Assessing Outcome from Therapies for Uterine Fibroids

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Background

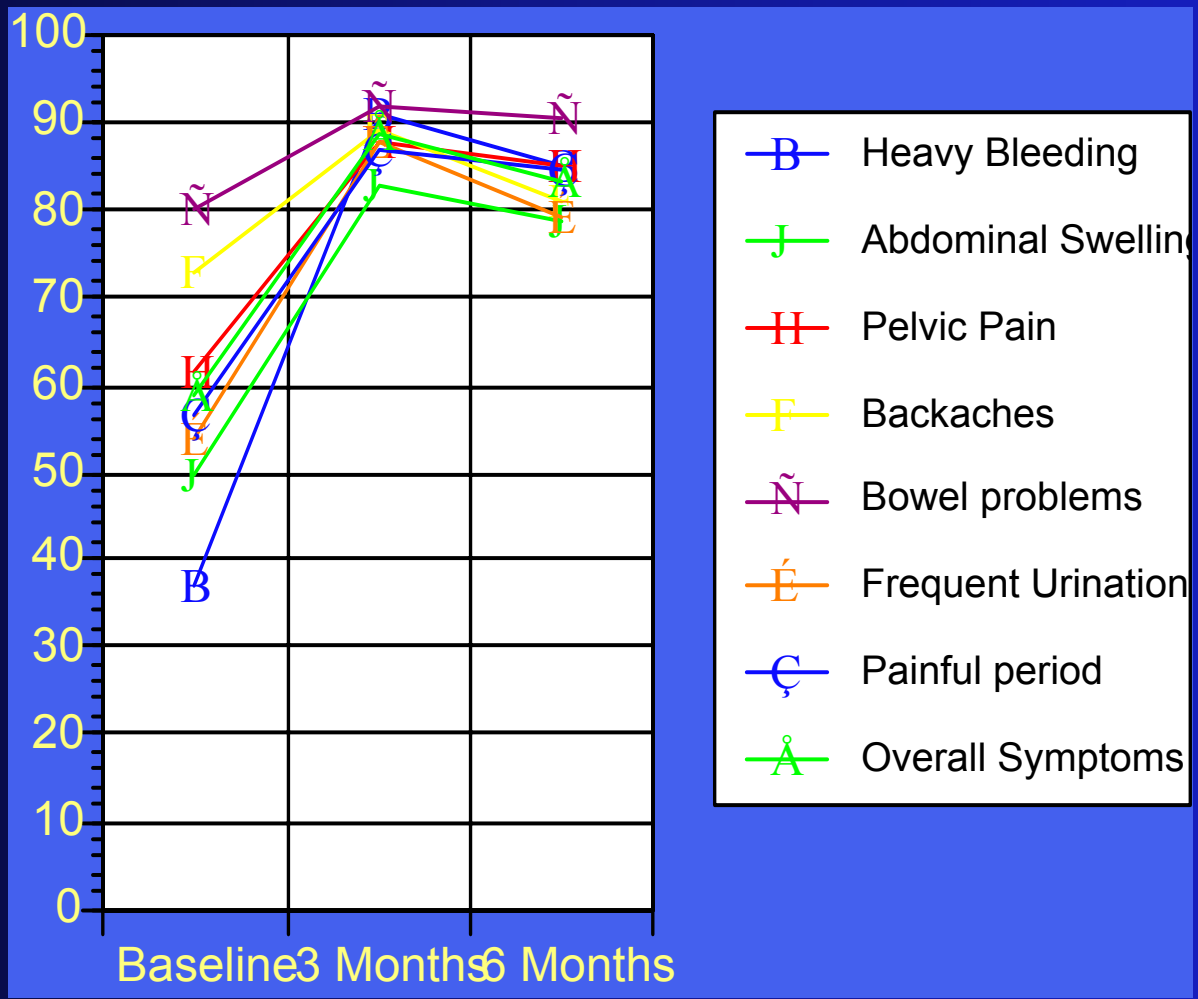
- There are few objective measures for outcome for various therapies for leiomyomata.
- Imaging outcome does not always correlate with symptom change. Imaging also subject to interobserver variability, the extent of which is not known.
- Symptoms from leiomyomata subjective and difficult to measure.
- Traditional treatment of hysterectomy definitive.
- With uterine-sparing therapies, need means of assessing success, failure and recurrence.

