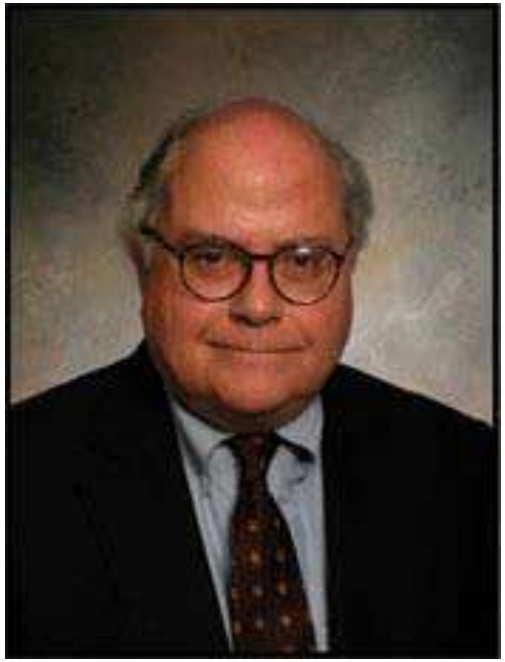
AAPM Special Symposium in Honor of Charles E. Metz

"Past, Present and Future Roles of ROC Analysis in Medical Imaging and Quantitative Image Analysis"

Kyle J. Myers
Division of Imaging and Applied Mathematics
CDRH/FDA

August 2013

Charles E. Metz: The Story of a Decades-long Relationship with the FDA



Charles E. Metz

Robert F. Wagner and David G. Brown

1981 Coded aperture paper

Reprinted from SPIE Vol. 314—Conference on Digital Radiography

On the multiplex advantage of coded source/aperture photon imaging

Robert F. Wagner, David G. Brown
Division of Electronic Products, Bureau of Radiological Health, Rockville, Maryland 20857
Charles E. Metz
Department of Radiology, University of Chicago, Chicago, Illinois 60637

Question: which gamma-ray aperture is best?

Image of point source is scaled, shifted version of aperture

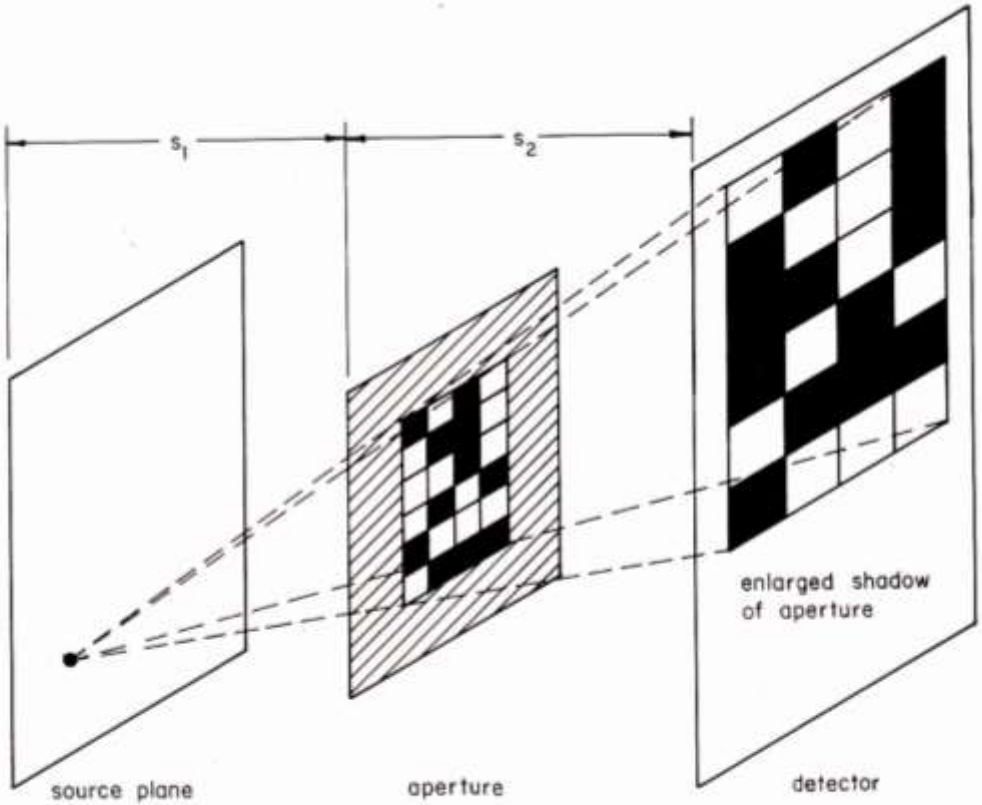


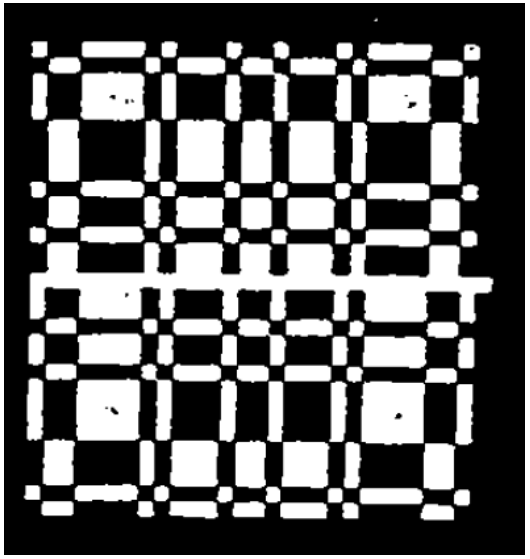
Fig. 8.3 Modification of Fig. 8.2 when the source point is not at infinity. The shadow magnification m_s can be used to determine the distance s_1 to the source plane since $m_s = (s_1 + s_2)/s_1$.

For ANY aperture:

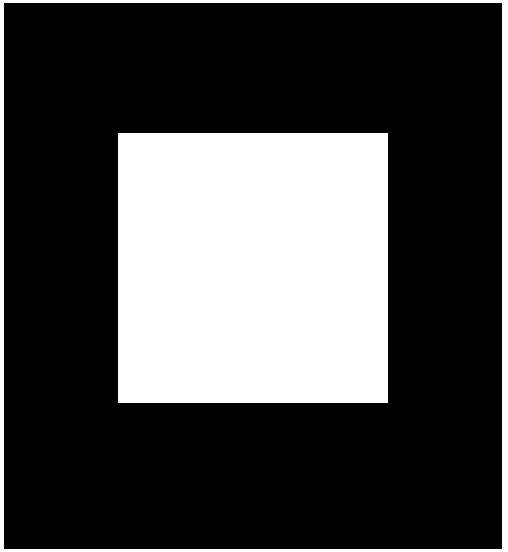
image of general object ("collection of point sources") is convolution with aperture

Film image (dark=exposed)

