

# Summary of Safety and Effectiveness Data

## I. General Information

<b><u>Device Generic Name</u></b>	Digital Mammographic X-ray System
<b><u>Device Trade Name</u></b>	SenoScan <sup>®</sup> Full Field Digital Mammography System
<b><u>Applicant's Name and Address</u></b>	Fischer Imaging Corporation 12300 North Grant St. Denver, CO 80026
<b><u>PMA Number:</u></b>	P010017
<b><u>Date of Good Manufacturing Practices Inspection:</u></b>	September 20, 2001
<b><u>Date of Notice of Approval to the Applicant:</u></b>	September 25, 2001

## II. Indications for use

The SenoScan<sup>®</sup> Full-Field Digital Mammography System is a dedicated mammography system intended to produce radiographic images of the human breast for the purpose of diagnostic and screening mammography. The SenoScan<sup>®</sup> Full-Field Digital Mammography system is intended to be used in the same clinical applications as traditional film-based mammographic systems.

## III. Device Description

The SenoScan<sup>®</sup> Full-Field Digital Mammography System (SenoScan<sup>®</sup>) includes a digital image receptor combined with a conventional mammographic X-ray device except for the collimator. The system consists of a dual filament x-ray tube, slit-collimator, x-ray generator, support arm, support assembly, compression device and CCD digital detector with readout equipment. The arm assembly consists of an X-ray tube on one end and a digital detector on the other end. The entire arm assembly pivots at the focal spot of the x-ray tube as the detector scans from left to right. The slit-collimator shapes the beam and limits the x-ray beam to the 1-cm active width of the detector. This results in images with very little scatter and no dose penalty associated with absorption of primary radiation by a grid.

The detector consists of an array of 4 charge-coupled devices (CCD). The CCDs have a sensitive element matrix of 405 x 2048 pixels. A cesium iodide (CsI) scintillator doped with thallium is chosen for its high detective quantum efficiency and its rapid decay time (less than 3  $\mu$ s). The overall detector size is approximately 1 cm x 22 cm. It is scanned over 30 cm, resulting in a 22 cm x 30-cm image.

The SenoScan<sup>®</sup> also includes an Acquisition Station and Review Station directly connected via Ethernet or Fiber Distributed Data Interface (FDDI). The Acquisition Station resides at the gantry for the purpose of image acquisition and quality control. Once accepted by the technologist, the image is sent to the Review Station. The softcopy image can then be reviewed on one or two 2K x 2.5K high-resolution monitors. The images are stored on a RAID array (redundant array of independent drives) which has a capacity from 45 gigabytes to 1.2 terabytes. Images can be printed on a laser printer using Dicom Print Services. Images can be archived either to a PACS using DICOM 3.0 or to a magneto-optical disk drive for long-term storage.

The following components are certified for use with SenoScan<sup>®</sup>. Certification is applicable when components are installed, calibrated, and serviced in accordance with all applicable instructions. Unauthorized modifications will invalidate certification.

- SenoScan<sup>®</sup> Gantry 94500G-2
- X-ray Tube 94518-2
- Collimator/Filter Assembly 947 LOM-2
- Detector 94767-1
- SenoScan<sup>®</sup> Generator 94100G-2
- HF/HV Transformer Assembly 94060M-2
- Inverter Assembly 94030M-2
- SenoScan<sup>®</sup> Acquisition Station 94830G-1
- SenoScan<sup>®</sup> Acquisition Station Computer 94502-1

The following laser film imaging systems have been qualified for use with SenoScan<sup>®</sup>. These hard copy film printers have been tested and found to be fully compatible with the SenoScan<sup>®</sup> system when installed, maintained, and operated in accordance with the manufacturer's instructions.

- Kodak Dry View 8610 Laser Imaging System/for Mammography
- Agfa Scopix LR 5200 Laser Imager

**Note:** Although a printer is listed as an option, facilities must have the ability to transfer usable images to other facilities and to patients. At this time, the indicated laser imagers are the only devices qualified for this task.

#### **IV. Contraindications**

None known.

#### **V. Warnings and Precautions**

- This equipment is not suitable for use in the presence of a flammable anesthetic mixture with air or oxygen or nitrous oxide.
- Operators should remain behind the provided lead-glass shielding during an x-ray exposure. To prevent exposure to x-ray, the operator must remain behind the technologist shield, in the zone of occupancy shown at the left, during the entire exposure.
- For U.S. only, until further direction is available from the FDA, the SenoScan<sup>®</sup> Full Field Digital Mammography System must only be used in MQSA screen-film accredited/certified facilities.
- The acquisition workstation should not be used for final interpretation of patient studies.
- For compatible Laser printers, see the Qualified Components listing in this section of the manual and the latest product data sheets. These sheets are available from your local sales representative.
- Operators should be trained to properly operate the user interface and review workstation. Only authorized trained personnel may operate this equipment. It is the responsibility of the site to ensure that proper operating techniques and procedures are followed when using mammographic x-ray equipment.
- Operators must ensure maximum radiological protection is provided to all persons present during x-ray operations. No unauthorized/unprotected person should be allowed in the room during x-ray operation.
- Quality control procedures must be followed to ensure continued high level of operation and be in compliance the MQSA regulations.
- Compression paddles must be carefully handled to prevent damage. Before use, compression paddles must be examined for the presence of cracks, sharp edges, roughness, and foreign matter, which may cause discomfort or injury to the patient. When not in use, compression paddles should be carefully stored in a manner that protects the paddles from damage.
- The provided on-screen ruler tool assumes that all measurements are made on a virtual surface located 2 cm above the breast support. Therefore, objects in the image which are above the virtual plane may be slightly larger than measured and those below the plane may be slightly smaller than measured.

- The 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), must not exceed 50 lux.
- This system contains no user serviceable parts. DO NOT remove any covers.
- Covers should be removed by qualified service personnel only. Installation and service should be performed only by qualified service personnel. Installation and Service manuals are available and should be consulted.
- Avoid touching the recording surface of any magnetic or optical storage media. Store recording media in approved manner and do not leave recording media exposed to any potentially harmful environments. Before usage, verify that there are no noticeable scratches or other imperfections that could potentially affect performance of the media.
- Unauthorized (third-party) software should not be added to the acquisition or review station computers. Addition of unauthorized software has the potential of affecting system performance or causing conflicts with system operation.
- DO NOT attempt to operate a system that has not been properly installed. The gantry, acquisition station/technologist shield, and generator must be properly anchored to the floor and all shielding and wiring must conform to the installation specifications.
- DO NOT use any accessories or other items not specifically intended for use with this x-ray system. Adverse effects may occur from foreign materials located in the x-ray beam.
- Before removing any component or assembly to be sent out for servicing:
  1. Determine if the component has been exposed to any body fluids. If so, wear proper personal protective equipment (gloves, gown, mask, goggles, etc.) when accomplishing steps 2 through 4.
  2. Clean and disinfect the component as described in the Cleaning and Disinfection section of this manual.
  3. Remove the component from the system and inspect any previously inaccessible surfaces for possible contamination. Clean and disinfect these surfaces as necessary
  4. Place the component in a standard Red Biohazard bag, bearing the proper biohazard symbols, and seal.
  5. Carefully package the component for shipping.

