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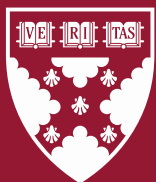
Case Histories of Transformational Advances

Mammography – Early Detection, Precise Diagnoses

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CASE HISTORIES OF TRANSFORMATIONAL ADVANCES

Mammography – Early Detection, Precise Diagnoses

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Abstract: This case history describes how the development of x-ray-based techniques and equipment (“mammography”) led 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: Like the other histories in this series, this advance 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 significant 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 thank Kirby Vosburgh for helpful information and suggestions.

Mammography

– Early Detection, Precise Diagnoses

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 relied on physical exams and surgical biopsies.¹ 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.²

Screening mammography has a greater impact, although diagnostic use came first. Screening in the United States, for instance, is thought to have helped reduce deaths from breast cancer by almost a quarter since 1990.³ By 2000, nearly three-quarters of American women over 50 (and nearly two-thirds of women in their 40s) were having regular mammograms.⁴ Screening has also created controversies about exposing healthy young women to X-ray radiation, as well as encouraging unwarranted treatment.⁵ Commercially, sales of screening mammography equipment are as much as ten times greater than the sales of diagnostic mammography equipment.⁶

The three main sections of this Note describe how: 1) the protocols and equipment, developed from 1950-1980, established a foundation for mammography; 2) improvements and new rules in the 1980s broadened use; and 3) digitization in the 1990s created a platform for more safety and accuracy.

1. Establishing the foundation (1950-1980)

Overcoming the Limitations of X-Rays. X-rays, discovered in 1895, were quickly adopted for 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, radiologists experimented⁷ with X-rays to detect breast cancer but could not sharpen blurry images.⁸ Physicians, therefore, relied on physical exams and biopsies.

In the 1950s, Raul Leborgne, a Uruguayan radiologist, developed a technique that significantly improved breast X-rays, revealing well-formed as well as emerging tumors. In a 1953 book, 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.⁹

Standardizing Diagnostic Mammography . Charles Gros, head of radiology at a cancer center affiliated with the University of Strasbourg (France), thought Leborgne's procedure was promising, but its description was inadequate for the typical radiologist. Gros, therefore, attempted to provide a more systematic description in his 1963 textbook *Diseases of the Breast*. Gros also collaborated with the French X-ray producer Compagnie Générale de Radiologie (CGR) to develop equipment to mechanize some steps.¹⁰ CGR introduced the equipment in Europe in 1966 and the U.S. in 1971.¹¹

This case history does not present original research or new thesis. Instead, it summarizes historical developments and includes questions to stimulate reflection and discussion.

Robert Egan, a radiologist at M.D. Anderson Hospital and Tumor Institute¹² 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 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 initially 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).

Egan's protocol, described in papers published in 1960 and 1962, had a ninety-seven percent correspondence with results of traditional diagnostic procedures (i.e., physical exam and biopsy). It also identified emerging tumors that traditional methods could not detect.¹³ (See box "How Robert Egan Developed and Tested Mammography Protocols").

While Egan was 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.¹⁴

Egan's work attracted the attention of the National Cancer Institute (NCI), which sponsored research, and the U.S. Public Health Service (USPHS), which organized prevention and treatment programs.¹⁵ To find out if radiologists at hospitals that lacked M.D. Anderson's resources and tradition of multi-specialty collaboration¹⁶ 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. Their results 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 large-scale screening of asymptomatic women.¹⁷ Jacob Gershon-Cohen's Philadelphia study¹⁸ and the NCI's own experience in the 1950s of promoting the so-called "Pap smear"^a test to screen women for early signs of cervical cancer also encouraged the NCI.¹⁹

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

^a 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.

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 studies suggested mammography could be used for screening because the procedure found tumors that 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).

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.²⁰ 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.²¹

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 physicians. 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.)²²

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.²³ 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 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.²⁴

Early results, published in 1971, suggested screening had dramatically reduced 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.²⁵

The HIP results helped spur a free screening program throughout the United States, which was co-sponsored^b by the NCI and the American Cancer Society (ACS).²⁶ By 1975, two years after the program was launched, over 280,000 women had been screened.²⁷

Concerns about Safety and Accuracy. In 1976 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).^c Thus, mammographic screening might cause as many deaths as it prevented.²⁸

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

	Study Group		Control Group	
	Total	Died of Breast Cancer	Total	Died of Breast Cancer
Total Selected	30,426	70	31,007	108
Screened	20,166	45		
Mammographic Exams	64,810			
Unscreened	10,260	25		
Breast Cancers Reported	299	70	285	108
Not Detected on Screening	167	53		
Screened at Least Once	93	28		
Refused Screening	74	25		
Detected on Screening	132	17		
Patient History or Physical Exam only or both	59	9		
Patient History or Physical Exam or both plus Mammography	29	7		
Mammography only	44	1		

Source: Bailar JC 3rd. "Mammography: a contrary view." *Ann Intern Med.* 1976 Jan;84(1):77-84. doi: 10.7326/0003-4819-84-1-77. PMID: 1106292.

Note: Bailar did not consider the slightly higher number of cancers reported in the screened group 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.^d The National

^b 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."

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

^d 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.

Institutes of Health (of which the NCI is a part) also convened its first ever “consensus conference”^e 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).²⁹

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.³⁰

Problems with Equipment, Film, and Human Error. A Food and Drug Administration (FDA) study published in 1979³¹ (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 the 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 started selling specialized CGR-style equipment. However, the controversy about screening that erupted in 1976 discouraged manufacturers from marketing or improving specialized equipment.³² As of 1979, more than half of American hospitals were using general-purpose equipment that increased radiation exposure when used for mammography.³³
2. *Not using specialized film.* As mentioned, Egan’s protocols 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.³⁴ (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.³⁵

^e 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.

Screening in Europe and Japan. Mammography did not gain the same support in Europe that it did in the United States.³⁶ By the mid-1970s, only Sweden and Scotland had trials for screening mammography under way.³⁷ Initial results from the Swedish trials suggesting that mammography could reduce breast cancer deaths led to more trials in Sweden and, by the end of the 1970s, nationwide screening. However, besides Austria, other European countries did not start screening programs.³⁸

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 scans³⁹ -- developed by Japanese researchers and Japanese companies^f -- for diagnosing breast cancer.⁴⁰

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.⁴¹ Therefore, the possibly fortuitous choice that Japanese companies had made later gave them advantages in selling ultrasound equipment for breast examinations abroad -- and improved the options available to many American and European women with unusually dense breast tissue.^g

Advances in Diagnostic Mammography. Physicians in the 1970s typically used the same mammographic equipment for screening and diagnosis. The equipment produced images that revealed the existence of lumps (or other such abnormalities) and indicated whether the lumps were likely to be malignant. However, the images did not provide a clear-cut diagnosis or much information about the precise location of lumps. Therefore, to perform a biopsy -- the next step in a more definitive diagnosis -- 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 Röntgencentralen, 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 for them to remain still during diagnostic procedures.⁴³ (See **Figure 1** on the next page)

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 diagnostic practice in the 1970s -- and besides Tekniska Röntgencentralen, no other producer offered stereoscopic imaging equipment at that time.⁴⁴

^f Hitachi for example was (as of 1980) one of the top X-ray producers in Japan, but when Hitachi developed breast imaging equipment, it invested primarily in ultrasound technology. The company did patent an X-ray mammography device in 1989 but did not market it. Instead, in the 1990s, the company formed an agreement to market and distribute U.S.-based Lorad's analog mammography equipment in Japan.

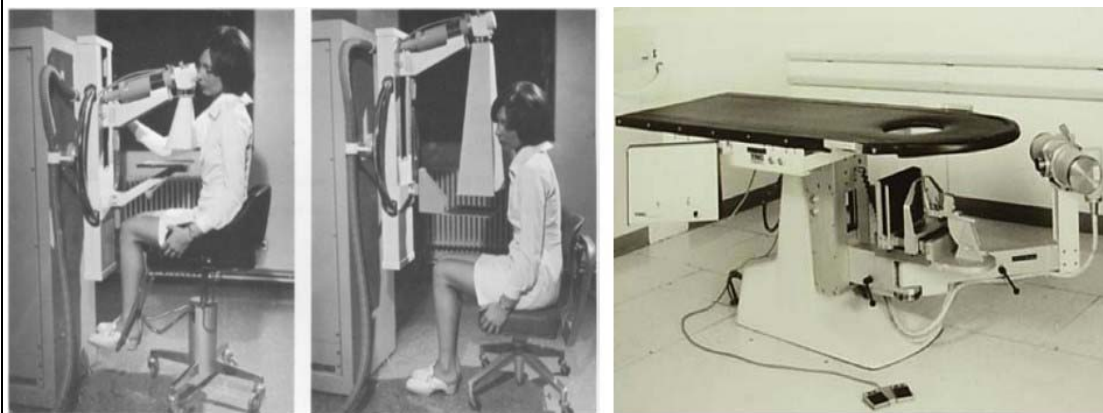
^g In the United States, researchers estimate that as many as 44% of women would benefit from breast cancer screening done with alternative imaging technologies.

Producers of Equipment and Film. As mentioned, French X-ray producer CGR was the first to sell specialized mammographic equipment. Except for one startup, Xonics,^h all the other companies that started selling specialized mammographic 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.⁴⁵ 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.⁴⁶

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 in the U.S.⁴⁷

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).⁴⁸

Figure 1 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).



Source: Arthur G. Haus, "Historical Technical Developments in Mammography," *Technology in Cancer Research & Treatment* 1, no. 2 (2002) and Henry M. Kuerer "Kuerer's Breast Surgical Oncology," *The McGraw-Hill Companies, Inc.* (2010).

^h Xonics, a 1972 California startup, secured a patent in 1973 for a process that produced X-ray images on thin plastic sheets that looked like 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.

Questions (for reflection and discussion):

Before reading further please write down (in less than ten words) which decision, event, or condition you found the most significant in establishing the foundations of mammography.

- _____

Be prepared to explain why you found this significant.

Also think about what would need to happen for the use of mammography to broaden.

