Working Paper 20-005

Case Histories of Transformational Advances

Gastrointestinal Endoscopy – Without Cutting In

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Abstract: This case history describes how endoscopy transformed the diagnosis of ulcers, cancerous polyps, and other alimentary canal diseases 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: 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.

Gastrointestinal Endoscopy —Without Cutting In

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, glass fiber-based endoscopes had therapeutic applications: they enabled "minimally invasive" surgeries on the throat, stomach, and intestines. Technological advances then continued to reshape endoscopy, most notably by introducing an ingestible capsule containing a miniature digital camera.[1]

The following three sections describe the development of 1) flexible glass fiber instruments in the 1950s and 1960s; 2) new diagnostic techniques and minimally invasive endoscopic surgeries in the 1970s and early 1980s 3) digitization and miniaturization through the end of the 20th century. A concluding section summarizes the competitive situation of equipment producers in 2000.

1. Flexible glass fiber endoscopes (1950-1970s)

Prior 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 complete examination, caused substantial discomfort, and posed risks of cuts and burns.[2]

In the early 1930s, the German medical device company Richard Wolf[3] 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, limiting their use. Over the next thirty years, physicians in Europe and the United States (where Schindler had emigrated to teach in 1934) bought more than a thousand of these devices.[4] 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 that bent fibers transmitted distorted images.[5] The two 1954 Nature articles, written by physicists from Britain and the Netherlands,[6] 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

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

- Coated glass fibers, packaged in flexible bundles, could be used in photography, microscopy, and endoscopy applications.[7]

The articles attracted the attention of Basil Hirschowitz, a South African gastroenterologist with a fellowship[8] 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 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 US patent[a] 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 the issuance of the patents for fourteen years.)[9]

By January 1957, Hirschowitz, Peters, and Curtiss had developed and started testing a prototype fiber endoscope. That May, they showed that it transmitted undistorted images at the American Gastroscopic Club[10] by letting attendees[11] read a telephone directory through its eyepiece. Shortly after that, Hirschowitz persuaded American Cystoscope Makers, Inc., which had been producing rigid endoscopes since 1908, to develop a flexible glass fiber device for clinical use.[12]

Diagnostic Applications. In 1960, Hirschowitz moved to the University of Alabama and began researching 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*" (italics 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 gastroscope 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.[13]

[a] 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. They did not however apply for a patent in Japan.

Hirschowitz conceded that the existing Wolf-Schindler gastroscope 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. Conversely, X-rays diagnosed problems not visible in endoscope examinations in up to forty percent of cases.[b] When used jointly, Hirschowitz suggested endoscopes and X-rays would produce accurate diagnoses ninety percent of the time.[14]

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 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 $1,600 (approximately $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 gastroscopes[c]and

- *Inability to extract tissue samples:* fiber endoscopes lacked the tools necessary to extract tissue samples for lab analysis, as gastroscopes could.[15]

These problems reinforced the reluctance of physicians to learn new procedures with fiber endoscopes.[16]

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[b] For instance, an X-ray would show problems with the outer surface of the stomach and ducts, while the fiber endoscope could only view the inside of the stomach and ducts.

[c] 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).

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)[17]; and
- Still and motion cameras designed for endoscopic examinations.[18]

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 of using fiber endoscopes in teaching gastroenterology.[19]

Thirty-four residency programs in gastroenterology (like Hirschowitz's) that had been started in American medical schools with National Institutes of Health[20] 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 US and Europe) in which they used endoscopes. Thus, the number of gastroenterologists who learned to use fiber endoscopes continued to multiply.[21]

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 had started widespread stomach cancer screening in the mid-1960s. In the screening procedures, Japanese gastroenterologists initially used "gastro cameras"[d] inserted into patients' stomachs at the end of long, flexible tubes.[22] However, gastro cameras 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 gastro cameras), therefore sold rapidly after they were introduced. By 1969, 15,000 were used in Japan (compared to 10,000 gastro cameras in 1966).[23]

Producers of Fiber Endoscopes. By the end of the 1960s, six companies were selling fiber endoscopes in the US, Europe, and Japan. (See Exhibit 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 after that, American Optical Company, a producer of eyeglasses and microscopes, offered a competing device.[e] American Optical had also been developing coated glass fibers for the US Central Intelligence Agency. In 1954, the company filed for a patent for the

[d] Japanese companies also made various rigid and semi-rigid endoscopes. Historians report that gastro cameras 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 gastro cameras in the U.S. before the device was discontinued.

[e] 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.

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 US patents and back royalties.[24]

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 Olympus, had been selling gastro cameras; the other, Machida, was a longtime producer of metal tubular endoscopes.[25]

Two German gastroscope producers – Richard Wolf (established in 1906 and 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; although the record does not explicitly state so, both companies presumably invented around the fiber coating and fiber endoscope patents.)[26]

Questions (for reflection and discussion):

Before reading further, please write down (in less than ten words) which innovation, event, or condition you found to be the most significant in developing fiber endoscopes – or would expect to have the most long-term impact. (Be prepared to explain why).

- ____

2. New diagnostic and surgical procedures (1970-1983)

Improvements Expand 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 and cameras) to develop devices for routine clinical use.[27]

Researchers used the improved endoscopes to study ulcers, chronic acid reflux, precancerous conditions in the throat and stomach, and diseases of the pancreas, gallbladder, and liver. Their research, in turn, spurred new diagnostic techniques and more diagnostic endoscopy.[28]

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, they encouraged clinicians to continue this collaboration.[29]

Improved endoscopes also enabled new "minimally invasive" surgeries in the 1970s. Previously, surgeons had to cut open stomachs and alimentary canals extensively to remove obstructions, gallstones, and tumors. Such "open" surgeries were disfiguring, dangerous, expensive, and required long recovery times.[30]

Minimally invasive procedures using laparoscopes inserted through incisions in the abdomen had been pioneered by European gynecologists in the 1930s.[f] However, physicians resisted laparoscopic surgeries because they did not want to operate through tubes that did not offer well-lit views of interior abdominal cavities.[31]

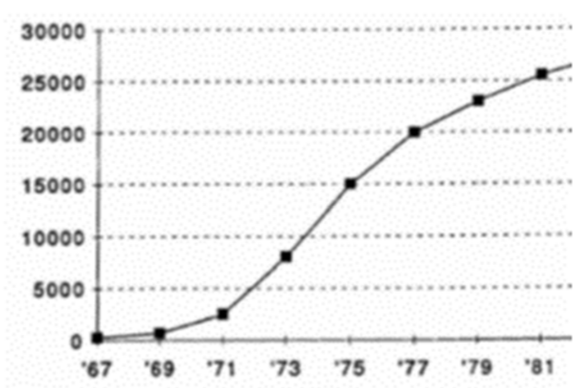
By the early 1970s, the wider, brighter views offered by improved endoscopes encouraged the development of new surgical techniques. For instance, a Japanese surgeon based in New York and an American colleague developed prototype endoscopes -- and related tools and techniques -- to remove tumors and abnormal 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 gallstones 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.[32]

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.[33]

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.[34]

Accelerated Adoption. Endoscope use started growing rapidly in the United States in the early 1970s (See Figure 1) as training provided by medical schools and associations supported the adoption of new endoscopic procedures.

