

Case Histories of Significant Medical Advances: Gastrointestinal Endoscopy

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Gastrointestinal Endoscopy

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Abstract: We describe how endoscopy transformed the diagnosis of ulcers, cancerous polyps and other diseases of the alimentary canal and enabled “minimally invasive” surgeries to treat such diseases. Specifically, we chronicle how: 1) flexible glass fiber endoscopes developed in the 1950s and 1960s provided the foundation; 2) technical advances – promoted by evangelical innovators – in the 1970s and early 1980s enabled new diagnostic techniques and minimally invasive abdominal surgeries; 3) radical and incremental improvements through the end of the 20th century sustained growth – although they did not enable many new procedures; and, 4) capsule endoscopes containing miniaturized cameras that patients swallowed provided another breakthrough in the first decade of the 21st century.

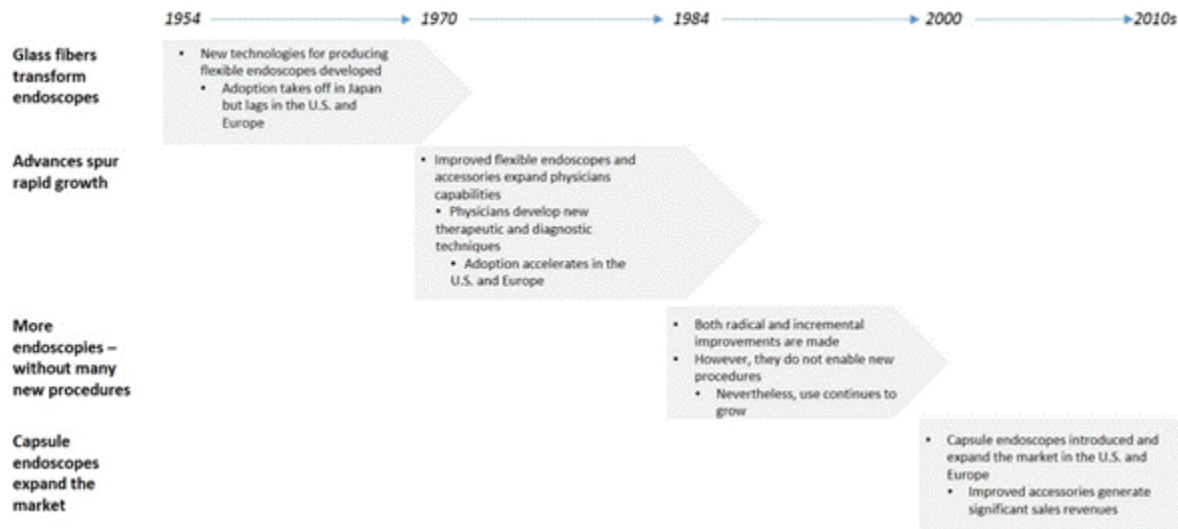
Note: This case history, like the others in this series, is included in a list compiled by Victor Fuchs and Harold Sox (2001) of technologies produced (or significantly advanced) between 1975 and 2000 that internists in the United States said had had a major impact on patient care. The case histories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

Gastrointestinal Endoscopy

Technology has transformed the centuries-old technique of endoscopy. Nineteenth century physicians had inserted metal tubes called endoscopes into bodily orifices to help diagnose problems in the alimentary canal, such as indigestion, bleeding, or obstructions. In 1957, a revolutionary flexible glass fiber-based endoscope enabled the diagnosis of many more gastrointestinal diseases, including ulcers and cancers. In addition to improving diagnoses, which was their initial application, glass fiber-based endoscopes had therapeutic applications: they enabled “minimally invasive” surgeries on the throat, stomach, and intestines that reduced infections, hospital stays, and recovery times. Technological advances then continued to reshape endoscopy, most notably with the introduction of an ingestible capsule containing a miniature digital camera.¹

The four main sections of this case study describe the progressive development of endoscopes and endoscopic techniques. (See **Figure 1**) An Epilogue reviews recent developments.

Figure 1 The Evolution of Endoscopy



1. Glass fibers transform endoscopes (1954-1970)

Early tubular and jointed devices

Nineteenth century endoscopes comprised metal tubes fitted with glass lenses and incandescent lamps. Physicians inserted them through mouths and rectums to inspect stomachs and colons. However, these endoscopes were too short and stiff to enable a full examination, caused substantial discomfort, and posed risks of cuts and burns.²

In the early 1930s, the German medical device company Richard Wolf^a collaborated with German gastroenterologist Rudolph Schindler to reduce these drawbacks. They developed a jointed, rubber-coated “gastroscope” that physicians could safely slide into patients’ stomachs and swivel around to view large parts of the organ’s interior. However, operating Wolf-Schindler gastroscopes required considerable skill,

^a The company was founded as Brukner and Wolf in 1906 and in the 1930s was known as Georg Wolf. In 1947, it became Richard Wolf.

limiting their use: over the next thirty years physicians in Europe and the United States (where Schindler had emigrated to teach in 1934) bought a little more than a thousand of these devices.³ Instead, most physicians used X-rays, which had been used for medical diagnoses since 1895, or relied on patient histories and symptoms to prescribe treatments.

Breakthrough advances

In January 1954, two articles published in the same issue of *Nature*, a prestigious interdisciplinary journal, provided a foundation for a breakthrough in endoscopes. Both articles described a similar (but independently conceived) method, still in an experimental stage, for transmitting images through bendable glass fiber bundles. Researchers already knew that thin glass fibers could transmit light -- even when bent -- thereby potentially allowing the transmission of images "around corners." A German medical student (who had studied under gastroscope pioneer Rudolph Schindler) had hoped to use this capacity in an endoscope in 1930 but discovered the bent fibers transmitted distorted images.^b The two 1954 *Nature* articles, written by physicists from Britain and the Netherlands,^c suggested:

- Bent fibers distorted the images they transmitted because light "leaked" out as it passed through;
- Coating the fibers to limit light leaking out would reduce distortions - and they offered experimental evidence supporting this suggestion; and
- Coated glass fibers, packaged in flexible bundles, could be used in applications such as photography, microscopy - and endoscopy.⁴

The articles attracted the attention of Basil Hirschowitz, a South African gastroenterologist with a fellowship^d at the University of Michigan Medical School. In the spring of 1954, a few months after reading the articles, Hirschowitz visited the British authors' lab. Hirschowitz then recruited a University of Michigan colleague, physicist C.W. Peters, and Peters' undergraduate student, Larry Curtiss, to help build a flexible glass fiber endoscope. No quality fibers were then commercially available, so they melted glass rods to draw out their own fibers, which they wound around an oatmeal can. Between the summer of 1954 and the fall of 1956, they experimented with different coatings for their glass fibers, discovering that most materials rapidly wore off. Finally, in December 1956, the undergraduate student, Curtiss, hit upon the idea of coating the glass fibers with a different, more durable glass. The researchers filed for a U.S. patent^e based on their conceptual design for a fiber endoscope in December 1956. Curtiss then took the lead in writing up the patent application for the glass-clad fibers, which they filed five months later. (However, as we will see, a legal dispute delayed issuance of the patents for fourteen years.)⁵

By January of 1957, Hirschowitz, Peters, and Curtiss had developed and started testing a prototype fiber endoscope. That May, they demonstrated that it transmitted undistorted images at the American

^b Schindler's student, Heinrich Lamm, described his experiment in an article in a German engineering journal. He wrote, "I ... hope that some optical firm possessed of more means, sources of supply, and experience than I have, could be induced by this report to build a serviceable flexible gastroscope" -- but none did, because the article was not widely read. Lamm abandoned his research shortly thereafter, finished his medical degree, and emigrated to the U.S. to practice medicine in 1937.

