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ORIGINAL PAPER

Uterine fibroid therapy using interventional radiology mini-invasive treatments: current perspective

Carlo Masciocchi[1] · Francesco Arrigoni[1] · Fabiana Ferrari[1] · Aldo Victor Giordano[1] · Sonia Iafrate[1] · Ilaria Capretti[1] · Ester Cannizzaro[1] · Alfonso Reginelli[2] · Anna Maria Ierardi[3] · Chiara Floridi[3] · Alessio Salvatore Angileri[4] · Luca Brunese[5] · Antonio Barile[1]

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Abstract Uterine fibroids are common benign tumors of unclear etiopathology that affect the female reproductive tract. They are responsible for considerable morbidity and deterioration of life quality, and may have a negative impact on the reproductive system as well. Besides surgery aided by uterus-saving techniques, several minimally invasive procedures are now available within the field of interventional radiology that represent a valid solution for women who desire pregnancy and relief from disease-specific symptomatology. The main advantages offered by these techniques are low grade of invasiveness and short times of hospitalization. The most diffuse techniques are uterine artery embolization (UAE) and magnetic resonance-guided high-intensity focused ultrasound (MRgFUS). UAE is an endovascular procedure whose goal is obtained by provoking ischemia of the uterine vessels. MRgFUS is a thermoablation procedure that selectively ablates the symptomatic fibroids. In this review study, both procedures will be described, including a description of technical details, indications, contraindications, complications, and outcomes.

Keywords Uterine fibroids · Interventional radiology · UAE · MRgFUS · Uterine artery embolization · HIFU

✉ Carlo Masciocchi
carlo.masciocchi@cc.univaq.it

[1] Diagnostic and Interventional Radiology, Department of Applied Clinical Science and Biotechnology, University of L'Aquila, L'Aquila, Italy

[2] Department of Internal and Experimental Medicine, Magrassi-Lanzara, Institute of Radiology, Second University of Naples, Naples, Italy

[3] Department of Radiology, Insubria University, Varese, Italy

[4] Diagnostic and Interventional Radiology Unit, University of Milan, Milan, Italy

[5] Department of Medicine and Health Science "V. Tiberio", University of Molise, Campobasso, Italy

Introduction

Uterine fibroids (UFs), also known as myomas or leiomyomas, are the most common benign tumors of the female reproductive tract [1, 2].

They are monoclonal tumors that arise from the uterine smooth muscular tissue of the myometrium and consist of abundant quantities of extracellular matrix containing collagen, fibronectin, and proteoglycan [3, 4]. The etiopathology of UFs is unclear, multifactorial, and enigmatic [5].

The cumulative incidence of UFs is 20–40% of women during their reproductive years. The prevalence is lower in Europe than in the USA, and this is probably due to racial differences. The incidence is 80% among black women and approaches 70% among white women. The incidence by age 35 is 60% among African-American women, increasing to 80% by age 50, whereas in Caucasian women the incidence is 40% by age 35, and almost 70% by age 50 [6–8].

Many affected women are asymptomatic (approximately 50%), nevertheless, UFs can cause significant morbidity and deterioration of life quality [9]. Symptomatic UFs can cause abnormal uterine bleeding (AUB), heavy menstrual bleeding (HMB), and complaints related to the impact of the enlarged uterus on the adjacent pelvic structures ("bulk" symptoms).

Moreover, UFs have a negative impact on the reproductive system because interfering with the embryo transfer and implantation, they may reduce fertility. The risk of early spontaneous abortion and complications during labor and birth are other disease-related adverse events. UFs are the sole cause of infertility in 2–3% of women but may contribute to infertility in 5–10% of women. They are also estimated to be the cause of approximately 7% of recurrent spontaneous abortions [8, 10, 11].

Diagnosis can be accomplished through clinical examinations, but the clinical suspicion of UF is confirmed by means of diagnostic imaging. Transvaginal and abdominal ultrasounds (US) are often the method of first choice due to availability and low costs. Their limitations, however, lie in the fact that they are operator-dependent and inadequate for definition of the number and position of UFs.

Magnetic resonance imaging (MRI) is the technique of choice in the evaluation of many diseases [12–24] and in particular when precise mapping of the UF is required for presurgical planning. MRI has 88–93% sensitivity and 66–91% specificity in the diagnosis of UFs. Other imaging techniques (CT) have a limited sensitivity in detecting fibroids [6].

According to their anatomical location, UFs are traditionally classified into submucous, intramural or subserosal.

In 1993, the European Society of Gynaecological Endoscopy (ESGE) subdivided submucous UFs into three subtypes: pedunculated (type 0, without myometrial extension); sessile with intramural extension of fibroid $<50\%$ (type I), and sessile with intramural extension $\geq 50\%$ (type II) [25]. In 2001, the International Federation of Gynaecology and Obstetrics (FIGO) used the same system for classification of submucous UFs but included other categories, namely the type III Lesions that are localized in the myometrium but do not cause deformation of the endometrial cavity. Fibroids protruding $\geq 50\%$ out of the serosal surface are considered subserosal [26].

