Case Histories of Significant Medical Advances: Mammography

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Mammography

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Abstract: We describe how the development of x-ray-based techniques and equipment ("mammography") lead to widespread screening for breast cancer and enabled “minimally invasive” biopsies of breast tumors. Specifically, we chronicle how: 1) new protocols and equipment catalyzed the first widespread screening programs and minimally invasive biopsies in the 1960s and 1970s; 2) concerns about safety and accuracy spurred technological advance in the 1980s; and, 3) digitization further improved the safety and accuracy of mammography in the 1990s and 2000s.

Note: This case history, like the others in this series, is included in a list compiled by Victor Fuchs and Harold Sox (2001) of technologies produced (or significantly advanced) between 1975 and 2000 that internists in the United States said had had a major impact on patient care. The case histories focus on advances in the 20th century (i.e. before this millennium) in the United States, Europe, and Japan -- to the degree information was available to the researchers. Limitations of space and information severely limit coverage of developments in emerging economies.

Acknowledgments: We would like to thank Kirby Vosburgh for helpful information and suggestions.
Mammography

Mammography, which combines specialized X-ray equipment with techniques for positioning breasts, is used both for the screening of women who have no signs or symptoms of breast cancer as well as for the diagnosis of lumps or tissues to determine whether they are cancerous. Before mammography physicians had relied on physical exams and biopsies. However, physical exams could not detect emerging tumors and biopsies (of lumps that could be detected by physical examination) were expensive, invasive, potentially disfiguring, and sometimes inaccurate. Mammography has made large-scale screening feasible and diagnosis through biopsy less invasive and more accurate.

Screening mammography has greater impact, although diagnostic use came first. Screening in the United States, for instance, is thought to have helped reduced deaths from breast cancer by almost a quarter since 1990. Screening has also created controversies about exposing healthy women to X-ray radiation, as well as encouraging unwarranted treatment. Commercially, sales of screening mammography equipment are as much as ten times greater than the sales of diagnostic mammography equipment.

The three main sections of this case history describe the intertwined development of screening and diagnostic mammography. (see Figure 1) An Epilogue reviews recent developments.

Figure 1 The Evolution of Mammography

1. Establishing the foundation (1950-1980)

Overcoming the Limitations of X-Rays

X-rays, discovered in 1895, soon transformed medical diagnosis and created the specialty of radiology, but were not immediately useful in diagnosing breast cancer. Although X-rays provided acceptably clear images of bone fractures and hard objects lodged in bodies (such as bullets), images of soft tissues – including tumors in breasts – were blurry. For more than four decades after the discovery of X-rays, radiologists from the United States, Europe, and South America experimented with X-rays to detect breast cancer, yet none could overcome the problem of blurry images. Physicians therefore relied on physical exams and biopsies.

In the 1950s, Raul Leborgne, a Uruguayan radiologist, developed a technique that significantly improved the sharpness of breast X-rays, revealing well-formed as well as emerging tumors. In a 1953 book, a biopsy is the surgical removal of tissue samples for further examination in a lab.
he described a procedure, which entailed adjusting the X-ray beam, flattening the breast during the X-ray, taking images from multiple angles, and using more sensitive film.7

**Standardizing Diagnostic Mammography**

Charles Gros, head of radiology at a cancer center affiliated with University of Strasbourg (France), thought Leborgne’s procedure promising but its description inadequate for the typical radiologist. Gros therefore attempted to provide a more systematic description in his 1963 textbook *Diseases of the Breast*. Gros also attempted to reduce the training radiologists would need by developing equipment with the French X-ray producer Compagnie Générale de Radiologie (CGR) that would mechanize some of the steps.8 CGR introduced the equipment in Europe in 1966, and in the U.S. in 1971.9 (See Figure 2 at the end of this section)

### How Robert Egan Developed and Tested Mammography Protocols

Egan first took X-rays of a thousand breasts of women seeking treatment at Anderson for a breast related complaint. By comparing his X-ray images with diagnoses produced by traditional physical examinations and surgical biopsies Egan chose settings that he expected to produce the same diagnostic results. At the same time, Egan took X-rays of breasts that had been diagnosed as cancer-free by Anderson’s physicians. For instance, if a woman had a lump in one breast that was detected through a physical exam, and the other breast had been found to have no lumps in a physical exam, Egan would X-ray both breasts. In 19 cases, the X-ray of the other, seemingly cancer-free breast showed signs of an emerging tumor.

Egan then validated his protocol by X-raying another 1,522 breasts (of women who had also come to Anderson with breast complaints) without prior communication with the physicians conducting the physical exam and biopsies. He then compared his diagnoses with those produced by traditional procedures, and his comparison showed an astonishing 97% correspondence. In addition, Egan identified another 58 tumors that had gone otherwise undetected.

Both the studies suggested mammography could be used for screening, because the procedure had found tumors that had produced no discomfort and had not been identified through physical examination. However, Egan was more interested in helping medical internists (who did physical exams) and surgeons (who performed biopsies). Egan’s first article emphasized how his protocol could help decide, for instance, whether a lump discovered through a physical exam warranted a surgical biopsy. His second article did suggest mammographic screening of patients who had been successfully treated (to check for recurrence of the disease) but did not propose screening the general population.

Egan went on to participate in research that showed his techniques could be used by other radiologists. In 1965, after moving from Anderson to Emory University in Atlanta, Georgia, he continued to enthusiastically promote mammography, lecturing widely and training radiologists and technicians well into the 1970s. However, Egan focused his research mainly on testing women who had breast complaints or prior histories of breast cancer rather than on population-wide screening (although, as we will see, he did help adapt his protocol for rapid, high-volume screening).

Robert Egan, a radiologist at M.D. Anderson Hospital and Tumor Instituteb in Houston, Texas, developed Leborgne’s technique in a different direction. In 1956, Anderson’s chief radiologist had asked Egan, then a new resident at the hospital, to investigate X-ray diagnosis of breast cancer. In about five years, Egan developed and tested protocols that specified: 1) lower power X-rays than those used for other kinds of diagnostic applications (e.g. for fractured bones); 2) different settings for breasts of different sizes, densities, and so on; 3) highly sensitive X-ray film that Kodak had originally developed to identify flaws in metal structures; and 4) cardboard cut-outs to position breasts (instead of Leborgne’s technique of flattening and immobilizing breasts).

This protocol, described in papers published in 1960 and 1962, had a ninety-seven percent correspondence with results produced by traditional diagnostic procedures (i.e. physical exam and biopsy).

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b Now M.D. Anderson Cancer Center.
It also identified emerging tumors that traditional procedures could not detect.\textsuperscript{10} (See box “How Robert Egan Developed and Tested Mammography Protocols”).

As Egan started developing his protocols, another radiologist, Jacob Gershon-Cohen, was X-raying the breasts of women with breast cancers at Albert Einstein Medical Center in Philadelphia. Gershon-Cohen intended to record changes in breast tissues that occur as the disease advances. However, the Philadelphia radiologist became interested in early detection and, in the late 1950s, X-rayed the breasts of over 1,300 women who displayed no symptoms. In 1961, he published results that, like Egan’s research suggested, X-rays could detect malignant tumors at a very early stage.\textsuperscript{11}

Egan’s work attracted the attention of two U.S. government agencies -- the National Cancer Institute (NCI), which sponsored research, and the U.S. Public Health Service (USPHS), which organized prevention and treatment programs.\textsuperscript{12} To find out if radiologists at hospitals that lacked M.D. Anderson’s resources and tradition of multi-specialty collaboration\textsuperscript{13} might be able to replicate Egan’s results, NCI and USPHS officials helped bring radiologists from twenty-four American hospitals to Anderson to train under Egan. The results of mammography performed by the radiologists after they returned to their own hospitals also had a high correspondence with traditional diagnoses – seventy-eight percent. The high correspondence rate, although below Egan’s, prompted the NCI’s cancer control unit to consider the feasibility of large-scale screening of asymptomatic women.\textsuperscript{14} Jacob Gershon-Cohen’s Philadelphia study\textsuperscript{15} and the NCI’s own experience in the 1950s of promoting the so-called “Pap smear”\textsuperscript{c} test to screen women for early signs of cervical cancer also encouraged the NCI.\textsuperscript{16}

\textbf{Testing Screening Mammography}

To test whether the Pap smear screening model could be adapted to breast cancer, NCI officials contracted with the Health Insurance Plan of New York (HIP) to run a large-scale trial.\textsuperscript{17} HIP insured and provided medical services to several hundred thousand “members” in New York through thirty-one physician groups. Researchers leading the HIP trial offered free screening to more than 30,000 randomly selected women aged between forty and sixty-four (from about 85,000 women in this age bracket that HIP insured). Screening, which included physical examinations and patient histories as well as mammograms, was to be repeated annually for four years.\textsuperscript{18}

The research team repeatedly contacted the selected women to secure a high response rate and offered screening in mobile vans close to where some of the women worked and not just in the clinics of HIP’s physician groups. They also used a simpler, faster, mammographic procedure designed by pioneer Robert Egan. (Egan’s "normal" protocol, which was intended for diagnosing women who had breast related complaints or had previously been treated for breast cancer, was more time consuming. Egan also helped train the radiologists and technicians who performed the screening in the trial.)\textsuperscript{19}

