

MR vezérelt Fokuszált Ultrahang sebészet (MR guided Focused Ultrasound Surgery, MRgFUS)

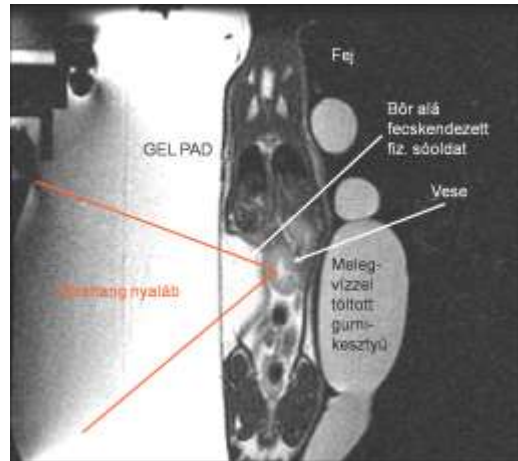
A tanulmányok a Semmelweis Egyetem És- és Szívsebészeti Klinika Radiológia Osztályán történtek a rendelkezésre álló Exablate 2000 klinikai MRgFUS rendszerrel és ezzel együttműködő GE 1.5T Signa MR szkennelrel.

Állatkísérletes adatok

Az MR-vezérelt fókuszált ultrahang vaszkuláris alkalmazási területeinek vizsgálata

Kutatásaink preklinikai részében egy állatkísérletes modell kidolgozása volt a cél az MRgFUS vaszkuláris alkalmazási lehetőségeinek felderítésére. Célunk a vese, mint jól perfundált szerv hőkezelése volt patkányban. A kísérletsorozatban összesen 85 állatot használtunk fel.

1. Első célunk egy olyan előkészítés és pozicionálás kidolgozása volt, amely altatott patkány esetében a vesét megfelelően célozhatóvá teszi, tehát nem esik se csont, se levegő az ultrahang útjába, valamint a céltér fogat és a bőr között elegendő a távolság. Ezeket az ismereteinket túllátott patkányokon szereztük. Sem intraperitonealisan befecskendezett sóoldat, sem a hasüregbe beültetett szilárd gél nem vezetett eredményre. A megoldást a **bőr alá fecskendezett nagy mennyiségű (20-50ml) sóoldat jelentette**, amely a kötőszöveti rostok közé bejutva azzal gélszerű állagot vesz fel, így megfelelő távolságot biztosít a bőr és célszerv között, valamint a közbeeső nem kívánatos szöveteket is félretolja. A módszert élő, altatott állatban is verifikáltuk.



2. A célzásnak egy hardware-es problémája is megoldásra szorult. A fókuszpont célzási pontosságát a koaguláció előtt kalibrálni kell, ugyanis méréseink szerint akár 1,5 cm-rel is eltérhet kalibráció előtt. A kalibrálást legalább 2, de inkább 3 síkban végezzük el. A 3. sík alapján megbizonyosodhatunk arról, hogy a kalibrált fókuszpont a hőtérképeken valóban ott jelenik meg, ahova céloztunk. A célzás kalibrációjához alkalmazott alacsony energiájú ultrahangimpulzus fókuszusa olyan szövetbe kell, hogy kerüljön, ahol a fókuszpont 1,5 cm-es esetleges eltérése esetén nem hagyja el a szövetet. Ilyen szövet a patkányban nem találunk kis mérete miatt, ezért leginkább egy **mellé helyezett kalibráló gélben végezzük el a kalibrációt**, majd ugyanabban a coronalis síkban lévő egy pontját kezeljük a vesének. Az után észlelhető eltérés 3mm-en belül marad méréseink szerint.



0034	0,25	0,758	6,0	48	1,2821	48,1	2,4	0,4	161,4%
0037	0,25	0,758	5,0	53	1,5443	57,0	2,5	0,4	271,4%
0043	0,25	0,781	6,5	51	1,0934	53,4	2,6	0,4	215,3%
0045	0,25	0,735	8,0	73	1,3709	29,8	2,7	0,4	46,1%
0055	0,25	0,735	7,5	76	1,6515	31,2	3,0	0,3	60,1%
0063	0,25	0,696	4,5	48	1,5308	59,9	1,5	0,7	158,5%
0065	0,125	0,344	4,5	75	2,7162	31,8	2,3	0,4	144,5%
0066	0,5	1,445	5,0	75	2,5755	51,1	1,7	0,6	255,5%
0073	0,25	0,576	5,5	64	1,6953	33,0	1,6	0,6	127,9%
0076	0,25	1,004	3,0	62	3,4262	37,8	1,2	0,8	167,3%
0085	0,25	0,912	3,5	75	3,2194	20,0	1,8	0,6	89,3%
Átlag	0,261	0,795	5,4	64	1,9816	41,2	2,1	0,5	132,2%

Kísérleti eredményeink.