^c One article was written by physicist Abraham van Heel, who was funded by the military in the Netherlands. The other was written by physicists Harold Hopkins and Narinder Kapany, who were funded by a grant from the Royal Society in the United Kingdom.

^d Hirschowitz's fellowship was sponsored by the American Cancer Society.

^e The U.S. patent would not be granted until 1971. However, the three researchers also applied for patents in Germany, France, and Canada, which they had received by the mid-1960s. Fatefully, they did not apply for a patent in Japan.

Gastroscopic Club^f by letting attendees^g read a telephone directory through its eyepiece. Shortly thereafter, Hirschowitz persuaded American Cystoscope Makers, Inc., which had been producing rigid endoscopes since 1908, to develop a flexible glass fiber device for clinical use.⁶

Clinical applications proposed

In 1960, Hirschowitz moved to the University of Alabama and began to research the diagnostic uses of American Cystoscope's fiber endoscope. In 1961, he published an article in *The Lancet*, a prestigious medical journal, describing how the "completely flexible" (emphasis in the original) fiber endoscope "readily displayed" not only the inside of the throat and stomach but also "areas not previously accessible": the duct coming out of the bottom of the stomach that leads to the gall bladder, liver, pancreas, and small intestine. In 1962, Hirschowitz published a study in the prestigious *Journal of the American Medical Association (JAMA)* comparing the results of five hundred fiber endoscope examinations with diagnoses made with X-rays and surgery. He concluded in the *JAMA* article that, in addition to more complete views of the stomach and ducts exiting the stomach, fiber endoscopes offered the following advantages over previous Wolf-Schindler jointed gastroscopes:

- *Brighter, projectable images*: the fiber endoscope lit the stomach with an incandescent lamp at the tip, just as the Wolf-Schindler gastroscopes did; however, it produced two and half times brighter images because less light was lost in transmission. The brighter images could be recorded or projected with still, television, or motion picture cameras, enabling viewing by a group, whereas the dimmer images produced by previous endoscopes only allowed viewing by individuals, one at a time, through eyepieces.
- *Patient comfort*: patients usually needed only minimal sedation to suppress gagging, allowing them to respond to physicians' questions and instructions during examinations; and
- *Shorter patient preparation times*: physicians needed less time to prepare patients who did not have to be fully sedated for examinations of the throat and stomach, allowing more time for diagnoses.⁷

Hirschowitz conceded that the existing Wolf-Schindler gastroscopes might be better for throat examinations. For diagnosing problems in the stomach and the duct exiting the stomach, however, Hirschowitz suggested that fiber endoscopes could complement traditional X-rays (the dominant mode of diagnosis, short of surgery) in two ways:

- *Bedside Diagnoses*: fiber endoscope procedures did not require removing patients from their beds, allowing physicians to examine severely ill patients with gastrointestinal bleeding who could not be moved for X-rays; and
- *Improved accuracy*: about a third of the problems discovered with the fiber endoscope could not be seen on X-rays at all. Conversely, in up to forty percent of cases, X-rays diagnosed problems that had not been visible in endoscope examinations.^h When used jointly, Hirschowitz suggested endoscopes and X-rays would produce accurate diagnoses ninety percent of the time.⁸

^f Gastroscopy pioneer Rudolph Schindler founded the American Gastroscopic Club in 1941. It became the American Society for Gastrointestinal Endoscopy in 1961.

^g The small audience of forty included Rudolph Schindler and physicist Narinder Kapany, an author of one of the pivotal 1954 *Nature* articles on bundling coated glass fibers. Both offered suggestions for improvement.

^h For instance, an X-ray would show problems with the outer surface of the stomach and ducts, whereas the fiber endoscope could only view the inside of the stomach and ducts.

Resistance in the United States and Europe

Hirschowitz's articles prompted several prominent American and European gastroenterologists to try fiber endoscopes – but their trials did not make the endoscopes more popular than gastroscopes (which, as mentioned, had also failed to enter mainstream clinical practice). Users reported many complaints, published in *The Lancet* and other medical journals, including:

- *Image quality*: lenses in fiber endoscopes did not focus easily and produced images with one-third less detail than gastroscopes. Image quality was further reduced by the inability to clean lenses during fiber endoscope procedures (whereas a gastroscope included a tube that injected bursts of air to clear the lens);
- *Maneuverability*: fiber endoscopes were hard to control as they moved through the throat into the stomach and hard to insert into the duct below the stomach;
- *Safety*: the curling or bending of fiber endoscopes sometimes caused tears and bleeding, and the use of incandescent lamps caused burns;
- *Fragility*: the glass fibers could easily break – especially if patients accidentally bit down on them;
- *Cost*: Gastroenterologists considered the fragile devices expensive – they cost about USD\$1,600 (approximately USD\$13,000 in today's dollars) and even more in Europe;
- *Limited improvements in accuracy*: fiber endoscopes did not always diagnose stomach problems more accurately than gastroscopesⁱ; and
- *Inability to extract tissue samples*: fiber endoscopes lacked the tools necessary to extract tissue samples for lab analysis, as gastroscopes could.^j

These problems reinforced the reluctance of physicians to learn new procedures with fiber endoscopes.⁹

The reluctance prompted American Cystoscope and other companies that had started selling fiber endoscopes to add a variety of improvements in the mid- to late-1960s, including:

- Tubes for air, water, and suction, to clean lenses during procedures;
- Devices specialized for specific examinations in the throat, the duct exiting the stomach, and the colon. (For instance, narrower devices for examining the duct exiting the stomach and shorter devices with more flexible tips for examining throats);
- Glass fibers that transmitted cool-to-the-touch light from an outside source into the body (replacing hot incandescent lamps, attached to the ends of endoscopes inserted into patients)^k; and
- Still and motion cameras optimized for endoscopic examinations.¹⁰

ⁱ However, in examinations of the duct exiting the stomach, where the gastroscope could not reach, researchers acknowledged that the fiber endoscope was superior (provided the examiner had the skill to maneuver the fiberscope into the duct).

^j The removal of a tissue sample for analysis in a lab is known as a "biopsy."

