

Fuji Computed Radiography Mammography Suite (FCRMS)

ESSENTIAL PRESCRIBING INFORMATION

PRESCRIPTION DEVICE

Caution: Federal law restricts this device to sale by or on the order of a physician.

DEVICE DESCRIPTION

In conventional screen-film mammography (SFM), a mammographic x-ray machine exposes the breast and projects an aerial x-ray intensity image onto a screen-film receptor which is then processed to produce an analog image. The Fuji Computed Radiography (FCR) system with FCRMS installed (FCR m) and a display device replaces the screen-film receptor and chemical processing system to produce a digital image.

FCR m should be used with mammographic x-ray machines and output display devices that are cleared by the United States Food and Drug Administration (FDA) for primary image interpretation in mammography. The requirements for these components are:

Mammographic X-ray Machine

An x-ray machine specifically designed for mammography and legally sold in the United States for mammography should be used.

The x-ray tube should have as a minimum a molybdenum target and molybdenum filter (Mo/Mo) combination for calibration of the FCR m image reader and optionally any of the following anode target and filter combinations: molybdenum target with rhodium filter (Mo/Rh), rhodium target with rhodium filter (Rh/Rh), and tungsten target with rhodium filter (W/Rh).

The x-ray system should have both manual exposure control and automatic exposure control (AEC). The AEC may be of the type controlling mAs only, or mAs and kVp, or mAs, kVp and filter, or mAs, kVp, filter, and target.

Fuji Computed Radiography System

FCR m consists of the following:

- Fuji dual-side Imaging Plates HR-BD in 18cm x 24 cm or 24cm x 30 cm sizes, for capturing the x-ray images and a corresponding number of Fuji IP Cassettes DM in the same sizes, for transporting the imaging plates;
- a Fuji ClearView image reader configured for dual-side reading and 50 micrometer sampling pitch; for reading the x-ray image from the imaging plate in the cassette; and
- a Fuji Flash Plus IIP CR console unit, the “acquisition” workstation with FCRMS installed.

With FCRMS installed in the Flash Plus IIP CR console unit, the console unit may be referred to as a Fuji Flash Plus IIP m (appending an italic m for mammography). Similarly, a connected image reader may be labeled with an italic m appended to the model name, e.g., a Fuji ClearView CS m or ClearView 1 m image reader. A complete FCR m system for mammography (HR-BD imaging plates, DM cassettes, ClearView m reader (for example ClearView CS m , ClearView 1 m , or other), and Flash Plus IIP m console) is also known as an FCR m system.

Softcopy or Hardcopy Display

Primary interpretation of softcopy images must be performed either on a:

- review work station consisting of a PC-based computer with FDA cleared mammography displays capable of handling DICOM MG “for presentation” images; or
- Fuji review workstation with FDA cleared mammography displays capable of handling DICOM MG “for presentation” or “for processing” images.

The review workstation should have a minimum of two displays, each with a minimum image array size of five megapixels.

For primary interpretation of hardcopy images, use a printer cleared for mammography that supports DICOM basic grayscale print management service with a pixel pitch of 50 micrometers or less and film maximum optical density of at least 3.6.

INDICATIONS FOR USE

The Fuji Computed Radiography Mammography Suite (FCRMS) is a software device that, in conjunction with a specified Fuji Computed Radiography system forms the Fuji Computed Radiography for mammography (FCR m) device. FCR m with a dedicated mammographic x-ray machine generates digital mammographic images that can be used for screening and diagnosis of breast cancer. It is intended for use in the same clinical applications as traditional screen-film based mammographic (SFM) systems. The mammographic images can be interpreted by a qualified physician using either hardcopy film or softcopy display at a workstation.

CONTRAINDICATIONS

There are no known contraindications.

WARNINGS AND PRECAUTIONS

Cautions and Warnings in the FCR m User Guide:

Warnings:

- For U.S. only: Until an accreditation body has been approved to accredit the FCR m unit, FDA will continue its process for extending the certification of an already certified facility to include these specific units. Until otherwise notified

by FDA, a facility with an FCR m unit (that does not have a corresponding approved accreditation body) will be exempt from the MQSA accreditation requirement but must request FDA to extend its current certification to cover its unaccredited FCR m unit.

- The mammographic x-ray system's automatic exposure control (AEC) should be calibrated for use with FCR m prior to use.
- The FCR m image reader must be calibrated with S value in mammography that is based on an exposure to the imaging plate of 20 mR at 25 kVp using a molybdenum (Mo) target and Mo filter (Mo/Mo 0.03 mm) with only air in the beam.
- The x-ray system must have a molybdenum (Mo) target and Mo filter for S value calibration.
- Insertion of a broken cassette into an FCR m reader can result in mechanical failure and system shutdown.

Cautions:

- FCR m does not emit radiation; however, it is used in conjunction with x-ray emitting equipment. Refer to the Cautions and Warnings associated with the x-ray emitting equipment.
- Do not use the Fuji reader and console in the presence of a flammable anesthetic or gaseous mixtures.
- The user should follow the x-ray exposure unit instructions in order to safely operate the exposure device.
- Do not use the Flash Plus IIP Computer Radiography (CR) console for primary interpretation of patient images.
- Only authorized, trained personnel should operate this equipment. The site is responsible for ensuring that proper operating techniques and procedures are followed when operating the FCR m .
- The softcopy review station should be located in a suitably dark environment to enhance image visibility during review. The ambient light level, measured at the surface of the monitor screen (with the monitor turned off), should not exceed 20 lux.
- DO NOT remove any covers or attempt to service the system. The system contains no user serviceable parts.
- Do not touch the recording surface of magnetic or optical storage media.
- Do not add unauthorized software to the CR console or soft copy review station computers. Unauthorized software may affect system performance or cause conflicts with system operation.

Fuji Computed Radiography Mammography Suite (FCRMS)
Essential Prescribing Information

- DO NOT insert a moist cassette into the CR reader. If necessary, remove the imaging plate from wet cassette and insert it (make sure the imaging plate is dry) into a dry cassette.
- Only use the HR-BD Imaging Plate and Fuji IP Cassette DM for mammography.
- Do not use water, screen cleaner, or isopropyl alcohol to clean the imaging plates. Anhydrous ethanol is the only solution suitable for wet cleaning of an imaging plate.
- A protective, plastic bag should be used to cover the cassette in the presence of blood or other body fluids.
- Always follow the facilities' infection control guidelines.
- Always wear appropriate protective clothing when handling blood or any cleaning solutions.
- Equipment contaminated with blood or other body fluids should be cleaned and disinfected with the appropriate agents.
- In a fixed site or mobile environment, after exposure, ensure that imaging plates are read without undue delay to preserve optimal image quality.