The ESGE and the expanded FIGO classification systems are valuable to evaluate therapeutic options, but present some limitations.

For these reasons, in 2005, a presurgical classification was designed taking into consideration 4 criteria: a) penetration of the UF into the myometrium (same as ESGE/FIGO system); b) extension of the UF base into the endometrial surface; c) size of the fibroid; d) location along the uterine wall, in the upper, middle or lower third of the corpus and its orientation (anterior-posterior or lateral) [27–29].

To date, surgical as well as medical treatments are available and their choice depends on number, size and location of UFs, patient's age and preferences, and pregnancy expectations.

Symptomatic UFs are most diffusely treated with radical surgery (hysterectomy) in women, who have completed childbearing, or conservative surgery (myomectomy and endometrial ablation), in women, who wish to preserve fertility.

Today the radiologist has a lot of interventional options in vascular and nonvascular field of application [30–34].

Regarding UFs, mini-invasive interventional radiology procedures include uterine artery embolization (UAE) and magnetic resonance-guided focus ultrasound surgery (MRgFUS) [6, 35].

Uterine artery embolization (UAE)

Uterine artery embolization (UAE) is a mini-invasive treatment of symptomatic UFs that uses embolic material to occlude the uterine arteries and reduce blood supply to the fibroids [36, 37] [Fig. 1].

Thanks to its safety and efficacy, UAE is accepted as a treatment option for UFs by the American Congress of Obstetricians and Gynaecologists [38].

The aim of UAE is the reduction or elimination of fibroid-related symptoms, but not the removal of the fibroids. With this technique, a reduction in volume of the UF is also achieved [39].

UAE was first employed in 1979, on a patient with pelvic hemorrhage after a failure hysterectomy [40], but transcatheter embolization of the uterine arteries for treatment of symptomatic leiomyomas was first reported by Ravina et al. only in 1995 [41, 42].

Indications and contraindications

The UK National Institute for Health and Clinical Excellence (NICE) recommends UAE as a treatment option in women who have disease-related symptoms such as heavy menstrual bleeding. NICE does not indicate a preference in subfertile women (NICE 2007) [43]. The role of UAE in women desiring pregnancy has not been sufficiently described in the existing literature [44].

Some authors describe high rates of miscarriage in patients submitted to UAE. In addition, they observe third trimester and peripartum complications, preterm deliveries, malpresentations, preeclampsia and intrauterine growth restrictions.

The results concerning fertility have been recently reported in a prospective cohort study of 66 patients treated with UAE. Notwithstanding good clinical results and good ovarian reserve, the reproductive outcomes in these patients after UAE were quite poor. These findings were observed in a preselected poor population of candidates for surgery. Nevertheless, the possible adverse effects of UAE on fertility

