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Prediction of distant relapse in patients with invasive breast cancer from deep learning models applied to digital pathology slides

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Background

Breast cancer (BC) has a favorable long-term prognosis, with an estimated average 5-year survival rate of 87%. Nevertheless, 10% of patients relapse after initial treatment each year. To better identify these patients, Owkin and Gustave Roussy conceived a diagnostic tool that applies deep learning (DL) to whole slide images (WSI) and clinical data, that could work as an aid in therapeutic decision.

Methods

1437 patients diagnosed with ER+HER2- BC between 2005 and 2013 were included. All patients underwent surgical resection, with full follow-up and an available hematoxylin-eosin stained glass slide, which was digitized, preprocessed and cut into small patches called *tiles*. These tiles were fed into the DL network along with survival information. A weighted average of tile features was computed to predict a risk of relapse. Cox models based on baseline clinical variables (BV) (age at surgery, tumor stage and size, number of positive nodes (N+), number of nodules, surgery type) and extended clinical variables (EV) (combining BV with ER/PR/HER2 Status, Grade, Ki67, Histological Type) were also considered. Performance was evaluated using cross-validation. Metastasis free interval was chosen as primary endpoint. Uno's time dependent AUC was used as a metric to quantify the discrimination capability of the models.

Results

The prediction of 5-year survival based solely on BV yielded an AUC of 0.77. DL algorithm based solely on WSI yields an AUC of 0.77. A model based on EV yielded an AUC of 0.80. Combining BV with our DL algorithm resulted in an improved AUC of 0.81. This model also predicted relapse in ER+HER2-N0 (AUC=0.77) and ER+HER2-N+ (AUC=0.80) subgroups. Validation will be carried out on large independent cohorts from external health care centers.

Conclusions

DL applied to WSI could predict the risk of relapse in early ER+HER2- BC patients. Coupled to BV, our model could be a promising tool for treatment decision-making at low cost. Our next steps are to unravel the most predictive tiles to discover new biomarkers, and to develop novel models for prediction of relapse, as an alternative to onerous techniques such as immunohistochemistry or molecular tests.

Legal entity responsible for the study

Gustave Roussy.

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Owkin.

Disclosure

C. Saillard, B. Schmauch, V. Aubert, A. Jaeger, A. de Lavergne, A. Kamoun, P. Courtiol: Financial Interests, Institutional, Full or part-time Employment: Owkin. F. André: Financial Interests, Institutional, Other, speaker/advisor: Roche; Financial Interests, Institutional, Other, speaker/advisor: AstraZeneca; Financial Interests, Institutional, Other, speaker/advisor: Daiichi Sankyo; Financial Interests, Institutional, Other, speaker/advisor: Pfizer; Financial Interests, Institutional, Other, speaker/advisor: Novartis; Financial Interests, Institutional, Other, speaker/advisor: Lilly. All other authors have declared no conflicts of interest.