Figure 1 Number of endoscopes in use by year in the United States



Source: William T. Kasumi, Asao Kasumi, and Benjamin Ishikawa, "The Spread of Upper Gastrointestinal Endoscopy in Japan and the United States: An International Comparative Analysis of Technology Diffusion," *International Journal of Technology Assessment in Health Care* 9, no. 3 (1993).

[f] Gynecologists conducted laparoscopic surgeries to remove growths and (by the 1970s) perform sterilizations.

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).[35] Moreover, the number of physicians specializing in gastroenterology was 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.[36]

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.[37]

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.[38]

New Producers. The growing use of endoscopes attracted nine new producers – most with medical device or camera businesses -- in the 1970s and early 1980s. (See **Exhibit 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.

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).[39] By 1983, these three Japanese producers had secured eighty-nine percent of the American endoscope market. Although comparable market data is unavailable for Japan and Europe, analysts suggested that the same three companies dominated in Japan and led European sales.[40]

Questions (for reflection and discussion):

Before reading further, please write down (in less than ten words) what you found most significant or surprising in the development of endoscopic procedures.

- ____

Be prepared to explain why you found this significant.
Also, think about what might have to happen for the wider use of endoscopy.

3. Digitization and Miniaturization (1984 -- 2000)

Semiconductor Sensors. Concerns about patient comfort prompted the development of thinner endoscopes with more fibers. Fears about the transmission of HIV/AIDS through bodily fluids also spurred the introduction of easily sterilized endoscopes and included disposable parts. These advances, however, did not enable new diagnostic and therapeutic procedures (unlike innovations in the 1970s)[41]

Welch Allyn, a longtime American medical device producer that had started selling fiber endoscopes in the late 1970s, tried a more radical "digitization" of endoscopes. As early as the 1970s, some consumer cameras had used semiconductor 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.[42]

US Food and Drug Administration (FDA) rules could have delayed sales of the digitized devices but did not. In 1976, Congress 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.[43]

European rules (the first introduced in 1985) that unified diverse national regulations across the continent also did not pose a significant barrier to digitization. These rules standardized manufacturing and safety standards across countries but did not require clinical trials to establish the efficacy of medical devices.[44]

High prices, however, posed a significant obstacle. Digitized endoscopes were nearly twice as expensive as analog fiber endoscopes (priced at between $5-15,000 per unit). Yet, unlike other devices that were also digitized in this period, digitized ultrasound did not apparently offer commensurably valuable clinical advantages to physicians[45]or support new applications. [46]

Ultrasound Alternative. 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.[47] The FDA again 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 a 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 two-dimensional 'slices' through the alimentary canal) that earlier endoscopes did not provide. However, very high prices – about ten times the price of an analog endoscope[g] – and the considerable skill required to use the ultrasound endoscopes discouraged widespread adoption.[48]

Capsule Endoscopes. In 1998, an Israeli startup, Given Imaging, announced a revolutionary alternative to endoscopes inserted through orifices: a "capsule" endoscope. (See **Exhibit 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 like those used by Welch Allyn in their 1984 digital endoscope with a new military technology developed to guide so-called "smart" bombs. A patient would swallow the 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.[49]

The capsule endoscopes were designed to dramatically improve views of the small intestine, which even very thin endoscopes could not penetrate deeply; decrease the risks of infection because they were disposable; and greatly reduce patient discomfort by making anesthetic sedation unnecessary. (Patients could continue their daily routines as the capsule passed through their alimentary canal, transmitting data

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[g] Endoscopic ultrasound devices cost as much as $100,000 per unit in 1991.

to the recording belt they wore.) And, along with the discomfort, capsules would eliminate the cost of administering anesthesia, which accounted for half the cost of endoscopic colon examinations.[50]

Given's capsules did face a regulatory obstacle, however -- in 2000, the FDA decided capsule endoscopes were not substantially equivalent to fiber endoscopes and would, therefore, have to undergo clinical trials.

Continued Growth. Although the new technologies had not (as in the 1970s) spurred the development of new uses for endoscopy, procedures developed in earlier decades continued to increase in the US in the 1980s:

- Concerns about colorectal cancer spurred training efforts that increased colonoscopies (that had, as mentioned, included the surgical removal of tumors since the 1970s).[51]
- Endoscopes were more widely used to diagnose ulcers. In the early 1980s, two Australian doctors used the then-new cell-extracting capabilities of endoscopes to show that bacterial infections caused ulcers.[52] And
- Many specialists – including gastroenterologists and general surgeons – started performing minimally invasive surgeries.[53]

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.[54] Similarly, more stomach cancer screening helped increase the number of endoscopes used in Japan by twenty-five percent.[h] [55] Although comparable European use data is unavailable, sales data suggests that use increased in some European countries in the late 1990s.[56] [57]

The number of companies selling endoscopes also increased. Sixty-six US and twenty-one European companies started selling endoscopes after 1984 (See **Exhibit 4**). Two-thirds specialized in devices for minimally invasive surgery. Many were capitalizing on the movement to perform more laparoscopic surgeries but then also added endoscopic devices.[58] About a quarter were diagnostics companies that may have been attracted by the easy availability of the technology after the expiration of the original fiber endoscope patent in 1988. Analysts recorded no exits during the period.[59] Despite the many new entrants that had started selling endoscopes, three Japanese incumbents had maintained their dominance – in the US and Europe (**Exhibit 5**) – as well as in their home markets. According to a study published by Frost & Sullivan, Japanese companies had maintained market leadership by offering high optical quality, broad product lines, reliable performance, and extensive sales and service support. They also rapidly matched any promising improvements offered by entrants.[60]

Questions (for reflection and discussion):

Please write (in less than ten words) what you found most significant or surprising about the development and use of endoscopes after 1984 (and be prepared to explain why).

