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Digital mammography: what do we and what don't we know?

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Abstract High-quality full-field digital mammography has been available now for several years and is increasingly used for both diagnostic and screening mammography. A number of different detector technologies exist, which all have their specific advantages and disadvantages. Diagnostic accuracy of digital mammography has been shown to be at least equivalent to film-screen mammography in a general screening population. Digital mammography is superior to screen-film mammography in younger women with dense breasts due to its ability to selectively optimize contrast in areas of dense parenchyma. This advantage is especially important in women with a genetic predisposition for breast cancer, where intensified early detection programs may have to start from 25 to 30 years of age. Tailored image processing and computer-aided diagnosis hold the potential to further improve the early detection of breast cancer. However, at present no consensus exists among radiologists on which processing is optimal for digital mammograms. Image processing may also vary significantly among vendors with so far limited interoperability. This review aims to summarize the available information regarding the impact of digital mammography on workflow and breast cancer diagnosis.

Keywords Digital mammography · Breast cancer screening · Image processing · Workflow · Quality assurance

Introduction

The concept of digital mammography with all its advantages including easier image storage and tailored image processing is not new. As early as 1967, Fred Winsberg from the University of Chicago proposed an algorithm for computer-aided breast cancer detection using digitized film mammograms [1]. Although film digitization can produce high-quality digital mammograms, this process is not only labor intensive and expensive, but primarily does not solve the limitations inherent to film mammography, mainly the narrow dynamic range caused by the non-linear characteristic curve of film. Initial experiments with digital mammography based on computed radiography (CR) started in the late 1980s [2]. However, image quality was inferior to state-of-the-art film-screen mammography at comparable dose due to the poor detective quantum efficiency (DQE) of these early CR systems [3]. For several years now, newer dedicated mammography CR systems as well as a number of different integrated full-field digital mammography systems have become available [4–6], many of which have received regulatory approval (Table 1). Increasingly these systems are replacing film-screen

Table 1 Digital mammography systems

Description	Detector type	Detector material	Signal generation	Pixel size	Image area	Pixel matrix	Name	Manufacturer (distributors)	Comments	FDA approval[a]
CCD mosaic	Integrated (area)	CsI:Tl phosphor-scintillator	CCD array (3×4 mosaic)	41 μm	18.6×24.8 cm	6,400×4,800	Digital Breast Imager	Trex (Lorad, Bennett)[b]	No longer available	15.3.2002
CCD slot scanning	Integrated (scanning)	CsI:Tl phosphor-scintillator	1.4-cm wide array of 4 CCDs	54 μm[c]	22.1×30.4 cm	4,096×5,625	Senoscan	Fischer (Philips)[d]	No grid necessary	25.9.2001
Phosphor flat panel	Integrated (area)	CsI:Tl phosphor-scintillator	Array of photo diodes/TFT	100 μm	19.2×23 cm	1,914×2,294	Senographe 2000D	General Electric	Images can be obtained in rapid sequence	28.1.2000
							Senographe DS	General Electric		19.2.2004
					24×30.7 cm	2,394×3,062	Senographe Essential	General Electric		11.4.2006
Selenium flat panel	Integrated (area)	Amorphous selenium	Array of electrode pads/TFT	70 μm	25×29 cm	3,584×4,096	Selenia	Lorad/Hologic (Agfa)	Direct conversion of X-ray photons to electric charge	2.10.2002
							Novation	Siemens (Agfa)		20.8.2004
				85 μm	17.4×23.9 cm or 23.9×30.5 cm	2,016×2,816 or 2,816×3,584	Giotto IMAGE	IMS		
							Nuance	Planmed		
Photon counter	Integrated (scanning)	Silicon strip	Array of X-ray photon counters	50 μm	24×26 cm	4,800×5,200	Micro-Dose Mammography	Sectra	Very high DQE, currently no AEC	
Computed radiography (CR)	Cassette-based (area)	Photostimulable phosphor	Laser scanning	50 μm	18×24 cm or 24×30 cm	Approx. 1,800×2,400 or 2,400×3,000	FCR Profect CSFCR 5000 MA	Fuji(Siemens, Philips)	Dual-sided readout	10.7.2006
							CR 75.0 CR 85-X	Agfa		
							CR 975	Kodak		
							REGIUS 190 Mammo	Konica Minolta		

Cs:Tl = thallium-activated cesium iodide; TFT = thin film transistor; CCD = charge-coupled device, AEC = automatic exposure control

[a]Information current as of 25 September 2006 [7]

[b]No longer produced, all installations replaced by Lorad/Hologic Selenia systems

[c]Additional high-resolution mode with pixel size of 27 μm available with limited field of coverage

[d]Intellectual property bought by Hologic in 2005, existing installations remain in service, however, no new systems are produced or distributed

[e]These systems are sometimes also called amorphous silicon systems, because the detector is mounted on an amorphous silicon substrate. However, this name is misleading, since this is true also for the selenium flat-panel systems.