Sixty-seven percent of the women contacted for screening responded, about half of whom completed the full four-year sequence of annual screening. Overall, between 1963 and 1968, HIP researchers screened 20,166 women – a number that might normally have taken up to twenty years.\textsuperscript{20} Women who showed signs of breast cancer were referred to specialists for further investigation and, if necessary, treatment. Researchers then compared the death rates of the women who had been screened with the same number of HIP-insured women in a “virtual” matched control group who had not been contacted for screening.\textsuperscript{21}

Early results, published in 1971, suggested screening had produced a dramatic decline in breast cancer deaths. Only thirty-one women who had been screened had died of breast cancer -- forty percent less than the fifty-two women who had died of breast cancer in the control group.\textsuperscript{22}

\textsuperscript{c} Pap smears are named for their inventor, Dr. George Papanicolaou. They entail taking a sample of cells on a swab from the opening at the bottom of the uterus and testing the cells in a lab for signs of cancer. Pap smears were the first large-scale attempt at early detection, and they provided a model for large-scale screening of asymptomatic women for breast cancer.
The HIP results helped spur a free screening program throughout the United States, which was co-sponsored\(^d\) by the NCI and the American Cancer Society (ACS).\(^{23}\) By 1975, two years after the program was launched, over 280,000 women had been screened.\(^{24}\)

**Concerns about Safety and Accuracy**

In 1976, however, an NCI statistician, John C. Bailar, published a reappraisal of the HIP trial suggesting that the radiation risks of screening might outweigh the benefits. Bailar noted that only forty-four cases of breast cancer had been found through mammography alone in the HIP trial. (In fifty-nine cases the patients’ physical exams and histories had provided a sufficient indication and another twenty-nine cancers had been identified through some combination of the patient’s medical history, physical exam, and mammography. See Table 1) And, because treatment after early detection did not cure all breast cancers, Bailar estimated mammography alone prevented only about a dozen deaths (out of the forty-four “additional” early detections). Meanwhile, mammography could itself have induced sixteen cancer deaths by exposing more than 20,000 healthy women to radiation (according to Bailar’s estimates).\(^e\) Thus, mammographic screening might cause as many deaths as it prevented.\(^{25}\)

**Table 1** Summary Data for the Health Insurance Plan (HIP) Study

<table>
<thead>
<tr>
<th></th>
<th>Study Group</th>
<th></th>
<th>Control Group</th>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>Died of Breast Cancer</td>
<td>Total</td>
<td>Died of Breast Cancer</td>
</tr>
<tr>
<td>Total Selected</td>
<td>30,426</td>
<td>70</td>
<td>31,007</td>
<td>108</td>
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<tr>
<td>Screened</td>
<td>20,166</td>
<td>45</td>
<td></td>
<td></td>
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<tr>
<td>Mammographic Exams</td>
<td>64,810</td>
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<td></td>
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<tr>
<td>Unscreened</td>
<td>10,260</td>
<td>25</td>
<td></td>
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<tr>
<td>Breast Cancers Reported</td>
<td>299</td>
<td>70</td>
<td>285</td>
<td>108</td>
</tr>
<tr>
<td>Not Detected on Screening</td>
<td>167</td>
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<td></td>
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<tr>
<td>Screened at Least Once</td>
<td>93</td>
<td>28</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Refused Screening</td>
<td>74</td>
<td>25</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Detected on Screening</td>
<td>132</td>
<td>17</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient History or Physical Exam only or both</td>
<td>59</td>
<td>9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient History or Physical Exam or both plus Mammography</td>
<td>29</td>
<td>7</td>
<td></td>
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<tr>
<td>Mammography only</td>
<td>44</td>
<td>1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Source: Bailar (1976).

Note: Bailar did not consider the slightly higher number of cancers reported in the screened group to be significant.

After the publication of Bailar’s report, the NCI asked three different groups of university-based researchers to review its screening program. By 1977, the researchers reported a variety of problems, including mistaken diagnoses that had led to fifty-three unnecessary mastectomies.\(^f\) The National Institutes

\(^d\) The U.S. Congress passed the National Cancer Act in 1971. The act increased funding for research and development of cancer diagnostics and treatments. The initiatives supported by this act are often referred to as part of then-President Richard Nixon’s “War on Cancer.”

\(^e\) Bailar also pointed out that the women would have a greater risk of developing other cancers, such as leukemia and lung cancer.

\(^f\) A mastectomy is the surgical removal of the whole breast and some surrounding chest muscles. For decades, it was the primary treatment for breast cancer.
of Health (of which the NCI is a part) also convened its first ever “consensus conference” in 1977 to recommend standards for screening; previously, the NCI and the ACS had published their own standards. However, attendees at the conference could not agree on how often women should be screened and whether women should begin screening before menopause (which typically starts around age fifty).  

Meanwhile, Public Citizen, an advocacy group run by consumer rights activist Ralph Nader, obtained and publicized government records that showed that equipment in some screening centers delivered radiation doses that exceeded federal safety limits.  

Problems with Equipment, Film, and Human Error

A Food and Drug Administration (FDA) study published in 1979 (after the Public Citizen report had been released - See Exhibit 1) attributed excessive radiation exposure and misdiagnoses from mammographic screening to three factors:

1. **Screening with general purpose X-ray equipment.** As mentioned, the French X-ray manufacturer CGR was first to develop specialized equipment in collaboration with radiologist, Charles Gros. Although the equipment had been designed to reduce the training necessary to produce sharp X-rays, it also happened to reduce radiation exposure. CGR had started selling this equipment for diagnostic use, first in France in 1966 and then in the U.S. in 1971. Possibly because mammography was not yet a common procedure, no other companies were selling specialized equipment when free screening was started in the U.S. in 1973. As the free screening program unfolded between 1973 and 1976, other companies did start selling specialized CGR-style equipment. However, the controversy about screening that erupted in 1976 discouraged manufacturers from marketing or improving specialized equipment. As of 1979, more than half of American hospitals were using general purpose equipment that increased radiation exposure when used for mammography.

2. **Not using specialized film.** As mentioned, Egan’s protocols had specified specialized X-ray film and low-powered X-rays. The specifications -- like Gros’s specialized equipment -- happened to reduce radiation exposure but were not always followed: some radiologists and technicians used standard X-ray film and power settings that reduced accuracy and exposed patients to more radiation. Others did not use X-ray film at all. Instead they used plates intended for general X-ray use and popularized in 1971 by the copier pioneer Xerox. The plates, which Xerox had developed as a substitute for traditional X-ray film, enabled X-ray images to be printed on paper. And, like standard film, they exposed patients undergoing mammography to more radiation than specialized film. (See Exhibit 2)

3. **Operator Error.** The FDA also reported that many operators made mistakes, such as putting film in backwards or using the wrong X-ray settings. Using specialized equipment and film reduced such errors. However, according to the FDA’s research, only fifteen percent of screening mammography was being performed on specialized equipment with specialized film.

Mammography in Europe and Japan

Mammography did not gain the same support in Europe that it did in the United States. Unlike Robert Egan, who not only developed his mammography protocol but also then devoted himself to promoting its widespread use, Charles Gros had largely focused on developing equipment. Europe also lacked organizations that championed screening, like the American Cancer Society and the NCI. By the mid-1970s, only Sweden and Scotland had trials for screening mammography under way. Initial results from the Swedish trials suggested that mammography could indeed help to reduce breast cancer deaths, leading to

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8 Consensus conferences brought leading authorities together for public discussions in “an experiment in quickening ... certain decisions about scientific matters that have important social dimensions” (as The New York Times reported in 1977). The series ran for thirty-six years, until its formal retirement in 2013.
more trials in Sweden and, by the end of the 1970s, nationwide screening. However, besides Austria, other European countries did not start screening programs.\(^3\)\(^5\)

**Xonics’ Mammography System**

Xonics, a 1972 California startup, secured a patent in 1973 for a process that produced X-ray images on thin plastic sheets that looked similar to traditional X-ray film with less radiation. Xonics’ devices adapted standard X-ray equipment and were intended to produce chest X-rays and mammograms. Lacking its own sales and marketing, Xonics acquired Standard X-ray, a longtime American X-ray manufacturer, in 1975. It also reached an agreement by 1977 with Belgium’s AGFA, an X-ray film producer, to help develop and sell its devices.

However, Xonics could not actually produce its chest X-ray equipment. And, despite promising results in studies of its mammography units, Xonics failed to secure more than a few hundred orders. In 1983, the company sold out to Elscint, an Israeli medical imaging company, and by 1985, Elscint had shut down the business it had acquired from Xonics.

