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Zooming method (× 2.0) of digital mammography *vs* digital magnification view (× 1.8) in full-field digital mammography for the diagnosis of microcalcifications

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ABSTRACT. The purpose of this study was to determine whether the interpretation of microcalcifications assessed on images zoomed (× 2.0) from digital mammograms is at least equivalent to that from digital magnification mammography (× 1.8) with respect to diagnostic accuracy and image quality. Three radiologists with different levels of experience in mammography reviewed each full-field digital mammography reader set for 185 patients with pathologically proven microcalcification clusters, which consisted of digital magnification mammograms (MAGs) with a magnification factor of 1.8 and images zoomed from mammograms (ZOOM) with a zoom factor of 2.0. Each radiologist rated their suspicion of breast cancer in microcalcific lesions using a six-point scale and the image quality and their confidence in the decisions using a five-point scale. Results were analysed according to display methods using areas under the receiver operating characteristic curves (A_z value) for ZOOM and MAGs to interpret microcalcifications, and the Wilcoxon matched pairs signed rank test for image quality and confidence levels. There was no statistically significant difference in the level of suspicion of breast cancer between the ZOOM and MAG groups (A_z=0.8680 for ZOOM; A_z=0.8682 for MAG; p=0.9897). However, MAG images were significantly better than ZOOM images in terms of visual imaging quality ($p<0.001$), and the confidence level with MAG was better than with ZOOM ($p<0.001$). In conclusion, the performance of radiologists in the diagnosis of microcalcifications using ZOOM was similar to that using MAGs, although image quality and confidence levels were better using MAGs.

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Magnification mammography produces better spatial resolution and signal-to-noise ratio than does contact mammography. It is well established as a valuable adjunct to contact mammography, especially for the diagnosis of microcalcifications, despite the additional radiation exposure and increased radiation dose because of the shorter distance between the breast and X-ray source during examination [1–4].

However, with respect to full-field digital mammography (FFDM), a few studies using zoomed images from contact mammograms have recently been reported and, as a result, a debate has arisen over whether a digital zooming system of FFDM can replace the magnification view of digital mammography [5–7]. Whereas Fischer et al [5] reported that zoomed images of a digital contact mammogram were equivalent to direct magnification of FFDM for the interpretation of microcalcifications, our previous report suggested that magnification mammography yielded better sensitivity and receiver operating characteristic (ROC) analysis than did zoomed images [7]. However, that study compared images zoomed by a factor of 1.3 with images magnified by a factor of 1.8. Therefore, we wondered whether using a zooming factor comparable to a magnification factor of 1.8 would yield the same results.

The purpose of this study was to determine whether the diagnostic accuracy and image quality of microcalcification assessments using images twice zoomed from contact mammograms were equivalent to those obtained using digital magnification mammography by a magnification factor of 1.8.

Methods and materials

Institutional Review Board approval was obtained for this retrospective study. Informed patient consent was not required.

Study population

From October 2006 to February 2008, 2648 percutaneous biopsies or localisations for surgical biopsy were referred and performed at our breast imaging division. Among them, masses were targeted regardless of the presence of microcalcifications in 2414 biopsies or localisations; the

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remaining 234 biopsies or localisations involved microcalcifications. Of these 234 patients, all underwent contact mammograms; most had also undergone magnification mammography before biopsy recommendation. Their medical and radiological records were reviewed retrospectively by one radiologist. Exclusion criteria were as follows: (i) cases of microcalcifications associated with possible masses, such as an asymmetry or focal asymmetry ($n=18$), on a retrospective review, (ii) cases without available magnification mammogram or contact mammography of FFDM performed within one month ($n=26$), (iii) cases without visible calcifications on specimen mammograms after biopsy ($n=1$), and (iv) cases with BB marker on mammograms because of clinical palpability ($n=4$). Only calcifications in lesions that underwent FFDM by both contact mammogram and magnification mammography within one month of each other, and that underwent subsequent biopsy, were included.

