

## 기관고유연구사업 최종보고서

연구분야(코드)	I-2	과제번호	1210170		지원 프로그램	창의 (일반연구)과제	
과제성격(기초,응용,개발)	개발	실용화 대상여부	실용화	공개가능여부 (공개,비공개)		공개	
연구과제명	(국문) 자연개구부무흉터내시경수술법(NOTES)의 개발 및 임상 적용 II						
	(영문) Development and clinical application of NOTES II						
과제책임자	소 속	의공학연구과	직 위	과장 (선임연구원)			
	성 명	손 대 경	전 공	외 과			
세부과제	구분	세부과제명		세부과제책임자			
		성명	소속(직위)	전 공			
	1	자연개구부무흉터내시경수술법(NOTES)의 개발 및 임상 적용	손대경	의공학연구과 (과장)	외과		
	2						
3							
총 연구기간	2012년1월 ~ 2014년12월 (총 3년)		참여연구원수 (단위: 명, MY)		13 명 ( 2.1 MY)		
연구기간 및 연구비 (단위:천원)	구분	연구기간	계	국립 암센터	기업부담금		
					소계	현금	현물
	계	2012.01~2014.12.	285,000	285,000			
	제1차	2012.01~2012.12.	95,000	95,000			
	제2차	2012.01~2012.12.	95,000	95,000			
제3차	2012.01~2012.12.	95,000	95,000				
참여기업	명칭		전화		FAX		
<p>기관고유연구사업관리규칙에 따라 본 연구개발사업을 성실히 수행하였으며 아래와 같이 최종보고서를 제출합니다.</p> <p style="text-align: center;">2014년 10 월 29 일</p> <p style="text-align: center;">과제책임자                  손 대 경                  (서명)</p>							
국립 암 센터 원 장    귀 하							
(첨부서류)							

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(한글)

(영문)

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※ 여러개의 세부과제로 과제가 구성된 경우 위 목차와 동일하게 세부과제별로 작성함

(I. 총괄과제, II. 제1세부과제, III. 제2세부과제.....)

## < 요약 문 >

<p>연구목표 (200자 이내)</p>	<p>&lt;최종목표&gt; 자연개구부무흉터내시경수술법(NOTES)의 개발 및 임상 적용을 통해 대장암으로 수술적 치료를 요하는 환자들의 삶의 질 향상에 기여할 수 있도록 하기 위함.</p> <p>&lt;당해연도목표&gt; 자연개구부무흉터내시경수술법(NOTES)의 전임상실험 및 임상실험</p>																		
<p>연구내용 및 방법 (500자 이내)</p>	<p><b>1) NOTES 전임상 실험</b></p> <p><b>1-1) NOTES rectosigmoidectomy human cadaver 실험</b></p> <hr/> <table style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 70%;">Cavadvr</td> <td style="text-align: right;">M:F = 11:1</td> </tr> <tr> <td colspan="2">Operation</td> </tr> <tr> <td style="padding-left: 20px;">Median op. time(min, range)</td> <td style="text-align: right;">120 (70-165)</td> </tr> <tr> <td style="padding-left: 20px;">Mean length of bowel ± SD (cm, range)</td> <td style="text-align: right;">34.7±6.9 (25-45)</td> </tr> <tr> <td colspan="2">TME quality</td> </tr> <tr> <td style="padding-left: 20px;">Complete</td> <td style="text-align: right;">7 (58%)</td> </tr> <tr> <td style="padding-left: 20px;">Nearly complete</td> <td style="text-align: right;">5 (42%)</td> </tr> <tr> <td colspan="2">Intraoperative complications</td> </tr> <tr> <td style="padding-left: 20px;">Urethra injury</td> <td style="text-align: right;">3 cases</td> </tr> </table> <hr/> <p><b>1-2) Pure NOTES rectosigmoidectomy (Endoscopic IMA Ligation) in Animal Models</b></p> <ul style="list-style-type: none"> <li>; Five live animals (four pigs 45 kg each, one dog 25 kg each)</li> <li>; Endoscopic dissection of the IMA: success 100%</li> <li>; Mean operation time: 125 minutes (range, 90-170 min)</li> <li>; No intraoperative complications or hemodynamic instability</li> <li>; The mean length of the resected specimen: 14.4 cm (range, 12-16 cm)</li> </ul> <p><b>2) NOTES rectosigmoidectomy clinical trial</b></p> <p>“A pilot study for the evaluation of the safety and the efficacy of transanal total mesorectal excision” (NCCCTS-13-681, NCT01938027)</p> <ul style="list-style-type: none"> <li>; Sep. 2013 to Oct 2014, 7 male and 5 female patients (Preop CRT 4 cases)</li> </ul>	Cavadvr	M:F = 11:1	Operation		Median op. time(min, range)	120 (70-165)	Mean length of bowel ± SD (cm, range)	34.7±6.9 (25-45)	TME quality		Complete	7 (58%)	Nearly complete	5 (42%)	Intraoperative complications		Urethra injury	3 cases
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	<p>; Mean age of patients was <math>62.3 \pm 10.1</math>, and BMI was <math>24.5 \pm 2.8</math></p> <p>; (<u>TME quality</u>) complete or near complete TME: 11 cases (91.7%) incomplete TME : 1 case</p> <p>; DRM: <math>2.6 \pm 2.4</math> cm, CRM: <math>9.5 \pm 0.4</math> mm</p> <p>; Mean number of harvested lymph nodes: <math>15.8 \pm 4.0</math></p> <p>; Mean length of hospital stay was <math>11.6 \pm 5.0</math> days</p> <p>; No postoperative mortality</p> <p>; Minor postoperative complication: 6 patients [urinary dysfunction (2), postoperative transient ileus (3), wound abscess (1)]</p> <p><b>3) LED-TEM 개선 및 임상 시험 준비</b></p> <p>; 개선된 2차 시제품 제작 및 동물실험을 통한 검증</p> <p>; KFDA 승인을 위해서는 기술이전이 우선적으로 필요함을 확인 ==&gt; 기술이전 추진</p> <p><b>4) NOTES platform 설계 및 제작</b></p> <p>; 1차 시제품 설계 제작 및 문제점 확인 후 2차 시제품 제작</p> <p>; 돼지실험 3회, human cadaver 2회를 통해 전임상실험 완료</p>																								
<p>연구개발에 따른 기대성과</p>	<p>&lt;정량적 성과<sup>1)</sup>&gt;</p> <table border="1" data-bbox="491 1193 1426 1391"> <thead> <tr> <th>구분</th> <th>달성치/목표치<sup>1)</sup></th> <th>달성도(%)</th> </tr> </thead> <tbody> <tr> <td>SCI 논문 편수</td> <td>10 / 6</td> <td>167</td> </tr> <tr> <td>IF 합</td> <td>24.2 / 24</td> <td>100</td> </tr> <tr> <td>기타 성과</td> <td>(특허 출원) 5 / 3</td> <td>167</td> </tr> </tbody> </table> <p>1) 총연구기간 내 목표연구성과로 기 제출한 값</p> <p>&lt;정성적 성과&gt;</p> <ul style="list-style-type: none"> <li>- NOTES 임상 시험 완료 (NCCCTS-13-681)</li> <li>- NOTES 동물 실험 경험 축적 및 국내외 다기관 공동 연구 시스템 구축</li> <li>- NOTES platform 및 robot 시제품 제작</li> </ul>	구분	달성치/목표치 <sup>1)</sup>	달성도(%)	SCI 논문 편수	10 / 6	167	IF 합	24.2 / 24	100	기타 성과	(특허 출원) 5 / 3	167												
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국문	무흉터수술	경항문수술	대장절제술																						
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	TEM																								