Cautions and Warnings in the FCR_m Quality Control Manual:

Cautions:

- Use only the Fuji IP Cassette DM and Fuji IP HR-BD for mammographic imaging and QC testing.
- Perform the Sensitivity Confirmation test prior to the Acceptance and QC tests, using only molybdenum (Mo) target and Mo 0.03 mm filter at 25kVp. Do not use any additional filter as the use of another filter may cause an error in sensitivity confirmation.
- If the mammography x-ray unit will not allow 20 mR exposures, the lowest MR exposure greater than 20 should be used. Always use 25 kVp for the sensitivity confirmation test.

POTENTIAL ADVERSE EFFECTS

The following potential adverse effects that apply to mammography using FCRm:

- excessive breast compression;
- excessive x-ray exposure;
- electrical shock;
- infection and skin irritation; or
- abrasion or puncture wound

SUMMARY OF NON-CLINICAL STUDIES

Sensitometric Response

The sensitometric response of the Fuji HR-BD imaging plate was assessed by exposing representative plates to x-ray beams with spectra typical of mammographic imaging with a polymethylmethacrylate (PMMA) phantom in the beam. No image processing was performed. The pixel values obtained from the central region of the images were recorded (see Figure 1). QL is the variable name used for the pixel value, in this case for an unprocessed image.

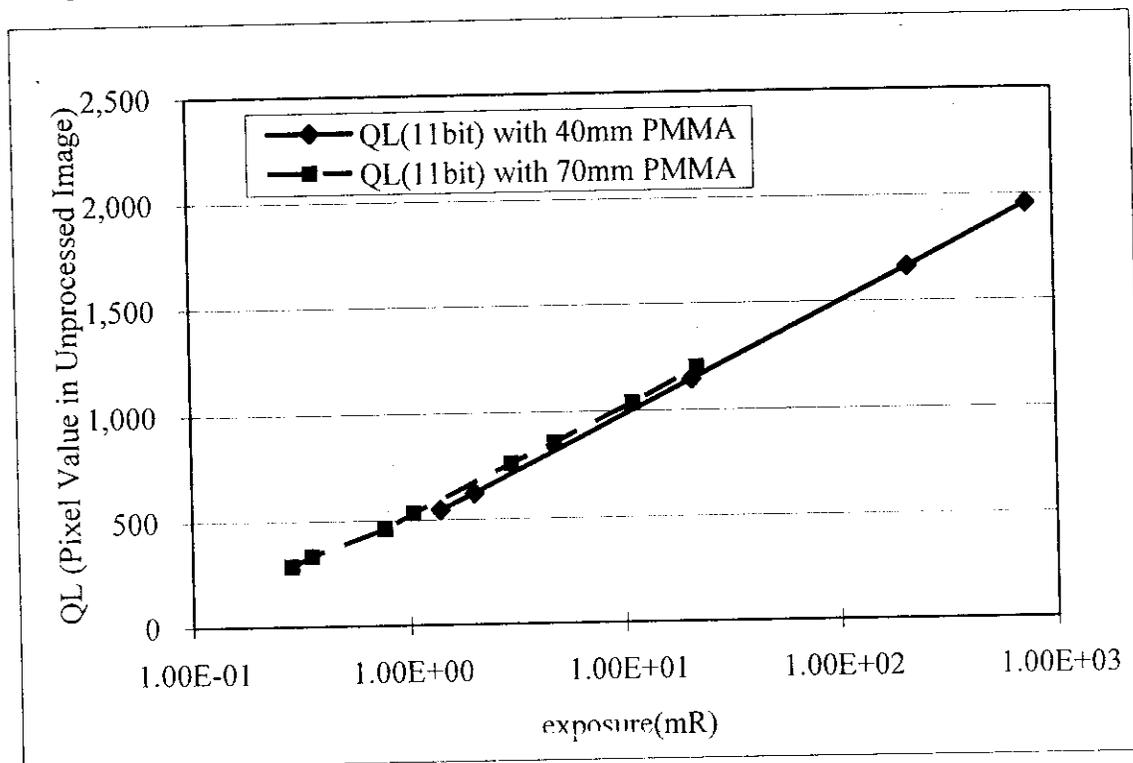


Figure 1. Sensitometric Response of Imaging Plate

Spatial Resolution

The spatial resolution of the HR-BD imaging plate with the image processing of FCRMS was measured by imaging contrast transfer function phantoms with mammographic x-ray spectra. The Modulation Transfer (MTF) was calculated from the Contrast Transfer Function (CTF) data. The results for processed and unprocessed images along with MTF for a SFM system are shown in Figure 2.

