



World Journal of Gastrointestinal Surgery

World J Gastrointest Surg 2010 June 27; 2(6): 177-230

A peer-reviewed, online, open-access journal of gastrointestinal surgery





Editorial Board

2009-2013

The *World Journal of Gastrointestinal Surgery* Editorial Board consists of 336 members, representing a team of worldwide experts in gastrointestinal surgery research. They are from 35 countries, including Australia (6), Austria (2), Belgium (6), Brazil (9), Bulgaria (2), Canada (8), China (30), Denmark (1), Finland (1), France (10), Germany (22), Greece (6), India (10), Ireland (3), Israel (3), Italy (48), Jamaica (1), Japan (47), Malaysia (1), Netherlands (9), Pakistan (1), Poland (1), Portugal (1), Russia (1), Singapore (6), Serbia (1), South Korea (9), Spain (5), Sweden (2), Switzerland (4), Thailand (2), Tunisia (1), Turkey (8), United Kingdom (7), and United State (62).

PRESIDENT AND EDITOR-IN-CHIEF

Lian-Sheng Ma, *Beijing*

STRATEGY ASSOCIATE EDITORS-IN-CHIEF

Elijah Dixon, *Calgary*
Antonello Forgione, *Milan*
Tobias Keck, *Freiburg*
Tsuyoshi Konishi, *Tokyo*
Natale Di Martino, *Naples*

GUEST EDITORIAL BOARD MEMBERS

Chao-Long Chen, *Kaohsiung*
Chien-Hung Chen, *Taipei*
Jong-Shiaw Jin, *Taipei*
Chen-Guo Ker, *Kaohsiung*
King-Teh Lee, *Kaohsiung*
Wei-Jei Lee, *Taoyuan*
Shiu-Ru Lin, *Kaohsiung*
Wan-Yu Lin, *Taichung*
Yan-Shen Shan, *Tainan*
Jaw-Yuan Wang, *Kaohsiung*
Li-Wha Wu, *Tainan*
Fang Hsin-Yuan, *Taichung*

MEMBERS OF THE EDITORIAL BOARD



Australia

Ned Abraham, *Coffs Harbour*
Christopher Christophi, *Melbourne*
M Michael, *Victoria*
David Lawson Morris, *Kogarah*
Jas Singh Samra, *St Leonards*
Matthias W Wichmann, *Millicent*



Austria

Harald R Rosen, *Vienna*
Franz Sellner, *Vienna*



Belgium

Giovanni Dapri, *Brussels*
Jean-François Gigot, *Brussels*
Lerut Jan Paul Marthe, *Brussels*
Gregory Peter Sergeant, *Leuven*
Hans Van Vlierberghe, *Gent*
Jean-Louis Vincent, *Brussels*



Brazil

Jose E Aguilar-Nascimento, *Cuiaba*
MR Álvares-da-Silva, *Porto Alegre*
Fernando M Biscione, *Minas Gerais*
Julio Coelho, *Curitiba*
Marcel A Machado, *São Paulo*
MAF Ribeiro Jr, *Santana de Parnaíba*
José Sebastião dos Santos, *São Paulo*
Marcus VM Valadão, *Rio de Janeiro*
Ricardo Zorron, *Rio de Janeiro*



Bulgaria

Krassimir D Ivanov, *Varna*
Belev Nikolai, *Plovdiv*



Canada

Runjan Chetty, *Toronto*

Laura A Dawson, *Toronto*
Mahmoud A Khalifa, *Toronto*
Peter Kim, *Toronto*
Peter Metrakos, *Quebec*
Reda S Saad, *Toronto*
Manuela Santos, *Montreal*



China

Yue-Zu Fan, *Shanghai*
Wen-Tao Fang, *Shanghai*
Yong-Song Guan, *Chengdu*
Shao-Liang Han, *Wenzhou*
Michael G Irwin, *Hong Kong*
Long Jiang, *Shanghai*
Wai Lun Law, *Hong Kong*
Ting-Bo Liang, *Hangzhou*
Quan-Da Liu, *Beijing*
Yu-Bin Liu, *Guangdong*
Ding Ma, *Wuhan*
Jian-Yang Ma, *Chengdu*
Kwan Man, *Hong Kong*
Tang Chung Ngai, *Hong Kong*
Yan-Ning Qian, *Nanjing*
Ai-Wen Wu, *Beijing*
Yin-Mo Yang, *Beijing*
Yun-Fei Yuan, *Guangzhou*



Denmark

Thue Bisgaard, *Lykkebæk*



Finland

Helena M Isoniemi, *Helsinki*



France

Chapel Alain, *Far*
 Mustapha Adham, *Lyon*
 Brice Gayet, *Paris*
 Jean-François Gillion, *Antony*
 D Heresbach, *Rennes Cedex*
 Romaric Loffroy, *Dijon Cedex*
 Jacques Marescaux, *Strasbourg Cedex*
 Yves Panis, *Clichy*
 Aurélie Plessier, *Clichy*
 Eric Savier, *Paris*



Germany

Vollmar Brigitte, *Rostock*
 Dieter C Broering, *Kiel*
 Hans G Beger, *Ulm*
 Ansgar M Chromik, *Bochum*
 Marc-H Dahlke, *Regensburg*
 Irene Esposito, *Neuherberg*
 Stefan Fichtner-Feigl, *Regensburg*
 Benedikt Josef Folz, *Bad Lippspringe*
 Helmut Friess, *München*
 Reinhart T Grundmann, *Burghausen*
 Bertram Illert, *Würzburg*
 Jakob R Izbicki, *Hamburg*
 Haier Jörg, *Münster*
 Jörg H Kleeff, *Munich*
 Axel Kleespies, *Munich*
 Uwe Klinge, *Aachen*
 Martin G Mack, *Frankfurt*
 Klaus Erik Mönkemüller, *Bottrop*
 Matthias Peiper, *Dusseldorf*
 Hubert Scheidbach, *Magdeburg*
 Joerg Theisen, *Munich*



Greece

Eelco de Bree, *Herakleion*
 Stavros J Gourgiotis, *Athens*
 Andreas Manouras, *Athens*
 Theodoros E Pavlidis, *Thessaloniki*
 George H Sakorafas, *Athens*
 Vassilios E Smyrniotis, *Athens*



India

Anil K Agarwal, *New Delhi*
 Shams-ul-Bari, *Kashmir*
 Somprakas Basu, *Varanasi*
 Pravin J Gupta, *Nagpur*
 Vinay Kumar Kapoor, *Lucknow*
 Chandra Kant Pandey, *Lucknow*
 Shailesh V Shrikhande, *Mumbai*
 Sadiq S Sikora, *Bangalore*
 Prod Rakesh K Tandon, *New Delhi*
 Imtiaz Ahmed Wani, *Srinagar*



Ireland

Kevin C P Conlon, *Dublin*

Prem Puri, *Dublin*
 Eamonn M Quigley, *Cork*



Israel

Tulchinsky Hagit, *Tel Aviv*
 Ariel Halevy, *Zerifin*
 Jesse Lachter, *Haifa*



Italy

Angelo Andriulli, *San Giovanni Rotondo*
 Giuseppe Aprile, *Udine*
 Gianni Biancofiore, *Pisa*
 Stefania Boccia, *Rome*
 Luigi Bonavina, *San Donato*
 Pier Andrea Borea, *Ferrara*
 Giovanni Cesana, *Milan*
 Stefano Crippa, *Verona*
 Giovanni D De Palma, *Napoli*
 Giovanni De Simone, *Napoli*
 Giuseppe Malleo, *Verona*
 Giorgio Ercolani, *Bologna*
 Carlo Feo, *Ferrara*
 Simone Ferrero, *Genova*
 Valenza Franco, *Milano*
 Leandro Gennari, *Rozzano*
 Felice Giuliant, *Roma*
 Salvatore Gruttadauria, *Palermo*
 Calogero Iacono, *Verona*
 Riccardo Lencioni, *Pisa*
 Dottor Fabrizio Luca, *Milan*
 Paolo Massucco, *Candiolo*
 Giorgio Di Matteo, *Roma*
 Giulio Melloni, *Milan*
 Manuela Merli, *Roma*
 Paolo Morgagni, *Forlì*
 Chiara Mussi, *Rozzano*
 Gabriella Nesi, *Florence*
 Angelo Nespoli, *Monza*
 Fabio Pacelli, *Rome*
 Corrado Pedrazzani, *Siena*
 Roberto Persiani, *Rome*
 Piero Portincasa, *Bari*
 Pasquale Petronella, *Napoli*
 Stefano Rauseri, *Varese*
 Carla Ida Ripamonti, *Milan*
 Antonio Russo, *Palermo*
 Giulio A Santoro, *Treviso*
 Stefano Scabini, *Genoa*
 Gianfranco Silecchia, *Roma*
 Guido AM Tiberio, *Brescia*
 Umberto Veronesi, *Milano*
 Bruno Vincenzi, *Rome*
 Marco Vivarelli, *Bologna*
 Alberto Zaniboni, *Brescia*
 Alessandro Zerbi, *Milan*



Jamaica

Joseph M Plummer, *Kingston*



Japan

Yasunori Akutsu, *Chiba*

Ryuichiro Doi, *Kyoto*
 Yosuke Fukunaga, *Sakai*
 Akira Furukawa, *Shiga*
 Shigeru Goto, *Oita*
 Kazuhiko Hayashi, *Tokyo*
 Naoki Hiki, *Tokyo*
 Takeyama Hiromitsu, *Nagoya*
 Tsujimoto Hironori, *Tokorozaawa*
 Tsukasa Hotta, *Wakayama*
 Yutaka Iida, *Gifu*
 Kazuaki Inoue, *Yokohama*
 Masashi Ishikawa, *Tokushima*
 Tatsuo Kanda, *Niigata*
 Tatsuyuki Kawano, *Tokyo*
 Keiji Koda, *Chiba*
 Hajime Kubo, *Kyoto*
 Iruru Maetani, *Tokyo*
 Yoshimasa Maniwa, *Kobe*
 Toru Mizuguchi, *Hokkaido*
 Zenichi Morise, *Toyoake*
 Yoshihiro Moriwaki, *Yokohama*
 Yoshihiro Moriya, *Tokyo*
 Satoru Motoyama, *Akita*
 Hiroaki Nagano, *Osaka*
 Masato Nagino, *Nagoya*
 Toshio Nakagohri, *Kashiwa*
 Kazuyuki Nakamura, *Yamaguchi*
 Shingo Noura, *Osaka*
 Kazuo Ohashi, *Tokyo*
 Yoichi Sakurai, *Toyoake*
 Hirozumi Sawai, *Nagoya*
 Masayuki Sho, *Nara*
 Yasuhiko Sugawara, *Tokyo*
 Hiroshi Takamori, *Kumamoto*
 Sonshin Takao, *Kagoshima*
 Kuniya Tanaka, *Yokohama*
 Masanori Tokunaga, *Shizuoka*
 Yasunobu Tsujinaka, *Kashiwa*
 Akira Tsunoda, *Kamogawa*
 Toshifumi Wakai, *Niigata*
 Jiro Watari, *Nishinomiya*
 Shinichi Yachida, *Kagawa*
 Yasushi Yamauchi, *Fukuoka*
 Hiroki Yamaue, *Wakayama*
 Yutaka Yonemura, *Osaka*



Malaysia

Way Seah Lee, *Kuala Lumpur*



Netherlands

Lee H Bouwman, *Hague*
 Wim A Buuman, *Maastricht*
 Robert Chamuleau, *Amsterdam*
 Miguel A Cuesta, *Amsterdam*
 Jeroen Heemskerk, *Roermond*
 Buis Carlijn Ineke, *Deventer*
 Wjhj Meijerink, *Amsterdam*
 Chj van Eijck, *Rotterdam*
 Alexander L Vahrmeijer, *Leiden*



Pakistan

Kamran Khalid, *Lahore*

**Poland**

Bogusław Machaliński, *Szczecin*

**Portugal**

Jorge Correia-Pinto, *Braga*

**Russia**

Grigory G Karmazanovsky, *Moscow*

**Singapore**

Brian KP Goh, *Singapore*
Salleh bin Ibrahim, *Singapore*
John M Luk, *Singapore*
Francis Seow-Choen, *Singapore*
Vishalkumar G Shelat, *Singapore*
Melissa Teo, *Singapore*

**Serbia**

Ivan Jovanovic, *Belgrade*

**South Korea**

Joon Koo Han, *Seoul*
Hyung-Ho Kim, *Seongnam*
Woo Ho Kim, *Seoul*
Sang Y Lee, *Gyeongangnam-do*
Woo Yong Lee, *Seoul*
Hyo K Lim, *Seoul*
Jae-Hyung Noh, *Seoul*
Sung Hoon Noh, *Seoul*
Hee Jung Wang, *Suwon*

**Spain**

Antonio M Lacy Fortuny, *Barcelona*
Laura L Garriga, *Barcelona*
Francisco José Vizoso, *Gijón*
David Parés, *Sant Boi de Llobregat*
Prieto Jesus, *Pamplona*

**Sweden**

Helgi Birgisson, *Uppsala*
Jörgen Rutegård, *Umeå*

**Switzerland**

Andrea Frilling, *Zürich*
Pascal Gervaz, *Genève*
Bucher Pascal, *Geneva*
Marc Pusztaszeri, *Carouge*

**Thailand**

Varut Lohsiriwat, *Bangkok*
Rungsun Rerknimitr, *Bangkok*

**Tunisia**

Nafaa Arfa, *Tunis*

**Turkey**

Ziya Anadol, *Ankara*
Unal Aydin, *Gaziantep*
Mehmet Fatih Can, *Ankara*
Gözde Kir, *Istanbul*
Adnan Narci, *Afyonkarahisar*
Ilgin Ozden, *Istanbul*
Mesut Abdulkrim Ünsal, *Trabzon*
Omer Yoldas, *Ordu*

**United Kingdom**

Graeme Alexander, *Cambridge*
Simon R Bramhall, *Birmingham*
Giuseppe Fusai, *London*
Najib Haboubi, *Manchester*
Gianpiero Gravante, *Leicester*
Aftab Alam Khan, *Kent*
Caroline S Verbeke, *Leeds*

**United States**

Eddie K Abdalla, *Houston*

Forse Robert Armour, *Omaha*
Samik K Bandyopadhyay, *Kolkata*
Marc D Basson, *Lansing*
James M Becker, *Boston*
Thomas D Boyer, *Tucson*
Michael E de Vera, *Pittsburgh*
Andrew J Duffy, *New Haven*
Kelli Bullard Dunn, *Buffalo*
Thomas Fabian, *New Haven*
P Marco Fisichella, *Maywood*
Raja M Flores, *New York*
Markus Frank, *Boston*
Niraj J Gusani, *Hershey*
Douglas W Hanto, *Boston*
John P Hoffman, *Philadelphia*
Scott A Hundahl, *California*
Michel Kahaleh, *Charlottesville*
David S Kauvar, *Maryland*
Mary M Kemeny, *New York*
Nancy E Kemeny, *New York*
Vijay P Khatri, *Sacramento*
Joseph Kim, *Duarte*
Andrew Klein, *Los Angeles*
Richard A Kozarek, *Seattle*
Robert A Kozol, *Farmington*
Sunil Krishnan, *Houston*
Atul Kumar, *New York*
Wei Li, *Seattle*
Keith D Lillemoe, *Indianapolis*
Henry T Lynch, *Omaha*
Paul Ellis Marik, *Philadelphia*
Robert C Miller, *Rochester*
Thomas J Miner, *Providence*
Ravi Murthy, *Houston*
Atsunori Nakao, *Pittsburgh*
Hirofumi Noguchi, *Dallas*
Jeffrey A Norton, *Stanford*
Timothy M Pawlik, *Baltimore*
Nicholas J Petrelli, *Newark*
Alessio Pigazzi, *Duarte*
James John Pomposelli, *Carlisle*
Mitchell C Posner, *Chicago*
Alexander S Rosemurgy, *Florida*
Ng Chaan S, *Houston*
Sukamal Saha, *Flint*
Reza F Saidi, *Boston*
Aaron R Sasson, *Omaha*
Christian M Schmidt, *Indianapolis*
Perry Shen, *Winston-Salem*
Ali A Siddiqui, *Dallas*
Frank A Sinicrope, *Rochester*
Thomas Earl Starzl, *Pittsburgh*
John H Stewart, *Winston-Salem*
Paul H Sugarbaker, *Washington*
Douglas S Tyler, *Durham*
Vic Velanovich, *Detroit*
Alan Wilkinson, *Los Angeles*
M Michael Wolfe, *Boston*
Christopher L Wolfgang, *Baltimore*
You-Min Wu, *Little Rock*
Zhi Zhong, *Charleston*

**EDITORIAL**

- 177 NOTES-Natural orifice transluminal endoscopic surgery: Why not?
Forgione A

TOPIC HIGHLIGHT

- 179 Natural orifice transluminal endoscopic surgery: The transvaginal route moving forward from cholecystectomy
Targarona EM, Maldonado EM, Marzol JA, Marinello F
- 187 Transgastric cholecystectomy: From the laboratory to clinical implementation
Dallemagne B, Perretta S, Allemann P, Donatelli G, Asakuma M, Mutter D, Marescaux J
- 193 Current experience and future directions of completely NOTES colorectal resection
Sylla P
- 199 Natural orifice transluminal endoscopic surgery and localized resection for colorectal neoplasia
Cahill RA, Mortensen NJ
- 203 NOTES: The question for minimal resection and sentinel node in early gastric cancer
Asakuma M, Cahill RA, Lee SW, Nomura E, Tanigawa N
- 207 Single access laparoscopic surgery: Complementary or alternative to NOTES?
Dapri G
- 210 Natural orifice transluminal surgery: Flexible platform review
Shaikh SN, Thompson CC
- 217 *In vivo* miniature robots for natural orifice surgery: State of the art and future perspectives
Tiwari MM, Reynoso JF, Lehman AC, Tsang AW, Farritor SM, Oleynikov D
- 224 Natural orifice transluminal endoscopic surgery: Educational challenge
Dunkin BJ

Contents

World Journal of Gastrointestinal Surgery
Volume 2 Number 6 June 27, 2010

ACKNOWLEDGMENTS I Acknowledgments to reviewers of *World Journal of Gastrointestinal Surgery*

APPENDIX I Meetings
I-IV Instructions to authors

ABOUT COVER Dunkin BJ. Natural orifice transluminal endoscopic surgery: Educational challenge.
World J Gastrointest Surg 2010; 2(6): 224-230
<http://www.wjgnet.com/1948-9366/full/v2/i6/224.htm>

AIM AND SCOPE *World Journal of Gastrointestinal Surgery* (*World J Gastrointest Surg*, *WJGS*, online ISSN 1948-9366, DOI: 10.4240), is a monthly, open-access, peer-reviewed journal supported by an editorial board of 336 experts in gastrointestinal surgery from 35 countries.
The major task of *WJGS* is to rapidly report the most recent results in basic and clinical research on gastrointestinal surgery, specifically including micro-invasive surgery, laparoscopy, hepatic surgery, biliary surgery, pancreatic surgery, splenic surgery, surgical nutrition, portal hypertension, as well as the associated subjects such as epidemiology, cancer research, biomarkers, prevention, pathology, radiology, genetics, genomics, proteomics, pharmacology, pharmacokinetics, pharmacogenetics, molecular biology, clinical trials, diagnosis and therapeutics and multimodality treatment. Emphasis is placed on original research articles and clinical case reports. This journal will also provide balanced, extensive and timely review articles on selected topics.

FLYLEAF I-III Editorial Board

EDITORS FOR THIS ISSUE

Responsible Assistant Editor: *Na Liu*
Responsible Electronic Editor: *Chuan Yang*
Proofing Editor-in-Chief: *Lian-Sheng Ma*

Responsible Science Editor: *Jin-Lei Wang*
Proofing Editorial Office Director: *Jin-Lei Wang*

NAME OF JOURNAL
World Journal of Gastrointestinal Surgery

LAUNCH DATE
November 30, 2009

SPONSOR
Beijing Baishideng BioMed Scientific Co., Ltd.,
Room 903, Building D, Ocean International Center,
No. 62 Dongsihuan Zhonglu, Chaoyang District,
Beijing 100025, China
Telephone: 0086-10-8538-1892
Fax: 0086-10-8538-1893
E-mail: baishideng@wjgnet.com
<http://www.wjgnet.com>

EDITING
Editorial Board of *World Journal of Gastrointestinal Surgery*,
Room 903, Building D, Ocean International Center,
No. 62 Dongsihuan Zhonglu, Chaoyang District,
Beijing 100025, China
Telephone: 0086-10-8538-1891
Fax: 0086-10-8538-1893
E-mail: wjgs@wjgnet.com
<http://www.wjgnet.com>

PUBLISHING
Beijing Baishideng BioMed Scientific Co., Ltd.,
Room 903, Building D, Ocean International Center,
No. 62 Dongsihuan Zhonglu, Chaoyang District,
Beijing 100025, China
Telephone: 0086-10-8538-1892

Fax: 0086-10-8538-1893
E-mail: baishideng@wjgnet.com
<http://www.wjgnet.com>

SUBSCRIPTION
Beijing Baishideng BioMed Scientific Co., Ltd.,
Room 903, Building D, Ocean International Center,
No. 62 Dongsihuan Zhonglu, Chaoyang District,
Beijing 100025, China
Telephone: 0086-10-8538-1892
Fax: 0086-10-8538-1893
E-mail: baishideng@wjgnet.com
<http://www.wjgnet.com>

ONLINE SUBSCRIPTION
One-Year Price 216.00 USD

PUBLICATION DATE
June 27, 2010

CSSN
ISSN 1948-9366 (online)

PRESIDENT AND EDITOR-IN-CHIEF
Lian-Sheng Ma, Beijing

STRATEGY ASSOCIATE EDITORS-IN-CHIEF
Elijah Dixon, Calgary
Antonello Forgione, Milan
Tobias Keck, Freiburg
Tsuyoshi Konishi, Tokyo
Natale Di Martino, Naples

EDITORIAL OFFICE
Jin-Lei Wang, Director
World Journal of Gastrointestinal Surgery
Room 903, Building D, Ocean International Center,
No. 62 Dongsihuan Zhonglu, Chaoyang District,
Beijing 100025, China
Telephone: 0086-10-8538-1891
Fax: 0086-10-8538-1893
E-mail: wjgs@wjgnet.com
<http://www.wjgnet.com>

COPYRIGHT
© 2010 Baishideng. All rights reserved; no part of this publication may be reproduced, stored in a retrieval system, or transmitted in any form or by any means, electronic, mechanical, photocopying, recording, or otherwise without the prior permission of Baishideng. Author are required to grant *World Journal of Gastrointestinal Surgery* an exclusive license to publish.

SPECIAL STATEMENT
All articles published in this journal represent the viewpoints of the authors except where indicated otherwise.

INSTRUCTIONS TO AUTHORS
Full instructions are available online at http://www.wjgnet.com/1948-9366/g_info_20100305152206.htm. If you do not have web access please contact the editorial office.

ONLINE SUBMISSION
<http://www.wjgnet.com/1948-9366office>

NOTES-Natural orifice transluminal endoscopic surgery: Why not?

Antonello Forgione

Antonello Forgione, AIMS Advanced International Mini-invasive Surgery Academy; Department of General and Emergency Surgery, Niguarda Ca' Granda Hospital, Piazza Ospedale 3, Milan 20162, Italy

Author contributions: Forgione A solely contributed to this paper. Correspondence to: Antonello Forgione MD, PhD, MBA, Department of General and Emergency Surgery, Niguarda Ca' Granda Hospital, Piazza Ospedale 3, Milan 20162, Italy. antonello.forgione@aimsacademy.org

Telephone: +39-2-64447600 Fax: +39-2-64447603

Received: May 26, 2010 Revised: June 20, 2010

Accepted: June 24, 2010

Published online: June 27, 2010

Abstract

Since natural orifice transluminal endoscopic surgery (NOTES) was first described by Anthony Kalloo, it has attracted tremendous interest from surgeons and gastroenterologist all around the world. This special issue of the *World Journal of Gastrointestinal Surgery* explores the current possibilities and future potential of the most disruptive revolution in the field of surgery represented by the NOTES approach. In the future, new technologies developed for this approach and deeper insight into several gastrointestinal diseases will lead to the design of completely new interventional procedures and change the way we will operate, bringing us to the previously unimaginable goal of "no scar surgery".

© 2010 Baishideng. All rights reserved.

Key words: Gastrointestinal surgery; Minimally invasive surgery; Natural orifice transluminal endoscopic surgery; Microrobotics

Forgione A. NOTES-Natural orifice transluminal endoscopic surgery: Why not? *World J Gastrointest Surg* 2010; 2(6): 177-178 Available from: URL: <http://www.wjgnet.com/1948-9366/full/v2/i6/177.htm> DOI: <http://dx.doi.org/10.4240/wjgs.v2.i6.177>

EDITORIAL

We, human beings, don't like to undergo surgical procedures, not only for the fear and effect of the disease, but also for the expected postoperative pain, the risks and side effects of anesthesia, the recovery time needed after an operation and the permanent visible scars that will forever leave an unpleasant reminder of the experience and alter the esthetic of the person^[1].

The revolutionary concept of natural orifice transluminal endoscopic surgery (NOTES) described by Kalloo *et al*^[2], promises to overcome many of the historical drawbacks of the surgical approach.

After a long period of testing in experimental settings the NOTES approach has now proven its feasibility and safety in preliminary clinical experience in the performance of basic surgical procedures^[3-5]. At same time, new fields of surgery and innovative approaches are being explored in order to allow more advanced procedures to be performed^[6,7].

So far, the major efforts in the field have been primarily concentrated on the use of natural orifice approaches to simply replicate traditional radical procedures whilst respecting established operative strategies. However, the NOTES approach is also stimulating the appreciation of complementary advanced technologies and new surgical concepts, that will allow us not only to perform the procedures *via* a minimal access, but also to minimize the extent or even the need for a surgical resection. These new concepts are represented for example by genetically driven gastrointestinal cancer treatment and manipulation of the gastrointestinal tract for the cure of metabolic disorders^[8-10].

In fact, Better genetic and physiopathological knowledge will help us to customize the surgical approach to the specific needs of the patient. This will avoid the usual "one size fits all" strategy that often relies on extended surgical resection of large specimens simply to perform the correct cancer staging. This approach rarely adds any clinical benefit to the patients while may impair their functional outcome and quality of life^[11].

In this special issue of the *World Journal of Gastrointestinal Surgery*, leading experts in the field report on their current experimental and clinical experience with this new approach, such as “Natural orifice transluminal endoscopic surgery: The transvaginal route moving forward from cholecystectomy” by Targarona *et al*^[12], “Transgastric cholecystectomy: From the laboratory to clinical implementation” by Dallemagne *et al*^[13], “Current experience and future directions of completely NOTES colorectal resection” by Sylla^[14], “Natural orifice transluminal endoscopic surgery and localized resection for colorectal neoplasia” by Cahill *et al*^[15], “NOTES: The question for minimal resection and sentinel node in early gastric cancer” by Asakuma *et al*^[16], “Single access laparoscopic surgery: Complementary or alternative to NOTES?” by Dapri^[17], “Natural orifice transluminal surgery: Flexible platform review” by Shaikh *et al*^[18], “*In vivo* miniature robots for natural orifice surgery: State of the art and future perspectives” by Tiwari *et al*^[19], and “Natural orifice transluminal endoscopic surgery: Educational challenge” by Dunkin^[20]. All The authors in their articles, highlight how technological developments and new concepts will definitively push forward this previously unimaginable frontier of “no scar surgery”, allowing for its widespread application and the conception of completely new techniques that will greatly impact the way we will address many diseases in the future.

REFERENCES

- 1 **Swanstrom LL**, Volckmann E, Hungness E, Soper NJ. Patient attitudes and expectations regarding natural orifice transluminal endoscopic surgery. *Surg Endosc* 2009; **23**: 1519-1525
- 2 **Kalloo AN**, Singh VK, Jagannath SB, Niiyama H, Hill SL, Vaughn CA, Magee CA, Kantsevov SV. Flexible transgastric peritoneoscopy: a novel approach to diagnostic and therapeutic interventions in the peritoneal cavity. *Gastrointest Endosc* 2004; **60**: 114-117
- 3 **Zorrón R**, Filgueiras M, Maggioni LC, Pombo L, Lopes Carvalho G, Lacerda Oliveira A. NOTES. Transvaginal cholecystectomy: report of the first case. *Surg Innov* 2007; **14**: 279-283
- 4 **Ujiki MB**, Martinec DV, Diwan TS, Denk PM, Dunst CM, Swanström LL. Video: natural orifice transluminal endoscopic surgery (NOTES): creation of a gastric valve for safe and effective transgastric surgery in humans. *Surg Endosc* 2010; **24**: 220
- 5 **Rao GV**, Reddy DN, Banerjee R. NOTES: human experience. *Gastrointest Endosc Clin N Am* 2008; **18**: 361-370; x
- 6 **Zorrón R**, Goncalves L, Leal D, Kanaan E, Cabral I, Saraiva P. Transvaginal hybrid natural orifice transluminal endoscopic surgery retroperitoneoscopy--the first human case report. *J Endourol* 2010; **24**: 233-237
- 7 **Sylla P**, Rattner DW, Delgado S, Lacy AM. NOTES transanal rectal cancer resection using transanal endoscopic microsurgery and laparoscopic assistance. *Surg Endosc* 2010; **24**: 1205-1210
- 8 **Cahill RA**, Asakuma M, Trunzo J, Schomisch S, Wiese D, Saha S, Dallemagne B, Marks J, Marescaux J. Intraperitoneal virtual biopsy by fibered optical coherence tomography (OCT) at natural orifice transluminal endoscopic surgery (NOTES). *J Gastrointest Surg* 2010; **14**: 732-738
- 9 **Cahill RA**, Lindsey I, Cunningham C. Address of early stage primary colonic neoplasia by N.O.T.E.S. *Surg Oncol* 2009; **18**: 163-168
- 10 **Rubino F**, Schauer PR, Kaplan LM, Cummings DE. Metabolic surgery to treat type 2 diabetes: clinical outcomes and mechanisms of action. *Annu Rev Med* 2010; **61**: 393-411
- 11 **Forgione A**, Leroy J, Cahill RA, Bailey C, Simone M, Mutter D, Marescaux J. Prospective evaluation of functional outcome after laparoscopic sigmoid colectomy. *Ann Surg* 2009; **249**: 218-224
- 12 **Targarona EM**, Maldonado EM, Marzol JA, Marinello F. Natural orifice transluminal endoscopic surgery: The transvaginal route moving forward from cholecystectomy. *World J Gastrointest Surg* 2010; **2**: 179-186
- 13 **Dallemagne B**, Perretta S, Allemann P, Donatelli G, Asakuma M, Mutter D, Marescaux J. Transgastric cholecystectomy: From the laboratory to clinical implementation. *World J Gastrointest Surg* 2010; **2**: 187-192
- 14 **Sylla P**. Current experience and future directions of completely NOTES colorectal resection. *World J Gastrointest Surg* 2010; **2**: 193-198
- 15 **Cahill RA**, Mortensen NJ. Natural orifice transluminal endoscopic surgery and localized resection for colorectal neoplasia. *World J Gastrointest Surg* 2010; **2**: 199-202
- 16 **Asakuma M**, Cahill RA, Lee SW, Nomura E, Tanigawa N. NOTES: The question for minimal resection and sentinel node in early gastric cancer. *World J Gastrointest Surg* 2010; **2**: 203-206
- 17 **Dapri G**. Single access laparoscopic surgery: Complementary or alternative to NOTES? *World J Gastrointest Surg* 2010; **2**: 207-209
- 18 **Shaikh SN**, Thompson CC. Natural orifice transluminal surgery: Flexible platform review. *World J Gastrointest Surg* 2010; **2**: 210-216
- 19 **Tiwari MM**, Reynoso JF, Lehman AC, Tsang AW, Farritor SM, Oleynikov D. *In vivo* miniature robots for natural orifice surgery: State of the art and future perspectives. *World J Gastrointest Surg* 2010; **2**: 217-223
- 20 **Dunkin BJ**. Natural orifice transluminal endoscopic surgery: Educational challenge. *World J Gastrointest Surg* 2010; **2**: 224-230

S- Editor Wang JL L- Editor Hughes D E- Editor Yang C

Antonello Forgione, MD, PhD, MBA, Series Editor

Natural orifice transluminal endoscopic surgery: The transvaginal route moving forward from cholecystectomy

Eduardo M Targarona, Edgar Mauricio Maldonado, Jose Antonio Marzol, Franco Marinello

Eduardo M Targarona, Edgar Mauricio Maldonado, Jose Antonio Marzol, Franco Marinello, Department of Surgery, Hospital Santpau, Autonomous University of Barcelona, Sant Quinti 89, 08041 Barcelona, Spain

Author contributions: Targarona EM conceived the idea, scripted and finally revised the manuscript; Maldonado EM, Marzol JA and Marinello F participated in reviewing the literature and writing the manuscript.

Correspondence to: Eduardo M Targarona, MD, Professor, Department of Surgery, Hospital Santpau, Autonomous University of Barcelona, Sant Quinti 89, 08041 Barcelona, Spain. etargarona@santpau.cat

Telephone: +34-93-5565671 Fax: +34-93-5565608

Received: December 26, 2009 Revised: February 1, 2010

Accepted: February 8, 2010

Published online: June 27, 2010

© 2010 Baishideng. All rights reserved.

Key words: Transvaginal approach; Cholecystectomy; Nephrectomy; Splenectomy; Segmental gastrectomy; Retroperitoneal exploration; Natural orifice transluminal endoscopic surgery; Bariatric surgery

Peer reviewer: Theodoros E Pavlidis, MD, PhD, Professor, Department of Surgery, University of Thessaloniki, Hippocraton Hospital, A Samothraki 23, Thessaloniki 54248, Greece

Targarona EM, Maldonado EM, Marzol JA, Marinello F. Natural orifice transluminal endoscopic surgery: The transvaginal route moving forward from cholecystectomy. *World J Gastrointest Surg* 2010; 2(6): 179-186 Available from: URL: <http://www.wjgnet.com/1948-9366/full/v2/i6/179.htm> DOI: <http://dx.doi.org/10.4240/wjgs.v2.i6.179>

Abstract

The advent of minimally invasive surgery and the advances in endoluminal flexible endoscopy have converged to generate a new concept in digestive surgery, whose acronym natural orifice transluminal endoscopic surgery (NOTES), has become a familiar term in the surgical community. NOTES has been performed through the mouth, the bladder, the rectum and the vagina. Of these four approaches, the vagina has gained most popularity for several reasons. It is not only readily accessible and easy to decontaminate but it also provides safe entry and simple closure. The transvaginal approach has been described in the experimental and the clinical setting as an option for cholecystectomy, nephrectomy, splenectomy, segmental gastrectomy, retroperitoneal exploration and bariatric surgery. However, larger series are needed to delineate the exact risks of this approach, and to transcend cultural barriers that impede its wider introduction. Prospective randomized trials will shed light on the definitive role of the vaginal approach in minimal invasive surgery of the future.

INTRODUCTION

The advent of minimally invasive surgery and the advances in endoluminal flexible endoscopy have converged to generate a new concept in digestive surgery in which the wall of a hollow organ is trespassed to gain access to the peritoneal cavity. This new approach, whose acronym natural orifice transluminal endoscopic surgery (NOTES) has become a familiar term in the surgical community, aims to reduce the effects and consequences of surgical trauma to a minimum. Since it was first defined by Kalloo *et al*^[1] in 2004, it has attracted tremendous interest from surgeons and flexible endoscopists all around the world^[2,3]. NOTES surgery poses many conceptual, physical and technical challenges that were thoroughly assessed in a "white paper" published in 2006^[4]. The most complex technical issues related to NOTES are access closure and the risk of microbial contamination. NOTES has been performed through the mouth, urinary bladder, rectum and vagina. Of these

four approaches, the vagina has gained most popularity for several reasons. It is not only readily accessible and easy to decontaminate but it also provides safe entry and simple closure^[5]. The aim of this paper is to describe the anatomical and technical considerations associated with this surgical procedure, and provide an overview of experimental and clinical evidence collected to date.

ANATOMIC BASIS

The transvaginal approach to the peritoneal cavity for diagnostic or therapeutic purposes is not new in the field of gynecology. It was named “ventroscopy” by Ott in 1901, culdoscopy by Decker and Cherry (1944) or colpolaparoscopy by Klatfen (1948)^[6]. Transvaginal hysterectomy has been performed successfully for many years. In 1998, Tsin^[6] described his experience with operative colpolaparoscopy for appendectomies and cholecystectomies. The vagina has also been used for years to retrieve organs such as the spleen or the kidney^[7,8] after laparoscopic dissection, so as to avoid a minilaparotomy or trocar site enlargement.

The anatomical basis for the transvaginal approach is the wide posterior fundus of the vagina formed as a result of the anteversion position of the uterus^[9]. The vaginal pouch is bounded by the posterior vaginal wall, the sacrouterine ligaments and the anterior rectum wall, and it forms the floor of the Douglas pouch (Figures 1 and 2). The fundus of the vagina is 3-4 cm wide. As it is not adherent to the anterior face of the rectum and has no interposed organ or anatomical structure, it allows direct entry to the peritoneum.

TRANSVAGINAL APPROACH

Technique

Colpotomy is a common, standardized and consolidated approach in gynecology. It is used to remove not only gynecologic lesions but also non-gynecological organs in mini-invasive general surgery. For this procedure, the patient is placed in dorsal decubitus with the legs in stirrups, in the Lloyd-Davies position. Antithrombotic prophylaxis is administered together with a single dose of antibiotic prophylaxis. A nasogastric tube and a Foley catheter are used under general orotracheal anesthesia. A bimanual gynecologic examination is recommendable to rule out masses or adhesions. After bladder catheterization, the vagina is decontaminated with betadine. The presence of a gynecologist is recommended when initially gaining experience with the technique. The colpotomy can be performed blindly without transumbilical laparoscopic control, or under laparoscopic control. If entry is blind, the patient is placed in the Trendelenburg position to reduce the risk of injuring the small bowel while gaining access to the abdominal cavity. The posterior fundus is then grasped two cm below the cervix and a sharp or electric scalpel is used to perform a colpotomy to reach the abdominal cavity. This procedure is only applicable for pure NOTES.

