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# Uterine Peristalsis Before and After Ultrasound-Guided High-Intensity Focused Ultrasound (USgHIFU) Treatment for Symptomatic Uterine Fibroids

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Data Collection B  
Statistical Analysis C  
Data Interpretation D  
Manuscript Preparation E  
Literature Search F  
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**Background:** This study investigated uterine peristalsis before and after ultrasound-guided high-intensity focused ultrasound (USgHIFU) treatment for symptomatic uterine fibroids by cine magnetic resonance imaging (cine MRI).

**Material/Methods:** A total of 30 patients with symptomatic uterine fibroids were treated by USgHIFU, who were subjected to cine MRI before and after USgHIFU treatment in the periovulatory phase. The images were analyzed for the existence, direction, and frequency of uterine peristalsis. The effects of uterine volume, the largest fibroid volume and location, and the fibroid number were examined before and after USgHIFU treatment.

**Results:** The incidence of uterine peristalsis was significantly increased after USgHIFU treatment. The main direction of uterine peristalsis before and after USgHIFU was cervix-to-fundus. In 12 cases, uterine peristalsis newly emerged after USgHIFU, and the largest fibroid volumes in these 12 cases were significantly smaller than in the remaining 18 cases before and after USgHIFU. The reduction rates of the largest fibroid volume in the 12 cases were significantly higher than in the remaining 18 cases. The largest fibroids were mainly located in the intramural area before and after USgHIFU.

**Conclusions:** USgHIFU treatment may contribute to the recovery of uterine peristalsis in patients with symptomatic fibroids, as detected by cine MRI. Uterine peristalsis recovery was related to the largest fibroid volume, especially for intramural fibroids.

**MeSH Keywords:** **Leiomyoma • Magnetic Resonance Imaging, Cine • Peristalsis • Ultrasound, High-Intensity Focused, Transrectal**

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## Background

Uterine fibroids are among the most common pelvic benign tumors in women. Approximately 25% of women of reproductive age have fibroids and 50% of these women have clinical symptoms [1]. One-third of these women with clinical symptoms receive treatment [2]. Traditional treatments include hysterectomy and myomectomy [3,4]. In recent years, non-surgical treatment of uterine fibroids has become an important research focus.

The ultrasound-guided high-intensity focused ultrasound (USgHIFU) is a non-invasive treatment [5–7] that can be used in the treatment of pelvic and abdominal solid tumors, especially uterine fibroids [5–8]. USgHIFU for uterine fibroids can preserve the uterus and improve the quality of life of patients, and is especially suitable for patients who are afraid of surgery and require uterus preservation. However, clinical pathology assessment is usually not performed before or after the USgHIFU treatment. Therefore, USgHIFU is not suitable for patients suspected to have uterine malignant tumors. The therapeutic effect of USgHIFU is usually evaluated by imaging methods. USgHIFU has been reported to be a safe and effective noninvasive treatment option for uterine fibroids [5–7]. Previous studies have evaluated the efficacy of USgHIFU in treating uterine fibroids through tissue structure, blood perfusion, and MRI signal characteristics [9–11].

Uterine peristalsis, the subtle and rhythmic wave-like movement of the inner myometrium, varies in frequency, direction, and amplitude during the menstrual cycle [12–17]. In the periovulatory phase, uterine peristalsis is most active and occurs in the cervix-to-fundus direction, allowing for the rapid transport of sperm to the fallopian tubes [12–14]. Uterine fibroids can block or inhibit the normal rhythm of uterine peristalsis [18–21]. Consequently, uterine peristalsis may be used as marker to evaluate the efficacy of uterine fibroids treatment.

In cine magnetic resonance imaging (cine MRI), fast sequences are used to repeatedly scan 1 or several tissue layers, with high temporal and spatial resolution. Therefore, cine MRI may be an effective method to capture the uterine movement. In this study, differences in uterine peristalsis and its relevant factors between before and after USgHIFU treatment for symptomatic uterine fibroids were investigated by cine MRI. The efficacy of USgHIFU in treating uterine fibroids by cine MRI was also evaluated.

