Multiparametric MRI Characterization of Funaki sub-types of Uterine Fibroids Considered for MRI-guided High-Intensity Focused Ultrasound (MR-HIFU) Therapy

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Target Audience: Researchers and clinicians interested in pelvic MRI and MRI- guided HIFU ablation therapy.

Purpose: The Funaki classification is currently used to assess the likelihood of uterine fibroids to respond to magnetic resonance (MR)-guided high-intensity focused ultrasound (MR-HIFU) ablation therapy [1]. Fibroids are characterized based on their signal intensity on T2-weighted images into 3 subtypes: Type 1, low signal intensity compared to skeletal muscle; Type 2, intermediate signal intensity, lower than myometrium but higher than skeletal muscle; and Type 3, signal intensity similar to or higher than that of myometrium. Type 3 fibroids are considered less likely to respond to MR-HIFU due to their inherent higher vascularity [2] and presumed decreased cellularity [3]. Our purpose was to correlate multiparametric magnetic resonance (MR) imaging data on symptomatic uterine fibroids being considered for MR-HIFU ablation with fibroid characterization based on the Funaki Classification scheme.

Methods: This prospective study was approved by the local institutional review board and informed patient consent was obtained prior to imaging. Sixty one fibroids in 31 patients (30-49 years) who underwent MR imaging consisting of T1WI, T2WI, DWI and DCE sequences between December 2013 to October 2014 were included in the analysis. Fibroids were characterized based on the Funaki classification by a single blinded MRI fellowship-trained radiologist: Images were acquired prone in a 3T Philips Achieva with a 16-channel XL torso coil or Ingenia with anterior and posterior torso coils. DCE-MRI data were analyzed using commercially available VersaVue Enterprise (iCAD, Inc., Nashua, NH) and open-source DICOM-viewer OsiriX software. A region of interest (ROI) was drawn to include most of the fibroid avoiding the outer boundary to minimize partial volume effects. Quantitative measures of K^{trans}, K_{ep} ,V_e, V_p, IAUC and $T1_0$ as well as monoexponential ADC (calculated with 9-10 b values between 0-1000), true diffusion coefficient (D), pseudodiffusion coefficient (Dp) and perfusion fraction (f) were calculated as mean± standard deviation. Differences in these parameters among the three Funaki types were determined using linear mixed model. All statistical analyses were considered to be significant with $p<0.05$.

Results: All fibroids were assigned a Funaki subtype based on previously defined criteria: Type 1 (n=15), Type 2 (n=34), and Type 3 (n=12). Type 1 fibroids ranged in size from 2.5-6.5cm, Type 2 fibroids from 2.5-9.5 cm and Type 3 fibroids from 3.0-11.0cm in maximum diameter respectively. K^{trans}, K_{ep}, V_p, monoADC and tissue diffusion coefficient of Type 3 fibroids were statistically higher than Type 1 and Type 2 fibroids ($p<0.05$) (Fig.1). No significant difference was found in the V_e, IAUC, $T1_0$, pseudodiffusion coefficient and perfusion fraction between the three types of fibroids. Significant differences in K^{trans} and V_p were shown between Type 1 and Type 3 fibroids; while significant differences in monoADC and tissue diffusion coefficient were shown between Type 1 and Type 3 and Type 2 and Type 3 fibroids ($p<0.05$) (Fig.1). Representative images depicting the parameters that demonstrated statistical differences are shown (Fig.2).

Discussion : Comparison of the DCE-MRI derived pharmacokinetic parameters based on Tofts model and diffusion-weighted imaging among the three fibroid types, demonstrated significant statistic differences of K^{trans}, K_{ep}, V_p, monoADC and tissue diffusion coefficient of Type 3 fibroids. The volume transfer constant of Gd-DTPA (K^{trans}) between the capillary and extravascular extracellular space (EES), transfer constant from the EES back to blood plasma (K_{ep}), Plasma Volume (V_p), Apparent Diffusion Coefficient (ADC) and perfusion-free diffusion (D) is higher in Type 3 fibroids. Increased vascularity and higher ADC values which may signify decreased cellularity in Type 3 fibroids would imply the need for higher energy deposition to achieve an ablative thermal dose with MR-HIFU, making them less suitable for this therapeutic option.

Conclusions: Use of pharmacokinetic and diffusion weighted imaging parameters can serve as an objective and sensitive method to discriminate differences in capillary permeability, blood flow, and cellularity among the three traditionally reported fibroid types described by Funaki to plan MR-HIFU treatment. This multi-parametric characterization may enable better selection of patients for MR-HIFU and other therapeutic options.

References: 1. Funaki K. American Journal of Obstetrics & Gynecology 2007. **2.** Chenaxi L. Proc. Intl. Soc. Mag. Reson. Med. 22 (2014). **3.** Marlijne E. Proc. Intl. Soc. Mag. Reson. Med. 22 (2014).

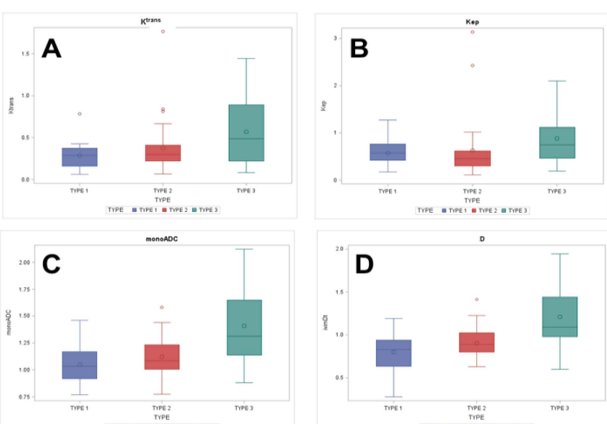

Fig.1: Box and Whisker plots summarizes the distribution of K^{trans}(A), K_{ep} (B), monoADC (C) and D (D) in the 3 fibroid types. Blue= Type 1, Red= Type 2, Green= Type 3 fibroids.

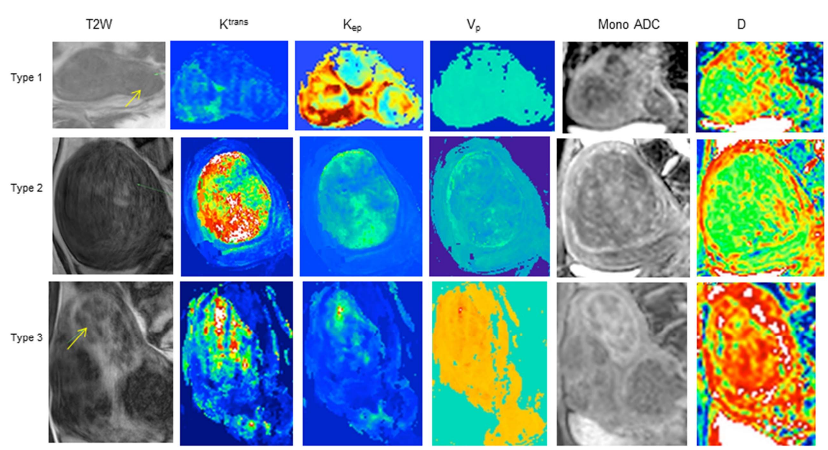

Fig.2: T2WI, K^{trans}, K_{ep}, V_p color maps, ADC, D maps of the 3 fibroid types.