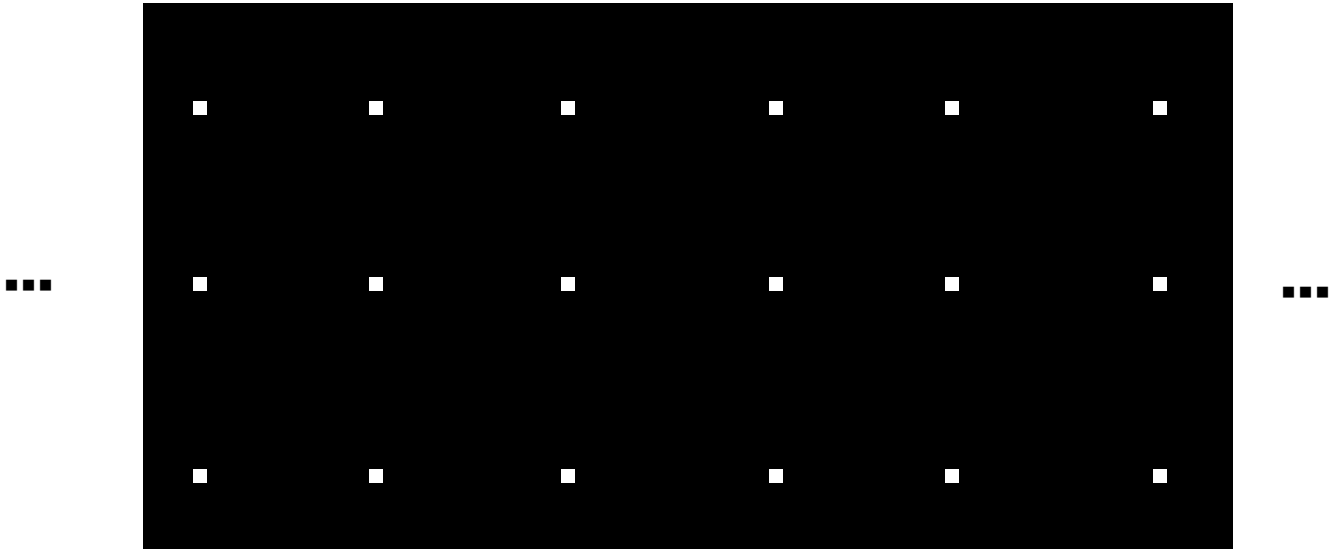
Barrett and Swindell, Academic Press,1981



URA = Uniformly Redundant Array

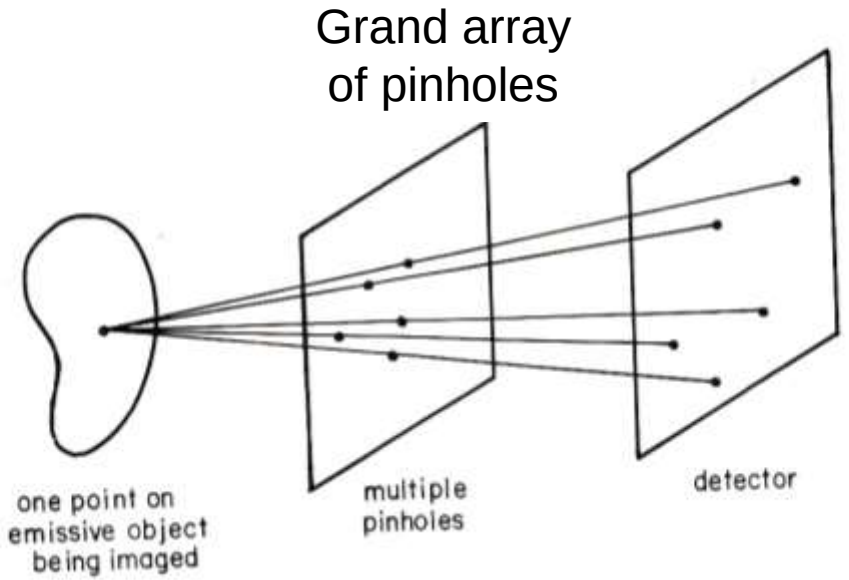


Square



Grand Array of Pinhole Apertures

Grand array gives set N of nonoverlapping images



Pinholes spaced far enough apart to ensure images of object don't overlap.

Barrett and Swindell, Academic Press,1981

Signal detection theory

There is a class of imaging applications for which an exact solution exists for the question of which aperture to use to collect photons via signal detection theory

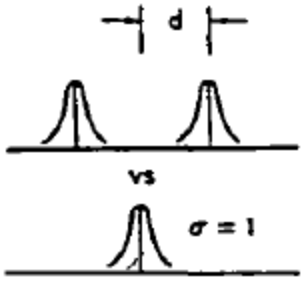
-- detection/discrimination tasks
-- observer is given raw, undecoded data (no display)
-- accounting for Poisson noise
-- optimal decision variable is the likelihood ratio

TASK SNR = ability of ideal observer to <u>discriminate:</u>

images of double Gaussian objects (class “a”)

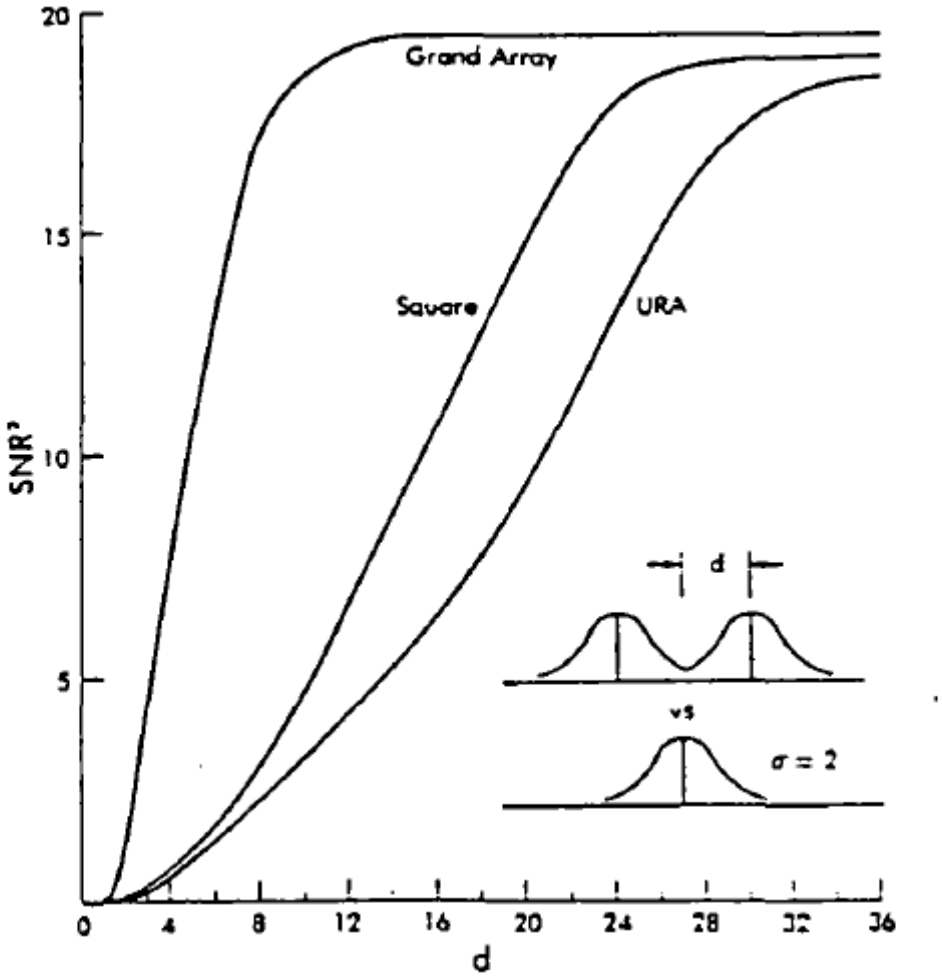
from

images of single Gaussian objects (class “b”)



$$SNR^2 = \frac{\left[\sum_{ij} (a_{ij} - b_{ij}) \ln\left(\frac{a_{ij}}{b_{ij}}\right)\right]^2}{\frac{1}{2}\sum_{ij} (a_{ij} + b_{ij})\left[\ln\left(\frac{a_{ij}}{b_{ij}}\right)\right]^2}$$

