

Blind Title Page

The impact of simulated motion blur on lesion detection performance in full field digital mammography

Running Head: Image blurring and lesion detection in mammography

Abstract

Objective: Motion blur is a known phenomenon in full-field digital mammography, but the impact on lesion detection is unknown. This is the first study to investigate detection performance with varying magnitudes of simulated motion blur.

Method: Seven observers (15±5 years' reporting experience) evaluated 248 cases (62 containing malignant masses, 62 containing malignant microcalcifications and 124 normal cases) for three conditions: no blurring (0 mm) and two magnitudes of simulated blurring (0.7 mm and 1.5 mm). Abnormal cases were biopsy proven. Mathematical simulation was used to provide a pixel shift in order to simulate motion blur. A free-response observer study was conducted to compare lesion detection performance for the three conditions. The equally weighted jackknife alternative free-response receiver operating characteristic (wJAFROC) was used as the figure of merit. Test alpha was set at 0.05 to control probability of Type I error.

Results: wJAFROC analysis found a statistically significant difference in lesion detection performance for both masses ($F(2,22) = 6.01, P=0.0084$) and microcalcifications ($F(2,49) = 23.14, P<0.0001$). The figures of merit reduced as the magnitude of simulated blurring increased. Statistical differences were found between some of the pairs investigated for the detection of masses (0.0mm v 0.7mm, and 0.0mm v 1.5mm) and all pairs for microcalcifications (0.0 mm v 0.7 mm, 0.0 mm v 1.5 mm, and 0.7 mm v 1.5 mm). No difference was detected between 0.7 mm and 1.5 mm for masses.

Conclusion: Mathematical simulation of motion blur caused a statistically significant reduction in lesion detection performance. These false negative decisions could have implications for clinical practice.

Advances in knowledge: This research demonstrates for the first time that motion blur has a negative and statistically significant impact on lesion detection performance digital mammography.

Introduction

Full-field Digital Mammography (FFDM) is the current standard imaging technique for the early detection of breast cancer¹⁻³ and high quality, artefact free, diagnostic images are crucial to the accuracy of this process. Unwanted motion during the image acquisition phase and subsequent image blurring is an unfortunate consequence in some FFDM images.⁴ It is thought that this could lead to a reduction in diagnostic performance. Figure 1 illustrates a typical example of motion blur in mammography.

