MR was performed. Subsequently, they underwent surgery. Then we restrospectively investigated the correspondence of the complete answers to the treatment evaluated first at the MRI (iCR) and then through the post-operative histological examination (pCR). Subsequently, we divided the sample of patients into three groups: luminal A/B (HER2 negative), triple negative (TN), HER2 positive. Finally, by examining patients in whom there was no iCR and/or pCR, we evaluated the correlation between the size of the residual tumour mass shown on MRI and those shown by the postoperative histological examination.

Results: MRI, in predicting a Complete Response (RC), has a sensitivity of 55%, a specificity of 86%, a VPP of 50% and a VPN of 88%. The analysis shows that for luminal subtypes the use of magnetic resonance imaging leads to non-specific and heterogeneous responses with a high number of false positivities in the face of a histological examination that shows a pCR. The other two subgroups, on the other hand, are more similar to each other in terms of predictivity of imaging with a comparable percentage of false positives and negatives. What distinguishes them, however, is the greater specificity of resonance in the HER2+ group with 71% compared to 33% in the triple-negative group, although among the latter imaging has shown greater sensitivity (90% vs 64%). The correlation between the size of the residual tumor seen through MRI and the size shown by the post-surgical histological examination is very low (0.23) in the group of luminals.

Conclusions: MRI is sensitive but not very specific, leading in 50% to the risk of over-treating patients and in 12% of cases to under-treating them. In the stratification by subtype, it has also emerged that this method could be useful and more reliable in the evaluation of the response of HER2+ and triple-negative tumors; instead, it is considered unreliable in the evaluation of luminal subtypes, where a histological examination is also necessary.

No conflict of interest.

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Deep learning enables fully automated mitotic density assessment in breast cancer histopathology

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Background: Mitosis counting is an important part of breast cancer grading, yet known to suffer from observer variability. Advances in machine learning enable fully automated analysis of digitized glass slides. The present study evaluated automatic mitosis counting and demonstrated applicability on triple negative breast cancers (TNBC).

Material and Methods: In entire scanned H&E slides of 90 invasive breast tumours, a deep learning algorithm (DLA) fully automatically detected all mitoses and determined the hotspot (area with highest mitotic density). Subsequently, two independent observers assessed mitotic counts on glass slides according to routine practice, and in the computer-defined hotspot.

Next, automated mitotic counting was performed in our TNBC cohort (n = 597). Multivariable Cox regression survival models were expanded with dichotomized mitotic counts. The c-statistic was used to evaluate the additional prognostic value of every possible cut off value.

Results: Automatic counting showed excellent concordance with visual assessment in computer detected hotspots with intraclass correlation coefficients (ICC) of 0.895 (95% CI 0.845–0.930) and 0.888 (95% CI 0.783–0.936) for two observers, respectively. ICC of fully automated counting versus conventional glass slide assessment were 0.828 (95% CI 0.750–0.883 and 0.757 (95% CI 0.638–0.839), respectively (Table 1).

In the TNBC cohort, automatic mitotic counts ranged from 1 to 269 (mean 57.6) in 2 mm^2 hotspots. None of the cut off values improved the models' baseline c-statistic.

Table 1 Linear weighted kappa scores and intra class correlation coefficients for mitotic scores between observer I, observer II and the CNN.

	Kappa	Intra class correlation coefficient (ICC)
Observer I glass versus CNN	0.604 (95% CI 0.477–0.731)	0.828 (95% CI 0.750–0.883; p < 0.001)
Observer II glass versus CNN	0.609 (95% CI 0.484–0.734)	0.757 (95% CI 0.638–0.839; p < 0.001)
Observer I hotspot versus CNN	0.654 (95% CI 0.530–0.777)	0.895 (95% CI 0.845–0.930; p < 0.001)
Observer II hotspot versus CNN	0.794 (95% CI 0.691–0.896)	0.888 (95% CI 0.783–0.936; p < 0.001)

Conclusion: Automatic mitosis counting is a promising complementary aid for mitoses assessment. Our method was capable of fully automatically locating the mitotic hotspot in tumours, and was capable of processing a large series of TNBC, showing that mitotic count was not prognostic for TNBC even when attempting alternative cut off points.

Conflict of interest:
Advisory Board: Jeroen van der Laak is member of the scientific advisory boards of Philips, the Netherlands and ContextVision, Sweden and receives research funding from Philips, the Netherlands and Sectra, Sweden.

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Prone, stereotactic, vacuum-assisted breast biopsy

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Background: Stereotactic VAB is the gold standard in the biopsy guidance of nonpalpable breast lesions which cannot be detected on ultrasound. The aim of this study is to learn about prone, stereotactic, vacuum-assisted core biopsy (PS VAB) systems through our experience:

- Basic concept, types, future advancements
- Utilization
- Advantages and disadvantages
- BI-RADS lesions

Material and Methods: Between 2010–2019, 1600 cases were documented, 90% due to microcalcifications. System: guidance-table combo and biopsy device. The patient lies prone, her breast is compressed. After targeting, sampling/excision is done under local anaesthesia with 7–9 G needles from multiple angles. Markers may be used at the end of the procedure to mark the site of the biopsied lesion.

