SCHOOL OF MEDICINE
SURGERY

Podium Presentation 1

Improving Predictive Accuracy of Artificial Intelligence Model of Response to Neoadjuvant Chemotherapy in Breast Cancer

Presenter: Sangeetha Prabhakaran MD, FACS

Sangeetha Prabhakaran MD, FACS; Kushal Virupakshappa PhD; Upasana Rai PhD; Nadja Falk MD; Jain Zhou MD; David Martin MD; Fred Schultz MA; Avinash Sahu PhD;

Background: Response to neoadjuvant chemotherapy in breast cancer with pathologic complete response (pCR) is associated with improved patient outcomes. The rates of pCR vary with breast tumor subtype and therapy given; however overall rates remain low (<30%). Predictive studies of pCR from core biopsy pre-treatment core needle biopsy samples, if successful, would lead to better patient selection and improved outcomes.

Methods: We used the HALO pathology system to train and validate an AI algorithm designed to predict pCR to neoadjuvant chemotherapy of breast cancer based on pre-treatment core needle biopsies. We performed retrospective chart review of clinical, demographic and treatment response variables, notably percent tumor cellularity which indicated residual tumor remaining after neoadjuvant systemic therapy. We used Surgery Research Investigator Award grant funding to train and test AI technology on core needle biopsies of breast cancer patients as an initial proof of concept.

Results: We previously reported our results that the algorithm identified patterns predictive of treatment response to neoadjuvant therapy (as evidenced by residual tumor on final surgical pathology). We initially used the median cut off residual tumor cellularity to define tumors as sensitive or resistant to neoadjuvant chemotherapy. AI analysis of 259 cases (126 Resistant, 133 Sensitive) was performed. After training on 155 cases (75 Resistant and 80 Sensitive), we ran the algorithm on a test set of 104 (51 Resistant and 53 Sensitive). The algorithm marked up the test images as either Resistant or Sensitive. We reviewed results using multiple magnification; tumor only; expanded mark-ups with both 5.5x as well as 10x magnification. The categorization was only slightly better than chance using this 50% correct-call cutoff. The algorithm however substantially performed better identifying Resistant than Sensitive cases.

We then addressed cellularity prediction as a 4-class classification task, categorizing tumor cellularity into: <25%, 25–50%, 50–75% and 75–100%.Using CLAM (a multiple instance learning framework with attention mechanisms) on whole-slide images (with and without tumor makers multimodal/unimodal) and we achieved a baseline accuracy of 56% AUC (for both multimodal and unimodal approach).

Conclusions: The AI algorithm can overall better predict cases resistant to neoadjuvant chemotherapy than sensitive cases. However, this deep learning approach faces challenges due to complicating model debugging and difficulty isolating failure modes in established architectures. To address these limitations, we're now exploring interpretable approaches: texture patterns, collagen density quantification, etc. as features for simple ML approaches

Podium Presentation 1

Improving Predictive Accuracy of Artificial Intelligence Model of Response to Neoadjuvant Chemotherapy in Breast Cancer

like logistic regression, decision trees, etc. This shift aims to improve interpretability through engineered biomarkers, reduce dependency on large training datasets and establish clearer performance baselines for comparison. In addition to the above, we are exploring incorporating radiologic response to systemic therapy using pre-treatment and post-treatment MRI breasts into our algorithm to improve its predictive capability.

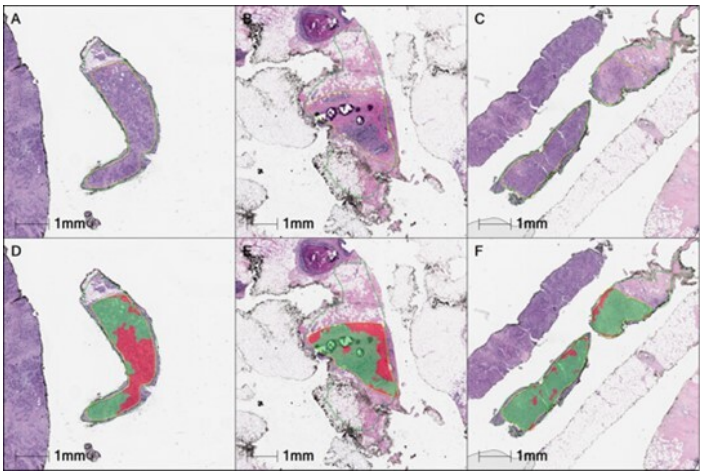

Figure 1a: Sensitive cases markup example. Pre-treatment core needle biopsies of cases predicted as sensitive to treatment by HALO. Green areas are more sensitive to treatment

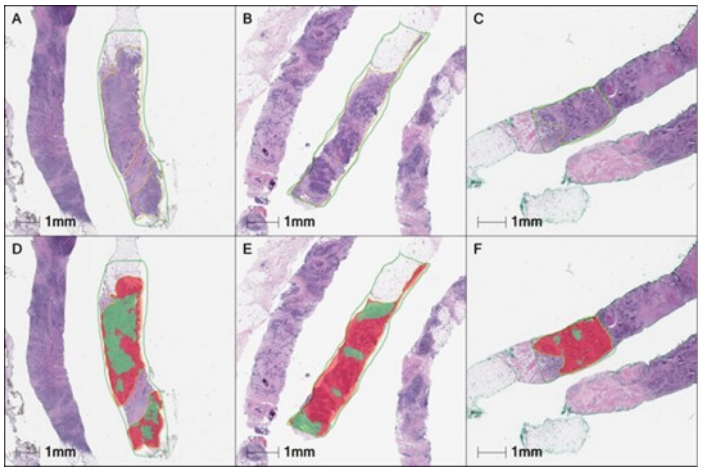

Figure 1b: Resistant cases markup example. Pre-treatment core needle biopsies of cases predicted as more resistant by HALO. Green areas are sensitive to treatment and red areas are resistant.