosis

|      | Focal adenomyosis +<br>(n = 122) |      | Focal adenomyosis -<br>(n = 170) |      |         |
|------|----------------------------------|------|----------------------------------|------|---------|
|      | N                                | %    | N                                | %    | p       |
| Osis | 119                              | 97.5 | 118                              | 69.4 | < 0.001 |

# Relationship between Endometriosis, DIE *and* MRI focal adenomyosis

|      | Focal adenomyosis +<br>(n = 122) |      | Focal adenomyosis -<br>(n = 170) |      |         |
|------|----------------------------------|------|----------------------------------|------|---------|
|      | N                                | %    | N                                | %    | p       |
| Osis | 119                              | 97.5 | 118                              | 69.4 | < 0.001 |
| DIE  | 110                              | 90.2 | 56                               | 36.2 | < 0.001 |

# Relationship between **DIE** ( $n = 166$ ) and **MRI adenomyosis appearance**

|                            | <b>Posterior Focal<br/>adenomyosis</b><br><br>( $n = 98$ ) | <b>No posterior focal<br/>adenomyosis</b><br><br>( $n = 68$ ) | <b>p</b>                        | <b>OR<br/>(95%CI)</b>       |
|----------------------------|--|---|---------------------------------|-----------------------------|
| <b>r AFS</b>               |  |   |                                 |                             |
| <b>Total</b>               | <b><math>60.3 \pm 34.6</math></b>                          | <b><math>21.2 \pm 21.8</math></b>                             | <b><math>&lt; 0.0001</math></b> |                             |
| <b>Implants</b>            | <b><math>19.9 \pm 15.7</math></b>                          | <b><math>10.3 \pm 10.1</math></b>                             | <b><math>&lt; 0.0001</math></b> |                             |
| <b>Adhesions</b>           | <b><math>41.8 \pm 27.3</math></b>                          | <b><math>10.9 \pm 16.7</math></b>                             | <b><math>&lt; 0.0001</math></b> |                             |
| <b>Stages III &amp; IV</b> | <b>87 (84.5%)</b>  | <b>56 (42.4%)</b>   | <b><math>&lt; 0.0001</math></b> | <b>7.4<br/>[3.9 - 13.9]</b> |

# Relationship between **DIE** ( $n = 166$ ) and **MRI** adenomyosis appearance

|                                     | Posterior<br>Focal<br>adenomyosis<br><br>( $N = 98$ ) | No posterior<br>focal<br>adenomyosis<br><br>( $n = 68$ ) | p          | OR [95%CI]       |
|-------------------------------------|---|--|------------|------------------|
| Mean Nb of DIE lesions              | $3.8 \pm 2.0$   | $2.5 \pm 1.8$  | $< 0.001$  |                  |
| Nb DIE lesions $> 3$ ( $n, \%$ )    | 52 (53.1)   | 13 (19.1)  | $< 0.001$  | 4.8 [2.3 - 9.9]  |
| Intestinal DIE ( $n, \%$ )          | 86 (87.8)   | 37 (54.4)  | $< 0.001$  | 6.0 [2.8 - 13.0] |
| Mean Nb of GI DIE lesions           | $2.1 \pm 1.8$   | $1.0 \pm 1.5$  | $< 0.001$  |                  |
| Nb GI DIE lesions $> 1$ ( $n, \%$ ) | 50 (51.1)   | 15 (22.7)  | $< 0.001$  | 3.5 [1.8 - 7.1]  |
| Nb GI DIE lesions $> 2$ ( $n, \%$ ) | 25 (25.5)   | 5 (7.6)  | 0.002      | 4.2 [1.5 - 11.7] |
| Associated OMA ( $n, \%$ )          | 52 (53.1)   | 14 (20.6)  | $< 0.0001$ | 4.4 [2.1 - 8.9]  |