## Material and Methods

### Study subjects

We enrolled 43 patients with symptomatic uterine fibroids who planned to undertake USgHIFU between March 2015 and

**Table 1.** Inclusion and exclusion criteria.

Inclusion	<p>Patients of childbearing age older than 18 years. Planning to undergo USgHIFU treatment for symptomatic fibroids. Agreeing to receive MRI examination before and after USgHIFU. Able to communicate fluently with doctors during surgery. Via preoperative simulated localization of USgHIFU, the sound channel was safe and the myoma was clearly visible under ultrasound guidance</p>
Exclusion	<p>Patients were in menopause or perimenopause or gestation. Suspected to have uterine malignant tumors. Presence of all general contraindications for MRI. Having received other methods treatment for uterine fibroids, e.g., medical or surgical treatment. Having other pelvic diseases or uncontrollable systemic diseases. Having the history of severe connective tissue disease or high-dose radiotherapy in the lower abdomen. Having scars in the lower abdominal vocal passage that affected the treatment of USgHIFU. Unable to lie prone for 2 hours. Taking oral contraceptives, or having intrauterine device or metal implants</p>

We enrolled 43 patients with symptomatic uterine fibroids who planned to undertake USgHIFU. However, 13 patients did not meet the inclusion criteria and were excluded. Therefore, 30 patients were included in this study.

October 2017. The most important inclusion and exclusion criteria are summarized in Table 1. Thirteen patients did not meet the inclusion criteria and were excluded. Therefore, 30 patients (age range 24–47 years, mean age 37 years) were included in this study. Informed consent was obtained from every patient and the study was approved by the local ethics review board.

### MRI examination

MRI was performed using a 1.5T scanner (Magnetom Essenza, Siemens, Munich, Germany). Patients underwent MRI examinations before and after USgHIFU. The interval between MRI examination and USgHIFU ranged from 2 to 30 days (with an average of 13 days), and the interval between USgHIFU and follow-up imaging ranged from 101 to 358 days (with an average of 206 days). MRI scans were also performed within 5 days before or after the anticipated date of ovulation. Ovulatory phase was defined as 14 days prior to the expected beginning of the next menstrual cycle. The dominant follicle size and endometrium thickness were also used to help determine the ovulatory phase [22,23], which were monitored by ultrasound before magnetic resonance examination and confirmed by MRI.

Pelvic MRI included the axial T1- and sagittal and axial T2-weighted turbo spin-echo sequences. Imaging parameters were: for the sagittal T2-weighted images, repetition time (TR)=4000 ms and echo time (TE)=92 ms; and for the axial T2-weighted images, TR=4330 ms and TE=88 ms. Half-Fourier acquisition single-shot turbo spin-echo (HASTE) sequences were used for the cine MRI, which included 30 images of the uterus in the mid-sagittal axis over a 2-min period. The cine MRI parameters were: TR=4000 ms, TE=86 ms, slice thickness=5 mm, field of view (FOV)=32 cm, and matrix=256×256.

### Image analysis

Thirty serial HASTE images were observed at the post-processing workstation (SyngoMMWP VE40A) and were displayed at 4 frames/s. These images were analyzed and evaluated by 2 independent radiologists (with more than 11 years of gynecologic MRI experience and 3 years of uterine peristalsis evaluation experience, respectively). The presence or absence of peristalsis, when peristalsis occurred, and the direction and frequency of peristalsis were observed and evaluated.

Occurrence of uterine peristalsis was defined the changes in configuration of the endometrium and/or inner myometrium during the cine sequence. Peristalsis direction was classified as: (A) cervix-to-fundus, (B) fundus-to-cervix, and (C) opposing peristalsis (co-existing of fundus-to-cervix and cervix-to-fundus). Peristalsis frequency was defined as the number of peristalsis waves in 2 min.

The volumes of the uterus and the largest fibroid, the largest fibroid location, and the fibroid number were recorded. The volumes of the uterus and the largest fibroid were measured on the sagittal and axial T2-weighted images and calculated using the formula for prolate ellipse [3]: volume (cm<sup>3</sup>)=length×width×height×0.523. The reduction rates were calculated as [24]: reduction rate=100×(volume before USgHIFU–volume after USgHIFU)/volume before USgHIFU. Based on locations, the largest fibroids were classified as either intramural fibroids, submucosal fibroids, or subserosal fibroids. The fibroid number was counted in all images of sagittal T2-weighted and were classified as 1, 2–5, 6–10, and >10 fibroids.