Finally, 185 cases of calcification, histologically proven by needle or surgical biopsy, from 185 patients (mean age, 49.9 years; range, 27–69 years) were included in this study. We observed 43 cases of cancer, representing 23.2% of the lesions. Patient age was recorded, and breast density according to the standard Breast Imaging Reporting and Data System (BIRADS) scale [8] was reviewed for each mammogram (*i.e.* extremely dense, heterogeneously dense, scattered fibroglandular densities or almost completely fat) by the radiologist who collected data of the study population.

FFDM and workstations

Mammography was performed using the Lorad/Hologic Selenia Full Field Digital Mammography System (Lorad/Hologic, Danbury, CT). This system, based on a detector with amorphous selenium, used a 70 μm pixel direct-capture device and yielded 2560× 3328 matrix images with 18× 24 cm paddle. The system produced images of 14 bits per pixel. Standard craniocaudal and mediolateral oblique views were obtained during routine mammography.

Magnification views on digital mammography were taken using a magnification factor of 1.8. The effective pixel size of digital magnification mammograms (MAGs) was approximately 39 μm. Craniocaudal and true lateral views were obtained during the magnification view.

Images were displayed on a pair of high-resolution 5 megapixel LCD monitors (SMD 21500; Siemens, Erlangen, Germany) that were part of the review workstation (Senoadvantage, GE, Milwaukee, Wisconsin, USA) with soft-copy reading software (Senoadvantage, GE, Milwaukee, Wisconsin, USA). The pixel size of the LCD monitors was 165 μm, and the matrix size was 2048× 2560. The monitor system was set to accept 14 bit images and display a 10 bit output. The square digital zooming frame used in this study was commercially available and had a zooming factor of 2.0 set as the default mode. The size of commercially available zooming frames applied with medium-sized settings was 11.5× 11.5 cm.

Reviewers and review round

Images were evaluated independently by three radiologists who were specialists in breast imaging at the academic institutions and who had not collected the original data from the study population. Reviewers were not shown any clinical information or pathological findings from the medical records, pathological results or ratios of malignant to benign lesions included in the study. No prior film or patient history was provided. Reviewers had an average of 7.0 years (4 years, 5 years and 12 years) of experience in interpreting mammograms and 4–5 years' experience in soft-copy review of digital mammography. The three reviewers worked for different institutions during the review process for the current study. One reviewer worked for the institution from which cases were included during the entire period of case collection. Another had worked for the same institution in the first three months of case collection; the remaining reviewer had not worked for the institution at any time. The number of mammograms read by each radiologist in his/her own practice varied from 300 to 400 mammograms per month.

Cases were divided into four groups according to the acquisition date of contact mammography (Figure 1), and therefore cases were reviewed randomly with respect to the density of the breast parenchyma and lesion type. The radiologists assigned scores to the images in four sessions. Sessions were conducted 5 weeks apart, and the same case was not seen twice in any one session; contact mammography using the zooming method and magnification views of digital mammography with contact mammography were alternated. Each patient case was seen once by each radiologist, with each patient's images zoomed from mammograms (ZOOM) and MAG studies presented at different reading sessions. Sessions were conducted as follows:

- Session A: 46 ZOOM and 46 MAGs (A in Figure 1a)
- Session B: 46 ZOOM and 46 MAGs (B in Figure 1b)
- Session C: 47 ZOOM and 46 MAGs (C in Figure 1c)
- Session D: 46 ZOOM and 47 MAGs (D in Figure 1d).

Review protocol

The radiologist who collected data marked the area included by magnification mammography on each view of the contact mammogram with a commercially available circle marker of annotation to avoid the possibility of inadvertent evaluation of the wrong lesion. Each mammogram was then captured with the annotation marker as a print-screen image to identify the area of interest and not to diagnose microcalcifications.