[f]Exact pixel matrix varies slightly among vendors

mammography both for screening as well as for diagnostic mammography. This review will summarize the current evidence on the advantages and disadvantages of digital mammography.

Measuring image quality in digital mammography

Image quality of conventional film-screen systems can be fairly accurately described by three parameters: (1) the characteristic curve of a film-screen system, (2) the sensitivity or "speed" and (3) the high-contrast line-pair resolution. All three concepts do not apply to digital imaging.

Digital mammography detectors have a linear relationship between detector dose and signal intensity, and no fixed characteristic curve as in film-screen mammography exists. Translation of detector signal intensities into monitor brightness is achieved by specific window settings and non-linear look-up tables, which can be modified to optimize the contrast in a certain image area of interest [8, 9].

While the sensitivity of a film-screen system defines the amount of dose required to reach a certain optical density of the developed film, there is no single optimal detector dose in digital mammography. With decreasing detector dose, image noise increases in the digital image and vice versa. By changing the X-ray beam energy spectrum, image noise can be exchanged against image contrast while keeping the parenchymal dose to the patient constant. In digital mammography, it is often beneficial to move to a higher energy spectrum than with film-screen mammography, since image noise is lower and the resulting loss in image contrast can be compensated for by adjusting the window setting [10, 11].

Due to the continuous course of the modulation transfer function (MTF) in film-screen mammography, the high-contrast line-pair resolution can be used to accurately predict the performance of the system at lower frequencies. At least with modern flat-panel digital mammography, the MTF abruptly declines at the nyquist limiting frequency defined by the pixel size of the detector [12, 13]. This results in a nominally lower spatial (line-pair) resolution, although the MTF at lower (clinically more relevant) frequencies may be significantly higher than with film-screen mammography. For digital mammography, line-pair resolution is therefore meaningless, and the performance of the system is better described by the so-called contrast-detail resolution, the ability to visualize object details of a certain size and radiation contrast. Contrast-detail resolution for a given dose is in turn determined by the DQE of the digital detector. A system with a higher DQE will reach the same contrast-detail resolution at a lower dose than an otherwise similar system with a lower DQE (Fig. 1). This can be used in clinical practice, where integrated digital mammography systems with a high DQE are usually operated at a mean glandular dose 20–30% lower than that of film-screen mammography [16–18]. Since the DQE of a digital system is difficult to measure in a standardized manner and may depend on a variety of factors such as X-ray beam quality and detector dose [19], acceptance testing for digital mammography systems is usually achieved by assessing the contrast-detail resolution of a system with certain phantoms such as the CDMAM phantom [14, 20]. However, contrast-detail phantoms such as the CDMAM phantom showing objects on a uniform background may not be ideal to predict the performance of a system in clinical practice. Such phantoms tend to favor digital systems by overestimating the detection performance for larger low-contrast objects due to unrealistically narrow window settings used when viewing the digital images, made possible by the lack of background structure [21]. By adding a structured background to the CDMAM phantom, Grosjean and Muller were able to show that while visibility of small details <0.4 mm was still limited by noise sources related to the image acquisition process, detection of larger low-contrast objects was mainly determined by the structured background [22]. This is in keeping with results from earlier experimental work based on digitized film [23, 24] and matches the experience from clinical practice. While adequate detector dose and low quantum noise levels are necessary to adequately show microcalcifications, visibility of larger masses is much less affected by image noise associated with lower dose or inferior DQE of the detector (Fig. 2). This effect can be used to significantly reduce the parenchymal dose for additional localization views, e.g., as part of interventional procedures in which the presence of a certain abnormality is already known (Fig. 3) [25, 26].

Digital mammography systems

There are now several different types of digital mammography systems available, which all are capable of producing high-quality digital mammograms, but all have specific advantages and disadvantages. Digital mammography systems can be grouped according to detector material, whether they are integrated or cassette-based systems, or whether they use an area detector or slot scanning technique (Table 1). Integrated systems usually allow for a higher throughput than cassette-based CR systems, but are more expensive. Slot scanning systems often can operate at a lower dose, since the slot collimation is effective in reducing scatter radiation, thus obliviating the need for an additional anti-scatter grid. Disadvantages of the slot scanning systems include longer scan times, high tube strain and the need for exact mechanical registration of the moving collimation slot and the detector. There are two different basic types of integrated area detectors, one on the bases of a phospor scintillator combined with an array of photo diodes capturing the light generated by the