Kulcs: Δt : szonikáció ideje (s) – m: az állat tömege (g) – Ren H: vese vastagsága (mm) – \emptyset : laesió átmérője (mm) – AP: hangteljesítmény (W) – SAR: specifikus abszorpciós ráta (W/kg) – ΔT : hőmérsékletnövekedés (K) – $\emptyset 2/\emptyset 1$: a laesiók átmérőinek aránya (önkontroll) – SAR2/SAR1: specifikus abszorpciós ráták aránya – $\Delta T 2/\Delta T 1$: hőmérsékletnövekedés, százalékban kifejezve.

A FUS kezelés mikrobuborékos UH-kontrasztanyaggal való potencírozása kísérletsorozatunkban sikeresnek tekinthető. A csúcshőmérséklet kontrollhoz képest mért 132%-os átlagos növekedése bizonyítja, hogy elvárásainknak megfelelően a mikrobuborékok felületén jelentős a hangenergia-elnyelődés. A vese jól perfundált szervként nagy koncentrációban tartalmazott mikrobuborékokat. A környező szövetek az esetek túlnyomó többségében nem károsodtak, így a szelektivitást is megfelelően értékelhetjük. A kísérleti anyag leközlése folyamatban van, Várallyay Cs, Tamás B, Simonffy L, Hubay M, Lénárd Zs, Paukovits TM, Bérczi V, Balázs Gy, Hüttl K, Jolesz FA: *Microbubble-augmentation of MR guided focused ultrasound surgery: ablative effect enhancement in rat kidney.*

AZ MR KÉPALKOTÁS SZEREPE MR VEZÉRELT FÓKUSZÁLT ULTRAHANGOS MÉHMIÓMA KEZELÉST KÖVETŐEN: KORAI ÉS KÖZÉP TÁVÚ EREDMÉNYEK

Abstract

Az MRgFUS egy kialakulóban lévő hőablációs technika jó- és rosszindulatú daganatok kezelésére. Tanulmányunk célja a méhmióma termoabláció hatékonyságának korai és középtávú kiértékelése volt MR képalkotás utánkötvetéses vizsgálatok alapján. Klinikánkon összesen 43 mióma kezelés történt 2004 és 2007 között. A kezelések az I. sz. Szülészeti és Nőgyógyászati klinikával kooperációban folytak. Klinikai, és ultrahangscreening, valamint az ultrahangos utánkötvetés, és életminőséget kiértékelő kérdőívek kitöltésére is itt történt. 3 és 6 hónapos MRI utánkötvetéses vizsgálatok során értékeltük a kezelt miómák teljes volumenének, valamint a nem perfundált térfogatok változását. Szignifikáns mióma volumen csökkenés volt megfigyelhető 3 és 6 hónappal a kezelést követően ($10\pm 19\%$, $p=0.022$ and $19\pm 29\%$, $p<0.001$) A csökkenés mértéke korrelációt mutatott a kezelést után közvetlenül mért nem perfundált térfogattal. Az 5,4 cm alatti átmérőjű miómáknál nagy hatékonyságúnak bizonyult az MRgFUS eljárás, minthogy ebben az alcsoportban a csökkenés mértéke $35\pm 18\%$ volt. Eredményeink arra engednek következtetni, hogy kisebb miómák esetében hatékonyabb kezelés várható, amely az arányában nagyobb kezelhető térfogattal magyarázható.

A kézirat elküldésre került az Academic Radiology folyóiratba, ahol nem fogadták el publikációra. Az alábbiakban csatolt kéziratot a European Journal of Radiology folyóiratban tervezzük közzélni.

THE ROLE OF MR IMAGING AFTER MR GUIDED FOCUSED ULTRASOUND SURGERY FOR UTERINE LEIOMYOMAS: EARLY AND MID TERM RESULTS

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Short running head: MR guided Focused Ultrasound Surgery

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THE ROLE OF MR IMAGING AFTER MR GUIDED FOCUSED ULTRASOUND SURGERY FOR UTERINE LEIOMYOMAS: EARLY AND MID TERM RESULTS

Abstract

Rationale and Objectives: MR-guided Focused Ultrasound Surgery (MRgFUS) is an evolving thermoablative technique for treatment of different benign and malignant tumors. The aim of the present study was to evaluate early and mid term effectiveness of MRgFUS in uterine leiomyoma (fibroid) treatment based on MR imaging follow-up exams and to determine MR based predictors, which can predict the treatment effectiveness.

Materials and Methods: 38 patients with uterine fibroids were treated in a single center by MRgFUS. MRI follow-up exams were performed 3, 6 months after the procedure. Fibroid total and nonperfused volumes were compared and evaluated over time.