The hanging protocol for the review round included a two-view print-screen image of a contact mammogram with the original image of the contact mammogram or magnification mammogram of the same case. The reviewer was allowed to briefly check areas of interest on print-screen images and then to open either the contact mammogram or the magnification mammogram directly according to the order. When contact mammograms were reviewed, two-view contact mammograms of one breast were hung on one monitor so that the reviewer could check the area of interest corresponding to the marked area on two-view print-screen images on the other monitor. Then mediolateral oblique and

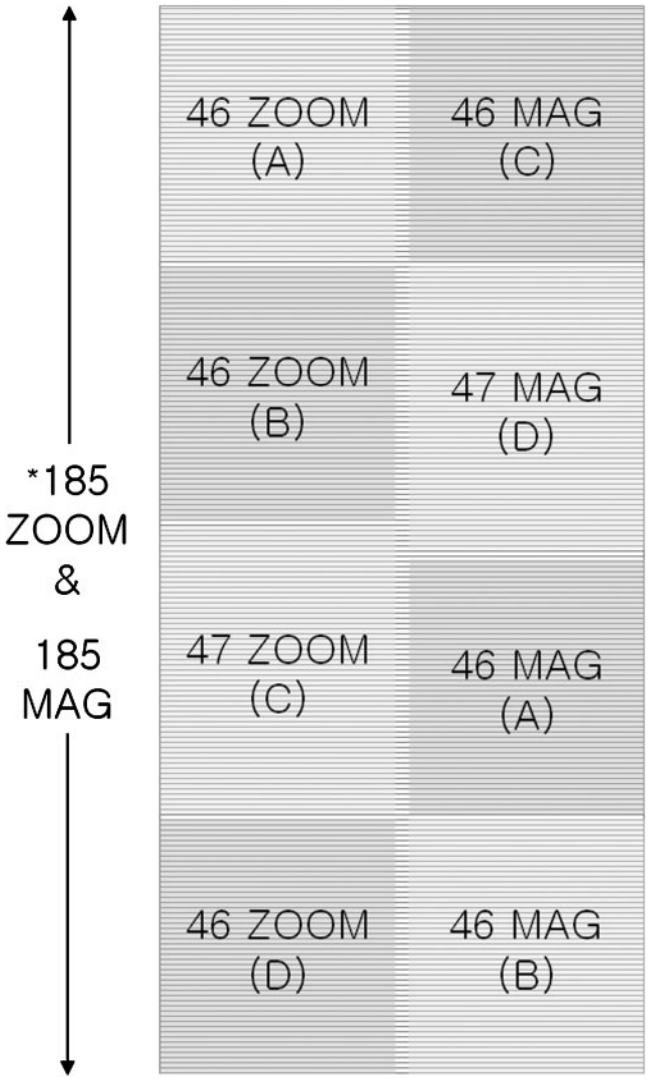

Figure 1. Diagram of the protocol for the review session (given in parentheses). ZOOM, images zoomed from digital contact mammography; MAG, geometric magnification digital mammography; *cases arranged according to acquisition date order of ZOOM.

craniocaudal views were hung simultaneously on the right and left monitors (fit to screen mode), and images on ZOOM were reviewed using a square digital zooming frame. In ZOOM, the zoomed area was always displayed with a twice-zoomed pixel pitch, without improving spatial resolution. When a magnification mammogram was reviewed, two-view magnification mammograms of one breast were displayed simultaneously on the right and left monitors (fit to screen mode) and reviewed; the print-screen images of contact mammograms were reviewed in limited cases, according to the reviewer's preference, to determine lesion distribution. The zooming frame was also used to review magnification mammography to ensure that results would reflect the accuracy of routine diagnostic work.

Each radiologist was given a questionnaire and instructed to check whether the reviewed mammogram was contact or magnification, the probability of malignancy (I), the shape (II) and distribution (III) of microcalcifications, and the image quality (IV). The probability of malignancy six-point scale was used to classify the likelihood of cancer as follows:

(1) Definitely not malignant, similar to BIRADS category 2 [7, 8].
(2) Probably not malignant, similar to BIRADS category 3.
(3) Low–possibly malignant, similar to BIRADS category 4a.
(4) Intermediate–probably malignant, similar to BIRADS category 4b.
(5) Probably malignant, similar to BIRADS category 4c.
(6) Definitely malignant, similar to BIRADS category 5.