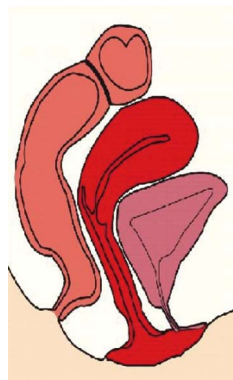


Figure 1 Sagittal view of the female pelvis showing the shape and location of the vaginal fundus that delineate the floor of the Douglas pouch.

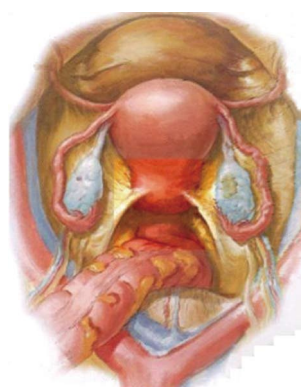


Figure 2 Draft of the deep pelvis and the Douglas pouch showing the free zone for transvaginal access to the peritoneal cavity.

For safety reasons, entry through the vagina is usually performed under transumbilical laparoscopic control. In this case, after exploratory laparoscopy to rule out adhesions or an impracticable Douglas pouch, entry is gained by sharp dissection or using a conventional laparoscopic trocar (12 mm of diameter), either with or without blades.

Contraindications

There are a number of potential contraindications and when transvaginal surgery is proposed, the patient should be clearly and fully informed and asked to sign a consent form. A preoperative gynecologic examination is recommended. Clinical contraindications are active infections, pregnancy or cervical cancer. Technical difficulties may be encountered in the case of previous gynecologic surgery, gynecologic infections, or previous inflammatory digestive diseases such as inflammatory bowel disease, diverticulitis or appendiceal peritonitis. In such cases a previous laparoscopy should be carried out. The presence of endometriosis should also be ruled out as this could shrink the rectovaginal wall or the Douglas pouch. Another point to consider is the practice of transvaginal surgery in a young nulliparous patient as the impact of transvaginal surgery on fertility is not yet known. A practical safeguard therefore is to offer this surgery only to postmenopausal women or patients who no longer want to have children.

Table 1 Transvaginal NOTES procedures reported to date

Author	Year	NOTES	NO. of patients	Operation
Pugliese	2009	Hybrid	18	Cholecystectomy
DeCarli	2009	Hybrid	12	Cholecystectomy
Gumbs	2009	Hybrid (3)/Pure (1)	4	Cholecystectomy
Zornig	2009	Hybrid	68	Cholecystectomy
Seven	2009	Hybrid	2	Cholecystectomy
Castro-Perez	2009	Hybrid	7	Cholecystectomy
Horgan	2009	Hybrid	9	Cholecystectomy
Horgan	2009	Hybrid	1	Cholecystectomy
Horgan	2009	Hybrid	1	Appendectomy
Targarona	2009	Hybrid	1	Splenectomy
Tabutsadze	2009	Hybrid	2	Appendectomy
Nakajima	2009	Hybrid	2	Partial Gastrectomy
De Sousa	2009	Pure	4	Cholecystectomy
Navarra	2009	Hybrid	6	Cholecystectomy
Noguera	2009	Hybrid	15	Cholecystectomy
Noguera	2009	Hybrid	1	Liver Resection
Palanivelu	2009	Hybrid	6	Cholecystectomy
Cardoso Ramos	2008	Hybrid	4	Sleeve Gastrectomy
Cardoso Ramos	2008	Hybrid	32	Cholecystectomy
Zorrón	2008	Pure	1	Cancer Diagnostic Staging
DeCarli	2008	Hybrid	1	Cholecystectomy
Lacy	2008	Hybrid	1	Sigmoidectomy
Palanivelu	2008	Hybrid (2)/Pure (1)	3	Appendectomy
Branco Filho	2007	Hybrid	1	Cholecystectomy
Dolz	2007	Hybrid	1	Cholecystectomy
Zornig	2007	Hybrid	20	Cholecystectomy
Forgione	2007	Hybrid	3	Cholecystectomy
Marescaux	2007	Hybrid	1	Cholecystectomy
Bessler	2007	Hybrid	1	Cholecystectomy
Zorrón	2007	Hybrid	1	Cholecystectomy

NOTES: Natural orifice transluminal endoscopic surgery.

Potential complications

The transvaginal approach appears to be safe. Potential complications with the transvaginal approach would logically resemble those of transvaginal hysterectomy and fertiloscopy. Figures show that there seems to be less pain after transvaginal hysterectomy than after open hysterectomy. Nassif *et al*^[10] found that the incidence of infection after transvaginal hysterectomy was as low as 3.9%, and less than 0.1% after fertiloscopy. Dyspareunia is reported in 2% of cases after the operation and normally improves with time in 81% of cases, leading to an overall incidence around 0.2% at distance from surgery. Rectal injury is estimated to be about 0.2%.

Other complications may arise from postoperative bleeding or chronic infection of the wound. Additional theoretical morbidity may be related to infertility. However, no adverse effects were found in a 12-mo follow up of a combined series of 70 patients who underwent transvaginal cholecystectomy^[11,12].

Types of transvaginal NOTES

“Totally”, “Pure” or “True” NOTES refer to procedures performed only with transluminally placed flexible or rigid tools, without laparoscopic assistance to gain access to the abdominal cavity. With currently available instruments these techniques imply a high degree of difficulty and they have

been performed in very few cases to date.

The term “Hybrid” NOTES is used to describe procedures that involve any type of transabdominal assistance. Hybrid NOTES can be divided into 2 categories: NOTES-assisted laparoscopy and Lap-assisted NOTES. In the former, most of the operation is conducted using transabdominal instruments while in the second category surgery is mainly transluminal but includes transabdominal assistance^[13,14].

Transvaginal NOTES: Current experimental and clinical uses

Cholecystectomy^[11-35]: Over a few months, starting in 2007, several groups around the world reported successful performance of transvaginal cholecystectomies performed either fully endoscopically with minimal laparoscopic assistance for retraction and clip application^[15-17] or NOTES assisted in which dissection was performed with laparoscopic tools^[18,19].

More than 214 cholecystectomies have since then been published using transvaginal NOTES^[11-35], Table 1.

Five cases were carried out using pure NOTES techniques, while the others were hybrid procedures. During the hybrid procedure, the vaginal access is used for visualization and to perform part of the operation by means of endoscopic maneuvers, whilst exposure, clipping and

dissection of the gallbladder is done using different technical options, such as transumbilical or transparietal access or by adding additional rigid or articulated instruments through the vagina.

The pure NOTES operations were performed by only two authors. Gumbs *et al.*^[34] reported a case in which they performed colpotomy and then introduced a trocar under direct vision into the abdominal cavity. A 15-mm port was then established through the colpotomy, and this was also used to create the pneumoperitoneum. A double channel gastroscope was introduced through the 15-mm port. An extra 5-mm port was placed beside the 15-mm port to allow placement of a reticulating retractor. Calot's triangle structures were dissected by means of the double channel endoscope. The cystic duct and artery were clipped endoscopically and the gallbladder was removed through the vagina. The colpotomy was then closed with absorbable suture. de Sousa *et al.*^[35] published 4 totally NOTES transvaginal cholecystectomies, performing posterior colpotomy under direct visualization. A single channel gastroscope with the insufflation tube attached was inserted through the vagina. A double channel colonoscope was placed next to the gastroscope. One endoscope was used for retraction and insufflation. Calot's triangle was dissected using endoscopic instruments such as hot-biopsy forceps, polypectomy snare, and endoscopic hook. The cystic duct and artery were clipped endoscopically. The gallbladder was retrieved through the colpotomy which was then closed with absorbable suture. Other authors have performed hybrid procedures, assisted by means of different laparoscopic instruments.

Appendectomy^[36-38]: Six appendectomies have been performed using this novel approach. Palanivelu *et al.*^[36] reported two hybrid transvaginal NOTES appendectomies and one pure transvaginal NOTES appendectomy. Pneumoperitoneum was achieved by means of a Veress needle in the umbilicus. A 3-mm port was placed through the umbilicus to receive a laparoscope in the first two cases. Colpotomy was made under laparoscopic guidance in the first two patients, and a double channel endoscope was then introduced into the cavity. The left working channel was used to provide traction while the right channel allowed dissection and closure of the appendix base with an endoloop. The specimen was removed through the colpotomy which was then closed with absorbable suture. The operative time was 103.5 min. Two patients complained of postoperative vaginal discomfort, but extra analgesics were not needed. The hospital stay was 48 h. Intraoperative hemorrhage from the appendicular artery was reported but was controlled endoscopically. Tabutsadze *et al.*^[37] published two transvaginal NOTES appendectomies and Horgan *et al.*^[38] performed one hybrid transvaginal NOTES appendectomy. The operative time averaged 78 min and hospital stay was 24 h. No complications were reported.

Sigmoidectomy and right colectomy^[39,40]: A hybrid

NOTES transvaginal sigmoidectomy has been reported^[39]. A needle scope in the right lower quadrant allowed insufflation with CO₂. Colpotomy was made under laparoscopic guidance. A 12 mm port was placed through the colpotomy to insert the flexible endoscope. Two 2-mm ports on the right flank and on the umbilicus were needed for traction. An anal dilator introduced through the rectum improved exposure of the surgical area. The inferior mesenteric pedicle was dissected and then transected with a 45-mm Endo GIA stapler introduced through the vagina. After sigmoid mobilization, a 45-mm Endo GIA stapler was introduced through the vagina and the upper rectum was sectioned. The specimen was extracted through the vagina. The proximal colon section was severed, a purse-string suture was applied, and a circular stapling anvil was inserted into the proximal end of the colon. The proximal colon was then reintroduced into the abdominal cavity. A 31-mm circular stapler was placed transanally to perform the anastomosis. Colpotomy was closed with absorbable suture. Histological diagnosis was adenocarcinoma. The operative time was 150 min. Minimal postoperative pain responded to oral paracetamol and ketoprofene in usual doses. The hospital stay was 96 h and no complications were reported.

A hybrid transvaginal assisted right colectomy has been described by Burghardt in 2008^[40].

Cancer diagnostic staging^[41]: A totally NOTES transvaginal abdominal exploration was performed to obtain histological diagnosis and tumor staging. Colpotomy was performed under direct vision. A flexible double channel colonoscope was introduced through the vagina and pneumoperitoneum was established through the smallest working channel. Sixteen biopsies were taken. The colpotomy was closed using absorbable suture. The operative time was 105 min, post-surgical analgesia was not required and hospital stay was 48 h. No complications were reported.

Liver resection^[42]: A transvaginal hybrid NOTES liver resection was described. Pneumoperitoneum was achieved through a Veress needle in the umbilicus, where a 5-mm trocar was located. A 3-mm trocar was inserted in the right upper quadrant. A 12-mm trocar was placed transvaginally to receive the single channel video gastroscope. The cystic duct and artery were clipped and sectioned. Cholecystectomy was performed with electrocautery. The liver transection required the use of a harmonic scalpel and tissue sealing was achieved with radiofrequency energy. The specimen was inserted into an endobag and extracted transvaginally. The colpotomy was closed with absorbable suture. The histological diagnosis was atypical adenoma. The operative time was 110 min and hospital stay was 48 h. No complications were reported.

Partial gastrectomy^[43]: Two transvaginal hybrid NOTES partial gastrectomies have been performed. A pneumoperitoneum was created through the 10 mm port introduced transumbilically. An additional port was needed in the left

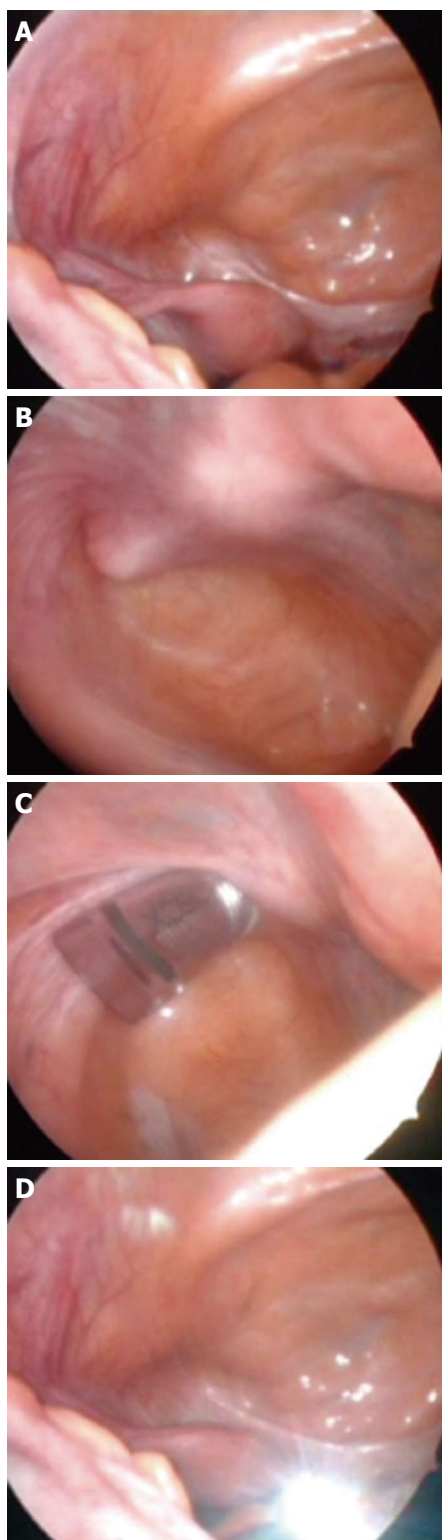


Figure 3 Images corresponding to the transvaginal access to the pelvis with the patient located in full lateral position, used for the transvaginal splenectomy. A: Intraoperative view of the Douglas pouch with the patient placed in full lateral decubitus; B and C: Insertion of the trocar through the lateral fundus of the posterior vaginal vault; D: Introduction of the scope ascending to the left hypochondrium.

midabdomen. Colpotomy was carried out through a single puncture with a 12-mm port under laparoscopic vision. A flexible endoscope was introduced through the port in

the colpotomy. A second flexible endoscope was advanced transorally into the stomach to determine the localization of the tumor. Once transvaginal gastric mobilization was achieved, the transvaginal endoscope was changed for a linear stapling device which was used to perform a partial gastrectomy, under laparoscopic guidance. The specimen was extracted transvaginally protected in an endobag. The colpotomy was closed with absorbable suture. Analysis of the specimen showed a hemorrhagic lipoma in one case and a gastrointestinal stromal tumor in the other. Operative time was 365 min for the former and 170 min in the latter case. Analgesia was not required. The hospital stay was 120 h in both cases and no complications were observed.

Sleeve gastrectomy^[44]: Four transvaginal hybrid NOTES Sleeve Gastrectomies have been reported in the literature so far. Pneumoperitoneum was made through a Veress needle in the umbilicus. A 10-mm port was then inserted and the laparoscope was introduced. Under laparoscopic vision, a 12-mm transvaginal port was placed. A further 5 mm port and a further 2 mm port were placed in the right upper quadrant and in the left upper quadrant, respectively. The stomach was mobilized using a harmonic scalpel and was calibrated with a 36F bougie. Using linear staplers, the sleeve was performed from the mid-antrum to the angle of his. The staple line was then reinforced with suture. The stomach was extracted transvaginally. The colpotomy was closed with absorbable suture and the total operative time was 95 min. One patient required further analgesic treatment on the second postoperative day. Hospital stay was 48 h and no complications were reported.

Splenectomy^[45]: Two transvaginal hybrid NOTES splenectomies have been reported so far. Patients were placed in right decubitus with the left leg in stirrups. The table was flexed at the flank. A pneumoperitoneum was made *via* a Veress needle. A 5-mm port was placed at the anterior axillary line and two 3 mm ports were positioned at the subxyphoid area and the posterior axillary line, respectively. Colpotomy was established in the left vaginal cul-de-sac, and a 15-mm trocar was introduced (Figure 3). This trocar was used for visualization *via* a colonoscope. Splenic mobilization was achieved through the transabdominal ports using a 5-mm harmonic scalpel. The splenic pedicle was stapled under laparoscopic guidance by using a linear stapler introduced through the vagina. The specimen was extracted transvaginally in an endobag. Colpotomy was closed with absorbable suture. The operative time was 180 min and no complications were reported.

Urological surgery and retroperitoneal exploration: In an experimental setting, Allemann *et al.*^[46-49] approached the retroperitoneal space through the lateral wall of the vagina and this access allowed visualization of the retroperitoneal structures. Removal of the adrenal gland, kidney and pancreatic tail was feasible, and lymph node sampling was also achieved^[46-49].

Urological surgery constitutes an emerging area of interest for transvaginal access. Pure NOTES and NOTES-assisted radical nephrectomies have been described and the outcome has been good both in the experimental and the clinical setting^[47,50-55].

Other indications: Lomanto *et al.*^[56] has recently proposed the experimental possibility of repairing abdominal wall hernias using transvaginal placement and fixation of a mesh.

PERCEPTION OF TRANSVAGINAL NOTES

Several surveys have been conducted to evaluate the perception of surgeons, gynecologists and female patients concerning the procedure^[57-61].

From a general point of view, findings show that women accept this procedure if they are assured it is as safe and painless as conventional laparoscopic surgery and will be performed by a surgeon who is skilled in the technique. There are some clearly age-related factors that play an important role in a patient's decision-making: nulliparous and younger women express concerns regarding sexual function, fertility and cosmesis, whilst postmenopausal women or women who do not want further children are more disposed to accept this type of surgery^[58,59].

The surveys found that the major concern for the total group of women was infection. Like women, surgeons and gynecologists are influenced by patient age but their most important concern was the increased risk of procedure-related complications^[60,61].

These findings suggest that as more evidence regarding safety emerges, the transvaginal route for NOTES procedures will be better accepted.

CONCLUSION

Current knowledge and experimental and clinical evidence support the potential advantages of the vagina as a NOTES approach. So far, this route represents the most successful and widely accepted among all the other possible NOTES approaches, and this is due mainly to the relative simplicity of access and closure. Larger series are needed to delineate the exact risks of this approach and to overcome cultural barriers to this concept.

Prospective randomized trials will shed light on the definitive role of the vaginal approach in minimal invasive surgery of the future.

ACKNOWLEDGMENTS

The authors thank Carolyn Newey for revising the English text.

REFERENCES

- 1 Kallou AN, Singh VK, Jagannath SB, Niiyama H, Hill SL, Vaughn CA, Magee CA, Kantsevov SV. Flexible transgastric peritoneoscopy: a novel approach to diagnostic and therapeutic

- 2 eutic interventions in the peritoneal cavity. *Gastrointest Endosc* 2004; **60**: 114-117
- 3 Gee DW, Rattner DW. Natural orifice transluminal endoscopic surgery: current status. *Adv Surg* 2009; **43**: 1-12
- 4 Targarona EM. [Transgastric endoscopic surgery: technological delirium or potential advance?] *Cir Esp* 2006; **80**: 1-2
- 5 Rattner D, Kalloo A. ASGE/SAGES Working Group on Natural Orifice Transluminal Endoscopic Surgery. October 2005. *Surg Endosc* 2006; **20**: 329-333
- 6 Lomanto D, Chua HC, Myat MM, So J, Shabbir A, Ho L. Microbiological contamination during transgastric and transvaginal endoscopic techniques. *J Laparoendosc Adv Surg Tech A* 2009; **19**: 465-469
- 7 Tsin DA. Culdolaparoscopy: a preliminary report. *JSLs* 2001; **5**: 69-71
- 8 Zornig C, Emmermann A, von Waldenfels HA, Felixmüller C. [Colpotomy for specimen removal in laparoscopic surgery] *Chirurg* 1994; **65**: 883-885
- 9 Ghezzi F, Raio L, Mueller MD, Gyr T, Buttarelli M, Franchi M. Vaginal extraction of pelvic masses following operative laparoscopy. *Surg Endosc* 2002; **16**: 1691-1296
- 10 Moran EA, Gostout CJ. Anatomical considerations for natural orifice transluminal endoscopic surgery. *Clin Anat* 2009; **22**: 627-632
- 11 Nassif J. Transvaginal access. *eats.fr* 2008; Available from: URL: <http://www.eats.fr/doi-10.1016/ennassif004.htm>
- 12 Zornig C, Mofid H, Siemssen L, Emmermann A, Alm M, von Waldenfels HA, Felixmüller C. Transvaginal NOTES hybrid cholecystectomy: feasibility results in 68 cases with mid-term follow-up. *Endoscopy* 2009; **41**: 391-394
- 13 Pugliese R, Forgione A, Sansonna F, Ferrari GC, Di Lernia S, Magistro C. Hybrid NOTES transvaginal cholecystectomy: operative and long-term results after 18 cases. *Langenbecks Arch Surg* 2010; **395**: 241-245
- 14 Chamberlain RS, Sakpal SV. A comprehensive review of single-incision laparoscopic surgery (SILS) and natural orifice transluminal endoscopic surgery (NOTES) techniques for cholecystectomy. *J Gastrointest Surg* 2009; **13**: 1733-1740
- 15 Sodergren MH, Clark J, Athanasiou T, Teare J, Yang GZ, Darzi A. Natural orifice transluminal endoscopic surgery: critical appraisal of applications in clinical practice. *Surg Endosc* 2009; **23**: 680-687
- 16 Zorrón R, Filgueiras M, Maggioni LC, Pombo L, Lopes Carvalho G, Lacerda Oliveira A. NOTES. Transvaginal cholecystectomy: report of the first case. *Surg Innov* 2007; **14**: 279-283
- 17 Marescaux J, Dallemagne B, Perretta S, Wattiez A, Mutter D, Coumaros D. Surgery without scars: report of transluminal cholecystectomy in a human being. *Arch Surg* 2007; **142**: 823-826; discussion 826-827
- 18 Forgione A, Maggioni D, Sansonna F, Ferrari C, Di Lernia S, Citterio D, Magistro C, Frigerio L, Pugliese R. Transvaginal endoscopic cholecystectomy in human beings: preliminary results. *J Laparoendosc Adv Surg Tech A* 2008; **18**: 345-351
- 19 Bessler M, Stevens PD, Milone L, Parikh M, Fowler D. Transvaginal laparoscopically assisted endoscopic cholecystectomy: a hybrid approach to natural orifice surgery. *Gastrointest Endosc* 2007; **66**: 1243-1245
- 20 Zornig C, Mofid H, Emmermann A, Alm M, von Waldenfels HA, Felixmüller C. Scarless cholecystectomy with combined transvaginal and transumbilical approach in a series of 20 patients. *Surg Endosc* 2008; **22**: 1427-1429
- 21 Dolz C, Noguera JF, Martín A, Vilella A, Cuadrado A. [Transvaginal cholecystectomy (NOTES) combined with minilaparoscopy] *Rev Esp Enferm Dig* 2007; **99**: 698-702
- 22 Branco Filho AJ, Noda RW, Kondo W, Kawahara N, Rangel M, Branco AW. Initial experience with hybrid transvaginal cholecystectomy. *Gastrointest Endosc* 2007; **66**: 1245-1248
- 23 Decarli L, Zorrón R, Branco A, Lima FC, Tang M, Pioneer

- SR, Zanin I Jr, Schulte AA, Bigolin AV, Gagner M. Natural orifice transluminal endoscopic surgery (NOTES) transvaginal cholecystectomy in a morbidly obese patient. *Obes Surg* 2008; **18**: 886-889
- 23 **Zorron R**, Maggioni LC, Pombo L, Oliveira AL, Carvalho GL, Filgueiras M. NOTES transvaginal cholecystectomy: preliminary clinical application. *Surg Endosc* 2008; **22**: 542-547
 - 24 **Ramos AC**, Murakami A, Galvão Neto M, Galvão MS, Silva AC, Canseco EG, Moyses Y. NOTES transvaginal video-assisted cholecystectomy: first series. *Endoscopy* 2008; **40**: 572-575
 - 25 **Decarli LA**, Zorron R, Branco A, Lima FC, Tang M, Pioneer SR, Sanseverino JL, Menguer R, Bigolin AV, Gagner M. New hybrid approach for NOTES transvaginal cholecystectomy: preliminary clinical experience. *Surg Innov* 2009; **16**: 181-186
 - 26 **Palanivelu C**, Rajan PS, Rangarajan M, Prasad M, Kalyanakumari V, Parthasarathi R, Senthilnathan P. NOTES: Transvaginal endoscopic cholecystectomy in humans-preliminary report of a case series. *Am J Gastroenterol* 2009; **104**: 843-847
 - 27 **Seven R**, Barbaros U. Needloscopy-assisted transvaginal cholecystectomy. *Surg Laparosc Endosc Percutan Tech* 2009; **19**: e61-e63
 - 28 **Asakuma M**, Perretta S, Allemann P, Cahill R, Con SA, Solano C, Pasupathy S, Mutter D, Dallemagne B, Marescaux J. Challenges and lessons learned from NOTES cholecystectomy initial experience: a stepwise approach from the laboratory to clinical application. *J Hepatobiliary Pancreat Surg* 2009; **16**: 249-254
 - 29 **Navarra G**, Rando L, La Malfa G, Bartolotta G, Pracanica G. Hybrid transvaginal cholecystectomy: a novel approach. *Am J Surg* 2009; **197**: e69-e72
 - 30 **Castro-Pérez R**, Acosta-González LR, Dopico-Reyes E, Robaina-Arias LE. [MANOS: Transvaginal cholecystectomies: preliminary report] *Cir Esp* 2009; **85**: 292-297
 - 31 **Noguera J**, Dolz C, Cuadrado A, Olea J, Vilella A, Morales R. Hybrid transvaginal cholecystectomy, NOTES, and minilaparoscopy: analysis of a prospective clinical series. *Surg Endosc* 2009; **23**: 876-881
 - 32 **Horgan S**, Mintz Y, Jacobsen GR, Sandler BJ, Cullen JP, Spivack A, Easter DW, Chock A, Savu MK, Ramamoorthy S, Bosia J, Agarwal S, Lukacz E, Whitcomb E, Savides T, Talamini MA. Video. NOTES: transvaginal cholecystectomy with assisting articulating instruments. *Surg Endosc* 2009; **23**: 1900
 - 33 **Sugimoto M**, Yasuda H, Koda K, Suzuki M, Yamazaki M, Tezuka T, Kosugi C, Higuchi R, Watayo Y, Yagawa Y, Uemura S, Tsuchiya H, Hirano A, Shoki R. Rendezvous gastrotomy technique using direct percutaneous endoscopic gastrotomy for transgastric cholecystectomy in hybrid natural orifice transluminal endoscopic surgery. *J Hepatobiliary Pancreat Surg* 2009; **16**: 758-762
 - 34 **Gumbs AA**, Fowler D, Milone L, Evanko JC, Ude AO, Stevens P, Bessler M. Transvaginal natural orifice transluminal endoscopic surgery cholecystectomy: early evolution of the technique. *Ann Surg* 2009; **249**: 908-912
 - 35 **de Sousa LH**, de Sousa JA, de Sousa Filho LH, de Sousa MM, de Sousa VM, de Sousa AP, Zorron R. Totally NOTES (T-NOTES) transvaginal cholecystectomy using two endoscopes: preliminary report. *Surg Endosc* 2009; **23**: 2550-2555
 - 36 **Palanivelu C**, Rajan PS, Rangarajan M, Parthasarathi R, Senthilnathan P, Prasad M. Transvaginal endoscopic appendectomy in humans: a unique approach to NOTES--world's first report. *Surg Endosc* 2008; **22**: 1343-1347
 - 37 **Tabutsadze T**, Kipshidze N. New trend in endoscopic surgery: transvaginal appendectomy NOTES (Natural Orifice Transluminal Endoscopic Surgery). *Georgian Med News* 2009; **7**: 10
 - 38 **Horgan S**, Cullen JP, Talamini MA, Mintz Y, Ferreres A, Jacobsen GR, Sandler B, Bosia J, Savides T, Easter DW, Savu MK, Ramamoorthy SL, Whitcomb E, Agarwal S, Lukacz E, Dominguez G, Ferraina P. Natural orifice surgery: initial clinical experience. *Surg Endosc* 2009; **23**: 1512-1518
 - 39 **Lacy AM**, Delgado S, Rojas OA, Almenara R, Blasi A, Llach J. MA-NOS radical sigmoidectomy: report of a transvaginal resection in the human. *Surg Endosc* 2008; **22**: 1717-1723
 - 40 **Burghardt J**, Federlein M, Müller V, Benhidjeb T, Elling D, Gellert K. [Minimal invasive transvaginal right hemicolectomy: report of the first complex NOS (natural orifice surgery) bowels operation using a hybrid approach] *Zentralbl Chir* 2008; **133**: 574-576
 - 41 **Zorrón R**, Soldan M, Filgueiras M, Maggioni LC, Pombo L, Oliveira AL. NOTES: transvaginal for cancer diagnostic staging: preliminary clinical application. *Surg Innov* 2008; **15**: 161-165
 - 42 **Noguera JF**, Dolz C, Cuadrado A, Olea JM, Vilella A. Transvaginal liver resection (NOTES) combined with minilaparoscopy. *Rev Esp Enferm Dig* 2008; **100**: 411-415
 - 43 **Nakajima K**, Nishida T, Takahashi T, Souma Y, Hara J, Yamada T, Yoshio T, Tsutsui T, Yokoi T, Mori M, Doki Y. Partial gastrectomy using natural orifice transluminal endoscopic surgery (NOTES) for gastric submucosal tumors: early experience in humans. *Surg Endosc* 2009; Epub ahead of print
 - 44 **Ramos AC**, Zundel N, Neto MG, Maalouf M. Human hybrid NOTES transvaginal sleeve gastrectomy: initial experience. *Surg Obes Relat Dis* 2008; **4**: 660-663
 - 45 **Targarona EM**, Gomez C, Rovira R, Pernas JC, Balague C, Guarner-Argente C, Sainz S, Trias M. NOTES-assisted transvaginal splenectomy: the next step in the minimally invasive approach to the spleen. *Surg Innov* 2009; **16**: 218-222
 - 46 **Perretta S**, Allemann P, Asakuma M, Dallemagne B, Marescaux J. Adrenalectomy using natural orifice transluminal endoscopic surgery (NOTES): a transvaginal retroperitoneal approach. *Surg Endosc* 2009; **23**: 1390
 - 47 **Perretta S**, Allemann P, Asakuma M, Cahill R, Dallemagne B, Marescaux J. Feasibility of right and left transvaginal retroperitoneal nephrectomy: from the porcine to the cadaver model. *J Endourol* 2009; **23**: 1887-1892
 - 48 **Zacharopoulou C**, Nassif J, Allemann P, Dallemagne B, Perretta S, Marescaux J, Wattiez A. Exploration of the retroperitoneum using the transvaginal natural orifice transluminal endoscopic surgery technique. *J Minim Invasive Gynecol* 2009; **16**: 198-203
 - 49 **Allemann P**, Perretta S, Asakuma M, Dallemagne B, Mutter D, Marescaux J. Multimedia manuscript. NOTES retroperitoneal transvaginal distal pancreatectomy. *Surg Endosc* 2009; **23**: 882-883
 - 50 **Kaouk JH**, Haber GP, Goel RK, Crouzet S, Brethauer S, Firoozi F, Goldman HB, White WM. Pure Natural Orifice Transluminal Endoscopic Surgery (NOTES) Transvaginal Nephrectomy. *Eur Urol* 2009; Epub ahead of print
 - 51 **Alcaraz A**, Peri L, Molina A, Goicoechea I, García E, Izquierdo L, Ribal MJ. Feasibility of transvaginal NOTES-assisted laparoscopic nephrectomy. *Eur Urol* 2010; **57**: 233-237
 - 52 **Kaouk JH**, White WM, Goel RK, Brethauer S, Crouzet S, Rackley RR, Moore C, Ingber MS, Haber GP. NOTES transvaginal nephrectomy: first human experience. *Urology* 2009; **74**: 5-8
 - 53 **Ribal Caparrós MJ**, Peri Cusi L, Molina Cabeza A, García Larrosa A, Carmona F, Alcaraz Asensio A. [First report on hybrid transvaginal nephrectomy for renal cancer] *Actas Urol Esp* 2009; **33**: 280-283
 - 54 **Aron M**, Berger AK, Stein RJ, Kamoi K, Brandina R, Canes D, Sotelo R, Desai MM, Gill IS. Transvaginal nephrectomy with a multichannel laparoscopic port: a cadaver study. *BJU Int* 2009; **103**: 1537-1541
 - 55 **Branco AW**, Branco Filho AJ, Kondo W, Noda RW, Kawahara N, Camargo AA, Stunitz LC, Valente J, Rangel M. Hybrid transvaginal nephrectomy. *Eur Urol* 2008; **53**: 1290-1294
 - 56 **Lomanto D**, Dhir U, So JB, Cheah WK, Moe MA, Ho KY. Total transvaginal endoscopic abdominal wall hernia repair: a NOTES survival study. *Hernia* 2009; **13**: 415-419

- 57 **Varadarajulu S**, Tamhane A, Drelichman ER. Patient perception of natural orifice transluminal endoscopic surgery as a technique for cholecystectomy. *Gastrointest Endosc* 2008; **67**: 854-860
- 58 **Peterson CY**, Ramamoorthy S, Andrews B, Horgan S, Talamini M, Chock A. Women's positive perception of transvaginal NOTES surgery. *Surg Endosc* 2009; **23**: 1770-1774
- 59 **Swanstrom LL**, Volckmann E, Hungness E, Soper NJ. Patient attitudes and expectations regarding natural orifice transluminal endoscopic surgery. *Surg Endosc* 2009; **23**: 1519-1525
- 60 **Volckmann ET**, Hungness ES, Soper NJ, Swanstrom LL. Surgeon perceptions of Natural Orifice Translumenal Endoscopic Surgery (NOTES). *J Gastrointest Surg* 2009; **13**: 1401-1410
- 61 **Thele F**, Zygmunt M, Glitsch A, Heidecke CD, Schreiber A. How do gynecologists feel about transvaginal NOTES surgery? *Endoscopy* 2008; **40**: 576-580

S- Editor Li LF **L- Editor** Hughes D **E- Editor** Yang C

Antonello Forgione, MD, PhD, MBA, Series Editor

Transgastric cholecystectomy: From the laboratory to clinical implementation

Bernard Dallemagne, Silvana Perretta, Pierre Allemann, Gianfranco Donatelli, Mitsuhiro Asakuma, Didier Mutter, Jacques Marescaux

Bernard Dallemagne, Silvana Perretta, Pierre Allemann, Gianfranco Donatelli, Mitsuhiro Asakuma, Didier Mutter, Jacques Marescaux, Department of Digestive and Endocrine Surgery, Pôle Hépat-Digestif, University Hospital of Strasbourg and IRCAD, 67091 Strasbourg Cedex, France

Author contributions: Dallemagne B was principal investigator and edited the paper; Perretta S, Alleman P, Donatelli G, Asakuma M, Mutter D and Marescaux J all contributed to the performance of the surgical procedures, the data collection and the analysis and the redaction of the paper.

Correspondence to: Bernard Dallemagne, MD, Department of Digestive and Endocrine Surgery, Pôle Hépat-Digestif, University Hospital of Strasbourg and IRCAD, 1 Place de l'Hôpital, 67091 Strasbourg Cedex, France. bernard.dallemagne@ircad.fr

Telephone: +33-388-19006 Fax: +33-388-119099

Received: December 26, 2009 Revised: March 30, 2010

Accepted: May 6, 2010

Published online: June 27, 2010

© 2010 Baishideng. All rights reserved.

Key words: Flexible surgery; Cholecystectomy; Natural orifice transluminal endoscopic surgery; Minimal invasive surgery; Endoscopic surgery

Peer reviewer: Miroslav N Milicevic, Professor, Department of HPB Surgery and Liver Transplant, The First Surgical Clinic University of Belgrade Clinical Center, Belgrade 11000, Yugoslavia

Dallemagne B, Perretta S, Allemann P, Donatelli G, Asakuma M, Mutter D, Marescaux J. Transgastric cholecystectomy: From the laboratory to clinical implementation. *World J Gastrointest Surg* 2010; 2(6): 187-192 Available from: URL: <http://www.wjgnet.com/1948-9366/full/v2/i6/187.htm> DOI: <http://dx.doi.org/10.4240/wjgs.v2.i6.187>

Abstract

After the first report by Kalloo *et al* on transgastric peritoneoscopy in pigs, it rapidly became apparent that there was no room for an under-evaluated concept and blind adoption of an appealing (r)evolution in minimal access surgery. Systematic experimental work became mandatory before any translation to the clinical setting. Choice and management of the access site, techniques of dissection, exposure, retraction and tissue approximation-sealing were the basics that needed to be evaluated before considering any surgical procedure or study of the relevance of natural orifice transluminal endoscopic surgery (NOTES). After several years of testing in experimental labs, the revolutionary concept of NOTES, is now progressively being experimented on in clinical settings. In this paper the authors analyse the challenges, limitations and solutions to assess how to move from the lab to clinical implementation of transgastric endoscopic cholecystectomy.