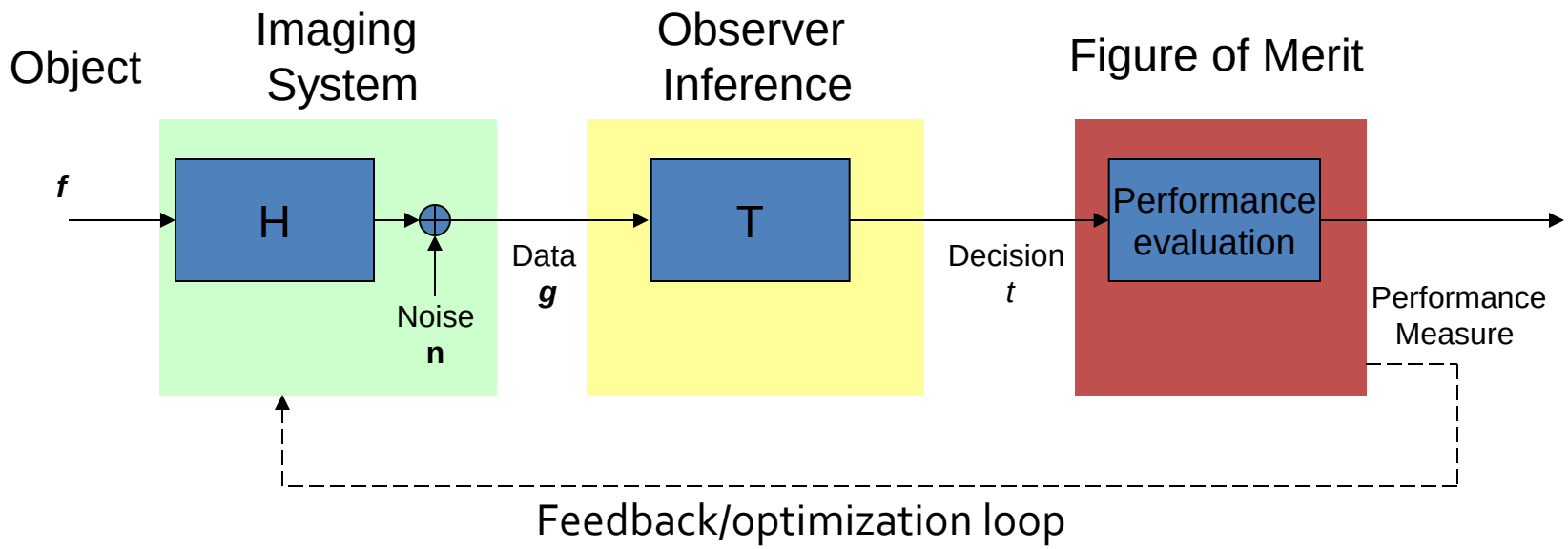
Example results



Square outperforms URA for this SKE/BKE task!

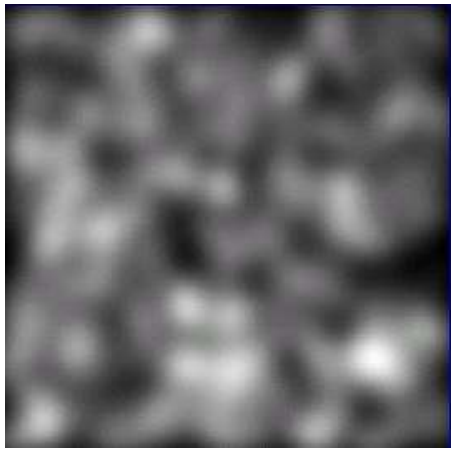
MANY important lessons learned, follow-on studies and changes to assessment culture

- Aperture OPTIMIZATION for task would find a <u>different</u> Coded Aperture that beats the Great Gaping Hole

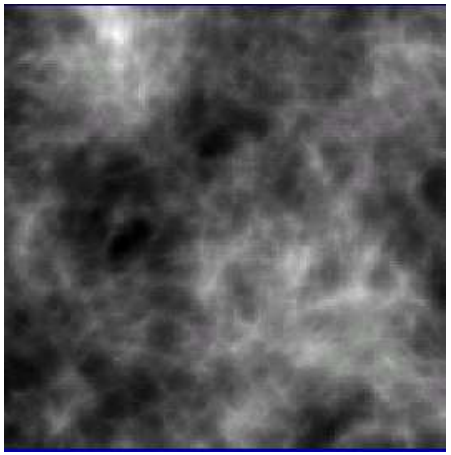


MANY important follow-on studies and changes to assessment culture – cont'd

- Comparison of SKE tasks to those with randomness in signal or background
  - Randomness in signal parameters (location)
  - Structured backgrounds (lumpy BGs)



Lumpy Background



Clustered Lumpy Background

State of the Art: AAPM TG234

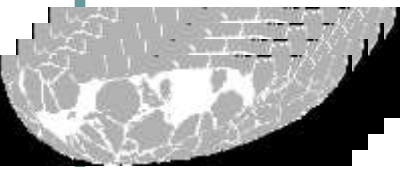
- Virtual Clinical Trials in 3D X-ray Breast Imaging
  - Special Session on Monday morning

- Predrag R. Bakic, U. of Pennsylvania:
  Real Time Simulation of Breast Anatomy
- Ingrid Reiser, U. of Chicago:
  Simulation of Small Scale Breast Tissue Structures for X-ray Imaging
- Nooshin Kiarashi, Duke U.:
  Generation of X-ray Relevant Software Breast Phantoms from Clinical Datasets
- Rongping Zeng, FDA:
  Task Based Assessment of X-Ray Breast Imaging Systems using In Silico Modeling Tools

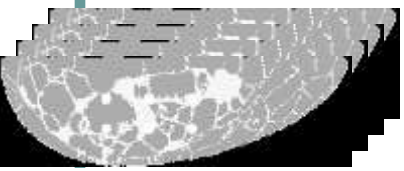
DBT virtual imaging chain (Zeng, AAPM'13)

- Simulated DBT image chain

Object



Lesion-absent (40)

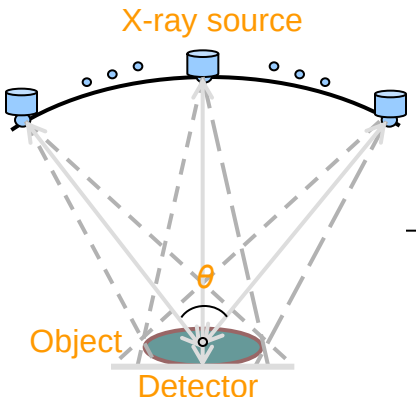


Lesion-present (40)

Numerical breast phantom*:
500 μm, cupsize B, 25% glandular density,
6 mm lesions (6 in each LP phantom)

*BakicEtAl-MedPhys2011-v38(6)

DBT data acquisition



Point and mono-energetic x-ray source; detector pixel size 500 μm; Separable footprints forward projector**; Poisson noise model, fixed total exposure.

