Tumor Angiogenesis Correlates with Metastasis in Human Prostate Cancer: An Arterial Spin-labeling MRI Study

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Purpose Angiogenesis plays a vital role in the growth, progression and metastasis process of prostate cancer (Pca), and microvessel density, a measure of tumor angiogenesis, correlates with metastasis in Pca.[1] Arterial spin labeling (ASL) MRI is a non-invasive, non-contrast enhanced imaging method capable of quantitatively measuring the blood flow (BF) which is specific to the microvascular perfusion characteristics.[2] Our previous researches[3,4] have identified that the ASL method could detect higher BF in Pca. Therefore the aim of this study is to explore the value of ASL MRI in the evaluation of incidence of metastasis in Pca with four different inversion times (TIs).

Methods The local ethics committee approved the study and 40 patients (mean 73±9 years; range 50-86 years) with pathologically confirmed prostate cancer were recruited. They were classified into two groups: localized Pca (n=22) and metastatic Pca (n=18). The MR scans were performed on a clinical 3.0T MR scanner (Signa HD; GE Healthcare, Milwaukee, Wisconsin, USA) with an 8-channel pelvic phased-array coil. The PASL protocol was performed with a fluid alternating inversion recovery (FAIR) sequence combined with a single-shot fast spin-echo (SSFSE) imaging, with four TIs (1000,1200,1400 and 1600msec) and the unchanged other parameters (TR/TRM$_0$= 3500/6000ms, flip angle = 90°, FOV=24 cm^2, slice thickness=5mm and phases=8). The regions of interest (ROIs) were placed in the prostate cancerous areas, and the average BF in these regions for each patient was measured.

Results The mean BFs in metastatic Pca were significantly higher than in localized Pca when TIs were 1000, 1200 and 1600ms, respectively (All P<0.05, Independent T-test) (Table 1, Figure 1a-d). When TI was 1400ms, the mean BF in metastatic Pca appeared higher than in localized Pca, but no statistic difference was detected (P=0.100).

Discussion The treatment options of Pca wary depending on the stage and knowing the stage helps define prognosis and survival time. This study shows a significant correlation between the BF value measured by ASL MRI and the incidence of metastases in Pca. These results are consistent with the known role of angiogenesis in the metastatic process of Pca, certificated by histopathologic and dynamic contrast-enhanced (DCE) MRI findings.[5,6] ASL is non-invasive, non-contrast enhanced method which may be an alternative to DCE MRI, significantly benefitting Pca patients with renal dysfunction or other contraindications to the administration of MR contrast-agent.

Conclusion The BF measured by ASL sequence offers a non-invasive, non-contrast enhanced marker of biologically aggressive Pca. The ASL MRI may prove valuable in selecting Pca patients for whole-body scan to detect potential metastatic lesion and for aggressive adjuvant therapies. Further work with a larger population is needed to determine the optimal TI and cut-off values of BF.

Group	BF (ml/100g/min)			
	TI=1000ms	TI=1200ms	TI=1400ms	TI=1600ms
Localized Pca	91.0±20.6	116.6±26.5	105.5±29.2	95.2±25.7
Metastatic Pca	120.2±34.3	144.7±45.9	123.6±38.7	122.3±44.5
P value	0.002	0.002	0.100	0.030

Table 1.Results of comparison of perfusion parameter (BF) between localized and metastatic Pca.
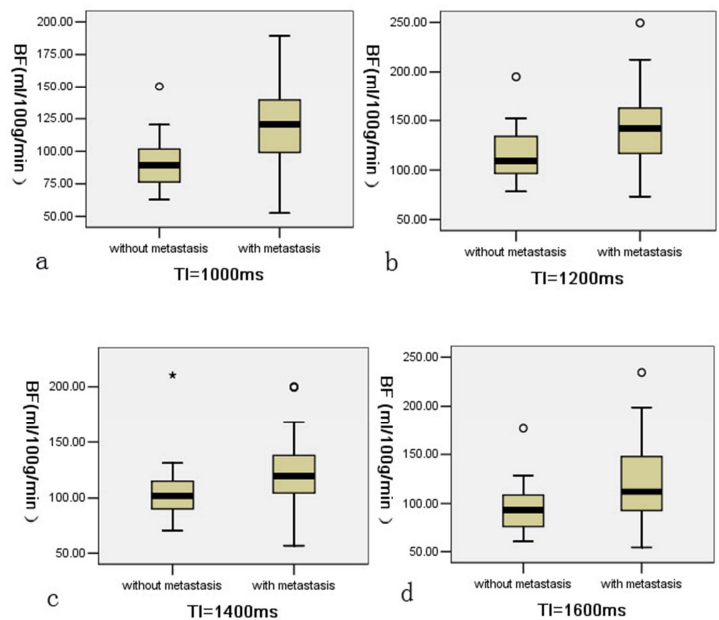
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Figure 1.Boxplots showing higher BF values in metastatic Pca compared to localized Pca.