DCE-MRI and DWI are Sensitive to Vascular Changes in Renal Cell Carcinoma Following Sunitinib Therapy  
Dania Daye1, Anil Chauhan1, Sarah Englander1, Thomas Ferrara1, Colleen Redlinger2, Naomie Haas2, Hee-Kwon Song1, Stephen Keefe2, and Mark Rosen1  
1Radiology, University of Pennsylvania, Philadelphia, PA, United States, 2Medicine, University of Pennsylvania, Philadelphia, PA, United States

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 response3-4. More recently, DWI has been used to characterize changes in RCC after anti-angiogenic therapy5. 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/mm²). 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 (Ktrans, kep, ve, and vp), and DWI parameters (ADC0-200, ADC200-800, Fp), were compared pre- and post-therapy by the Students t-test. Pearson correlations among DWI and DCE-MRI parameters were also evaluated.  

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 Ktrans, kep, and vp by 60%, 52%, and 63%, respectively after therapy (p<0.05 for all comparisons). ADC0-200 and Fp demonstrated post-treatment declines of 18% and 42%, respectively (p<0.05 for each), but there was no significant change in ADC200-800 (Fig 2). A strong positive correlation was seen between vp and ADC0-200 before therapy (r=0.45, Fig 3) and more modest correlation after therapy (r=0.33). Positive correlations were also noted between ve and Fp pre-therapy (r=0.28) and post-therapy (r=0.30). Modest positive correlations were also noted between changes in Ktrans and Fp(r=0.32) and changes in Ktrans and ADC0-200 (r=0.25, Fig 3)  
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.  