Available Measures of Outcome

- Simple questionnaires on symptom severity, improvement and satisfaction.
- Symptom-specific validated questionnaire
  - Ruta menorrhagia questionnaire
    - Ruta, DA. Qual Life Res, 1995 Feb:4:33-40
- Pictorial Blood Loss Assessment Chart
  - Higham J. Brit J of Ob and Gyn 1990;97:734-739.
  - Janssen CAH. Obstet Gynecol 1995;85:977-982.
- General health-related quality of life (HRQOL) questionnaires
  - SF-36, SF-12, Nottingham Health Profile
- Proprietary fibroid specific HRQOL questionnaires.

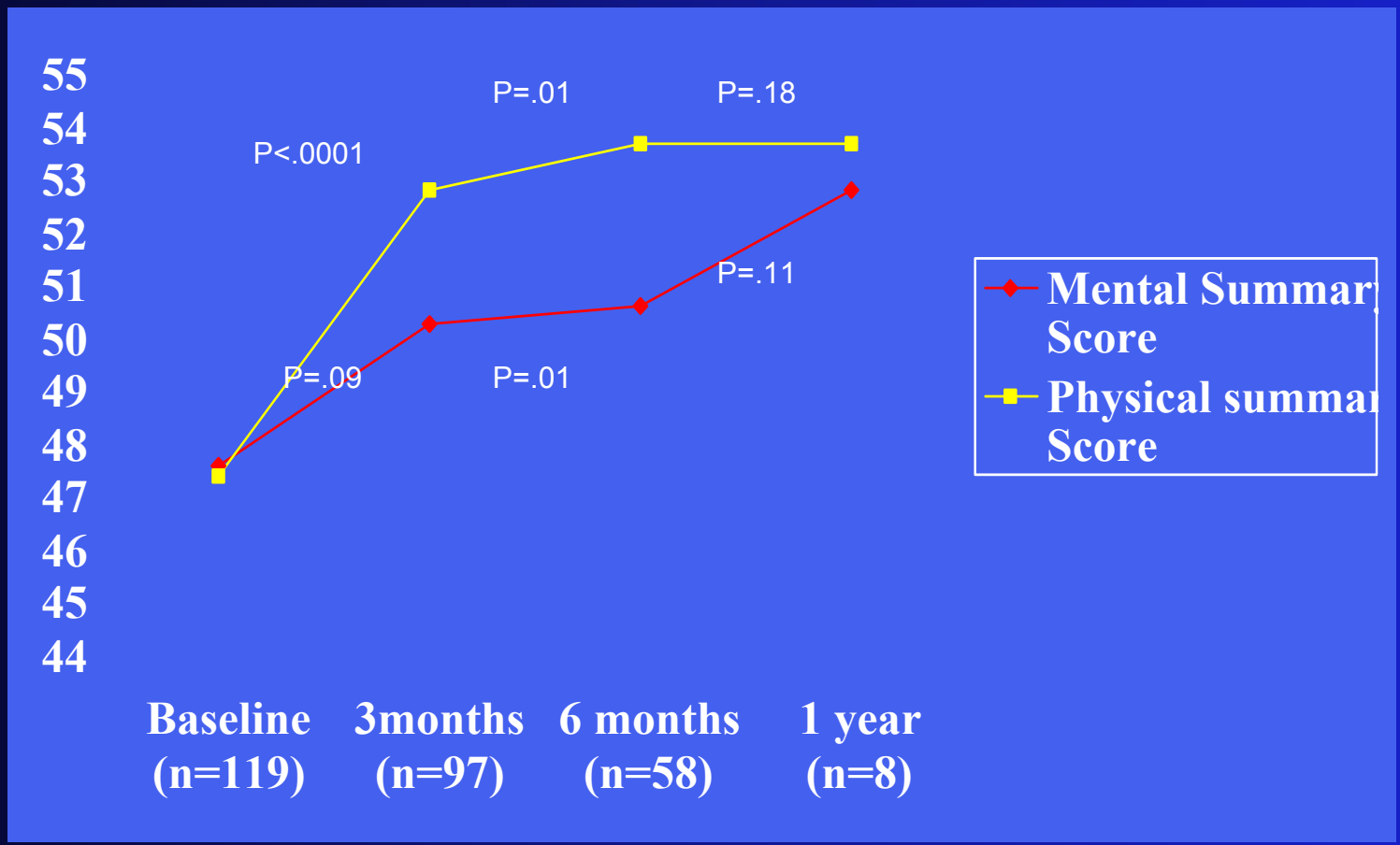
Uterine Embolization and Symptoms

Spies JB. J Vasc. Intervent Radiol.1999;10:1293-1303.



