

## 24<sup>th</sup> Seah Cheng Siang Lecture\*: Seeing Better, Doing Better—Evolution and Application of Gastrointestinal (GI) Endoscopy

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### Abstract

Gastrointestinal (GI) endoscopy has evolved tremendously from the early days when candlelight was used to illuminate scopes to the extent that it has now become an integral part of the practice of modern gastroenterology. The first gastroscope was a rigid scope first introduced by Adolf Kussmaul in 1868. However this scope suffered from the 2 drawbacks of poor illumination and high risk of instrumental perforation. Rudolf Schindler improved on this by inventing the semiflexible gastroscope in 1932. But it was Basil Hirschowitz, using the principle of light conduction in fibreoptics, who allowed us to “see well” for the first time when he invented the flexible gastroscopy in 1958. With amazing speed and innovation, instrument companies, chiefly Japanese, had improved on the Hirschowitz gastroscope and invented a flexible colonoscope. Walter McCune introduced the technique of endoscopic retrograde cholangiopancreatography (ERCP) in 1968 which has now evolved into a sophisticated procedure. The advent of the digital age in the 1980s saw the invention of the videoendoscope. Videoendoscopes have allowed us to start seeing the gastrointestinal tract (GIT) “better” with high magnification and resolution and optical/digital enhancements. Fusing confocal and light microscopy with endoscopy has allowed us to perform an “optical biopsy” of the GI mucosa. Development of endoscopic ultrasonography has allowed us to see “beyond” the GIT lumen. Seeing better has allowed us to do better. Endoscopists have ventured into newer procedures such as the resection of mucosal and submucosal tumours and the field of therapeutic GI endoscopy sees no end in sight.

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### The Early Beginnings

Man’s innate curiosity to study the internal organs of the human body dates back to the time of Hippocrates where basic speculums were invented to peer into the buccal cavity and vagina. The first instruments used to intubate the oesophagus and stomach in the 16<sup>th</sup> and 17<sup>th</sup> centuries were designed for the purpose of extracting foreign bodies stuck in the oesophagus (or pushing them down into the stomach).

The first scopes used candlelight for illumination (Bozzini, 1806) and subsequently gasogen which is a mixture of alcohol and turpentine (Desormeux, 1853).<sup>1</sup> These scopes were, however, mainly designed as urethro-cystoscopes. Desormeux was the first to call such instruments, “endoscopes”.<sup>1</sup>

### Development of Rigid Scopes

Adolf Kussmaul is credited with inventing the first gastroscope in 1868. Taking the cue from sword swallows who were popular entertainers at that time, Kussmaul attempted to insert a long rigid hollow tube into a professional sword swallower at a meeting of the Society of Naturalists in Freiburg, Germany. Illumination was provided by a gasogen lamp but it was poor and as a result, the examination was unsatisfactory.<sup>1</sup> Water-cooled and electrically-heated wire platinum loops were then used by Nietze for providing light but these were found to be cumbersome and impractical. The “enlightenment” of endoscopy followed Edison’s invention of the incandescent lamp in 1879. A miniaturised or “mignon” light bulb was

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used with oesophagoscopes by Leiter and Mickulicz (1887).<sup>1</sup> Despite much effort at developing a gastroscope by many workers, the first fully usable rigid gastroscope was produced by Elsner in 1911. Rudolf Schindler, who more than anyone else had popularised upper gastrointestinal (GI) endoscopy at that time, called the Elsner instrument “the mother of all instruments”. He himself modified this rigid scope in 1922 by adding an air-channel into the scope to clean the lens. Through numerous examinations and assiduous recording by colour drawings, he published his classic book, “Lehrbuch und Atlas der Gastroskopie” (Textbook and Atlas of Gastroskopy) in 1923.<sup>1</sup>

