Research in Digital Mammography and Tomosynthesis at The University of Toronto

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Introduction
My first exposure to digital medical imaging came in 1972 with the landmark publication by Ambrose and Hounsfield\textsuperscript{1,2} of the results with the first CT scanner and my discovery of the earlier work by Oldendorf\textsuperscript{3} on CT. While, in many ways more sophisticated than modern digital mammography, the CT application was actually very appropriate as a first start in digital imaging because it provided an enormous benefit, excellent contrast discrimination, with coarsely spaced, i.e. low spatial resolution measurements – possible with the technology available then. It was several years later that the first digital radiographic systems were introduced for subtraction angiography\textsuperscript{4}.

My interest in digital mammography (DM) arose from a visit to a mammography facility, in the late 1970s with my PhD supervisor, Harold E. Johns, a giant in the physics of radiation therapy, who had only recently begun research in medical imaging physics. We observed the poor contrast and high radiation doses of the direct film mammography used at the time. Although there was a progression of improved analog devices including xeroradiography and early screen-film detectors, I began to think that perhaps digital methods could be applied to improve contrast performance while allowing reduction of doses. But the detection of breast cancer required not only good contrast, but also excellent spatial resolution and detector technology at that time was still quite primitive.

Early developments – line scanning
The first publication that suggested the possibility of digital mammography to me was by Paul Bjorkholm, who worked for a company called AS&E (now Hologic). He described a single-line detector that scanned across the body in synchrony with a finely collimated line-beam of x rays\textsuperscript{5}. With my graduate student, Robert Nishikawa (now at The University of Chicago) we began to analyze the limitations of film mammography\textsuperscript{6} and to consider how we could meet the demanding imaging requirements of mammography with a digital system using components that were available in the 1980s. There were several challenges: achieving high spatial resolution over a field of view as large as the breast, digitizing the signal precisely over a wide range and displaying the image.

Our first experimental system employed a Siemens high-resolution CsI x-ray image intensifier. This was a special device designed for coronary catheterization and provided a spatial resolution of 5 line-pairs per mm. Employing a modest amount of geometric magnification with a small-focus x-ray tube, we achieved 7 line-pairs per mm. We coupled this device optically through lenses to a self-scanned linear photodiode array and with digital sampling electronics wired by us, were able to capture a signal from a line-beam of x rays. Scanning this assembly across a phantom produced our first digital "mammogram".\textsuperscript{7} The narrow beam of radiation employed and the ability to apply Pb collimation at the detector surface, provided an efficient way to reduce the effects of scattered radiation from the breast, unlike area methods, where an antiscatter grid is used, necessitating an increase in dose. The superior imaging performance of the digital system compared to what was then a state-of-the art screen film system, in imaging small, low-contrast structures is seen in Figure 1.
Figure 1 Comparison of images of a contrast-detail detectability phantom for L) a screen-film mammography detector and R) a prototype digital detector constructed in our laboratory.7 The superior depiction of both lower contrast discs and smaller discs with the digital system is evident.

But, clearly such a system was impractical, in part due to the bulkiness of the detector assembly. A viable system would provide image coverage right to the chest wall of the patient, a wide dynamic range and good immunity against scattered radiation and low noise. We began to explore the use of a fan-beam geometry in which multiple lines of the image were acquired simultaneously. Due to lack of a suitable large-area detector technology, we maintained the scanning approach, but opening the collimation to a width of a few millimetres. The detector consisted of a strip of CsI phosphor bonded to the surface of a fibre-optic taper bundle. X-rays absorbed in the phosphor produced an optical image which was demagnified by the tapered fibres and coupled to a multi-line CCD array. This was more efficient than using lenses and the pixels of the CCD were small enough to represent the equivalent of 50 micrometres in the breast. The image was acquired in “time-delay integration (TDI) mode in which the electronic signal was shifted from column to column of the CCD at the same speed, but in the opposite direction to the linear scanning motion of the x-ray source and detector array across the breast. This caused a relatively noise-free integration of the CCD charge signal pertaining to a given path through the breast and when the charge reached the final column it was converted to a digital image pixel value and stored. A system based on this design was manufactured commercially by Fischer Imaging in the US (Figure 2).

In 1992, following a conference in the Capitol Building in Washington focusing on how to make an impact on finding breast cancer earlier89, the National (soon to become International) Digital Mammography Development Group was formed. This group consisting of imaging scientists,
radiologists and industry partners pooled their efforts to accelerate the development and introduction of DM.

**Area detectors for digital mammography**

At the same time, industry gradually began to introduce full-field detector systems. For example, Fuji developed a photostimulable phosphor flat plate which was exposed in a cassette in a conventional mammography unit similar to the way a screen-film system would be used. The plate was not divided into discrete pixels. The phosphor contained a high density of electron traps. During x-ray exposure, the absorbed x rays would liberate energetic photoelectrons which would lose their energy within a few tens of micrometres. The energy would cause electrons in the crystal lattice of the phosphor to be excited and then, with a fairly high probability, be trapped. Electrons could remain in the traps for a long period of time (hours to days) forming a latent image of the x-ray exposure. In a separate reading device the plate was slowly scanned in one direction while a red laser beam scanned back and forth in the orthogonal direction to form a raster. The energy of the laser light discharged the traps and the electrons were temporarily liberated. As they descended to their ground states they caused the emission of blue light from the phosphor. This light was collected by an optical detector whose signal was digitized to form the image. The size of the laser beam and the distance between measurements defined the nominal pixel size and spacing and the location of the laser beam on the plate at the time when the light was emitted from the phosphor gave the x-y location of each pixel.