Results: 53.4% B2, 10.8% B3 and 35.2% B4-5 lesions in concordance to the literature. Enough sample for the extremely precise diagnosis leads to 55% less surgeries and 75% less two-step surgeries. Digital breast tomosynthesis might further facilitate targeting, sampling and might broaden the scope of lesion identification. This is currently under investigation.

PS-VAB in particular, compared to seated variants, offers more comfort to the patient, meanwhile eliminating collapses and promoting effortless, precise targeting shortening diagnostic workup. No specific preparation is needed from the patient, even anticoagulation-therapies are not necessary to be suspended.

Conclusions: VAB is the gold standard in lesions that are not palpable and cannot be detected on ultrasound (mostly microcalcifications).

Provides enough sample for the extremely precise preoperative diagnosis.

- Can be therapeutic (papillomas, radial scars, smaller fibroadenomas)
- Site markers can be used, when necessary (might migrate)
- Surgeries are reduced by 55%, two-stage surgeries by 75%
- Prone systems are more comfortable and eliminate collapses, while promoting precise targeting
- Few prone systems are operating in Hungary (only one with tomosynthesis), it is expensive and underfinanced (2400 cases annually, 200 financed)

No conflict of interest.

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The relative eosinophil count in breast cancer as an emerging prognostic biomarker

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Background: Cancer outcome appears to be affected by circulating immune cells in several tumor types. The role of peripheral eosinophils was widely studied in melanoma, while less data are available for breast cancer (BC) so far. In a previous study, we showed an association between baseline relative eosinophil count (REC), pathological complete response and survival rate in triple negative and hormone receptor negative/HER2 positive breast cancer. In this retrospective study we analyzed the role of REC in all breast cancer subtypes at time of diagnosis and during follow-up.

Material and Methods: Stage I-III BC patients (pts) treated between 1999 and 2018 were included in the study. REC and relative lymphocyte count (RLC) at seven different timepoints were collected. The pts were divided into two groups according to REC, using 1.5% as threshold, and according to RLC,

using 17.5% as threshold. The co-primary endpoints were the BC specific survival (BCSS) and the time to treatment failure (TTF) according to REC. The secondary endpoints were: BCSS and TTF according to RLC, the association between REC and RLC with relapse; the variation of REC during follow-up and at relapse. Statistical analysis was done with SPSS v25 software.

Results: Overall 930 early BC pts were included in the study. The median age of the whole cohort was 61 years (25–97). The pts were well balanced according to the TNM stage in the group REC-low (393 pts) and in the group REC-high (597 pts): 30.5% and 32.9% stage I; 45.3% and 45.1% stage II; 22.6% and 21.4% stage III respectively; 1.4% unknown. After a median follow-up of 91 months (range 1–245) we observed a benefit in TTF (HR 0.610–95% CI 0.458–0.812, p 0.001) and BCSS (HR 0.632–95%CI 0.433–0.923, p 0.018) in REC-high *vs* REC-low group. A survival benefit was observed also in the RLC-high *vs* RLC-low group (TTF: HR 0.421–95% CI 0.262–0.677, p 0.001; BCSS: HR 0.350–95% CI 0.2–0.614, p 0.001). A lower rate of relapse was observed in the REC-high *vs* REC-low group (17.1% *vs* 24.7%, p 0.005) and in the RLC-high *vs* RLC-low group (19.4% *vs* 35.8%, p 0.004). We observed a lower median REC at baseline before surgery (1.8% and 1.4% in pts without and with relapse respectively), compared to the median value after surgery (2.7% and 2.5% respectively), that remain stable until 10 years of postsurgical follow up in cancer free pts. A decrease in median REC was detected at time of relapse (1.5%). All the differences observed in the groups of pts with and without tumor recurrence were statistically significant ($p < 0.0001$), suggesting a role of the presence of cancer in the modulation of eosinophil count.

Conclusions: REC could be a new promising, affordable and accessible predictive and prognostic biomarker in all BC subtypes. Mechanistic studies, ongoing in our laboratory, are needed to understand eosinophils' physio-pathological role.

No conflict of interest.

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Diagnostic work-up in women suspect for breast cancer in the Netherlands

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Introduction: The goal of this study is to outline the hospital-based work-up during the diagnostic care pathway of women suspect for breast cancer in the Netherlands and to identify factors which influence this diagnostic work-up.

Method: Two cohorts have been analyzed: the "benign" cohort (n = 30,334 women suspect for breast cancer from ten hospitals) and the "malignant" cohort (n = 2,236 breast cancer patients from five hospitals). Hospital-based financial data in combination with tumor data (malignant cohort) from the Netherlands Cancer Registry was used. Patterns within the diagnostic care pathway were analyzed for both the benign and malignant cohort. For the women with finally diagnosis of breast cancer factors influencing the number of diagnostic care activities number of days until diagnosis of breast cancer were identified in the malignant cohort using multivariable Poisson regression models. To determine the factors influencing the number of days until diagnosis of breast cancer in the malignant cohort multivariable Cox regression models were used.

