

# ADVANCES IN ENDOSCOPY

Current Developments in Diagnostic and Therapeutic Endoscopy

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## Current Status of Natural Orifice Transluminal Endoscopic Surgery



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### G&H How did the idea of natural orifice transluminal endoscopic surgery come about?

**MK** There were a number of similar-thinking minimally invasive surgeons and, so to speak, maximally invasive gastroenterologists who shared a desire to expand the continuum that occurred with the change from laparotomy to laparoscopy. This change basically eliminated the large scar from the long incision, replacing it with smaller scars from a few small incisions. The question that followed was how could scars be completely avoided. The answer to that was to use a natural orifice. There are multiple different examples of surgery being performed through a natural orifice. One example is gynecologic surgery that occurs transvaginally; oral surgery and some transnasal surgeries are other examples. So, the thought was, why not expand that into the abdomen and potentially the chest. There were good suggestions that if one could decrease pain, improve the recovery, decrease analgesics, and decrease hospital stay or even avoid hospital stay, the likely result would be cost-savings and patient acceptance. Another part of the goal, which this group of physicians was thinking about, was the ability to have organ-sparing surgeries or procedures. Instead of resecting the organ to take the pathology, the surgeon could either remove the pathology and leave the organ, or correct the pathology, depending upon exactly what the issue was.

### G&H What were the opportunities and challenges of natural orifice transluminal endoscopic surgery?

**MK** For innovators, challenges are an opportunity. I will say that the barriers to adoption and expansion of prac-

tice are multiple but not insurmountable. One of the key issues is to think about whether we—meaning physicians and those who are interested in minimally invasive procedures—are opening new avenues and new procedures as opposed to replicating procedures. A little bit of the challenge component is that much of the enthusiasm for natural orifice transluminal endoscopic surgery (NOTES) was spent trying to replicate procedures instead of creating new procedures, and new opportunities were not initially targeted. So, for many of us the opportunities and challenges are on the same coin, different sides.

We need devices to enable and empower us to be able to perform whatever procedure it is that we desire to do. The other challenges, which can be seen with a lot of innovation, are acceptance of the paradigm shift and going against accepted dogma. Those can be somewhat difficult to easily surmount. Then there are the unknowns, which I will not discuss here in detail. The key dogma issues became somewhat difficult because of the need to have devices that require a regulatory pathway and a reimbursement pathway. It is also important to have procedures that provide a clinical pathway and pay-or approval, meaning Centers for Medicare and Medicaid Services, insurance companies, and hospitals or ambulatory centers where these procedures are performed need to be able to justify the expenses.

The biggest hurdles that we have faced with NOTES—beyond the question, *what is the killer app?*—have been the tools and the US Food and Drug Administration (FDA) regulatory pathways to approve the tools. A lot of the devices that were being used were intended for intraluminal use and were then being used to go extraluminally, a purpose for which the FDA wanted data that were difficult to generate. Reimbursement

pathways are difficult, as there is a significant discrepancy when one is trying to take an established procedure and have it performed by a method that may not be written into the reimbursement coding. That has led to many of the NOTES procedures and even some of the current intraluminal procedures being uncovered or covered by incorporation into under-reimbursed coding groups.

### G&H What has limited the growth and adoption of NOTES in gastroenterology, and what are the offshoots of the NOTES experience?

**MK** Part of what has limited growth and adoption is the tools. Part of it is the reimbursement. But having the tools and reimbursement is predicated also on having outcome studies showing safety, efficacy, and long-term outcomes, and outcome studies are not necessarily easy to run and are very difficult to execute as investigator-initiated trials. I would say that device companies must be able to develop tools and perform, run, or fund the studies necessary to show the safety and efficacy of the device as well as the long-term outcome of the procedure. This process is a long runway with potentially relatively small return on investment (ROI). For this reason, for many companies (and some of the venture capital funds even), as soon as they hear *NOTES* or the phrase *natural orifice surgery*, their reaction is to back away. That response is unfortunate but has not really stymied investigator-initiated innovation.

I mentioned, *what is the killer app?* One of the things that we did through the Natural Orifice Surgery Consortium for Assessment and Research (NOSCAR) was rather novel in that as a society group we obtained independent funding from multiple different companies to fund a study of NOTES. With that, we picked transorifice cholecystectomy, which was 1 of the 2 early targets—the other target being appendectomy. We developed a protocol by a consensus amongst the few groups that were performing NOTES, and we successfully proved the hypothesis. Cholecystectomy via NOTES could be done, it could be done safely, patients liked it, and the complication rate was essentially nil. The problem was that the devices were not being fully marketed or made available from the device companies and health systems did not see an ROI, and this led to adoption issues as there were not clear reimbursement and revenue pathways. In addition, it was unknown whether there were enough operators who were able to understand the anatomy and deal with potential altered anatomy and complications.