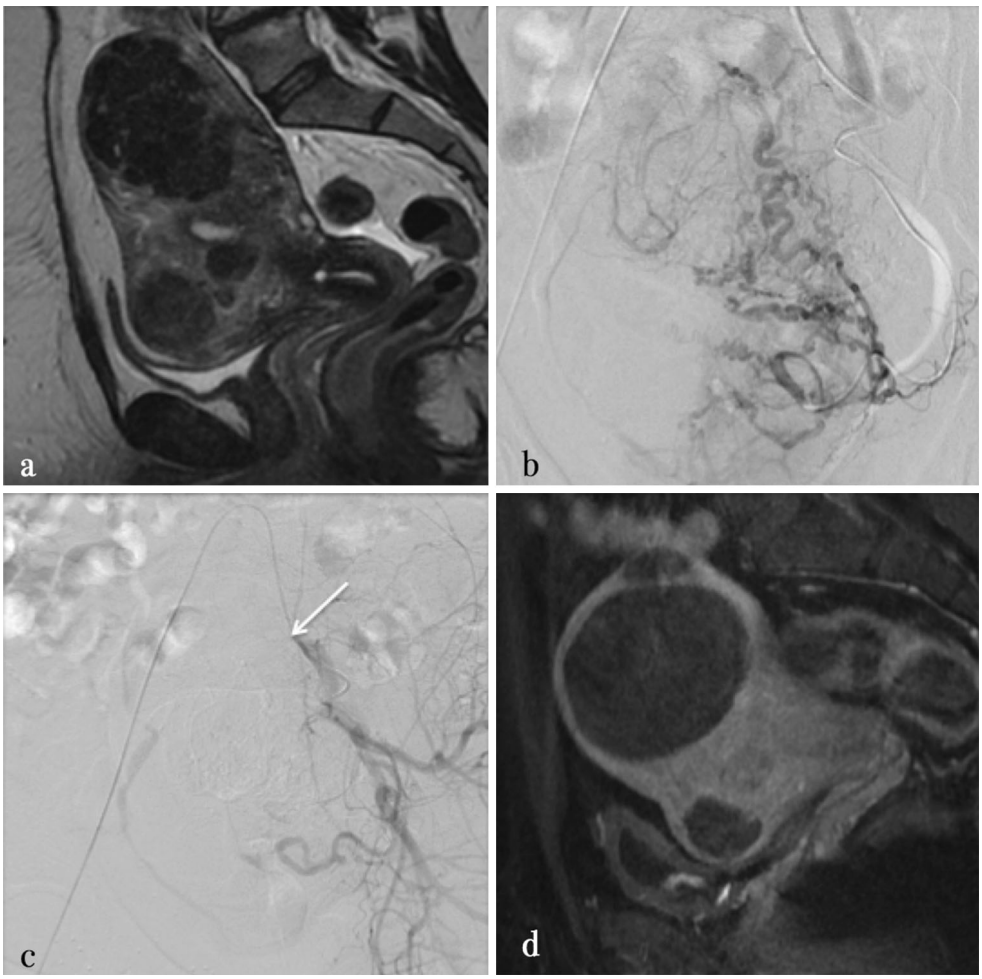

Fig. 1 42-year-old woman with uterine fibroids treated with embolization; **a** before treatment, multiple intramural hypointense fibroids of the uterus are identified at sagittal T2-weighted image; **b** hypervascularization of the fibromatous uterus demonstrated thanks to a selective injection of the *left* uterine artery; **c** selective injection of the left hypogastric artery (*arrow*) shows exclusion of the *left* uterine artery using microspheres; **d** sagittal GE T1w with fat suppression, after 24 months, shows complete infarction of the fibroids and normal perfusion of the surrounding myometrium

potential should be carefully evaluated for women in childbearing age. However, the mechanism of the adverse fertility outcome after UAE still remains enigmatic [45].

By means of UAE, it is possible to treat single and multiple UFs. All fibroid locations (submucosal, intramural, and subserosal) are eligible for embolization. In patients with pedunculated fibroids, UAE is relatively contraindicated, because fibroid degeneration and infection are possible complications [36, 38].

UAE is particularly indicated in women with UF associated with heavy menstrual bleeding or with history of multiple surgical treatments or other failed therapies [46].

However, the low vascularization of the target UF poses some problems when performing the UAE. Therefore, a preoperative MRI study of the arterial vascularization is suggested. The absence of enhancement after gadolinium injection is indicative of a poor vascularization of the UF [46].

Absolute contraindications include pregnancy, suspicion of gynecologic malignancy and current uterine or adnexal infection, and over hyperthyroidism/florid thyroiditis. Relative contraindications include documented allergic reactions to iodine-based contrast media, postmenopause, allergic reaction to local anesthesia, latent hyperthyroidism, fertility desire, and renal insufficiency. The latter represents a contraindication, unless the patient is undergoing dialysis.

Other typical exclusion criteria are history of pelvic radiation, acute vasculitis and immune-compromised conditions [39, 47].

Technique

UAE is an angiographic procedure that provokes the complete occlusion of both uterine arteries with embolic material, followed by ischemic necrosis of the UF without

permanent adverse effects on the otherwise normal uterus. The normal myometrium, in fact, rapidly establishes a new blood supply through collateral vessels from the ovarian and vaginal circulations, while the reduction in blood supply results in a decrease in UF volume with improvement in the gynecologic symptoms [43].

This procedure is always performed using general, epidural, spinal anesthesia or conscious sedation because the induced necrosis can be painful.

UAE is typically performed from a femoral artery puncture using 4 or 5 Fr catheters followed by an angiographic evaluation of the uterine and ovarian arteries [48, 49].

The most commonly used particulate embolic agent for occlusion is polyvinyl alcohol (PVA), a nonbiodegradable agent available in a variety of sizes (normally 150–1000 micrometers for this procedure), which is suspended in a contrast solution to be visualized while entering the uterine arteries. Its reflux is observed once the complete occlusion of the vessel is achieved. To avoid the accidental embolization of the ovarian arteries, it is suggested to perform a selective embolization of the anastomosis between the uterine and the ovarian vessels, if present. Blood supply to the ovary, after this preventive embolization, is guaranteed by collateral vessels.

A final angiography is performed to confirm the occlusion of the uterine arteries. The procedure takes from 45 to 135 min. The estimated ovarian dose is approximately 20 rads (20 cGy) [43]. The patients are subsequently submitted to 24-hour post-procedural observation and treated with narcotics for pain relief [50].

Complications

Common complications from UAE can be acute ($\leq$24 h after UAE), subacute (>24 h to up to 1 week after UAE), and chronic (>1 week postoperatively). Acute complications include pain [47], post-embolization syndrome (PES), septic bleeding, groin hematoma, reaction to contrast medium, vasovagal response, and pulmonary embolus.