Mammography also lagged in Japan. A small-scale breast cancer screening program launched in 1977 relied on physical exams. Radiologists did sometimes X-ray breasts after discovering abnormalities in physical exams. However, Japanese physicians usually preferred ultrasound\(^h\) technology -- developed by Japanese researchers and Japanese companies\(^i\) -- when diagnosing breast cancer.\(^3\)\(^6\)

The preference for ultrasound in Japan would turn out to have unexpected advantages. Research later showed that dense breast tissues reduced the accuracy of mammograms. And, although dense breast tissue is more common in Japan, it is also found in women in other parts of the world.\(^3\)\(^7\) Therefore, the possibly fortuitous choice that Japanese companies had made later gave them advantages in selling ultrasound equipment for breast examinations abroad – and gave many American and European women with unusually dense breast tissue better options for diagnosis.\(^j\)

**Producers of Equipment and Film**

Producers of traditional X-ray equipment and film dominated the sales of the specialized mammographic equipment and film in the United States. As mentioned, French X-ray producer CGR was the first to sell specialized mammographic equipment. Except for one startup (See box “Xonics’ Mammography System”), all the other companies that started selling mammography equipment in the U.S. in the 1970s also sold X-ray and other medical devices. For instance, General Electric (GE), a multinational conglomerate that started selling mammography equipment in 1974, had been selling X-ray equipment since 1896. By the mid-1970s, GE had a large medical diagnostic business that included computed tomography (CT) equipment (which was also X-ray based) and ultrasound.\(^3\)\(^8\) Likewise, Siemens, GE’s longstanding German competitor, started selling mammography equipment in 1973. Siemens had also been selling X-ray equipment since 1896, and, by the mid-1970s, Siemens also had a large medical diagnostic business that, like GE’s, included CT equipment and ultrasound. Similarly, the three companies selling specialized film for mammography in the U.S., namely Kodak, Du Pont, and AGFA, were large, longtime producers of traditional X-ray film.\(^3\)\(^9\)

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\(^h\) Ultrasound devices use sound waves to create images of the soft tissues and organs inside the body.

\(^i\) Hitachi is a striking example: as of 1980, it was one of the top X-ray producers in Japan and had a small share of Japanese ultrasound sales. When Hitachi developed breast imaging equipment, it invested primarily in ultrasound technology rather than X-ray. The company did patent an X-ray mammography device in 1989 but did not market it. In the 1990s, the company formed an agreement to market and distribute U.S.-based Lorad’s analog mammography equipment in Japan.

\(^j\) In the United States, researchers estimate that as many as 44% of women would benefit from breast cancer screening done with alternative imaging technologies.
Four companies that sold mammographic equipment in the U.S. (including CGR) also served the European market, as did three small European X-ray producers that did not sell in the United States. Likewise, Kodak, Du Pont, and AGFA sold specialized film – and Xerox its plates that could be used instead of film – in Europe as well as the U.S. 40

Only three companies sold mammographic equipment or film in Japan by the end of the 1970s: Toshiba, a Japanese multinational that, like GE and Siemens, was a longtime producer of traditional X-rays and other medical devices; Du Pont (selling film); and Xerox (selling plates). 41 (See Exhibit 3)

**Advances in Diagnostic Mammographic Equipment**

Most mammographic equipment sold by CGR and its competitors in the 1970s did not distinguish between screening and diagnosis: it simply produced images that revealed the existence of lumps (or other such abnormalities) and indicated whether the lumps were likely to be malignant. However, these images did not provide much information about the precise location of lumps. Therefore, to perform a biopsy – the next step in diagnosing potential tumors -- surgeons had to cut open breasts extensively. And extensive cutting made biopsies disfiguring and dangerous. 42

In the mid-1970s, a Swedish radiologist collaborated with Tekniska Rontgencentralen, a Swedish producer of industrial X-ray equipment, to develop equipment that produced “stereoscopic” images that provided more precise information about the location of lumps. The equipment also included a table for patients to lie down on. Previously, patients sat upright making it difficult to remain still during diagnostic procedures. 43 (See Figure 2)

Radiologists could use the stereoscopic images to insert a thin wire that guided surgeons to where the biopsy was taken. Alternatively, radiologists could themselves extract suspect cells using a very fine needle instead of having surgeons cut open breasts. However, although the fine needle procedures were “minimally invasive” and produced less discomfort and scarring, they required more expertise, which many radiologists did not have. And, even experts made mistakes. Therefore, the Swedish innovation did not significantly change normal diagnostic practice in the 1970s – and besides Tekniska Rontgencentralen, no other producer offered stereoscopic imaging equipment at that time. 44

In the following decade, however, diagnostic practices changed, and more companies sold equipment targeted for diagnostic use that provided stereoscopic images and positioned patients horizontally. Thus, diagnostic equipment and screening equipment (that did not produce stereoscopic images and continued to position patients upright) would emerge as distinct categories. 45

**Figure 2** A woman seated in position for screening mammography in front of CGR’s Senographe, circa 1970 (left and middle), and a breast biopsy table circa 1987, on which a woman would lie prone with her breast and arm positioned through the hole (right).

2. Use Broadens (1980s)

**New Equipment and Rules**

In the 1980s, companies developed equipment with controls and filters that (when used with newly-available, more sensitive film) reduced radiation exposure. The improvements also reduced the risks of misdiagnosis by producing more detailed images. In addition, companies introduced basic, low-end devices priced at $16,000 in 1989, down from $65,000 in the early 1980s.46

New rules encouraged the use of the new equipment. Laws passed by the U.S. federal and state governments between 1986 and 1992 established quality standards for and required regular inspections of equipment. These standards and inspections forced hospitals to stop adapting general purpose X-ray equipment for mammography, as many had previously done.47 Some states also passed laws requiring insurance companies to reimburse for screening mammography – and radiologists to perform the screening on equipment that met the new quality standards. A newly-formed breast cancer advocacy group that had lobbied for the laws also educated women about the benefits of such screening.48 (See Exhibit 4) By 1991, the number of women who were regularly screened nearly doubled, to almost fifty-five percent of American women over age forty, up from less than thirty percent in 1987.49

Mammographic installations in the U.S. also received an unintended boost from cost-containment rules introduced to limit hospitals’ purchases of expensive computed tomography1 (CT) and magnetic resonance imagingm (MRI) units. These rules encouraged radiologists to open imaging centers that were exempt from purchasing restrictions because they were not affiliated with hospitals. These new imaging centers had then bought mammographic equipment to round out their diagnostic offerings. By 1990, forty-seven percent of centers offered screening and diagnostic mammography.50

The introduction of better, cheaper equipment combined with the new rules helped to increase installations of mammographic units by nearly twenty-fold in the United States between 1983 and 1990.51 (See Figure 3)

**Figure 3** Estimated Number of Mammographic Units Installed in United States

![Image of Figure 3](image-url)


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k Although experts disagreed for decades about when women should begin to get regular mammograms, the American Cancer Society and American College of Radiology maintained that regular screening should begin at age 40, and the Centers for Disease Control and Prevention tracked utilization by women aged 40 and older.

1 As previously mentioned, CT is an advanced digital X-ray technique.

m MRI uses magnetic fields and radio wave pulses to obtain data used to construct images.

n For a full explanation of these regulations, please refer to our computed tomography, magnetic resonance imaging, and ultrasound case studies.
Mammography in Europe and Japan

The results of large-scale trials conducted in Sweden (published in 1985) suggested that regular screening could reduce breast cancer deaths by about thirty percent, while a small-scale trial in the Netherlands (published in 1984) suggested screening could halve deaths. These trials were apparently influential. Belgium, Denmark, Greece, Ireland, France, Luxembourg, Portugal, and Spain started national screening programs in 1986. By 1991, Finland, Italy, the Netherlands, and the United Kingdom also had programs. And, because national health insurance plans covered the cost, screening was free for the women undergoing the procedure.

In Japan, mammography use continued to lag. The small-scale program to screen healthy women that had started in 1977 had been turned into a national program in 1987; however, physicians continued to rely primarily on physical examination for screening. Mammography was used – if at all – when there was a question about whether an abnormality found by a physical examination warranted a biopsy.

Producers of Equipment and Film

Twenty-four companies entered the rapidly growing American market for mammographic equipment in the 1980s – two and a half times as many as in the 1970s. Two thirds of the entrants specialized in screening equipment that did not include stereoscopic imaging. (Stereoscopic imaging was offered in diagnostic equipment by 1970s-era producers, like GE and Fischer who also sold screening equipment.)

Although, as in the 1970s, a majority of entrants had existing X-ray businesses, now about a third were startups. Meanwhile, four companies, including pioneer CGR, sold out their entire medical diagnostic businesses (including mammography) to competitors, mainly large industrial conglomerates like General Electric. In addition, Xerox shut down its plate business in 1989.

Far fewer companies entered the European market in the 1980s (just six) and only three companies started selling in Japan. Meanwhile, three companies that had exited the American market (including CGR and Xerox) also stopped selling in Europe and Japan. (See Exhibit 5)

Advances in Diagnostic Mammography

In 1988, a group of radiologists in Colorado (who were not affiliated with an equipment manufacturer or a university research group) adapted a so-called “biopsy gun,” previously used to diagnose kidney and prostate cancer, for diagnosing breast tumors. Developed in Sweden in the early 1980s, the “gun” was a small box containing a thin, spring-loaded needle that was shot into tissue suspected to contain malignant cells. The needle would pierce the tissue, scrape a sample, and then retract, leaving only a small hole to heal. By the mid-1980s, urologists commonly used the gun. The Colorado radiologists combined the gun with the diagnostic mammographic equipment developed in Sweden in the late 1970s. As previously described, the 1970s Swedish innovation (which combined stereoscopic images and tables) could be used in “minimally invasive” fine needle biopsies of suspect cells. The needles shot from guns extracted more cells, resulting in fewer missed cancers, than biopsies performed with fine needles. However, although the new minimally-invasive biopsies were now at least as good (or better) than open surgical biopsy, the gun-based devices were slow to catch on, possibly due to radiologists’ reluctance to try the new procedure. Companies continued to sell diagnostic equipment without biopsy guns for another decade.

(Equipment without biopsy guns did however incorporate the controls, filters, and film used to improve screening equipment in the 1980s. This made images of suspect lumps that were sharper, could be magnified with less blurring, and required less radiation exposure.)