※ 요약문의 총분량은 2page 이내로 제한함

## Project Summary

<b>Title of Project</b>	Development and clinical application of NOTES II
<b>Key Words</b>	NOTES; Transanal surgery; Colectomy; TEM
<b>Project Leader</b>	Dae Kyung Sohn
<b>Associated Company</b>	none

### Background and purpose:

Natural orifice transluminal endoscopic surgery (NOTES) is the integration of laparoscopic minimally invasive surgery techniques with flexible endoscopy technology. It has emerged as a promising new alternative to conventional minimal invasive surgery such as laparoscopic or robotic surgery. Our research project was performed to develop the NOTES procedures and devices for clinically application of NOTES in mainly colorectal cancer surgery.

### Methods & outcomes

#### 1) NOTES preclinical study

##### 1-1) NOTES rectosigmoidectomy human cadaver experiments

Cavader	M:F = 11:1
Operation	
Median op. time(min, range)	120 (70-165)
Mean length of bowel $\pm$ SD (cm, range)	34.7 $\pm$ 6.9 (25-45)
TME quality	
Complete	7 (58%)
Nearly complete	5 (42%)
Intraoperative complications	
Urethra injury	3 cases

##### 1-2) Pure NOTES rectosigmoidectomy (Endoscopic IMA Ligation) in Animal Models

- ; Five live animals (four pigs 45 kg each, one dog 25 kg each)
- ; Endoscopic dissection of the IMA: success 100%
- ; Mean operation time: 125 minutes (range, 90-170 min)
- ; No intraoperative complications or hemodynamic instability
- ; The mean length of the resected specimen: 14.4 cm (range, 12-16 cm)

## **2) NOTES rectosigmoidectomy clinical trial**

“A pilot study for the evaluation of the safety and the efficacy of transanal total mesorectal excision” (NCCCTS-13-681, NCT01938027)

- ; Sep. 2013 to Oct 2014, 7 male and 5 female patients (Preop CRT 4 cases)
- ; We used GelPOINT® Path (Applied Medical) for transanal approach. For transabdominal approach, Octoport™ (Dalim) was used at the presumed ileostomy site, and additional ports were used if necessary.
- ; Mean age of patients was  $62.3 \pm 10.1$ , and BMI was  $24.5 \pm 2.8$
- ; (TME quality) complete or near complete TME: 11 cases (91.7%)  
incomplete TME : 1 case
- ; DRM:  $2.6 \pm 2.4$  cm, CRM:  $9.5 \pm 0.4$  mm
- ; Mean number of harvested lymph nodes:  $15.8 \pm 4.0$
- ; Mean length of hospital stay was  $11.6 \pm 5.0$  days
- ; No postoperative mortality
- ; Minor postoperative complication: 6 patients [urinary dysfunction (2), postoperative transient ileus (3), wound abscess (1)]

## **3) LED-TEM development**

- ; upgrade of LED-TEM prototype and function test in animal model
- ; KFDA approval after knowledge transfer

## **4) NOTES platform development**

- ; design and making of multi-articulating NOTES platform
- ; ensure technology patent
- ; animal test and human cadaver test

## **Conclusions**

Transanal rectal resection with TME is a promising new approach in the treatment of rectal cancer in patients, especially with a poorly accessible pelvis for traditional laparoscopic TME. Currently, short-term outcomes of small clinical series suggest that transanal endoscopic TME is not only feasible but safe in carefully selected patients when carried out by trained surgeons. We expect this new approach has developed continuously and expanded to the clinical applications of pure NOTES.

## 1. 연구의 최종목표

자연개구부무흉터내시경수술법(NOTES)의 개발 및 임상 적용을 통해 대장암으로 수술적 치료를 요하는 환자들의 삶의 질 향상에 기여할 수 있도록 하기 위함.