## **VI. Potential Adverse Effects of the Device on Health**

The following list of potential adverse events apply to mammography and are also applicable to digital mammography using the SenoScan<sup>®</sup>. No adverse events were observed during the clinical trials.

Excessive breast compression  
Excessive X-ray exposure  
Electric shock  
Infection  
Skin irritation, abrasion, or puncture wounds.

## **VII. Alternative Practices and Procedures**

There are several methods available for screening and diagnosing cancer in the breast. These include clinical breast examination, screen-film mammography, digital mammography, ultrasound examination and magnetic resonance imaging. After an abnormality is determined, a biopsy may be performed to diagnose the cancer.

## **VIII. Marketing History**

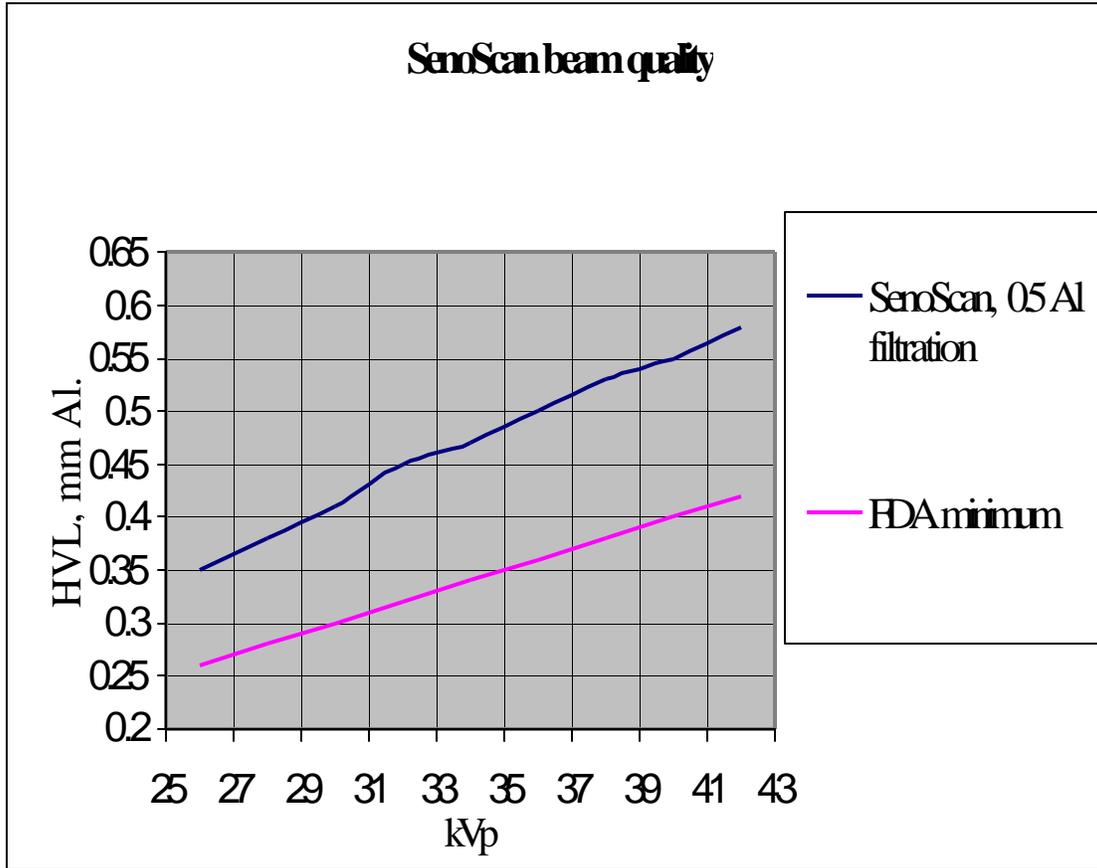
SenoScan<sup>®</sup> has only been used in clinical trials. SenoScan<sup>®</sup> has not yet been made available for commercial distribution anywhere in the world. The x-ray portion, excluding the collimator, has been used for film-screen mammography for many years.

## **IX. Summary of Nonclinical Studies**

The x-ray portion of the equipment is comparable to that found in traditional screen-film mammographic systems. A series of laboratory studies were undertaken to evaluate the SenoScan<sup>®</sup> physics performance with respect to the digital receptor and image display. The following characteristics were investigated: x-ray beam quality; detector sensitometric response, overall system resolution, signal-to-noise ratio, detective quantum efficiency, and radiation dose as mean glandular dose.

## X-ray Beam Quality

A typical measurement of the beam half-value layer (HVL) as a function of peak kilo-voltage (kVp) is presented in Figure 1. The SenoScan<sup>®</sup> beam quality exceeds the FDA minimum at all relevant values for kVp.

