Could contrast ultrasound replace contrast pelvic MRI in the follow-up of patients with symptomatic fibroids treated with uterine artery embolization (UAE)?

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Aims and objectives

Leiomyomas, also known as fibroids or myomas, are the most common gynecologic neoplasm, occurring in 20%-30% of women of reproductive age. (1) Fibroids are composed of smooth muscle with varying amounts of fibrous connective tissue. Fibroids are benign and, the most part of them, asymptomatic. Unfortunately, patients with fibroids can suffer symptoms such as menorrhagia, dysmenorrhea, urinary frequency, pelvic and back pain, dyspareunia, constipation, or bulk-related symptoms. The symptomatic patients are suitable to be treated with medical or Surgical treatments. For well over a decade, uterine fibroid embolization (UFE) has been proven as an effective minimally invasive treatment for symptomatic patients. (1)

The Uterine Fibroid Embolization (UFE) is a well known and effective method of treating symptomatic fibroids. This percutaneous minimal technique selectively catheterizing both uterine arteries, where microspheres are injected to occlude the distal arterioles that vascularize the fibroids. It causes necrosis of the tumours, decreasing patients' symptoms and eventually decreasing tumours' size. Multiples articles in the literature had shown very good results of the technique, without observing statistical differences with miomectomy or hysterectomy. Therefore, it is a good option for women who wish to avoid surgery, are poorly surgical candidates, or wish to retain their uterus (1)

Ultrasonography (US scan) remains the Gold standard diagnostic imaging technique for patients with suspicious of symptomatic uterine fibroids. However, magnetic resonance (MRI) imaging is the most accurate imaging technique for detection and evaluation of them.

Even MRI is more extensive than US, it can show both uterine artery origins, its variants and a possible ovarian artery fibroid vascular supply, decreasing patient's and operator's radiation dose during the procedure. It is also superior to differentiate adenomyosis and leiomyomas. Therefore, it has become the modality of choice for diagnosis and follow up of patients treated with UAE.

The evaluation in gray scale and with color Doppler has low sensitivity in the detection of alterations in microvascularization. The use of intravenous ultrasound contrast (in our case, Sonovue), is a simple technique, not nephrotoxic and without the adverse effects of iodinated contrasts and ionizing radiation, which provides information on the vascularization of the fibroid in real time, in addition to allow better definition of the boundaries of the tumour thus improving the diagnostic yield. (10)
The aim of this study is to evaluate the powerful of post-UAE iv contrast US scan vs post- iv contrast MRI scan in order to detect the success and complications of the percutaneous technique.

**Contrast Enhanced Ultrasound (CEUS)**

There are several contrast enhanced ultrasound (CEUS) drugs licensed in Europe, such as Levovist®, Optison®, Sonovue®, Definity®. In our case, SonoVue was the drug used, which is currently the CEUS most frequently used. It is a high molecular weight gas, whose microbubbles contain sulfur hexafluoride stabilized with several surfactants (phospholipids and palmitic acid). The average diameter of the microbubbles is 2.5 microns and 90% is less than 8 microns. It remains viable in the vial for 6 h after preparing it. The usual dose is 2.4 ml when administered intravenously. (2) (3).

Ultrasound scans with Sonovue pre- and post UAE were performed with a Siemens ultrasound, B-mode with pulse inversion and a low-frequency convex probe (up to 5Mhz).

Follow up c-US scans were performed one month after the percutaneous procedure was done. Differences in the size of the biggest tumours and the lack or persistence of myomas' contrast enhancement were recorded. If contrast enhancement of the lesions persisted, they were classified as 1) Peripheral enhancement, 2) Partial enhancement, but less than 50% 3) Partial enhancement, but more than 50%, 4) Avascular. Preservation of uterus vascularity was also checked.

We considered a successful treatment by imaging if a lack of tumour enhancement and a preservation of uterus vascularity was observed. The decrease of tumours' size compared with the pre treatment c-US scan was not necessary to evaluate the success of UAE.

These ultrasounds were performed and reported by trained radiologists of the interventional radiology department. Those radiologists did not know the result of the pelvic MRI and vice versa.