^k A roughly concurrent, parallel line of development to glass fiber endoscopes entailed the use of glass rods to transmit light into the body. In an 1889 *Lancet* article, Viennese scientists described using a glass rod to channel exterior light into the nose and throat during endoscopic diagnoses. They reported the rod was cool to the touch and therefore safer than the hot incandescent bulbs typically used to light endoscopes. In 1952, French scientists built a prototype endoscope that incorporated this so-called "cold light," and, by 1960, two German endoscope companies offered rigid endoscopes lit with "cold light." However, none of these researchers or companies had tried to transmit images with the glass rods or fibers prior to Hirschowitz's experiments. By 1967, fiber endoscope makers had replaced the incandescent lamp with a second glass fiber bundle that transmitted light from an outside source into the stomach. This use of "cold light" further increased the intensity of light in the stomach 10- to 50-fold while reducing the likelihood of burns.

Use in teaching gastroenterology

Hirschowitz started a residency program to train physicians specializing in gastroenterology at the University of Alabama after he moved there in 1960 (along with conducting the clinical research described earlier). The program taught diagnostic procedures that used fiber endoscopes. Hirschowitz also used the endoscopes to project images on a screen in his teaching (instead of requiring students to look through eyepieces one-by-one) – and published articles promoting this advantage to using fiber endoscopes in teaching gastroenterology.¹¹

Thirty-four residency programs in gastroenterology (like Hirschowitz's) that had been started in American medical schools with National Institutes of Health¹ funding also used fiber endoscopes extensively. These programs attracted both American and European medical students. Many of the graduates of these programs later secured teaching appointments (in the U.S. and Europe), in which they used endoscopes. Thus the number of gastroenterologists who learned to use fiber endoscopes continued to multiply.¹²

Popularity in Japan

Japanese physicians adopted fiber endoscopes more rapidly than their counterparts in the United States and Europe. Japan had a high incidence of stomach cancer and therefore had started widespread stomach cancer screening in the mid-1960s. In the screening procedures, Japanese gastroenterologists initially used “gastrocameras”^m inserted into patients' stomachs at the end of long, flexible tubes.¹³ However, gastrocameras recorded images on traditional film that had to be developed before diagnoses could be made. Fiber endoscopes, which provided immediate viewing (thereby eliminating the delays associated with gastrocameras), therefore sold rapidly after they were introduced. By 1969, 15,000 were in use in Japan (compared to 10,000 gastrocameras in 1966).¹⁴

Producers of fiber endoscopes

By the end of the 1960s, six companies were selling fiber endoscopes in the U.S., Europe, and Japan. (See Table 1) As mentioned, a fifty-year-old endoscope producer, American Cystoscope, became the first in 1960, using technology licensed from Hirschowitz and his University of Michigan colleagues. Shortly thereafter, a producer of eyeglasses and microscopes, American Optical Company, offered a competing device.ⁿ American Optical had also been developing coated glass fibers for the U.S. Central Intelligence Agency. In 1954, the company had filed for a patent for the coated fibers, which it received in 1958. Therefore, when American Cystoscope started selling fiber endoscopes, American Optical sued for patent infringement (on their patent for the coated glass fibers, not for the endoscope itself). The long-running patent dispute would continue until 1971, when Hirschowitz's team won on a technicality, and finally obtained their U.S. patents, in addition to back royalties.¹⁵

While the dispute continued, American Optical licensed its technology to two companies in Japan, where Hirschowitz and his colleagues had not applied for a patent. One of the companies, camera producer

¹ The division of the National Institutes of Health (a U.S. government agency that funds medical research) that oversaw the funding for gastroenterology programs was the National Institute for Arthritis and Metabolic Diseases, now known as National Institute of Diabetes and Digestive and Kidney Diseases.

^m Japanese companies also made various rigid and semi-rigid endoscopes. Historians report that gastrocameras were introduced in the U.S. at the First World Congress of Gastroenterology in Washington, D.C., in 1958. However, the devices were “overshadowed by Basil Hirschowitz's paper on the fiberscope, which had been first used in the previous year.” Olympus sold only about 200 gastrocameras in the U.S. before the device was discontinued.

ⁿ Hirschowitz had previously pitched the fiber endoscope to American Optical, Eder Instrument Company (U.S.), and Genito-Urinary Manufacturing Ltd. (UK) before reaching an agreement with ACMI.

Olympus, had been selling gastrocameras, and the other, Machida, was a longtime producer of metal tubular endoscopes.¹⁶

Two German gastroscope producers – Richard Wolf (established in 1906, which had helped develop jointed gastroscopes) and Karl Storz (established in 1945) – also introduced fiber endoscopes in the 1960s. (Both companies also already offered laparoscopes -- tubular instruments inserted through small incisions, rather than through orifices, into patients’ abdomens; and although the record does not explicitly state so, both companies presumably invented around the fiber coating and fiber endoscope patents.)¹⁷

Table 1 Companies that sold fiber endoscopes in the 1960s (including domiciles, source of technology, innovations introduced, and pathologies diagnosed)

Company (Domicile)	Source of Technology	Innovations Introduced	Pathologies Diagnosed
American Cystoscope Makers Inc. (USA)	Licensed from Curtiss, Peters, and Hirschowitz	Channel for air, water, and suction; longer devices	Throat, stomach, duct exiting the stomach
American Optical (USA)	Developed glass fibers for U.S. government		Stomach
Karl Storz Instruments (Germany)	Worked with UK physicist who first proposed fiber endoscopes	Improved controls and lighting in endoscopic cameras	Throat, stomach
Machida Endoscopes Co. (Japan)	Licensed from American Optical		Throat, stomach, duct exiting the stomach, colon
Olympus Corp. (Japan)	Licensed from American Optical	Longer, more durable devices; longer, narrower devices; shorter, more flexible devices; improved optics in endoscopic cameras	Throat, stomach, duct exiting the stomach, ducts to the pancreas and gall bladder, colon
Richard Wolf Instruments (Germany)	Had previously used glass fibers to light traditional rigid endoscopes	Devices with external light sources	Throat, stomach

Sources: Morrissey (1972), Edmonson (1991), Kasumi et al (1993), Lintynski (1996), Hecht (1999), Hirschowitz (2003), and Gelijns and Rosenberg (2010).

Note: One other American company, Eder Instrument Company, had tried to develop fiber endoscopes but failed to produce devices for routine clinical use.

