The Future of Interventional Endoscopy

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It's tough to make predictions, especially about the future
Yogi Berra

Take-Home Points:

- The field of GI endoscopy will continue to evolve but progress is expected to be more incremental and less revolutionary
- The higher complexity of new endoscopic interventions, and the high capital expenditures for some new technologies will drive the development of advanced interventional endoscopy units at select referral centers
- Endoscopic submucosal dissection (ESD), peroral endoscopic myotomy (POEM) procedures for achalasia, bariatric endoscopy techniques, EUS-guided gallbladder drainage and anastomoses, and full-thickness resection of polyps and subepithelial tumors are examples of new interventions that provide tangible benefits, but often to only a small subgroup of patients
- Non-invasive colorectal cancer screening tests and "optical biopsy" technologies are likely to eventually decrease the number of colonoscopies and biopsies being performed by gastroenterologists
- In the U.S., high provider costs, significant provider shortages and the development of easier-to-maneuver colonoscopes may result in an increase in the number of endoscopies performed by non-physicians

The Past

Since the development of the first fully flexible endoscopes in the late 1950s, the field of gastrointestinal endoscopy has evolved at a rapid pace. Here are a few of the revolutionary milestones in procedure development over the last 60 years [1]:

- **1958** Upper endoscopy (Hirschowitz)
- **1963** Flexible sigmoidoscopy (Overholt)
- **1969** Colonoscopy (Overholt, Wolff, Shinya, and others)
- **1974** ERCP/sphincterotomy (Kawai, Classen)
- **1980** Endoscopic ultrasound
- **2000** Capsule endoscopy
- **2001** Balloon enteroscopy (Yamamoto)

There has been a parallel development of accessory devices and techniques that have allowed us to perform a number of interventions to include polypectomy (Wolfff & Shinya, 1973), biliary

stenting (Soehendra, 1975), stricture dilation, hemostasis, fine needle aspiration and drainage of fluid collections, Barrett's ablation, and many more.

Imaging capabilities have also advanced with the two biggest quantum leaps represented by the adoption of fiberoptics in the 1950s and video chips in 1984, the latter effectively untethering the endoscopist's eye from the endoscope and allowing others to observe live images of endoscopic exams on monitors. Image resolution continues to be improved and new technologies such as narrow-band imaging, endo-microscopy, high frequency ultrasonography, optical coherence tomography, etc. are being studied and suggested for adoption into everyday clinical practice.

Before trying to predict the future...

This presentation provides one endoscopist's subjective opinion as to where our field might be heading, and it will provide a small potpourri of evolving trends in interventional endoscopy. Before doing so, it is worth emphasizing the well-recognized fact that "predicting the future is easy... getting it right is the hard part".

For your enjoyment, here is a short list of some "massive fail"-predictions related to the future of technology and music. A more extensive list can be found here [2]:

- **1876** "This 'telephone' has too many shortcomings to be seriously considered as a means of communication." - William Orton, President of Western Union
- **1903** "The horse is here to stay but the automobile is only a novelty - a fad." - President of the Michigan Savings Bank advising Henry Ford's lawyer, Horace Rackham, not to invest in the Ford Motor Company.
- **1921** [about radio] "The wireless music box has no imaginable commercial value. Who would pay for a message sent to no one in particular?"
- **1946** "Television won't be able to hold on to any market it captures after the first six months. People will soon get tired of staring at a plywood box every night." - Darryl Zanuck, 20th Century Fox.
- **1962** "Guitar groups are on their way out, Mr. Epstein." - Dick Rowe of Decca Music to the manager of the Beatles when turning down the 'Fab Four' for a record contract.
- **1966** "Remote shopping, while entirely feasible, will flop." - Time Magazine.
- **1995** "I predict that Internet will soon go spectacularly supernova and in 1996 catastrophically collapse." Robert Metcalfe, founder of 3Com.
- **2005** "There is just not that many videos I want to watch." - Steve Chen, CTO and co-founder of YouTube expressing concerns about his company's long-term viability.
- **2006** "Everyone's always asking me when Apple will come out with a cell phone. My answer is, 'probably never'." - David Pogue, The New York Times.

And we have certainly had our own share of incorrect predictions in GI endoscopy, to include the tsunami that was supposed to hit us with new techniques for endoscopic anti-reflux

therapies, natural orifice transluminal endoscopic surgery (NOTES), injectable therapies for cancers, and others. Few of the anticipated advances touted by a well-known innovator in our field in an editorial in the early 2000s have materialized [3]. This has not prevented that same innovator from providing an updated list of predictions in a more recent article [4].