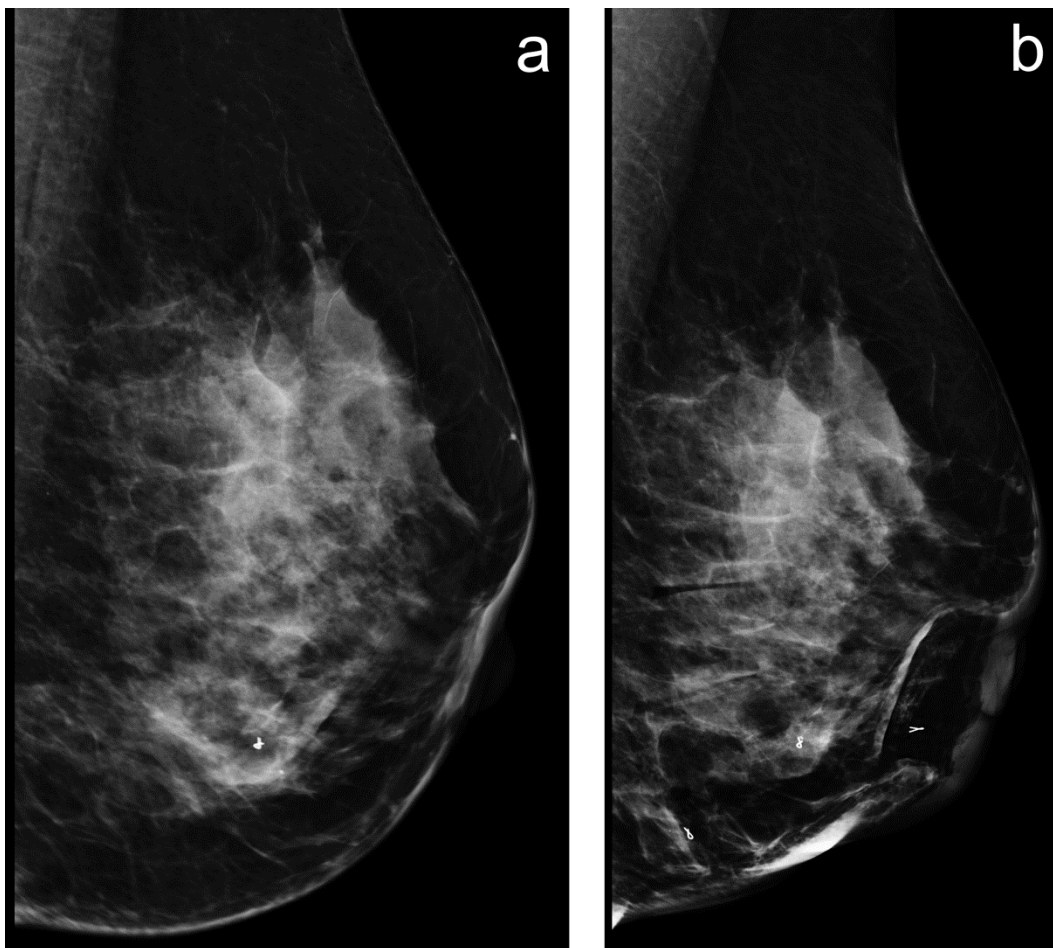


Figure 1a&b: blurred image 1a - the internal breast anatomical structures show no clearly defined edges or borders but appear unfocused and a single metallic marker within the breast resembles two (one superimposed on another) as a result of motion occurring during image acquisition. Image 1b shows no significant blurring as the breast structures are much sharper, focused and three metallic markers within the breast have clearly defined borders.

The causes of image blur can be patient-based (e.g. breast and/or chest wall motion), or technology-based (e.g. paddle movement).^{5,6} This can lead to distortion of the image in one or more directions.⁷ Chest wall motion could be due to respiration⁸ but we hypothesise that breast motion could be more complex, and could be the outcome of a combination of paddle movement, thixotropic behaviour and blood being forced away from the breast due to the applied compression force. Thixotropic behaviour⁹ can be defined as a time-dependent reduction of viscosity and modulus induced by deformation when mechanical loading changes breast volume and results in motion of fixed structures (glandular and adipose tissues).

Compression paddle motion has been reported to occur during the 'clamping' phase¹⁰ and it has been hypothesised that this may cause image blur.¹¹ Recent research identified paddle motion to be present in a number of FFDM machines during the clamping phase, with estimates of motion being as high as 1.7 mm.^{12,13} Further reports suggest that the visual impact of simulated image blurring can be detected from 0.4mm of movement.¹⁴

Anecdotal evidence within the National Health Service Breast Screening Programme (NHSBSP) suggests that image blurring may require images to be repeated, thus increasing patient radiation dose, anxiety, and service costs. The paucity of literature on this topic suggests that this technical issue continues to be under-reported. Some studies^{15,16} have calculated the repeat and technical recall rates with direct reference to image blurring. Several studies report image blurring to be a dominating factor in overall recall rates,^{18,19} causing up to 90 % of all recalls.¹⁹ Results from another screening service found that 0.86 % of all screening candidates were recalled due to image blurring;¹⁶ a high proportion of the 3% maximum NHSBSP permissible rate for repeated images.¹⁶

Recent research¹² suggests blurring is visible at sub-millimetre levels, but presently we do not know the impact of blurring on breast cancer detection. Consequently, our current study seeks to understand whether blurring has an impact on cancer detection performance in FFDM. Our approach uses novel software to perform a pixel shift simulation of motion to introduce blurring to clinical FFDM images.