### <1차년도(2012): NOTES 전임상시험 + 임상시험 준비 >

- NOTES pre-clinical study (Human cadaver 및 animal experiments)
- Transanal rectosigmoidectomy 임상시험 준비
- LED-TEM 개선 및 임상 시험 준비

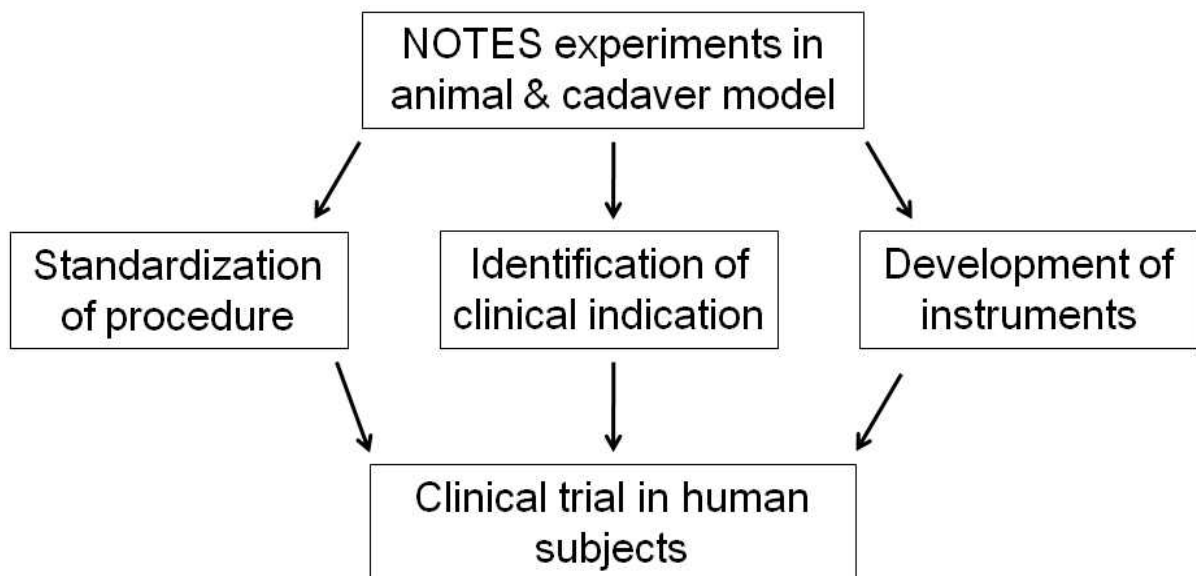
### <2차년도(2013): NOTES 전임상시험 + 임상시험>

- NOTES pre-clinical study
- Transanal rectosigmoidectomy 임상시험 시작
- LED-TEM 기술 이전 준비, NOTES 기기 개발
- NOTES platform 시제품 제작 및 실험

### <3차년도(2014): NOTES 전임상시험 + 임상시험>

- NOTES pre-clinical study
- Transanal rectosigmoidectomy 임상시험 완료
- NOTES platform 제작 및 실험, NOTES 기기 개발

## 2. 연구의 내용 및 결과

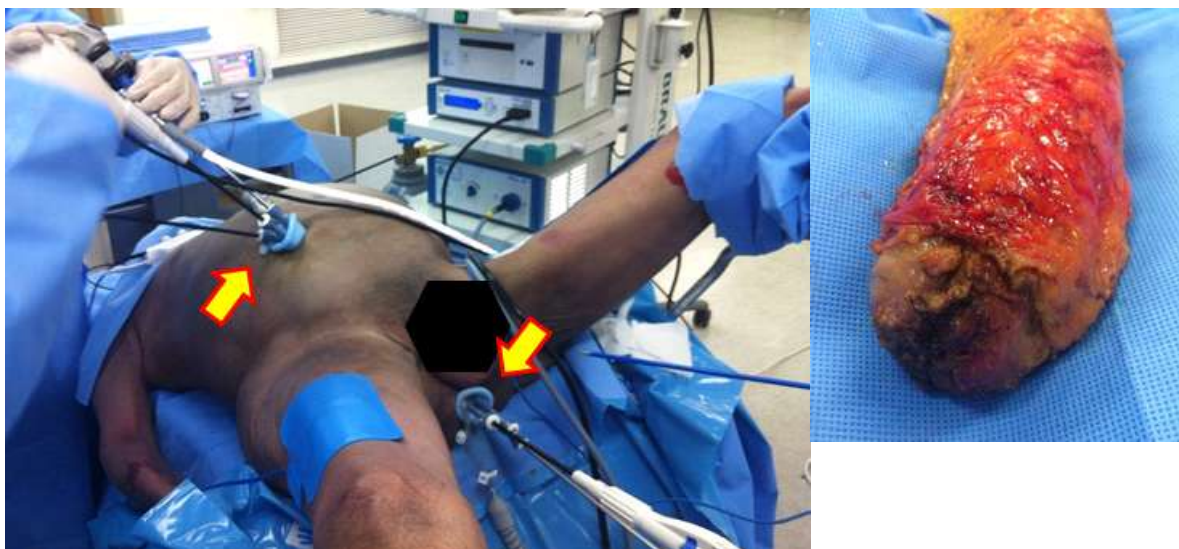


## 1) NOTES 전임상 실험

### 1-1) NOTES rectosigmoidectomy clinical trial을 위한 Human cadaver 실험

#### a. 연구 방법

- Primary oncologic outcome measurement: TME (total mesorectal excision) quality
- Secondary parameters: operation time, complications
- Operation methods
  - (1) full-thickness circumferential incision about 1cm above the dentate line
  - (2) rectal lumen was closed with a purse-string suture
  - (3) a multiple instrument access single-port was placed in the anus
  - (4) the rectum was mobilized cephalad with conventional laparoscopic instruments to the level of anterior peritoneal reflection
  - (5) after placing the lower right quadrant port as diverting stoma site, single-port laparoscopic mobilization of left colon and splenic flexure was performed
  - (6) specimen was delivered transanally or transabdominally and transected
  - (7) intestinal continuity was restored by hand-sewn coloanal anastomosis and diverting ileostomy was created





b. 연구 결과

Table 1. Results of cadaver series

Cavadder	M:F = 11:1
Operation	
Median op. time(min, range)	120 (70-165)
Mean length of bowel $\pm$ SD (cm, range)	34.7 $\pm$ 6.9 (25-45)
Additional port (case)	8
TME quality	
Complete	7 (58%)
Nearly complete	5 (42%)
Intraoperative complications	
Urethra injury	3 cases

Table 2. Details of cadaver experiments

Case No.	Sex	Op time (min)	Additional port	Specimen length (cm)	TME quality	Complication
#1	M	100	No	40	Complete	Urethral injury with bladder laceration
#2	M	165	No	25	Nearly complete	
#3	M	140	Yes	30	Complete	Urethral injury
#4	M	145	Yes	40	Nearly Complete	
#5	M	98	No	30	Nearly Complete	
#6	M	120	Yes	30	Complete	
#7	F	165	Yes	40	Nearly Complete	
#8	M	90	Yes	35	Complete	
#9	M	120	Yes	45	Complete	Urethral injury
#10	M	70	Yes	43	Nearly Complete	
#11	M	95	No	25	Complete	
#12	M	135	Yes	33	Complete	

