

Reclassification of Full-Field Digital Mammography Systems:

Background and Motivation

Robert Phillips

Chief, Radiological Devices Branch, ODE

Radiological Devices Panel Meeting

May 23, 2006

Reclassification process

- Either Agency or publicly initiated
- Requires justification and development of “special controls” (guidance)
- Concept and proposal presented to advisory panel for recommendation
- Proposal and draft guidance made available for public comment (published in Federal Register)
- Final action and guidance (published in Federal Register). Device placed into either Class 1 or 2

Outline

- Background
- Current Situation
- Device History
- Device Premarket Application History
- Basis of Device Approvals
- Equipment Problems
- What has changed?
- Process

Background

- Film/screen (F/S) systems are analog in that they use a film/screen system to directly convert x-rays into an image on a piece of film
- Digital systems (FFDM) convert x-rays into a number that is part of an numerical image matrix. A computer then processes the matrix into an image that is either displayed on an imaging device or printed to a piece of film or paper.

Background (2)

- FFDM systems are intended as replacements for F/S Mammography systems
- Both are intended to “to generate mammographic images for screening and diagnosis of breast cancer”

Background (3)

- New devices, entering the market after May 28, 1976, are automatically Class 3 (need Premarket Application approval [PMA]) unless they can be shown to be substantially equivalent to a device marketed prior to May 28, 1976 or undergo a *de novo* process.

Current Situation

- F/S mammography systems are in Class 2. They secure marketing approval through the 510(k) (substantially equivalence) process
- FFDM, including computed, mammography systems are in Class 3. They secure marketing approval through the PMA process (demonstration of safety and effectiveness).

History

- From the 1980s: Development of FFDM systems
- 1996 – Panel meeting to discuss FFDM mammography approval process.
- Several 510(k) FFDM submissions, using ROC analysis, did not show “Substantial Equivalence”
- Thus, FFDM systems for screening and diagnosis needed to be approved under PMA process

History (2)

- To date, 4 FFDM devices have been approved using the PMA process
- The agency has published guidance for FFDM PMA submissions
- Digital Mammography Imaging Screening Trial (DMIST) completed

Approved FFDM Systems

- January 28, 2000: Senographe 2000D, General Electric Medical Systems
 - Detector: flat panel amorphous silicon with deposited cesium iodide
- September 25, 2001: SenoScan Full-Field Digital Mammography System, Fischer Imaging Corporation
 - Detector: array of 4 charge-coupled devices (CCDs) optically coupled to a cesium iodide (CsI) scintillator doped with thallium
- March 15, 2002: Lorad Digital Breast Imager, Hologic Inc.
 - Detector: array of 12 charge-coupled devices (CCDs) optically coupled to a thallium activated cesium iodide (CsI:TI) scintillator plate, later changed to amorphous selenium (a-Se)
- August 20, 2004: Siemens Mammomat Novation, Siemens Medical Solutions USA, Inc.
 - Detector: Hologic amorphous selenium (a-Se)

Basis for Device PMA Approvals

- Physical device description
- Physical performance data
 - Dynamic range and sensitometric response
 - Image Sharpness, Modulation Transfer Function (MTF)
 - Image noise vs. exposure, Noise Power Spectrum (NPS)
 - Detective Quantum Efficiency (DQE)
 - Patient radiation dose
 - Phantom scoring
- Clinical data
 - Reader performance analysis, i.e., sensitivity and specificity
 - Side-by-side mammographic feature analysis
 - Comparison to F/S systems

FFDM System Problems

- 4 recalls
 - all occurring between 2003-2005
- Reasons for recall:
 - Software truncated images
 - X-ray tube overheated
 - Lack of technical specifications for minimum filtration and maximum line current
 - Network node overload caused interruption in image acquisition

What has Changed?