With respect to the shape and distribution of microcalcifications, the reviewer was allowed to choose one of 14 microcalcification shapes (skin, vascular, popcorn-like, large rod-like, round, lucent-centre, milk of calcium, suture, dystrophic, punctate, coarse heterogeneous, amorphous or indistinct, fine pleomorphic, fine linear/branching) and 6 types of distribution (clustered, linear, segmental, regional, multiple grouped, diffuse). The reviewers were also asked to rate their confidence on a scale from 5 to 1 for the above three items (I, II and III), except for image quality, among questionnaire items. The meaning of the confidence numbers, in order from 5 to 1, was ''absolutely confident'', ''very confident'', ''somewhat confident'', ''not too confident'' and ''not at all confident''. The image quality of ZOOM or MAGs was evaluated and grades of 1 to 5 awarded:

(1) Not acceptable.
(2) Intermediate.
(3) Moderate.
(4) Good.
(5) Excellent.

Each reviewer was allowed to choose the most worrisome shape of microcalcifications in an area of interest.

Statistical analysis

The area under curve (A_z value) of ROC analysis was calculated for each individual reviewer and for all reviewers together with histopathological examination as the reference standard using the six-point malignancy scale for ZOOM and MAG images. Parametric estimates of the areas under ROC curves (A_z) were calculated and compared to measure reader performance with the two techniques by using Dorfman-Berbaum-Metz multi-reader, multicase method (DBM MRMC) [9, 10]. DBM MRMC used the DBM algorithm to compare multiple modalities by using data from multiple readers and multiple cases. This program employed jack-knifing and analysis of variance techniques. Statistical significance of the results was reported at 95% confidence intervals for mean differences in A_z values for reader performance using the two techniques. Mean differences were regarded as statistically significant at the 5% level when the corresponding confidence interval did not encompass zero. Inter-reviewer agreement between the three radiologists was also calculated for each display technique in terms of the probability of malignancy using

pairwise comparisons of ROC curves. For descriptive purposes, estimates of sensitivity, specificity and the positive and negative predictive values of the two display methods were computed on the basis of the six-point malignancy scale using histopathological examination as the reference standard. For this purpose, malignancy scores were dichotomised as negative (scores of 1 or 2) or positive (scores of 3, 4, 5 or 6). Values were then compared to the McNemar test. Two-tailed *p*-values less than 0.05 were considered statistically significant.

The agreement between display techniques in describing calcification shape and distribution was calculated using kappa statistics (κ). A κ-value of 0.20 or less was considered slight; 0.21–0.40, fair; 0.41–0.60, moderate; 0.61–0.80, substantial; and 0.81–1.00, almost perfect [11]. Confidence levels for shape, distribution and probability of malignancy were also calculated for ZOOM and MAG images using a Wilcoxon matched pairs signed-rank test.

To compare the image quality of the two display methods, data were evaluated using the Wilcoxon matched pairs signed-rank test. A *p*-value was calculated for cases where the reviewers did not rate the methods as equivalent. Two-tailed *p*-values of <0.05 were considered statistically significant.

A_z values were compared between ZOOM and MAGs for pre-specified subgroups, which were defined according to age (<50 years *vs* ⩾50 years), breast density (heterogeneously dense or extremely dense *vs* less dense), image quality (a rating better than 3 on the five-point scale of ZOOM image quality *vs* a rating of 3 or less), probability of malignancy (greater than 3 on the six-point malignancy scale of ZOOM *vs* 3 or less) and the confidence level of the probability of malignancy (greater than 3 on the confidence level of ZOOM *vs* 3 or less). A pairwise comparison of ROC curves was performed using statistical software (Medicalc for Windows®, version 7.4.0.0; Medicalc Software, Mariakerke, Belgium) to compare the radiologists' performance using the two techniques. DBM MRMC, as used above, was not appropriate for comparison in the pre-specified subgroups (image quality, probability of malignancy and confidence level) because the number of cases included for each reviewer was not identical. The statistical significance of results for reader performance when using the two techniques was reported as 95% confidence intervals for mean differences in A_z values. Mean differences were regarded as statistically significant at the 5% level when the corresponding confidence interval did not encompass zero.

