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Reproductive impact of MRI-guided focused ultrasound surgery for fibroids: a systematic review of the evidence

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Abstract

Purpose of review—Magnetic-resonance-guided focused ultrasound surgery (MRgFUS) is a minimally invasive technique for the treatment of uterine fibroids. The purpose of this review is to highlight the impact of MRgFUS on fertility and reproductive outcomes.

Recent findings—The role of MRgFUS in the treatment of fibroids has been evolving since its introduction in 2004. Several new devices and techniques including location-specific treatment, volumetric therapy, and vessel-targeted therapy have been introduced over the last few years. Several case series report uncomplicated pregnancy following MRgFUS; however, results of the ongoing studies will further elucidate the utility of MRgFUS in patients planning future fertility. A systematic review of the literature was completed and studies that reported quality of life at baseline and after 6 months were included in a meta-analysis.

Summary—MRgFUS represents a minimally invasive treatment for uterine fibroids that is able to improve the quality of life and fibroid size with durability. It is possible that MRgFUS could be the treatment of choice for patients desiring future fertility; however, further investigation is needed.

Keywords

fertility; fibroids; HIFU; MRgFUS; pregnancy

Conflicts of interest

There are no conflicts of interest.

INTRODUCTION

Uterine fibroids (leiomyoma and myoma) represent the most common benign neoplasm of reproductive age women and increase in incidence with age [1,2]. Although the majority of women are asymptomatic, clinical manifestations of fibroids include menstrual disorders, reproductive dysfunction, and bulk-related symptoms [3[■],4]. The incidence of fibroids in infertile patients is estimated to be 1–2.4%, and the resultant endometrial distortion is associated with impaired implantation and increased mis-carriage [5]. In pregnancy, intramural fibroids are associated with miscarriage [6] and large fibroids can cause fetal malposition and labor dystocia and impair myometrial contractility, potentially leading to hemorrhage, uterine rupture, and cesarean delivery [7,8].

Although medical treatments for fibroids exist, many treatments have unattractive side-effect profiles and are of limited utility for improving reproductive outcomes. Myomectomy, particularly hysteroscopic myomectomy, is the treatment of choice for reproductive age women and can increase the chance of pregnancy and live birth [9]. Myomectomy, however, is not without risk and adverse outcomes including hemorrhage, conversion to hysterectomy, uterine rupture and abnormal placentation have been associated with surgical intervention [7,9]. Recently, new minimally invasive treatments have been introduced, including uterine artery embolization (UAE) and magnetic-resonance-guided focused ultrasound surgery (MRgFUS). UAE, although effective, has limitations for patients desiring future fertility because of increased risks of diminished ovarian reserve, miscarriage, cesarean delivery, and postpartum hemorrhage [6,10]. Here, we describe the mechanics of MRgFUS and optimal patient selection, as well as review the recent literature focusing on the impact of MRgFUS on the quality of life and reproductive outcomes.

MATERIALS AND METHODS

A systematic literature search of the MEDLINE and Cochrane databases was performed using the keywords ‘MRgFUS’, ‘magnetic resonance guided focused ultrasound’, ‘HIFU’, and ‘high frequency focused ultrasound’, cross referenced with the search terms ‘myoma’, ‘fibroid’, ‘pregnancy’, ‘fertility’, and ‘reproductive outcome’ on 1 September 2013 (Fig. 1). These results and their references were analyzed to find those articles excluded from the primary search. Eligible articles were selected including all case reports, case series, reviews and retrospective evaluations, focusing on those published within the last 2 years. This search yielded 1123 articles. Initial screening excluded 1084 articles based on title, abstract, and removal of duplicates. Only studies focusing on the use of MRgFUS for the treatment of uterine fibroids and examining subsequent reproductive outcomes were included in the final review. A total of 39 articles were included in final qualitative analysis, with 10 included in the meta-analysis.

