Evaluate the efficacy of intravoxel incoherent motion imaging in predicting treatment outcome in patients with head and neck cancer

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Introduction

Intravoxel incoherent motion imaging (IVIM) holds the promise of characterizing diffusion and perfusion simultaneously within biological tissue without the need for injection of a contrast agent[1]. IVIM was applied early in the investigation of diseases such as chronic brain ischemia, liver cirrhosis, and muscle inflammatory myopathy. Recently the use of IVIM has been expanded to characterize tumor biology and has shown its superiority over conventional diffusion weighting imaging (DWI) in the detection and differentiation of prostate[2], pancreas[3] and breast tumors[4]. The purpose of the present study was to evaluate whether IVIM measures can be used to quantify tumor microcirculation in head and neck cancers, and to determine if these measures predict patient outcome.

Methods

MRI data acquisition: Sixteen patients with both primary tumor and metastatic nodes were enrolled in this retrospective study approved by local institutional review board (age: 38-64 years; M/F: 15/1; primary cancer: 11 oropharynx, 4 oral cavity and 1 nasopharynx). All patients underwent IVIM study on a GE 1.5T Excite scanner with an 8-channel neurovascular phased-array coil prior to treatment. IVIM images was acquired using a single-shot echo planar imaging (SS-EPI) spin echo sequence with 17 b values: b = 0, 13, 17, 23, 30, 40, 53, 70, 92, 122, 161, 212, 280, 369, 488, 644, and 850 s/mm^2, respectively. Other parameters were as follows: TR (repetition time) = 4000 ms, TE (echo time) = 90~104 ms, NEX (number of excitation) = 4, matrix = 128 × 128, FOV (field of view) = 20~22 cm, slices = 4~6, and slice thickness = 6-8 mm.

ROI based data analysis: IVIM based measures (ADC-apparent diffusion coefficient, f-vascular volume fraction, D-pure diffusion coefficient and D*-pseudo-diffusion coefficient) were quantified by the two compartment model[1]. Regions of interest (ROI) were drawn on both primary tumor and metastatic node for each patient (see Fig.1) excluding necrotic area by an experienced neuroradiologist. For each ROI, the values of all measures were calculated on a voxel-by-voxel basis, and summarized by the mean and standard deviation (std). The Spearman correlation coefficients (ρ) were calculated to analyze the correlation between measures of the primary tumor and neck nodal metatases, and Rank sum test was used to compare the group difference. Probabilities of progression-free survival (PFS) and overall survival (OS) were estimated using the Kaplan-Meier method.

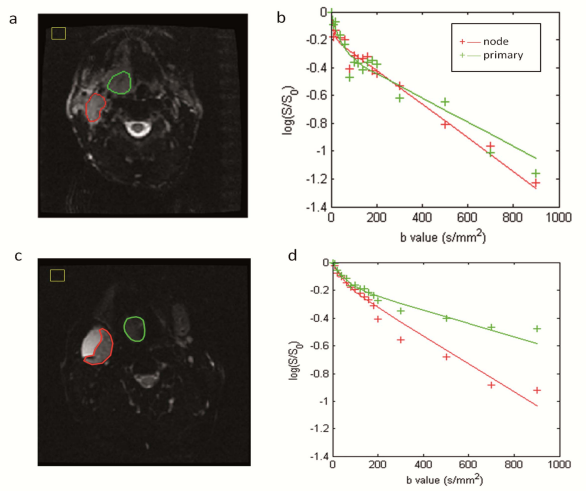

Fig.1. IVIM images and model fits from two representative patients. (a) and (b) for a patient without necrotic node (male, 54 years old, oropharynx tumor); and (c) and (d) for a patient with necrotic node (male, 56 years old, oropharynx tumor). The primary tumors and metastatic nodes excluding necrotic areas (outlined as green and red, respectively) were prescribed on IVIM images at b=0 s/mm2 in (a) and (c). IVIM model fits for the primary tumors and metastatic nodes are shown in (b) and (d). In (a) and (c), the yellow boxes depict the noise ROIs for estimating image noise.

Results

Figure 1 shows the IVIM images and model fitting plots from two representative patients, having metastatic nodes with and without necrosis, respectively. It was found that f and D was significantly different between primary tumors and metastatic nodes, and there was significant correlation of all measures (ADC, f, D and D*) between primary tumors and metastatic nodes (ρ ranged from 0.60 to 0.71; p values < 0.013; Table 1). The analysis by the Kaplan-Meier method showed that patients with lower standard deviation of diffusion coefficient (std(D)) from both primary tumors and metastatic nodes had prolonged PFS (p<0.001 for primary tumor; p=0.017 for metastatic node) and OS (p=0.037 for primary tumor; p=0.037 for metastatic node). Figure 2 displays the PFS curves for std(D) from primary tumors and metastatic nodes.

Table 1 Paired Student's t-test and correlation analysis for 16 primary tumors and metastatic nodes. (ρ - correlation coefficient, and * denotes p value<0.05)

Parameters	Primary tumor N=16 (mean±std)	Metastatic node N=16 (mean±std)	p value	Correlation coefficient ρ (p value)
ADC (10^{-3} m^2/s)	1.05±0.31	1.10±0.26	0.38	0.66(0.004)*
f	0.30±0.10	0.23±0.08	0.0009*	0.60(0.013)*
D (10^{-3} m^2/s)	0.49±0.24	0.70±0.25	0.0002*	0.71(0.0018)*
D* (10^{-3} m^2/s)	45.61±24.12	50.47±26.98	0.41	0.70(0.002)*

Discussion and Conclusion

The results demonstrate that primary tumors have distinct in vivo MR signatures with significantly higher vasculature and lower diffusion than those in metastatic nodes in head and neck cancer. All IVIM measures between primary tumors and metastatic nodes were highly correlated. It was also observed that measures of std(D) in both primary tumors and metastatic nodes were predictors of outcome (PFS and OS). However, std(D) from primary tumors had higher sensitivity in predicting PFS than from metastatic nodes. After appropriate validation in larger patient population, these findings may provide better understanding of the underlying tumor biology, and might be useful in optimizing treatment planning and improving patient care.

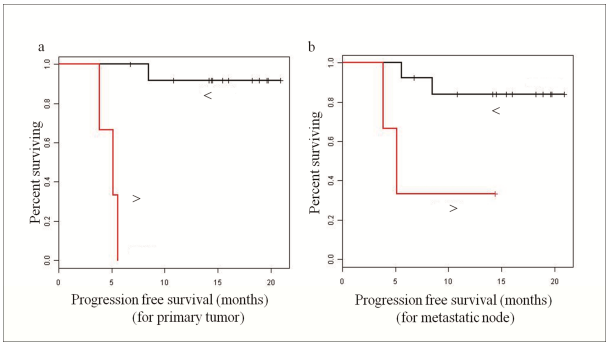

Fig 2. Kaplan-Meier progression-free survival (PFS) plots: (a) Patients stratified at median std (D) of primary tumor, and (b) patients stratified at median std (D) of metastatic node. Note: In both Figure (a) and (b), red lines represent the plot with std (D) > median, and the black lines represent the plot with std (D) < median. The dots above each line represent censored observations.

Acknowledgments

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References

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