



Automated detection of breast cancer in false-negative screening MRI studies from women at increased risk



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ABSTRACT

Purpose: To evaluate the performance of an automated computer-aided detection (CAD) system to detect breast cancers that were overlooked or misinterpreted in a breast MRI screening program for women at increased risk.

Methods: We identified 40 patients that were diagnosed with breast cancer in MRI and had a prior MRI examination reported as negative available. In these prior examinations, 24 lesions could retrospectively be identified by two breast radiologists in consensus: 11 were scored as visible and 13 as minimally visible. Additionally, 120 normal scans were collected from 120 women without history of breast cancer or breast surgery participating in the same MRI screening program. A fully automated CAD system was applied to this dataset to detect malignant lesions.

Results: At 4 false-positives per normal case, the sensitivity for the detection of cancer lesions that were visible or minimally visible in retrospect in prior-negative examinations was 0.71 (95% CI = 0.38–1.00) and 0.31 (0.07–0.59), respectively.

Conclusions: A substantial proportion of cancers that were misinterpreted or overlooked in an MRI screening program was detected by a CAD system in prior-negative examinations. It has to be clarified with further studies if such a CAD system has an influence on the number of misinterpreted and overlooked cancers in clinical practice when results are given to a radiologist.

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1. Introduction

Dynamic Contrast Enhanced-Magnetic Resonance Imaging (DCE-MRI) has been used for almost 15 years to screen women with increased risk of developing breast cancer [1–3]. DCE-MRI has shown to be more sensitive for breast cancer than mammography [1,4–8], especially in women with dense breasts [9]. Nowadays, breast DCE-MRI is recommended in screening programs for women with cumulative lifetime breast cancer risk of more than 20–25% (US and EU guidelines) [10,11]. In screening, it is common to perform systematic analysis of observer errors by retrospectively examining prior screenings for visible signs of cancer. In mammography observer errors are frequent [12–14] and it was estimated that by better interpretation of screening mammograms 20–30% of

the cancers could be detected earlier without increasing the recall rate to an unacceptable level [15,16].

Only a few studies on observer error have been performed for breast MRI [17,18]. These studies investigated the causes of false-negative results on prior DCE-MRI exams of patients in whom breast cancer was revealed on a follow-up positive MRI examination. In the retrospective evaluation of Pages et al. [17], 58 pairs of positive and prior-negative MRI exams (60 cancers) were assessed. In 28 (47%) of these 60 cancers, the authors reported potential observer error. Similarly, Yamaguchi et al. [18] reviewed 15 pairs of positive and prior-negative MRI exams (16 cancers) from 15 patients screened with MRI. Of the 16 reviewed breast cancers, 9 (56%) were identifiable on the prior scan. The main causes for false-negative evaluations were small lesion size, extensive background enhancement and the presence of malignant lesions with smooth margins, which are typically found in benign masses. Furthermore, although it has not been reported, it is likely that fatigue while analyzing 4-dimensional data, and lack of experience also lead to observer errors.

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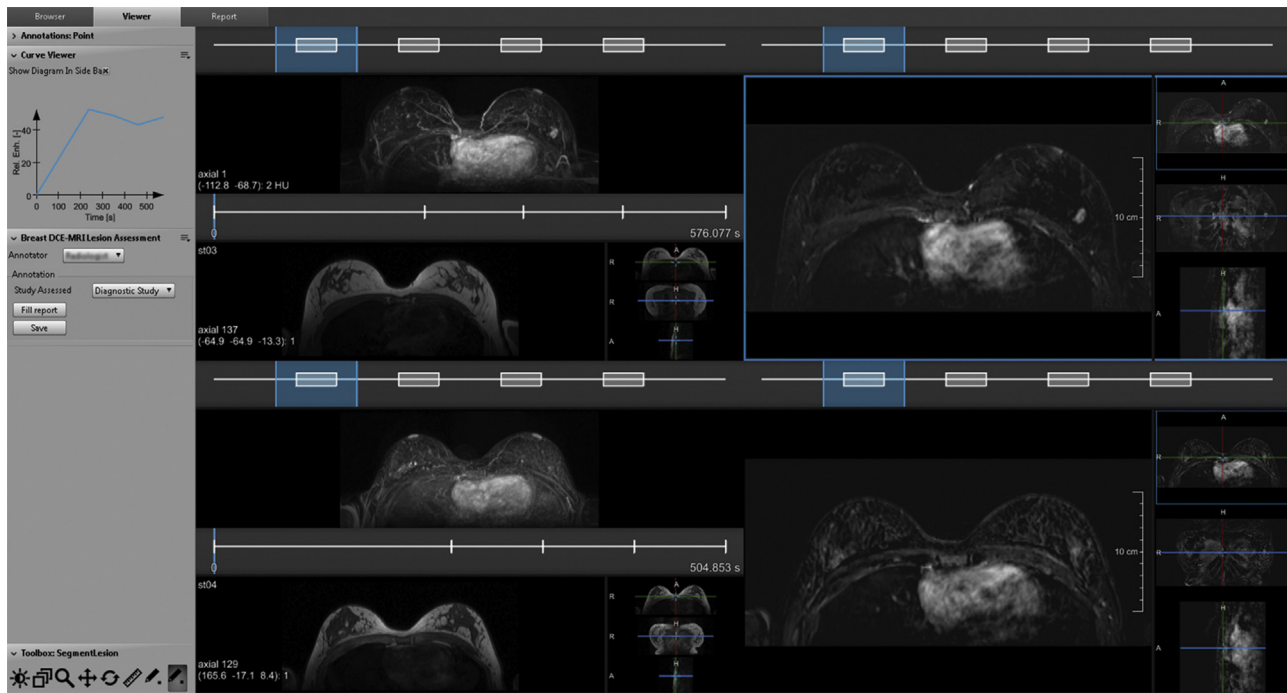