Magnetic-resonance-guided focused ultrasound surgery

MRgFUS is a thermal ablation technique approved by the United States Food and Drug Administration (FDA) in 2004 for the ExAblate 2000. The method uses MRI to direct ultrasonic energy to a focal point within a fibroid, resulting in tissue necrosis with minimal damage to surrounding tissue. This is afforded through quantitative temperature mapping,

allowing for detection of small temperature elevations in surrounding tissues prior to irreversible damage.

The current platforms used in the United States, Canada, Europe, Asia, and Australia for MRgFUS are the ExAblate 2000 (InSightec, Haifa, Israel), ExAblate 2100 (InSightec, Haifa, Israel) and Sonal-leve MR-HIFU (Philips Medical Systems, Vantaa, Finland). An alternative technique that uses ultrasound guidance [ultrasound-guided focused ultrasound surgery (USgFUS)] to direct the energy beam is used in Asia, Mexico, and parts of Europe; however, this is not approved by the United States FDA. The MRgFUS platform is integrated in a table docked within a compatible magnetic resonance (MR) scanner. The patient lies prone upon a gel pad coupled to a water tank that is used to propagate the ultrasound beam. Immediately prior to treatment, T2-weighted MR is used to identify target fibroids and assess proximity to critical structures including the bowel, spine, and neurovascular bundles. The fibroid is then outlined and a sonication plan is developed. After a low-energy test dose, therapeutic sonications are commenced. MR is used to monitor tissue temperature to ensure adequate power delivery and avoid surrounding tissue damage. At treatment completion, repeat contrast MR is used to determine the area of nonperfusion volume (NPV), which is represented as a volume and percentage ablation of the targeted fibroid. The patient is subsequently discharged home.

Patient selection criteria

MRgFUS candidates are screened with MR to determine whether they meet the selection criteria. Factors considered include fibroid imaging characteristics and location, the number and size of myomas, and proximity of critical structures. Patients are typically excluded if they weigh more than 115 kg, have serious health complications, have contraindications to MR such as claustrophobia or implants, have abdominal scarring, uterine size greater than 24 weeks, or have pedunculated, nonenhancing or heavily calcified fibroids [11■,12]. Initial studies excluded patients desiring future fertility; however, this exclusion has come into question after a number of uncomplicated pregnancies after MRgFUS have been reported.

RESULTS

Experience with magnetic-resonance-guided focused ultrasound surgery

Since the approval of MRgFUS, a number of publications have assessed its safety and efficacy. These studies and their results are summarized in Table 1 [13-26,27■,28■,29■] and Fig. 2 [14-17,19-22,24,26,27■,28■,29■,30,31]. The association of increased NPV with diminished fibroid symptoms, as measured by the standardized Symptom Severity Score (SSS) included within the Uterine Fibroid Symptom and Quality of Life (UFS-QOL) scale, has been noted by several authors [20,24,32]. Additionally, increased NPV is associated with a greater decrease in fibroid size and decreased reintervention rate [20,24,32]. Studies that reported mean SSS at baseline and after 6 months were included in a meta-analysis to evaluate the overall mean SSS after 6 months (Fig. 3) [33]. This included 10 studies. A random-effects model was used to estimate the overall mean SSS observed in these studies to account for potential heterogeneity among studies in addition to sampling error. The overall mean improvement in SSS at 6 months following MRgFUS was estimated

to be 31.0 (95% confidence interval 23.9–38.2). Current studies examine location-specific treatment, T2 intensity, and volumetric techniques.

Location-specific treatment

Whereas initial studies examined fibroid treatment by size and ablation volume, two recent studies have examined location-specific treatment. Wang *et al.* [27] prospectively examined the use of USgFUS in 76 women with 78 submucosal fibroids. Women were treated with a mean NPV ratio of 80% and followed for 30 months. Fibroid size was reduced by 46.7, 68.2, 78.9, and 90.1% at 3, 6, 12, and 24 months, respectively (Table 1). Menstrual bleeding diminished at each follow-up point and SSS decreased over this time period (Fig. 3). Interestingly, 58% of women experienced vaginal expulsion of necrotic tissue after USgFUS that resolved within 2–3 menses. Although USgFUS may be a well tolerated and minimally invasive treatment for submucosal fibroids, its advantages over hysteroscopic myomectomy have yet to be demonstrated.