### Statistical analysis

Inter-observer agreement of radiologists for the incidence of uterine peristalsis before and after USgHIFU was determined using the weighted kappa coefficient. Incidences of uterine peristalsis before and after USgHIFU were compared by the Pearson's chi-square test. The differences in uterine peristalsis direction, the location of the largest fibroid, and the fibroid numbers before and after USgHIFU were compared using Fisher's exact probability test. The volumes of the uterus and

the largest fibroid, and the uterine peristalsis frequency, before and after USgHIFU were compared by the 2-sample *t* test. The uterine volume before and after USgHIFU, the reduction rates of the uterus volume, and the largest fibroid volume between patients with uterine peristalsis newly emerging after USgHIFU and patients without were compared by the 2-sample *t* test. The largest fibroid volume before and after USgHIFU between patients with uterine peristalsis newly emerging after USgHIFU and patients without was compared by the separate variance estimation *t* test. Differences in the largest fibroid location and fibroid number between patients with uterine peristalsis newly emerging after USgHIFU and patients without were compared by Fisher's exact probability test. Statistical analysis was performed with SPSS 19.0 software. *P*<0.05 was considered as statistically significant.

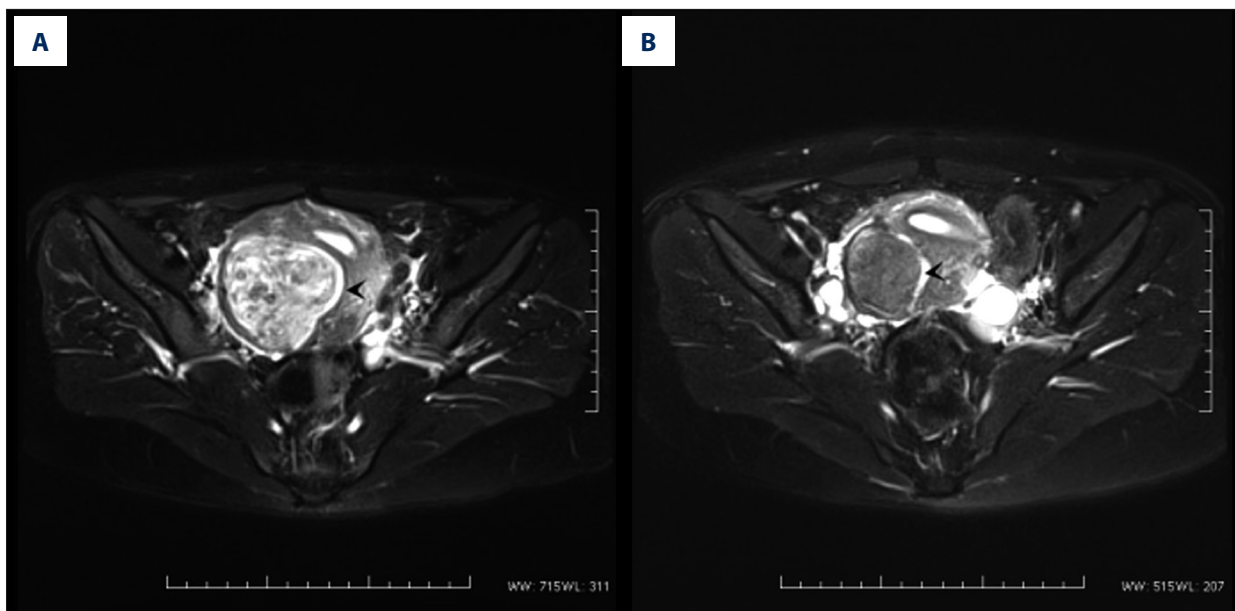
## Results

### Uterine peristalsis evaluation

To investigate uterine peristalsis before and after successful USgHIFU treatment, the rate of existence, frequency, and direction of uterine peristalsis were analyzed. All the patients with symptomatic fibroids underwent successful USgHIFU treatment (Figure 1), with no adverse effects reported. After the USgHIFU treatment, according