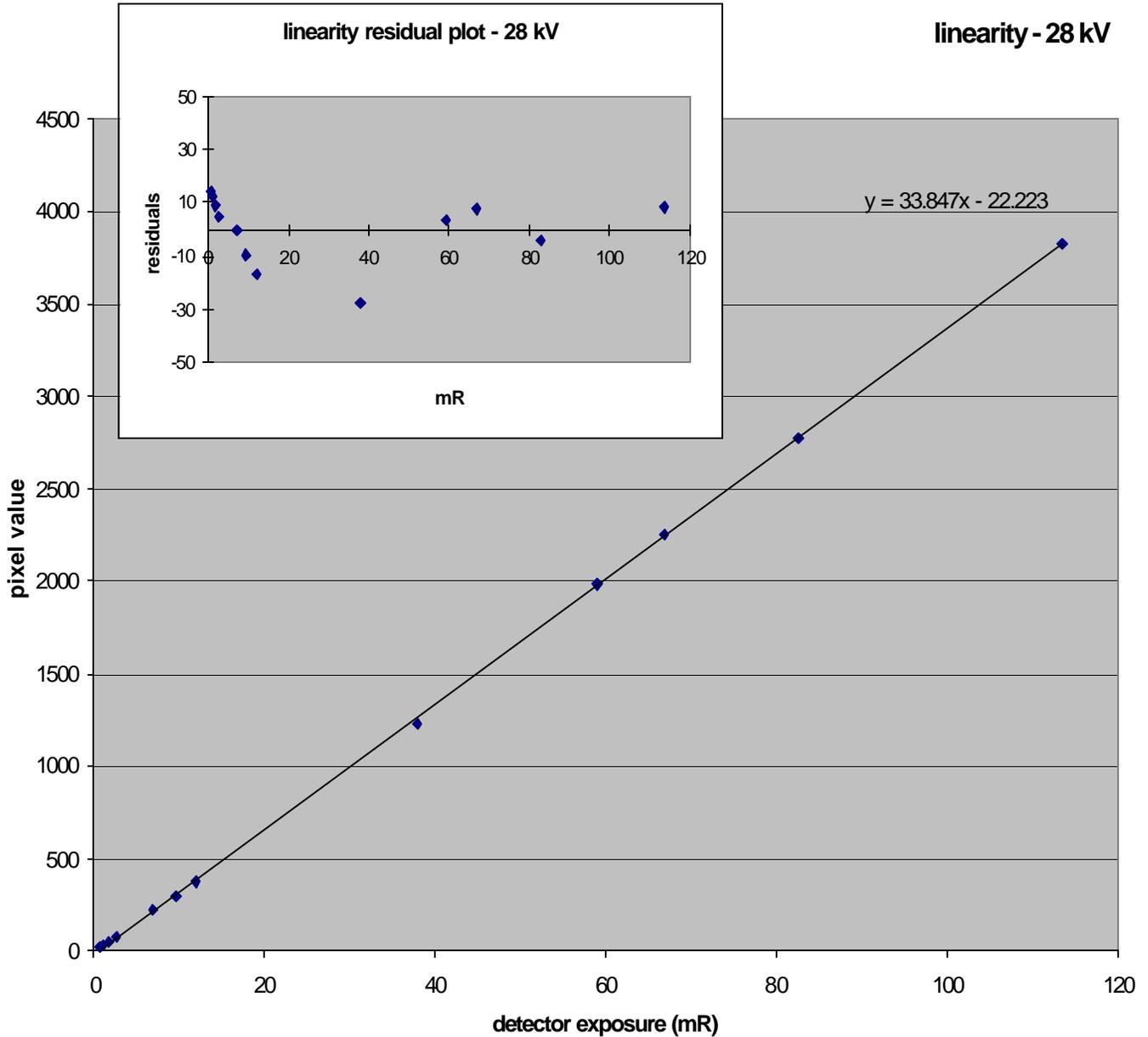


**Figure 1. SenoScan<sup>®</sup> incident x-ray beam quality as a function of kVp. (Half value layer, mm Aluminum, obtained with compression paddle in the beam)**

## Detector Sensitometric Response

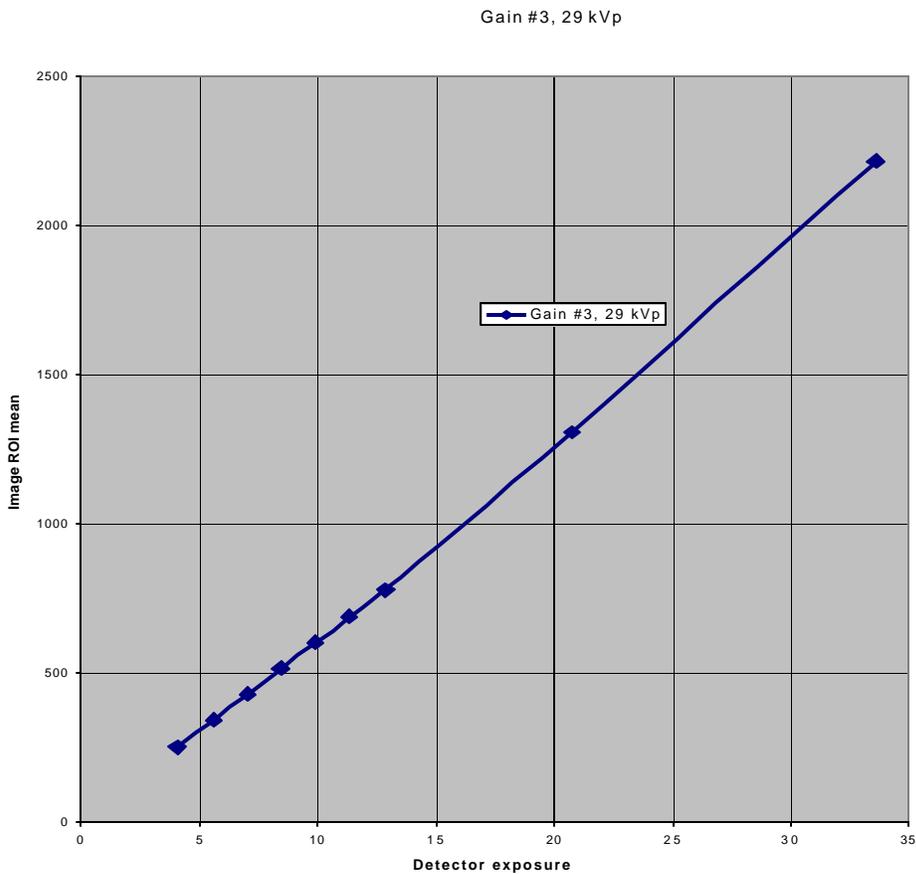
X-rays attenuated by the detector scintillator are converted into light energy. The CCD transforms the light energy into an electric charge. The electric charge forms an analog voltage that is then converted into digital values by the data acquisition system. That system offers a number of gain settings that provide various sensitometric responses (i.e. digital value vs. radiation exposure curve). Gain settings are selected for optimal imaging characteristics and allow for optimal exposure. The benefit of multiple gain settings can be seen particularly in the high-resolution mode of operation. Figure 2 shows a typical detector sensitometric response curve as a function of incident exposure, in the Standard mode. The curves demonstrate linear

response over the system practical dynamic ranges.