Pedunculated fibroids had previously been an exclusion factor for MRgFUS [11,12]. Park *et al.* [34] retrospectively examined the utility of a stalk-sparing treatment in nine women with a single pedunculated subserosal fibroid. Mean fibroid volume was 197.8 cm³ and mean stalk diameter was 3.5 cm. Fibroids were treated with a mean NPV ratio of 67%. At 6-month follow-up, fibroid volume had decreased by 30% and stalk diameter had decreased by 13%. SSS diminished from 30.0 at baseline to 14.6 at 6 months. Without reported stalk separation or adverse outcomes, it appears MRgFUS can safely treat pedunculated fibroids. Combined, these studies indicate that image-guided focused ultrasound can treat fibroids of different locations with high accuracy and improvement in symptomatology.

T2 intensity

T2-weighted MR is used for pretreatment MRgFUS planning, and fibroids can be categorized as hyperintense or hypointense based upon T2 signal intensity relative to the myometrium and endometrium. Prior studies have demonstrated that NPV, resultant fibroid size, and SSS are reduced in patients with hyperintense fibroids [32,35]. Fibroid hyperintensity correlates with vascularization [36] and is responsive to gonadotrophin-releasing hormone (GnRH) agonist pretreatment, potentially improving MRgFUS success [17]. Two current studies retrospectively examine MRgFUS outcomes based upon T2 imaging.

In a retrospective analysis of 81 patients, Machtinger *et al.* [25] examined the factors associated with long-term MRgFUS efficacy (Table 1). Hypointense fibroids were associated with increased treatment success compared with hyperintense fibroids. Additionally, women with long-term treatment success were significantly older at treatment (46.3 versus 43.6 years). Not surprisingly, younger women (36–40 years) had a higher incidence of hyperintense fibroids (59%) compared with older women. Zhao *et al.* [37] retrospectively examined MRgFUS outcomes in 282 patients based upon T2 intensity. Hyperintense fibroids were subdivided into three categories (heterogeneous, slightly homogeneous, and markedly homogeneous) and NPV ratios were compared. Whereas hypointense fibroids achieved a mean NPV ratio of 86.3%, NPV of hyperintense fibroids

was 67.6% and NPV of slightly homogeneous hyperintense was only 55.8%. It appears that slightly homogeneous hyperintense fibroids respond less well to MRgFUS and may represent the exclusion criteria. These studies reflect the difficulty of treating hyperintense fibroids, particularly fibroids that are slightly homogeneous in appearance; however, a standardized grading criterion and high-quality prospective analysis is needed.

New equipment

Since the introduction of the ExAblate 2000 in 2004, new platforms including the Sonalleve MR-HIFU (Philips Healthcare, Vantaa, Finland) and the ExAblate 2100 (InSightec, Haifa, Israel) have emerged and recent studies examined their safety and efficacy.

A major advance of the Sonalleve system is volumetric MRgFUS, a novel technique that temporally switches focal point position along outward-moving concentric circles in an attempt to improve treatment efficacy and ablation homogeneity. Three current studies examine the efficacy of the Sonalleve system. In a prospective multicenter study of 33 patients with 36 fibroids, Voogt *et al.* [31] assessed the safety and technical feasibility of volumetric MRgFUS. No adverse outcomes occurred, and concordance between predicted treatment volume and NPV was 92%. Kim *et al.* [38] treated 10 women with volumetric MRgFUS in a prospective multicenter study and noted increased energy efficiency, independent of target depth or T2 intensity. To histologically ascertain Sonalleve safety and accuracy, Venkatesan *et al.* [39] examined hysterectomy specimens of 11 patients within 30 days of MRgFUS. MR images were examined alongside hysterectomy specimens to facilitate identification. All fibroids demonstrated treatment in the expected location with a mean ablation volume of 6.92 cm³. Although these studies are limited by small numbers, it appears Sonalleve does provide well tolerated and effective ablation with a high level of accuracy and energy efficiency.