==> 연구 결론: Transanal rectosigmoidectomy is feasible and safe in carefully selected patients when carried out by trained surgeons. (*\*manuscript in submission*)

## 1-2) Pure NOTES rectosigmoidectomy (Endoscopic IMA Ligation) in Animal Models

### a. 연구방법

- The same procedures in transanal approach.
- When the peritoneal reflection was visualized, the peritoneum of the rectosigmoid was kept intact until subsequent IMA dissection was completed.
- Proximal dissection was continued along the retroperitoneal avascular plane via transanal endoscopic dissection alone, which was facilitated by CO<sub>2</sub> insufflation.
- Mesocolic dissection and IMA pedicle isolation were achieved using a coagrasper (FD-410LR, Olympus, Tokyo, Japan) and clipped using endoscopic clips (hx-600-90, Olympus, Tokyo, Japan).
- After completion of the IMA dissection, the peritoneal lateral attachments of the rectosigmoid, sigmoid, and descending colon were divided using a needle knife (Wilson-Cook Medical Inc., Winston-Salem, NC, USA).
- When the rectosigmoid colon was fully mobilized, it was exteriorized and transected. A colorectal anastomosis was performed using a circular stapler with a single stapling technique.

### b. 연구 결과

- ; Five live animals (four pigs 45 kg each, one dog 25 kg each)
- ; Endoscopic dissection of the IMA: success 100%
- ; Mean operation time: 125 minutes (range, 90-170 min)
- ; No intraoperative complications or hemodynamic instability
- ; The mean length of the resected specimen: 14.4 cm (range, 12-16 cm)

	<b>1st</b>	<b>2nd</b>	<b>3rd</b>	<b>4th</b>	<b>5th</b>
Animal	Dog	Pig	Pig	Pig	Pig
Sex	F	F	F	M	M
BW (kg)	25	45	45	45	45
OP time (min)	125	170	90	150	90
Specimen length (cm)	12	16	16	13	15
Transanal port	SILS™		GelPOINT™		
IMA ligation	<b>Endoclip</b>				

## 2) NOTES rectosigmoidectomy clinical trial

“A pilot study for the evaluation of the safety and the efficacy of transanal total mesorectal excision” (NCCCTS-13-681, 2013-08-08 IRB승인, Clinicaltrial.gov 등록 (NCT01938027) )

### a. 연구 방법

- Inclusion criteria; Rectal cancer (cT1/T2 + N0) located in AV 4-12cm

Age: 60-75yrs, Tumor: W/D or M/D

ECOG performance status 2 or less

- Exclusion criteria;

- Synchronous colon cancer or other malignancy
- Obstructing rectal cancer
- Pregnant or breast-feeding
- Receiving any other study agents
- Fecal incontinence
- History of prior colorectal cancer or inflammatory bowel disease
- BMI > 30
- T3 rectal cancer not treated preoperatively with full-course chemoradiation

- Primary end point: TME quality (N=12)

### A. 복강경 수술 단계

- (기존 시행하고 있는 복강경 직장암 수술과 차이 없음)
- 복벽에 트로카를 삽입 후 CO2 가스를 주입하여 기복을 형성함.
- 하장간막동맥(IMA) 및 정맥(IMV)를 확인하고, 복강경 수술기구를 사용하여 림프절 절제를 시행한 후 혈관 절단함.
- 에스결장을 수술면을 따라 박리하고, 필요시 비만곡부위의 박리하여 결장의 충분한 길이를 확보함.

### B. 경항문 수술 단계

- (경항문 수술은 복강경 수술과 동시에 또는 순차적으로 시행할 수 있음)
- 경항문으로 종양의 위치를 확인하고, 충분한 절제연을 확보한 후 직장 봉합을 시행함.
- 경항문으로 복강경 및 내시경 수술 기구를 이용하여 직장의 박리를 시행함.
- 직장간막의 수술적 절제연을 따라 복강 내로 연결되는 위치까지 박리를 시행함.
- 결장 및 직장의 박리가 완료되면, 창상보호용 수술기구 등을 이용하여 안전하게 항문을 통해 박리된 결장을 뽑아내고, 종양으로부터 5cm 이상의 안전한 거리를 두고 절제함.
- 남은 결장 및 직장은 수기 또는 자동문합기를 이용하여 단단문합술을 시행함.
- 필요시 복벽 트로카 삽입 부위를 통해 회장루를 만들고, 배액관을 삽입한 후 수술을 마침.

#### Statistical Consideration :

- Pilot study로 10명에서 결과를 확인할 예정이며 약 20%의 탈락율을 예상하여, 총 12명의 환자를 대상으로 연구를 진행함.
- TME quality, 30-day postoperative complications, No. of harvested LN 등의 결과에 대해 서술적으로 기술함.
- Oncologic outcome (2-year local recurrence free survival, 5-year survival)은 Kaplan-Meier survival curve를 통해 결과를 도출



<그림> Transanal TME clinical trial

b. 연구 결과 (Early outcome)

; From September 2013 to October 2014, 7 male patients and 5 female patients

; The location of tumors was  $6.7 \pm 2.1$  cm from the anal verge

; 4 (33.3%) of the patients underwent preoperative chemoradiotherapy

; Mean age of patients was  $62.3 \pm 10.1$ , and BMI was  $24.5 \pm 2.8$

; Mean operation time was  $119.2 \pm 48.5$  min

; Estimated blood loss was  $117.8 \pm 135.5$  ml

; No intraoperative complication and conversion.

; **TME quality** : 11 cases (91.7%) of complete or near complete TME

1 case of incomplete TME

; Distal resection margin:  $2.6 \pm 2.4$  cm, circumferential resection margin:  $9.5 \pm 0.4$  mm

; Mean number of harvested lymph nodes:  $15.8 \pm 4.0$

; Mean length of hospital stay was  $11.6 \pm 5.0$  days

; No postoperative mortality

; Minor postoperative complication occurred in 6 patients.

