Zoomed image of contact mammography versus magnification mammography in the diagnosis of microcalcifications with soft-copy full field digital mammography

Min Jung Kim

Department of Medicine

The Graduate School, Yonsei University

Zoomed image of contact mammography versus magnification mammography in the diagnosis of microcalcifications with soft-copy full field digital mammography

Directed by Professor Eun-Kyung Kim

The Doctoral Dissertation
submitted to the Department of Medicine,
the Graduate School of Yonsei University
in partial fulfillment of the requirements for the degree
of Doctor of Philosophy

Min Jung Kim

December 2008

This certifies that the Doctoral

Dissertation of Min Jung Kim is approved.

Thesis Supervisor : Eun-Kyung Kim

Thesis Committee Member #1

Thesis Committee Member #2

Thesis Committee Member #3

Thesis Committee Member #4

The Graduate School
Yonsei University

December 2008

ACKNOWLEDGEMENTS

I would like to express my gratitude to Prof. Eun-Kyung Kim, thesis supervisor, for her tireless support during my Doctor's Degree course. I cannot thank her enough. I also acknowledge helpful comments of Profs. Byeong-Woo Park, Hee-Joung Kim, Deok Won Kim and Tae-Suk Roh. They have helped me with sincere directions, encouragements, advice, and revisions from the start of my research to the finish of writing this thesis.

My grateful thanks also are extended to colleagues, Profs. Ji Hyun Youk, Seon Hyeong Choi, Eun Ju Son, Jin Young Kwak, Soo Jin Kim, and Sung Hee Park for their patience and help in reviewing the enormous cases for this thesis. I want to thank Profs. Dae Ryong Kang and Joon Seok Lim. for their help in statistical analysis and interpretation of this thesis. This thesis would not have been possible without their kind help.

Finally, I deeply appreciate my husband, Prof. Byung Moon Kim for being beside me with endless love and encouragement, my parents for showing their spirit of sacrifice, and my lovely kids for giving me boundless joy.

<TABLE OF CONTENTS>

LIST OF FIGURES

LIST OF TABLES

<ABSTRACT>

Zoomed image of contact mammography versus magnification mammography in the diagnosis of microcalcifications with soft-copy full field digital mammography

Min Jung Kim

Department of Medicine
The Graduate School, Yonsei University

(Directed by Professor Eun-Kyung Kim)

PURPOSE: The purpose of this study was to determine whether the diagnostic accuracy and image quality of microcalcifications of zoomed images from contact mammograms (1.3 of zooming factor) of digital mammography were equivalent to those of soft-copy digital magnification mammography. And this study was also designed to compare the diagnostic accuracy and image quality of microcalcifications when different zooming factors (2.0 of zooming factor) are used in contact mammograms with digital magnification mammography.

MATERIALS AND METHODS:

I. Comparison of x1.3 zooming method (ZOOM-1.3) and digital magnification view (magnification factor 1.8;MAG) in full-field digital mammography: image quality and diagnostic performance for characterization of microcalcifications

Three radiologists with different levels of experience in mammography reviewed 120 microcalcification clusters in 111 patients with a full field digital mammography (FFDM) system using digital magnification mammogram (MAG) images and zoomed images from contact mammography (ZOOM) with commercially available zooming systems on

monitors. Each of three radiologists estimated the probability of malignancy and rated the image quality and confidence level. Performance was evaluated by sensitivity, specificity, positive predictive value, negative predictive value, and receiver operating characteristic (ROC) analysis.

II. Comparison of x 2.0 zooming method (ZOOM-2.0) with MAG in FFDM: image quality and diagnostic performance for microcalcifications

Three radiologists with different levels of experience in mammography reviewed each FFDM reader set for 185 patients with pathologically-proven microcalcification clusters, which consisted of MAG with a magnification factor of 1.8 and ZOOM with a zoom factor of 2.0. Each radiologist rated their suspicion of breast cancer in microcalcific lesions using a 6-point scale and used a 5-point scale to rate image quality and confidence level in their decisions. Results were analyzed according to display methods using areas under the ROC curves (A_z value) for ZOOM and MAG to interpret microcalcifications. DBM MRMC and Wilcoxon matched-pairs signed rank test were used for statistical analysis.

RESULTS:

I. All three radiologists rated MAG images higher than ZOOM-1.3 images for sensitivity (average value, 92% vs. 87%, $P<0.05$) and performance by ROC analysis improved with MAG imaging. The confidence level of diagnosis decision and the assessment of lesion characteristics were also better in MAG images than those in ZOOM images with statistical significance ($P<0.0001$).

II. A_z value for ZOOM-2.0 were 0.8680 and were similar to that of MAG (0.8682, 95% confidence interval for a mean difference (CI): -0.02973 to 0.02934; $p=0.9897$). 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 ZOOM ($p<0.001$).

CONCLUSIONS:

I. MAG can enhance diagnostic performance when characterizing microcalcifications. ZOOM-1.3 cannot serve as an alternative to MAG.

II. Radiologist performance in the diagnosis of microcalcifications using ZOOM -2.0 was comparable to MAG. Thus, ZOOM-2.0 might be an alternative tool for MAG in the diagnosis of microcalcifications although image quality and confidence levels were not as good as MAG.

Key words: Digital Mammography, Magnification, Zooming

Zoomed image of contact mammography versus magnification mammography in the diagnosis of microcalcifications with soft-copy full field digital mammography

Min Jung Kim

Department of Medicine
The Graduate School, Yonsei University

(Directed by Professor Eun-Kyung Kim)

I. INTRODUCTION

Magnification mammography supplies higher spatial resolution and signal-to-noise ratio (SNR). It is well established as a valuable adjunct to contact mammography, especially for the diagnosis of microcalcifications despite additional radiation exposure with increased radiation dose due to the shorter distance between breast and X-ray source during examination[1-4].

However, with respect of full-field digital mammography (FFDM), several investigations have indicated that digital mammography may have equivalent or improved object detection compared to screen-film mammography [5-7]. Skaane et al. suggested that digital mammography with soft-copy interpretation was better at detecting breast cancers than screen-film mammography. They strongly recommended the post-processing of images, including adjustment of window level and zoom, during soft-copy interpretation [8, 9]. Obenauer et al. reported that further studies of tools in soft-copy reading were needed for its potential benefits [10]. Moreover, a few studies using zoomed images from contact mammograms have recently been reported and brought a debate whether a digital zooming system of FFDM can

replace the magnification view of digital mammography [11, 12] With regard to post-processing tools, Fisher et al. reported that monitor zooming of a digital contact mammogram is equivalent to direct magnification FFDM in the interpretation of microcalcifications [11]. However, they used hard-copy reading with a small number of subjects.

The purpose of this study was to determine whether the diagnostic accuracy and image quality of microcalcifications of zoomed images from contact mammograms (1.3 of zooming factor) of digital mammography were equivalent to those of soft-copy digital magnification mammography. And this study was also designed to compare the diagnostic accuracy and image quality of microcalcifications when different zooming factors (2.0 of zooming factor) are used in contact mammograms with digital magnification mammography.

II. MATERIALS AND METHODS

Institutional Review Board approval was obtained for this retrospective study and informed patient consent was not required. The authors have no declared conflicts of interest.

II-1. Comparison of x1.3 zooming method (ZOOM-1.3) and digital magnification view (magnification factor 1.8;MAG) in FFDM: image quality and diagnostic performance for characterization of microcalcifications

Case Selection

From May 2005 to October 2006, 917 MAG were performed at my institution, and the data were retrieved from the radiological database files. Subjects' medical and radiologic records were retrospectively reviewed by a

radiologist (MJK). Exclusion criteria were as follow: no available contact mammogram of FFDM performed no earlier than one month prior to when the magnification mammogram was taken (n=409), subjects with clinical symptoms (n=108), probably benign microcalcifications that were not surgically proven and were not followed up for a minimum of 2 years after initial diagnosis (n=221), and lesions of microcalcifications associated with a mass (n=31).

120 mammograms in 111 patients were selected to maintain the expected rate of malignancy among lesions referred for biopsy. Twenty-eight cases of cancer were observed, representing 23% of the lesions. Fifty-one benign lesions were surgically proven and 41 lesions were found in 39 patients who underwent at least 2 years of mammographic follow-up for probable benign microcalcifications. Among those 41 lesions, 28 lesions underwent mammogrphic follow up for more than three years. Surgically-proven benign lesions included three atypical ductal hyperplasia.

