Assessment of Intratumoral Heterogeneity of Vascularity in Renal Masses with Arterial Spin Labeling (ASL) and Dynamic Contrast Enhanced (DCE) MRI at 3T

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INTRODUCTION: Renal cell carcinoma (RCC) growth and metastatic potential has been linked tightly to the ability of the tumor to induce the formation of new blood vessels (i.e. angiogenesis). While dynamic contrast enhanced (DCE) MRI has been proposed to measure tumor perfusion in a variety of tumors, contraindications to receive I.V. contrast due to impairment in the renal function are common in RCC patients. Furthermore, the contributions of both blood flow and vascular permeability to tissue enhancement may lead to erroneous estimations of tumor perfusion with DCE MRI. Alternatively, quantitative arterial spin labeling (ASL) MRI can be used to measure renal mass perfusion at 1.5T without the need for I.V. contrast [1]. However the correlation between ASL signal and DCE-derived vascular parameters in renal masses has not been yet described. Moreover, the theoretical advantage of ASL MRI at 3T due to increased signal-to-noise ratio and the prolonged T1 values in tissues has not been investigated. The purpose of this study was to measure the intratumoral heterogeneity in renal mass perfusion with ASL MRI at 3T and to correlate these findings with those on DCE MRI.

MATERIALS AND METHODS

Patients and MRI Protocol: This was a prospective, IRB-approved, HIPAA-compliant study. After signing an informed consent, 24 patients scheduled for surgical resection of a known renal mass underwent 3T dual-transmit MRI with a 16-channel SENSE-XL-Torso coil (Achieva, Philips Medical System, Cleveland, OH). A 2D ASL coronal acquisition (16 label-control pairs and proton density–weighted reference image) was obtained through the kidneys with pseudocontinuous labeling (pCASL), background suppression and superior saturation of inflowing blood after labeling with a single shot turbo spin echo [2]. Labeling was performed axially 8–10cm above the center of FOV for 1500 ms followed by a 1500ms post-labeling delay [3]. FOV=40cm×40cm, matrix=176×176, TR=6s. DCE MRI was then performed using a coronal 3D spoiled gradient echo acquisition with a temporal resolution of 5 sec. To minimize respiratory motion during DCE MRI, three consecutive dynamic phases were obtained within each 15-sec breath-held acquisition period. A 15-sec period of free-breathing was allowed between consecutive acquisition periods. Three baseline dynamic phases were acquired, followed by a bolus of 0.1 mmol/kg of gadobutrol (Gadavist; Bayer Healthcare Pharmaceuticals, Wayne, NJ) using a power injector at a rate of 2 cc/sec followed by a 20 cc saline flush at 2 cc/sec. The same MRI sequence was used to generate a T1 map ($T1_0$) prior to contrast injection with three separate acquisitions (flip angle 10°, 5°, and 2°). *Image Reconstruction:* ASL label-control pairs were subtracted and averaged in k-space and then converted to quantitative perfusion (*P*) maps. DCE images were analyzed using commercial software VersaVue Enterprise (iCAD, Inc., Nashua, NH), to perform voxel-by-voxel fitting with Tofts model and generate quantitative maps of K^{trans}, *Kep*, *Ve* and *Vp*. The $T1_0$ and initial area under the concentration curve (iAUC) were also calculated. *Image Analysis:* All images were analyzed with a DICOM viewer (Osirix X, version 5.6, 64bit, Bernex, Switzerland). Regions of interest (ROI) of entire tumor, and of high flow and low flow areas within the tumor, as well as within the ipsilateral and contralateral renal cortex were drawn on ASL *P* map and on the DCE-derived maps K^{trans}, *Kep*, *Ve* and *Vp*, $T1_0$ and iAUC. *Histopathology:* The analysis of the tumor after surgical resection served as the gold-standard. All tumors were classified into one of the following categories: *(a)* low-grade (LG) clear cell RCC (ccRCC), *(b)* high-grade (HG) ccRCC, *(c)* papillary RCC (pRCC), *(d)* chromophobe RCC (chrRCC), *(e)* oncocytoma (ONC), or *(f)* angiomyolipoma (AML). *Statistics:* The Spearman rank-order correlation was used to assess the correlation between ASL perfusion and DCE parameters ($p<0.05$ considered statistically significant).