### Rudolf Schindler and the Semiflexible Gastroscope

But the rigid scope had serious drawbacks. Instrumental perforations were not uncommon and as a result, the initial enthusiasm for the procedure waned. Schindler set about to invent a semiflexible gastroscope with the collaboration of a Berlin instrument maker, Georg Wolf. Working on the optical principle proposed by Hoffmann in 1911 that lenses attached to a flexible wire at short focal intervals from one another would bend light, Wolf and Schindler produced such a scope in 1932.<sup>2,3</sup> It had a flexible distal 30-cm tip which was made of a bronze wire spiral and which incorporated a number of short convex lenses. This instrument was a major advance at that time, as not only was it much safer, it also provided significantly more information about the stomach. Despite the temporary setback of World War II and the incarceration of Schindler himself in a Nazi concentration camp, the semiflexible scope gained many ardent followers. This was in no small measure due to Schindler who was an enthusiastic and indefatigable teacher. Following his release from prison in 1934, Schindler and his family emigrated to the United States, where he was given an academic position at the University of Chicago. He continued his good work there and Chicago soon became a mecca for gastroenterologists and endoscopists. In 1941, Schindler started, at a meeting in his own house, the American Gastroscopic Club, the forerunner of the American Society of Gastrointestinal Endoscopy (ASGE). The ASGE chose to recognise his exceptional contributions in 1962 by creating the Schindler Award, the society’s highest tribute for contributions to the field of gastrointestinal endoscopy.<sup>4</sup>

### Dawn of a New Era: Fibreoptic Endoscopy—Seeing Well

The Schindler-Wolf semiflexible gastroscope was the standard bearer for gastroscopes until 1957 when a further dramatic innovation, that of fibreoptics, was introduced into endoscopes. The inspiration for the making of a fibrescope was a 1954 paper appearing in *Nature* entitled “A flexible fibrescope using static scanning” coauthored by Harold

Hopkins and Nirmal Kapany.<sup>5</sup> In this paper, Hopkins and Kapany showed that light could be transmitted through a single glass fibre based on the principle of total internal reflection. Basil Hirschowitz who was then a GI fellow at Ann Arbor, University of Michigan with Professor Marvin Pollard, was fascinated about the possibility of using fibreoptics in endoscopes and with the encouragement of his former mentor, Sir Francis Avery Jones of Middlesex Hospital, London, he paid a visit to Hopkins and Kapany at the Imperial College, London. On his return, Hirschowitz enlisted the help of Wilbur Peters, a physicist, and Larry Curtis, a sophomore student at the University of Michigan. Working feverishly with his coworkers, Hirschowitz was able to develop the first fibreoptic gastroscope, which he presented to the American Gastroscopic Society in Colorado Springs in May 1957. Before the year was out, the American Cystoscopic Makers Inc (ACMI) contracted to manufacture fibrescopes under license and in October 1960, the ACMI 4990 Hirschowitz gastroduodenal fibrescope was available for sale and use. Hirschowitz reported his initial experience with the fibreoptic scope in the *Lancet* in 1961.<sup>6</sup> By the late 1960s, fibreoptics had almost completely displaced lens-optic gastroscopes. The Olympus Optical Company’s (Tokyo, Japan) first fibre gastroscope was introduced in 1968. ACMI produced the panendoscope in 1970. Japanese and American manufacturers rapidly and competitively improved fibreoptic instruments. In the words of Hirschowitz, “There seemed to be no end to the ingenuity of endoscopists and instrument makers and the application of fibreoptic instruments to diagnosis and therapy”<sup>7</sup> (Professor Basil Hirschowitz, circa 2004, Fig. 1).

While developments were taking place in the United States, Dr Tatsuno Uji and engineers from the Olympus Optical Company, Japan, had developed a gastrocamera in 1952. In essence, it consisted of a miniaturised intragastric camera which could take high quality pictures. It was presented to Western endoscopists at the World Congress in Washington DC in 1958. Olympus Optical Company

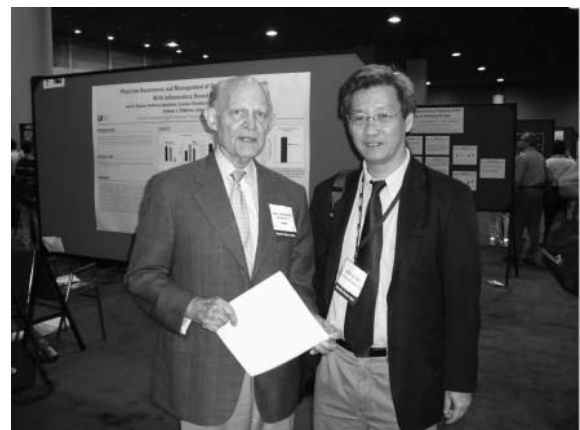


Fig. 1. Professor Basil Hirschowitz with author, May 2004, Digestive Disease Week, New Orleans, USA.