2. Broadening Use (1980s)

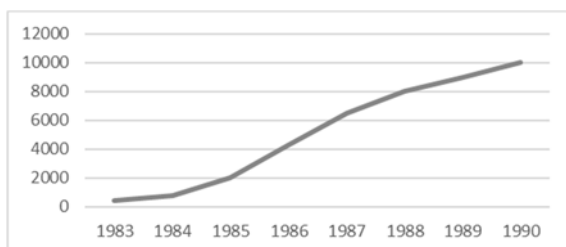
New Screening Equipment and Rules. In the 1980s, companies developed equipment with controls and filters that (when used with newly available, more sensitive film) reduced radiation exposure. The improvements also reduced the risks of misdiagnosis by producing more detailed images. In addition, companies introduced basic, low-end devices priced at \$16,000 in 1989, down from \$65,000 in the early 1980s.⁴⁹

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.⁵⁰ 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.⁵¹ (See **Exhibit 3**). Although experts would continue to disagree (See **Exhibit 4**) about when women should begin to get regular mammograms, by 1991, the American Cancer Society was recommending regular screening for women over 40 (who did not have any symptoms).⁵² And by then, the number of women who were regularly screened had nearly doubled to almost fifty-five percent of American women over age forty, up from less than thirty percent in 1987.⁵³

Mammographic installations in the U.S. also received an unintended boost from cost-containment rules introduced to limit hospitals' purchases of expensive computed tomography⁵⁴ (CT) and magnetic resonance imaging⁵⁵ (MRI) units. These rules encouraged radiologists to open imaging centers that were exempt from purchasing restrictions because they were not affiliated with hospitals.⁵⁶ These new imaging centers then bought mammographic equipment to round out their diagnostic offerings. By 1990, forty-seven percent of centers offered screening and diagnostic mammography.⁵⁷ The introduction of better, cheaper equipment combined with the new rules helped to increase installations of mammographic units by nearly twenty-fold in the U.S. between 1983 and 1990.⁵⁸ (See **Figure 2**).

Figure 2 Estimated Number of Mammographic Units Installed in the United States



Source: 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).

Screening 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,⁵⁹ while a small-scale trial in the Netherlands (published in 1984) suggested screening could halve deaths.⁶⁰ These trials were apparently influential.⁶¹ 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.⁶² And, because national health insurance plans covered the cost, screening was free for women undergoing the procedure.⁶³

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.⁶⁴

Advances in Diagnostic Mammography. As mentioned, stereoscopic imaging, pioneered in Sweden in the 1970s to improve the precision of diagnostic biopsies, had not been widely adopted. Diagnostic practices, however, changed in the 1980s as more companies sold equipment 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) emerged as distinct categories.⁶⁵

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 stereoscopic imaging for "minimally invasive" fine needle breast biopsies. The needles shot from guns extracted more cells, resulting in fewer missed cancers. However, although the new minimally invasive biopsies were now at least as good (or better) than open surgical biopsies, 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.⁶⁶

(Diagnostic equipment without biopsy guns did, however, incorporate the controls, filters, and film used to improve screening equipment in the 1980s. The improved diagnostic equipment produced images of suspect lumps that were sharper, could be magnified with less blurring, and required less radiation exposure.)⁶⁷

New Producers and Exits. 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 Imaging, who also sold screening equipment).⁶⁸

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 GE.⁶⁹ In addition, Xerox shut down its plate business in 1989.⁷⁰

Far fewer companies entered the European market in the 1980s (just six), and only three companies started selling in Japan. (See **Appendices**). Meanwhile, three companies that had exited the American market (including CGR and Xerox) also stopped selling in Europe and Japan.⁷¹

Questions (for reflection and discussion):

Before reading further please write down (in less than ten words) which decision, event, or condition you found the most significant or surprising in broadening the use of mammography.

- _____

Be prepared to explain why you found this significant or surprising.

3. Digitizing Mammography (1990-2000)

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 tumors⁷² and that computers would save radiologists time by flagging suspicious lumps.⁷³ Researchers also believed digitized images could be produced with less radiation.⁷⁴

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.⁷⁵ Researchers also tried to directly record images with electronic sensors, but sensors at the time, like scanners, also could not produce sharp images.⁷⁶ Screening mammography presented an additional problem: it required equipment that could X-ray a whole breast at once. However, sensors could not produce large ("full field") images without distortion.⁷⁷

Participants at a 1991 NCI workshop agreed that improved electronic sensors were more likely to increase sharpness and reduce distortion than improved scanners.⁷⁸ 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.⁷⁹

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 undistorted, 'full field' images of the whole breast (needed for screening). In about a year, developers were able to introduce digital equipment that produced detailed 'small field' images more rapidly than analog diagnostic equipment. The sensor-based diagnostic equipment (introduced in 1992)ⁱ 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.⁸⁰ (See Exhibit 5)

ⁱ Lorad, a manufacturer of low-radiation screening equipment, was first to introduce the new digital diagnostic equipment.

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 for 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 U.S. companies – Fischer Imaging, GE, and Trex Medical^j – which had already started selling digital diagnostic equipment, were testing prototypes for full field screening.⁸¹

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.⁸² 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. Fuji also did not get FDA approval to sell the plates and laser scanners (for general X-ray use) in the U.S. until 1989.⁸³ (Coincidentally, as mentioned, Xerox 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 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.⁸⁴

Regulatory Obstacles. 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.⁸⁵ 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^k to earlier analog devices.⁸⁶ The exemptions helped the rapid adoption of digital (small-field) diagnostic mammography.

Developers of digitized, full-field screening 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.⁸⁷ 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 – including Fuji’s plate-based system -- undergo large-scale

^j Trex had been acquired by Thermo-Electron, a diversified producer of analytical and scientific products, which had also acquired Lorad.

^k 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.

clinical trials to demonstrate its safety and effectiveness (rather than just “agreement” with prior analog equipment).⁸⁸

GE immediately conducted large-scale trials for its full-field, sensor-based screening equipment and secured approval from the FDA for its digitized products in 2000. Trex Medical, however, did not have the financial resources to meet the new FDA requirement. Its sales had slowed in 1998 after losing an OEM agreement with U.S. Surgical and continued to decline in 1999. The company’s CEO left the company two days before the FDA rejected its ‘substantial equivalence’ exemption application in December 1999.⁸⁹ About nine months later, bone-densitometry manufacturer Hologic announced its purchase of the struggling Trex (from its parent, Thermo-Electron) for \$55 million. (Just a few months earlier, Hologic had acquired Direct Radiography Corp. a manufacturer of digital X-ray systems for medical imaging that was also developing a digital screening product.)

Digitization in Europe and Japan. Although European and Japanese companies were not leaders in digitizing diagnostic mammography, American companies had introduced their digital diagnostic products in Europe and Japan by the mid-1990s. And by the late 1990s, digital diagnostic equipment accounted for nearly ninety percent of total diagnostic equipment sales in Japan and Europe (as it also did in the United States).⁹⁰

In the much larger category of screening mammography, 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.⁹¹ Therefore, Fujifilm had been able to offer its plates and laser scanners in 1998. Similarly, Trex Medical and GE were able to introduce digitized screening equipment in Europe in 1998 and 1999, respectively.⁹²

In Japan, radiologists started using Fujifilm’s plates and laser scanners for screening mammography in the mid-1990s, whereas sensor-based digital screening equipment was not available in Japan until 2000.⁹³ 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 were negligible – as of 2000, only two sensor-based units had been sold in all of Japan.⁹⁴

New Producers and Exits. Entry into the American mammography equipment market slowed in the 1990s. Whereas in the 1980s (before any digitization had occurred), twenty-four companies had started selling mammographic equipment, only seventeen started selling in the 1990s. Meanwhile, nearly twice as many companies departed as in the 1980s.

Most entrants offered improved analog screening equipment (where technological advances had continued alongside efforts to develop full-field digitized products), while a few others focused on the smaller diagnostic equipment market.

Fewer companies started selling mammography equipment in Europe in the 1990s 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. (American producers that exited their domestic market also stopped selling in Europe, and two European companies also exited.)⁹⁵

Entrants into the Japanese market increased in the 1990s, but the total number of producers remained small. 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.

The Situation at the end of 2000

A Frost & Sullivan report estimated that analog screening equipment accounted for \$222.2 million – or nearly 80% -- of worldwide mammographic equipment sales in 2000. And North American and European buyers accounted for 48.8% and 41.8% of the worldwide analog screening equipment sold.⁹⁶

Analog screening equipment sales in the US had fallen by more than a third in 2000. Frost & Sullivan attributed the decline to a “flurry of regulation-prompted sales,” spurred in the previous year by the Mammography Quality Standards Act passed in 1992. The Act had mandated minimum specifications for many features (such as image receptor sizes, exposure control, and compression paddle devices) that the equipment used in many facilities did not meet. As the first effective date for compliance approached in 1999, purchases to replace sub-standard equipment jumped.⁹⁷ Between 1997 and 1999, sales of screening units jumped by nearly 24% (from \$136 million to \$168.3 million), while the total number of installations increased by less than 1%.⁹⁸ The sales, however, reduced replacement purchases that might have been made in 2000. And with a sharp fall in its largest segment, worldwide sales of mammographic equipment had also declined, albeit to a much smaller extent (to \$282.5 million in 2000 from \$292.5 million in 1999).⁹⁹

Frost & Sullivan expected worldwide sales to rebound after their 2000 decline and grow at more than 10% a year to \$567.2 million in 2007. The report also predicted a significant shift from analog to digital mammography, particularly in North America and Western Europe. The report predicted analog sales (mainly screening equipment) to fall by nearly 20% in North America to \$91 million between 2000 and 2007 and by about 6% to \$88.4 million in Western Europe. Meanwhile, digital mammography sales were expected to grow by 373% in North America to \$162.9 million in 2007 and by over 700% to \$130 million in Western Europe.¹⁰⁰

According to the Frost and Sullivan report, the global mammography market was “mature,” with “the vast majority of sales coming from the replacement of outdated or obsolete equipment. The principal markets for mammography equipment, the United States and Western Europe, [we]re practically saturated.” Moreover, mammography facilities weren’t even replacing equipment, which had an average life span of nine years, “until they absolutely ha[d] to.”¹⁰¹ One reason was low utilization: In the U.S., the average number of procedures performed per machine in 2000 was just over 2100, compared to a potential capacity of more than 9000 procedures. And, with reimbursement rates often below operating costs, most U.S. facilities offered mammography as a “loss leader.” Hundreds were closing. In Germany and France, radiologists organized strikes to protest low reimbursement rates.¹⁰²

Reduced demand – and an increased preference for cheaper and more basic units was also expected to reduce prices, from \$75,500 per unit in 2000 to \$71,000 in North America.¹⁰³ Lower prices would, in turn, further limit the total revenues from analog screening equipment. Prices in Western Europe (where Frost & Sullivan expected smaller declines in total revenue), however, were expected to rise from \$76,700 per unit in 2000 to \$81,000 in 2007.¹⁰⁴