to both radiologists, the rate of existence of fibroids, and the frequency of fibroids were significantly increased (radiologist A: *P*=0.004, and *P*=0.025; radiologist B: *P*=0.004 and *P*=0.018) (Table 2; Figures 2, 3; Supplementary Videos 1, 2). The inter-observer agreement for these radiologists for the presence of peristalsis before and after USgHIFU was excellent (*k*=0.927 and *k*=0.911) (Table 2). According to radiologists A and B, additional 12 patients had uterine peristalsis after USgHIFU (the same 12 patients for both these 2 radiologists). There were no significant differences in the peristalsis direction before and after USgHIFU. The main direction of uterine peristalsis before and after USgHIFU was cervix-to-fundus (Table 2).

### Uterine and fibroids characteristics

To investigate the characteristics of uterine and fibroids before and after USgHIFU, the volume of the uterus and the largest fibroid, the location of the largest fibroid, and the number of fibroids were analyzed. The volume of the largest fibroid was significantly decreased after USgHIFU (*P*=0.034) (Table 3). No statistically significant differences were found in uterus volume between before and after USgHIFU, or in the location of the largest fibroid between before and after USgHIFU. The largest fibroid before and after USgHIFU was mainly located in the intramural area. The size of the largest fibroid located in the submucosal area was decreased after USgHIFU (Table 3).

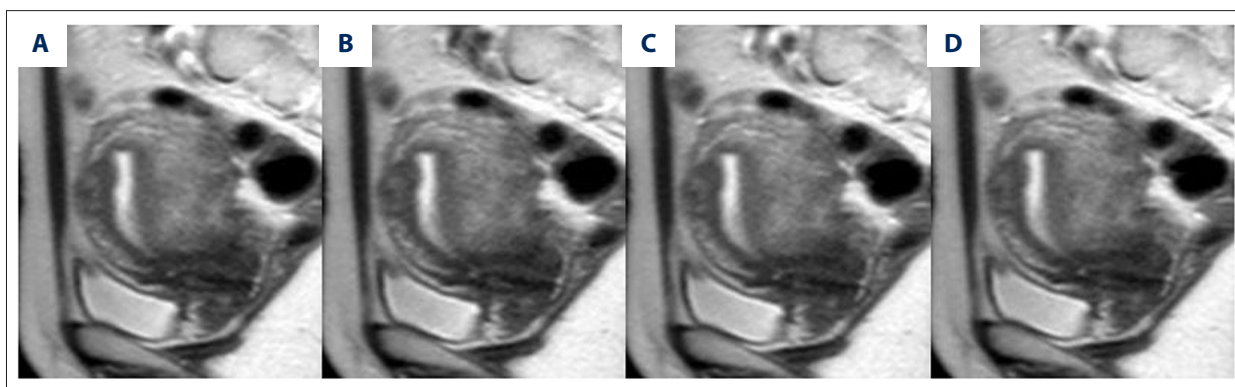


**Figure 1.** A 42-year-old woman with fibroids receiving USgHIFU treatment. (A, B) Representative pictures indicating fibroids (arrowheads) before (A) and 6 months after (B) USgHIFU treatment.

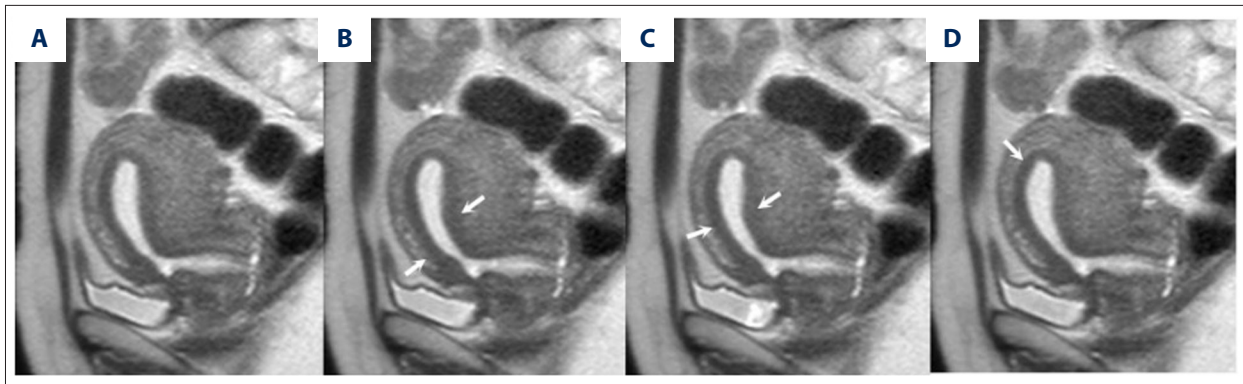
**Table 2.** Uterine peristalsis evaluation before and after USgHIFU.