**Figure 2. Detector system sensitometric response in the Standard mode, 54-mm pixels, obtained after offset correction at 28 kVp, gain #1.**

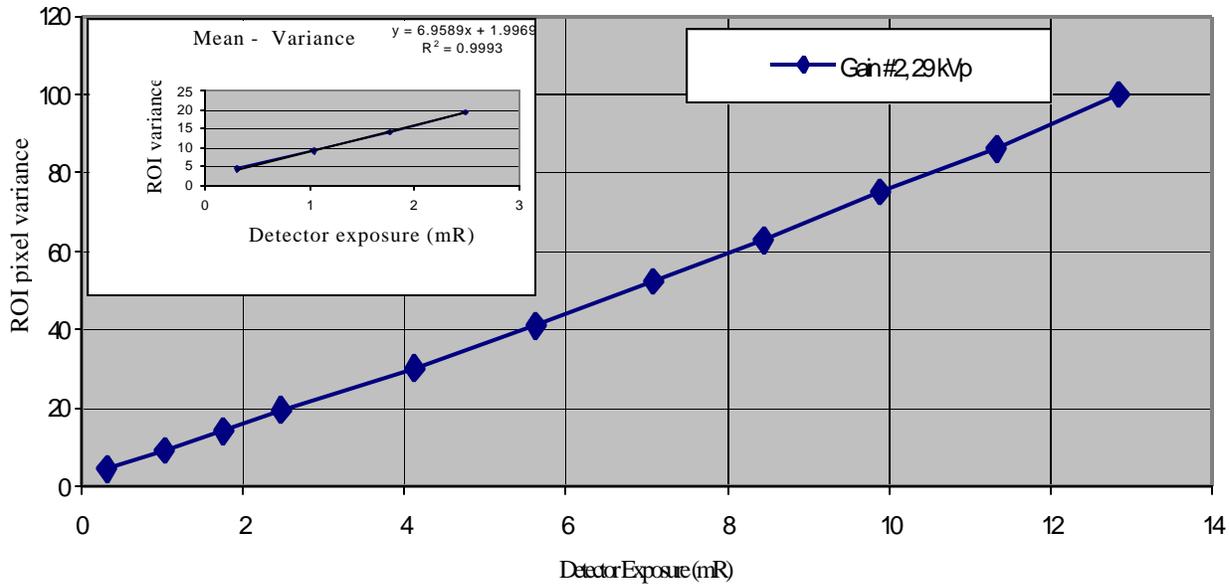
Figure 3 presents the sensitometric response associated with gain number 3. Higher gain in this mode makes more efficient use of the available quantum energy. In High-resolution mode, the pixel size is  $\frac{1}{4}$  of the available pixel area in the standard imaging mode.



**Figure 3. Detector system sensitometric response with gain number 3, obtained after offset correction, at 29 kVp. Gain 3 is used in high-resolution mode.**

Finally, Figure 4 presents an image noise-variance versus exposure plot for gain #2 at 29 kVp. The linearity of the graph demonstrates that the SenoScan<sup>®</sup> operates in a quantum-limited mode over a wide range of detector exposures, including exposures well below those expected in routine clinical imaging.

### Image variance as a function of exposure (gain2, 29 kVp)



**Figure 4. Image noise variance as a function of detector exposure, gain #2, 29 kVp**

#### Detective Quantum Efficiency

The detective quantum efficiency (DQE) provides a quantitative measure of the efficiency of SNR transfer of the image acquisition system. While the radiologist is the ultimate judge of diagnostic content of medical images, the detective quantum efficiency (DQE) is widely accepted as the most relevant figure of merit to quantitatively characterize the image quality of medical x-ray systems. Medical imaging system performance can often be evaluated in terms of detection performance characteristics. The DQE characterizes a detection system, and can be interpreted as the efficiency of such system in transmitting the information it receives. Specifically, the DQE can be described as the fraction of incident photons that would have to be detected without additional (detector) noise to yield the same signal-to-noise (SNR) ratio as is actually observed<sup>1</sup>. Therefore, it is a measure of detection performance (SNR) as a function of frequency that accounts for dose. The noise factor derived from the DQE,  $NF=1/(DQE)^{1/2}$  is the decrease in SNR that accompanies the detection process.

Accordingly, the DQE, defined as:

$$(SNR_{out}(v)/SNR_{in}(v))^2$$

- Includes combined effects of the modulation transfer function (MTF) and all relevant noise.
- Remains stable under spatial filtering that affects the MTF.
- Facilitates the comparison of different imaging systems.

The DQE as measured on an imaging system will always be less than the DQE of the detector alone. Indeed, the system measurement necessarily includes MTF reducing factors such as the finite focal spot aperture, off-focal radiation, and other components such as grids that reduce scattered radiation but require increased patient dose.

It should be noted that this evaluation was conducted using a complete imaging system. Readers should use caution in comparing DQE measurements. Other published DQE measurements may represent 'detector only' calculations. 'Detector only' calculations may not include important contributing factors to resolution or dose degradation. Further DQE exposure measurements obtained on a laboratory system demonstrate DQE as a function of exposure.

### Sensitometry and Mean-Variance

X-ray sensitometry was evaluated by performing a series of imaging exposures under a variety of conditions of kilovoltage (kV) and tube current settings. To extend the range of measurement, observations were also recorded with different thicknesses of polymethyl methacrylate (PMMA) attenuating slabs placed in the beam. The exposure time was fixed by the scanning time of the system. A region of interest is selected in the image and the mean image digital signal pixel value (referred to hereafter as P) is recorded as well as the variance of signal within the region. In addition, the tube current (mA) and the exposure in mR incident on the detector were recorded.

The variance of the digital signal is also plotted vs the mean value to assess the contribution to the image noise from quantum and nonquantum sources and to estimate the dynamic range.

### X-ray Spectrum

The purpose of this measurement is to estimate the shape of the spectrum so that the number of input quanta to the detector can be used in the calculation of DQE. A CdZnTe room temperature spectrometer, with a 100  $\mu$ m pinhole at its entrance, was located at a distance of approximately 20 cm from the detector and aligned with the central ray of the x-ray beam. Spectra were measured to estimate the shape of the spectrum. At least 500 counts were acquired at the peak of the spectrum.

Exposure was measured with a Keithley mammographic ionization chamber, corrected for temperature and pressure. The measured exposure was used to obtain an absolute calibration of the spectrum.

### MTF

Modulation transfer function was evaluated by imaging a slanted edge composed of a sheet of niobium foil with ground edges mounted on a larger sheet of aluminum. This was placed at a location 4 cm from the detector. This provided a moderate contrast transition. The slanted edge  $\sim$ 1:16, provided approximately 10x oversampling.

MTF was determined in both the direction along the slot detector and in the scanning direction at several kilovoltages. In addition, to assess possible hysteresis effects, MTF was measured in both the rising and falling directions of signal.

## NPS

The noise power spectra were measured from images of a uniformly attenuating PMMA phantom. After standard flat-fielding, the image is segmented into multiple sections, each of size 32x32 pixels. These are integrated in one dimension (x or y) to synthesize “slit” images. A standard, one-dimensional Fourier-transform based noise power spectrum is calculated in both x and y directions. The spectra from each region are then averaged to reduce the uncertainty in the final NPS. NPS data were acquired at four kilovoltages and at several intensity levels obtained by varying tube current (mA) and the thickness of PMMA attenuator in the x-ray beam.

