Focus on DWI in Cancer

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Highlights

- **DWI can be readily used for cancer treatment response assessment.**
- **Applications include assessment of mouse tumor models along with clinical patients.**
- **Quantification can be accomplished by using whole tumor and voxel-based metrics.**

Introduction

Diffusion-weighted imaging (DWI) offers insight into cellular edema, density and cyto-architecture by way of sequences sensitive to water mobility affected by these features [1, 2]. This feature provides an opportunity to apply this imaging modality for assessing cancer treatment response. Single-shot echo-planar imaging is the most widely used technique [3], although specialized multi-shot approaches may offer advantages [4]. Outside of the brain, however, greater tissue motion usually necessitates use of single-shot techniques. Baseline SNR and diffusion anisotropy drive the choice of diffusion sensitivity (i.e. "b-value") and multiplicity in gradient directions. There is also a variety of techniques to analyze diffusion data driven by the specific clinical/scientific application. Basic analyses to exhibit relative mobility as normalized DWI and apparent diffusion coefficient (ADC) maps are useful for lesion detection and diagnosis. However, more elaborate quantitative analyses are typically employed in oncology where the distinction between viable cellular, edema, and necrotic zones are desirable for treatment planning. Serial changes in tissue cellularity in response to therapy are also measurable by diffusion using various quantitative methods that can be used to extract quantitative metrics using whole-tumor ADC average, histogram analysis, and pre-treatment vs post-treatment voxel-by-voxel differences. Applications of DWI in both preclinical cancer animal models as well as in the clinical setting provide for outstanding translational applications of this imaging modality. This lecture will provide an overview of basic methodologies and applications of DWI to oncology.

Acquisition Issues

The vast majority of human neuro DWI studies to date have been performed using a diffusion sensitivity range of b≈0 to 1000sec/mm^2 since it offers good contrast across tissue water mobility environments and provides consistent ADC values across multiple field strengths and platforms. Greater b-values can be achieved on clinical systems (e.g. 2000 - 5000 sec/mm^2) but such heavy diffusion weighting is only useful for the minority of tissues where signal persists above the noise floor. Several studies have demonstrated tissue exhibiting multi-exponential diffusion behavior which is best observed over an extended b-value range [5-8]. This phenomenon may represent a means to further segregate pathology and response on a more fundamental biophysical scale. In the abdomen, higher tissue ADC values and lower baseline SNR, typically limit DWI protocols to lower b-values (<500 sec/mm^2). Furthermore, contrast from "hyper" diffusion-like motions, such as blood flow, can be manipulated at very low b-values.

Neuro tissue is highly anisotropic and requires multi-directional diffusion-weighted scans. If one is only interested in average diffusivity, a minimum of 3-orthogonal DWI scans are required plus one b≈0 for calculation of ADC. Typically, for following treatment-induced changes in ADC values the average diffusivity is used. If maps of diffusion anisotropy (e.g. fractional anisotropy) or white matter fiber track integrity are desired for assessment of the impact of a brain tumor on adjacent brain tissue, then greater directional sampling by diffusion tensor imaging (DTI) is required with at least 6 directions plus one b≈0. Neuro tissue exhibits strong anisotropy whereas anisotropy in nearly all other soft tissues is relatively modest [9-14].

Analysis Issues

ADC maps generated from DWI and DTI data have proven helpful in defining solid enhancing tumor, non–enhancing lesion, peritumoral edema, and necrotic or cystic regions from normal surrounding brain tissue. ADCs of cellular dense brain tumors, such as medulloblastoma and meningioma, range 0.6 to 0.8 x 10^{-3} mm^2/s, whereas the ADCs for solid enhancing high-grade glioma span 0.8 to 1.3 x 10^{-3} mm^2/s; and greater for necrotic cyst. Serial whole-tumor average ADC values as a function of time following therapy are also being used as a potential biomarker of therapy response. Given inevitable tumor heterogeneity, some have adopted histogram analysis techniques to stratify tumor based on water mobility which infers cellularity [15]. Alternatively, voxel-by-voxel subtraction of spatially-registered pre-treatment from post-treatment ADC maps provides not only the change in whole-tumor average ADC, but also the spatial pattern ADC change and the fractional volume of tumor exhibiting this change [16, 17]. These indices are all being investigated as biomarkers of response. Merit and challenges of these methods applied to mouse models along with clinical examples of brain and body DWI will be presented [18-21].

References:

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