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● *Original Contribution*

EFFECT OF BIOLOGICAL CHARACTERISTICS OF DIFFERENT TYPES OF UTERINE FIBROIDS, AS ASSESSED WITH T2-WEIGHTED MAGNETIC RESONANCE IMAGING, ON ULTRASOUND-GUIDED HIGH-INTENSITY FOCUSED ULTRASOUND ABLATION

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Abstract—The aims of this study were to assess the effects of the biological characteristics of different types of uterine fibroids, as assessed with T2-weighted magnetic resonance imaging (MRI), on ultrasound-guided high-intensity focused ultrasound (USgHIFU) ablation. Thirty-five patients with 39 symptomatic uterine fibroids who underwent myomectomy or hysterectomy were enrolled. Before surgery, the uterine fibroids were subdivided into hypo-intense, iso-intense, heterogeneous hyper-intense and homogeneous hyper-intense categories based on signal intensity on T2-weighted MRI. Tissue density and moisture content were determined in post-operative samples and normal uterine tissue, the isolated uterine fibroids were subjected to USgHIFU, and the extent of ablation was measured using triphenyltetrazolium chloride. Hematoxylin and eosin staining and sirius red staining were undertaken to investigate the organizational structure of the uterine fibroids. Estrogen and progesterone receptor expression was assayed via immunohistochemical staining. The mean diameter of uterine fibroids was 6.9 ± 2.8 cm. For all uterine fibroids, the average density and moisture content were 10.7 ± 0.7 mg/mL and 75.7 ± 2.4%, respectively; and for the homogeneous hyper-intense fibroids, 10.3 ± 0.5 mg/mL and 76.6 ± 2.3%. The latter subgroup had lower density and higher moisture content compared with the other subgroups. After USgHIFU treatment, the extent of ablation of the hyper-intense fibroids was 102.7 ± 42.1 mm^2, which was significantly less than those of the hypo-intense and heterogeneous hyper-intense fibroids. Hematoxylin and eosin staining and sirius red staining revealed that the homogeneous hyper-intense fibroids had sparse collagen fibers and abundant cells. Immunohistochemistry results revealed that estrogen and progesterone receptors were highly expressed in the homogeneous hyper-intense fibroids. This study revealed that lower density, higher moisture content, sparse collagen fibers, abundant cells and overexpression of estrogen and progesterone receptors are important biological characteristics that resulted in poor efficacy in the treatment of homogeneous hyper-intense fibroids. (E-mail: chenwz@haifu.com.cn)

Key Words: **Biological characteristics, Ultrasound-guided high-intensity focused ultrasound, Uterine fibroids, Effect.**

INTRODUCTION

Such factors as tissue density, moisture content, internal structure and estrogen receptor (ER) and progesterone receptor (PR) expression reflect the biological characteristics of uterine fibroids. Ultrasound-guided high-intensity focused ultrasound (USgHIFU) can produce a region of coagulative necrosis by converting sound energy into thermal energy within uterine fibroids via the use of tightly and precisely focused sound waves without harming tissues outside the focus. Different types of biological characteristics create different acoustic environments in the location of the intended ultrasound reaction and ultimately affect the deposition of ultrasound energy. Uterine fibroids with different signal intensities on T2-weighted magnetic resonance imaging (MRI) have different biological characteristics (Yamashita et al. 1993) that result in different HIFU ablation effects (Funaki et al. 2009;

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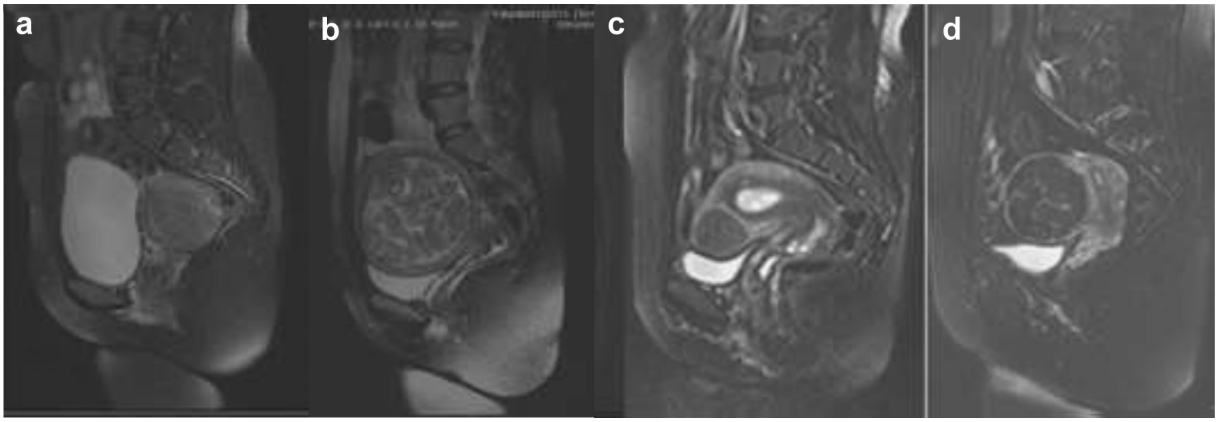