General HRQoL Instruments

SF 12 and UFE



UFE vs. Hysterectomy
Quality of Life results at 12 months

P-Values for SF-12 comparison results between the groups

Two Sample t-test	% Change Baseline to 3 M	% Change Baseline to 6 M	% Change Baseline to 12 M
SF-12 Physical	.61	.59	.69
SF-12 Mental	.11	.46	.19

Developing a QoL Instrument

- Determine the universe of potential symptoms.
  - Focus Groups
- Develop set of items to inquire about the identified symptoms and test the quality of the items.
  - Cognitive debriefing of several patients
  - Expert review
- Develop twice as many items as are estimated to be needed in a final instrument.

Validation Study

- Initially cross sectional
  - Can the instrument distinguish individuals with varying severities of symptoms or QoL impact.
- Use previously validated questionnaires such as SF-36 in addition to the new questionnaire.
- Where possible also use objective measures (eg physician exam, imaging findings)
- Test on both normals and patients with the condition.
- Retest 1 to 3 weeks later to test reliability

UFS-QOL

- 110 patients with fibroids, 30 normals.
- Standards: SF-36, Ruta menorrhagia questionnaire, sexual functioning scale.
- Patient self-assessment of severity and also physician assessment of severity.
- Retest in 40 subjects (random subset)

Data Analysis

- Initial exploratory data analysis of created items.
  - Detect floor effects and ceiling effects, difference between normals and abnormals, internal consistency of similar constructs or ideas.
  - Discard obvious outlyers
- Identify subscales, which are groups of items that score similarly and are related in concepts.