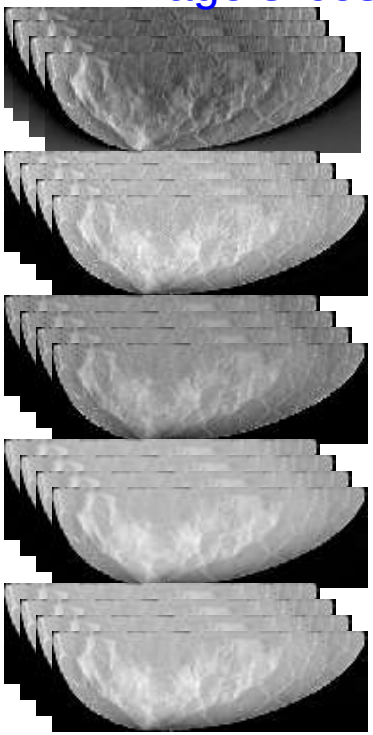
**Long&FesslerEtAl-IEEE-TMI2010-v29p1839

Reconstruction

- FBP
- SART
- ML
- TV-LS-mild
- TV-LS-strong

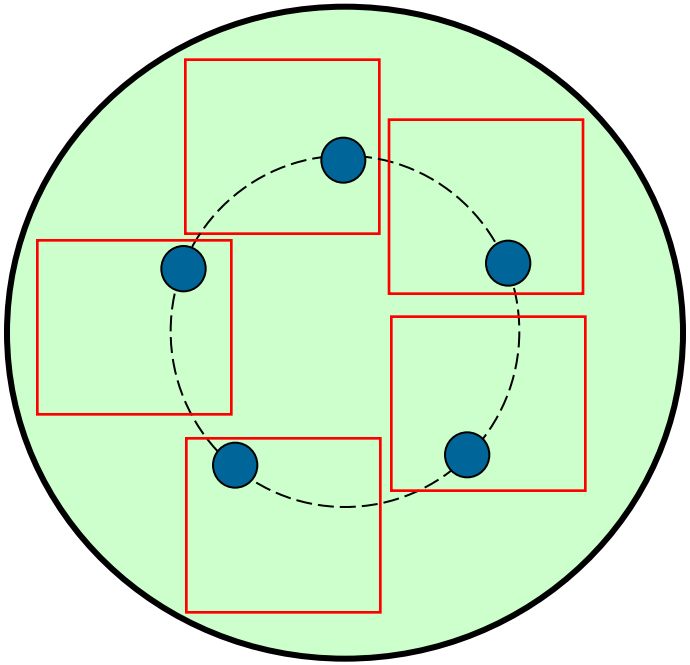
Step size was tuned to obtain relatively fast convergence; Number of iterations was decided to have optimal lesion detectability in a small ensemble of breast phantoms.

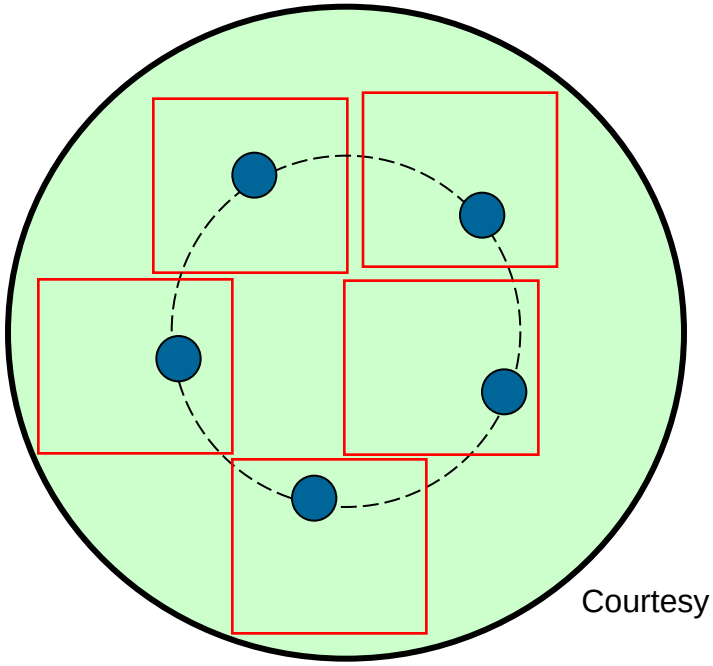
DBT image slices



Recon. Voxel size: 500 μm in-plane, 2 mm slice interval

Need for new phantom designs for OAIQ* studies





Courtesy L. Popescu

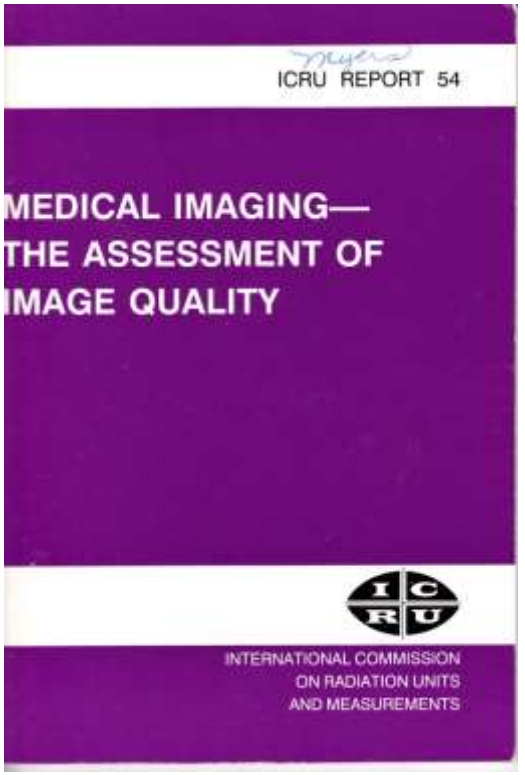
- Objects at same radial location with randomly placed ROIs
  ➔ search task
- Uncertainty in signal location (or size, shape) allows for more "dynamic range" in task SNRs available for a given image set

*Objective Assessment of Image Quality

ICRU report

Peter Sharp, Chris Taylor, David Barber, Charles Metz, Kyle Myers

Ideal observer
Task SNR and
Imaging Chain!



In Brief: ATL High Definition Imaging breast ultrasound

By The Gray Sheet / *Dec. 4, 1995*
News in Brief / Word Count: 54 / Article # 01210490033 / Posted: December 4 1995 5:00 AM