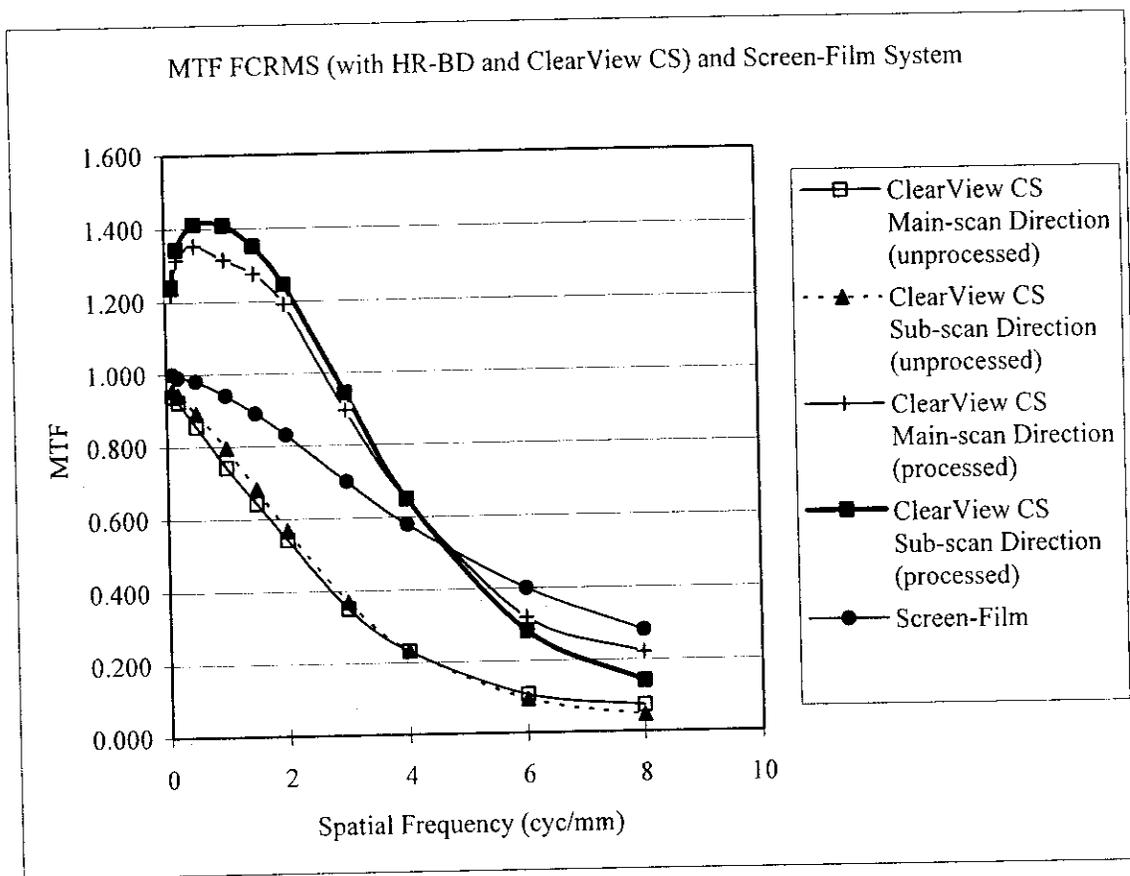


Figure 2. MTF Measurements With and Without Image Processing

Signal to Noise Transfer and Dynamic Range

Quantitative measure of the efficiency of signal to noise ratio (SNR) transfer and dynamic range of the image acquisition system were measured by the noise equivalent quanta (NEQ) and the detective quantum efficiency (DQE) as a function of spatial frequency and radiation exposure level. These qualities of the combination of the HR-BD imaging plate and FCRMS were measured by combining noise and spatial resolution measurements made at several different radiation exposures and are expressed as NEQ and DQE as a function of spatial frequency as shown in Figures 3 and 4.

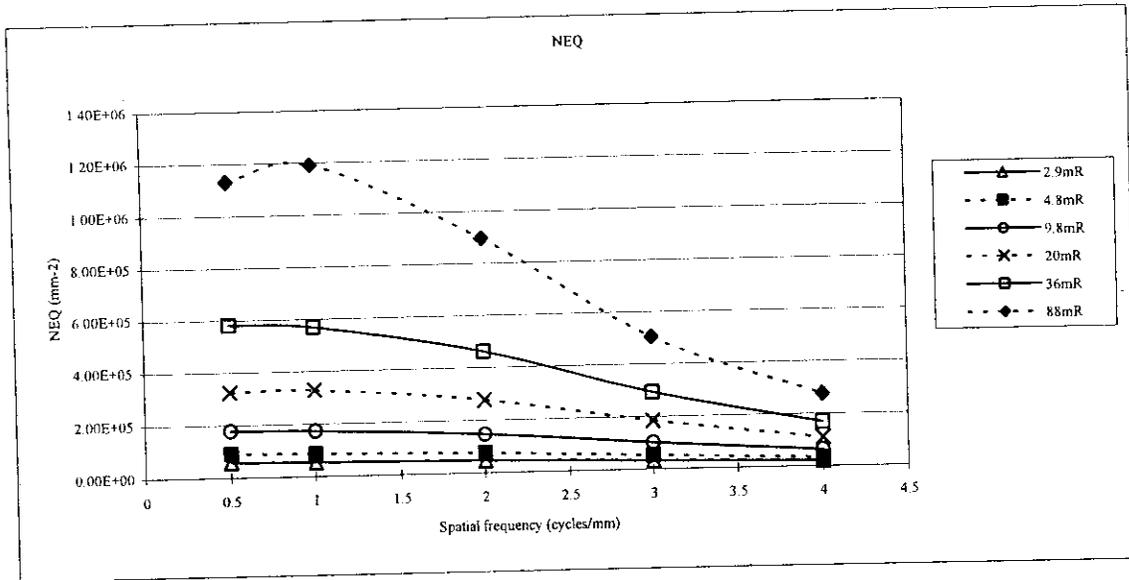


Figure 3. Relationship between NEQ and X-ray Exposure

The relationship between DQE, x-ray exposure, and spatial frequency are shown below in Figure 4.

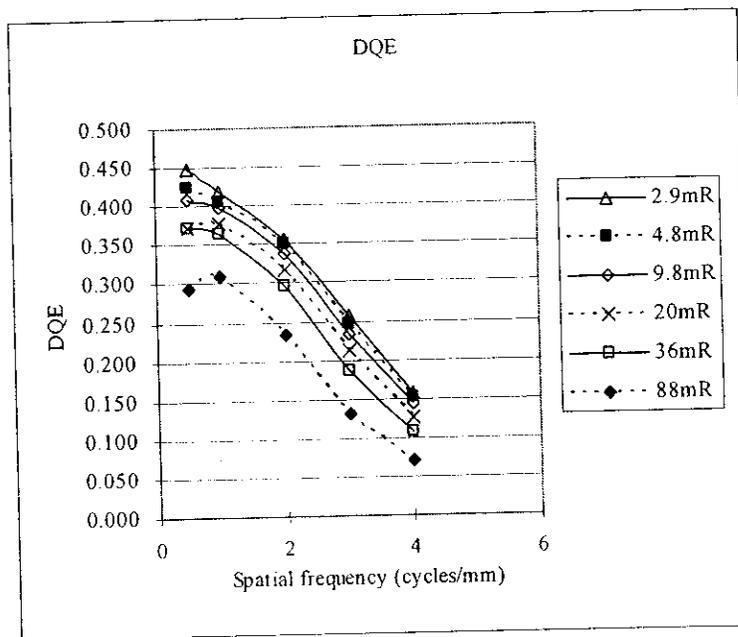


Figure 4. Relationship Between DQE and X-ray Exposure

Phantom Tests

The imaging performance of FCRMS with the HR-BD imaging plate was tested with two types of phantoms. One was a contrast-detail mammography (CDMAM) phantom manufactured by Nuclear Associates. This phantom contains a square array of circular test objects which are constant in diameter and vary in contrast in the direction of one

side of the square and are constant in contrast and vary in diameter in the orthogonal direction. An x-ray image of the phantom is made and the contrast (or gold thickness) of the lowest contrast visible test object at each value of object diameter is noted. Images were obtained with a Fuji IP Cassettes DM cassette and a HR-BD imaging plate. The images from the imaging plate were processed both with and without the Pattern Enhancement for Mammography (PEM) image processing software. The results are displayed in Table 1 and Figures 5 and 6. The k-values are the product of the disk diameter and the thickness. Ideal k-values that a system should detect are 60 -80 μm^2 . The image quality factor (IQF) is the sum of the products of the diameters of each of the smallest scored objects and their relative contrast. The lower the value of IQF, the better is the image quality.

