MINIMAL INVASIVE PROCEDURES & HIGH FREQUENCY FOCUSED ULTRASOUND

(WM GEDROYC, SECTION EDITOR)

An Update on Magnetic Resonance Guided Focused Ultrasound Surgery (MRgFUS) of Uterine Fibroids

Fiona M. Fennessy · Clare M. Tempany

Abstract Magnetic resonance-guided high focused ultrasound surgery (MRgFUS) is a non-invasive treatment option for uterine fibroids. In addition to offering excellent anatomical depiction of the uterine fibroids and uterus, magnetic resonance imaging offers functional imaging and thermal guidance for safe delivery of the focused ultrasound beam. Once appropriately selected for treatment, this out patient treatment option is well tolerated by patients and results in sustained symptom relief. More recent advances in this technology allows for quicker treatment times, allowing for greater nonperfused volumes to be attainable within the allotted scanner time. Also, upon review of fibroid and patient characteristics, the optimal candidates for successful MRgFUS are becoming more established.

Keywords MRgFUS · Focused ultrasound surgery · Uterine fibroids · Image guided therapy · Leiomyomas

Introduction

Uterine Fibroids

Uterine fibroids (leiomyomas) are benign clonal tumors of the smooth muscle cells [1], categorized by their locations as either intramural (entirely or mostly contained within the myometrium), submucosal (projecting into the endometrial cavity), or subserosal (projecting outwards from the serosal surface of uterus). The estimated cumulative incidence by 50 years of age is greater than 80 % for black women and nearly 70 % for white women [2]. The precise pathophysiology of uterine fibroids is not clearly elucidated, although there are well-established risk factors such as delayed menopause, exogenous hormone replacement therapy, and race [3]. Fibroids can be subject to a variety of degenerative changes, especially during periods of rapid growth. The types of degeneration include myxoid, hyaline, cystic, red (hemorrhagic), and fatty degeneration. This variety of degenerative phenomena combined with calcification and necrosis all contribute to the complexity and variability of fibroid imaging appearances.

The symptoms associated with fibroid disease are generally grouped into one of three categories—bulk, bleeding and fertility related. Symptoms include pelvic pain, menorrhagia, dysmenorrhagia, pressure-related symptoms such as pelvic fullness and urinary frequency, and dyspareunia. Submucosal fibroids may be associated with early pregnancy loss. Treatment of large fibroids is associated with symptom improvement [4], but even small uterine fibroids, especially those in a submucosal location, can be very symptomatic.

Ultrasound is usually the first imaging modality of choice for the detection and diagnosis of fibroids that typically appear as well-defined hypoechoic masses within the uterine wall. However, large uterine fibroids, especially pedunculated subserosal ones, may cause enlargement and lobulation of the uterus, or at times may simulate an adnexal mass. Areas of calcification within the fibroid may cause shadowing foci or curvilinear echoes. Complete pelvic imaging with MRI is often required to confirm the diagnosis of uterine fibroids (and exclude adenomyosis, which may result in

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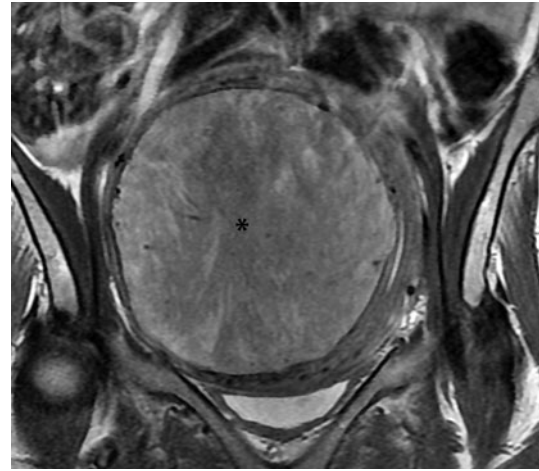e-mail: ffennessy@partners.org

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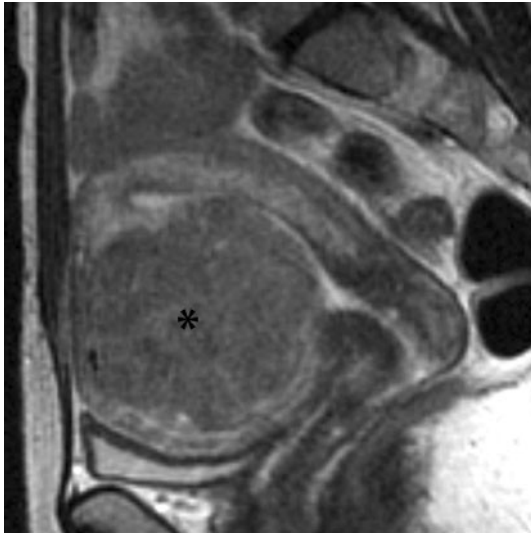
Fig. 1 Sagittal T2 WI demonstrating the imaging characteristics of a typical uterine fibroid (*asterisk*), which is well defined and of low SI compared to myometrium

Fig. 2 Coronal T2 WI demonstrating the MR appearance of a cellular uterine fibroid (*asterisk*), which is of predominantly high SI compared to myometrium