- DMIST study results have been published
- Our understanding of FFDM technology has improved to the point that we can develop appropriate special controls so that we can assure adequate safety and effectiveness through the 510(k) process

Proposed Indications for Use

“to generate full-field digital mammographic images for screening and diagnosis of breast cancer”

Presentations

- Sophie Paquerault – DMIST study
- Robert Jennings – Risks to Health and Special Controls
- Panel Questions

Reclassification of Full-Field Digital Mammography Systems:

Digital Mammography Imaging Screening Trial

Sophie Paquerault

Office of Science Engineering Laboratories, and

Office of Device Evaluation

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Digital Mammography Imaging Screening Trial (DMIST)

- Funded by the National Cancer Institute through the American College of Radiology Imaging Network
- Principal investigator: Etta Pisano, M.D.
- Clinical trial comparing reader performance for FFDM and SFM in detection and characterization of breast cancer in the screening setting
- Sept. 2005: Outcome of the trial published in New England Journal of Medicine, “*Diagnostic Performance of Digital versus Film Mammography for Breast-Cancer Screening*”

Digital Mammography Imaging Screening Trial: Protocol

- Trial enrolled 49,528 asymptomatic women presenting for screening mammography at 33 clinical sites, a total of 335 diagnosed breast cancers
- All patients underwent both FFDM and SFM acquisition
- Readers' tasks:
 - Rated mammograms using a BIRADS scale, a seven-point scale
 - Provided a binary workup recommendation
 - Rated breast density according to BIRADS lexicon

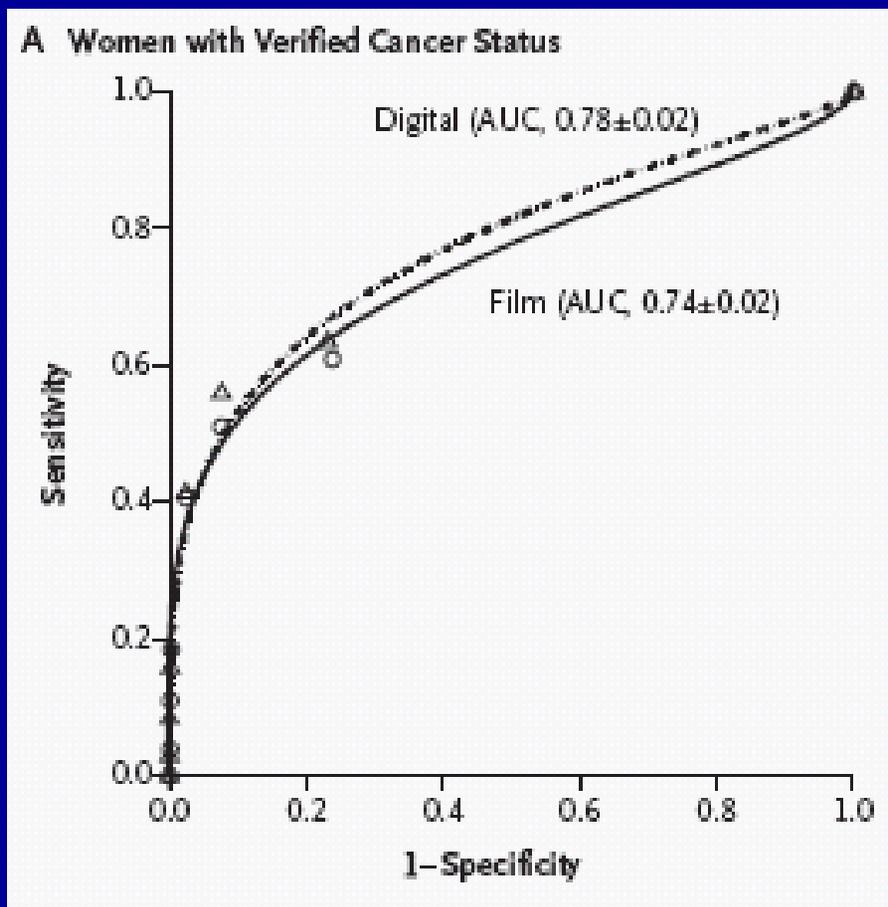
Digital Mammography Imaging Screening Trial: Protocol

- Five digital mammography systems:
 - Senoscan (Fischer Medical)
 - Computed Radiography System for Mammography (Fuji Medical)
 - Senographe 2000D (General Electric Medical Systems)
 - Digital Mammography System (Hologic)
 - Selenia Full-Field Digital Mammography System (Hologic)
- Trial not intended for individual comparison of these digital systems

