Diffusion-weighted MRI using different *b*-value combinations for the evaluation of treatment results after volumetric MR-guided high-intensity focused ultrasound ablation of uterine fibroids

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Target audience: Clinicians, researchers, and MR technicians with interest in MR-HIFU ablation of uterine fibroids.

Purpose: Uterine fibroids are the most common benign gynecological tumors. In the past decade, the demand for conservative treatments has progressively increased. [1] MR-HIFU is a noninvasive outpatient image-guided technique that uses heat generated by convergent high-intensity ultrasound waves. [2] As with other non-invasive techniques, there is a need for methods to evaluate the therapeutic effect during the interventional procedure. To assess the extent of tissue ablation (i.e. non-perfused volume), the periprocedural application of contrast-enhanced T1-weighted MRI (CE-T1w) should be limited, given the possible side effects, the unknown safety profile of the contrast agent after heating, the relatively long clearance time of the agent, and the fact that the acceptable total dose of contrast agent is limited. An imaging method that has been suggested is diffusion-weighted MRI (DWI). Especially in well-perfused tissues, like uterine fibroids, [3] the apparent diffusion coefficient (*ADC*) is known to reflect not only the diffusion of water molecules, but also information about the microcirculation of blood in the capillaries. The aim of our study was to investigate the influence of the choice of *b*-values on the *ADC*-maps of fibroids, and to determine what combination of *b*-values allows the best differentiation between ablated fibroid tissue and untreated tissue immediately after MR-HIFU ablation of uterine fibroids.

Methods: A total of 56 patients with 67 uterine fibroids were treated with volumetric MR-HIFU (Sonalleve, Philips Healthcare, Finland). Post-treatment images were obtained using CE-T1w imaging and DWI using a fat-suppressed single-shot spin-echo echo-planar imaging (SE-EPI) with b=0, b=200, b=400, b=600, and b=800 s/mm^2. The ablated regions inside the fibroids, defined as non-perfused volume (NPV), were identified on post-contrast T1w MRI. *ADC*-maps were generated using subsets of *b*-values to investigate the effects of tissue ablation on perfusion and water diffusion in fibroids treated with MR-HIFU. Four combinations of *b*-values were used: (1) all *b*-values, (2) b=0 and 200 s/mm^2; (3) b=400, 600 and 800 s/mm^2; and (4) b=0 and 800 s/mm^2. This study was approved by our local institutional review boards, all patients gave written informed consent for the use of clinical and imaging data. Tests of four different *b*-value combinations were conducted using Bonferroni adjusted alpha levels of 0.0125 per test (0.05/4).

Results: Using the lowest *b*-values (b=0 and 200 s/mm^2), a significant decrease ($p<0.001$) in the mean *ADC* of the ablated tissue ($1.53\pm0.28\cdot10^{-3}$ mm^2/s) was observed, compared to baseline ($2.16\pm0.33\cdot10^{-3}$ mm^2/s). Calculating the *ADC*-value with the highest *b*-values (b=400, 600, 800 s/mm^2), the *ADC*-value increased significantly post-treatment ($p<0.001$), although the increase was much lower than the decrease observed at b=0 and 200 s/mm^2 (Table 1). The *ADC*-value of the other *b*-value combinations and normal *myometrium* did not change after MR-HIFU treatment. *ADC*-maps calculated with the lowest *b*-values resulted in the best visual agreement of non-perfused fibroid tissue detected on CE-images. An example of pre- and post-treatment *ADC*-maps in a patient calculated using the different *b*-value combinations is shown in Figure 1.

Table 1. *ADC*-values ($\cdot10^{-3}$ mm^2/s) calculated with different combinations of *b*-values, pre- and post-treatment

Different *b*-value combinations	Treated fibroid tissue			Normal *myometrium*		
	Pre-treatment	Post-treatment	*P*	Pre-treatment	Post-treatment	*P*
0, 200, 400, 600, and 800 s/mm^2	1.27±0.23	1.20±0.25	0.034	1.85±0.34	1.88±0.37	0.207
0 and 200 s/mm^2	2.16±0.33	1.53±0.28	<0.001	2.82±0.55	2.82±0.58	0.918
400, 600, and 800 s/mm^2	0.76±0.18	0.92±0.21	<0.001	1.02±0.19	1.07±0.23	0.053
0 and 800 s/mm^2	1.09±0.23	1.11±0.24	0.492	1.55±0.24	1.57±0.26	0.355

Discussion & Conclusion: DWI and *ADC*-mapping may be useful for direct evaluation of MR-HIFU ablation of uterine fibroids. Our results demonstrate that the measured *ADC*-value in fibroid tissue is influenced by the choice of *b*-values used for *ADC*-calculation. We believe that the apparently restricted diffusion in the NPV, observed immediately after treatment, is in part related to the reduced perfusion effect. Using low *b*-values (b=0 and 200 s/mm^2) might be the best choice to emphasize such perfusion changes in *ADC*-maps. The observed change in *ADC* based on the highest *b*-values suggests that the reduced perfusion may be accompanied by an increase in extracellular fluid volume directly after ablation. This may be due to direct thermal damage done to the cell membranes.

References: [1] Merrill RM. Med Sci Monit 2008 January;14(1):CR24-CR31. [2] Tempany CM *et al*. Radiology 2003 March;226(3):897-905. [3] Walocha JA *et al*. Hum Reprod 2003 May;18(5):1088-93.

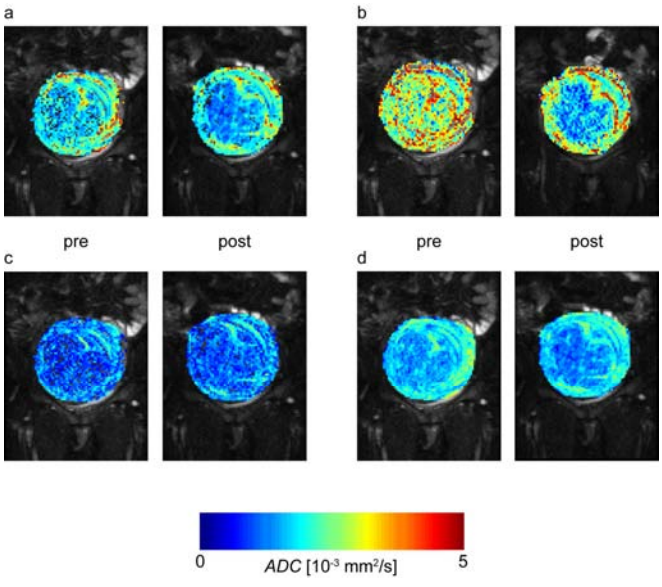

Figure 1. Reconstructed pre- and post-treatment *ADC*-maps using four different approaches: (a) all *b*-values; (b) b=0 and 200 s/mm^2, indicating a significant decrease in *ADC*-value; (c) b=400, 600 and 800 s/mm^2, indicating a significant increase in *ADC*-value; (d) b=0 and 800 s/mm^2.