Materials and Methods

Case Selection

Ethical approval for this study was granted by the University of Salford (HSCR15-107) and with consent from The University Hospital of North Manchester, Nightingale Centre. This was a retrospective study of breast screening images drawn from the PROCAS database²⁰. Initially 150

cases containing microcalcification, 150 cases containing masses and 150 normal cases were made available. These were reviewed visually to identify a range of BIRADS density grades and to ensure that the cases did not contain blurring. Cases were chosen from a bank of 300 to ensure a representative distribution of breast density (A=10%, B=40%, C=40%, D=10%) while also excluding cases where the pathology was too obvious, to control difficulty, and also excluding cases that contained artefacts other than blurring. The FFDM system used for image acquisition was the GE Seno Essential. This FFDM unit has a 23x19.2 cm² field of view alpha-Si flat panels coupled with a CsI(Tl) scintillator image receptor with 100-micron pixel size. This system was operating within the NHSBSP quality assurance guidelines.²¹ All images from clients deemed to be mammographically normal had gone through a subsequent breast screening cycle (3 years) to confirm that no cancer was present. Images demonstrating either malignant microcalcifications or masses were biopsy proven cancers. A mammography image reader with 17 years of mammography reporting experience re-confirmed the location(s) of masses and microcalcifications in all images. This acted as the truth for the observer study.

In total, 248 cases (124 normal; 62 containing microcalcifications; 62 containing masses) were evaluated by the observers at 0 mm (no blurring), and two magnitudes of simulated blurring, 0.7 mm and 1.5 mm. Sample size was guided by tables provided by Obuchowski.²⁸ Free-response data was analysed separately for microcalcifications and masses. All images were assessed visually by an experienced mammography advanced practitioner to exclude any images which may have contained blur.

Simulated Blurring and Image Display

A mathematical model^{22, 23} was used to simulate motion in the FFDM images.¹³ Simulated motion blur was applied using a convolution mask that provided a 3 standard deviation (3SD) distribution of blur over the desired blur radius. The 3SD range is consistent with the application of a Gaussian blur mask, typically used to generate generic blur effects (equivalent to a semi-transparent film being placed over an image). However, the Gaussian distribution profile did not match the characteristics of a typical blur effect. To determine an appropriate blur distribution function a simulation of image pixel motion, under elastic restitution, was made. This allowed an individual pixel to be displaced by a random vector (within the range of the blur effect) and the pixel contribution to the overall image sampled by sub-steps, as the pixel returned to the central position. Sampling of the motion pixel was enacted as a pixel sized Gaussian distribution within a super-sampled image frame to allow for fractional motion within each sub-step. Repeated iterations of this process enabled a representative

distribution profile to be generated that showed a sharper central peak, more rapid initial distribution decay, and longer continuation, than with a traditional Gaussian function. Multiple applications of the simulation were made to define an average distribution function. To ensure that the intensity window of the pixel values remained the same after blurring, the pre-blurring minimum and maximum pixel intensities were corrected post-blurring through intensity scale and shift.

An initial face validity check with 8 mammography practitioners suggested the visual appearance of simulated blur was comparable to real blur. Subsequently, 5 mammography practitioners who had been trained to identify image blur were presented with 20 real and 20 simulated (10 at 0.7mm and 10 at 1.5mm) blurred images in a randomised and anonymised fashion. The images were displayed on a 5MP monitor calibrated to the DICOM greyscale standard; ambient lighting was set below 10 lux²⁴. For images containing simulated blurring the average incorrect rate was 34% (SD=13.8); for real blur, the average incorrect rate was 34% (SD=20). The incorrect rate refers to the proportion of images incorrectly identified as either real blur or simulated blur. On this basis, we propose the visual appearance of simulated blur to be comparable to that of a real blur.

In accordance with observations made by Ma et al.,^{12, 13} two levels of simulated blurring were used in our study and images were evaluated under 3 conditions - without blurring (0 mm), and with two magnitudes of simulated blurring (0.7 mm & 1.5 mm). Ma et al. (2014) concluded that the extent of paddle motion, through the acquisition of mammographic images, could be as much as 1.5 mm in the vertical plane. Ma et al. (2015) illustrated that image blurring at 0.7 mm is the minimum amount of simulated breast movement required for visually detection of soft edge mask estimation of blurring; as used in this study.