INTRODUCTION

Breaching the lumen of a healthy organ to perform an operation without surgical incision raises several scientific and ethical concerns. Preservation of the abdominal wall is the single obvious inherent advantage. Complications related to the breach in organs can be disastrous. After the first report by Kalloo *et al*^[1] on transgastric peritoneoscopy in pigs, it rapidly became apparent that there was no room for an under-evaluated concept and blind adoption of an appealing (r)evolution in minimal access surgery. Systematic experimental work became mandatory before any translation to the clinical setting. Choice and management of the access site, techniques of dissection, exposure, retraction and tissue approximation-sealing were the basics that needed to be evaluated before considering any surgical procedure or study of the relevance of natural orifice transluminal endoscopic surgery (NOTES). The second step was to identify the surgical procedures that would benefit the most from this new approach in terms of

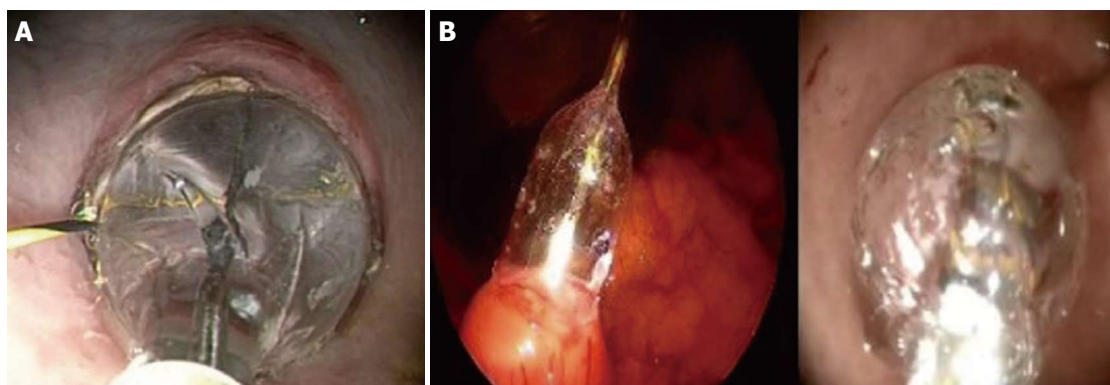


Figure 1 Balloon dilatation of the gastrotomy in the animal model (A) and in a patient (B).

outcome and acceptance by the surgical community. The third step was to analyze the physiological consequences of NOTES and compare it to open and laparoscopic similar operations. Then, once all these issues were overcome, translation to the clinical setting was considered.

In parallel, each of these challenges stimulated technological innovation to overcome the inherent difficulties associated with the utilization of instruments that were originally developed to work inside and not outside the lumen of hollow organs.

In 2005, IRCAD strasbourg established an intensive research program on NOTES. A step by step analysis of the challenges of NOTES was performed. The value and adequacy of the different natural orifices and various surgical procedures were studied. This experimental work provided essential information about the feasibility and potentialities of NOTES and extensive surgical training.

Between 2005 and 2008, over 400 experimental procedures were performed on inanimate models, *ex-vivo* tissues, animal models and human cadavers. A systematic analysis of the steps of the transgastric route was carried out from the introduction of the endoscope into the oropharynx to the closure of the stomach after various surgical procedures. Transgastric cholecystectomy was identified as the procedure that would initiate the translation to humans. Translation from the laboratory to human application is reported.

TRANSGASTRIC ACCESS AND CLOSURE TECHNIQUES

Although most believe that the transgastric route will dominate NOTES in the future, a factor limiting the transgastric route is the lack of a secure and reliable method for creating and closing the gastrotomy required by the procedure. Indeed, creating a gastrotomy from within the stomach requires a blind entry to the peritoneal cavity making it hard to avoid damage to neighbouring structures^[2] and to ensure the gastrotomy is sited in the best possible position.

Several gastrotomy techniques were evaluated and the most used method is based on the established safety of percutaneous endoscopic gastrotomy placement with balloon dilatation^[3]. A flexible wire is passed through the ante-

rior abdominal wall and guides the stomach incision at the level of the antrum and dilatation of the gastrotomy. This method was used extensively in the experimental setting and provided efficient, reliable and reproducible access to the peritoneal cavity.

In the clinical setting, this method of small gastrotomy with guided balloon dilatation was elected. At this point, gastric incision was still a blind manoeuvre and the clinical protocol imposed a visual control of this step. Therefore, transgastric access was obtained under laparoscopic visual control by means of a 5-mm rigid laparoscope introduced in an umbilical trocar^[4]. An endoscopic monopolar needle-knife was used to create a 0.5-cm gastrotomy on the anterior gastric wall in the antrum of the stomach. A guide-wire was passed through the gastrotomy to guide a 18 mm balloon dilator which expanded the gastrotomy and allowed for the passage of the 12 mm gastroscope (KARL STORZ® Endoskope, Germany) (Figure 1). This method was successfully utilized in a series of 11 transgastric cholecystectomies. No bleeding or injuries to adjacent organs were observed.

Closure of the gastrotomy is crucial. There is general agreement that there must be near-zero tolerance for leaks. The ideal closure should be rapid, reproducible and safe, ideally performed under vision to avoid any injury to the adjacent organs and should grant a full thickness bite.

Different methods have been tested in the laboratory^[5-14]. The simple application of current endoclips enables only a single-layer mucosal approximation. In addition, their application might sometimes be difficult due to tangential orientation of the tissue or because of tissue edema. Using two endoscopes to provide layer-by-layer endoscopic clip closure was another alternative that uses current endoscopic instruments^[15]. An original technique using a cardiac septal occluder has demonstrated a zero leak rate^[16]. The system was widely used for survival studies on animal models but it was not transferable to the clinical setting for cost issues and concerns about the long term outcome of the intraperitoneal, non absorbable part of the mechanism made with nitinol.

In patients, the gastrotomy was closed with extracorporeal interrupted 3/0 Vicryl stitches by means of a 2-mm laparoscope and a 3-mm needle holder that were inserted



Figure 2 Retraction of the gallbladder with a laparoscopic micro-instrument introduced in the right hypochondrium.

side by side into the 5 mm umbilical port. Gastroscopy was carried out in order to inspect the closure and to confirm an airtight seal by the attainment of a satisfactory pneumogastrium.

This method of creation and closure of the gastrotomy was successfully used in a series of transgastric cholecystectomies. Neither bleeding nor injuries to adjacent organs were observed. No gastric or biliary leaks occurred.

EXPOSURE AND RETRACTION

Dissection of the critical view of safety is a basic rule for laparoscopic cholecystectomy. This requires retraction of the gallbladder and exposure of the triangle of Calot which cannot be offered by current flexible endoscopes and instrumentation. The different methods experimented with in the laboratory such as retracting needle, suspension thread and T-tags provided adequate exposure thanks to a transparietal element. Magnetic retraction eliminates this necessity but poses several problems in bringing the internal part of the system in the peritoneal cavity and grabbing the gallbladder^[17,18]. The transoral dual scope technique brings more instruments in the peritoneal cavity. A single channel endoscope serves as a surgical assistant and provides retraction of the gallbladder. Another scope performs the dissection and clipping of the pedicle. This method raises several problems in terms of manoeuvrability and tolerance of the oesophagus to the movements of the two endoscopes.

Whilst a transvaginal grasper can be used in a transvaginal cholecystectomy to provide retraction^[19], this is not possible in the transgastric route. Transparietal assistance is obligatory and a micro-laparoscopic grasper was inserted alternatively through the umbilicus or the right hypochondrium in patients (Figure 2).

DISSECTION

Once exposure of the gallbladder is obtained, the dissection can be carried out using exclusively flexible instruments inserted *via* the two working channels of the endoscope (Figure 3). Feasibility of this method has been extensively

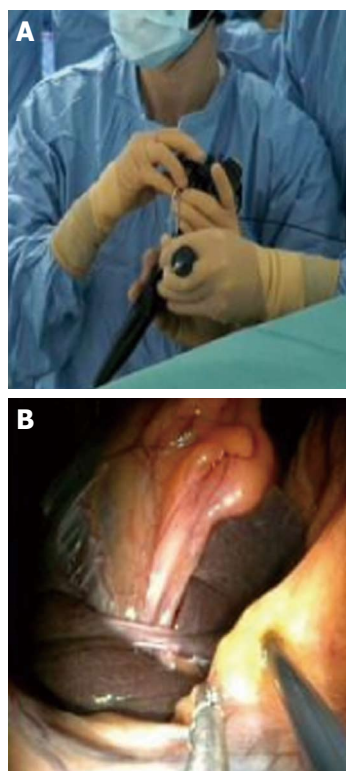


Figure 3 Dissection of the cystic pedicle with a flexible endoscope: “four hands” technique. External view (A) and endoscopic view (B).

studied in the animal model^[17] (Figure 4). However, these instruments are obviously not designed or adapted to perform such tasks and, as a result, the dissection becomes time consuming.

As a laparoscopic trocar was inserted systematically at the umbilicus to monitor the creation of the gastrotomy, the operating time improved dramatically by using standard laparoscopic instruments such as a hook inserted through this trocar which was also necessary for the clip applicator.

TISSUE SEALING

Currently there is no flexible device that can be introduced orally to seal vessels or biliary structures. This is one of the major current limitations of NOTES. Although flexible endoclips have been used successfully in the laboratory, postoperative bleeding was observed in one patient after the description of transvaginal cholecystectomy^[20]. At this point, sealing the cystic duct and artery necessitates a laparoscopic clip applicator introduced through a 5-mm laparoscopic trocar. An alternative is the flexible endoloop whose development was not intended to sealing these elements.

CONTROLLING CONTAMINATION

Controlling contamination is a rather contentious issue. One of the biggest concerns associated with NOTES surgery is the risk of intra-abdominal infection due to intraoperative spillage or *via* inadequate closure of the gastrointestinal

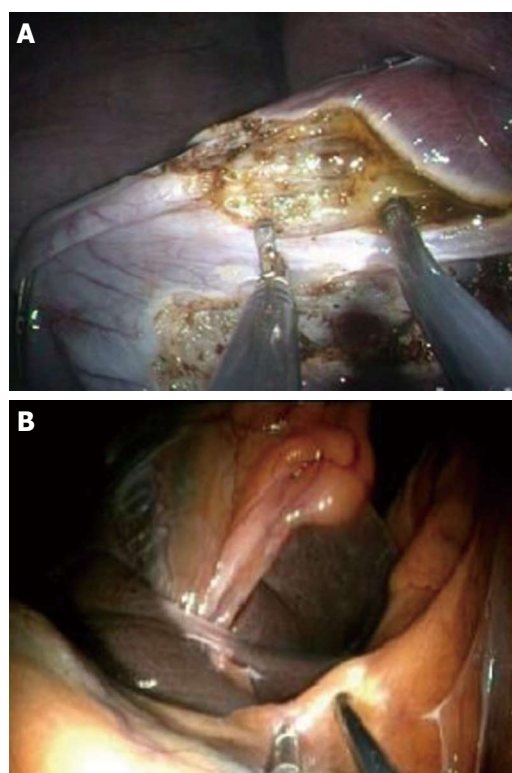


Figure 4 Dissection of the cystic pedicle with a flexible endoscope in the animal model (A) and in a patient (B).

tract. Perforation may occur inadvertently during abdominal surgery as well as endoscopic procedures. This issue has been addressed in studies that investigate the bacterial load and contamination in patients during laparoscopic Roux-en-Y gastric bypass and transgastric staging peritoneoscopy^[21,22]. These findings demonstrated that while transgastric access does contaminate the abdominal cavity, introduced pathogens are clinically insignificant due to species or bacterial load. A systematic study of the bacteria content of peritoneal fluid samples before and after transgastric cholecystectomy confirmed these findings.

EXTRACTION OF SPECIMEN

Extraction of a specimen such as the gallbladder is a minor concern in the animal model. The gallbladder is normal and thin and is passed easily through the gastrotomy and esophagus. In humans, an unexpected limitation of the transgastric access was the size of the gallbladder stones. Indeed, if passage inside the stomach is not a real problem, large stones may cause esophageal laceration when the gallbladder is extracted through the mouth. A maximum size of 20 mm seems to be the upper limit and fragmentation of large stones may be challenging in a NOTES setting.

TRANSGASTRIC CHOLECYSTECTOMY IN HUMAN BEINGS

From September 2007 to June 2009, 11 patients (7 men

and 4 women) with a mean age of 48.5 years (range 28-65 years) and a mean BMI of 23.3 (range: 21-31) were enrolled in the study. Three patients had a past surgical history of appendectomy and one of hysterectomy.

All procedures were completed using a hybrid approach with a 5-mm umbilical trocar. In one patient, there was a need to switch to a laparoscopic procedure (conversion) because of lack of exposure of the triangle of calot.

Transgastric peritoneal access was achieved without complication or injury to adjacent organs. The site chosen for the creation of the gastrotomy was the gastric antrum in all patients to facilitate access to the right hypochondrium and the gallbladder. Additional transparietal assistance was mandatory in all patients to retract the gallbladder and to achieve a safe exposure of Calot's triangle. Dissection of the gallbladder was completely achieved with flexible endoscopic instruments in 2 patients while a combination with laparoscopic hook dissector was used in the other patients. A 5-mm laparoscopic clip applier was systematically used to secure the cystic pedicle. Single port gastric closure was successfully achieved in 10/11 patients. One patient required an additional 5 mm trocar because of technical failure of the instrumentation.

No trauma, vascular or biliary injury to the adjacent organs occurred during the procedure.

The mean operative time was 132 min (range 90-180 min) and this was mainly due to the longer time needed to accomplish the dissection of the gallbladder and closure of the gastrotomy without any new dedicated technology.

All patients recovered promptly. Postoperative pain evaluated using the VAS, Visual Analog Scale, a tool that allows to objectify pain intensity on a 0-10 scale (0 being no pain, 10 being extreme pain), was 2/10 at 24 h and 0/10 at 48 h under usual immediate postoperative analgesia with paracetamol. One patient required additional analgesia with morphine on day 1. They were allowed fluids the very evening of the procedure and resumed a normal diet on the first postoperative day. No gastric or biliary leaks occurred. Mean hospital stay was 2 d (range 2-3 d). The bacteriological analysis of the peritoneal aspirates showed no significant contamination of the peritoneal cavity for both aerobic and non-aerobic species. One patient was readmitted 8 d after the operation for epigastric pain. Workup, including gastroscopy, did not reveal any complications.

PERSPECTIVE AND FUTURE PROSPECTS

One of the most frequent criticisms of laparoscopy in the early 1990s was the absence of scientific background based on experimental work and the fact that the majority of surgeons entered this new surgical approach without any previous training. One of the most popular and frequent operations, cholecystectomy, rapidly became the procedure to be done laparoscopically. There was no scientific evidence of the superiority of the laparoscopic approach over the open operation but every single surgeon thought that if he was not performing laparoscopic surgery he would be brought off a market driven and largely supported by

the industry. Some years later, it became evident that the rate of iatrogenic injuries of the biliary tract had more than doubled compared to open surgery. This finding stimulated the surgical scientific community and teaching programs were started all over the world. Scientific societies were created to drive education and training and stimulate scientific support and criticism. Guidelines were established.

Twenty years later, after the first report on transgastric peritoneoscopy using a flexible endoscope, the lesson was learned. There was no question about starting this new technique in a clinical setting without a strong and systematic evaluation of the feasibility and safety of the technique and consistent training in the laboratory. Scientific societies reacted immediately and organized joint associations between gastroenterologists and laparoscopic surgeons which proposed prerequisites and guidelines for experimental development and clinical implementation^[23].

An extensive research program was developed in IRCAD Strasbourg to evaluate the feasibility and potential of NOTES. The numerous challenges generated an impressive number of experiments that provided endoscopic and surgical training to gastroenterologists and surgeons involved in the program. All natural orifice access and potential surgical procedures were reviewed and studied^[24-31]. Transgastric access was the most widely used and several surgical applications were tested. Cholecystectomy was then defined as the application that would be transferred to human application.

Various transgastric surgical procedures *via* natural orifices have proven to be feasible in animal models. Survival studies on cholecystectomy were a prerequisite before clinical implementation^[17]. These procedures are technically challenging given the current instrumentation that is available. The choice of the adequate gastric exit site and the creation and closure of the gastrotomy are all parameters that still need to be standardized. An additional challenge is obtaining adequate spatial orientation and retraction with the endoscope in a retroflexed position when the image is upside down and an off-axis manipulation is required^[32]. Although some of this spatial incongruity can be overcome with experience and exposure, interpretation of the anatomy and identification of the structural landmarks are still quite challenging. In cholecystectomy, one of the major limitations is to obtain satisfactory exposure of the gallbladder and Calot's triangle. Research programs have identified possible solutions but none is currently available for clinical application^[18]. So transparietal assistance is still mandatory. These "hybrid" techniques are a cross between NOTES and laparoscopy.

The passage to the clinical setting relied on the experimental work and the surgical steps reproduced closely the techniques that were performed many times in the laboratory: creation of the gastrotomy, introduction of the endoscope in the peritoneal cavity, exposure of the gallbladder and technique of dissection with the flexible double channel endoscope^[4]. For obvious safety reasons, all these steps were completed under the surveillance and

assistance of a 5-mm umbilical trocar. Indeed, clipping of the cystic elements and closure of the gastrotomy were achieved with laparoscopic instruments. In two of our patients, a laparoscopic view was necessary to verify the biliary anatomy that was not clearly understood. One of the lessons of this experience is that there can be some distortion of the anatomical landmarks related to a different angle of view.

Bacterial contamination of the abdomen was also of great concern. The peritoneal fluid samples taken before and after the gastrotomy's closure did not reveal any significant contamination of the peritoneal cavity and no clinical infection occurred. These findings confirm the results reported by Narula *et al*^[21,22] who investigated the bacterial load and contamination in patients during laparoscopic Roux-en-Y gastric bypass and transgastric diagnostic peritoneoscopy.

Finally, an unsuspected limitation of the transgastric cholecystectomy technique may be related to the size of the gallstone which should not be over 20 mm in diameter. Retrieval of larger stones, although feasible by enlarging the gastrotomy, could result in impaction and/or injury of the oesophagus and oro-pharynx. In one patient we had to change the 5 mm umbilical trocar to a 10-mm one to extract the gallbladder containing a 25-mm stone. In all but this patient, the gallbladder was extracted orally through the gastrotomy. No complications occurred during our initial clinical series and this is more than probably related to the intensive training program in the laboratory.

CONCLUSION

Although NOTES hybrid techniques seem to diverge from the philosophy pursued at the beginning in the lab, they have the great merit of allowing the application of this revolutionary approach in clinical settings to explore the potential benefits for patients waiting for technological development that will facilitate the performance of pure NOTES "no scar surgery".

REFERENCES

- 1 **Kalloor AN**, Singh VK, Jagannath SB, Niiyama H, Hill SL, Vaughn CA, Magee CA, Kantsevov SV. Flexible transgastric peritoneoscopy: a novel approach to diagnostic and therapeutic interventions in the peritoneal cavity. *Gastrointest Endosc* 2004; **60**: 114-117
- 2 **Sohn DK**, Turner BG, Gee DW, Willingham FF, Sylla P, Cizginer S, Konuk Y, Brugge WR, Rattner DW. Reducing the unexpectedly high rate of injuries caused by NOTES gastrotomy creation. *Surg Endosc* 2010; **24**: 277-282
- 3 **Sumiyama K**, Gostout CJ. Techniques for transgastric access to the peritoneal cavity. *Gastrointest Endosc Clin N Am* 2008; **18**: 235-244; vii
- 4 **Dallemagne B**, Perretta S, Allemann P, Asakuma M, Marescaux J. Transgastric hybrid cholecystectomy. *Br J Surg* 2009; **96**: 1162-1166
- 5 **Dray X**, Giday SA, Buscaglia JM, Gabrielson KL, Kantsevov SV, Magno P, Assumpcao L, Shin EJ, Reddings SK, Woods KE, Marohn MR, Kalloor AN. Omentoplasty for gastrotomy closure after natural orifice transluminal endoscopic surgery procedures (with video). *Gastrointest Endosc* 2009; **70**: 131-140

- 6 **Katsarelis D**, Polydoru A, Tsaroucha A, Pavlakis E, Dedemadi G, Pistiolis L, Karakostas N, Kondi-Paphiti A, Mallas E. Endoloop application as an alternative method for gastrotomy closure in experimental transgastric surgery. *Surg Endosc* 2007; **21**: 1862-1865
- 7 **Magno P**, Giday SA, Dray X, Chung SS, Cotton PB, Gostout CJ, Hawes RH, Kalloo AN, Pasricha PJ, White JJ, Assumpcao L, Marohn MR, Gabrielson KL, Kantsevov SV. A new stapler-based full-thickness transgastric access closure: results from an animal pilot trial. *Endoscopy* 2007; **39**: 876-880
- 8 **McGee MF**, Marks JM, Jin J, Williams C, Chak A, Schomisch SJ, Andrews J, Okada S, Ponsky JL. Complete endoscopic closure of gastric defects using a full-thickness tissue plicating device. *J Gastrointest Surg* 2008; **12**: 38-45
- 9 **Meireles OR**, Kantsevov SV, Assumpcao LR, Magno P, Dray X, Giday SA, Kalloo AN, Hanly EJ, Marohn MR. Reliable gastric closure after natural orifice transluminal endoscopic surgery (NOTES) using a novel automated flexible stapling device. *Surg Endosc* 2008; **22**: 1609-1613
- 10 **Sporn E**, Bachman SL, Miedema BW, Loy TS, Calaluze R, Thaler K. Endoscopic colotomy closure for natural orifice transluminal endoscopic surgery using a T-fastener prototype in comparison to conventional laparoscopic suture closure. *Gastrointest Endosc* 2008; **68**: 724-730
- 11 **Trunzo JA**, Mcgee MF, Cavazzola L. A Comparison of Three Endoscopic Suturing Devices for Natural Orifice Transluminal Endoscopic Surgery Gastrotomy Closure. *Gastrointest Endosc* 2009; **69**: AB304
- 12 **Voermans RP**, Worm AM, van Berge Henegouwen MI, Breedveld P, Bemelman WA, Fockens P. In vitro comparison and evaluation of seven gastric closure modalities for natural orifice transluminal endoscopic surgery (NOTES). *Endoscopy* 2008; **40**: 595-601
- 13 **von Renteln D**, Schmidt A, Vassiliou MC, Gieselmann M, Caca K. Natural orifice transluminal endoscopic surgery gastrotomy closure with an over-the-endoscope clip: a randomized, controlled porcine study (with videos). *Gastrointest Endosc* 2009; **70**: 732-739
- 14 **Chiu PW**, Lau JY, Ng EK, Lam CC, Hui M, To KF, Sung JJ, Chung SS. Closure of a gastrotomy after transgastric tubal ligation by using the Eagle Claw VII: a survival experiment in a porcine model (with video). *Gastrointest Endosc* 2008; **68**: 554-559
- 15 **Asakuma M**, Perretta S, Cahill RA, Solano C, Pasupathy S, Dallemagne B, Tanigawa N, Marescaux J. Peroral dual scope for natural orifice transluminal endoscopic surgery (NOTES) gastrotomy closure. *Surg Innov* 2009; **16**: 97-103
- 16 **Perretta S**, Sereno S, Forgione A, Dallemagne B, Coumaros D, Boosfeld C, Moll C, Marescaux J. A new method to close the gastrotomy by using a cardiac septal occluder: long-term survival study in a porcine model. *Gastrointest Endosc* 2007; **66**: 809-813
- 17 **Perretta S**, Dallemagne B, Coumaros D, Marescaux J. Natural orifice transluminal endoscopic surgery: transgastric cholecystectomy in a survival porcine model. *Surg Endosc* 2008; **22**: 1126-1130
- 18 **Scott DJ**, Tang SJ, Fernandez R, Bergs R, Goova MT, Zeltser I, Kehdy FJ, Cadeddu JA. Completely transvaginal NOTES cholecystectomy using magnetically anchored instruments. *Surg Endosc* 2007; **21**: 2308-2316
- 19 **Forgione A**, Maggioni D, Sansonna F, Ferrari C, Di Lernia S, Citterio D, Magistro C, Frigerio L, Pugliese R. Transvaginal endoscopic cholecystectomy in human beings: preliminary results. *J Laparoendosc Adv Surg Tech A* 2008; **18**: 345-351
- 20 **Marescaux J**, Dallemagne B, Perretta S, Wattiez A, Mutter D, Coumaros D. Surgery without scars: report of transluminal cholecystectomy in a human being. *Arch Surg* 2007; **142**: 823-826; discussion 826-827
- 21 **Narula VK**, Happel LC, Volt K, Bergman S, Roland JC, Dettorre R, Renton DB, Reavis KM, Needleman BJ, Mikami DJ, Ellison EC, Melvin WS, Hazey JW. Transgastric endoscopic peritoneoscopy does not require decontamination of the stomach in humans. *Surg Endosc* 2009; **23**: 1331-1336
- 22 **Narula VK**, Hazey JW, Renton DB, Reavis KM, Paul CM, Hinshaw KE, Needleman BJ, Mikami DJ, Ellison EC, Melvin WS. Transgastric instrumentation and bacterial contamination of the peritoneal cavity. *Surg Endosc* 2008; **22**: 605-611
- 23 **Rattner D**, Kalloo A. ASGE/SAGES Working Group on Natural Orifice Transluminal Endoscopic Surgery. October 2005. *Surg Endosc* 2006; **20**: 329-333
- 24 **Allemann P**, Perretta S, Asakuma M, Dallemagne B, Mutter D, Marescaux J. Multimedia manuscript. NOTES retroperitoneal transvaginal distal pancreatectomy. *Surg Endosc* 2009; **23**: 882-883
- 25 **Allemann P**, Perretta S, Marescaux J. Surgical access to the adrenal gland: the quest for a "no visible scar" approach. *Surg Oncol* 2009; **18**: 131-137
- 26 **Cahill RA**, Asakuma M, Perretta S, Dallemagne B, Marescaux J. Gastric lymphatic mapping for sentinel node biopsy by natural orifice transluminal endoscopic surgery (NOTES). *Surg Endosc* 2009; **23**: 1110-1116
- 27 **Cahill RA**, Perretta S, Leroy J, Dallemagne B, Marescaux J. Lymphatic mapping and sentinel node biopsy in the colonic mesentery by Natural Orifice Transluminal Endoscopic Surgery (NOTES). *Ann Surg Oncol* 2008; **15**: 2677-2683
- 28 **Leroy J**, Cahill RA, Perretta S, Forgione A, Dallemagne B, Marescaux J. Natural orifice transluminal endoscopic surgery (NOTES) applied totally to sigmoidectomy: an original technique with survival in a porcine model. *Surg Endosc* 2009; **23**: 24-30
- 29 **Nassif J**, Zacharopoulou C, Wattiez A. Staging of gynaecological malignancies by natural orifice transluminal endoscopic surgery (N.O.T.E.S.). *Surg Oncol* 2009; **18**: 147-152
- 30 **Perretta S**, Allemann P, Asakuma M, Dallemagne B, Marescaux J. Adrenalectomy using natural orifice transluminal endoscopic surgery (NOTES): a transvaginal retroperitoneal approach. *Surg Endosc* 2009; **23**: 1390
- 31 **Perretta S**, Allemann P, Dallemagne B, Marescaux J. Natural orifice transluminal endoscopic surgery (N.O.T.E.S.) for neoplasia of the chest and mediastinum. *Surg Oncol* 2009; **18**: 177-180
- 32 **Swanstrom L**, Zheng B. Spatial orientation and off-axis challenges for NOTES. *Gastrointest Endosc Clin N Am* 2008; **18**: 315-324; ix

S- Editor Wang JL L- Editor Roemmele A E- Editor Yang C

Antonello Forgione, MD, PhD, MBA, Series Editor

Current experience and future directions of completely NOTES colorectal resection

Patricia Sylla

Patricia Sylla, Department of Surgery, Massachusetts General Hospital, 15 Parkman Street, WACC 460, Boston, MA 02114, United States

Author contributions: Sylla P contributed solely to this review. Correspondence to: Patricia Sylla, MD, Department of Surgery, Massachusetts General Hospital, 15 Parkman Street, WACC 460, Boston, MA 02114, United States. psylla@partners.org

Telephone: +1-617-7261893 Fax: +1-617-7240355

Received: December 26, 2009 Revised: January 28, 2010

Accepted: February 4, 2010

Published online: June 27, 2010

Abstract

Clinical implementation and widespread application of natural orifice transluminal surgery (NOTES) has been limited by the lack of specialized endoscopic equipment, which has prevented the ability to perform complex procedures including colorectal resections. Relative to other types of transluminal access, transanal NOTES using transanal endoscopic microsurgery (TEM) provides a stable platform for endolumenal and direct transluminal access to the peritoneal cavity, and specifically to the colon and rectum. Completely NOTES transanal rectosigmoid resection using TEM, with or without transgastric endoscopic assistance, was demonstrated to be feasible and safe in a swine survival model. The same technique was successfully replicated in human cadavers using commercially available TEM, with endoscopic and laparoscopic instrumentation. This approach also permitted complete rectal mobilization with total mesorectal excision to be performed completely transanally. As in the swine model, transgastric and/or transanal endoscopic assistance extended the length of proximal colon mobilized and overcame some of the difficulties with TEM dissection including limited endoscopic visualization and maladapted instrumentation. This extensive laboratory experience with NOTES transanal rectosigmoid resection served as the basis for the first human NOTES transanal rectal cancer excision using

TEM and laparoscopic assistance. Based on this early clinical experience, NOTES transanal approach using TEM holds significant promise as a safe and substantially less morbid alternative to conventional colorectal resection in the management of benign and malignant colorectal diseases. Careful patient selection and substantial improvement in NOTES instrumentation are critical to optimize this approach prior to widespread clinical application, and may ultimately permit completely NOTES transanal colorectal resection.

© 2010 Baishideng. All rights reserved.

Key words: Colorectal diseases; Transanal endoscopic microsurgery; Natural orifice transluminal endoscopic surgery

Peer reviewers: Wai Lun Law, MS, FRCS, FACS, Professor, Chief, Division of Colorectal Surgery, Queen Mary Hospital, The University of Hong Kong, Pokfulam Road, Hong Kong, China; Marcus Vinicius Motta Valadão, MD, Instituto Nacional de Câncer, Hospital do Câncer Unidade I, Hc2, Rua do Equador 831, Santo Cristo, Rio de Janeiro 20220-410, RJ, Brasil

Sylla P. Current experience and future directions of completely NOTES colorectal resection. *World J Gastrointest Surg* 2010; 2(6): 193-198 Available from: URL: <http://www.wjgnet.com/1948-9366/full/v2/i6/193.htm> DOI: <http://dx.doi.org/10.4240/wjgs.v2.i6.193>

INTRODUCTION

Since the report of the first human transgastric endoscopic appendectomy in India in 2004, natural orifice transluminal surgery (NOTES) has represented the next step in the evolution of minimally invasive surgery since laparoscopy. Given the right transluminal route, endoscopic platform and instrumentation, surgical procedures ranging in complexity from cholecystectomy to colorectal resections could

theoretically be performed entirely endoscopically without the need for abdominal incisions^[1,2]. The advantages of such an approach include reduced incisional pain, decreased wound complications including infection and hernias, improved cosmetic results, and faster recovery and return to work. Until recently, endoscopic access to the abdominal cavity using transoral/transgastric route was the most intensely investigated type of transluminal access. However, this type of access has been hampered by difficulties in achieving easily reproducible and secure gastrotomy closure. Over the last few years, significant effort has been spent exploring alternate access routes such as transesophageal, transvaginal, transvesical and transcolonic/transanal access. Of all these approaches, transvaginal access has become the preferred type of access for NOTES procedures and has rapidly evolved from the experimental setting to human application with the first human cases described in 2007^[3,4]. The international experience now counts several hundred cases of successfully performed hybrid transvaginal NOTES procedures including cholecystectomy, nephrectomy, and sleeve gastrectomy^[5-9]. Access through and closure of the vagina is routinely performed by gynecologists, and when performed to access the peritoneal cavity for NOTES procedures, it is relatively safe. Downsides of this approach include the fact that it is restricted to female patients. The long-term effects of vaginal access have not yet been investigated.

ADVANTAGES OF TRANSCOLONIC/ TRANSANAL NOTES ACCESS

Relative to other types of transluminal access, transcolonic/transanal NOTES has been described in few reports, mainly due to concerns related to fecal contamination of the abdominal cavity and the potential for infectious complications. The first reports described transcolonic peritoneoscopy^[10,11] ($n = 6$) and cholecystectomy^[12] ($n = 5$) in swine survival models with septic complications occurring in 1 animal (9%) following incomplete closure of the anterior colotomy^[12]. Subsequent reports have described transcolonic surgical procedures of increasing complexity such as ventral hernia repair^[13] and distal pancreatectomy^[14] in survival swine models with good results. The cited advantages of the transrectal approach include the relative ease of colotomy creation and closure, and the ability to visualize abdominal organs in line with the endoscope without the need for retroflexion^[13,14]. All authors agree that the viability of this approach relies on the adequacy of the colotomy closure, with the incidence of septic complications directly correlating with the integrity of the closure.

Another advantage of NOTES transcolonic/transanal access to the peritoneal cavity is the current availability of a specialized platform to perform endorectal and transrectal procedures. As described by Wilhelm *et al*^[10], transcolonic peritoneoscopy is facilitated by the use of the transanal endoscopic microsurgery (TEM) platform through which specialized instruments can be introduced. TEM was first introduced in 1983 as a technique to excise mid- to high

rectal adenomas not amenable to colonoscopic or transanal resection due to location, size, or risk of incomplete resection or colonic perforation. The platform consists of a 4-cm wide rigid beveled proctoscope sealed with a face plate with several air-tight ports through which an angled scope and adapted dissecting instruments can be inserted and CO₂ insufflated to distend the rectum and create a working space. TEM permits precise endoscopic mucosal or full-thickness excision of mid- and high rectal lesions following which the rectal defect can be closed with a suturing device. It represents an attractive minimally invasive alternative to more radical resection of solitary rectal ulcers, adenomas and carcinoid tumors as well as early rectal cancers^[15].

Based on series published over the past two decades, conversion rates to open surgery during TEM procedures have remained below 1% with a less than 5% incidence of major complications^[16]. The latter include inadvertent entry into the peritoneal cavity during full-thickness excision of high rectal lesions located above the peritoneal reflection^[17]. While this occurrence was originally considered a major complication of TEM and was managed by conversion to laparotomy in an effort to prevent intraabdominal infection^[18], a study comparing the morbidity associated with full-thickness excision with and without peritoneal entry in 34 TEM full-thickness excisions demonstrated that in all 11 cases where the peritoneal cavity was inadvertently entered and subsequently closed, no infectious complications were noted^[19]. In addition, no significant differences in the complication rates were noted between the groups with or without peritoneal entry^[19]. These results strongly support the concept that purposeful entry into the peritoneal cavity during transcolonic/transanal NOTES procedures is safe, granted adequate closure of the enterotomy can be achieved.

Despite these findings, most surgeons remain significantly more reluctant to puncture the colon or rectum than the vagina to perform intraabdominal NOTES procedures. With regards to the applicability of NOTES in the field of colorectal surgery however, transcolonic/transanal access is intuitively better suited than other access routes. First, rather than creating an opening through an otherwise healthy organ to perform transgastric and transvaginal cholecystectomy, the enterotomy is created through the diseased organ itself. Second, the enterotomy created is ultimately closed by incorporating it into a standard colorectal anastomosis, which would be required regardless of whether the procedure was achieved *via* NOTES or standard surgery. Finally, a NOTES approach can be anticipated to have substantial benefits over a standard transabdominal approach. Despite significantly reducing incisional pain and recovery time relative to open surgery, standard and single port laparoscopic colorectal resections still require one or more sizeable abdominal incisions to exteriorize specimens, with various degrees of incisional pain and substantial incidence of short and long-term wound complications. Based on the published colorectal literature comparing outcomes following perineal proctosigmoidectomy *vs* abdominal approaches in the

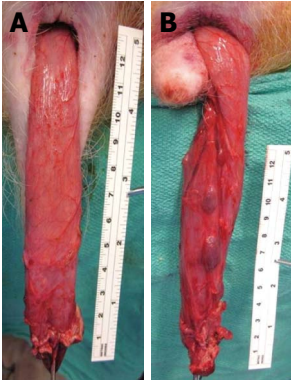


Figure 1 Transanal exteriorization of the rectosigmoid colon mobilized using transanal endoscopic microsurgery (TEM) only (A), and TEM with transgastric endoscopic assistance (B) in a swine survival model. Transgastric endoscopic assistance significantly increased the length of specimen that could be mobilized transanally.

management of full-thickness rectal prolapse, perineal repair is associated with a higher incidence of recurrence but significantly less pain and peri- and postoperative morbidity^[20]. Hence, the potential benefits of a transanal NOTES approach over standard colorectal resections can be extrapolated from this experience, particularly if a pure transanal endoscopic approach can be used.

TRANSCOLONIC/TRANSANAL NOTES COLORECTAL RESECTION: EXPERIMENTAL EVIDENCE

Radical sigmoidectomy using a pure NOTES transanal approach was first described in 3 human cadavers in 2007 by Whiteford *et al*^[21] who used TEM as an endoscopic platform without the need for any abdominal incisions. Although adequate colon and mesenteric dissection could be achieved transanally, the authors were limited in the length of sigmoid colon that could be mobilized due to difficulties in overcoming the acute angle at the sacral promontory with TEM instrumentation. Based on this preliminary experience, a pure transanal NOTES approach to colorectal resection was further investigated in an experimental model using swine. In a pilot study using swine cadavers and non-survival animals, transanal endoscopic rectosigmoid resection using TEM could be replicated in that model^[22]. Purse String closure of the distal rectum at the start of the procedures was effective at preventing fecal outflow and contamination during the procedure. Following full-thickness incision of the rectal wall, the presacral space could be entered and circumferential *en-bloc* resection of the rectosigmoid colon and its mesentery could be performed endoscopically. The peritoneal reflection was reached and the peritoneal cavity entered, and dissection of the sigmoid was continued proximally until further advancement of the proctoscope into the pelvis was limited by the narrow size of the swine pelvis. The colon was subsequently pulled out through the anus, transected, and stapled colorectal anastomosis was performed. In an attempt to overcome

difficulties negotiating the sharp angle of the sacral promontory and narrow swine pelvis, dual transanal and transgastric endoscopic access was used to improve visualization, retraction, and mobilization of the proximal colon. Relative to a transanal approach alone, combined transgastric and transanal endoscopic dissection prolonged operative time but permitted additional length of sigmoid colon to be mobilized and resected transanally^[22].

The safety of this NOTES approach was recently demonstrated in a 2-wk survival study using 20 swine that evaluated and compared outcomes of pure transanal endoscopic rectosigmoid resection versus combined transanal and transgastric rectosigmoid resection^[23]. All procedures were completed successfully without transabdominal assistance and pneumoperitoneum was closely monitored and titrated intraoperatively using the CO₂ insufflator connected to the TEM platform. There were no mortalities in either group and two major complications were noted at necropsy in the combined transanal/transgastric group which included an abdominal abscess and abdominal wall hematoma resulting from a T-tag misfire during gastrotomy closure. Again, combined transgastric and transanal endoscopic rectosigmoid mobilization was demonstrated to significantly prolong the operative time but extend the length of rectosigmoid mobilized transanally (Figure 1), where transgastric endoscopic assistance extended the average length of specimen mobilized by 54% and resected by 45% relative to a pure transanal NOTES approach^[23]. All specimens resected were grossly intact with respect to the integrity of the colonic wall, attached mesentery and lymph nodes (Figure 1), which suggests that this approach could be a viable alternative to open or laparoscopic rectosigmoid resection in the clinical setting.