Results: Patients finally diagnosed with malignant disease had their diagnosis less often in one day (62% versus 67%) and on average had an equal number of average hospital visits (1.6) and a higher average number diagnostic care activities (4.7 versus 2.6) compared to patients with benign breast lesions. Of patients with malignant disease receiving triple-diagnostics, 87% were diagnosed during their first hospital visit. Factors influencing the number of diagnostic care activities were: individual hospital (IRR ranged between 0.89, 95%CI 0.84–0.95 to 1.22, 95%CI 1.16–1.29), higher age at diagnosis (continuous; IRR 0.998, 95%CI 0.996–0.999), palpable tumor (yes vs no; IRR 0.96, 95%CI 0.93–1.00), metastasis suspect lymph nodes (cN2 vs cN0; IRR 1.3, 95%CI 1.0–1.7; cN3 vs cN0; IRR 1.16, 95%CI 1.0–1.3), localization (central vs inner quadrant; IRR 0.93, 95%CI 0.88–0.99) and histology (other vs ductal; IRR 0.92, 95%CI 0.86–0.99). Factors influencing the number of days until (malignant) diagnosis were: hospital (IRR ranged between 1.12, 95%CI 1.09–1.35 and 1.3, 95%CI 1.19–1.42), higher BIRADS score (2/3 versus 0/1/unknown IRR 0.79 95%CI 0.66–0.95), detected by screening (yes vs no IRR 1.13, 95%CI 1.04–1.22), metastasis (cM1 vs cM0; IRR 0.70, 95%CI 0.54–0.91), and cT stage (cT2 vs cT1 IRR 1.16, 95%CI 1.05–1.28).

Conclusion: The diagnostic work-up of patients finally diagnosed with malignant disease demanded more time and diagnostic care activities than for those with benign lesions and was influenced by hospital, tumor and patient characteristics. This knowledge can improve the diagnostic care pathway and decrease variation.

No conflict of interest.

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Is sentinel lymph node biopsy necessary in the setting of microinvasive DCIS?

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Background: Breast cancer treatment guidelines recommend the surgeon perform a sentinel lymph node biopsy (SLNB) for patients with ductal carcinoma in situ (DCIS) who have a high risk of invasive cancer or for whom a mastectomy is planned.

Material and Methods: Our retrospective review evaluates patients diagnosed with DCIS or DCIS with microinvasion who were clinically node negative and had SLNB from 2005–2017. A diagnosis of DCIS does not routinely merit SLNB. However, a diagnosis of DCIS with microinvasion is considered a more aggressive form of DCIS and surgeons at our institution routinely perform SLNB in this setting, even though the patients are clinically node negative. SLNB is performed due to the concern for possible understaging of DCIS at the time of core needle biopsy in order to exclude the possibility of occult axillary metastatic disease. Our hypothesis is that metastatic disease is not routinely diagnosed in patients with DCIS with microinvasion. SLNB is not without morbidity; the literature quotes about a 5% chance of postoperative lymphedema (McLaughlin et al. J Clin Oncol. 2008 Nov 10;26(32):5213–9).

Results: At this time in our ongoing data collection, we have looked at a total of 75 patients who had DCIS with microinvasion and 56 patients who had DCIS only. Sixty four (85.3%) of patients with DCIS with microinvasion had SLNB. Sixteen patients (28.6%) with DCIS only had SLNB, which we surmise was due to surgeon preference. The SLNB results for the 64 patients with DCIS with microinvasion are as follows: 89.1% were pN0, 3.1% were pN0i, 3.1% were pN1mi, and 4.7% were pN1a. Both pN1mi and pN1a are considered clinically significant metastatic disease to the axillary lymph nodes. Of the 75 patients who had DCIS with microinvasion, 92.2% of the patients did not have clinically significant axillary metastatic disease. Of the 16 patients who had DCIS only and SLNB, none had axillary metastatic disease.

Conclusions: Given the low rate of significant metastatic disease to the axillary lymph nodes, even in the setting of DCIS with microinvasion, our preliminary results support our hypothesis that SLNB could be omitted in these patients. These results correlate with Roozendaal's study of 910 patients in the Netherlands (Breast Cancer Research Treatment 2016 156:517–525); Roozendaal's study found that 79.5% of the patients with DCIS with microinvasion were pN0, 4.9% were pN0i+, 6.6% were pN1mi, and 9% were pN1. Clinical relevance: Our results support the omission of SLNB for patients with DCIS with microinvasion; this will reduce the morbidity of postoperative side effects such as lymphedema in this patient population. Additionally, even though there were few patients with DCIS who underwent SLNB, this study reinforces the fact that these patients should not have SLNB.

No conflict of interest.

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Reconsidering the management of palpable DCIS: a single institution audit

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Background: Ductal carcinoma in situ (DCIS) identified by screening mammography accounts for 20% of breast cancer diagnoses, and microinvasion (DCIS-M) is found in 5%–10%. There are no defined treatment guidelines for palpable DCIS or DCIS-M. The role of screening