0 Only one company, 3M, started selling specialized film, and none of the three established film producers exited.
3. Mammography Digitized (1990s and 2000s)

Technological Challenges and Advances

As far back as the 1970s, researchers had believed digitized X-ray images that could be processed by computers would improve the safety and effectiveness of mammography. They anticipated for instance that computerized enhancement of images would help precisely locate and identify the boundaries of small tumors and that computers would save radiologists time by flagging suspicious lumps. Researchers also believed digitized images could be produced with less radiation.

Researchers first tried using scanners to digitize X-ray images produced on paper from Xerox’s plates, but the low resolution scanners then available could not reproduce the sharpness of the original paper printouts. Researchers also tried to directly record images with electronic sensors, but sensors at the time, like scanners, also could not produce sharp images. Screening mammography presented an additional problem: it required equipment that could X-ray a whole breast at once. However, sensors could not produce large images without distortion.

Participants at a 1991 NCI workshop agreed that improved electronic sensors were more likely to increase sharpness and reduce distortion than improved scanners. Therefore, the NCI promoted collaboration between developers of mammographic equipment and government agencies that had already developed advanced sensors for military, space, and energy applications.

NCI-sponsored collaborations first applied new sensor technologies to diagnostic equipment that required detailed images of only a part of a breast, and thus avoided the problem of producing large undistorted images of the whole breast (needed for screening). In about a year, developers were able to introduce digital equipment that produced detailed images more rapidly than analog diagnostic equipment. The new sensor-based digital equipment (introduced in 1992) also typically incorporated computer-controlled biopsy guns -- previously, radiologists aimed the guns by hand. The new computer-controlled units increased the accuracy and speed of biopsies. By 1997, digital diagnostic equipment accounted for seventy-five percent of diagnostic mammography sales in the United States, and by 2000, digital units accounted for almost ninety percent of sales (See Exhibit 6).

Developers of sensor-based diagnostic equipment also attempted to solve the distortion problems that had limited the digitization of screening equipment – for which the market was much larger. (Screening equipment sales in the U.S. amounted to $134.5 million compared to $7 million of diagnostic equipment in 1997). Efforts to reduce distortion included using image-capturing panels with more (and sometimes larger) sensors, as well as computers with faster processors, more storage capacity, and better software. By the mid-1990s, three companies, which had already started selling digital diagnostic equipment, had developed and started to test prototypes for screening.

While most developers focused on using electronic sensors to digitize images, Fujifilm, a longtime Japanese producer of X-ray film, took a different approach. By the early 1980s, Fujifilm had developed plates that (like Xerox’s plates) substituted for X-ray film in existing X-ray equipment. Images recorded by the plates were digitized with laser scanners. Fujifilm first marketed the plates and laser scanners for general X-ray use. They quickly proved popular in Japan, but adoption in Europe and the U.S. grew more slowly. Although existing X-ray equipment could be retrofitted for plates, few radiology departments were equipped with the computer networks, electronic storage systems, and video monitors necessary to support digitized X-rays. (As mentioned, Xerox had stopped selling its image recording plates in 1989.)

Initially, images produced by Fujifilm’s plates-and-scanner alternative also lacked the detail necessary for screening mammography. By the mid-1990s, Fujifilm was able to produce more detailed images by

---

P Lorad, a manufacturer of low-radiation screening equipment, was first to introduce the new digital diagnostic equipment.
using faster processors and more memory in their scanners. However, by the time Fujifilm could produce satisfactory images for screening, changes in U.S. regulations created a new problem.\textsuperscript{75}

**Regulatory Barriers**

The 1976 Medical Device Regulation Act had given the FDA authority to require clinical trials to demonstrate safety and effectiveness for new devices deemed not “substantially equivalent” to existing devices.\textsuperscript{8} In the 1980s, the FDA had classified new mammographic equipment (then all analog) as substantially equivalent to pre-1976 equipment and thus exempt from clinical trials. And, in the early 1990s, the FDA again exempted digitized devices developed for minimally invasive, “gun”-based biopsies, deeming them as substantially equivalent to earlier analog devices.\textsuperscript{76} The exemptions helped the rapid adoption of digital diagnostic mammography.

Developers of digitized screening mammographic equipment also lobbied the FDA for a “substantially equivalent” exemption even before they had products ready to sell. In 1996, the FDA said it would exempt new digital screening equipment – if companies could show that it produced results that agreed with those produced by analog equipment.\textsuperscript{8} Two years later, GE and Trex Medical duly submitted what they believed was evidence of agreement for their newly developed digital screening products. However, in 1999 the FDA ruled that the data submitted by the two companies did not show sufficient agreement and therefore did not support a substantial equivalence exemption. The FDA further required that all digital equipment developed for mammographic screening undergo large-scale clinical trials to demonstrate its safety and effectiveness (rather than just “agreement” with prior analog equipment).\textsuperscript{77}

Trex Medical did not have the financial resources to meet the new FDA requirement,\textsuperscript{78} whereas GE immediately conducted more trials and secured approval from the FDA in 2000. A third American company, Fischer, also conducted trials and secured FDA approval in 2001. In addition, Siemens, which had started selling digitized diagnostic and screening equipment in the European market, applied for and secured FDA approval in 2004.\textsuperscript{79}

Meanwhile, the NCI and the American College of Radiology (ACR) conducted a large-scale trial evaluating the effectiveness of digital screening. The trial tested five devices and enrolled almost 50,000 women at thirty-three centers across the United States. Some devices included in the NCI/ACR trial had not acquired FDA approval: rather they were tested under an Investigational Device Exemption (which companies must secure from the FDA to run trials on their devices).\textsuperscript{80}

The results of the NCI/ACR trial published in 2005 suggested that the FDA’s previous determination that digital equipment did not produce the same results as analog equipment was technically correct -- but for reasons that may not have substantively supported the trial requirements that regulators had imposed. The NCI/ACR trial found that in some cases -- such as for (presumptively pre-menopausal) women under age fifty -- digital screening equipment produced more accurate results that therefore did not agree with the (less accurate) analog screening results.\textsuperscript{81}

Another result from the NCI/ACR trial published in 2006 showed that most digital equipment exposed patients to less radiation. The FDA later corroborated the safety advantages at a conference in 2009. The agency revealed that its analysis of data obtained during the mammography facility inspections required by law had shown that digital units reduced radiation exposure by up to forty percent.\textsuperscript{82} Nonetheless, the

\textsuperscript{8} Previously the FDA only had such authority over new drug introductions.

\textsuperscript{7} Analog screening and digital diagnostic equipment may have also been considered equivalent because they used the same or similar X-ray generators. In the 1990s, digital screening equipment with integrated sensors sometimes featured new, computer-controlled X-ray generators that borrowed technologies from CT scanners.

\textsuperscript{8} By requiring evidence of “agreement,” the FDA held digital mammography to a standard similar to that of Egan’s early test of mammography’s “correspondence” to diagnoses made via traditional physical exams and surgical biopsies.
FDA declined to revise its 1999 rule requiring clinical trials, and between 2005 and 2010, just two other companies applied for FDA approval, and only one obtained it in 2006.\(^8^3\)

(The successful applicant in 2006 was Fujifilm, whose prototypes had been included in the NCI/ACR trial, under an Investigational Device Exemption. As mentioned, the company used plates and scanners, not sensors, to digitize images.)\(^8^4\)

**Effects of Digitization in the U.S.**

FDA trial requirements that restricted entry (combined with one exit) limited competition: by 2005, there were only three manufacturers offering digital screening equipment, compared with approximately forty companies selling analog equipment. Limited competition and the benefits of digitized screening allowed manufacturers to charge much higher prices for digital equipment than for analog equipment – up to six times more. Nonetheless, digital screening mammography sales caught up to analog by 2005 and, after the publication of the NCI/ACR results, digital displaced analog at an even faster rate. (See Figure 4 and Exhibit 7).

**Figure 4** Screening Mammography Units Sold (North America, predominantly United States)

![Figure 4](image1)


**Digitization in Europe and Japan**

Although European companies were not leaders in digitizing diagnostic mammography, American companies had introduced their digital diagnostic products in Europe by the mid-1990s. By the late 1990s, digital diagnostic equipment accounted for nearly ninety percent of total diagnostic equipment sales (as they did in the United States as well).\(^8^5\) (See Exhibit 7)

As in the U.S., screening equipment continued to significantly outsell diagnostic equipment in Europe.\(^8^6\) (See Exhibit 6) And, in this larger category, less stringent rules gave European users earlier access to digitized equipment. Unlike the FDA, European regulators did not require trials to establish the effectiveness of new medical devices: companies only had to satisfy safety standards.\(^8^7\) Therefore, Trex Medical was able to introduce its digitized screening equipment in Europe in 1998 – but, as mentioned, was never able to secure FDA approval to sell in the U.S. Similarly, GE could sell its digital screening equipment in Europe in 1999, a year before it had permission to sell in the U.S.\(^8^8\)

Most notably, Fujifilm could offer its plates and laser scanners in Europe as an alternative to Trex’s and GE’s sensor-based equipment in 1998 – eight years before receiving FDA approval to sell in the United States. By 2005, two other multinational film producers – Kodak and AGFA – had also taken advantage of Europe’s less stringent requirements to introduce their own plates and scanners. And earlier availability made plates more popular in Europe than in the U.S. In 2007, plates and scanners accounted for a third of
digital screening mammography sales in Europe, whereas in the United States, they only accounted for two percent of sales that year.\textsuperscript{1}\textsuperscript{89}

