Mammographic Density and Cancer Detection:

Does Digital Imaging Challenge our Current Understanding?

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Rationale and Objectives: To investigate the impact of breast density on the performance of radiologists when mammograms are digitally acquired and displayed.

Materials and Methods: A total of 150 craniocaudal digital mammograms including 75 cases with cancer were examined by 14 radiologists divided into two groups: those who read more (six) and less (eight) than 2000 mammograms per year. Cases were classified as low or high mammographic density. For both types of cases, detection of cancers within and outside the dense fibroglandular tissue was investigated. The performance of radiologist was measured using jack-knife free-response receiver operating characteristic (JAFROC) figure of merit (FOM).

Results: Radiologists with over 2000 annual reads had significantly higher JAFROC FOM (P = .03) for high (0.76) mammographic density compared to low (0.70) mammographic density cases. When lesions overlaid the fibroglandular tissue, cases with high mammographic density compared to low mammographic density displayed increased location sensitivity for all radiologists (P = .03) and for those radiologists reading more than 2000 mammograms annually (P = .04), whereas JAFROC FOMs increased for all radiologists (P = .05). No significant changes were observed when the lesion was outside the fibroglandular region.

Conclusions: Increased mammographic density improves the performance of experienced radiologists when using digital mammograms. This finding, which does not align with those previously reported for film screen systems, may be because of windowing/leveling opportunities available with digital images.

Key Words: Digital mammography; mammographic density; breast cancer; cancer detection; radiologists' performance.

Mammography is the leading imaging modality for early detection of breast cancer, and as a screening tool it has significantly decreased breast cancer mortality (1–6). Mammographic images depict adipose and fibroglandular tissues, with the latter appearing as visually bright because of its higher attenuation coefficient compared to the more radiolucent adipose tissue (7,8). The visual representation of increased amounts of fibroglandular tissue is often referred to as mammographic density (7,9,10).

Previous studies have shown that increased mammographic density is associated with higher risk of missed malignancies (11,12) and interval cancers (13,14), with sensitivity dropping from 80%–98% in fatty breasts to 29%–75% in mammographically dense breasts (13,15–19). In addition, increased numbers of large screen-detected tumors (>15 mm) (10,20–22), higher recall rates (23–25), and decreased efficiency of breast screening programs (17) have all been linked to high levels of mammographic density.

However, a key element that is often neglected when one considers the potential deleterious effects of high mammographic density in breast cancer detection is that most of the previous work was performed with screen-film (13,16,20,26) or digitized screen-film mammographic images (19). More recent studies, which have compared digital to screen-film mammography (27,28), have suggested that sensitivity may increase marginally in high-density mammographic images (83.6%) compared to low-density mammographic images (68.1%) in digital mammograms. This potential increase in performance in high mammographic density images was also shown in a very recent prospective study looking at the performance of radiologists in two-dimensional (2D) versus integrated 2D and "3D digital mammography" (also known as digital breast tomosynthesis). In this study, Ciatto et al. (29) reported that false-positive rates were higher in the mammograms

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depicting less dense breast parenchyma. However, these findings were incidental, as these studies did not specifically focus on investigating the impact of mammographic density on breast cancer detection. The precise impact of density in the digital era therefore remains underexplored, although the radiologic and clinical importance of this common image appearance is substantial (9,30–32).

In addition, there is a great lack of understanding about the mechanisms underlying the impact of mammographic density on cancer detection. Anecdotally, it is often assumed that increased mammographic density superimposed on the cancer masks the clues required for optimal visualization of the lesion. If this "masking hypothesis" is correct, high mammographic density images should reduce detection of cancers that are presented overlaying the dense regions of the breast parenchyma, whereas detection of cancers located outside these regions should not be adversely affected. To date this has not been investigated, and thus it needs to be studied to further the understanding of the impact of increased mammographic density on the interpretative process of radiologists.

The purpose of this study is twofold. On the one hand, we sought to investigate the performance of radiologists with digitally acquired and displayed mammograms depicting a variety of mammographic densities, aiming at characterizing the effects of high mammographic density on the performance of radiologists. On the other hand, we sought to determine whether the masking hypothesis is supported when using digital technology.

MATERIALS AND METHODS

Institutional ethical approval was obtained, patient consent waived, and all radiologists signed a consent form to participate before any images were presented. This study was performed at the 14th Asian Oceanian Congress of Radiology combined with The Royal Australian and New Zealand College of Radiologists (RANZCR) 63rd Annual Scientific Meeting (2012) held in Sydney, Australia. Fourteen radiologists voluntarily participated, and demographic details describing the radiologists are presented in Table 1.

Although all radiologists read mammograms as part of their clinical practice, they were subdivided into those radiologists who read over 2000 mammograms per year and radiologists who read under 2000 mammograms per year. The number of mammographic cases read per year has been previously determined as a factor that can affect mammographic screen reader performance and reader practice (33–35), and the 2000 cases chosen here align with Australian National Accreditation Standards (36).

Selection of Images

A digitally acquired set of 150 craniocaudal mammographic images with a range of different mammographic densities was selected from BreastScreen NSW, Australia. Patient consent was waived, and all patients' identification details were removed from the images. Images were acquired from each of the following six digital mammographic units: Sectra Medical Systems (Linkoping, Sweden), Fuji Medical Systems (Tokyo, Japan), General Electric Healthcare (Waukesha, IL), Agfa HealthCare (Mostsel, Belgium), Philips Healthcare (Amsterdam, the Netherlands), and Carestream Health systems (Rochester, New York). The mammographic units acquired images with a median resolution of 4740 $\times$ 3540 pixels (minimum 2294 $\times$ 1914 pixels; maximum 5928 $\times$ 4728 pixels).

The test set contained 75 cases with 78 biopsy-proven malignant lesions, whereas the remaining cases were malignancy-free. Forty-eight cancers were mass lesions, 12 were architectural distortions, 14 were focal asymmetry, and four calcification only presentations. Lesions had a median diameter of 12 mm (minimum 8 mm; maximum 20.6 mm). The "true" locations of all malignant lesions were delineated by two expert high-volume radiologists who screen read for BreastScreen New South Wales and who had access to additional imaging and the relevant pathology reports. These two radiologists did not participate as observers in this study. Malignancy-free images were confirmed after a routine 2-year follow-up.

The two breast imaging experts, working in conjunction, also allocated the images to four specific breast density categories, with an agreement of 100%. The allocation method was based on the mammographic density classification described in the Synoptic Breast Imaging Report of the National Breast Cancer Centre (NBCC, now Cancer Australia), endorsed by the RANZCR (37). This is similar to the new fourth edition American College of Radiology Breast Imaging Reporting and Data System (38) and is described subsequently:

1. RANZCR/NBCC first level <25% glandular tissue (37 cases).
2. RANZCR/NBCC second level 25%–50% glandular tissue (38 cases).
3. RANZCR/NBCC third level 51%–75% glandular tissue (38 cases).
4. RANZCR/NBCC fourth level >75% glandular tissue (37 cases).

We grouped the classifications for mammographic density as follows:

1. Low mammographic density images: RANZCR/NBCC first level <25% glandular tissue and second level 25%–50% glandular tissue (Fig 1a).
2. High mammographic density images: RANZCR/NBCC third level 51%–75% glandular tissue and fourth level >75% glandular tissue (Fig 1b).

The mammograms with malignant lesions were selected according to whether the lesion was completely overlaying fibroglandular regions (Fig 2), and thus no lesions were located partially between the fibroglandular and the fatty areas of the parenchyma. Only one case was excluded from this grouping, because it contained three malignant lesions, two