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FULL PAPER

Feasibility study on energy prediction of microwave ablation upon uterine adenomyosis and leiomyomas by MRI

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Objective: To evaluate the feasibility of energy prediction of percutaneous microwave ablation (PMWA) upon uterine leiomyomas and adenomyosis by MRI.

Methods: 63 patients (49 patients with 49 uterine leiomyomas and 14 patients with adenomyosis) who underwent ultrasound-guided PMWA treatment were studied during the period from June 2011 to December 2012. Before PMWA, contrast-enhanced MRI (ceMRI) was performed for all of the patients. Based on the signal intensity (SI) of T_2 weighted MRI, uterine leiomyomas were classified as hypointense, isointense and hyperintense. During ablation, the output energy of the microwave was set at 50 W, and T11a microwave antennas were

used. ceMRI was performed within 7 days after PMWA treatment. Non-perfused volume and energy required per unit volume were analysed statistically.

Results: When unit volume of lesions was ablated, uterine adenomyosis needed more energy than did uterine leiomyomas, and hyperintense uterine leiomyomas needed more energy than did hypointense pattern.

Conclusions: MRI SI of uterine leiomyomas and uterine adenomyosis can be used to predict PMWA energy.

Advances in knowledge: The conclusions indicate that MRI SI can be used to perform pre-treatment planning, which will make the treatment more precise.

Uterine leiomyomas and adenomyosis are benign lesions that occur most commonly in females of childbearing age. Although many females with uterine leiomyomas and adenomyosis are asymptomatic, as many as 20–65% of them have symptoms^{1,2} such as abnormal uterine bleeding, dysmenorrhoea, pelvic pressure, low abdominal pain and infertility. These symptoms often lead to reduced quality of life, as well as loss of work and increased medical costs.³ Hysterectomy has been the main mode of therapy for leiomyomas and adenomyosis. However, medical technology advancements have made less invasive treatment options available, such as uterine artery embolization (UAE),^{4–6} high-intensity focused ultrasound (HIFU),^{7–9} radiofrequency (RF)¹⁰ and percutaneous microwave ablation (PMWA).^{11,12} PMWA is a minimally invasive technique for the treatment of uterine leiomyomas and adenomyosis by inducing tissue necrosis through heat. Previous reports^{11,12} have indicated that PMWA provides a feasible, safe and reliable alternative for the treatment of uterine leiomyomas and adenomyosis. However, until now, the energy required per unit volume (EPV) of PMWA in uterine lesions has been unclear, which has limited the widespread use of PMWA therapy. In this study, we sought

to investigate the relationship between the MRI signal intensity (SI) of uterine lesions and the EPV of PMWA to better predict PMWA energy before treatment and to make the PMWA procedures standardized.

METHODS AND MATERIALS

Patients

The study was approved by the institutional ethics committee (Chinese PLA General Hospital, Beijing, China). Informed consent was obtained from all patients. From June 2011 to December 2012, 63 patients (49 patients with 49 uterine leiomyomas and 14 patients with adenomyosis) who underwent PMWA treatment at the PLA General Hospital were examined. Patients were 30–48 years of age (average age, 41.3 ± 3.9 years).

The inclusion criteria were as follows: patients with uterine leiomyomas and adenomyosis who had been diagnosed by ultrasonography and contrast-enhanced MRI (ceMRI) in our hospital; patients who had experienced one of the following symptoms for more than 1 year: menorrhagia or metrorrhagia, dysmenorrhoea, lower abdominal pain, bulk pressure or urinary frequency; patients who were above 18

years of age, but in pre-menopausal status; patients with no reproductive needs; in leiomyoma lesions, the average diameter of the intramural or subserous myoma of the uterus ≥ 5 cm and of the submucous myoma ≥ 3 cm, and in adenomyosis lesions, the width of the junctional zone of the uterus ≥ 5 mm and the thickness of the lesion ≥ 3 cm; patients who underwent ceMRI before and after microwave (MW) ablation within 7 days; and patients who had never received other treatments, such as myomectomy, HIFU, UAE, cryoablation, RF or ethanol injection, before PMWA.