The ExAblate 2100 includes additional safety mechanisms and a transducer that can be elevated closer to the abdominal wall, allowing for reduced energy density, a decreased focal distance, and an increased maximum energy level. Trumm *et al.* [28] retrospectively analyzed 115 consecutive patients treated with ExAblate 2100 at a single center (Table 1; Fig. 2). Mean NPV ratio was 88% and 6.5-month follow-up demonstrated decrease in SSS scores from 62.5 at baseline to 37.5. With a high NPV and no adverse outcomes, it appears the ExA-blade 2100 may provide improved outcomes compared to the ExAblate 2000.

New techniques

In addition to new equipment, new MRgFUS techniques have been introduced. Whereas prior studies have commented on bladder and rectal filling [40] to move critical structures as well as the use of scar patches [21], we focus on the technological advances of the last 2 years.

To improve treatment efficacy and safety, Yoon *et al.* [29] retrospectively examined the use of thermal dose maps (Table 1) created and overlaid on MR. Maps were displayed to the treating physician as thermal dose volumes (TDVs), and comparison between NPV, TDV,

and initial treatment volume was used to judge treatment efficacy. Correlation was found between TDV and NPV with a mean ratio of 1.5, providing physicians with a real-time estimate of treatment efficacy and allowing for adjustments to achieve desired NPV.

In another attempt to improve NPV, Voogt *et al.* [41[■]] used a vessel-targeted technique focusing ablation on fibroid arterial supply in a series of three fibroids treated in two patients. NPV ratios were 84, 68, and 86% in the three fibroids treated, and all patients had improvement in SSS and fibroid volume at 6-month follow-up. Although this is an isolated series of two patients, it represents a novel method providing high relative NPV.

PREGNANCY FOLLOWING MAGNETIC-RESONANCE-GUIDED FOCUSED ULTRASOUND SURGERY

Initial studies of MRgFUS excluded women desiring future fertility; however, now that case reports of 35 pregnancies following MRgFUS exist (Tables 2 and 3; [5,7,8,21,42-45,46[■], 47-49]), multicenter studies have commenced for patients desiring future fertility [45]. The prenatal treatment of fibroids with MRgFUS in each of these patients is described in Table 2, whereas Table 3 describes the individual outcomes of each of these pregnancies. In the largest published case series of pregnancy after MRgFUS, Rabinovici *et al.* [7] described 54 pregnancies in 51 women after MRgFUS. Three previously published case reports were included in this series [5,47,48]. Mean time to conception after MRgFUS was 8 months. Twenty-two patients (41%) carried their pregnancy to term, eleven pregnancies were ongoing at study completion, seven patients electively terminated, and fourteen miscarried. Of the patients who carried to term, 64% delivered vaginally (Table 3).

A subsequent case series followed 24 women with unplanned pregnancy following USgFUS [46[■]]. Seven carried their pregnancies to term and all patients delivered via cesarean section. Of the remaining pregnancies, two miscarried and fifteen were electively terminated. It is noted that the preference for cesarean section in China, the location of this case series, was high related to sociocultural considerations.

Several additional cases of pregnancy following MRgFUS have been reported. In 2007, Gavrilova-Jordan *et al.* [8] described a nulligravida who was treated with MRgFUS and spontaneously conceived. Despite an increase in myoma size during pregnancy, she carried the pregnancy to 39 weeks and was delivered by vacuum-assisted vaginal delivery. Rowe and Nebgen [42] reported a 40-year-old who underwent ablation of two fibroids with a NPV of 86% and subsequently delivered vaginally at 36 weeks. Zaher *et al.* [50] described a 39-year-old with a prior 28-week delivery attributed to fibroids who underwent MRgFUS following GnRH agonist pretreatment, and after an uncomplicated pregnancy underwent a postdates induction of labor. A final pregnancy was reported by Yoon *et al.* [43], in which a 31-year-old nulligravida conceived 4 months after MRgFUS and delivered a 3190 g infant without complications.