In digital screening, Frost & Sullivan based its forecast of growth in North America and Europe on technical advantages such as “increased contrast resolution” and “real-time image enhancement,” providing “sharper, more detailed views” and thus “improved early detection rates for hard-to-detect cancers.” If it were “conclusively demonstrated” that digital screening saved more lives than analog screening, this would “provide an enormous impetus for facilities to invest in the digital modality.” Digital screening also had the potential for reducing false positives and radiation doses and for enabling tele-mammography in remote areas.¹⁰⁵

Outside North America and Western Europe, Frost & Sullivan expected increased sales of both analog and digital equipment. In Japan, the report noted a “strong possibility” that a national screening program would be passed into law, which would increase analog screening equipment sales from \$14.8 million (from 199 units) in 2000 to \$33.2 million (from 471 units) in 2007. Meanwhile, digital mammography would also increase from \$2.3 million in 2000 to \$21 million.¹⁰⁶

In the rest of the world, Frost & Sullivan expected analog screening equipment sales to grow from \$5.7 million (from 75 units) to \$16.7 million (from 225 units) in 2007 and digital equipment sales to rise from \$2.7 million to \$23.8 million in 2007. The report also expected rapid increases in the sales of refurbished (analog) equipment, which was often priced at less than half the price of new units, in Latin America, Eastern Europe, and other developing regions that did not enforce stringent technical standards.¹⁰⁷

According to the report, there were only seven “active competitors” worldwide in the mammography equipment market in 2000. Three – GE, Siemens, and Toshiba – were multinational industrial conglomerates that sold a wide range of medical devices.¹ The other four – Hologic, Instrumentarium Imaging, Picker International, Fischer Imaging, and Planmed – were “niche-players” that focused on medical imaging. Seven “active competitors” exited between 1997 and 2000: two multinational conglomerates (Phillips and Hitachi) and four medical imaging specialists (Acoma, Picker International, Elscint, and Soredex.).

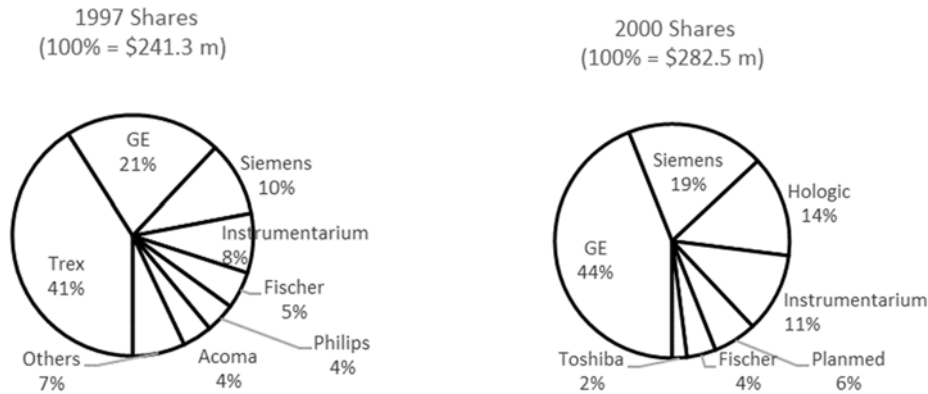
GE, the market leader in 2000, had more than doubled its share of 1997 global sales (See Figure 4). Trex Medical, the leader in 1997, had stumbled, as mentioned, and been acquired by Hologic. GE had taken advantage of the erstwhile leader’s difficulties “to undercut its pricing and capture a substantial portion of its market share.” Two Scandinavian niche-players, Instrumentarium and Planmed, had also benefitted from Trex’s decline.¹⁰⁸

GE had secured a 53% share of the analog equipment sold in North America. According to Frost & Sullivan, GE, then the world’s largest corporation (with nearly \$500 billion in market capitalization), had “pioneered... internet promotions offering mammography equipment at prices far below list price.” Its “access to economies of scale and capitalization” gave GE’s mammography business a “considerable advantage in this highly price-conscious market.”¹⁰⁹ GE was also the market leader in European analog equipment sales (with a 37% share), followed by Siemens (29%).¹¹⁰ In Japan, GE was slightly behind market leader Toshiba (which had a 33% share) with 31% of the market.¹¹¹

GE was also, as mentioned, the only company in the U.S. that had received FDA approval for digital screening. However, Fischer Imaging and Hologic were preparing to apply for approval. Three of the other four “active competitors” in the analog market, namely Siemens, Instrumentarium Imaging, and Planmed, were also developing digital screening products.¹¹² Developing and marketing digital screening, according to Frost & Sullivan, was necessary to remain a viable competitor in mammography because end-users wanted suppliers on the cutting-edge of imaging technology.¹¹³

¹ Frost & Sullivan’s list apparently excluded Fuji’s plate and scanner systems, as well as very small producers of ancillary mammographic equipment and systems.

Figure 4 Shares of World Mammographic Equipment Sales in 1997 and 2000



Source: Frost & Sullivan, *World X-ray Mammography Market* (2001).

High R&D costs for digital screening had, according to Frost & Sullivan, driven many niche producers with limited financial resources out of the market, whereas large conglomerates, such as Phillips, had probably decided the returns did not justify the investment. Expensive components, such as detectors, workstations, and display monitors, also contributed “substantially” to the prices of digital screening systems. Unless the R&D and component costs were controlled, predicted Frost & Sullivan, prices would remain high, financial returns would remain low and more niche producers would be forced out of mammography.¹¹⁴

Questions (for reflection and discussion):

Have Hologic and the other “niche-players” made a mistake in attempting to develop and sell digital screening products? And why or why not?

- Made a Mistake/Not made a mistake
Because (in less than 10 words)
-

Also, think about what you found significant or surprising about the digitization of mammography.

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 survey 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, operating errors occurred over fifty percent of the time. In contrast, specialized equipment used with specialized film reduced errors to just six percent.

Source: R. G. Jans et al., "The Status of Film/Screen Mammography. Results of the BENT Study," *Radiology* 132, no. 1 (July 1979): 197-200, <https://doi.org/10.1148/132.1.197>.

Exhibit 2 Xerox's "Xeromammography"

In 1955, two American physicians working on civil defense medical services reported on a new method for producing X-ray images like 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.

Source: See endnote 115.¹¹⁵

Exhibit 3 Breast Cancer Advocacy

Before the 1970s, treatment for breast cancer was limited to radical mastectomies that removed entire breasts. This disfiguring surgery kept a 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, the President’s wife, 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, the Susan G. Komen Foundation provided another boost. Nancy Brinker started the foundation in 1982 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.

Source: Paraphrased from Susan Braun, “The History of Breast Cancer Advocacy,” *The Breast Journal* 9 (May 1, 2003).

Exhibit 4 Questions about 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.”

Source: Excerpted from *Health Care Technology and Its Assessment in Eight Countries, International Differences in Health Care Technology and Costs* (Washington, DC: Office of Technology Assessment, United States Congress: For sale by the Supt. of Docs., U.S. G.P.O., 1995).

Exhibit 5 Mammography Equipment Markets: Selected statistics

	2000 Estimates			2007 (Predicted)		
	Screening	Diagnostic	Total	Screening	Diagnostic	Total
<u>North America</u>						
Sales (\$m)						
Analog	108.5	1.4	109.9	90.6	0.4	91
Digital	22.7	11.5	34.2	145.8	17.1	162.9
Prices (\$ '000s/unit)						
Analog	75.5	35.9	-	71.1	27.6	-
Digital	473.1	107.4	-	324.7	91.6	-
Installed base (Units)						
Analog	15,287	-	-	14,712	-	-
Digital	48	-	-	1054	-	-
<u>Western Europe</u>						
Sales (\$m)						
Analog	93.2	1.1	94.3	88.3	0.1	88.4
Digital	9.6	6.5	16.1	117.4	12.6	130
Prices (\$ '000s/unit)						
Analog	76.7	37.1	-	81	26	-
Digital	452.9	110.4	-	324.4	95.2	-
Installed base (Units)						
Analog	10,273	-	-	10,690	-	-
Digital	12	-	-	726	-	-
<u>Japan</u>						
Sales (\$m)						
Analog	14.8	0.42	15.22	33.2	0.12	33.32
Digital	0.9	3.3	4.2	15.9	5.1	21
Prices (\$ '000s/unit)						
Analog	74.6	37.2	-	70.4	30.4	-
Digital	474.7	107.4	-	325.6	91.7	-
<u>Rest of the World</u>						
Sales (\$m)						
Analog	5.7	0.26	5.96	16.7	0.03	16.73
Digital	1.9	0.8	2.7	18.8	5	23.8
Prices (\$ '000s/unit)						
Analog	75.6	36.7	-	74.1	28	-
Digital	466.9	108.4	-	324.9	92.8	-
<u>Worldwide</u>						
Sales (\$m)						
Analog	222.2	3.1	225.3	228.7	0.6	229.3
Digital	35.1	22.1	57.2	298	39.8	337.8
Prices (\$ '000s/unit)						
Analog	75.6	36.7	-	72.8	26	98.8
Digital	466.9	108.4	-	325	92.8	417.8

Source: Frost & Sullivan, *World X-Ray Mammography Market* (2001).

Note: Analog screening sales pertain just to the "add-ons" to a basic mammography unit.

Appendix 1: Mammography Timeline

Year	Event
1895	X-rays discovered
1913	First X-ray images taken of breast cancer tumors. Radiologist Raul Leborgne publishes a new technique for producing sharp breast X-rays.
1950s	Radiologist Charles Gros begins experiments in Strasbourg, France. Radiologist Robert Egan begins experiments in Houston, Texas.
1956	Radiologist Jacob Gershon-Cohen begins studies on early detection in Philadelphia, Pennsylvania.
1960-62	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.
1963	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.
1964	Kodak produces industrial X-ray films and screens vacuum-sealed together for high-quality, high-contrast breast X-ray images.
1966	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.
1971	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.
1973	Breast Cancer Detection and Demonstration Project (BCDDP) launched.
1975	The BCDDP grows to 29 centers across the U.S.
1976	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. Federal limits on radiation exposure lowered.
1977	The Food and Drug Administration (FDA) surveys mammography machines nationwide. National Institutes of Health convenes a public consensus building conference but fails to reach full consensus. Lazlo Tabar begins controlled trials of mammography in multiple towns across Sweden.
1981	The BCDDP ends.
1982	The Susan G. Komen Foundation founded by Komen's sister, Nancy Brinker.
1983	The Komen Foundation holds its first fundraising race in Dallas, Texas.
1985	Lazlo Tabar publishes initial data from Swedish trials confirming mammography reduces mortality rates and detects cancers at an earlier stage.
1986	National Breast Cancer Awareness Month established.
1987	GE acquires pioneer CGR.
1988	Partial coverage of mammograms begins nationally under Medicare, but not Medicaid.