For the free-response receiver operating characteristic (FROC) study, images were displayed on a 5-Megapixel reporting grade monitor calibrated to the DICOM Grey Scale Display Function (GSDF) Standard.²⁴ Ambient room lighting was set to below 10 lux. ROCview²⁵, which provides zoom up to 100%, was used to provide a randomised order of cases for each observer in each evaluation and to record the observer data from the free-response study.

Observer Performance Study

Seven observers (15±5 years' clinical reporting experience in mammography) evaluated image sets containing malignant masses, microcalcifications and normal cases for the three conditions. All observers participate in the NHSBSP approved biannual external audit which evaluates their performance for difficult cases specifically selected by expert radiologists.^{26, 27} It was agreed that

local directors of screening would be notified of any outliers regarding poor performance; however, no outliers were identified and this was not required.

All observers were provided with relevant training prior to beginning the free-response study. Observers were shown 15 images, not used in the main study, comprising of 5 normal images, 5 containing masses and 5 containing microcalcifications. This introduced the observers to the task and familiarised them with creating mark-rating pairs²⁸ (localisation and confidence score) using mouse clicks and a slider-bar confidence scale. Observers were instructed to move the slider-bar (scale 1-10) further to the right for an increasing suspicion of malignancy. Observer ratings were then displayed alongside the case. All observers were advised of the importance of localising the centre of each lesion, as all localisations are compared to a reference map (truth) and determined as lesion localisation (LL) or non-lesion localisation (NL) by an acceptance radius emanating from the centre of each lesion/cluster. A minimum period of 2-weeks was imposed between image evaluations to reduce the influence of case memory. Each observer completed the evaluations (0 mm, 0.7 mm, and 1.5 mm) in a different order to reduce the dependence of evaluation order on the overall figure of merit (FOM).

Statistical Analysis

Free-response data was analysed primarily using the equally weighted jackknife alternative free-response receiver operating characteristic (wJAFROC) FOM. This represents the empirical probability that a lesion localisation is rated higher than a non-lesion localisation on normal cases.^{29,30} Data analysis was performed using Rjafroc³¹ where we also used alternative FOMs to provide us with values of sensitivity (FOM = HrSe) and specificity (FOM = HrSp). Test alpha was set at 0.05 to control probability of Type I error.

Separate analyses were performed for the detection of microcalcifications and masses. For each analysis, an acceptance radius was used based on the maximum size of the mass or spread of an individual cluster of microcalcifications. The acceptance radius was set at 42 pixels (11 mm) for masses and 50 pixels (13 mm) for microcalcifications.

The wJAFROC FOM was calculated to reward correct localisations and penalise errors. It provides a single value summarising performance which can be compared statistically. For instance, comparing two magnitudes of simulated blurring, one calculates a FOM for each method and a statistical test is performed to identify the difference between two FOMs; if the difference is large enough to be different in consideration of the pre-test value of alpha (0.05) then there is a statistical difference if

the result of the overall F-test is also significant.³² We report the result of the overall F-test, p-values for FOM pairs, and the observer averaged FOM and 95% confidence interval (CI) for each magnitude of simulated blurring.

Results

Free-response data were collected for the detection of malignant microcalcifications and masses for three conditions; (i) no simulated blurring (0 mm), and for two magnitudes of simulated blurring (ii) 0.7 mm, and (iii) 1.5 mm. A statistically significant difference was found for the detection of masses ($F(2,21) = 6.01, P=0.0084$) and for the detection of microcalcifications ($F(2,49) = 23.14, P<0.0001$). For both analyses, a significant difference was observed between 0 mm and 0.7 mm, and between 0 mm and 1.5 mm of simulated blurring, and also between 0.7 mm and 1.5 mm for microcalcifications. No significant difference was detected between 0.7 mm and 1.5 mm for masses. Rjafroc was also used to calculate observer averaged sensitivity (FOM = HrSe) and specificity (FOM = HrSp) as the FOM for all conditions for microcalcifications and masses, Table 1 & Table 2.