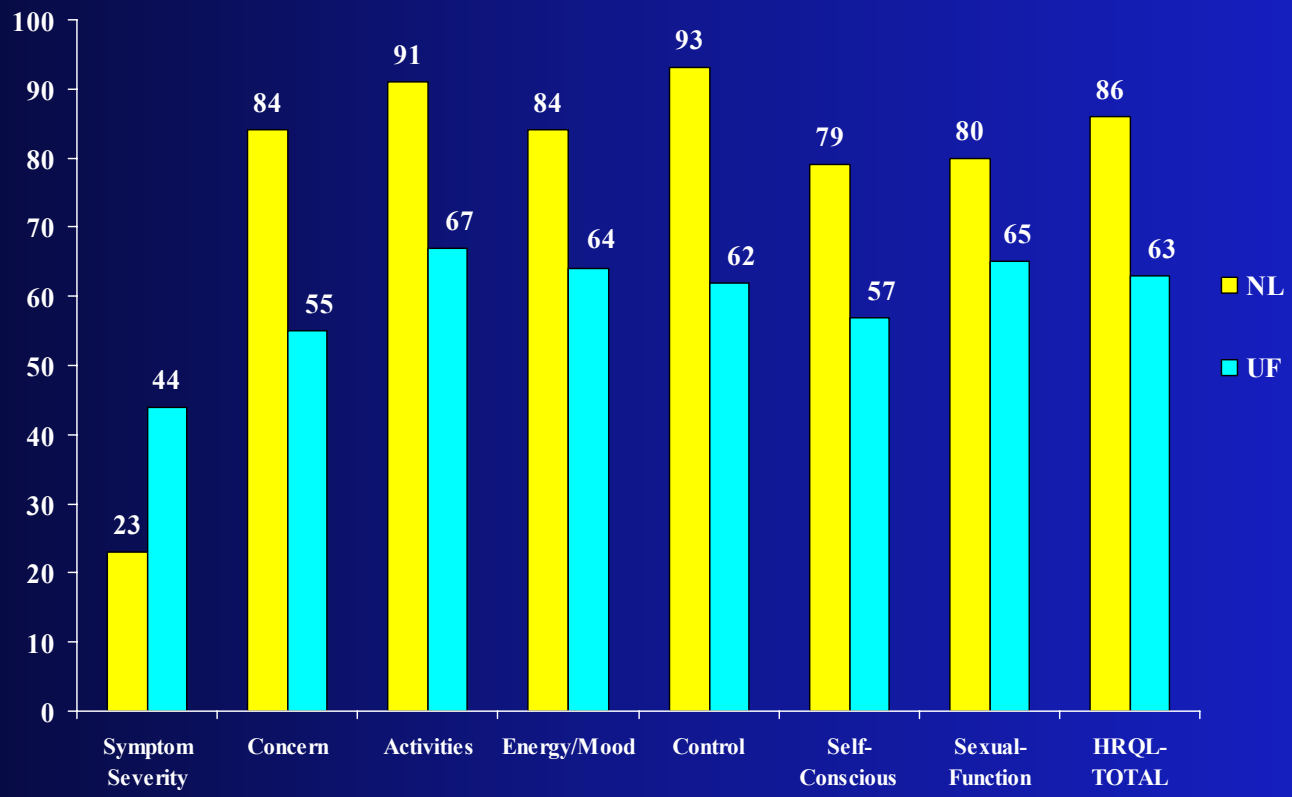
Data Analysis

- May develop two sets of subscales and repeat analysis to determine which items can be discarded.
- Discard final items to create final questionnaire.
- Assess internal validity of final instruument
- Score the QoL and compare results to the standard instruments to determine the external validity
- Compare the test-retest to determine the reliability.