Disk Diameter (mm)	Disk Thickness (μm)	
	Screen-Film Fuji UM-Mammo Fine with UM-MA HC	FCRm
0.1	1	1
0.13	0.8	0.8
0.16	0.63	0.5
0.2	0.4	0.4
0.25	0.31	0.25
0.31	0.2	0.2
0.4	0.16	0.16
0.5	0.13	0.13
0.63	0.13	0.1
0.8	0.13	0.08
1	0.1	0.08
1.25	0.08	0.06
1.6	0.06	0.06
2	0.06	0.06
2.5	0.06	0.06
3.2	0.06	0.06
IQF	1.60	1.46

Table 1. IQF Results with SFM and FCRm

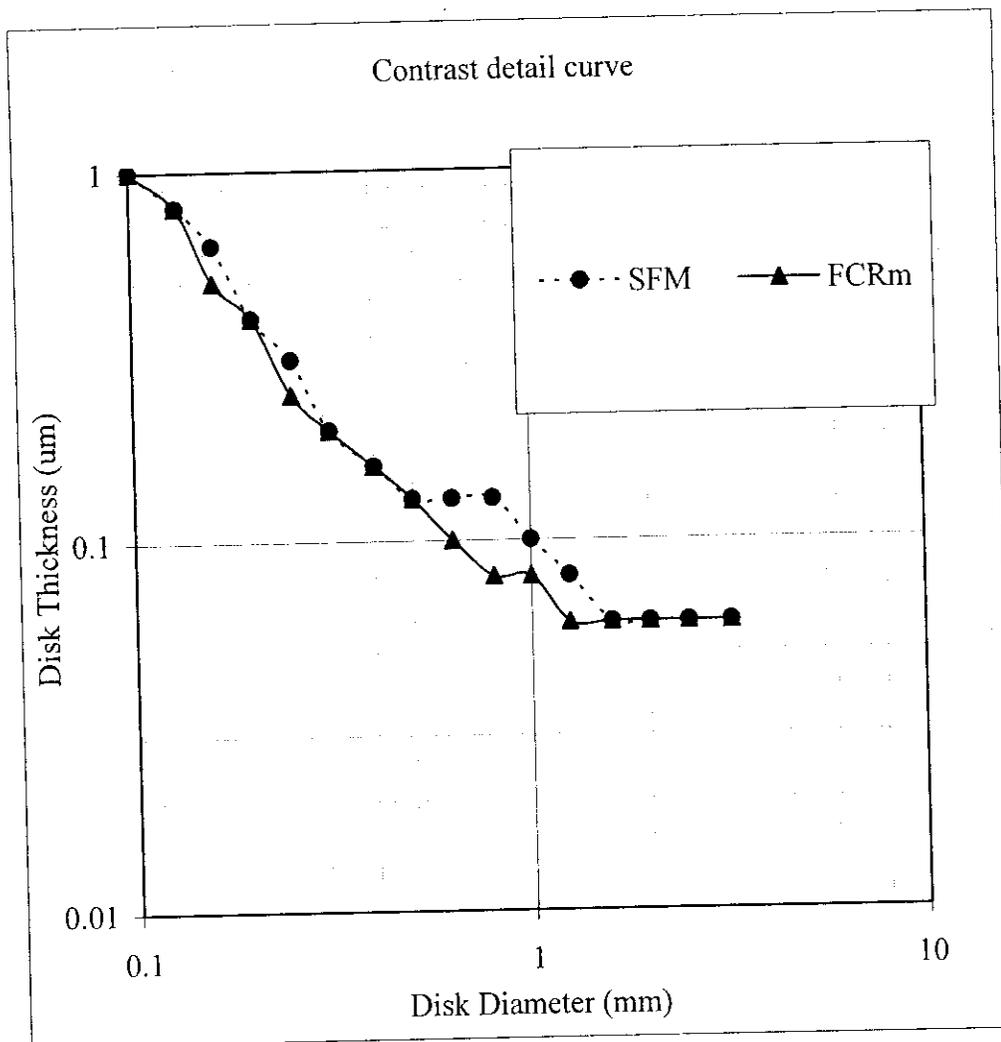


Figure 5. Contrast Detail Curve for SFM and FCRm

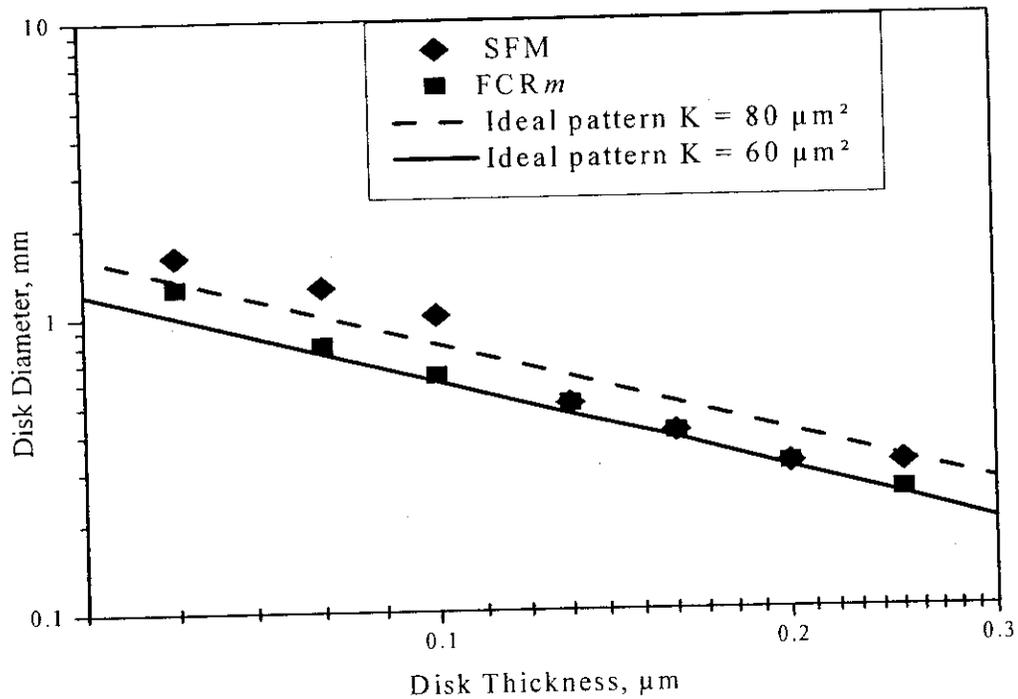


Figure 6. Contrast Detail Curve for SFM and FCRm with Ideal k Values

In another phantom image experiment, an FDA approved American College of Radiology (ACR) Mammography Accreditation Phantom (RMI-156) was used for image quality evaluation. Both HR-BD imaging plates and a SFM cassette were used to acquire the images and score them. The scores are shown in Table 2.