## DQE

The spatial frequency dependent DQE was calculated from the x-ray spectrum, MTF and NPS using the definition:

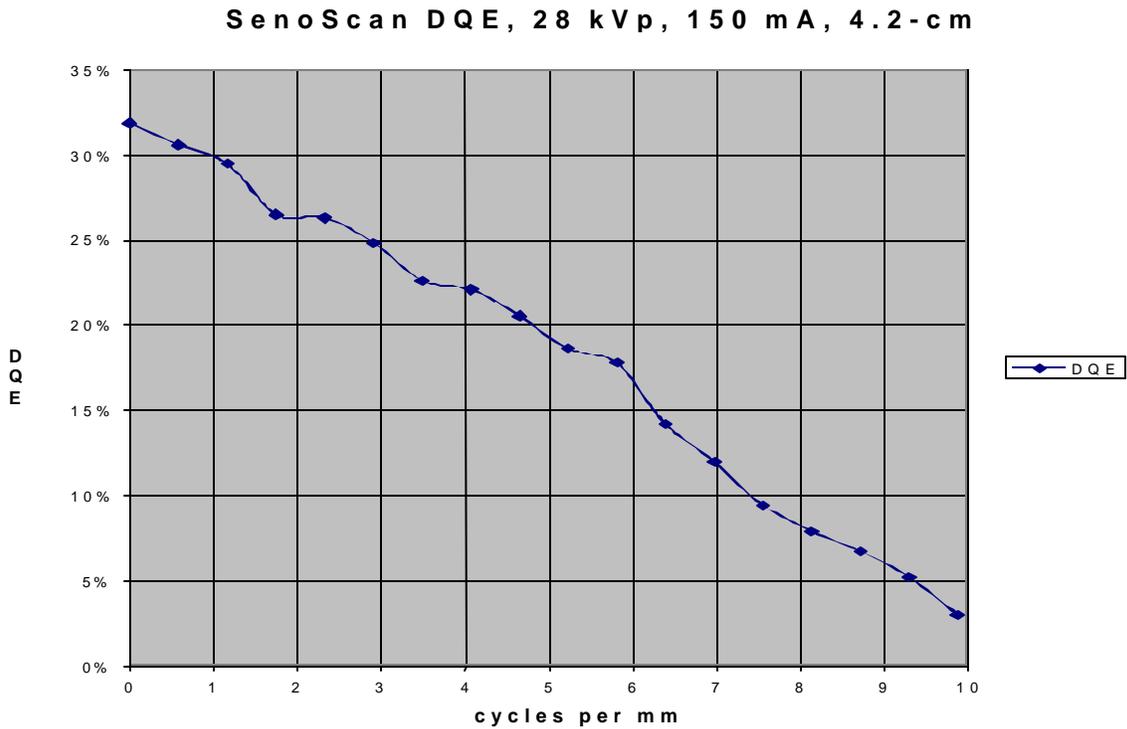
$$DQE(f) = \frac{P^2 \cdot MTF^2(f)}{(n/a) \cdot NPS(f)}$$

where a is the area of the detector element, and n is the number of x-ray quanta incident on the detector element. Therefore (n/a) is the entrance x-ray quantum fluence to the detector (obtained from the exposure and the spectral measurement).

DQE(0) was estimated by extrapolating the mean of the DQE values in the slot and scan directions from the two lowest frequency points measured.

## DQE Performance Characterization

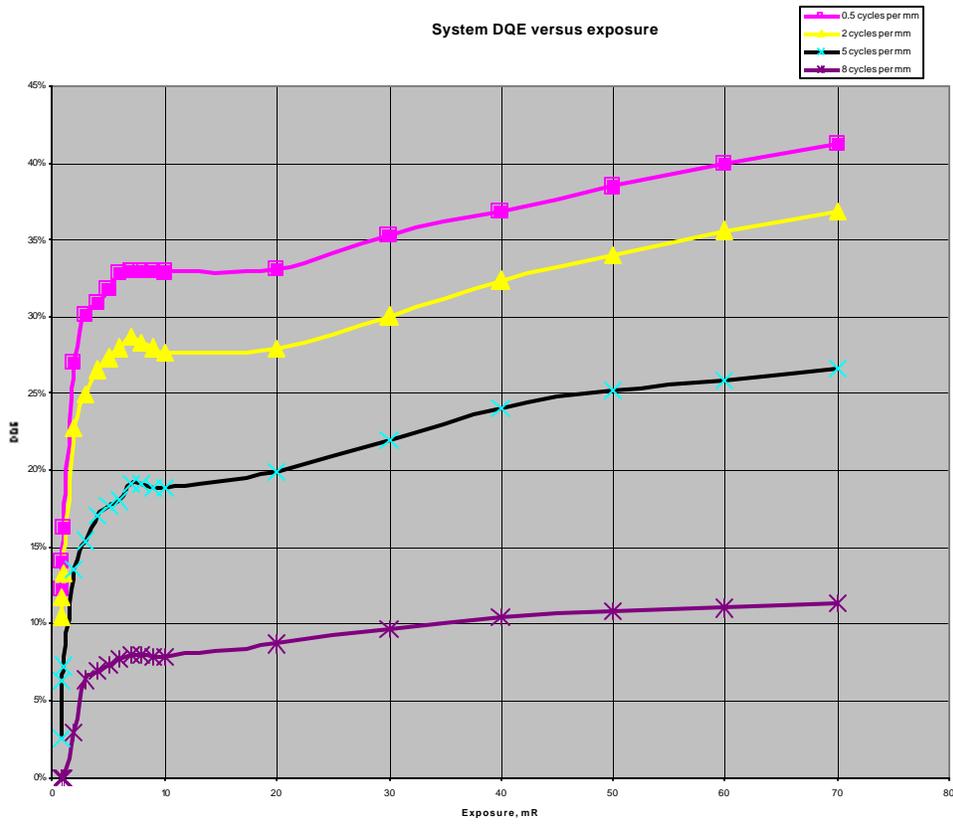
The smaller pixel size of the SenoScan<sup>®</sup> system extends the effective detection capability for this system well beyond a frequency of 5 cycles per mm. Measurable DQE between 5 and 10 cycles per mm means that SenoScan<sup>®</sup> is capable of distinguishing much smaller objects. Also, the SenoScan<sup>®</sup> system exhibited a zero spatial frequency DQE of 32% for 28 kVp. This is shown in Figure 5.