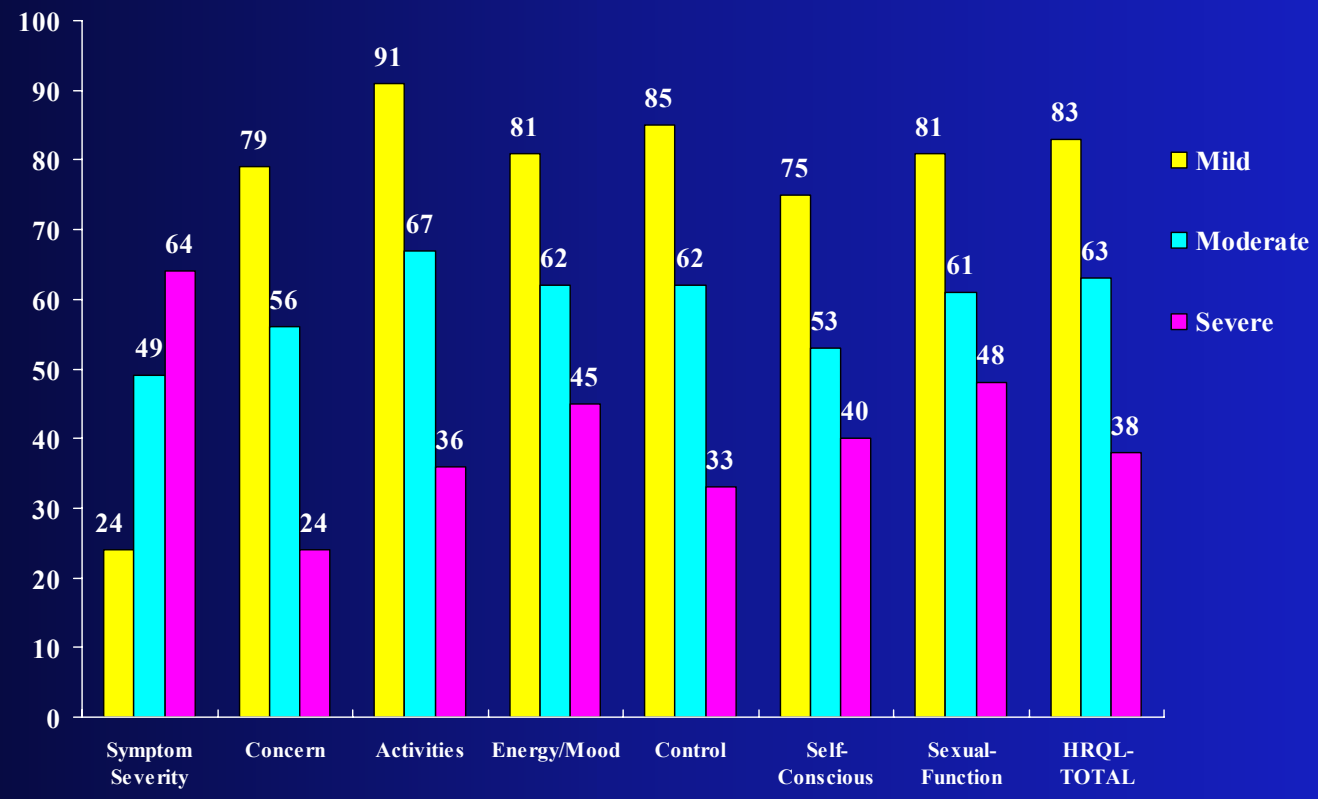
Concurrent Validity

- Small to moderate correlations with the SF-36 subscales (0.10 to 0.64).
- Bodily pain subscale of the SF-36 had the strongest correlation with the activities subscale of the UFS-QOL ($r = 0.64$).
- Moderate correlations between the UFS-QOL subscales and the Menorrhagia questionnaire ($r = 0.49 – 0.76$) and Revicki-Wu scale ($r = 0.14 – 0.78$)
- Subscale to subscale correlations were 0.45 to 0.75

Discriminant Validity: NL vs UF



Discriminant Validity: Patient-Rated Severity Levels



Uterine Fibroid Symptom and Quality of Life Questionnaire

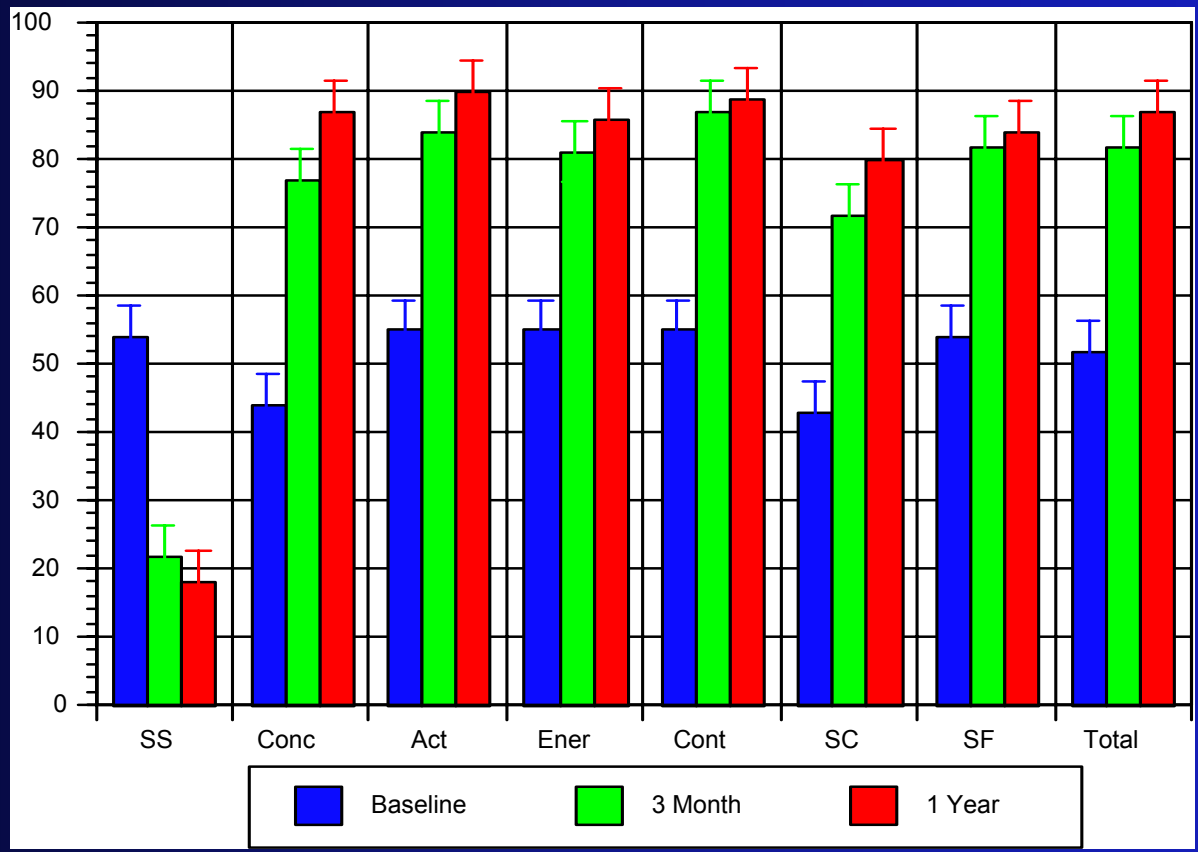
UFS-QoL

- Yields a symptom summary score and a overall QoL score, normalized to a 100 point scale.
- Symptom scale: lower score better
- Q0L Score: higher score better
  - Overall QoL is derived from the individual subscale scores.
    - To score, the subscales must be scored individually then combined for the final score. This is to protect against missing data. If less than 50% of any subscale is missing then the score can be imputed for the missing items from the mean of the other answers in the subscale.