Principles of MRgFUS

For many surgical procedures, image-guided ablative therapy (IGT) has been accepted as a less invasive alternative to open surgery. In IGT, tumor ablation typically occurs through percutaneous placement of a probe (cryo- or laser-therapy) to induce focal thermal ablation where tissue destruction occurs secondary to rapid thermal changes. Imaging is used to identify the lesion for targeting, to guide

similar symptomatology), fully characterize all fibroids and accurately demonstrate fibroid location, size and volume. Administration of intravenous contrast can determine fibroid viability, and evaluate for the presence or absence of necrosis. This is essential for patients who wish to be treated with either uterine artery embolization (UAE) or magnetic resonance-guided high focused ultrasound surgery (MRgFUS), where it is necessary to determine the vascular perfusion pattern prior to treatment.
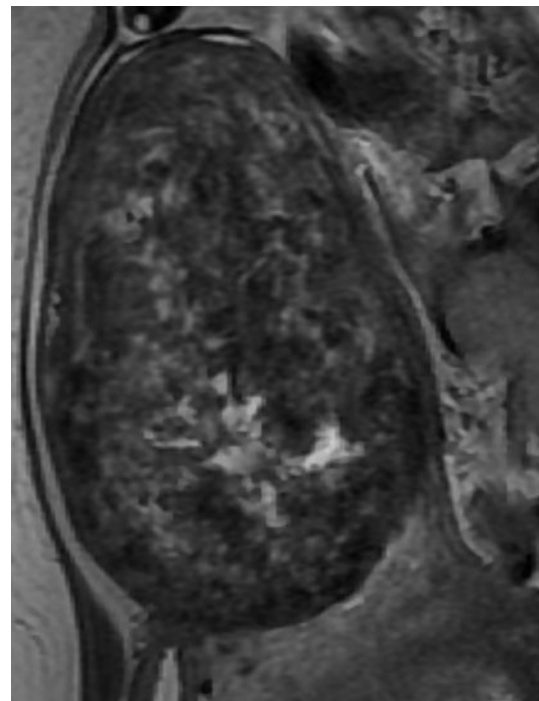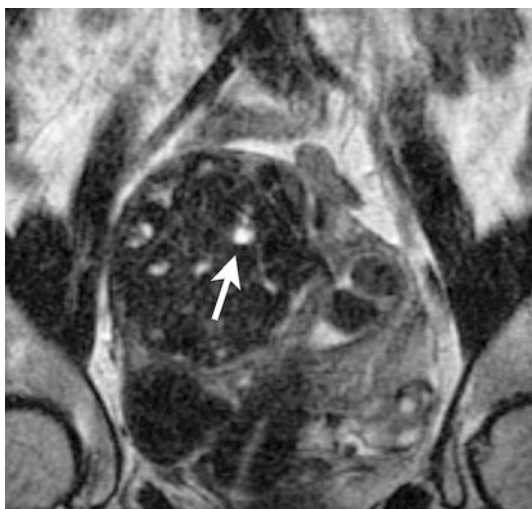
Many types of fibroids can be identified on MRI. The *classical* fibroids typically appear as well-defined uterine masses of low signal on a T2-weighted image compared to myometrium (Fig. 1), and enhance after administration of IV gadolinium. By contrast, *hypercellular* fibroids, a variation of uterine fibroid that is composed of compact smooth muscle cell without any or few intervening collagen fibers, usually shows a high signal intensity on T2-weighted imaging (Fig. 2). A rare type of fibroid is one that contains fat, known as a lipoleiomyoma. The fat is usually in focal aggregates, but may be diffuse. Different forms of fibroid degeneration can also occur: Hyaline degeneration is the most common, whereby smooth muscle is replaced by fibroid connective tissue. On MR imaging, this is recognized as areas of lower signal intensity (SI) on T2 weighted images (WI) (Fig. 3) and less enhancement after administration of intravenous gadolinium agents compared to classical fibroids. With cystic degeneration, areas of fluid are seen within the fibroid, which is of high SI on T2 WI (Fig. 4) and does not enhance after contrast. Hemorrhagic degeneration (also termed red or carneous degeneration) usually shows diffuse or peripheral high SI on T1 WI, with variable SI on T2 WI, where there may also be a low SI rim. There is lack of enhancement after administration of IV gadolinium.

Fig. 3 Sagittal T2 WI demonstrating typical appearance of hyaline degeneration within a uterine fibroid. Hyaline degeneration typically appears heterogeneous with distinct areas of very low SI

Fig. 4 Coronal T2 WI demonstrating small areas of high SI (*arrow*) within the uterine fibroid, consistent with cystic degeneration

safe placement of the probe and to monitor treatment response. In addition to providing anatomical information for guiding ablation, the ideal source of image guidance also provides real-time thermometry with tissue temperature change feedback. Using proton resonance frequency techniques, MR has the unique capability of providing accurate and rapid thermometry, making it reliable for real-time temperature monitoring.

Focused ultrasound surgery (FUS), is a totally non-invasive of ablative therapy that causes an increase in temperature within tissue when ultrasound waves interact with tissue and loose energy through tissue absorption. When the temperature elevation is therapeutic (above 55 °C) for thermal ablation (cell-kill), protein denaturation and tissue thermo-coagulation results. The first therapeutic use of FUS was in 1942 in the liver [5]. There have been broad applications of ultrasound guided FUS or "high intensity focused ultrasound (HIFU)" which has been used in many centers for successful treatments in a wide number of diseases, such a liver metastases, prostate cancer and bone tumor ablation [6]. However, due to poor visualization of the target, and lack guidance and monitoring with thermometry, clinical acceptance of FUS has been slow in the US.