![Figure 2 Detector used in the Fischer slot-scan digital mammography system. X rays are absorbed by a CsI(Tl) phosphor and the light produced is conducted along a fibre optic bundle to a multiline CCD. Readout is accomplished in TDI mode by scanning the detector and the x-ray source across the breast.](image-url)
The technology used to make flat-panel video displays could also be used in reverse as a large-area detector readout. Typically a glass plate would have a matrix of “pixels” formed on it. Electronic charge proportional to the image signal would be collected on these elements. On the corner of each element is a thin film transistor (TFT) switch that would read out the charge on that element onto a readout line running along each row of the matrix whenever that switch was activated by a signal along that particular column line. In DM there are two ways of converting x-ray energy being used in flat-panel systems. One produced by General Electric uses a CsI crystal material coated over the entire plate as the x-ray absorber and an array of photodiodes, one on each detector element, to convert the phosphor light to electronic charge.

The other technology produced by at least two companies, Hologic and Analogic, employs a coating of amorphous selenium as the x-ray absorber. The energy of the x rays is directly converted into charge which is stored on the detector elements until they are read out by means of the TFT switches. A strong electric field causes the electrons to drift directly to the collection surface (detector elements) with negligible spreading. This allows use of a thick absorber to attain high x-ray quantum absorption efficiency without loss of spatial resolution due to spreading sideways of the charge.

**Signal and Noise Considerations**

One of the fundamental limitations in the performance of a radiographic imaging system is noise and an important goal is achieving a satisfactory signal difference to noise level (SDNR). This is done in part by ensuring that the exposure to the breast is high enough and that x rays are used as efficiently as possible. This implies that the quantum efficiency of the detector must be high, which is achieved by utilizing a detector material with high atomic number and density and/or making the absorbing layer thicker. As thickness is increased there is a loss of spatial resolution, especially in phosphors, so a compromise between resolution and quantum efficiency occurs. In addition, detectors should introduce as little additional noise into the image as possible and this implies that the electronic readout circuitry must be of very low-noise design and the signal levels be reasonably high.

An early limitation in the development of DM was the availability of high-speed analogue to digital converting electronics with a sufficient number of bits to record the wide range of signal from x-ray transmission through different parts of the breast and to do this with adequate precision. For systems whose signal was linear with the transmitted x-ray energy fluence 13 or 14 bit A/D converters were required, although if, as in CR systems, the signal range was first compressed by logarithmic transformation, then fewer bits were needed.

Another type of noise in screen-film imaging, structural noise, comes from the granularity of the film emulsion and spatial nonuniformity of the sensitivity of the screen. In digital imaging, because the same detector is used repeatedly, it is possible to measure this nonuniformity as well as any shifts in sensitivity over time and to perform a “flat-field” correction. In this way much of the structural noise can be removed (Figure 3).

Most detectors used in DM (eg phosphors, amorphous selenium) operate by integrating the signal from the absorbed energy of interacting x rays. Since there is a spectrum of x rays of different energy there is a mixture of signals from low-energy x rays that contain higher contrast information and from higher energy x rays that produce a lower contrast image. This causes additional fluctuation and reduces the quality of information in the image. A recently introduced technology
overcomes this problem and that of noise in the readout electronics by counting x rays absorbed by the detector. Each x-ray gives one count regardless of the energy that it carries. This not only reduces noise but also reduces the weighting of the image due to high-energy x rays improving SDNR.\textsuperscript{10,11} Interestingly, because of the challenges in designing a quantum counting detection system, the device described here manufactured by Philips (formerly SECTRA) is configured as a multi-line detector, so that in addition to the SDNR advantages, this geometry, which does not require an antiscatter grid, also provides a dose efficient means of rejecting scattered radiation that would otherwise expose the detector.

**Clinical evaluation**

In 2001 the Digital Mammography Imaging Screening Trial (DMIST) began under the leadership of Dr. Etta Pisano and almost 50,000 women were recruited to receive both DM and screen-film mammography. The results of detection accuracy were compared and in 2005 a paper appeared in The New England Journal of Medicine showing that while overall the diagnostic accuracy of DM was statistically equivalent to that of screen-film mammography, for women who had dense breasts and those under the age of 50, it was more accurate, i.e., its sensitivity was higher without loss of specificity.\textsuperscript{12} Since that time the clinical use of DM has ramped up quickly and in many countries it has now largely replaced film mammography.

![Figure 3](image-url)  
**Figure 3** Illustrating the reduction of structural noise (nonuniformity of detector response and x-ray field intensity) by flat-field correction. L) uncorrected  R) corrected.
Image processing and display

Digital mammograms presented both advantages and challenges. The advantages were the wide dynamic range of image information and the ability to adjust brightness and contrast while viewing, to sharpen images. But images are displayed on monitors, which are analogue devices with limited range. The challenge of display was met through image processing and a number of adaptive algorithms were introduced to allow good display of relevant contrast, for example by compensating for breast thickness (Figure 4). At the same time, the commercial introduction of high resolution 5 Mpixel displays and ergonomic workstation design greatly facilitated the task of image viewing.

The Future

Digital mammography has improved both the accuracy and the efficiency of breast cancer detection and diagnosis and allowed us to dispense with the environmental issues of film processing chemistry. But I see DM as a launching pad for even more powerful applications, some which are already in use and others to come. These include contrast-enhanced imaging, CAD, tomosynthesis and fusion with other modalities like ultrasound and molecular imaging, providing high spatial resolution to complement the functional information of the second modality.

Currently my lab is very interested in tomosynthesis. We are working on approaches for dose reduction, on improved image reconstruction methods, on the combination of contrast injection imaging with tomosynthesis and on developing a metric for image quality that will correlate strongly with diagnostic accuracy. We are also planning a large trial, "TMIST", that will compare the performance of tomosynthesis with digital mammography and we are developing the tools for quality assurance during that study. It is an exciting time!