An alternative NOTES approach to sigmoid resection that also combines transgastric and transcolonic access was described by Leroy *et al*^[24] and shown to be both feasible and safe in a 2-wk survival study using 5 swine. Endolumenal access was used to retract the colon during transgastric endoscopic sigmoid dissection, and introduce the anvil of the circular stapler into the proximal colon. Transcolonic access was subsequently obtained to introduce an endoscopic linear stapler into the peritoneal cavity and divide the colon. Of note, a transabdominal Berci needle (2.7 mm) was still required to establish and monitor pneumoperitoneum and to assist with anvil positioning during completion of the intracorporeal stapled anastomosis^[24].

TRANSCOLONIC/TRANSANAL NOTES COLORECTAL RESECTION: TRANSITIONING TO CLINICAL PRACTICE

In preparation for transitioning to human application, the same completely NOTES approach described in swine was successfully replicated in human cadavers using commercially available TEM, laparoscopic and NOTES instrumentation. In a series of 7 male and female cadavers, our group demonstrated that transanal NOTES rectosig-

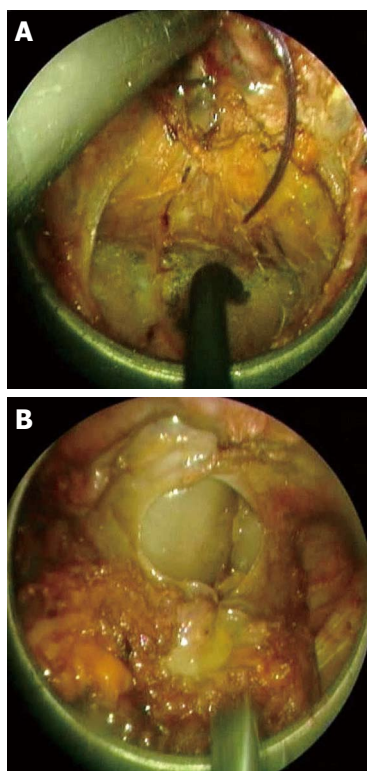


Figure 2 Transanal endoscopic rectal dissection using TEM in a male human cadaver. A: Following full-thickness transection of the rectal wall, the presacral plane was entered posteriorly and total mesorectal excision was completed; B: Following mobilization of the anterior rectal wall from the posterior aspect of the prostate, the peritoneal cavity was entered.

moid resection could be achieved using the same steps as described in swine, with the added benefit of being able to complete a totally endoscopic mesorectal excision transanally with TEM^[25]. Circumferential dissection of the rectum was initiated at the level of the anorectal ring, above the anal sphincter complex, and posterior entry into the presacral space with mesorectal dissection was greatly facilitated by CO₂ insufflation and the use of flexible instruments (Figure 2A). Following posterior and lateral dissection of the rectum and mesorectum, the peritoneal reflection was divided after carefully mobilizing the posterior vagina or prostate from the anterior rectal wall (Figure 2B). Once the peritoneal cavity was entered, more cephalad colon mobilization required longer and more flexible optics and instruments to improve visualization of pelvic and abdominal structures and provide effective bowel retraction, tissue manipulation, vascular division and hemostasis respectively.

Commercially available TEM, laparoscopic, single-port and endoscopic instrumentation is currently maladapted for this type of NOTES approach and is the major limiting factor for achieving more proximal colon mobilization and splenic flexure takedown transanally. Combining transgastric and/or transanal endoscopic assistance by inserting flexible endoscopes through a gastrotomy and/or the TEM faceplate, was found to overcome some of those technical limitations by improving endoscopic visualiza-

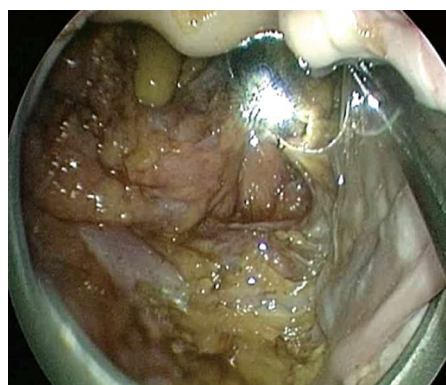


Figure 3 Transanal endoscopic mobilization of the rectosigmoid colon using TEM with combined transgastric endoscopic assistance in a human cadaver. A double channel colonoscope was inserted transgastrically and used to help dissect the peritoneal attachments of the sigmoid colon.



Figure 4 Specimen exteriorization following transanal endoscopic mobilization of the rectosigmoid colon using TEM in a male human cadaver. Total mesorectal excision and sigmoid mesenteric dissection could be achieved.

tion and assisting with endoscopic dissection (Figure 3). Overall, the average length of rectosigmoid colon mobilized transanally in this series of 7 human cadavers was 38.7 cm (range, 15-75 cm, Figure 4)^[25]. Other important technical limitations encountered with this approach in this model include morbid obesity and adhesions from prior abdominal or pelvic surgery. Both factors were found to markedly increase the difficulty of the dissection, risk of bowel perforation, and limit the proximal extent of colon mobilized^[25].

Although the experimental experience described has demonstrated that transgastric access and gastrotomy closure using T-tags is feasible and safe in a survival study in swine, the consensus remains that until significant technological improvements are made to standardize techniques for and ensure safety of gastrotomy closure, early clinical application of NOTES rectosigmoid resection should employ either pure transanal endoscopic access or a hybrid approach with laparoscopic assistance. This will ensure that the procedures are performed safely, are technically easier to perform during the steep portion of the learning curve, and simpler to standardize for potential widespread application. In addition, all NOTES colorectal procedures should be performed under IRB protocol at centers with experience with NOTES and TEM.

TRANSCOLONIC/TRANSANAL NOTES: HUMAN EXPERIENCE

In addition to the growing international experience with single-port laparoscopic colorectal resection, laparoscopic colorectal resection using transrectal assistance, where transrectal access is used for specimen extraction^[26], insertion of the anvil of a circular stapler for intracorporeal double-stapled anastomosis^[27,28], or both^[29] has been described. Transvaginal access has also been used as an extraction site following colorectal resection^[30] as well part of a hybrid NOTES laparoscopic rectosigmoid dissection^[31] where significant portions of the dissection are performed transvaginally.

A pure NOTES approach to colorectal resection, either using transvaginal or transanal/transcolonic access, has not been reported to date. However, the first clinical case of a NOTES transanal resection for rectal cancer using TEM and laparoscopic assistance was just recently performed at the Hospital Clinic in Barcelona^[32]. After obtaining institutional review board approval, transanal endoscopic rectal resection with total mesorectal excision using the TEM platform was performed in a 76-year-old female with a T2N1 mid-rectal cancer treated with preoperative chemoradiation. Laparoscopic visualization and assistance with retraction and exposure during rectosigmoid mobilization was provided through one 5-mm right lower quadrant port which was later used as the stoma site for a diverting loop ileostomy and two 2-mm needle ports, one of which was later used as a drain site. The specimen was transected transanally followed by hand-sewn coloanal anastomosis. The total procedure time was under 5 h, the patient's recovery was uneventful, and she was discharged on the fifth postoperative day. The final pathology demonstrated a ypT1N0 tumor with intact mesorectum that included 23 negative lymph nodes and negative proximal, distal and radial margins^[32].

TRANSCOLONIC/TRANSANAL NOTES COLORECTAL RESECTION: FUTURE DIRECTIONS

Based on this first clinical report, NOTES transanal endoscopic rectal cancer resection using TEM appears to be feasible and safe in the clinical setting. Careful patient selection with respect to pathology and patient characteristics will be critical for the technical success of these procedures. Major rate-limiting factors in the widespread applicability of this approach include: (1) the lack of specialized equipment required to perform transanal NOTES procedures; and (2) experience with TEM and advanced endoscopic skills. Until substantial improvement in NOTES instrumentation is made to optimize this approach, these procedures should be completed under laparoscopic assistance.

With respect to indications for transanal NOTES procedures, this approach is an attractive minimally invasive

alternative for the management of benign and pre-malignant lesions of the rectum and sigmoid colon such as large unresectable polyps, dysplastic lesions, and resectable cancers of the rectum. Complete or partial mesorectal excision with lymph node sampling can be achieved, which is a significant advantage relative to transanal local excisions and TEM. Because this approach involves initial full-thickness circumferential rectal and mesorectal dissection starting 4-5 cm from the anal verge, patients selected for this approach should have clear indications for low anterior resection with a low colorectal anastomosis, which is associated with a worse functional outcome than if the rectum was preserved. This is particularly important when evaluating patients with benign pathology. The potential deleterious effect of prolonged placement of the 4-cm wide TEM platform on anal sphincter function and fecal continence will also need to be investigated. With respect to potential oncologic applications of this approach in rectal cancer, although our experience with human cadavers and this first clinical case demonstrate that an adequate oncologic rectal resection can be achieved, the long-term oncologic outcomes of this approach, in terms of local recurrence and survival, need to be formally evaluated. Until such results are available, this approach for rectal cancer should be considered investigational and be performed under IRB protocol by colorectal surgeons with extensive NOTES and TEM experience.

CONCLUSION

Review of the experimental evidence to date suggests that completely NOTES rectosigmoid resection using transanal access with TEM with or without transgastric endoscopic assistance, is feasible and safe. The importance of developing better adapted tools such as a modified flexible transanal endoscopic platform, longer and more flexible dissecting instruments, and staplers and hemostatic devices to permit safe completion of these procedures without the need for transabdominal assistance is critical. As demonstrated with the clinical case of NOTES transanal rectal cancer resection using TEM, laparoscopic assistance is currently needed to compensate for the limitations in NOTES instrumentations and to ensure safety. Based on this preliminary clinical experience, NOTES transanal approach with TEM has significant potential applications in the treatment of both benign and malignant colorectal diseases, as well as potential advantages over conventional colorectal resection. With respect to oncologic applications, careful patient selection is critical and oncologic outcomes will need to be followed closely.

REFERENCES

- 1 **Rattner D**, Kalloo A. ASGE/SAGES Working Group on Natural Orifice Translumenal Endoscopic Surgery. October 2005. *Surg Endosc* 2006; **20**: 329-333
- 2 **ASGE, SAGES**. ASGE/SAGES Working Group on Natural Orifice Translumenal Endoscopic Surgery White Paper October 2005. *Gastrointest Endosc* 2006; **63**: 199-203

- 3 **Marescaux J**, Dallemagne B, Perretta S, Wattiez A, Mutter D, Coumaros D. Surgery without scars: report of transluminal cholecystectomy in a human being. *Arch Surg* 2007; **142**: 823-826; discussion 826-827
- 4 **Bessler M**, Stevens PD, Milone L, Parikh M, Fowler D. Transvaginal laparoscopically assisted endoscopic cholecystectomy: a hybrid approach to natural orifice surgery. *Gastrointest Endosc* 2007; **66**: 1243-1245
- 5 **Ramos AC**, Zundel N, Neto MG, Maalouf M. Human hybrid NOTES transvaginal sleeve gastrectomy: initial experience. *Surg Obes Relat Dis* 2008; **4**: 660-663
- 6 **Zorron R**, Maggioni LC, Pombo L, Oliveira AL, Carvalho GL, Filgueiras M. NOTES transvaginal cholecystectomy: preliminary clinical application. *Surg Endosc* 2008; **22**: 542-547
- 7 **Gumbs AA**, Fowler D, Milone L, Evanko JC, Ude AO, Stevens P, Bessler M. Transvaginal natural orifice transluminal endoscopic surgery cholecystectomy: early evolution of the technique. *Ann Surg* 2009; **249**: 908-912
- 8 **Horgan S**, Cullen JP, Talamini MA, Mintz Y, Ferreres A, Jacobsen GR, Sandler B, Bosia J, Savides T, Easter DW, Savu MK, Ramamoorthy SL, Whitcomb E, Agarwal S, Lukacz E, Dominguez G, Ferraina P. Natural orifice surgery: initial clinical experience. *Surg Endosc* 2009; **23**: 1512-1518
- 9 **Salinas G**, Saavedra L, Agurto H, Quispe R, Ramírez E, Grande J, Tamayo J, Sánchez V, Málaga D, Marks JM. Early experience in human hybrid transgastric and transvaginal endoscopic cholecystectomy. *Surg Endosc* 2010; **24**: 1092-1098
- 10 **Wilhelm D**, Meining A, von Delius S, Fiolka A, Can S, Hann von Weyhern C, Schneider A, Feussner H. An innovative, safe and sterile sigmoid access (ISSA) for NOTES. *Endoscopy* 2007; **39**: 401-406
- 11 **Fong DG**, Pai RD, Thompson CC. Transcolonic endoscopic abdominal exploration: a NOTES survival study in a porcine model. *Gastrointest Endosc* 2007; **65**: 312-318
- 12 **Pai RD**, Fong DG, Bundga ME, Odze RD, Rattner DW, Thompson CC. Transcolonic endoscopic cholecystectomy: a NOTES survival study in a porcine model (with video). *Gastrointest Endosc* 2006; **64**: 428-434
- 13 **Fong DG**, Ryou M, Pai RD, Tavakkolizadeh A, Rattner DW, Thompson CC. Transcolonic ventral wall hernia mesh fixation in a porcine model. *Endoscopy* 2007; **39**: 865-869
- 14 **Ryou M**, Fong DG, Pai RD, Tavakkolizadeh A, Rattner DW, Thompson CC. Dual-port distal pancreatectomy using a prototype endoscope and endoscopic stapler: a natural orifice transluminal endoscopic surgery (NOTES) survival study in a porcine model. *Endoscopy* 2007; **39**: 881-887
- 15 **Cataldo PA**. Transanal endoscopic microsurgery. *Surg Clin North Am* 2006; **86**: 915-925
- 16 **Swanstrom L**. Transanal endoscopic microsurgery: current indications and techniques. *J Gastrointest Surg* 2000; **4**: 342-343
- 17 **de Graaf EJ**, Doornebosch PG, Stassen LP, Debets JM, Tetteroo GW, Hop WC. Transanal endoscopic microsurgery for rectal cancer. *Eur J Cancer* 2002; **38**: 904-910
- 18 **Smith LE**, Ko ST, Saclarides T, Caushaj P, Orkin BA, Khanduja KS. Transanal endoscopic microsurgery. Initial registry results. *Dis Colon Rectum* 1996; **39**: S79-S84
- 19 **Gavagan JA**, Whiteford MH, Swanstrom LL. Full-thickness intraperitoneal excision by transanal endoscopic microsurgery does not increase short-term complications. *Am J Surg* 2004; **187**: 630-634
- 20 **Tou S**, Brown SR, Malik AI, Nelson RL. Surgery for complete rectal prolapse in adults. *Cochrane Database Syst Rev* 2008; CD001758
- 21 **Whiteford MH**, Denk PM, Swanström LL. Feasibility of radical sigmoid colectomy performed as natural orifice transluminal endoscopic surgery (NOTES) using transanal endoscopic microsurgery. *Surg Endosc* 2007; **21**: 1870-1874
- 22 **Sylla P**, Willingham FF, Sohn DK, Gee D, Brugge WR, Rattner DW. NOTES rectosigmoid resection using transanal endoscopic microsurgery (TEM) with transgastric endoscopic assistance: a pilot study in swine. *J Gastrointest Surg* 2008; **12**: 1717-1723
- 23 **Sylla P**, Sohn DK, Cizginer S, Konuk Y, Turner BG, Gee DW, Willingham FF, Hsu M, Mino-Kenudson M, Brugge WR, Rattner DW. Survival study of natural orifice transluminal endoscopic surgery for rectosigmoid resection using transanal endoscopic microsurgery with or without transgastric endoscopic assistance in a swine model. *Surg Endosc* 2010; Epub ahead of print
- 24 **Leroy J**, Cahill RA, Perretta S, Forgione A, Dallemagne B, Marescaux J. Natural orifice transluminal endoscopic surgery (NOTES) applied totally to sigmoidectomy: an original technique with survival in a porcine model. *Surg Endosc* 2009; **23**: 24-30
- 25 **Sylla P**, Kim MC, Dursun A, Sohn DK, Ajari I, Konuk Y, Turner BG, Gee D, Brugge WR, Rattner DW. Completely NOTES rectosigmoid resection using Transanal Endoscopic Microsurgery (TEM): Experience in human cadavers. Poster presentation at the ASCRS meeting; 2010 May; Minneapolis, USA
- 26 **Franklin ME**, Kazantsev GB, Abrego D, Diaz-E JA, Balli J, Glass JL. Laparoscopic surgery for stage III colon cancer: long-term follow-up. *Surg Endosc* 2000; **14**: 612-616
- 27 **Cheung HY**, Leung AL, Chung CC, Ng DC, Li MK. Endo-laparoscopic colectomy without mini-laparotomy for left-sided colonic tumors. *World J Surg* 2009; **33**: 1287-1291
- 28 **Leroy J**, Cahill RA, Asakuma M, Dallemagne B, Marescaux J. Single-access laparoscopic sigmoidectomy as definitive surgical management of prior diverticulitis in a human patient. *Arch Surg* 2009; **144**: 173-179; discussion 179
- 29 **Akamatsu H**, Omori T, Oyama T, Tori M, Ueshima S, Nakahara M, Abe T, Nishida T. Totally laparoscopic sigmoid colectomy: a simple and safe technique for intracorporeal anastomosis. *Surg Endosc* 2009; **23**: 2605-2609
- 30 **Franklin ME Jr**, Kelley H, Kelley M, Brestan L, Portillo G, Torres J. Transvaginal extraction of the specimen after total laparoscopic right hemicolectomy with intracorporeal anastomosis. *Surg Laparosc Endosc Percutan Tech* 2008; **18**: 294-298
- 31 **Lacy AM**, Delgado S, Rojas OA, Almenara R, Blasi A, Llach J. MA-NOS radical sigmoidectomy: report of a transvaginal resection in the human. *Surg Endosc* 2008; **22**: 1717-1723
- 32 **Sylla P**, Rattner DW, Delgado S, Lacy AM. NOTES transanal rectal cancer resection using transanal endoscopic microsurgery and laparoscopic assistance. *Surg Endosc* 2010; **24**: 1205-1210

S- Editor Li LF L- Editor Hughes D E- Editor Yang C

Antonello Forgione, MD, PhD, MBA, Series Editor

Natural orifice transluminal endoscopic surgery and localized resection for colorectal neoplasia

Ronan A Cahill, Neil J Mortensen

Ronan A Cahill, Neil J Mortensen, Department of Colorectal Surgery, John Radcliffe Hospital, Headley Way, Headington, Oxford OX3 9DU, United Kingdom

Author contributions: Both authors contributed significantly to this work and met the qualifications for authorship in every respect.

Correspondence to: Ronan A Cahill, MD, Department of Colorectal Surgery, John Radcliffe Hospital, Headley Way, Headington, Oxford OX3 9DU, United Kingdom. cahillra@gmail.com
Telephone: +44-1865-220937 Fax: +44-1865-851173

Received: December 26, 2009 Revised: February 4, 2010

Accepted: February 11, 2010

Published online: June 27, 2010

Abstract

Modern methods of surgical intervention have the potential to provide effective, definitive management of early stage colorectal neoplasia by truly minimally invasive means. Margin-free clearance of early colonic neoplasia from within the intestinal lumen can already now be effected by endoscopic submucosal dissection in the colon and transluminal endoscopic microsurgery (TEM) in the rectum. Natural orifice transluminal endoscopic surgery (NOTES) offers the potential for providing transmural, full thickness excision as TEM does but at sites in the colon proximal to the rectum. The next conceptual advance required to make this practice an effective reality lies in evolving surgical regional staging strategies to effectively partner localized resective approaches and allow their deployment as definitive curative therapy. As the most compelling modality for nodal status ascertainment in the absence of lymphatic basin excision for other malignant disease processes, it seems timely to reconsider sentinel node biopsy in cancer of the colon and rectum. Whether by this means or indeed any other, such an ability to confidently identify patients with node negative disease would allow nascent innovative techniques flourish as definitive management for confined (N0) T1 and T2 cancers and so allow the application of available advanced tech-

nology for clinical benefit. Conversely, the development of a specific clinical niche for NOTES (whether, as here, for full thickness localized colonic excision or nodal staging alone) would greatly benefit the evolution and incorporation of this surgical strategy into clinical care paradigms.

© 2010 Baishideng. All rights reserved.

Key words: Natural orifice transluminal endoscopy; Early stage colorectal neoplasia; Colorectal cancer; Minimal invasive surgery; Laparoendoscopic surgery; Endoscopy

Peer reviewer: Paolo Massucco, MD, Department of Surgical Oncology, IRCC, Str Stat 142, Candiolo 10060, Italy

Cahill RA, Mortensen NJ. Natural orifice transluminal endoscopic surgery and localized resection for colorectal neoplasia. *World J Gastrointest Surg* 2010; 2(6): 199-202 Available from: URL: <http://www.wjgnet.com/1948-9366/full/v2/i6/199.htm> DOI: <http://dx.doi.org/10.4240/wjgs.v2.i6.199>

INTRODUCTION

As much as representing an alternative access route, natural orifice transluminal endoscopic surgery (NOTES) may prompt re-evaluation of the operative blueprint for intra-abdominal operations for colorectal neoplasia. This is because it poses a stimulating challenge to expert groups intent on surmounting the technical aspects of confined operative space but also, and, more importantly, as a means of making this potential advance relevant to clinical practice. By minimizing operative access alone, laparoscopy has already provided clear short-term benefits to patients in terms of postoperative pain and convalescence rates^[1-3]. Combining focused intra-abdominal operation with minimized access may add synergistically to patient outcome if oncological providence can be assured so that cure rates are not compromised. From the alternative perspective, exact replication

of the entire radical operation as conventionally performed is frustrating for the development of NOTES-type (and indeed single port laparoscopic) operations^[4]. Tailoring the operative approach to the individualized needs of any particular patient with colorectal cancer and thereafter specifically selecting the least invasive suitable approach seems likely to be the next major step change in surgical progress for this disease^[5].

LOCALISED FULL THICKNESS

RESECTION OF THE COLON BY NOTES

Provision of a facility to provide full thickness, partial circumference localized resection of a segment of large intestine would seem an ideal niche for the nascent technique of NOTES as currently there is a gap between the capability to provide partial thickness mural resection by endoscopic means (i.e. mucosal and submucosal endoscopic dissection) and conventional radical operation (including resection of sites of potential but unproven nodal metastases). Transluminal endoscopic microsurgery (TEM) can provide partial circumference full thickness resection for the rectum^[6,7], but there is no similar approach available in clinical practice for the colon. However, selected expert groups have already developed methods and means of assuring safe resection of a segment of intestine in survival animal studies using NOTES approaches using both conventional and innovative technology. While the TEM platform can be adapted for use to provide rigid instrumentation through the rectum^[8], standard, flexible endoscopic and laparoscopic equipment can also be employed *via* combined transgastric and transcolonic routes to allow two expert surgeons to work in concert to provide full thickness segmental excision^[9]. By including the colotomy within the resected specimen, this approach leaves only the gastrotomy site as the single peritoneal access site. While further technological development to ensure safe visceral access sites is still required, there is sufficient promise in the techniques under evaluation to suggest this concern will be surmounted in the near future^[10]. In addition, many of the elements developed for employment in this method can be directly transposed to laparoscopic operations for benign disease^[11].

ONCOLOGICAL ASPECTS OF LOCALISED RESECTION

The current requirement for radical mesocolonic and mesorectal excision in combination with resection of the colorectal primary is predominantly based on the need to ensure nodal staging in every case and resection of all disease containing sites in node-positive patients. Despite advances in preoperative imaging, the majority of nodes bearing cancer deposits in colorectal cancer patients lie beneath the size threshold of resolution (5 mm) of both computerized tomograms and magnetic resonance imaging. Already, a small group of patients (10% of the total, a figure equating to 9555 people per year in England

alone and 11500 per year in the United Kingdom) are undergoing a full operation when their entire cancer burden is in fact potentially removable (and curable) by an endoscopic procedure that would not entail removal of any significant length of bowel and that could be performed potentially as a day-case procedure. This figure is set to increase with increasing awareness of early surveillance of higher risk groups (e.g. family history) while the advent of systematic wide-spread screening programmes is expected to further shift the incidence of node-negative disease up to 50%^[12,13]. If nodal status could be assured without radical surgery, the current requirement to perform radical mesenteric resection in every case may then be viewed as exposing the truly node negative patients to additional unnecessary risks of injury during their operation^[14].

Because of this, certain groups have already begun to suggest that limiting operative extent should indeed pay considerable dividend for the patient and indeed the health-care provider and reduce the relatively high morbidity rates associated with radical operation for early stage disease^[15]. Standard surgical staging alone in such node negative patients introduces increased intraoperative risks (e.g. injuries of root mesenteric and paracolic structures such as the ureters, para-aortic nerves and duodenum and spleen). As complete nodal resection requires high arterial ligation, this intraoperative step also induces ischemia on a wider area of intestine than would otherwise be induced by narrow margin excision of the primary lesion. Thus, such radical resection may be implicated at least theoretically in incidences of anastomotic leak (which remain unacceptably frequent across the spectrum of colorectal resection) and postoperative ileus (a major factor in both patient convalescence and hospital stay as well as a cause of readmission in enhanced recovery programmes). Furthermore, postoperative bowel dysfunction complicates patients' recovery after colorectal resection at least in the first postoperative year. Finally, operative extent and lymphatic clearance is directly related to the need for both temporary and permanent stoma formation in cancers of the rectum.

SENTINEL NODE BIOPSY AND COLORECTAL CANCER

Surgeons involved in the care of breast cancer^[16], melanoma^[17] and, more recently, early stage gastric cancer^[18] have recognized the concept of sentinel nodes (SNs) as first order draining nodes and therefore the first possible site of metastasis *via* lymphatic drainage from a primary tumor. Moreover, they have proved that the absence of metastases in these SNs is correlated with the absence of metastases in downstream lymph nodes. Embracing this concept has allowed selection of patients without nodal involvement for simplified operation in these specialties. In this way, for breast cancer, melanoma and, more recently, gastric cancer, surgeons have begun offering limited operations with functional preservation for those patients with node negative disease without oncological compromise.

By contrast, in colorectal cancer this concept has so far been confined to pathological upstaging after conventional operation. Return to its original purpose of selecting node negative patients and its use as an oncological support for minimal resective techniques could therefore pay dividends for selected patients with colorectal malignancy. Further confining lymphatic mapping to patients with early stage disease could also allow it to function with maximum efficiency and effectiveness as it is clear from experience in cancers at other sites, that this technique functions best in those whom can benefit from it the most (i.e. those with localized disease). Supportive evidence for this concept has already been provided by rigorous systematic reviews of the literature^[19] and secondary intention analysis of prospective, high quality databases^[20]. Experimental study has also demonstrated that lymphatic mapping and sentinel node excision can be performed with high accuracy without conventional operative approaches (see below). The proof of the validity of this premise now requires prospective *a priori* analysis in the clinical setting.

The immediate clinical niche for a minimally invasive approach to SN biopsy within the current clinical care setting is the after-treatment of patients undergoing endoscopic resection (either polypectomy or endoscopic mucosal/submucosal resection) of a lesion in their colon that is subsequently determined to be a completely excised invasive cancer. Conventionally, the gold standard further treatment for such patients is radical resection although this is usually overtreatment as most such patients have truly node negative disease. Sentinel node mapping and biopsy could provide a means for laparoendoscopic determination of nodal burden and hence obviate further radical operations in those proven node negative. For this indication, the ideal mapping agent would be injected immediately prior to the initial endoscopic resection. The agent would then persist both in the colon wall and in the first draining ("sentinel") nodes and so allow subsequent laparoscopic detection of both the site of the primary and SNs. Analysis of nodes (ideally intraoperatively) would then allow determination of the oncological adequacy of the index procedure and indicate whether further resection is required.

A second role for NOTES with considerable clinical resonance is in the upgrading of endoscopic resective techniques to a definitive surgical treatment of localised (N0) colorectal primary lesions with diameters within their effective range. This would probably entail a combined NOTES/laparoendoscopic approach. Indeed laparoscopic assistance in intraluminal resection has already been advocated by certain experts^[21]. As well as determining the appropriateness of endoscopic resection in the selected case, peritoneal access would also provide a ready means for performing full-thickness localised resection of the primary. Thirdly, proof of capability could subsequently be applied to advancing the role of minimized access operations such as single port operations and ultimately perhaps pure NOTES-type procedures^[22].

SENTINEL NODE BIOPSY AND NOTES

Considerable preclinical work has been expended to demonstrate the feasibility and safety of sentinel node biopsy from the colonic mesentery by NOTES^[23]. Both the concept and practice of the use of the surgical access technique are straightforward either as a nodal biopsy technique alone or in combination with a NOTES segmental resective technique^[24]. A transgastric approach is made to allow a double channel flexible endoscope to access the peritoneum. Thereafter, an intraluminal magnetic frame allows display of the sigmoid colon and mesentery, allowing the *in situ* peritoneoscope to observe the performance of lymphatic mapping by a sigmoidoscope. Choice of a mapping agent that is rapidly taken up by the lymphatics allows the NOTES optic to follow the efferent lymphatics in real-time so that the first order draining node(s) is identified. Thereafter, the sentinel node(s) can be "cherry-picked" from the mesentery and retrieved to the exterior for analysis by either standard pathological evaluation or possibly by rapid intraoperative RT-PCR determination. Additionally, innovative optical biopsy technologies such as Optical Coherence Tomography may in future allow direct *in situ* analysis of nodal status^[25].

CONCLUSION

These developments in surgical capability and shifts in patient demographics mean that there is now, as never before, an opportunity to consider a range of resective options depending on stage of disease at presentation. An ability to confidently direct NOTES development towards the resection of the primary alone, rather than including resection of nodal sites of unproven dissemination, would greatly simplify its progression by sharpening its focus. In addition, a means to ensure correct nodal staging ahead of operative resection would therefore greatly enhance the evolution of the discipline of colorectal surgery overall. Whether or not this role can be fulfilled to absolute satisfaction by SN biopsy is at the moment unproven. Even if definitively proven as not suitable for routine clinical use in this field, the admission that operative surgical extent could be individualized to the disease stage of the patient at presentation would encourage additional work in this field to focus on the basic issues presented here and to work to hone the current surgical paradigm. Therefore, the most important issues are the acceptance of the concept of moving towards individualized surgical extent of resection and the need for appropriate, assiduous evaluation of the potential of new technologies to make this a reality.

ACKNOWLEDGEMENTS

RA Cahill holds a Career Development Award from the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES). The authors also gratefully acknowledge the support of the Oxford Colon Cancer Trust (OCCTO-PUS) and the Pharsalia Trust in furthering the advancement of this work

REFERENCES

- 1 **Tjandra JJ**, Chan MK. Systematic review on the short-term outcome of laparoscopic resection for colon and rectosigmoid cancer. *Colorectal Dis* 2006; **8**: 375-388
- 2 **Schwenk W**, Haase O, Neudecker J, Müller JM. Short term benefits for laparoscopic colorectal resection. *Cochrane Database Syst Rev* 2005; CD003145
- 3 **Murray A**, Lourenco T, de Verteuil R, Hernandez R, Fraser C, McKinley A, Krukowski Z, Vale L, Grant A. Clinical effectiveness and cost-effectiveness of laparoscopic surgery for colorectal cancer: systematic reviews and economic evaluation. *Health Technol Assess* 2006; **10**: 1-141, iii-iv
- 4 **Cahill RA**, Marescaux J. Natural orifice transluminal endoscopic surgery (N.O.T.E.S.) for oncologic disease. *Surg Oncol* 2009; **18**: 91-93
- 5 **Cahill R**, Lindsey I, Cunningham C. NOTES for colorectal neoplasia--surgery through the looking glass. *Gut* 2009; **58**: 1168-1169
- 6 **Bretagnol F**, Merrie A, George B, Warren BF, Mortensen NJ. Local excision of rectal tumours by transanal endoscopic microsurgery. *Br J Surg* 2007; **94**: 627-633
- 7 **Tytherleigh MG**, Warren BF, Mortensen NJ. Management of early rectal cancer. *Br J Surg* 2008; **95**: 409-423
- 8 **Whiteford MH**, Denk PM, Swanström LL. Feasibility of radical sigmoid colectomy performed as natural orifice transluminal endoscopic surgery (NOTES) using transanal endoscopic microsurgery. *Surg Endosc* 2007; **21**: 1870-1874
- 9 **Leroy J**, Cahill RA, Perretta S, Forgione A, Dallemagne B, Marescaux J. Natural orifice transluminal endoscopic surgery (NOTES) applied totally to sigmoidectomy: an original technique with survival in a porcine model. *Surg Endosc* 2009; **23**: 24-30
- 10 **Perretta S**, Sereno S, Forgione A, Dallemagne B, Coumaros D, Boosfeld C, Moll C, Marescaux J. A new method to close the gastrotomy by using a cardiac septal occluder: long-term survival study in a porcine model. *Gastrointest Endosc* 2007; **66**: 809-813
- 11 **Leroy J**, Cahill RA, Asakuma M, Dallemagne B, Marescaux J. Single-access laparoscopic sigmoidectomy as definitive surgical management of prior diverticulitis in a human patient. *Arch Surg* 2009; **144**: 173-179; discussion 179
- 12 **Fazio L**, Cotterchio M, Manno M, McLaughlin J, Gallinger S. Association between colonic screening, subject characteristics, and stage of colorectal cancer. *Am J Gastroenterol* 2005; **100**: 2531-2539
- 13 **Pignone M**, Rich M, Teutsch SM, Berg AO, Lohr KN. Screening for colorectal cancer in adults at average risk: a summary of the evidence for the U.S. Preventive Services Task Force. *Ann Intern Med* 2002; **137**: 132-141
- 14 **Cahill RA**. Regional nodal staging for early stage colon cancer in the era of endoscopic resection and N.O.T.E.S. *Surg Oncol* 2009; **18**: 169-175
- 15 **Cahill RA**, Leroy J, Marescaux J. Localized resection for colon cancer. *Surg Oncol* 2009; **18**: 334-342
- 16 **Mabry H**, Giuliano AE. Sentinel node mapping for breast cancer: progress to date and prospects for the future. *Surg Oncol Clin N Am* 2007; **16**: 55-70
- 17 **Balch CM**, Morton DL, Gershenwald JE, McMasters KM, Nieweg OE, Powell B, Ross MI, Sondak VK, Thompson JF. Sentinel node biopsy and standard of care for melanoma. *J Am Acad Dermatol* 2009; **60**: 872-875
- 18 **Kitagawa Y**, Saikawa Y, Takeuchi H, Mukai M, Nakahara T, Kubo A, Kitajima M. Sentinel node navigation in early stage gastric cancer--updated data and current status. *Scand J Surg* 2006; **95**: 256-259
- 19 **Cahill RA**, Leroy J, Marescaux J. Could lymphatic mapping and sentinel node biopsy provide oncological providence for local resectional techniques for colon cancer? A review of the literature. *BMC Surg* 2008; **8**: 17
- 20 **Cahill RA**, Bembenek A, Sirop S, Waterhouse DF, Schneider W, Leroy J, Wiese D, Beutler T, Bilchik A, Saha S, Schlag PM. Sentinel node biopsy for the individualization of surgical strategy for cure of early-stage colon cancer. *Ann Surg Oncol* 2009; **16**: 2170-2180
- 21 **Cahill RA**, Asakuma M, Perretta S, Leroy J, Dallemagne B, Marescaux J, Coumaros D. Supplementation of endoscopic submucosal dissection with sentinel node biopsy performed by natural orifice transluminal endoscopic surgery (NOTES) (with video). *Gastrointest Endosc* 2009; **69**: 1152-1160
- 22 **Cahill RA**, Lindsey I, Cunningham C. Address of early stage primary colonic neoplasia by N.O.T.E.S. *Surg Oncol* 2009; **18**: 163-168
- 23 **Cahill RA**, Perretta S, Leroy J, Dallemagne B, Marescaux J. Lymphatic mapping and sentinel node biopsy in the colonic mesentery by Natural Orifice Transluminal Endoscopic Surgery (NOTES). *Ann Surg Oncol* 2008; **15**: 2677-2683
- 24 **Cahill RA**, Perretta S, Forgione A, Leroy J, Dallemagne B, Marescaux J. Multimedia article. Combined sentinel node biopsy and localized sigmoid resection entirely by natural orifice transluminal endoscopic surgery: a new challenge to the old paradigm. *Dis Colon Rectum* 2009; **52**: 725
- 25 **Cahill RA**, Asakuma M, Trunzo J, Schomisch S, Wiese D, Saha S, Dallemagne B, Marks J, Marescaux J. Intraoperative virtual biopsy by fibered optical coherence tomography (OCT) at natural orifice transluminal endoscopic surgery (NOTES). *J Gastrointest Surg* 2010; **14**: 732-738

S- Editor Li LF L- Editor Hughes D E- Editor Yamg C

Antonello Forgione, MD, PhD, MBA, Series Editor

NOTES: The question for minimal resection and sentinel node in early gastric cancer

Mitsuhiro Asakuma, Ronan A Cahill, Sang-Woong Lee, Eiji Nomura, Nobuhiko Tanigawa

Mitsuhiro Asakuma, Ronan A Cahill, Sang-Woong Lee, Eiji Nomura, Nobuhiko Tanigawa, Department of General and Gastroenterological Surgery, Osaka Medical College, Osaka 569-8686, Japan

Author contributions: Asakuma M and Lee SW conceived the idea, designed the study, collected and analysis the data; Asakuma M and Cahill RA were involved in drafting the manuscript; Asakuma M, Nomura E and Tanigawa N approved the final version.

