DCE-MRI and DWI are Sensitive to Vascular Changes in Renal Cell Carcinoma Following Sunitinib Therapy

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Target Audience: Clinical scientists, MRI physicists, and tumor biologists interested in monitoring anti-angiogenic therapy in tumors.

Purpose: To compare the ability of dynamic contrast-enhanced (DCE-)MRI and multi B-value diffusion weighted imaging (DWI) to delineate functional changes in renal cell carcinoma early after the initiation of sunitinib therapy.

Background: Anti-angiogenic agents such as sorafenib and sunitinib, are approved for therapy of renal cell carcinoma (RCC)[1-2]. DCE-MRI can document vascular changes in RCC after initialization of therapy, and pre-therapy DCE-MRI has been shown to be a biomarker of tumor response[3-4]. More recently, DWI has been used to characterize changes in RCC after anti-angiogenic therapy[5]. However, direct comparison between these MRI techniques for detecting therapy-induced changes in RCC is lacking.

Methods: Ten patients with metastatic RCC underwent DWI and DCE-MRI at 1.5T before and early (26±7 days) after the start of sunitinib therapy. DWI was performed at four B values (0, 200, 500, and 800 sec/mm^2). DCE-MRI was performed using large volume hybrid-radial imaging, with two second temporal resolution, with IV injection of 0.07 mmol/kg gadobenate. All visible tumors were manually segmented separately on DWI and DCE-MRI image sets by a single radiologist, blinded to time point (pre- or post-therapy). Tumors greater than 2.5 cm in diameter that could be identified on both imaging sets were included in the analysis. Tumor T1 values, DCE-MRI parameters (K^{trans}, k_{ep}, v_e, and v_p), and DWI parameters ($ADC_{0\text{-}200}$, $ADC_{200\text{-}800}$, F_p), were compared pre- and post-therapy by the Students t-test. Pearson correlations among DWI and DCE-MRI parameters were also evaluated.

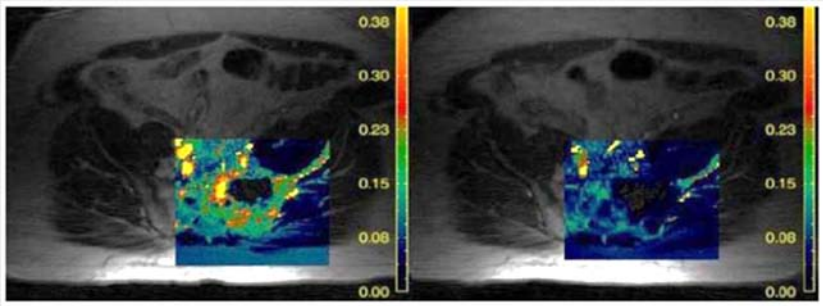

Figure 1: K^{trans} maps of an RCC metastasis to the sacrum before (left) and after (right) sunitinib therapy, demonstrating the effects of anti-angiogenic therapy on tumor perfusion.

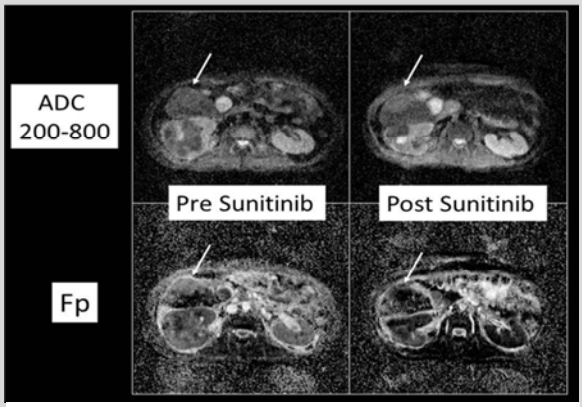

Figure 2: RCC metastasis to the liver (arrow) before and after sunitinib therapy. Functional DWI maps demonstrate the profound decrease in perfusion fraction (Fp), with more modest post-therapy elevation of diffusion ($ADC_{200\text{-}800}$).

Results: A total of 21 tumors in ten patients were identified. Mean tumor T1 values decreased after therapy (1028 vs. 747 ms, $p<0.0002$). Significant changes in DCE-MRI parameters were seen (**Fig 1**), with mean declines in K^{trans}, k_{ep}, and v_p by 60%, 52%, and 63%, respectively after therapy ($p<0.05$ for all comparisons). $ADC_{0\text{-}200}$ and F_p demonstrated post-treatment declines of 18% and 42%, respectively ($p<0.05$ for each), but there was no significant change in $ADC_{200\text{-}800}$ (**Fig 2**). A strong positive correlation was seen between v_p and $ADC_{0\text{-}200}$ before therapy ($r=0.45$, **Fig 3**) and more modest correlation after therapy ($r=0.33$). Positive correlations were also noted between v_p and F_p pre-therapy ($r=0.28$) and post-therapy ($r=0.30$). Modest positive correlations were also noted between changes in K^{trans} and F_p.($r=0.32$) and changes in K^{trans} and $ADC_{0\text{-}200}$ ($r=0.25$, **Fig 3**)

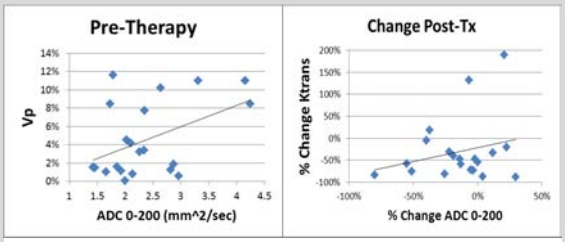

Figure 3: Correlation between DCE-MRI and DWI in RCC. L: Baseline $ADC_{0\text{-}200}$ vs. v_p. R: Change $ADC_{0\text{-}200}$ vs. K^{trans}.

Discussion/Conclusion: While conventional ADC measures by DWI does not reveal changes in RCC tumor diffusion following anti-angiogenic therapy, analysis of multi-B-value DWI reveals changes related to tumor devascularization, similar to those demonstrated with DCE-MRI. Multi-B-value DWI may prove to be a useful surrogate marker for anti-vascular tumor effects of targeted therapy in RCC. While DCE-MRI metrics of tumor vascularity undergo greater changes after therapy, DWI can be performed as a whole body technique without IV contrast, and may prove useful in monitoring therapy in RCC.

References: 1) Escudier, et al., N Engl J Med. 2007;356:125–134. 2) Motzer, et al., N Engl J Med. 2007;356:115–124 3) Flaherty, et al., Cancer Biol Ther. 2008;7:496–501. 4) Hahn, et al., J Clin Oncol. 2008;26:4572–4578 5) Desar, et al., Cancer Imaging. 2011;11:259–265