Mammography in Japan gradually increased in the 1990s and 2000s. Japanese studies published in the 1990s showed that screening with mammography identified more tumors than screening with physical examinations alone.\textsuperscript{90} The studies, along with rising deaths from breast cancer, convinced the Japanese government to launch a national screening program in 2000 that recommended women over age forty have both a mammogram and a physical examination every two years – both of which would be paid for by the country’s health insurance program.\textsuperscript{91} More screening identified more tumors and lumps which in turn increased diagnostic mammography, typically using digitized equipment. By the late 1990s, digital diagnostic equipment accounted for almost ninety percent of total diagnostic equipment sales in Japan, as it did in Europe and the United States.\textsuperscript{92}

As in Europe and the U.S., screening equipment continued to significantly outsell diagnostic equipment in Japan. But the overall usage of both was much smaller in Japan.\textsuperscript{93} (See Exhibit 8). And, the digitization of screening in Japan took a different path. Japanese radiologists had started using Fujifilm’s plates and laser scanners for mammography in the mid-1990s, whereas sensor-based digital screening equipment was not available in Japan until 2000.\textsuperscript{94} Additionally radiologists continued to favor analog equipment (which itself had been improving) to a much greater degree than their American and European counterparts. Therefore, the sales and usage of sensor-based digital screening in Japan was negligible – as of 2003, only three sensor-based units had been sold in all of Japan.\textsuperscript{95} (See Exhibits 7 and 8)

**Producers of Equipment and Film**

Entry into the American mammography equipment market progressively declined in the 1990s and 2000s. Whereas in the 1980s (before any digitization had occurred), twenty-four companies had started selling mammographic equipment, only seventeen started selling in the 1990s, and nine started selling in the 2000s. Meanwhile, twice as many companies departed between 1990 and 2010 as had in the 1980s: eleven shut down or were acquired, most by 2000.\textsuperscript{96} But, because entrances exceeded exits, the total number of producers increased.

Most entrants (See Table 2) offered improved analog screening equipment – the sales of which were declining – while a few others specialized in diagnostic equipment – the sales of which had always been relatively small. Therefore, even though the number of competitors increased, so did concentration, with two companies offering digitized equipment dominating the market: long-standing producer GE, and a newcomer, Hologic. Hologic, which had started as a producer of bone density scanners, had acquired the digital mammography businesses from Trex Medical and Fischer in the 2000s. The acquisitions enabled Hologic to outsell GE in North America.\textsuperscript{11} By 2007, Hologic accounted for over sixty percent of screening mammography sales and over eighty percent of diagnostic mammography sales.\textsuperscript{97}

\textsuperscript{1} Sensor-based systems significantly “outsold” plate-and-scanner combinations both in Europe and the U.S. because sensor-based units included X-ray generators, making their prices significantly higher. Plate and laser scanner combinations did not. Instead, they were used to retrofit existing analog X-ray equipment. Plates and laser scanner combinations cost about a quarter of the cost of sensor-based units.

\textsuperscript{11} North American revenues were based predominantly on U.S. sales.
Table 2  Categorization of entrants into the U.S. Market (from 1990 to 2010)

<table>
<thead>
<tr>
<th>Target Market</th>
<th>Technology</th>
<th>Analog</th>
<th>Digital</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screening</td>
<td></td>
<td>17</td>
<td>3</td>
</tr>
<tr>
<td>Diagnosis</td>
<td></td>
<td>3</td>
<td>3</td>
</tr>
</tbody>
</table>


Note:  A small number of companies, most notably Giotto, Instrumentarium, Trex, and Hologic, occupied more than one cell in the table above. In addition to the companies counted in the table, two companies produced digital workstations and accessories, three produced film digitizers, and products could not be identified in the case of five companies.

Fewer companies started selling mammography equipment in Europe in the 1990s and 2000s than had in the United States. Large companies that started selling in the U.S. also sold in Europe, but many small American entrants did not, and Europe had only a few new domestic producers. (American producers that exited their domestic market also stopped selling in Europe, but there were no significant exits by European companies.)

GE and Siemens accounted for about seventy percent of the European mammography equipment sales revenues in the late 2000s, while Hologic failed to make inroads in Europe as it had done in the United States.

Entrants into the Japanese market increased in the 1990s and 2000s, however, the overall number of producers remained small -- about a dozen in all. (See Exhibit 8) Half the post-1990 entrants offered digital equipment (mostly plates and scanners for screening, as previously mentioned), and the other half sold analog screening equipment. As in the U.S., the market was highly concentrated, with just four companies accounting for over eighty percent of sales revenues by 2002. And, Fujifilm, which had previously not been a significant player in mammography before the mid-1990s, had secured well over half the share.

4. Epilogue (post-2010)

Screening mammography use and mammographic equipment installations, having reached a high level, plateaued. Old controversies about the frequency of screening and the screening of pre-menopausal women that had first surfaced with the publication of John Bailar’s 1976 report could not be resolved, despite numerous studies over several decades in many countries. New controversies about whether the detection and removal of very early-stage breast cancers (particularly in older women) reduced deaths emerged. Another large-scale trial is under way, but it remains to be seen whether it will “…break the deadlock in [the] debate and advance towards a new, dynamic approach to breast cancer screening,” as its researchers hope. (See Exhibit 9)

In addition, ultrasound and MRI, which did not pose radiation risks, came into increased use on women with dense breast tissues. In developing economies, where mammography installations had not reached a high level and breast cancer deaths were rising, expansion of mammography was limited by the prevalence of dense breast tissue and by the cost of the procedure.

The United States remained the largest market, although prices and revenues declined there by almost thirty percent. The declines came about after the FDA issued new rules for digital mammography in 2010, increasing competition. By then regulators considered the technology mature enough to treat any new equipment as an extension of existing equipment (and thus exempt from clinical trials). Shortly thereafter,
six companies – predominantly producers of X-ray and cameras based outside the U.S. – offered digital mammographic equipment for screening and helped drive down prices.\textsuperscript{106}

Meanwhile, efforts to improve digital mammography by reducing misdiagnoses and unnecessary treatment continue. Using technologies similar to those used in CT scanners, Hologic developed screening mammography equipment that produces detailed three-dimensional (or “3D”) breast X-rays.\textsuperscript{107} Since its introduction in 2011, 3D mammography improved diagnosis and treatment for women with dense breasts.\textsuperscript{108} Some startups are using artificial intelligence in an effort to make it feasible for computers to assist physicians with diagnoses by accurately identifying suspicious lumps. Others (who are not selling mammography equipment themselves) are developing genetic tests that could help doctors identify and aggressively treat malignant tumors that are likely to grow quickly while reducing the overtreatment of slow-growing and less deadly malignancies. These tests could potentially reduce concerns that discourage mammographic screening.\textsuperscript{109}
Exhibit 1

The FDA’s Mammography Survey

The U.S. Food and Drug Administration (FDA) surveyed mammography procedures and equipment in forty-two states in 1977 and 1978.

The FDA found that about 550 installations used specialized mammographic equipment (first developed by Charles Gros and CGR), typically with highly sensitive, specialized mammographic film, as recommended by Robert Egan and sold at that time by Kodak and Du Pont.

The rest (about 2,230 units) were general purpose units. Some used standard film, others used specialized film, and yet others used Xerox’s plates instead of film.

The FDA’s survey showed wide variations in safety and accuracy depending on the equipment and film used.

- General purpose equipment used with standard X-ray film was the most unsafe and inaccurate option: it exposed patients to the most radiation and produced the blurriest images. Inspectors found that eighty-eight percent of general purpose units used with standard film worked incorrectly, often because of operator error.

- Xerox’s plates (used to retrofit general purpose equipment) worked correctly more often, but incorrect operation was still high — over twenty-five percent.

- Use of specialized mammographic film exposed patients to the least radiation and produced the sharpest images. However, if the specialized film was used with general purpose units, the equipment operating errors occurred over fifty percent of the time. In contrast, specialized equipment used with specialized film reduced errors to just six percent.

In 1955, two American physicians working on civil defense medical services reported on a new method for producing X-ray images similar to those used in Xerox’s newly-available photocopiers. The plates required no special, costly chemicals to produce very detailed, lasting images (in blue ink on white paper). “Although our initial interest in xeroradiography came about because of civil defense,” the physicians wrote, “we have been impressed from the start with the possibility of using the method in routine clinical radiography.”

Within a few years, researchers had tested xeroradiography for several applications, including mammography, and found the images rivaled and sometimes surpassed those made on X-ray film. In 1966, the American College of Radiology began working with Xerox to develop a commercial device.

Xerox’s xeroradiographic units were introduced in 1971 for use with general purpose X-ray equipment, but its cost-effectiveness, quality, and ease-of-use made it immediately popular for mammography. By the mid-1970s, over half the mammograms made in the United States were xeromammograms, and the device was being tested in Swedish clinical trials.

Critics questioned the safety of mammographic screening in 1976, and subsequent tests revealed that xeromammography was not as safe as mammography performed with specialized mammographic equipment and film (as noted in Exhibit 1). Despite improvements made in the 1980s, sales dwindled, and Xerox discontinued the device for general as well as mammographic uses in 1989.