Correspondence to: Mitsuhiro Asakuma, MD, Department of General and Gastroenterological Surgery, Osaka Medical College, Osaka 569-8686, Japan. sur105@poh.osaka-med.ac.jp

Telephone: +81-726831221 **Fax:** +81-726852057

Received: December 26, 2009 **Revised:** February 28, 2010

Accepted: March 7, 2010

Published online: June 27, 2010

Abstract

Surgical therapy for gastric cancer involves both removal of the cancer lesion and complete lymph node dissection. Natural orifice transluminal endoscopic surgery (NOTES) is considered to represent the next revolution in surgery. Many surgeons and endoscopists believe that NOTES may be a superior alternative for early gastric cancer treatment. Sentinel node (SN) navigation surgery for gastric cancer: Single institution results of SN mapping for early gastric cancer are increasingly being considered acceptable. Furthermore, a major large-scale clinical trial of SN mapping for gastric cancer has recently been completed by The Japan Society of SN Navigation Surgery study group. They reported false negative rate of 7.0% while the sensitivity of metastasis detection based on SN status was 93%. Combination of SN biopsy and NOTES: This concept was first described by Cahill *et al* who proved the feasibility of lymphatic mapping and SN biopsy by NOTES. Lymphatic channel filling was immediately observable *via* the intraperitoneal optics. Partial resection of the stomach by hybrid NOTES: Several centers have already reported gastrectomy assisted by NOTES using the transvaginal route. However, the main problem of full-thickness resec-

tion of gastric wall remains endoscopic gastric closure. Establishing an endoscopic suturing method would be an important step toward expanding potential indications. NOTES is met with both enthusiasm and skepticism but will gain its own place as human creativity eventually provides solutions to its technical limitations. In the near future, NOTES can evolve the capacity to complement the existing armamentarium for gastric cancer surgery.

© 2010 Baishideng. All rights reserved.

Key words: Early gastric cancer; Lymphatic mapping; Endoscopic submucosal dissection; Sentinel node biopsy; Natural orifice transluminal endoscopic surgery

Peer reviewer: Jae-Hyung Noh, MD, PhD, Department of Surgery, Sungkyunkwan University School of Medicine, 50 Irwon-Dong, Gangnam-gu, Seoul 135-710, South Korea

Asakuma M, Cahill RA, Lee SW, Nomura E, Tanigawa N. NOTES: The question for minimal resection and sentinel node in early gastric cancer. *World J Gastrointest Surg* 2010; 2(6): 203-206 Available from: URL: <http://www.wjgnet.com/1948-9366/full/v2/i6/203.htm> DOI: <http://dx.doi.org/10.4240/wjgs.v2.i6.203>

INTRODUCTION

Surgical therapy for gastric cancer involves both removal of the cancer lesion and complete lymph node dissection, in the belief that removal of all the lymph nodes which might contain metastases should contribute to the patient's survival. In addition, these resected lymph nodes provide important information to predict recurrence and survival and to guide adjuvant therapy decisions. Although this procedure is still a gold standard in clinical practice, since the advent of laparoscopic surgery patient expectations in combination with improved instrumentation and increasing surgeon experience have generated the possibility of less

invasive treatment such as laparoscopic gastrectomy and endoscopic submucosal dissection (ESD). Recently, natural orifice transluminal endoscopic surgery (NOTES) has been considered to represent the next revolution in surgery. As flexible endoscopy has been developed initially in order to examine the stomach, many surgeons and endoscopists may believe that NOTES will become a superior alternative for early gastric cancer treatment.

SENTINEL NODE NAVIGATION SURGERY FOR GASTRIC CANCER

Lymphatic mapping and sentinel node (SN) biopsy is progressing towards clinical applicability for early-stage gastric carcinoma. Evidence of its technical feasibility at laparoscopy and laparotomy, coupled with advances in intraoperative methods of nodal analysis, has encouraged advocates to propose it as appropriate for patients with localized disease who could be cured by limited resection rather than conventional radical surgery thus avoiding unnecessary lymph node dissection.

In Japan, clinical applications of this novel, minimally invasive approach have had great impact on patient care for gastric cancer as more than half of gastric cancer cases in major institutions are now treated this way. The clinical applications of SN mapping for GI cancer have previously been controversial. However, single institution results of SN mapping for early gastric cancer are increasingly being considered acceptable in terms of detection rate and accuracy in determining regional lymph node status^[1-3]. Furthermore, a major large-scale clinical trial of SN mapping for gastric cancer in conventional open surgery has recently been completed. The Japan Society of Sentinel Node Navigation Surgery study group conducted this multicenter prospective trial for SN mapping by combined blue dye and radioactive tracer (Technetium-99 m tin colloid) injection. They reported at ASCO 2009 that in this trial 433 early gastric cancer cases (≥ 4 cm cT1N0M0 or cT2N0M0) were enrolled at 12 major hospitals. After 36 cases dropped out due to pre or intra-operative diagnosis, the detection rate was 97.5% (387/397). Among the detected cases, 57 (15%) had pathologically-detected metastasis, of whom 53 showed SN positivity^[4] (Table 1). Overall, therefore the false negative rate was 7.0% while the sensitivity of metastasis detection, based on SN status was 93%, and the accuracy of metastatic status based on SN was 99% (383/387).

This study is the first prospective multicenter trial for the gastric cancer SN biopsy. While the method is not easy to practice and not feasible in all hospitals as it requires intra-operative endoscopic skills and specific instruments such as gamma probe, the study proves the concept of SN in gastric cancer. To maximize the utility of the technique in the manner we propose, reliable intraoperative analysis (to the level attainable by immunohistochemistry) of the SNs is required. Rapid intraoperative pathological diagnosis is indeed already available for other malignancies^[5-8]. Furthermore advanced optical imaging may soon

Table 1 Result of the clinical trial of SN mapping for gastric cancer conducted by The Japan Society of Sentinel Node Navigation Surgery study group^[4]

Factors	n (%)
SN identification (n = 397)	
Undetected	10 (2.5)
Detected	387 (97.5)
Mean No. of identified SN	5.5/case
pN factor (n = 387)	
pN (+)	57 (15)
pN (-)	330 (85)
SN metastasis (n = 57)	
pSN (+)	53 (93)
pSN (-)	4 (7)
SN/non-SN metastatic status (n = 387)	
SN (+)/non-SN (-)	32 (8)
SN (+)/non-SN (+)	21 (5)
SN (-)/non-SN (-)	330 (85)
SN (-)/non-SN (+)	4 (1)

SN: Sentinel node.

allow *in vivo* assessment^[9]. Thus, SN navigation seems a very promising method for individualized, minimally invasive surgery.

COMBINATION OF SN BIOPSY AND NOTES

The initial idea behind NOTES was that of an incisionless surgery, which would de facto eliminate scars by accessing the peritoneal cavity *via* natural orifices. On the other hand, endoscopic treatments for early gastric cancer such as ESD have already been established as a “no scar treatments”. Given that a considerable number of standard gastrectomy with lymphnode dissections are being performed worldwide which in fact are unnecessary (although presently this is known only after the operation), it is clear for the surgeons and endoscopists that the concepts of NOTES, ESD and SN navigation should be combined.

The first step towards this concept was first described by Cahill *et al.*^[10,11] who separately proved the feasibility and reliability of lymphatic mapping and SN biopsy by NOTES for the sigmoid colon and stomach in an animal model. For both organs, lymphatic channel filling was immediately observable by the intraperitoneal optics after the methylene blue dye was injected. Furthermore they also demonstrated SN biopsy followed by ESD^[12] (Figure 1).

It seems clear that NOTES-SN biopsy may augment and thereby extend the role of ESD. Such a combined approach may be particularly useful for those unfit or unsuitable for “gold standard” operative resection. It is furthermore intriguing to suggest that NOTES could also allow full-thickness transmural localized resection, meaning that this approach could perhaps provide definitive surgical treatment for small T2 or even T3, N0 cancers^[13]. A means of secure gastrotomy closure is however crucial^[14-18]. Different techniques have been explored varying from “no closure” through suture closure to the use of percutaneous

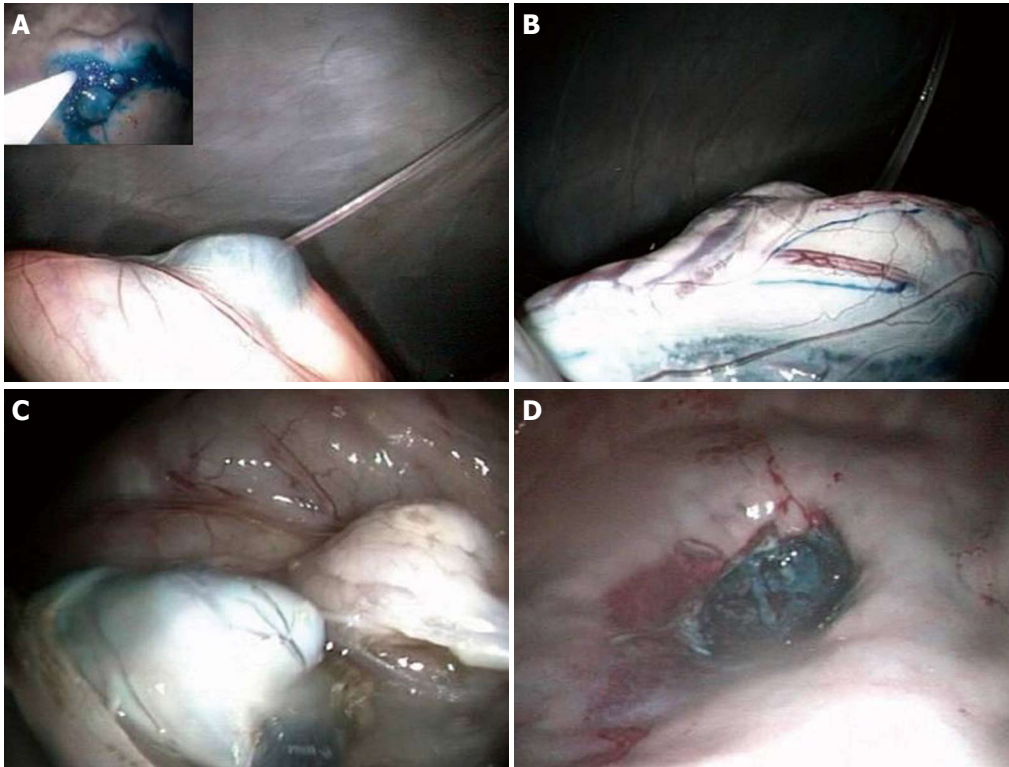


Figure 1 Lymphatic mapping of the stomach. To allow for a straight approach to the stomach and its lymphatic basin by the natural orifice transluminal endoscopic surgery (NOTES) endoscope, a transvaginal access was used. A space in the retroperitoneum was made by blunt dissection so that the double-channel endoscope could be advanced through the retroperitoneum and into the peritoneum proper. A: The intraperitoneal NOTES endoscope observes lymphatic mapping as performed by the intraluminal gastroscopy on either side of the pseudolesion (see insert). One point five millilitre of methylene blue dye was used for each submucosal injection; B: The blue stained efferent lymphatic channels from these injection sites are seen to run to and then along the greater curvature; C: Torque on the gastroscopy allows these channels to be followed by fully exposing both the stomach's posterior surface and allowing access of the NOTES endoscope to the retrogastric space. A single sentinel node is found in this case just behind the pylorus. The faint blue tinge of the node as it takes up the dye is evident. An excisional biopsy of the node was performed and the specimen retrieved to the exterior by grasping and withdrawing the entire endoscope; D: View of the stomach, after removal of a 1.5 cm specimen by endoscopic submucosal dissection.

endoscopic gastrostomy tubes, endoclips, prostheses and tissue glues. However, no-one method has yet been universally accepted or adopted although considerable work is ongoing.

PARTIAL RESECTION OF THE STOMACH BY HYBRID NOTES

NOTES may further advance by combination with laparoscopic surgery as well as ESD. By combining with more conventional methods, the application of NOTES can potentially cover a wider range of diseases. EGC is undoubtedly a good candidate for this kind of surgery. NOTES-related surgery can play a role between the two generally accepted standard treatments for EGC, endoscopic surgery and laparoscopic surgery. Laparoscopic local resection (full-thickness resection) has been reported as a useful alternative to total or subtotal gastrectomy with EGC. This is usually done from outside the stomach using a multifiring stapling device and it is occasionally difficult to obtain adequate surgical margin even with intraoperative endoscopic control. Therefore, the substitution of ESD by the endoscopic full-thickness resection may improve the patient's post operative quality of life. Abe *et al*^[19] have already reported

the use of this technique although their procedure uses 4 trocars, which might be reduced in the future by developing a "hybrid" NOTES technique. The transvaginal route might be a good candidate for access to the stomach and indeed several centers have already reported sleeve gastrectomy assisted by NOTES^[20-23]. Similar methods might therefore be applicable to partial or wedge resection for the primary lesion alone in the case of small, early gastric cancer with the resected specimen then being removed *via* the breached organ. Certain gastrointestinal stromal lesions may also be resectable by such an approach^[13,24]. Potentially magnetic anchoring and guidance systems may also be enrolled to further reduce trocar number with the magnetic component within the viscus being removed with the specimen^[25-27].

The main problem with full-thickness resection of gastric wall remains, however, endoscopic endoscopic gastric closure. As mentioned earlier, even methods for closure of the small gastric hole for transgastric NOTES procedure are not yet established and so endoscopic suture for a relatively larger area is much more challenging. Although several groups have used endoscopic suture for animal stomach^[28,29], the method it is not yet easy to apply in clinical settings. Thus establishing an effective endoscopic suturing

method would be an important step toward expanding potential indications for NOTES related procedure.

CONCLUSION

NOTES is met with both enthusiasm and skepticism but will gain its own place in the field of surgery as, sooner or later, human creativity will eventually provide solutions to its technical limitations. In the near future therefore, we believe, that NOTES will evolve the capacity to complement the existing armamentarium for gastric cancer surgery.

REFERENCES

- 1 **Hiratsuka M**, Miyashiro I, Ishikawa O, Furukawa H, Motomura K, Ohigashi H, Kameyama M, Sasaki Y, Kabuto T, Ishiguro S, Imaoka S, Koyama H. Application of sentinel node biopsy to gastric cancer surgery. *Surgery* 2001; **129**: 335-340
- 2 **Kitagawa Y**, Fujii H, Mukai M, Kubota T, Otani Y, Kitajima M. Radio-guided sentinel node detection for gastric cancer. *Br J Surg* 2002; **89**: 604-608
- 3 **Miwa K**, Kinami S, Taniguchi K, Fushida S, Fujimura T, Nonomura A. Mapping sentinel nodes in patients with early-stage gastric carcinoma. *Br J Surg* 2003; **90**: 178-182
- 4 **Kitagawa Y**, Takeuchi H, Takagi Y, Natsugoe S, Terashima M, Murakami N, Fujimura T, Sakamoto J, Aikou T, and Kitajima M. Prospective multicenter trial of sentinel node mapping for gastric cancer. *Journal of Clinical Oncology*, ASCO Annual Meeting Proceedings 2009; **27**: 4518
- 5 **Tew K**, Irwig L, Matthews A, Crowe P, Macaskill P. Meta-analysis of sentinel node imprint cytology in breast cancer. *Br J Surg* 2005; **92**: 1068-1080
- 6 **Ali R**, Hanly AM, Naughton P, Castineira CF, Landers R, Cahill RA, Watson RG. Intraoperative frozen section assessment of sentinel lymph nodes in the operative management of women with symptomatic breast cancer. *World J Surg Oncol* 2008; **6**: 69
- 7 **Tsujimoto M**, Nakabayashi K, Yoshidome K, Kaneko T, Iwase T, Akiyama F, Kato Y, Tsuda H, Ueda S, Sato K, Tamaki Y, Noguchi S, Kataoka TR, Nakajima H, Komoike Y, Inaji H, Tsugawa K, Suzuki K, Nakamura S, Daitoh M, Otomo Y, Matsuura N. One-step nucleic acid amplification for intraoperative detection of lymph node metastasis in breast cancer patients. *Clin Cancer Res* 2007; **13**: 4807-4816
- 8 **Hughes SJ**, Xi L, Raja S, Gooding W, Cole DJ, Gillanders WE, Mikhitarian K, McCarthy K, Silver J, Ching J, McMillan W, Luketich JD, Godfrey TE. A rapid, fully automated, molecular-based assay accurately analyzes sentinel lymph nodes for the presence of metastatic breast cancer. *Ann Surg* 2006; **243**: 389-398
- 9 **Cahill RA**. Regional nodal staging for early stage colon cancer in the era of endoscopic resection and N.O.T.E.S. *Surg Oncol* 2009; **18**: 169-175
- 10 **Cahill RA**, Perretta S, Leroy J, Dallemagne B, Marescaux J. Lymphatic mapping and sentinel node biopsy in the colonic mesentery by Natural Orifice Transluminal Endoscopic Surgery (NOTES). *Ann Surg Oncol* 2008; **15**: 2677-2683
- 11 **Cahill RA**, Asakuma M, Perretta S, Dallemagne B, Marescaux J. Gastric lymphatic mapping for sentinel node biopsy by natural orifice transluminal endoscopic surgery (NOTES). *Surg Endosc* 2009; **23**: 1110-1116
- 12 **Cahill RA**, Asakuma M, Perretta S, Leroy J, Dallemagne B, Marescaux J, Coumaros D. Supplementation of endoscopic submucosal dissection with sentinel node biopsy performed by natural orifice transluminal endoscopic surgery (NOTES) (with video). *Gastrointest Endosc* 2009; **69**: 1152-1160
- 13 **Abe N**, Takeuchi H, Yanagida O, Masaki T, Mori T, Sugiyama M, Atomi Y. Endoscopic full-thickness resection with laparoscopic assistance as hybrid NOTES for gastric submucosal tumor. *Surg Endosc* 2009; **23**: 1908-1913
- 14 **Asakuma M**, Perretta S, Cahill RA, Solano C, Pasupathy S, Dallemagne B, Tanigawa N, Marescaux J. Peroral dual scope for natural orifice transluminal endoscopic surgery (NOTES) gastrotomy closure. *Surg Innov* 2009; **16**: 97-103
- 15 **Meireles OR**, Kantsevov SV, Assumpcao LR, Magno P, Dray X, Giday SA, Kalloo AN, Hanly EJ, Marohn MR. Reliable gastric closure after natural orifice transluminal endoscopic surgery (NOTES) using a novel automated flexible stapling device. *Surg Endosc* 2008; **22**: 1609-1613
- 16 **Perretta S**, Allemann P, Dallemagne B, Marescaux J. Natural orifice transluminal endoscopic surgery (N.O.T.E.S.) for neoplasia of the chest and mediastinum. *Surg Oncol* 2009; **18**: 177-180
- 17 **Sporn E**, Miedema BW, Astudillo JA, Bachman SL, Loy TS, Davis JW, Calaluce R, Thaler K. Gastrotomy creation and closure for NOTES using a gastropexy technique (with video). *Gastrointest Endosc* 2008; **68**: 948-953
- 18 **Sumiyama K**, Gostout CJ, Gettman MT. Status of access and closure techniques for NOTES. *J Endourol* 2009; **23**: 765-771
- 19 **Abe N**, Mori T, Takeuchi H, Ueki H, Yanagida O, Masaki T, Sugiyama M, Atomi Y. Successful treatment of early stage gastric cancer by laparoscopy-assisted endoscopic full-thickness resection with lymphadenectomy. *Gastrointest Endosc* 2008; **68**: 1220-1224
- 20 **Vix M**, Solano C, Asakuma M. NOTES sleeve gastrectomy. Available from: URL: <http://www.websurg.com>
- 21 **Fischer LJ**, Jacobsen G, Wong B, Thompson K, Bosia J, Talamini M, Horgan S. NOTES laparoscopic-assisted transvaginal sleeve gastrectomy in humans—description of preliminary experience in the United States. *Surg Obes Relat Dis* 2009; **5**: 633-636
- 22 **Marchesini JC**, Cardoso AR, Nora M, Galvão Neto M, Mottin CC, Baretta G, Padoin AV, Moretto M, Maggioni L, Alves LB, Kupski C. Laparoscopic sleeve gastrectomy with NOTES visualization—a step toward NOTES procedures. *Surg Obes Relat Dis* 2008; **4**: 773-776
- 23 **Ramos AC**, Zundel N, Neto MG, Maalouf M. Human hybrid NOTES transvaginal sleeve gastrectomy: initial experience. *Surg Obes Relat Dis* 2008; **4**: 660-663
- 24 **Nakajima K**, Nishida T, Takahashi T, Souma Y, Hara J, Yamada T, Yoshio T, Tsutsui T, Yokoi T, Mori M, Doki Y. Partial gastrectomy using natural orifice transluminal endoscopic surgery (NOTES) for gastric submucosal tumors: early experience in humans. *Surg Endosc* 2009; Epub ahead of print
- 25 **Raman JD**, Bergs RA, Fernandez R, Bagrodia A, Scott DJ, Tang SJ, Pearle MS, Cadeddu JA. Complete transvaginal NOTES nephrectomy using magnetically anchored instrumentation. *J Endourol* 2009; **23**: 367-371
- 26 **Raman JD**, Scott DJ, Cadeddu JA. Role of magnetic anchors during laparoendoscopic single site surgery and NOTES. *J Endourol* 2009; **23**: 781-786
- 27 **Ryou M**, Thompson CC. Magnetic retraction in natural-orifice transluminal endoscopic surgery (NOTES): addressing the problem of traction and countertraction. *Endoscopy* 2009; **41**: 143-148
- 28 **Ikedo K**, Mosse CA, Park PO, Fritscher-Ravens A, Bergström M, Mills T, Tajiri H, Swain CP. Endoscopic full-thickness resection: circumferential cutting method. *Gastrointest Endosc* 2006; **64**: 82-89
- 29 **Ikedo K**, Fritscher-Ravens A, Mosse CA, Mills T, Tajiri H, Swain CP. Endoscopic full-thickness resection with sutured closure in a porcine model. *Gastrointest Endosc* 2005; **62**: 122-129

S- Editor Li LF L- Editor Hughes D E- Editor Yang C

Antonello Forgione, MD, PhD, MBA, Series Editor

Single access laparoscopic surgery: Complementary or alternative to NOTES?

Giovanni Dapri

Giovanni Dapri, Department of Gastrointestinal Surgery, European School of Laparoscopic Surgery, Saint-Pierre University Hospital, 1000 Brussels, Belgium

Author contributions: Dapri G solely contributed to this paper. Correspondence to: Giovanni Dapri, MD, Department of Gastrointestinal Surgery, European School of Laparoscopic Surgery, Saint-Pierre University Hospital, 322, Rue Haute, 1000 Brussels, Belgium. giovanni@dapri.net

Telephone: +32-2-5354115 Fax: +32-2-5353166

Received: December 26, 2009 Revised: February 3, 2010

Accepted: February 10, 2010

Published online: June 27, 2010

Abstract

In recent years, single access laparoscopic surgery (SALS) and natural orifice transluminal endoscopic surgery (NOTES) have gained interest from both clinical and industrial point of view, with the increased development of different laparoscopic instruments, production of various access ports, and improvement of operative endoscopes. The main advantages stimulating these two approaches are the cosmetic result, the rapid recovery of the patient, and the reduced need for pain killers. SALS and NOTES are in part complementary and in part alternative techniques. Currently, SALS is much simpler and technically easier than NOTES.

© 2010 Baishideng. All rights reserved.

Key words: Single port; Single incision; Single access; Laparoscopy; Transumbilical; Natural orifice transluminal endoscopic surgery

Peer reviewers: Luigi Bonavina, MD, Professor, Department of Surgery, University of Milano Medical School, San Donato Milanese, Piazza Malan 20097, Italy; Jorge Correia-Pinto, MD, PhD, Professor, School of Health Sciences, University of Minho, Campus de Gualtar, Braga 4710-057, Portugal

Dapri G. Single access laparoscopic surgery: Complementary or alternative to NOTES? *World J Gastrointest Surg* 2010; 2(6): 207-209 Available from: URL: <http://www.wjgnet.com/1948-9366/full/v2/i6/207.htm> DOI: <http://dx.doi.org/10.4240/wjgs.v2.i6.207>

INTRODUCTION

Single access laparoscopic surgery (SALS) consists of performing laparoscopic procedures through a unique access, usually the umbilicus, because it represents a natural scar and constitutes a well-healing site of access to the peritoneal cavity. This approach was reported for the first time in 1996 by Kala *et al*^[1] during laparoscopic appendectomy, and in 1997 by Navarra *et al*^[2] during laparoscopic cholecystectomy. With the advent of natural orifice transluminal endoscopic surgery (NOTES), the umbilicus has gained more importance, being recognized as an “embryonic natural orifice”.

NOTES is a term first coined by a joint group of surgeons and gastroenterologists organized by the Society for American Gastrointestinal Endoscopic Surgeons (SAGES) and the American Society of Gastroenterologists (ASGE). It describes the fusion of minimally invasive surgery and interventional endoscopy, in order to perform flexible endoscopic procedures by the transgastric, transvaginal, transenteric, transvesical or transrectal approach. The first NOTES report was made in experimental animals in 2004 by Kalloo *et al*^[3], and in human during a transgastric appendectomy by Rao and Reddy^[4].

In the recent years, SALS and NOTES have received both clinical and industrial investment, with an increased development of different instruments, production of various ports for SALS, and research into operative endoscopes for NOTES. The main advantages stimulating these two approaches are the cosmetic results, and probably the decreased abdominal trauma, the improved recovery of the patient, and the reduced need for pain killers.

COMPLEMENTARY

SALS and NOTES currently share similar technical limitations: lack of triangulation between instruments, poor working ergonomics, restricted visual axis and reduced operative field.

The difficulty with working through a small single access, *via* an organ during NOTES, or the umbilicus during most SALS procedures, can be summarized by the limited triangulation obtained with the classic straight instruments, the restricted degrees of freedom of their movements, and the contact/proximity between the instruments during the operation.

These issues have been fully resolved in SALS, by the introduction of articulating instruments, where the straight shaft is supported by flexible tips and rotatable handles.

Unfortunately using articulating instruments, surgeons have to cross their hands or the instruments' tip in order to reach a working triangulation, because the specific direction of the handles corresponds to fixed movements of the tools' tips. This enables surgeons to use the ergonomics of classic laparoscopy. Moreover, all articulating instruments are currently only available as disposables, and this has the consequence of increasing costs compared to standard laparoscopic procedures.

Because of this, we participated in the development of curved instruments for SALS, where the classic shafts have different curves in order to reach a working triangulation inside the abdomen and at the same time maintain an ergonomic position of the surgeon's hands outside the access. The curved instruments are mostly available as reusables, maintaining the costs at a similar level to classic laparoscopy.

The instruments were also modified for NOTES, giving consideration to the target to be reached from the natural orifice, and the difficulty of working in parallel positions. Long and flexible tools were developed for new operative endoscopes. These operative endoscopes are again mostly under research and not widely available. They are based on the concept of permitting the gastroenterologist and the surgeon to work together in an ergonomic position without conflict between the four hands, whilst allowing them to reach a triangulation at the target area.

In SALS, the limited visual axis can be resolved by the use of new optic-camera systems, which are equipped with optics allowing 360° rotation or a flexible camera. Hence the conflict between the optic and the instruments' tips inside the abdomen, as well as the conflict between the surgeon's hands outside the cavity can be avoided. During NOTES, the visual axis is much improved thanks to the use of new endoscopes, which are provided with articulation of the working channels. These new endoscopes continue to be supported by the optical washing system and by some channels for operative field exposure. Contrary to SALS, in NOTES procedures problems still remain concerning spatial orientation, which is quite difficult with flexible endoscopes.

The problem of having reduced operative field in SALS, as in NOTES, is mainly due to the exposure of the

operative field. This can be improved by the placement of stitches or by the use of some grasping anchors. These anchors are applied for one extremity to the viscera, and for the other one to the peritoneal sheet, increasing the operative field. Furthermore, the grasping anchors can also be maneuvered by external magnets in both SALS^[5] and NOTES^[6] approaches.

ALTERNATIVE

SALS and NOTES are alternatives if we consider their current and probable future application in humans.

SALS, given its similar character to standard laparoscopy, is overall technically easier than NOTES, because the learning curve is much less. The transvaginal approach obviously cannot be offered to male patients, hence the restriction for male patients of the remaining transgastric, transentric, transvesical or transrectal procedures. Moreover, in females, a problem persists for pregnant patients, where the NOTES procedure can be attempted, in contrast to SALS.

In patients with a BMI > 35 kg/m², SALS may be quite difficult although still easier than NOTES, because the fatty tissue does not compromise the route of the scope and instruments through the single access^[7], and ports are added as necessary as during NOTES^[8].

In comparison to SALS, NOTES has advantages because of the possibility to perform not only transluminal, but also endolumenal procedures. For the esophagus, classic endoscopic mucosectomy can be safely performed with endolumenal suturing. Furthermore the performance of endolumenal fundoplication, already reported as feasible and reliable^[9], offers patients with symptomatic gastroesophageal reflux or small hiatal hernia, the option of being treated by scarless surgery.

Another application area favouring NOTES is the endolumenal approach for bariatric revisional surgery. Thanks to the new operative endoscopes, already developed^[10-12] or under development^[13], surgeons can offer patients these endolumenal techniques, thus avoiding new transabdominal surgeries. Patients with gastric pouch dilation, gastrojejunal anastomosis enlargement, or early complications such as bleeds and leaks, can be submitted to this new transoral intra-gastric surgery with obvious benefits.

Similarly, the old strategy of treating rectal lesions by transanal endoscopic microsurgery, is nowadays incorporated in NOTES procedures. This not only avoids extended and incapacitating resection of the rectum, but also has the option of suturing and closure of potential rectal defects, thanks to the improvement of these dedicated instruments^[14]. Thanks to NOTES and to the development of the new operative colonoscopes, some urgent cases such as colic perforation during diagnostic colonoscopy, will be treated through this access with no more open or laparoscopic surgery.

In future, thanks to the introduction of the new operative endoscopes, NOTES will be useful to transorally correct some congenital agenesis of the gastrointestinal tract, e.g. esophageal and duodenal (Jeffrey Ponsky, commu-

nication at SAGES 2009). The new operative endoscopes should permit both opening the visceral lumen, and suturing of the new gastrointestinal continuity endoluminally.

At present, NOTES retains some limitations when compared to SALS. First, is the intrinsic risk for abdominal spillage of gastric, vaginal, enteric, vesical or colonic contents during the NOTES procedures. The second issue is the difficult task of viscerotomy closure with increased risk for leakage during the post-procedure course.

Finally, the application of standard laparoscopy or open surgery remains available for patients with previous open surgeries, as both transluminal and single access may difficult to achieve in these conditions. In addition, the resection of huge benign and malignant tumors or solid organs, cannot be performed by either SALS or NOTES approaches, and the use of standard laparoscopy or open surgery is indicated.

COMMON FUTURE

The classic operative endoscopes have undergone a revolution, and are currently under continue research in terms of long instrument stability, overtube diameter, port-access safety, spatial orientation, and working handle changes. These endoscopes will be supported by free rotation of the tools' tips, simplified instrument change through the working channel, more controlled flexibility of the instrument shaft, and external handle modifications similar to standard laparoscopy. In the near future they will be available for NOTES, and if they are modified in length and in some other parts, like port access, these endoscopes will also be applicable for SALS procedures. Obviously a learning process will be required for laparoscopic surgeons performing SALS with new operative flexible endoscopes. Once research and development is completed, the ideal platform for NOTES and SALS will probably be similar in terms of principles and instruments' action.

CONCLUSION

NOTES and SALS have stimulated innovative efforts invested in surgery in recent years. With the advent of NOTES, SALS has been reconsidered because the umbilicus is considered as the embryological natural access. At present, SALS is actually more applicable than NOTES, because of the lack of new operative endoscopes, absence of visceral access and closure of openings. In the future, the

ideal platform will not be very different between the two approaches in terms of principles and instruments' action.

REFERENCES

- 1 **Kala Z**, Hanke I, Neumann C. [A modified technic in laparoscopy-assisted appendectomy--a transumbilical approach through a single port] *Rozhl Chir* 1996; **75**: 15-18
- 2 **Navarra G**, Pozza E, Occhionorelli S, Carcoforo P, Donini I. One-wound laparoscopic cholecystectomy. *Br J Surg* 1997; **84**: 695
- 3 **Kaloo AN**, Singh VK, Jagannath SB, Niiyama H, Hill SL, Vaughn CA, Magee CA, Kantsevoy SV. Flexible transgastric peritoneoscopy: a novel approach to diagnostic and therapeutic interventions in the peritoneal cavity. *Gastrointest Endosc* 2004; **60**: 114-117
- 4 **Rattner D**, Kaloo A. ASGE/SAGES Working Group on Natural Orifice Transluminal Endoscopic Surgery. October 2005. *Surg Endosc* 2006; **20**: 329-333
- 5 **Dominguez G**, Durand L, De Rosa J, Danguise E, Arozamena C, Ferraina PA. Retraction and triangulation with neodymium magnetic forceps for single-port laparoscopic cholecystectomy. *Surg Endosc* 2009; **23**: 1660-1666
- 6 **Raman JD**, Scott DJ, Cadeddu JA. Role of magnetic anchors during laparoendoscopic single site surgery and NOTES. *J Endourol* 2009; **23**: 781-786
- 7 **Saber AA**, Elgamal MH, Itawi EA, Rao AJ. Single incision laparoscopic sleeve gastrectomy (SILS): a novel technique. *Obes Surg* 2008; **18**: 1338-1342
- 8 **Ramos AC**, Zundel N, Neto MG, Maalouf M. Human hybrid NOTES transvaginal sleeve gastrectomy: initial experience. *Surg Obes Relat Dis* 2008; **4**: 660-663
- 9 **Cadière GB**, Rajan A, Gernay O, Himpens J. Endoluminal fundoplication by a transoral device for the treatment of GERD: A feasibility study. *Surg Endosc* 2008; **22**: 333-342
- 10 **Mikami D**, Needleman B, Narula V, Durant J, Melvin WS. Natural orifice surgery: initial US experience utilizing the StomaphyX device to reduce gastric pouches after Roux-en-Y gastric bypass. *Surg Endosc* 2010; **24**: 223-228
- 11 **Horgan S**, Jacobsen G, Weiss GD, Oldham JS Jr, Denk PM, Borao F, Gorcey S, Watkins B, Mobley J, Thompson K, Spivack A, Voellinger D, Thompson C, Swannstrom L, Shah P, Haber G, Brengman M, Schroder G. Incisionless revision of post-Roux-en-Y bypass stomal and pouch dilation: multicenter registry results. *Surg Obes Relat Dis* 2010; **6**: 290-295
- 12 **Thompson CC**, Slattery J, Bundga ME, Lautz DB. Peroral endoscopic reduction of dilated gastrojejunal anastomosis after Roux-en-Y gastric bypass: a possible new option for patients with weight regain. *Surg Endosc* 2006; **20**: 1744-1748
- 13 **Torquati A**, Kernodle SS, Kaiser JL, Attwell AR. Transoral revision of dilated gastro-jejunoanastomosis after gastric bypass surgery. *Surg Obes Relat Dis* 2008; **4**: 306
- 14 **Burghardt J**, Buess G. Transanal endoscopic microsurgery (TEM): a new technique and development during a time period of 20 years. *Surg Technol Int* 2005; **14**: 131-137

S- Editor Li LF L- Editor Hughes D E- Editor Yang C

Antonello Forgione, MD, PhD, MBA, Series Editor

Natural orifice transluminal surgery: Flexible platform review

Sohail N Shaikh, Christopher C Thompson

Sohail N Shaikh, Christopher C Thompson, Division of Gastroenterology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA 02115, United States

Author contributions: Shaikh SN created the manuscript; Thompson CC performed the editing and aided in the final manuscript creation.

Correspondence to: Christopher C Thompson, MD, Assistant Professor, Division of Gastroenterology, Brigham and Women's Hospital, Harvard Medical School, 75 Francis Street, Boston, MA 02115, United States. ccthompson@partners.org

Telephone: +1-617-5258266 Fax: +1-617-5258740

Received: December 26, 2009 Revised: February 18, 2010

Accepted: February 25, 2010

Published online: June 27, 2010

Abstract

Natural orifice transluminal surgery (NOTES) has garnered significant attention from surgeons and gastroenterologists, due to the fusion of flexible endoscopy and operative technique. Preliminary efforts suggest that NOTES holds potential for a less invasive approach with certain surgical conditions. Many of the hurdles encountered during the shift from open to laparoscopic surgery are now being revisited in the development of NOTES. Physician directed efforts, coupled with industry support, have brought about several NOTES specific devices and platforms to help address limitations with current instrumentation. This review addresses current flexible platforms and their attributes, advantages, disadvantages and limitations.

© 2010 Baishideng. All rights reserved.

Key words: Direct drive endoscopic system; Incisionless operating platform; Natural orifice transluminal surgery; Natural orifice transluminal surgery scope; Challenges; Attributes

Peer reviewer: Tang Chung Ngai, MB, BS, Professor, Department

of Surgery, Pamela Youde Nethersole Eastern Hospital, 3 Lok Man Road, Chai Wan, Hong Kong, China

Shaikh SN, Thompson CC. Natural orifice transluminal surgery: Flexible platform review. *World J Gastrointest Surg* 2010; 2(6): 210-216 Available from: URL: <http://www.wjgnet.com/1948-9366/full/v2/i6/210.htm> DOI: <http://dx.doi.org/10.4240/wjgs.v2.i6.210>

INTRODUCTION

Advances in the fields of laparoscopy and interventional endoscopy have ushered in a new era of minimally invasive surgery. Natural orifice transluminal endoscopic surgery (NOTES) is a new technique that permits flexible endoscopic "scarless" trans-visceral peritoneal access and may be the next evolutionary stride towards progressively less invasive procedures. To date, several important steps have been taken, from simple abdominal exploration in animal models to trans-visceral cholecystectomy in humans^[1,2]. As this nascent field matures, technology has produced several platforms that address basic needs and strive to match their surgical counterparts. This article reviews currently available flexible platforms, their advantages, disadvantages and comparisons with currently available tools.