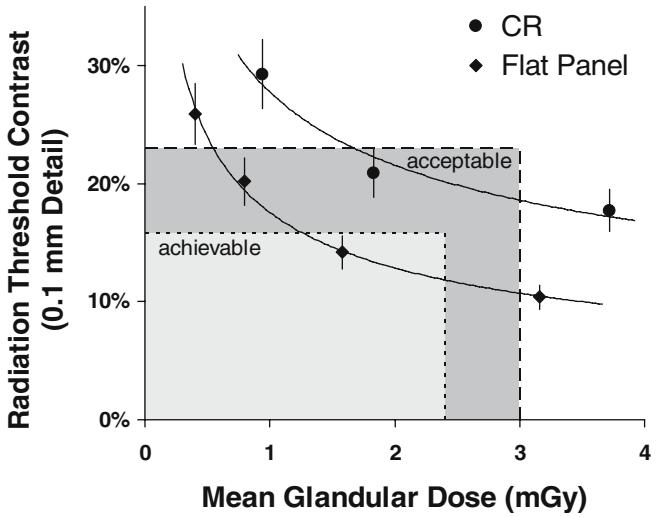

Fig. 1 Relationship between mean glandular dose at 6-cm compressed breast thickness and radiation threshold contrast for 0.1-mm details with a CR (Fuji Profect) and a flat panel (Siemens Novation) digital mammography system. Data points outside the grey acceptable/achievable area do not fulfill the minimum criteria for contrast-detail resolution or are associated with a mean glandular dose above the maximum acceptable dose level as defined by the European guidelines for quality assurance in breast cancer screening and diagnosis [14]. Results are averaged from three human readers each scoring four CDMAM phantom images. Threshold contrast values shown are nominal at 28 kV Mo/Mo, actual exposure parameters were 26 kV Mo/Rh for the CR system and 28 kV W/Rh for the flat-panel system. Compared to the CR system, the flat-panel system can alternatively be operated at the same dose with higher image quality or at the same image quality with lower dose. Source: Young et al. [15]

phosphor layer and the second type using an amorphous selenium layer with direct conversion of the X-ray photons to an electric charge. Both systems use a TFT

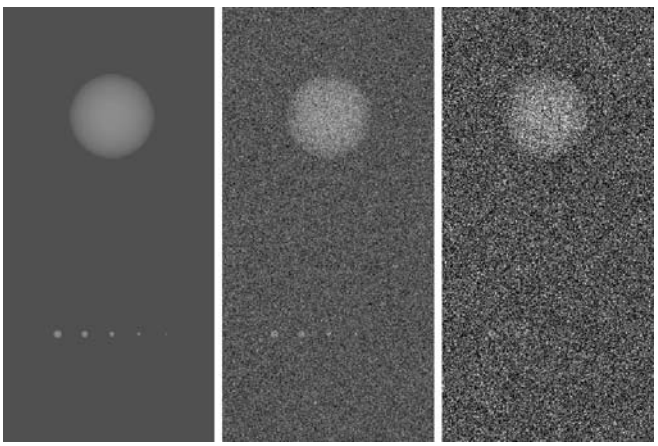

Fig. 2 Influence of various degrees of superimposed random Gaussian noise (increasing from left to right) on visibility of objects with different size. The large low-contrast object (top row) simulating a mass is almost unaffected by the image noise and is well seen on all images. The five smaller objects (bottom row) simulating microcalcifications are rapidly lost with increasing image noise

array mounted on a amorphous silicon base for signal read-out. Detector elements in the phosphor flat-panel systems with a pixel size of 100 μm are usually slightly larger than in the selenium-based systems (70–85 μm). Reduction in detector element size in phosphor flat-panel systems is difficult, since with a decreasing size of the detector elements, the relative portion of the active detector area would decrease rapidly compared to the relatively fixed inactive portion of the detector related to the signal read-out, resulting in a lower DQE and higher parenchymal dose for the patient. An advantage of phosphor flat-panel systems is that images can be obtained in relatively short sequence, which is useful for patient throughput and advanced applications such as tomosynthesis and contrast-enhanced mammography [27, 28]. A disadvantage of selenium-based systems compared to phosphor flat-panel systems is the higher amount of image lag (image signal carried over from a previous to a subsequent exposure) and ghosting (temporary change in sensitivity base on prior exposure history). However, detector development in this area is ongoing, and both lag and ghosting have been reduced significantly in newer clinical selenium-based systems [29].

The value of CR mammography systems compared to integrated full-field systems has recently been under intense discussion. One major selling point of CR systems is the lower investment cost, especially if existing mammography equipment can be used for acquiring the mammographic images. This cost advantage, however, is significantly smaller when considering a new installation. One argument brought forward against CR mammography is that the dose necessary to operate CR systems at acceptable image quality levels is higher than that of integrated full-field systems. Although there is no doubt that CR systems have a slightly lower DQE than integrated full-field systems, part of this dose disadvantage may be explained by other factors. Integrated systems usually optimize the entire imaging chain including choice of the exposure parameters such as kVp and the anode/filter combination. It has been shown that the major dose savings with digital mammography systems are achieved in patients with larger breasts by switching to a higher energy beam spectrum earlier than with conventional film-screen systems [16, 30]. Since CR mammography systems are used with standard mammography equipment traditionally designed for film-screen mammography, this optimization of exposure parameters often does not occur. Another common problem with CR mammography is that imaging processing algorithms developed for other radiographic exams (e.g., chest films) are used. Image noise with digital images is higher in areas of lower detector dose, e.g., the mediastinum. Since this noise may be perceived as disturbing, special processing algorithms have been developed for CR images to suppress noise in bright (underexposed) image areas [31]. In mammography, such