Table 2. ACR Phantom Results

	SFM Score	FCRm Score
Fibers	4.7	5.0
Specks	3.5	3.8
Masses	3.4	3.6

SUMMARY OF CLINICAL STUDIES

Study 1 Comparative Accuracy of FCRm Compared to Screen-Film Mammography (SFM) in Detection of Breast Cancer

Study Objective

To test the non-inferiority of FCRm compared to SFM among patients from diagnostic and screening populations.

Primary Objective

To compare the accuracy of FCR m and SFM mammography in detection of breast cancer among women undergoing screening or diagnostic mammography using hard copy film.

Secondary Objectives

To compare the sensitivity and specificity of FCR m and SFM.

Design

A prospective, multi-center, cohort study was conducted in the United States in which patients underwent both FCR m and SFM at the acquisition site. Two sites participated as image acquisition sites and one site participated as the core reading center (CRC). Patients were enrolled from screening and diagnostic populations whose mammograms were interpreted as American College of Radiology (ACR[®]) Breast Imaging Reporting and Database System (BI-RADS[®]) assessment category 1, 2, or 3. In addition, the study was enriched by enrolling patients with BI-RADS[®] assessment category 4 or 5.

FCR m and original SFM hard copy examinations of the four standard views: right mediolateral oblique (RMLO), left mediolateral oblique (LMLO), right craniocaudal (RCC), and left craniocaudal (LCC) were provided to the CRC for independent interpretation by six MQSA-qualified radiologist readers. CRC readers completed standardized image interpretation forms for each mammography examination. Readers reported the anticipated final ACR[®] BI-RADS[®] assessment category and were asked to record their assessment of the probability of cancer on a continuous scale ranging from 0 (no chance of cancer) to 100 (certainty of cancer).

Patient Population

Women were eligible for the study provided they fulfilled all of the following criteria:

- underwent or were scheduled to undergo a screening or diagnostic SFM examination^a at one of the acquisition sites;
- at least 40 years of age;
- provided written informed consent indicating willingness to participate in this research study prior to performance of the FCR[®] mammogram; and
- met none of the exclusion criteria.

Women were not eligible for enrollment if they had any of the following:

- a breast implant;

^a For a single patient, the terms “examination”, “mammogram”, and “study” have been used interchangeably to mean four standard views with or without special views. The four standard views are right craniocaudal (RCC), left craniocaudal (LCC), right mediolateral oblique (RMLO), and left mediolateral oblique (LMLO).

- a unilateral mammogram or an incomplete SF mammogram;
- excisional breast biopsy with a finding of carcinoma;
- pregnancy or possibility of pregnancy;
- self-reported, non-focal or bilateral breast pain;
- penal incarceration; or
- inability to undergo follow-up mammography examinations.

Variables

The primary analysis variables included the receiver operating characteristic (ROC) area, sensitivity, and specificity.

- The primary endpoint was the area under the ROC curve (AUC). AUC was based on the CRC readers' subjective assessments of the probability that a breast had cancer using a continuous scale ranging from 0 (no chance of cancer) to 100 (certainty of cancer).
- Sensitivity and specificity were secondary endpoints. Sensitivity and specificity were based on the CRC readers' BI-RADS™ category assessments.

Processes

Each SFM and FCR_m examination was interpreted by the radiologist at the acquisition site who reported finding location, finding characterization, finding conspicuity, and diagnostic work-up. In addition, the acquisition sites reported brief medical history and image acquisition parameters.

Each SFM and FCR_m examination was also interpreted independently by six readers at the CRC. CRC readers' subjective impression about the absence or presence of cancer was reported, by quadrant, on a continuous scale from 0 (no chance of cancer) to 100 (certainty of cancer). Additionally, the CRC readers reported the BI-RADS™ category by quadrant. The primary analysis was based on CRC data.

Statistical Methods

The analysis of AUC, sensitivity, and specificity of SFM compared to FCR_m were performed using the individual breast, rather than the patient or the quadrant, as the unit of analysis.

The AUC for SFM and FCR_m were estimated for each of the six CRC readers using the readers' highest assessment of the probability of cancer in each breast. A nonparametric method [Obuchowski, 1997¹] was used that takes into account the clustered nature of the data (that is, two breasts per patient). The upper 95% confidence limit for the difference in the AUC areas of SFM compared to FCR_m was constructed using the random-effects model of Dorfman, Berbaum, and Metz [Dorfman, 1992²].

The sensitivity and specificity of SFM and FCR m were estimated for each CRC reader based on the BI-RADS[®] category. In calculation method 1, BI-RADS[®] categories 1 and 2 were considered negative and categories 0, 3, 4, and 5 were considered positive. In calculation method 2, BI-RADS[®] categories 0, 1, 2 and 3 were considered negative, and categories 4 and 5 were considered positive. For each breast, the BI-RADS[®] category for the quadrant with the highest probability of cancer was used for the analysis of sensitivity and specificity. The method of Generalized Estimating Equations (GEE), as described by Diggle, Heagerty, Liang, and Zeger [Diggle, 2002³], was used to estimate the difference in sensitivity and specificity between SFM and FCR m while taking into account the correlation between breasts in a single patient.

The difference in conspicuity between SFM and FCR m was evaluated by the acquisition site radiologist based on the most suspicious mammographically detectable finding per patient. This included the main feature that makes the finding most conspicuous (specifically, calcification, mass only, mass with calcifications, architectural distortion, or focal asymmetry); the breast, quadrant, and view with the most conspicuous feature; the conspicuity scale (ranging from 0 to 11, where 0 = no finding identifiable and 11 = highly conspicuous); and whether a difference in conspicuity between SFM and FCR m was due to a difference in patient positioning. Findings that were not detectable on SF, but were detectable on FCR m (or vice versa), were assigned a conspicuity scale value of zero for the modality (SFM or FCR m on which the finding was not detectable). The difference in conspicuity between SFM and FCR m was tested using the Wilcoxon signed rank test.

Test of Equivalent Effectiveness

SFM and FCR m were determined to have equivalent effectiveness if: (a) the upper 95% confidence limit on the observed difference in AUC for SFM versus FCR m was less than or equal to 0.10; or (b) the upper 95% confidence limits on the observed differences in sensitivity and specificity for SFM versus FCR m are less than or equal to 0.10.

Case Selection Bias Adjustment

An analytical approach was developed to estimate the magnitude of the case selection bias, which resulted from enrolling patients in the study based on the results of their SFM examinations at the acquisition sites. The expectation, in light of this case selection bias, was that the sensitivity of FCR m would be less than SFM in the study. The AUC, sensitivity, and specificity analyses were implemented using this approach to estimate the magnitude of the case selection bias.