Year	Event
	Radiologists develop new mammographic equipment designed to facilitate minimally invasive biopsies.
1989	Lazlo Tabar publishes additional data confirming mammography reduces mortality rates and catches cancers at an earlier stage.
1990	Full coverage of mammography begins for those on Medicare, but not for Medicaid recipients.
1991	Blue Cross Blue Shield becomes the first major private insurance company to cover mammographic screening for women over 40.
1992	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.
1993	The NCI returns to discouraging mammograms for women under 50; the American Medical Association follows, but eventually reinstates recommendations that screening should start when women are 40.
1996	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.
1998	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 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.
	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).

Appendix 2: Companies entering mammographic equipment markets (and country of their domicile)

Year	Market Entered (from 1966 -1970)		
	United States	Europe	Japan
1966	Kodak (US)	Compagnie Générale de Radiologie (France)	
1971	Xerox (US) CGR (France)	Kodak (US)	
1972	Du Pont (US)	Siemens (Germany) Picker (US) Xerox (US)	
1973	Siemens (Germany) Philips (The Netherlands) Picker (US) Fischer (US)	Philips (Netherlands) Du Pont (US)	
1974	General Electric (US)		
1975	Technicare (US)	AGFA/Gevaert (Belgium)	
1976	Xonics (US)	Valmet (Finland)	
1977	AGFA/Gevaert (Belgium)	Elema-Shonander (Sweden) Tekniska Röntgencentralen (Sweden)	Xerox (US) Toshiba (Japan) Du Pont (US)

Source: See endnote 116.¹¹⁶

Year	Market Entered (1980-1989)		
	United States	Europe	Japan
1980	Soredex (Finland)	Soredex (Finland);	
1981	Elscint (Israel)	Elscint (Israel). The General Electric Company (GEC, UK)	Siemens (Germany)
1982			GE/Yokogawa (US/Japan)
1983	Ohmic (US)	GE (US)	Shimadzu (Japan)
1984	3M (US)	Gilardoni (Italy) 3M (US)	
1988	Custom Medical Products (US)		
1989	AS&E (US); Amerisys (US). Ausonics Corp. (Australia). Bennett X-ray Corp. (US). Continental X-ray Corp. (US). International Radiographic Inc. (US). Kramex Corp. (US). Lorad Medical Systems (US). MammoCare USA (US). MinXRy Inc. (US); Moti (US). National X-ray (US). Planmed (Finland); Porta Ray (US). Raytheon Medical Systems Shimadzu Medical Systems (Japan) Spectrascan Imaging Services (US) Supertech Inc. (US) Transworld X-ray (US)	Planmed (Finland)	

Sources: Sarah A. Fox, Carolyn Kimme-smith, and Dennis S. Kios, "The Technology Of Mammography: Misunderstood and Underutilized," *International Journal of Technology Assessment in Health Care* 4, no. 4 (1988): 521-544, <https://doi.org/10.1017/S0266462300007601>; Anderson (1990); Haus (1990, 2002); the Health Device Sourcebooks; the Medical Device Registers; and the FDA 510(k) database.

Year	Market Entered (1990-2000)		
	United States	Europe	Japan
1990	Giotto (Italy)	International Medico Scientific (Italy)	
	Acoma Medical Imaging (Japan)	Giotto (Italy)	Acoma Medical Imaging (Japan)
	BG Imaging Specialties (US)		Hitachi (Japan)
	International Medico Scientific (Italy)		
1991	York X-ray (US)		
	American Shared Curecare (US)	Instrumentarium (Finland)	
	Camp-Ray (US)		
	Coastal Medical Systems (US)		
	Instrumentarium (Finland)		
	LogETronics (US)		
	RP Kincheloe (US)		
1992	Universal Medical Systems (US)		
	Vision Ten (US)		
	Dynarad Corp. (US)		
1993	Medical Systems Engineering (US)		
	Trex (US)	Sectra Imtec (US)	
1997	Sterling Diagnostic Imaging (US)		Fujifilm (Japan)
			Planmed (Finland)
			Instrumentarium (Finland)
			Fischer (United States)
1998		Trex (United States)	
		Fujifilm (Japan)	
2000	Vidar Systems Corp (US)	Cintec Medical (Israel)	
	Dbi Systems (US)	Hologic (United States)	Hologic (United States)
	Hologic (US)		

Sources: The *Health Device Sourcebook*; the *Medical Device Register*; FDA 510(k) database; and Frost & Sullivan reports; (2000) *World X-Ray and Computed Tomography Markets*; (2001) *World X-ray Mammography Market*; (2003) *X-Ray Mammography Markets in North America and Japan and the Rest of the World*, and (2008) *European Mammography Systems Market*.

Endnotes

¹ A biopsy is the surgical removal of tissue samples for further examination in a lab.

² Physical exams included visual assessment but primarily entailed systematic assessment by touch. Adrian M. K. Thomas and Arpan K. Banerjee, *The History of Radiology* (OUP Oxford, 2013); Arthur G. Haus, "Historical Technical Developments in Mammography," *Technology in Cancer Research & Treatment* 1, no. 2 (2002): 119–26; A. G. Haus, "Technological Improvements in Mammography over the Past 20 Years," *Medical Progress through Technology* 19, no. 1 (1993): 31–42; W. R. Hendee, "History and Status of X-Ray Mammography," *Health Physics* 69, no. 5 (1995): 636–48; Bonnie N. Joe and Edward A. Sickles, "The Evolution of Breast Imaging: Past to Present.," *Radiology* 273, no. 2 Suppl (November 2014): S23-44, <https://doi.org/10.1148/radiol.14141233>; Sophia Zackrisson and Nehmat Houssami, "Chapter 13 - Evolution of Mammography Screening: From Film Screen to Digital Breast Tomosynthesis" (Elsevier Inc, 2016); Siddhartha Mukherjee, *The Emperor of All Maladies: A Biography of Cancer*. (Scribner, 2010); Richard H. Gold, Lawrence W. Bassett, and Bobbi E. Widoff, "Highlights from the History of Mammography.," *Radiographics* 10, no. 6 (1990): 1111–1131; L. W. Bassett and R. H. Gold, "The Evolution of Mammography," *AJR. American Journal of Roentgenology* 150, no. 3 (1988): 493–98.

³ 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.

⁴ U.S. Department of Health and Human Services. *Health United States 2015*. Table 70. Use of mammography among women aged 40 and over, by selected characteristics: United States, selected years 1987–2015. Excel version downloaded from: <https://www.cdc.gov/nchs/hus/contents2017.htm#070> .

⁵ Studies have produced a wide range of estimated impacts of screening mammography on mortality, and the exact impact continues to be debated. See, for example: Donald A. Berry et al., "Effect of Screening and Adjuvant Therapy on Mortality from Breast Cancer," *New England Journal of Medicine* 353, no. 17 (October 27, 2005): 1784–92, <https://doi.org/10.1056/NEJMoa050518>; H. Gilbert Welch et al., "Breast-Cancer Tumor Size, Overdiagnosis, and Mammography Screening Effectiveness," *New England Journal of Medicine* 375, no. 15 (October 13, 2016): 1438–47, <https://doi.org/10.1056/NEJMoa1600249>; Mukherjee, *The Emperor of All Maladies*; "Mammograms More Likely to Cause Unneeded Treatment than to Save Lives," *STAT*, October 12, 2016, <https://www.statnews.com/2016/10/12/mammogram-overdiagnose-breast-cancer/>.

⁶ "Breast Biopsy Device Market Size | Industry Report, 2024," accessed September 26, 2018, <https://www.grandviewresearch.com/industry-analysis/breast-biopsy-device-market>; "Mammography Market Size, Share | Industry Analysis Report 2018-2025," accessed May 18, 2018, <https://www.grandviewresearch.com/industry-analysis/mammography-market>.

⁷ By the 1950s, results of these experiments had been presented to radiologists who met regularly through the International Club of Radiotherapists, which had been formed in Europe in 1953 and had active members based in in Brazil, Canada, Colombia, Cuba, Guatemala, India, Mexico, Peru, the United States, Uruguay, and Venezuela.

⁸ In 1913, a German surgeon, Albert Salomon, was able to identify the distinctive shapes of large tumors in X-ray images of breasts (after the breasts had been surgically removed). Salomon was able to see breast cancer in these early X-rays in part because breast cancers were denser than other soft tissues and sometimes contained calcium deposits, which are hard, like bone. Mukherjee, *The Emperor of All Maladies*; Thomas and Banerjee, *The History of Radiology*; Gold, Bassett, and Widoff, "Highlights from the History of Mammography.,"; Bassett and Gold, "The Evolution of Mammography"; Stephen A. Feig, "Mammographic Screening: An Historical Perspective," *Seminars in Roentgenology, Carcinoma of the Breast*, 28, no. 3 (July 1, 1993): 193–203, [https://doi.org/10.1016/S0037-198X\(05\)80079-3](https://doi.org/10.1016/S0037-198X(05)80079-3); Barron H. Lerner, *The Breast Cancer Wars: Hope, Fear, and the Pursuit of a Cure in Twentieth-Century America* (New York: Oxford University Press, 2001), http://nrs.harvard.edu/urn-3:hul.ebook:EBSCO_187172; Robert A. Aronowitz, *Unnatural History?: Breast Cancer and American Society* (New York: Cambridge University Press, 2007). Egan contends in his 1962 article on mammography that there are 75 articles on the technique published by that date. In a 1960 article, he cites or discusses the research done by Stanford Warren (U.S.), Charles Gros (France), and Raul Leborgne (Uruguay). In a 1965 article, he also mentions Jacob Gershen-Cohen (U.S.), Edwin Lame and Eugene Pendergrass (U.S.), and Ira Lockwood (U.S.). Lame and Pendergrass cite 120 articles as of 1947. Gros and Leborgne discuss research not published in English by other South American researchers, as well. Robert L. Egan, "Mammography, An Aid to Diagnosis of Breast Carcinoma," *JAMA* 182, no. 8 (November 24,

1962): 839–43, <https://doi.org/10.1001/jama.1962.03050470017004>. Robert L. Egan, “Experience with Mammography in a Tumor Institution: Evaluation of 1,000 Studies,” *Radiology* 75, no. 6 (1960): 894–900, <https://doi.org/10.1148/75.6.894>. R. Lee Clark et al., “Reproducibility of the Technic of Mammography (Egan) for Cancer of the Breast,” *The American Journal of Surgery* 109, no. 2 (1965): 127–133, [https://doi.org/10.1016/S0002-9610\(65\)80133-7](https://doi.org/10.1016/S0002-9610(65)80133-7); Edwin L. Lame and Eugene P. Pendergrass, “An Addition to the Technic of Simple Breast Roentgenography,” *Radiology* 48, no. 3 (March 1, 1947): 266–68, <https://doi.org/10.1148/48.3.266>.

