



## Natural orifice transluminal endoscopic surgery: Where are we going?

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Received: May 11, 2010 Revised: June 8, 2010

Accepted: June 15, 2010

Published online: September 21, 2010

### Abstract

The foundation for natural orifice transluminal endoscopic surgery (NOTES) is to access the peritoneal and other body cavities through the wall of the alimentary tract *via* natural orifices, with the goal of performing procedures within the peritoneum and other cavities, without the need to make incisions in the abdominal wall. We have made great progress in the field of NOTES since the publication of the White Paper in 2006. There are still major fundamental goals as outlined by the Society of American Gastrointestinal and Endoscopic Surgeons/American Society for Gastrointestinal Endoscopy joint committee that need to be evaluated and answered before NOTES is ready for widespread clinical use. These include prevention of infection, instrument development, creation of a multitasking platform, and the ability to recognize and treat intraperitoneal complications such as hemorrhage and other physiological adverse events. In response to this need, recent abstracts and papers have focused on the management of intraoperative complications. The next phase is to focus on controlled prospective multicenter clinical trials that compare defined NOTES procedure to standard laparoscopy. The goal is to produce reliable and convincing data for the United States Food and Drug Administration, insurance companies, the physician community and the general public. At the present time, we still

have many important milestones that still need to be met. Most investigators agree that a hybrid technique and not a pure NOTES practice should be advocated until devices can meet the current and new challenges in this field.

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**Key words:** Natural orifice transluminal endoscopic surgery; Endoscopic surgery; Gastrointestinal surgery; Laparoscopy

**Peer reviewers:** Eric S Hungness, MD, FACS, Assistant Professor, Division of Gastrointestinal and Oncologic Surgery, Northwestern University Feinberg School of Medicine, 676 N. St. Clair St., Suite 650, Chicago, IL 60611-2908, United States; Hoon Jai Chun, MD, PhD, AGAF, Professor, Department of Internal Medicine, Institute of Digestive Disease and Nutrition, Korea University College of Medicine, 126-1, Anam-dong 5-ga, Seongbuk-gu, Seoul 136-705, South Korea

Whang SH, Thaler K. Natural orifice transluminal endoscopic surgery: Where are we going? *World J Gastroenterol* 2010; 16(35): 4371-4373 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v16/i35/4371.htm> DOI: <http://dx.doi.org/10.3748/wjg.v16.i35.4371>

### INTRODUCTION

"Surgery, gaining much from the general advance of knowledge, will be rendered both knifeless and bloodless." (John Hunter, 1762). Dr. John Hunter, an accomplished anatomist and surgeon during the 18th century was many years ahead in his thinking. The foundation for natural orifice transluminal endoscopic surgery (NOTES) is to access the peritoneal and other body cavities through the wall of the alimentary tract *via* natural orifices. This allows one to perform procedures within the peritoneum and other cavities, without the need to make any incisions in the abdominal wall. The concept has generated much excitement and controversy over the past decade and has

revolutionized our thinking about what is possible, from simple peritoneoscopy to resection of solid organs.

## WHERE HAVE WE BEEN

In 2005, members of the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) and the American Society for Gastrointestinal Endoscopy (ASGE) met to form the Natural Orifice Consortium for Assessment and Research (NOSCAR). This led to the production of the White Paper on NOTES in 2006, which laid down the fundamental objectives and goals that need to be addressed before NOTES will be ready for clinical application<sup>[1]</sup>. Since then, it has become clear that the field of NOTES research would create quite a stir in the gastroenterology and surgical worlds. This is reflected by the number of abstracts devoted to NOTES at the annual Digestive Disease Week (DDW), which has demonstrated a 20-fold increase from 2004 to 2007. There were 55 NOTES-related abstracts presented at DDW/Society for Surgery of the Alimentary Tract in 2009, which was the highest number reported over the last 6 years<sup>[2]</sup>. This indicates that numerous investigators have performed fundamental and noteworthy advances in a short period of time.

There have been some 60 human NOTES cases reported in the United States; the majority in the context of transgastric and transvaginal appendectomy and cholecystectomy<sup>[3]</sup>, all approved by review boards to be performed under research conditions. In South America, this number has already reached the hundreds. The Brazilian NOTES Registry from 2008 highlights their experience with 116 institutional-review-board-approved procedures<sup>[4]</sup>. The majority of the procedures (94) were transgastric and transvaginal cholecystectomies. Other procedures reported in the database are transvaginal appendectomy, nephrectomy, and gynecological procedures. The bulk of reported human NOTES procedures have been limited to hybrid, laparoscopic-assisted approaches in the setting of case reports and phase I studies. Most of these studies have demonstrated safety and feasibility with variable completion rates. The major criticism to current NOTES research is the heavy emphasis on "proof of concept" without addressing management of potential complications and providing solid data on its benefits compared to laparoscopic surgery. A recent study by a German group completed a retrospective case-controlled study which compared transvaginal cholecystectomy (47 patients) to conventional laparoscopic cholecystectomy (46 patients)<sup>[5]</sup>. Hensel *et al*<sup>[5]</sup> reported similar complication rates but the NOTES group had a lower need for postoperative analgesia, faster recovery, and better cosmetic results compared to their laparoscopic counterparts. Although this was a retrospective study, the group aimed to evaluate the presumed benefits of NOTES compared to conventional laparoscopic procedures through a comparative study. These results are very exciting but will need to be confirmed and reproduced through prospective clinical trials. In addition, a recent study by Federlein *et al*<sup>[6]</sup> has combined the use of NOTES with traditional laparoscopy by performing video-assisted