- ____

[h] 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.

The Competitive Situation in 2000

Given Imaging's new capsule endoscopes had not yet challenged Japanese dominance of the US endoscope market because it had not received FDA approval. Given had also not attempted to sell its products in Europe. Instead, after raising capital from several sources -- a large Israeli technology company, the Israeli government, and private equity firms in the US and Europe – Given Imaging had started clinical trials in the US (the FDA had required) and in its home country (Israel).

Questions (for reflection and discussion):

Based just on this case (and exhibits) – and without hindsight – would you expect the market shares of companies selling endoscopes to change significantly by 2010?

o Expect significantly different US market shares

o Expect significantly different European market shares

o Expect significantly different Japanese market shares

o Do not expect significant changes in any of the three major markets

(Pick one or more options from the list and be prepared to explain why)

Exhibit 1 Companies selling fiber endoscopes in the 1960s and their domiciles, sources 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 US 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: See endnotes).[61]

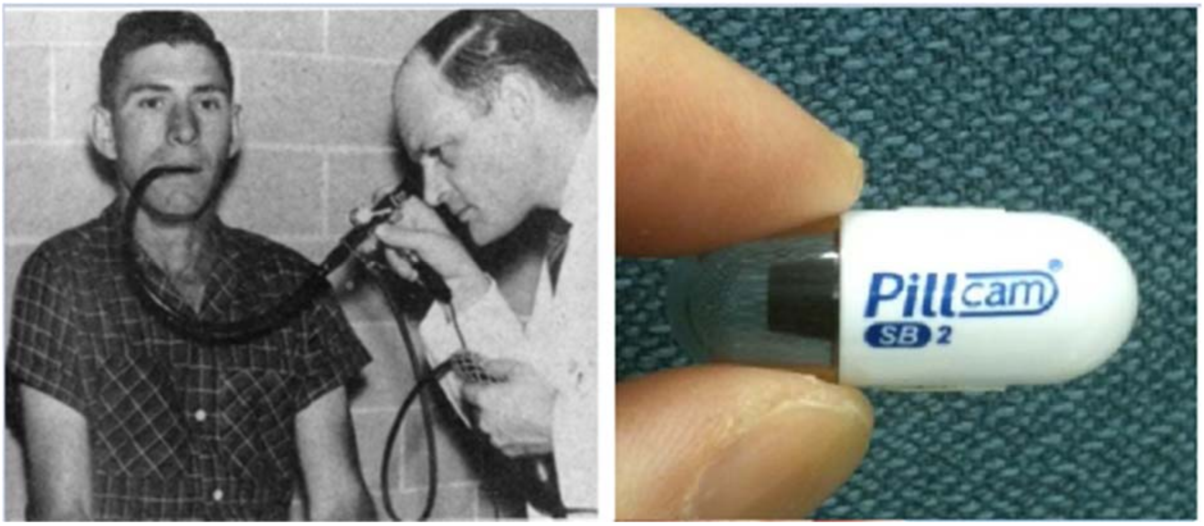
Note: Improved versions of these tools are still standard laparoscopic instrumentation.

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

		Sales Region		
Company	**Originating Industry**	**US**	**Europe**	**Japan**
V. Meuller (US.)	Diagnostic and Therapeutic devices	x		
C. R. Bard (U.S.)	Diagnostic and Therapeutic devices	x		
Fujinon (Japan)	Cameras and Film (incl. X-ray film)	x	x	x
Pentax (Japan)	Cameras and Film	x	x	x
Warner-Lambert (US.)	Pharmaceuticals	x		
Eder Instruments I US.)	Rigid Endoscopes	x		
Reichert Instruments (U.S.)	None (investment group)	x		
Welch Allyn (US.)	Medical devices and supplies	x		
American Hospital Supply ((US.)	Medical devices and supplies	x	x	x

Sources: Frost & Sullivan. (June 1984), Gelijns and Rosenberg (2010), the US Food & Drug Administration's 510(k) database, the Health Devices Sourcebooks, and the Medical Device Registries.

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



Source: James M. Edmonson, "History of the Instruments for Gastrointestinal Endoscopy," *Gastrointestinal Endoscopy* 37 (1991) and "File:GivenimagingKK.JPG" TMKO, https://commons.wikimedia.org/wiki/File:GivenimagingKK.JPG. CC BY 3.0, https://creativecommons.org/licenses/by/3.0/deed.en.

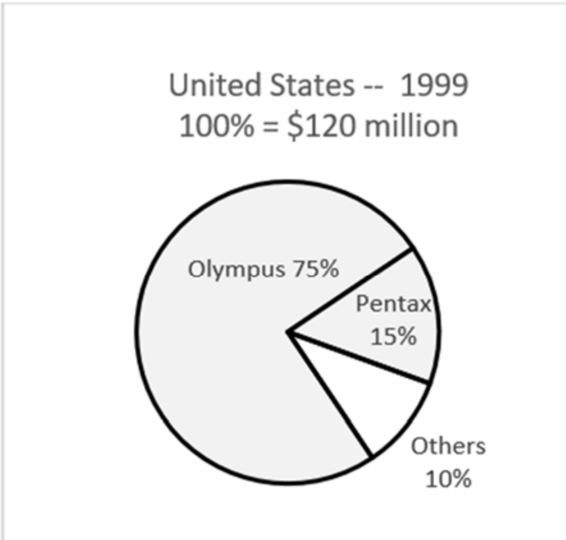
Exhibit 4 Companies entering the flexible endoscopy market 1984-2000 (including domiciles, originating industries, and sales regions, with startups in bold)

