Enhancement Pattern Mapping (EPM) Signatures in pre-diagnostic MRIs Associate with Hepatocellular Carcinoma Time-to-Disease and Differentiate Cases/Controls

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Cancer early detection research aims to improve survival rates of highly lethal cancers such as Hepatocellular Carcinoma (HCC). We used a previously described voxel-wise image processing method called Enhancement pattern mapping (EPM) to test the hypothesis that EPM can predict risk of HCC prior to clinical diagnosis. We collected Magnetic Resonance Imaging (MRI) scans from patients undergoing liver surveillance due to high HCC risk from cirrhosis, identified cases (developed HCC, n=42), controls (no HCC, n=61), and analyzed at least two MRIs for each patient (median time between MRIs of 43.2 months, range of 111 months) with EPM. Here, we analyzed EPM as a method to differentiate cases from controls and evaluated changes in EPM as a predictor of time-to-disease (measured from date of MRI to date of HCC diagnosis). Preliminary results from log rank and cox proportional hazard models indicate that cases with high absolute changes in lesion EPM mean per day have shorter times-to-disease (median time 184 days) compared to those with low absolute changes per day (median time 286.5 days) (p=0.0007, HR=3.44). Similarly, cases with high absolute changes in lesion EPM mode per day have shorter times-to-disease (median time 189.5 days) compared to cases with lower absolute EPM mode changes per day (median time 311.5 days, Figure 1) (p=0.001, HR=3.03). Internal validations of log rank and cox proportional hazards model results were performed using receiver operating characteristic (ROC) curve analysis using absolute changes of EPM mean and mode per day to differentiate cases from controls. Validation results using ROC area under the curve (AUC) indicate the proportional hazards model's ability to differentiate controls from cases (AUC=0.97, Figure 2) and that absolute changes of EPM mean and mode per day may be able to predict those most at risk of developing HCC. Ongoing work will incorporate clinical factors, such as cirrhosis etiology, age, and sex, into a multivariable model to predict HCC risk. With proper validation, our work may help identify those at the highest risk of HCC at earlier, curable stages.

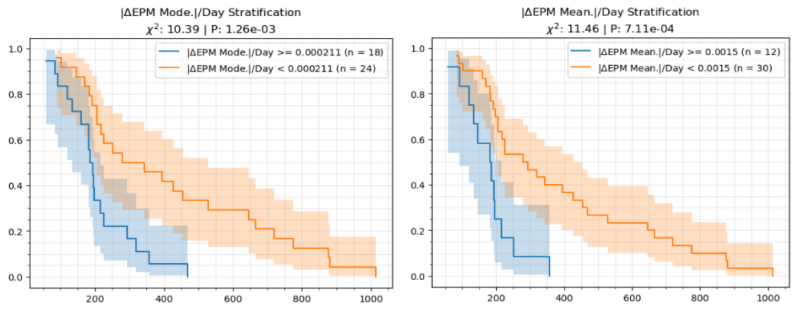

Figure 1. Kaplan-Meier analysis of EPM changes in cases illustrates that cases with higher absolute changes in EPM mean and EPM mode per day are more likely to have shorter times-to-disease than cases which do not have these EPM signals.

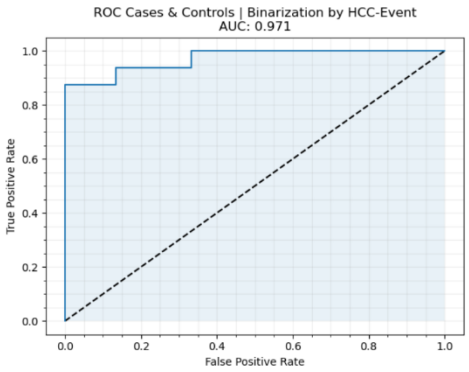

Figure 2. Receiver operating characteristics (ROC) curve of proportional hazards model indicates absolute changes in EPM mean and mode per day are capable of differentiating patients who develop HCC from those who do not. ROC curve was created using a 70% to 30% split of training to testing data.