Fortunately, a current randomized controlled trial (NCT00730886, clinicaltrials.gov) offers MRgFUS to infertile patients with uterine fibroids. The first report published from this study was a 37-year-old unable to conceive with donor insemination. MR demonstrated a

submucosal and several intramural fibroids. The patient underwent MRgFUS on two successive days and subsequently conceived 3 months after treatment. She progressed to have an uncomplicated pregnancy and vaginally delivered a 3450 g infant at term [45].

A case report from the United Kingdom [44] described the first successful case of in-vitro fertilization (IVF) after MRgFUS. A 45-year-old underwent MRgFUS for a single anterior intramural myoma with a NPV ratio of 90%. She became pregnant in her first cycle of IVF, 10 months after MRgFUS. Her pregnancy was uncomplicated and she delivered a 3050 g infant via cesarean section for fetal distress.

The minimally invasive nature of MRgFUS, allowing for fibroid ablation while avoiding surrounding tissue damage and hysterotomy, suggests MRgFUS could be a well tolerated approach for patients desiring fertility and may not increase obstetric risk [50]. If MRgFUS can decrease myoma size and resolve endometrial architecture, it is possible that subsequent fertility may be improved; however, further studies are needed.

MAGNETIC-RESONANCE-GUIDED FOCUSED ULTRASOUND SURGERY LIMITATIONS

Despite the promises of MRgFUS, limitations remain. Although MRgFUS is a novel, minimally invasive technique, only a fraction of patients meet the inclusion criteria. In a 2010 review of 169 premenopausal women with symptomatic uterine fibroids, Behera *et al.* [12] found only 16% met MRgFUS criteria. The most common preliminary screening exclusions were financial difficulty and desire for future fertility, whereas the most common anatomical contraindications were large fibroid volume and the presence of intracavitary fibroids. In 2013, Fröling *et al.* [11[■]] found when screening premenopausal women with symptomatic uterine fibroids for UAE versus MRgFUS, 99.2% of patients met the UAE inclusion criteria, whereas only 38.0% met the inclusion criteria for MRgFUS. The most common contraindication to MRgFUS was bowel obstructing the sonication site. It is encouraging that in three years, the number of patients meeting the inclusion criteria has doubled (16–38%); however, this is based upon limited data. It is also likely that advances allowing for treatment of fibroids in previously disadvantageous locations [27[■],34] and patients desiring future fertility [45] will continue to amend the exclusion criteria.

When considering MRgFUS for reproductive age women, it is critical to note the average age in previously published studies was approximately 43, an age after which most women complete childbearing and after which most clinics offer IVF. Furthermore, women who have successful MRgFUS are generally older, and younger women have a higher incidence of hyperintense fibroids, which increase treatment difficulty [25]. Although there are single reports of intrauterine insemination [45] or IVF [44] after MRgFUS, data remain limited and the ideal timing of IVF after MRgFUS remains unknown.

Regarding pregnancy, there are only 35 published reports of live birth following MRgFUS and the heterogeneity of these data is great. Although 53% (19 of 35) of pregnancies resulted in vaginal delivery, the power of this case series is too low to detect rare but serious outcomes, such as uterine rupture and placenta accreta. It is reassuring that studies [45] are

underway to further elucidate the use of MRgFUS in patients desiring future fertility; however, the past clinical trials of MRgFUS have encountered low enrollment. Although interest in MRgFUS is generally high, the financial aspects of MRgFUS remain complicated and MRgFUS is rarely covered by insurance in the United States. As many study protocols require randomization along with out-of-pocket payment for MRgFUS, many interested patients cannot afford to participate.

