Diffusion Basis Spectrum Imaging Detects Microstructural Heterogeneity in Human Glioma

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Introduction

MRI is the preferred imaging modality for high-grade gliomas but is limited in characterizing tumor microenvironment. Diffusion basis spectrum imaging (DBSI), based on diffusion tensor, has previously been utilized to quantitate axonal disturbances and CNS inflammation. We hypothesized DBSI can quantitatively visualize the glioma microenvironment.

Methods

Glioma samples (n=20) were fixed and subjected to traditional MRI and DBSI ex vivo. DBSI parameters—anisotropic diffusion fraction (fiber fraction), restricted isotropic diffusion fraction (restricted fraction), and hindered isotropic fraction (hindered fraction) maps—were generated. Immunohistochemistry was performed on sections. Digitized histology images were quantified to generate tumor density maps and compared with DBSI measures. High-throughput analysis was performed with support vector machine (SVM) learning utilizing a training subset that was then applied to a validation set of remaining samples. Three patients underwent preoperative DBSI.

Results

Using a representative tumor sample, a neuropathologist compared DBSI maps with the tumor density map. We discovered that the DBSI restricted fraction map correlated with hematoxylin nuclear counts as well as GFAP-positive cells. The DBSI restricted fraction map predicted the quantitative histology map (90.2% correlation, $P<0.01$), suggesting DBSI can predict cell density in high-grade glioma. We next employed SVM learning for high-throughput analysis to validate these findings and also to extend our analysis to DBSI fiber and hindered fractions. We found fiber fraction correlated with white matter tracts and hindered fraction with tumor necrosis. SVM analysis correctly predicted areas of hypercellularity (97.3%), necrosis (100%), and white matter disruption (85.0%) within a tumor. Finally, in three tumor patients, DBSI-defined tumor heterogeneity was observed.

Conclusions

DBSI parameters correlate with specific aspects of tumor microstructure. DBSI can predict tumor microenvironment quantitatively and can successfully be applied to tumors in vivo. These results have implications for noninvasive interrogation of tumor microenvironment, which may prove useful for diagnosis and for monitoring treatment response versus recurrence.

Learning Objectives

By the conclusion of the session, participants should be able to:

1) Understand diffusion basis spectrum imaging

2) Identify differences in tumor microenvironment

3) Apply diffusion basis spectrum imaging to gliomas

4) Understand support vector machine learning application to large pathology data sets

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