**Pelvic MRI with contrast.**

In our case we used a 1.5 T Siemens MRI machine, and all the MRIs were performed under the same protocol, which included turbo-spin echo and fat saturation sequences in T2 and 2D FLASH with dynamic sequential study, post intravenous gadolinium injection (0.1 mmol / kg) in the sagittal and axial planes and, in some cases coronal plane was also included.

During Pre UAE c-MRI, size, number and location of fibroids were reported (only transmural and transmural myomas with submucosal component were embolized in
our case). Uterine arteries anatomy and the possible ovarian artery hypertrophy and involvement were also described.

Follow-up c-MRI was performed in the majority of patients between the 1st and 2nd month post UAE procedure. Differences in the size of the biggest tumours and the lack or persistence of myomas' contrast enhancement were recorded. If contrast enhancement of the lesions persisted, they were classified as 1) Peripheral enhancement, 2) Partial enhancement less than 50% 3) Partial enhancement, but more than 50%, 4) Avascular. The preservation of uterus vascularity was also checked.

We considered a successful treatment by imaging if a lack of tumour enhancement. The decrease of tumours' size compared with the pre treatment c-MRI was not necessary to evaluate the success of UAE.

Once more, these MRI were reported by consultant interventional radiologists. Those radiologists did not know the result of the pelvic c-US scan findings
Methods and materials

Between 2004 and 2007, 39 patients with symptomatic uterine transmural myomas were treated with UAE in our department. All of them were enrolled in a comparative prospective study to evaluate the diagnostic power of c-US scan vs c-MRI scan in order to evaluate patients follow up. (figure 1)

UAE was always performed at the interventional radiology suite. Both uterine arteries were successfully catheterized and embolised with particles in all cases. No ovarian artery embolisation was performed during the first procedure attempt. All patients were admitted for 24-48 hours post-procedure to evaluate and treat probable post procedure pain.

Clinical and analytical (HB, FSH and LH) follow up at the gynecology and interventional radiology service were also performed at 6-12-24 months post UAE.

Patient's type of symptoms referred, c-US and c-MRI pre and post procedure findings, immediate or late complications, improvement of the symptoms post treatment, need of second embolisation, need of second hospital admission, hysterectomy required and analytic data were collected.
Fig. 1: Performance Algorithm

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Results

39 patients were included in the study, with a mean age of 44.5 years (36-55). 24 months follow up was completed in 18 cases (46.2%), 21 patients were followed up during 12 month (53.8%) and all them during 6 months (100%).

Pre-embolization ultrasound was performed at 27 (69.2%), pre-embolization MRI at 39 (100%), c-US scan and c-MRI scan follow up were performed in all cases (100%). 26% of patients had a single myoma (Figure 2). 77% of treated myomas were transmural, while the remaining 23% were transmural with a submural component. Of the total sample, 8 patients (17.9%) were re-admitted post UAE: 4 for severe pain, 3 for expulsion of myoma (2 ended in hysterectomy) (Figure 3) and 1 for high fever.

Post-treatment Sonovue ultrasonography as well as contrast-enhanced MRI demonstrated avascular tumor in 30 patients (82.1%) and persistence of tumor vascularization in 9 patients (17.9%). (Figures 4, 5, 6, 7, 8, 9, 10, 11 and 12) those results showed a 100% PPV and 100% NPV of Sonovue ultrasound findings vs c-MRI findings (Figure 13).

Studying the 9 patients with persistent vascularization, 7 had transmural myomas and 2 transmural myomas with serous component. The type of persistence vascularity was 2/9 peripheral uptake, 6/9 partial uptake less than 50% and 1/9 presented partial uptake vascularization but greater than 50% of the myoma. Clinical review of these 9 patients showed persistent symptoms in 5 patients. A second UAE was performed in all 5 cases, and in 4 of them, one or both ovarian arteries were now embolised. Unfortunately, one of these 5 patients required hysterectomy even though the second UAE was attempted.

Figure 14 shows initial patients’ symptomatology. Figure 15 shows clinical symptoms evolution at 6, 12, 24 months Post UAE, recording whether the patient presented 1) improvement 2) failure 3) asymptomatic 4) menopause. Clinical evolution shows improvement of symptoms after 6-12 months post treatment with tendency to increase menopause and asymptomatic symptoms after 12-24 months, as expected.

