Egyptian Journal of Radiology and Nuclear Medicine

RESEARCH

Open Access

Preliminary insights into high-intensity focused ultrasound ablation for symptomatic uterine fibroids: a first look in Egypt

Mohamed Fawzi[1], Safaa ElMandouh[1], Alaa Eid Elbanna[1], Micheal Ezzat Narouz[1], Menna Habib[1], Shrouk Shady Mahmoud[1] and Ahmed Said Badr[1*]

Abstract

Background Uterine fibroids are common gynecological conditions that affect a significant number of women of reproductive age and may necessitate surgical intervention for their removal. However, there is a rising trend toward minimally invasive procedures, such as magnetic resonance-guided high-intensity focused ultrasound (MRgHIFU) ablation. This report provides the first experience in Egypt and North Africa on the use of MRgHIFU ablation as a therapeutic option for uterine fibroids.

Results This study demonstrates a correlation between post-operative NPV% and symptom improvement. Following a three-month follow-up period, a significant reduction in pain scores and excessive bleeding was observed. Importantly, there was no significant elevation in hemoglobin levels (11.23 ± 2.23 to 11.25 ± 1.71 g/dL) after treatment. Furthermore, the mean non-perfused volume ratio in the treated fibroids was 46 ± 27.3% (SD) among the 20 participants. These findings suggest a favorable therapeutic outcome of MRgHIFU, with no serious adverse effects reported.

Conclusion MRgHIFU is a noninvasive therapeutic approach for the treatment of uterine myomas, offering significant benefits in terms of pain reduction and improved quality of life. This particular study represents the pioneering clinical experience of this innovative therapy in Egypt.

Keywords Uterine fibroid, High-intensity focused ultrasound (HIFU), Efficacy

Background

Uterine fibroids are benign, encapsulated uterine lesions that typically result in hysterectomy in women before menopause [1]. This kind of tumor is age-related, with a 20% prevalence at the age of 35 and a cumulative prevalence of 80% at the age of 50%; However, it is extremely rare in girls under the age of 25 [2]. Uterine fibroids generally reduce the quality of life due to symptoms such as excessive prolonged menstrual bleeding, pelvic dullness, dysmenorrhea, and anemia, which are caused by intramural and sub-mucosal lesions. Constipation, sacral discomfort, and urine urgency are other manifestations of the large intra-mural and interstitial myomas [3].

High-intensity focused ultrasound (HIFU) treatment is a non-invasive, non-ionizing ablation procedure that uses high-intensity focused ultrasound for the absorption of acoustic energy locally.

As a non-invasive treatment, magnetic resonance-guided high-intensity focused ultrasound (MRgHIFU) therapy necessitates medical imaging for procedure planning and targeting, real-time therapy monitoring, and post-operative evaluation. Magnetic Resonance Imaging (MRI) is considered the gold standard approach for regulating HIFU thermal ablations due to its ability to deliver

*Correspondence:
Ahmed Said Badr
Ahmedsaidbadr40@gmail.com
[1] Radiology Department, National Hepatology and Tropical Medicine Research Institute, Cairo, Egypt

tissue temperature in real time using MR Thermometry [4]. According to Funaki et al., UFs are divided into three kinds based on the signal intensity of T2-weighted magnetic resonance imaging (T2WI), with hyperintense fibroids being more difficult to be ablated than hypointense and isointense fibroids [3]. During MRgHIFU thermal ablation, an ultrasound transducer produces a focused beam of high-intensity ultrasound waves. The acoustic energy is absorbed by the targeted tissue within the focused region, causing a temperature rise and coagulative necrosis [5].

Thermal ablation is accomplished by a series of sonications, the number and duration of which are determined by the size and tissue properties of the fibroid. A contrast-enhanced T1 weighted imaging of an MRI scan is employed immediately after MRgHIFU to visualize the ablated tissue, which may be seen on such scans as a non-perfused volume (NPV). A high NPV to total fibroid volume (NPV%) ratio is a technical predictor of favorable clinical results and low re-intervention rates [6]. The current study provides our experience with this novel therapeutic option of symptomatic uterine fibroid.

Methods

Study design

We included women in reproductive age group who took part in our hospital (National Hepatology and Tropical Medicine Research institute, Diagnostic & Interventional Radiology Department, HIFU Unit). Eligibility for MRgHIFU treatment was determined by a screening MRI-scan (performed on a 1.5 T MRI-scanner, Ingenia, Philips Healthcare, Eindhoven, The Netherlands). Several parameters were collected from the patients during the study, including age, hemoglobin (HB) level, multiplicity of fibroids, target fibroid size, target tumor location, FUNAKI type, pain score, excessive bleeding, HB level, red blood cell (RBC) count, and non-perfused volume (NPV) percentage.