Full-Field Digital Mammograms and Workstation

Mammograms were obtained using FFDM system (Lorad/Hologic, Danbury, CT). The system, based on a amorphous selenium detector, used a direct-capture device of 70 μm pixel size and yielded an image size of 2560 x 3328 matrix with 18 x 24 cm paddle. The system was set to allocate 16-bit images and store them at 12 bits. Standard craniocaudal and mediolateral oblique views were obtained during routine mammography (focal spot size 0.3 mm).

MAG with magnification factor 1.8 was obtained using geometric magnification digital mammography (focal spot size of 0.1 mm). The breast was elevated from the detector and moved closer to the X-ray source of the mediolateral and craniocaudal projections. An 18 x 24 cm as the active image receptor was used for these projections. With respect to the paddles used for

magnification, the 7.5cm coned-down spot compression device was used. If the extent of microcalcifications was regional or diffuse on contact mammograph and the evaluation of microcalcifications, a 10-cm rectangular paddle was used instead by decision of the supervising radiologist. The effective pixel size of MAG was approximately 39 μm with a magnification factor of 1.8.

These images were displayed on a pair of high resolution, 5 megapixel (MP) LCD monitors (MFGD 5621HD, Barco, NV) that were part of the review workstation (Selenia Softcopy Workstation, Lorad/Hologic) with soft-copy reading software (MeVis BreastCare, MeVis Bremen). The pixel pitch of the LCD monitors was 165 μm and the matrix size was 2048 x 2560. The monitor system was set to accept 8-bit gray images and display them as such.

The hanging protocol of contact mammogram included a 4-view mammograms that were shown on a monitor. So the reviewer could check the areas of interest with an annotation marker, and then marked mediolateral oblique and craniocaudal views that were shown simultaneously on the right and left monitors (single tilting mode). Reviewers were allowed to use commercially available zooming methods on the contact mammogram and a square digital zooming frame with a zooming factor of about 1.3, that was calculated by dividing image pixel matrix by screen pixel matrix. ZOOM is always displayed in full resolution where one acquisition pixel on the digital detector matches one display pixel on the monitor as the default option. The size of commercially available zooming frames applied with medium-sized settings (matrix size, 850 x 850 pixel size, 70 micron) was 5.95 x 5.95 cm with a zoomed ruler that supplied by the workstation on a zoomed area. This zooming frame was also allowed to review MAG to ensure that the results would reflect the accuracy of routine diagnostic work because this frame would be also available on the reading of a MAG in practice.

Image Review

The study group was evaluated independently by three radiologists who were specialists in breast imaging and who had not collected data of the study populations. The reviewers were not given the medical records or pathological results of the subjects nor the ratio of malignant to benign lesions included in the study. The reviewers had an average of 6.3 years (1, 2, and 10 years) of experience in interpreting mammogram and 1-3 of years experience in soft-copy review of digital mammography at the same academic institution.

The radiologists assigned scores to the images in two sessions that were 5weeks apart such that the same case was not see twice in any session; session A (60 ZOOM-1.3 and 60 MAG) and session B (the other 60 MAG and 60 ZOOM-1.3). The cases were reviewed in order of acquisition date order so that they were random with respect to density of the breast parenchyma and lesion type. Reviewers were allowed to review ZOOM-1.3 first at the odd-row cases on the list of the study population arranged according to acquisition date order and evaluate MAG at the even-row cases in the A session. In the B session, reviewers looked at the other mammogram (ZOOM-1.3 vs.MAG) of patients. The cases were interpreted in a standard reviewing room without ambient light. To avoid the possibility of inadvertent evaluation of the wrong lesion, the radiologists were directed to the area of interest with a commercially available marker of annotation on contact mammogram. If a reviewer reviewed briefly a contact mammogram without zooming method and clicked on an annotation marker at the upper corner of the monitor, a circle was designed to appear on the monitor. It was identical to the area that was taken by MAG and was previously described on the monitor by the radiologist who had collected the cases of this study. The reviewer could then interpret the visible microcalcifications limited to the circle with zooming display. The annotation marker was commercially available at the workstation used.

Prior to a review of MAG, a reviewer was allowed to review briefly a contact mammogram without zooming method and to open MAG that corresponded to the contact mammogram. No prior films or patient history were provided.

Each radiologist was given a questionnaire (See Appendix). They were instructed to check whether the reviewed mammogram was ZOOM or MAG in the questionnaire and fill out the columns in the questionnaire.

Questionnaire: The microcalcification features on ZOOM-1.3 or MAG were analyzed according to shape, distribution, and the probability of malignancy. The probability for malignancy based on a 6-point scale were used to classify the likelihood of cancer; 1, definitely not malignant, similar to BI-RADS category 2 [13]; 2, probably not malignant, similar to category 3; 3, low-possibly malignant, similar to category 4a; 4, intermediate-probably malignant, similar to category 4b; 5, probably malignant, similar to category 4c; and 6, definitely malignant, similar to category 5. The BI-RADS standard scale for the likelihood of cancer classification was not used because it does not readily lend itself to receiver operating characteristic (ROC) analysis since it is not a continuous scale [14]. The quality of ZOOM-1.3 or MAG was evaluated, and one of the following five grades were given: “Excellent,” “Good,” “Moderate,” “Intermediate,” or “Not-acceptable.” Each reviewer was allowed to pick the most worrisome shape of microcalcifications when there were several types in an interesting area. The reviewers were also asked to choose the most appropriate confidence level from 1 to 5 for each questionnaire item except for imaging quality; 5 meaning “Absolutely confident,” 4 meaning “Very confident,” 3 meaning “Somewhat confident,” 2 meaning “Not too confident,” and 1 meaning “Not at all confident.”

Reproducibility test

For evaluation of inter-reviewer validity and intra-reviewer validity,

another review round with the same 120 ZOOM-1.3 used in the previous review round and the same questionnaire was reviewed using by each radiologist seven weeks apart from the previous rounds.

Statistical Analysis

The sensitivities, specificities, and positive and negative predictive values for ZOOM-1.3 and MAG images were calculated by each reviewer with histopathologic examination and follow-up data as the reference standard. Sensitivity was defined as the percentage of cancer detected among all 28 cancers included. Specificity was defined as the percentage of benign result by reviewers among the cases with final benign diagnosis. The positive predictive value was defined as the percentage of cancers detected among the cases positive results by reviewers. And the negative predictive value was defined as the percentage of the cases with final benign diagnosis among the cases negative results by reviewers. The values were then compared to the McNemar test. Two-tailed p values less than 0.05 were considered to indicate a statistically significant difference. A cutoff between level 2 of the probability of malignancy and level 3 of the probability of malignancy was used to define a positive versus a negative result. For example, in cancer cases, the assignment of probability of malignancy of level 3 or higher was considered to be an interpretation with a true-positive result. In addition, ROC analysis using the probability of malignancy based on a 6-point scale was conducted to assess and compare the radiologists' performance for the characterization of microcalcifications with MAG and ZOOM-1.3 images. To analyze performance, I calculated and compared parameter estimates of the area under the ROC curve (A_z value).

The agreement between display techniques for descriptions of shape of calcifications, distribution, and the probability of malignancy and image quality was calculated using kappa statistics (κ). A kappa 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 [15]. The inter-reviewer agreement between the three radiologists was also calculated for each display technique in terms of the shape, distribution, image quality and probability of malignancy. And then the intra-reviewer agreement for each radiologist was calculated in terms of the same items using κ statistics.

For comparison of image quality of the both display methods, the data were evaluated using a paired t-test. A 95% confidence interval and p value were calculated for which the reviewers did not rate the mammography as equivalent. Two-tailed p values less than 0.05 were considered to indicate a statistically significant difference.

Confidence levels for the four categories of shape, distribution of calcifications, and the probability of malignancy were also calculated for the ZOOM and MAG using a paired t-test. I compared the confidence level for the probability of malignancy between the accurate and inaccurate diagnosis using unpaired t-test. An accurate diagnosis was defined when a reviewer had classified a case as level 3 or higher in probability of malignancy and the case turned out to be malignant. When a reviewer had classified a case as level one or two and the case turned out to be benign. Otherwise, an inaccurate diagnosis was defined. All statistical analysis including ROC analysis, were performed with statistical software (SAS system for Windows, version 9.1; SAS institute, Cary, NC).