INITIAL ENDEAVORS

The first published NOTES procedure used a standard forward viewing endoscope, biliary sphincterotome, guide wire, and an esophageal dilatation balloon for transgastric access and liver biopsy^[3]. This re-purposed equipment, although rudimentary for these purposes, has been used by gastroenterologists and surgeons alike. More complex trans-gastric procedures were performed in the pre-clinical setting with standard endoscopic equipment including:

tubal ligation, hysterectomy/simulated appendectomy^[4], cholecystectomy^[5] and splenectomy^[6]. In this early work, several methodological and technical limitations were identified. An alternative approach from the inferior abdomen was explored for cholecystectomy^[7] and pancreatic work^[8], and proved useful in addressing certain limitations of upper abdominal surgery, however, other unique problems were revealed.

In 2005, leaders of the ASGE and SAGES (NOSCAR-Natural Orifice Surgery Consortium for Assessment and Research) reviewed the early work and identified several fundamental challenges to NOTES in a manuscript known as the White Paper^[9]. Peritoneal access and closure, infection, spatial orientation, management of complications and multi-tasking platforms were identified as critical areas of focus. Further NOTES experience subsequently confirmed the limitations of current instrumentation and identified new problems, which were not initially experienced with the transition from open to laparoscopic surgery.

Laparoscopy introduced several challenges related to visualization and tissue manipulation, however, unlike NOTES, laparoscopy mimics the surgical perspective, maintaining remote visualization using rigid, short length instruments optimally positioned for triangulation, traction, dissection, target mobilization and tissue approximation. Additionally, ports allow for 5, 10, 12 mm and larger access to the peritoneum. Since the initial cholecystectomy by Muhe in 1985^[10], laparoscopy has become the gold standard for minimally invasive surgery and is the benchmark to which NOTES is compared.

EQUIPMENT-GENERAL ATTRIBUTES AND LIMITATIONS

Purpose-specific equipment and technology is sorely lacking compared to specialized laparoscopic paraphernalia. Current endoscopic technology and design have several shortcomings when applied to more complex surgical procedures and can be framed in the context of basic platform elements, including guide tube attributes, spatial orientation and imaging characteristics.

Guide tube and user interface attributes

Shaft: Originally purposed for gastrointestinal procedures, flexibility is desirable for atraumatic endolumenal movement; although this may aide in intra-abdominal navigation it also poses a challenge for maneuvering in open space or when attempting to achieve traction or counter-traction. Conversely, laparoscopic tools are rigid, and the combination of spaced ports of entry with transabdominal fulcrum points allow for a stable platform. Alternative means of target fixation, apart from the physical platform, may aide in stability and organ manipulation and help address current limitations of traction and angles of tissue engagement^[11]. Additionally, the increased distance between operator and

end-effectors, which is typical with flexible endoscopy, limits its haptic feedback.

Working channels: Maximal size on commercially available endoscopes is 3.7 mm, limiting the size of available equipment and contrasts greatly to variable size laparoscopic ports. The proximity and parallel orientation of channels limit triangulation, robust tissue manipulation and traction. Furthermore, current endoscopes are restricted to two working channels that are inadequate for some procedures^[4].

Ancillary channels: Channels dedicated for insufflation, irrigation and suction are sub-optimal for routine needs of intra-abdominal surgery and may be inadequate in the event of an emergency.

User interface: Current endoscopes are designed for the endoscopist to control field of view and positioning/orientation. The working channels and navigational/field control elements are in close proximity and lead to complicated team interactions.

Spatial orientation and image characteristics

Site of access: NOTES entry point (transgastric, transcolonic, transurethral or transvaginal) is often selected for proximity or best en-face view, however, this does not ensure direct or adequate visualization of the desired site. Additionally, trans visceral peritoneoscopy may have limited reach and stability in certain orientations; for example targeting the spleen *via* the transgastric approach. Considerable maneuvering of the endoscope is often required to achieve acceptable positioning and stability. A “bounce-off” technique, utilizing internal structures to redirect scope vectors and trajectory is often necessary, yet technically challenging. This may be due to several reasons, including inter-patient variability and inherent mobility of internal structures. Conversely, procedure specific transabdominal port placement allows optimal laparoscopic site selection and stability.

Visual orientation: While endoscopists accustomed to the confines of the gastrointestinal tract are typically comfortable with inverted positioning, surgeons prefer a fixed horizon. With the camera married to the endoscope shaft, horizon is at the mercy of the endoscope’s final position. Laparoscopic visualization is divorced from the effectors allowing remote imaging with maintenance of the horizon. This may diminish work load and prove beneficial when dealing with complex surgeries^[12]. Vantage point is yet another issue; the close proximity and magnified endoscopic views may prove advantageous for meticulous dissection, while a remote view of the operative field may be essential for other tasks and harder to achieve with current flexible platforms. Ancillary visualization technologies with co-

Table 1 NOTES prototype specifications

Prototype	Paradigm	Working Length (cm)	Channels/ Size (mm)	Diameter (mm)	Visualization	Positioning mechanism	Specializations	Procedures performed
DCE (EGD/ Colonoscope)	Endoscopic	103/168	Two: 3.7, 2.8/Two: 3.7, 3.2	12.6/13.7	Standard endoscopic	Standard scope shaft	Two small parallel channels	Animal and human NOTES (Hybrid procedures)
NOTES scope	Endoscopic	133	Two: 2.8, 2.8	14.3	Standard endoscopic	Two bending segments, one lockable	Dual bending segments, orthogonal lifting gates	Animal hybrid NOTES
IOP	Endoscopic/ Flexible-laparoscopic	110	Four: 7, 6, 4, 4	18	N-scope	Built in shaft-stiffening system	2.5cm gasping forceps with tissue anchors	Human NOTES, endoluminal bariatrics, anti-reflux procedures
EndoSAMURAI	Flexible-laparoscopic	103	Three: 2.8, 2.8, 2.8	15.7	Endoscopic	Uses a stiffening overtube system	Bimanual control enables 5 degrees of freedom for 2 end effectors	Animal NOTES
DDES	Flexible-laparoscopic	55	Three: 7, 4.2, 4.2	16 × 22	N-scope	Articulating guide sheath	Bimanual control with 7 degrees of freedom for 2 end effectors	Bench top EMR, ESD and skills assessment models

NOTES: Natural orifice transluminal surgery; DCE: Dual channel endoscope; EGD: Esophagogastroduodenoscope; IOP: Incisionless operating platform; DDES: Direct drive endoscopic system.

computer tomography and 3D image registration may help mitigate these limitations in the future^[13] (Figure 1).

Imaging: Current endoscopic depth of field, although excellent for near vision, lacks the needed distant visualization that would aid in complex procedures and abdominal exploration. Additionally, there may be insufficient light for certain procedures, including exploration and cancer staging. A 10-mm laparoscope provides 380 lumens while a typical endoscope with a 3-mm light bundle provides only 25 lumens. Conversely, the magnified endoscopic images may be superior to laparoscopic images for certain procedures.

Work load

There is a fundamental difference in work load between laparoscopic and endoscopic paradigms. Laparoscopically, the field of view is maintained by an assistant while instruments are maneuvered and executed by the surgeon. Endoscopically, positioning and field of view are maintained by a complex coordination of positioning-wheels, torque, placement, and locking mechanisms. The endoscopic tools are also positioned by the endoscopist (in unison with the endoscope) while actuated by an assistant. Additionally, mental workload will likely be increased by fluctuating visual frames of reference and angles of approach associated with NOTES procedures.

While many of these differences pose disadvantages compared to the current laparoscopic paradigm, flexible endoscopy's added reach and close visualization of an operative field may confer advantages still unknown, for example, inspection of the lesser sac and the suprahepatic/intra diaphragmatic space in cancer staging, which are not readily attainable with current minimally invasive techniques.

FLEXIBLE PLATFORMS

NOSCAR's second meeting included industry participation and several platform solutions were proposed. These have evolved into two broad systems: rigid, mimicking single incision laparoscopic surgery (SILS) and flexible, emulating endoscopy. Flexible platforms may be further divided into two groups: A traditional endoscopic model where the endoscopist controls navigation and instrument position while the assistant exchanges and actuates instruments, and a flexible-laparoscopic paradigm where the interventionalist has complete control of the instruments and the assistant provides visualization and maintains the operative field.

NOTES scope

One of the first platforms to be used in NOTES animal models was the "R-scope" (XGIF-2TQ160R; Olympus, Tokyo, Japan) later modified to the NOTES scope. It has been used to perform several procedures in the pre-clinical setting including cholecystectomy^[14,15]. This device falls under the traditional endoscopic paradigm. It is a modified dual channel endoscope (DCE) with additional elevator toggles and a larger wheel further down the handle to control a second bending segment (Figure 2). The primary segment is lockable, allowing for a better angle of approach and more precise tissue manipulation with maneuvering of the second segment. Additionally, the two working channels have lifting gates that are orthogonally positioned allowing for simultaneous lifting (vertical motion) and dissection (horizontal motion) (Figure 3). This configuration allows more accurate tissue manipulation off-axis to the visual plane. See Table 1 for device specifics. This endoscope addresses several of the DCE shortcomings, including positioning and to a small degree triangulation. The second bending segment, although useful, can be technically dem-

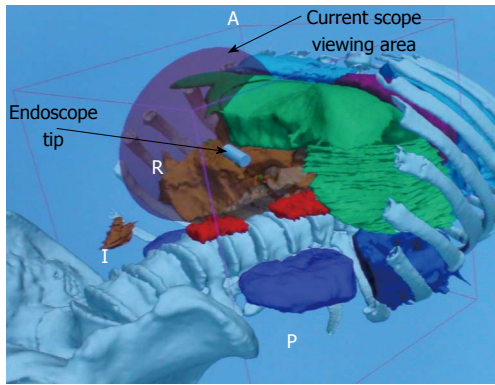


Figure 1 Image registration illustrating tracking of the endoscope tip within a 3D reconstruction of the subject's abdomen.



Figure 2 Natural orifice transluminal surgery (NOTES)/R scope user interface.

anding. These features may lead to increased physical and mental work load. Furthermore, the image is still married to the effectors and, as such, has a limited field of view. Essentially the NOTES scope further refined what the current standard endoscope is capable of while partially tackling some tasks germane to complex surgery.

Incisionless operating platform

The incisionless operating platform (IOP; USGI Medical, San Capistrano, CA) was initially designed to function within the traditional endoscopic paradigm, with recent modifications bridging to the flexible-laparoscopic model. This device was developed through collaboration of physicians and industry and addresses several NOTES requirements. It has been successfully used in a variety of procedures, and is the first specialized platform to be used in clinical NOTES cases, including human transgastric cholecystectomy^[16]. In appearance, the IOP is similar to, but larger than a standard endoscope, with multiple ports and directional wheels at the user interface (Figure 4). Based on endoscopic ergonomics, this platform consists of a 110 cm × 18 mm overtube-like design with a steerable shaft and several channels (Table 1). In some models, the overtube-shaft is capable of stiffening, providing enhanced stability. Its four channels (7, 6, 4 and 4 mm in size) allow

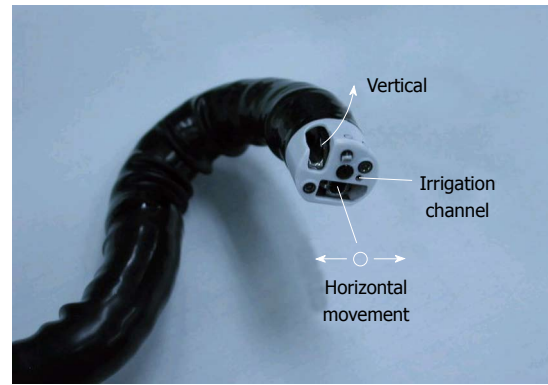


Figure 3 NOTES/R scope distal tip arrangement.

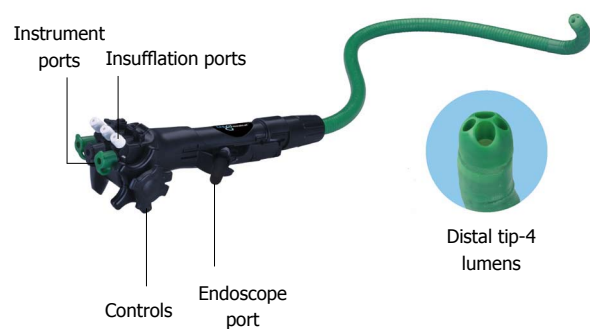


Figure 4 Incisionless operating platform.

for an N-scope (Olympus, Tokyo, Japan) and specialized equipment^[17]. The N-scope is independently rotatable within the channel allowing for an adjustable horizon while maintaining instrument position. The other channels can be used for instruments as well as high flow carbon dioxide insufflation^[14]. Several specialized tools have been designed for this system including a 2.5-cm grasping jaw, capable of performing tissue plications with unique anchors and several accessories for tissue manipulation. Compared to the DCE, the IOP has enhanced deflection and improved triangulation due to the large channels and effectors' ability to enter the operative field. However, the IOP's in-line channel orientation is still subject to parallelism. This may be overcome with instrument modifications. This device presents a new paradigm for the endoscopist as visualization is divorced from the primary operator. Work load for the IOP is high and requires skilled assistants as the primary operator interchanges responsibilities for instrument exchange, device orientation and scope positioning. This is increasingly challenging when the device is in an unstable position. Newer versions of this device allow for bimanual instrument control and are more consistent with the flexible-laparoscopic model.

EndoSAMURAI

The EndoSAMURAI (Olympus Corp., Tokyo, Japan)

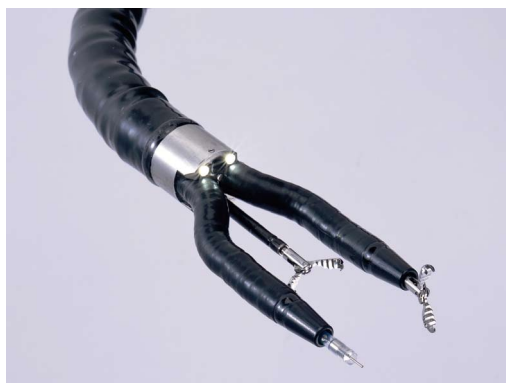


Figure 5 EndoSAMURAI end effectors.



Figure 6 EndoSAMURAI user interface.

was designed to operate within the flexible-laparoscopic paradigm. It has been tested in animal models for cholecystectomy^[18]. It consists of a specialized endoscope with a remote working station and a locking overtube. The distal end of the scope has two short modified independent arms, which upon entry remain parallel with the scope shaft, however, open in an elbow-like fashion when in position (Figure 5). These serve as conduits for different effectors, including standard endoscopic accessories, and are manipulated from a control unit apart from the traditional endoscopic user interface (EVIS EXERA II Universal Platform-Olympus Corp; Figure 6). With 5 degrees of freedom and triangulation capabilities, the arms can tie sutures as well as provide traction and counter traction. In addition to the two conduits, it has a third working channel that may be used for ancillary equipment or suction/irrigation. Stiffened by a locking overtube, the scope articulates in the same manner as a standard endoscope with identical visualization. Although essentially a modified DCE, the EndoSAMURAI overcomes parallelism by the angle at which its effectors are positioned. Additionally, it has better stability compared to the DCE because of the locking overtube. As the arms are married to the camera/scope, it still bears the same image-perspective limitations as the standard endoscope. Interestingly, this system employs a “drive, park and move” methodology. Where the user navigates to the

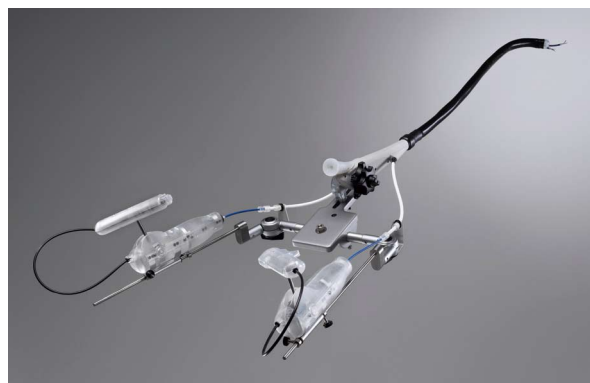


Figure 7 Direct drive endoscopic system (DDES).



Figure 8 DDES-distal end.

target with the endoscope, locks the overtube system and scope in position and then proceeds to the user interface. This effectively allows one operator to perform most of the work load as the image is theoretically kept in place with the locking system with subsequent maintenance of the image by the assistant, which is somewhat similar to traditional laparoscopy.

Direct drive endoscopic system

The direct drive endoscopic system (DDES; Boston Scientific, Natick, MA) is a flexible-laparoscopic multitasking platform that consists of a 55-cm steerable guide sheath that houses 3 lumens extending from a rail-based platform with interchangeable 4 mm instruments (Figure 7, Table 1). The user interface consists of ergonomic rail-guided drive handles situated above the surgeon's waist level. A unique system in the handle allows for seven degrees of freedom: surge, pitch, yaw, roll, tool action, heave and sway. Equipment currently available consists of graspers, scissors, needle pushers and cautery devices. These effectors can traverse a distance from the sheath tip independent of the image (Figure 8). While specialized tools are passed through channels in the guide tube, an N-scope is used for visualization. The N-Scope is freely rotatable and positioned independent of the DDES end effectors. The sheath serves as a guide that can be “docked” once in position. Maintenance of visualization may require adjustment of the

endoscope as well as the sheath while tissue is manipulated. This system accomplishes much of what is desired to mimic a laparoscopic approach, including cutting, grasping, suturing, triangulation and knot tying. Of note, current iterations of the DDES do not have a dedicated channel for irrigation and suction and rely on the endoscope's capabilities, which may not be adequate for intra-abdominal procedures. This system has been tested *ex-vivo* and *in-vivo* with suturing tasks accomplished commensurate with laparoscopy, as well as endoscopic mucosal resection and sub-mucosal dissection^[15,19].

Parallel to these technical developments, the human NOTES experience has continued to broaden. Early human work out of Ohio State University used standard endoscopic equipment for diagnostic human peritoneal exploration^[20]. This study confirmed that the initial steps of NOTES procedures were safe and feasible in humans. A variety of other human NOTES procedures have been performed to date including: transvaginal and transgastric cholecystectomy^[21], transgastric appendectomy^[22], sleeve gastrectomy^[23], and several others. Many of these procedures have been hybrid in nature with laparoscopic components. As tools are further enhanced, current hybrid procedures may evolve to pure NOTES. However, the hybrid approach may be the best course for the near term to maximize patient safety. In addition to the above prototypes, many others are under development and are in various stages of testing. Currently, the best training tools to acquire skills necessary for NOTES, and develop a comfort level with novel instrumentation, are a combination of animal models and human cadavers, which can only approximate the human surgical experience. NOTES simulators are currently under development and may in the future offer a better means of training.

CONCLUSION

More sophisticated tools are needed to better equip NOTES interventionalists to accomplish tasks that currently fall under the purview of laparoscopic surgery. Acknowledging the inadequacies of current endoscopic equipment in 2006, NOSCART outlined the ideal attributes of a NOTES platform. Although no current platform meets all of these desired attributes, much progress has been made. It may also be true that we are asking too much of a NOTES platform. It may be more realistic to have specialized platforms that optimally address specific access sites, organs or individual procedures. Endeavors to improve NOTES equipment will likely continue to improve the endolumenal and SILS armamentarium. Additionally, as imaging and proprioception obstacles are encountered, it may become necessary to employ alternative technologies for navigation and orientation. As issues addressed in the original White Paper are investigated, including new platform technology, a word of caution is warranted as the zeal of performing pure NOTES procedures must be tempered with patient safety. Many advances have been made to date. As time has allowed the laparoscopic equipment to evolve, becoming

more mature and task-specific, the many NOTES advances over just 5 years are encouraging. With continued oversight and participation of NOSCART and similar organizations, future progress in flexible platforms holds great potential.

REFERENCES

- 1 **Swanstrom L.** USGI announces first NOTES Transgastric Cholecystectomy procedures, using the USGI Endosurgical Operating System, performed by Dr. Lee Swanstrom at Legacy Hospital in Portland, OR. USGI Medical, Inc. 2007. Available from: URL: <http://www.usgimedical.com/news/releases/062507.htm>
- 2 **Dallemagne B,** Perretta S, Allemann P, Asakuma M, Marescaux J. Transgastric hybrid cholecystectomy. *Br J Surg* 2009; **96**: 1162-1166
- 3 **Kaloo AN,** Singh VK, Jagannath SB, Niiyama H, Hill SL, Vaughn CA, Magee CA, Kantsevov SV. Flexible transgastric peritoneoscopy: a novel approach to diagnostic and therapeutic interventions in the peritoneal cavity. *Gastrointest Endosc* 2004; **60**: 114-117
- 4 **Merrifield BF,** Wagh MS, Thompson CC. Peroral transgastric organ resection: a feasibility study in pigs. *Gastrointest Endosc* 2006; **63**: 693-697
- 5 **Wagh MS,** Thompson CC. Surgery insight: natural orifice transluminal endoscopic surgery—an analysis of work to date. *Nat Clin Pract Gastroenterol Hepatol* 2007; **4**: 386-392
- 6 **Tagaya N,** Kubota K. NOTES: approach to the liver and spleen. *J Hepatobiliary Pancreat Surg* 2009; **16**: 283-287
- 7 **Pai RD,** Fong DG, Bundga ME, Odze RD, Rattner DW, Thompson CC. Transcolonic endoscopic cholecystectomy: a NOTES survival study in a porcine model (with video). *Gastrointest Endosc* 2006; **64**: 428-434
- 8 **Ryou M,** Fong DG, Pai RD, Tavakkolizadeh A, Rattner DW, Thompson CC. Dual-port distal pancreatectomy using a prototype endoscope and endoscopic stapler: a natural orifice transluminal endoscopic surgery (NOTES) survival study in a porcine model. *Endoscopy* 2007; **39**: 881-887
- 9 **Rattner D,** Kaloo A. ASGE/SAGES Working Group on Natural Orifice Transluminal Endoscopic Surgery. October 2005. *Surg Endosc* 2006; **20**: 329-333
- 10 **Litynski GS.** Erich Mühe and the rejection of laparoscopic cholecystectomy (1985): a surgeon ahead of his time. *JLS* 1998; **2**: 341-346
- 11 **Ryou M,** Thompson CC. Magnetic retraction in natural-orifice transluminal endoscopic surgery (NOTES): addressing the problem of traction and countertraction. *Endoscopy* 2009; **41**: 143-148
- 12 **Swanstrom L,** Zheng B. Spatial orientation and off-axis challenges for NOTES. *Gastrointest Endosc Clin N Am* 2008; **18**: 315-324; ix
- 13 **Vosburgh KG,** Stylopoulos N, Estepar RS, Ellis RE, Samset E, Thompson CC. EUS with CT improves efficiency and structure identification over conventional EUS. *Gastrointest Endosc* 2007; **65**: 866-870
- 14 **Bardaro SJ,** Swanström L. Development of advanced endoscopes for Natural Orifice Transluminal Endoscopic Surgery (NOTES). *Minim Invasive Ther Allied Technol* 2006; **15**: 378-383
- 15 **Astudillo JA,** Sporn E, Bachman S, Miedema B, Thaler K. Transgastric cholecystectomy using a prototype endoscope with 2 deflecting working channels (with video). *Gastrointest Endosc* 2009; **69**: 297-302
- 16 **Swanström L,** Swain P, Denk P. Development and validation of a new generation of flexible endoscope for NOTES. *Surg Innov* 2009; **16**: 104-110
- 17 **Swanstrom LL,** Whiteford M, Khajanchee Y. Developing essential tools to enable transgastric surgery. *Surg Endosc* 2008; **22**: 600-604
- 18 **Spaun GO,** Zheng B, Swanström LL. A multitasking platform

- for natural orifice transluminal endoscopic surgery (NOTES): a benchtop comparison of a new device for flexible endoscopic surgery and a standard dual-channel endoscope. *Surg Endosc* 2009; Epub ahead of print
- 19 **Thompson CC**, Ryou M, Soper NJ, Hungess ES, Rothstein RL, Swanstrom LL. Evaluation of a manually driven, multitasking platform for complex endoluminal and natural orifice transluminal endoscopic surgery applications (with video). *Gastrointestinal Endosc* 2009; **70**: 121-125
 - 20 **Hazey JW**, Narula VK, Renton DB, Reavis KM, Paul CM, Hinshaw KE, Muscarella P, Ellison EC, Melvin WS. Natural-orifice transgastric endoscopic peritoneoscopy in humans: Initial clinical trial. *Surg Endosc* 2008; **22**: 16-20
 - 21 **Salinas G**, Saavedra L, Agurto H, Quispe R, Ramírez E, Grande J, Tamayo J, Sánchez V, Málaga D, Marks JM. Early experience in human hybrid transgastric and transvaginal endoscopic cholecystectomy. *Surg Endosc* 2010; **24**: 1092-1098
 - 22 **Palanivelu C**, Rajan PS, Rangarajan M, Parthasarathi R, Senthilnathan P, Prasad M. Transvaginal endoscopic appendectomy in humans: a unique approach to NOTES--world's first report. *Surg Endosc* 2008; **22**: 1343-1347
 - 23 **Ramos AC**, Zundel N, Neto MG, Maalouf M. Human hybrid NOTES transvaginal sleeve gastrectomy: initial experience. *Surg Obes Relat Dis* 2008; **4**: 660-663

S- Editor Li LF **L- Editor** Lutze M **E- Editor** Yang C

Antonello Forgione, MD, PhD, MBA, Series Editor

***In vivo* miniature robots for natural orifice surgery: State of the art and future perspectives**

Manish M Tiwari, Jason F Reynoso, Amy C Lehman, Albert W Tsang, Shane M Farritor, Dmitry Oleynikov

Manish M Tiwari, Jason F Reynoso, Albert W Tsang, Dmitry Oleynikov, Department of Surgery, University of Nebraska Medical Center, 985126 Nebraska Medical Center Omaha, NE 68198-5126, United States

Amy C Lehman, Shane M Farritor, Department of Mechanical Engineering, University of Nebraska-Lincoln, N104 Scott Engineering Center, Lincoln, NE 68588-0656, United States

Author contributions: Lehman AC, Farritor SM and Oleynikov D were involved in concept and design of the study, data acquisition, data analysis and interpretation; Tiwari MM, Reynoso JF and Tsang AW participated in data acquisition and preparation of the manuscript.

Supported by NASA EPSCoR, Nebraska Research Initiative, Telemedicine and Advanced Technology Research Center, NASA-Nebraska Space Grant Consortium grants and National Science Foundation Graduate Research Fellowship

Correspondence to: Dmitry Oleynikov, MD, FACS, Director, Associate Professor, Department of Surgery, University of Nebraska Medical Center, 985126 Nebraska Medical Center Omaha, NE 68198-5126, United States. doleynik@unmc.edu

Telephone: +1-402-5594581 Fax: +1-402-5596749

Received: February 4, 2010 Revised: March 11, 2010

Accepted: March 18, 2010

Published online: June 27, 2010

a laparoscopic or NOTES procedure is the use of small robotic devices that can be implanted in an intracorporeal manner. Multiple, independent, miniature robots can be simultaneously inserted into the abdominal cavity to provide a robotic platform for NOTES surgery. The capabilities of the robots include imaging, retraction, tissue and organ manipulation, and precise maneuverability in the abdominal cavity. Such a platform affords several advantages including enhanced visualization, better surgical dexterity and improved triangulation for NOTES. This review discusses the current status and future perspectives of this novel miniature robotics platform for the NOTES approach. Although these technologies are still in pre-clinical development, a miniature robotics platform provides a unique method for addressing the limitations of minimally invasive surgery, and NOTES in particular.

© 2010 Baishideng. All rights reserved.

Key words: Robotic surgery; *In vivo* robots; Natural orifice surgery; Robotic surgical platforms

Peer reviewer: Dr. Simone Ferrero, San Martino Hospital and University of Genoa, Largo R. Benzi 1, Genoa 16131, Italy

Tiwari MM, Reynoso JF, Lehman AC, Tsang AW, Farritor SM, Oleynikov D. *In vivo* miniature robots for natural orifice surgery: State of the art and future perspectives. *World J Gastrointest Surg* 2010; 2(6): 217-223 Available from: URL: <http://www.wjgnet.com/1948-9366/full/v2/i6/217.htm> DOI: <http://dx.doi.org/10.4240/wjgs.v2.i6.217>

Abstract

Natural orifice transluminal endoscopic surgery (NOTES) is the integration of laparoscopic minimally invasive surgery techniques with endoscopic technology. Despite the advances in NOTES technology, the approach presents several unique instrumentation and technique-specific challenges. Current flexible endoscopy platforms for NOTES have several drawbacks including limited stability, triangulation and dexterity, and lack of adequate visualization, suggesting the need for new and improved instrumentation for this approach. Much of the current focus is on the development of flexible endoscopy platforms that incorporate robotic technology. An alternative approach to access the abdominal viscera for either

INTRODUCTION

Minimally invasive surgery represents a significant shift in surgical approach from the conventional open surgery methods, offering patient benefits including reduced morbidity, shorter hospital stays, and better cosmetic results.

The safety and efficacy of laparoscopic techniques has been demonstrated in several abdominal surgeries^[1-4]. Adequate access to target organs in the abdominal space, either for diagnostic or therapeutic purposes, is critical for surgical intervention. In contrast to traditional laparotomy, laparoscopic techniques employ strategic arrangement of limited ports for abdominal cavity access depending on the surgical procedure. The notion that safety and efficacy of current laparoscopic techniques can be further enhanced by reducing the number of laparoscopic port incisions^[5,6] has resulted in the renewed interest in single incision laparoscopic surgery for several surgical procedures such as cholecystectomy, appendectomy and nephrectomy^[7-10]. However, outcomes of single incision surgery are still being evaluated.

Consistent with a push towards further reducing surgical invasiveness, natural orifice surgery is a novel surgical approach. Natural orifice transluminal endoscopic surgery (NOTES) involves the use of natural orifices to gain access to the abdominal cavity^[11]. This effectively eliminates the need for any external incisions for visceral access, and thus NOTES represents the least invasive surgical technique. Successful application of NOTES technology has been demonstrated in several pre-clinical studies using either a transgastric, transvesical or transcolonic approach^[12-14]. A NOTES approach has also been used for various abdominal surgical procedures such as organ resection^[15], gastrojejunostomy and gastrojejunal anastomosis^[16,17], and oophorectomy and tubectomy^[18]. Recently, NOTES has shown promise in clinical studies of cholecystectomy and appendectomy^[19,20]. Despite several studies, NOTES experience remains largely experimental with limited clinical studies.

FLEXIBLE ENDOSCOPY PLATFORM FOR NOTES

Although several experimental studies have clearly demonstrated the feasibility and successful application of NOTES^[12-18], inherently the approach appears to be surgically challenging. NOTES approach, in principle, shows an amalgamation of laparoscopic minimally invasive surgery techniques with endoscopic technology. Recent advances in fiberoptics and endoscopic technology allow for enhanced imaging and manipulation of visceral organs. A typical NOTES procedure incorporates a flexible endoscopy platform to obtain access to the peritoneal cavity. Current flexible video-endoscopes are specifically designed to traverse through hollow intraluminal structures and provide image-guided navigation through body cavities. With the help of a trans-visceral surgical incision, an entry into the abdominal space is accomplished. Subsequently, the accessory channels of the flexible endoscope are utilized to insert devices for manipulation of the target abdominal organ. Upon completion of the surgical tasks, the visceral incision is repaired and the scope manually withdrawn through the natural orifice^[11]. However, several questions regarding the technique still remain unanswered. The optimal visceral site for access to the peritoneal cavity remains

unclear. Consequently, there is lack of a standardized approach for creating this trans-visceral opening. Additionally, lack of adequate closure techniques for the NOTES visceral incision site has resulted in limited applications of this surgical endoscopic technique^[11].

NOTES INSTRUMENTATION

Despite the advances in NOTES technology, this novel surgical approach exhibits a unique instrumentation paradox. Progressive propagation of instruments first through the hollow visceral lumen followed by maneuverability to different parts of the abdomen through a visceral incision requires the design and development of endoscopic entry tools that are flexible in their entirety. However, once within the anatomic space, the same instruments are required to provide a stable platform for organ and tissue manipulation. As a result endoscope fixation and stiffening may be optimal for such tasks^[21]. In addition, there is inadequate visualization of the surgical environment during the NOTES procedure. The prospect of working through a small orifice and within a closed lumen while also performing tasks that require precision is surgically challenging. The problem is further compounded by two-dimensional imaging of the operating field and limited intuitive knowledge of the exact orientation of the scope within the lumen. Furthermore, organ and tissue manipulation require precise articulation and triangulation capabilities of surgical tools. These capabilities, in addition, should not be restricted in any fashion by the movement of the endoscope. However, current flexible video-endoscopes offer minimal triangulation and hence impair surgical manipulation. Current flexible endoscopy platforms allow for accessory instrumentation through the endoscope channels that are in the same geometric plane as the endoscope. This single-planar instrumentation further restricts the ability to apply off-axis forces for organ manipulation^[11]. Thus, inadequate visualization and lack of triangulation with existing instruments limits surgical dexterity. Therefore, there is a need for new and improved surgical tools and instrumentation for NOTES.

FLEXIBLE ROBOTICS PLATFORM FOR NOTES

Limited visualization and surgical dexterity constraints were similarly seen during the early development of laparoscopic surgery. Robotic technology significantly influenced laparoscopic surgery and alleviated some of these constraints of traditional laparoscopic surgery. The commercially available da Vinci Surgical System (Intuitive Surgical Inc., Sunnyvale, CA) incorporated features such as articulating end effectors and increased degrees of freedom that significantly increased surgical dexterity during laparoscopic surgery. In addition, stereoscopic three-dimensional vision and tremor abolition enabled sophisticated visual feedback during surgical tasks^[22]. These enhancements and the development of robotic instruments and devices fur-

ther improved tissue and target organ manipulation during laparoscopic surgical tasks.

Similarly, the application of robotic technology to existing NOTES technique can revolutionize natural orifice surgery. As with laparoscopic surgery, robotics can help address some of the classical constraints of the flexible endoscopy platform used during NOTES. Better visualization through robotic stereoscopic visualization and significant improvement in surgical dexterity by enhancing degrees of freedom for complex surgical tasks can be accomplished with a flexible robotics platform^[23]. Another critical area that could benefit from a flexible robotics platform is the mechanical control of endoscope movement within the tubular lumen. Existing flexible video-endoscopes used in the NOTES approach allow for manual control of endoscope motion. This is best suited for traversing less complex, tubular, hollow structures during endoscopy procedures and is certainly suboptimal for complex, small anatomic spaces. Manual control of existing endoscopic technology is also not suitable for navigation through a three-dimensional, complex abdominal cavity that requires several maneuvers and fine control of the endoscope tip. Constant positioning and re-positioning of the manual endoscope in several desired locations of the abdominal cavity remains troublesome. As a result, current manipulation and steering technologies are crude and do not offer the surgical precision required for complex surgical tasks during NOTES. Thus, development of a flexible robotics platform capable of providing better visualization, precision maneuverability in large cavities, fine motor control of endoscope distal tip during complex tasks and enhanced surgical dexterity is necessary^[24].

MINIATURE *IN VIVO* SURGICAL ROBOTS FOR NOTES

Although a flexible robotics platform can offer significant advantages over the current platform, there are specific limitations that may hamper this technology. Current surgical robotics is largely an exoluminal technology that is further constrained by the large size of the robot. Despite the advantages of increased degrees of freedom, robotics technology still remains, to some extent, constrained by the fulcrum effect at the abdominal wall incision. Animal studies in a porcine model of NOTES nephrectomy have noted some of these limitations. A transvaginal NOTES approach for porcine pyeloplasty and nephrectomy with the da Vinci robotic platform has demonstrated frequent collisions of robotic arms and raised the issue of appropriateness of the da Vinci surgical platform for NOTES^[25]. These results suggest that in the present form, any application of surgical robotics for NOTES seems inappropriate because the available technology is too large for the natural orifice and does not conform to the geometry of the lumen. Miniaturization of the robotic technology can significantly enhance the degrees of freedom in either a laparoscopic or NOTES procedure^[21]. A fundamentally different and alternative approach to

access the abdominal viscera for either a laparoscopic or NOTES procedure is the use of small robotic devices that can be introduced in an intracorporeal fashion. These robots can be inserted in the abdominal cavity and are thus not constrained by the abdominal wall incision. Additionally multiple, independent, miniature robots each with a specific, specialized purpose can be inserted in the abdominal cavity.

This novel robotics platform is the result of significant cross-talk between flexible endoscopy and surgical robotics platforms. It appears that the da Vinci surgical platform may not be suitable for NOTES. Miniature surgical robotics provides an alternative robotic platform that is considerably smaller and task-specific for NOTES. This novel miniature robotics platform provides specific robot-assist devices for NOTES surgical tasks such as surgical environment imaging, tissue and organ manipulation and precise maneuverability in the abdominal cavity. Many robots can be simultaneously deployed into the peritoneal cavity providing enhanced imaging from multiple angles and improved dexterity due to loss of the abdominal wall fulcrum effect^[21]. Categorized as either fixed-base or mobile, the miniature *in vivo* robots can act as a family to perform complex surgical tasks. A miniature robot with improved optics and the ability to reposition the camera in an arbitrary fashion within the peritoneal cavity would furnish the surgeon with three-dimensional imaging, improved depth perception and quality video feedback^[26]. Additionally, these *in vivo* robots can be controlled externally in a remote fashion thus eliminating the need for an external tether required in the existing flexible endoscopic platform. Thus, the characteristic challenges and constraints of NOTES have presented an opportunity for development of novel robotic surgical platforms.