Uterine fibroids ranging from 2 to 10 cm in size are generally considered suitable for MRgHIFU treatment. However, several factors need to be taken into account. Scarring of the abdominal wall, such as that resulting from previous cesarean section or laparotomy, can pose relative contraindications for MRgHIFU. This is because the ultrasound beam cannot effectively pass through scar tissue using dynamic focusing or movement of the HIFU probe. Therefore, careful attention should be paid when treating uterine fibroids located near the lumbar plexus to minimize the risk of nerve damage.

It is important to note that the MRgHIFU beam has a limited depth of penetration, reaching a maximum depth of 11 cm. As a result, uterine fibroids located deeper than this threshold cannot be effectively targeted. In such cases, a technique involving the filling of the rectum with ultrasound gel can be employed. This method helps to reposition the uterus ventrally and mobilize the fibroid into the focus of the HIFU beam. It is worth mentioning that the relatively long treatment times associated with MRgHIFU can present challenges in clinical practice. In situations where adequate heating cannot be achieved or if the bowels are obstructing the path of the beam and cannot be moved, these cases are considered treatment failures. It is crucial to base clinical decisions on sound scientific evidence and individual patient characteristics. Close monitoring and careful consideration of these factors will help ensure the safe and effective use of MRgHIFU for treating uterine fibroids.

HIFU: application methods

The primary principle of HIFU involves delivering mechanical energy to tissue by transmitting ultrasound waves through a medium, whether solid or liquid. Unlike diagnostic ultrasound probes that disperse ultrasound waves, HIFU probes are designed with a spherical curvature to focus and concentrate the ultrasound waves at a central point, thereby intensifying the ultrasound energy. The underlying physical mechanism of HIFU revolves around the absorption of ultrasound by tissues, which is then converted into heat. This thermal energy leads to the formation of necrotic foci, referred to as the NPV. HIFU treatments can be guided by sonographic or MRI techniques. The NPV and tissue temperature distribution can be visualized and assessed using contrast-enhanced MRI (as demonstrated in Fig. 1). The destruction of necrotic tissue in uterine fibroids results in volume reduction and alleviation of various clinical symptoms. Achieving high NPVs is a crucial predictor of therapeutic success in MRgHIFU treatment for uterine fibroids, indicating effective ablation of the targeted tissue.

HIFU therapy: treatment cells and temperature mapping

Prior to HIFU treatment, a T2-weighted planning MRI is performed with the patient in the prone position. This imaging technique is employed to identify the precise anatomical location of the uterine fibroid (UF). It allows for an assessment of the UF size, target volume, and the feasibility of accessing the UF with the HIFU beam. The treatment procedure involves sonicating the UF in a step-by-step manner, using a cluster of treatment cells measuring between 4–16 mm in diameter (as shown in Fig. 2). Real-time multiplanar MR thermometry is utilized during the procedure to monitor the ablation temperatures and identify structures that may be at increased risk, particularly in cases involving large-volume UF ablations. This allows for efficient temperature tracking and adjustment of the HIFU beam's energy during the ablation