**Figure 5. SenoScan<sup>®</sup> DQE at 28 kVp, 150 mA, and 4.2 cm PMMA in the beam.**

These DQE data indicate clearly the detection efficiency achieved by a combination of slot scanning (and associated scatter rejection) and digital detector, over a range of frequencies that extend out through 10 LP/mm. The true system performance indicated by these measurements should translate into improved conspicuity of minute lesions requiring non-vanishing DQE at relatively high frequencies. Published DQE measurements are often “detector only”, that is do not include the effect of a scatter-rejection grid. Generally speaking, DQE measurements with a grid will be about 50% of those obtained without a grid, although the actual variation will depend on the amount of scattered radiation generated by the object being imaged and rejected by the grid. The SenoScan<sup>®</sup> System DQE measurement supports the claim that SenoScan<sup>®</sup> could significantly reduce dose in a patient population.

Figure 6 presents system SenoScan<sup>®</sup> DQE measurements as a function of detector exposure, for four different spatial frequencies.



**Figure 6. DQE data for the SenoScan<sup>®</sup> System as a function of exposure.**

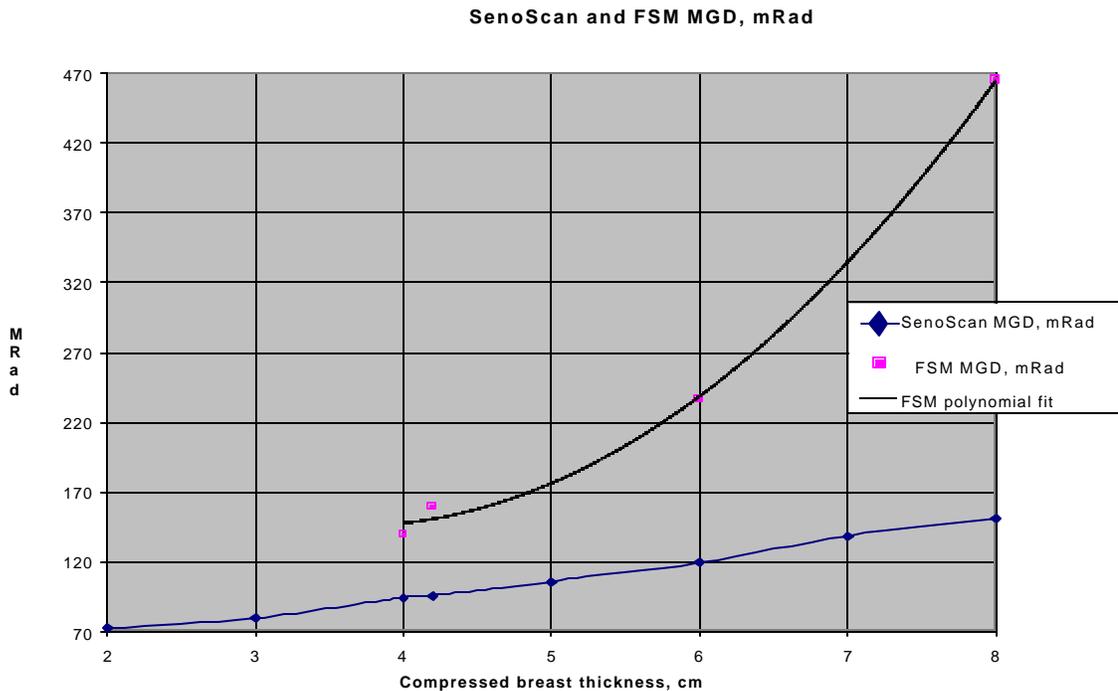
Patient Radiation Dose Studies

Table 1 shows the calculated mean glandular dose for the production SenoScan<sup>®</sup> system based on the technique chart for a 50/50 adipose/fibroglandular breast composition. The technique chart is derived by setting technique factors to achieve a constant ADU response. A constant ADU response assures that the exposure is adequate across a complete range of compressed thicknesses. The 4.2-cm SenoScan<sup>®</sup> dose was interpolated from the available data for direct comparison with the data given in Tesic et al.<sup>2</sup>, Suleiman et al.<sup>3</sup>, and Rothenberg<sup>4</sup>. Figure 7 presents the same information in a graphical form.

**Table 1. Mean glandular dose for the recommended exposure techniques for 50/50 breast composition.**

Breast thickness, cm	kVp	mA	<i>SenoScan</i> <sup>®</sup> MGD, mRad	FSM MGD, mRad	% decrease in dose
2	26	110	72		
3	27	140	80		
4	29	160	94	140	33
4.2			96	160	40
5	31	170	106		
6	33	180	119	237	50
7	35	200	139		
8	37	200	152	465	67

From Table 1, it is apparent that for the techniques recommended in the operator manual, the *SenoScan*<sup>®</sup> system provides dose savings that varies from 33% for a 4-cm compressed breast to more than 67% for an 8-cm compressed breast. At 4.2-cm, the dose savings is 40%.



**Figure 7. *SenoScan*<sup>®</sup> and Film-Screen mean glandular dose as a function of compressed breast thickness.**

The *SenoScan*<sup>®</sup> dose was also calculated from the *SenoScan*<sup>®</sup> technique chart provided with prototype systems used during the clinical trial. Table 2 presents the corresponding *SenoScan*<sup>®</sup> dose data.

**Table 2. SenoScan<sup>®</sup> dose as calculated from the technique chart used on clinical evaluation systems.**

Breast Thickness, cm	kVp	mA	<i>SenoScan<sup>®</sup> Dose, mRd</i>
2	26	160	105
3	29	170	128
4	31	190	142
4.2			144
5	33	200	151
6	35	200	163
7	38	200	184
8	40	190	183

The significantly reduced dose values for the production SenoScan<sup>®</sup> system as compared to the dose values of the prototype systems used in the clinical trials result from design changes that enabled imaging at lower techniques with a somewhat softer beam. Dose calculations and comparisons in Table 2 are based solely on the recommended technique chart, and do not necessarily imply equal image quality relative to film-screen mammography at large breast thicknesses. However, recent research on beam optimization in digital mammography indicates that dose-constrained image quality should not decrease significantly as the kVp is increased. Williams et al.<sup>5</sup> suggest that for digital mammography a figure of merit appropriate for beam optimization is related to SNR per unit radiation dose. Using SNR<sup>2</sup>/MGD as indicative of image quality constrained by dose, the authors find that the performance of all three referenced digital mammography systems (including SenoScan<sup>®</sup>) remains fairly flat as a function of kVp.

## **X. Summary of Clinical Studies**

Two reader studies were conducted using images acquired with the SenoScan<sup>®</sup> system. Study A compared reader performance of digital mammography exams printed on laser film with screen-film mammography for the same patient. Study B compared reader performance with softcopy diagnosis against hardcopy diagnosis (laser printed film) of digitally acquired mammograms.

