AI in combination with the global counting methodology by the International Ki67 in Breast Cancer Working Group identifies more patients eligible for treatment and increases diagnostic speed by 5x-8x.

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Introduction

Assessment of Ki-67, ER, PR, and HER2 expression by immunohistochemistry (IHC), as the most established predictive biomarkers in breast cancer, is the important basis for oncologic treatment decisions.

Ki-67 proliferation plays a role in overall prognosis and prediction of chemotherapy benefits and high and low results are very helpful in the decision of oncology treatments in Sweden. This marker may emerge as a companion diagnostic for CDK4/6 inhibitors and even for patients classified as low proliferative.

However, quantification of Ki-67 positivity and lack of standardization leads to substantial inter-observer variability. In Sweden, the new national guidelines recommend the use of a global counting methodology by the International Ki67 in Breast Cancer Working Group (IKWG). New cut-offs according to the published data of IKWG were implemented in all of Sweden (Global Score weighted, Ki-67-low <6 %, Ki-67-medium 6-29 %, and Ki-67-high > 29 %) since substantial inter-observer/laboratory variability is observed in the range of >5 to <30%, which is where most investigators have selected cut-offs according to this study.

The development of deep-learning artificial intelligence (AI) algorithms may diminish some of the challenges associated with manual assessment and improve the accuracy of Ki-67 expression scoring. The use of AI-based approaches to biomarker scoring is not common worldwide, primarily due to the lack of large-scale clinical validation studies. We used an algorithm from the AI-development company Mindpeak to evaluate the Ki-67 expression of tumor cells on IHC-stained whole slide images using manual IHC scoring and comparing it with the AI algorithm's automatic counting (Mindpeak) in breast cancer patients.

Objectives

1. Implementation of AI algorithm in clinical practices at our Department
2. Evaluation of Mindpeak algorithm in the quantification of Ki67 in comparison with manual quantification.

Materials and Methos

In a prospective study, 113 Ki-67 slides from breast cancer patients were analyzed, 102 from hospital Sankt Görans and 11 from Elskinstuna, using manual counting, and using Mindpeak's AI algorithm for global counting including the following criteria: quality assurance (EQA) in pre-analytical and analytical factors. The entire glass slide section (WSI) was examined using low-power magnification (10x objectives). The manual assessment was performed (counting 400 cells, 4 areas) of the percentages of the invasive tumor in the glass slide that exhibit the following Ki-67 scores (excluding carcinoma in-situ and non-tumor tissue such as necrosis and fibrosis): Negative i.e. contains invasive cells but a very low (including zero), percentage of positive invasive cells with the following estimation: low, medium and high according to the protocol published by IKWG. The same methodology was chosen with the Mindpeak AI algorithm but here the software counted the cells automatically, did the mathematical calculations, and gave the Global Score weighted and Global Score unweighted as readout.

Results

The quantification of Ki-67 expression on tumor cells with the AI software identified more Ki-67 positive samples at cut-offs of ≥1% and ≥5% compared with manual scoring. Four additional patients were classified as low >5 % when more cells were considered by the AI software Figure 1. Similarly, two additional patients were re-categorized into the medium range with 6%-29 %. In addition, the diagnostic time needed for quantification and calculation was 8 times lower when using the AI software compared to the manual process as shown in figure 2. We found a correlation between manual counting and AI automatic counting, but the AI was able to count more cells. Figure 3.
The AI output is visualized including the complete set of results as the Global Score weighted, the scores for the four representative areas and their weights based on overall invasive tumor composition on the WSI as well as single-cell dot annotations on top of the tumor cells in the representative areas Figure 4.

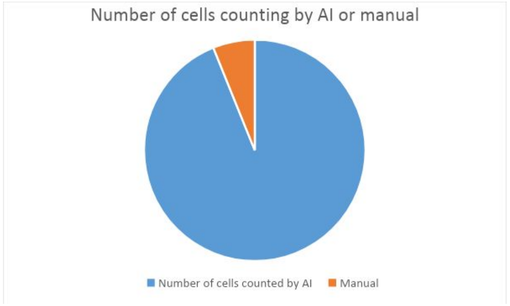


Figure 1.

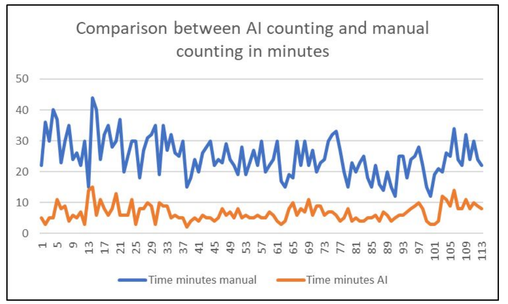


Figure 2.

Figure 3.

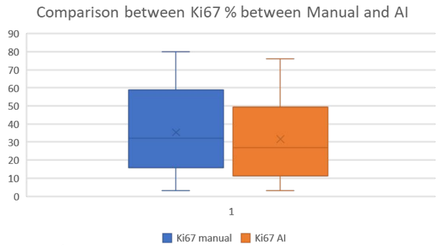
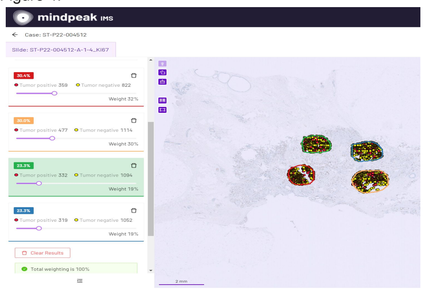


Figure 4.



Conclusions

Our prospective study on 113 Ki-67-stained slides from breast cancer patients demonstrates the benefit of implementing digital pathology-AI-based methods in clinical practice to identify more patients who would benefit from treatment with immuno-oncology therapy compared with manual assessment. In addition, diagnostic effectiveness is increased eight-fold as well as standardization is achieved.

References

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