subsequently developed a model incorporating fibrescope and a gastrocamera in 1963 and this was used widely in Japan for mass screening for gastric cancer. But the gastrocamera had already by then, been quickly rendered obsolete by fibreoptic scopes.<sup>8</sup>

Fibreoptics was soon introduced for the examination of organs other than the upper gastrointestinal tract (GIT). Bergein Overholt, who also worked in the University of Michigan, Ann Arbor, presented his experience with the first fibreoptic sigmoidoscopy in 1967 at the ASGE meeting.<sup>1</sup> Subsequently in 1969 fiber optic colonoscopy and shortly thereafter, endoscopic polypectomy was performed by Wolff and Shinya in New York.<sup>9</sup> Colonoscopy opened up a whole unexplored field of endoscopy. This was particularly significant in the face of widespread skepticism at that time. Comments included: “It requires a tricky skill that few will be able to acquire”, “It will tell you nothing a good radiologist couldn’t show” etc. Time has however, proven otherwise.

### Further Innovations—Seeing More

One of the most exciting and elegant innovations of fibreoptic endoscopy was the cannulation of the ampulla of Vater. WC Watson of Glasgow in 1966 reported in the *Lancet*, his observations of the ampulla of Vater with a flexible duodenoscope and concluded that “endoscopic examination of the ampulla of Vater could be helpful in the diagnosis of biliary and pancreatic disorders”. McCune and colleagues from George Washington University reported in 1968 the first successful cannulation of the pancreatic duct using an Eder duodenoscope with a makeshift housing for a canula.<sup>10</sup> But the Japanese were responsible for developing the endoscopic retrograde cholangiopancreatography (ERCP) as a standard diagnostic procedure. Itaru Oi, and Kunio Takagi and colleagues, together with engineers from the Machida Manufacturing Company and Olympus Optical Company, developed specially designed ERCP scopes: the FDS and JF and JFB-2 models respectively.<sup>11,12</sup> Peter Cotton reported on his series of patients undergoing ERCP in 1972.<sup>13</sup> In 1973, Keichi Kawai from Japan and Meinhard Classen and Ludwig Demling from Germany simultaneously reported endoscopic electrosurgical sphincterotomy of the papilla for the non-operative extraction of common bile duct stones.<sup>14,15</sup> In 1980, Nib Soehendra from Hamburg, Germany introduced stenting of the biliary system with plastic tubes.<sup>16</sup> The range of innovations that have come out in this field from pioneer ERCP-dedicated endoscopists such as Kees Huibregtse from Amsterdam have been truly amazing.<sup>17</sup>

Endoscopic ultrasonography, a more recently developed innovation in the late 1980s combines the diagnostic

capability of an ultrasound probe and that of a fibreoptic scope. Lutz and Rosch from Germany was the first to report on a transgastroscopic ultrasonography<sup>18</sup> and subsequently Strohm et al<sup>19</sup> and Eugene DiMagno from Mayo Clinic<sup>20</sup>, improved on the applicability of these instruments. The first mechanical sector scanning instruments for endoscopic ultrasound displayed 180° images. The subsequent introduction of a full 360° image endoscope, the Olympus GF-UM3, provided the first commercially available echoendoscope.