### A. Study Comparing SenoScan<sup>®</sup> Full Field Digital Mammography to Screen-Film Mammography

Women were enrolled into the study at six clinical sites (Table 3). The clinical study was designed to determine the diagnostic accuracy of the SenoScan<sup>®</sup> system compared to standard screen-film mammography in a population of women presenting for screening and diagnostic mammography.

## 1. Study Inclusion / Exclusion Criteria

Only women who were medically eligible for screening or diagnostic mammographic examination were included in the clinical studies. Women who were unable or unwilling to understand or execute the patient consent form were excluded from the study.

Digital mammography case acquisition for this study was completed in three phases. The first phase involved the enrollment of women who had been recommended for breast biopsy, who had had abnormal screen-film mammograms, or who had symptoms which led to their referral for diagnostic mammography at 4 of the participating institutions. The second phase involved the enrollment of women who were scheduled to undergo breast biopsy, either percutaneous or open surgical biopsy, at 2 of the participating institutions. In the third phase, cases were drawn from the case files of two additional institutions. These mammograms were obtained on women who were not recruited to the SenoScan<sup>®</sup> approval trial per se, but to other clinical trials that had the same eligibility criteria as this study at 2 participating institutions. All of the women whose mammograms were included in Phase 3 of case acquisition had signed consent forms that allowed the use of their images in additional research, as needed. In total, case acquisition was driven by the desire to obtain a representative sample from both a screening and diagnostic population.

**Table 3. Institutions and the phase of case acquisition in which they participated**

<b>Institution</b>	<b>Phase(s)</b>
University of North Carolina	1 and 2
Sally Jobe Clinic	1 and 2
Brooke Army Hospital	1
Thomas Jefferson University	1
University of California at San Francisco	3
University of Toronto	3

## 2. Study Population

Case acquisition in the initial phase of the study was terminated when a total of 560 women were enrolled. Additional patients were enrolled in the next two phases of the study with the intent being to enroll subjects until a total of 100 biopsy-proven breast cancer cases were available for inclusion in the planned reader study.

All cases of patients with cancer were included in the reader study. Non-cancer cases were selected by taking a stratified random sample from the remaining cases. The stratification was by institution, so that cases would be included in proportion to the number of cancer cases recruited to the protocol at each institution.

There were 248 cases selected for inclusion in the reader study. All 248 cases consisted of both a unilateral or bilateral digital and screen-film mammograms of the same patient. The 248 cases included 125 cases with cancer.

As the study progressed, a subset of screen-film mammograms were removed either for patient care purposes or because the originating site requested their return so some readers did not read all screen-film mammograms that were initially selected for inclusion in the study. No digital cases were removed from the reader study once it began. No significant adverse events occurred during the film acquisition phase.

### 3. Cancer Size and Stage Distribution

The Agency for Healthcare Research and Quality (formerly the Agency for Health Care Policy and Research) Clinical Practice Guidelines, Number 13, AHCPR Publication Number 95-0632: Quality Determinants of Mammography suggests that a good mammography program should have at least 30% of detected cancers that are less than or equal to 1 cm in size. With 42% of cancers being equal to or less than 1cm in size, this study was well within the suggested guidelines. Some cancers were positively identified as cancer via fine-needle aspiration (FNA) and therefore no size information was available. The AHCPR guidelines suggest that 50% of detected cancers should be Stage 0 or 1. With 75% of cancers being stage 0 or 1, this study population fell well within this guideline.

**Table 4. Distribution of Cancer Stages Found in the Clinical Trial with SenoScan<sup>®</sup>**

<b>Size</b>	<b>Frequency Count</b>	<b>Percent</b>	<b>Cumulative Frequency</b>	<b>Cumulative Percent</b>
<b>Tis</b>	15	20.8	15	20.8
<b>T1</b>	11	15.3	26	36.1
<b>T1A</b>	4	5.6	30	41.7
<b>T1B</b>	11	15.3	41	56.9
<b>T1c</b>	13	18.1	54	75.0
<b>T2</b>	11	15.3	65	90.3
<b>T3</b>	4	5.6	69	95.8
<b>T4</b>	2	2.8	71	98.6
<b>TX</b>	1	1.4	72	100.0

### 4. Image interpretation

A total of 8 radiologists participated in this reader study. Of those, 6 had extensive experience in interpreting digital mammograms. The remaining 2 readers were trained in interpreting SenoScan<sup>®</sup> digital mammograms by reading 10 printed digital mammograms that were not part of this study, and receiving immediate instructive feedback regarding pathologically proven lesions present in the images. All readers also trained in the use of the forms used in the study just before interpreting examinations.

The 248 digital mammograms and the 248 screen-film mammograms were randomly assigned to one of two groups, A or B. Each group contained a mixture of digital and screen-film examinations. If the digital mammogram for a given patient were assigned to group A, then the screen-film mammogram for that same patient would be assigned group B. All readers read group A cases first. After a minimum of 4 weeks, group B cases were then read.

The study was designed to detect differences of 0.05 in the ROC area under the curve (AUC). The 95% confidence interval for the difference of the mean AUC's (digital and film) was determined by applying the approach described by Obuchowski in *Academic Radiology*, 1995, 2:S22-S29.

As noted by Lewin et al. In *Diagnostic Imaging 9/99*, area under the curve, sensitivity and specificity can be affected by using suspicion of cancer on the initial screen-film mammogram, as an enrollment criterion. Using recruitment criteria such as a BIRADS score of 3, 4, or 5 results in a bias towards higher sensitivity for screen-film mammography and a higher specificity for digital mammography. The amount of bias cannot be easily quantified.

The calculation of sensitivity and specificity was accomplished by defining a level of suspicion (LOS) 1-5 scale used to classify the likelihood of cancer in each case into two categories. The categories used were LOS 1 and 2 and LOS 3, 4 and 5. The scale is as follows:

- 1 – definitely not malignant
- 2 – probably not malignant
- 3 – possibly malignant
- 4 – probably malignant
- 5 – definitely malignant

The BIRADS standard scale for classifying was not used because of the confounding of likelihood of cancer with “abnormality”.

## 5. Results

There was no statistically significant difference in the average areas under the curve (AUC) for SenoScan<sup>®</sup> and screen-film mammography (Table 5). The standard error and size of the confidence interval confirmed that the study achieved the predicted power, based on the choice of number of readers and number of cases to be included. The true, but unknown mean difference between digital and film AUC included zero.