	Before USgHIFU (n=30)		After USgHIFU (n=30)	
	Radiologist A	Radiologist B	Radiologist A	Radiologist B
Peristalsis present	10 (33.3%)	11 (36.7%)	22 (73.3%)	23 (76.7%)
Direction				
C-F	6	6	19	20
F-C	1	2	2	2
OP	3	3	1	1
Frequency	3.60±0.70	3.64±0.92	4.32±0.84	4.43±0.84

C-F – cervix-to-fundus; F-C – fundus to cervix; OP – opposing peristalsis.



**Figure 2.** Uterine peristalsis in a 42-year-old fibroid patient before undergoing USgHIFU treatment in the periovulatory phase. (A–D) Static images of uterine peristalsis. The patient showed no peristalsis. No changes were observed in the signal intensities of both the junctional zone and the configuration of the endometrium.



**Figure 3.** Uterine peristalsis in the same patient showing uterine peristalsis recovery. (A–D) Static images of recovered uterine peristalsis. The peristalsis was in the cervix-to-fundus direction, in the periovulatory phase, 6 months after USgHIFU treatment. The conduction of low signal intensity in the junctional zone and the stripping movement of the endometrium from cervix to fundus (arrow) are shown.

**Table 3.** Characteristics of uterine and fibroids before and after USgHIFU.

	Before USgHIFU	After USgHIFU	P
Volume			
Uterine	341.90±44.31	262.00±36.74	0.17
The largest fibroid	119.03±125.28	59.92±81.58	0.034
Location of the largest fibroid			0.08
Intramural	20	21	
Submucosal	7	2	
Subserosal	3	3	
Disappeared	0	4	
Number of fibroids			0.772
1	19	17	
2–5	4	5	
6–10	5	5	
>10	2	1	
None	0	2	

No significant differences were observed in the number of fibroids between before and after USgHIFU ( $P=0.772$ ) (Table 3). Patients with solitary fibroids predominated. Moreover, fibroids disappeared in 2 patients with a solitary fibroid after USgHIFU.

#### Comparison between patients with and without uterine peristalsis newly emerging after USgHIFU

To investigate the differences between fibroid patients with uterine peristalsis newly emerging after USgHIFU and those without, the uterine volume, the reduction rate of the largest fibroid, the location of the largest fibroid, and the number of fibroids were analyzed. The largest fibroid volume before and after USgHIFU in patients with uterine peristalsis newly

emerging after USgHIFU was significantly smaller than in those without ( $P=0.022$  and  $P=0.018$ ) (Table 4). The reduction rate of the largest fibroid volume in patients with uterine peristalsis newly emerging after USgHIFU was significantly larger than in those without ( $P=0.008$ ) (Table 4). The uterus volume before and after USgHIFU, and the reduction rate of the uterus volume, showed no statistically significant differences between patients with uterine peristalsis newly emerging after USgHIFU and patients without. Additionally, no significant differences were observed in the location of the largest fibroid, or in the number of fibroids, between patients with uterine peristalsis newly emerging after USgHIFU and patients without. Fibroids in patients with uterine peristalsis newly emerging after USgHIFU were mainly intramural and submucosal (Table 4).



