Automated prognosis marker assessment in 2,004 breast cancers using an artificial intelligence-based framework for BLEACH&STAIN mHIC

Introduction and Objectives

The assessment of prognostic markers in routine clinical practice of breast cancer is currently performed using multi-gene RNA panels. However, the unknown proportion of normal breast tissue in relation to malignant breast tissue can reduce the predictive value of such tests. Multiplex fluorescence immunohistochemistry holds the potential for a better assessment of tumors because tumor cells can be separately analyzed.

Materials & Methods

To enable automated prognosis marker detection (i.e. TROP2, GATA3, androgen receptor [AR], progesterone receptor [PR], estrogen receptor [ER], HER2, PD-L1, K87, TOP2A), we have developed and validated a framework for automated breast cancer characterization, which comprises three different artificial intelligence analysis steps and an algorithm for cell-distance analysis of 11+1 markers. BLEACH&STAIN multiplex fluorescence immunohistochemistry staining in 2,004 breast cancers in a TMA format.

Image analysis was performed using a previously trained deep learning-based framework (U-Net) for cell detection followed by single cell intensity measurement of the fluorophores. Cell-to-cell distance analysis was then used to calculate the distance from epithelial cells to Myosin+ basal cells. Epithelial cells close to Myosin+ basal cells (> 25μm) were classified as benign epithelial cells and excluded from the study. This approach was combined with a deep-learning based framework (DeepLabV3) for automated breast cancer detection resulting in an improved prognostic performance.

The analysis framework was validated by the concordance with well-characterized biological findings, such as the identification of 1% HER2, 74% PR/ER+, and 15% triple negative cases in the study cohort.

Results

Conclusions

- A deep learning-based framework for automated breast cancer identification using BLEACH&STAIN multiplex fluorescence IHC facilitates automated prognosis marker quantification in breast cancer.
- Automated tumor cell identification improves prognostic performance of prognosis marker quantification.

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