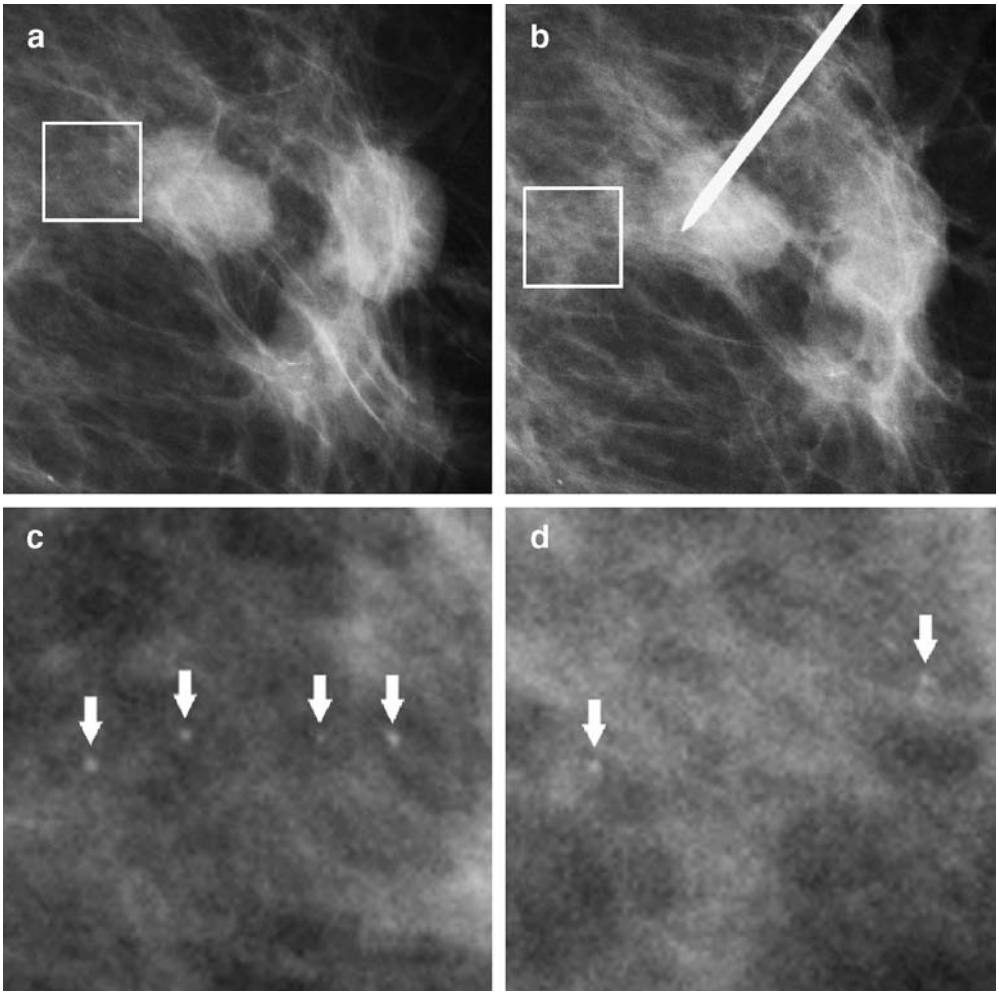

Fig. 3 Example of a breast interventional procedure using reduced dose mammographic images. A 76-year-old patient with bifocal invasive-ductal carcinoma surrounded by high-grade DCIS. Normal-dose mammographic image (**a**) and needle localization image at 50% reduced dose (**b**) with enlarged area of microcalcifications (**c,d**) in the vicinity of the main tumor. Both masses are equally well seen on the reduced dose image during the localization procedure. However, the individual microcalcifications (arrows) are less well depicted on the lower dose image (**d**) than on the normal dose image (**c**) due to a slightly higher amount of image noise in the lower dose image

algorithms will lead to impaired visibility of microcalcifications in areas of dense parenchyma and should therefore not be used.

Clinical comparison of digital and film-screen mammography

Early clinical studies comparing digital mammography with film-screen mammography were inconclusive (Table 2). None of the clinical trials so far has demonstrated significant differences in detection performance in a general screening population between film-screen and digital mammography. While in the study of Lewin et al. [33], the recall rate with digital mammography was significantly lower than with film-screen mammography, both the Oslo I and II studies found a higher recall with digital mammography [34, 36]. These results are difficult to compare, since the recall rates in the US are in general much higher than in European screening programs (Table 2).

One reason for the variable results of clinical mammography trials is that differences in positioning and reader performance far outweigh any difference in the acquisition technique, be it between screen-film and digital mammography or between different digital mammography systems [39]. This is easily demonstrated by the fact that in paired screening trials with two separate mammographic exams obtained at the same time (one film-screen and one digital) the number of detected cancers increases by 30% and more (Table 3), just by obtaining a second set of mammographic images independently read by one or more additional radiologists, while differences in cancer detection between digital and film-screen mammography on the whole are negligible.