II-2. Comparison of x 2.0 zooming method (ZOOM-2.0) and MAG in FFDM: image quality and diagnostic performance for microcalcifications:

Study population

From October 2006 to February 2008, 2648 percutaneous biopsy or localization for surgical biopsy were referred and performed in my breast imaging division. 2414 biopsies or localizations were for mass associated with/without microcalcifications, and the remaining 234 biopsies or localizations were for microcalcifications. All 234 patients had undergone contact mammograms and most of them had also undergone magnification mammogram prior to the recommendation of biopsy. Their medical and radiologic records were retrospectively reviewed by one radiologist. Exclusion criteria were as follows; cases of microcalcifications associated with possible mass such as a asymmetry or focal asymmetry (n=18) on a retrospective review, cases without available magnification mammogram or contact mammogram of FFDM performed within onemonth each other (n=26), cases without visible calcifications on specimen mammogram after biopsy (n=1), and cases with BB marker on mammograms due to clinical palpability (n=4). Only calcifications in lesions that had undergone FFDM with both a contact mammogram and magnification mammogram within onemonth and that had undergone subsequent biopsy were included.

Finally, 185 cases of calcification, histologically proven by needle or surgical biopsy, from 185 patients (mean age, 49.9 years old; range 27-69) were included in this study. Forty-three cases of cancer were observed, representing 23.2% of the lesions. Patient age was recorded and breast density, reported according to the standard Breast Imaging Reporting and Data System (BIRADS) scale [13], was reviewed for each mammogram (extremely dense, heterogeneously dense, scattered fibroglandular densities, and almost completely fat) by the radiologist who collected data of the study population.

Workstation

Images were displayed on a pair of high-resolution, 5MP LCD monitors (SMD 21500, Siemens) that were part of the review workstation

(Senoadvantage, GE) with soft-copy reading software (Senoadvantage, GE). The pixel pitch of the LCD monitors was 165 μm, and the matrix size was 2048 x 2560. The monitor system was set to accept 14-bit images and display 10-bit output. The square digital zooming frame used in this study was commercially available and had a zooming factor of 2.0 fixed as the default mode. The size of commercially available zooming frames applied with medium-sized settings was 11.5 x 11.5 cm.

Reviewers and Review round

Images were evaluated independently by three radiologists who were specialists in breast imaging at the same academic institution and who had not collected the original data from the study population. Reviewers were not given any clinical information or pathologic findings from the medical records, pathological results, or ratios of malignant to benign lesions included in the study. No prior films or patient history were provided. Reviewers had an average of 7.0 years (4, 5 and 12 years) of experience in interpreting mammograms and 4-5 years of experience in soft-copy review of digital mammography. Each of three reviewers worked for different institution when the review for the current study was going on. One of three reviewers has worked for the institution in which cases were included in this study for the entire case-collection period. Another reviewer had worked for the same institution in early 3months when the cases were included and the remaining reviewer had not worked for the institution, where the cases included, during case-collection period. The number of mammogram read by each radiologist in their own practice varied from 300 to 400 mammograms per month.

Cases were divided into 4 groups according to the acquisition date order of contact mammogram (Figure 1); 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; session A (46 ZOOM-2.0 and

other 46 MAG, A in Figure 1), session B (46 ZOOM-2.0 and other 46 MAG, B in Figure 1), session C (47 ZOOM-2.0 and other 46 MAG, C in Figure 1), and session D (46 ZOOM-2.0 and other 47 MAG, D in Figure 1). In each session, ZOOM and MAG with print-screen images were alternated. The cases were reviewed in acquisition date order of contact mammogram so that they were random with respect to the density of the breast parenchyma and lesion type.

Review protocol

The radiologist who had collected data marked the area included by MAG on each view of contact mammogram with a commercially available circle-shaped marker of annotation in each case 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 for identification of the area of interest, not for diagnosis of microcalcifications.

The hanging protocol for the review round included a 2-view print-screen image of a contact mammogram with original image of the contact mammogram or MAG of the same case. The reviewer was allowed to briefly check the areas of interest on the print-screen images and then open either the contact mammogram or to open the MAG directly according to the given order. When a ZOOM was reviewed, 2-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 2-view print-screen images on the other monitor. Then mediolateral oblique and craniocaudal views were hung simultaneously on the right and left monitors (fit to screen mode), and ZOOM were reviewed using a square digital zooming frame. In ZOOM-2.0, the zoomed area was always displayed with a twice zoomed pixel pitch without improving spatial resolution. When a MAG was reviewed, 2-view magnification mammograms of one breast were hung simultaneously on the right and left monitors (fit to screen mode) and reviewed. The print-screen

image of contact mammogram was reviewed in limited cases, according to the reviewer's preference, to determine the lesion distribution. The zooming frame was also used to review MAG to ensure that the results would reflect the accuracy of routine diagnostic work.

Each radiologist was given a questionnaire and instructed to check whether the reviewed mammogram was ZOOM or MAG and to fill out the remaining items, including probability of malignancy, shape and distribution of microcalcifications, and image quality. The probability of malignancy based on a 6-point scale was used to classify the likelihood of cancer; 1, definitely not malignant, similar to BI-RADS category 2 [13, 16]; 2, probably not malignant, similar to category 3; 3, low-possibly malignant, similar to category 4a; 4, intermediate-probably malignant, similar to category 4b; 5, probably malignant, similar to category 4c; and 6, definitely malignant, similar to category 5. With respect to the shape and distribution of microcalcifications, the reviewer was allowed to choose one of 14 types of shape and 6 types of distribution as follows: shape--skin, vascular, popcorn like, large rod-like, round, lucent-center, milk of calcium, suture, dystrophic, punctuate, coarse heterogeneous, amorphous or indistinct, fine pleomorphic, fine linear/branching; distribution--clustered, linear, segmental, regional, multiple grouped, and diffuse. The reviewers were also asked to choose the most appropriate confidence level from 1 to 5 for the above three questionnaire items. The meaning of the confidence numbers, in order from 5 to one, was "Absolutely confident", "Very confident", "Somewhat confident", "Not too confident" and "Not at all confident". The image quality of ZOOM-2.0 or MAG was evaluated, and one of five grades was given: "Not-acceptable" was one, followed by "Intermediate," "Moderate," "Good," and "Excellent" in order from 2 to 5. Each reviewer was allowed to choose the most worrisome shape of microcalcifications in an interesting area.

Statistical Analysis

A_z value of ROC analysis was calculated using the probability of malignancy based on a 6-point scale for ZOOM-2.0 and MAG images for each individual reviewer and for all reviewers together with histopathologic examination as the reference standard. Parametric estimates of A_z value were calculated and compared for reader performance with the two techniques by using DBM MRMC [17, 18]. The statistical significance of the results was reported at 95% confidence intervals for the mean differences in Az values for reader performance with use of 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 comparison of ROC curves. For descriptive purposes, estimates of sensitivity, specificity, and the positive and negative predictive value of the two display methods were computed on the basis of the six-point malignancy scale using histopathologic examination as the reference standard. Sensitivity was defined as the percentage of cancer detected among all 43 cancers included. Specificity was defined as the percentage of benign result by reviewers among the cases with final benign diagnosis. The positive predictive value was defined as the percentage of cancers detected among the cases positive results by reviewers. And the negative predictive value was defined as the percentage of the cases with final benign diagnosis among the cases negative results by reviewers. For this purpose, malignancy scores were dichotomized as negative (score of 1 or 2) or positive (score 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 kappa 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 [15]. Confidence levels for shape, distribution, and the probability of malignancy were also calculated for ZOOM-2.0 and MAG images using a Wilcoxon matched paired signed rank test.

To compare the image quality of the two display methods, data were evaluated using a Wilcoxon matched paired signed rank test. A 95% confidence interval and p value were calculated for cases where the reviewers did not rate the methods as equivalent. Two-tailed p values less than 0.05 were considered statistically significant.