The PES is one of the most common complications after UAE. It is characterized by flu-like symptoms, including malaise, fever, local pain, nausea and vomiting. Antiemetic agents, pain reducers, and rest are the possible typical options to treat PES. The patients should also be evaluated for infection, including a complete physical examination, diagnostic imaging studies, laboratory tests, and blood cultures [51].

Subacute and chronic complications include transient or permanent amenorrhea, endometritis, urinary retention, delayed reaction to contrast media, passage of fibroid tissue, tubo-ovarian abscess, uterine necrosis, and rupture [46].

A relatively common complication of UAE is vaginal expulsion of an infarcted fibroid. The transcervical passage of myomas occurs in 2.2–7.7% of cases. The myomas are expelled spontaneously, and no additional treatment is required. This expulsion has been reported as occurring even after 3 years from the procedure [52].

The reasons of pregnancy and neonatal complications in women treated with uterine arterial embolization are still unclear [53].

Potential post-procedural complications are ovarian ischemia due to reduction in ovarian blood flow, and infection leading to fallopian tube damage with subsequent infertility [43].

Other reported risks of infertility following UAE include postpartum hemorrhage, cesarean delivery, abnormal placentation, malpresentation, and adverse effects on the placental blood flow [54, 55].

Outcomes

The clinical response to UAE is high. A significant accomplishment is the reduction in menorrhagia (in 80–93% of patients) and the decrease in fibroid volume (from 50 to 78%. Reduction in uterine volume of 50% at 3 months after embolization and 67% at 6 months). In a study carried out in 2011, the authors observed improvement in life quality (UFS-QOL) after 6 years. Symptom severity and life quality score after a short-term follow-up was 93.97 versus a median value of 62.93 before UAE. In the long-term follow-up, HRQOL total value was 100 [49].

MRI follow-up studies showed that in the UFs treated with UAE, the volume reductions exceeded 50% in case of submucosal UFs [56].

The complication rate of UAE is low, and the results are rapid and impressive. For these reasons, embolization can be suggested to replace conventional medical and surgical treatments of UFs, although at present there is still controversy about its indication for women seeking pregnancy or wishing to preserve their fertility [57].

MRgFUS

Magnetic resonance-guided high-intensity focused ultrasound (MRgFUS) is a mini-invasive procedure which uses the thermal ablation power of ultrasounds (HIFU) combined with the radiological guidance of magnetic resonance (MR) [58].

MRgFUS is safe, effective, and feasible in clinical applications and was approved in 2004 by the US Food and Drug Administration (FDA) for the treatment of symptomatic uterine fibroids [59].

Focused ultrasonic energy induces coagulation necrosis of a target lesion with a noninvasive thermal ablation modality [60].

HIFU is also used in different clinical fields such as neurological diseases [61], bone tumors [62–65], and adenomyosis [66].

Indications and contraindications

MRgFUS is a valid alternative to other uterus-preserving therapies in particular for women affected by UFs and desiring pregnancy [Fig. 2].

The lack of radiation exposure and the possibility to perform a selective treatment of the target fibroids alone, without damaging the endometrium are all advantages of the technique, particularly suitable for women with disease-related problems of fertility. MRgFUS is also a valuable tool to perform the "bridging therapy," indicated for premenopausal women with painful menstrual cycles and debilitating metrorrhagia. In these cases, the treatment of symptomatic UFs allows significant improvement in the disabling symptomatology and prevents the patients from undergoing surgical or medical therapies [67].

The indication for MRgFUS depends on size, number, and position of symptomatic UFs. An elective indication is the low number of fibroids, measuring no more than 10 cm in their maximum diameter. MRgFUS is a time-consuming procedure, so the extended period of immobilization on the MRI table may increase the risk of deep venous thrombosis reducing the overall compliance of the patients to the