Use of UFS-QoL in Longitudinal Research

- FIBROID Registry
  - Voluntary registry of 3000 women undergoing uterine artery embolization for fibroids.
  - Now assessing 1 year follow-up; 3 year follow-up intended.
- High-frequency ultrasound ablation of fibroids.
  - Proposed also for use in randomized comparison of UAE and HiFU.
  - Several translations created.
- Efficacy of selective progesterone receptor modulators

Use in Studies Comparing Techniques



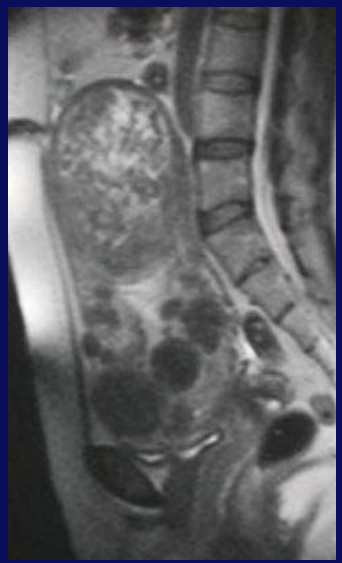
Particle PVA vs Tris Acryl Gelatin Microspheres.
Randomized Comparative Study (N=100)

Additional Needs for Clinical Studies

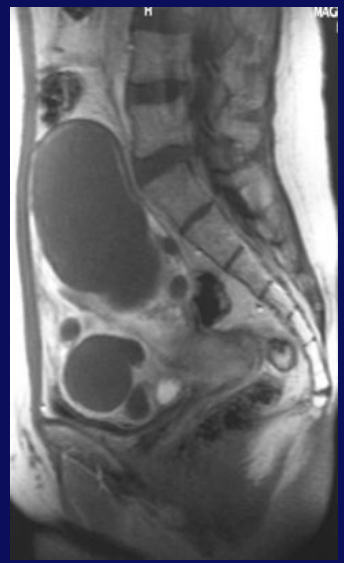
- Accepted system for classifying disease severity
  - Imaging based, encompass uterine size, # of fibroids, size of primary fibroids, degree of endometrial deviation.
  - Easily and reliably applicable.
- Accepted definitions of outcome
  - Failed procedure:
    - No persisting substantive improvement, hysterectomy, definitive myomectomy or re-embolization in first 12 months.
  - Short-term recurrence:
    - Hysterectomy, definitive myomectomy or re-treatment from 12 to 36 months.
  - Long-term recurrence:
    - Hysterectomy, definitive myomectomy, or re-embolization 36 months or greater.
- Uniform standards for assessing anatomic (imaging) outcome for ablative and uterine sparing therapies.
  - Based on fibroid perfusion (contrast-enhanced MRI).
  - Ultrasound of little utility as a follow-up imaging tool.