**Table 4.** Comparison of fibroid patients with uterine peristalsis newly emerging after USgHIFU and those without.

	Newly emerged	No change or not present	P
Number of cases	12	18	–
Age	38.25±6.85	37.78±6.73	0.47
Uterine volume, cm <sup>3</sup>			
Before USgHIFU	263.40±88.25	394.24±297.00	0.151
After USgHIFU	192.82±54.05	308.12±248.09	0.126
The largest fibroid volume, cm <sup>3</sup>			
Before USgHIFU	64.39±35.97	155.45±149.75	0.022
After USgHIFU	23.09±21.97	84.47±97.19	0.018
Volume reduction rate, %			
Uterine	22.63±23.14	18.90±21.67	0.656
The largest fibroid	69.79±24.08	48.18±17.09	0.008
Location of the largest fibroid			0.377
Intramural	8	12	
Submucosal	4	3	
Subserosal	0	3	
Number of fibroids, n			0.586
1	7	12	
2–5	2	2	
6–10	3	2	
>10	0	2	

**Table 5.** Reduction rates of the largest fibroid volume in different locations after USgHIFU.

The largest fibroid location	N	Volume reduction rate
Submucosal	7	71.61%
Intramural	20	53.67%
Subserosal	3	33.37%

### Reduction rates

To investigate the reduction rates of the largest fibroid volume in different locations, the reduction rate of the largest fibroid volume and its location were analyzed. Our results showed that the volume of the largest fibroid was significantly reduced after USgHIFU. Submucosal fibroids showed the most obvious differences, followed by intramural fibroids and, lastly, subserosal fibroids (Table 5).

### Discussion

Previous studies have suggested that uterine fibroids reduced and disturbed the subtle wave conduction within the normal uterine muscle, which can interfere with fertility by affecting the rapid transport of sperm to the fallopian tubes in the periovulatory phase [18–20]. Kido et al. [25] reported that the incidence of uterine peristalsis is increased after uterine artery embolization (UAE), and successful UAE can induce the recovery of uterine muscle function by decreasing the fibroid and uterine volumes. In our study, the incidence of uterine peristalsis was significantly increased after USgHIFU during the periovulatory phase, suggesting that successful USgHIFU treatment is helpful for patients with fibroids. Additionally, the main directions of uterine peristalsis before and after USgHIFU were consistent with previous reports [18,25,26].

In this study, the volumes of the largest fibroid before and after USgHIFU, and the related changes between patients with uterine peristalsis newly emerging after USgHIFU and those without, were investigated. Our results show that the recovery of uterine peristalsis after USgHIFU may be affected by the

volume of the largest fibroid. In particular, the smaller the largest fibroid volume was, the larger the decreasing magnitude in the largest fibroid volume would be, and uterine peristalsis newly emerging after USgHIFU was more likely to occur in the smaller of the largest fibroids. Moreover, these were no statistically significant differences in uterus volume before and after USgHIFU, or between the patients with uterine peristalsis newly emerging after USgHIFU and those without. Some women had smaller uterus volume after USgHIFU, while others had larger volume. The reduced uterine volume may be due to coagulation necrosis of the fibroid, which reduces the volume of the fibroid. Reduced fibroid volume can reduce the effect on uterine peristalsis. Thus, uterine peristalsis can be recovered in those patients. The enlarged uterine volume may be due to inflammation related to the USgHIFU therapy, which is similar to the pseudoprogression in patients with glioblastoma multiforme after radiotherapy and temozolomide chemotherapy [27,28]; this is therapy-induced inflammation, not tumor recurrence [27,28]. The inflammatory tissue is softer than the fibrous tissue, so the inflammatory tissue may have less effect on uterine peristalsis than the fibrous tissue, which is the main component of uterine fibroids. Therefore, uterine peristalsis recovery may be found in patients with enlarged uterine volume. Further in-depth studies are needed to address these issues.

No significant differences were found in the location of the largest fibroid, perhaps because the largest fibroid before and after USgHIFU was mainly located in the intramural area in this study. The largest fibroid volume was significantly reduced after USgHIFU, especially for the submucosal fibroids, which is similar to previous reports [24,29]. In line with our findings, Kido et al. [18,25] reported that patients with submucosal fibroids have no peristalsis during the periovulatory phase. The volume of submucosal fibroids was decreased most after USgHIFU, but patients with submucosal fibroids still showed no peristalsis during the periovulatory phase. Otherwise, the submucosal fibroids disappeared or were observed in other regions. The recovery of uterine peristalsis after USgHIFU may be associated to the decreased volume of intramural fibroids and the number of the largest fibroids in the submucosal region.