FIXED *IN VIVO* IMAGING ROBOTS

Fixed-base *in vivo* miniature robots remain in the location of deployment and are unable to self-navigate away from this intraperitoneal position. The pan and tilt camera robot is a prototypical fixed-base imaging robot. This imaging robot was developed for *in vivo* use during standard laparoscopic surgery and successfully employed for surgical visual feedback in a porcine model^[27]. This conically designed, aluminum robot measures 15 mm in diameter and rests on retractable, spring loaded platform legs that are abducted after entry into the abdominal cavity. Illumination is provided by light-emitting-diodes (LED). It is equipped with 360 degree panning capability and a 45 degree tilt mechanism controlled by two independent motors. These movements allow for better visualization and depth perception during laparoscopic surgery. Visual feedback from this robot has been used to perform a porcine laparoscopic cholecystectomy and canine laparoscopic prostatectomy^[26,27]. This robot was inserted through a small abdominal incision and the visual feedback from the robot allowed for placement of additional trocars and other laparoscopic tools during surgery. The robot enabled better visualization



Figure 1 Mobile *in vivo* imaging robot.

of the surgical environment by providing additional viewing angles and reference frames in conjunction with a standard laparoscope. However, the first generation prototype had a set focal length for the camera lens and thus showed reduced adaptability to focus at varying distances in the peritoneal cavity. An adjustable focus lens was added in the next generation prototype which used the motor previously used for the panning mechanism. Secondary views provided in addition to the standard laparoscope during canine prostatectomy significantly enhanced visualization during the surgical procedure. This imaging robot prototype is wired for power and future designs are planned for wireless communication and battery power.

MOBILE *IN VIVO* IMAGING ROBOTS

In contrast to the fixed-base miniature robots, mobile robots possess the capability to navigate the abdominal cavity for tissue manipulation and organ exploration. Mobile robots are specifically designed to navigate the smooth and deformable terrain of the abdominal cavity with the help of two independently driven helical-profiled wheels. This wheel design affords sufficient traction without causing any trauma to the tissues. This mobile robot is 15 mm in diameter and 75 mm in length and the safety and mobile capabilities of this robot in the abdominal cavity have been demonstrated in porcine tests^[28].

A second generation prototype of this mobile robot, shown in Figure 1, integrated the navigation capability of this robot with an adjustable-focus robotic camera system. The mobile adjustable-focus robotic camera is 20 mm in diameter and has two independently motor-driven wheels and a counter-rotation preventing tail. This system is capable of forward, reverse and turning motion within the abdominal cavity. The capability of this mobile imaging robot to navigate and explore various abdominal organs was tested in an *in vivo* porcine model^[28]. After insertion through a modified laparoscopic port, the mobile camera system safely navigated the abdominal organs and provided a focused view of various abdominal regions. The mobile robotic camera system also provided sole visual feedback and enhanced depth perception during a porcine cholecystectomy. Insertion of such a mobile imaging robot through a standard laparoscopic port could eliminate the need for a separate camera port during abdominal surgeries.

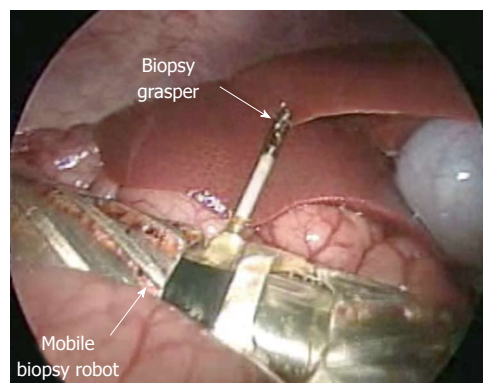


Figure 2 *In vivo* biopsy robot with biopsy grasper.

MOBILE *IN VIVO* BIOPSY ROBOT

A modified prototype of the mobile imaging robot is the mobile *in vivo* biopsy robot, shown in Figure 2. This *in vivo* biopsy robot is essentially similar in design to the mobile *in vivo* imaging robot and possesses independently controlled wheels for mobility, a camera system for surgical imaging and a 2.4 mm wide robotic grasper for biopsy. The biopsy robot is designed to generate sufficient extraction force for tissue biopsy. The mobile imaging camera system on this robot provided visual feedback and helped select a suitable biopsy site. The biopsy graspers were then successfully applied and hepatic tissue biopsy was accomplished^[29]. The biopsy robot was then retracted through the entry incision and thus demonstrated successful one-port biopsy and tissue manipulation. This robot provides the added advantage of surgical task assistance and tissue manipulation compared to the previous mobile imaging robots that solely provided visualization assistance during abdominal surgery.

MOBILE ENDOLUMINAL ROBOT

The mobile endoluminal robot is 12 mm in diameter and 75 mm long with two independently driven wheels that provide forward, reverse and turning capability in the abdominal cavity. The ability of the mobile endoluminal robot for transgastric exploration under esophagogastroduodenoscopic (EGD) control was successfully demonstrated in porcine models^[30,31]. The robot was advanced into the gastric cavity through an overtube placed under EGD control. The robot was introduced into the peritoneal cavity through a transgastric incision performed with an endoscopic needle-knife. A robot-assisted abdominal cavity exploration including liver and small bowel manipulation was successfully completed. Subsequently, the robot was retracted and an endoscopic closure of transgastric incision site was achieved. The robot was eventually retrieved with an endoscopic snare demonstrating the potential ability of these *in vivo* robots to perform natural orifice surgery.

IN VIVO COOPERATIVE ROBOTS

In vivo robots confirm to the geometry of the lumen and

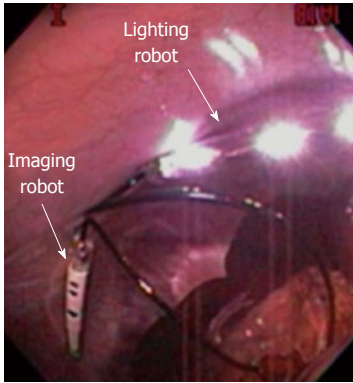


Figure 3 Cooperative robots: Imaging and lighting robot used together.

their size specifications are in accordance with natural orifice size presenting the potential that a family of miniature *in vivo* robots could be synchronously deployed in the abdominal cavity for natural orifice surgery. The concept of cooperative robots, shown in Figure 3, each providing spatial orientation and specific task assistance during surgical procedures has been demonstrated in a non-survival porcine model^[32]. Three miniature *in vivo* robots, including a peritoneum-mounted imaging robot, a lighting robot and a retraction robot, are designed for specific surgical tasks. The imaging robot is a 12 mm robot consisting of an outer tube that houses an inner tube with a lens, camera board and three direct current (DC) micromotors for rotation. The robot is fitted with LED for illumination and enables the device to provide video feedback without supplemental light source. The imaging robot can be re-positioned in the abdominal cavity by manipulating external magnetic handles that attract magnets in the robot's body. This magnetically anchored imaging robot is designed to provide video feedback on a standard monitor during surgical procedures. The lighting robot has an outer tube that houses six white LEDs and is attached to the interior abdominal wall with external magnetic handles. The retraction robot consists of two embedded magnets and a tethered grasping device. A magnetic DC micromotor in the body of the robot coupled with a drum provides rotational movement and activates a grasping device. All three robots are appropriately sized to be inserted through a standard laparoscopic trocar or through a natural orifice during NOTES procedure.

These three robots in conjunction with a standard upper endoscope have been used in a non-survival porcine NOTES procedure^[32]. For this procedure, initially an overtube was placed with the assistance of an endoscope and advanced into the peritoneal cavity. The three robots were then deployed in the peritoneal cavity and magnetically positioned along the upper abdominal wall. In this cooperative procedure, the imaging robot was able to provide high quality video feedback for peritoneal cavity exploration. The retraction robot was specifically used for manipulation of surgical targets such as bowel and gallbladder. Thus, stable imaging by the imaging robot, adequate illumination

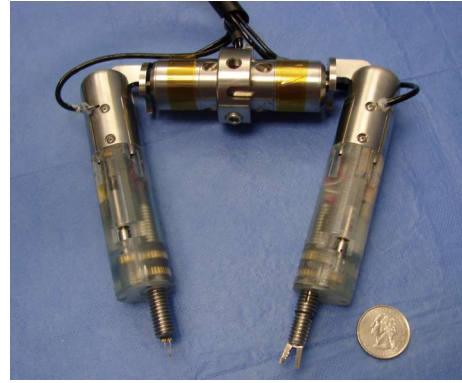


Figure 4 Prototype *in vivo* dexterous robot with grasper and cautery end effector arms.

by the lighting robot and tissue manipulation by the retraction robot provide proof of concept for the use of multiple, independent, specialized robotic devices in a NOTES approach.

IN VIVO DEXTEROUS ROBOT

The dexterous miniature *in vivo* robot for NOTES is a multi-functional robot with ability for tissue retraction and manipulation, stereovision imaging, cautery, and tissue grasping capability. The design of the robot consists of two arms connected to a central body as shown in Figure 4. Each arm consists of upper and lower segments. The upper arm is connected to the central body by a rotational shoulder joint. Retraction and extension is achieved by a lower arm that telescopes in and out of an upper arm. The lower arm is fitted with either a grasper forceps or a cautery end effector. This robot has a remote surgeon interface console. The surgeon control interface is remote in location and comprises of two controllers, a display, and a foot pedal. Each robot arm movement is controlled by the movement of the controllers that are located remotely. Grasper and cautery extensions can be activated when required, at the push of a button. The video feedback from a standard laparoscope is displayed on a screen between the two controllers. Using the surgeon interface console, positioning of the dexterous robot arms with adequate workspace can be performed remotely. Each quadrant of the abdomen can be imaged and surgically accessed through this technique without requiring additional incisions. This robot has been used to perform cholecystectomy and small bowel dissection in a porcine model^[33]. This robotic device was endoscopically deployed in the peritoneal cavity through a gastrotomy incision. On-board video feedback from the robot enabled visualization of the small bowel for further manipulation. A small bowel dissection was then performed with the help of forceps on one arm and cautery on the other arm. The small bowel was grasped and retracted with one arm allowing for access of the cautery. The cautery arm was then extended and was able to cauterize the bowel. The positioning of the arms allows for off-axis forces to be applied during tissue retraction

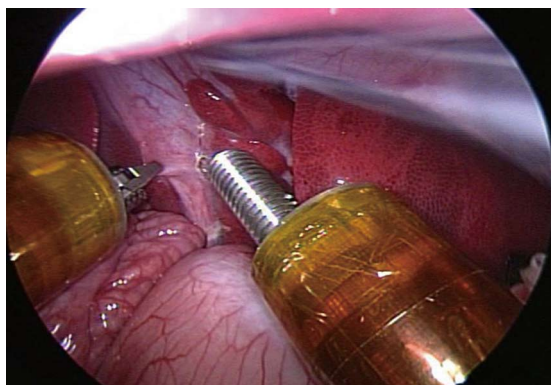


Figure 5 *In vivo* dexterous robot performing tissue manipulation during porcine cholecystectomy.

and dissection. Once in the peritoneal cavity, this robot provided a stable platform for visualization, dexterous capability to apply off-axis forces, and better triangulation capability for tissue manipulation. Tissue manipulation capability of the *in vivo* dexterous robot is shown in Figure 5. Presently, the initial prototype of this robot is large and hence an abdominal incision was utilized for adequate access for a cholecystectomy. Further miniaturization of the robot for performing a NOTES procedure in a remote fashion is ongoing.

NOTES FUTURE PERSPECTIVES

Miniature *in vivo* robotics is a novel platform and an alternative approach for NOTES. Although successful application of several distinct *in vivo* robots has been demonstrated in animal models, limitations of their use remain. Currently, some of these robots are best suited for use in conjunction with laparoscopic and endoscopic instruments. To be completely NOTES-compatible, further refinement of these robotic devices is necessary. Nevertheless, successful application of some of these *in vivo* robots for NOTES has been shown in animal models. For robots that are large in size, further miniaturization is necessary for NOTES approach. Additionally, some of these robots still remain externally tethered for power. Future tether-free applications will be adequately battery-powered and use wireless technology^[21]. Development of *in vivo* robotic assistants with a range of end effectors for specialized complex tasks such as tissue dissection, tissue manipulation and organ retraction, better cauterization, enhanced stereoscopic visualization, surgical suturing capability, and closure of visceral incision endoscopically is necessary for translation into NOTES technology.

Future flexible robotics platform for NOTES will require development of robotic endoscopes with the ability to develop a stable platform for complex surgical tasks without compromising endoscope tip maneuverability. A computer-controlled robotic platform may benefit tasks requiring surgical precision, navigation through peritoneal cavity, and complex maneuvers of the endoscope tip. This computerized robotic platform would allow for surgically

precise, accurately controlled and complex maneuvers of the endoscope during surgical procedures. Advances in instrumentation for NOTES would include flexible robotics platform-specific graspers, forceps, scissors, needle-drivers, coagulators and other surgical instruments with easy insertion and quick exchangeability^[23,24].

In addition to these robotic platform-specific developments, several issues specific to NOTES such as the optimal site for visceral incision, a standardized technique for NOTES procedures and adequate closure techniques need to be addressed^[11]. These issues along with technology development will ultimately determine if the scope of NOTES can be broadened to include complex surgical procedures.

CONCLUSION

A miniature *in vivo* robotics platform represents a novel and alternative approach for NOTES. Such a platform affords several advantages such as enhanced visualization, better surgical dexterity and significantly improved triangulation capability for NOTES procedures. Development of task-specific *in vivo* robotic devices for use during NOTES provides enhanced surgical dexterity. Development of a totally intraperitoneal team of robots that cooperatively perform surgical procedures in animal models has been accomplished. Currently, robots that can perform NOTES and other laparoscopic procedures in a remote fashion are being developed. Although these technologies are still in pre-clinical development, a miniature robotics platform provides a unique method for addressing the limitations of minimally invasive surgery, and NOTES in particular.

REFERENCES

- 1 Colak T, Akca T, Kanik A, Aydin S. Randomized clinical trial comparing laparoscopic totally extraperitoneal approach with open mesh repair in inguinal hernia. *Surg Laparosc Endosc Percutan Tech* 2003; **13**: 191-195
- 2 Roumm AR, Pizzi L, Goldfarb NI, Cohn H. Minimally invasive: minimally reimbursed? An examination of six laparoscopic surgical procedures. *Surg Innov* 2005; **12**: 261-287
- 3 Zacks SL, Sandler RS, Rutledge R, Brown RS Jr. A population-based cohort study comparing laparoscopic cholecystectomy and open cholecystectomy. *Am J Gastroenterol* 2002; **97**: 334-340
- 4 Wei HB, Huang JL, Zheng ZH, Wei B, Zheng F, Qiu WS, Guo WP, Chen TF, Wang TB. Laparoscopic versus open appendectomy: a prospective randomized comparison. *Surg Endosc* 2010; **24**: 266-269
- 5 Munro MG. Laparoscopic access: complications, technologies, and techniques. *Curr Opin Obstet Gynecol* 2002; **14**: 365-374
- 6 Cugura JE, Kirac I, Kulis T, Janković J, Beslin MB. First case of single incision laparoscopic surgery for totally extraperitoneal inguinal hernia repair. *Acta Clin Croat* 2008; **47**: 249-252
- 7 Desai MM, Rao PP, Aron M, Pascal-Haber G, Desai MR, Mishra S, Kaouk JH, Gill IS. Scarless single port transumbilical nephrectomy and pyeloplasty: first clinical report. *BJU Int* 2008; **101**: 83-88
- 8 Kaouk JH, Haber GP, Goel RK, Desai MM, Aron M, Rackley RR, Moore C, Gill IS. Single-port laparoscopic surgery in urology: initial experience. *Urology* 2008; **71**: 3-6
- 9 Ponsky TA, Diluciano J, Chwals W, Parry R, Boulanger S. Early experience with single-port laparoscopic surgery in chil-

- dren. *J Laparoendosc Adv Surg Tech A* 2009; **19**: 551-553
- 10 **Tacchino R**, Greco F, Matera D. Single-incision laparoscopic cholecystectomy: surgery without a visible scar. *Surg Endosc* 2009; **23**: 896-899
- 11 **McGee MF**, Rosen MJ, Marks J, Onders RP, Chak A, Faulx A, Chen VK, Ponsky J. A primer on natural orifice transluminal endoscopic surgery: building a new paradigm. *Surg Innov* 2006; **13**: 86-93
- 12 **Fong DG**, Pai RD, Thompson CC. Transcolonic endoscopic abdominal exploration: a NOTES survival study in a porcine model. *Gastrointest Endosc* 2007; **65**: 312-318
- 13 **Kalloo AN**, Singh VK, Jagannath SB, Niiyama H, Hill SL, Vaughn CA, Magee CA, Kantsevov SV. Flexible transgastric peritoneoscopy: a novel approach to diagnostic and therapeutic interventions in the peritoneal cavity. *Gastrointest Endosc* 2004; **60**: 114-117
- 14 **Lima E**, Rolanda C, Pêgo JM, Henriques-Coelho T, Silva D, Carvalho JL, Correia-Pinto J. Transvesical endoscopic peritoneoscopy: a novel 5 mm port for intra-abdominal scarless surgery. *J Urol* 2006; **176**: 802-805
- 15 **Wagh MS**, Merrifield BF, Thompson CC. Endoscopic transgastric abdominal exploration and organ resection: initial experience in a porcine model. *Clin Gastroenterol Hepatol* 2005; **3**: 892-896
- 16 **Bergström M**, Ikeda K, Swain P, Park PO. Transgastric anastomosis by using flexible endoscopy in a porcine model (with video). *Gastrointest Endosc* 2006; **63**: 307-312
- 17 **Kantsevov SV**, Jagannath SB, Niiyama H, Chung SS, Cotton PB, Gostout CJ, Hawes RH, Pasricha PJ, Magee CA, Vaughn CA, Barlow D, Shimonaka H, Kalloo AN. Endoscopic gastrojejunostomy with survival in a porcine model. *Gastrointest Endosc* 2005; **62**: 287-292
- 18 **Wagh MS**, Merrifield BF, Thompson CC. Survival studies after endoscopic transgastric oophorectomy and tubectomy in a porcine model. *Gastrointest Endosc* 2006; **63**: 473-478
- 19 **Horgan S**, Cullen JP, Talamini MA, Mintz Y, Ferreres A, Jacobsen GR, Sandler B, Bosia J, Savides T, Easter DW, Savu MK, Ramamoorthy SL, Whitcomb E, Agarwal S, Lukacz E, Dominguez G, Ferraina P. Natural orifice surgery: initial clinical experience. *Surg Endosc* 2009; **23**: 1512-1518
- 20 **Decarli LA**, Zorron R, Branco A, Lima FC, Tang M, Pioneer SR, Sanseverino JI, Menguer R, Bigolin AV, Gagner M. New hybrid approach for NOTES transvaginal cholecystectomy: preliminary clinical experience. *Surg Innov* 2009; **16**: 181-186
- 21 **Shah BC**, Buettner SL, Lehman AC, Farritor SM, Oleynikov D. Miniature in vivo robotics and novel robotic surgical platforms. *Urol Clin North Am* 2009; **36**: 251-263, x
- 22 **Oleynikov D**. Robotic surgery. *Surg Clin North Am* 2008; **88**: 1121-1130, viii
- 23 **Canes D**, Lehman AC, Farritor SM, Oleynikov D, Desai MM. The future of NOTES instrumentation: Flexible robotics and in vivo minirobots. *J Endourol* 2009; **23**: 787-792
- 24 **Aron M**, Haber GP, Desai MM, Gill IS. Flexible robotics: a new paradigm. *Curr Opin Urol* 2007; **17**: 151-155
- 25 **Haber GP**, Crouzet S, Kamoi K, Berger A, Aron M, Goel R, Canes D, Desai M, Gill IS, Kaouk JH. Robotic NOTES (Natural Orifice Translumenal Endoscopic Surgery) in reconstructive urology: initial laboratory experience. *Urology* 2008; **71**: 996-1000
- 26 **Rentschler ME**, Platt SR, Dumpert J, Farritor SM, Oleynikov D. In vivo laparoscopic robotics. *Int J Surg* 2006; **4**: 167-171
- 27 **Oleynikov D**, Rentschler M, Hadzialic A, Dumpert J, Platt SR, Farritor S. Miniature robots can assist in laparoscopic cholecystectomy. *Surg Endosc* 2005; **19**: 473-476
- 28 **Rentschler ME**, Dumpert J, Platt SR, Ahmed SI, Farritor SM, Oleynikov D. Mobile in vivo camera robots provide sole visual feedback for abdominal exploration and cholecystectomy. *Surg Endosc* 2006; **20**: 135-138
- 29 **Rentschler ME**, Dumpert J, Platt SR, Farritor SM, Oleynikov D. Mobile in vivo biopsy and camera robot. *Stud Health Technol Inform* 2006; **119**: 449-454
- 30 **Rentschler ME**, Dumpert J, Platt SR, Farritor SM, Oleynikov D. Natural orifice surgery with an endoluminal mobile robot. *Surg Endosc* 2007; **21**: 1212-1215
- 31 **Lehman AC**, Rentschler ME, Farritor SM, Oleynikov D. Endoluminal minirobots for transgastric peritoneoscopy. *Minim Invasive Ther Allied Technol* 2006; **15**: 384-388
- 32 **Lehman AC**, Berg KA, Dumpert J, Wood NA, Visty AQ, Rentschler ME, Platt SR, Farritor SM, Oleynikov D. Surgery with cooperative robots. *Comput Aided Surg* 2008; **13**: 95-105
- 33 **Lehman AC**, Dumpert J, Wood NA, Redden L, Visty AQ, Farritor S, Varnell B, Oleynikov D. Natural orifice cholecystectomy using a miniature robot. *Surg Endosc* 2009; **23**: 260-266

S- Editor Li LF L- Editor Hughes D E- Editor Yang C

Antonello Forgione, MD, PhD, MBA, Series Editor

Natural orifice transluminal endoscopic surgery: Educational challenge

Brian J Dunkin

Brian J Dunkin, Department of Clinical Surgery, Weill Cornell Medical College, The Methodist Hospital, 6550 Fannin Street, Houston, TX 77030, United States

Author contributions: Dunkin BJ contributed all to this paper. Correspondence to: Brian J Dunkin, MD, FACS, Professor, Department of Clinical Surgery, Weill Cornell Medical College, The Methodist Hospital, 6550 Fannin Street, Houston, TX 77030, United States. bjdunkin@tmhs.org

Telephone: +1-713-4416382 Fax: +1-713-7902992

Received: December 26, 2009 Revised: March 31, 2010

Accepted: April 7, 2010

Published online: June 27, 2010

Peer reviewer: Rungsun Rerknimitr, MD, Division of Gastroenterology, Internal Medicine, King Chulalongkorn Memorial Hospital, Rama IVC Rd Lumpini, Bangkok 10310, Thailand

Dunkin BJ. Natural orifice transluminal endoscopic surgery: Educational challenge. *World J Gastrointest Surg* 2010; 2(6): 224-230 Available from: URL: <http://www.wjgnet.com/1948-9366/full/v2/i6/224.htm> DOI: <http://dx.doi.org/10.4240/wjgs.v2.i6.224>

Abstract

Natural orifice transluminal endoscopic surgery (NOTES) training is unique in that it crosses specialty lines and most practitioners do not possess both the knowledge and skill to perform the procedures in their current form. The learning process becomes even more complex because the field is in constant evolution with advances in technology and technique being introduced almost daily! The challenges of learning NOTES illustrates a larger problem in all procedurally based medical specialties today-the pace of change has become so rapid that a practicing physician's technical skills become out of date within five to ten years of completing residency or fellowship training. As a result, practicing physicians must develop a strategy to rapidly learn about a new technique or technology and introduce it safely into their practice while satisfying the concerns of their hospital's credentialing committee. This chapter will explore the options for learning new procedures and discuss the rapidly expanding armamentarium of education institutes and the developing technology to measure procedural competence.

© 2010 Baishideng. All rights reserved.

Key words: Simulation; Training; Preceptor; Telemedicine; Natural orifice transluminal endoscopic surgery

INTRODUCTION

In 1989 Dr. Eddie Joe Reddick became the first surgeon in the US to remove a diseased gallbladder from a patient using a miniaturized camera system, long narrow instruments and four half inch incisions in the abdominal wall. This new technique of laparoscopic surgery would revolutionize abdominal and thoracic surgery forever. Within three years nearly all general surgeons in the US would move from performing gallbladder surgery using an open technique (a term never used before the era of laparoscopy) to laparoscopic surgery. Most had never even seen a laparoscopic procedure before, much less used the technique to perform a complex operation. This created an unprecedented demand for new procedure training in surgery. Nearly overnight practicing surgeons needed to learn an entirely new set of surgical skills and offer them to their patients in a safe manner. As predicted, there was significant variation in the types of training experiences offered and, unfortunately, some patients suffered complications from undergoing operations by inadequately prepared surgeons.

In 2004, Kalloo *et al*^[1] reported on a series of transgastric peritoneoscopies done in a porcine model-a procedure to be later termed natural orifice transluminal endoscopic surgery (NOTES). That same year Reddy and Rao presented a video of the first human transgastric appendectomy at the Annual Conference of the Society of Gastrointestinal Endoscopy of India^[2]. As with the laparoscopy revolution,

the introduction of NOTES caused a stir among general surgeons and many scrambled to learn more in anticipation of the next possible wave of minimally invasive surgery. Interestingly, a subgroup of advanced therapeutic gastroenterologists was also intrigued by this new field and equally interested in learning more. By 2005 the first NOTES hands-on training course was conducted at Case Western Reserve School of Medicine in Cleveland, Ohio despite the fact that only one human case had been done in the world! Multiple courses followed both in the US and Europe.

NOTES training is unique in that it crosses specialty lines (general and thoracic surgery, gynecology, gastroenterology) and most practitioners do not possess both the knowledge and skill to perform the procedures in their current form. The flexible endoscopy instruments used in NOTES are not familiar to most surgeons while surgical technique and procedures are not familiar to most gastroenterologists. Adding unique points of access such as transvaginal, transcolonic or transesophageal further adds to the learning curve and the whole process becomes even more complex because the field is in constant evolution with advances in technology and technique being introduced almost daily!

The challenges of learning NOTES illustrates a larger problem in all procedurally based medical specialties today—the pace of change has become so rapid that a practicing physician's technical skills become out of date within five to ten years of completing residency or fellowship training. As a result, practicing physicians must develop a strategy to rapidly learn about a new technique or technology and introduce it safely into their practice while satisfying the concerns of their hospital's credentialing committee. This chapter will explore the options for learning new procedures and discuss the rapidly expanding armamentarium of education institutes and the developing technology to measure procedural competence.

CURRENT CHALLENGES IN PERFORMING NOTES

The introduction of laparoscopic cholecystectomy fostered the development of a myriad of educational programs focused on helping practicing surgeons to learn this new technique and begin performing these procedures. The experience from course to course was variable but a model of presenting didactic material coupled with live demonstration of technique followed by rehearsal in an inanimate or animate model was established. With time and standardization of the laparoscopic cholecystectomy technique, surgeons successfully transitioned to this new mode of surgery.

Training to learn NOTES is different from laparoscopy. When laparoscopic cholecystectomy was introduced, surgeons had expert knowledge about the disease process they were treating and the goals of the surgical procedure. Even the laparoscopic instruments looked like long extensions of open ones. Thus they only had to focus on the technical aspects of this new mode of entry into the abdominal

cavity. In a NOTES cholecystectomy, the surgeon again has expert knowledge of the disease process but use of the flexible endoscopic tools is more challenging than in laparoscopy. Now, not only does the surgeon have to learn about the variety of flexible tools but he must also master advanced flexible endoscopy just to deliver these tools to their target location. The tools and the endoscope are also linked which makes manipulation of both difficult to coordinate and results in relying on an assistant more than with most procedures. If transvaginal access is added to the procedure, a whole new understanding of anatomy must be mastered as well.

The gastroenterologist is equally challenged by NOTES. He or she has an advantage when manipulating the endoscope and flexible tools but does not have mastery of surgical principles, technique and anatomy which may have a longer learning curve than the technical issues facing a surgeon. In addition, the gastroenterologist is unaccustomed to working under sterile conditions in the operating room environment and potentially spending a number of hours to perform a single procedure. Alternative access points—such as the transvaginal route—are as equally unfamiliar as they are to the general surgeon.

Finally, both surgeons and gastroenterologists are handicapped in learning NOTES because of the rapid pace of change in the field. Laparoscopic cholecystectomy was disseminated to the majority of general surgeons once the technique had become standardized. In fact, the natural evolution of minimally invasive procedures is to standardize the technique which often results in eventually moving them out of a surgical environment and into another procedure area in the hospital. Percutaneous endoscopic gastrostomy (PEG) tube placement is an excellent example of this evolution having first been performed in the operating room but now done in the endoscopy unit or even at the patient's bedside. The technology and technique of NOTES is evolving so quickly that it is impossible to settle on a standard approach for a particular procedure. As a result, what is learned and even mastered today may not apply tomorrow.

OPTIONS FOR LEARNING A NEW SURGICAL TECHNIQUE

Having identified the challenges for a practicing surgeon to learn a new technique or technology, let us review current options for accomplishing this. The first option is to attend a “continuing medical education (CME)-type” event. CME programs are learning opportunities designed to enhance the knowledge and skills of practicing physicians in their care of patients. A surgeon attending such a program is granted CME credits. These credits document the number of hours the surgeon committed to the activity and are designed to track this type of effort for purposes of reporting to credentialing bodies such as state licensing boards and medical specialty boards. While CME requirements are a motivational element to encourage surgeons to continually update their knowledge and skills,

they are a poor mechanism for gaining procedural competence. The credits usually reflect attendance only and are not an accurate measure of knowledge or skill. There is also variable acceptance of CME credits alone as an indication of procedural competence by hospital credentialing bodies.

As a result, many surgeons follow attendance of a CME-type activity with a preceptorship. A preceptor is a coach in an educational relationship who structures the learning process to achieve a set of formally identified skills. A role model and teacher, the preceptor operates in an environment that closely resembles the normal work setting for the learner. There are three types of preceptorships^[3]. The first is an experience where the preceptor comes to the learner's institution to help perform the operation. This is the most efficient method of transferring skill because the preceptor can help guide the learner surgeon through the procedure on their own patient working with their own operative team and in their own hospital. The entire operative team learns during this experience and system-based barriers to the procedure can be identified and corrected. It is also convenient for the patient. Despite these advantages, there are significant barriers to this type of preceptorship. First, the preceptor may be limited in his or her ability to direct or even take over the procedure. This is because of potential limitations in gaining privileges at the host institution to "scrub-in" to the case. Such a limitation is more concerning when the legal community may view the preceptor as the most qualified person in the operating room and thus responsible for the outcome of the procedure which in turn leads to questions of malpractice liability. Also, many institutions require state licensure for even temporary privileges-a process that can take many months and significant commitment to accomplish. Finally, the ability for a preceptor to teach at institutions outside of their own is limited and disruptive to their own surgical practice.

A second type of preceptorship involves the learner visiting the preceptor's institution. This has the advantage of allowing the preceptor complete control of the case without exposing them to unusual privileging, licensing or malpractice issues. The down side is that most of the challenges put on the preceptor in the first model are now shifted to the learner. There are also issues about patient travel if the learner wants to operate on his own case, and ensuring continuity of the postoperative follow-up.

The third and most effective method of preceptorship is a mini fellowship. Such fellowships offer the most structured experience with time for the preceptor to monitor progress and ensure successful transfer of skills. The obvious disadvantage is that the learner must leave their practice for a significant period of time. There are also obstacles with licensing, privileging and malpractice. Finally, the learner may interfere with the training of residents and fellows at the preceptor's institution.

measures of procedural competence. A practicing surgeon would benefit most by being able to spend a short, concentrated, well structured period of time at an educational institute learning a new procedure and walk away from the experience with a validated objective measure of his or her skills that could be used to convince a credentialing body that they are now prepared to perform that procedure at their home institution. A number of developments are occurring to move surgical education closer to this goal.

One of the most basic advances in surgical training is the development of a new classification system which will give credentialing bodies a better understanding of the type of educational activity in which a surgeon has engaged. The American College of Surgeons developed the System for Verification of Knowledge and Skills which has five levels. A Level I educational event simply requires verification of attendance-much like CME. Level II requires verification of satisfactory completion of course objectives usually done by having the learner take a didactic examination. Level III requires verification of knowledge and skills which, to date, has been accomplished by using a combination of a written examination coupled with evaluation of skills by an expert proctor in a hands-on laboratory experience. Level IV requires verification of a preceptorial experience and Level V requires verification of satisfactory patient outcomes. This classification system clarifies the degree of training and will help credentialing bodies better understand a surgeons credentials and set standards for allowing a performance of new procedures.

Another advance in surgical training is the development of objective measures of knowledge and skill in basic laparoscopy. The Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) has developed a program called the fundamentals of laparoscopic surgery (FLS) which is a training and verification program for laparoscopic surgery. FLS includes on-line didactic material covering the fundamental knowledge-base required for any surgeon performing laparoscopy or thoracoscopy. It also entails a written examination as well as a hands-on skills test using the McGill Inanimate System for Training and Evaluation of Laparoscopic Skills (MISTELS) physical laparoscopy simulator. The MISTELS simulator consists of five exercises performed in a trainer box. A camera and LED lighting system provide visualization and the surgeon works through two trocars placed in fixed positions through an opaque cover on top of the box (Figure 1). The system was designed to be inexpensive and easily portable so that it could be used at home for practice. FLS has gone through extensive testing to prove reliability and validity and is the first commercially available program which provides a benchmark for knowledge and skills in a surgical technique^[4]. Because of the validation work that has been done on FLS, it has withstood the scrutiny of a high stakes exam and is now required by the American Board of Surgery (ABS) to become Board certified. SAGES has partnered with the American College of Surgeons and industry to provide FLS testing at no charge for every graduating general surgery resident in the US.

CURRENT ADVANCES IN SURGICAL TRAINING

What are most needed in surgical training are objective



Figure 1 A camera and LED lighting system provide visualization and the surgeon works through two trocars placed in fixed positions through an opaque cover on top of the box.

Following closely on the heels of FLS is another SAGES program called the Fundamentals of Endoscopic Surgery (FES). FES is modeled after FLS as a validated training and testing program of knowledge and skills in flexible gastrointestinal (GI) endoscopy. Like FLS, FES consists of web-based didactic material covering the fundamental knowledge required to perform flexible endoscopy as well as a written exam and a hands-on skills test. Because there is no equivalent of the MISTELS trainer for flexible endoscopy, the FES task force chose to use a computer based simulation platform for the hands-on skills test. There are five skills sets for FES including endoscope navigation, loop reduction, mucosal evaluation and targeting. FES is currently undergoing rigorous reliability and validity testing and will be rolled out at the SAGES annual meeting in April 2010. Once validated, it is expected that FES will take its place alongside FLS as another requirement by the American Board of Surgery to become certified.

While validated simulator training and testing is important, meaningful measures of real clinical performance are crucial to verifying that a practicing surgeon has the skills that he or she say they have. Validated clinical measures of procedure performance are also required to demonstrate that simulator training has a positive effect on clinical performance. Such an effect is called predictive validity in that performance on the simulator predicts performance in the real clinical domain. Predictive validity is the "Holy Grail" of simulation technology but is missing for almost all current surgical simulators. While developing FES it was envisioned that predictive validity would be a crucial component to its evaluation. As a result, the FES Task Force developed and validated a clinical assessment tool for GI endoscopy called GAGES-the Global Assessment of Gastrointestinal Endoscopic Skills. GAGES was developed by expert endoscopists and educators who defined the fundamental skills required to perform flexible GI endoscopy and then distilled the evaluation of these skills into 2 global assessments: GAGES Upper Endoscopy (GAGES-UE) and GAGES Colonoscopy (GAGES-C). A multi-institutional trial was then conducted to establish the validity of GAGES proving that experts and novices

achieved different scores when evaluated by expert observers. This exciting work provided the first validated clinical assessment tool for performing flexible endoscopy and may replace the practice of using procedure numbers as a surrogate for procedural competence.

In 2002 the American College of Surgeons (ACS) established its Division of Education which is pursuing a spectrum of educational programs to promote patient safety and help surgeons meet the requirements for Maintenance of Certification (MOC) while addressing core competencies^[5]. One of the visions of this Division was the creation of a network of accredited simulation centers that could offer educational support to practicing surgeons on a local and regional level to enhance the quality of surgical care. Some have even suggested that in the future, surgeons may be required by their specialty board to intermittently take a sabbatical during their career and go to an educational institute like that envisioned by the ACS to update their knowledge and skills. In 2005 the ACS began accrediting simulation centers based on strict criteria defined by the Division of Education. These centers are now known as Accredited Education Institutes (AEIs) of which there are currently 46. Most are located in North America, but there are also Institutes in Sweden, Greece and the United Kingdom. Recently the ACS has added to the power of the AEI network by forming the Research and Development Committee of the Consortium of ACS-Accredited Education Institutes. The charge of this Committee is to facilitate and govern the conceptualization, development and implementation of multi-institutional research programs across the AEIs. Such collaboration will foster the development of validated metrics of skills acquisition in a manner that has not been possible before.

While the establishment of a coordinated network of AEIs is a unique ACS program, the concept of providing procedurally based medical training in a comprehensive education institute is not. In 1994 the European Institute of Telesurgery (EITS) was established in Strasbourg, France. This institute has become a model of procedural training in minimally invasive surgery and is responsible for the education of thousands of practicing surgeons over the last 15 years. In 2008 EITS exported their training model to Taiwan with the formation of the Asian Institute of Telesurgery (AITS) which is already having a significant impact on surgeons in Asia. World class institutes have been established in other parts of the world as well including the Minimal Access Therapy Training Unit (MATTU) in Surrey, England and the Advanced Mini Invasive Surgery Academy (AIMS) in Milan, Italy which are a contemporary of EITS having been developed around the same concept and responsible for training many surgeons across multiple specialties in minimally invasive surgical techniques.

So, now surgeons and gastroenterologists have a growing world wide network of education institutes to help them learn new procedures and technologies in an efficient manner. As more validated metrics of procedural competence develop, they will be incorporated into the training of these institutes so that meaningful measures of technical



Figure 2 A novel method of measuring procedural competence using thermal imaging of the face.

proficiency can be given to credentialing bodies for hospital privileging, state and board licensure and MOC.