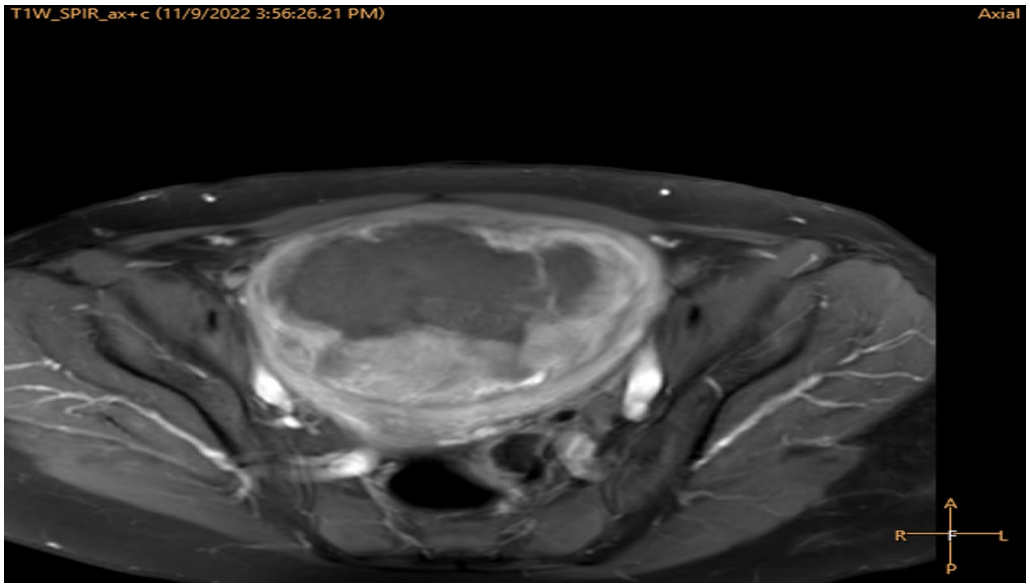

Fig. 1 Axial T1 MRI Image post-contrast shows non-enhancing (ablated) areas of the uterine fibroid post-HIFU therapy

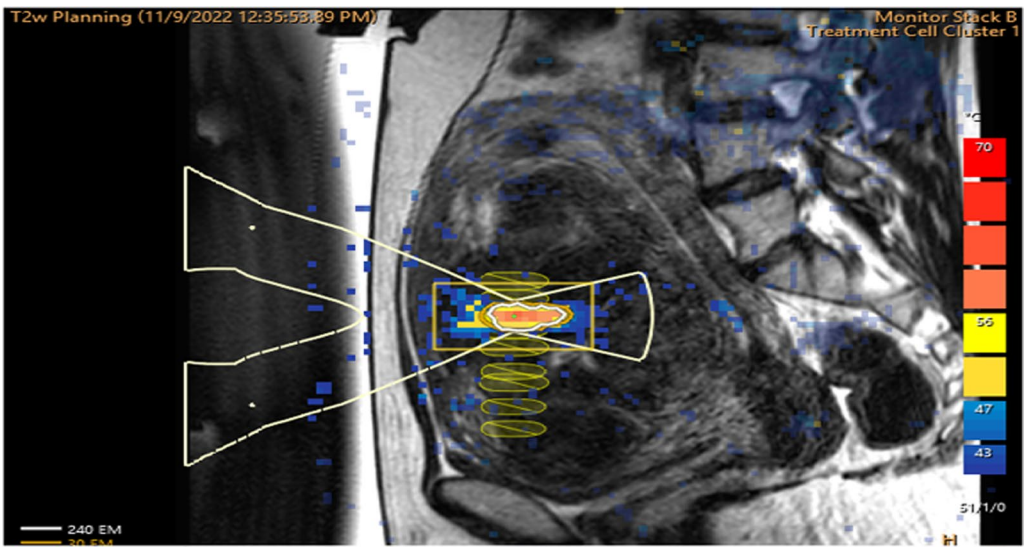

Fig. 2 Sagittal T2 showing virtual sonication probe directed at a column of clustered cells. The red area indicates the maximum thermal dose

process, ensuring optimal tissue heating while minimizing patient risk. The temperature curve (as depicted in Fig. 3) serves as a guide to adapt the energy of the HIFU beam as needed, enhancing the effectiveness of the treatment and reducing the overall treatment time.

MR-HIFU treatment

Pre-treatment

When subjects were met the eligibility criteria for MR-HIFU treatment and expressed their willingness to participate, they were examined by the anesthesiologist and received information about the conscious sedation during the MR-HIFU procedure. The evening before the treatment, women were instructed to shave their lower abdomen and observe an overnight fast, or at least refrain from eating for a minimum of 6 h. Upon admission to the day care facility in the morning, a bladder catheter was inserted, and an intravenous line was established. Pre-medication was administered, including Tiemonium Methyl Sulfate (5 mg/2 ml), Esomeprazole (40 mg),