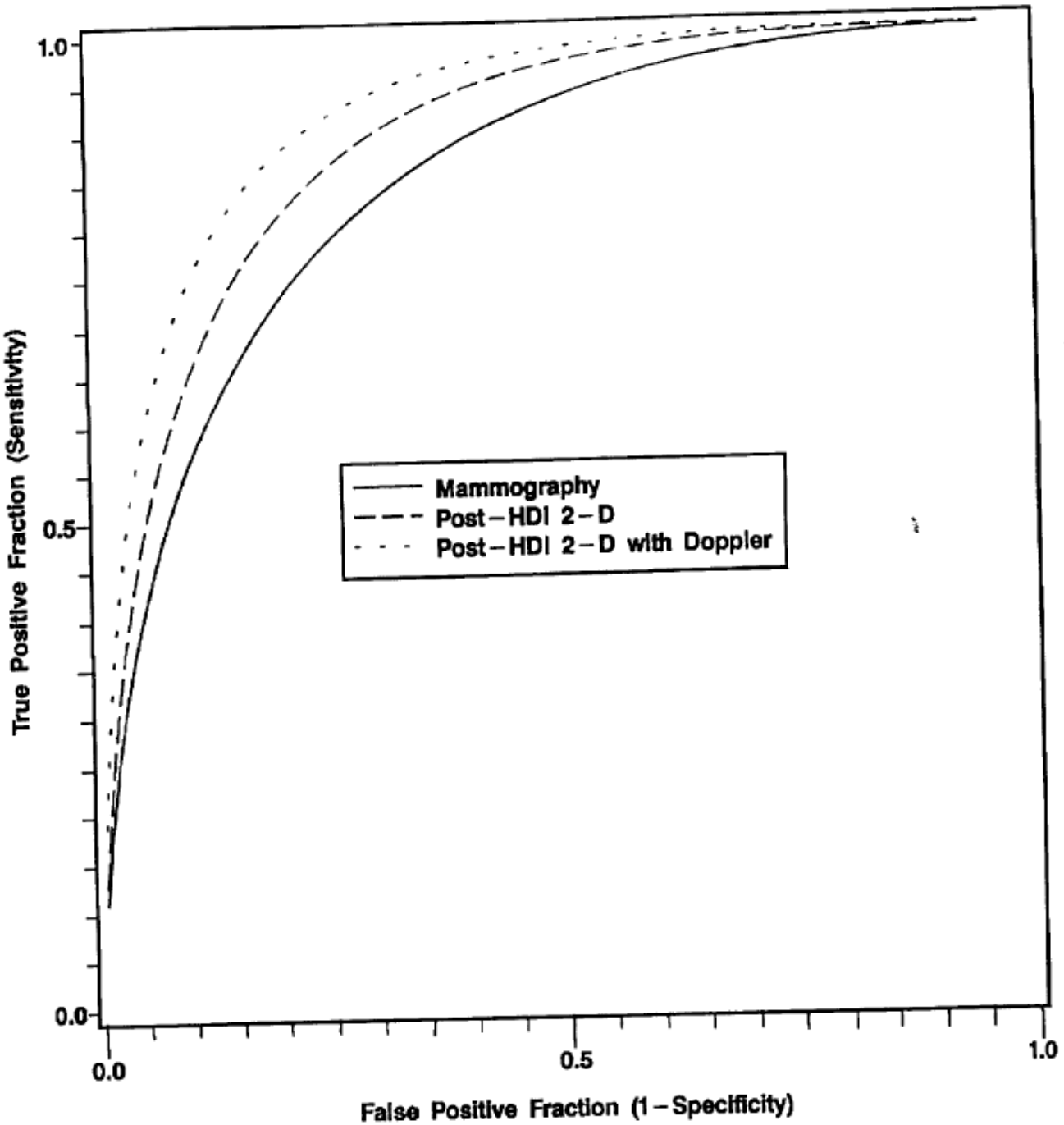
Executive Summary

ATL High Definition Imaging breast ultrasound: Premarket approval application for Advanced Technology Laboratories' HDI breast ultrasound system is slated for review Dec. 11 by FDA's Radiological Devices Panel in Gaithersburg, Maryland. The PMA, the first submitted to FDA for distinguishing benign from malignant disease by ultrasound, has been under "expedited review" by the agency...

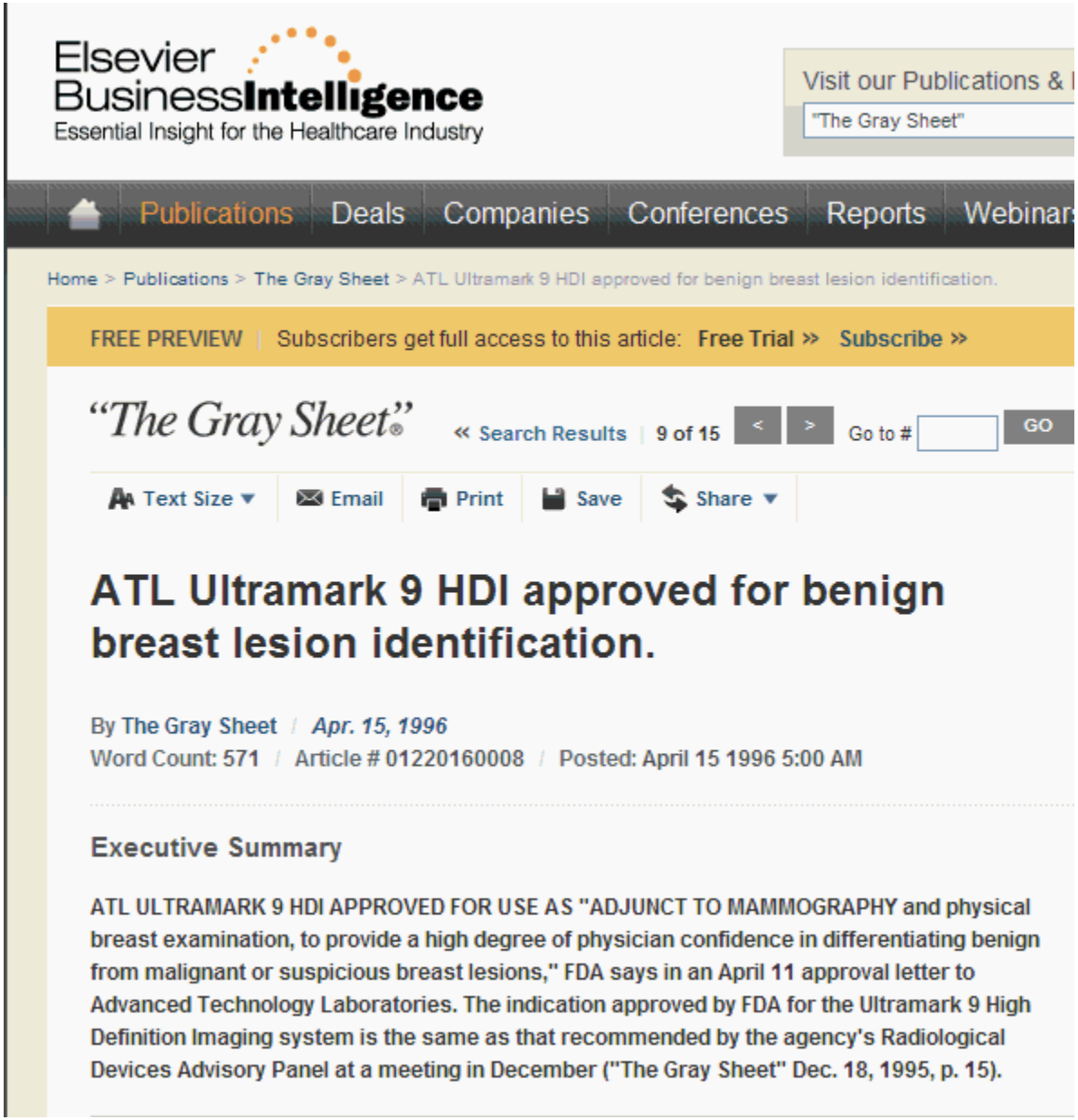
Table III. Assignment of LOS based on HDI-2D Image Criteria

HDI-2D LOS	Number of criteria observed	Assessment based on HDI-2D alone
5	5 malignant criteria	malignant
4	3-4 malignant criteria	probably malignant
3	1-2 malignant criteria	indeterminate
2	0 malignant criteria	probably benign
1	0 malignant criteria and all benign criteria	benign

Patients from nine U.S. and five non-U.S. sites entered into this study. This was a representative group of women who presented for diagnostic work-up or breast cancer screening and were recommended for breast biopsy. A total of 1270 patients, with 1334 masses were enrolled. Data from all patients who entered into this study were used to assess the safety of this device.