Digital mammography with the possibility to locally optimize image contrast has, however, a clear advantage in younger patients with dense breasts, as was impressively demonstrated by the Digital Mammographic Screening Trial (DMIST) [38]. Interestingly, the rapid decline in sensitivity as typically seen with film-screen mammography in denser breasts [40] was not observed with digital mammography in the DMIST trial, where the

Table 2 Prospective clinical screening trials comparing film-screen and digital mammography

	Study design	Number of sites	Digital system	Age (years)		Number of exams	Recall rate	Cancer detection rate	ppv
Lewin [32, 33]	Paired, single-reading	2	GE phosphorflat panel prototype[a]	>40	Film-screen	6,736	14.9%*	4.9‰	3.3%
					Digital	6,736	11.8%*	4.0‰	3.4%
OSLO I [34, 35]	Paired, double-reading with consensus	1	[GE Senographe 2000D]	50–69	Film-screen	3,683	3.5%	7.6‰	21.9%
					Digital	3,683	4.6%	6.2‰	13.7%
OSLO II [36]	Randomized,double-reading with consensus	1	GE Senographe 2000D	50–69	Film-screen	10,304	2.5%*	5.4‰	22.1%
					Digital	3,985	3.8%*	8.3‰	21.6%
				45–49	Film-screen	7,607	3.0%*	2.2‰	7.4%
					Digital	3,012	3.7%*	2.7‰	7.1%
DMIST [37, 38]	Paired, single-reading	33	GE Senographe 2000 D (45%)Fischer Senoscan (23%)Fuji FCR (22%)Lorad Digital Breast Imager and Hologic Selenia(together around 10%)[b]	all	Film-screen	42,745	8.4%	4.0‰	5%
					Digital	42,570	8.4%	4.3‰	5%
				< 50	Film-screen	14,355	10%	2.2‰*	2%
					Digital	14,355	10%	3.3‰*	3%

*Differences statistically significant
[a]Prototype predecessor of the Senographe 2000D (General Electric) using the same phosphor flat-panel detector.
[b]During the course of the trial, the Lorad/Trex Digital Breast Imager units were all replaced by Lorad/Hologic Selenia systems. Exam numbers for both systems are not specified separately

sensitivity of digital mammography in the subgroup of women with dense breasts was identical to the sensitivity in the entire group [38]. This advantage of digital mammography in women with dense breasts will be especially valuable in patients with a genetic predisposition for breast cancer, in whom intensified early detection measures including mammography may have to start as early as 25 to 30 years of age [41, 42]. However, it is uncertain whether the DMIST results can be translated into the European situation, where screening mammography exams are usually double-read and recall rates are much lower. Per Skaane in the Oslo II study at a recall rate of 3.7% for digital and 3.0% for film-screen mammography (compared to around 10% for women <50 years of age in the DMIST trial) found a much smaller, statistically not significant advantage for digital mammography in women below the age of 50 (Table 2). To be able to take full advantage of digital mammography in women with dense breasts, it may therefore be necessary to aggressively recall even subtle findings, so-called "minimal signs" as defined in the Dutch screening program [43]. In European population-based screening programs, however, there is a tendency to initially ignore these minimal signs in order to keep the recall rate at an acceptable low level [43].

Table 3 Impact of double examination on cancer detection in paired screening trials

	Age (years)	Number of exams	Number of cancers[a] detected by mammography				Gain by adding the second modality[b]	
			All	Film-screen	Digital	Both	Film-screen only	Digital only
Lewin [33]	>40	6,736	42	33 (78.6%)	27 (64.3%)	18 (42.9%)	15 (+55.6%)	9 (+27.3%)
OSLO I [34]	50–69	3,683	31	28 (90.3%)	23 (74.2%)	20 (64.5%)	8 (+34.8%)	3 (+10.7%)
DMIST [35]	All	42,555[c]	237	174 (73.4%)	185 (78.1%)	122 (51.5%)	52 (+28.1%)	63 (+36.2%)
	≥50	28,200	183	142 (77.6%)	137 (74.9%)	96 (52.5%)	46 (+33.6%)	41 (+28.9%)
	<50	14,355	54	32 (59.3%)	48 (88.9%)	26 (48.1%)	6 (+12.5%)	22 (+68.8%)

[a]All breast malignancies including invasive and in-situ breast cancers
[b]Percentage values are relative to the number of cancers found by the other modality
[c]Excluding 205 women who underwent only one type of mammography exam