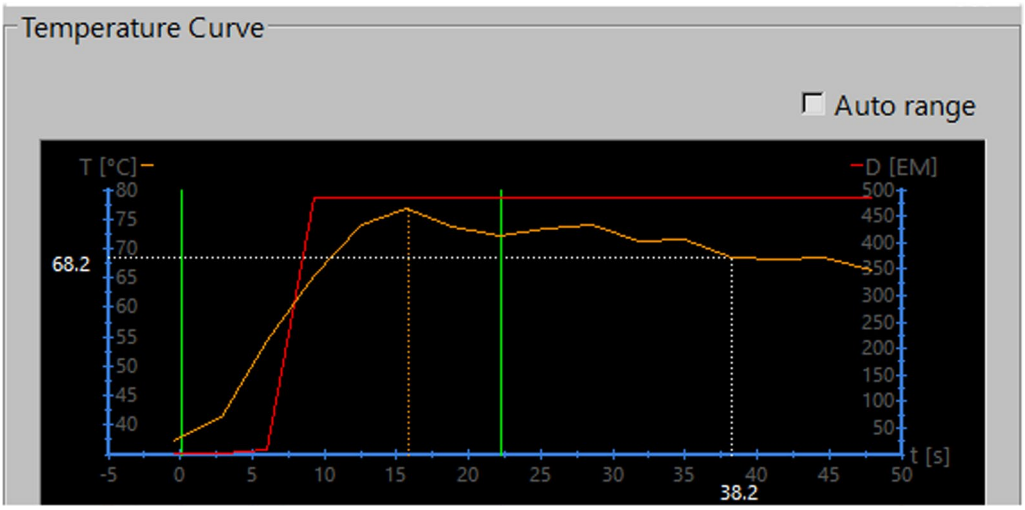

Fig. 3 Temperature curve of the selected sonication cell, where the two green line represent duration of the sonication. The orange curve represents a rapid rising temperature

Ondansetron hydrochloride (8 mg/ 4 ml), Dexamethasone Phosphate (8 mg/ 2 ml amp), Diclofenac Sodium (75 mg/ 3 ml), Synthetic Oxytocin (10 I. Units/1 ml).

Women were positioned in the prone position within the MRI scanner, and a pre-treatment MRI scan was conducted to verify the final position of the fibroid. The MR-HIFU procedure was performed using the Sonalleve V1 system (Profound Medical Inc., Mississauga, Canada), which was integrated into a 1.5-T Ingenia MRI scanner (Philips Healthcare, Best, The Netherlands).

Our sedation protocol involved administering a fentanyl bolus of either 20 µg/0.5 ml or 25 µg/1.0 ml, depending on the level of pain experienced by the patient. The purpose of the sedation was to alleviate pain to a manageable degree while still allowing for pain scoring to accurately adjust the heating dose.

Treatment

MR-HIFU fibroid ablation is a treatment approach that combines high-intensity focused ultrasound with real-time MRI guidance. The procedure involves directing a focused ultrasound beam toward the uterine fibroid, resulting in coagulative necrosis of the targeted tissue. To ensure safety, MR thermometry is utilized, enabling the measurement of heating in almost real-time within the targeted tissue and critical surrounding structures. Our treatment strategy involves sequentially ablating different parts of the fibroid. We begin by completely ablating the posterior part, followed by the middle and anterior parts of the fibroid. Throughout the procedure, if the patient experiences significant pain in the back or lower limbs, they have the option to immediately abort the procedure by pressing an emergency button. Additionally, the responsible radiologist has the authority to halt the sonication if they observe abnormal scattered heat.

Following the completion of the procedure, a contrast agent (gadoteric acid or gadoterate meglumine at a concentration of 0.1 mmol/kg) is administered. Subsequently, another MRI scan is performed with post-contrast T1 series to evaluate the non-perfused volume percentage (NPV%). The fibroid and NPV volumes are quantified using IntelliSpace K.J. Portal software (Philips Healthcare) through semi-automatic segmentation in the tumor tracking function. Manual corrections and review of the segmentation are carried out as necessary (as shown in Fig. 4). Generally, the NPV ratio is calculated by comparing the non-NPV within the targeted tissue to the total volume of the tissue. The NPV is measured and then divided by the total volume of the tissue to obtain the non-perfused volume ratio.

Post-treatment

Following the MRgHIFU procedure, patients remained under observation at the daycare facility for a few hours. During this time, the urinary bladder was washed with cold saline to aid in further cooling. Subsequently, the bladder catheter was removed. Before discharge, vital signs were monitored, and thorough assessments were conducted to identify any adverse events, such as pain or potential signs of skin burns in the lower abdominal region. If no abnormalities or complications were detected, patients were allowed to leave the hospital on the same day.