1.0
0.5
0.0
True Positive Fraction (Sensitivity)
Mammography
Post-HDI 2-D
Post-HDI 2-D with Doppler
0.0
0.5
1.0
False Positive Fraction (1-Specificity)

Landmark approval of ATL device – April 1996.



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ATL Ultramark 9 HDI approved for benign breast lesion identification.

By The Gray Sheet / *Apr. 15, 1996*
Word Count: 571 / Article # 01220160008 / Posted: April 15 1996 5:00 AM

Executive Summary

ATL ULTRAMARK 9 HDI APPROVED FOR USE AS "ADJUNCT TO MAMMOGRAPHY and physical breast examination, to provide a high degree of physician confidence in differentiating benign from malignant or suspicious breast lesions," FDA says in an April 11 approval letter to Advanced Technology Laboratories. The indication approved by FDA for the Ultramark 9 High Definition Imaging system is the same as that recommended by the agency's Radiological Devices Advisory Panel at a meeting in December ("The Gray Sheet" Dec. 18, 1995, p. 15).

FDA

XIV. REFERENCES

1. Smith, S.W., Wagner, R.F., Sandrik, J.M., Lopez, H., "Low Contrast Detectability and Contrast-Detail Analysis in Medical Ultrasound", IEEE Transactions on Sonics and Ultrasonics, Vol. 30, No.3, May, 1983, pp.164-173.

2. Lopez, H., Loew, M.H.,Butler, P.F., Hill, M.C., Allman, R.M., "A Clinical Evaluation of Contrast-Detail Analysis for Ultrasound Images", Medical Physics, Vol 17, No. 1, Jan/Feb. 1990, pp.48-57.

3. Lopez, H., Loew, M.H., Goodenough, D.J., "Objective Analysis of Ultrasound Images by Use of a Computational Observer", IEEE Transactions on Medical Imaging, Vol. 11, No. 4, December, 1992.

4. Charles E. Metz, "Basic Principles of ROC Analysis", *Seminars in Nuclear Medicine, Vol. VIII*, No.4. (Oct. 1978), pp. 283-298.

FDA Advisory Panel meeting for 1st 3D automated breast ultrasound system (April 2012)

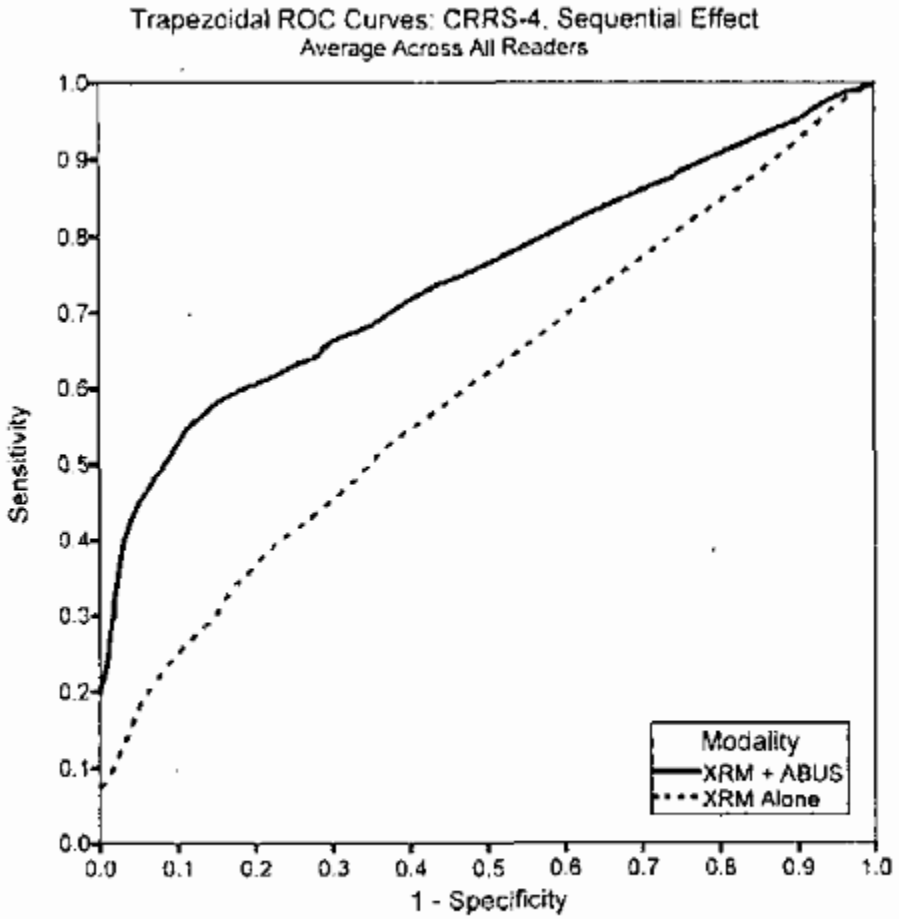
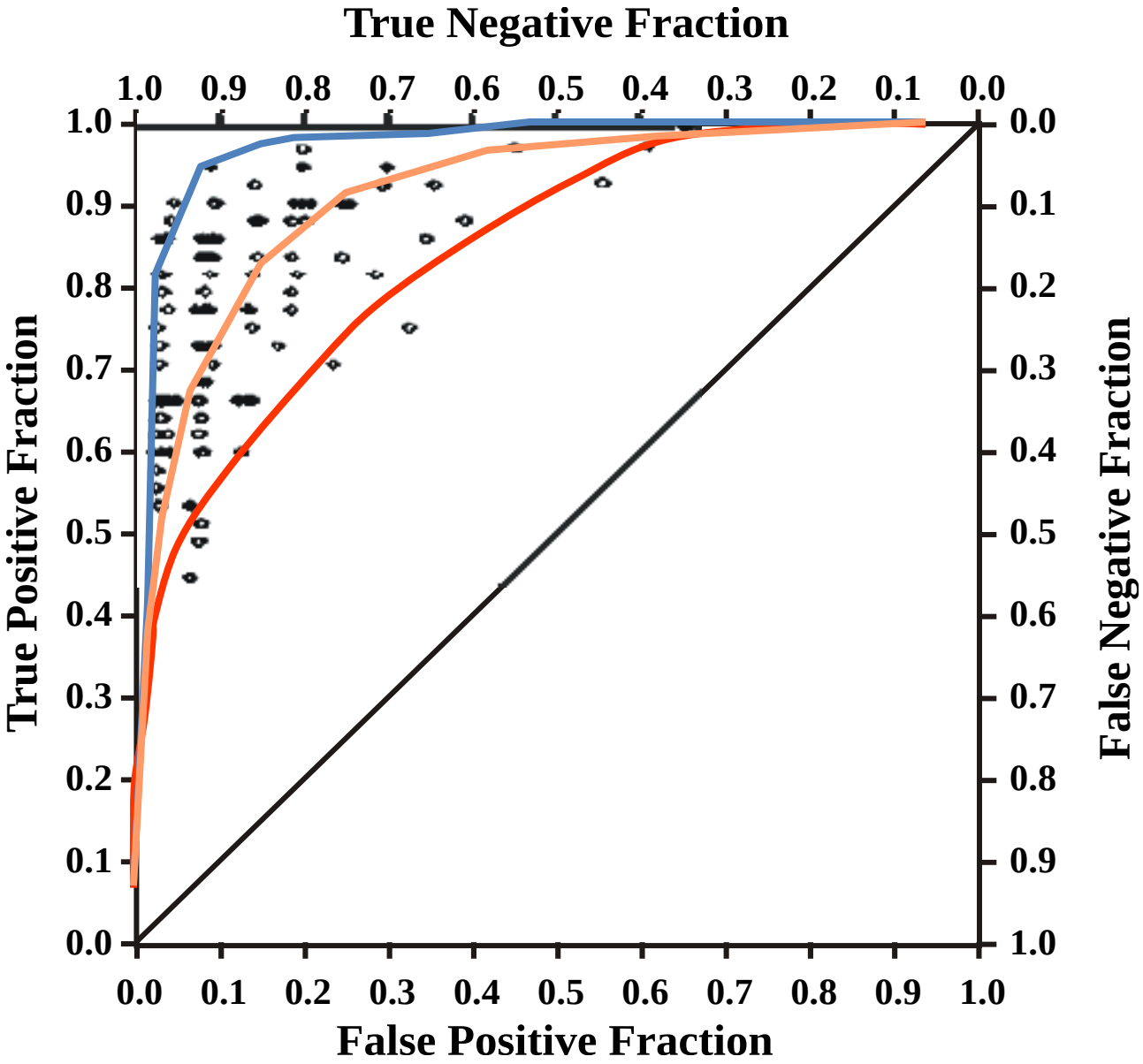