MR thermometry with clear guidance of the local temperature change in vivo was first described in 1992 [7], and has led to the advent of MRgFUS, where anatomical, functional and thermal guidance for delivery of the FUS beam is available. In addition to the excellent anatomical resolution and continuous imaging of the fibroid and adjacent structures (such as bowel, sacral nerves and bladder) during treatment that is offered by MRI, MR-based temperature mapping is possible. MR Temperature mapping occurs by exploiting the temperature sensitivity of the water proton chemical shift [8] based on the

fact that an increase in temperature leads to a corresponding increase in Brownian motion of the water molecules and a breakdown in hydrogen bonding, which results in a linear shift in the water proton resonance frequency. Phase imaging is used to estimate the proton resonance frequency shift using a fast spoiled gradient-recalled-echo sequence (FSPGR) before, during and after each sonication to monitor tissue temperature elevations within the targeted tissue to be treated and also in the surrounding normal tissue, to monitor for inadvertent thermal deposition.

MRgFUS System

The ExAblate 2000 (Insightec Inc., Haifa, Israel) was the first commercial MRgFUS device for treatment of uterine fibroids, and received FUS Food and Drug Administration (FDA) clearance in 2004. Developed in collaboration with investigators at Brigham and Women's Hospital, Boston, the ExAblate 2000 system houses the electronics, the phased-array transducer and a sealed water bath, and docks into a standard 1.5T or 3T magnet from general electric (General Electric Healthcare, Milwaukee, WI). The Philips MR HIFU device (Sonaleve) is a more recent device, which integrates with the Philips Achiva MR platform. It also consists of a patient tabletop containing the ultrasound transducers and a therapy-planning console that performs the surgical planning and real-time temperature tracking via MR during the procedure. In contrast to the ExAblate 2000 system, which uses a point-by-point method of ablating fibroid volumes, the Phillips system uses a volumetric ablation strategy. It is in the clinical trials phase and has yet to receive FDA clearance.

In the ExAblate MRgFUS system, energy originates from multiple electronically controlled transducer elements (phased arrays) arising from spherically curved ultrasound transducers. This system can focus to an operator defined point deep within the body, with each element driven by radiofrequency signals of a specified phase and amplitude so that waves emitted are all in phase at the focal point, and subsequently, at the point of convergence there is substantial temperature rise. Instead of focusing the ultrasound beams on a single point within the targeted organ, sonicating the desired point, then moving on to the next point, the Sonaleve system constantly moves the focal point within the targeted lesion [9]. The transducer assembly is mounted on a positioning system, which is sealed in a plastic chamber filled with degassed, deionized water and installed in a specially designed MR compatible table, replacing the standard MR table. For fibroid treatments a gel pad is placed on top of the window in this plastic chamber (Fig. 5) and acoustic coupling with the skin of the anterior abdominal wall is obtained through use of degassed water.

MRgFUS as a Treatment Option for Uterine Fibroids

As recently as 15–20 years ago, the choices for a woman with symptomatic fibroids were confined to conventional abdominal hysterectomy and conventional abdominal myomectomy. Hysterectomy has always been considered the "gold standard" definitive treatment for symptomatic uterine fibroids, as it removes the entire uterus and all uterine fibroids, and is the leading cause for preforming hysterectomy in the United States [10]. However, this surgical procedure is associated with surgical complications, risks, lengthy recovery times, absenteeism and potentially negative quality-of-life outcomes [11, 12•]. Typical recovery times range from 4 to 8 weeks [13]. Absenteeism and disability from hysterectomy have been shown to be important components of the cost burden of surgical fibroid treatment for women, their employers, and the healthcare system [14].

Today, many women are increasingly seeking less invasive treatment options for their uterine fibroids. Reasons are complex and maybe motivated by a trend towards later childbearing and interest in fertility preservation options, and the need for reduced recovery time. One option that has seen significant growth and interest since its first introduction in 1995 [15] is UAE. This involves selective catheterization of the uterine arteries and embolization under fluoroscopic control in an angiographic suite, followed by one night hospital stay. UAE has a lower rate of major complications than hysterectomy or myomectomy, albeit with a higher rate of minor complications. Two large European studies, the multicenter randomized EMbolization versus hysterectomY (EMMY) trial [16] and the HOPEFUL study [17] found that from a societal economic perspective, UAE is the superior treatment strategy to hysterectomy in women with symptomatic uterine

Fig. 5 The MRgFUS transducer assembly is mounted on a positioning system, all of which is sealed in a plastic chamber filled with de-gassed de-ionized water and installed in a specially designed MR compatible table. For fibroid treatments a gel pad is placed on *top* of the window in this plastic chamber, as depicted in this photograph. (Photograph, courtesy of Insightec Ltd.)

fibroids, although the need to improve the management of expectations following UAE, particularly regarding fertility, was emphasized.

Magnetic resonance guided focused ultrasound surgery is a novel non-invasive outpatient thermo-ablative treatment option. MRgFUS is currently being examined for use in treatment of a diverse range of both benign and malignant conditions throughout the body. This was first introduced in multi-center clinical trials for treatment of symptomatic uterine fibroids, beginning in 2000. More than 8,500 treatments have been performed to date with the ExAblate 2000 system, including multiple clinical trials and worldwide commercial treatments. MRgFUS offers several potential advantages over conventional options: it is a completely noninvasive outpatient procedure which typically takes 3 hours to complete, under minimal conscious sedation; patients usually return to their normal activities within 24 hours (compared to 10 days with UAE and 6 weeks with hysterectomy); it has a low risk of post-procedure complications such as post-embolization syndrome, as the ablated tissue is absorbed by the body.