Two cases (Figure 2a & 2b) illustrate the impact of the simulated blurring on the visual task. Figure 2a demonstrates a spiculated mass of irregular shape, low density, and indefinite borders. The percentage of observers detecting this abnormality reduced from 100% (7/7) to 71% (5/7) for 0.7 mm of simulated blurring, and to 71% (5/7) for 1.5 mm of simulated blurring. Figure 2b illustrates a case with a single cluster of granular microcalcifications of varying shape and density in the outer half of the right breast representing ductal carcinoma in situ. Again, this case saw a reduction in the number of observers detecting this cluster, from 100% (7/7) to 43% (3/7) for 0.7 mm of simulated blurring, and to 29% (2/7) for 1.5 mm of simulated blurring.

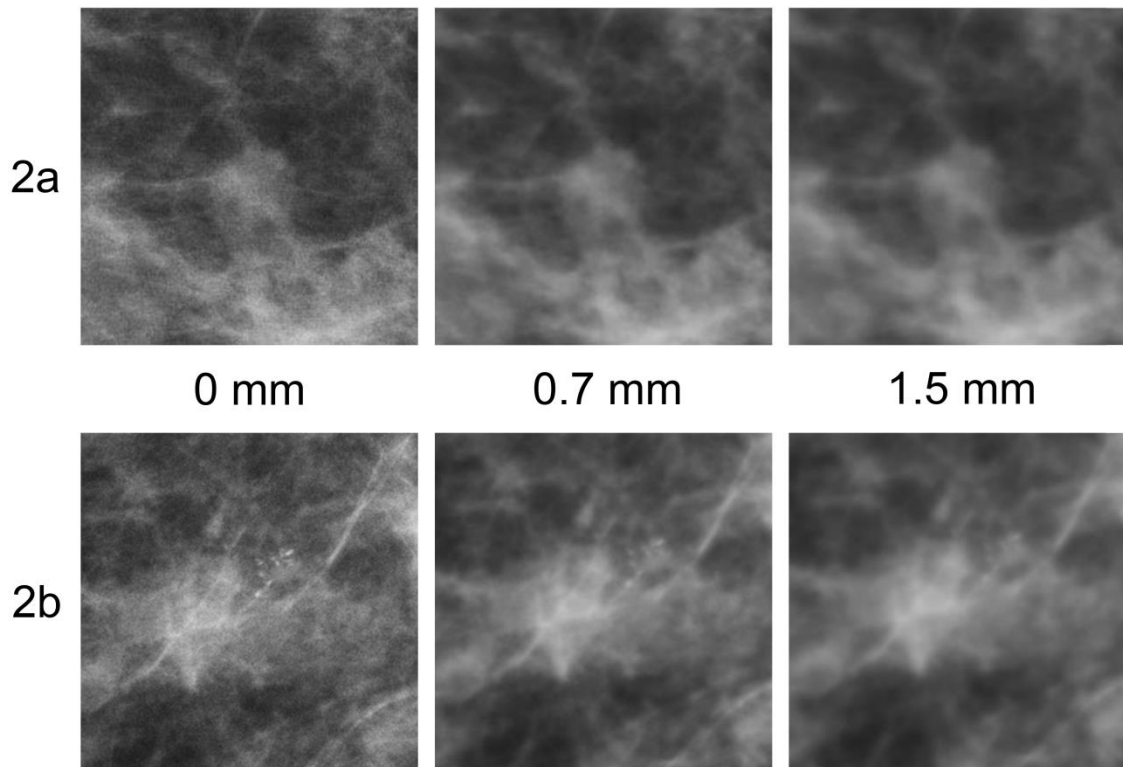


Figure 2a&b: Zoomed areas of FFDM images at 0 mm, 0.7 mm, and 1.5 mm of simulated blurring. A) Demonstrates a spiculated mass of irregular shape with indefinite borders. B) Illustrating a single cluster of granular microcalcifications with different shape, density, and size. While the mass becomes increasingly difficult to visualise, the microcalcifications are no longer visible with 1.5 mm of simulated blur.