Exclusion criteria were as follows: menstruating, pregnant or breastfeeding females; and patients with pelvic infection, coagulation disorders, heart or brain disease or malignant tumours.

Instruments

A MW tumour coagulator, KV2000-MW tumour coagulator (Kangyou Medical Instruments, Nanjing, China), was used with a frequency of 2450 MHz and was capable of continuous and pulse MW emission modes. The needle antenna was 15 gauge in diameter and 18 cm in length. The distance from the aperture of the MW emission to the needle tip was 11 mm, and the emission aperture was 1 mm. For the antenna, an internal water cycle cooling system was used to lower the temperature of the needle shaft.¹³

MRI was performed with a 1.5-T clinical MR system (TwinSpeed Signa EXCITE HD; GE Healthcare, Milwaukee, WI) by using torso phased-array coils. The routine MRI protocol consisted of a series of T_2 weighted fast spin echo sequence [repetition time (TR)/echo time (TE), 4000/102 ms; slice thickness (ST) = 5.0 mm; field of view (FOV) = 34×34 cm]; axial T_1 weighted spin echo images (TR/TE, 200/23 ms; ST = 5.0 mm; FOV = 38×38 cm); and sagittal, axial and coronal T_1 weighted spin echo sequences after administering contrast material. In all patients, 0.2 mmol kg^{-1} gadobutrol (Gadovist®; Bayer Schering Pharma, Berlin, Germany) was administered intravenously.

Contrast-enhanced (CE) ultrasonography was performed with 2.0 ml of SonoVue® (Bracco, Milan, Italy) to evaluate the perfusion of the fibroid. The microbubble contrast agent was mixed with 5 ml of normal saline, and, after vibration blending, 2.0 ml (5 mg ml^{-1}) was used for a quick bolus infusion into the median cubital vein followed immediately by a flush with 5 ml of normal saline.

Percutaneous microwave ablation procedures

The ablation was performed under intravenous conscious sedation (intravenous infusion of 2 mg kg^{-1} of flurbiprofen ester, supplemented by pumping 4 mg kg^{-1} of propofol per hour). The patients were placed in a supine position. Under ultrasound guidance, the MW antenna was inserted into the lesions. The output energy of the MW was set at 50 W. A single antenna was used for leiomyomas with mean diameters < 5 cm; double antennas were used with mean diameters > 5 cm, which were inserted at a distance of 1 cm in leiomyomas.¹¹ Generally, two antennas were used for adenomyosis when the lesions were > 5 cm thick. For large lesions with mean diameters > 5 cm, the ablation was first performed using two antennas with 50 W for

300 s, and the antennas was then withdrawn along the long axis or re-inserted into the unablated zone for another ablation session. During the ablation, variations in the echo from the lesions were monitored by real-time ultrasonography.¹¹ The MW therapy was stopped when the hyperecho (caused by microbubbles generated during MW emission and representing roughly the ablation zone) covered the entire lesion. Finally, CE ultrasonography was performed to evaluate ablation effects. The number of needle insertions and the time of every insertion ablation were recorded.

Methods

Uterine leiomyomas were classified into three types on pre-treatment T_2 weighted MRI: (1) hypointense, when the SI is the same as that of the skeletal muscle; (2) isointense, when the SI is lower than that of the myometrium but higher than that of the skeletal muscle; and (3) hyperintense, when the SI is the same as or higher than that of the myometrium. The images were reviewed by two radiologists. When they had different interpretations, a third radiologist became involved, and the image result was decided by vote. Finally, 28 hypointense leiomyomas, 13 isointense leiomyomas and 8 hyperintense leiomyomas were confirmed.