Az values were compared between ZOOM-2.0 and MAG for pre-specified subgroups, which were defined according to age (younger than 50 years vs. 50 years or older), breast density (heterogeneously dense or extremely dense vs. less dense), image quality (greater than 3 of image quality of ZOOM-2.0 vs. 3 or less), probability of malignancy (greater than 3 on the six-point malignancy scale of ZOOM-2.0 vs. 3 or less), and confidence level of the probability of malignancy (greater than 3 on the confidence level of ZOOM-2.0 vs. 3 or less). A pairwise comparison of ROC curves was performed using statistical software (Medicalc for Windows®, version7.4.0.0; Medicalc software, Belgium) to compare the radiologist performance with two techniques. DBM MRMC used above was not appropriate for comparison in the prespecified subgroups (image quality, probability of malignancy and confidence level). The number of cases included in each reviewer was not identical. The statistical significance of the results was reported at 95% confidence intervals for the mean differences in Az values for reader performance with use of the two techniques. 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).

III. **RESULTS**

III-1. Comparison of ZOOM-1.3 and MAG in full-field digital mammography: image quality and diagnostic performance for characterization of microcalcifications

Sensitivity, Specificity, ROC Analysis, and Image quality

For all three reviewers, MAG images were better than or equal to ZOOM-1.3 images in terms of sensitivity and negative predictive values (Table 1). However, with regard to specificity and positive predictive value, MAG images were worse than ZOOM-1.3 images in two of three radiologists although the remaining one radiologist showed improved specificity and positive predictive value with MAG images. All of the reviewers found that MAG images were better than ZOOM-1.3 images in terms of A_z value (p >0.05, Table 1, Figure 1). These differences were only statistically significant for reviewer 1 (p value =0.01).

Table 1. Performance of Three Reviewers Assessing 360 Microcalcifications[1] with ZOOM-1.3 and MAG Images

Reader	Sensitivity (%)		Specificity (%)		Positive Predictive Value (%)		Negative Predictive Value (%)		A_z value	
	[2]ZOOM-1.3	[3]MAG	ZOOM-1.3	MAG	ZOOM-1.3	MAG	ZOOM-1.3	MAG	ZOOM-1.3	MAG
1	27/28 (96)	27/28 (96)	31/92 (34)	40/92 (43)	27/88 (31)	27/79 (34)	31/32 (97)	40/41 (98)	0.822*	0.864*
2	24/28 (86)	25/28 (89)	62/92 (67)	56/92 (61)	24/54 (44)	25/61 (41)	62/66 (94)	56/59 (95)	0.823	0.839
3	22/28 (79)	25/28 (89)	79/92 (86)	61/92 (66)	22/35 (63)	25/56 (45)	79/85 (93)	61/64 (95)	0.849	0.862
All	73/84* (87)	77/84* (92)	172/276* (62)	157/276* (57)	73/177 (41)	77/196 (39)	172/183 (94)	157/164 (96)	0.825	0.852

Note: [1]number of lesions (n=120) X number of reviewer (n=3); [2]ZOOM-1.3 = images zoomed from digital contact mammogram with 1.3 of zooming factor; [3]MAG = geometric magnification digital mammogram with 1.8 of magnification factor; *$p<0.05$

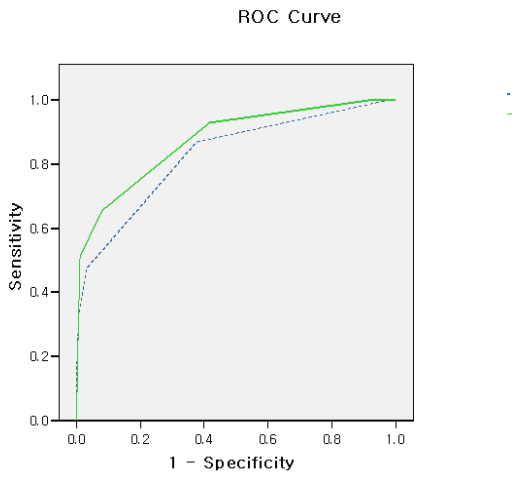

Figure 1. ROC curves for the diagnosis of microcalcifications: ZOOM-1.3 (dot line) vs MAG.-1.8 (solid line). A_z value of ZOOM-1.3 is 0.825 (95% confidence intervals 0.771 to 0.879) and that of MAG is 0.852 (95% confidence intervals 0.804 to 0.900).

In terms of image quality, MAG images (mean value 4.13 for MAG images, 95% CI 4.05 to 4.18) were better than ZOOM-1.3 images (mean value, 3.85 for ZOOM-1.3 images, 95% CI: 3.81 to 3.91,*p* value <0.0001).

Agreement on Imaging Findings

Between ZOOM-1.3 and MAG

The radiologists showed substantial agreement on mammographic findings between ZOOM -1.3 and MAG images but showed far less agreement on image quality of mammograms (Table 2).

Table 2 Agreement between Display Techniques for characterization of microcalcifications in 120 breast microcalcifications between ZOOM-1.3 and MAG

	Reviewer 1	Reviewer 2	Reviewer 3	Mean
Shape	0.6857	0.5052	0.5090	0.5735
	(0.0602)	(0.0759)	(0.0720)	(0.0407)
Distribution	0.8735	0.7685	0.7894	0.8094
	(0.0335)	(0.0489)	(0.0501)	(0.0264)
Probability of	0.6406	0.7117	0.6742	0.6839
malignancy	(0.0442)	(0.0519)	(0.0527)	(0.0279)
Image quality	0.0536	0.1031	0.0976	0.0635
	(0.0498)	(0.0665)	(0.0641)	(0.0349)

Note: Data are κ values; numbers in parentheses are standard errors.

For the two techniques, descriptions of the shapes of microcalcifications were the most discordant ($\kappa = 0.5735 \pm 0.0407$ [standard error]), followed by the probability of malignancy ($\kappa = 0.6839 \pm 0.0279$) and the distribution of microcalcifications ($\kappa = 0.8094 \pm 0.0264$). The radiologists showed just slight agreement on image quality values of ZOOM-1.3 and MAG images ($\kappa = 0.0635 \pm 0.0349$).

Confidence level

The radiologists had higher confidence in mammographic findings from MAG images than from ZOOM-1.3 images (p value <0.0001). The mean

confidence level was 3.547 for ZOOM-1.3 images and 4.172 for MAG images for the shape of calcifications; 4.108 for ZOOM-1.3 images and 4.467 for MAG images for the distribution of calcifications; and 3.364 for ZOOM-1.3 images and 4.111 for MAG images in the probability of malignancy. The mean confidence level for probability of malignancy was 3.787 in accurate diagnosis including both ZOOM-1.3 and MAG, and 3.636 in inaccurate diagnosis. The confidence level for probability of malignancy in accurate diagnosis was higher than that in inaccurate diagnosis with statistical significance (p value <0.05).

Reliability test

Inter-reviewer agreement between the three radiologists for the probability of malignancy in microcalcifications was fair for ZOOM-1.3 images ($\kappa = 0.384 \pm 0.067$) and MAG images ($\kappa = 0.381 \pm 0.062$). Table 3 showed the inter- and intra-reviewer agreement. While inter-reviewer agreement was fair to moderate in each round, the intra-reviewer agreement was moderate to substantial in terms of shape, distribution and probability of malignancy. However, the agreement for the image quality was fair agreement for both inter- and intra-reviewer agreement.

Table 3. inter- and intra-reviewer agreement on characterization of microcalcifications in 120 microcalcification clusters

Items	Inter-reviewer agreement		Intra-reviewer agreement		
	First round	Second round	Reviewer 1	Reviewer 2	Reviewer 3
Shape	0.384±0.067	0.447±0.028	0.596±0.054	0.778±0.049	0.637±0.050
distribution	0.381±0.062	0.357±0.030	0.632±0.059	0.787±0.049	0.656±0.052
Probability of malignancy	0.401±0.056	0.484±0.031	0.604±0.058	0.669±0.055	0.516±0.057
Image quality	0.224 ±0.084	0.313±0.044	0.201±0.065	0.206±0.065	0.248±0.071

III-2. Comparison of ZOOM-2.0 and MAG in full-field digital mammography: image quality and diagnostic performance for microcalcifications:

For probability of malignancy, the diagnostic accuracies of ZOOM-2.0 and MAG were similar for each individual reviewer (Figure 2) and for all reviewers together (A_z = 0.8644 for ZOOM-2.0 and A_z = 0.8667 for MAG).