Results: There was a significant fibroid volume reduction at 3- and 6-month follow-up ($10\pm 19\%$, $p=0.022$ and $19\pm 29\%$, $p<0.001$, respectively). The volume decrease correlated with the nonperfused volume (NPV) measured immediately after treatment. Fibroids smaller than 5.4 cm in diameter can be ablated with high efficacy, in this subgroup of patients $35\pm 18\%$ volume reduction was found after 6 months. . There was also correlation found between the early nonperfused volume and the fibroid volume decrease on the 3 and 6 months follow-ups.

Conclusion: In summary, this study suggests that MRgFUS can be an effective alternative in uterine fibroid treatment in selected patients. Patients with small, single uterine fibroids can be treated most effectively with the currently available equipment.

Keywords: Uterine fibroid, MR guided Focused Ultrasound Surgery, FUS

Introduction

Uterine fibroids are the most common, benign tumors in women of childbearing age, often asymptomatic, but can also cause excessive bleeding, pain and discomfort, urinary symptoms, as well as infertility. Symptomatic or rapid growing fibroids are usually treated with open abdominal surgery: hysterectomy or myomectomy of the fibroid. There are alternative, less invasive techniques also available, such as laparoscopic surgery¹ or endovascular uterine artery embolization².

Magnetic Resonance guided Focused Ultrasound Surgery (MRgFUS) is a completely non invasive thermoablative modality, and its potential applications are being extensively studied in various fields of the tumor therapy³⁻⁶. After the initial feasibility of this ablative methods was demonstrated in uterine fibroids, several prospective multi-center trials began^{4,7,8}. The first multicenter study in the treatments of uterine fibroids⁴ investigated 109 symptomatic patients, and found a significant improvement in their uterine fibroid symptoms on follow-up health-related quality-of-life questionnaires, but only a moderate volume decrease (13.5%) after 6 months. The use of Gonadotropin releasing hormone (GnRH) agonists can reduce the tumor size before MRgFUS thus improve the thermoablative effect, was studied in 49 symptomatic patients, in whom 21% of volume reduction was found after 6 months and 37% after one year⁹. Both studies enrolled only symptomatic patients with a symptom severity score more than 40 (in a 0-100 range) based upon questionnaires regarding menstrual bleeding and discomfort in the everyday life.

In our present study MRgFUS treatment was offered to patients as an alternative of surgical myomectomy or hysterectomy. The effectiveness of the treatment was studied as fibroid volume reduction. For this aim early (3 months) and mid-term (6 months) results of volume changes were evaluated using MRI. A secondary aim of this study was to find predictors which could foresee the

treatment effectiveness prior to the procedure, providing better criteria in the future for patient selection.

Materials and Methods

MRI-guided Focused Ultrasound treatment: The technique of MRI-guided Focused Ultrasound has been described in detail before ^{4,7}. In brief: The patients were treated under conscious sedation and analgesia, was induced by diazepam (Seduxen) 10mg i.m., 0.25 mg alprazolam (Frontin, Egis) per os, and during the treatment 75mg diclofenac-natrium (Neodolpasse, Fresenius Kabi) was given as slow iv. infusion. The patients were placed in prone position and the fibroid was positioned directly above a water bath within the MR bed, containing the multiple elements ultrasonic transducer of the focused ultrasound system (Exablate 2000, Haifa, Israel). Acoustic coupling was accomplished by placing a coupling gel pad between the patient and the chamber containing the transducer. The lower abdominal skin was carefully shaved in order to avoid any air bubbles trapped in the hair that could absorb the ultrasonic beam. A urinary catheter was inserted and in some cases bladder filling of saline was used to ensure the suitable position of the fibroid. A set of MR images confirmed the patient's position and was used for planning the treatment parameters: (i) Drawing the treatment area borders on the MR images, (ii) Defining the number of adjacent sonications required for the thermal ablation of the marked target, (iii) Analyzing the energy beam pathway for avoidance of any heat-sensitive organ within it (bowel, nerve) and areas of surgical scarring. Pretreatment verification of accuracy was carried out by a few low-energy, sub-therapeutic sonications followed by the required adjustments of the system parameters. When a mild increase of temperature was seen exactly at the targeted volume using MR images, the actual treatment was started at a full therapeutic power. Each sonication was monitored in real time using MRI thermometry, on the basis of proton resonance frequency (PRF) shift method of temperature mapping ¹⁰. In response to the resulting temperature map and verbal communication with the patient, sonication parameters could be modified including power, length of sonication, spot size and frequency. Moving the focal point according to the treatment plan, one fibroid was treated within a maximum time of 3.5 hours. Following the completion of the last sonication spot, I.V. Gadolinium contrast enhanced scans were

performed and the nonperfused area was assessed in the target fibroid. Following treatment the patient was hospitalized and observed till next morning.