I would say the beauty of NOSCAR is the ability to pivot. Dr Jay Pasricha, amongst some of the thought leaders, looked at peroral endoscopic myotomy (POEM) as a natural outgrowth. POEM technically is in the wall of the esophagus and the stomach and not extraluminal,

meaning completely through the wall of the gastrointestinal (GI) tract into the chest or abdominal cavity. The NOSCAR experience has decreased the fear of accidentally entering those spaces with the knowledge that one can close openings into those spaces and violate what was surgical dogma with no significant concern or consequences to the patient when appropriately handled. So, the beauty of NOSCAR has been not only the ability to pivot but also to expand the real horizon of what can be done transorally and transrectally, and POEM is a beautiful example. Other clear examples are the procedures of third-space endoscopy, including resection of tumors, for submucosal lesions of the GI tract as well as the ability to utilize other devices, including endoprosthesis, to perform various anastomoses and to consider using the suturing devices for bariatric surgery and other potential applications. So, I do think the NOTES experience was ground-breaking and absolutely has led to procedures seen every day in practice now.

### G&H How has the role of NOTES evolved since its inception almost 2 decades ago?

**MK** I think it is critical to appreciate that medicine is a moving target. Pharmaceuticals change. Disease therapies change or are discovered. With that, our diagnostic strategies need to change as well as our approach to therapeutic interventions and diagnostic interventions. Endoscopic ultrasound (EUS), for example, was developed pre-NOTES. At Indiana University in the early phases of this procedure, when we were performing EUS-guided biopsies of mediastinal nodes and the pancreas, we were considered heretics for violating the gastric, esophageal, and duodenal walls. As providers gained more experience performing EUS and began using companion therapeutics, they have greatly helped patients. I think NOTES has played a role in accelerating the adoption of EUS therapeutics with enterostomies.

### G&H What have studies revealed about the clinical application of NOTES?

**MK** The studies looking at actual NOTES, for example, with cholecystectomy as a target, revealed that NOTES is clearly able to be performed. So, the proof of the hypothesis is there. The issue is whether the devices are there for widespread adoption and whether there are enough trained operators for that. The answer unfortunately is it did not disseminate widely. There were clear difficulties with reimbursement.

### G&H Does current endoscope technology enable transluminal endoscopic procedures?

**MK** Again, morphing natural orifice surgery into third-space endoscopy and intraluminal surgery, the endoscopes do enable it, but additional changes to devices and ancillary devices are critical. One major area where change is needed is visualization and maintenance of insufflation. The operator must be able to maintain visualization of the operative field. Intraluminally, when using water or insufflation gas, visualization is easy. When we violate the wall of the esophagus or stomach or the small bowel or colon to enter the peritoneum, there is no longer an ability to maintain that easy visualization for access. Some overtubes and other devices have been created not only for endoluminal surgery but also for extraluminal procedures. There are some regulatory issues with the extraluminal devices that have limited corporate investment in those spaces. However, there has been real progress in devices for closure (eg, endoscopic suturing and various types of suturing). Different closure devices, large clips, staples, and other devices are available and have allowed for the performance of transluminal procedures when necessary as well as the safe handling of intraluminal procedures when accidental penetration or perforation occurs into the extraluminal space. Although there has been improvement in the devices, there are always unmet needs that everyone wants addressed.

### **G&H** Does current endoscopy training include aspects that are needed if one wanted to perform transluminal endoscopic procedures?

**MK** Most programs at this point are not, per se, looking at targets that are extraluminal organs for their advanced training programs. However, there is no question that endoscopic surgery is occurring. For example, endoscopic submucosal dissection, various anastomoses, gastrojejunostomy applications, and various bariatric procedures (including endoscopic sleeves) are available and taught within the advanced training programs both surgical and GI. The current endoscopy training will enable the future generation to move quickly into transluminal endoscopic procedures and to be comfortable when performing anastomoses or connections between lumens through which one enters the extraluminal space.

### **G&H** How does NOTES fit in GI endoscopy practice today?

**MK** I would say that NOTES in the traditional use of transluminal endoscopic surgery is not in any of the everyday practices. However, third-space endoscopy or intraluminal and intramural surgical and endoscopic procedures are performed routinely at this point. Again, NOSC

AR led to a mindset revolution and helped push the paradigms to allow for what is being seen now, which is advanced organ-sparing procedures.

### **G&H** How can the experience with NOTES inform future development of GI endoscopic procedures?

**MK** I think the entire NOTES experience has led us to recognize that it probably is best not to replicate procedures that already can be performed with a high degree of efficacy and safety but to look at procedures that are not able to be easily reproduced or have potential significant morbidity for patients. The experience with POEM has been a huge paradigm shift in the management of patients with achalasia and patients with other motor disorders of the esophagus. Overall, what the NOTES experience has done to inform future development is to define the need for better devices to be able to resect lesions, perform anastomoses, and achieve secure closure. In addition, it has led to some interesting thought and device development in fusion technologies, where one can use image-guided and computer-aided procedures. The operator can fuse imaging from radiographic studies along with, for example, EUS or non-white light visualization modalities, to be able to look through the wall and into other organs or spaces and be able to perform procedures that otherwise would be extraordinarily difficult by other measures.

### **Disclosures**

*Dr Kochman is a consultant for Olympus, Dark Canyon Labs, Boston Scientific Corporation, Virgo Systems, and ACI (Adjudication Committee) and has consulted for Castle Biosciences. He has stock in Dark Canyon Labs, Virgo Systems, Endosound, and Endiatx, from which he also receives share-based payment, and has equity in AGA-Varia and Varia.*

### **Suggested Reading**

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