Microcalcifications

For a long time, the question whether digital mammography with a spatial resolution lower than film-screen mammography systems can adequately visualize small microcalcifications has been at the center of an intense debate. In theory, digitization with a limited spatial resolution may impair visualization of small details in two ways. Objects smaller than the pixel size of a digital detector will be shown larger and with lower contrast. In addition, the shape information of small objects may be lost, since objects slightly larger than the pixel size will be depicted by a few square pixels [4, 44]. However, both experimental studies [45, 46] as well as clinical trials [47–49] have shown this to be irrelevant both for detection and characterization of microcalcifications. This is due to the fact that in overview (unmagnified) mammographic images, only microcalcifications larger than approximately 130 μm can be detected [2, 50]. With these small microcalcifications just at the detection threshold, also with film-screen mammography no real shape information is discernible due to screen unsharpness, scatter radiation and geometric blur associated with the larger focus. Although on average there may be no differences in the depiction of microcalcifications between film-screen and digital mammography, both systems may have advantages and disadvantages in certain patient populations. Integrated digital systems with a high DQE imaged at sufficient dose may be superior to film-screen mammography in depicting microcalcifications in dense parenchyma due to higher contrast. This is not true for CR systems, which at clinically acceptable dose levels have a relatively high noise level in areas of dense parenchyma, limiting the visualization of subtle microcalcifications. While in general the lower spatial resolution of digital mammography will not play a role in clinical practice, digital mammography may be at a slight disadvantage in older patients with small and transparent breasts, in whom film-screen mammography may depict details smaller than the usual visibility threshold of around 130 μm. Although not analyzed separately, there may have been a slight advantage for film-screen mammography in the DMIST trial in patients ≥50 years of age and with transparent breasts [51, 52], which could support this hypothesis.

Some authors have suggested that with digital mammography fewer magnification views may be necessary [53]. Based on theoretical considerations and our own clinical experience with digital mammography for more than 7 years now, this theory cannot be supported. Electronic magnification (zooming) of digital mammograms contains less rather than more additional information compared to using a strong magnifying glass with high spatial resolution film-screen mammography. With digital mammography systems, due to the limited spatial resolution, small microcalcifications will be depicted by just a few individual pixels. Electronic magnification can be done in two ways, pixel replication or interpolation. When pixel replication is used, small microcalcifications will always be shown with a ragged border due to the blown-up square pixels. Both with bilinear and bicubic interpolation, the two most common forms, small microcalcifications will always appear round on the electronically magnified images. In both cases, no relevant additional information is provided by the electronic magnification other than that the microcalcifications are easier to see. Both with conventional film-screen and digital mammography, additional small-focus spot views with geometric (e.g., ×1.8) magnification are necessary for more detailed analysis of microcalcifications. Due to the higher spatial resolution related to the magnification as well as the reduced geometric unsharpness offered by the smaller focus, true geometric magnification views will show additional smaller microcalcifications not seen on the overview mammogram and the shape of the individual microcalcifications will be more clearly depicted (Fig. 4). Both with film-screen and digital mammography, it may sometimes be difficult to reliably distinguish subtle amorphous microcalcifications at the detection threshold from image noise. Again, electronic magnification will not help in this situation, since both noise as well as microcalcifications will be shown enlarged, and true geometric magnification views will be necessary to resolve this question.

Impact on workflow

Introduction of digital imaging into mammography has significant workflow implications. Most of the advantages of digital mammography are related to getting rid of film. With integrated digital systems, the lack of film cassette handling allows for a higher patient throughput [54] and lets the technologist concentrate more on the patient. Especially interventional procedures such as preoperative wire localizations are much faster with integrated digital systems without the need for films to be developed between each step of the procedure. Digital images can automatically be transferred, stored and retrieved without the need for human interaction. There are no lost or misplaced films and digital images can be viewed by several different people at the same time. Film library space and personnel are freed up, and the higher investment costs for digital mammography are at least in part compensated for by these savings [55]. When considering the impact of digital mammography on the reading of mammographic studies, the picture is less clear-cut. There is no doubt that images acquired digitally should best be read as soft-copy on a monitor. Only in this way can the main advantages of digital mammography such as tailored image processing and contrast optimization be harvested. However, depending on detector area and pixel size, digital mammograms may have an image matrix of up to 4,800×6,000 pixels with a file size of more than 50 MByte. These images are