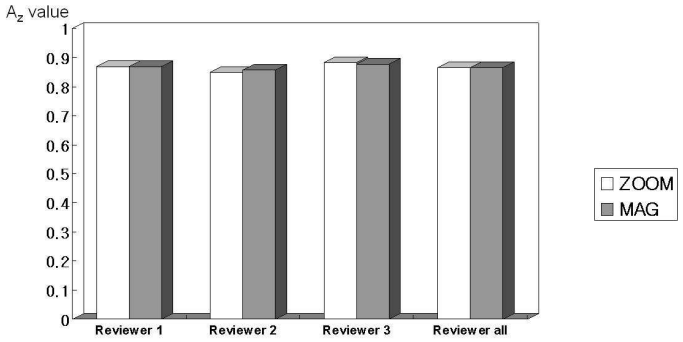

Figure 2. Receiver operator characteristics for the diagnosis of microcalcifications: ZOOM-2.0 vs MAG. A_z values of ZOOM-2.0 were 0.8692 for reviewer 1; 0.8504 for reviewer 2; and 0.8844 for reviewer 3. Values for MAG were 0.8692 (95% confidence interval for mean difference for ZOOM-2.0-MAG, -0.06913 to 0.06896) for reviewer 1; 0.8580 (95% confidence interval for mean difference for ZOOM-2.0-MAG, -0.07396 to 0.05873) for reviewer 2; and 0.8773 (95% confidence interval for mean difference for ZOOM-2.0-MAG, -0.06112 to 0.07536) for reviewer 3. There was no statistical significant difference between ZOOM-2.0 and MAG for any of the reviewers. Overall, A_z values for all 3 reviewers were 0.8680 for ZOOM-2.0 and 0.8682 for MAG (95% confidence interval for mean difference for ZOOM-2.0-MAG, -0.02973 to 0.02934, p=0.9897). Note: ZOOM-2.0 = images zoomed from digital contact mammography; MAG = geometric magnification digital mammography; A_z value =area under curves.

The difference of A_z value for ZOOM-2.0-MAG ranged -0.0071 to 0.0076 (95% confidence interval, -0.02973 to 0.02934; p=0.9897). A_z value of overall including ZOOM-2.0 and MAG were 0.8683 for reviewer 1; 0.8497 for reviewer 2; and 0.8797 for reviewer 3. The difference of A_z value for reviewer ranged 0.001 to 0.003. The inter-reviewer difference in diagnostic accuracy was insignificant for both overall cases and each display method (p>0.05, respectively).

There were no statistically significant differences between ZOOM-2.0 and MAG in diagnostic performance, including sensitivity specificity, and positive and negative predictive values (Table 4, p>0.05).

Table 5 lists the case characteristics for each of the prespecified subgroups.

The A_z value of MAG did not vary significantly from that of ZOOM-2.0 according to age, breast density, image quality of ZOOM-2.0, confidence level of ZOOM-2.0, or the probability of malignancy (p>0.05, Figure 3).

Table 4. Performance of 3 Reviewers Assessing 555 Microcalcifications[1] with ZOOM-2.0 and MAG Images

Reader	Sensitivity (%)		Specificity (%)		Positive Predictive Value (%)		Negative Predictive Value (%)		A_z value	
	[2]ZOOM-2.0	[3]MAG	ZOOM-2.0	MAG	ZOOM-2.0	MAG	ZOOM-2.0	MAG	ZOOM-2.0	MAG
1	40/43 (93)	40/43 (93)	70/142 (49)	82/142 (58)	40/112 (38)	40/100 (40)	70/73 (96)	82/85 (96)	0.8692	0.8692
2	38/43 (88)	39/43 (91)	95/142 (67)	67/142 (47)	38/85 (48)	39/114 (34)	95/100 (95)	67/71 (94)	0. 8504	0.8580
3	41/43 (95)	40/43 (93)	77/142 (54)	66/142 (46)	41/106(39)	40/116 (34)	77/79 (97)	66/69 (96)	0.8844	0.8773
All	119/129 (92)	119/129 (92)	242/426 (57)	215/426 (50)	119/303 (39)	119/330 (36)	242/252 (96)	215/225 (96)	0.8680	0.8682

Note: [1]number of lesions (n=185) x number of reviewer (n=3),

[2]ZOOM-2.0 = images zoomed from digital contact mammogram;

[3]MAG = geometric magnification digital mammogram; Numbers are percentages, and raw data are in parentheses.

Table 5. Characteristics of prespecified subgroups in 555 microcalcifications[1]

Characteristic	n	A_z value			
		[2]ZOOM-2.0	[3]MAG	95% CI of Mean difference	p value
Age at enrollment -yr					
younger than 50	303	0.847	0.836	0.011 (-0.052 to 0.074)	0.735
50 or older	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-2.0					
>3 of confidence level (4,5)	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-2.0					
>3 of image quality (4, 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-2.0					
>3 of probability of malignancy of ZOOM-2.0 (4,5,6)	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

Note: [1]number of lesions (n=185) X number of reviewer (n=3), [2]ZOOM-2.0 = images zoomed from digital contact mammogram; [3]MAG = geometric magnification digital mammogram.

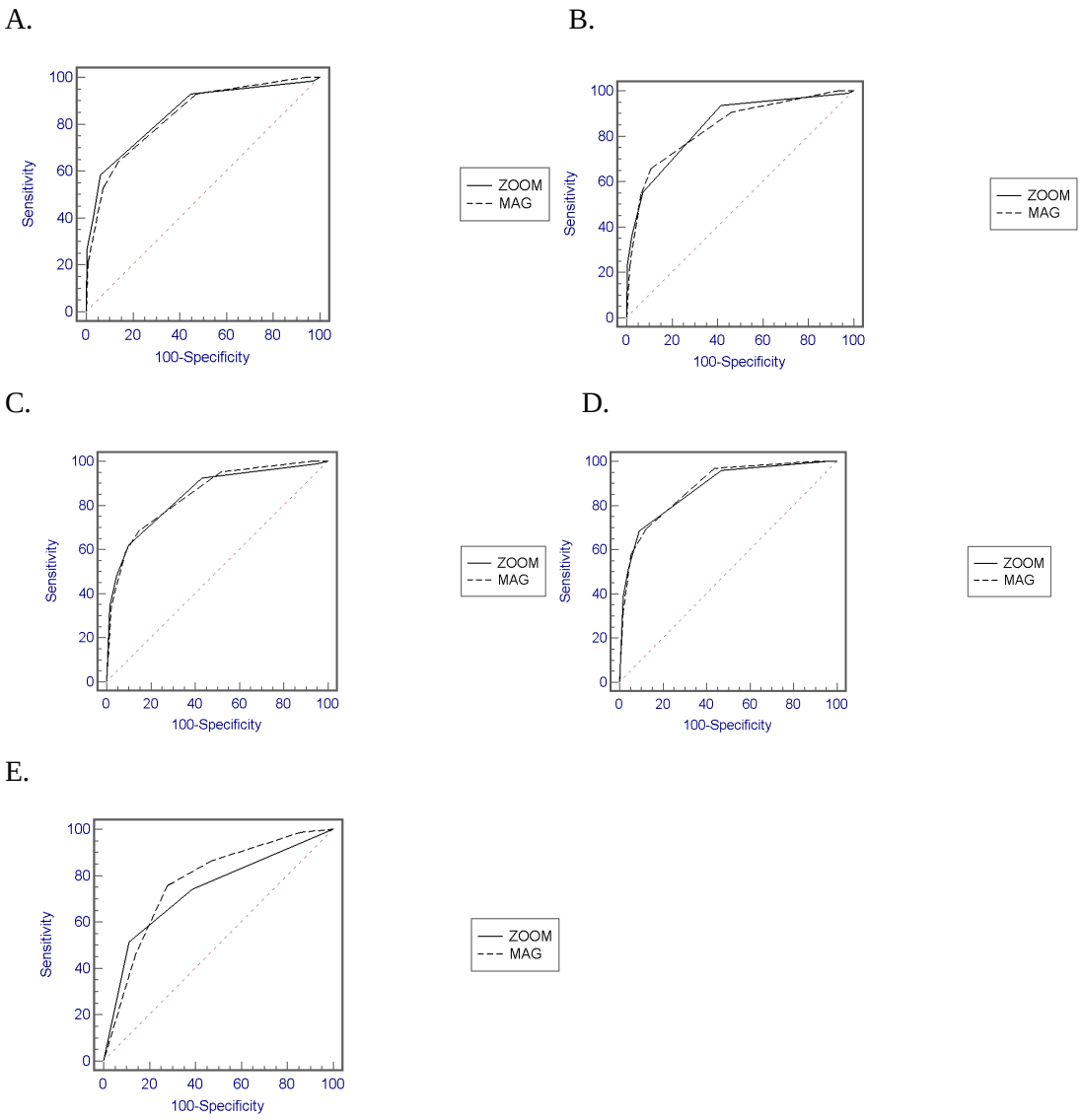

Figure 3. Receiver operator characteristics for the diagnosis of microcalcifications: ZOOM-2.0 vs. MAG in subgroups. A: Patients younger than 50 years. B: Patients with heterogeneously dense or extremely dense breasts. C: Patients with high image quality of ZOOM-2.0. D: patients with a high confidence interval of ZOOM-2.0. E: Patients with a high probability of malignancy of ZOOM-2.0.

