

Automatic image analysis of Sentinel Nodes in Breast cancer

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The aim of this study was to evaluate whether automated image analysis can substitute the manual assessment of metastases in SNs in breast cancer patients.

INTRODUCTION

Breast cancer is one of the most common cancer diseases in women with more than 1.67 million cases each year worldwide (2012). In breast cancer, the sentinel lymph node (SN) pinpoints the first lymph node(s) into which the tumor spreads and it is usually located in the ipsilateral axilla. In cases where ultrasound analysis or a needle biopsy shows no signs of metastatic disease in the axilla, a SN biopsy is performed.

Assessment of metastases in the SN is done in a conventional microscope by manually measuring the size and/or counting the number of tumor cells, to categorize the type of metastases; macro metastases, micro metastases or isolated tumor cells to determine which treatment the breast cancer patient will benefit from.

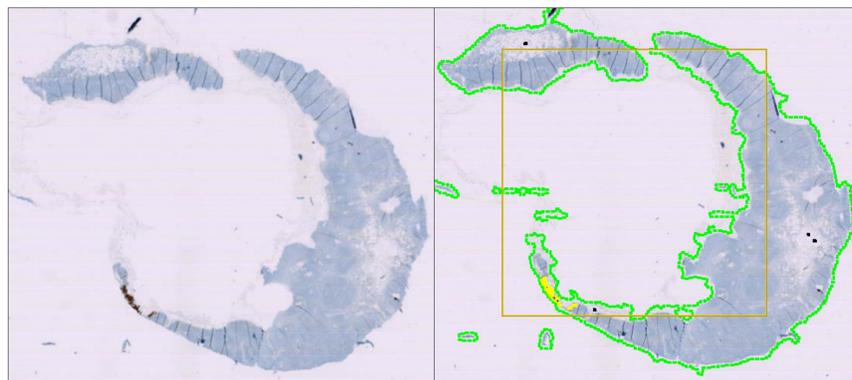


Figure 2. Image analysis sentinel node. Region of interest (Green), tumor detection (yellow)

RESULTS

We used conventional manual review as golden standard for assessment of positive tumor cells and compared with automated image analysis.

	Patients included	Image Analysis vs. Manual Reading Agreement	Cohen's kappa
Rigshospitalet	30	96.7 %	0.923
Odense Hospital	14	85.7 %	0.720

DISCUSSION

In three cases a disagreement between manual and automated assessment was observed. The automated analysis assessed three cases as positive whereas the manual assessments were negative. The three false positive cases were in one case due to folds in the tissue section and for the last two due to staining variations (figure 3). No false negative was observed.

Using this method as a screening tool pathologists would easily pick up on false positive results and areas with folds and staining variations could be excluded in a new image analysis run.

CONCLUSION

Application of automated image analysis will remove the need for time consuming manual counting of tumor cells and will have a significant impact on turn-around-time for SNs in breast cancer.

In addition to a faster turnaround time it will provide an objective, reproducible and more accurate assessment of the SNs in breast cancer.

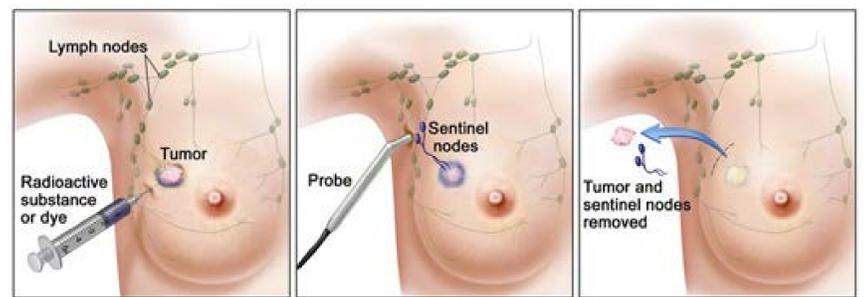


Figure 1. Removal of sentinel node

MATERIALS AND METHODS

Consecutive SNs from 44 patients with early breast cancer receiving surgery in the period of February to August 2015 were collected and included in this study.

FFPE tissue sections were analyzed by IHC using the BenchMark ULTRA from Ventana.

A mixture of CK7 and CK19 and CAM5.2 was used for detection of positive epithelial tumor cells.

SN sections were assessed in a conventional microscope according to national guidelines regarding SNs in breast cancer patients (www.DBCG.dk).

IHC sections were scanned in a NanoZoomer-XR digital slide scanner and the images were analyzed in Visiopharm's software using a custom made algorithm for SN in breast cancer.

The algorithm evaluates staining reaction of CK7/19 and CAM5.2 and was fine tuned for each stain based on stain intensity and background.

Metastases	Positive Cells	Tumor Area
MacroMetastases		> 2mm
MicroMetastases	> 200 cells	> 0,2mm and/or ≤ 2mm
Single Cells/Clusters	≤ 200 cells	< 0,2 mm

Table 1. National guidelines in Denmark for Sentinel Nodes

The automatic assessment translates into number of positive cells, size of positive tumor area and biggest diameter in each area. Based on positive tumor cells and diameter the algorithm estimates and categorizes patient samples into macro metastases, micro metastases or isolated tumor cells according to national guidelines (Table 1).

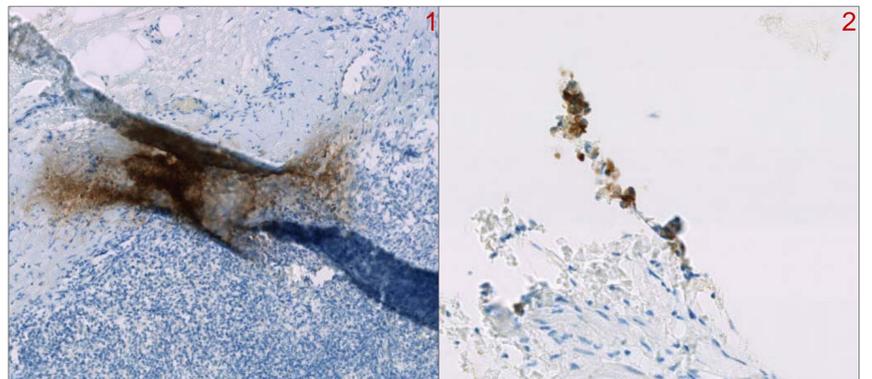


Figure 3. (1) False positive result illustrated by a fold in the tissue section. (2) False negative illustrated by few isolated tumor cells.