All statistical analyses, including ROC analysis, were performed using statistical software (SAS system for Windows, version 9.1; SAS institute, Cary, NC).

Results

For the probability of malignancy on the basis of the six-point malignancy scale, the diagnostic accuracies of ZOOM and MAG were similar for each individual reviewer (Table 1) and for all reviewers together (A_z=0.8680 for ZOOM and A_z=0.8682 for MAG). The difference in A_z values for the reviewers ranged from 0.001 to 0.003. The inter-reviewer difference in diagnostic accuracy was not statistically significant for both the overall cases and each display method ($p>0.05$).

Table 1. Diagnostic performance for the diagnosis of microcalcifications: ZOOM *vs* MAG

	A_z value		
	ZOOM	MAG	95% CI of mean difference
Reviewer 1	0.8692	0.8692	−0.06112 to 0.07536
Reviewer 2	0.8504	0.8580	−0.07396 to 0.05873
Reviewer 3	0.8844	0.8773	−0.06112 to 0.07536
Reviewer all	0.8680	0.8682	−0.02973 to 0.02934

A_z value, area under receiver operating characteristic curve; ZOOM, images zoomed from digital contact mammography; MAG, geometric magnification digital mammography; CI, confidence interval.

There were no statistically significant differences between ZOOM and MAG in diagnostic performance based on the dichotomised probability of malignancy, including sensitivity, specificity and positive and negative predictive values ($p>0.05$). The sensitivity, specificity, positive predictive value and negative predictive value were 92.25 (119/129), 56.8% (242/426), 39.3% (119/303) and 96.0% (242/252) for ZOOM, and 92.2% (119/129), 50.5% (215/426), 36.1% (119/330) and 95.6% (215/225) for MAG.

Table 2 lists the case characteristics of the pre-specified subgroups. The A_z value of MAG did not vary significantly from that of ZOOM according to age, breast density, image quality of ZOOM, confidence level of ZOOM or probability of malignancy ($p>0.05$, Figure 2).

Number of lesions (n=185) × number of reviewers (n=3).Between ZOOM and MAG, the description of microcalcification shape and distribution showed fair agreement ($\kappa=0.523\pm0.042$ and $\kappa=0.563\pm0.042$, respectively). The confidence level for MAG was, however, significantly better than ZOOM at describing microcalcification shape and distribution, as well as in assigning the probability of malignancy ($p<0.0001$; Table 3).

In terms of imaging quality, MAG images were better than ZOOM images ($p<0.0001$).

Discussion

Magnification mammography is used to improve diagnostic accuracy, especially in the evaluation of microcalcifications, by imaging a particular region of the breast. Magnification increases spatial resolution and the signal-to-noise ratio. Therefore, it is a valuable adjunct to contact mammography despite the increased radiation dose and additional radiation exposure [1–4]. However, a few investigators have suggested that ZOOM, a post-processing method of digital mammography, can be a potential benefit not available with film–screen mammography [5–7]. Fischer et al [5] reported that zoomed images of digital contact mammograms were equivalent to geometric magnification FFDM in hard copy reading.