- urinary dysfunction (2), postoperative transient ileus (3), wound abscess (1)

==> **Conclusions:**

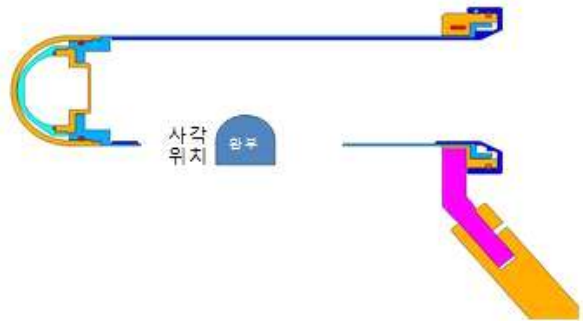
“In this pilot study, a high-quality of TME was possible in most of patients without serious complication. Transanal TME for rectal cancer patients was feasible and oncologically safe procedure. Further investigations are necessary to evaluate its long-term oncologic safety and to clarify its indications.”

*(\*SAGES 2015 meeting, abstract submission)*

### 3) LED-TEM 개선 및 임상 시험 준비

#### ○ 경향문 수술 장치 1차 시제품의 문제점 분석

- 1차년도에 개발한 경향문 수술 장치 시제품은 측면 수술창을 가지며 회전 가능한 경통들과 LED 조명 장치를 내장하고 있었음 (그림 좌)



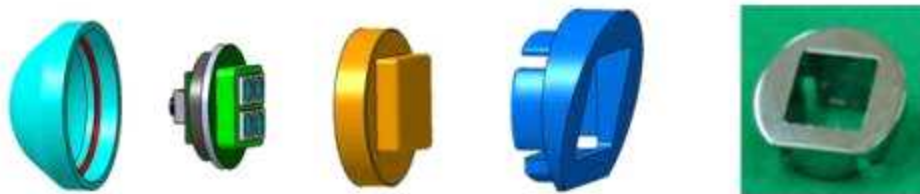
<그림> 사각 위치

<그림> 경향문 수술 장치 1차 시제품

- 개발한 1차 시제품은 집도의의 눈과 측면 수술창의 상대적인 위치로 인해 환부의 조명 측은 경우에 따라 사각 위치(그림 우)에 있게 됨
- 이를 해결하기 위한 한 방안으로 경통 내측에 반사판을 설치하여 집도의가 반사판을 통해 사각 위치를 볼 수 있도록 하도록 하는 아이디어를 구현함

#### ○ LED 조명장치 연동 반사판의 설계 및 제작 (반사판 1차 시제품)

- 기 제작된 LED 조명 장치와 함께 사용될 수 있도록 반사판의 1차 시제품을 제작함.
- 설계의 특성 : 조명을 방해하지 않으면서 최대의 면적을 갖도록 설계
  - (1) 반사판의 내면은 LED 조명창을 둘러싸는 형상을 갖도록 함.
  - (2) 외경은 내부 경통의 내경과 거의 일치하도록 함 (그림 참조).
  - (3) 반사판의 경사각은 수직면을 기준으로 15° 기울어지도록 함.
- 제작을 통한 검증: 실제 반사판을 제작하여 실험해 본 결과, 사각 위치의 일부분을 볼 수 있기는 하였으나, 반사판이 조명창 둘레로 배치되어 있어 사각 위치를 전체적으로 보는 것에 어려움 존재.

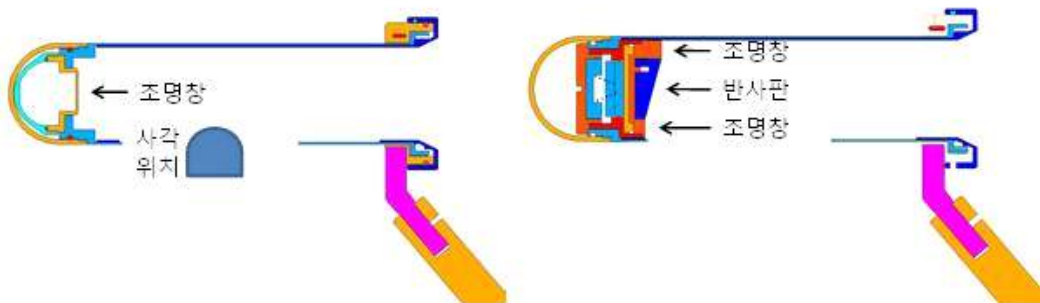


<그림> 반사판 1차 시제품

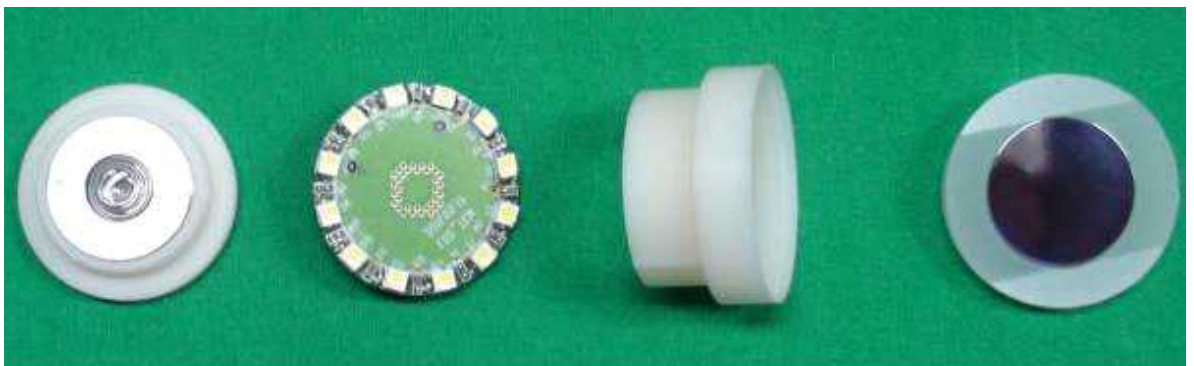
#### ○ LED 조명장치 연동 반사판의 설계 및 제작 (반사판 2차 시제품)