No Symptom Recurrence

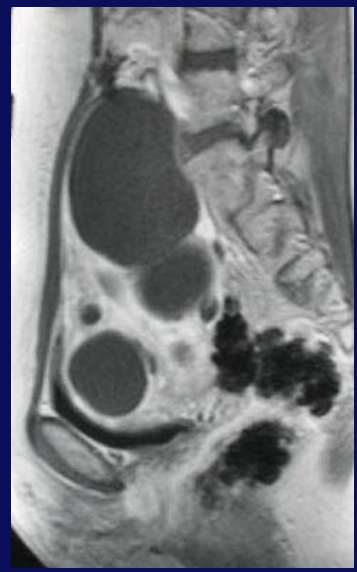
Complete Fibroid Infarction



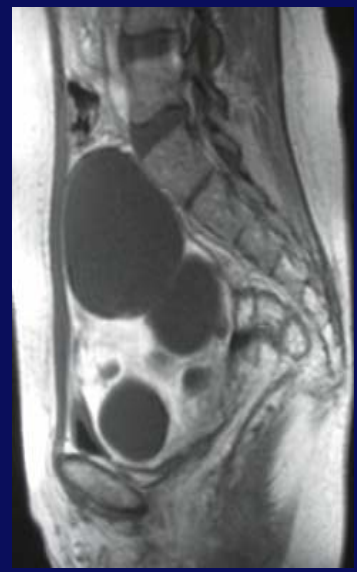
Baseline



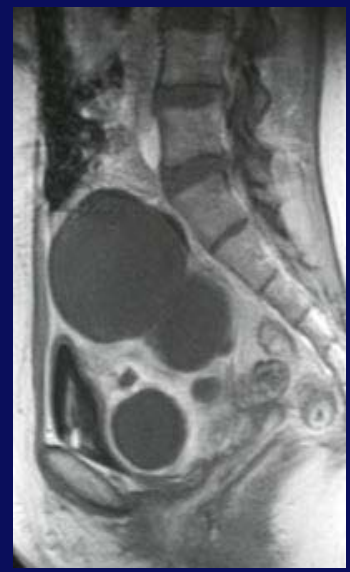
3 Months



1 Year



2 Years

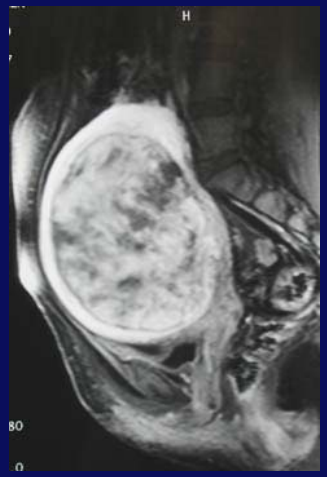


3 years

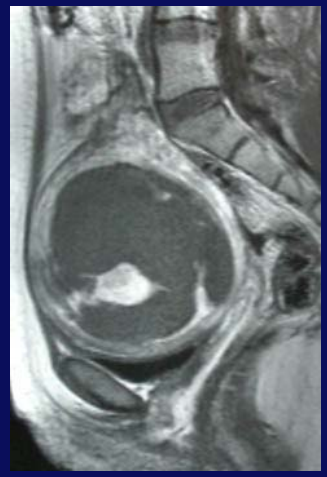
Early Recurrence

Incomplete Fibroid Infarction

Recurrent symptoms at 2.5 years post-embolization



Pre



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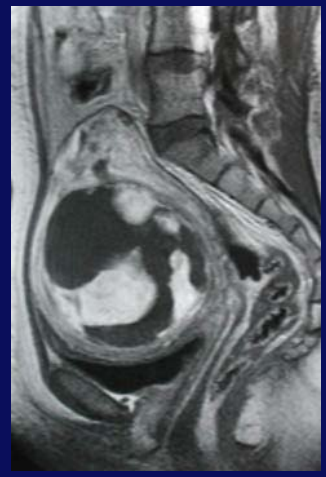
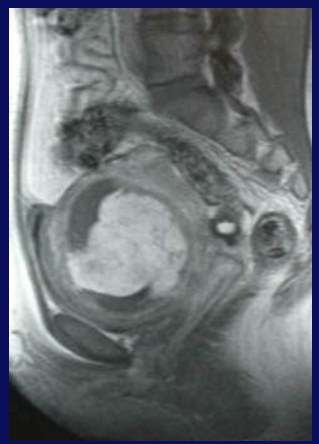
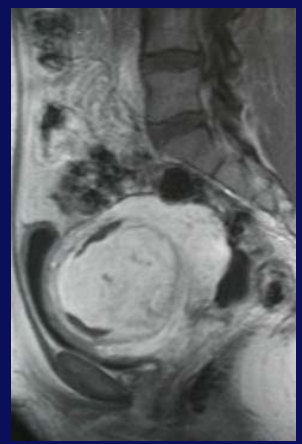