Study Results

Patient Disposition and Demography

A total of 218 patients were enrolled in the investigation (161 at the Mayo Clinic and 57 at the University of California - Los Angeles (UCLA)). Five patients were excluded from

the analyses, 3 protocol deviations at enrollment and 2 patients classified as not evaluable. Of the remaining 213 patients:

- mean age was 57.9 years
- 86.4 % (n=184) were Caucasian;
- 37% (n=79) had dense breast tissue composition;
- 54% (n=115) were from a screening population and 46% (n=98) were from a diagnostic population;
- distribution of final ACR® BI-RADS® assessments was as follows: 10% category 1, 14% category 2, 9% category 3, 53% category 4, and 14% category 5;
- 28% (n=59) were determined by tissue sampling to have cancer:
 - 42% (n=25) of the cancers were from a screening population;
 - 58% (n=34) of the cancers were from a diagnostic population;
 - 54% (n=32) of cancers had a final assessment of BI-RADS® category 4;
 - 46% (n=27) of cancers had a final assessment of BI-RADS® category 5;
 - 63% (n=37) of cancer patients were enrolled at Mayo Clinic; and
 - 37% (n=22) of cancer patients were enrolled at UCLA.

Mammography Findings

- There were 176 mammographically detectable findings among the 213 patients.
- The most suspicious mammographically detectable findings^b were characterized as follows: 44% mass without calcifications; 37% calcifications; 8% mass with calcifications; 8% focal asymmetry; and 5% architectural distortion.
- The percentage of International Union Against Cancer (UICC) tumor, node, and metastasis (TNM) classification Stage 0 or I tumors found was 54% (desirable goal for a screening program > 50% [Bassett, 1994⁴]). The percentage of minimal cancers found was 41%, where minimal cancers are defined as ductal carcinoma *in situ* (TNM Stage 0) or invasive cancers less than or equal to 1.0 cm (TNM Stage IA or IB) (desirable goal for a screening program > 30% [Bassett, 1994]).

ROC Analysis-

The overall areas under the ROC curves were 0.8622 for SFM and 0.8025 for FCR_m with a difference of 0.0597 (see Figure 7). The 95% confidence interval of the difference was

^b The most suspicious mammographically detectable finding for each patient is defined as the finding with the highest probability of cancer. If two or more findings are equally suspicious (that is, equal probabilities of cancer), then the most conspicuous finding (that is, prominent finding) is reported. The total across findings exceeds 100% because several patients had, for example, architectural distortion with calcifications.

0.0351 to 0.0843. In other words, with 95% confidence, the area under the ROC curve for SFM could be as much as 0.0843 greater than for FCRm. Because the upper 95% confidence limit on the observed difference in the area under the ROC curve for SFM versus FCRm is less than or equal to 0.10, the null hypothesis can be rejected ($p < 0.001$) in favor of the alternative hypothesis that the overall ROC area of SFM was no more than 0.10 greater than FCRm.

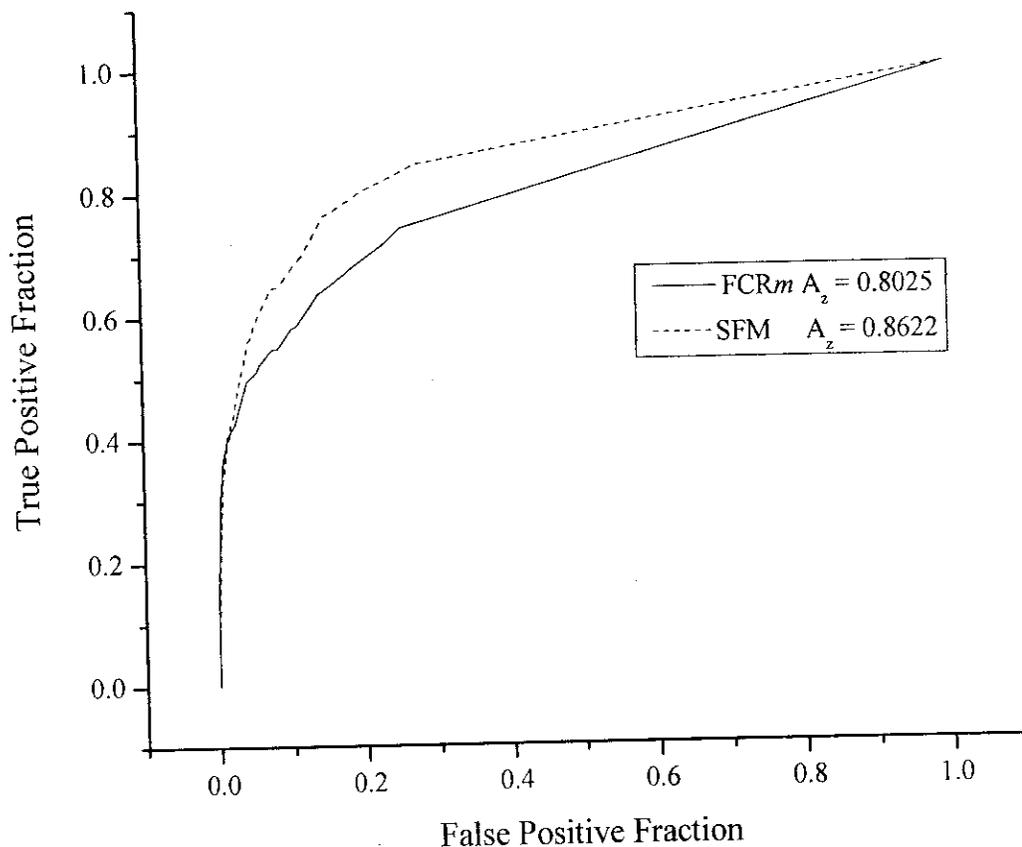


Figure 7. Receiver Operating Characteristic (ROC) Curves
FCRm and Screen-Film (SF)

Sensitivity

Where BI-RADS[®] category 0 and 3 cases were categorized as positive (calculation 1), the overall sensitivity for SFM and FCRm was 0.806 and 0.687, respectively, with a mean difference of 0.119 and a 95% confidence interval of 0.052 to 0.187.

Where BI-RADS[®] category 0 and 3 cases were categorized as negative (calculation 2), the overall sensitivity for SFM and FCRm was 0.764 and 0.631, respectively, with a mean difference of 0.133 and a 95% confidence interval of 0.065 to 0.202.

In other words, with 95% confidence, the sensitivity of SFM could be as much as 0.202 greater than for *FCRm*. This difference in sensitivity between SFM and *FCRm* is consistent with the case selection bias. Because the upper 95% confidence limit on the observed difference in sensitivity between SFM and *FCRm* was greater than 0.10, the null hypothesis cannot be rejected in favor of the alternative hypothesis that the sensitivity of SFM was no more than 0.10 greater than *FCRm*.