Microcalcifications

For microcalcifications, the observer averaged wJAFROC FOM and 95% confidence intervals (CIs) are displayed in Table 1. Differences between FOM pairs (magnitudes of simulated blurring) are displayed in Figure 3a with the p-values to indicate significance. For a difference in FOMs to be declared significant, the 95% CI of the FOM pair must not include zero, in addition to the result of the overall F-test being significant. The observer averaged wAFROC curves for microcalcifications are displayed in Figure 4a.

When sensitivity (HrSe) was used as the FOM, a significant difference was found between all pairs of magnitudes of simulated blurring ($F(2,18) = 10.48, p=0.0010$). This implies that the false negative rate was increasing significantly as the magnitude of simulated motion blur was increased. When specificity (HrSp) was used as the FOM, there was no significant difference between magnitudes of

simulated blurring ($F(2,13) = 0.21, p=0.8110$). This reveals that the false positive rate did not increase significantly with image blurring.

Masses

For masses, the observer averaged wJAFROC FOM and 95% confidence intervals (CIs) are displayed in Table 2. Differences between FOM pairs (magnitudes of simulated blurring) are displayed in Figure 3b with the p-values to indicate significance. The observer averaged wAFROC curves for masses are displayed in Figure 4b.

When sensitivity (HrSe) was used as the FOM, there was no significant difference between magnitudes of simulated blurring ($F(2,16) = 0.43, p=0.6575$). This implies that the false negative rate was not changing significantly as a result of simulated motion blur. When specificity (HrSp) was used as the FOM, again there was no significant difference between magnitudes of simulated blurring ($F(2,12) = 1.31, p=0.3043$).

Magnitude of Simulated Blurring (mm)	wJAFROC FOM (95% CI)	Sensitivity (%)	Specificity (%)
0	0.899 (0.859,0.939)	97.9	84.8
0.7	0.813 (0.757,0.870)	86.4	84.3
1.5	0.746 (0.679,0.812)	76.5	86.6

Table 1: The wJAFROC FOM and 95% CI, sensitivity, and specificity for each magnitude of simulated blurring for the detection of microcalcifications.

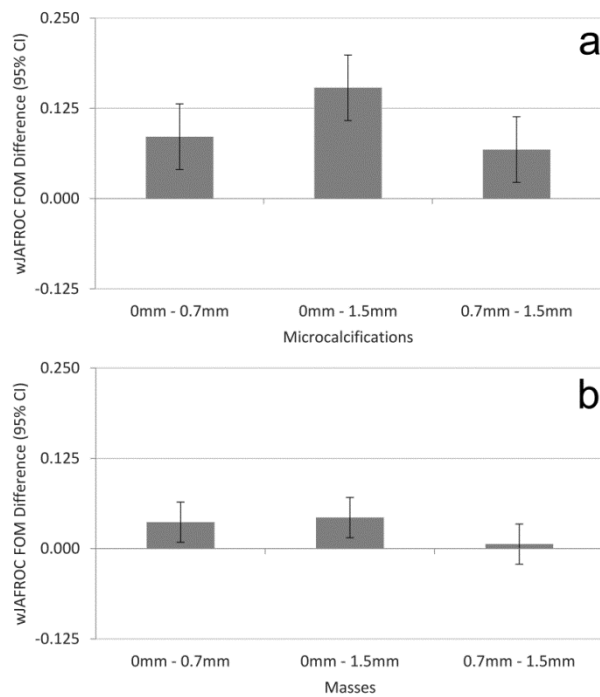


Figure 3a&b: The magnitude difference for all pairs of simulated blurring for microcalcifications (a) and for masses (b). For a difference between pairs of FOMs to be declared significant, the result of the overall F-test must be significant, and the 95% CI of the pair must not include zero. Statistical differences are evident between all pairs except between 0.7mm and 1.5mm for masses.