FUTURE OF PROCEDURAL TRAINING

Exciting developments are on the horizon for verifying procedural competence in medical procedures and supporting physicians through the early part of their learning curve with these new techniques. One example comes from the Methodist Institute for Technology, Innovation and Education (MITIE) in Houston, Texas. MITIE has teamed up with the computer science department at the University of Houston (UH) to develop a novel method of measuring procedural competence using thermal imaging of the face (Figure 2). The UH team had developed a method of quantitatively measuring stress by monitoring the thermal signature of the face and other parameters such as perspiration build-up on the upper lip and intercantonal fold distance. When the MITIE team saw this technology, they hypothesized that expert surgeons should be less stressed while performing complex surgical tasks when compared to a novices and will thus have different thermal signatures. It was proposed to use this technology to monitor novice and expert surgeons while performing laparoscopic drills in a FLS trainer. Preliminary data indicates that these groups can be differentiated by their thermal monitoring. These results are exciting because such a monitoring device is unobtrusive and independent of the actual procedure being performed. Perhaps in the future, a credentialing body will ask for a surgeon's thermal signature before granting privileges for a new procedure!

Other recent innovations in simulation include motion tracking of the hands. At the Imperial College in London, Datta *et al*^[6] have used magnetic trackers in the Imperial College Surgical Assessment Device (ICSAD) to demonstrate that it is possible to quantitatively track the motion of a surgeon's hands and generate a "motion signature" which has a different pattern in experts versus novices (Figure 3). A similar approach has been taken by Rosen *et al*^[7] at the University of Washington using real laparoscopic instruments with a mechanical device called the Blue Dragon (Figure 4). Noble *et al*, working in MITIE,

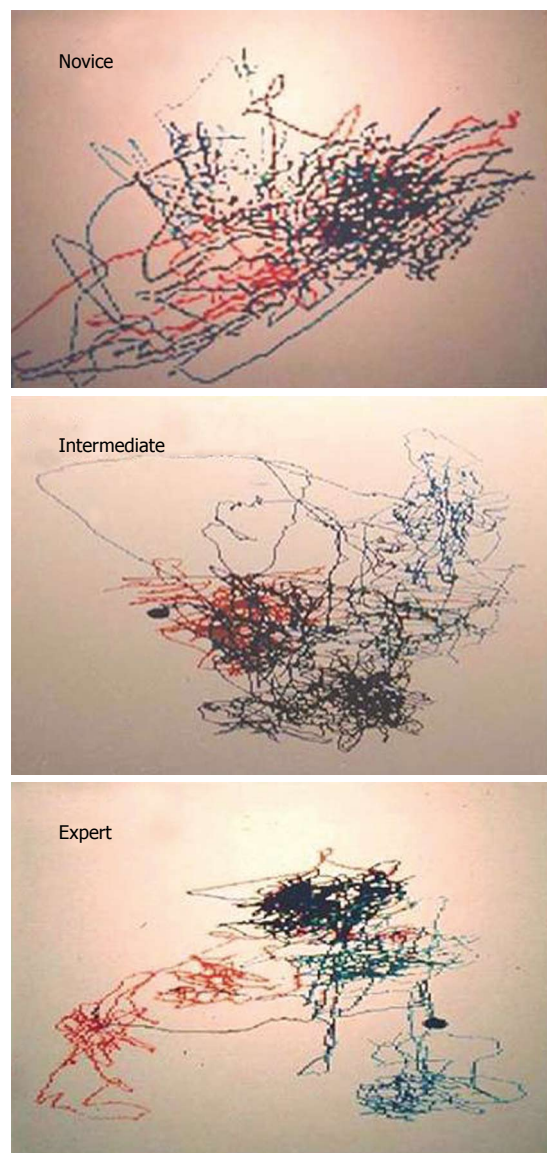


Figure 3 Magnetic trackers demonstrate that it is possible to quantitatively track the motion of a surgeon's hands and generate a "motion signature" which has a different pattern in experts vs novices.

are using motion capture camera technology like that used for video games to monitor orthopedic surgeons during joint replacement surgery (Figure 5). Not only are the tools used by the orthopedic surgeon tracked in space but also the joint prosthesis themselves and the patient's boney surfaces. Using this type of tracking, a surgeon can receive feedback about whether or not their surgical performance fell within acceptable parameters and, if not, what elements require correction. Another advance in simulation on the immediate horizon is termed patient specific simulation. This type of simulation allows for real clinical imaging data sets from specific patients to be programmed into a simulator for the purposes of rehearsing a procedure prior to its actual clinical performance. In this way, surgical teams may rehearse procedures using real patient data for their planning, running scenarios over and over until a satisfactory outcome is achieved. Such simulators are already available in endovascular surgery.

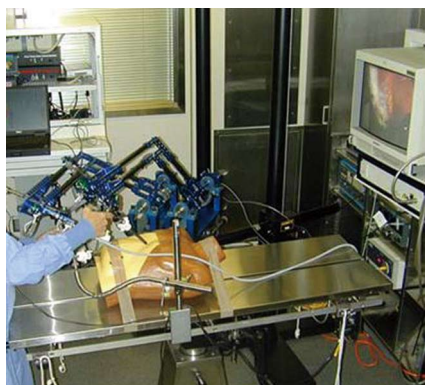


Figure 4 Real laparoscopic instruments with a mechanical device called the Blue Dragon.



Figure 5 Motion capture camera technology.

To maximize procedural adoption, it is imperative that a surgeon receives support from a preceptor after returning to their own hospital. This support during the early part of the learning curve is imperative to ensure smooth procedural adoption while maximizing patient safety. In an effort to address the challenges faced by traveling preceptors outlined earlier in this paper, some have turned to telecommunications as a means of providing support without requiring the preceptor to travel. Telemedicine has certainly gained acceptance in a number of areas but has been difficult to effectively implement in the operating room. Ideally, for teleproctoring to be effective, a meaningful linkage to the OR could be established at a moment's notice when the operating surgeon desires a real time consultation. Until recently, this type of communication has not been available. However, In Touch Health Inc., a leader in medical telepresence *via* the wide area network (WAN) and a remotely manipulated robot, has partnered with Karl Storz Endoscopy to develop the VisitOR1™ telecommunications platform (Figure 6). This platform allows a preceptor working from a laptop computer to link into a VisitOR1™ operating room and manipulate a video monitor with built-in camera and laser pointer. By remotely controlling the camera and video platform the proctor can see what the surgeon sees, point to areas on the operating field, telestrate on the video monitor and push pre-recorded content out to the operative field. With this type of communication



Figure 6 Remote surgeon on control station and VisitOR1™ in operating room environment.

an experienced surgeon working through the early part of their learning curve for a new procedure could be guided safely to deliver quality care in a short period of time with excellent outcomes.

If NOTES progresses to become a common surgical approach, multiple types of NOTES training environments will be created. Ideally, these environments will incorporate the above elements in order to confirm procedural competence. For example, once the learner has prepared for a hands-on training experience, they would come to an accredited training institute to work in a simulated environment. This environment would reproduce patient specific anatomy and pathology for accurate pre-procedure rehearsal. The surgeon's performance would also be closely monitored with both thermal imaging and motion tracking to ensure proper technique. Finally, when the surgeon has been deemed competent in this simulated environment, they would return to their own hospital where telemedicine technology could allow a mentor surgeon to join them remotely and counsel them through their first procedures.

CONCLUSION

In the end, the real question is not who is going to be performing NOTES – gastroenterologists or surgeons? The real question is how do practicing health care professionals learn new techniques and technology and introduce them safely into their practice to optimize patient care? NOTES is an example of the ever quickening pace of change in medical technology putting unprecedented pressure on

health care providers to stay current. The advent of an international network of educational institutes coupled with the development of validated metrics of procedural competence will help procedurally based physicians adopt new techniques safely with maximum patient benefit. In this way surgery continues to move away from an apprentice model of skills acquisition to a criterion-based one. Such a move is required to address the fast pace of change in health care.

REFERENCES

- 1 **Kalloor AN**, Singh VK, Jagannath SB, Niiyama H, Hill SL, Vaughn CA, Magee CA, Kantsevov SV. Flexible transgastric peritoneoscopy: a novel approach to diagnostic and therapeutic interventions in the peritoneal cavity. *Gastrointest Endosc* 2004; **60**: 114-117
- 2 **Reddy N**, Rao P. Per oral transgastric endoscopic appendectomy in human. Abstract presented at 45th Annual Conference of the Society of Gastrointestinal Endoscopy of India; February 28-29, 2004; Jaipur, India
- 3 **Sachdeva AK**. Acquiring skills in new procedures and technology: the challenge and the opportunity. *Arch Surg* 2005; **140**: 387-389
- 4 Fried GM, Feldman LS, Vassiliou MC, Fraser SA, Stanbridge D, Ghitulescu G, Andrew CG. Proving the value of simulation in laparoscopic surgery. *Ann Surg* 2004; **240**: 518-525; discussion 525-528
- 5 **Sachdeva AK**, Pellegrini CA, Johnson KA. Support for simulation-based surgical education through American College of Surgeons--accredited education institutes. *World J Surg* 2008; **32**: 196-207
- 6 **Datta V**, Mackay S, Mandalia M, Darzi A. The use of electromagnetic motion tracking analysis to objectively measure open surgical skill in the laboratory-based model. *J Am Coll Surg* 2001; **193**: 479-485
- 7 **Rosen J**, Brown JD, Barreca M, Chang L, Hannaford B, Sinanan M. The Blue DRAGON--a system for monitoring the kinematics and the dynamics of endoscopic in minimally invasive surgery for objective laparoscopic skill assessment. *Stud Health Technol Inform* 2002; **85**: 412-418

S- Editor Wang JL **L- Editor** Roemmele A **E- Editor** Yang C



ACKNOWLEDGMENTS

Acknowledgments to reviewers of *World Journal of Gastrointestinal Surgery*

Many reviewers have contributed their expertise and time to the peer review, a critical process to ensure the quality of *World Journal of Gastrointestinal Surgery*. The editors and authors of the articles submitted to the journal are grateful to the following reviewers for evaluating the articles (including those published in this issue and those rejected for this issue) during the last editing time period.

Runjan Chetty, MB, BCh, Professor, Department of Pathology, University of Glasgow, McGregor Building, Western Infirmary, Dumbarton Road, Glasgow G11 6NT, Scotland, United Kingdom

Reinhart T Grundmann, Professor, Wissenschaftlich Medizinischer Direktor, Kreiskliniken Altötting-Burghausen, Krankenhausstr 1, D- 84489 Burghausen, Germany

Niraj J Gusani, MD, Professor, Department of Surgery and Public Health Sciences, 500 University Drive, MC H070, Hershey, PA 17033, United States

Tatsuo Kanda, MD, PhD, Division of Digestive and General Surgery, Niigata University, Graduate School of Medical and Dental Sciences, Niigata 951-8510, Japan

Chen-Guo Ker, MD, PhD, Professor, Department of Surgery,

Kaohsiung Medical University, No 100, Tz-You 1st Rd, Kaohsiung, Taiwan, China

Uwe Klinge, MD, Professor, Institute for Applied Medical Engineering AME, Helmholtz Institute, RWTH Aachen Pauwelsstrabe 30, Aachen 52074, Germany

Paolo Massucco, MD, Department of Surgical Oncology, IRCC, Str Stat 142, Candiolo 10060, Italy

Tang Chung Ngai, MB, BS, Professor, Department of Surgery, Pamela Youde Nethersole Eastern Hospital, 3 Lok Man Road, Chai Wan, Hong Kong, China

Giulio A Santoro, Professor, Pelvic Floor Unit and Colorectal Unit, Department of Surgery, Regional Hospital, Treviso 31000, Italy

Sonshin Takao, MD, PhD, Professor, Division of Advanced Medicine, Kagoshima University, Frontier Science Research Center, 8-35-1 Sakuragaoka, Kagoshima 890-8544, Japan

Guido Alberto Massimo Tiberio, Professor, Department of Medical and Surgical Sciences, University of Brescia, Viale Europa 17, Brescia 25100, Italy

Ibeto Zaniboni, MD, UO di Oncologia, Fondazione Poliambulanza, Via Bissolati 57, Brescia 25124, Italy



Meetings

Events Calendar 2010

January 15-16, 2010

AGA Clinical Congress of Gastroenterology and Hepatology
The Venetian And Palazzo, 3355 Las Vegas Blvd South, Las Vegas, United States
<http://www.gilearn.org/clinical-congress>

January 27-31, 2010

Alpine Liver & Pancreatic Surgery Meeting
Carlo Magno Zeledria Hotel, Madonna di Campiglio, Italy
<http://www.alpsphbmeeting.soton.ac.uk>

February 25, 2010

Multidisciplinary management of acute pancreatitis symptoms
The Royal Society of Medicine, 1 Wimpole Street, London, United Kingdom
<http://www.rsm.ac.uk/academ/pancreatitis10.php>

March 4-7, 2010

2010 Annual Meeting of the Society of Surgical Oncology
Renaissance® St. Louis Grand Hotel, 800 Washington Avenue, St. Louis, Missouri, United States
<http://www.surgonc.org/>

March 25-28, 2010

20th Conference of the Asian Pacific Association for the Study of the Liver
Beijing, China
<http://www.apasl2010beijing.org/en/index.aspx>

April 14-18, 2010

The International Liver Congress™ 2010
Vienna, Austria

May 1-5, 2010

2010 American Transplant Congress
San Diego Convention Center, 111 West Harbor Drive, San Diego, United States
<http://www.atcmeeting.org/2010>

May 1-5, 2010

Digestive Disease Week 2010
Ernest N Morial Convention Center, 900 Convention Center Blvd, New Orleans, United States
<http://www.ddw.org/>

May 15-19, 2010

Annual Meeting of the American Society of Colon and Rectal Surgeons
Hilton Minneapolis Hotel & Convention Center, Minneapolis, Minnesota, United States
<http://www.fascrs.org/>

September 16-18, 2010

Prague Hepatology Meeting 2010
Prague, Czech Republic
<http://www.congressprague.cz/en/kongresy/phm2010.html>

September 23-25, 2010

2010 Gastrointestinal Oncology Conference
The Sheraton Philadelphia City Center, Philadelphia, United States
<http://www.isgio.org/isgio2010/program.htm>

October 20-23, 2010

Australian Gastroenterology Week
Melbourne, Australia
<http://www.gesa.org.au/agw.cfm>

November 13-14, 2010

Case-Based Approach to the Management of Inflammatory Bowel Disease
San Francisco, United States



Instructions to authors

GENERAL INFORMATION

World Journal of Gastrointestinal Surgery (*World J Gastrointest Surg*, *WJGS*, online ISSN 1948-9366, DOI: 10.4240), is a monthly, open-access (OA), peer-reviewed journal supported by an editorial board of 336 experts in gastrointestinal surgery from 35 countries.

The biggest advantage of the OA model is that it provides free, full-text articles in PDF and other formats for experts and the public without registration, which eliminates the obstacle that traditional journals possess and usually delays the speed of the propagation and communication of scientific research results. The open access model has been proven to be a true approach that may achieve the ultimate goal of the journals, i.e. the maximization of the value to the readers, authors and society.

The role of academic journals is to exhibit the scientific levels of a country, a university, a center, a department, and even a scientist, and build an important bridge for communication between scientists and the public. As we all know, the significance of the publication of scientific articles lies not only in disseminating and communicating innovative scientific achievements and academic views, as well as promoting the application of scientific achievements, but also in formally recognizing the "priority" and "copyright" of innovative achievements published, as well as evaluating research performance and academic levels. So, to realize these desired attributes of *WJGS* and create a well-recognized journal, the following four types of personal benefits should be maximized. The maximization of personal benefits refers to the pursuit of the maximum personal benefits in a well-considered optimal manner without violation of the laws, ethical rules and the benefits of others. (1) Maximization of the benefits of editorial board members: The primary task of editorial board members is to give a peer review of an unpublished scientific article via online office system to evaluate its innovativeness, scientific and practical values and determine whether it should be published or not. During peer review, editorial board members can also obtain cutting-edge information in that field at first hand. As leaders in their field, they have priority to be invited to write articles and publish commentary articles. We will put peer reviewers' names and affiliations along with the article they reviewed in the journal to acknowledge their contribution; (2) Maximization of the benefits of authors: Since *WJGS* is an open-access journal, readers around the world can immediately download and read, free of charge, high-quality, peer-reviewed articles from *WJGS* official website, thereby realizing the goals and significance of the communication between authors and peers as well as public reading; (3) Maximization of the benefits of readers: Readers can read or use, free of charge, high-quality peer-reviewed articles without any limits, and cite the arguments, viewpoints, concepts, theories, methods, results, conclusion or facts and data of pertinent literature so as to validate the innovativeness, scientific and practical values of their own research achievements, thus ensuring that their articles have novel arguments or viewpoints, solid evidence and correct conclusion; and (4) Maximization of the benefits of employees: It is an iron law that a first-class journal is unable to exist without first-class editors, and only first-class editors can create a first-class academic journal. We insist on strengthening our team cultivation and construction so that every employee, in an open, fair and transparent environment, could contribute their wisdom to edit and publish high-quality articles, thereby realizing

the maximization of the personal benefits of editorial board members, authors and readers, and yielding the greatest social and economic benefits.

The major task of *WJGS* is to rapidly report the most recent results in basic and clinical research on gastrointestinal surgery, specifically including micro-invasive surgery, laparoscopy, hepatic surgery, biliary surgery, pancreatic surgery, splenic surgery, surgical nutrition, portal hypertension, as well as the associated subjects such as epidemiology, cancer research, biomarkers, prevention, pathology, radiology, genetics, genomics, proteomics, pharmacology, pharmacokinetics, pharmacogenetics, molecular biology, clinical trials, diagnosis and therapeutics and multimodality treatment. Emphasis is placed on original research articles and clinical case reports. This journal will also provide balanced, extensive and timely review articles on selected topics.

The columns in the issues of *WJGS* will include: (1) Editorial: To introduce and comment on major advances and developments in the field; (2) Frontier: To review representative achievements, comment on the state of current research, and propose directions for future research; (3) Topic Highlight: This column consists of three formats, including (A) 10 invited review articles on a hot topic, (B) a commentary on common issues of this hot topic, and (C) a commentary on the 10 individual articles; (4) Observation: To update the development of old and new questions, highlight unsolved problems, and provide strategies on how to solve the questions; (5) Guidelines for Basic Research: To provide guidelines for basic research; (6) Guidelines for Clinical Practice: To provide guidelines for clinical diagnosis and treatment; (7) Review: To review systemically progress and unresolved problems in the field, comment on the state of current research, and make suggestions for future work; (8) Original Article: To report innovative and original findings in gastrointestinal surgery; (9) Brief Article: To briefly report the novel and innovative findings in gastrointestinal surgery; (10) Case Report: To report a rare or typical case; (11) Letters to the Editor: To discuss and make reply to the contributions published in *WJGS*, or to introduce and comment on a controversial issue of general interest; (12) Book Reviews: To introduce and comment on quality monographs of gastrointestinal surgery; and (13) Guidelines: To introduce consensus and guidelines reached by international and national academic authorities worldwide on basic research and clinical practice in gastrointestinal surgery.

CSSN

ISSN 1948-9366 (online)

Published by

Beijing Baishideng BioMed Scientific Co., Ltd.

SUBMISSION OF MANUSCRIPTS

Manuscripts should be typed in 1.5 line spacing and 12 pt. Book Antiqua with ample margins. Number all pages consecutively, and start each of the following sections on a new page: Title Page, Abstract, Introduction, Materials and Methods, Results, Discussion, Acknowledgements, References, Tables, Figures, and Figure Legends. Neither the editors nor the publisher are responsible for the opinions expressed by contributors. Manuscripts formally accepted for publication become the permanent property of Beijing Baishideng BioMed Scientific Co., Ltd, and may not be reproduced by any means, in whole or in part, without the written permission of both the authors and the publisher. We reserve the right to copy-edit and

Instructions to authors

put onto our website accepted manuscripts. Authors should follow the relevant guidelines for the care and use of laboratory animals of their institution or national animal welfare committee. For the sake of transparency in regard to the performance and reporting of clinical trials, we endorse the policy of the International Committee of Medical Journal Editors to refuse to publish papers on clinical trial results if the trial was not recorded in a publicly-accessible registry at its outset. The only register now available, to our knowledge, is <http://www.clinicaltrials.gov> sponsored by the United States National Library of Medicine and we encourage all potential contributors to register with it. However, in the case that other registers become available you will be duly notified. A letter of recommendation from each author's organization should be provided with the contributed article to ensure the privacy and secrecy of research is protected.

Authors should retain one copy of the text, tables, photographs and illustrations because rejected manuscripts will not be returned to the author(s) and the editors will not be responsible for loss or damage to photographs and illustrations sustained during mailing.

Online submissions

Manuscripts should be submitted through the Online Submission System at: <http://www.wjgnet.com/1948-9366office>. Authors are highly recommended to consult the ONLINE INSTRUCTIONS TO AUTHORS (http://www.wjgnet.com/1948-9366/g_info_20100305152206.htm) before attempting to submit online. For assistance, authors encountering problems with the Online Submission System may send an email describing the problem to wjgs@wjgnet.com, or by telephone: +86-10-85381891. If you submit your manuscript online, do not make a postal contribution. Repeated online submission for the same manuscript is strictly prohibited.

MANUSCRIPT PREPARATION

All contributions should be written in English. All articles must be submitted using word-processing software. All submissions must be typed in 1.5 line spacing and 12 pt. Book Antiqua with ample margins. Style should conform to our house format. Required information for each of the manuscript sections is as follows:

Title page

Title: Title should be less than 12 words.

Running title: A short running title of less than 6 words should be provided.

Authorship: Authorship credit should be in accordance with the standard proposed by International Committee of Medical Journal Editors, based on (1) substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; (2) drafting the article or revising it critically for important intellectual content; and (3) final approval of the version to be published. Authors should meet conditions 1, 2, and 3.

Institution: Author names should be given first, then the complete name of institution, city, province and postcode. For example, Xu-Chen Zhang, Li-Xin Mei, Department of Pathology, Chengde Medical College, Chengde 067000, Hebei Province, China. One author may be represented from two institutions, for example, George Sgourakis, Department of General, Visceral, and Transplantation Surgery, Essen 45122, Germany; George Sgourakis, 2nd Surgical Department, Korgialenio-Benakio Red Cross Hospital, Athens 15451, Greece

Author contributions: The format of this section should be: Author contributions: Wang CL and Liang L contributed equally to this work; Wang CL, Liang L, Fu JF, Zou CC, Hong F and Wu XM designed the research; Wang CL, Zou CC, Hong F and Wu XM performed the research; Xue JZ and Lu JR contributed new reagents/analytic tools; Wang CL, Liang L and Fu JF analyzed the data; and Wang CL, Liang L and Fu JF wrote the paper.

Supportive foundations: The complete name and number of

supportive foundations should be provided, e.g., Supported by National Natural Science Foundation of China, No. 30224801

Correspondence to: Only one corresponding address should be provided. Author names should be given first, then author title, affiliation, the complete name of institution, city, postcode, province, country, and email. All the letters in the email should be in lower case. A space interval should be inserted between country name and email address. For example, Montgomery Bissell, MD, Professor of Medicine, Chief, Liver Center, Gastroenterology Division, University of California, Box 0538, San Francisco, CA 94143, United States. montgomery.bissell@ucsf.edu

Telephone and fax: Telephone and fax should consist of +, country number, district number and telephone or fax number, e.g., Telephone: +86-10-59080039 Fax: +86-10-85381893

Peer reviewers: All articles received are subject to peer review. Normally, three experts are invited for each article. Decision for acceptance is made only when at least two experts recommend an article for publication. Reviewers for accepted manuscripts are acknowledged in each manuscript, and reviewers of articles which were not accepted will be acknowledged at the end of each issue. To ensure the quality of the articles published in *WJGS*, reviewers of accepted manuscripts will be announced by publishing the name, title/position and institution of the reviewer in the footnote accompanying the printed article. For example, reviewers: Professor Jing-Yuan Fang, Shanghai Institute of Digestive Disease, Shanghai, Affiliated Renji Hospital, Medical Faculty, Shanghai Jiaotong University, Shanghai, China; Professor Xin-Wei Han, Department of Radiology, The First Affiliated Hospital, Zhengzhou University, Zhengzhou, Henan Province, China; and Professor Anren Kuang, Department of Nuclear Medicine, Huaxi Hospital, Sichuan University, Chengdu, Sichuan Province, China.

Abstract

There are unstructured abstracts (no more than 256 words) and structured abstracts (no more than 480). The specific requirements for structured abstracts are as follows:

An informative, structured abstracts of no more than 480 words should accompany each manuscript. Abstracts for original contributions should be structured into the following sections. AIM (no more than 20 words): Only the purpose should be included. Please write the aim as the form of "To investigate/study/...; MATERIALS AND METHODS (no more than 140 words); RESULTS (no more than 294 words): You should present *P* values where appropriate and must provide relevant data to illustrate how they were obtained, e.g. 6.92 ± 3.86 vs 3.61 ± 1.67 , $P < 0.001$; CONCLUSION (no more than 26 words).

Key words

Please list 5-10 key words, selected mainly from *Index Medicus*, which reflect the content of the study.

Text

For articles of these sections, original articles, rapid communication and case reports, the main text should be structured into the following sections: INTRODUCTION, MATERIALS AND METHODS, RESULTS and DISCUSSION, and should include appropriate Figures and Tables. Data should be presented in the main text or in Figures and Tables, but not in both. The main text format of these sections, editorial, topic highlight, case report, letters to the editors, can be found at: http://www.wjgnet.com/1948-9366/g_info_20100312191047.htm.

Illustrations

Figures should be numbered as 1, 2, 3, etc., and mentioned clearly in the main text. Provide a brief title for each figure on a separate page. Detailed legends should not be provided under the figures. This part should be added into the text where the figures are applicable. Figures should be either Photoshop or Illustrator

files (in tiff, eps, jpeg formats) at high-resolution. Examples can be found at: <http://www.wjgnet.com/1007-9327/13/4520.pdf>; <http://www.wjgnet.com/1007-9327/13/4554.pdf>; <http://www.wjgnet.com/1007-9327/13/4891.pdf>; <http://www.wjgnet.com/1007-9327/13/4986.pdf>; <http://www.wjgnet.com/1007-9327/13/4498.pdf>. Keeping all elements compiled is necessary in line-art image. Scale bars should be used rather than magnification factors, with the length of the bar defined in the legend rather than on the bar itself. File names should identify the figure and panel. Avoid layering type directly over shaded or textured areas. Please use uniform legends for the same subjects. For example: Figure 1 Pathological changes in atrophic gastritis after treatment. A: ...; B: ...; C: ...; D: ...; E: ...; F: ...; G: ...*etc.* It is our principle to publish high resolution-figures for the printed and E-versions.

Tables

Three-line tables should be numbered 1, 2, 3, *etc.*, and mentioned clearly in the main text. Provide a brief title for each table. Detailed legends should not be included under tables, but rather added into the text where applicable. The information should complement, but not duplicate the text. Use one horizontal line under the title, a second under column heads, and a third below the Table, above any footnotes. Vertical and italic lines should be omitted.

Notes in tables and illustrations

Data that are not statistically significant should not be noted. ^a*P* < 0.05, ^b*P* < 0.01 should be noted (*P* > 0.05 should not be noted). If there are other series of *P* values, ^c*P* < 0.05 and ^d*P* < 0.01 are used. A third series of *P* values can be expressed as ^e*P* < 0.05 and ^f*P* < 0.01. Other notes in tables or under illustrations should be expressed as ¹F, ²F, ³F; or sometimes as other symbols with a superscript (Arabic numerals) in the upper left corner. In a multi-curve illustration, each curve should be labeled with ●, ○, ■, □, ▲, △, *etc.*, in a certain sequence.

Acknowledgments

Brief acknowledgments of persons who have made genuine contributions to the manuscript and who endorse the data and conclusions should be included. Authors are responsible for obtaining written permission to use any copyrighted text and/or illustrations.

REFERENCES

Coding system

The author should number the references in Arabic numerals according to the citation order in the text. Put reference numbers in square brackets in superscript at the end of citation content or after the cited author's name. For citation content which is part of the narration, the coding number and square brackets should be typeset normally. For example, "Crohn's disease (CD) is associated with increased intestinal permeability^[1,2]". If references are cited directly in the text, they should be put together within the text, for example, "From references^[19,22-24], we know that..."

When the authors write the references, please ensure that the order in text is the same as in the references section, and also ensure the spelling accuracy of the first author's name. Do not list the same citation twice.

PMID and DOI

Please provide PubMed citation numbers to the reference list, e.g. PMID and DOI, which can be found at <http://www.ncbi.nlm.nih.gov/sites/entrez?db=pubmed> and <http://www.crossref.org/SimpleTextQuery/>, respectively. The numbers will be used in E-version of this journal.

Style for journal references

Authors: the name of the first author should be typed in bold-faced letters. The family name of all authors should be typed with the initial letter capitalized, followed by their abbreviated first and middle initials. (For example, Lian-Sheng Ma is abbreviated

as Ma LS, Bo-Rong Pan as Pan BR). The title of the cited article and italicized journal title (journal title should be in its abbreviated form as shown in PubMed), publication date, volume number (in black), start page, and end page [PMID: 11819634 DOI: 10.3748/wjg.13.5396].

Style for book references

Authors: the name of the first author should be typed in bold-faced letters. The surname of all authors should be typed with the initial letter capitalized, followed by their abbreviated middle and first initials. (For example, Lian-Sheng Ma is abbreviated as Ma LS, Bo-Rong Pan as Pan BR) Book title. Publication number. Publication place: Publication press, Year: start page and end page.

Format

Journals

English journal article (list all authors and include the PMID where applicable)

- 1 **Jung EM**, Clevert DA, Schreyer AG, Schmitt S, Rennert J, Kubale R, Feuerbach S, Jung F. Evaluation of quantitative contrast harmonic imaging to assess malignancy of liver tumors: A prospective controlled two-center study. *World J Gastroenterol* 2007; **13**: 6356-6364 [PMID: 18081224 DOI: 10.3748/wjg.13.6356]

Chinese journal article (list all authors and include the PMID where applicable)

- 2 **Lin GZ**, Wang XZ, Wang P, Lin J, Yang FD. Immunologic effect of Jianpi Yishen decoction in treatment of Pixu-diarrhoea. *Shijie Huaren Xiaohua Zazhi* 1999; **7**: 285-287

In press

- 3 **Tian D**, Araki H, Stahl E, Bergelson J, Kreitman M. Signature of balancing selection in Arabidopsis. *Proc Natl Acad Sci USA* 2006; In press

Organization as author

- 4 **Diabetes Prevention Program Research Group**. Hypertension, insulin, and proinsulin in participants with impaired glucose tolerance. *Hypertension* 2002; **40**: 679-686 [PMID: 12411462 PMCID:2516377 DOI:10.1161/01.HYP.0000035706.28494.09]

Both personal authors and an organization as author

- 5 **Vallancien G**, Emberton M, Harving N, van Moorselaar RJ; Alf-One Study Group. Sexual dysfunction in 1, 274 European men suffering from lower urinary tract symptoms. *J Urol* 2003; **169**: 2257-2261 [PMID: 12771764 DOI:10.1097/01.ju.0000067940.76090.73]

No author given

- 6 21st century heart solution may have a sting in the tail. *BMJ* 2002; **325**: 184 [PMID: 12142303 DOI:10.1136/bmj.325.7357.184]

Volume with supplement

- 7 **Geraud G**, Spierings EL, Keywood C. Tolerability and safety of frovatriptan with short- and long-term use for treatment of migraine and in comparison with sumatriptan. *Headache* 2002; **42** Suppl 2: S93-99 [PMID: 12028325 DOI:10.1046/j.1526-4610.42.s2.7.x]

Issue with no volume

- 8 **Banit DM**, Kaufer H, Hartford JM. Intraoperative frozen section analysis in revision total joint arthroplasty. *Clin Orthop Relat Res* 2002; **(401)**: 230-238 [PMID: 12151900 DOI:10.1097/00003086-200208000-00026]

No volume or issue

- 9 Outreach: Bringing HIV-positive individuals into care. *HRS-A Careaction* 2002; 1-6 [PMID: 12154804]

Books

Personal author(s)

- 10 **Sherlock S**, Dooley J. Diseases of the liver and biliary system. 9th ed. Oxford: Blackwell Sci Pub, 1993: 258-296

Chapter in a book (list all authors)

- 11 **Lam SK**. Academic investigator's perspectives of medical treatment for peptic ulcer. In: Swabb EA, Azabo S. Ulcer disease: investigation and basis for therapy. New York:

Instructions to authors

Marcel Dekker, 1991: 431-450

Author(s) and editor(s)

- 12 **Breedlove GK**, Schorffheide AM. Adolescent pregnancy. 2nd ed. Wicczorek RR, editor. White Plains (NY): March of Dimes Education Services, 2001: 20-34

Conference proceedings

- 13 **Harnden P**, Joffe JK, Jones WG, editors. Germ cell tumours V. Proceedings of the 5th Germ cell tumours Conference; 2001 Sep 13-15; Leeds, UK. New York: Springer, 2002: 30-56

Conference paper

- 14 **Christensen S**, Oppacher F. An analysis of Koza's computational effort statistic for genetic programming. In: Foster JA, Lutton E, Miller J, Ryan C, Tettamanzi AG, editors. Genetic programming. EuroGP 2002: Proceedings of the 5th European Conference on Genetic Programming; 2002 Apr 3-5; Kinsdale, Ireland. Berlin: Springer, 2002: 182-191

Electronic journal (list all authors)

- 15 Morse SS. Factors in the emergence of infectious diseases. Emerg Infect Dis serial online, 1995-01-03, cited 1996-06-05; 1(1): 24 screens. Available from: URL: <http://www.cdc.gov/ncidod/EID/eid.htm>

Patent (list all authors)

- 16 **Pagedas AC**, inventor; Ancel Surgical R&D Inc., assignee. Flexible endoscopic grasping and cutting device and positioning tool assembly. United States patent US 20020103498. 2002 Aug 1

Statistical data

Write as mean \pm SD or mean \pm SE.

Statistical expression

Express *t* test as *t* (in italics), *F* test as *F* (in italics), chi square test as χ^2 (in Greek), related coefficient as *r* (in italics), degree of freedom as *v* (in Greek), sample number as *n* (in italics), and probability as *P* (in italics).

Units

Use SI units. For example: body mass, *m* (B) = 78 kg; blood pressure, *p* (B) = 16.2/12.3 kPa; incubation time, *t* (incubation) = 96 h, blood glucose concentration, *c* (glucose) 6.4 ± 2.1 mmol/L; blood CEA mass concentration, *p* (CEA) = 8.6 $24.5 \mu\text{g/L}$; CO_2 volume fraction, 50 mL/L CO_2 , not 5% CO_2 ; likewise for 40 g/L formaldehyde, not 10% formalin; and mass fraction, 8 ng/g, *etc.* Arabic numerals such as 23, 243, 641 should be read 23 243 641.

The format for how to accurately write common units and quantums can be found at: http://www.wjgnet.com/1948-9366/g_info_20100312191949.htm.

Abbreviations

Standard abbreviations should be defined in the abstract and on first mention in the text. In general, terms should not be abbreviated unless they are used repeatedly and the abbreviation is helpful to the reader. Permissible abbreviations are listed in Units, Symbols and Abbreviations: A Guide for Biological and Medical Editors and Authors (Ed. Baron DN, 1988) published by The Royal Society of Medicine, London. Certain commonly used abbreviations, such as DNA, RNA, HIV, LD50, PCR, HBV, ECG, WBC, RBC, CT, ESR, CSF, IgG, ELISA, PBS, ATP, EDTA, mAb, can be used directly without further explanation.

Italics

Quantities: *t* time or temperature, *c* concentration, *A* area, *l* length, *m* mass, *V* volume.

Genotypes: *gyrA*, *arg 1*, *c myc*, *c fos*, *etc.*

Restriction enzymes: *EcoRI*, *HindIII*, *BamHI*, *Kho I*, *Kpn I*, *etc.*

Biology: *H. pylori*, *E. coli*, *etc.*

SUBMISSION OF THE REVISED MANUSCRIPTS AFTER ACCEPTED

Please revise your article according to the revision policies of *WJGS*. The revised version including manuscript and high-resolution image figures (if any) should be copied on a floppy or compact disk. The author should send the revised manuscript, along with printed high-resolution color or black and white photos, copyright transfer letter, and responses to the reviewers by courier (such as EMS/DHL).

Editorial Office

World Journal of Gastrointestinal Surgery

Editorial Department: Room 903, Building D, Ocean International Center, No. 62 Dongsihuan Zhonglu, Chaoyang District, Beijing 100025, China

E-mail: wjgs@wjgnet.com

<http://www.wjgnet.com>

Telephone: 0086-10-85381891

Fax: 0086-10-85381893

Language evaluation

The language of a manuscript will be graded before it is sent for revision. (1) Grade A: priority publishing; (2) Grade B: minor language polishing; (3) Grade C: a great deal of language polishing needed; and (4) Grade D: rejected. Revised articles should reach Grade A or B.

Copyright assignment form

Please download a Copyright assignment form from http://www.wjgnet.com/1948-9366/g_info_20100312191901.htm.

Responses to reviewers

Please revise your article according to the comments/suggestions provided by the reviewers. The format for responses to the reviewers' comments can be found at: http://www.wjgnet.com/1948-9366/g_info_20100312191818.htm.

Proof of financial support

For paper supported by a foundation, authors should provide a copy of the document and serial number of the foundation.

Links to documents related to the manuscript

WJGS will be initiating a platform to promote dynamic interactions between the editors, peer reviewers, readers and authors. After a manuscript is published online, links to the PDF version of the submitted manuscript, the peer-reviewers' report and the revised manuscript will be put on-line. Readers can make comments on the peer reviewer's report, authors' responses to peer reviewers, and the revised manuscript. We hope that authors will benefit from this feedback and be able to revise the manuscript accordingly in a timely manner.

Science news releases

Authors of accepted manuscripts are suggested to write a science news item to promote their articles. The news will be released rapidly at EurekaAlert/AAAS (<http://www.eurekaalert.org>). The title for news items should be less than 90 characters; the summary should be less than 75 words; and main body less than 500 words. Science news items should be lawful, ethical, and strictly based on your original content with an attractive title and interesting pictures.

Publication fee

Authors of accepted articles must pay a publication fee.

EDITORIAL, TOPIC HIGHLIGHTS, BOOK REVIEWS and LETTERS TO THE EDITOR are published free of charge.