CONCLUSION

MRgFUS represents an evolving technology to treat fibroids in a minimally invasive manner. Current data support the ability of MRgFUS to improve both quality of life and fibroid size (Fig. 2, Fig. 3, and Table 1). These data indicate that by 6 months, most patients have responded to MRgFUS treatment (Fig. 2). There is an average improvement in SSS to half of pretreatment values (Fig. 3). For pregnancy, the average time to diagnosis from MRgFUS was 8.2 months and most pregnancies were carried to term with an average fetal weight of 3273 g. Given the minimally invasive approach, MRgFUS could become the treatment of choice for patients desiring future fertility; however, further investigation is needed.

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KEY POINTS

- MRgFUS is a minimally invasive treatment for uterine fibroids that results in improved quality of life and diminished fibroid size.
- New techniques and platforms for MRgFUS are in development and may provide a greater treatment response.
- Thirty-five reports of pregnancy after MRgFUS have been reported in the literature to date, and ongoing studies will further elucidate the utility of MRgFUS in women desiring future fertility.
- Existing data suggest that pregnancy after MRgFUS is indeed well tolerated, and protocols should be extended to women desiring future fertility.

FIGURE 1.

Schematic diagram of results of literature search. A total of 39 studies were included in the qualitative analysis and 10 studies provided sufficient detail to be included in the quantitative analysis.

FIGURE 2.

Patient-reported Symptom Severity Score (y-axis) at 3, 4, 6, and 12 months (x-axis) after MRgFUS treatment. Mean and median patient-reported Symptom Severity Score from 15 studies on MRgFUS from 2004 to 2013 are depicted. MRgFUS, magnetic-resonance-guided focused ultrasound surgery.

FIGURE 3.

Quantitative analysis of 10 studies that reported mean Symptom Severity Score (SSS) after 6 months. A random-effects model was used to estimate the overall mean SSS observed in these studies to account for potential heterogeneity among studies in addition to sampling error. The overall mean SSS at baseline was 56.3 and after 6 months SSS was estimated to be 31.0 (95% confidence interval 23.9–38.2). Bars above represent calculated 95% confidence intervals assuming normal distribution.

Table 1
Summary of 17 studies reporting follow-up results after treatment of fibroids by magnetic-resonance-guided focused ultrasound surgery

Study and year ^a	n	Age	Volume treated (cm ³)	NPV%	% Shrinkage					Treatment after MRgFUS			% Requiring additional treatment
					1 month	3 months	4 months	6 months	12 months	MRgFUS	Myomectomy	Hysterectomy	UAE
Hesley 2006 [13]	42	46	<150						6	6	2	6	1
^b Hindley 2004 [14]; Stewart 2006 [15]; Taran 2009 [16]	109	45	285	9				14			23 with additional treatment [3 hysterectomy; 1 UAE]		
Smart 2006 [17]	49	41						21	37		3	1	1
Rabinovici 2007 [18]	35	46	216	31	12			15				6	
Fennessy 2007 [19]	96	46	<150	16						23 with additional treatment			
	64	46	<150	26						7 with additional treatment			
Stewart 2007 [20]	359	45	290	19						13 with additional treatment			
Zaher 2010 [21]	25	37	740	64						2 with additional treatment			
Kim 2011 [22]	40	46	337	32		19		26			2	2	5
Gorny 2011 [23]	130	46	350	45							1	7	
Dobrowir 2012 [24]	100	42	185	67		29		38			4	2	1
Machtinger 2012 [25]	80	46	213	41					5		4	13	2
Desai 2012 [26]	50	36	120	88		30							
Wang 2012 [27]	75	38	140	80		46.7		68.2	78.9	4			
Trumm 2013 [28]	115	42	89	88					8				

Study and year ^a	n	Age	Volume treated (cm ³)	NPV%	% Shrinkage					Treatment after MRgFUS				% Requiring additional treatment ^b
					1 month	3 months	4 months	6 months	12 months	MRgFUS	Myomectomy	Hysterectomy	UAE	
Yoon 2013 [29]	60	41	200	40				29	32	6 With additional treatment				11.0
Average		43.1	263.8	46.1	12	46.7	29	28	42.4					14.5

MRgFUS, magnetic-resonance-guided focused ultrasound surgery; NPV, nonperfusion volume; UAE, uterine artery embolization.