2. Advances spur rapid growth (1970-1983)

Improvements expand diagnostic uses

By the 1970s, improved fiber endoscopes had completely displaced gastroscopes for gastrointestinal diagnoses and become an important complement to X-rays. One significant improvement enabled the extraction of cells from the throat, stomach, and duct exiting the stomach for lab analysis: Japanese gastroenterologists and surgeons developed endoscopes with tools that scraped off (or pinched) and then extracted clusters of cells. Another significant improvement magnified views of inflamed, bleeding, or damaged areas: a gastroenterologist and a surgeon from Los Angeles added zoom lenses to endoscopes. Both teams collaborated with Japanese companies (that produced endoscopes as well as cameras) to develop devices for routine clinical use.¹⁸

Researchers used the improved endoscopes to study ulcers, chronic acid reflux, pre-cancerous conditions in the throat and stomach, and diseases of the pancreas, gall bladder, and liver. Their research in turn spurred new diagnostic techniques and more diagnostic endoscopy.¹⁹

Endoscopes' new diagnostic uses complemented, rather than replaced, existing X-ray procedures, helping to reduce resistance to the device. Gastroenterologists – including, as mentioned, Hirschowitz, the fiber endoscope's developer and popularizer -- had long encouraged their fellow specialists to collaborate with radiologists by comparing the results of endoscopies with X-ray examinations. As researchers developed new diagnostic techniques, the researchers encouraged clinicians to continue this collaboration.²⁰

Surgical uses

Improved endoscopes enabled new “minimally invasive” surgeries in the 1970s. Previously, surgeons had to cut open stomachs and alimentary canals extensively to remove obstructions, gall stones, and tumors. Such “open” surgeries were disfiguring, dangerous, expensive, and required long recovery times.²¹

Minimally invasive procedures using laparoscopes inserted through incisions in the abdomen had been pioneered by European gynecologists in the 1930s.^o However, physicians resisted laparoscopic surgeries because they did not want to operate through tubes inserted through orifices that did not offer well-lit views of interior abdominal cavities.²²

By the early 1970s, the wider, brighter views offered by improved endoscopes encouraged the development of new surgical techniques. For instance, a Japanese surgeon based in New York and an American colleague developed prototype endoscopes -- and related tools and techniques -- to remove tumors and abnormal growths as they were identified during diagnostic examinations of the colon (“colonoscopies”). Engineers from Olympus, a Japanese producer of endoscopes, turned the prototypes into devices for routine clinical use. Similarly, American surgeons based in Washington DC developed prototype endoscopes to remove gall stones during examinations of bile ducts. Eder Instrument Company, a longtime producer of laparoscopes and gastroscopes based in Chicago, turned those prototypes into devices for routine clinical use.²³

The new endoscopic surgeries offered three advantages over “open” surgeries: first, they eliminated delays between diagnosis and treatment; second, they were cheaper, more patient-friendly, and could be performed in physicians' offices (instead of hospital operating theaters); and third, gastroenterologists, who lacked surgical training and qualifications, as well as access to operating theaters, could learn to perform many of the procedures.²⁴

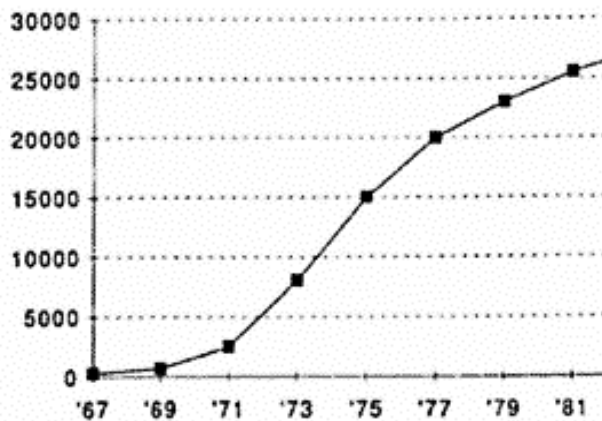
Surgeons, also performed these minimally invasive treatments, and, by 1981, they had formed their own professional association, the Society of American Gastrointestinal Endoscopic Surgeons, to provide training, organize conferences, and develop additional surgical techniques that used endoscopes.²⁵

Adoption accelerates

Endoscope use started growing rapidly in the United States in the early 1970s (See Figure 2) as training provided by medical schools and associations supported the adoption of new endoscopic procedures.

^o Gynecologists conducted laparoscopic surgeries to remove growths and (by the 1970s) perform sterilizations.

Figure 2 Number of endoscopes in use by year in the United States



Source: Kasumi et al (1993).

Endoscopic training in American residencies increased to the extent that, by 1980, some leading gastroenterologists complained it had crowded out all other diagnostic training (including X-ray).²⁶ Moreover, the number of physicians specializing in gastroenterology was itself multiplying: overall, the number of gastroenterologists emerging from American residency programs increased over four-fold in the 1970s. Membership in the American Gastroenterological Association increased over three-fold at the same time. Nearly half of the members of the Association also belonged to the American Society for Gastrointestinal Endoscopy. Both the Association and the Society offered courses in endoscopy and organized national conferences on the topic, and, in 1980, made endoscopy training a requirement for certification as a gastroenterologist.²⁷

Endoscopy also likely grew in Europe in the 1970s and early 1980s, although comparable data on endoscope use is unavailable. Some European medical schools had offered training in endoscopy since the 1960s, as had the European Society of Gastrointestinal Endoscopy. Overall, membership in the European Society was similar in size to comparable American groups by the 1980s.²⁸

Japan continued to lead, however. Between 1969 and 1981, the number of endoscopes used by physicians there had doubled (to about 30,000 devices). And, per-capita, the Japanese numbers were more than twice the number of endoscopes being used in the United States in 1981.²⁹

New producers – and market leaders

The growing use of endoscopes attracted nine new producers – most with medical device or camera businesses -- in the 1970s and early 1980s. (See Table 2) Overall, however, the number of companies selling endoscopes grew from six to just ten, because three 1960s- and two 1970s-vintage producers sold out to their competitors.

Table 2 Companies entering the flexible endoscopy market 1970-1983 (including domiciles, originating industries, and sales regions)

Company (Domicile)	Originating Industries	Sales Region		
		U.S.	Europe	Japan
V. Meuller (U.S.)	Diagnostic and therapeutic devices	X		
C.R. Bard (U.S.)	Diagnostic and therapeutic devices	X		
Fujinon (Japan)	Cameras and film (including X-ray film)	X	X	X
Pentax (Japan)	Cameras and film	X	X	X
Warner Lambert (U.S.)	Pharmaceuticals	X		
Eder Instruments (U.S.)	Rigid endoscopes	X		
Reichert Instruments (U.S.)	None (investment group)	X		
Welch Allyn (U.S.)	Medical devices and supplies	X		
American Hospital Supply (U.S.)	Medical devices and supplies	X	X	X

Sources: Frost & Sullivan (1984), Gelijns and Rosenberg (1999), the U.S. Food & Drug Administration’s 510(k) database, the Health Devices Sourcebooks and the Medical Device Registries.