In contrast to the study by Fischer et al [5], which used a zoom factor of 1.8, another study [7] reported that magnification mammography was better than contact mammogram images when zoomed with a factor of 1.3,

Table 2. Characteristics of pre-specified subgroups in 555 microcalcifications[a]

Characteristic	n	A_z value		95% CI of mean difference	*p*-Value
		ZOOM	MAG		
Age at enrolment (years)					
<50 years	303	0.847	0.836	0.011 (−0.052 to 0.074)	0.735
⩾50 years	252	0.889	0.856	0.033 (−0.031 to 0.096)	0.310
Breast density					
Heterogeneously dense or extremely dense	411	0.848	0.839	0.009 (−0.045 to 0.063)	0.751
Almost entirely fat or scattered fibroglandular densities	144	0.828	0.844	0.016 (−0.069 to 0.101)	0.711
Confidence level of ZOOM					
>3 of confidence level for ZOOM (*i.e.* 4 or 5)	317	0.875	0.879	0.005 (−0.037 to 0.046)	0.828
3 or less	238	0.717	0.734	0.017 (−0.101 to 0.135)	0.776
Image quality of ZOOM					
>3 of image quality of ZOOM (*i.e.* 4 or 5)	392	0.846	0.849	0.002 (−0.046 to 0.051)	0.931
3 or less	163	0.805	0.775	0.029 (−0.088 to 0.147)	0.625
Probability of malignancy of ZOOM					
>3 of probability of malignancy of ZOOM (*i.e.* 4, 5 or 6)	110	0.736	0.772	0.036 (−0.062 to 0.135)	0.471
3 or less	445	0.717	0.748	0.031 (−0.058 to 0.121)	0.490

A_z value, area under receiver operating characteristic curve; ZOOM, images zoomed from digital contact mammography; MAG, geometric magnification digital mammography; CI, confidence interval.
[a]Number of lesions (n=185) × number of reviewers (n=3).

with respect to sensitivity and ROC analysis. In our study, we used a zoom factor of 2.0, which is higher than the magnification factor of MAG (1.8), to assess whether the discrepancy between the two previous studies could have arisen from the difference in zooming factors. A larger population was also used in this study when compared with previous work. The current study showed that the diagnostic performance of ZOOM using a factor of 2.0 was similar to that of 1.8 MAG. Furthermore, one of the three reviewers (reviewer 3) obtained higher A_z values from ZOOM than from MAG. However, in terms of image quality and confidence level for assigning a probability of malignancy from mammogram images, MAG was still significantly better than ZOOM. These findings suggest that the earlier discrepancy in diagnostic performance might have been caused by the difference in zooming factor. However, further studies using the same population to compare the different zooming factors should follow in order to clarify this. With currently available digital contact and magnification mammography units, we conclude that the higher spatial resolution and signal-to-noise ratio of MAG did not affect diagnostic performance, but had a significant impact on image quality and confidence in assigning a probability of malignancy.

There was fair agreement between ZOOM and MAGs in our study, as well as in previous studies [7], for the description of microcalcification shape. However, for lesion distribution, only fair agreement was noted in this study, whereas almost perfect agreement was reported in the previous study ($\kappa=0.8094\pm0.0264$ [7]). When a MAG was reviewed, a review of contact mammograms using ZOOM from the same case was not allowed, but a review of the print screen images was allowed according to the reviewer's preference. A brief review of the contact mammogram or print screen images prior to interpretation of magnification mammography could be useful for the determination of distribution. The confidence level for MAG was rated superior to that of ZOOM for diagnosis by all three reviewers This result is consistent with the previous study that used a zooming factor of 1.3 [7].

In this study, A_z values were compared between ZOOM and MAG in pre-specified subgroups of cases, which were sorted by age, breast density, image quality, probability of malignancy and confidence level in the probability of malignancy. However, the A_z value for MAG did not differ significantly from that of ZOOM in any of the subgroups. Digital mammography is known to be more useful in women under the age of 50 years, in women with heterogeneously dense or extremely dense breasts on mammography, and in pre- or peri-menopausal women [12]. However, we found no difference in the A_z value between MAG and ZOOM in women under the age of 50 years or in women with heterogeneously dense or extremely dense breasts on mammography. Although we did not evaluate the difference between pre- and post-menopausal women, it is reasonable to postulate that the effect of those differences on MAG and ZOOM were reflected in the age and breast density subgroups.