Patients: 38 patients were enrolled in the study and treated with MRgFUS. Eligibility criteria were age over 18 years, premenopausal, with anatomically reachable uterine fibroid, as defined on MR imaging. All patients were referred to surgical removal of the fibroid for various reasons, including bleeding disorders, urinary symptoms, infertility or other subjective symptoms, and could chose MRgFUS as an alternative. Women, who were unsuitable for MRI, such as those with cardiac pacemakers, were ineligible for the study. A clear pathway from the anterior abdominal wall to the fibroid without passing through the bowel was required by the protocol. Patients who had other pelvic or uncontrolled systemic disease were excluded, as were postmenopausal women. All women had negative pregnancy tests both at recruitment and immediately before the treatment. Informed consent was obtained from patients in the study after the nature of the procedure had been fully explained. The study was approved by the local Ethical Committee.

Follow-up: Patients were scheduled to the 3 months, 6 months or both 3 and 6 months follow-up MR scans. The fibroid volumes, the nonperfused volumes (NPV) were measured and compared to the initial scans.

Volume Measurements: Fibroid volumes were measured by two of the authors (C.V. and Z.L) on T2-weighted images immediately before treatment and at the follow-up time points by using three perpendicular length measurements and applying the ellipsoid formula. (product of the three diameter measurements x 0.52)¹¹ Nonperfused volume (NPV) was estimated similarly, using T1 weighted post contrast images before MRgFUS, immediately post-MRgFUS and at the follow-up visits.

Data Analysis: Data are presented as mean \pm standard deviation if otherwise not indicated.

Statistically significant differences between groups were determined by performing one-way (time) and two-way (time and fibroid diameter) repeated measurement of ANOVA and post hoc Tukey test.

Differences were considered to be significant at $P \leq 0.05$. Relationships between variables were determined by simple linear regression analyses. Statistical analysis was performed by the SigmaStat for Windows Version 2.03 (SPSS Inc.) program package.

Results

38 patients, aged 39.2 ± 7 years (range 26-56 years), with MR confirmed uterine fibroids were enrolled in this study (Table 1). The size of the fibroids was 5.4 ± 2 cm in diameter (range 2-10.6 cm) and 118 ± 132 cm³ in volume (range 4.1-618 cm³). 21 patients had single fibroid and 17 patients had multiple fibroids. Most of the treated fibroids were intramural (n=31), while 5 were submucosal and 2 were subserosal.

Because of the long treatment time, in 4 patients treatments were performed in two sessions on separate days to reduce the chance of potential adverse effects and discomfort to the patient caused by the prone and motionless position. With conscious sedation and continuous intravenous analgesia, most of the patients tolerated the procedure well. In two cases the treatment was interrupted because of a skin redness (n=1) and a second-third degree (n=1) skin burn, most likely caused through air bubbles being trapped because of inadequate shaving of the pelvic region. In both cases the skin healed completely and later fibroids were removed surgically. There were no other adverse events potentially related to the MRgFUS procedure.

Nonperfused tissue on gadolinium-enhanced scans, was $24 \pm 27\%$ (range 0-90%) of the total fibroid volume (Table 2). Generally, in smaller fibroids, larger percentages of nonperfused areas were achieved within the recommended maximum of 3.5 hours "in bore" time (Figure 1). Fibroids smaller than 5.4 cm (the mean fibroid diameter of our patient group) showed $34 \pm 30\%$, while fibroids larger than 5.4 cm in diameter demonstrated $17 \pm 18\%$ of necrosis.

3 and 6 months follow-up MR exams were performed 3.5 ± 0.4 months, and 6.4 ± 0.6 months (mean \pm standard error) after FUS procedure respectively. 8 patients participated at 3 months follow-up, six at 6 months follow-up and 16 at both follow-up exams. Four patients left the study and had surgery before the first follow-up visit, contact was lost with two patients and they did not appear on follow-up visits.

The 3 months follow-up showed a $10\pm 19\%$ volume decrease ($p=0.022$), while at 6 months follow-up we found a further 9% volume decrease; totally 6 months after the treatment the fibroid volume was $19\pm 29\%$ smaller than before the treatment ($p<0.001$). Further analyzing our data we found that this volume decrease results from the shrinkage of the smaller fibroids. Fibroids smaller than the mean 5.4 cm in diameter showed a significant volume decrease of $21\pm 16\%$ (0.002) at 3 months follow-up, and $35\pm 18\%$ decrease at 6 months follow-up ($p<0.001$) (Figure 2), whereas the fibroids larger than 5.4 cm showed no significant changes (Figure 3). Statistically significant correlation was found between the extent of the early nonperfused volume and the follow-up results, as Figure 4 describes.

More than half of the patients were considered to be non symptomatic according to the criteria used in previous works⁴. Thus, the study was not intended to evaluate the improvement of the clinical symptoms. Answering a single question at the follow-up visits, 11 patients reported improved, 14 stable and 2 worsening symptoms (see Table 1).

