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Panakeia

Evaluation of a predictive method for the H&E-based molecular profiling of breast cancer with deep learning

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BACKGROUND & AIMS

Growing pathology workforce shortages, increased incidence of cancers and increasing requests for molecular testing have resulted in demanding pathology workloads across the NHS. The primary techniques for profiling the molecular biomarkers of breast cancer are immunohistochemistry (IHC) and in-situ hybridization (ISH). These tests pose a great challenge for the current standard practice, as they account for a large proportion of the high turnaround time for breast cancer biopsy diagnosis due to IHC/ISH preparation requiring specialised, quality-assured, laboratory work with dedicated equipment, expensive reagents and additional pathologist time **Figure 1.**

OUR APPROACH TO THIS PROBLEM

To address this issue, Panakeia has developed an AI-based, CE-marked medical device which can provide pathologists with accurate cancer biomarker status, simply by analysing diagnostic H&E biopsy images. The first device focuses on breast cancer and provides Oestrogen Receptor (ER), Progesterone Receptor (PR) and Her2 status as text output by analysing H&E biopsy images of breast cancer tissue.

METHODS

A proprietary convolutional neural network (CNN) model was used to determine the status of molecular profiles for breast cancer. The workflow of the prediction of breast cancer molecular profiles from H&E images with deep learning is illustrated in **Figure 2.** Each model was trained on a set of 256x256 tiles acquired from whole slide images (WSI) stained with H&E. In the first step of the pipeline, the image is broken down into tiles. A standard deviation filter is used to eliminate the background tiles which do not contain any relevant information. Then, an independent tumour segmentation model is used to detect the tumour regions and discard non-tumour regions. Data was acquired from 1) the Cancer Genome Atlas (TCGA) open-access dataset for the breast adenocarcinoma (BRCA) study (i.e TCGA-BRCA) and 2) a proprietary dataset by a private clinical data provider (e.g. BioIVT). To ensure confounder independence and show generalisability during validation, different TCGA labs were chosen for model selection and validation. For the clinical evaluation study, a subset of the TCGA-BRCA dataset was used, which only contained images from laboratories that were not included in model selection.

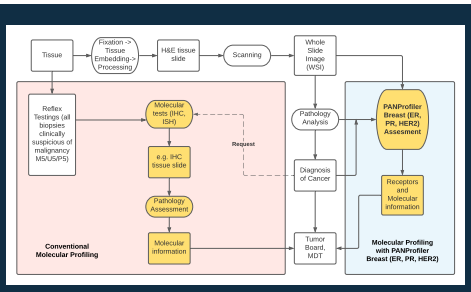

Figure 1. Breast cancer diagnostic pathway with the traditional molecular testing (red) and with PANProfiler Breast (ER, PR, HER2) (blue).

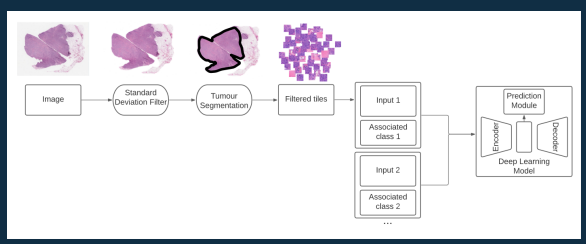

Figure 2. Visualisation of the training pipeline demonstrating filtering and cancer segmentation.

Biomarker	TRR	Accuracy	PPV	NPV
ER	89%	87%	87%	86%
PR	48%	83%	83%	79%
HER2	78%	87%	N/A*	87%
HER2-ISH§	82%	90%	N/A*	90%

Table 1. Final performance metrics for each biomarker. The final method is only allowed to predict negative results for HER2

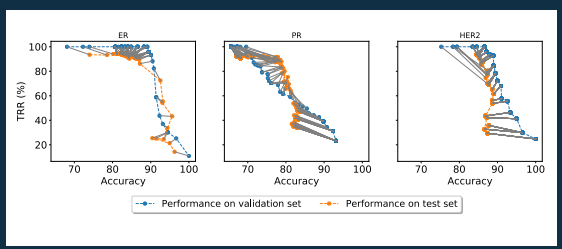

Figure 3. The relationship between accuracy and TRR in accordance with the predictive thresholds computed on a validation set (blue line) and applied to a test set (orange line).

DISCUSSION OF RESULTS

Table 1. For ER, the device achieved good performance for every considered metric. PR follows a very comparable trend with regards to accuracy, PPV, and NPV. Despite a relatively low TRR (Test Replacement Rate), its effectiveness is similar to that of ER. A high level of TRR was seen for HER2 and its general performance was on par with ER. As the method was only allowed to predict negative results for HER2, PPV was not applicable. During validation, a noticeable tradeoff between TRR and Accuracy was observed **Figure 3**.

CONCLUSION

PANProfiler Breast (ER, PR, HER2) is built upon deep-learning models that can be used to infer the status of ER, PR and HER2 directly from digitally scanned H&E-stained biopsy/resection slides. Clinical validation results show the effectiveness of the device as a predictive tool that can reduce the need for the current standard tests used for profiling the molecular biomarkers of breast cancer.