IntraVoxel Incoherent Motion MRI for the characterization of uterine fibroids before MR-guided high-intensity focused ultrasound ablation

Marlijne Elisabeth Ikink[1], Johanna MM van Breugel[1], Robbert J Nijenhuis[1], Marianne J Voogt[1], Maurice AAJ van den Bosch[1], Koen L Vincken[2], and Lambertus W Bartels[2]
[1]*Radiology, University Medical Center Utrecht, Utrecht, Utrecht, Netherlands,* [2]*Radiology and Image Sciences Institute, University Medical Center Utrecht, Utrecht, Utrecht, Netherlands*

Target audience: Clinicians and scientists interested in MR-HIFU ablation of uterine fibroids.

Purpose: In the past decade, MR-guided high-intensity focused ultrasound (MR-HIFU) has evolved as a non-invasive treatment for symptomatic uterine fibroids. Although MR-HIFU is applicable to a substantial number of patients, multiple clinical and anatomical factors influence patient eligibility, and must be taken into account to ensure patient safety and treatment efficacy. Funaki *et al.* [1] have previously reported a correlation between T2-weighted (T2w) signal intensity of uterine fibroids and the efficacy of MR-HIFU ablation. According to the signal intensity, fibroids were classified as type 1 (very low signal intensity – comparable with the abdominal muscle), type 2 (intermediate signal intensity), and type 3 (very high signal intensity – equal or higher than the *myometrium*). Morphological and functional features, such as cellularity, vascularity, perfusion, necrosis, edema, and calcification that are reflected in the signal intensity on T2w MRI, may influence the clinical outcome. What exactly causes the differences in signal intensity on T2w MRI is not well-known. Diffusion-weighted MRI (DWI) with subsequent mapping of the apparent diffusion coefficient (*ADC*) allows tissue characterization based upon differences in the motion of water molecules. In the intravoxel incoherent motion (IVIM) theory, [2] tissue is assumed to incorporate a perfusion fraction (f) of water flowing in capillaries, with a flow-related pseudodiffusion coefficient (D^*) and a fraction ($1-f$) of static perfusion-free diffusion (D) of intracellular and extracellular water. Although IVIM has been a subject of controversy in tissues with small perfusion fractions like the brain, the IVIM theory has recently been verified in (abdominal) organs with much higher values of the perfusion fraction f. [3] The purpose of our study was to use IVIM MRI to determine the perfusion fraction (f) and the true diffusion coefficient (D) of uterine fibroids and to investigate whether these DWI characteristics differ for fibroids with different signal intensities on T2w MRI.

Methods: This study was approved by our local institutional review board, all patients gave written informed consent for the use of clinical and imaging data. Sixty-three uterine fibroids in 52 patients were prospectively included and treated on a clinical MR-HIFU system (Sonalleve, Philips Healthcare, Finland) integrated into a 1.5-T MRI (Achieva, Philips Healthcare, The Netherlands). Patients were treated in prone position with a standardized procedure. [4] For adequate planning of treatment and DWI scans, anatomical T2w 3D TSE and T1-weighted (T1w) 3D fat-suppressed spoiled gradient echo MR images were acquired after localizer scans at the start of the MR-HIFU procedure. The DWI series were additionally performed in the coronal plane using a fat-suppressed single shot SE-EPI sequence with b=0, b=200, b=400, b=600, and b=800 s/mm^2. Diffusion coefficient maps were calculated by voxel-wise non-linear least squares fitting of the signal decay function to the DWI data, acquired at different b-values using in-house developed software (imageXplorer, iX 2.0, Image Sciences Institute, The Netherlands). Analysis was performed in a circular region of interest (ROI), drawn to include most of the target fibroid. An *ADC*-map was calculated from the images b_0=0 s/mm^2 and b_1=400 s/mm^2, the perfusion free diffusion parameter D was determined from the images b_1=400 s/mm^2, b_2=600 s/mm^2 and b_3=800 s/mm^2. Following, using $f = 1 - \exp[-b_1 \cdot (ADC - D)]$, [2] the perfusion fraction f was calculated. Differences were assessed after the uterine fibroids were classified into three types based on their signal intensity on T2w MRI, by an experienced radiologist, as explained above.