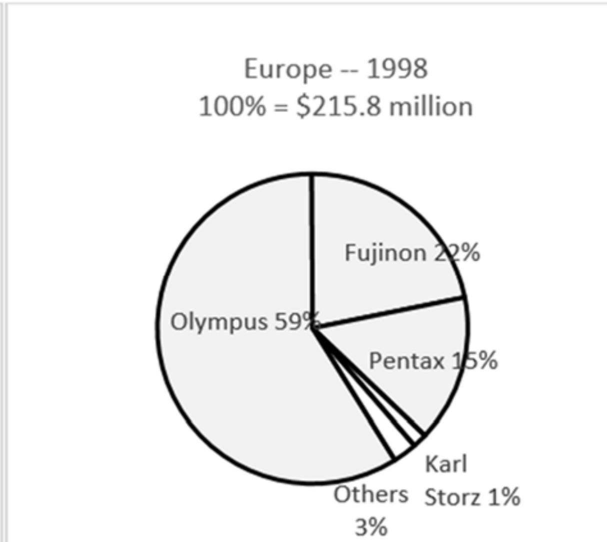
		Sales Region		
Company (Domicile)	**Originating Industries**	**US.**	**Europe**	**Japan**
Advanced Biomedical Instruments (USA)	Rigid and semi-flexible endoscopes and surgical equipment	X[62]		
Aesculap Instruments Corp. (USA)	Rigid and semi-flexible endoscopes and surgical equipment	X[63]		
Akos Biomedical (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)	Unknown	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)	Unknown	X		
Electro Surgical Instruments Company (USA)	Surgical equipment	X		
Ethicon (USA)	Surgical equipment	X	X	X
Fiberoptic Medical Products Inc. (USA)	Unknown	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

		Sales Region		
Company (Domicile)	**Originating Industries**	**US.**	**Europe**	**Japan**
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)	Unknown	X		
Miltex (USA)	Surgical equipment	X		
Misdom-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 (unknown)	Unknown	X		
Omnisonics Technologies (USA)	**Startup**	X		
Opto Vision Inc. (USA)	Optical devices	X		
Oswald Lebringer (unknown)	Unknown	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)	Unknown	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 (unknown)	Unknown	X		
Welch Allyn (USA)	Diagnostic devices	X		
William Cook (Denmark)	Startup specializing in fiber endoscopes and surgical equipment		X	
Max Wocher and Son (USA)	Surgical equipment	X		
XOMED (USA)	Surgical equipment	X		
Zeiss (Germany)	Endoscopic cameras and video monitors, surgical equipment	X	X	

Source: Frost & Sullivan. (1999) *European Endoscopes and Peripheral Endoscopic Equipment Markets. Chapter 3,* Frost & Sullivan (2001) *US Endoscopes Market, Chapter 5*, the US Food & Drug Administration's 510(k) database, the Health Devices Sourcebooks, and the Medical Device Registries.

Exhibit 5 Market shares of companies selling endoscopes in the US (1999) and Europe (1998)





Sources: Frost & Sullivan. (2001 and 1999).

Endnotes

[1] Basil I. Hirschowitz, "Historical Perspectives on Technology in GI Endoscopy," *Techniques in Gastrointestinal Endoscopy* 5, no. 2 (2003): 56–64, https://doi.org/10.1053/tgie.2003.1; Annetine C. Gelijns and Nathan Rosenberg, "From the Scalpel to the Scope: Endoscopic Innovations in Gastroenterology, Gynecology, and Surgery" (World Scientific Publishing CoPteLtd, 2010); Tetsuya Nakamura and Akira Terano, "Capsule Endoscopy: Past, Present, and Future," *Journal of Gastroenterology* 43, no. 2 (2008): 93–99, https://doi.org/10.1007/s00535-007-2153-6.

[2] James M. Edmonson, "History of the Instruments for Gastrointestinal Endoscopy," *Gastrointestinal Endoscopy* 37 (1991): S27–S56, https://doi.org/10.1016/S0016-5107(91)70910-3.

[3] 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.

[4] Hirschowitz, "Historical Perspectives on Technology in GI Endoscopy"; Leon Morgenstern, "From the Sword to Schindler: A Saga of Gastroscopy," *Surgical Innovation* 16, no. 2 (2009): 93–96, https://doi.org/10.1177/1553350609336844; Edmonson, "History of the Instruments for Gastrointestinal Endoscopy."

[5] 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.

[6] One article was written by physicist Abraham van Heel, who was funded by the military in the Netherlands. The other was written by London's Imperial College physicists Harold Hopkins and Narinder Singh Kapany, who were funded by a grant from the Royal Society in the United Kingdom. (Kapany, a native of India, who later emigrated to the United States and started several companies in Silicon Valley, was often described as the "father of fiber optics". See: https://news.ucsc.edu/2020/12/narinder-kapany-in-memoriam.html)

[7] A. C. S. Van Heel, "A New Method of Transporting Optical Images without Aberrations," *Nature* 173, no. 4392 (January 2, 1954): 39–39, https://doi.org/10.1038/173039a0; H. H. Hopkins and N. S. Kapany, "A Flexible Fibrescope, Using Static Scanning," *Nature* 173, no. 4392 (January 2, 1954): 39–41, https://doi.org/10.1038/173039b0; Jeff Hecht, *City of Light: The Story of Fiber Optics* (New York: Oxford University Press, 1999).

[8] Hirschowitz's fellowship was sponsored by the American Cancer Society.

[9] Hirschowitz, "Historical Perspectives on Technology in GI Endoscopy"; Gelijns and Rosenberg, "From the Scalpel to the Scope."

[10] Gastroscope pioneer Rudolph Schindler founded the American Gastroscopic Club in 1941. It became the American Society for Gastrointestinal Endoscopy in 1961.

[11] 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.

[12] Hirschowitz, "Historical Perspectives on Technology in GI Endoscopy"; Gelijns and Rosenberg, "From the Scalpel to the Scope"; Patsy Gerstner, "The American Society for Gastrointestinal Endoscopy: A History," *Gastrointestinal Endoscopy* 37 (1991): S1–S26, https://doi.org/10.1016/S0016-5107(91)70909-7; Hecht, *City of Light;* B. I. Hirschowitz et al., "Demonstration of a New Gastroscope, the Fiberscope," *Gastroenterology* 35, no. 1 (1958): 50.

[13] Although he did not mention it, reducing sedation had the additional advantage of significantly reducing costs for throat and stomach examination, because sedation required the services of anesthesiologists. Physicians that later used fiber endoscopes for examinations of the colon, however, continued to sedate patients.

[14] Hirschowitz, "Historical Perspectives on Technology in GI Endoscopy"; Gelijns and Rosenberg, "From the Scalpel to the Scope"; Gerstner, "The American Society for Gastrointestinal Endoscopy"; BasilI. Hirschowitz, "ENDOSCOPIC EXAMINATION OF THE STOMACH AND DUODENAL CAP WITH THE FIBERSCOPE," The Lancet, Originally published as Volume 1, Issue 7186, 277, no. 7186 (May 20, 1961): 1074–78, https://doi.org/10.1016/S0140-6736(61)92308-X; "Gastroduodenal Endoscopy with Fiberscope: Analysis of 500 Examinations," *JAMA* 183, no. 9 (March 2, 1963): 217–217, https://doi.org/10.1001/jama.1963.03700090177170.