Discussion

In this study the MR findings of the uterine fibroid MRgFUS treatment on follow-up visits were investigated. Our results suggest that MRgFUS treatment causes a significant tumor volume reduction both at 3 and 6 months post-treatment. The volume decrease is slightly larger in our study than in the previously published multicenter study (at 6 mo 19% vs. 13.5%, respectively)⁴ which could be due to different patient enrollment criteria, as in our study patients with less symptoms could also be enrolled. Being a relatively new technique, there are still no long term outcome data available. It seems that subtle treatment effects can rather manifest in symptom reduction, than tumor shrinkage. There might be a higher pressure in the tumor contributing to the symptoms, and a slight volume decrease could cause a considerable intratumoral pressure decrease, and subsequent clinical improvement. With an average of less than 30% nonperfused tissue there is a concern whether the remaining tumor tissue can keep growing and the symptoms come back after years. While this remains to be proven, it seems prudent to reach the highest possible percentage of the thermally coagulated area.

One of the most limiting factors is the procedure length, specifically the total “in bore” time, which should not exceed 3.5 hours to reduce the potential adverse effects caused by the motionless position. In smaller tumors even shorter time could be sufficient to achieve a large percentage of nonperfused volume. Another limitation is the safety margin, which should be kept at the serosal and endometrial borders. Although in our study we tried not to treat close to the endometrium and serosa, in some cases the nonperfused area extended to almost the whole tumor volume, beyond the original treatment plan. This finding was reported earlier, as a result of heat accumulation in the tissue and/or small vessel damage within the fibroid¹². Based on Multicenter Phase I, II and III trials, MRgFUS is considered to be a safe procedure¹³, pregnancy and delivery after treatment was reported without adverse events¹⁴.

There are also intrinsic limiting factors, such as the amount of fat tissue in the lower abdominal wall, which can distort the ultrasound beams, or anatomic location of the fibroid limiting the access of the fibroid, or the ultrasound beam can heat the pelvic bone, causing pain, which can result in early termination of the treatment and end up with low percentage of nonperfused volume. Also the histology of the fibroid can differ; Table 1 suggests that fibroids with high signal intensity and inhomogeneous appearance on T2 weighted images were treated with the less success. Higher cellularity/vascularity was found in fibroids with hyper intense T2 signal ^{11,15}. High cellularity increases the water content of the tissue, which lessens the ultrasound absorption, higher vascularity could be in charge of decreased heat accumulation through vascular cooling effect ¹⁶.

Consistent with previous works, our results showed that having the limitations of the new modality, patient selection is one of the most crucial factors which determine the clinical success of MRgFUS on uterine fibroids. There is a correlation between the early nonperfused volume and the later decrease of the fibroid, emphasizing the importance of treating as large volume as possible. Better results can be achieved in small, solitary fibroids.

This study was intended to report the imaging results of the MRgFUS uterine fibroid treatments performed in a single center, and to help understanding the advances and limitations of this new non-invasive method. We believe that further technical development will expand the indications of MR-guided Focused Ultrasound Surgery, and besides uterine fibroids, in the future this treatment modality will be a valuable tool in various fields of the medicine.

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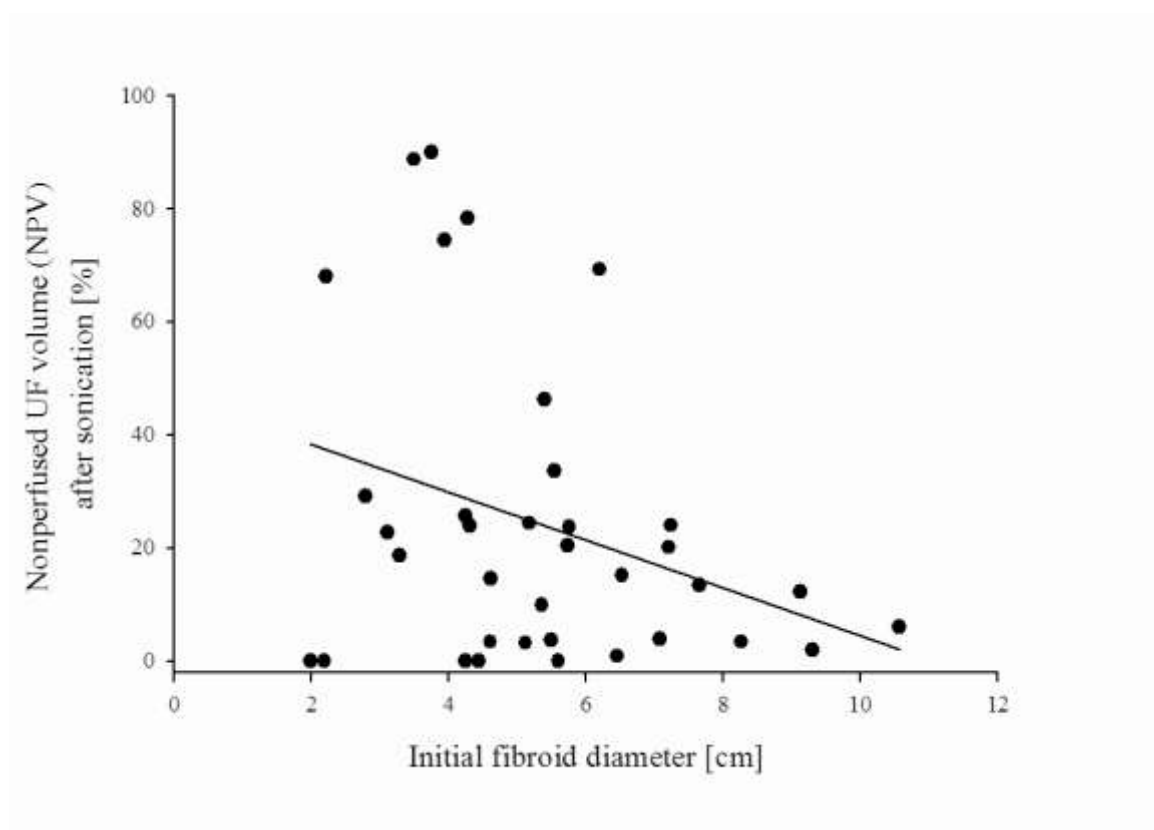