Patient Selection for Treatment

All women that present for treatment with MRgFUS are screened though a full history and fibroid symptom review and physical examination, with particular attention being paid to the skin of the anterior wall to evaluate for scar tissue. Fibroid symptomology is commonly assessed the validated uterine fibroid symptom and quality of life questionnaire (UFSQoL) [18]. This allows establishment of a baseline fibroid "symptom score" preprocedure, and is useful for post-procedure follow up and monitoring of response to treatment. Candidates for MRgFUS must have no contra-indications to MR such as metallic implanted devices, berry aneurysm clips, cardiac pacemakers or severe claustrophobia, and pregnancy needs to be excluded at screening. Patients need to have the ability to communicate with MR staff, and the patient's girth and weight need to be compatible with the specific magnet requirements. Also, in the United States, the current FDA-labeling requires that patients should be "family complete", which needs to be taken into consideration in that country.

After the history and physical examination, all candidates must undergo a screening IV contrast-enhanced MRI examination to assess for MR imaging features of fibroids and suitability for treatment. Whenever possible, MR images should be obtained in the prone position, which is how the patient is positioned for treatment. Screening in this way allows the candidate to experience the position they will be in on the day of treatment, as they need to be able to lie prone with conscious sedation for up to 3 hours on the day of treatment. Screening in the prone position

also allows the physician to evaluate how pelvic structures, such as bowel loops, are likely to relate to the position of the uterine fibroids on treatment day. The screening MR utilizes a routine protocol with multiplanar T2 WI and T1 WI before and after intravenous gadolinium chelate administration as previously described [19, 20]. MR confirms the presence of uterine fibroids, and excludes other potential causes of the patient's symptoms, such as adenomyosis. The number, size and position of uterine fibroids within the uterus are all recorded. In addition, the SI of the fibroids compared with the surrounding myometrium on T2 WIs is noted.

As outlined in Table 1, there are many important treatment limitations that can be identified on the MR screening examination. We consider the ideal MRgFUS candidate to have <5 accessible, solid, enhancing fibroids of low SI on T2 WI's, measuring approximately 6 cm in size. The goal of the treatment is to treat the source of the patient's symptoms—thus while it is often possible to treat more than one fibroid in a single session, it can be challenging when there are a large number to determine which particular fibroid is the most symptomatic. As described later in this chapter, there are recent technical developments that allow a greater fibroid treatment volume in a shorter time frame, however multiple small fibroids scattered throughout a small uterus may be better treated with other options.

Fibroids whose centers are more than 12 cm from the skin of the anterior abdominal wall, or more than 20 cm from the transducer cannot be treated, as they will be out of range of the transducer (Fig. 6). In patients with a symptomatic uterine fibroid of >10 cm in diameter, we recommend pretreating these patients with a gonadotropin releasing hormone agonist (GnRHa). The reason for this is that treatment of a uterine fibroid of greater than 10 cm in diameter would require extended time in the magnet or additional treatment sessions, which may be unacceptable to the patient. Pretreatment with a GnRHa 3-months prior to MRgFUS treatment will shrink the estrogen-dependent fibroid by 30–40 % by interfering with the hypothalamic–pituitary–ovarian axis, reducing fibroid vascularity and allowing a greater % of the fibroid to be treated with MRgFUS in one session. In addition, it has been found that the response to each individual sonication is greater post-treatment with GnRHa, with a 50 % larger area of targeted tissue destruction per unit of energy applied [21]. We therefore also consider pretreatment of patients with highly cellular fibroids (hyperintense SI on T2 WI) with a GnRHa, as it has been reported that MRgFUS of T2 hyperintense fibroids results in lower non-perfused volumes compared to iso- or hypointense fibroids [22]. GnRHa's potentiate the thermal effects of MRgFUS [23], and may have an important role in treating fibroids which otherwise have been found to respond poorly to MRgFUS [24]. It has also been noted (in a case report) that dynamic contrast-enhanced MR may be used to select a subpopulation of uterine fibroid patients suitable for MRgFUS despite high

Table 1 Fibroid treatment limitations with MRgFUS, and possible solutions

Factor	Limitation	Solution
Fibroid number		
Too many (without dominant fibroid)	Cannot treat all in one session	More than one treatment session?
Fibroid size		
Greater than 10 cm	Small treatment volume	Pretreatment with GnRH agonist
Fibroid location		
Posterior	Upper limit of treatment depth is 12 cm from anterior abdominal wall, or 20 cm from transducer. Cannot treat fibroid tissue <4 cm from the anterior spine due to risk of nerve injury	None
Fibroid MR imaging characteristics		
High SI on T2 WI	Difficult to obtain high treatment temperatures	Role for pretreatment with GnRH agonist?
Areas of calcification	Interferes with ultrasound beam propagation	Change beam pathway?
Areas of nonperfusion	Poor treatment effect	
Acoustic window		
Scarring of anterior abdominal wall	May cause skin burn and interfere with beam propagation	Change beam pathway
Intervening bowel loops	Could result in visceral organ damage	Change beam pathway/use of gel pad to displace bowel loops

From [37], with permission

signal on T2 WIs [25]. However, further verification studies are warranted.

Procedure

Preparation for Treatment

Prior to the procedure, the patient is asked to ensure that the skin of the lower anterior abdominal wall to the level of the pubic symphysis is hair and cream/oil free, any of which may obstruct the US beam passage and cause the ultrasound beam to become unfocused. A serum pregnancy test is performed on the morning of the treatment, and an intravenous line is sited to administer fluids and conscious sedation throughout the procedure, as necessary. A Foley catheter is placed in the bladder to prevent bladder and patient movement throughout the procedure. Once in the MR suite, the patient is positioned in the prone position, such that the skin of the lower anterior abdominal wall lies directly over the degassed water and gel pad, which is coupled to the transducer. The necessary monitoring leads (oxygen saturation and heart rate) are attached and titrated IV doses of midazolam and fentanyl are administered to alleviate any position-related discomfort or procedure-related pain and anxiety. Clear audio communication with the patient in the bore of the magnet by the operator must be well established at the outset of the procedure.