[15] The removal of a tissue sample for analysis in a lab is known as a "biopsy."

[16] Hirschowitz, "Historical Perspectives on Technology in GI Endoscopy"; Gelijns and Rosenberg, "From the Scalpel to the Scope"; Edmonson, "History of the Instruments for Gastrointestinal Endoscopy"; Norman N. Cohen, Rollin W. Hughes, and Hector E. Manfredo, "Experience with 1000 Fibergastroscopic Examinations of the Stomach," *The American Journal of Digestive Diseases* 11, no. 12 (December 1, 1966): 943–50, https://doi.org/10.1007/BF02233083; Robert Kemp, "A NOTE ON THE FIBERSCOPE," The *Lancet*, Originally published as Volume 2, Issue 7246, 280, no. 7246 (July 14, 1962): 88–89, https://doi.org/10.1016/S0140-6736(62)92775-7; Brian Stanford, "THE FIBERSCOPE," *The Lancet,* Originally published as Volume 2, Issue 7255, 280, no. 7255 (September 15, 1962): 558, https://doi.org/10.1016/S0140-6736(62)90425-7; Brian Stanford, "THE FIBERSCOPE," *The Lancet,* Originally published as Volume 2, Issue 7268, 280, no. 7268 (December 15, 1962): 1274, https://doi.org/10.1016/S0140-6736(62)92839-8; Edward B. Benedict, "THE FIBERSCOPE," *The Lancet,* Originally published as Volume 2, Issue 7203, 278, no. 7203 (September 16, 1961): 664, https://doi.org/10.1016/S0140-6736(61)90341-5; F. Avery Jones, T. D. Kellock, and Brian Stanford, "THE FIBERSCOPE," *The Lancet,* Originally published as Volume 1, Issue 7189, 277, no. 7189 (June 10, 1961): 1285, https://doi.org/10.1016/S0140-6736(61)92791-X; Ian S. Campbell, Joel D. Howell, and H. Hughes Evans, "Visceral Vistas: Basil Hirschowitz and the Birth of Fiberoptic Endoscopy," *Annals of Internal Medicine* 165, no. 3 (August 2, 2016): 214, https://doi.org/10.7326/M16-0025.

[17] 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.

[18] John F. Morrissey, Gastrointestinal Endoscopy, Gastroenterology, V. 62, I. 6, 1972, p. 1241-1268, https://doi.org/10.1016/S0016-5085(72)80094-5: 28

[19] Campbell, Howell, and Evans, "Visceral Vistas"; Basil Hirschowitz, "Photography through the Fiber Gastroscope," The *American Journal of Digestive Diseases* 8, no. 5 (1963): 389–395, https://doi.org/10.1007/BF02231991; Basil Hirschowitz, "Endoscopic Photography Using Fiber Optics," *Society of Motion Picture and Television Engineers,* Journal 73, no. 8 (1964): 625; Basil I. Hirschowitz, "Use of Motion Pictures in Teaching & Diagnosis*," *Annals of the New York Academy of Sciences* 142, no. 2 (March 1, 1967): 455–60, https://doi.org/10.1111/j.1749-6632.1967.tb14357.x; Kemp, "A NOTE ON THE FIBERSCOPE."

[20] 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.

[21] G. A. Scheele and G. Kitzes, "Analysis of Academic Training Programs in Gastroenterology for the 10-Year Period 1957 to 1967," *Gastroenterology* 57, no. 2 (1969): 203–24; Campbell, Howell, and Evans, "Visceral Vistas"; T. P. Almy, "Current Trends in Graduate Training in Gastroenterology," *Gastroenterology* 41 (1961): 153–55; Morrissey, "Gastrointestinal Endoscopy." Morrissey notes in the early 1970s that there was only one training program specializing in teaching flexible endoscopy alone (at the University of Wisconsin), and it trained 20 students a year. By contrast, there were 110 training centers teaching flexible endoscopy throughout Japan at the time. (The centers had been put in place during the roll out of the gastro camera in the 1950s.) Morrissey suggested that students wishing to specialize in flexible endoscopy travel to Japan for training if they could not find programs in the U.S. By the late 1970s, however, flexible endoscopy had overtaken all other forms of training in gastroenterology in the U.S., so much so that some complained the U.S. training was out of balance. Morrissey also noted that few institutions could afford color television 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.

[22] Japanese camera producer Olympus had developed the devices in the early 1950s in collaboration with physicians at the University of Tokyo.

[23] Hirschowitz, "Historical Perspectives on Technology in GI Endoscopy"; John F. Morrissey, "The 1982 A/S/G/E Distinguished Lecture: Gastrointestinal Endoscopy—20 Years of Progress," *Gastrointestinal Endoscopy* 29, no. 1 (February 1, 1983): 53–56, https://doi.org/10.1016/S0016-5107(83)72506-X; Gelijns and Rosenberg, "From the Scalpel to the Scope"; Morrissey, "Gastrointestinal Endoscopy"; Edmonson, "History of the Instruments for Gastrointestinal Endoscopy."

[24] Hecht, *City of Light;* Gelijns and Rosenberg, "From the Scalpel to the Scope."

[25] Morrissey, "Gastrointestinal Endoscopy."

[26] In fact, British physicist Harold Hopkins, an author of one of the two 1954 *Nature* articles, had by that time developed and patented a new endoscope design that used glass rods (instead of coated glass fibers) to transmit light and images along a tube. Hopkins licensed his glass rod technology to Storz, and Storz used it to produce laparoscopes for gynecological procedures. Hirschowitz, "Historical Perspectives on Technology in GI Endoscopy"; William T. Kasumi, Asao Kasumi, and Benjamin Ishikawa, "The Spread of Upper Gastrointestinal Endoscopy in Japan and the United States: An International Comparative Analysis of Technology Diffusion," *International Journal of Technology Assessment in Health Care* 9, no. 3 (1993): 416–425, https://doi.org/10.1017/S0266462300004670; Edmonson, "History of the Instruments for Gastrointestinal Endoscopy"; Gelijns and Rosenberg, "From the Scalpel to the Scope"; Annetine C. Gelijns, "Diagnostic Devices: An Analysis of Comparative Advantages," 1999; Morrissey, "Gastrointestinal Endoscopy"; Grzegorz S. Litynski, "Endoscopic Surgery: The History, the Pioneers," *World Journal of Surgery* 23, no. 8 (1999): 745–753, https://doi.org/10.1007/s002689900576; Grzegorz S. Litynski, *Highlights in the History of Laparoscopy: The Development of Laparoscopic Techniques-- a Cumulative Effort of Internists, Gynecologists, and Surgeons* (Frankfurt/Main: Barbara Bernert Verlag, 1996).