We found no significant differences in the number of fibroids, perhaps because most of the patients in this study has solitary fibroids. Patients with a solitary fibroid were more likely to have restored uterine peristalsis after USgHIFU. This could be because uterine peristalsis is the subtle movement of the inner myometrium, and a uterine fibroid may interfere with the conduction of uterine peristalsis by causing uterine deformation. Patients with a solitary fibroid may be more likely to have restores uterine morphology by decreasing the fibroid volume after successful USgHIFU treatment.

Our study has several limitations. First, the time interval for patients to undergo an MRI after USgHIFU was not consistent, ranging from 3 months to 1 year, but the follow-up time was at least 3 months, which can be used to evaluate the efficacy of USgHIFU in treating uterine fibroids. We plan to conduct further research on peristalsis after USgHIFU at different time-points. Second, there may be some deviation in the calculation of the ovulation phase. The examination of follicle sizes and endometrial thickness were performed to minimize potential errors in determining the ovulation phase. Third, we used the 1.5T MRI, not the 3.0T MRI, but images from the 1.5T MRI were able to clearly show uterine peristalsis. Lastly, the evaluation of uterine peristalsis was subjective; however, 2 experienced radiologists evaluated all the images, and the inter-observer agreement was excellent.

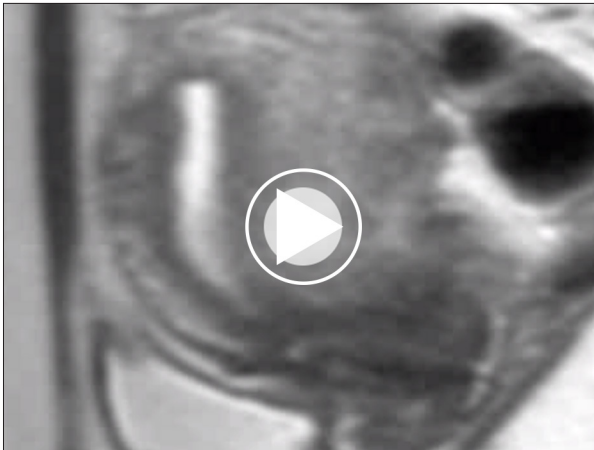
## Conclusions

The incidence of uterine peristalsis is significantly increased after USgHIFU during the periovulatory phase. Cine MRI showed recovery of uterine peristalsis after successful USgHIFU. The recovery of uterine peristalsis was associated with the largest fibroid volume and the related changes, especially for intramural fibroids.

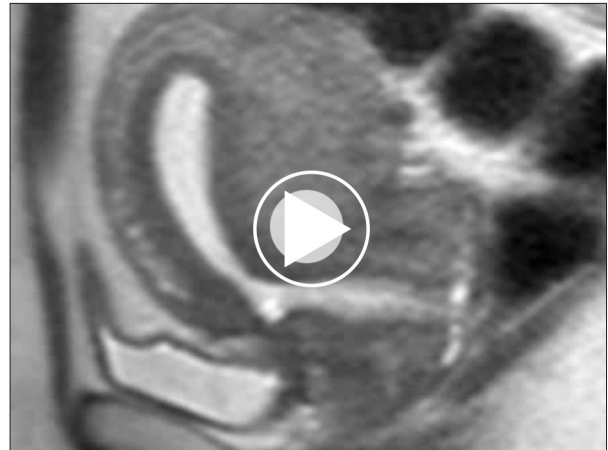
## Conflicts of interest

None.

## Supplementary Videos



**Supplementary Video 1.** Uterine peristalsis in a 42-year-old fibroid patient before undergoing USgHIFU treatment in the periovalutary phase. The patient showed no peristalsis.



**Supplementary Video 2.** Uterine peristalsis in the same patient showing uterine peristalsis recovery. The peristalsis was in the cervix-to-fundus direction, in the periovalutary phase, 6 months after the USgHIFU treatment.

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