- 반사판 1차 시제품의 문제점을 극복하기 위해, 2차 시제품에서는 아래 그림에 나타난

- 것과 같이 LED 및 조명창의 위치를 중심에서 외곽으로 옮기고 반사판을 중심에 설치하는 것으로 설계를 변경함
- 또한 1차 시제품에서는 LED 조명 어셈블리가 이미 완성된 상태에서 반사판을 추가했었으나, 2차 시제품에서는 LED 조명 어셈블리와 반사판을 일체로 제작하여 LED 조명 및 반사판 어셈블리(그림 참조)가 되도록 설계.
  - LED 조명 어셈블리는 그림4에서 알 수 있듯이 단품으로 조립된 후 경통 외부로부터 삽입해 체결하였고, 경통에 걸림턱을 두어 조명창 부분만 경통 내부로 삽입되도록 함.
  - LED 조명 및 반사판 어셈블리의 경우 경통에 걸림턱을 두는 동일한 체결 방식을 사용하면 반사판의 면적을 최대한 크게 한다는 관점에서 경통 내부의 공간을 충분히 활용하지 못하는 문제가 발생.
  - 따라서 LED 조명 및 반사판 어셈블리가 단품 상태로 조립되는 것이 아니라, 일부는 경통 외부로부터 삽입되고, 나머지 부분은 경통 내부로부터 삽입되어 경통과 함께 조립되는 방식으로 결합 방식을 변경하여 반사판의 면적을 최대화하고자 하였는데, 실제 구현된 반사판의 지름은  $\phi 21.8$ 임.



<그림> 반사판 2차 시제품 체결 방식



<그림> LED 조명 및 반사판 어셈블리

반사판 1차 시제품은 수직면에 대한 설치 각도가 15°가 되도록 하였고, 평면



반사판으로 제작하였는데, 2차 시제품에서는 그림6에 나타난 바와 같이 수직면에 대해 10°, 15°, 20°의 설치 각도를 가지는 평면 반사판과 15°의 설치 각도를 가지는 볼록 반사판을 제작.

- 측면 수술창 내 환부의 위치에 따라 적합한 반사판의 설치 각도가 변경되는 것이므로 시술에 앞서 환부의 위치에 맞는 반사판을 조립하여 사용하는 것이 필요할 것으로 판단됨.
- 볼록 반사판이 약간의 왜곡은 있으나 평면 반사판에 비해서는 더 넓은 사각 지대를 볼 수 있게 하므로 반사판 설치 목적에 조금 더 부합하는 것을 제작된 시제품으로부터 확인할 수 있었음.



<그림> 볼록 및 평면 반사판

아래 그림은 측면 수술창을 가지며 회전 가능한 경통들과 LED 조명 장치 및 반사판을 내장한 경향문 수술 장치 2차 시제품을 보여줌

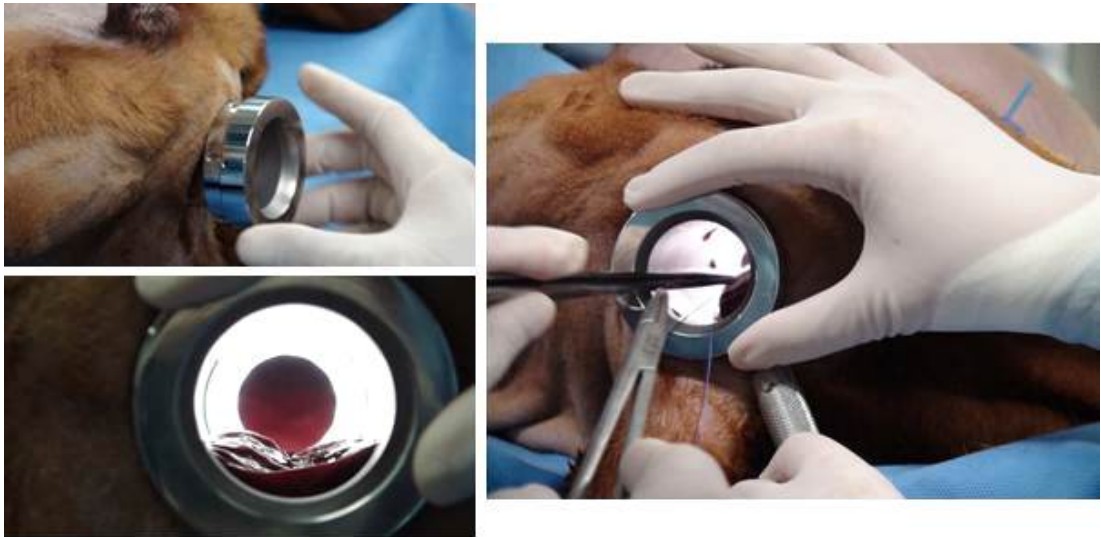


<그림> 경향문 수술 장치 2차 시제품



○ 동물실험을 통한 2차 시제품의 검증

- 아래 그림은 개를 대상으로 한 동물 실험에 제작한 시제품을 적용하는 장면을 보여주고 있음. 동물 실험은 성공적이었으며, 향후 임상 적용을 준비 중임.
- 2차 시제품은 EO 가스 소독 및 방수 테스트에서 좋은 결과를 보였으며, 임상시험을 위해 필요한 추가 실험 및 서류를 준비 중임

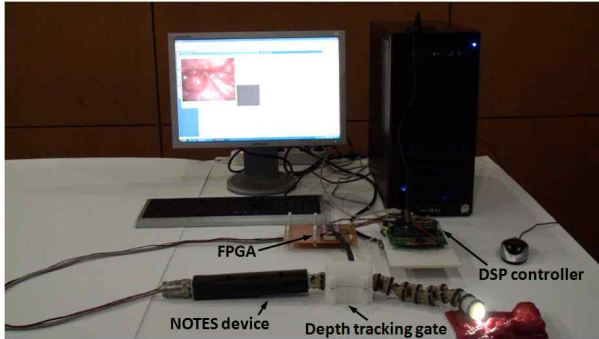


<그림> 경향문 수술 장치 동물 실험

- ; KFDA 승인을 위해서는 기술이전이 우선적으로 필요함을 확인하고, 기술이전을 우선 진행하기로 함
- ; 향 후 기술이전을 위한 적극적인 노력 필요