Fig. 1. Workstation used for lesion annotation and BI-RADS lexicon reporting in the DCE-MRI scan were the lesions was reported in screening (upper row) and in the prior-negative DCE-MRI examination (lower row).

The high frequency of positive findings in prior MRI scans reported to be negative (BI-RADS 1 or 2) indicates the importance of developing additional tools to aid radiologists in analyzing DCE-MRI. A computer-aided detection (CAD) system that automatically highlights abnormalities could draw the attention of the radiologist to a tumor that might otherwise be overlooked or misinterpreted. Automated computer-aided detection systems are currently being developed for this purpose [19–21].

The aim of this study is to evaluate the performance of an automated computer-aided detection (CAD) system to detect breast cancers that were overlooked or misinterpreted in a breast MRI screening program for women at increased risk for developing breast cancer.

2. Materials and methods

2.1. Study dataset

This retrospective study was approved by our institutional board and the requirement for informed consent was waived. A cross search of our MR imaging and pathology records between January 2003 and January 2014 identified 40 women at increased risk (≥ 20 –25% lifetime risk) that were diagnosed with breast cancer (42 tumors) with MRI and had a prior-negative DCE-MRI examination performed before the one in which the cancer was diagnosed. The time interval between examinations was 11.64 ± 1.95 months (average $\pm$ standard deviation). In 37 women, the cancer was detected in the screening examination. In the remaining 3 women, the cancer was detected between screening rounds (interval cancer). Note that we only considered prior DCE-MRI studies with a Breast Imaging Reporting and Data System (BI-RADS) score of 1 and 2 as prior-negative DCE-MRI examinations. Indications for MRI screening in these 40 women (median age: 48, range: 33–77) included family ($n=8$) or personal ($n=10$) history of breast cancer, BRCA1 ($n=10$), BRCA2 ($n=10$) or BRCA1 and 2 ($n=1$) carriers and radiation to the chest at young age ($n=1$). The distribution of breast cancer lesions was 33 invasive ductal carcinoma, 5 ductal

carcinoma in situ, 3 invasive lobular carcinoma and 1 secretory carcinoma, and the size (average $\pm$ standard deviation) as estimated in MRI and pathology was 1.69 ± 1.09 cm and 1.48 ± 1.10 cm, respectively.

The 40 DCE-MRI examinations in which the cancer was diagnosed (positive DCE-MRI scan) and the 40 prior-negative DCE-MRI scans were retrospectively evaluated side-by-side and in consensus by two radiologists with 8 and 12 years of experience in breast MR imaging using an in-house-developed dedicated breast DCE-MRI workstation. The workstation provided T1-weighted images without fat suppression for all the time points of prior-negative and positive DCE-MRI scans. Furthermore, it visualized subtraction images and their maximum intensity projection. An option to display the average contrast enhancement versus time curve in a region of interest specified by the user was also provided. Images were corrected for motion using the algorithm described in Ref. [21]. No T2-weighted or diffusion-weighted images were used, since these sequences were not available in the majority of the cases. Fig. 1 shows a screenshot of the workstation used in this study.

For each pair of DCE-MRI scans, as described in the clinical report, first the radiologists identified the breast lesion in the positive MRI examination. Subsequently, the prior-negative MRI examination was analyzed. Lesions were retrospectively detected in 24 prior-negative MRI scans. Based on their size, morphology, and enhancement characteristics as defined in the BI-RADS lexicon [22], 13 lesions (13 scans; including 1 interval cancer) were scored as “minimally visible” (BI-RADS 2/3) and 11 lesions (11 scans) were scored as “visible” (BI-RADS 4/5). These 24 prior examinations in which the lesion was minimally visible or visible were considered as prior false-negative MRI scans. In this study, we did not investigate possible causes for overlooking or misinterpreting these lesions during MRI screening. The remaining 18 lesions (16 scans) were scored as “not visible”. Fig. 2 shows an example of each category. Locations of the lesions and their extent were marked by the radiologists using a semi-automatic tool [21] in both the positive and prior DCE-MRI examinations.

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