### Videoendoscopy—Seeing Better

Videoendoscopy provided perhaps the latest innovation in GI endoscopy. It is certainly not a new technique of performing endoscopy but a new way of viewing, acquiring and storing images in the digital form. The mechanical control and internal lumen subsystems remained essentially unchanged. Videoendoscopy is made possible following the discovery of the charged couple device (CCD) or electronic chip as it is commonly called.<sup>21</sup> The first videoendoscope system was developed by Welch Allyn Incorporated (Skaneateles, USA) and exhibited at the ASGE meeting in 1983 and the first clinical report on its use in colonoscopy by Sivak and Fleischer in 1984.<sup>22</sup> It drew little interest then as the prevailing attitude was “why replace something that is perfectly good with one that provided an image of lesser definition and at greater cost?”. Again, time has been the best judge. With further development and refinement of the system predominantly by the Japanese companies—Olympus Optical Company, Pentax and Fujinon—videoendoscopy has achieved not only “supra-maximum” quality imaging with ease of storage and transfer of images, it has also become the standard system for all forms of endoscopy today.

Videoendoscopy has also meant that endoscopists have now moved away from viewing through an “eyepiece” and to viewing images on a “television” screen (Fig. 2). This has made it ergonomically better for endoscopists as well as improving visualisation, and has also made teaching of endoscopy trainees more efficient.

### Seeing Even Better

Videoendoscope instruments with even better imaging reaching a million pixels have been produced. Magnifying endoscopes and chromoendoscopy have enhanced the details of the GI mucosa. Recent innovations by the instrument companies included enhanced optical and digital modalities including narrow band imaging (Olympus, Optical company, Tokyo, Japan), Flexible spectral imaging colour enhancement (Fuji Film, Japan) and i-scan technology (Pentax, Hoya Corporation, Japan)<sup>23</sup> (Fig. 3).



Fig. 2. Fiberoptic gastroscope using an eyepiece (left); videoendoscope using a television monitor (right) with a trainee and instructor by his side.

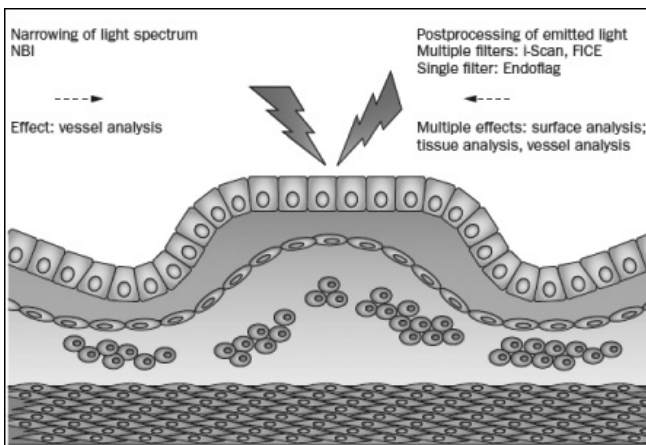


Fig. 3. This figure explains the principles of digital or virtual chromoendoscopy. NBI uses distinct filters to narrow the light that is emitted to the tissue. The ‘blue’ light leads to improved visualisation of surface vessel architecture. Emitted light from the tissue can be postprocessed, with many different effects modulated. FICE: Fuji intelligent chromoendoscopy; NBI: Narrow band imaging. Figure reproduced with permission from Elsevier<sup>®</sup>. Sauk J, Hoffman A, Anandasabapathy S, Kiesslich R. High-definition and filter-aided colonoscopy. *Gastroenterol Clin North Am* 2010;39:859-81.

Several technologies have now emerged that allow high resolution examination of the GI mucosa. These innovations have enabled an “optical biopsy” of the GI mucosa at the cellular and even the subcellular level. These technologies include confocal endoscopy, endocytoscopy and optical coherence tomography endoscopy.

Confocal endoscopy is perhaps the best established of these techniques and is already in routine clinical use. Essentially, it is a fusion of endoscopy and confocal microscopy techniques and was originally invented by Pentax as a scope-based technology.<sup>24</sup> In more recent years Mauna Kea Technologies has introduced a probe-based confocal endoscopy.<sup>25</sup> Endocytoscopy (EC) can be simply described as the application of a light microscope on the lining of the GIT and provides an ultra-high magnification of cells of the GI epithelium.<sup>26</sup> Again this technology can be scope-based or probe-based. Currently however, it is only available in prototype forms. Optical coherence tomography techniques for the GIT borrows the application

from examination of the retina in ophthalmology and relies on the back scattering of light to obtain cross-sectional image of tissues.<sup>27</sup> Again, this technology is still in the prototype form. These examinations are carried out in vivo with real-time image display. These optical biopsy techniques would be most useful in diagnosing dysplasia in patients with Barrett’s oesophagus and ulcerative colitis for example, and allows an immediate decision to be made on endoscopic therapy.