Three Japanese camera companies – Olympus, Pentax, and Fujinon – made several investments in the United States to increase endoscope sales. Olympus built a repair and refurbishing facility, and all three hired sales forces of thirty to fifty people (about three times the size of their competitors’ sales forces).³⁰ By 1983, these three Japanese producers had secured eighty-nine percent of the American endoscope market. Although comparable market data is not available for Japan and Europe, analysts suggested the same three companies dominated in Japan and also led sales in Europe.³¹

3. More endoscopies – without many new procedures (1984-2000)

Improving and digitizing endoscopes

Concerns about patient tolerance and comfort spurred companies to produce thinner endoscopes containing more fibers. The deadly transmission of HIV/AIDS through contaminated bodily fluids also spurred companies to produce easily sterilized endoscopes and include disposable parts, improving the safety of the devices. These advances, however, did not enable new diagnostic and therapeutic procedures (unlike innovations in the 1970s that, as mentioned, had improved the understanding and diagnosis of more diseases and enabled minimally invasive surgeries).³²

Welch Allyn, a longtime American medical device producer that had started selling fiber endoscopes in the late 1970s, attempted a more radical “digitization” of endoscopes. As early as the 1970s, some consumer cameras had used semi-conductor sensors to convert images into digitized “bits” (1s and 0s) that could be stored and processed electronically (instead of recording the images on film). In 1984, Welch Allyn introduced an endoscope with a camera-like sensor at its tip. The sensor converted images to digitized bits that the endoscope’s fiber bundles transmitted to an external computer. The computer would then process the bits to produce digital images for display on a video terminal or electronic storage.³³

U.S. Food and Drug Administration (FDA) rules could have delayed sales of the digitized devices but did not. In 1976, Congress had authorized the FDA to require clinical trials for new devices – previously the FDA only had such authority over new drug introductions. The FDA could, however, exempt new devices from clinical trials if it decided the devices were “substantially equivalent” to existing devices. And, after review, the FDA classified all new fiber endoscopes (including sensor-tipped devices that used fiber

bundles to transmit digitized bits) as substantially equivalent to pre-1976 endoscopes, exempting them from potentially costly and time-consuming trials.³⁴

European rules (the first of which was introduced in 1985) that unified diverse national regulations across the continent also did not pose a significant barrier to the introduction of digitized endoscopes. These rules standardized manufacturing and safety standards across countries but did not require clinical trials to establish the efficacy of medical devices.³⁵

High prices, however, posed a significant obstacle to widespread use. Digitized endoscopes were nearly twice as expensive as analog fiber endoscopes^p However, they did not seem to offer commensurably valuable clinical advantages to physicians.^q In addition, digitized endoscopes (like the new, cheaper, incrementally-improved analog fiber endoscopes) did not spur the development of new applications (as new devices had in the 1970s).³⁶

Ultrasound endoscopes

In 1991, Pentax, a Japanese camera company that had made fiber endoscopes since the early 1970s, introduced endoscopes that used ultrasound (rather than optical lenses) to produce images. Physicians had started using ultrasound scanners to produce diagnostic images in the 1960s. These scanners included “transponders” placed outside patients’ bodies that emitted high-frequency sound waves and recorded the reflections or “echoes” produced by internal organs and blood vessels. The echoes were then converted into images that showed two-dimensional “slices” through the body on a television monitor. In 1983, a California startup introduced a new scanner that converted echoes into digitized bits and used computers to construct optimized images from the bits. Pentax’s 1991 ultrasound device also produced computer optimized images from digitized echoes but from inside the patient’s alimentary canal rather than from outside the body. It did this by placing a transponder (instead of an optical lens) at the end of an endoscope.³⁷

As in the case of digitized endoscopes, the FDA deemed the ultrasound endoscope an extension of prior technology and therefore exempt from clinical trial requirements (which European rules also did not require). Japanese regulators did require Pentax’s device to undergo more extensive review. However, Pentax had considerable experience with the regulators and was able to satisfy these requirements easily. And, unlike Welch Allyn’s 1984 digitized endoscope, Pentax’s ultrasound device produced diagnostic information (such as the two-dimensional slices through the alimentary canal) that previous endoscopes did not provide. However, very high prices – about ten times the price of an analog endoscope^r – and the considerable skill required to operate the ultrasound endoscopes discouraged their widespread use.³⁸

Endoscopic procedures continue to increase

Procedures developed in earlier decades continued to increase use in the U.S. in the 1980s:

- Greater concerns about colorectal cancer spurred training efforts that increased colonoscopies (that had, as mentioned, included the surgical removal of tumors since the 1970s) among both gastroenterologists and general physicians;³⁹
- Endoscopes were more widely used to diagnose ulcers. In the early 1980s, two Australian doctors had used the then-new cell extracting capabilities of endoscopes to demonstrate that bacterial

^p In the mid-1990s, fiber endoscopes cost about USD\$5,000-USD\$15,000.

^q In contrast, ultrasound scanners that happened to be digitized at the time offered advantages such as markedly better image quality and faster procedure times.

^r Endoscopic ultrasound devices cost as much as USD\$100,000 per unit in 1991.

infections caused ulcers. This breakthrough finding was not widely accepted – and therefore not used in diagnosis -- until the mid-1990s, after corroboration by numerous trials;⁴⁰ and

- Physicians from a variety of specialties – including gastroenterologists, gynecologists, neurologists, orthopedists, and general surgeons – started performing minimally invasive surgeries.⁴¹

More colonoscopies, ulcer tests, and minimally invasive surgeries helped increase the number of endoscopes used in the United States by twenty percent in the 1980s.⁴² Similarly, more stomach cancer screening helped increase the number of endoscopes used in Japan by twenty-five percent.^{s 43} Although comparable European use data is unavailable, sales data from the 1990s suggests use increased in some European countries in the late 1990s.^{t 44}

Japanese producers continue to dominate

Sixty-six companies in the U.S. and twenty-one companies in Europe started selling endoscopes in the late 1980s and 1990s. (See Exhibit 1) Two thirds of these companies specialized in devices for minimally invasive surgery. Many were capitalizing on the movement to perform more laparoscopic surgeries but then also added endoscopic devices to their product lines.^u (The entrants may have stimulated the growing interest in minimally invasive surgery, as noted above.) About a quarter were established diagnostics companies that may have been attracted by the easy availability of the technology after the expiration of the original fiber endoscope patent (which had been issued in 1971 and expired in 1988). Remarkably, analysts recorded no exits during the period.⁴⁵

Longtime Japanese endoscope producers did not cede much share to the entrants, however. They continued to dominate the market by offering high optical quality, broad product lines, reliable performance, and extensive sales and service support, and they rapidly copied any promising improvements offered by entrants. By the end of the 1990s, two Japanese producers – Olympus and Pentax -- held ninety percent share of the American gastrointestinal endoscope market, and, along with a third Japanese producer, Fujinon, held ninety-six percent share of the European gastrointestinal endoscope market.⁴⁶

4. Capsule endoscopes expand the market (after 2000)

Capsules spur a second revolution

In 1998, an Israeli startup, Given Imaging, announced a revolutionary alternative to endoscopes inserted through orifices: a “capsule” endoscope. (See Figure 3) The startup’s founders (an engineer and high-tech executive) developed the capsule with the help of a British gastroenterologist. The capsule blended an optical lens and electronic sensors similar to those used by Welch Allyn in their 1984 digital endoscope with a new military technology developed to guide so-called “smart” bombs. A patient swallowed the