Scheduled follow-up appointments were planned for three months after the treatment. During these follow-up visits, the patient's recovery progress, potential adverse

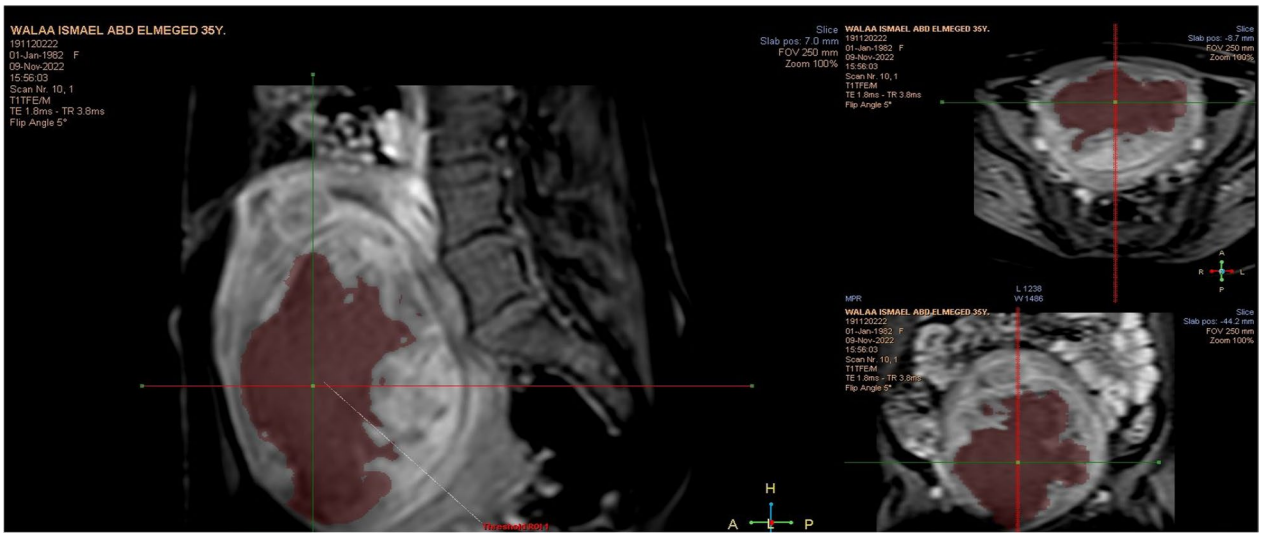

Fig. 4 IntelliSpace K.J. Portal software (Philips Healthcare) with red areas are showing the calculated NPV

events, and the reduction of symptoms were discussed and evaluated. These discussions provided an opportunity to address any concerns or complications that may have arisen post-treatment.

Statistical analysis

Data analysis was performed using IBM SPSS Statistics (Version 26.0, IBM Corp., USA). Quantitative parametric data were presented as mean ± standard deviation (SD), while categorized data were reported as numbers and percentages. Descriptive statistics, including the number of cases, mean, standard deviation, range (minimum to maximum), and the number and percentage, were calculated for both quantitative and qualitative measures. The Wilcoxon matched-pairs test was employed in this study to compare the pain score, excessive bleeding occurrences, hemoglobin (HB) levels, and red blood cell (RBC) counts before and after a 3-month treatment period. This non-parametric statistical test is suitable for paired data analysis when the distribution of variables is not assumed to be normal. P-value was considered significant at < 0.05.

Results

The study included a total of 20 patients who underwent MRI-guided HIFU procedures. As depicted in Table 1, the age of the patients ranged from 30 to 51 years, with a mean age of 40.45 years and a standard deviation of 6.35 years. All patients were premenopausal at the time of the procedure. Among the patients, 50% [10] had a single fibroid, while the remaining 50% [10] had multiple fibroids. The volume of the fibroids varied significantly, ranging from 13 to 1170 cc, with a mean volume of 202.15 cc and a standard deviation of 266.63 cc.

Table 1 Baseline characteristics of the studied patients (N = 20)

Parameters	Mean ± SD (min–max)
Age (years), Mean ± SD (min–max)	40.45 ± 6.35 (30–51)
HB level (gm/dl), Mean ± SD (min–max)	11.23 ± 2.23 (6.6–14.9)
Multiplicity of fibroid, N (%)	
Single	10 (50)
Multiple	10 (50)
Target Fibroid Size (cc), Mean ± SD (min–max)	202.15 ± 266.63 (13–1170)
Target tumor location, N (%)	
Anterior wall	10 (50)
Posterior wall	9 (45)
Sub mucous	1 (5)
Target FUNAKI type, N (%)	
I	10 (50)
II	4 (20)
III	6 (30)

Regarding the classification of the fibroids, 50% [10] were categorized as FUNAKI I, 20% [4] as FUNAKI II, and 30% [6] as FUNAKI III. In terms of location, 50% [10] of the uterine fibroids were found on the anterior wall, 45% [9] on the posterior wall, and 5% [1] were identified as submucosal fibroids. The preoperative hemoglobin (Hb) levels of the patients ranged from 6.6 mg/dl to 14.9 mg/dl, with a mean Hb level of 11.23 mg/dl and a standard deviation of 2.23 mg/dl.