[27] I. Oi, S. Kobayashi, and T. Kondo, "Endoscopic Pancreato-cholangiography," *Endoscopy* 02, no. 02 (May 1970): 103–6, https://doi.org/10.1055/s-0028-1098441; Edmonson, "History of the Instruments for Gastrointestinal Endoscopy"; Morrissey, "Gastrointestinal Endoscopy"; Morrissey, "The 1982 A/S/G/E Distinguished Lecture"; Hirschowitz, "Historical Perspectives on Technology in GI Endoscopy"; Gelijns and Rosenberg, "From the Scalpel to the Scope"; Gelijns, "Diagnostic Devices"; Per M. Hellström, "This Year's Nobel Prize to Gastroenterology: Robin Warren and Barry Marshall Awarded for Their Discovery of Helicobacter Pylori as Pathogen in the Gastrointestinal Tract," *World Journal of Gastroenterology* 12, no. 19 (2006): 3126, https://doi.org/10.3748/wjg.v12.i19.3126; Bernard M. Schuman, "The Evolution of Diagnostic ERCP," *Gastrointestinal Endoscopy* 36, no. 2 (March 1, 1990): 155–56, https://doi.org/10.1016/S0016-5107(90)70976-5.

[28] Oi, Kobayashi, and Kondo, "Endoscopic Pancreato-cholangiography"; Edmonson, "History of the Instruments for Gastrointestinal Endoscopy"; Morrissey, "Gastrointestinal Endoscopy"; Morrissey, "The 1982 A/S/G/E Distinguished Lecture"; Hirschowitz, "Historical Perspectives on Technology in GI Endoscopy"; Gelijns and Rosenberg, "From the Scalpel to the Scope"; Gelijns, "Diagnostic Devices"; Hellström, "This Year's Nobel Prize to Gastroenterology"; Schuman, "The Evolution of Diagnostic ERCP."

[29] Hirschowitz, "Historical Perspectives on Technology in GI Endoscopy"; F A Mettler, "Diagnostic Radiology: Usage and Trends in the United States, 1964-1980.," *Radiology* 162, no. 1 (January 1, 1987): 263–66, https://doi.org/10.1148/radiology.162.1.3786774; F. A. Mettler et al., "Use of Radiology in U.S. General Short-Term Hospitals: 1980-1990," *Radiology* 189, no. 2 (November 1993): 377–80, https://doi.org/10.1148/radiology.189.2.8210363; Schuman, "The Evolution of Diagnostic ERCP."

[30] Gelijns, "Diagnostic Devices"; Edmonson, "History of the Instruments for Gastrointestinal Endoscopy."

[31] Grzegorz S. Litynski, "Raoul Palmer, World War II, and Transabdominal Coelioscopy. Laparoscopy Extends into Gynecology," *JSLS: Journal of the Society of Laparoendoscopic Surgeons* 1, no. 3 (1997): 289–92; Gelijns, "Diagnostic Devices"; Edmonson, "History of the Instruments for Gastrointestinal Endoscopy"; Litynski, "Endoscopic Surgery"; By the mid-to-late 1960s, laparoscopes' optics had been improved with a rod-lens system designed by Harold Hopkins, an author of one of the 1954 *Nature* articles. However, gastroenterologists had by that time begun to develop minimally invasive techniques that used fiber endoscopes. For a description of the Hopkins rod-lens system, see: Willia S. Cockett and Abraham T. K. Cockett, "The Hopkins Rod-Lens System and the Storz Cold Light Illumination System," *Urology* 51, no. 5, Supplement 1 (May 1, 1998): 1–2, https://doi.org/10.1016/S0090-4295(98)00060-0.

[32] Surgery on the throat, stomach, and intestines was not performed by general surgeons, rather it was considered a specialty requiring additional training. Gastroenterologists had previously diagnosed problems and then turned patients over to surgeons specializing in gastrointestinal surgery for treatment. Oi, Kobayashi, and Kondo, "Endoscopic Pancreato-cholangiography"; Edmonson, "History of the Instruments for Gastrointestinal Endoscopy"; Morrissey, "Gastrointestinal Endoscopy"; Morrissey, "The 1982 A/S/G/E Distinguished Lecture"; Hirschowitz, "Historical Perspectives on Technology in GI Endoscopy"; Gelijns and Rosenberg, "From the Scalpel to the Scope"; Gelijns, "Diagnostic Devices"; Michael V. Sivak, "Polypectomy: Looking Back," *Gastrointestinal Endoscopy* 60, no. 6 (December 1, 2004): 977–82, https://doi.org/10.1016/S0016-5107(04)02380-6; Schuman, "The Evolution of Diagnostic ERCP"; Michael V. Sivak, "ERCP at Thirty Years: An Interview with Dr. William S. McCune (1909–1998)," *Gastrointestinal Endoscopy* 48, no. 6 (December 1, 1998): 643–44, https://doi.org/10.1016/S0016-5107(98)70054-9; William S. McCune, "ERCP—the First Twenty Years," *Gastrointestinal Endoscopy* 34, no. 3 (May 1, 1988): 277–78, https://doi.org/10.1016/S0016-5107(88)71331-0.

[33] Edmonson, "History of the Instruments for Gastrointestinal Endoscopy"; Morrissey, "Gastrointestinal Endoscopy"; Morrissey, "The 1982 A/S/G/E Distinguished Lecture"; Hirschowitz, "Historical Perspectives on Technology in GI Endoscopy"; Gelijns and Rosenberg, "From the Scalpel to the Scope"; Gelijns, "Diagnostic Devices."

[34] Litynski, "Endoscopic Surgery."

[35] F. Kern, "Clinical Training in Gastroenterology: A Proposal for Restoring Balance," *Gastroenterology* 76, no. 6 (1979): 1489–92; Joel F. Panish and Paul Sherlock, "Training in Gastroenterology: The New Balance," *Gastroenterology* 78, no. 1 (1980): 170–174; Fred Kern, "More on Balance" (Elsevier Inc, 1980).