Although our results showed that digital mammography using ZOOM could obviate the need for magnification mammography in the diagnosis of microcalcification, further studies should be undertaken to confirm our results. Furthermore, zooming display in soft-copy reading may not attenuate the role of magnification mammography in other clinical situations, including the evaluation of mammographic abnormalities, such as asymmetry and distortion, and evaluation of the lesion once again under different positions [13, 14]. Magnification mammography would still be useful for the characterisation of asymmetry or distortion using a spot-compression paddle and for the confirmation of layering calcification in cases of ''milk of calcium'' using a true lateral view.

Our study has some limitations. First, our study population was larger than those of previous studies comparing MAG and ZOOM [5, 7], but the size of our series was still too small to confirm any similarity in diagnostic performance between MAG and ZOOM and to draw reliable statistical power. Further studies with a larger population and various types of equipment should be undertaken, particularly for the analyses of pre-specified subgroups. Second, this study was

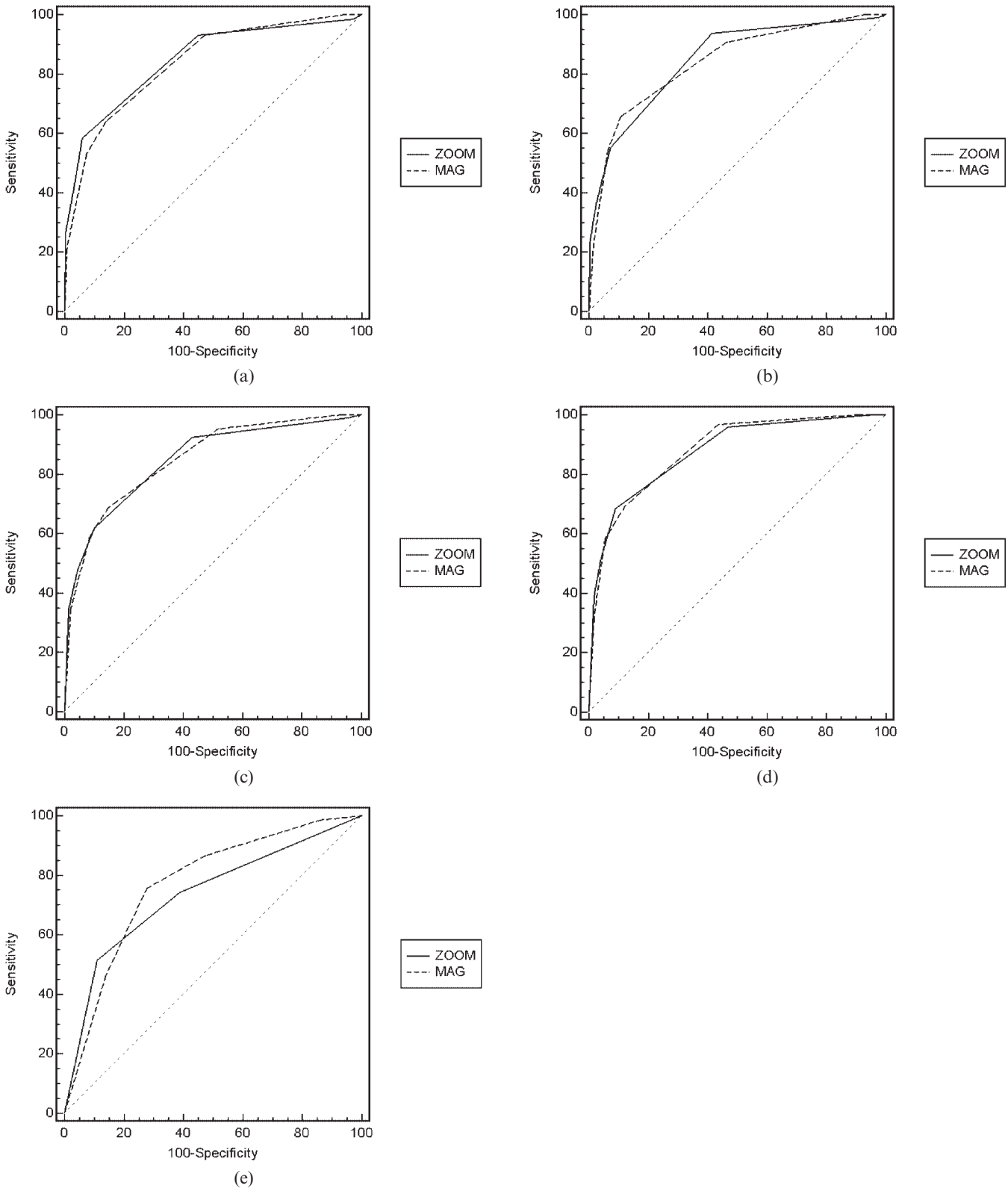

Figure 2. Receiver operating characteristic curves for the diagnosis of microcalcifications: ZOOM *vs* MAG in subgroups. (a) Patients younger than 50 years. (b) Patients with heterogeneously dense or extremely dense breasts. (c) Patients with high image quality of ZOOM. (d) Patients with a high confidence level of ZOOM. (e) Patients with a high probability of malignancy of ZOOM. ZOOM, images zoomed from digital contact mammography; MAG, geometric magnification digital mammography.

reviewed by three radiologists who had been qualified in academic institutions for several years and showed acceptable diagnostic performance when compared with that in previous studies [12, 15]. However, the small number of observers could reduce the ability to generalise from the results found. Further studies involving more reviewers with various degrees of experience are necessary. Another limitation is the possibility of case

Table 3. The confidence level[a] for the three questionnaire items

	Mean value		Median value		Difference (MAG – ZOOM)				
	MAG	ZOOM	MAG	ZOOM	Mean	Median	Min	Max	*p*-value
Shape of microcalcifications	4.03	3.75	4.00	4.00	0.28	0.00	−2.00	3.00	
Distribution of microcalcifications	4.15	3.92	4.00	4.00	0.23	0.00	−3.00	3.00	<0.0001