Treatment Planning

Once the patient is correctly positioned such that the uterine fibroid to be treated overlies the location of the ultrasound beam (confirmed by single-shot fast spin-echo locator sequences), T2 WI in axial, sagittal and coronal
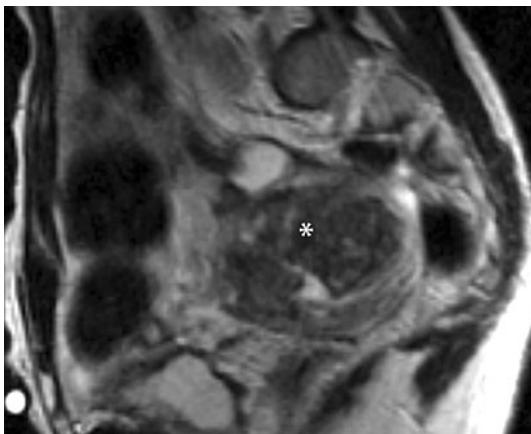
Fig. 6 Sagittal T2 WI demonstrating low SI posterior uterine fibroid (*asterisk*) which is too posterior to treat as the *center* is more than 12 cm from the skin of the anterior abdominal wall. In addition, multiple loops of bowel are seen coursing anterior to the uterus

planes are acquired by the MR scanner and transferred to the ExAblate program for treatment planning. Using the system software, a region of treatment is manually drawn within the fibroid, usually on coronal images. The outlined volume is also displayed on axial and sagittal images, and is filled in with multiple sonication pathways. The treating physician reviews all the outlined beam pathways for each treatment sonication to ensure the beam passage is safe, and that no unintended structures (such as bowel loops) are in the beam path. Should any beam trajectory involve bowel loops, the sonication spots can be moved or deleted, or they may be pushed out of the treatment field. This is usually performed by use of a thick gel pad that displaces the bowel loops superiorly and out of the beam pathway (Fig. 7). Likewise, should the beam trajectory be too close to bone such that it would have an undesirable effect on boney energy deposition (and subsequent inadvertent sciatic nerve injury), sonication spots can be swapped for spots that converge on the same area, but through a different pathway after beam angulation. The presence of an ostomy and anterior abdominal wall scarring (Fig. 8) are not contraindications to treatment, but successful treatment in such cases requires careful pre-treatment planning [26].

After treatment planning, a low-energy (50–100 W or 50–100 J/s) test sonication is delivered to a location within the target volume. Temperature rise during this test sonication can be detected through use of a fast spoiled gradient echo sequence, even though this sonication is not of sufficient energy to cause tissue damage. The location of the temperature rise is then used to precisely align the MRI and ultrasound beam co-ordinates.

Treatment

After confirming that the test sonication is located in the planned position, therapeutic sonications are delivered. These consist of high-power bursts of typically 20 s in duration. The energy of the sonications delivered is slowly increased until a therapeutic thermal dose is achieved (usually greater than 60 °C) to induce tissue coagulation. A series of images are acquired before, during and after the sonications to map the temperature history of the sonicated tissue volume. On the ExAblate system, these temperature-sensitive images are automatically triggered for each sonication selected, and temperature and dose distribution maps are displayed within seconds. The thermal maps are closely studied to confirm ablation in the targeted area, and to determine where additional sonication spots should be placed to obtain complete dose coverage of the targeted volume.

During the treatment continuous communication with the patient is necessary and very important. At our site we have a nurse remain in the room beside the MR device, and