[36] Paul Sherlock, "The Challenge of the 1980s," *Gastrointestinal Endoscopy* 25, no. 3 (August 1, 1979): 85–87, https://doi.org/10.1016/S0016-5107(79)73380-3; Charles J. Lightdale, "Notes on the Development of the American Society for Gastrointestinal Endoscopy," *Gastrointestinal Endoscopy* 29, no. 1 (February 1, 1983): 51–53, https://doi.org/10.1016/S0016-5107(83)72505-8; Donald M. Switz, "American Gastroenterological Association: Results of a Membership Poll," *Gastroenterology* 90, no. 2 (February 1986): 482–85, https://doi.org/10.1016/0016-5085(86)90951-0; Gabriel F. Tucker et al., "Standards for Training in Endoscopy: Statement of the Committee on Bronchoesophagology: Statement of the Committee on Bronchoesophagology," *Chest* 69, no. 5 (1976): 665–666, https://doi.org/10.1378/chest.69.5.665; Melvin Schapiro, "Who Should Be Doing Gastrointestinal Endoscopy?," *JAMA* 245, no. 6 (1981): 577–577, https://doi.org/10.1001/jama.1981.03310310019014; B. F. Overholt, "A/S/G/E Guidelines for Standards of Training and Practice," *Gastrointestinal Endoscopy* 22, no. 1 (1975): 46–47. Frost & Sullivan. (June 1984) *The Endoscopy Products Market in the U.S.*

[37] Francisco Vilardell, "European Society of Gastrointestinal Endoscopy," *Gastrointestinal Endoscopy* 19, no. 4 (May 1, 1973): 196–97, https://doi.org/10.1016/S0016-5107(73)74002-5; G. Hellers, "Education and Training in Gastroenterology. A Report from Europe," *Scandinavian Journal of Gastroenterology.* Supplement 144 (1988): 80–81; Sverre Emas, "Gastroenterology in Europe 1983," *Digestive Diseases and Sciences* 29, no. 8 (August 1, 1984): 758–59, https://doi.org/10.1007/BF01312950; W. S. Haubrich, "Gastroenterology Flourishes in Europe," *Gastrointestinal Endoscopy* 26, no. 3 (August 1, 1980): 110–11, https://doi.org/10.1016/S0016-5107(80)73291-1.

[38] Kasumi, Kasumi, and Ishikawa, "The Spread of Upper Gastrointestinal Endoscopy in Japan and the United States."

[39] According to a Frost & Sullivan market research report, the sales forces had helped the Japanese producers incorporate American physicians' feedback into the endoscopes that could extract cells or magnify diseased or damaged areas. Olympus and Machida, as mentioned, had also led development of the endoscopes and tools used in minimally invasive surgeries. However, by the end of the decade, Machida had been absorbed into Pentax. Gelijns, "Diagnostic Devices." Frost & Sullivan. (June 1984) *The Endoscopy Products Market in the U.S.*; 177.

[40] Gelijns. Frost & Sullivan. (June 1984) *The Endoscopy Products Market in the U.S.*; 177.

[41] Gelijns. Frost & Sullivan. (Winter 1990/1991) The U.S. Market for Endoscopes and Endoscopic Products, Volumes I & II.

[42] Gelijns, "Diagnostic Devices"; "Welch Allyn Company History," accessed July 6, 2015, http://www.welchallyn.com/en/about-us/history.html. Frost & Sullivan. (Winter 1990/1991) *The U.S. Market for Endoscopes and Endoscopic Products, Volumes I & II.*

[43] "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.*

[44] The rules, however, did not mandate strict conformity to standards, as historians have noted, "because of concerns that this might hinder innovation." Later, manufacturers were required to report adverse effects or incidents to a central authority. Daniel B. Kramer, Shuai Xu, and Aaron S. Kesselheim, "Regulation of Medical Devices in the United States and European Union," *The New England Journal of Medicine* 366, no. 9 (2012): 848–855, https://doi.org/10.1056/NEJMhle1113918; "European Union Regulation of In Vitro Diagnostic Medical Devices," accessed January 3, 2019, https://www.cov.com/en/news-and-insights/insights/2010/01/european-union-regulation-of-in-vitro-diagnostic-medical-devices; Chai, "Medical Device Regulation in the United States and the European Union"; Christa Altenstetter, "Medical Device Regulation in the European Union, Japan and the United States. Commonalities, Differences and Challenges," *Innovation: The European Journal of Social Science Research* 25, no. 4 (December 1, 2012): 362–88, https://doi.org/10.1080/13511610.2012.723328.

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

[46] Frost & Sullivan. (Winter 1990/1991) The U.S. Market for Endoscopes and Endoscopic Products, Volumes I & II.

[47] 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. Sources: 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.

[48] "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; Ellen Koch, "Managing the Medical Arms Race: Innovation and Public Policy in the Medical Device Industry (Book Review)," 1993; See also: Altenstetter, "Medical Device Regulation in the European Union, Japan and the United States. Commonalities, Differences and Challenges." Prices based on reporting in Frost & Sullivan. (Winter 1990/1991) *The U.S. Market for Endoscopes and Endoscopic Products, Volumes I & II.*

[49] Judy Skatssoon, "NSW - Science Fiction Becomes Medical Reality with Pillcam.," *Australian Associated Press,* October 16, 2000, http://global.factiva.com/redir/default.aspx?P=sa&an=aap0000020020307dwag026du&cat=a&ep=ASE; Nakamura and Terano, "Capsule Endoscopy"; Samuel N. Adler, "The History of Time for Capsule Endoscopy," *Annals of Translational Medicine* 5, no. 9 (May 2017), https://doi.org/10.21037/atm.2017.03.90; Mark Appleyard, Arkady Glukhovsky, and Paul Swain, "Wireless-Capsule Diagnostic Endoscopy for Recurrent Small-Bowel Bleeding.(Letter to the Editor)," *The New England Journal of Medicine* 344, no. 3 (2001): 232; Kathleen Fackelmann, "Capsule Takes Fantastic Voyage Pill with Tiny Camera Films Small Intestine, Looking for Trouble," *USA Today,* January 18, 2001, FINAL edition, sec. LIFE.

[50] Skatssoon, "NSW - Science Fiction Becomes Medical Reality with Pillcam."; Nakamura and Terano, "Capsule Endoscopy"; Adler, "The History of Time for Capsule Endoscopy"; Appleyard, Glukhovsky, and Swain, "Wireless-Capsule Diagnostic Endoscopy for Recurrent Small-Bowel Bleeding.(Letter to the Editor)"; Fackelmann, "Capsule Takes Fantastic Voyage Pill with Tiny Camera Films Small Intestine, Looking for Trouble"; RICHARD PHILLIPS, "TINY CAMERA GIVES INSIDE VIEW OF INNARDS.," *The Express on Sunday,* February 18, 2001, http://global.factiva.com/redir/default.aspx?P=sa&an=thexsu0020010715dx2i001iy&cat=a&ep=ASE; ROSIE MESTEL, "Pill-Size Gastro-Cam Is Just a Swallow Away," *Los Angeles Times,* June 1, 2000, http://articles.latimes.com/2000/jun/01/local/me-36233.