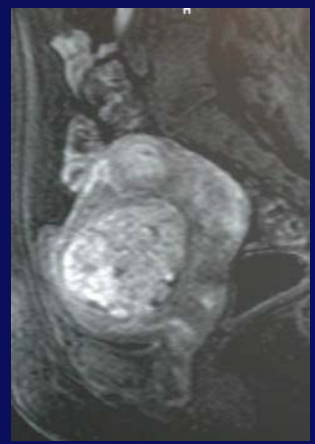
1 year



2 years



3 years



4 years

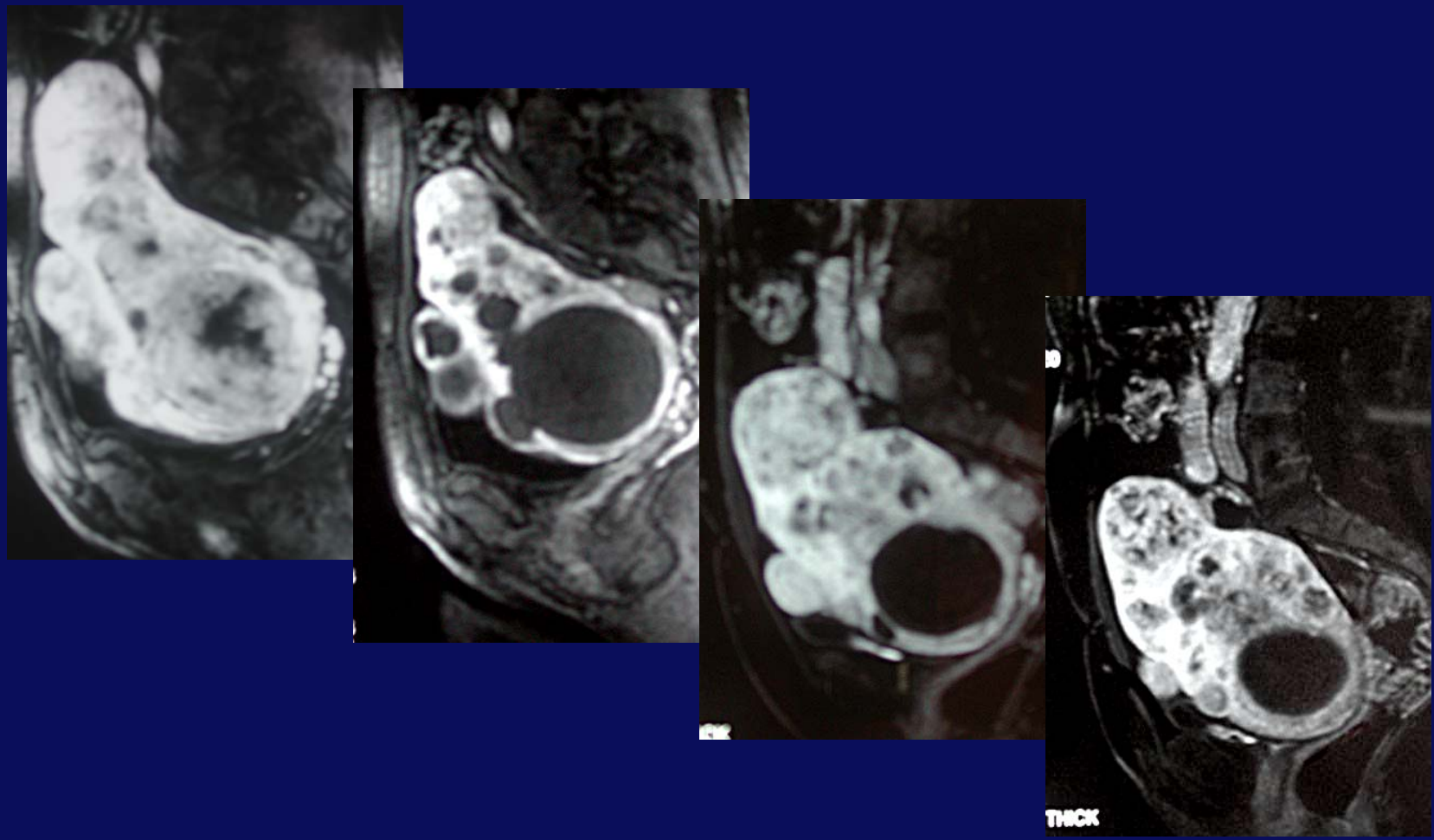
Late Recurrence

Old and New Fibroids

53 months

Late Recurrence

Old and New Fibroids



46 months

Conclusions

- Many medical conditions are symptom driven, with poor objective measures.
- Available objective measures only indirectly measure outcome and may mislead investigator.
- Modern outcome standards require consideration of symptom severity, quality of life impact.
- The use of validated condition-specific questionnaire and imaging may provide best analysis.