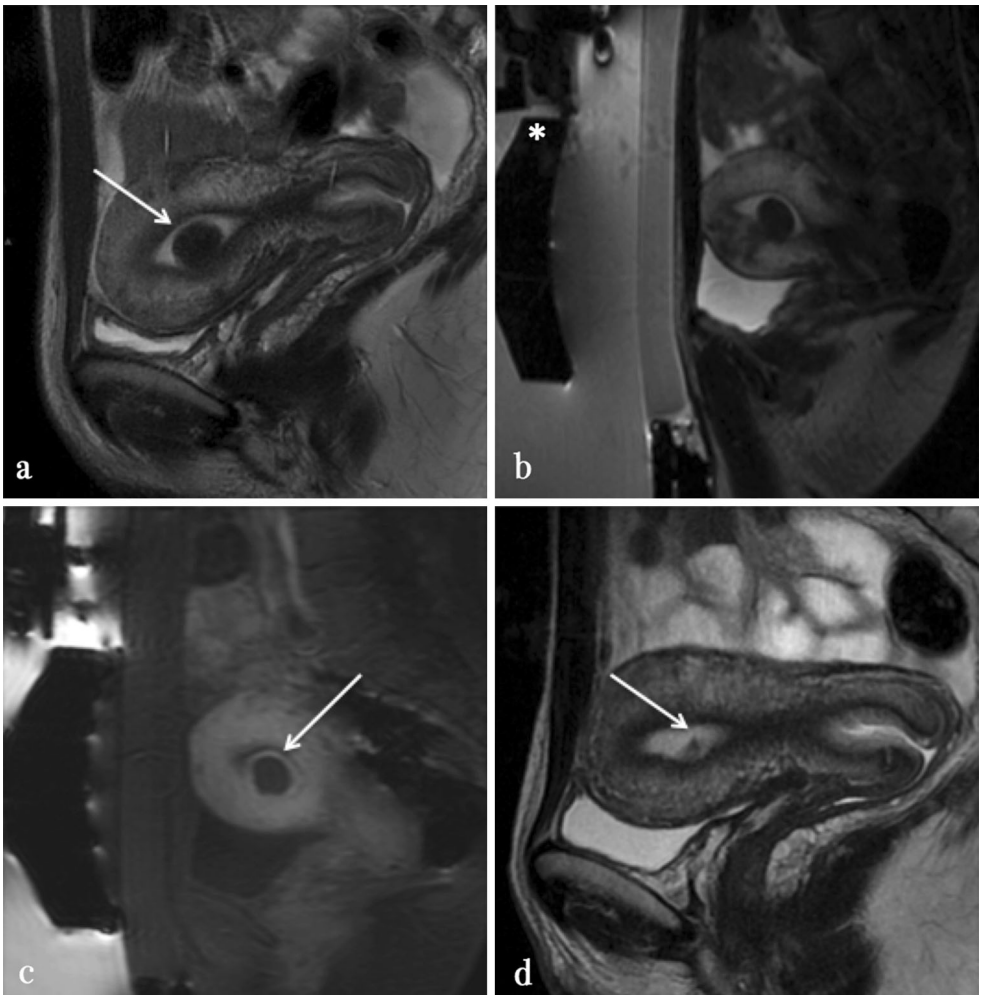

Fig. 2 38-year-old woman with uterine myoma treated with MRI-guided high-intensity focused ultrasound ablation (MRgFUS); **a** T2-weighted image from screening MRI examination shows a submucosal uterine fibroid (*arrow*) in anterior wall of anteverted uterus; **b** sagittal T2-weighted MR image acquired during treatment planning shows prone patient on the MRI table top and the HIFU transducer (*); the bladder is not completely empty to optimize the position of the uterus for the treatment; **c** sagittal T1-weighted gadolinium-enhanced image acquired at the end of the treatment demonstrates the effect of the ablation, as an area of non-perfusing volume corresponding to coagulative necrosis (*arrow*); **d** posttreatment (24 months) sagittal T2w image shows the quite complete disappearance of the treated fibroid; the endometrial line appears normal (*arrow*)

treatment. This is one of the reasons why it is strongly suggested to concentrate the treatment on the dominant fibroid alone [67, 68]. The fibroids are defined "dominant" when associated with symptomatology [Fig. 2]. In the presence of multiple fibroids, it will be more likely that one or more are not responsible for symptomatology.

The presence of an accessible acoustic window is a considerable precondition for treatment. The acoustic window is the conical pathway between the transducer, which generates the ultrasound beam, and the target lesion. This pathway must be free from obstacles (bone, air, scars, etc.) to obtain the proper penetration and concentration of the ultrasound beam [Fig. 3].

Necrotic degenerative alterations and/or fibroid vascularity, documented on MRI by hyperintense signal on the T2-weighted imaging may limit the increase in temperature thus impairing the success of the treatment. Nearby vital structures, such as bladder, bowel or sacral bone can be damaged when too close to the target fibroids [67, 69].

One limitation to the use of HIFU is represented by the presence of pedunculated fibroids that can detach into the peritoneal cavity.

Absolute contraindications include pregnancy, suspicion of gynecologic malignancy, and acute inflammatory diseases. The absence of a proper acoustic window is an exclusion criterion for treatment (bowel or bladder interpositions are an example).

General contraindications to MRI are the presence of cardiac pacemakers, intrauterine devices, sensitivity to MR contrast agents, severe claustrophobia, and patient's size [70, 71].

Technique

HIFU is a low-risk procedure because there is no need for surgical resection. The patients should be previously evaluated according to the guidelines issued by the American College of Cardiology and American Heart Association [72]. Prior to treatment, the patients are clinically examined and submitted to MR imaging to determine their eligibility and plan the treatment.

During MR imaging examination and procedure, the patients lie on the prone position. A water bath or gel pad is placed over the transducer. MR examination and procedure can take up to 3–5 h. The restrictions to the procedural time have been defined in the USA by the Food and Drug Administration (FDA), owing to the high risk of deep vein thrombosis due to prolonged patients' immobilization.