The volume of the lesions before PMWA on T_2 weighted images and the volume after PMWA on ceMRI were calculated according to the following formulae: $4/3\pi (d/2)^3$, where $d = (\text{length} + \text{width} + \text{height})/3$. The length was measured parallel to the endometrium on the sagittal MRI sequences, the height was measured perpendicularly to the length on the same MRI sequence and the width was measured parallel to the endometrium on the axial MRI sequences.

$$\begin{aligned} \text{The total energy of PMWA} &= \text{power of PMWA} \\ &\quad \times \text{total time of PMWA} \end{aligned}$$

$$\text{EPV} = \text{the total energy of PMWA/PMWA volume}$$

Statistical analysis

Statistical analysis was performed using SPSS® v. 13.0 (SPSS Inc., Chicago, IL). The comparison of ordinal classification information was completed with Kruskal–Wallis H -test; the comparison of multiple means with analysis of variance, after the equal check of variance, and the two-two comparisons among the means were carried out using the least significant difference (LSD) method; a standard t -test was used for the comparison of the two quantitative data sets, of which, the rank-sum test was performed if the normal distribution was not obeyed.

RESULTS

Balance test

The balance test was performed to rule out the influence of the number of needle insertions in a single lesion and the PMWA time of every insertion. No significant difference was found, neither between the leiomyoma and adenomyosis groups (Table 1) nor among the three patterns of the leiomyoma groups (Table 2). There was good comparability among these groups.

The EPV was compared between the leiomyoma and adenomyosis groups. There was a significant difference between the

Table 1. The result of the balance test between the leiomyoma and adenomyosis groups

Lesions	Number of lesions	Number of needle insertions in single lesions			Microwave ablation time of every insertion (s)		
		1	2–3	>3	<300	300–600	>600
Adenomyosis	14	1	10	3	1	30	7
Leiomyomas	49	11	33	5	9	77	10
Sum	63	12	43	8	10	107	17
<i>H</i>		2.41			2.93		
<i>p</i> -value		0.12			0.09		

two groups (Table 3, Figures 1 and 2). When unit volumes of lesions were ablated, the uterine adenomyosis needed more energy than did the uterine leiomyomas.

The EPVs were compared among the three patterns of uterine leiomyoma groups using analysis of variance. A significant difference was found among groups ($F = 3.296$; $p = 0.046$). The two-two comparisons were carried out using the LSD method, and a significant difference was found between the hypointensity and hyperintensity groups ($p = 0.015$) (Table 4, Figures 2 and 3). When unit volumes of lesions were ablated, hyperintense uterine leiomyomas needed more energy than those of the hypointense pattern.

DISCUSSION

Uterine leiomyomas and adenomyosis are the most common pathological changes that occur in the uterus. In recent years, increasing attention has been paid to the study of minimally invasive or non-invasive therapies. As one of the minimally invasive therapies, PMWA is an easy and fast procedure with the advantage of security, effectiveness and reliability.¹¹ In the course of PMWA, the number of antennas and their placement depend on the ablation zones obtained from *ex vivo* porcine musculature models. So far, there is no quantitative clinical study about ablation zones of PMWA of uterine leiomyomas or adenomyosis. In the present study, the relationship between EPV and MRI was studied to evaluate the feasibility of prediction energy of PMWA on

uterine leiomyomas and adenomyosis by MRI and lay the groundwork for clinical study of ablation zones of different MRI SIs.

In our study, the ablation for large lesions with mean diameters >5 cm was first performed using two antennas with 50 W for 300 s. Based on the experience from our previous study,¹⁴ after MWA with 50 W for 300 s by one or two antennas, the coagulation zones in porcine musculature *in vivo* can be induced covering $4.30 \times 3.00 \times 2.80$ cm or 19.98 cm³, $4.41 \times 4.19 \times 3.89$ cm or 37.78 cm³ (two antennas, 300 s). On ablation with two antennas, there would be small regions that receive significant energy deposition from more than one antenna. A third antenna insertion was always used as supplementary ablation and the ablation was stopped when the hyperecho joined with what was made by the two antennas before, so regions that receive significant energy deposition from a third antenna are very small or none. This will make the EPV a little high with two or more antennas compared with one antenna. In our study, balance tests of the number of antenna insertions and the PMWA time of every insertion were performed among groups; no significant difference was found; the distribution of antenna numbers and the PMWA time among groups were balanced; and the result was reliable.