Fig. 7 Challenging treatment-planning scenarios. **a** *Left* In this patient, bowel loops are in *front* of the fibroid (*arrows*), thus initially reducing the size of the acoustic window (*box*). *Right* To move these loops aside, a larger gel pad is placed *below* the abdomen (*star*), allowing access to most of the fibroid. **b** *Left* In another patient, even with this larger gel pad, bowel loops are still in *front* of the fibroid (*arrows*), thus severely limiting the acoustic window (*box*). *Right* To displace the loops further, normal saline is instilled into the urinary bladder via a Foley catheter, displacing the bowel loops superiorly and creating a wider acoustic window. **c** *Left* The third patient has a scar directly in *front* of the fibroid (*circle*). *Right* By tilting the ultrasound beam, the scar can be avoided. From [36], with permission
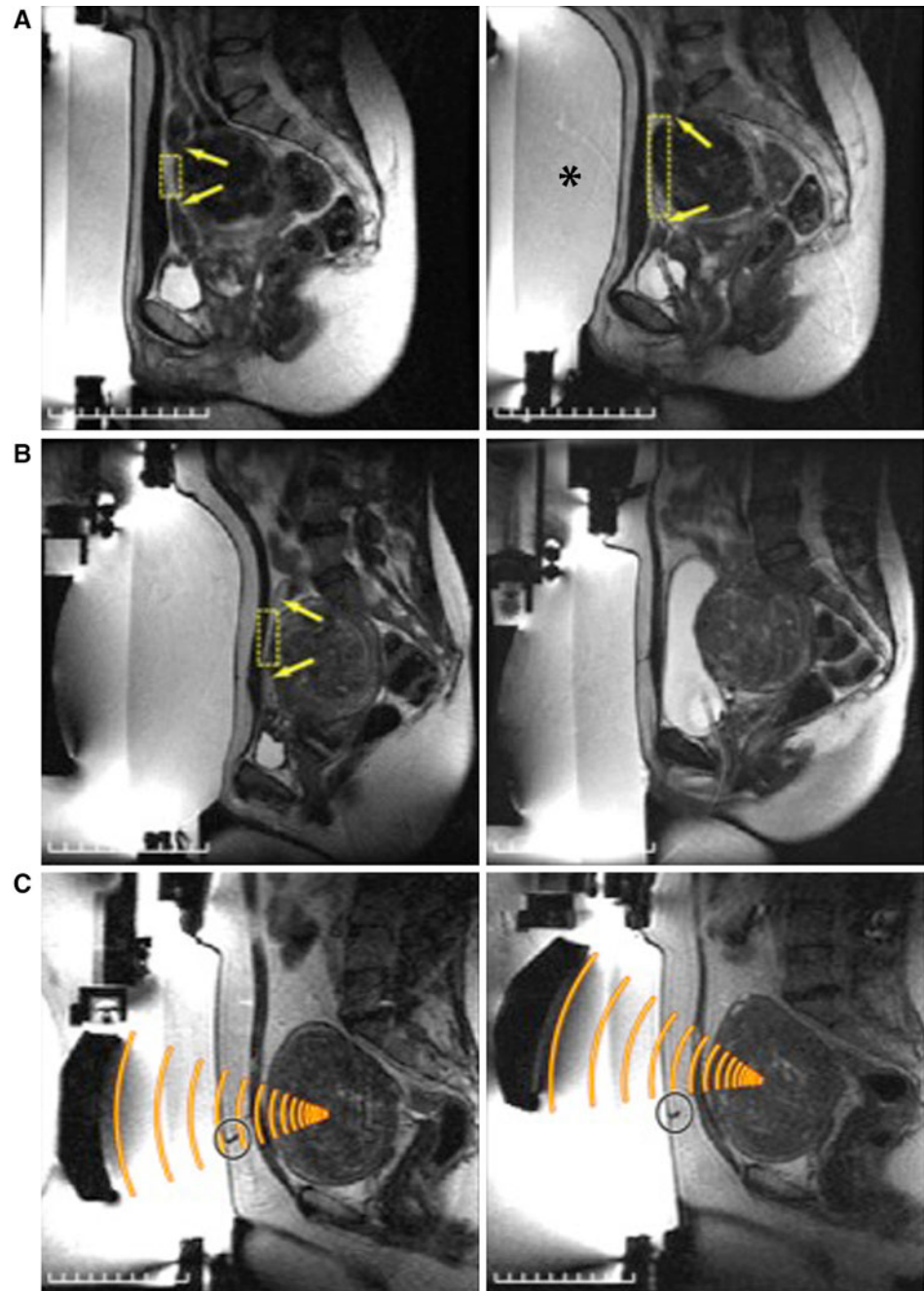
the physician operator is outside in direct communication at all times regarding location of any discomfort or pain, early knowledge of which helps avoid inadvertent heat build-up in the anterior abdominal wall skin or within bone. In the anterior abdominal wall location, inadvertent heat build-up is more likely to occur if there is scarring (such as prior C-section incision scar), which can cause the ultrasound beam to become unfocused. The procedure may be stopped prematurely if the imaging is substandard, or there are targeting difficulties (due to persistent patient motion, for example) or if the patient reports intolerable

sonication-related pain (such as sciatica), or unacceptable positional-related discomfort. Sciatica is a very important symptom, which if reported by the patient must be addressed, by either changing sonication angle or power. As the procedure progresses, the device will cumulatively display all therapeutic sonications and the treated volume can be monitored carefully.

Once finished, the final step of the procedure is administration of contrast-enhanced T1 WI to confirm an area of non-enhancement within the fibroid, indicating tissue necrosis (Fig. 9). This so-called non-perfuse volume (NPV)
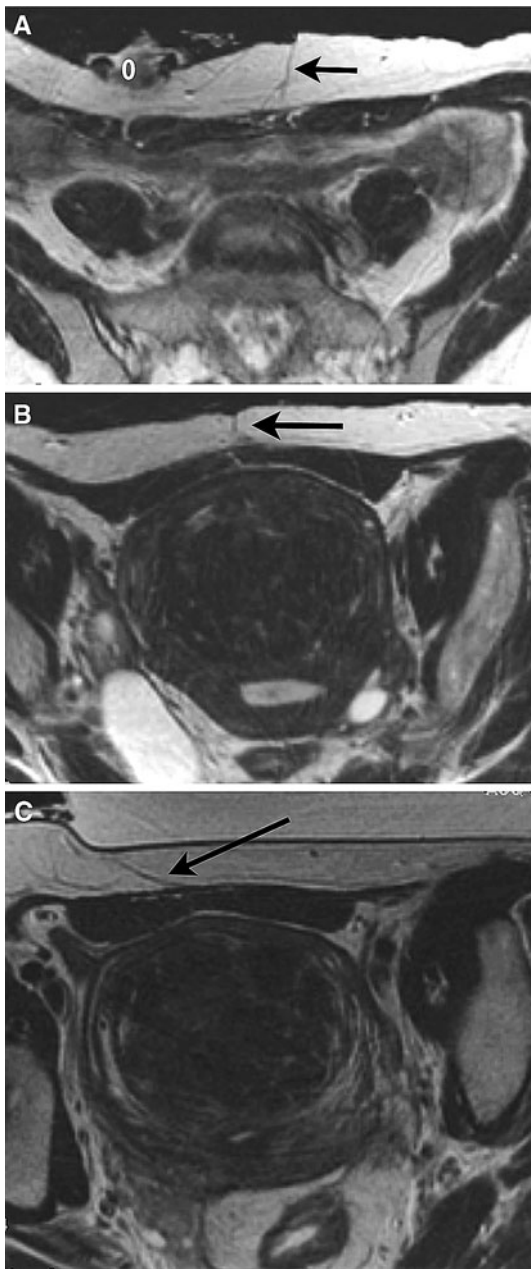
Fig. 8 Screening axial T2 WIs (**a** and **b**) demonstrating a *right lower quadrant* ostomy (O) and longitudinal anterior abdominal wall scarring (*arrow*), which overlies the uterine fibroid. Due to multiple prior surgeries and a history of adhesions, MRgFUS was an attractive option. On the treatment day, the ostomy bag was placed off to the side and the skin of the anterior abdominal wall was pulled off to the *right* side such that the scar was placed outside the treatment window, as can be seen on treatment day axial T2 WI (**c**), allowing access to the fibroid for treatment