The clinical and laboratory outcomes of 20 patients before and after 3 months of MRgHIFU therapy were

Table 2 Clinical and Laboratory outcomes before and after 3 months of HIFU therapy

Parameters	Before treatment (N = 20)	After treatment (N = 20)	P value
Pain score, Mean ± SD	6.5 ± 1.91	5 ± 2.16	0.0018
Excessive bleeding, N (%)	19 (95)	2 (10)	< 0.001
HB level (gm/dl), Mean ± SD	11.23 ± 2.17	11.25 ± 1.71	0.99
RBCs count (m/ul), Mean ± SD	4.45 ± 0.53	4.61 ± 0.45	0.0168

Table 3 NPV of the ablated fibroid lesion 3 months after HIFU treatment

Parameters	(N = 20)
NPV ratio percentage, Mean ± SD (Range)	46 ± 27.3 (1–85)
NPV ratio grade	
I (1%–25%)	5 (25)
II (25%–50%)	5 (25)
III (50%–75%)	7 (35)
IV (above 75%)	3 (15)

assessed. The results are presented in Table 2. Before treatment, the patients had a mean pain score of 6.5 ± 1.91, which significantly decreased to 5 ± 2.16 after treatment (p = 0.0018). This indicates a significant improvement in pain management following HIFU therapy. Excessive bleeding was reported by 19 out of 20 patients (95%) before treatment, but after HIFU therapy, only 2 patients (10%) experienced excessive bleeding (p < 0.001). This demonstrates a substantial reduction in bleeding episodes after treatment. The mean hemoglobin (HB) level before treatment was 11.23 ± 2.17 gm/dl, which remained relatively unchanged at 11.25 ± 1.71 gm/dl after treatment (p = 0.99). No significant difference was observed in HB levels before and after HIFU therapy. Regarding the red blood cell (RBC) count, the mean value before treatment was 4.45 ± 0.53 m/ul, which increased to 4.61 ± 0.45 m/ul after treatment (p = 0.0168). This indicates a statistically significant increase in RBC count following HIFU therapy.

NPV of the ablated fibroid lesion was evaluated in 20 patients 3 months after HIFU treatment. The results are summarized in Table 3. The mean NPV percentage was found to be 46 ± 27.3%, with a range of 1% to 85%. This indicates the average proportion of the ablated fibroid lesions that did not show any perfusion after HIFU treatment.

The NPV grades were categorized as follows: Grade I (1%—25%), Grade II (25%—50%), Grade III (50%—75%), and Grade IV (above 75%). Among the patients, 5 (25%) had Grade I NPV, 5 (25%) had Grade II NPV, 7 (35%) had Grade III NPV, and 3 (15%) had Grade IV NPV. No serious adverse effects were reported.

Discussion

Usually, the conventional treatment for symptomatic uterine fibroids is open or laparoscopic hysterectomy or myomectomy with potential subsequent hysterectomy. The operative drawbacks discourage women from the treatment options; especially those who are in the childbearing period. The surgical approach complications include hematomas, hemorrhages, bowel or urinary tract injury, wound infection and cystitis. [7] In a study done to assess the complication rates for open, laparoscopic, and hysteroscopic myomectomy operations, the results were 10.8%, 2.94%, and 6.25%, respectively. [8] On the other hand, our study and other studies conducted on MRgHIFU treatment for uterine fibroids stated low complication rates.

Interventional radiology intervened in this situation by offering different minimally invasive treatment options like uterine fibroid embolization UFE, uterine artery embolization UAE, and high-intensity focused ultrasound wave ablation of the uterine fibroids HIFU; with great outcomes and some limitations of each. The HIFU tissue ablation takes place due to the intracellular organelles and intra-organ fluid expansion and contraction by the ultrasound waves energy, forming bubbles that burst causing resonance that push the temperature to destroy the tissue. [9] The ultrasound ablation is usually guided by an ultrasound scan or MR real-time imaging. MRI offers outstanding soft tissue delineation of the fibroids, opposed to the ultrasound scan that has poor conspicuity between different soft tissues. Additionally, MRI is the only imaging modality that provides real-time thermal maps, necessary for regulating the thermal ablating effects, providing ideal mass ablation and avoiding detrimental outcomes on surrounding structures. [10].