Specificity

Where BI-RADS® category 0 and 3 cases were categorized as positive (calculation 1), the overall specificity for SFM and *FCRm* was 0.808 and 0.826, respectively, with a difference of -0.017, and a 95% confidence interval of -0.036 to 0.001.

Where BI-RADS® category 0 and 3 cases were categorized as negative (calculation 2), the overall specificity for SFM and *FCRm* was 0.857 and 0.872, respectively, with a difference of -0.015, and a 95% confidence interval of -0.033 to 0.002.

In other words, with 95% confidence, the specificity of SFM could be as much as 0.036 less than *FCRm* to as much as 0.002 greater than *FCRm*. Because the upper 95% confidence limit on the observed difference in specificity between SFM and *FCRm* was less than 0.10, the null hypothesis can be rejected in favor of the alternative hypothesis that the specificity of SFM was no more than 0.10 greater than *FCRm*.

Conspicuity

Among patients with visible findings on SFM and/or *FCRm* where a difference in conspicuity was not due to improper positioning (n=174), the mean conspicuity ratings for SFM and *FCRm* were 8.5 and 8.8, respectively (p=0.007), using an 11-point Likert scale where 0 = no finding identifiable and 11 = highly conspicuous.

Case Selection Bias Adjustment

The post-hoc analysis adjusting for case selection bias resulted in the mean difference in ROC area between SFM and *FCRm* decreasing by approximately 42.5% (from 0.0597 to 0.0343) and the mean difference in sensitivity decreasing by 42.9% (from 0.119 to 0.068). The mean difference in specificity remained similar.

Safety

No adverse events were reported for patients enrolled during the study.

Study Conclusions -

Based on the results of the ROC analysis (the primary endpoint), SFM and *FCRm* have equivalent effectiveness given that the upper 95% confidence interval limit of the difference in the area under the ROC curve for SFM compared to *FCRm* was less than or equal to 0.10. These ROC analysis results support the conclusion that *FCRm* was not inferior to SFM in the detection of breast cancer.

The post-hoc analysis adjustment for case selection bias resulted in the mean difference in ROC area between SFM and FCR m decreasing by approximately 42.5% and the mean difference in sensitivity decreasing by 42.9%.

Among patients with visible findings on SFM and/or FCR m where a difference in conspicuity was not due to improper positioning, the mean conspicuity ratings for FCR m were significantly greater ($p=0.007$) than SFM among all patients.

Because the statistical analysis of the primary endpoint treated patients and readers as random effects and the study sample consisted of samples of cancer and non-cancer patients from screening and diagnostic populations, the results are generalizable to the population of similar patients undergoing mammography.

Study 2 – Comparative Feature Analysis of FCR m Soft Copy Display Compared to FCR m Hard Copy

Study Objective

The objective of this study was to demonstrate diagnostically equivalent performance between the soft and hard copy displays.

Design

The study was conducted as a side-by-side feature comparison using one site as a Core Reading Center (CRC). Six radiologist readers independently performed a side-by-side feature comparison of FCR m soft copy display and FCR m hard copy film. The CRC readers did not have access to patient information such as medical history and clinical diagnosis.

Patient Population

One hundred FCR m mammography examinations were acquired from Study 1 (four standard views only; CC and MLO for each breast). The patients' mammography examinations were included in this study if they met the following inclusion criteria:

- evaluable under the Study 1 protocol, defined as a patient with known true clinical status and with complete SFM and FCR m mammography examinations (four standard views), in which there was sufficient anatomical coverage, sufficient contrast, no significant motion or other artifacts, no over or underexposure of film, limited noise, and clinically insignificant difference in patient positioning between SFM and FCR m and
- none of the exclusion criteria was met.

A patient's mammography examination was not eligible for inclusion in this study if the patient had a protocol violation of the Study 1 protocol.

The FCR m mammography examinations were chosen to include 50 tissue-proven cancers and 50 non-cancers, with the diagnoses of non-cancers determined by tissue sampling, mammography special views and/or ultrasound, or one-year follow-up. In addition, the cases were chosen to provide a distribution of: (1) cancers and non-cancers from both

screening and diagnostic populations; (2) ACR[®] BI-RADS[™] categories; (3) finding types, e.g., calcifications, masses with or without spiculations, architectural distortion, and focal asymmetry; and (4) breast tissue composition, e.g., patients with heterogeneously or extremely dense breast tissue composition.

Variables

The primary analysis variables were the three endpoints of the comparative feature analysis: (1) conspicuity; (2) tissue visibility at or near the skin line; and (3) tissue visibility at or near the chest wall.

Assessments

Each FCR[®] examination was evaluated on both soft copy display and hard copy film independently by six readers at the CRC. They were asked to identify, by display format (specifically, FCR^m soft copy display and FCR^m hard copy film), the one main feature by which the finding was identifiable (specifically, calcification, mass with or without spiculations, architectural distortion, or focal asymmetry between the two breasts).

The readers also were asked to indicate, using an 11-point Likert scale, the following, by view (CC and MLO): (1) finding conspicuity; (2) visibility of tissue at or near the skin line of the breast; and (3) visibility of tissue at or near the chest wall. The 11-point Likert scale was defined where 1 was FCR^m soft copy display superior, 6 was equally visible on FCR^m soft copy display and FCR^m hard copy film, and 11 was FCR^m hard copy film superior.

Statistical Methods

The CRC readers' characterization of the one main feature that makes the finding most conspicuous (suspicious) between FCR^m soft copy display and FCR^m hard copy film was summarized using frequency tabulations. The one main feature was reported for all patients and, separately, for cancer patients and non-cancer patients. This included whether there was calcification only, mass only, mass with calcification, architectural distortion, focal asymmetry, or no finding identifiable. Additionally, if there was a calcification, the characteristics of the calcification (specifically, typically benign, intermediate concern, or high probability of malignancy) were compared descriptively between FCR^m soft copy display and FCR^m hard copy film. If there was a mass, margins (specifically, circumscribed, microlobulated, obscured, indistinct, or spiculated) were compared descriptively between FCR^m soft copy display and FCR^m hard copy film.

A comparative feature analysis was performed to determine comparable image quality. Three endpoints were examined for the comparative feature analysis: 1) conspicuity, 2) tissue visibility at or near the skin line, and 3) tissue visibility at or near the chest wall.