is the standard metric used to assess treatment outcome. The goal is to achieve as high an NPV as possible in an individual fibroid. Before discharge, the treating physician examines the skin of the anterior abdominal wall, paying particular attention if scarring is present, to evaluate for any

heat-induced skin changes. The patient is then discharged home with an escort, usually 1–2 hours after the procedure, and at least in our practice, the patient is followed up by phone 24 hours later. Upon discharge, the patient is aware of what to expect post-procedure, including mild menstrual-type cramping or nausea due to sedation.

Clinical Outcome with MRgFUS

The first results of the initial phase I/II trial of the ExAblate 2000 device, (treating a subvolume of a fibroid prior to hysterectomy), demonstrated MRgFUS to be a safe and feasible treatment through pathological correlation [23]. Subsequent multicenter phase III clinical trials demonstrated a majority (71 %) of patients to have reached the targeted symptom improvement at 6 months post-therapy, maintained in 51 % by 12 months post-therapy [27]. However a proportion of the patients in the phase III trials were treated with a less restrictive protocol, which resulted in a greater nonperfused volume (NPV) (25.8 vs 16.7 % with the more restricted protocol), and a significantly greater reduction in symptom score [19]. This finding was echoed in a review of almost 300 patients treated in Japan [28] where the patient groups were divided according to the chronological treatment time. In this study it was found that those treated earlier on had a NPV of 39 %, whereas those treated later on had a NPV of 54 %. Interestingly, procedural-related complications fell as the NPV rose. This study underscored the importance of the learning process on treatment optimization, and the need to achieve large NPVs for sustained symptom relief.

Side effects of treatment with MRgFUS are minimal. Transient abdominal pain related to the sonication, sciatica, or pain related to position within the magnet, are the most common side effects seen [19]. Sciatica can occur due to absorption of energy by bone in the far field of the sonication, with transfer of heat from the adjacent pelvic bones causing irritation, stimulation or even injury to the adjacent nerve. Mitigating steps have been established as follows— all abdominal wall scars must be identified and should not be crossed by the beam path during treatment, and fibroid tissue lying within 4 cm immediately anterior to the sacral spine cannot be treated. Minor skin burns [27] and a single case of a more serious full thickness abdominal skin burn [29] were reported early in the development of this technique, leading to a fastidious need for examination of the treatment path and to confirm the absence of skin oils, hairs and especially scar tissue. Some operators are now using ultrasound masking scar tape over significant scars to great benefit. There also was a report of a sciatic nerve palsy which resolved clinically of its own accord without treatment [27], thought to be due to transfer of heat from the
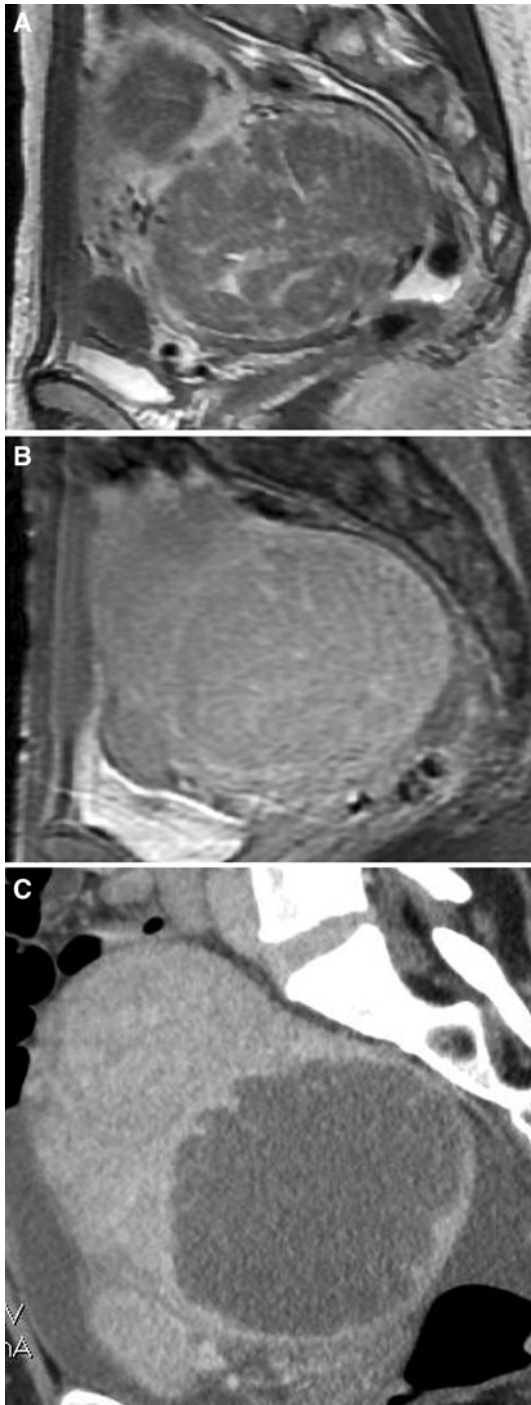
Fig. 9 Screening sagittal T2 WI (**a**) and sagittal T1 post administration of intravenous gadolinium chelate (**b**) demonstrating a well-defined dominant uterine fibroid that demonstrates diffuse homogenous enhancement. After MRgFUS, sagittal images from a pelvic CT (**c**) demonstrating lack of enhancement in the targeted fibroid, consistent with ablation of the entire fibroid volume

adjacent bone causing heat buildup and injury to the adjacent nerve.