On 3-month follow up, a significant reduction in pain score and menstrual bleeding were observed. However, there was no remarkable elevation in hemoglobin levels, yet. Grade III group (NPVR = 50%-75%) represented 35% of the cases, while the grade I group (NPVR = < 25%) were 25% of the cases, the grade II group (NPVR = 25%-50%) represented 25% and, grade IV group ((NPVR = 75%-100%) were 5%. The mean NPVR for these results was 46% after one session of MRgHIFU. After which, some of the patients required further sessions with subsequently higher NPVR.

K. J. Anneveldt et al. in their study; lessons learned during implementation of MRgHIFU treatment of uterine fibroids came out with a median NPVR = 66.5%. [11] On the other hand, the meta-analysis done by liang et al.

in 2021 stated that of the 20 papers in the MRgHIFU and the 10 in the USgHIFU the mean NPVR was 58.92% and 81.07% in the MRgHIFU group and the USgHIFU group, respectively. However, Liang et al. also reported that the complications rates were much less in the MRgHIFU; The rate of post-operative skin thermal injury in the MRgHIFU group reached 4.5% and 14.4% in the US-HIFU group, where, the percent of post-operative sciatic nerve pain was 8.9% and 15.7% in the MRgHIFU group and USgHIFU group, respectively, and, the percent of post-operative abnormal vaginal discharge was 20.3% in the MRgHIFU group and 11.3% in the USgHIFU group. [12].

MRgHIFU complications might happen, namely skin burn, sciatic nerve temporary or permanent damage, thermal damage of the abdominal wall muscle and subcutaneous fat, hematuria, intestinal injury, uterine hemorrhage, and others. However, most of the relevant studies have not reported any of these, except for, minor skin burns. [13]. during the 3-month follow-up, our study has not reported any complications, yet. The complications were successively avoided by the use of the rapid cooling technique after the session by using the already placed urinary catheter to flush a fair amount of cold fluid to rapidly cool the pelvic area.

During defining our inclusion criteria, we concluded some situations that might be considered as contraindications for an optimal MRgHIFU. They are uncontrolled bleeding, sub-serosal pedunculated fibroids, metallic or plastic objects in the uterus or the field of the sonication, like IUCD and metallic stitches, patients with claustrophobia, active malignancies or metastases, and, unreachable fibroids of distance more than 11 cm from the anterior abdominal wall as this is the maximum depth the HIFU beam can reach.

The major challenge faced during HIFU sessions was motion; whether coarse motion like respiratory movements or fine motion like the simple abdominal wall tension reflex of the patients to the sound of beam or even just the peristaltic movements or the fine motion of patients with claustrophobia who request mild sedation during the procedure. However, a motion compensation was successfully established by the help of the multiplanar real-time MR thermometry. Thus, ultrasound energy dispersion was prevented, avoiding the higher energy needed to overcome the dispersion, thus preventing any damage for the surrounding structures, and providing precise focus of the ultrasound beam on the targeted lesion.

A limitation that faced us was that there is no pathological specimen. Another one, that could be overcome, is the short period of the follow-up. Longer period of post-interventional follow up is recommended to assess the need for re-intervention. However, we support having re-intervention as some of the patients included in the study underwent multiple sessions with doubled and even higher success rates. Re-intervention concept gives the opportunity for a wider range of patients to undergo uterine fibroids MRgHIFU. The reasons that faced us to have multiple sessions were huge fibroid, recurrence after 1 year, technical difficulties, and combined FUNAKI type II/III with cystic degeneration and high vascularity. Quinn et al. supports re-intervention as they stated that if the NPV% is less than 50% or the uterine fibroid was FUNAKI type III, the risk of needing intervention is higher. Also, the re-intervention rate was 42.8% within 3 years, and 59.3% within 5 years. [14] Also, the meta-analysis by liang et al. in 2021 revealed a 13.4% intervention rate after one year in the MR-HIFU subjected patients. [12].

Conclusion

MR-HIFU is a completely non-invasive, less painful therapeutic option for uterine myomas that has demonstrated an improvement in quality of life due to the reduction in myomas-related symptoms. This study is the first to represent the clinical experience of MR-guided HIFU therapy of symptomatic uterine fibroids in Egypt. With more cases being done and with the increase in the learning curve better results will be expected in our next study.