⁹ Mukherjee, *The Emperor of All Maladies*; Thomas and Banerjee, *The History of Radiology*; Gold, Bassett, and Widoff, “Highlights from the History of Mammography.”; Bassett and Gold, “The Evolution of Mammography”; Feig, “Mammographic Screening”; Lerner, *The Breast Cancer Wars*; Aronowitz, *Unnatural History*.

¹⁰ 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.

¹¹ Sarah A. Fox, Carolyn Kimme-smith, and Dennis S. Kios, “The Technology Of Mammography: Misunderstood and Underutilized,” *International Journal of Technology Assessment in Health Care* 4, no. 4 (1988): 521–544, <https://doi.org/10.1017/S0266462300007601>; Gold, Bassett, and Widoff, “Highlights from the History of Mammography.”; Bassett and Gold, “The Evolution of Mammography.”

¹² Now the M.D. Anderson Cancer Center.

¹³ R. L. Egan, “Evolution of the Team Approach in Breast Cancer,” *Cancer* 36, no. 5 (1975): 1815–22; Robert L. Egan, *Mammography*, American Lecture Series, Publication No. 568 (Springfield, Ill, CCThomas 1964, 1964); Robert L. Egan, “Mammography,” *The American Journal of Nursing* 66, no. 1 (1966): 108–111, <https://doi.org/10.2307/3419514>; Robert L. Egan, *Mammography* (Springfield, Ill: Thomas, 1972); Robert L. Egan, *Technologist Guide to Mammography*, (Baltimore, Williams & Wilkins, 1968); Robert L. Egan, “Roles of Mammography in the Early Detection of Breast Cancer,” *Cancer* 24, no. 6 (1969): 1197–1200, [https://doi.org/10.1002/1097-0142\(196912\)24:6<1197::AID-CNCR2820240622>3.0.CO;2-S](https://doi.org/10.1002/1097-0142(196912)24:6<1197::AID-CNCR2820240622>3.0.CO;2-S); Robert L. Egan, “Present Status of Mammography,” *Annals of the New York Academy of Sciences* 114, no. 2 (1964): 794–802, <https://doi.org/10.1111/j.1749-6632.1964.tb40998.x>; Robert L. Egan, “Mammography,” *The American Journal of Surgery* 106, no. 3 (1963): 421–429, [https://doi.org/10.1016/0002-9610\(63\)90125-9](https://doi.org/10.1016/0002-9610(63)90125-9); Egan, “Experience with Mammography in a Tumor Institution”; Egan, “Mammography, An Aid to Diagnosis of Breast Carcinoma”; Clark et al., “Reproducibility of the Technic of Mammography (Egan) for Cancer of the Breast.”

¹⁴ Gershon-Cohen JJ and Berger SM, “Detection of Breast Cancer by Periodic X-Ray Examinations: A Five-Year Survey,” *JAMA* 176, no. 13 (July 1, 1961): 1114–16, <https://doi.org/10.1001/jama.1961.63040260015013a>; Helen Ingleby, *Comparative Anatomy, Pathology, and Roentgenology of the Breast*, (Philadelphia, 1960), <http://hdl.handle.net/2027/mdp.39015072254553>; Gold, Bassett, and Widoff, “Highlights from the History of Mammography.”

¹⁵ The U.S. Public Health Service had been founded in 1798, and the National Cancer Institute had been founded in 1937

¹⁶ 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.

¹⁷ Clark et al., “Reproducibility of the Technic of Mammography (Egan) for Cancer of the Breast.”

¹⁸ 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.”

¹⁹ Clark et al., “Reproducibility of the Technic of Mammography (Egan) for Cancer of the Breast.”

²⁰ 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 a Personal Involvement with the National Cancer Institute, 1938 to 1978* / ([Bethesda, Md.]?., 1983), <http://hdl.handle.net/2027/pur1.32754076368780>; Lewis C. Robbins, "The Public Health Service's Program in Cancer Control," *Public Health Reports* (1896-1970) 76, no. 4 (1961): 341-43, <https://doi.org/10.2307/4591137>; Sam Shapiro and Health Insurance Plan of Greater New York, *Periodic Screening for Breast Cancer: The Health Insurance Plan Project and Its Sequelae, 1963-1986*, Johns Hopkins Series in Contemporary Medicine and Public Health (Baltimore: Johns Hopkins University Press, 1988).

²¹ Sam Shapiro, Philip Strax, and Louis Venet, "Evaluation of Periodic Breast Cancer Screening With Mammography: Methodology and Early Observations," *JAMA* 195, no. 9 (February 28, 1966): 731-38, <https://doi.org/10.1001/jama.1966.03100090065016>; H. David Banta and United States, eds., *Health Care Technology and Its Assessment in Eight Countries, International Differences in Health Care Technology and Costs* (Washington, DC: Office of Technology Assessment, United States Congress: For sale by the Supt. of Docs., U.S. G.P.O., 1995).

²² Shapiro, Strax, and Venet.

²³ Mukherjee, *The Emperor of All Maladies*, 295

²⁴ Shapiro, Strax, and Venet, "Evaluation of Periodic Breast Cancer Screening With Mammography."

²⁵ Lerner, *The Breast Cancer Wars*; Shapiro, Strax, and Venet, "Evaluation of Periodic Breast Cancer Screening With Mammography"; Sam Shapiro, Philip Strax, and Louis Venet, "Periodic Breast Cancer Screening in Reducing Mortality From Breast Cancer," *JAMA* 215, no. 11 (March 15, 1971): 1777-85, <https://doi.org/10.1001/jama.1971.03180240027005>; Mukherjee, *The Emperor of All Maladies*; Bassett and Gold, "The Evolution of Mammography"; Philip Strax et al., "Mammography and Clinical Examination in Mass Screening for Cancer of the Breast," *Cancer* 20, no. 12 (1967): 2184-2188, [https://doi.org/10.1002/1097-0142\(196712\)20:12<2184::AID-CNCR2820201217>3.0.CO;2-3](https://doi.org/10.1002/1097-0142(196712)20:12<2184::AID-CNCR2820201217>3.0.CO;2-3).

²⁶ Radiologists affiliated with the American Cancer Society had also been involved in planning the study that tested the reproducibility of Egan's technique.

²⁷ Lerner, *The Breast Cancer Wars*; Mukherjee, *The Emperor of All Maladies*; Shapiro, Strax, and Venet, "Periodic Breast Cancer Screening in Reducing Mortality From Breast Cancer"; L. H. Baker, "Breast Cancer Detection Demonstration Project: Five-Year Summary Report," *CA: A Cancer Journal for Clinicians* 32, no. 4 (July 1, 1982): 194-225, <https://doi.org/10.3322/canjclin.32.4.194>; Bettyann Kevles, *Naked to the Bone: Medical Imaging in the Twentieth Century*, The Sloan Technology Series (Reading, Mass: Addison-Wesley, 1998), Chapter 10.

²⁸ Bailar critiqued other methods of cancer control, not just mammography, in articles written throughout his career. Barron H. Lerner, "To See Today with the Eyes of Tomorrow': A History of Screening Mammography," *Canadian Bulletin of Medical History* 20, no. 2 (2003): 299; Lerner, *The Breast Cancer Wars*; Barron H. Lerner and Phil Plait, "John Bailar's Righteous Attack on the 'War on Cancer,'" *Slate*, January 12, 2017, http://www.slate.com/articles/health_and_science/medical_examiner/2017/01/john_bailar_reminde_us_of_the_value_of_evidence.html; Mukherjee, *The Emperor of All Maladies*; Aronowitz, *Unnatural History*; R. G. Jans et al., "The Status of Film/Screen Mammography. Results of the BENT Study," *Radiology* 132, no. 1 (July 1979): 197-200, <https://doi.org/10.1148/132.1.197>; Lawrence W. Bassett, "The Regulation of Mammography," *Seminars in Ultrasound, CT, and MRI* 17, no. 5 (1996): 415-423, [https://doi.org/10.1016/S0887-2171\(96\)90028-1](https://doi.org/10.1016/S0887-2171(96)90028-1).

²⁹ The debate about when and how often women should be screened has persisted to the present day. Lerner, "To See Today with the Eyes of Tomorrow"; Lerner, *The Breast Cancer Wars*; Lerner and Plait, "John Bailar's Righteous Attack on the 'War on Cancer'"; Mukherjee, *The Emperor of All Maladies*; Aronowitz, *Unnatural History*; Jans et al., "The Status of Film/Screen Mammography. Results of the BENT Study"; Bassett, "The Regulation of Mammography"; Laura J. Esserman, "The WISDOM Study: Breaking the Deadlock in the Breast Cancer Screening Debate," *NPI Breast Cancer* 3 (September 13, 2017),

<https://doi.org/10.1038/s41523-017-0035-5>; Welch et al., “Breast-Cancer Tumor Size, Overdiagnosis, and Mammography Screening Effectiveness”; Berry et al., “Effect of Screening and Adjuvant Therapy on Mortality from Breast Cancer”; “Mammograms More Likely to Cause Unneeded Treatment than to Save Lives.”

³⁰ Public Citizen obtained the records through a Freedom of Information Act request. Broad federal standards limiting radiation exposure from electronic products had been developed after the passage of the Radiation Control for Health and Safety Act of 1968. Lerner, “To See Today with the Eyes of Tomorrow”; Lerner, *The Breast Cancer Wars*; Lerner and Plait, “John Bailar’s Righteous Attack on the ‘War on Cancer’”; Mukherjee, *The Emperor of All Maladies*; Aronowitz, *Unnatural History*; Jans et al., “The Status of Film/Screen Mammography. Results of the BENT Study”; Bassett, “The Regulation of Mammography.”

³¹ Jans et al., “The Status of Film/Screen Mammography. Results of the BENT Study.”

³² Philips may have introduced an improved version of its Mammostest equipment in the late 1970s, but generally equipment manufacturers turned to developing dual spot and other advancements that would not be available until the 1980s. Mammographic film companies continued to offer incremental improvements to their film that helped to lower the amount of radiation required. Jans et al.; J. E. Jensen and P. F. Butler, “Breast Exposure: Nationwide Trends; a Mammographic Quality Assurance Program--Results to Date,” *Radiologic Technology* 50, no. 3 (December 1978): 251–57; Bassett, “The Regulation of Mammography”; Gold, Bassett, and Widoff, “Highlights from the History of Mammography.”; Bassett and Gold, “The Evolution of Mammography”; Feig, “Mammographic Screening”; A. Van Steen and R. Van Tiggelen, “Short History of Mammography: A Belgian Perspective,” *JBR-BTR: Organe de La Société Royale Belge de Radiologie (SRBR) = Orgaan van de Koninklijke Belgische Vereniging Voor Radiologie (KBVR)* 90, no. 3 (2007): 151–53.