Fig. 1. T2-weighted magnetic resonance images obtained before treatment: (a) homogeneous hyper-intense fibroid; (b) heterogeneous hyper-intense fibroid; (c) iso-intense fibroid; (d) hypo-intense fibroid.

Lenard et al. 2008). Moreover, our previous work found that uterine fibroids with different hyper-intensities on T2-weighted MRI also result in different high-intensity focused ultrasound (HIFU) ablation effects, and other studies have observed poor efficacy for homogeneous hyper-intense fibroids (Zhao et al. 2013). The different biological characteristics of different hyper-intense uterine fibroids and the effects of these characteristics on USgHIFU ablation were investigated in the present study. The growth of uterine fibroids is stimulated primarily by ERs and PRs, regardless of whether there are differences in the rates of positivity for ERs and PRs across different hyper-intense uterine fibroid tissues. This issue warrants further research and development.

METHODS

Specimens and reagents

The ethics committee of Chongqing Medical University approved this study. Written informed consent was provided by all patients before the procedure. Thirty-nine uterine fibroid specimens from 35 patients who underwent hysterectomy or myomectomy were included in this study. To be included in this study, all patients with uterine fibroids agreed to undergo pre-treatment MRI to delineate the fibroids and had not undergone any treatment, such as a gonadotrophin-releasing hormone agonist, uterine artery embolization or radiofrequency treatment. All specimens were divided into four parts: three parts were used to determine tissue density, tissue moisture content and organizational structure of the uterine fibroids, and the fourth was subjected to USgHIFU.

The applied reagents included triphenyltetrazolium chloride (TTC) and picric–sirius red dye liquor from Sigma (St. Louis, MO, USA), streptavidin–horseradish peroxidase immunohistochemical kits from Cowin Biotech (Beijing, China) and rabbit anti-human ER and rabbit anti-human PR antibodies from Abcam (Cambridge, England).

USgHIFU therapeutic system and main parameters

The treatments were performed with a JC200 HIFU tumor therapy system (Chongqing Haifu [HIFU] Tech,

Table 1. Baseline data of patients with different types of uterine fibroids as assessed with T2-weighted magnetic resonance imaging

Variable	Normal myometrium	Heterogeneous hyper-intense fibroids	Homogeneous hyper-intense fibroids	Iso-intense fibroids	Hypo-intense fibroids
Number of patients	14	8	7	8	12
Number of fibroids	14	10	7	8	14
Age (y)					
Mean ± SD	39.6 ± 6.2	39.6 ± 8.5	34.7 ± 8.8	37.0 ± 5.0	41.5 ± 6.8
Range	(36–52)	(27–50)	(21–47)	(29–42)	(30–52)
Body mass index (kg/m^2)					
Mean ± SD	23.2 ± 2.3	23.3 ± 2.6	21.7 ± 2.4	22.5 ± 1.9	23.5 ± 2.9
Range	(20.4–28.7)	(9.1–27.2)	(18.4–25.4)	(20.4–26.4)	(18.8–28.7)
Fibroid location (AW/PW/LW)	3/5/6	3/4/3	2/4/1	2/2/4	6/2/6
Fibroid diameter (cm)					
Mean ± SD	6.9 ± 2.8	6.8 ± 2.5	7.4 ± 3.0	5.5 ± 2.0	5.2 ± 1.5
Range	(5.1–12.1)	(3.9–12.1)	(3.7–11.5)	(3.5–9.6)	(3.2–8.8)

SD = standard deviation; AW = anterior wall; PW = posterior wall; LW = lateral wall.