Abbreviations

MRgHIFU	Magnetic resonance-guided high-intensity focused ultrasound
HIFU	High-intensity focused ultrasound
MRI	Magnetic resonance imaging
NPV	Non-perfusion volume
UF	Uterine fibroid
SD	Standard deviation.
HB	Hemoglobin.
RBCs	Red blood cells

Acknowledgements

Not applied.

Author contributions

MF and AS authored the manuscript and handled correspondence with the journal. SE and AE were responsible for collecting and processing patient data and images. ME, MH, and SS contributed to the study's design and conducted the statistical analysis. The study was conceptualized by AE and SE, who also contributed to its design and coordination. Eventually, MF and AS reviewed the draft from a clinical perspective. All authors have read and approved the manuscript.

Funding

This research did not receive specific grants from public, commercial, or not-for-profit funding agencies.

Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
The Institutional Review Board (IRB) of the National Hepatology and Tropical Medicine Research Institute approved the study with ethical committee approval. Informed written consent was taken from all subjects.

Consent for publication
All patients included in this research gave written informed consent to publish the data contained within this study.

Competing interests
No financial or non-financial competing interests.

Received: 7 November 2023 Accepted: 21 February 2024
Published online: 26 February 2024

References

1. Wiggermann A, Beldoch M, Hoellen F, Hunold P (2016) MR-guided high-intensity focused ultrasound treatment of uterine fibroids. Res Rep Focused Ultrasound 4:9
2. Baird DD, Dunson DB, Hill MC, Cousins D, Schectman JM (2003) High cumulative incidence of uterine leiomyoma in black and white women: ultrasound evidence. Am J Obstet Gynecol 188(1):100–107
3. Jiang L, Yu JW, Yang MJ, Zhong Q, Chen JY (2022) Ultrasound-guided HIFU for uterine fibroids of hyperintense on T2weighted MR imaging with or without GnRH-analogue-pretreated: a propensity score matched cohort study. Front Surg 9:975839
4. Tempany CM, McDannold NJ, Hynynen K, Jolesz FA (2011) Focused ultrasound surgery in oncology: overview and principles. Radiology 259(1):39
5. Verpalen IM, Anneveldt KJ, Nijholt IM, Schutte JM, Dijkstra JR, Franx A, Bartels LW, Moonen CT, Edens MA, Boomsma MF (2019) Magnetic resonance-high intensity focused ultrasound (MR-HIFU) therapy of symptomatic uterine fibroids with unrestrictive treatment protocols: a systematic review and meta-analysis. Eur J Radiol 1(120):108700
6. Duc NM, Keserci B (2018) Review of influential clinical factors in reducing the risk of unsuccessful MRI-guided high-intensity focused ultrasound treatment outcome of uterine fibroids. Diagn Interv Radiol 24:283–291
7. Paul GP et al (2010) Complications of laparoscopic myomectomy: a single surgeon's series of 1001 cases. Aust N Z J Obstet Gynaecol 50:385–390
8. Alharbi AA et al (2020) Intraoperative and postoperative complication for open, laparoscopic, and hysteroscopic myomectomies in Saudi Arabia. PMC. https://doi.org/10.7759/cureus.7154
9. Vaughan MG, ter Haar GR, Hill CR, Clarke RL, Hopewell JW (1994) Minimally invasive cancer surgery using focused ultrasound: a pre-clinical, normal tissue study. Br J Radiol 67:267–274
10. Sapareto SA, Dewey WC (1984) Thermal dose determination in cancer therapy. Int J Radiat Oncol Biol Phys 10:787–800
11. Anneveldt KJ et al (2021) their study; lessons learned during implementation of MRgHIFU treatmen of uterine fibroids. Insights Imaging 12:188
12. Yu L, Zhu S, Zhang H et al (2021) The efficacy and safety of MR-HIFU and US-HIFU in treating uterine fibroids with the volume <300 cm3 a meta-analysis. Int J Hyperthermia 38(1):1126–1132
13. Jeong J-H, Hong GP et al (2016) Clinical consideration of treatment to ablate uterine MRgFUS (Sonalleve). J Menopausal Med 22:94–107
14. Quinn SD, Vedelago J, Gedroyc W, Regan L (2014) Safety and five-year re-intervention following magnetic resonance guided focused ultrasound (MRgFUS) for uterine fibroids. Eur J Obstet Gynecol Reprod Biol 182:247–251

Publisher's Note