The skin between umbilicus and pubic bone must be prepared by removing accurately any hair, dirt or topical creams that can cause deflection of the ultrasonic beams.

Moderate sedation to control pain and anxiety during the treatment is often necessary, but, if the patients are highly compliant, as it happened in our experience, it is possible to perform a complete treatment without administration of any drugs.

A Foley catheter is inserted into the bladder to keep it empty and avoid the movement of the uterus due to bladder filling. However, some authors prefer to treat the fibroids with a full bladder: This last has the aim of removing the bowel (and so the air contained) from the acoustic pathway.

Rectal filling can be required to push the uterus toward the anterior abdominal wall and obtain optimal acoustic access to the target fibroid, by increasing the distance between the target fibroid and the sacral bone.

Preliminary images are acquired to localize the UF. The margins of the target area are subsequently drawn on the acquired images by the operator. A computerized module generates a treatment plan after calculating the energy, location, and number of ultrasound sonications, or energy bursts, needed to treat the fibroid volume. The treatment consists of multiple single releases of energy called sonications that have a narrow cylindrical shape. The sum of the single sonications must cover the entire fibroid volume.

To obtain a temperature sufficient to induce coagulative necrosis (57 °C for at least one second), different parameters must be considered: delivered energy, time spent to deliver energy, and cooling. Typically, the sonications employed are short and multiple (60–90 sonications lasting 20 s each; 1.000–7.000 joules of energy each one) with continual thermal feedback. Between the sonications are pauses, during which the skin is cooled to avoid thermal damage to nontarget organs. However, both patient and operator can stop the procedure at any time [71–76].

Technicalwise, many restrictions have been imposed over the years to the use of MRgFUS by the FDA aimed at balancing procedural safety with effectiveness. In the past, it was possible to treat one single fibroid at a time, and the maximum duration allowed for the treatment was 3 h, without permission to repeat the procedure.

The FDA has gradually retired these technical restrictions, and in April 2009, 100% ablation of the target lesion was declared possible [77].

Complications

The posttreatment adverse events are rare [78] but possible.

During the sonication, transient pain or uterine cramping may occur and can be reduced by moderate sedation. Usually, posttreatment discomfort is minimal, and the patients are discharged from the hospital in the evening of the day of treatment. Small and superficial skin burns may occur due to trapping of air between the transducer and the patient's skin. Abdominal scars are more serious events, and their risk can be mitigated by cleaning and shaving the