4) NOTES platform 설계 및 제작

- 1차 시제품 제작 및 문제점 확인 후 2차 시제품 제작
- 2차 시제품 개선사항
  - ; 타기관에서의 동물실험 등을 위해 노트북을 이용할 수 있도록 프로그램 변경
  - ; Portable device controller 제작 및 3D mouse 사용
  - ; 방수 가능하도록 고무 cover 제작
  - ; Endoscopy 삽입 가능하도록 channel 직경 확대 등
- 전임상 실험
  - ; 돼지실험 3회, human cadaver 2회를 통해 전임상실험 진행
  - ; 전임상 실험 결과 논문 작성

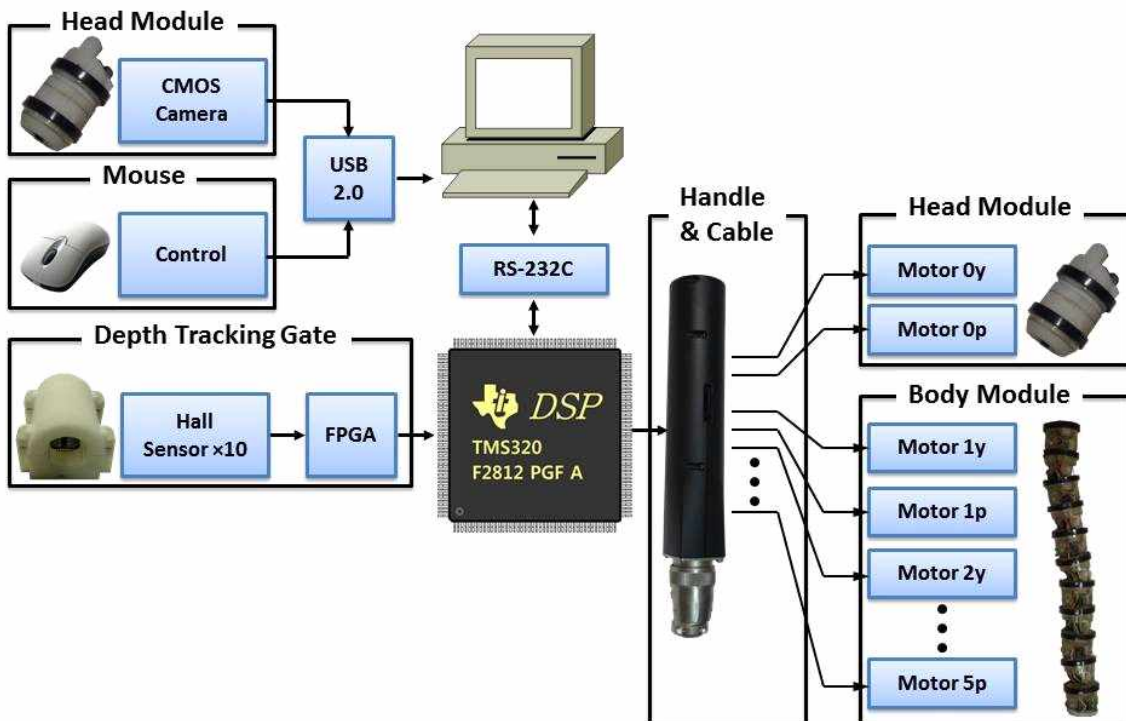


<그림> 1차 시제품



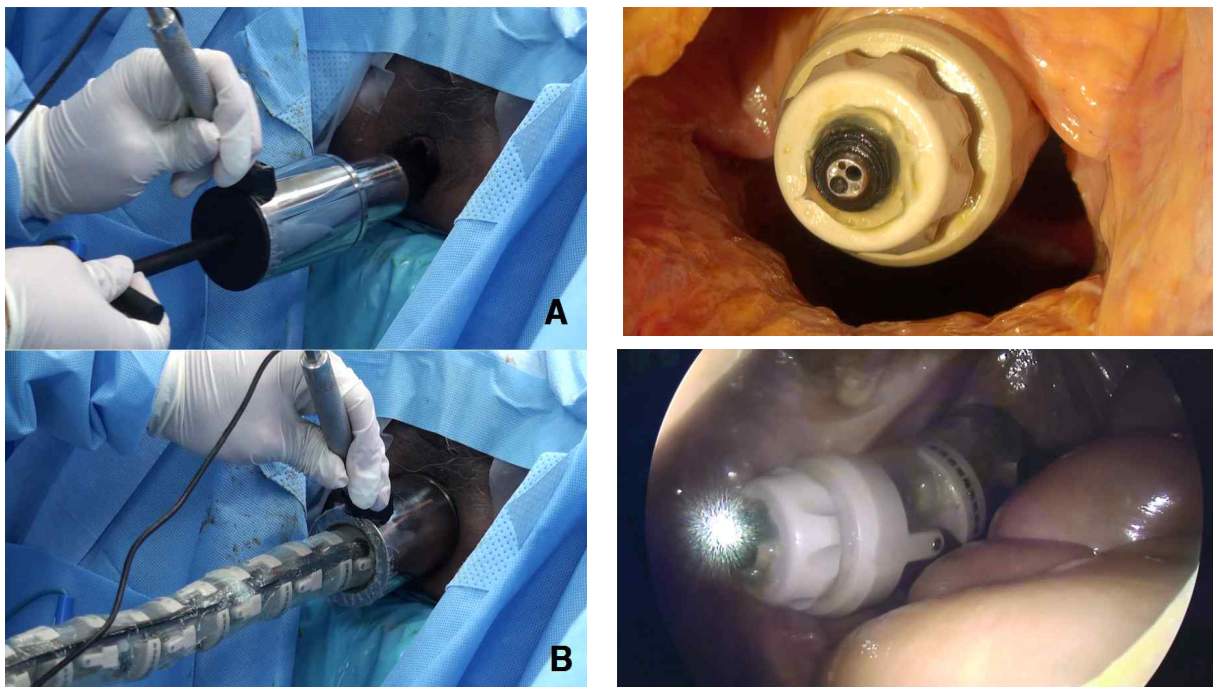
<그림> 개선된 2차 시제품

## NCC NOTES Platform의 제어 시스템





<그림> NOTES platform 시제품을 이용한 동물실험



<그림> NOTES platform 시제품을 이용한 Cadaver 실험

*Son et al. Surg Endosc 2014 Oct 8. [Epub ahead of print] (IF: 3.313)*

## 5) NOTES instruments 등의 개발

- 다기능 주사침 (내시경용 주사장치 {Endoscopic Injection Apparatus})

10-2013-0123509 (출원일: 2013.10.16.)