Analytical blood test follow up (HB, FSH, and LH) shows an increase in hemoglobin levels after UAE in patients with clinical and imaging successful treatment (Figure 16). Interestingly, patients with therapeutic failure had minimal increase in hemoglobin levels until a new embolization was performed. Analytical data evolution evaluation of FSH and LH demonstrated a tendency to menopause hormone patron in the group of patients with therapeutic success (Figure 17).
**Fig. 2:** The graph shows the number of embolized fibroids. 26% of the embolized patients had 1 fibroid.

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**Fig. 3:** Complications, A) One of the 3 cases of expulsion of fibroid after UAE, was a fibroid of about 15 cm B) Hysterectomy.

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**Fig. 4:** A) Ultrasound without contrast pre-UAE showing fibroid of 46x41mm, B) Ultrasound image after UAE showing fibroid with absence of color Doppler signal. C) Sonovue contrast ultrasound post-UAE showing avascular fibroid.

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**Fig. 5:** MRI images before and after UAE showing successful treatment, these findings coincide with the results of pre and post UAE ultrasound (see previous image). A) Pre-EAU MRI showing vascularized fibroid. B) Post-UAE MRI demonstrating avascular fibroid.

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**Fig. 6:** A) and a) Pre-UAE ultrasound with contrast showing fibroid with homogenous enhancement (vascularized) B) Post-UAE ultrasound with contrast (Sonovue) showing avascular fibroid C) Pelvic MRI with contrast that shows absence of fibroid enhancement (successful treatment)

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**Fig. 7:** Images showing successful embolization. A) and B) Pelvic MRI with contrast 1 month post UAE, dynamic sequential study with fat suppression demonstrating avascular fibroid. C) Ultrasound with contrast (Sonovue) a month after UAE showing the same avascular fibroid

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Fig. 8: Images show successful embolization. A) and a) Angiographic study showing both uterine arteries before embolization with PVA microparticles. B) Ultrasound with contrast (Sonovue) post-embolization showing avascular fibroid C) MRI with contrast, dynamic sequential study with fat suppression, showing the same avascular fibroid

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**Fig. 9:** Images of a failure of the UAE. A) Sonovue contrast ultrasound post- UAE shows enhancement of more than 50% of the fibroid, B) pelvic MRI with contrast also showed enhancement of more than 50% of the myoma. C) and c) Angiographic study showing both permeable uterine arteries with irrigation of fibroid. D) and d) Post-embolization angiographic study with PVA showing amputation / occlusion of both uterine arteries

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**Fig. 10:** Images show peripheral enhancement / vascularization of the fibroid after UAE. A) MRI post embolization with peripheral enhancement of the fibroid. B) Ultrasound with contrast (Sonovue) post embolization, that also shows peripheral vascularization of the myoma.

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**Fig. 11:** ultrasound images of a post embolized transmural myoma with persistence of peripheral vascularization A) Pre-contrast ultrasound shows image of anechogenic myoma B) Ultrasound with contrast (Sonovue) showing peripheral enhancement of myoma.

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**Fig. 12:** Post-embolization MRI of the same patient of the previous figure, where peripheral fibrous enhancement of the fibroid is also shown

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**Fig. 13:** Results show a sensitivity and specificity of ultrasound contrast Sonovue 100%, with NPV and PPV of ultrasound Sonovue 100%

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**Fig. 14:** Initial Symptomatology of the 39 patients included in the study

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**Fig. 15:** Graph showing the clinical evolution of patients at 6, 12, and 24 post UAE.

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**Fig. 16:** The graph shows the evolution of hemoglobin in patients before and after UAE, with improvement of anemia in patients with successful treatment, while patients with treatment failure do not.

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**Fig. 17:** Graph showing tendency to increase FSH and LH levels in patients with therapeutic success in relation to evolution to menopause as expected

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Conclusion

This study shows that pelvic Contrast Enhanced Ultrasound (CEUS) is a sensible and specific follow up imaging technique to assess treatment responses in patients with uterine fibroids treated with UAE, being it cheaper and more easily accessible than cMRI (gold standard).
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