The unit of analysis was the view (CC and MLO). The analysis of each endpoint was performed by aggregating the data across 6 readers, 100 patients, and 2 views (total of 1,200 evaluations). For conspicuity, only views (CC and MLO) with an identifiable finding were analyzed. A view was defined as having comparable image quality on FCR^m hard copy film and FCR^m soft copy display if the reader scored it as ≤ 6 on the

Likert scale (1= FCR m soft copy is superior, 6=equally visible on FCR m soft copy display and FCR m hard copy film, and 11= FCR m hard copy is superior). A view was defined as non-comparable if the reader scored it as > 6 on the Likert scale.

The data were clustered in that for each patient there was an observation from each of the six readers for each view (CC and MLO). The probability ($\hat{\pi}$) that FCR m soft copy display was comparable to FCR m hard copy and its variance was estimated using methods for clustered binary data [Rao, 1992]⁵.

A Wald statistic (z) was calculated to test whether the probability that FCR m soft copy display was comparable to FCR m hard copy film (score of ≤ 6 on the Likert scale) exceeded the predefined level π_0 (where $\pi_0=0.80$). If z exceeded 1.645 (that is, $p<0.05$), then it was concluded that FCR m soft copy display and FCR m hard copy film have comparable image quality. This statistic was computed for each comparative feature analysis endpoint (conspicuity, tissue visibility at or near the skin line, and tissue visibility at or near the chest wall).

Study Results

Patient Disposition and Demography

Among the 100 FCR[®] examinations, 67% of the examinations were acquired at the Mayo Clinic and 33% were acquired at UCLA (Study 1 image acquisition sites). Overall, 49% of patients were from a screening population and 51% percent were from a diagnostic population. Among patients with cancer, 42% were from a screening population and 58% were from a diagnostic population.

The distribution of BI-RADS[™] categories was: 9% category 1, 6% category 2, 10% category 3, 48% category 4, and 27% category 5. Among patients with cancer, 50% were BI-RADS[™] category 4 and 50% were BI-RADS[™] category 5.

The one main feature was characterized as follows: calcification only 22%, mass only 39%, mass with calcification 14%, architectural distortion 7%, focal asymmetry 12%, and no finding identifiable 6%. For 6 patients, the one main feature was identifiable on only the CC view. For 6 other patients, the one main feature was identifiable on only the MLO view.

The mean age was 58 years (range 40 to 93) and approximately one-half of patients (51%) had dense breast tissue composition.

Characterization of One Main Feature

The most suspicious mammographically detectable findings for FCR m soft copy display and FCR m hard copy film were characterized similarly by the six readers.

Among patients with cancer, the percentage of patients with a high probability of malignancy (for calcifications) and with spiculated margins (for mass only or mass with calcifications) were generally similar between FCR m soft copy display and FCR m hard copy film.

Conspicuity -

An identifiable finding on either the CC or MLO view was reported on 1,057 of the 1,200 evaluations (6 readers, 100 patients, 2 views). Among the 1,057 evaluations, the mean conspicuity of the one main feature was 5.2 (range: 1 to 10) on the 11-point Likert scale. The estimated probability that FCR*m* soft copy display was comparable to FCR*m* hard copy film was 0.946 (1,000 comparable views out of 1,057 evaluations) with a z-statistic of 5.109. The p-value was less than 0.0001.

Tissue Visibility At or Near the Skin Line

Among the 1,200 evaluations, the mean tissue visibility at or near skin line was 5.2 (range: 1 to 7). The estimated probability that FCR*m* soft copy display was comparable to FCR*m* hard copy film was 0.999 (1,199 comparable views out of 1,200 evaluations) with a z-statistic of 239.0. The p-value was less than 0.0001.

Tissue Visibility At or Near the Chest Wall

Among the 1,200 evaluations, the mean tissue visibility at or near chest wall was 5.9 (range: 2 to 6). The estimated probability that FCR*m* soft copy display was comparable to FCR*m* hard copy film was 1.0 (1,200 comparable views out of 1,200 evaluations). The z-statistic could not be calculated because all readers scored all views as having comparable image quality.

Study Conclusions

FCR*m* soft copy display and FCR*m* hard copy film have comparable image quality based on each of the three endpoints: feature conspicuity, tissue visibility at or near the skin line, and tissue visibility at or near the chest wall.

The results from Studies 1 and 2 provide a reasonable assurance of the safety and effectiveness of FCR*m* in screening and diagnosis of breast cancer.

Additional Literature Data

The performance of FFDM systems were compared to SFM in a fifty thousand patient multi-center trial; the Digital Mammography Imaging Screening Trial (DMIST)⁶. Five FFDM systems, including Fuji FCR*m* were studied. Study results showed similar accuracy of FFDM and SFM systems in detecting breast cancer for the general population of women in the trial. Also, the performance of FFDM did not vary significantly from film mammography according to race, the risk of breast cancer, or the type of machine used. The performance of FFDM was significantly better than film mammography among women under the age of 50 years, with dense breasts, or women who are pre- or perimenopausal.

CONFORMANCE TO STANDARDS

The Fuji Computed Radiography Mammography Suite conforms to the following voluntary standards:

- ISO13485:2003 Medical devices - Quality management systems - Requirements for regulatory purposes
- ISO14971:2000 Medical devices - Application of risk management to medical devices
- DICOM (Digital Imaging and Communication in Medicine)

FCR m image readers contain a laser and conform to the applicable requirements of the United States Radiation for Health and Safety Act of 1968 found in 21 CFR Subchapter J, Part 1040, Performance Standards for Light-Emitting Products.

The CR console current conformance to the evolving Digital Imaging and Communications in Medicine (DICOM) Standard is detailed on the Fujifilm Medical Systems U.S.A., Inc. Internet site <http://www.fujimed.com>.

TRAINING PROGRAM

MQSA regulations require interpreting physicians to complete at least eight hours of modality-specific training before independently interpreting mammograms from FCR m . Similarly, radiologic technologists must complete at least eight hours of modality-specific training before performing mammographic examinations using FCR m . For FCR m , Fuji's training program addresses both of these MQSA personnel requirements for training in a new modality.

Under MQSA, the physicist must receive at least 8 hours of training in surveying units of the new mammographic modality before performing surveys independently.

OPERATION MANUAL / DIRECTIONS FOR USE

Users should refer to the operation manuals and user guides for directions on how to use the FCR m and associated devices.

PRODUCT COMPLAINTS

Health care professionals who have complaints or have experienced dissatisfaction in the identity, quality, durability, reliability, safety, effectiveness, or performance of this device should notify Fuji. Facilities using this device must report deaths and serious injuries to which this device has or may have caused or contributed should notify Fujifilm Medical Systems, USA, Inc. immediately by telephone (203-324-2000), fax (203-353-0926), or written correspondence (Fujifilm Medical Systems USA, Inc. 419 West Avenue, Stamford, CT 06902)

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