Figure 1. Relationships between the initial fibroid mean diameter and the nonperfused volume (NPV) of the uterine fibroid (UF) determined after the sonication. NPV is expressed as the percentage of the total fibroid volume determined before the sonication. Best results were achieved in fibroids between 2 and 6 cm in diameter.

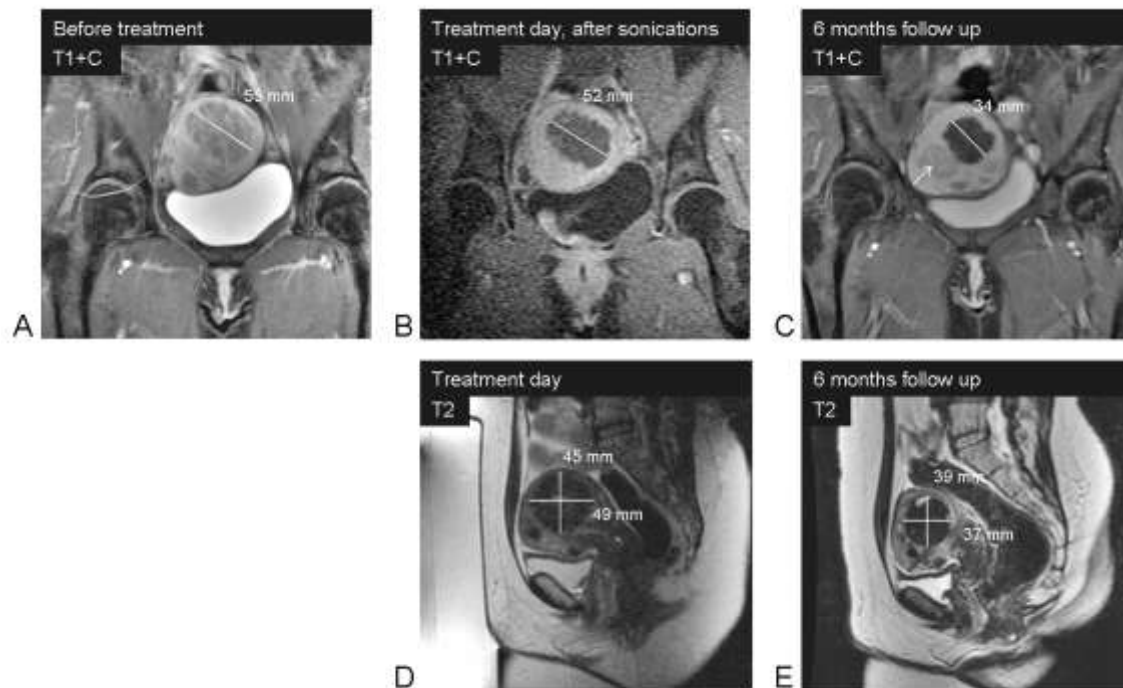


Figure 2. MR images of a 44 year-old female with a small uterine fibroid.

Contrast enhancement before treatment (panel A). After sonications the nonperfused volume represents the necrotized tissue (panel B), which decreases over time, as panel C describes. Since high percentage of the fibroid volume was treated, the overall volume of the tumor shrank after 6 months (panel E) compared to the initial scan (panel D). On panel C, the arrow is pointing at a non treated fibroid, which has grown beside the treated one.