Compared with leiomyomas, adenomyosis ablation required more energy when ablating unit volume of lesions. Leiomyomas¹⁵ and adenomyosis^{16,17} are different types of

Table 2. The result of the balance test among three patterns of uterine leiomyoma groups

Signal intensity patterns	Number of lesions	Number of needle insertions			Microwave ablation time of every insertion (s)		
		1	2–3	>3	<300	300–600	>600
Hypointense leiomyomas	28	6	19	3	7	41	8
Isointense leiomyomas	13	5	6	2	3	20	3
Hyperintense leiomyomas	8	1	5	2	2	16	2
Sum	49	12	30	7	12	77	13
<i>H</i>		1.68			0.034		
<i>p</i> -value		0.43			0.980		

Table 3. The comparison of energy required per unit volume (EPV) (J cm^{-3}) between leiomyoma and adenomyosis groups

Lesions	Number	EPV (median)	P25–P75
Adenomyosis	14	1026.47 ^a	637.26–1404.64
Leiomyomas	49	680.39 ^a	533.52–881.77

P25, 25th percentile; P75, 75th percentile.

^aWilcoxon $W = 1409.50$; $Z = -2.620$; $p = 0.009$.

diseases; they have different tissue structure, which will affect the penetration depth of MW and heat conduction. The mechanisms causing the different EPV results between the two diseases are still unclear. One potential mechanism may be the presence of a pseudocapsule; leiomyomas have a pseudocapsule, whereas adenomyosis does not. Further study is required to understand the role of pseudocapsule in the PMWA process.

MRI is based on proton shift, and the SI depends on the proton density in a tissue, resulting in characteristic tissue T_1 and T_2 relaxation times. Specific sequence imaging can provide some information about tissue directly^{18,19} and can reveal the pathological character of lesions to a certain extent.²⁰ Hyperintense leiomyomas have been categorized as either cellular leiomyomas or degenerated leiomyomas. The cellular leiomyoma is predominantly composed of densely packed cellular fascicles of smooth muscle with little intervening collagen; this leiomyoma has more tissue fluid content, resulting in homogeneous hyperintense SI on T_2 weighted images, and most of

the contrast-enhanced MR images show remarkable and homogeneous contrast enhancement.^{18,19} For the degenerated leiomyomas composed of ordinary leiomyoma cells with extensive degenerative changes (hyaline degeneration, myxomatous degeneration, haemorrhage, cystic change, fatty change etc.), the T_2 weighted images show heterogeneous hyperintense SI, and the ceMRI shows irregular, peripheral or minimal enhancement.¹⁸ Hypointense leiomyomas were predominantly composed of typical whorls of smooth muscle cells and had less tissue fluid content, producing hypointense SIs on T_2 weighted images and irregular, peripheral, minimal or homogeneous enhancement on ceMRI.¹⁹ T_2 weighted images can reveal the tissue structure to a certain extent, which can be used to decide the MW ablation energy. So, T_2 weighted images were used to evaluate EPV in the study.

The results from this study indicate that the hyperintense group needs more energy than does the hypointense group when ablating unit volume of uterine leiomyomas. A significant difference in EPV was found between the hypointense

Figure 1. MR images of adenomyosis before and after percutaneous microwave ablation (PMWA) in a 41-year-old female with a lesion located in the posterior uterine wall. (a) T_2 weighted sagittal MR image of adenomyosis before PMWA (arrow). (b) Contrast-enhanced MRI (ceMRI) of the same lesion before PMWA showing homogeneous contrast enhancement (arrow). (c) ceMRI of the same lesion after PMWA; the length and height of the non-perfusion area were measured on sagittal ceMRI. (d) ceMRI of the same lesion after PMWA; the width of the non-perfusion area was measured on axial ceMRI.