Digital Mammography Imaging Screening Trial: **Analysis**

- Performance evaluation using the area under the Receiver Operating Characteristic (ROC) curve (AUC)
- Performance evaluation using sensitivity, specificity, positive predictive value

Digital Mammography Imaging Screening Trial: Results

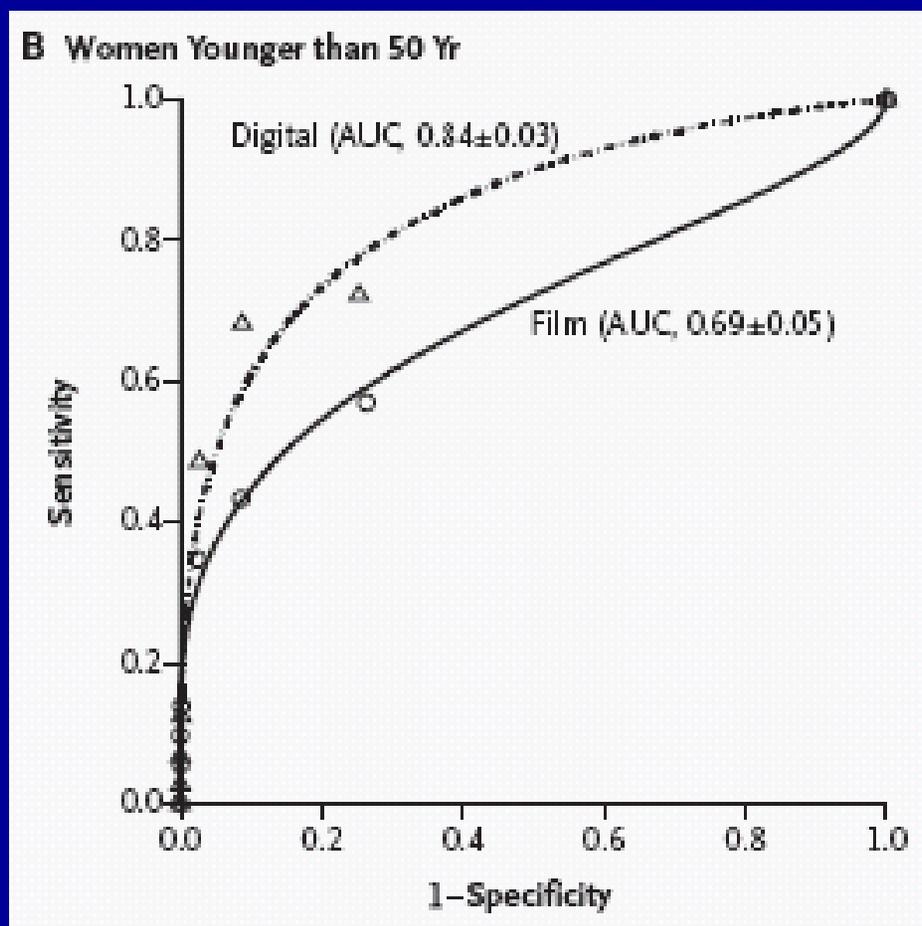


Δ AUC = 0.03 (95% CI 0.02-0.08)

P=0.18

42,760 Women with Fully Verified
Breast-Cancer Status

Digital Mammography Imaging Screening Trial: Results



Δ AUC = 0.15 (95% CI 0.05-0.25)

P=0.002

14,335 Women under the Age of
50 Years

Digital Mammography Imaging Screening Trial: **Summary**

- Overall, FFDM is similar to SFM
- FFDM is more accurate in women under the age of 50 years, women with dense breasts, and premenopausal or perimenopausal women
- Call-back rate of 8.4 percent for both FFDM and SFM is similar to, or lower, than those reported elsewhere for U.S. screening programs
- Neither digital nor screen-film mammography finds all cancers

Reclassification of Full-Field Digital Mammography Systems:

Risks to Health and Mitigation of Risks

Robert J. Jennings

Office of Science Engineering Laboratories,
Division of Imaging and Applied Mathematics

Radiological Devices Panel Meeting

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Outline

- Risks to Health
- Mitigation of Risks

Risks to Health

- Misdiagnosis
 - False negative
 - False positive
- Image retakes
 - Due to loss of data during acquisition or archiving
 - Due to incorrect positioning of the patient because of receptor/detector dimensions
- Excessive x-ray exposure
- Excessive breast compression
- Electrical shock
- Infection, skin irritation