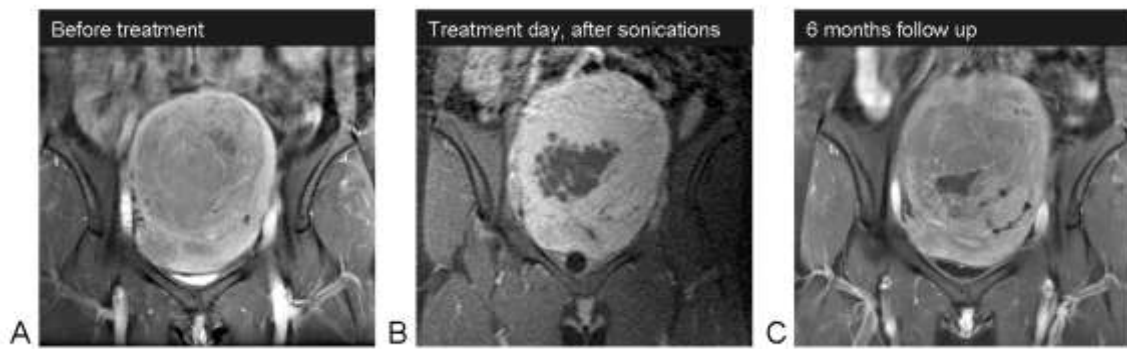


Figure 3. T1 weighted contrast enhanced coronal plane MR images of a 34 year-old female patient with large uterine fibroid; before FUS treatment (panel A), large nonperfused area indicates the non necrotized tissue after sonications (panel B). Although the non enhancing area decreased, the large amount of viable tissue causes an overall growth in the tumor volume, as the 6 months follow-up scan shows (panel C).

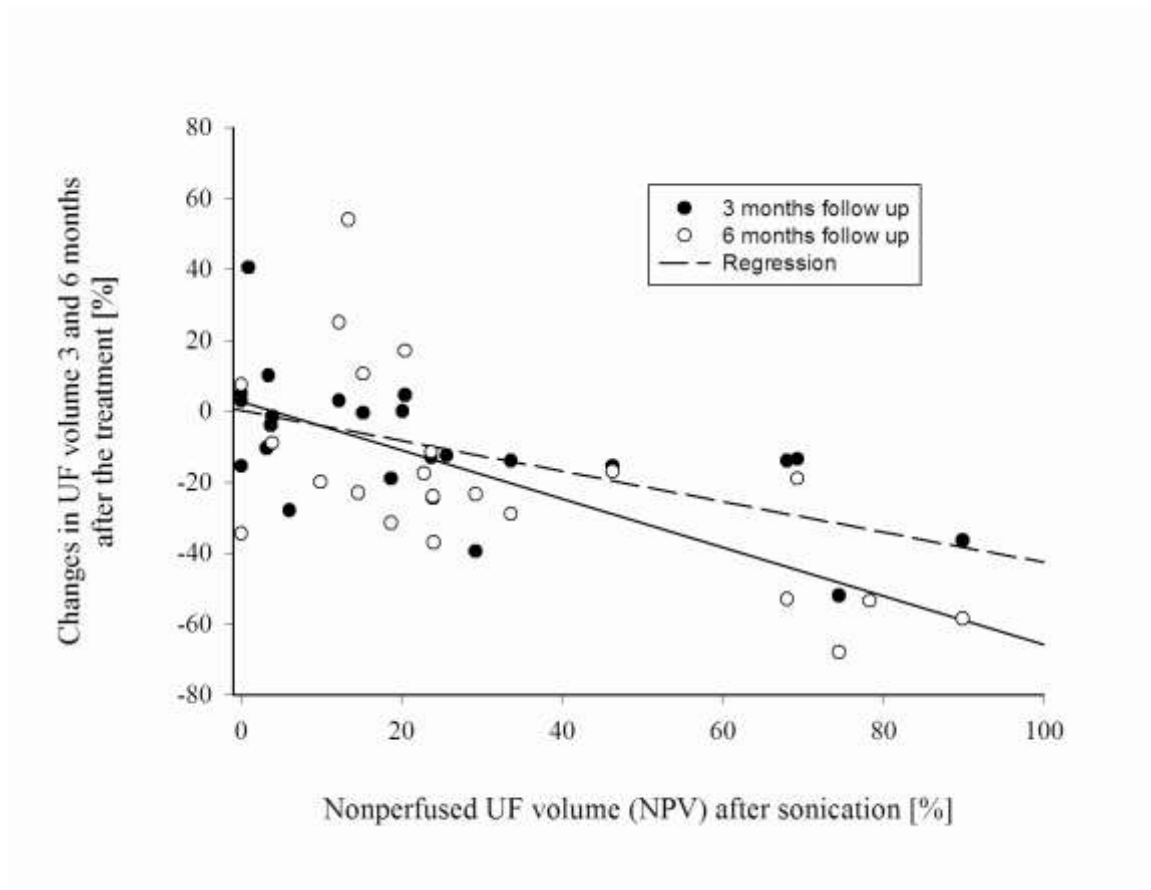


Figure 4. Linear relationships between the nonperfused volume (NPV) of the uterine fibroid (UF) determined after the sonication and fibroid volumes 3 and 6 months after the MRg-FUS treatment (TV_3 and TV_6 , respectively). NPV, TV_3 and TV_6 are expressed as the percentage of the total fibroid volume determined before the sonication.