Magnitude of Simulated Blurring (mm)	wJAFROC FOM (95% CI)	Sensitivity (%)	Specificity (%)
0	0.905 (0.859,0.952)	92.3	82.7
0.7	0.869 (0.814,0.924)	91.9	73.3

Table 2: The wJAFROC FOM and 95% CI, sensitivity, and specificity for each magnitude of simulated blurring for the detection of masses.

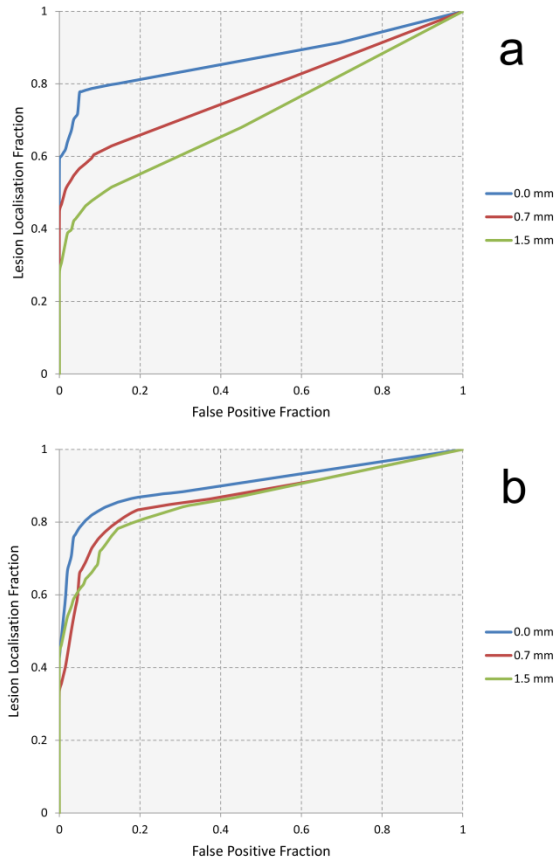


Figure 4a&b: The wAFROC curves for all magnitudes of simulated image blurring for microcalcifications (a) and masses (b).

Discussion

This study has investigated the impact of computer simulated motion by means of shifting accumulated pixel points to blur the resultant image. We have found simulated motion blur to have a significant effect on observer performance, with performance becoming statistically worse for the detection of microcalcifications as simulated blurring was increased from 0 mm to 0.7 mm, and then on to 1.5 mm. For masses, a statistical difference in detection performance was also observed when blurring was applied to the images at 0.7 mm. However, in this instance, observer performance did not become incrementally worse when the higher magnitude of blurring (1.5 mm) was applied. To be clear, there was no significant difference in detection performance between images blurred with a magnitude of 0.7 mm and those with 1.5 mm,

for cases containing masses. This was not the case for microcalcifications, where detection performance became statistically worse as the magnitude of blurring was increased. The previous work¹³ has suggested that motion blur is visible at 0.7 mm for a soft-edged blur, and our work seems to confirm this. This could have implications for practice as it could mean that when blur is observed in an image, repeat imaging should be considered as in clinical work one would simply not know how much blurring is present and what impact it is having.

An example is provided in Figure 2b. Here, 7/7 observers detected the lesion in Figure 2b when there was no simulated blurring (0 mm); this decreased to 3/7 observers at 0.7 mm and only 2/7 detected the lesion at 1.5 mm. This is a typical example of the reduction in detection performance, and this trend was observed over a large number of cases containing microcalcifications.

Conversely, we found that mass lesions that have higher contrast with their background, and/or have defined borders (oval or round), do not cause difficulties for detection in the presence of simulated blurring. This means that motion blur has less impact on higher contrast and well-defined masses.