More recently, there has been an effort to determine imaging and clinical predictors of success with MRgFUS

fibroid treatment. A very recent study has determined that older patients (mean age 46) were more likely to be associated with long-term treatment success [30]. We and others [30, 31] have also shown that fibroids of low SI on pretreatment T2-weighted MR images are more likely to decrease in size post-MRgFUS compared with more cellular fibroids of high SI on T2 WI.

In the USA, the current FDA-labeling of the ExAblate 2000 for fibroid treatment is for women who should be 'family complete'. This has since been removed, as there have been more than 54 post FUS pregnancies reported world-wide, with a high rate of successful full term delivered pregnancies [32]. This data would suggest that MRgFUS is a safe fibroid treatment option in women who decide to become pregnant, as there are no significant complications from the procedure in women seeking pregnancy as with existing fibroid therapies. Considering this data is based on a small number of patients, a randomized clinical trial (NCT00730886, clinicaltrials.gov) comparing MRgFUS with ExAblate 2000 to myomectomy in women with unexplained infertility and who have non-hysteroscopically resectable uterine fibroids was undertaken, the data of which is now being analyzed.

MRgFUS Technology Assessment

Multicenter clinical trials have shown MRgFUS to be a safe, acceptable and effective treatment for uterine fibroids that leads to long-term symptom relief. However, for MRgFUS to be widely accepted and approved by insurance companies, it must be shown to improve net health outcome and be deemed as beneficial as any established alternatives. It needs to be evaluated with respect to patient preferences for treatment and outcome of treatment with regards to quality of life, offset against the cost of treatment, both to the individual and society as a whole. Performing a cost–utility analysis is an integral part of this new technology assessment. We have shown that fibroid utility values increase after MRgFUS treatment, and that perceived patient morbidity for the noninvasive MRgFUS treatment option is far less than that for hysterectomy [12•], indicating a patient preference for MRgFUS. There have been no prospective randomized controlled trials comparing MRgFUS, and many would argue that such a study is necessary to evaluate this novel therapy in an appropriate comparable context. Based upon clinical trial data to date however, a number of retrospective decision analysis studies have been performed and have shown that MRgFUS, as a first-line fibroid treatment strategy, is likely to be cost-effective in comparison to UAE, myomectomy and hysterectomy [13, 33]. The key efficacy outcomes of quality of life and symptom improvement, in addition to

patient preference for noninvasive interventions were recently listed as the reasoning behind the favorable guidelines announcement by NICE (the National Institute for Health and Clinical Excellence of the NHS in the UK), for the treatment of uterine fibroids using MR-guided focused ultrasound. The new guidelines state that the current evidence on the efficacy of magnetic resonance image-guided transcutaneous focused ultrasound treatment for uterine fibroids and evidence on safety are adequate to support the use of this procedure under normal arrangements (http://guidance.nice.org.uk/IPG413).

Summary of Recent Techniques to Optimize Increase in Ablation Volume

As the goal of MRgFUS is to treat as much of the fibroid as possible within acceptable treatment times, there is much current investigation into how to optimize treatment strategies. The initial point-by-point strategy used in preliminary trials of the ExAblate 2000 created a small ablation zone of approximately 5 mm in size, and the user selected each subsequent sonication. There have been many developments in this front of recent times, such as development and FDA clearance of an "interleaved mode" for the ExAblate 2000 which allows the system to target different parts of the fibroid, allowing the recently ablated tissue area to cool while the focus moves onto other areas of the fibroid, thereby reducing the cooling time required. The interleaved mode also permits a greater number of sonications to be delivered during the same treatment window. In a similar vein, the Phillips system has demonstrated a method of volumetric ablation (versus single-cell ablation) which comprises of multiple outward moving concentric circles, thought to be more energy efficient as it uses heat that is already deposited in the inner part of the trajectory to pre-heat the outer parts [9]. Furthermore, it has been shown that near-field heat accumulation can be exploited and is effective in the treatment of large fibroids, the so-called "one layer" strategy [34•]. There has also been some very preliminary investigation into targeted vessel ablation, where MRgFUS is aimed at the blood vessel supplying the fibroid, with resultant greater non-perfused volumes obtained [35].

Conclusion

MRgFUS is a noninvasive treatment option for benign and malignant tumors, the potential for which is tremendous. Technological improvements in MRgFUS are ongoing, with the goal of optimizing ablation volume in as little treatment time as possible. Robust technology assessment of MRgFUS remains a necessity, taking into consideration key efficacy outcomes of quality of life and symptom improvement, in addition to patient preference for noninvasive interventions. Our knowledge about MRgFUS is continually evolving as treating physicians learn to use it more efficiently and effectively, and as we begin to make use of technological improvements and continue to understand which patients, which fibroids and which symptoms are the most likely to benefit from MRgFUS. A potentially disruptive technology, MRgFUS has the potential to alter the way we evaluate and treat patients suffering with fibroid symptoms. For the moment, however, each patient requires a customized treatment strategy when considering fibroid treatment options available.

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