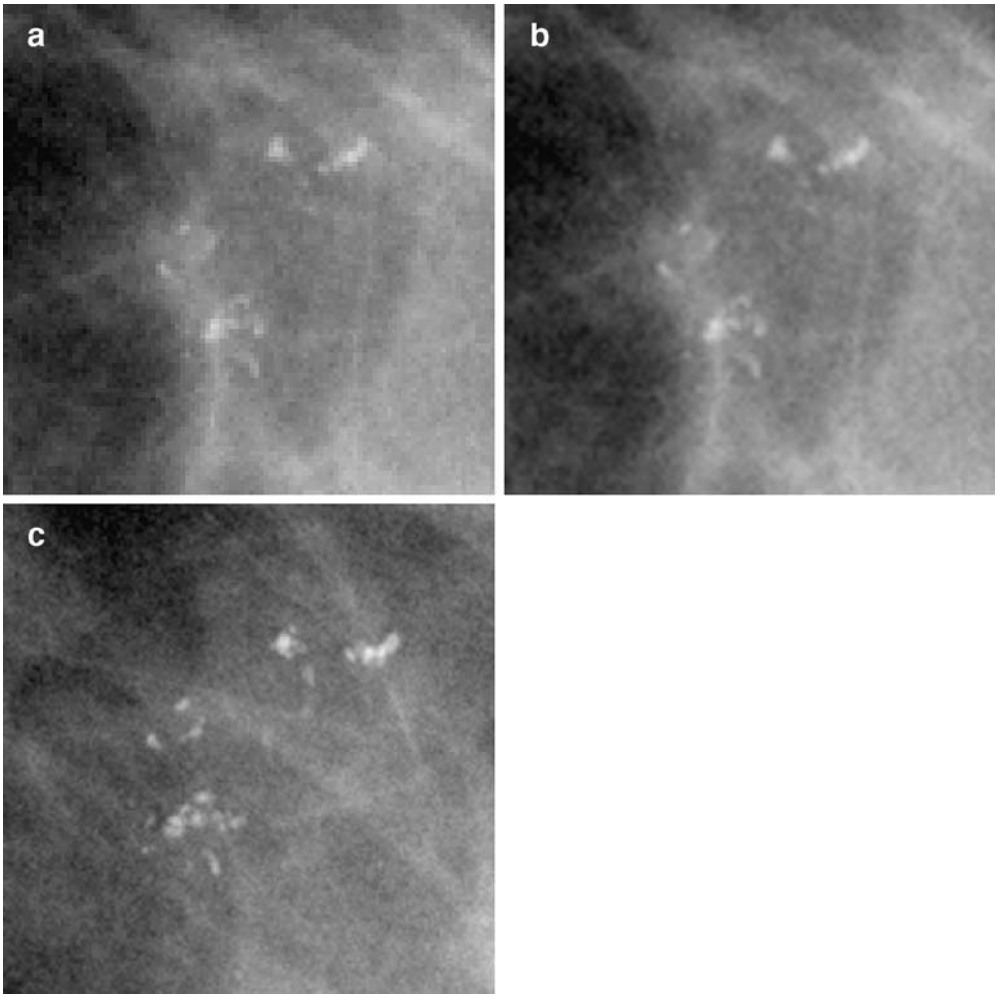

Fig. 4 Impact of true geometric magnification on the visibility of microcalcifications. A 52-year-old patient with a suspicious cluster of microcalcifications on mammography (diagnosis: high-grade DCIS). Electronic magnification of the overview digital mammogram using pixel replication (**a**) and bicubic interpolation (**b**) compared to the geometric ×1.8 spot magnification view (**c**). The shape of the individual microcalcifications is much better defined on the geometric magnification view, in addition several additional smaller microcalcifications are seen. The images shown correspond to an area of approximately 1×1 cm

too large to be displayed at full 1:1 resolution on a high-resolution 5-megapixel monitor, the current standard for mammography review workstations. Both hard- and software of mammography review stations has improved significantly over the last few years. Dedicated mammography review stations now allow to switch almost instantaneously between different image layouts including a sequential magnified quadrant zoom, with softcopy reading speed approaching or even surpassing that of batch film reading [56, 57]. Viewing the entire image piece by piece in full resolution may be tedious, but necessary to ensure that no microcalcifications are overlooked. There has been some discussion recently about the use of computer-aided diagnosis (CAD) techniques, which have a near perfect sensitivity for microcalcifications of more than 98%, as a preprocessing tool, only showing those areas of the image in full resolution to the radiologist, where the CAD system has detected possible microcalcifications [58]. This concept has the potential for significantly speeding up softcopy reading of digital mammograms.

Different opinions exist on how to handle prior mammographic films when reading digital mammogram softcopy. Digitization of prior films is expensive, and image characteristics of digitized films are different from primary digital mammograms, making direct comparison difficult. Keeping a film viewer next to the computer workstation is not only cumbersome, but light from the view box may interfere with the image display on the monitor. Some groups have therefore decided with softcopy reading not to offer prior mammographic films during the primary reading session, but only in the consensus conference in case abnormal findings exist on the current exam requiring comparison with older exams [36].

Another limitation of softcopy reading is related to the lower maximum contrast of monitors compared to viewing film in front of a high luminance alternator. Most vendors try to compensate for this disadvantage of monitor reading by specialized non-linear image processing, compressing the dynamic range of the mammographic image so that the entire breast from the chest wall to the skin can be viewed simultaneously at maximum contrast [59, 60]. Key to this technique is a so-called thickness compensation or density