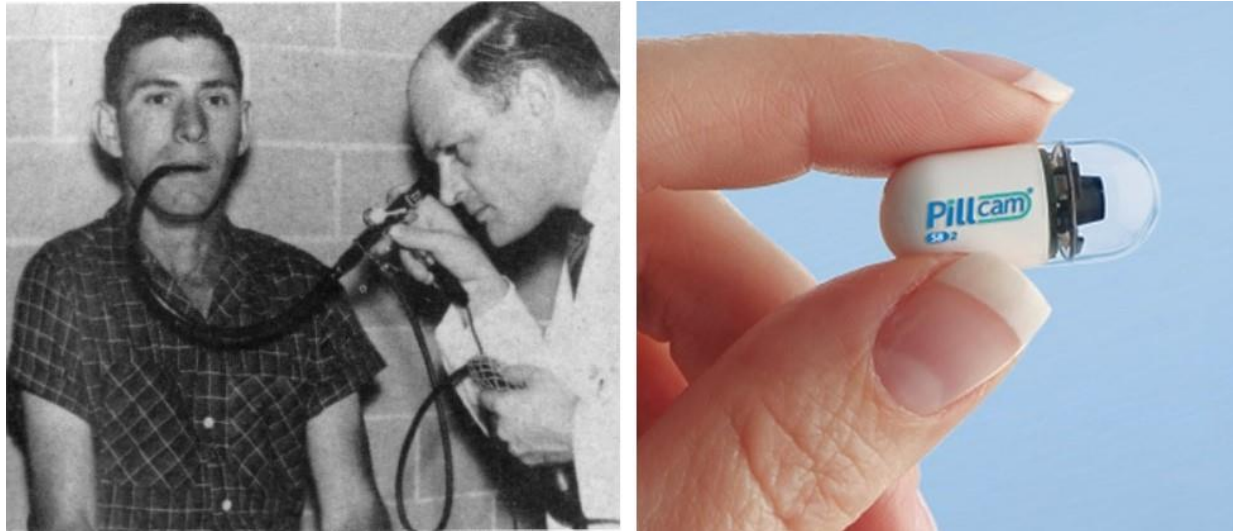
^s As of 1993, Japan had four times as many gastroenterologists trained on endoscopes as in the U.S. (around 20,000), and they performed two to three times as many upper gastrointestinal procedures than American gastroenterologists did during the same period.

^t France accounted for a disproportionate share of the increased use (as determined by increases in sales) in Europe. Frost & Sullivan attributed increased sales in France to the indirect effect of new sterilization rules passed there in the wake of scandals about transfusions made with HIV-contaminated blood. The rules required rigid endoscopes be heat sterilized for three times as long as required elsewhere in Europe. The long period of sterilization tended to wear devices out faster, spurring frequent replacement. Although fiber endoscopes were not heat sterilized (they were cleaned with solvents instead), and therefore the new French rules did not apply, Frost & Sullivan analysts believed that French physicians voluntarily replaced fiber endoscopes frequently to limit the transmission of communicable diseases.

^u In addition to greater familiarity with the technique, increases were driven by the large number of entrants who invested in developing and marketing new devices during a big boom in laparoscopy in 1989 and 1990. Please see our case study on the evolution of laparoscopy for more information.

capsule, and, as it traveled through the patient's alimentary canal, the sensors inside the capsule converted images produced by the lens into digitized bits. The capsule then wirelessly transmitted the bits to a storage unit worn on patients' belts. Finally, a computer enhanced and displayed the stored images.⁴⁷

Figure 3 Basil Hirschowitz demonstrating his flexible fiber endoscope circa 1960 (left) and the Given capsule endoscope (right)



Source: Edmonson (1991) and Mathworks.com.

Given Imaging's capsule endoscopes dramatically improved views of the small intestine, which even very thin endoscopes could not penetrate deeply. The capsules also decreased the risks of infection, because they were disposable. Furthermore, they greatly reduced patient discomfort by making anesthetic sedation unnecessary. (In fact, patients went about their routine activities for the day while the capsule passed through their alimentary canal, transmitting data to the recording belt they wore.) And, because anesthesia accounted for half the cost of endoscopic examinations of the colon, the capsules reduced costs as well.⁴⁸

From 1998 to 2001, Given Imaging raised capital from several sources -- a large Israeli technology company, the Israeli government, and private equity firms in the United States and Europe. The company used the funds to start clinical trials its home country (Israel) and the United States in 2000, and a year later in Australia and four countries in Europe in 2001 -- even though Australian and European regulators did not require the trials. The company also opened sales offices in the countries where it had started trials and formed distribution partnerships in China, Japan, Taiwan, South Korea, and Chile.⁴⁹

Securing exemption from U.S. trials

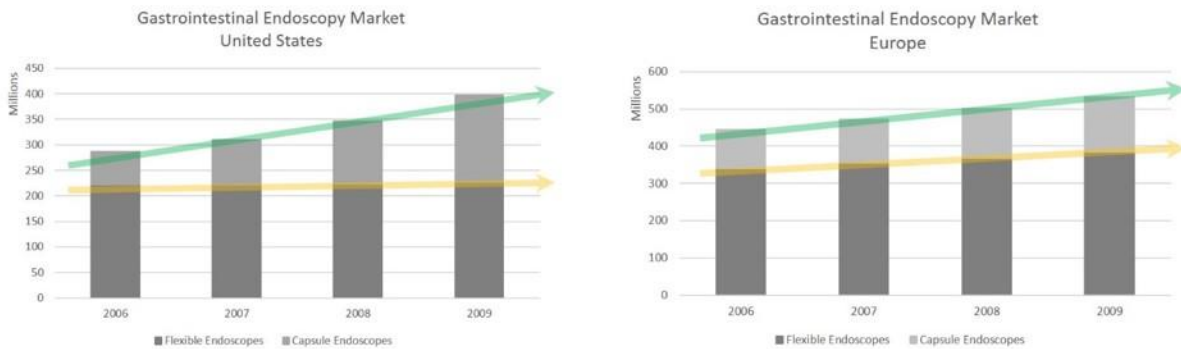
Rules in Europe and Australia allowed Given Imaging to start selling its capsule endoscopes there in July 2001 even though clinical trials had been only recently initiated.⁵⁰ The company was able start selling in the United States just a month later -- after persuading the FDA to exempt it from clinical trial requirements. Earlier, in 2000, the FDA had decided capsule endoscopes were not substantially equivalent to fiber endoscopes and would therefore have to undergo clinical trials -- which Given then immediately initiated (as mentioned). However, Given took nearly a year to collect data on seventy-seven patients. Given then petitioned the FDA to reclassify their capsules as "substantially equivalent" to digitized endoscopes that also used electronic sensors and thus exempt from trial requirements. Given's claim -- and favorable results from the relatively few patients that Given had tested (which Given had included in its petition) -- persuaded the FDA. In January 2002, less than a year after Given had submitted its petition, the

FDA exempted capsule endoscopes from trial requirements, permitting the company to immediately start selling its products.⁵¹

Adoption of capsules accelerates

Use of capsule endoscopes – as reflected by their sales revenues – grew rapidly in the 2000s in the U.S. and Europe. Between 2006 and 2009, capsule revenues in the United States nearly tripled, while use of (and revenues from) traditional fiber endoscopes remained flat. Growth in Europe was less dramatic but still substantial: sales revenues for capsules increased there by about thirty percent, outpacing fiber endoscope sales, which increased by about twenty percent during the same period. (See Figure 4) By 2009 – just eight years after their approval – capsule revenues totaled about USD\$170 million in the U.S. and USD\$150 million in Europe.