Frost & Sullivan. (1983) *The Diagnostic Radiology Market in the U.S.* Section VI, 29-31.

³³ Jans et al., “The Status of Film/Screen Mammography. Results of the BENT Study”; Jensen and Butler, “Breast Exposure”; Bassett, “The Regulation of Mammography”; Gold, Bassett, and Widoff, “Highlights from the History of Mammography.”; Bassett and Gold, “The Evolution of Mammography”; Feig, “Mammographic Screening”; Van Steen and Van Tiggelen, “Short History of Mammography.” Frost & Sullivan. (1983) *The Diagnostic Radiology Market in the U.S.* Section VI, 29-31.

³⁴ Jans et al., “The Status of Film/Screen Mammography. Results of the BENT Study”; Jensen and Butler, “Breast Exposure”; Bassett, “The Regulation of Mammography”; Gold, Bassett, and Widoff, “Highlights from the History of Mammography.”; Bassett and Gold, “The Evolution of Mammography”; Feig, “Mammographic Screening”; Van Steen and Van Tiggelen, “Short History of Mammography.” Frost & Sullivan. (1983) *The Diagnostic Radiology Market in the U.S.* Section VI, 29-31. Xerox introduced the plates in 1971 as a low-cost substitute for X-ray film, but, after two studies showed they also happened to produce sharper images of breasts than even the specialized X-ray film stipulated by Egan, the plates were widely used for mammography See: Goro Inada, Shozo Fujita, and Mineko Ishizaki, “Comparative Studies on Film-, Xeroradio- and Ultrasound-Mammography of Breast Tumors,” *Nagoya Medical Journal* 15, no. 4 (1969): 187–190; Robert L. Egan, “Mammography, Xeroradiography, and Thermography,” *Clinical Obstetrics & Gynecology* 18, no. 2 (June 1975): 197–210; William D. Hayford, “Xeromammography,” *JAMA* 235, no. 7 (1976): 707–707, <https://doi.org/10.1001/jama.1976.03260330017011>; Lester Kalisher and Derace L. Schaffer, “Xeromammography in Early Detection of Breast Cancer,” *JAMA* 234, no. 1 (1975): 60–63, <https://doi.org/10.1001/jama.1975.03260140062016>.

³⁵ Jans et al., “The Status of Film/Screen Mammography. Results of the BENT Study”; Jensen and Butler, “Breast Exposure”; Bassett, “The Regulation of Mammography.”

³⁶ Two reasons have been suggested: 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. although he did found a journal and a professional organization devoted to mammography in the 1970s. Wackenheim, A. “Obituary: Charles Marie Gros.” In *Clinical Radiology*. (1985) 36:477-478. Europe also lacked organizations that championed screening, like the American Cancer Society and the NCI.

³⁷ Mukherjee, *The Emperor of All Maladies*. And, as Mukherjee points out, the Scottish trials would turn out to be flawed in design.

³⁸ E. Altobelli and A. Lattanzi, “Breast Cancer in European Union: An Update of Screening Programmes as of March 2014 (Review),” *International Journal of Oncology* 45, no. 5 (September 1, 2014): 1785–92, <https://doi.org/10.3892/ijo.2014.2632>.

³⁹ Ultrasound devices use sound waves to create images of the soft tissues and organs inside the body.

⁴⁰ Goro Inada, Shozo Fujita, and Mineko Ishizaki, "Comparative Studies on Film-, Xeroradio- and Ultrasound-Mammography of Breast Tumors"; Rikiya Abe et al., "Mobile Unit for Use in Mass Screening for Breast Cancer," *The Japanese Journal of Surgery* 17, no. 3 (May 1, 1987): 151-55, <https://doi.org/10.1007/BF02470590>.

⁴¹ Ian Munroe for EURObiZ Japan, "Breast Cancer: Low Screening Has Rates on the Rise in Japan," *Japan Today*, accessed January 17, 2017, <https://www.japantoday.com/category/health/view/breast-cancer-low-screening-has-rates-on-the-rise-in-japan>; Catherine Sauvaget et al., "Challenges in Breast and Cervical Cancer Control in Japan," *The Lancet Oncology* 17, no. 7 (July 1, 2016): e305-12, [https://doi.org/10.1016/S1470-2045\(16\)30121-8](https://doi.org/10.1016/S1470-2045(16)30121-8); Jong-Myon Bae et al., "Distribution of Dense Breasts Using Screening Mammography in Korean Women: A Retrospective Observational Study, Distribution of Dense Breasts Using Screening Mammography in Korean Women: A Retrospective Observational Study," *Epidemiology and Health* 36 (November 4, 2014): e2014027, <https://doi.org/2014.36.0.e2014027>; Brian L. Sprague et al., "Prevalence of Mammographically Dense Breasts in the United States," *JNCI Journal of the National Cancer Institute* 106, no. 10 (September 12, 2014), <https://doi.org/10.1093/jnci/dju255>; Thomas M Kolb, "Ultrasound Boosts Cancer Detection in Dense Breasts," *Diagnostic Imaging* 22, no. 11 (November 2000): 103.

⁴² F. Burbank, "Stereotactic Breast Biopsy: Its History, Its Present, and Its Future," *The American Surgeon* 62, no. 2 (February 1996): 128-50.

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

⁴⁶ Fox, Kimme-smith, and Kios, "The Technology Of Mammography"; Frost & Sullivan (1983) *The Diagnostic Radiology Market in the U.S.*

⁴⁷ Kodak had started selling mammographic film in Europe by 1969, and Du Pont had followed suit by 1975. By the end of the decade, AGFA-Gaevert (Belgium/Germany) also offered mammographic film in Europe and had an agreement with Xonics to produce and distribute its mammographic plates. In addition, Xerox offered its devices (that enabled general purpose X-ray equipment to produce accurate mammograms) in England. J. W. Boag, "Xeroradiography," *Physics in Medicine & Biology* 18, no. 1 (1973): 3, <https://doi.org/10.1088/0031-9155/18/1/001>. Fox, Kimme-smith, and Kios, "The Technology Of Mammography"; Frost & Sullivan (1983) *The Diagnostic Radiology Market in the U.S.*

⁴⁸ Goro Inada, Shozo Fujita, and Mineko Ishizaki, "Comparative Studies on Film-, Xeroradio- and Ultrasound-Mammography of Breast Tumors"; Abe et al., "Mobile Unit for Use in Mass Screening for Breast Cancer"; B. A. Arnold, "Evaluation of Mammographic Screen-Film Systems," *Japanese Journal of Radiological Technology* 34, no. 6 (March 1, 1979): 761, <https://doi.org/10.6009/jjrt.KJ00003104821>.

⁴⁹ Fox, Kimme-smith, and Kios, "The Technology Of Mammography"; Haus, "Technological Improvements in Mammography over the Past 20 Years"; Rothenberg; Gina Kolata, "Mammograms: Safer and More Accurate: Preliminary Diagnoses of Cancer Are Correct 75% of the Time.," *New York Times*, October 17, 1987, sec. NATIONAL NEWS; Haus, "Technological Improvements in Mammography over the Past 20 Years"; Haus, "Historical Technical Developments in Mammography"; Hendee, "History and Status of X-Ray Mammography"; M. J. Yaffe, "AAPM Tutorial. Physics of Mammography: Image Recording Process," *Radiographics: A Review Publication of the Radiological Society of North America, Inc* 10, no. 2 (1990): 341-63; C. Kimme-Smith et al., "New Mammography Screen-Film Combinations," 1988, http://inis.iaea.org/Search/search.aspx?orig_q=RN:21006927; K. T. Karila, "Performance of Automatic Exposure Controls in Mammography," *Medical Physics* 9, no. 6 (December 1982): 898-903; K. T. Karila, "Performance of X-Ray Generators and Unnecessary Dose in Mammography," *Radiology* 144, no. 2 (July 1982): 395-401, <https://doi.org/10.1148/radiology.144.2.7089296>. *Health Devices Sourcebook, 1990: The Hospital Purchasing Guide; a Directory of Medical Devices, Trade Names, Manufacturers, and Service Companies*, n.d.; Heidi M. Siegenthaler (Ed) Garrett, *Medical Device Register, 1993: The Official Directory of Medical Suppliers*, n.d.; L. N. Rothenberg, "Mammography Instrumentation: Recent Developments," *Medical Progress Through Technology* 19, no. 1 (1993): 1-6.

⁵⁰ Bassett, "The Regulation of Mammography"; Ruth Fischer et al., "The Impact of the Mammography Quality Standards Act on the Availability of Mammography Facilities," *Preventive Medicine* 27, no. 5 (September 1, 1998): 697-701, <https://doi.org/10.1006/pmed.1998.0347>; Lou Fintor, Marianne Haenlein Alciati, and Ruth Fischer, "Legislative and Regulatory Mandates for Mammography Quality Assurance," *Journal of Public Health Policy* 16, no. 1 (1995): 81-107, <https://doi.org/10.2307/3342978>; Haus, "Technological Improvements in Mammography over the Past 20 Years"; Haus, "Historical Technical Developments in Mammography." "pmb6_13_r10_Mammography_(JLaw).pdf." Accessed December 12, 2016. [http://www.sprmn.pt/pdf/pmb6_13_r10_Mammography_\(JLaw\).pdf](http://www.sprmn.pt/pdf/pmb6_13_r10_Mammography_(JLaw).pdf).

"1998 MQSA (Mammography Quality Standards Act) Final Rule Released. American College of Radiology." *Radiology Management* 20, no. 4 (1998): 51-55.

⁵¹ Susan Braun, "The History of Breast Cancer Advocacy," *The Breast Journal* 9 (May 1, 2003): S101-3, <https://doi.org/10.1046/j.1524-4741.9.s2.13.x>.

⁵² "History of ACS Recommendations for the Early Detection of Cancer in People Without Symptoms. Downloaded on September 28, 2020 from "https://www.cancer.org/health-care-professionals/american-cancer-society-prevention-early-detection-guidelines/overview/chronological-history-of-acs-recommendations.html

⁵³ Bassett, "The Regulation of Mammography"; Nadine Brozan, "Cost of Mammography Is a Major Deterrent," *New York Times*, September 22, 1986, sec. Style; "How to Make Mammography Affordable," *New York Times*, December 7, 1987, sec. NATIONAL NEWS, <http://search.proquest.com.ezp-prod1.hul.harvard.edu/docview/110695484/abstract/37DEFF8F72524911PQ/15?accountid=11311>; "New Law Requires Insurers To Pay Mammogram Costs," *New York Times*, September 7, 1988, sec. WASHINGTON TALK, <http://search.proquest.com.ezp-prod1.hul.harvard.edu/docview/110478903/abstract/67A4A9995991436EPQ/271?accountid=11311>; Valerie Andolina, *Mammographic Imaging: A Practical Guide*, 3rd ed. (Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins, 2011); Mukherjee, *The Emperor of All Maladies*.

