Artificial intelligence-based breast cancer detection facilitates automated prognosis marker assessment using multiplex fluorescence immunohistochemistry

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Background

Prognostic markers in routine clinical practice of breast cancer are often assessed using RNA based multi-gene panels that are depending on a fluctuating tumor purity. Multiplex fluorescence immunohistochemistry (mIFHC) holds the potential for improved risk assessment.

Materials & Methods

To enable automated prognosis marker quantification, we developed and validated a framework for automated breast cancer detection involving three different artificial intelligence analysis steps and an algorithm for cell-distance analysis using BLEACH&STAIN multiplex fluorescence immunohistochemistry. Pan-cytokeratin (panCK) antibodies were used to detect epithelial cells and antibodies directed against Myosin and p63 were used to identify basal cells.

Distance calculation between basal cells and benign epithelial cells

The optimal distance between Myosin+ and p63+ basal cells and benign panCK+ cells was identified as 25 µm in breast cancer and used – combined with deep learning-based algorithms – to exclude benign glands from the analysis. Our framework discriminated normal glands from malignant glands with an accuracy of 98.4% (95% confidence interval [CI]: 97.4 – 99.3).

Marker distribution and MCL cluster

The analysis framework was validated by the concordance with well-characterized biological findings, such as the identification of 11% HER2+, 74% PR+/ER+, and 15% triple negative cases in the study cohort.

Results

Kaplan–Meier estimates for overall survival in breast cancer of no special type.

Unsupervised cluster analysis

Association between biomarkers and breast cancer NPY phenotype

Conclusions

- The combined assessment of up to 5 markers in a prognosis score showed strong prognostic relevance (p<0.001) and was an independent risk factor in multivariate analysis (p=0.005).
- Automated tumor cell identification improves prognostic performance of prognosis marker quantification and enables rapid and reliable analysis of multiple prognostic markers.

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