For those interested in the general topic of predicting the future, be it in the tech sector, or in politics, or even the weather, here are a couple of great reads for a rainy day:

a. Philip Tetlock and Dan Gardner: "Superforecasting: The Art and Science of Prediction" [5] - Because expertise allows pundits to construct plausible explanations for past events, they have too much confidence about their ability to predict future events.

b. Nassim Taleb: "Black Swan: The Impact of the Highly Improbable" [6] - A black swan is a highly improbable event with three principal characteristics: It is unpredictable, it carries a massive impact, and, after the fact, we concoct an explanation that makes it appear less random, and more predictable, than it was.

Recent Developments, Current Trends and the Near Future

When looking at GI endoscopy, the pace of innovation appears to be slowing as our field has matured. Advances still occur at a decent pace, but most of them are happening in an incremental fashion and not as "quantum leaps".

Areas that appear ripe for further innovation relate to those aspects of our work where current endoscopic techniques are either extremely cumbersome, or very costly, or they remain relatively ineffective. Here are some examples:

Small bowel enteroscopy - examination of the entire small bowel with a conventional endoscope remains extremely cumbersome. Single or double balloon enteroscopy may allow for complete small bowel inspection, but only after hours of struggling. Efforts are underway to develop self-propelled devices and pilot studies of the "Spirus" enteroscope reported early successes with complete enteroscopies achieved in an anterograde fashion after less than 30 minutes of examination time [7]. Bowel trauma from the motorized spiral device has been a significant obstacle and has slowed commercialization of this device.

Endoscopic submucosal dissection (ESD) - ESD involves expanding the submucosal layer of the GI tract via injection with a high-viscosity solution and subsequently entering this expanded layer with the endoscope to perform a very controlled dissection of the submucosa with the use of dedicated needle-knife devices. Originally developed in Japan (because of the high incidence of early gastric cancers in Asian countries), these techniques are increasingly being adopted in Western countries and applied to resect large polyps and early cancers from esophagus, stomach and colon, and for removal of select subepithelial tumors (e.g. carcinoid tumors, some gastrointestinal stromal tumors, Schwannomas) [8]. This technique requires specialized equipment and considerable training and expertise. Depending on the location and

size of the resection targets, procedures may take several hours. At least in the U.S., ESD is poorly reimbursed (if it is reimbursed at all). For all of these reasons adoption of ESD has occurred at a very slow rate and the technique is currently available at only a few select centers (including in Vancouver, BC).

Per-Oral Endoscopic Myotomy (POEM) - a variation on ESD techniques, POEM procedures are increasingly being used to perform myotomy of the lower esophageal sphincter in a minimally invasive fashion in patients with achalasia. The technique has been well studied and in experienced hands is very effective with an acceptable risk profile [9]. Just as with ESD, training takes a long time and specialized equipment is needed. In centers with POEM expertise, the intervention is replacing open Heller myotomies as the initial surgical intervention for achalasia.

Endoscopic Full-Thickness Resection (EFTR) - While conventional polypectomy techniques, EMR, and ESD are useful techniques for the removal of polyps and other lesions, they can be cumbersome to apply and they are generally restricted to superficial layers of the GI wall. Devices are now becoming available to perform EFTR of the gastrointestinal wall in a single step procedure [10]. While several prototype devices are being developed and studied, the only FDA approved device in the U.S. is the Ovesco EFTR device. It consists of a large circular clip with a grasping forceps that allows a lesion to be pulled into the cap thereby creating a full-thickness duplication of the intestinal wall. The over-the-scope clip is then deployed and the tissue above the clip is resected with a snare that is integrated in the device. This device has been used to perform full thickness resections in esophagus, stomach, small and large intestine. Targets have included polyps, early cancers, and submucosal tumors. Some of the current limitations have to do with the difficulties of maneuvering the endoscope with the EFTR device attached, the more limited field of view, and the diameter of the cap/clip assembly limiting the size of the resection target. Further improvements of endoscopic clipping and stapling devices may eventually allow for simple, quick and complete resection of a defined area of the intestinal wall.

Lumen-apposing metal stents (LAMS) and related applications - Endoscopic drainage of pancreatic pseudocysts was first described in the mid 1980s and since the early 1990s is often done under EUS guidance. Initially, the accessories needed for puncture and drainage of the pseudocyst were "rigged" from other biliary procedures, with small caliber double pigtail plastic stents commonly used to drain the fluid collection. Over the past decade, a new type of self-expandable metal stent has been developed, initially by the company Xlumena which subsequently was bought by Boston Scientific. This "Axios" stent attempts to overcome the limitations of prior endoscopic accessories with a removable, fully covered, nitinol, braided stent deployed via a dedicated catheter which allows cautery-enhanced cyst puncture. A "dumbbell" configuration with two large flanges aims to avoid stent migration and the large inner diameter of the stent (10mm or 15mm) even allows access of the fluid collection with a standard upper endoscope [11]. Several large case series now exist documenting the benefits of this stent for pseudocyst drainage, and several centers have begun reporting the use of the Axios stent for EUS-guided gallbladder drainage, and even for the EUS-guided creation of gastro-jejunal anastomoses as seen on the cover of the May 2018 issue of *Gastrointestinal Endoscopy*.

