The Utility of Diffusion-Weighted MRI in Cervical Cancer

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Introduction:

Apparent Diffusion Coefficient (ADC) maps derived from Diffusion-Weighted MR imaging (DWI) provide a quantitative measure which reflects all forms of intravoxel incoherent motion [1]. Tumor oxygenation (pO_2) and interstitial fluid pressure (IFP) are examples of microenvironment parameters which may influence ADC and have been shown to be significant prognostic factors in cervical cancers treated with radiation and surgery [2]. We examined differences in ADC between cervix carcinoma and normal cervix tissue, the correlation between ADC and invasive microenvironment measures such as IFP and tumor pO_2, and tested the ability of ADC measurements to predict early response to chemoradiation therapy.

Methods:

Diffusion-Weighted MRI was performed in 47 patients with cervical cancer (37 squamous carcinoma) undergoing chemoradiation therapy and 26 normal controls on a 1.5T system (Signa LX Echospeed Plus, GE Healthcare) using an 8 channel body coil. Axial and sagittal T2 weighted images were acquired for anatomical registration. An axial echo planar DWI pulse sequence was employed with the same slice locations as the T2 images (b-val 600 s/mm^2, TR 4000ms, TE 68ms) using the optimized TE option and ASSET (Array Spatial Sensitivity Encoding Technique) parallel imaging. IFP was measured using a wick-in-needle apparatus, and oxygen tension was measured using a polarographic needle electrode system (Eppendorf-Netheler-Hinz, Hamburg, Germany) [2].

Results:

The average mADC value (mean of all individual patient mADC values) of the cervical carcinomas was found to be $1.09\pm0.20\text{x}10^{-3}$mm^2/s, and that of the control cervical tissue to be $2.09\pm0.46\text{x}10^{-3}$mm^2/s. The difference in mADC between the two groups was significant ($P<0.001$). The mADC of FIGO stage T1b/T2a disease was significantly lower than that of all other stages ($P=0.002$). In a sub-analysis of only squamous cell carcinoma cases, the 90th percentile of the ADC histogram was found to be significantly lower in patients who responded to therapy compared to those who showed progressive disease ($P=0.039$). Within the entire study population, there was no observed correlation between ADC and nodal status, tumor volume/grade, or any of the microenvironment parameters (IFP, mO_2, HP5).

Discussion:

Diffusion in tumor tissues was found to be significantly lower than in normal cervical tissue, possibly reflecting greater cell density. A relative shift of water from the extracellular (ECV) to intracellular (ICV) compartments has been identified with the drop in ADC observed in ischemic stroke as there are fewer barriers to free diffusion in the ECV. It follows that an increase in local cellularity will cause a decrease in the ECV/ICV ratio, lowering the measured ADC. While we observed no distinction between histologic tumor grades based on ADC, grading includes factors such as nuclear size and necrosis which may have competing influences on ADC. Necrotic areas present in high-grade tumors may raise the ADC due to an increase in ECV, while the smaller nuclei of low-grade tumors reduce intracellular resistance to water diffusion. Our study did not find any relationship between ADC and tumor oxygenation, nor between ADC and IFP. It is possible that such a relationship does not exist, however since tumor physiology is known to be a dynamic process we expect spatial and temporal variation in the oxygenation and interstitial fluid pressure over the course of hours. As the MR imaging was not conducted on the same day as the invasive measurements, the degree to which these correlations were affected is not known. The significant separation between early and late FIGO stage disease may prove a useful factor in treatment planning; early FIGO stage disease (below IIb) is more amenable to surgical resection and ADC measurements could better inform cases where the extent of progression is uncertain.

References:

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2. Fyles A. **Radiother Oncol**; 80:132-137 (2006).