For microcalcifications, we can be less predictive of the impact of simulated blurring on different presentations, other than to say that the impact is greater (higher level of significance) than for masses. The variation in presentation of microcalcifications may be a factor in detection performance and the influence of motion blur, but we have been unable to establish any trend.

There are many factors related to the appearance of breast lesions within FFDM images that can affect lesion detection performance: location within the breast; lesion size, shape, and contrast; the texture and complexity of the surrounding tissue. Lesions located within fibro-glandular regions of high-density breast or those complicated by overlapping anatomical structures are more challenging to detect. Small calcification clusters with indefinite edges are considered the most difficult lesions to identify due to size and poor contrast. Lesion shape can be used as a predictor of malignancy,³³ so it is important that this can be adequately characterised.

We also analysed the observer data using sensitivity and specificity as FOMs to obtain a better understanding of the impact of simulated motion blur. For both microcalcifications and masses there was a reduction in sensitivity as the magnitude of simulated image blurring was increased. For masses, this was not statistically significant and the values in Table 2 demonstrate that the false negative rate changed little as blurring increased. For microcalcifications, this was not the case and there was a statistically significant reduction in sensitivity, Table 1, suggesting that the increase in motion blur caused the smaller lesions to become visually imperceptible. Figure 2b provides a typical

example of this. The change in specificity was not significantly different for masses or microcalcifications.

There are some limitations to our work. In clinical mammography, the operator does not know what magnitude of motion blur they are inspecting, so it could be suggested that it was superfluous to investigate two different magnitudes of motion blur. However, we know from previous work¹² that image blurring is visible at about the level of 0.7 mm for the soft edge mask used in this simulation, so it is of interest to understand if this caused a reduction in observer performance; if it didn't, we needed to understand whether a higher magnitude of motion blur did cause an effect. Of course, the image blurring in this study is a simulation, and it has a global effect on the image. In clinical mammography, the motion blur may be global or regional and for regional blurring, we are not able to predict the impact of this on lesion detection performance from our current work. Additionally, image noise may be blurred by our mathematical simulation, while real movement blur would not affect quantum mottle. To overcome a potential smoothing effect on quantum mottle, brought about by mathematical simulation, it may be possible to adapt our method by adding noise back into the newly created blurred image. Despite this, our method gives us a certain level of control on motion blur that could not be achieved with blurred images from a clinical setting. In respect of the power of the study, it should also be noted that the prevalence of disease in our study is much higher than would be expected in a screening population, but this is difficult to overcome in observer studies.

A further limitation of the blurring process is also worth raising. The blurring process is enacted as a convolution mask that, in effect spreads each pixel, redistributing its intensity into the neighbouring pixels based on a function and mask size determined by the modelling of the pixel motion as a random vector path parameterised by the characteristics of breast tissue (generalised) elastic coefficient, required duration and required displacement. The latter two factors act as input to the simulation to determine the magnitude of the blur effect. This creates a controllable blur mask for convolution that has a distribution curve reflective of the intensity spread within a collimated light (energy) propagation system reflective of the X-ray system used. Without modelling actual motion within the breast it is not possible to determine direction of motion at a specific locality within the breast, so this is an approximation to the blur effect that is uniform for the entire image region. Localisation is possible, but requires each source image to have a specific region of blur

defined and in this case motion is assumed to be radial, and the mask application adjusted accordingly on a per pixel basis, from the centre of the defined region, with maximum motion at the centre, reducing to zero motion at the perimeter of the region. Given the large number of source images processed for this study, and the requirement for a consistent blur effect on all the generated image sets, regional blurring was not used in this study. This is a limitation in that the blur effect is indicative of the blur that would be present within a 'real' patient image in terms of magnitude and effect, but does not replicate the directional nature of the blur that would occur for a 'real' image.

Conclusion

Simulated motion blur has a statistically significant and negative impact on lesion detection performance for the detection of malignant microcalcifications and masses in FFDM imaging. In view of this, caution should be exercised when making decisions about the acceptability of images that appear to contain blur as false negative decisions could be reached.

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