Results: The median age of the patients was 45 (IQR [42, 47]) years, the median Body Mass Index was 22.8 (IQR [21.4, 24.8]) kg/m^2. The median baseline fibroid volume was 245 (IQR [121, 482]) cm^3, with a maximum diameter of 8.6 (IQR [6.7, 11.1]) cm. The uterine fibroids were predominantly intramurally located (n=38), with a low signal intensity on T2w MRI (n=39). The median perfusion fraction f over the ROI was 33% (IQR [29%, 37%]), the median diffusion coefficient D was $0.71 \cdot 10^{-3}$ (IQR [$0.64 \cdot 10^{-3}$, $0.89 \cdot 10^{-3}$]) mm^2/s. When these parameters were categorized into the three types of fibroids, [1] we found a significantly higher diffusion coefficient D in the high-intensity type 3 uterine fibroids ($0.89 \cdot 10^{-3}$ (IQR [$0.81 \cdot 10^{-3}$, $1.08 \cdot 10^{-3}$]) mm^2/s) when compared to low-intensity type 1 fibroids ($0.69 \cdot 10^{-3}$ (IQR [$0.62 \cdot 10^{-3}$, $0.76 \cdot 10^{-3}$]) mm^2/s; P<0.001). The differences between the three types of fibroids are shown in Figure 1. No significant difference in the perfusion fraction f was observed between the three groups (P=0.370).

Discussion & Conclusion: We observed that high-intensity type 3 uterine fibroids had a significantly higher diffusion coefficient D. This may indicate less restriction of water molecules in these fibroids, probably representing more fluid-rich tissue compared to low-intensity type 1 fibroids. Although, we have measured a high median perfusion fraction f of 33% (IQR [29%, 37%]) in the overall group of uterine fibroids, no significant difference in perfusion fraction was found between the three types of uterine fibroids. The difficulty to obtain an adequate thermal dose with MR-HIFU ablation in high-intensity type 3 fibroids appears to be related to the cellularity and the extracellular water content, rather than the perfusion state. However, further studies with MRI-based perfusion measurement techniques are needed to confirm this hypothesis.

References: [1] Funaki K *et al*. Am J Obstet Gynecol 2007;196(2):184-6. [2] Le Bihan D *et al*. Radiology 1988;168(2):497-505. [3] Lemke A *et al*. Magn Reson Med. 2010 Dec;64(6):1580-5. [4] Ikink ME *et al*. Eur Radiol. 2013 Nov;23(11):3054-61.

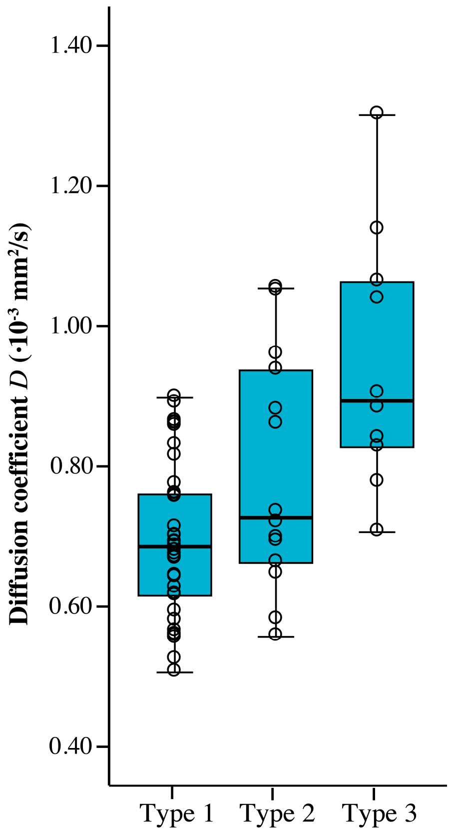

Figure 1. Representation of scatter plot, full range, interquartile range, and median value of the diffusion coefficient D for type 1, type 2, and type 3 uterine fibroids. The diffusion coefficient D was significantly higher in type 3 fibroids (n=10) compared with type 1 (n=39, P<0.001) and type 2 (n=14, P=0.048) uterine fibroids. There was no significant difference found between type 1 and type 2 uterine fibroids.