⁵⁴ As previously mentioned, CT is an advanced digital X-ray technique.

⁵⁵ MRI uses magnetic fields and radio wave pulses to obtain data used to construct images.

⁵⁶ For a full explanation of these regulations, please refer to the Notes on development of computed tomography, magnetic resonance imaging, and ultrasound.

⁵⁷ 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.

⁵⁸ 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).

⁵⁹ L. Tabár et al., "Reduction in Mortality from Breast Cancer after Mass Screening with Mammography. Randomised Trial from the Breast Cancer Screening Working Group of the Swedish National Board of Health and Welfare," *Lancet* (London, England) 1, no. 8433 (April 13, 1985): 829-32.

⁶⁰ A. L. M. Verbeek et al., "Reduction of Breast Cancer Mortality through Mass Screening with Modern Mammography: First Results of the Nijmegen Project, 1975 - 1981," *The Lancet* 323, no. 8388 (June 2, 1984): 1222-24, [https://doi.org/10.1016/S0140-6736\(84\)91703-3](https://doi.org/10.1016/S0140-6736(84)91703-3). A second study in the Netherlands also suggested mortality could be reduced or delayed through regular mammography screenings: H. J. A. Collette et al., "Evaluation for Screening for Breast Cancer in a Non-Randomised Study (The DOM Project) by Means of a Case-Controlled Study," *The Lancet*, Originally published as Volume 1, Issue 8388, 323, no. 8388 (June 2, 1984): 1224-26, [https://doi.org/10.1016/S0140-6736\(84\)91704-5](https://doi.org/10.1016/S0140-6736(84)91704-5).

⁶¹ 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](https://doi.org/10.1016/0168-8510(94)00683-6). However, comprehensive adoption data does not exist for Europe.

⁶² Altobelli and Lattanzi, "Breast Cancer in European Union"; P. Autier et al., "Mammography Screening and Breast Cancer Mortality in Sweden," *Journal of the National Cancer Institute* 104, no. 14 (July 18, 2012): 1080-93, <https://doi.org/10.1093/jnci/djs272>; Cornelis Biesheuvel, Stefanie Weige, and Walter Heindel, "Mammography Screening: Evidence, History and Current Practice in Germany and Other European Countries," *Breast Care* 6, no. 2 (2011): 104-109, <https://doi.org/10.1159/000327493>; L. Von Karsa, "Mammography Screening - What Is Going on in Europe," *Ejc Supplements* 8, no. 3 (2010): 189-189; Karen Birchard, "Mammography Benefits Seen in Europe," *Medical Post* 39, no. 20 (May 20, 2003): 58; R. Ballard-Barbash et al., "Breast Cancer Screening in 21 Countries: Delivery of Services, Notification of Results and Outcomes Ascertainment," *European Journal of Cancer Prevention: The Official Journal of the European Cancer Prevention Organisation (ECP)* 8, no. 5 (October 1999): 417-26.

⁶³ David H. Howard, Lisa C. Richardson, and Kenneth E. Thorpe, "Cancer Screening And Age In The United States And Europe," *Health Affairs* 28, no. 6 (November 1, 2009): 1838-47, <https://doi.org/10.1377/hlthaff.28.6.1838>; Ballard-Barbash et al., "Breast Cancer Screening in 21 Countries," 21.

⁶⁴ 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.")

⁶⁵ 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.

⁶⁶ 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."

⁶⁷ Burbank, "Stereotactic Breast Biopsy." Rothenberg, "Mammography Instrumentation"; Kolata, "Mammograms"; Haus, "Technological Improvements in Mammography over the Past 20 Years"; Haus, "Historical Technical Developments in Mammography"; Hendee, "History and Status of X-Ray Mammography"; Yaffe, "AAPM Tutorial. Physics of Mammography"; Kimme-Smith et al., "New Mammography Screen-Film Combinations"; Karila, "Performance of Automatic Exposure Controls in Mammography"; Karila, "Performance of X-Ray Generators and Unnecessary Dose in Mammography."

⁶⁸ Howard Anderson, "Trends in Equipment Acquisition," *Trustee* 43, no. 11 (November 1990): 18, 21; Haus, "Technological Improvements in Mammography over the Past 20 Years"; Haus, "Historical Technical Developments in Mammography"; Kimme-Smith et al., "New Mammography Screen-Film Combinations"; Andrew Pollack, "Two Giants Swap Ambitions: G.E. Grows in A Tough Field G.E. Expands in Tough Medical Imaging Business," *New York Times*, July 24, 1987, sec. Business Day, <http://search.proquest.com.ezp-prod1.hul.harvard.edu/docview/110652028/abstract/67A4A9995991436EPQ/190?accountid=11311>. See the *Health Devices Sourcebooks* for 1980, 1989-1992, which register companies making devices for the US Market. ECRI, and Emergency Care Research Institute. *Health Devices Sourcebook*. Plymouth Meeting, PA: ECRI, 1979-2005. Some of the companies listed in the Health Devices Sourcebook, however, are dealers or service companies. See also the *Medical Device Registers: The Official Directory of Medical Suppliers*. In addition, the FDA 510(k) database lists companies intending to market in the US. Vision Ten started with devices but then switched to building film digitizers. "pmb6_13_r10_Mammography_(JLaw).pdf." Accessed December 12, 2016. [http://www.sprnm.pt/pdf/pmb6_13_r10_Mammography_\(JLaw\).pdf](http://www.sprnm.pt/pdf/pmb6_13_r10_Mammography_(JLaw).pdf).

⁶⁹ Only one company, 3M, started selling specialized film, and none of the three established film producers exited.

⁷⁰ Anderson, "Trends in Equipment Acquisition"; Haus, "Technological Improvements in Mammography over the Past 20 Years"; Haus, "Historical Technical Developments in Mammography"; Kimme-Smith et al., "New Mammography Screen-Film Combinations"; Pollack, "Two Giants Swap Ambitions." See also the *Health Devices Sourcebooks* for 1980, 1989-1992, and the *Medical Device Registers*. In addition, the FDA 510(k) database lists companies intending to market in the U.S.

⁷¹ Information about the European market has been gleaned from Frost & Sullivan (1983) *The Diagnostic Radiology Market in the U.S.*

⁷² Researchers were particularly interested in testing computed tomography's capacity to improve diagnostic breast X-rays. Some were initially interested in screening with CT but, when tested, found it practical for diagnostic use only. Researchers used contrast agents and alternative views (such as multiple "slices" through the breast and chest) as well as computerized processing to enhance the digital images of breasts and locate hard-to-find cancers. Later, researchers also noted that digital magnification made minimally-invasive biopsies more accurate. See: Ch Chang et al., "Computed Tomographic Mammography Using a Conventional Body Scanner," *American Journal of Roentgenology* 138, no. 3 (March 1, 1982): 553-58, <https://doi.org/10.2214/ajr.138.3.553>; C. H. Joseph Chang et al., "Computed Tomography in Detection and Diagnosis of Breast Cancer," *Cancer* 46, no. S4 (n.d.): 939-46, [https://doi.org/10.1002/1097-0142\(19800815\)46:4+<939::AID-CNCR2820461315>3.0.CO;2-L](https://doi.org/10.1002/1097-0142(19800815)46:4+<939::AID-CNCR2820461315>3.0.CO;2-L); HEANG-PING Chan et al., "Digital Mammography: ROC Studies of the Effects of Pixel Size and Unsharp-Mask Filtering on the Detection of Subtle Microcalcifications," *Investigative Radiology* 22, no. 7 (July 1987): 581-89; G D Dixon, "Preoperative Computed-Tomographic Localization of Breast Calcifications.," *Radiology* 146, no. 3 (March 1, 1983): 836-836, <https://doi.org/10.1148/radiology.146.3.6828704>; X. H. Zhou and R. Gordon, "Detection of Early Breast Cancer: An Overview and Future Prospects," *Critical Reviews in Biomedical Engineering* 17, no. 3 (1989): 203-55; Burbank, "Stereotactic Breast Biopsy"; Andrew D. A Maidment, "Digital Mammography," *Seminars in Roentgenology, Digital Imaging*, 38, no. 3 (July 2003): 216-30, [https://doi.org/10.1016/S0037-198X\(03\)00048-8](https://doi.org/10.1016/S0037-198X(03)00048-8).

⁷³ Laurens Ackerman, "Computer Classification of Radiographs and Xerograms of the Breast" (ProQuest Dissertations Publishing, 1971), <http://search.proquest.com/docview/302549978/>; Laurens V. Ackerman and Earl E. Gose, "Breast Lesion Classification by Computer and Xeroradiograph," *Cancer* 30, no. 4 (n.d.): 1025-35, [https://doi.org/10.1002/1097-0142\(197210\)30:4<1025::AID-CNCR2820300425>3.0.CO;2-7](https://doi.org/10.1002/1097-0142(197210)30:4<1025::AID-CNCR2820300425>3.0.CO;2-7); C. Kimme-Smith, "New and Future Developments in Screen-Film Mammography Equipment and Techniques," *Radiologic Clinics of North America* 30, no. 1 (1992): 55-66; Chan et al., "Digital Mammography."

⁷⁴ Joerg W. Oestmann et al., "A Comparison of Digitized Storage Phosphors and Conventional Mammography in the Detection of Malignant Microcalcifications," *Investigative Radiology* 23, no. 10 (October 1988): 725-28; Carolyn Kimme-Smith et al., "Digital Mammography A Comparison of Two Digitization Methods," *Investigative Radiology* 24, no. 11 (November 1989): 869-75; Andrew D. A. Maidment and Martin Joel Yaffe, "Scanned-Slot Digital Mammography," in *Medical Imaging IV: Image Formation*, vol. 1231 (Medical Imaging IV: Image Formation, International Society for Optics and Photonics, 1990), 316-27, <https://doi.org/10.1117/12.18808>; T. Yamada and Y. Muramatsu, "Computed Radiography for Breast Cancer," *Japanese Journal of Clinical Oncology* 20, no. 2 (June 1990): 164-68.

