

Tissue dynamics spectroscopic imaging: functional imaging of heterogeneous cancer tissue

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Abstract

Significance: Tumor heterogeneity poses a challenge for the chemotherapeutic treatment of cancer. Tissue dynamics spectroscopy captures dynamic contrast and can capture the response of living tissue to applied therapeutics, but the current analysis averages over the complicated spatial response of living biopsy samples.

Aim: To develop tissue dynamics spectroscopic imaging (TDSI) to map the heterogeneous spatial response of tumor tissue to anticancer drugs.

Approach: TDSI is applied to tumor spheroids grown from cell lines and to *ex vivo* living esophageal biopsy samples. Doppler fluctuation spectroscopy is performed on a voxel basis to extract spatial maps of biodynamic biomarkers. Functional images and bivariate spatial maps are produced using a bivariate color merge to represent the spatial distribution of pairs of signed drug-response biodynamic biomarkers.

Results: We have mapped the spatial variability of drug responses within biopsies and have tracked sample-to-sample variability. Sample heterogeneity observed in the biodynamic maps is associated with histological heterogeneity observed using inverted selective-plane illumination microscopy.

Conclusion: We have demonstrated the utility of TDSI as a functional imaging method to measure tumor heterogeneity and its potential for use in drug-response profiling.

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1 Introduction

Tumor heterogeneity presents a challenge for the successful treatment of cancer using chemotherapeutics.¹ For instance, genetic variability in tumors caused by clonal outgrowth of selected genotypes within a tumor may cause subsets of cells with genetic variations to be resistant even while the majority of the tumor responds to treatment. Selective pressure and genetic drift of the cancer cell population during treatment often lead to patient relapse and the

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