Mitigation of Risks

- Special Controls
 - Guidance documents
 - Voluntary Standards
 - Other special controls
- Quality System Regulations (QSRs)

Guidance Documents

- Guidance for 510(k) submissions for FFDM systems is under development
- Guidance for FFDM accessories is also under development
- Guidance for software contained in medical devices is already available

Device 510(k) Clearance Guidance

- Physical device description
 - Similar requirements to those in the guidance for FFDM PMAs
- Physical performance data
 - Similar requirements to those in the existing PMA guidance document, with the following differences:
 - Performance compared to that of cleared devices
 - More relevant Automatic Exposure Control (AEC) system evaluation criteria will be developed
 - Phantom scoring will be more extensive
- Clinical data
 - Reader evaluation of clinical films, as in ACR accreditation

Physical Performance Data

Imaging Performance

- Sensitometry (dynamic range, linearity, temporal effects)
- Image sharpness, Modulation Transfer Function (MTF)
- Image noise vs. exposure, Noise Power Spectrum (NPS)
- Detective Quantum Efficiency (DQE) (vs. exposure and spatial frequency)

Physical Performance Data

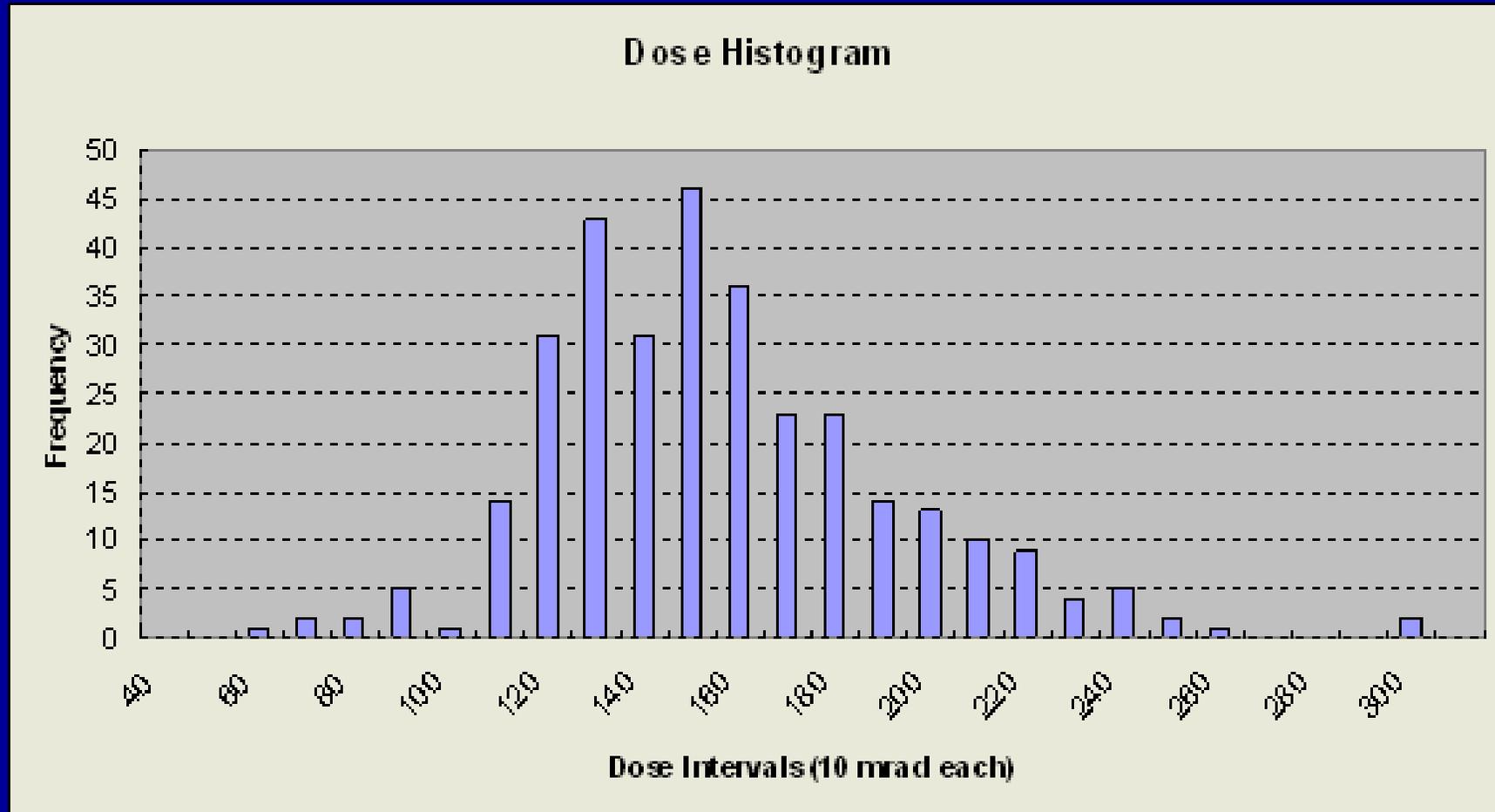
- Automatic Exposure Control (AEC)
 - Tracking of signal-to-noise ratio (SNR) and/or contrast-to-noise ratio (CNR) with breast thickness
 - Technique factor selection (kVp, mA, anode, filter), for all available AEC modes
 - Patient dose vs. breast thickness and AEC mode

