Tumor Volume Measurement in Prostate Cancer using Diffusion-Weighted Imaging: Initial Results

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Introduction: Accurate non-invasive measurement of prostate cancer tumor volume could significantly contribute to the determination of tumor prognosis and the selection of appropriate treatment. This has been indicated by findings that pathologic tumor volume correlates with pathologic stage, pathologic Gleason grade, margin status, and disease progression after radical prostatectomy [1][2]. Moreover, tumors smaller than about 0.5 cm^3 are considered to be insignificant [3] and potentially appropriate for deferred therapy. Previous studies of tumor volume assessment by magnetic resonance imaging (MRI) alone [4] and MRI combined with MR spectroscopic imaging (MRSI) [5] were limited by measurement variability, particularly for small tumors. Recent reports have suggested that apparent diffusion coefficient (ADC) maps calculated from diffusion-weighted imaging (DWI) may have clinical utility in prostate cancer diagnosis. The purpose of this study was to present a method to measure tumor volume from ADC maps and to assess the accuracy of the measurements, using whole-mount step-section pathology after radical prostatectomy as the gold standard.

Method: This retrospective study included 26 prostate cancer patients with no prior treatment who underwent preoperative MRI/DWI. The clinical characteristics of the patient population were: age 42-72 years (median 61 yrs.), PSA level at diagnosis 0.58-9.6 ng/mL (median 5.7 ng/mL), surgical Gleason score 6-9 (median 7). Thirty-two lesions had pathological volume $\geq$ 0.1 cm^3 and were evaluated. At surgical pathology, tumor volumes ranged from 0.12 to 12.79 cm^3 (median 0.49 cm^3); Gleason scores were: 3+3: 14/32 (44%); 3+4: 11/32 (34%); 4+3 or greater: 7/32 (22%).

***MR Acquisition*:** MR examinations were performed on 1.5T GE whole-body MRI units. For signal reception, endorectal receiver coils were used. DW images were obtained using single-shot spin-echo EPI. Imaging parameters were: TR/TE = 4000/99.8 ms, FOV = 14×14 cm^2, 72×72, 3-mm slice thickness, 0 gap, 4-8 NEX. The b-values were 0 and 800 s/mm^2.

Image Analysis: ADC maps were generated from the original DW images after convolution with a Gaussian blur function (FWHM=2 mm). To correct for susceptibility-related distortions affecting the ADC maps, affine transformation was used with 12 parameters (3 shifts + 3×3 matrix for rotation, scaling, and shearing) to warp the ADC map to match the corresponding T2w image. Clusters of voxels (contiguous regions) were designated as tumor if they met the following criteria: 1) The cluster was located in the peripheral zone; 2) ADC values of the voxels were within the threshold limits specified by our prior study [5]; 3) voxels that satisfied the ADC criteria were located within 5 mm of each other; 4) 165+ voxels in the cluster satisfied the above criteria (i.e., the cluster volume was $\geq$ 0.15 cm^3). A convex hull contour was drawn to include all voxels in each cluster. Tumor volumes measured by DWI were compared to the measurements on histopathological slides using paired t-tests, after correction for prostate shrinkage after surgery. Mean tumor cluster ADCs were also measured and compared to the threshold ADC criteria (Fig. 1).

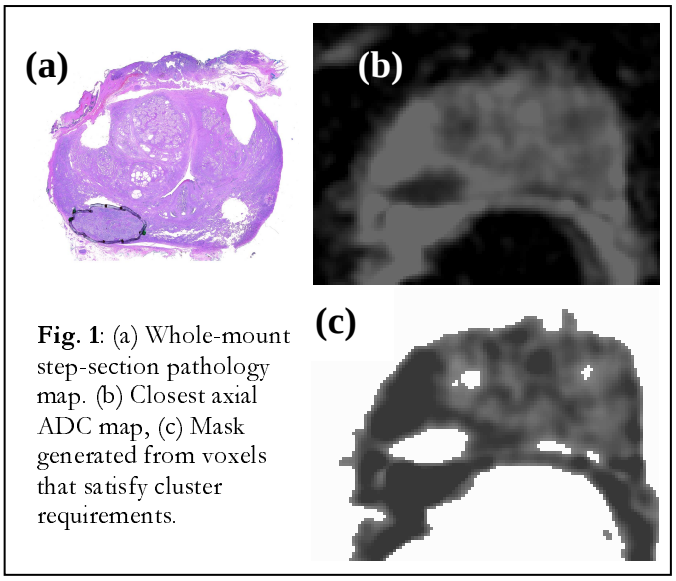

Fig. 1: (a) Whole-mount step-section pathology map. (b) Closest axial ADC map, (c) Mask generated from voxels that satisfy cluster requirements.

Results and Discussion: Tumor volumes measured as clusters of voxels on ADC maps correlated significantly with tumor volumes measured on histopathology (p value=0.021) (see Table). These initial findings suggest that the approach used here (combining a statistical ADC threshold and other specific criteria to define tumor-containing voxel clusters) is a robust method to measure prostate tumor volume by DWI.

Cluster Volume (mm^3)	Pathology Lesion Volume (mm^3)	p value		ADC Threshold ($x10^{-3}$) mm^2/s	Cluster ADC ($x10^{-3}$) mm^2/s
1.21 (0.18-13.2)	**1.05 (0.12-12.79)**	**0.021**		**1.39 (0.97-1.74)**	**1.46 (1.2-1.42)**

References: [1] McNeal JE, et al. Cancer 1990; 66:1225-1233. [2] Epstein JI, et al. Cancer 1993; 71:3582-3593. [3] Egevad L, et al. Urology 1998; 52:653-658. [4] Ponchietti R, et al. Eur Urol 1999; 35:32-35. [5] Coakley FV, et al. Radiology 2002; 223:91-97. [5] Mazaheri, et al. ISMRM, 2006; p. 3497.