

# Deep Learning-Based, Fully Automated Analysis of Whole Slide Images Can Detect Invasive Breast Carcinoma and Count Ki-67 Easily and Precisely

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**Background:** The basic treatment of hormone-receptor (HR) positive breast carcinoma (BC) is anti-hormonal therapy. Chemotherapy or CDK 4/6 inhibitors would be added for **high-risk** patients, who are partly defined by **high Ki-67**. Since there remains concerns about reproducibility, we aimed to develop an automated image analysis.

**Design:** Random **100 cases** were collected from a previous study [Histopathology. 2020;77(3):471-480]. Resected specimen of primary **invasive BC** (HR+ and HER2-) had been stained with Ki-67 (MIB-1; Dako) and digitized by NanoZoomer-XR (Hamamatsu Photonics K.K.). Two board-certified pathologists evaluated Ki-67 following the recommendations from the International Working Group. We also performed original scoring using a deep learning (DL)-based Ki-67 (Breast, AI APP; Visiopharm) **in a fully automated approach** with no manual input or review. We compared the continuous output score and validated the accuracy of positive/negative counting or invasive cancer detection as good ( $\geq 80\%$ )/ fair/ poor ( $< 50\%$ ) among preselected square of  $1\text{mm}^2$ .

**Results:** Median/mean value of each pathologist and automated analysis were 11.7/15.1 (AIH, Path 1), 8.4/12.0 (TW) and 6.5/9.4 respectively. Every pair showed **statistically positive correlations** of Ki-67, and the highest value was yielded by Path 1 and the software ( $R=0.93$ ). When the same AI-APP was used by a laboratory technician, the correlation was perfect ( $R=1.0$ ). The software counted 385,985 cells on average within the full-face slides, and the sensitivity and specificity of our new algorithm is **88.9%** and **97.6%** respectively. Out of annotated 7301 positive cells, the APP misses 330 cells, and every single 3886 negative cells were judged as negative by the APP. Invasive cancer detection was regarded as good/fair/poor by

another pathologist at 82/16/2 cases respectively, and APP seems to be **superior** to Path 1 on three “fair” cases.

**Conclusion:** Here, we have created a fully automated software to analyze Ki-67, which proved to have **concordant result** with experienced breast pathologists. Besides some attentions needed for clinical use, it could allow pathologists to focus on another task and help clinicians to select the optimal treatment based on **precise tumor biology**.