^a First author only is listed with year of publication. Reference numbers in brackets.

^b Results presented in three reports on the group of 109 patients are summarized.

Table 2
Characteristics of fibroids treated by magnetic-resonance-guided focused ultrasound surgery in 34 patients prior to pregnancy

Study and year ^b	n	Age	No. of fibroids	Fibroid volume (cm ³)	No. treated	Location	NPV%
Gavrilova-Jordan 2007 [8]	1	38	1	947	1		
Rowe 2008 [42]	2	40	3	452	2		86
Zaher 2010 ^a [21]	3	39	5			I	90
Yoon 2010 [43]	4	31	2	201	2	I	
Zaher 2011 [44]	5	45	1	396	1	I	90
Bouwsma 2011 [45]	6	37	4	144	2	SM, I	68
Qin 2012 ^c [46■■]	7-13			66			84
Rabinovici 2010 [7]	14	42	1	18	1	I	44
	15	37	1	43	1	I	
	16	36	1	65	1	I	6
Rabinovici 2006 ^e [47]	17	37	d	84			39
	18	29	6	230	3	SM, SS	36
	19	37	>6	740	2	I, SS	33
Morita 2007 ^e [48]	20	30	1	215	1	SS	52
Hanstede 2007 ^e [5]	21	42	>6	396	2	SM, I	18
	22	45	1	480	1	I	20
	23	44	1	179	1	SM	95
	24	42	1	377	1	SS	16
	25	40	3	420	2	SS	83
	26	38	1	249	1	I	54
	27	32	2	173	1	I	57
	28	36	>6	340	4	T, I, SM, SS	100
	29	43	2	297	2	SM, I	
	30	37	2				
	31	36	3	65	1	I	
	32	41	1	160	1	T	47
	33	39	1	52	1	I	38
	34	35	2	248	1	T	29
Means		38	2	272.9	1.5		53.86

GnRH, gonadotrophin-releasing hormone; I, intramural; MRgFUS, magnetic-resonance-guided focused ultrasound surgery; NPV, nonperfusion volume; SM, submucosal; SS, subserosal; T, transmural.

^aGnRH agonist pretreatment.

^bFirst author only is listed with year of publication. Reference numbers in brackets.

^cMeans reported.

^d Adenomyosis.

^e Case reports included in Rabinovici *et al.* [7].

Table 3
Outcomes of 35 pregnancies in 34 patients after undergoing prenatal magnetic-resonance-guided focused ultrasound surgery