Figure 4. The overall ROC curves averaged across all readers trapezoidal ROC curves.

The Complication of Reader Variability:



TPF *vs* FPF for 108 U.S. radiologists all reading same images

No unique ROC curve

No unique (TPF, FPF) or (Se, Sp) point

TPF *vs* FPF for 108 mammographers in study by Beam et al.

Arch Intern Med 1996

GE files PMA for new digital mammography unit

By Brian Casey, AuntMinnie.com staff writer

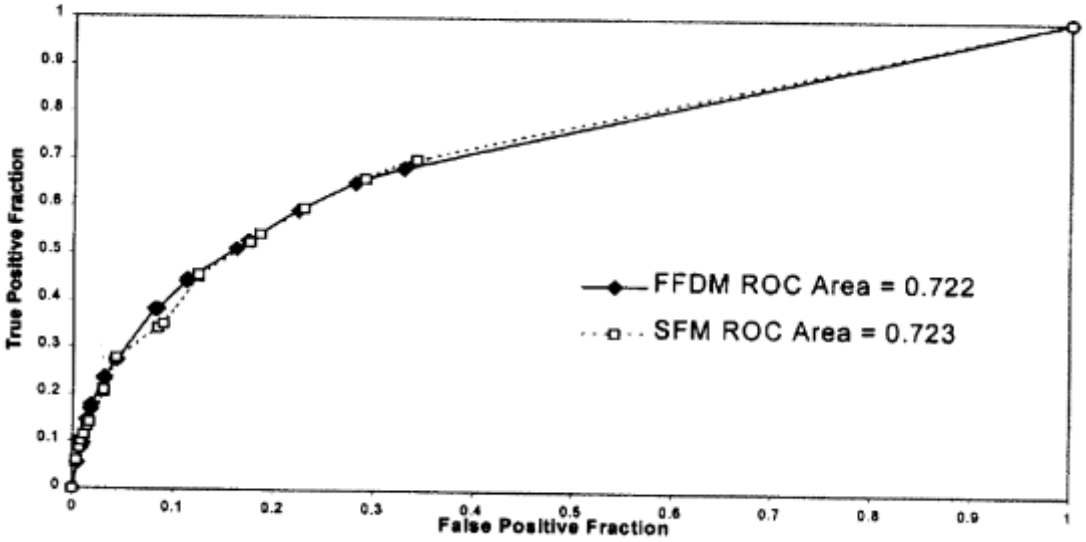
November 29, 1999 --

CHICAGO - GE Medical Systems announced at this week's RSNA meeting that it has already filed a premarket approval (PMA) application for its Senographe 2000D full-field digital mammography system. The Food and Drug Administration has granted the filing expedited review status, and will discuss the application at a committee meeting Dec. 16.

The FDA originally told vendors that it would allow full-field digital mammography systems to go through the less-rigorous 510(k) process, with submissions supported by clinical trials comparing digital mammography to film-screen mammography. But problems ensued with that approach after reader variability made it difficult to make an apples-to-apples comparison of the two technologies.

FDA Advisory Panel meeting for 1st FFDM system (Dec. 1999)

Figure 9: ROC Curves for All 5 Readers Combined in Reader Study #2



Sponsor's data analysis done using Metz LABMRMC software to account for reader variability

FDA approves GE's full-field digital mammography system

By Brian Casey, AuntMinnie.com staff writer

January 31, 2000 --

GE Medical Systems achieved a major milestone today, becoming the first company to receive Food and Drug Administration approval for a digital mammography system.

The Waukesha, WI, vendor reported that the FDA has signed off on GE's premarket approval (PMA) application for its Senographe 2000D product, which uses a digital detector rather than a film-screen system to acquire images. The agency's approval brings the U.S. into line with most of the rest of the world, where Senographe 2000D is already being sold.

Breast imaging advocates have touted digital mammography as one of the biggest technology advances in the field in decades. Digital systems have better contrast resolution and dynamic range than film, and it is easier for digital images to be manipulated and transmitted to other locations. Digital systems are also better than analog systems for imaging women with dense breasts.

Despite the potential advantages of digital technology, the FDA has taken a measured approach to approving full-field digital systems, and changed its regulatory approach to the technology several times. GE competitor Trex Medical of Danbury, CT, spent years trying to navigate the FDA's approval process, only to have its 510(k) application rejected by the agency.

GE filed its PMA not long after Trex's rejection, and encountered a much easier time. The FDA placed Senographe 2000D's application under fast-track review, and the application was recommended for approval by an FDA advisory panel on Dec. 16. It's not yet clear what indications are included in the FDA's approval.

Senographe 2000D uses digital detectors made from amorphous silicon, which collects x-rays and converts them into digital data. GE has spent 13 years and more than $100 million developing the technology, according to the company.

By Brian Casey
AuntMinnie.com staff writer
January 31, 2000

MIPS 2001: The CAD meeting

Contemporary Issues for Experimental Design in Assessment of Medical Imaging and Computer-Assist Systems

Robert F. Wagner, Ph.D.[+], Sergey V. Beiden, Ph.D.[+], Gregory Campbell, Ph.D.*,
Charles E. Metz, Ph.D.[++], William M. Sacks**, Ph.D., M.D.

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* Office of Surveillance and Biometrics, CDRH/FDA
** Office of Device Evaluation, CDRH/FDA
Center for Devices & Radiological Health, FDA,
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[++] Rossmann Laboratories, Department of Radiology,
The University of Chicago,
5841 South Maryland Ave
Chicago IL 60637

BACKGROUND

The dialog among investigators in academia, industry, NIH, and the FDA has grown in recent years on topics of historic interest to attendees of these SPIE sub-conferences on Image Perception, Observer Performance, and Technology Assessment. Several of the most visible issues in this regard have been the emergence of digital mammography and modalities for computer-assisted detection and diagnosis in breast and lung imaging. These issues appear to be only the "tip of the iceberg" foreshadowing a number of emerging advances in imaging technology. So it is timely to make some general remarks looking back and looking ahead at the landscape (or seascape).

