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Therapeutic response assessment of high intensity focused ultrasound therapy for uterine fibroid: Utility of contrast-enhanced ultrasonography

Xiao Dong Zhou *,[1], Xiao Long Ren **,[1], Jun Zhang, Guang Bin He, Min Juan Zheng, Xue Tian, Li Li, Ting Zhu, Min Zhang, Lei Wang, Wen Luo

Department of Ultrasonography, Xijing Hospital, The Fourth Military Medical University, No. 17 West Changle Road, Xi'an 710032, China

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Abstract

Purpose: To assess the utility of contrast-enhanced ultrasonography (ceUS) in the assessment of the therapeutic response to high intensity focused ultrasound (HIFU) ablation in patients with uterine fibroid.

Materials and methods: Sixty-four patients with a total of 64 uterine fibroids (mean: 5.3 ± 1.2 cm; range: 3.2–8.9 cm) treated with HIFU ablation under the ultrasound guidance were evaluated with ceUS after receiving an intravenous bolus injection of a microbubble contrast agent (SonoVue) within 1 week after intervention. We obtained serial ceUS images during the time period from beginning to 5 min after the initiation of the bolus contrast injection. All of the patients underwent a contrast enhanced MRI (ceMRI) and ultrasound guided needle puncture biopsy within 1 week after HIFU ablation. And as a follow-up, all of the patients underwent US at 1, 3, 6 and 12 months after HIFU treatment. The volume change was observed and compared to pre- and post-HIFU ablation. The results of the ceUS were compared with those of the ceMRI in terms of the presence or absence of residual unablated tumor and pathologic change in the treated lesions.

Results: On ceUS, diagnostic accuracy was 100%, while residual unablated tumors were found in three uterine fibroids (4.7%) and failed treatment was found in eight uterine fibroids (12.5%). All the 11 fibroids were subjected to additional HIFU ablation. Of the 58 ablated fibroids without residual tumors on both the ceUS and ceMRI after the HIFU ablation, the volumes of all the fibroids decreased in different degrees during the 1 year follow-up USs. And histologic examinations confirmed findings of necrotic and viable tumor tissue, respectively.

Conclusion: CEUS is potentially useful for evaluating the early therapeutic effect of percutaneous HIFU ablation for uterine fibroids.

Keywords: Contrast media; Uterine disease; High intensity focused ultrasound; Magnetic resonance imaging; Ultrasonography

1. Introduction

Uterine fibroids are common benign tumors in women of child-bearing age with an incidence of 20–40%. In 10–20% of women these uterine fibroids lead to symptoms such as bleeding, pain, and bulk-related symptoms [1]. Standard methods of treatment comprise medical treatment or surgery such as myomectomy or hysterectomy. Recently, several minimally invasive techniques have been introduced for the purpose of providing local control of uterine fibroids and for the purpose of preserving the uterine. One of these techniques, High intensity focused ultrasound (HIFU) has been widely used for the treatment of solid tumors including uterine fibroids [2,3]. Even though every effort is made to achieve complete therapy, residual viable tumor foci sometimes remain. In terms of the post procedural assessment, the accurate evaluation of tumor response to therapy using imaging modalities is important for determining whether the tumor is completely treated or needs additional treatment. Although contrast-enhanced computed tomography (CT) and magnetic resonance (MR) imaging have some limitations when it comes to using them as a standard of reference for detecting viable tumor foci after thermal therapy, they have generally been used to assess the therapeutic response to thermal therapy [4,5]. More recently, however, many new US imaging techniques have been introduced which make use of the signals from the microbubbles of contrast agents, and which have improved the depiction of the intratumoral vascularity or the therapeutic effects of nonsurgical treatments for liver tumors

* Corresponding author. Tel.: +86 29 84775443; fax: +86 29 83244121.
** Cocorresponding author.
E-mail addresses: zhouxd@fmmu.edu.cn (X.D. Zhou), renxiaolong70@hotmail.com (X.L. Ren).
[1] These authors contributed equally.

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[6,7]. To our knowledge, there has been no study, which has specifically focused on the use of contrast-enhanced ultrasonography (ceUS) for the assessment of the therapeutic response in uterine fibroids treated with HIFU ablation during the long-term follow-up period. The purpose of this study was to investigate the utility of CEUS in the early assessment of the therapeutic response to HIFU ablation in patients with uterine fibroids, using contrast enhanced MRI (ceMRI) as a standard of reference.