Between ZOOM-2.0 and MAG, the description of microcalcification shape and distribution showed moderate agreement (κ=0.523 ± 0.042, and κ=0.563±0.042, respectively). The confidence level for MAG was, however, significantly better than that for ZOOM-2.0 in describing microcalcification shape and distribution, as well as in assigning the probability of malignancy (*p* value <0.0001, Table 6).

Table 6. The mean confidence level for the three questionnaire items

	ZOOM-2.0	MAG	mean difference ±standard deviation	p
shape of microcalcifications	3.7387	4.0054	0.2667 ± 0.8795	
distribution of microcalcifications	3.9045	4.1351	0.2306 ± 0.9293	<0.0001
probability of malignancy	3.6270	4.0468	0.4198 ± 0.8360	

Note: ZOOM-2.0 = images zoomed from digital contact mammogram; MAG = geometric magnification digital mammogram.

For imaging quality, MAG images (mean value 4.23, 95% CI 4.16 to 4.30) were better than ZOOM-2.0 images (mean value 3.78, 95% CI: 3.72 to 3.84; p value <0.001).

IV. DISCUSSION

IV-1. Comparison of ZOOM-1.3 and MAG in full-field digital mammography: image quality and diagnostic performance for characterization of microcalcifications:

Several investigations have shown that interpretation with soft-copy display is likely to be useful with digital mammography and is unlikely to change accuracy or speed compared to interpretation using hard-copy display of digital mammography [10, 19] . This is the case despite the fact that the spatial resolution of a workstation monitor is lower than that of film for printing [20-22]. Moreover, workstation displays of digital mammograms allow the presentation of several versions of an image instantaneously, such as windowing, leveling, zooming, inversion, and computer-assisted diagnosis. A film mammogram can only be adjusted through the use of a magnifying glass or bright light. These post-processing tools and the ability to avoid the high costs of film, processing, and hard-copy image storage and retrieval, are potential benefits of soft-copy reading [6, 23, 24].

Magnification mammography is used to image a particular region of the breast and improve diagnostic accuracy in the evaluation of microcalcifications. Magnification mammography supplies higher spatial resolution and higher SNR. So, it is well established as a valuable adjunct to contact mammography examination despite increased radiation dose due to closer distance between breasts and X-ray source during the examination and additional radiation exposure [1-4]. However, Kuzmiak et al. reported no statistically significant difference in the diagnostic accuracy of microcalcifications for magnified screen-film mammogram versus

unmagnified soft-copy digital mammogram in a study of breast tissue biopsy specimens [12]. This suggested the possibility that digital mammography can obviate the need for MAG in the diagnosis of microcalcifications. In 2002, the same year when Kuzmiak et al.'s study [12] was reported, Fisher et al. reported that ZOOM were equivalent to FFDM MAG in hard-copy reading [11]. If MAG could be avoided in the diagnosis of microcalcification, the radiation exposure to the patient could be reduced and workflow could be accelerated by not requiring additional mammography.

In this study, I compared ZOOM-1.3 and MAG in soft-copy reading. While Fisher et al. reported that MAG images did not improve the diagnostic accuracy of hard-copy reading [11], this study with a larger series of subjects showed that MAG images increased sensitivity by 5% and A_z value by 0.03 despite decreased specificity by 5%. One of three radiologists did not only see improved sensitivity but also improved PPV and specificity with MAG. Moreover, the imaging quality of MAG was rated as superior to that of ZOOM-1.3, showing the agreement between the display technique as 0.1 or less than 0.1. Although the agreement of characterization of microcalcifications such as shape and distribution by each radiologist between display techniques was fair to substantial, MAG was also rated as superior to ZOOM-1.3 for confidence level in diagnosis by all 3 reviewers. In the diagnosis of microcalcifications, it is important not only how much suspicion for malignancy a radiologist consider for the microcalcification but also how much confidence the radiologist puts in rating the probability of malignancy. I could consider that MAG could give a radiologist more confidence for the diagnosis of microcalcification. In this study, an increase of confidence was also noted in the characterization classifying the shape and distribution of microcalcifications.

Therefore, this study suggests that digital MAG provides better diagnostic performance, image quality, and increased confidence for the

diagnosis of microcalcifications than the ZOOM-1.3, which is contrary to the results by Fisher et al [11]. One possible explanation for the discrepancy between the results of Fisher et al. and these results may be due to the magnification factor itself between 1.8 times of MAG and around 1.3 times of ZOOM-1.3. I used the commercially available zooming factor with zooming frame at the single tilting mode in the digital mammography unit used in my study. It showed the same spatial resolution with an non-zoomed area of full resolution mode where one acquisition pixel on the digital detector matches one display pixel on the monitor. Furthermore, MAG increase the size of calcification relative to the background noise pattern in the image while ZOOM-1.3 increase the size of both calcification and background noise pattern. The same is true for film except for the noise pattern added by film processing. SNR on MAG images increases due to a reduction in both scatter-related image degradation and noise. The lesion is projected over more pixels so that it can be seen in greater detail [25]. While the pixel size of contact mammography used in the current study is 70.0 microns, that the effective resolution of MAG is approximately 39 microns (70/1.8). Based on this theory, ZOOM in soft-copy reading may not attenuate the role of MAG. However, higher resolution monitors are continuously being developed and further studies for the role of zooming in soft-copy reading are necessary.

This study has several limitations. The results from one machine type with one pixel size and one zooming power cannot be generalized to those from other machines and zooming powers. Further studies with other mammographic machines and workstations with other zooming powers should be performed to generalize this result. I also plan to repeat this experiment shortly with other zooming powers larger than 1.8 times of the MAG [5]. Second, I evaluated diagnostic performance (sensitivity, specificity, PPV, NPV, and A_z value of ROC analysis) in this study given that the readers were directed to the area of the lesion of interest in both MAG and ZOOM-1.3

images. Although marking the area of interest in each view seems to invalidate evaluation of detection accuracy, that indication was inevitable in the current study. However, that bias, from pointing out the area of concern, could have been lessened by having the reviewers fill out either the ZOOM-1.3 or MAG sheets first according to their odd or even order, arranged by acquisition date, rather than always filling out the ZOOM-1.3 sheets first. Another, any of the parameters sensitivity, specificity, PPV or NPV does not alone tell us about goodness of the image because the diagnostic criteria may be stricter with other method. I did not suggest the objective evidence of goodness of the MAG but suggest only a few subjective evidences evaluated by three reviewers. This study was reviewed by 3 radiologists. The possibility to generalize from the results found is reduced when so few observers are used. Further study with more reviewers having various degrees of experience is necessary. In terms of the follow-up period for probably benign microcalcifications, I included cases that underwent at least 2 years of mammographic follow up although more than 3 years of follow-up could be acceptable. However, this does not interfere with the main results and conclusions of this study and is not very important.

With part 1 study, we have got the result that ZOOM-1.3 could not replace MAG in the diagnosis of microcalcifications. We have wondered whether there was any change in the result with a larger zooming factor.

IV-2. Comparison of ZOOM-2.0 and MAG in full-field digital mammography: image quality and diagnostic performance for microcalcifications:

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 SNR. So it

has been a valuable adjunct to contact mammography despite 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 from film-screen mammography [11, 12, 16]. Fisher et al. reported that ZOOM were equivalent to MAG of FFDM in hard-copy reading [11].