**Table 5. ROC Curve Comparison**

	<i>Area Under ROC Curve (AUC)</i>		
	<b>Digital</b>	<b>Film</b>	<i>95% CI for difference in AUC's</i>
<b>AVERAGE</b>	.715	.765	(-.101, .002)

The average specificity of SenoScan<sup>®</sup> is somewhat higher than the specificity of screen-film mammography (Table 6). Differences in sensitivity and specificity are consistent with selection bias as noted by Lewin et al.

**Table 6. Sensitivity and Specificity for Film and Digital Mammograms**

	Film	Digital
<b>Average</b>		
Sensitivity	0.74	0.66
Specificity	0.60	0.67

## 6. Study conclusions

The results of the study confirm that SenoScan<sup>®</sup> is safe and effective for use in screening and diagnostic mammography. Given that the confidence interval on the difference between areas under the curve includes zero, SenoScan<sup>®</sup> is comparable to screen-film mammography. No adverse events were observed.

### B. Study Comparing Reader Performance with Softcopy and Hardcopy Images

This study compared the speed and accuracy of interpretations by radiologists of SenoScan<sup>®</sup> digital mammograms displayed using two different media: 1) laser-printed on film and 2) a softcopy workstation.

#### 1. Study Inclusion / Exclusion Criteria for Mammograms

SenoScan<sup>®</sup> digital mammograms were selected from University of North Carolina case files. Digital mammograms were deemed suitable for inclusion in this study if 1) the patient had had at least one prior screen-film mammogram available for comparison between 10 and 65 months previously and 2) there were a total of four standard digital mammograms (two craniocaudal views and two mediolateral oblique views) that included all portions of both breasts. If more than one such eligible comparison mammogram existed, only the most recent comparison screen-film mammogram was used in the study. Otherwise suitable digital mammograms were excluded if they had been used in another digital mammography reader study that was occurring at the same time as this study, involving many of the same readers.

#### 2. Study Population

A total of 63 Fischer digital mammograms were identified for use in the study. These cases contained 7 biopsy-proven cancers and 13 biopsy-proven benign lesions. The remaining cases were of 23 patients who underwent six-month follow-up for probably benign findings and 20 cases without apparent findings. Of the 43 patients whose mammograms were included in the study who did not undergo biopsy, 42 had normal follow-up mammograms at one year after their study digital mammogram. The remaining patient had an unchanged mammogram at six months after her study digital mammogram.

#### 3. Demographics

The racial profile for these patients was 51 (81%) white, 9 (14%) African American, 1 (2%) Hispanic, 1 (2%) Asian, 1 (2%) unknown. The age breakdown of patients included in this study was 17 (26.9%) women ages 40-49 years, 23 (36.5%) women ages 50-59 years, 16 (25.4%)

women ages 60-69 years, 3 (4.8%) women ages 70-79 years, 1 (1.6%) woman ages 80-89 years, and 3 (4.8%) women of undetermined age.

#### 4. Image Interpretation

All readers were radiologists trained specifically in the tasks of the study, both printed film and softcopy digital mammography interpretation. Each reader was asked to provide his or her “hanging” preference so that the printed and softcopy images could be displayed in the order and site preferred by the reader.

A total of 8 other radiologist readers participated in the reader study. Seven of the 8 readers had been trained in the interpretation of digital mammography through participation in prior reader studies at the University of North Carolina. The eighth reader was trained in digital mammography interpretation using the 10 SenoScan® digital mammogram cases included in the set of 28 printed digital mammograms with pathologically proven lesions used to train the other readers prior to their participation in the other study. All participating readers are considered eligible for screen-film mammography interpretation under Food and Drug Administration MQSA regulations.

The 63 cases were divided into two sets of cases, set A and set B, for each of the two modalities, softcopy display and printed film, so that there were 4 sets of cases altogether (softcopy A, printed A, softcopy B, printed B). Four readers read all 63 cases in softcopy first, two readers starting with the cases in softcopy A, two readers starting with softcopy B. Similarly, the remaining four readers read all 63 cases on printed film first, two readers beginning with printed A, two readers beginning with printed B.

At least one month passed before each of the two groups of four readers read the cases in the other display condition. Again, half the readers were randomly assigned to begin with the cases in set A first. The other half began with set B. This counterbalancing of case display was intended to mitigate the effects of learning and fatigue.

#### 5. Results

No statistically significant difference in speed or accuracy of detection was noted. The following table shows the mean value and 95% confidence intervals.

**Table 7. Summary Results for Digital Mammograms in Hardcopy and Softcopy**

	Film	Softcopy	Difference	Bonferroni Corrected 95% Confidence Intervals	P Value
AUC	0.673	0.647	0.026	-0.060 - 0.112	0.393
Sensitivity	0.708	0.687	0.021	-0.111 - 0.153	0.598
Specificity	0.528	0.563	-0.035	-0.243 - 0.172	0.572
Time	1.607	1.532	0.076	-0.058 - 0.209	0.088

## 6. Study conclusions

The results of this study demonstrated the equivalence of softcopy and film interpretation of digital mammograms. The data suggest that viewing times for film and softcopy mammograms are comparable. Less certainty surrounds the diagnostic accuracy estimates because of the small sample size, although the data exclude very large differences.

## **XI. Conclusions Drawn from Nonclinical and Clinical Studies**

The results of the clinical and nonclinical studies conducted by the sponsor and described above provide a reasonable assurance of the safety and effectiveness of the SenoScan<sup>®</sup> Full Field Digital Mammography System for screening and diagnostic mammography. These findings therefore support FDA approval of the Fischer SenoScan<sup>®</sup> Full Field Digital Mammography System for clinical use in screening and diagnostic mammography.

## **XII. Panel Recommendation**

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Radiological Devices Advisory Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

## **XIII. FDA Decision**

The applicant's manufacturing facility was inspected on September 20, 2001 and was found to be in compliance with the Quality Systems Regulations. FDA issued an approval order on September 25, 2001.

## **XIV. Approval Specifications**

Directions for use: See the attached labeling.

Hazards to Health from Use of the Device: See Contraindications, Warnings, Precautions and Adverse Reactions in the attached labeling.

Post-Approval Requirements and Restrictions: See approval order.

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## References

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- <sup>3</sup> O.H. Suleiman, D.C. Spelic, J.L McCrohan, G.R. Symonds, F Hond, "Mammography in the 1990s: the United States and Canada," *Radiology* 1999, 210:345-5 1.
- <sup>4</sup> L.N. Rothenberg, "Exposures and Doses in Mammography," in *Categorical Course in Diagnostic Radiology Physics: Physical Aspects of Breast Imaging — Current and Future Considerations*, A.G. Haus and M.J. Yaffe, Eds. RSNA 1999, pp. 91-7.
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