A NOVEL AI-DERIVED METRIC IDENTIFIES OPTIMAL CANDIDATES FOR FOCAL THERAPY OF PROSTATE CANCER AND ACCURATELY PREDICTS TREATMENT MARGIN EFFICACY

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BACKGROUND, **INTRODUCTION, AND AIMS**: Successful prostate cancer focal therapy (FT) requires careful candidate selection and application of a treatment margin around MRI regions of interest (ROIs). Existing tools and guidelines are imperfect, contributing to appreciable rates of residual disease in FT trials to date. A data-driven tool for identifying optimal FT candidates and predicting margin efficacy is needed.

A machine learning algorithm was developed to estimate voxel-level risk of clinically significant prostate cancer (csPCa), resulting in a 3D cancer probability map (CPM). A novel metric, the Marks Confidence Score (MCS), was developed to predict the probability that a CPM-derived margin encapsulates all csPCa. The study objective was to predict margin efficacy and to select optimal FT candidates using the MCS metric.

MATERIALS AND METHODS: A machine learning model was developed using multi-institutional data from 875 patients. Input data consisted of T2-weighted MRI, surface models of the prostate and PI-RADS region(s) of interest, and tracked biopsy cores. The model combined a convolutional neural network with a gradient-boosted decision tree, and was trained using 5-fold cross validation. CPMs (Fig-A) were generated for 50 whole mount (WM) prostatectomy cases with localized GG2-3 csPCa. The MCS was defined as the proportion of these cases with complete csPCa encapsulation at each CPM threshold.

A second set of comparable WM data from an external institution (N = 50, Stanford University) was used to validate the MCS (Fig-B). Observed csPCa encapsulation rates were compared to MCS predictions for this held-out data. Furthermore, for each case the area under the Marks Confidence curve (mAUC) was computed after plotting MCS versus margin volume (Fig-C). It was hypothesized that patients with a high mAUC (≥ 0.6, N = 24/50) would be more optimal FT candidates.

RESULTS: There was no significant difference (Kolmogorov-Smirnov, p = 0.99) between the observed and MCS-predicted csPCa encapsulation rate (Fig-D), with a median error of 4% (IQR 2%-6%). Using mAUC to identify FT-optimal candidates, the mean margin volume required for csPCa encapsulation was lower for FT-optimal (31%) versus suboptimal (52%) cases (p = 0.001, Mann-Whitney). In the 25%-50% margin volume range (Fig-E, yellow), csPCa encapsulation rates were 40%-50% higher for FT-optimal versus suboptimal cases.

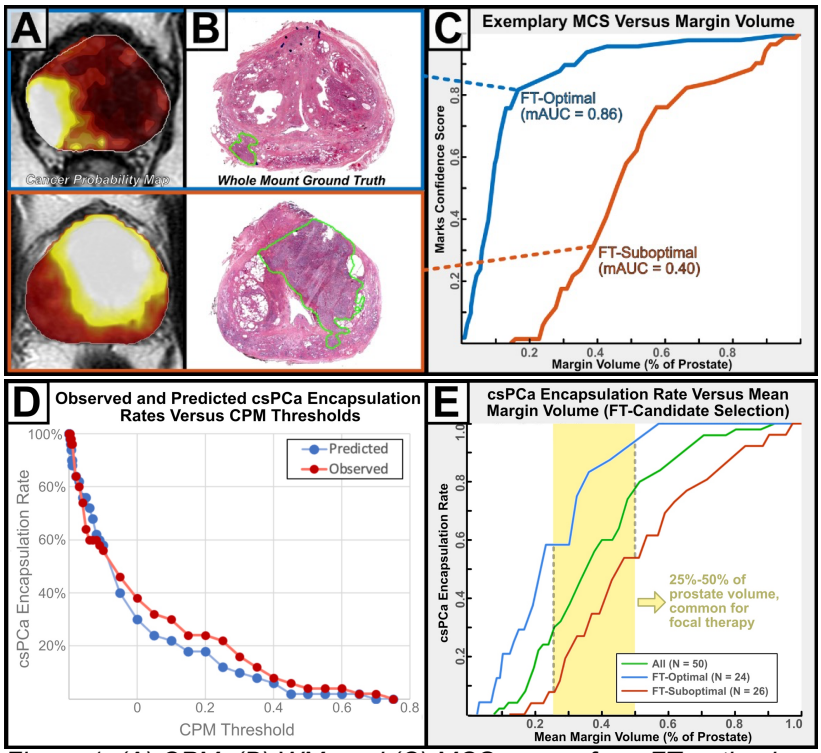

Figure 1: (A) CPM, (B) WM, and (C) MCS curves for a FT-optimal and FT-suboptimal case. (D) shows that csPCa encapsulation closely matches MCS predictions, and (E) compares FT-optimal and FT-suboptimal mean margin volumes necessary for csPCa encapsulation.

DISCUSSION AND CONCLUSION: The Marks Confidence Score accurately predicted csPCa encapsulation probability in an independent population of intermediate-risk prostate cancer patients, demonstrating its utility to assess FT suitability and margin efficacy. The MCS was also used to identify a FT-optimal subpopulation for whom substantially smaller margins would be required for treatment. This metric could be used to improve and standardize patient selection and margin definition for prostate cancer focal therapy.

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