# Relationship between DIE and adenomyosis

## Risk factors of severity ( $n = 166$ )

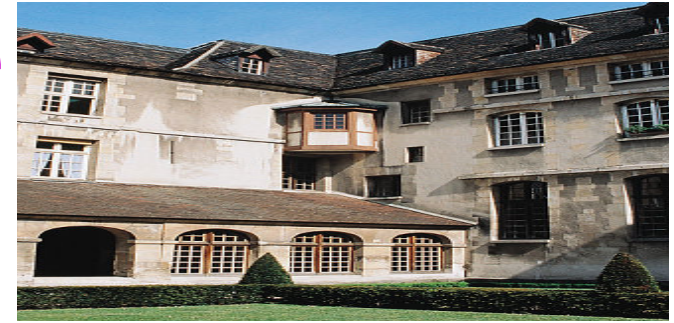
|   | DIE Ad OR [95% CI] |
|---|--------------------|
| Prediction of GI DIE lesions                  |                    |
| OMA   | 2.0 [0.8- 4.9]     |
| Post Focal ADM                                | 5.5 [2.2 -11.0]    |
| Prediction of number of GI DIE lesions > 1    |                    |
| OMA   | 3.7 [1.8- 7.5]     |
| Post Focal ADM                                | 2.4 [1.2 -5.2]     |
| Prediction of number of GI DIE lesions >2     |                    |
| OMA   | 1.6 [0.7- 3.8]     |
| Post Focal ADM                                | 3.6 [1.3 -10.4]    |
| Prediction of total number of DIE lesions > 3 |                    |
| OMA   | 2.3 [1.2- 4.7]     |
| Post Focal ADM                                | 3.8 [1.8 -8.0]     |

# Relationship between OMA and MRI adenomyosis appearance

|   | OMA +<br>(N=97) | OMA -<br>(N=140) | p      | OR<br>[95%CI] |
|---|-----------------|------------------|--------|---------------|
| Diffuse adenomyosis (n, %)                  | 42 (43.3%)      | 39 (27.9%)       | 0.01   | 2.1 [1.1 3.4] |
| Focal adenomyosis (n, %)                    | 60 (61.9%)      | 59 (42.1%)       | 0.002  | 2.2 [1.3 3.8] |
| Associated F and D Adosis (n, %)            | 24 (24.7%)      | 22 (15.7%)       | 0.06   | 1.8 [1.0-3.4] |
|   |                 |                  |        |               |
| Mean size of Junction Zone (JZ) mm          | 10.3 ± 4.9      | 7.9 ± 5.1        | <0.001 |               |
| % JZ / Myometrium                           | 0.63 ± 0.39     | 0.48 ± 0.27      | 0.001  |               |
| Mean size of<br>posterior focal adenomyosis | 16.2 ± 6.2      | 14.6 ± 5.1       | 0.169  |               |



# Take home messages



## Strategy

- **Global** approach

Endometriosis

and

Patients

SUP

OMAs

DIE

Adenomyosis



Pelvic pain



Infertility

- **Multidisciplinary** management

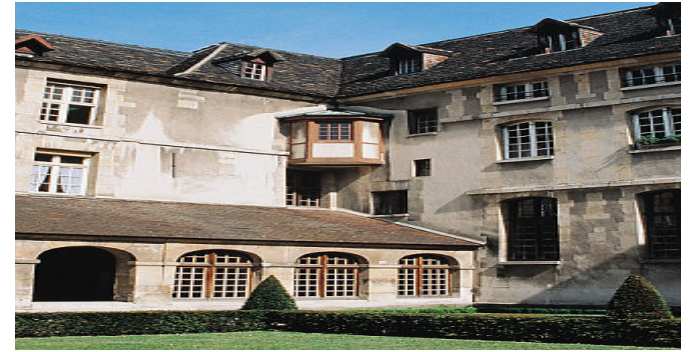
Surgery

ART

Medical Ttt



# Take home messages



- Signification of *diffuse* Adenomyosis ?
- *Focal* adenomyosis:
  - Marker for DIE severity
  - TVUS diagnosis ?
- Adenomyosis pathogenesis: *2 different entities* ?
  - *Diffuse:* Junction Zone
  - *Focal:* Implantation

# Diffuse adenomyosis

## Pathogenesis



# Focal adenomyosis

## Pathogenesis