RESULTS: Histopathologic diagnosis and ASL perfusion *P* and K^{trans} measurements for each subtype are shown in **Table 1**. Statistically significant differences in tumor perfusion were found among different histopathologic diagnoses **(Table legend)**. **Fig.1** shows representative ASL *and* DCE-derived perfusion maps in the same patient. Significant correlations were found between ASL *P* and K^{trans} in entire tumor (r=0.53, p=0.0083), *P* and *Kep* in entire tumor (r=0.67, p=0.0004), *P* and *Vp* in entire tumor (r=0.43, p=0.0379), *P* and *Ktrans* in high flow region (r=0.55, p=0.0081), *P* and *Kep* in high flow region (r=0.53, p=0.0003), *P* and *Vp* in high flow region (r=0.46, p=0.0285), and between *P* and iAUC in ipsilateral renal cortex (r=-0.46, p=0.0307).

CONCLUSION: ASL MRI at 3T allows for noninvasive assessment of tumor perfusion in renal masses without the need for administration of exogenous contrast. The perfusion measurements by ASL in entire tumor and in high flow region correlate with vascularity-related measurement by DCE MRI.

Table 1		LG ccRCC (n=10)	HG ccRCC (n=5)	pRCC (n=4)	chrRCC (n=1)	ONC (n=3)	AML (n=1)
ASL Perfusion (mL/min/100g)	Entire Tumor	152.80±114.31	165.29±83.21	88.66±34.69	123.84	151.48±91.87	150.56
	High Flow	295.08±178.64	253.2±183.62	107.34±28.03 (**a**)	296.757	244.81±87.49	308.848
K^{trans} (min^{-1})	Entire Tumor	1.03±0.75	0.82±0.55	0.22±0.10 (**b**)	0.32	1.14±0.62	1.22
	High Flow	2.36±1.82	1.40±0.58	0.31±0.13 (**c**, **d**)	0.37	2.04±0.77	2.02

Table legend: (**a**) Significantly lower than high flow perfusion of (LG+HG) ccRCC (p=0.0258); (**b**) significantly lower than entire K^{trans} of (LG+HG) ccRCC (p=0.0036); (**c**) significantly lower than high flow K^{trans} of (LG+HG) ccRCC (p=0.0005); (**d**) significantly lower than high flow K^{trans} of LG ccRCC (p=0.002) and than that of HG ccRCC(p=0.0159).

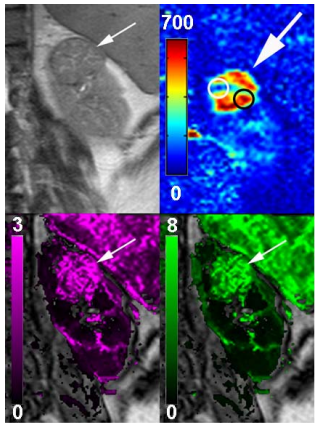
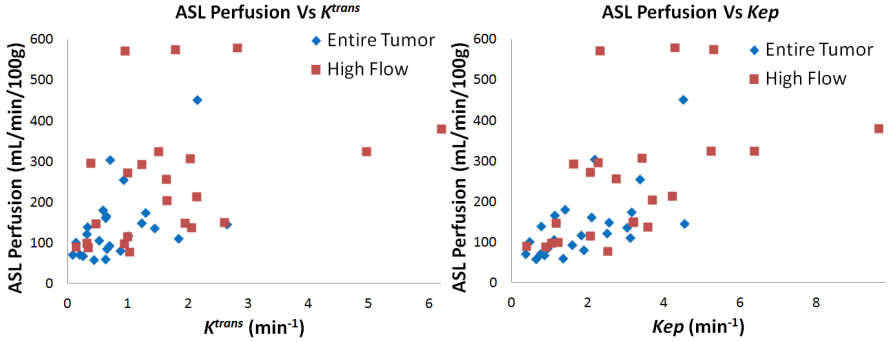


Fig.1: Above: PDW image (left) and ASL *P* map (right) in mL/min/100g for a patient with LG ccRCC. Black circle indicated high flow region and white circle indicated low flow region. Below: K^{trans} (Left) and *Kep* (Right) maps in min^{-1}.

Fig 2: Scatterplots of ASL perfusion and K^{trans} and *Kep*.



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