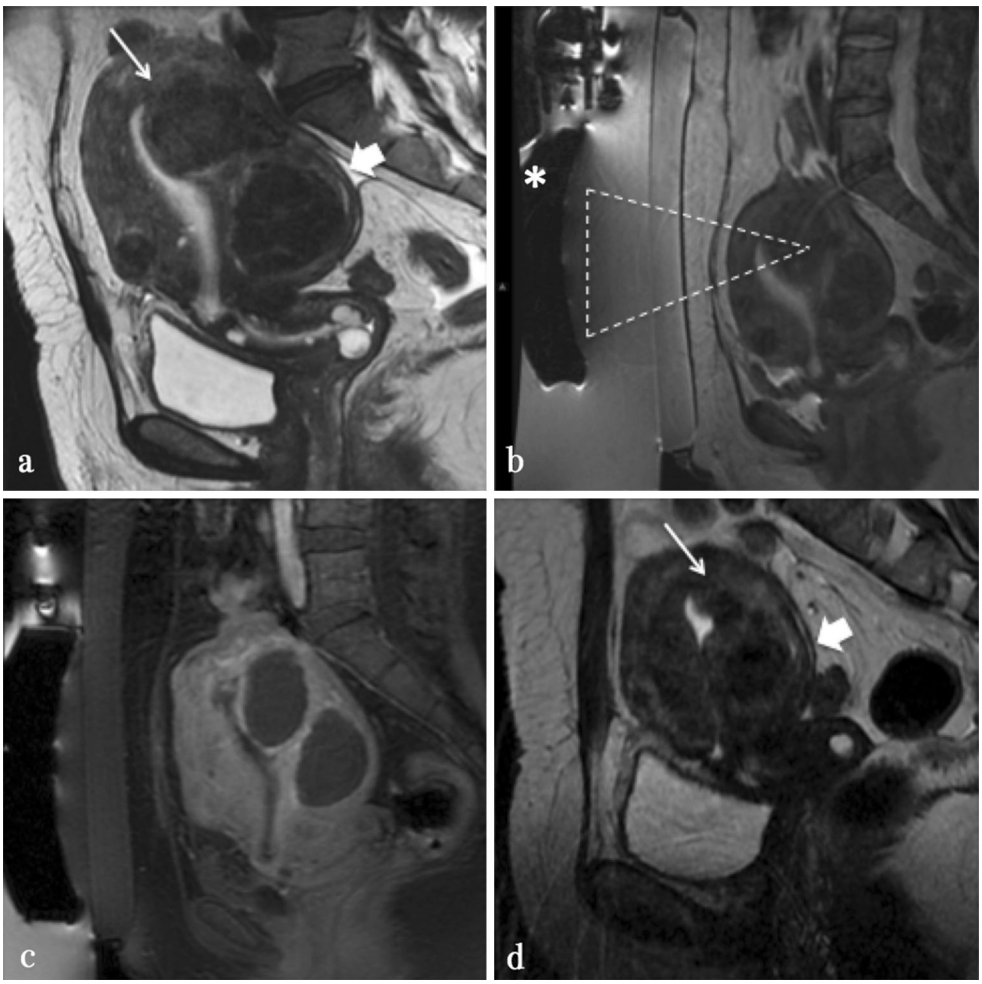

Fig. 3 Magnetic resonance imaging findings at baseline and 24 months after MRgFUS treatment in a 47-year-old woman: **a** sagittal T2w image showing almost three fibroids, greatest intramural in the posterior uterus wall (*small arrow* and *large arrow*); **b** MR image during MRgFUS treatment: patient prone (feet first) on the MR table; ultrasound beam pathway is focused on fibroid (*dashed line*, transducer *); c) sagittal contrast-enhanced fat-saturated MR image after treatment shows a complete ablation of both fibroids; **d** posttreatment sagittal T2w image after 12 months shows decrease in volume of both fibroids (small *arrow* and large *arrow*)

skin before treatment, to optimize acoustic access. Paresthesia of the leg is also observed, due to sciatic nerve damage and resolves over several months.

Deep vein thrombosis of the leg is infrequently seen. Bowel perforations are serious complications, but extremely rare, and require laparotomy and resection of the bowel. For these reasons, it is important to evaluate the space between the abdominal wall and the uterus to exclude that the bowel is located in front of the uterus [71, 79].

Outcomes

On post-gadolinium images, obtained immediately after the procedure, the efficacy of treatment is documented by an unenhanced area within the fibroid. Gadolinium is administered after the procedure to visualize and measure the non-perfused volume (NPV) [80].

Recent studies suggest that a NPV ratio exceeding 80% is sufficient to define clinical success [81]; instead, a NPV ratio of 45% brings a 15% risk of undergoing an alternative treatment [82].

Clinical effectiveness of MRgFUS is measured by improvement in symptomatology and is quantitatively assessed through the symptom and health-related quality-of-life scores from the Uterine Fibroid Symptom and Quality of Life questionnaires (UFS-QOL) [83, 84]. In an experience carried out in 2011 [83] on 29 patients, the 3-year follow-up study after MRgFUS showed a NPV mean value of 32.1%, gradually decreasing to 16.5% after 6 months and to 13.4% at 3 years. The mean tQOL grew from the baseline value of 44.1–68.8% after three months, and to 83.9% after 3 years.

Age-related outcomes were also observed, and long-term success was related to increasing age.

The heterogeneous structure of the fibroid, which makes ablation more difficult, was more frequently found in younger patients than in the age groups 41–45 and 46–53 [84]. This age-related factor must be taken into great consideration during the treatment, administering, if necessary, higher levels of energy to the patient.

Our experience showed more chances to obtain satisfying ablations and devascularizations in fibroids documented by hypointense signal on the T2-weighted MRI than in the hyperintense fibroids.

However, a great advantage of MRgFUS over other treatments is the possibility to repeat the procedure in case of partial or incomplete results [85].

Quite encouraging results have been published in patients desiring future pregnancy. In a review study issued in 2014, Clark et al. described pregnancies ascertained 8.2 months after MRgFUS of UFs. The pregnancies were carried to term with an average fetal weight of 3273 gr [86].

In another study, a satisfying number of patients were able to conceive after MRgFUS treatment of UFs, with spontaneous abortion rates almost similar to the baseline rate of 28%. No cases of uterine rupture, preterm labor, placental abruption, abnormal placentation or fetal growth restrictions were reported in the study. The success of IVF pregnancy after MRgFUS was described [87].

HIFU/MRgFUS treatments should replace surgical fibroid removal as the method of choice for women who require treatment of their fibroids to improve fertility. There is no evidence of any relevant impairment of fertility after MRgFUS procedure; on the other hand, the data collected are still insufficient to answer the question whether a "latency period" before becoming pregnant is needed [88].

Discussion and conclusions

Uterine fibroids or myomas are the commonest benign tumors of the uterus, with an estimated incidence of 20–40% in women during their reproductive years [28, 29]. Uterine myomas are associated with significant morbidity in up to 40% of women during their life. The emerging noninvasive techniques have modified the management of uterine fibroids preserving the uterus integrity.

UAE and MRgFUS are two mini-invasive procedures for the treatment of uterine fibroids and are possible alternatives to surgery.

These procedures require good radiological equipment and material, trained personnel and cooperation between interventional radiologists and gynecologists. When all these requirements are met, remarkable benefits for the patients are guaranteed [87]. The procedure is cost-effective. In 2014, a review study carried out in Germany compared UAE and MRgFUS with conventional surgery pointing out that mini-invasive interventional radiology procedures require shorter times of hospitalization.