Study and year ^a	n	Age	GP at MRgFUS	Treated	Time after MRgFUS (months)	Pregnancy complications	Delivery mode	Weeks	Weight (g)	Intrapartum/postpartum complications
Gavrilova-Jordan 2007 [8]	1	38	G0P0	1		GDM, HTN	VAVD	39		3420cm ³ myoma visible during second stage
Rowe 2008 [42]	2	40		2	1	None	NSVD	36	2898	None
Zaher 2010 [21]	3	39	G1P0	5	10	None	NSVD	42	3580	None
Yoon 2010 [43]	4	31	G1P0	2	4	None	NSVD	39	3190	None
Zaher 2011 [44]	5	45	G1P0	1	10	None	LTCS	40	3050	None
Bouwma 2011 [45]	6	37	G1P0	5	3		NSVD	40	3450	Endomyometritis
Qin 2012 [46]	7				3.25	None	LTCS	39	3200	Myomectomy at LTCS
	8				4.5	None	LTCS	39	3500	Nonpalpable fibroid
	9				6	None	LTCS	39	3000	Small fibroid (1.5 cm ³)
	10				6	ITM bleeding	LTCS	39	3200	Myomectomy at LTCS
	11				6	None	LTCS	37	3700	Nonpalpable fibroid
	12				1.25	ITM bleeding	LTCS	38	2500	Nonpalpable fibroid
	13				8	None	LTCS	39	2500	Small fibroid (0.5 cm ³)
Rabinovici 2010 [7]	14	42	G1P1	1	13	ITM bleeding	NSVD		3800	None
	15	37	G2P2	1	18	ITM bleeding	NSVD	40	3830	None
	16	36	G1P1	1	8	Chlamydia	LTCS	38	3480	Breech
Rabinovici 2010 [7] ^b	17	37	G2P1	Adenomyosis	3	Suspected persistent R umbilical vein	NSVD		3050	Manual removal of placenta
	18 ^c	29	G0P0	6	4	Hospitalization at 35 weeks for contractions	LTCS	38	2660	Breech, myomectomy at LTCS, hemorrhage requiring reoperation, DIC, ARDS
	18 ^c	31	G0P0	6	27	ITM bleeding, hospitalization at 28–30 weeks secondary to placenta previa	LTCS	39	2860	Placenta previa, complicated uterine scar, postpartum respiratory difficulty
	19	37	G1P0	>6	6	Vaginal bleeding	LTCS	41	3970	None
Morita 2007 [48] ^b	20	30	G0P0	1	4	None	NSVD	39	3210	None
Hansted 2007 [5] ^b	21	42	G3P3	>6	12	ITM bleeding, new diagnosis	NSVD	39	3170	Lochia

Study and year ^a	n	Age	GP at MRgFUS	Treated	Time after MRgFUS (months)	T2DM				
						Pregnancy complications	Delivery mode	Weeks	Weight (g)	Intrapartum/postpartum complications
	22	45	G0P0	1	8	GDM	VAVD	40	3350	Chorioamnionitis
	23	44	G2P2	1	23	None	LTCs		3430	Planned repeat LTCs, NICU admission for lung collapse
	24	42	G0P0	1	18	GDM, HTN	VAVD	38	3650	None
	25	40	G0P0	3	1	Oligohydramnios, placental insufficiency	NSVD	38	2890	Endometritis
	26	38	G2P1	1	10	None	LTCs	38	2990	Myomectomy at LTCs
	27	32	G0P0	2	5	None	NSVD	39	3190	None
	28	36	G1P0	>6	9	None	NSVD	42	3580	None
	29	43	G1P1	2	11	Myomectomy at 21 weeks	LTCs	36	3410	Placenta previa
	30	37		2	5	None	NSVD		3760	None
	31	36		3	5	None	NSVD		3100	None
	32	41	G4P2	1	1	Myoma growth to 9.6 × 9.3 cm	NSVD		3190	None
	33	39	G1P1	1	18	ITM bleeding, hospitalization at 14–16 weeks because of threatened AB	NSVD			
	34	35	G5P1	2	8	None	LTCs	40	3680	None
Means		37.8			8.2			39	3273	

Fifty-three percent of patients delivered vaginally. 1TM, first trimester; AB, abortion; ARDS, acute respiratory distress syndrome; DICl, disseminated intravascular coagulation; G, gravida; GDM, gestational diabetes mellitus; HTN, hypertension; LTCs, low transverse cesarean section; MRgFUS, magnetic-resonance-guided focused ultrasound surgery; NSVD, normal spontaneous vaginal delivery; P, para; T2DM, type 2 diabetes mellitus; VAVD, vacuum-assisted vaginal delivery.

^aFirst author only is listed with year of publication; reference numbers are in brackets.

^bCase reports included in Rabinovici *et al.* [7].

^cSubsequent pregnancy in same patient.