Figure 2. MR images of hypointense leiomyomas before and after percutaneous microwave ablation (PMWA) in a 32-year-old female, measuring $5.5 \times 5.2 \times 4.9$ cm and $5.4 \times 5.0 \times 4.6$ cm, respectively. (a) T_2 weighted sagittal MR image of a patient before PMWA shows two hypointense leiomyomas (arrows). (b) Two hypointense leiomyomas show minor enhancement on contrast-enhanced MRI (ceMRI) before PMWA (arrows). (c) ceMRI of the same patient after PMWA; the length and height of the non-perfusion area of a leiomyoma were measured on sagittal ceMRI. (d) ceMRI of the same patient after PMWA; the width of the non-perfusion area of a leiomyoma was measured on axial ceMRI.

and hyperintense leiomyoma groups ($p < 0.05$). This difference can be explained by the fact that the blood supply of leiomyomas can be represented by SI. In general, hyperintense SI on T_2 weighted MR images represents vascularization and fluid-rich tissues, and hypointense SI reflects low vascularity and low cellularity.^{19,20} Moreover, hyperintense leiomyomas enhanced prominently in the early dynamic phase of ceMRI, which indicated arterial blood supply.²¹ As high perfusion decreases heat accumulation through the

vascular cooling effect on hyperintense uterine leiomyomas, it is difficult to obtain adequate temperature elevation.^{22,23} Consequently, the EPV of hyperintense SI uterine leiomyomas was higher than that of hypointense SI uterine leiomyomas.

The study showed that uterine adenomyosis and hyperintense uterine leiomyomas needed more energy when ablating unit volume of lesions. It revealed the relationship between SI on MRI and the EPV of PMWA. So, MRI SI of uterine

Table 4. The comparison of energy required per unit volume (EPV) among three patterns of uterine leiomyoma groups

Signal intensity patterns	Number of lesions	Percutaneous microwave ablation volume (cm^3)	Total energy of microwave ablation (J)	EPV (J cm^{-3}) ^a
Hypointense leiomyomas	28	68.99 ± 11.05	$42,402.50 \pm 5623.37$	681.45 ± 224.90 ^b
Isointense leiomyomas	13	57.88 ± 12.30	$39,700.98 \pm 8526.33$	700.62 ± 255.92
Hyperintense leiomyomas	8	78.76 ± 20.18	$70,876.98 \pm 13,789.26$	957.61 ± 266.39 ^b

^aAnalysis of variance, $F = 3.879$; $p = 0.028$.

^bTwo-two comparisons, $p = 0.009$.

Figure 3. MR images of hyperintense leiomyomas before and after percutaneous microwave ablation (PMWA) in a 36-year-old female, measuring $6.4 \times 5.9 \times 6.4$ cm, and the method of measurement for non-perfusion area after PMWA. (a) T_2 weighted sagittal MR image of hyperintense leiomyomas before PMWA (arrow). (b) Contrast-enhanced MRI (ceMRI) of the same leiomyoma before PMWA shows homogeneous contrast enhancement (arrow). (c) ceMRI of the same leiomyoma after PMWA; the length and height of the non-perfusion area were measured on sagittal ceMRI. (d) ceMRI of the same leiomyoma after PMWA; the width of the non-perfusion area was measured on axial ceMRI.

leiomyomas and uterine adenomyosis can be used to predict PMWA energy.

Our study is limited because it is a retrospective study and mainly focused on the feasibility of energy prediction by MRI. The EPV values in the study cannot be used to predict PMWA

energy, and a study of precise quantitative PMWA energy is necessary in the future.

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