Figure 4 The Gastrointestinal Endoscopy Market in the United States (left) and Europe (right), 2006-2009



Source: Frost & Sullivan (2009, 2010)

However, Japan lagged in adoption of capsule endoscopes, which were not approved for use there until 2007. In 2010, capsule endoscope sales revenues for Japan and the Asia Pacific region totaled only about USD\$24 million – which was about a third of European capsule endoscope revenues and one-sixth of American capsule endoscope revenues at the time.⁵²

Entrants gain market share

Given Imaging’s founders had filed for U.S. patents before organizing their startup, but their start-up did not effectively use them to stop rivals from offering competing products. An American startup, SmartPill, and Japanese market leader Olympus both started selling their capsule endoscopes in the U.S. in 2006 and 2007 respectively. However, Given did not immediately challenge either in court: rather, Olympus first filed a patent infringement claim against Given. Given then countersued and eventually reached a settlement obtaining \$2.3 million in royalties and agreeing to cross-license some of its technologies with Olympus.⁵³

Yet neither SmartPill nor Olympus could take advantage of the legal opening, and as of 2009 Given’s capsule endoscopes accounted for nearly all of the capsule endoscopes sold in the United States. However, in fiber endoscopes, Olympus continued to dominate, and none of the many entrants from the previous decade had apparently been able to make significant inroads. Overall, therefore, Given and Olympus accounted for nearly the same share, with Olympus having about forty-three percent and Given having about forty-two percent. Pentax accounted for nearly all of the rest of sales revenues.⁵⁴

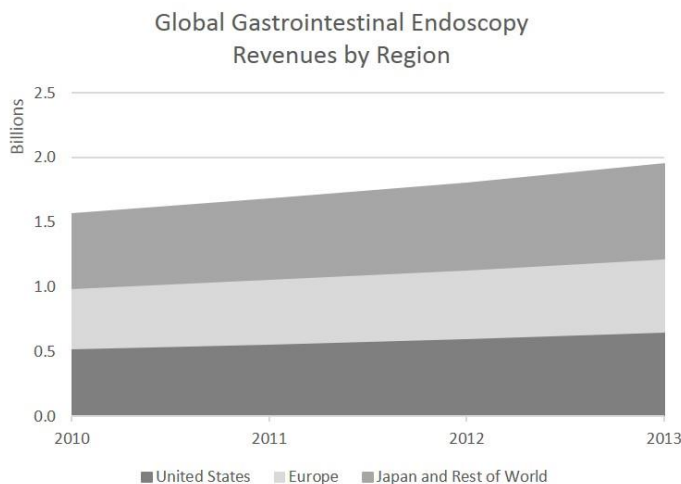
Given's capsule endoscopes had less success in Europe and Japan. In Europe, the company secured only six percent share of all endoscope sales revenues in 2009.^v And, Given did not make significant inroads in Japan, because capsule endoscopes were not approved for use there until 2007 (as previously mentioned).⁵⁵

Meanwhile, the tools and accessories that complemented the more complicated endoscopes used for minimally invasive surgeries had grown into a significant market of their own by the 2000s. Between 2004 and 2006, sales of tools alone generated revenues that matched (in Europe) or exceeded (in the U.S. and Japan) the revenues generated from sales of fiber and capsule endoscopes.⁵⁶

5. Epilogue

Combined global revenues of fiber and capsule endoscopes continued to grow in the 2010s. (See Figure 5)

Figure 5



Source: Frost & Sullivan (2014).

Note: The above figures include both capsule and fiber endoscopes, but not revenues from the sales of surgical tools and accessories.

Growth was sustained by new surgical procedures and more screening. By the 2010s, gastroenterologists performed minimally invasive endoscopic stomach surgery more frequently to treat obesity and manage diabetes. In the U.S. and Europe, government agencies rolled out national colorectal cancer screening programs that also increased demand for diagnostic endoscopy.⁵⁷

To meet these demands, researchers sought to develop more accurate and convenient endoscopic devices. For instance, they designed “ultra thin” fiber endoscopes with improved lighting and optics that produce highly detailed images to facilitate diagnosis and surgery. Researchers are also testing capsules containing miniature X-ray machines that use low doses of radiation to produce digitized two-dimensional “slices” of the entire alimentary canal. Capsule X-rays would be easier to use than endoscopic ultrasound (which also provides cross-sectional images, though not of the whole alimentary canal). They would also drastically improve patient comfort by eliminating the fasting and bowel cleansing currently required before all types of endoscopic examinations.⁵⁸

^v Frost and Sullivan analysts noted that physicians in Europe preferred fiber endoscopes. One reason might be because many there had already stopped sedating patients during colonoscopies, thus reducing patient preparation times and costs significantly.

Exhibits

Exhibit 1 Companies entering the flexible endoscopy market 1984-2000 (including domiciles, originating industries, and sales regions, with startups in bold)

Company (Domicile)	Originating Industries	Sales Region		
		U.S.	Europe	Japan
Advanced Biomedical Instruments (USA)	Rigid and semi-flexible endoscopes and surgical equipment	X*		
Aesculap Instruments Corp. (USA)	Rigid and semi-flexible endoscopes and surgical equipment	X**		
Akos Biomedical (USA)	Startup	X		
American Edwards Laboratories (USA)	Artificial heart valves and surgical equipment	X		
American Endoscopy, Inc. (USA)	Startup specializing in rigid, semi-flexible, and fiber endoscopes and surgical equipment	X		
Angio Laz (USA)	Endoscopic cameras and video monitors	X		
Astralite Corp. (USA)	Startup specializing in rigid, semi-flexible, and fiber endoscopes and surgical equipment	X		
Baxter (USA)	Blood bank and related medical devices and supplies	X		
B. Braun (Germany)	Surgical equipment and endoscopic surgical tools	X	X	
BFW (USA)	Endoscopic cameras and video monitors, surgical equipment	X		
Boehm Surgical (USA)	Rigid and semi-flexible endoscopes and surgical equipment	X		
Boston Scientific (USA)	Endoscopic cameras and video monitors, diagnostic devices	X	X	
Bovina Scientific, Inc. (USA)	<i>Unknown</i>	X		
Burnett Diagnostic Products (USA)	Diagnostic devices	X		
Busse Hospital Disposables (USA)	Surgical equipment and tools	X		
Cameron-Miller (USA)	Surgical equipment and tools	X		
Circon (The Netherlands)	Endoscopic cameras and video monitors, surgical equipment	X	X	
Codman & Shurtleff (USA)	Diagnostic devices, surgical equipment, and patient monitoring equipment	X		
Cogent Light Technologies (USA)	Startup specializing in surgical equipment	X		
Conmed Corp. (USA)	Surgical equipment	X		X