⁷⁵ Ackerman and Gose, "Breast Lesion Classification by Computer and Xeroradiograph"; Kimme-Smith et al., "Digital Mammography A Comparison of Two Digitization Methods"; Kimme-Smith, "New and Future Developments in Screen-Film Mammography Equipment and Techniques."

⁷⁶ S. L. Fritz et al., "A Digital Radiographic Imaging System for Mammography," *Investigative Radiology* 21, no. 7 (July 1986): 581-83; Rothenberg, "Mammography Instrumentation"; Maidment and Yaffe, "Scanned-Slot Digital Mammography"; F Shtern, "Digital Mammography and Related Technologies: A Perspective from the National Cancer Institute.," *Radiology* 183, no. 3 (June 1, 1992): 629-30, <https://doi.org/10.1148/radiology.183.3.1584908>.

⁷⁷ 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."

⁷⁸ 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 Breast Cancer Imaging," *Acta Astronautica* 41, no. 4 (1997): 515-523, [https://doi.org/10.1016/S0094-5765\(98\)00054-X](https://doi.org/10.1016/S0094-5765(98)00054-X); Maidment, "Digital Mammography."

⁷⁹ The development group began as a national group but expanded to work with international researchers by the end of the 1990s. In 1996, the USPHS funded an expansion of the program that enabled additional agencies within the U.S. federal government to participate. Shtern, "Digital Mammography and Related Technologies"; Winfield, "Aerospace Technology Transfer to Breast Cancer Imaging"; Maidment, "Digital Mammography"; "UNC-CH Scientists Study Improved Mammography," accessed August 21, 2018, <http://www.unc.edu/news/archives/mar97/bcancer.html>.

⁸⁰ Burbank, "Stereotactic Breast Biopsy." Frost & Sullivan. (2001) *World X-Ray Mammography Market*. See also: Frost & Sullivan. (2003) *X-Ray Mammography Markets in North America and Japan and the Rest of the World*. 3-35.

⁸¹ Although computer-assisted diagnoses did not develop as earlier researchers had hoped, researchers did find that digital screening systems exposed patients to less radiation and improved the accuracy of diagnoses in women with dense breasts. Daniel Winfield et al., "Technology Transfer in Digital Mammography: Report of the Joint National Cancer Institute-National Aeronautics and Space Administration Workshop of May 19-20, 1993," *Investigative Radiology* 29, no. 4 (April 1994): 507-15; Richard L. Morin and Andrew D. A. Maidment, "Digital Mammography: Coming of Age," *Journal of the American College of Radiology: JACR* 2, no. 9 (September 2005): 798-801, <https://doi.org/10.1016/j.jacr.2005.06.008>; Etta D. Pisano, "Current Status of Full-Field Digital Mammography," *Radiology* 214, no. 1 (January 1, 2000): 26-28, <https://doi.org/10.1148/radiology.214.1.r00ja5226>; Stephen A Feig and Martin J Yaffe, "Current Status of Digital Mammography," *Seminars in Ultrasound, CT and MRI, Breast Imaging: An Update*, 17, no. 5 (October 1, 1996): 424-43, [https://doi.org/10.1016/S0887-2171\(96\)90029-3](https://doi.org/10.1016/S0887-2171(96)90029-3); "Report of the Working Group on Digital Mammography: Digital Displays and Workstation Design. Washington DC, USA. March 19-10, 1998," *Academic Radiology* 6 Suppl 4 (April 1999): S195-219; "Report of the Working Group on Digital Mammography: Computer-Aided Diagnosis and 3D Image Analysis and Display. Cambridge, Massachusetts, USA. October 8-9, 1998," *Academic Radiology* 6 Suppl 5 (June 1999): S223-256; Maidment, "Digital Mammography"; "UNC-CH Scientists Study Improved Mammography." Frost & Sullivan. (2000) *World X-Ray and Computed Tomography Markets*. Chapter 5. Frost & Sullivan. (2001) *World X-Ray Mammography Market*.

⁸² Kodak was first to develop the phosphor-coated plates in 1973, patenting them in 1975. After 1975, Xerox, AGFA/Gaevent, Fujifilm, 3M, Siemens, and Toshiba all had similar plates in development. Fujifilm was the first of these companies to introduce a commercial plate for routine clinical use. H Kangaroo et al., "Two-Year Clinical Experience with a Computed Radiography System," *American Journal of Roentgenology* 151, no. 3 (September 1, 1988): 605-8, <https://doi.org/10.2214/ajr.151.3.605>; R. M. Dawood, "Radiology about to Go Digital.," *BMJ: British Medical Journal* 299, no. 6695 (August 5, 1989): 340-41; Rachot Yodnin, "CR History," (Technology, 03:54:40 UTC), https://www.slideshare.net/Ag_Silver/cr-history-2939116. See also: "Transitioning to

Digital Radiography – When Does It Make Sense?” by S.A. Mango, Aerial and Industrial Materials, Eastman Kodak Company, Rochester, USA.

⁸³ G. S. Lodwick, “Radiology Systems of the 1990s--Meeting the Challenge of Change,” *The Western Journal of Medicine* 145, no. 6 (December 1986): 848–52; Greg Freiherr, “Digital X-Ray: The Big Picture,” *Diagnostic Imaging*; San Francisco, November 1999, D4. Frost & Sullivan. (2004) *World Digital Radiography (DR) Markets*. 5-2. See also: the FDA’s 510(k) clearances database.

⁸⁴ “Fuji CR Mammo Approval Offers New Option for Breast Imaging,” AuntMinnie.com, accessed April 5, 2017, <http://www.auntminnie.com/index.aspx?sec=ser&sub=def&pag=dis&itemid=71682>; “FUJIFILM Computed Radiography for Mammography Progresses From Market Entrant to Market Leadership Worldwide,” *PR Newswire*; New York, July 28, 2002. “FUJIFILM’S FCR Velocity Enables High Productivity Digital X-Ray Affordably,” *PR Newswire*; New York, December 2, 2002.

⁸⁵ Previously the FDA only had such authority over new drug introductions.

⁸⁶ Niels, Morgan “FDA & Digital Mammography Why Has FDA Required Full Field Digital Mammography Systems to Be Regulated as Potentially Dangerous Devices for More Than 10 Years?,” *Academic Radiology* 17, no. 5 (2010): 652–657, <https://doi.org/10.1016/j.acra.2010.01.012>; Pisano, “Current Status of Full-Field Digital Mammography”;

Barbara Galen et al., “American College of Radiology Imaging Network: The Digital Mammographic Imaging Screening Trial—An Update,” *Academic Radiology* 9, no. 3 (March 2002): 374–75, [https://doi.org/10.1016/S1076-6332\(03\)80382-3](https://doi.org/10.1016/S1076-6332(03)80382-3); “Digital Sensors to Launch Revolution in Medical Imaging | MDDI Medical Device and Diagnostic Industry News Products and Suppliers,” accessed February 13, 2017, <http://www.mddionline.com/article/digital-sensors-launch-revolution-medical-imaging>.

⁸⁷ 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.

⁸⁸ Niels, “FDA & Digital Mammography Why Has FDA Required Full Field Digital Mammography Systems to Be Regulated as Potentially Dangerous Devices for More Than 10 Years?”; Pisano, “Current Status of Full-Field Digital Mammography”; Galen et al., “American College of Radiology Imaging Network”; “Digital Sensors to Launch Revolution in Medical Imaging | MDDI Medical Device and Diagnostic Industry News Products and Suppliers.”

⁸⁹ See: Thermo Electron Corporation, “Trex Medical Submits 510(K) for Full-Field Digital Mammography System,” accessed February 2, 2017, <http://www.prnewswire.com/news-releases/trex-medical-submits-510k-for-full-field-digital-mammography-system-77745572.html>; Thermo Electron Corporation, “FDA Notifies Trex Medical That 510(k) for Digital Mammography System Has Been Withdrawn,” accessed January 11, 2017, <http://www.prnewswire.com/news-releases/fda-notifies-trex-medical-that-510k-for-digital-mammography-system-has-been-withdrawn-77816787.html>; “Turbulence Hits Trex as Kirshner Quits, FDA Rejects Digital Mammography Filing | Diagnostic Imaging,” January 13, 1999, <http://www.diagnosticimaging.com/articles/turbulence-hits-trex-kirshner-quits-fda-rejects-digital-mammography-filing>.

⁹⁰ 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 and 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. Ishibashi et al.; Frost & Sullivan (2001). *World X-Ray Mammography Market*.

⁹¹ Chai, “Medical Device Regulation in the United States and the European Union”; Niels, “FDA & Digital Mammography Why Has FDA Required Full Field Digital Mammography Systems to Be Regulated as Potentially Dangerous Devices for More Than 10 Years?” Frost & Sullivan (2001). *World X-Ray Mammography Market*; Frost & Sullivan (2008) *European Mammography Systems Market*.

⁹² Corporation, “Trex Medical First To Receive Certification To Market Digital Mammography System In Europe”; “Trex CE Mark Gives European Patients Access to Digital Mammography before Those in the U.S. | Diagnostic Imaging”; “FDA Clears GE’s Digital Mammography System | Diagnostic Imaging”; “GE Medical Systems Begins European Shipments of Senographe 2000D Digital Mammography Unit | OBGYN.Net.” Frost & Sullivan (2001). *World X-Ray Mammography Market*; Frost & Sullivan (2008) *European Mammography Systems Market*.

⁹³ Frost & Sullivan (2001). *World X-Ray Mammography Market*.

⁹⁴ Frost & Sullivan. (2003) *X-Ray Mammography Markets in North America and Japan and the Rest of the World* B. Jouan, "Digital Mammography Performed with Computed Radiography Technology," *European Journal of Radiology* 31, no. 1 (July 1999): 18-24; Yamada and Muramatsu, "Computed Radiography for Breast Cancer"; Morimoto et al., "A Comparison of Mass Screening for Breast Cancer Using Mammography and Physical Examination Alone in Japan"; Takayuki Yamada, "Current Status and Issues of Screening Digital Mammography in Japan," *Breast Cancer* 17, no. 3 (July 1, 2010): 163-68, <https://doi.org/10.1007/s12282-009-0191-z>. When Yamada states that "Digital mammography has become more widespread. Digital systems are replacing screen-film systems and now account for more than half of mammographic equipment in Japan," he may be including both sensor-based and plate-based equipment in his estimate. See Uematsu, "Digital Mammography in Japan."

⁹⁵ 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?"

⁹⁶ Frost & Sullivan (2001). *World X-Ray Mammography Market*

⁹⁷ Frost & Sullivan (2001). *World X-Ray Mammography Market*, 3-5

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⁹⁹ Frost & Sullivan (2001). *World X-Ray Mammography Market*, 2-10

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