However, in contrast to Fisher's study with zoom factor of 1.8, a prior part 1 study documented that magnification mammography was better than ZOOM-1.3, with respect to sensitivity and ROC analysis, I used a zooming factor 2.0, higher than the magnification factor of MAG (1.8), to assess whether the discrepancy between the previous study could have arisen from the difference in the zooming factor. A larger study population was also used. The current study showed that the diagnostic performance of ZOOM-2.0 using a factor of 2.0 was similar to that of MAG. Furthermore, one of the three reviewers (reviewer 3) obtained higher A_z values from ZOOM-2.0 than from MAG. However, in terms of image quality and the confidence level for assigning a probability of malignancy from mammogram images, MAG was still significantly better than ZOOM-2.0. These findings suggest that the prior discrepancy in diagnostic performance might be mainly due to the difference in the zooming factor. However, further study should be followed to compare different size of zooming using the same population to clarify this. With the currently available digital contact and magnification mammography units, I could infer, the higher spatial resolution and SNR of MAG did not affect the diagnostic performance, but had a significant impact on image quality and confidence in assigning a probability of malignancy.

For the description of microcalcification shape, there was moderate agreement between ZOOM-2.0 and MAG in this study as well as in the prior study. However, for lesion distribution, while almost perfect agreement was reported in the prior study ($\kappa = 0.8094 \pm 0.0264$), only moderate agreement

was noted in this study. When a MAG was reviewed, a review of ZOOM-2.0 from the same case was not allowed. But the review of the print-screen images was just allowed according to reviewer's preference, not mandatory either. A review of the print-screen images was not mandatory, but 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. With respect to the confidence level of interpretation by reviewers, the confidence level for MAG was rated to be superior to that of ZOOM-2.0 for diagnosis by all 3 reviewers This result is consistent with that of the previous study with a zooming factor of 1.3 [16].

In this study, A_z values were compared between ZOOM-2.0 and MAG in pre-specified subgroups of cases, which were sorted by age, breast density, image quality, probability of malignancy, and confidence level in probability of malignancy. However, the A_z value for MAG did not differ significantly from that of ZOOM-2.0 in any of the subgroups. Digital mammography is known to be more useful in women under the age of 50, women with heterogeneously dense or extremely dense breasts on mammography, and pre- or perimenopausal women [26]. However, I found no difference in the A_z value between MAG and ZOOM-2.0 among women under the age of 50 or women with heterogeneously dense or extremely dense breasts on mammography. Although I did not evaluate the difference between pre- and postmenopausal women, it is reasonable to postulate that the effect of those differences on MAG and ZOOM-2.0 were reflected in the age and breast density subgroups.

Although my results showed the possibility that digital mammography using ZOOM-2.0 could obviate the need for magnification mammography in the diagnosis of microcalcification, further studies should be undertaken to confirm my results. Furthermore, ZOOM may not attenuate the role of MAG in other clinical situations, including evaluating mammographic abnormalities

such as asymmetry and distortion, and evaluating the lesion once again under different position [27, 28]. Magnification mammography using a spot-compression paddle would still be useful for the characterization of asymmetry or distortion.

This study has some limitations. First, this study population was larger than those of the previous studies comparing MAG and ZOOM-2.0 [11, 16], but the size of this series was still too small to confirm the similarity of diagnostic performance between MAG and ZOOM-2.0. Further study with a larger series should be undertaken. Second, this study was reviewed by 3 radiologists who were qualified in the academic institution for several years and showed acceptable diagnostic performance in comparison with that of other previous studies [7, 26]. However, the small number of observers could reduce the ability to generalize from the results found. Further study by more reviewers having various degrees of experience is necessary. Another, the study population consisted of the cases, pathologically proven at a few years ago or several months ago. Two of three reviewers have worked for the institution in which cases were included in this study, entire time or early 3 months of case-collection period, so the diagnostic performance could have been affected by case-recognition. However, all three reviewers showed no statistically significant difference in diagnostic accuracy. Therefore, the effect by case-recognition on the diagnostic performance was not significant on the conclusion of this study. Another, 142 microcalcifications among the 185 patients were benign at surgical or percutaneous biopsy in the current study. The follow-up period for those pathologically-proven microcalcifications was not acceptable as the cases included were biopsied several months to a few years ago. However, as considering the reported frequency of missed carcinomas averaged 2.8% [29], the possibility of false diagnosis could be similar for both ZOOM-2.0 and MAG. So, this does not interfere with the main results and conclusions of this study and is not very important.

V. CONCLUSION

V-1. The results of this study suggest that MAG images can provide better diagnostic performance, image quality, and confidence level for diagnosis than ZOOM-1.3 images during soft-copy reading. Therefore, ZOOM-1.3 cannot replace MAG in patients with microcalcification

V-2. The diagnostic performance of the radiologist evaluating microcalcifications with ZOOM-2.0 was comparable to that with MAG (X 1.8). ZOOM-2.0 might therefore be an alternative tool to MAG for the diagnosis of microcalcifications, although the imaging quality and confidence level were worse than with MAG.

References

1. Law J. Breast dose from magnification films in mammography. Br J Radiol 2005;78:816-20.
2. Sickles E, Doi K, Genant H. Magnification film mammography: image quality and clinical studies. Radiology 1977;125:69-76.
3. Sickles E. Further experience with microfocal spot magnification mammography in assessment of clustered breast microcalcifications. Radiology 1980;137:9-14.
4. Sickles EA. Microfocal spot magnification mammography using xeroradiographic and screen-film recording systems. Radiology 1979;131:599-607.
5. Lewin JM, Hendrick RE, D'Orsi CJ, Isaacs PK, Moss LJ, Karellas A, et al. Comparison of full-field digital mammography with screen-film mammography for cancer detection: results of 4,945 paired examinations. Radiology 2001;218:873-80.
6. Obenauer S, Luftner-Nagel S, von Heyden D, Munzel U, Baum F, Grabbe E. Screen film vs full-field digital mammography: image quality, detectability and characterization of lesions. Eur Radiol 2002;12:1697-702.
7. Lewin JM, D'Orsi CJ, Hendrick RE, Moss LJ, Isaacs PK, Karellas A, et al. Clinical comparison of full-field digital mammography and screen-film mammography for detection of breast cancer.

AJR Am J Roentgenol 2002;179:671-7.
8. Skaane P, Balleyguier C, Diekmann F, Diekmann S, Piguet JC, Young K, et al. Breast lesion detection and classification: comparison of screen-film mammography and full-field digital mammography with soft-copy reading--observer performance study. Radiology 2005;237:37-44.
9. Skaane P, Skjennald A. Screen-film mammography versus full-field digital mammography with soft-copy reading: randomized trial in a population-based screening program--the Oslo II Study. Radiology 2004;232:197-204.
10. Obenauer S, Hermann KP, Marten K, Luftner-Nagel S, von Heyden D, Skaane P, et al. Soft copy versus hard copy reading in digital mammography. J Digit Imaging 2003;16:341-4.
11. Fischer U, Baum F, Obenauer S, Funke M, Hermann KP, Grabbe E. [Digital full field mammography: comparison between radiographic direct magnification and digital monitor zooming]. Radiologe 2002;42:261-4.
12. Kuzmiak CM, Millnamow GA, Qaqish B, Pisano ED, Cole EB, Brown ME. Comparison of full-field digital mammography to screen-film mammography with respect to diagnostic accuracy of lesion characterization in breast tissue biopsy specimens. Acad Radiol 2002;9:1378-82.
13. American College of Radiology. Breast Imaging Reporting and Data System (BI-RADS). 4th ed. VA: Reston; 2003.
14. Kim HH, Pisano ED, Cole EB, Jiroutek MR, Muller KE, Zheng Y, et al. Comparison of calcification specificity in digital mammography using soft-copy display versus screen-film mammography. AJR Am J Roentgenol 2006;187:47-50.
15. Landis J, Koch G. The measurement of observer agreement for categorical data. Biometrics 1977;33:159-74.
16. Kim MJ, Kim EK, Kwak JY, Son EJ, Youk JH, Choi SH, et al. Characterization of microcalcification: Can digital monitor zooming replace magnification mammography in full-field digital mammography? Eur Radiol 2008:Epub ahead of print.
17. Kurt Rossmann Laboratories for Radiologic Image Research DoR, University of Chicago. http://www-radiology.uchicago.edu/krl/KRL_ROC/software_index.htm. Accessed July 22, 2008.
18. Wagner RF, Metz CE, Campbell G. Assessment of medical imaging systems and computer aids: a tutorial review. Acad Radiol 2007;14:723-48.
19. Pisano ED, Cole EB, Kistner EO, Muller KE, Hemminger BM, Brown ML, et al. Interpretation of digital mammograms:

comparison of speed and accuracy of soft-copy versus printed-film display. Radiology 2002;223:483-8.
20. Blume H, Roehrig H, Ji TL. Very high-resolution CRT display systems: update on state of the art of physical and psychophysical performance. SID Digest 1992;92:699-702.
21. Blume H, Roehrig H, Ji TL. High-resolution high-brightness CRT display systems:update on the state of the art. . SID Digest 1994;94:219-22.
22. Roehrig H, Blume H, Ji TL, Browne M. Performance tests and quality control of cathode ray tube displays. J Digit Imaging 1990;3:134-45.
23. Shtern F, Winfield D, eds. Report of the Working Group on Digital Mammography: digital displays and workstation design. Acad Radiol 1999;6:S197-S218.
24. Grabbe E, Fischer U, Funke M, Hermann KP, Obenauer S, Baum F. [Value and significance of digital full-field mammography within the scope of mammography screening]. Radiologe 2001;41:359-65.
25. Kopans DB. Mammography: equipment and basic physics. In: imaging B, editor. 3rd ed. Baltimore, MD: Lippincott Williams & Wilkins; 2007. p.243-65.
26. Pisano ED, Gatsonis C, Hendrick E, Yaffe M, Baum JK, Acharyya S, et al. Diagnostic performance of digital versus film mammography for breast-cancer screening. N Engl J Med 2005;353:1773-83.
27. Faulk RM, Sickles EA. Efficacy of spot compression-magnification and tangential views in mammographic evaluation of palpable breast masses. Radiology 1992;185:87-90.
28. Hall FM. Magnification spot compression of the breast. Radiology 1989;173:284.
29. Liberman L. Percutaneous image-guided core breast biopsy. Radiol Clin North Am 2002;40:483-500, vi.

<APPENDIX>

Case number					Contact mammography				Magnification mammography	
Image quality										
Excellent		Good		Moderate		Intermediate			Not acceptable	
The shape of clustered calcifications					Confidence rate	1	2	3	4	5
Typically benign										
Skin	Vascular	Coarse or papcorn like	Large rod-like	round	Lucent-center	Egg shell or rim	Milk of calcium	Suture	dystrophic	
Morphology of intermediate or highly suspicious calcifications for malignancy										
Punctate	Coarse heterogeneous		Amorphous or indistinct		Fine pleomorphic		Fine linear/branching			
Distribution					Confidence rate	1	2	3	4	5
Clustered	Linear		Segmental		Regional		Multiple groups		Diffuse	
Probability of malignancy					Confidence rate	1	2	3	4	5
1. Definitely not malignancy			2. Probably not malignant				3. Low-possibly malignant			
4. Intermediate-probably malignant			5. Moderate-probably malignant				6. Definitely malignant			

< ABSTRACT(IN KOREAN)>

소프트카피 디지털 유방촬영술로 시행한 석회화의 진단: 1배 유방촬영술의 줌 영상과 확대유방촬영술

<지도교수 김 은 경>

연세대학교 대학원 의학과

김 민 정

연구목적: 이 연구의 목적은 미세석회화의 진단적 정확도와 영상질이 디지털 유방촬영술의 1배 유방촬영술에서 줌했을 때(줌인수 1.3)와 디지털 유방촬영술의 확대유방촬영술에서 유사한지를 알아보고자 한다. 또한 1배 유방 촬영술에서 또 다른 줌인수를 사용한 경우(줌인수 2.0) 확대유방촬영술에서의 미세석회화의 진단적 정확도 및 영상질을 비교하고자 한다.

연구대상 및 방법:

Part1. 미세석회화의 특성화의 진단수행평가와 영상질에 있어 디지털 유방촬영술에서 1.3배 줌한 방법과 확대유방촬영술 (1.8배 확대인자)의 비교: 유방촬영술에 대한 서로 다른 정도의 경험을 가진 3명의 영상의학과 의사들이 디지털 확대 유방촬영술과 1배 유방촬영술로 모니터에서 상업적으로 사용가능한 방법을 이용한 줌영상을 이용하여 디지털 유방촬영술의 111명의 120 미세석회화 무리를 재고하였다. 각 영상의학과 의사는 악성가능성, 영상의 질과 신뢰수준을 측정하였다. 수행평가는 민감도, 특이도, 양성예측도 음성예측도, 그리고 수신자판단특성곡선 분석으로 평가하였다.

Part2. 미세석회화의 특성화의 진단수행평가와 영상질에 있어 디지털

유방촬영술에서 2.0배 줌한 방법과 확대유방촬영술의 비교:
유방촬영술에 대한 서로 다른 정도의 경험을 가진 3명의 영상의학과 의사가 185명의 환자에서 병리학적으로 확진된 미세석회화의 디지털 유방촬영술 판독세트를 평가하였다. 판독세트는 1.8배 확대인자를 갖는 디지털 확대 유방촬영술과 2배 줌인자를 갖는 줌한 영상으로 구성되어있다. 각 영상의학과 의사는 미세석회화병변에 있어서의 유방암의 의심정도를 6단계 척도로 평가하였고. 영상의 질과 그들의 결정에 대한 신뢰정도는 5단계 척도로 평가하였다. 미세석회화의 판독에 따른 결과는 수신자판단특성곡선에 따라 분석하였고 영상의 질과 신뢰수준은 윌콕슨 부호순위검정을 이용하였다.

연구결과:

Part1. 미세석회화의 특성화의 진단수행평가와 영상질에 있어 디지털 유방촬영술에서 1.3배 줌한 방법과 확대유방촬영술(1.8배 확대인자)의 비교: 3명의 영상의학과 의사 모두, 1.3배 줌영상에 비해 확대유방촬영영상으로 통계적으로 유의하게 높은 민감도를 보였다 (평균, 92% 대 87%, $P<0.05$). 또한 확대 유방촬영영상으로 향상된 수신자판단특성곡선을 보였다. 진단의 결정에 있어서의 신뢰수준과 병변특성화에 있어서도 모두 줌영상보다는 확대영상이 우수했다($P<0.0001$).

Part2. 미세석회화의 특성화의 진단수행평가와 영상질에 있어 디지털 유방촬영술에서 2.0배 줌한 방법과 확대유방촬영술의 비교: 2.0배 줌영상의 곡선하면적은 0.8680으로 확대영상과 유사하다(0.8682, 평균차이에 관한 95% 신뢰구간: -0.02973 에서 0.02934; $p=0.9897$). 그러나 영상의 질($p<0.001$)과 신뢰수준($p<0.001$)에 있어서는 확대영상이 줌영상에 비해 우수했다.

결론:

Part1. 미세석회화의 특성화의 진단수행평가와 영상질에 있어 디지털 유방촬영술에서 1.3배 줌한 방법과 확대유방촬영술(1.8배 확대인자)의 비교: 디지털 확대 유방촬영술은 미세석회와의 특성화시에 진단적 수행을 향상시킨다. 1.3배 줌영상으로 디지털 확대유방촬영술을 대체할 수 없다.

Part2. 미세석회화의 특성화의 진단수행평가와 영상질에 있어 디지털 유방촬영술에서 2.0배 줌한 방법과 확대유방촬영술의 비교: 2.0배 줌영상을 이용한 미세석회화의 진단에 있어서 영상의학과 의사의 수행은 확대영상을 이용했을 때와 유사했다. 이와 같이 2.0배 줌영상은 비록 영상의 질과 신뢰수준은 확대영상에 비해 떨어지더라도 미세석회화의 진단에 있어 대체수단으로 쓰일 수 있다.

핵심되는 말 :디지털 유방촬영술, 확대촬영, 줌

PUBLICATION LIST

Kim MJ, Kim EK, Kwak JY, Son EJ, Youk JH, Choi SH, et al. Characterization of microcalcification: Can digital monitor zooming replace magnification mammography in full-field digital mammography? European Radiology 2008:Epub ahead of print.