Miniaturisation of electronic components may allow the construction of new types of endoscopes that no longer require external wires, cables, or optical fibres. A “video pill” would allow the operator to perform a “drive through” endoscopy. The invention of capsule endoscopy in 2000 by Iddan et al<sup>28</sup> opened up the examination of a whole new frontier of the GIT—all 6 metres of the small intestine. Again, various technological advances over time have gradually allowed better capsule endoscopy imaging and more complete capture of images.

## Seeing Better, Doing Better

Seeing better has inevitably allowed us to do better. New generation and braver endoscopists have ventured into procedures such as resection of mucosal and submucosal tumours, and the field of therapeutic endoscopy sees no end in sight. Endoscopic submucosal dissection was first described for early gastric tumours by Japanese endoscopists in 2001<sup>29</sup> and is now an established technique for early cancers of the oesophagus, stomach and the colon.<sup>30</sup> Submucosal tunneling can now be performed safely and confidently, and experts like Haruhiro Inoue have described the technique of per-oral endoscopic myotomy (POEM) for achalasia of the cardia.<sup>31</sup> Braver endoscopists now routinely perform endoscopic dissection and removal of submucosal tumours, and there have been reports of full thickness endoscopy resection of GI tumours done together with laparoscopy or by endoscopy alone.<sup>32</sup>

Visualisation of the biliopancreatic tracts have improved with the introduction of ultrathin scopes or probes directly into the bile duct and pancreatic ducts. The “mother-baby” ERCP scope set up has been in use for a long time but recent innovations utilising an intraductal biliary balloon by Moon et al has allowed ultrathin gastroscopes to be introduced directly into the bile duct.<sup>33</sup> This has allowed biopsy of biliopancreatic tumours, and in the bile duct, it has permitted the use of electrohydraulic and pulsed laser therapies to fragment large stones and to remove stones from intrahepatic ducts.

## Epilogue—What of the Future?

The development and the subsequent widespread use and application of GI endoscopy ranks as one of the landmarks in the annals of medicine. GI endoscopy is indispensable to the field of gastroenterology and GI surgery. The “endoscope” has evolved from a candlelit instrument in the early 19th century to its current state of sophistication. Procedures are now performed in well planned dedicated endoscopy units (Fig. 4). Training, credentialing, audit, retraining and maintenance of standards of practice are important issues. The field of GI endoscopy has developed into a distinct and separate field, with journals, workshops, international meetings and a global fraternity of its own. With continuing advances and technical sophistication, GI endoscopy will remain an exciting field stimulating further research and spearheading advances in the diagnosis and treatment of GI diseases. Man’s ingenuity in the development of endoscopy has brought gastroenterology into the forefront of diagnosis and treatment of human diseases.



Fig. 4. A modern therapeutic endoscopy room with a digital fluoroscopy unit, University of Malaya Medical Centre (UMMC), Kuala Lumpur, Malaysia, 2014. The GI Endoscopy unit at the UMMC has been accorded the Centre of Excellence Award, by the World Endoscopy Organization from 2008 to 2014, an award which has now been renewed from 2015 to 2020.

## Postscript

*Professor Seah Cheng Siang, whom I did not have the chance to meet in his lifetime, was a teacher, doctor and pioneer gastroenterologist par excellence. Above all, he was a humane man who contributed immensely to the development of medicine and gastroenterology in Singapore. Many Malaysian doctors benefited from his teaching in the earlier days, as the only medical school then was the University of Malaya, which was based in Singapore before it moved to Kuala Lumpur, Malaysia in 1962. It is truly a privilege to deliver this lecture in his name in 2014. Younger physicians and gastroenterologists have been fortunate and as Sir Isaac Newton quoted, “[they] could see further by standing on the shoulders of giants”—a giant such as Professor Seah.*

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