Probability of malignancy	4.05	3.64	4.00	4.00	0.41	0.00	−2.00	3.00	

MAG, geometric magnification digital mammography; ZOOM, images zoomed from digital contact mammography; min, minimum; max, maximum.
[a]5-point scale.

recognition by the reviewers. The study population consisted of cases that were pathologically proven in a time period ranging from several months to a few years ago. Two of the three reviewers have worked for the institution from where the cases included in this study were chosen, either for the entire review period or for the first three months of the case collection period, and so the diagnostic performance could be affected by case recognition. However, all three reviewers showed no statistically significant difference in diagnostic accuracy. Therefore, the effect of case recognition on the diagnostic performance did not significantly impact on the conclusions of this study. In addition, 142 microcalcifications among the 185 patients were benign at surgical or percutaneous biopsy in our study. The follow-up period for patients with pathologically proven benign microcalcifications is limited, as the cases included were biopsied over a long time period, *i.e.* several months to a few years ago. However, as the reported frequency of missed carcinomas averaged 2.8% [16], the possibility of false diagnosis would be similar for both ZOOM and MAGs. Therefore, this possibility should not affect the main results and conclusions of this study. This study used an observational dataset, whereby the images were taken during routine clinical practice. This could be a potential source of bias, *e.g.* (i) selection bias associated with which patients were most likely to have both types of imaging; (ii) bias associated with the timing of mammography; and (iii) bias associated with the radiologist's experience at the time of imaging rather than review. Additionally, for statistical methodology, we used DBM MRMC to reflect the effect of multiple reviewers. However, we did not consider such conditions with multiple reviewers in other analyses. It is possible that the standard error could have been underestimated, leading to tighter confidence intervals. It is also possible that there were too few reviewers to incorporate this as a factor in the model.

In conclusion, the diagnostic performance of the radiologist evaluating microcalcifications with ZOOM (× 2.0) was similar to that with MAG (× 1.8), although image quality and confidence levels were better with MAG.

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