MRgFUS is the technique with the lowest grade of invasiveness. In fact, it is possible to achieve resolution of symptomatology (pain and menstrual bleeding) without even cutting the skin of the patient; a very important point is that it is possible to obtain the disappearance of the symptomatic fibroids without any damage to the endometrium [Fig. 2]: This is of capital importance for women seeking pregnancy. Other advantages include the absence of severe adverse effects, and short hospitalization and recovery times.

The main limits of MRgFUS are linked to the choice of the fibroids suitable for treatment, since the latter have to meet some fundamental requirements, in fact, they must be a few, poorly vascularized fibroids, not too large in diameter and easily accessible by the ultrasound beam.

The procedure is uterus sparing and represents the best solution for women desiring pregnancy and can be repeated and does not exclude further and more invasive therapies, when deemed necessary. Interestingly, Rabinovici et al. reported about 54 pregnancies in 51 women after MRgFUS treatment of uterine leiomyomas. This study describes that the mean time to conception after MRgFUS was 8 months. Other results were that live births occurred in 41% of pregnancies, the spontaneous abortion rate was 28%, with a 11% rate of elective pregnancy termination, and 20% ongoing pregnancies beyond 20 gestational weeks [89]. More recently, similar results have been shown in a systematic review [90] suggesting the safety of MRgFUS treatment of uterine fibroids in a substantial percentage of women carrying out pregnancy. To date, these data slightly differ from those reported in the series of pregnancies after UAE in terms of maternal age, time to conception, and miscarriage rate [91–93]; in a series of 187 patients treated with UAE for symptomatic uterine fibroids, 15 spontaneous pregnancies were observed. Of these, 12.5% were miscarriages ($n = 2$), and 87.5% were successful live births ($n = 14$) [94].

As to the clinical effectiveness of MRgFUS, most patients reported substantial symptomatic improvement, mainly regarding fibroid-related abdominal pain, menorrhagia, and urinary symptoms [95]. In a prospective study, MRgFUS ablation of uterine fibroids was performed in 35 symptomatic women scheduled for hysterectomy. Clinical symptoms and patient satisfaction were determined at 1 and 6 months after the procedure showing that 69% (24/35) of the treated patients reported either significant or partial improvement in symptoms. This study showed the clinical efficacy of MRgFUS ablation of uterine fibroids suggesting that this noninvasive surgical approach may be an

alternative therapy for women with uterine fibroids [96]. Several papers have shown reductions in symptoms, even 5 years after thermal ablation [97].

A prospective cohort study investigated on the long-term changes in health-related quality of life (HRQOL) after UAE for symptomatic fibroids. Eighty-two patients treated with UAE showed durable relief of disease-specific symptoms (abdominal pain and menorrhagia) and marked improvement in health-related quality of life [49].

As to number and size of fibroids, there is no restriction for UAE, after which the fibroid size reduces by about 50% and patients' symptoms improve markedly. However, the procedure brings the risk of subclinical deterioration of the ovarian function, particularly in women over 45 years of age. In fact, to date, UAE is not suitable for the treatment of women who wish to preserve their fertility [88]. UAE periprocedural complications include post-embolization syndrome, which can be disabling and delay the patient's discharge from the hospital, complete amenorrhea in 3.9% of cases, and a reintervention rate ranging from 7 to 34.6% [89].

MRgFUS and UAE are comparable in terms of Symptom Severity Score (SSS) and total health-related quality-of-life (HRQOL) scores. Comparing both score groups between the treatments, the score improvement from baseline to follow-up did not differ significantly. These data parallel with a systematic review of 38 studies reporting outcomes in 2500 patients, where MRgFUS is described as a safe, efficient, and cost-effective minimal invasive technique for treatment of uterine fibroids [98].

In conclusion, uterine fibroids have an enormous economic impact on modern society and the surgical procedures with materials and hospitalization times contribute significantly to the total annual costs of this disease [29]. Although myomectomy is generally regarded as the standard of care for uterine-preserving procedural treatments, UAE and MRgFUS have also been shown to provide a comparable clinical symptom relief and may reduce the time of hospitalization [90, 91]. To date, MRgFUS-treated patients experience a strong reduction in hospitalization times and a faster return to normal life when compared with the other procedures.

Conclusions

Patients affected by uterine fibroids may benefit from alternative minimally invasive or noninvasive treatments, and MRgFUS represents one of these options. The future task of researchers, however, should be to take into consideration the possibility to extend MRgFUS treatment protocols for treatments of greater fibroid volumes and achievement of higher infarction rates.

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Compliance with ethical standards

Conflict of interest None.

Informed consent All procedures performed in this study were in accordance with the Helsinki Declaration and its later amendments; an informed consent was obtained from all individual participants included in the study.

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