Endoscopic treatment of obesity - The obesity epidemic continues to sweep the world. In Canada, more than 25% of adults, or approximately 7 million people, are obese (defined by a BMI of >30 kg/m^2). Numerous comorbidities have been linked to obesity, including diabetes, cardiovascular and respiratory diseases, cancer, etc), and attributable costs have been estimated to be as high as 20-25% of all health expenditures. While management requires a multi-disciplinary approach, obesity surgery, while effective, is utilized by <1% of 'eligible' patients [12]. Endoscopic bariatric therapies may be more appealing to some patients, may serve as a bridge to bariatric, orthopedic or transplant surgeries, or might work in otherwise poor operative candidates.

In the U.S., there are currently 4 FDA-approved devices [12]: they include three intragastric balloons and an aspiration device. An endoscopic suturing device with approval for the general indication of tissue apposition is being used for endoscopic sleeve gastroplasty. At present, none of these interventions are being reimbursed by major insurers in the U.S.

Of the intragastric balloons, the "Orbera" device has the most data. Studies have shown a modest average Excess Weight Loss (EWL) of 25% with average Total Body Weight Loss (TBWL) of 11%. Numerous other space-occupying devices are currently being studied. The "Aspire" aspiration device essentially consists of a 26FR PEG which an aspiration pump and reservoir used to remove gastric contents 20min after each meal. In individuals who continue with the device, EWL of 30-50% has been documented. Using the Apollo Endosurgery "Overstitch" suturing device, an endoscopic sleeve gastroplasty technique has been developed, in essence constricting the stomach internally with endoscopically placed sutures. Early trials suggest an EWL of 30-50% with TBWL of 15-20%. A host of other devices are currently being developed, including gadgets for suturing, stenting (and thus internally bypassing the absorptive areas of duodenum), magnets to create intestinal bypass anatomy, stretching devices to induce satiety, and several others [12]. Whether any of these devices and techniques will prove effective, safe, and durable remains to be determined.

Other Things On The Horizon

Clips - Current hemoclips are not optimally constructed. They do not allow the application of high traction forces and are therefore not ideal for the approximation of fibrotic edges or large defects. There is no "multi-clip" applicator, and the currently available clips are expensive. Several companies are in the process of developing new types of clips to address these shortfalls.

Making colon polyps jump out at you - Colon polyps are easily identified on a background of melanosis coli because the neoplastic tissue does not take up the pigment and thus stands out as a whitish lesion on a brown background. Efforts are underway to create a similar contrast in patients without melanosis, for example, with the use of an ingestible pill for chromoendoscopy. Other research is focusing on the use of artificial intelligence to automatize the detection of colon lesions.

Automated colonoscopes - An Israel based company continues to work on a partially self-propelled colonoscope [13] which could find its way to the cecum with minimal steering by a (non-physician) operator. The endoscope also features a 360-degree true circular optics allowing for complete visualization of the entire colonic circumference upon withdrawal. Statistically, fewer than half of all screening colonoscopies yield a clinically relevant polyp. One could therefore envision several such screening exams being performed in parallel by non-physician providers with a physician endoscopist standing by to perform polyp removal when necessary. It is worth noting that this semi-self propelled endoscope, as well as endoscopes from other companies, are fully disposable and meant for one time use. While this has few, if any, widespread applications at present, the issue of endoscope-transmitted infections is worth following very closely as further reports of significant reprocessing lapses and/or transmission of potentially deadly organisms may quickly change the interest in these disposable devices, and the regulatory requirements for scope reprocessing.

More than anything else... - More than anything discussed so far, it seems likely that our routine workdays as GI endoscopists will be affected more by any disruptive innovations related to the detection and management of colon polyps and colorectal cancers. This presentation will conclude with a few remarks on "optical biopsies", "resect and discard" techniques for small colon polyps, and new serologic tests and biomarkers such as the ones recently reported [14]. These blood tests may eventually enable accurate non-invasive identification of early cancers and polyps, as well as risk stratifications of patients, and thus lead to a paradigm shift in colorectal cancer screening.

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