### Exhibit 3  Companies entering mammographic equipment markets (and the country of their domicile) from 1966-1979

<table>
<thead>
<tr>
<th>Year of Entry</th>
<th>United States</th>
<th>Europe</th>
<th>Japan</th>
</tr>
</thead>
<tbody>
<tr>
<td>1966</td>
<td>Kodak (US)</td>
<td>Compagnie Générale de Radiologie (France)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Xerox (US)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1971</td>
<td>CGR (France)</td>
<td>Kodak (US)</td>
<td>Siemens (Germany)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Picker (US)</td>
<td></td>
</tr>
<tr>
<td>1972</td>
<td>Du Pont (US)</td>
<td>Xerox (US)</td>
<td></td>
</tr>
<tr>
<td>1973</td>
<td>Siemens (Germany)</td>
<td>Philips (Netherlands)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Philips (The Netherlands)</td>
<td>Du Pont (US)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Picker (US)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fischer (US)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1974</td>
<td>General Electric (US)</td>
<td>AGFA/Gevaert (Belgium)</td>
<td></td>
</tr>
<tr>
<td>1975</td>
<td>Technicare (US)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1976</td>
<td>Xonics (US)</td>
<td>Valmet (Finland)</td>
<td>Elema-Shonander (Sweden)</td>
</tr>
<tr>
<td>1977</td>
<td>AGFA/Gevaert (Belgium)</td>
<td>Tekniska Rontegencentralen (Sweden)</td>
<td>Xerox (US)</td>
</tr>
</tbody>
</table>

Exhibit 4

Breast Cancer Advocacy

Before the 1970s, treatment for breast cancer was limited to radical mastectomies that removed entire breasts. This disfiguring surgery kept few women alive for more than five years.

Explicit mention of the disease was avoided; conversations referred to women who had “The Big C.”

In November 1972 Shirley Temple Black, a former child movie star who had become a diplomat, came forward with her breast cancer diagnosis. In 1974, First Lady Betty Ford and the vice-president’s wife, “Happy” Rockefeller, followed Black’s lead. The publicity helped promote early detection via screening mammography sponsored by the NCI and the American Cancer Society. Later, other celebrities revealed their cancer diagnoses to promote screening and raise funds for research.

In the early 1980s, Susan G. Komen Foundation provided another boost. Nancy Brinker had started the foundation in 1982 by to honor her sister Susan Komen, who had died of breast cancer in 1980. By 1985, the Texas-based organization had raised over a million dollars for research through luncheons, cocktail parties, dinner dances, polo matches, and a road race. The foundation also sponsored educational seminars and an award named for First Lady Betty Ford.

By the late 1980s, the Komen Foundation had become a powerful advocacy group, lobbying for state and federal laws that spurred advances in mammographic equipment, required insurance coverage for screening, increased funding for research, and created another federally-funded free screening program (instituted in the 1990s). The foundation also taught women how to self-examine their breasts and recommended when and how often women should undergo screening mammography.

In 1991, the Komen Foundation started its Pink Ribbon Campaign, which is credited with raising millions of dollars for breast cancer advocacy, research, and education.

Exhibit 5  Companies entering mammographic equipment markets (and the country of their domicile) from 1980-1989

<table>
<thead>
<tr>
<th>Year of Entry</th>
<th>United States</th>
<th>Europe</th>
<th>Japan</th>
</tr>
</thead>
<tbody>
<tr>
<td>1980</td>
<td>Sorodex (Finland)</td>
<td>Sorodex (Finland)</td>
<td>Siemens (Germany)</td>
</tr>
<tr>
<td></td>
<td>Elscint (Israel)</td>
<td>The General Electric Company (GEC, UK)</td>
<td></td>
</tr>
<tr>
<td>1981</td>
<td>Ohmic (US)</td>
<td>GE (US)</td>
<td>GE/Yokogawa (US/Japan)</td>
</tr>
<tr>
<td>1982</td>
<td>3M (US)</td>
<td>Gilardoni (Italy)</td>
<td>Shimadzu (Japan)</td>
</tr>
<tr>
<td>1983</td>
<td>Custom Medical Products (US) AS&amp;E (US) Amerisys (US) Ausonics Corp. (Australia)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1988</td>
<td></td>
<td>Planmed (Finland)</td>
<td></td>
</tr>
<tr>
<td>1989</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Source: Kimme-Smith et al (1988); Anderson (1990); Haus (1990, 2002); the Health Device Sourcebooks; the Medical Device Registers; and the FDA 510(k) database.

Exhibit 6  Mammography Sales Revenues in Major Markets in 2000

<table>
<thead>
<tr>
<th>Region</th>
<th>Diagnostic (% digital)</th>
<th>Screening (% digital)</th>
</tr>
</thead>
<tbody>
<tr>
<td>North America (predominantly the U.S.)</td>
<td>$12.9 million (89%)</td>
<td>$131.2 million (17%)</td>
</tr>
<tr>
<td>Europe (predominantly Western Europe)</td>
<td>$7.6 million (86%)</td>
<td>$102.8 million (9%)</td>
</tr>
<tr>
<td>Japan</td>
<td>$3.7 million (89%)</td>
<td>$15.7 million (6%)</td>
</tr>
</tbody>
</table>

### Exhibit 7 Number of digital screening units installed in major markets (and digital screening units as a percentage of total screening units)

<table>
<thead>
<tr>
<th></th>
<th>2000</th>
<th>2003</th>
<th>2007</th>
<th>2010</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>United States</strong></td>
<td>48 (&lt;1%)</td>
<td>465 (3%)</td>
<td>3,805 (28%)</td>
<td>8,957 (72%)</td>
</tr>
<tr>
<td><strong>Europe</strong></td>
<td>12 (&lt;1%)</td>
<td></td>
<td>~4000 (50%)*</td>
<td></td>
</tr>
<tr>
<td><strong>Japan</strong></td>
<td>2 (&lt;1%)</td>
<td>3 (&lt;1%)</td>
<td>143 (~5%)</td>
<td>~400 (10%)**</td>
</tr>
</tbody>
</table>

*Comparison does not include plates and laser scanners. *Based on 2014 and 2015 installations. **Based on 2011 installations.

### Exhibit 8
Companies entering mammographic equipment markets (and country of their domicile) from 1990-2009

<table>
<thead>
<tr>
<th>Year of Entry</th>
<th>United States</th>
<th>Europe</th>
<th>Japan</th>
</tr>
</thead>
<tbody>
<tr>
<td>1990</td>
<td>Giotto (Italy)</td>
<td>International Medico Scientific (Italy)</td>
<td>Acoma Medical Imaging (Japan)</td>
</tr>
<tr>
<td></td>
<td>Acoma Medical Imaging (Japan)</td>
<td>Giotto (Italy)</td>
<td>Hitachi (Japan)</td>
</tr>
<tr>
<td></td>
<td>BG Imaging Specialties (US)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>International Medico Scientific (Italy)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>York X-ray (US)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1991</td>
<td>American Shared Curecare (US)</td>
<td>Instrumentarium (Finland)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Camp-Ray (US)</td>
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<td></td>
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<tr>
<td></td>
<td>Coastal Medical Systems (US)</td>
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<td></td>
<td>Instrumentarium (Finland)</td>
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<td></td>
<td>LogETronics (US)</td>
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<td>RP Kincheloe (US)</td>
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<td>Universal Medical Systems (US)</td>
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<td></td>
<td>Vision Ten (US)</td>
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</tr>
<tr>
<td></td>
<td>Dynarad Corp. (US)</td>
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<tr>
<td>1992</td>
<td>Medical Systems Engineering (US)</td>
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</tr>
<tr>
<td></td>
<td>Trex (US)</td>
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<td>1993</td>
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<td>Sectra Imtech (US)</td>
<td>Fujifilm (Japan)</td>
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<tr>
<td>1997</td>
<td>Sterling Diagnostic Imaging (US)</td>
<td></td>
<td>Planned (Finland)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Instrumentarium</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>(Finland)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Fischer (United States)</td>
</tr>
<tr>
<td>1998</td>
<td></td>
<td>Trex (United States)</td>
<td>Fujifilm (Japan)</td>
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<td></td>
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<td></td>
<td>Hologic (United States)</td>
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<tr>
<td>2000</td>
<td>Vidar Systems Corp (US)</td>
<td>Cintec Medical (Israel)</td>
<td>Hologic (United States)</td>
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<td></td>
<td>Dba Systems (US)</td>
<td>Hologic (United States)</td>
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<td></td>
<td>Hologic (US)</td>
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<tr>
<td>2004</td>
<td>Barco (Belgium)</td>
<td>Barco (Belgium)</td>
<td>Totoku Electric (Japan)</td>
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<tr>
<td>2006</td>
<td>Electronic Business Machine Co. (US)</td>
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<td></td>
<td>Fujifilm (Japan)</td>
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<tr>
<td>2007</td>
<td>Onex (US)</td>
<td>Konica (Japan)</td>
<td>Konica (Japan)</td>
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<tr>
<td>2008</td>
<td>Dexela (US)</td>
<td>Metaltronica (Italy)</td>
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<td></td>
<td></td>
<td>Xcounter (Sweden)</td>
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<tr>
<td></td>
<td></td>
<td>Imaging Dynamics (Canada)</td>
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</table>

Exhibit 9

The Uncertain Benefits of Breast Cancer Screening

In 1995 a U.S. Office of Technology report, *Health Care Technology and Its Assessment in Eight Countries*, noted:

“...A large, well-designed randomized trial carried out in the Health Insurance Plan (HIP) of Greater New York during the 1970s, [showed] clear benefits from routine screening in terms of mortality from breast cancer in women over the age of 50.