The advances have been facilitated and documented in several forums. The major role of the SPIE Medical Imaging Conferences is well-known to all of us. Many of us were also present at the Medical Image

BACKGROUND

The dialog among investigators in academia, industry, NIH, and the FDA has grown in recent years on topics of historic interest to attendees of these SPIE sub-conferences on Image Perception, Observer Performance, and Technology Assessment. Several of the most visible issues in this regard have been the emergence of digital mammography and modalities for computer-assisted detection and diagnosis in breast and lung imaging. These issues appear to be only the "tip of the iceberg" foreshadowing a number of emerging advances in imaging technology. So it is timely to make some general remarks looking back and looking ahead at the landscape (or seascape).

The advances have been facilitated and documented in several forums. The major role of the SPIE Medical Imaging Conferences is well-known to all of us. Many of us were also present at the Medical Image Perception Conference IX (1) sponsored by the Medical Image Perception Society and co-sponsored by CDRH and NCI in September of 2001 at Airlie House VA. The workshops and discussions held at that conference addressed some critical contemporary issues related to how society—and in particular industry and FDA—approach the general assessment problem. A great deal of inspiration for these discussions was also drawn from several workshops in recent years sponsored by the Biomedical Imaging Program of the National Cancer Institute on these issues, in particular the problem of "The Moving Target" of imaging technology.

Another critical phenomenon deserving our attention is the fact that the Fourth National Forum on Biomedical Imaging in Oncology was recently held in Bethesda MD, February 6-7, 2003. These Forums are presented by the National Cancer Institute (NCI), the Food and Drug Administration (FDA), the Centers for Medicare and Medicaid Services (CMS), and the National Electrical Manufacturers Association (NEMA). They are sponsored by the National Institutes of Health/Foundation for Advanced Education in the Sciences (NIH/FAES). These Forums led to the development of the NCI's Interagency Council on Biomedical Imaging in Oncology (ICBIO) about two and a half years ago. The purpose of the ICBIO is to assist developers of

Medical Imaging 2003: Image Perception, Observer Performance, and Technology Assessment,
Dev P. Chakraborty, Elizabeth A. Krupinski, Editors, Proceedings of SPIE Vol. 5034 (2003)

2010 FDA/MIPS workshop

- "Evaluating Imaging and Computer-aided Detection and Diagnosis Devices at the FDA"
  - Followed by questionnaire to speakers and panelists probing consensus statements for a workshop summary paper

- "This is an *excellent* questionaire overall, in my opinion."
- "This document is very, VERY good, in my opinion."
- "This sentence strikes me as not only awkward, but impenetrably opaque."

Special Review

Evaluating Imaging and Computer-aided Detection and Diagnosis Devices at the FDA

Brandon D. Gallas, PhD, Heang-Ping Chan, PhD, Carl J. D'Orsi, MD, Lori E. Dodd, PhD, Maryellen L. Giger, PhD, David Gur, ScD, Elizabeth A. Krupinski, PhD, Charles E. Metz, PhD, Kyle J. Myers, PhD, Nancy A. Obuchowski, PhD, Berkman Sahiner, PhD, Alicia Y. Toledano, ScD, Margarita L. Zuley, MD

Acad Radiol 2012; 19:463–477

Software

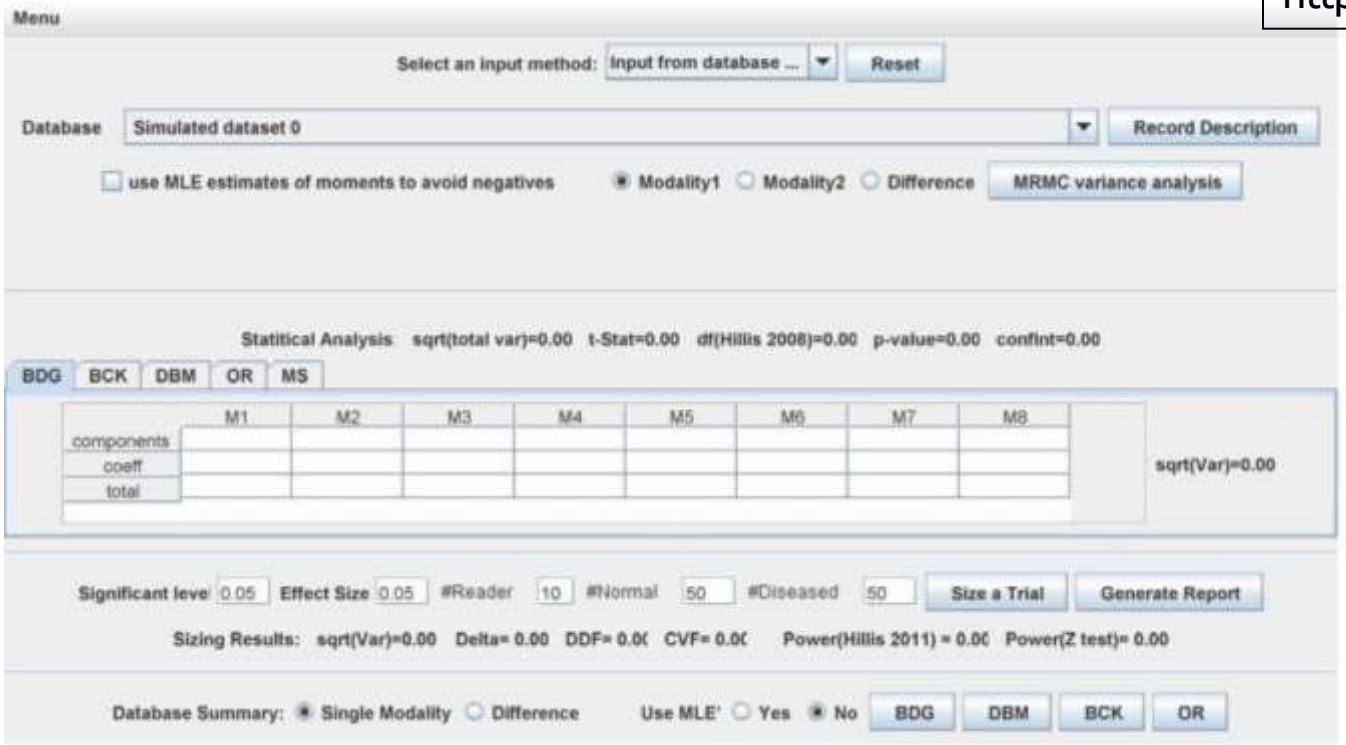
- http://metz-roc.uchicago.edu/
- 

- http://js.cx/~xin/index.html
- iMRMC — Analyzing and Sizing Multi-reader Multi-case ROC Trials

  Xin He, Brandon Gallas

iMRMC: Webpage and Software for Sizing an MRMC Clinical Trial

http://js.cx/~xin/index.html



Incl. Database of Components of Variance

Send us your reader data!

- A resource for investigators designing a trial to compare two imaging modalities.
- Uses datasets from previous imaging trials to estimate power of new trial designs.
- Over time, database growth will benefit wide community of clinical trialists.

iMRMC 2.0

in development

iMRMC Analyzing and Sizing Multi-reader Multi-case ROC Trials

Xin He, Brandon Gallas

- Allow for arbitrary study design
- Roe and Metz App in development
  - Simulate MRMC experiments
  - Allow variance to differ across truth and modality
  - Numerically calculate components of variance

Charlie's Impact

- Major influence on the culture of imaging system assessment at the FDA

- Facilitated bringing significant innovations to patients in Breast Imaging (FFDM, US, and CAD) and beyond!

Heang-Ping Chan's Research updates: U Michigan, Charlie, FDA