2. Materials and methods

2.1. Patients

Between May 2004 and June 2005, 119 consecutive patients with 187 uterine fibroids were referred to our institution for US-guided HIFU ablation. Of these, all 64 patients with 103 uterine fibroids who underwent both ceUS and ceMRI in the next week after HIFU ablation were included in this study. The remaining 55 patients with 84 fibroids were excluded because ceMRI was not performed. Of these 64 patients, 27 patients had multi fibroids and only one largest fibroid was chosen to perform US-guided percutaneous needle biopsy for these patients. Thus, of these 103 uterine fibroids, we excluded 39 fibroids, because US-guided percutaneous needle biopsy was not performed. The remaining 64 (34.2%) of 187 treated uterine fibroids in 64 patients (53.8%) formed the study population. The mean age was 39.1 ± 5.6 years (range from 26 to 51 years). The mean diameter of uterine fibroids was 5.3 ± 1.2 cm (range from 3.2 to 8.9 cm).

This study was approved by the institutional review board, and written informed consent was obtained from all patients. The diagnosis of uterine fibroids was confirmed by US-guided percutaneous needle biopsy in all these 64 patients.

2.2. HIFU therapy system

HIFUNIT 9000 tumor therapy system (Shanghai Aishen Technology, Shanghai, China) was used. This device, which was designed and manufactured for clinical tumor therapy, comprised an ultrasonic therapeutic unit and an ultrasonic diagnostic unit under the control of a central processing unit. It has six self-focusing acoustic therapeutic transducers which can focus ultrasound beam through two times focalization. A diagnostic transducer was localized in the center of the therapeutic transducers. Thus, tissues in the path of therapeutic ultrasound waves could be viewed in diagnostic ultrasonic images. Ultrasonography was used to guide HIFU treatment and monitor therapeutic effects in real time. The integrated transducers are immersed in a water bag which is filled with degassed water. The water bag has an acoustic transparent membrane bottom for HIFU to transmit without obstruction, and ultrasound coupling gel was applied to eliminate air pockets trapped between the membrane and the patient's skin. The focal intensity (I_{SATA}) of the therapeutic transducers, which was calibrated by a radiation force assay in degassed water, was 0–3000 W/cm^2. The frequency of ultrasound wave was 1.0 MHz. The focal region of the therapeutic transducers was an ellipsoid with dimensions of 8 mm along the beam axis and 3 mm in the transverse direction at the 17 cm focal distance from each therapeutic transducer.

All HIFU ablations were performed percutaneously by one experienced radiologist, using real-time US guidance. HIFU ablation was performed under intravenous conscious sedation. Our strategy for complete tumor ablation was to ablate the entire fibroid itself.

2.3. US examinations

All patients were evaluated with ceUS within 1 week after HIFU ablation by two ultrasonographers experienced in ceUS. A Toshiba Aplio 80 (Toshiba, Tokyo, Japan) and a 3.5-MHz harmonic-imaging transducer with standardized US device parameters were used. A microbubble US contrast agent, SonoVue (Bracco, Milan, Italy) was used and a low MI (0.01–0.12) was selected to avoid the disruption of microbubbles. CEUS studies were performed after the administration of 2.4 ml of SonoVue as a bolus by using a 20- or 22-gauge peripheral intravenous cannula, followed by a 5-ml normal saline flush. Before the contrast agent injection, the lesion was localized on gray scale imaging, and color Doppler imaging was then activated with a color box enclosing the lesion. A preliminary sweep was then performed in the plane that was optimal for the visualization of the lesion and the resulting image was stored as a baseline cine loop. The machine settings, such as the focal zone and time-gain compensation, were optimized. After the contrast agent injection, we obtained serial ceUS images during the period ranging from beginning to 5 min. We evaluated the vascularity within the ablation zones by means of a continuous scan after the initiation of contrast injection. After obtaining the whole images, the radiologists reviewed the images frame by frame from cine loop memory and stored them digitally on the hard disc. Focal areas with irregular peripheral enhancement within the ablation zones were considered as residual tumor foci. Final decisions on the existence of residual unablated tumors required a consensus to be reached by two radiologists.

As follow-up, a baseline examination including B-scan and CDFI was performed and analyzed. All the uterine fibroids were measured by one experienced ultrasonographer in three dimensions and mean diameters and volumes were calculated using the formula $(D_1 + D_2 + D_3)/3$ and $(0.5233 D_1 D_2 D_3)$, respectively [8]. The sizes of fibroids were compared before and 1, 3, 6 and 12 months after HIFU treatment.

2.4. Contrast-enhanced MRI

Contrast enhanced MRI was performed within 1 week after HIFU ablation. Philips Gyroscan Intera 1.5 T superconducted Magnetic Resonance Image system was used. Routine axial TSE/T2W1 plain scan was conducted before the contrast enhanced MRI examination. Technique parameter: TR: 1500 ms; TE: 75 ms; matrix: 256 mm × 128 mm; FOV: 28–36 mm; slice thickness: 5 mm; slice spacing: 1 mm; contrast media gadolinium-diethylenetriamine pentaacetic acid (Magnevist, Schering, Berlin, Germany) was used to perform contrast enhanced MRI. The image collection began just at the