$$TV_3 = 100.2 - (0.43 * NPV) \quad p=0.002 \quad r=0.603 \text{ (dashed line)}$$

$$TV_6 = 102.645 - (0.69 * NPV) \quad p<0.001 \quad r=0.643 \text{ (solid line)}$$

Pt#	Age (yrs)	UF MR appearance on T2-w images	Average UF diameter before Tx (cm)	UF volume before Tx (cm ³)	NPV (%)	NPV (cm ³)	ΔV_3 (%)	ΔV_6 (%)	ΔS
UF patients without follow-up exams									
1	34	dark/bright, inhomogenous	4.3	40	0	0	had myomectomy		
2	27	bright, homogenous	9.3	422	2	8.4	had myomectomy		
3	40	dark, homogenous	4.4	46	0	0	had myomectomy		
4	39	dark/bright, inhomogeneous	4.6	51	3	1.5	had myomectomy		
5	30	bright, homogenous	7.9	253	0	0	skinburn - Tx stopped		
6	43	dark, homogenous	5	65	0	0	skin redness -Tx stopped		
7	28	dark, homogenous	5.2	72	24	17.3	lost contact		
8	42	dark, homogenous	3.5	22	89	19.6	lost contact		
UF patients with follow-up at 3 months									
9	26	dark, inhomogenous	2.2	5.5	0	0	5	-	0
10	36	bright homogenous	8.3	295	3	8.9	10	-	+
11	38	dark, adenomyosis	5.5	87	4	3.5	-4	-	0
12	42	bright, inhomogenous	6.5	141	1	1.4	41	-	+
13	38	bright, inhomogenous	7.2	196	20	39.2	0	-	+
14	44	bright, adenomyosis	5.1	70	3	2.1	-11	-	+
15	40	dark, homogenous	4.2	40	26	10.4	-13	-	+
16	41	dark, inhomogenous	10.6	618	6	37.1	-28	-	0
UF patients with follow-up at 6 months									
17	48	dark, homogenous	5.4	80	10	8.0	-	-20	0
18	51	dark, inhomogenous	7.6	234	13	30.4	-	54	0
19	44	dark, homogenous	4.3	41	78	32.0	-	-54	++
20	43	dark, homogenous	3.1	15.8	23	3.6	-	-18	+
21	38	dark, homogenous	4.6	52	15	7.8	-	-23	0
22	49	bright, inhomogenous	7.2	199	24	47.8	-	-37	n/a
UF patients with follow-up at 3 and 6 months									
23	42	dark, inhomogeneous	5.6	92	0	0	3	8	-
24	40	dark, homogenous	2.2	6	68	4.1	-14	-53	0
25	56	dark, homogenous	3.3	18.6	19	3.5	-19	-32	0
26	33	dark, inhomogeneous	5.7	98	20	19.6	5	17	-
27	46	dark, inhomogeneous	5.4	82	46	37.7	-16	-17	0
28	34	middle bright, inhom,	9.1	398	12	47.8	3	25	n/a
29	33	dark, inhomogeneous	7.1	186	4	7.4	-2	-9	n/a
30	40	dark, inhomogeneous	4.3	42	24	10.1	-25	-24	0
31	26	bright, inhomogeneous	6.5	146	15	21.9	-1	11	0
32	37	dark, homogenous	2.8	11.3	29	3.3	-40	-24	+
33	36	dark, homogenous	2	4.1	0	0	-16	-35	+
34	32	dark, homogenous	3.9	32	74	23.7	-52	-68	0
35	48	bright, homogenous	5.8	100	24	24.0	-13	-12	+
36	46	dark, homogenous	3.7	28	90	25.2	-37	-59	++
37	44	dark, inhomogeneous	5.5	89	34	30.3	-14	-29	0
38	37	dark, homogenous	6.2	125	69	86.3	-14	-19	0

Table 1. Summary of our MRg-FUS treated uterine fibroid patients and characteristics of the fibroids at treatment and at 3 and 6 month follow-up exams. UF – uterine fibroid; NPV – nonperfused volume of the fibroid expressed as a volume (cm³) and also as a percentage of

the total volume; ΔV_3 and ΔV_6 —changes of the fibroid volume 3 and 6 months after the treatment respectively, expressed as a percentile change of the total volume; ΔS indicates the subjective changes in symptoms based on a single question at the follow-up visits. “-“: worse, “0”: no change, “+” better “++” much better, “n/a”: not available