Cooper (USA)	Endoscopic cameras and video monitors, ophthalmic devices, and surgical equipment	X		
Cuda Products (USA)	Endoscopic cameras and video monitors, surgical equipment	X		
Dittmar & Penn (USA)	Diagnostic devices and surgical equipment	X		
Downs Tabard Ltd. (UK)	Diagnostic and prosthetic devices, surgical equipment	X	X	
Dyonics (USA)	Diagnostic devices and surgical equipment	X		
Electro Fiber Optics Corp. (USA)	<i>Unknown</i>	X		
Electro Surgical Instruments Company (USA)	Surgical equipment	X		
Ethicon (USA)	Surgical equipment	X	X	X
Fiberoptic Medical Products Inc. (USA)	<i>Unknown</i>	X		
Galenica (Switzerland)	Pharmaceuticals	X	X	
Gebrueder Martin OHG (Germany)	Surgical equipment	X	X	
Henke-Sass Wolf (Germany)	Rigid and semi-rigid endoscopes, surgical equipment, endoscopic cameras and video monitors	X	X	
Imagyn Medical (USA)	Surgical equipment	X		
IsoLux (Spain)	Endoscopic cameras and video monitors	X	X	
Jarit (USA)	Startup specializing in surgical equipment	X		
JVC (Japan)	Endoscopic cameras and video monitors	X	X	X
Linvatec (Belgium)	Diagnostic devices and surgical equipment		X	
Luxtech Corp. (USA)	Endoscopic cameras and video monitors	X		
Medicon (Germany)	Surgical equipment	X	X	X
Micro Medical Devices (USA)	Diagnostic devices	X		
Microvasive (Italy)	Surgical equipment	X	X	
Mi-Lor Corp. (USA)	<i>Unknown</i>	X		
Miltex (USA)	Surgical equipment	X		
Misdorn-Frank and Sklar Instruments (USA)	Surgical equipment	X		
Mitsubishi Cable America (Japan/USA)	Diagnostic devices	X		X
Monarch Molding (USA)	Endoscopic surgical tools	X		
MTW (Germany)	Diagnostic devices and surgical equipment		X	
Narco Scientific, Pilling Division (USA)	Surgical equipment	X		
Northgate Technologies Inc. (USA)	Surgical equipment	X		

Oktas (<i>unknown</i>)	<i>Unknown</i>	X	
Omnisonics Medical Technologies (USA)	Startup	X	
Opto Vision Inc. (USA)	Optical devices	X	
Oswald Lebringer (<i>unknown</i>)	<i>Unknown</i>	X	
Precise Optics (USA)	Diagnostic devices	X	
Propper Manufacturing (USA)	Diagnostic devices, surgical equipment, and endoscopic surgical tools	X	
Scholly Fiberoptic GmbH (Germany)	Surgical equipment		X
Schott Fiber Optics (Germany)	Optical devices	X	X
Sharplan Lasers (USA)	Surgical equipment	X	
Smith & Nephew (UK)	Surgical equipment		X
Solos Endoscopy (USA)	Startup specializing in endoscopic cameras and video monitors, surgical equipment	X	
Stryker Endoscopy (Germany)	Endoscopic cameras and video monitors, surgical equipment		X
Technology Marketing Group (USA)	<i>Unknown</i>	X	
Ueth & Haug (Germany)	Surgical equipment	X	X
United States Surgical (USA)	Surgical equipment	X	
Vision Sciences (USA)	Startup specializing in endoscopic cameras and video monitors, surgical equipment	X	
Vista Medical Technologies (USA)	Startup specializing in endoscopic cameras and video monitors, surgical equipment	X	
Weck Endoscopy (<i>unknown</i>)	<i>Unknown</i>	X	
Welch Allyn (USA)	Diagnostic devices	X	
William Cook (Denmark)	Startup specializing in fiber endoscopes and surgical equipment		X
Max Woche and Son (USA)	Surgical equipment	X	
XOMED (USA)	Surgical equipment	X	
Zeiss (Germany)	Endoscopic cameras and video monitors, surgical equipment	X	X

*ABI had a partnership with MTO in Paris, France.

**Aesculap is now an American division of B. Braun, Germany.

Sources: Frost & Sullivan (1999, 2001, 2001), the U.S. Food & Drug Administration's 510(k) database, the Health Devices Sourcebooks and the Medical Device Registries.

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projection for teaching, so most of the 1960s use in teaching likely involved live demonstrations with black and white televisions or prerecorded color still and motion pictures taken with the fiber endoscopes.

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- ³⁴ "Managing the Medical Arms Race," accessed November 10, 2018, <https://publishing.cdlib.org/ucpressebooks/view?docId=ft5489n9wd&chunk.id=d0e5241&toc.depth=1&toc.id=d0e5241&brand=ucpress;query=japan%20regulations#1>; John Y. Chai, "Medical Device Regulation in the United States and the European Union: A Comparative Study," *Food and Drug Law Journal* 55 (2000): 57-80. Frost & Sullivan. (Winter 1990/1991) *The U.S. Market for Endoscopes and Endoscopic Products, Volumes I & II.*
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- ³⁷ Gelijns, "Diagnostic Devices" Frost & Sullivan. (Winter 1990/1991) *The U.S. Market for Endoscopes and Endoscopic Products, Volumes I & II.* See also our case study of the evolution of ultrasound devices, such as Acuson's "computed sonography," which is described briefly here.
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⁵⁶ “Sage Sourcebook of Modern Biomedical Devices: Business Environments in a Global Market.” Accessed June 6, 2017. http://go.galegroup.com.ezp-prod1.hul.harvard.edu/ps/eToc.do?tabID=&searchId=&searchType=AdvancedSearchForm&docId=1RBI&userGroupName=camb55135&action=DO_BROWSE_ETOC&inPS=true&contentSegment=&source=&prodId=GPS&etocId=GALE%7CCX2660299001&isD ownLoadOptionDisabled=true. Japanese companies had long led in endoscope sales, but after 2000, American and European producers led in sales of tools, which helped them gain substantial shared of overall sales revenues. In Europe, American tool makers accounted for one-third of overall sales revenues (of all endoscopes and surgical tools) by 2004. In Japan, fifteen companies – including ten large American and European tool makers – accounted for two-thirds share of overall sales revenues by 2004. And, in the U.S., American tool makers accounted for about forty-five percent of overall sales revenues by 2006.

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