[51] Robert D. Schertz, William N. Baskin, and James T. Frakes, "Flexible Fiberoptic Sigmoidoscopy Training for Primary Care Physicians: Results of a 5-Year Experience," *Gastrointestinal Endoscopy* 35, no. 4 (1989): 316–320, https://doi.org/10.1016/S0016-5107(89)72800-5; Wm. MacMillan Rodney, "Flexible Sigmoidoscopy and the Despecialization of Gastrointestinal Endoscopy an Environmental Impact Report," *Cancer* 70, no. S3 (September 1, 1992): 1266–71, https://doi.org/10.1002/1097-0142(19920901)70:3+<1266::AID-CNCR2820701512>3.0.CO;2-I; R. J. Ackermann, "Performance of Gastrointestinal Tract Endoscopy by Primary Care Physicians. Lessons from the US Medicare Database," *Archives of Family Medicine* 6, no. 1 (February 1997): 52–58. Frost & Sullivan. (Winter 1990/1991) *The U.S. Market for Endoscopes and Endoscopic Products, Volumes I & II.*

[52] As described in our another Note in this series., ;Hirschowitz, "Historical Perspectives on Technology in GI Endoscopy"; Hellström, "This Year's Nobel Prize to Gastroenterology"; Barry J. Marshall, "One Hundred Years of Discovery and Rediscovery of Helicobacter Pylori and Its Association with Peptic Ulcer Disease," in *Helicobacter Pylori: Physiology and Genetics,* ed. Harry LT Mobley, George L. Mendz, and Stuart L. Hazell (Washington (DC): ASM Press, 2001), http://www.ncbi.nlm.nih.gov/books/NBK2432/; Barry Marshall, "A Brief History of the Discovery of Helicobacter Pylori," in *Helicobacter Pylori,* ed. Hidekazu Suzuki, Robin Warren, and Barry Marshall (Springer Japan, 2016), 3–15, https://doi.org/10.1007/978-4-431-55705-0_1; John Robin Warren, "The Discovery and Pathology of H Pylori / Papers Published by John Robin Warren." (Thesis, 1999), https://digital.library.adelaide.edu.au/dspace/handle/2440/38453.

[53] Hirschowitz, "Historical Perspectives on Technology in GI Endoscopy"; Frost & Sullivan. (Winter 1990/1991) *The U.S. Market for Endoscopes and Endoscopic Products, Volumes I & II.,* Sections 1.1.2, 1.2.2, and 3. Frost & Sullivan. (2001) *U.S. Endoscopes Market,* Chapter 5. Frost & Sullivan. (1999) *European Endoscopes and Peripheral Endoscopic Equipment Markets.* Chapter 3. See also our case study on laparoscopy.

[54] Kasumi, Kasumi, and Ishikawa, "The Spread of Upper Gastrointestinal Endoscopy in Japan and the United States"; Schertz, Baskin, and Frakes, "Flexible Fiberoptic Sigmoidoscopy Training for Primary Care Physicians"; Rodney, "Flexible Sigmoidoscopy and the Despecialization of Gastrointestinal Endoscopy an Environmental Impact Report"; Ackermann, "Performance of Gastrointestinal Tract Endoscopy by Primary Care Physicians. Lessons from the US Medicare Database." Frost & Sullivan. (Winter 1990/1991) *The U.S. Market for Endoscopes and Endoscopic Products, Volumes I & II.*

[55] Kasumi, Kasumi, and Ishikawa, "The Spread of Upper Gastrointestinal Endoscopy in Japan and the United States."

[56] 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.

[57] Frost & Sullivan. (1999) European Endoscopes and Peripheral Endoscopic Equipment Markets. Chapter 3.

[58] 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.

[59] Frost & Sullivan. (Winter 1990/1991) *The U.S. Market for Endoscopes and Endoscopic Products,* Volumes I & II., Sections 1.1.2, 1.2.2, and 3. Frost & Sullivan. (2001) *U.S. Endoscopes Market,* Chapter 5. Frost & Sullivan. (1999) *European Endoscopes and Peripheral Endoscopic Equipment Markets.* Chapter 3. Estimates of entrants are also based on records in the FDA's 510(k) database, in addition to the Health Devices Sourcebooks and the Medical Device Registries.

[60] Frost & Sullivan. (2001) U.S. Endoscopes Market, Chapter 5. Frost & Sullivan. (1999) European Endoscopes and Peripheral Endoscopic Equipment Markets. Chapter 3.

[61] Compiled by casewriter from John F. Morrissey, Gastrointestinal Endoscopy, Gastroenterology, V. 62, I. 6, 1972, p. 1241-1268, https://doi.org/10.1016/S0016-5085(72)80094-5 James M. Edmonson, "History of the Instruments for Gastrointestinal Endoscopy," *Gastrointestinal Endoscopy* 37 (1991): S27–S56, https://doi.org/10.1016/S0016-5107(91)70910-3, Kasumi et al "The Spread of Upper Gastrointestinal Endoscopy in Japan and the United States: An International Comparative Analysis of Technology Diffusion," *International Journal of Technology Assessment in Health Care* 9, no. 3 (1993), Litynski GS, Paolucci V. The history of surgery. World J Surg. 1998 Oct;22(10):1108-9. doi: 10.1007/s002689900526. PMID: 9747176, Jeff Hecht, *City of Light: The Story of Fiber Optics* (New York: Oxford University Press, 1999), Basil I. Hirschowitz, "Historical Perspectives on Technology in GI Endoscopy," *Techniques in Gastrointestinal Endoscopy* 5, no. 2 (2003): 56–64, https://doi.org/10.1053/tgie.2003.1, and Annetine C. Gelijns and Nathan Rosenberg, "From the Scalpel to the Scope: Endoscopic Innovations in Gastroenterology, Gynecology, and Surgery" (World Scientific Publishing CoPteLtd, 2010).

[62] ABI had a partnership with MTO in Paris, France.

[63] Aesculap became an American division of B. Braun, Germany.