...The HIP randomized trial offered the interventional group, approximately 31,000 women aged 40 to 64 years, four successive annual screenings with two-view mammography and breast physical examination. About 67 percent of the women accepted, and approximately 50 percent of those received at least three screenings. The trial showed a statistically significant reduction in mortality in women who were over 50 years of age at entry into the study. Five years after entry, the reduction in mortality was about 50 percent, falling to about 20 percent at 18 years after entry. For women 40 to 50 years of age at entry, the reduction in mortality was small (about 5 percent at five years, and not statistically significant).

[The HIP study was] ...followed up by two randomized studies in Sweden, one in the United Kingdom, and a number of nonrandomized studies. These studies in total seem to demonstrate benefit from screening but leave a number of unanswered questions. One problem is that each one has used a different screening regimen, so the independent contribution of the two methods of examination cannot be estimated... Another problem is that the studies have been done at different times with different X-ray technologies; the question of the usefulness of modern technology cannot then be answered. Nonetheless, it is widely assumed that modern X-ray mammography screening alone is of benefit.

A contentious issue is the question of screening women under the age of 50 years. In the United States some groups do not recommend screening women under 50 years of age, but others do. In Canada the Task Force on the Periodic Health Examination does not recommend screening younger women, but the province of British Columbia does support this practice.

A number of cost-effectiveness analyses of breast screening have been carried out... [One US study] estimated that a program that screened 25 percent of American women between the ages of 40 and 75 would cost $US 4.2 billion for annual breast physical examination alone and $US15 billion for examination plus mammography. Using outcomes from the HIP study, the marginal cost of adding a year of life with both examination and mammography would be $US 134,081 in the age group from 40 to 50 years; $US83,830 in the age group from 55 to 65 years; and $US92,412 in the 65 to 75 year-old group. Other studies have found lower costs per year of life added with breast cancer screening. Typical figures range between $US13,200 and $US28,000 per year of life saved.”

Twenty years later, many of the same concerns about the medical benefits remained unresolved:

- One American study (published in 2016) reported that “women were more likely to have breast cancer that was overdiagnosed than to have earlier detection of a tumor that was destined to become large.” The authors concluded, the reduction in breast cancer deaths was due to improved treatment rather than early detection.

- These results were corroborated by a similar study conducted in the Netherlands (published in 2017) that concluded that screening had little influence on mortality there, and older women were frequently overdiagnosed.

- As previously noted in the Epilogue, another large study is under way in the United States. As its lead researchers have observed, “There are few medical issues that have generated as much controversy as screening for breast cancer. In science, controversy often stimulates innovation; however, the intensely divisive debate over mammographic screening has had the opposite effect and has stifled progress. The same two questions—whether it is better to screen annually or bi-annually, and whether women are best served by beginning screening at 40 or some later age—have been debated for 20 years ...The WISDOM Study (Women Informed to Screen Depending On Measures of risk) is a pragmatic, adaptive, randomized clinical trial [that aims to] ...break the deadlock in this debate and advance towards a new, dynamic approach to breast cancer screening.”

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
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<tbody>
<tr>
<td>1895</td>
<td>X-rays discovered</td>
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<tr>
<td>1913</td>
<td>First X-ray images taken of breast cancer tumors.</td>
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<tr>
<td>1960-62</td>
<td>Egan reports a 97% correspondence rate and high rates of early detection for his mammography technique. Gershon-Cohen also reports on accuracy of early detection using mammography.</td>
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<tr>
<td>1963</td>
<td>Gros authors a textbook based on his mammographic technique and findings. National Cancer Institute (NCI) contracts with Health insurance Plan of New York (HIP) to run a clinical trial testing screening mammography.</td>
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<tr>
<td>1964</td>
<td>Kodak produces industrial X-ray films and screens vacuum-sealed together for high-quality, high-contrast breast X-ray images.</td>
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<tr>
<td>1966</td>
<td>CGR introduces the Senograph, an X-ray machine designed by Gros and engineer Emille Gabbay specifically for mammography, in Europe. Robert Egan moves to Emory University, where he trains radiologists from across the U.S. Xerox begins research into xeroradiography.</td>
</tr>
<tr>
<td>1971</td>
<td>Initial results from the HIP trial suggest that mammography reduces breast cancer deaths by forty percent. Congress passes the National Cancer Act, enabling the NCI to join with the American Cancer Society to fund a national free screening mammography program. Xerox brings xeroradiography to market. CGR’s Senograph introduced in U.S.</td>
</tr>
<tr>
<td>1973</td>
<td>Breast Cancer Detection and Demonstration Project (BCDDP) launched.</td>
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<tr>
<td>1975</td>
<td>The BCDDP grows to 29 centers across the U.S.</td>
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<tr>
<td>1976</td>
<td>John Bailar at the NCI raises questions about mammography’s accuracy and safety. Medical Device Act passed. Surgeons and radiologists propose the use of mammography to perform wire-guided localizations to prepare for biopsies.</td>
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<tr>
<td>1981</td>
<td>The BCDDP ends.</td>
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<tr>
<td>1982</td>
<td>The Susan G. Komen Foundation founded by Komen’s sister, Nancy Brinker.</td>
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<tr>
<td>1983</td>
<td>The Komen Foundation holds its first fundraising race in Dallas, Texas.</td>
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<tr>
<td>1985</td>
<td>Lazlo Tabar publishes initial data from Swedish trials confirming mammography reduces mortality rates and detects cancers at an earlier stage.</td>
</tr>
<tr>
<td>1986</td>
<td>National Breast Cancer Awareness Month established.</td>
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<tr>
<td>1987</td>
<td>GE acquires pioneer CGR.</td>
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<tr>
<td>1988</td>
<td>Partial coverage of mammograms begins nationally under Medicare, but not Medicaid. Radiologists develop new mammographic equipment designed to facilitate minimally invasive biopsies.</td>
</tr>
<tr>
<td>1989</td>
<td>Lazlo Tabar publishes additional data confirming mammography reduces mortality rates and catches cancers at an earlier stage.</td>
</tr>
<tr>
<td>1990</td>
<td>Full coverage of mammography begins for those on Medicare, but not for Medicaid recipients.</td>
</tr>
<tr>
<td>1991</td>
<td>Blue Cross Blue Shield becomes the first major private insurance company to cover mammographic screening for women over 40.</td>
</tr>
<tr>
<td>1992</td>
<td>Activists succeed in lobbying Congress for unprecedented levels of funding for breast cancer research. Mammography Quality Standards Act passed by Congress; the law requires inspections of mammography facilities and equipment. Lorad introduces diagnostic mammographic equipment for performing minimally invasive surgeries that features digital components. Within two years, competitors Fischer and Bennett will offer similar devices.</td>
</tr>
<tr>
<td>1993</td>
<td>The NCI returns to discouraging mammograms for women under 50; the American Medical Association follows, buts eventually reinstates recommendations that screening to start when women are 40.</td>
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<tr>
<td>1996</td>
<td>The FDA provisionally agrees to allow 510(k) approval of digital mammographic equipment for screening, provided companies submit data showing its equivalency to analog equipment.</td>
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<tr>
<td>1998</td>
<td>Trex Medical introduces sensor-based digital mammographic equipment for screening in Europe. Within a year, GE will introduce its sensor-based digital mammographic equipment for screening in Europe. Fujiﬁlm introduces plates that adapt analog equipment to produce digital images in Europe, where they quickly...</td>
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</table>
become a popular alternative to sensor-based digital mammographic equipment. (Radiologists in Japan had already been using Fujifilm’s plates for mammography.)

1999  The FDA rejects equivalency data submitted by GE and Trex Medical and requires clinical trials before approval to market digital mammographic equipment for screening.

2000  Hologic acquires Trex Medical.

2000  GE receives FDA approval to market its digital mammographic equipment for screening. In the next six years, only four other companies will receive approval: Fischer, Hologic, Siemens, and Fujifilm.

2005  Results of trial sponsored by NCI shows digital mammographic equipment for screening equivalent to standard mammography, except in use on patients under 50 years of age, when digital diagnoses women more accurately than analog.

2010  FDA changes rules for digital screening mammographic equipment and no longer requires clinical trials before marketing.

2011  Hologic introduces 3-D mammographic equipment under old FDA rules (already in trials when rule change made).

Source: Casewriter.
Endnotes


2 The mortality improvements in this study and others cited herein are thought to have been a combination of early detection and early treatment, unless otherwise mentioned.


5 By the 1950s, these results would have been presented to a large number of radiologists who met regularly through the International Club of Radiotherapists, which had been formed in Europe in 1953 and had active members based in Brazil, Canada, Colombia, Cuba, Guatemala, India, Mexico, Peru, the United States, Uruguay, and Venezuela.


8 Gros also recommended contrast agents (chemicals injected into the breast) be used to further improve the detail of X-ray images taken with Leborgne’s technique. However, such an improvement made the procedure more time consuming, invasive, and difficult to learn and execute. Jean Dalsace, *Gynecologic Radiography* (New York: Hoeber-Harper, 1959). Nonetheless, researchers in the 1980s did experiment with mammography conducted with digital X-ray fluoroscopic equipment and contrast agents that were usually used for coronary angiography – a process similar to what Gros had imagined in the 1950s.