Physical Performance Data

Patient Dose Data

- From June 2, 2000 to September 2, 2003, the agency certified 337 FFDM units.
- The average dose recorded for these FFDM units was about 15% lower than the average dose for film-screen units measured by government inspectors during the same period.

FFDM Patient Dose Data



Physical Performance Data Recommendations

- That sensitometry, MTF, NPS, and DQE be measured by methods supported by standards such as those developed by the IEC or by recommendations such as those of the AAPM.
- That AEC performance (patient dose as a function of breast thickness) conform to EUREF “acceptable” or equivalent.

Device 510(k) Clearance Guidance

- Clinical Data

- Sets of patient films will be evaluated by CDRH staff who are trained in the evaluation of clinical films for the ACR mammography accreditation program.
- While ACR requires only two sets of films, FDA will request that the sponsor submit several sets of films covering a range of patient characteristics and machine settings

Device 510(k) Clearance Guidance

- Clinical Data

Requirements for clinical image attributes:

1. Positioning
2. Compression
3. Exposure level*
4. Contrast*
5. Sharpness
6. Noise
7. Artifacts

* For softcopy, “Ability to obtain optimal contrast/exposure”

Voluntary Standards

- ACR/NEMA Generic FFDM QA Program
- Voluntary Standards (electrical, mechanical, electromagnetic,...)
- Voluntary Material Standards
- Voluntary Biocompatibility Standards

Other Special Controls

- Labeling, which should contain the following:
 - A detailed quality assurance program to assure that imaging performance and patient dose remain acceptable
 - Explicit summary including physical device description and physical performance data
 - Appropriate cleaning and disinfection procedure
 - Device labeling should recommend that each clinical facility maintain an adverse event log book
- Medical Device Reporting (MDR Database)

Quality System Regulations (QSRs)

- QSRs require that domestic and foreign manufacturers have a quality system for the design, manufacture, packaging, labeling, storage, installation, and servicing of finished medical devices intended for commercial distribution in the United States
- QSRs help assure that medical devices are safe and effective for their intended use
- QSRs provide for the monitoring of device problems and for inspections of the operations and records of device manufacturers

Reclassification of Full-Field Digital Mammography Systems:

Panel Questions

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Chief, Radiological Devices Branch, ODE

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Question 1: Risks to Health and Controls

Do you believe that the risks to health from the device have been identified and that the mitigations for these risks are appropriate?

If not, what additional risks to health are presented by the device? What mitigations for these risks would provide a reasonable assurance of safety and effectiveness?

Question 2: Data requirements

Do you believe that the information to be required for 510(k) clearance will be sufficient for determining substantial equivalence between a new device and the predicates?

Question 3: Reclassification

Do you believe the materials presented support reclassification of FFDM devices?

Question 4: Labeling

If reclassified, are there any concerns that you believe need to be addressed in the labeling (includes direction for use, indications, and contraindications) of these devices?