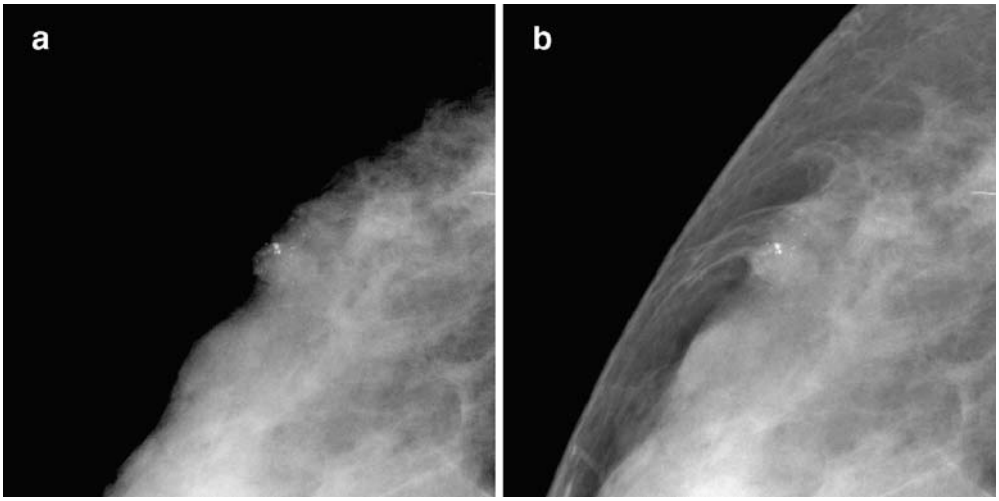

Fig. 5 Peripheral density correction in digital mammography. A 57-year-old patient with low-grade DCIS. The relatively superficial lesion with internal microcalcifications is only partially seen on the raw unprocessed image (**a**), which is similar to conventional film-screen mammography. On the processed image (**b**) the skin and subcutaneous tissue are shown with the same contrast and brightness as the central areas of the breast, and the lesion is shown in its entirety

equalization, which increases the brightness of the dark peripheral breast areas closer to the skin to match the brightness of the central parts of the breast (Fig. 5). In digital mammography, a variety of other image processing algorithms are available, e.g., to enhance the conspicuity of certain relevant findings such as masses or microcalcifications. Image processing may vary substantially among different digital mammography vendors, even endangering interoperability between mammography review workstations. Not surprisingly, there is also no agreement on the optimal image processing among radiologists [61], and care has to be taken not to prolong reading times by switching too much between different image processing and window settings.

Computer-aided diagnosis

Computer-aided diagnosis (CAD) can be defined as a diagnosis made by a radiologists taking into account the computer output as a second opinion, similar to the use of a spell-checker program. The concept of computer-aided diagnosis in mammography has now been around for more than 40 years [1]. Much of the earlier research as well as the first FDA-approved clinical system introduced in 1998 were based on digitized film-screen mammograms. However, integration of CAD into the workflow is much easier with digital mammography, where the CAD output can be shown directly on the mammography review workstation [62]. Although mammography CAD systems have received wide-spread adoption in the US, where there is additional reimbursement for the use of CAD, the clinical value of CAD is still being debated [63]. Several clinical studies have demonstrated that by using CAD more and smaller cancers can be detected, usually at the expense of a slightly higher recall rate [64–66]. The usefulness of CAD will vary with the mammography experience of the reader, and thorough training in the use of the CAD system will improve results [63]. One major problem of CAD is the still relatively high number of false-positive computer marks, on average between one and two per case [67], which means that in a screening situation often less than 1 in 100 computer prompts actually represents cancer (Table 4). It is important to realize that the sensitivity of CAD systems is different for masses and microcalcifications. While microcalcifications can be reliably detected by the computer with a sensitivity of more than 98%, the sensitivity of CAD systems for mammographic masses is significantly lower [68]. Even with high sensitivity/low specificity settings, current CAD systems miss around 10% of masses, which can be detected by a human observer [67]. Due to the very high sensitivity for microcalcifications, CAD systems may in the future be used to improve the reading workflow of digital mammograms. Radiologists would no longer need to look at the entire mammographic image at full resolution, something that depending on the pixel matrix of the image may take a long time, but would only need to look in full resolution at areas with possible microcalcifications detected by the CAD system [58]. Other future applica-

Table 4 Positive predictive value of CAD marks in a screening setting

Average number of CAD marks per normal case	Positive-predictive value (ppv)[a]	Number of positive CAD marks/abnormal readings to detect one cancer
5	0.001	1,000
1[b]	0.005	200
0.1	0.05	20
Radiologist[c]	0.1–0.5	2–10

CAD = computer-aided diagnosis
[a]Assuming a cancer detection rate of 5 per 1,000 screening exams
[b]Performance of current commercial CAD systems
[c]Based on a range of radiologists' recall rates between 1% and 5%

tions of CAD include prescreening, where a radiologist would no longer need to look at all at a mammogram with no computer-detected abnormalities, and double reading with CAD, where one of the human readers in the double reading process would be replaced by the computer.

Conclusion

Digital mammography has established itself as a true alternative to film-screen mammography offering significant workflow improvements, and there is no doubt that in the long run digital mammography will replace film-screen mammography. Although in general the diagnostic accuracy of digital mammography is similar to that of film-screen mammography, digital mammography may have specific advantages in younger women due to the possibility to selectively enhance image contrast in areas of dense parenchyma. Digital mammography enables an array of advanced applications such as contrast-enhanced mammography, tomosynthesis and computer-aided diagnosis, although the value of these new techniques in clinical practice has yet to be shown. Future efforts should aim to further optimize image acquisition parameters in digital mammography resulting in the lowest possible radiation exposure to the breast as well as to improve and standardize image processing techniques.

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