transvaginal cholecystectomy with rigid instruments<sup>[6]</sup>. They have determined that transvaginal cholecystectomy is safe and easy to learn but the potential complications are different from those of standard laparoscopy. The authors acknowledge that future studies including randomized trials need to be done to delineate the exact advantages of this procedure over standard laparoscopy.

## FUTURE GOALS

We have made great progress in the field of NOTES since the inception of the White Paper. It is fair to state that major goals outlined by the SAGES/ASGE joint committee, such as safe access to the peritoneal cavity and closure techniques, have been sufficiently addressed. However, there are many fundamental challenges as outlined in the White Paper that need to be evaluated and answered before NOTES is ready for widespread clinical use. These include prevention of infection, instrument development, creation of a multitasking platform, and the ability to recognize and treat intraperitoneal complications such as hemorrhage and other physiological adverse events<sup>[1]</sup>. In response to this need, recent abstracts and papers have focused on the management of intraoperative complications. Investigators have offered novel strategies and techniques to manage complications such as the use of a flexible bipolar forceps to obtain hemostasis in a quick and reliable fashion<sup>[7]</sup>. Furthermore, additional studies need to be performed to address the role of NOTES in the setting of intraperitoneal contamination and infection, ensuring the maintenance of spatial orientation, and assessing the safest method of specimen retrieval. Advanced flexible platforms and endoscopic suturing devices still need to be developed, which is heavily dependent on industry collaboration. Training has been assessed recently in this novel area of minimally invasive approaches, with the first abstract presented at DDW on the development of a skills assessment model for NOTES by Vassiliou *et al*<sup>[8]</sup>. Clearly, this is an exciting time and must be balanced by healthy skepticism and caution to ensure patient safety and maximum benefit. These efforts should be undertaken by experienced multidisciplinary teams with the interest of patients and societal gain at heart.

Our group has recently completed our experience with transvaginal flexible peritoneoscopy with laparoscopic assistance in women with chronic pelvic pain<sup>[9]</sup>. A complete diagnostic peritoneoscopy was performed in five women with a mean intra-abdominal insufflation pressure of 7 mmHg to visualize pelvic and abdominal structures, with minimal postoperative pain and high cosmetic satisfaction. However, we discovered that the flexible biopsy forceps was not sharp enough alone to achieve a reliable peritoneal biopsy and required laparoscopic assistance in three of four patients. Other therapeutic interventions that were undertaken included appendectomy, simply ovarian cyst drainage, and lysis of adhesions. We concluded that transvaginal peritoneoscopy might provide advantages over standard laparoscopy specifically as it applies to visualization, pelvic accessibility, and postoperative outcome. How-

ever, we recognize the need for improved instrumentation to forgo laparoscopic assistance. Potential advantages such as minimal anesthesia requirements, shorter recovery time, and integration into an ambulatory procedure can only be implemented once we have the means to answer these looming questions with solid evidence.

## CONCLUSION

Is NOTES ready for prime time? At present, the answer is no because we still have many important milestones that need to be met. What we have learned from past research is that the human NOTES experience is feasible but limited by current instruments and techniques. Many procedures have been tested in animal models but very few have confirmed their safety and feasibility in humans. We do know that in the current state, longer operative times and a steep learning curve are part of the package when it comes to NOTES procedures. Most investigators agree that a hybrid technique and not a pure NOTES practice should be advocated until devices can meet the current and new challenges in this progressive field. As we have learned from the introduction of past new innovative surgical techniques, such a feat is naturally met with heavy scrutiny. Such undertakings require a large amount of effort, time, and cost to be taken on by investigators, collaborating industry and society. We believe it will be paramount to find the complementary value of NOTES to existent minimally invasive and endoscopic procedures as we continue to make advances in this field.

The first NOSCART research grants were awarded in 2006, and since then, four rounds of NOTES funding has been completed by NOSCART for a total of 63 grants<sup>[10]</sup>. These have mainly been preclinical studies and some human phase I studies. The next phase is to focus on controlled prospective multicenter clinical trials to compare defined NOTES procedure to standard laparoscopy. The goal is to produce reliable and convincing data for the United States Food and Drug Administration, insurance companies, the physician community, and the general public. We are at a crucial crossroads to develop a systematic

and strategic plan to address fundamental complexities if NOTES is to move forward. Only then will we be able to take the next important and final step and implement NOTES into clinical practice.

As we make strides towards Hunter J's prophecy and apply it to the current state of minimally invasive surgery, we must proceed with healthy optimism balanced with sound caution.

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