12 The U.S. Public Health Service had been founded in 1798, and the National Cancer Institute had been founded in 1937.

13 Anderson was founded in 1941 as a cancer hospital and research center. Although affiliated with the University of Texas, the Institute emphasized collaboration across specialties in treating patients to a greater degree than most traditional teaching hospitals.

14 Clark et al., Reproducibility of the Technic of Mammography (Egan) for Cancer of the Breast.

15 The lead researcher on the Philadelphia study was far more optimistic than Egan about mammography’s capacity to serve as a screen. The article describing their results began: “Can delayed diagnosis and treatment of breast tumors be avoided by periodic x-ray examinations of women over 40 years of age? The results of a 5-year study, reported and interpreted here, indicated ‘yes.’” Gershon-Cohen JJ and Berger SM, “Detection of Breast Cancer by Periodic X-Ray Examinations.”

16 Clark et al., Reproducibility of the Technic of Mammography (Egan) for Cancer of the Breast.

17 The idea for the study was developed by Louis Robbins, who worked on cancer control for the U.S. Public Health Service, and Michael Shimkin, who headed a branch of the NCI devoted to statistical studies and epidemiology. (Shimkin is famous for conducting research that linked cigarette smoking to lung cancer.) They selected HIP because its director of research had been a statistician for the Public Health Service and one of its radiologists had already been trained in Egan’s mammography. HIP was also chosen because of its very large member pool (about 700,000 people) and its advanced electronic data system. The team that ran the study included Sam Shapiro, the statistician, Philip Strax, the radiologist, and Louis Venet, a clinician who handled referrals (and was needed, Shimkin recalls, to persuade surgeons to conduct surgery on patients who had no palpable cancers). Michael Boris Shimkin, As Memory Serves: Six Essays on Clinical Medicine and Public Health (Baltimore: Johns Hopkins University Press, 1986).


19 Shapiro, Strax, and Venet.

20 Mukherjee, The Emperor of All Maladies, 295.

21 Shapiro, Strax, and Venet, “Evaluation of Periodic Breast Cancer Screening With Mammography.”


23 Radiologists affiliated with the American Cancer Society had also been involved in planning the study that tested the reproducibility of Egan’s technique.


28 Jans et al., “The Status of Film/Screen Mammography. Results of the BENT Study.”


34 Mukherjee, The Emperor of All Maladies. And, as Mukherjee points out, the Scottish trials would turn out to be flawed in design.


38 Downloaded on June 5, 2018 from http://newsroom.gehealthcare.com/x-rays-and-ge-innovation-in-radiological-imaging/


43 Through the 1980s and 1990s, a few companies – most notably, GE – produced analog stereotactic diagnostic mammographic equipment that positioned patients upright. However, more companies made the table-based systems, and their sales overshadowed the sales of the upright units. Burbank. Frost & Sullivan (2001) World X-ray Mammography Market.

44 Burbank.

45 Both Leborgne and Egan had originally experimented with having women lie down during mammographic X-ray, but by the 1970s, screening mammography was performed on patients seated or standing upright. See: Gold, Bassett, and Widoff, “Highlights from the History of Mammography.”; Bassett and Gold, “The Evolution of Mammography”; Burbank.


According to a 1990 brief in *Medical Economics*, “After tremendous growth throughout the ’80s, the number of diagnostic imaging centers opening annually has leveled off. Many of the existing 1,195 centers have expanded the services they offer, however.” The accompanying chart showed ultrasound as the top service offered, with 49% of centers offering ultrasound imaging, and listed mammography next at 47%—both well above CT, MRI, X-ray, and other services. See: “Diagnostic Imaging Centers: Broadening Their Patient Bases.” *Medical Economics* 67, no. 23 (1990): 13. Imaging centers continued to proliferate in the 1990s. By 1997, there were approximately 2,500 imaging centers in the U.S. See: Frost & Sullivan. (4 January 1999) *World Ultrasound Equipment Markets*. Accessed March 2016; Section 3, Figures 3-01 and 3-02. McCue, P. “Marketing Considerations for Diagnostic Imaging Centers.” *Applied Radiology* 16, no. 10 (1987): 21-24.

51 Martin L. Brown, Larry G. ScD Kessler, and Fred G. DSc Rueter, “Is the Supply of Mammography Machines Outstripping Need and Demand? An Economic Analysis,” *Annals of Internal Medicine* 113, no. 7 (October 1990): 547-52, https://doi.org/10.1059/0003-4819-113-7-547; Bassett, “The Regulation of Mammography.” Brown, et al, acknowledge that they may be underestimating the total installed base in 1983-1984 and overestimating the base in 1989-1990 (both by small percentages of the whole—less than 10%), but they feel the overall rate of change is basically correct. In addition, there is a decline in use of general X-ray devices for mammography (to 1% of exams performed, down from an estimated 25+% of exams performed in late 1970s/early 1980s).


54 Specific examples of adoption in different European countries are discussed in, for example: H. David Banta, “Health Care Technology as a Policy Issue,” *Health Policy, Special Issue: Health care technology and its assessment in eight countries: Australia, Canada, France, Germany, Netherlands, Sweden, United Kingdom, United States*, 30, no. 1 (October 1, 1994): 1-21, https://doi.org/10.1016/0168-8510(94)00683-6. However, comprehensive adoption data does not exist for Europe.


57 Despite the limited use of mammography, however, the Japanese government did establish quality standards for mammographic equipment and educational standards for technicians operating the equipment and physicians interpreting the mammograms by the late 1980s. (See Abe et al., “Mobile Unit for Use in Mass Screening for Breast Cancer.” Ballard-Barbash et al., “Breast Cancer Screening in 21 Countries.”)

The most popular versions of these diagnostic mammography units were like those developed by Fischer: Fischer had acquired the rights to Tekniska Rontegencentralen’s device and incorporated the gun into the biopsy table, on which patients lay prone with their breasts immobilized. Researchers had initially tried the guns with GE’s diagnostic mammography equipment, which had seated patients upright, and found that some patients squirmed or fainted during the procedure. Burbank, “Stereotactic Breast Biopsy.”


Researchers were able to produce detailed and undistorted digital breast X-rays with modified computed tomography (CT) equipment, but the procedure was lengthy and costly, and it exposed patients to more radiation than standard mammography and required the use of contrast agents. Ackerman, “Computer Classification of Radiographs and Xerograms of the Breast”; Chang et al., “Computed Tomography in Detection and Diagnosis of Breast Cancer”; Kimme-Smith et al., “Digital Mammography A Comparison of Two Digitization Methods”; Maidment and Yaffe, “Scanned-Slot Digital Mammography”; Kimme-Smith, “New and Future Developments in Screen-Film Mammography Equipment and Techniques”; Chan et al., “Digital Mammography”; Chang et al., “Computed Tomographic Mammography Using a Conventional Body Scanner”; Zhou and Gordon, “Detection of Early Breast Cancer.”

Workshop attendees also noted that sensors might do the most to improve mammography for U.S. women in their 30s and 40s, who had benefited the least from standard mammography and who researchers were finding were more likely to have dense breast tissues. Shtern, “Digital Mammography and Related Technologies”; Daniel L. Winfield, “Aerospace Technology Transfer to


As noted above, the trial did not compare digital systems with each other, but against the so-called “gold standard” of analog screen-film mammography. However, the Fujifilm, GE, and Fischer systems performed very similarly. Hendrick et al., “Accuracy of Soft-Copy Digital Mammography versus That of Screen-Film Mammography According to Digital Manufacturer.”


84 By 1997, digital diagnostic equipment accounted for seventy-nine percent of diagnostic mammography sales revenues in Europe - slightly more than in the U.S., where they accounted for seventy-five percent. By 2000, digital units accounted for almost eighty-six percent of diagnostic mammography sales revenues in Europe - slightly less than in the U.S., where they accounted for ninety percent. Frost & Sullivan (2001). World X-Ray Mammography Market.


93 Japanese radiologists started using digitized diagnostic equipment around the same time as their European and American counterparts, after American companies introduced it in the mid-1990s. Likewise, Japanese radiologists adopted digital diagnostic equipment at about the same rate that their European and American counterparts had in the late 1990s. By 1997, digital diagnostic equipment accounted for seventy-one percent of diagnostic mammography sales revenues in Japan—slightly less than in the U.S., where they accounted for seventy-five percent, and Europe, where they accounted for seventy-nine percent. By 2000, digital units accounted for almost eighty-nine percent of diagnostic mammography sales revenues in Japan—about the same as the U.S., where they accounted for ninety percent, and a little more than in Europe, where they accounted for eighty-six percent. Frost & Sullivan (2003) *X-Ray Mammography Markets in North America and Japan and the Rest of the World,* Chapter 4, especially 4-22; Frost & Sullivan (2001). *World X-Ray Mammography Market,* 4-18, 4-55.


98 European entrants were also more likely to offer digitized equipment, and some focused on a relatively small domestic market. Four of the companies that exited the U.S. market also concurrently stopped selling in Europe. One, Philips, exited only temporarily, returning to the market in the early 2000s. Frost & Sullivan (2001). *World X-Ray Mammography Market.* Frost & Sullivan (2008) *European Mammography Systems Market,* 4-12. Nields, “FDA & Digital Mammography Why Has FDA Required Full Field Digital Mammography Systems to Be Regulated as Potentially Dangerous Devices for More Than 10 Years?”