10-2014-0136540 (출원일: 2014.10.10.)

“본 발명은 내시경용 주사장치에 관한 것으로, 더욱 상세하게는 주사 대상부위 조직을 내시경용 집게로 파지한 상태에서 주사침을 삽입하여 주사 용액을 안전하게 주입함은 물론 출혈 발생시에는 그 출혈 부위를 지혈할 수 있도록 한 다목적 내시경용 주사장치에 관한 것이다.”

*(\*현재 국내 및 PCT 출원 증으로 자세한 도면은 생략함)*

- 레이저 빔을 이용한 수술기구

10-2012-0115882 (출원일: 2012.10.18.)

“본 발명은 병변부가 클립 조립체에 파지된 상태에서 조사부에서 방출되는 광원이 병변부를 조사하여 치료하도록 구성되어, 클립 조립체로 병변부를 파지할 수 있고, 또한, 광원으로 병변부만 치료할 수 있기 때문에 광원으로 인한 주변 조직의 손상을 방지할 수 있는 의료용 수술 기구를 제공하는 것에 목적이 있음”

*(\*현재 국내 출원 증으로 자세한 도면은 생략함)*

- 다목적용 의료 영상 표지자 및 이의 제조방법

10-2014-0043485 (출원일: 2014.04.11.)

“본 발명은 의료 영상 표지자에 관한 것으로, 더욱 상세하게는 형광 염료 및 MRI 조영제 또는 CT 조영제를 하나 이상 포함하는 다목적용 의료 영상 표지자 및 이의 제조방법에 관한 것이다. 또한, 본 발명은 다목적용 의료 영상 표지자를 포함하는 내시경용 결찰기에 관한 것이다.”

*(\*현재 국내 출원 증으로 자세한 도면은 생략함)*

### 3. 연구결과 고찰 및 결론

#### 1) NOTES preclinical study

- NOTES rectosigmoidectomy cadaver experiments를 통해 기존 동물실험을 통해 표준화한 NOTES 수술법을 검증할 수 있었음. Rectum의 post. wall dissection은 비교적 쉽게 진행할 수 있었으나, anterior wall의 dissection 시 기존의 dissection plane 보다 깊게 진행되어 남성의 경우 urethra injury 의 위험성이 있음을 확인함. rectum을 closure 후 posterior wall의 dissection을 먼저 시행하는 것이 유리할 수 있음을 확인함. 남성 환자의 경우 foley catheter를 삽입 후 dissection을 시행하면 urethra injury의 가능성을 줄일 수 있을 것으로 예상됨.
- Transanal approach에 의한 수술을 위해서 surgeon은 어느 정도 이상의 animal study와 cadaver study 등을 통한 preclinical experiences가 필요할 것으로 생각됨. 향후 다기관 연구 등을 위해서는 공동의 preclinical study 참여 또는 video review 등을 통한 사전 교육이 필요할 것으로 생각됨.
- 현재 진행되고 있는 모든 transanal NOTES rectosigmoidectomy 수술법은 복강경 수술 보조 하에서 시행되고 있음. 기존의 복강경 수술로는 시야 확보나 접근이 어려운 좁은 골반강 내에서의 수술은 경항문 접근법이 장점을 가질 수 있으나, 추 후 pure NOTES 수술법을 위해서는 IMA(inferior mesenteric artery)의 경항문 접근법에 의한 박리와 결찰이 필수적임.
- 이러한 한계점을 극복하기 위해서는 flexible endoscopy를 이용하여 retroperitoneal approach에 의한 IMA의 dissection이 필요하며, 이를 검증하고 필요한 기기 및 술기 등을 확인하기 위해 동물 실험을 진행하였음.
- 동물실험 결과 총 5마리의 실험동물 모두에서 abdominal port의 보조없이 flexible endoscopy와 endoscopic instruments만으로 성공적으로 수술을 시행할 수 있었으며, 이를 통해 pure NOTES rectosigmoidectomy 의 가능성을 확인할 수 있었음.
- 보다 나은 환경에서의 수술을 위해서는 CO2 압력 조절 장치와 air suction장치의 정교한 control이 필수적이며, 이를 자동화할 수 있는 기기 개발이 필요함. Flexible endoscopy를 수술 범위까지 진행하여 지지할 수 있는 platform의 개발도 필수적임.
- 동물실험에서의 결과를 추 후 human cadaver test를 통해 검증해야 하며, 이를 위해서는 보다 힘을 강하게 전달할 수 있는 instrument 개발도 필수적임.

## 2) NOTES rectosigmoidectomy clinical trial

- 기존 TEM을 이용한 rectosigmoidectomy의 최초 증례는 2010년 Sylla 등에 의해 보고되었음. 이후 유럽과 남미, 미국 등에서 다양한 형태의 case series가 보고되기 시작하였으며, 최근에는 기존의 복강경 수술과의 간접적인 비교 연구 결과 또한 보고되고 있음.

- 또한 TEM장비의 비용이 고가인 점이 단점으로 지적되어, 최근의 많은 연구에서는 이에 대한 대안으로 SILS port 또는 transanal GELPOINT path 등의 flexible port를 이용한 transanal approach가 보고되고 있음.

- 본 연구는 직장암 환자의 수술에서 경향문 접근법의 안정성 및 효용성을 검증하고자 하며, 본 연구(2상 & 3상 임상시험)에 앞서 이를 위한 예비 연구(pilot study)로 진행되었음.

본 연구에서는 primary outcome으로서 TME quality, 30-day postoperative complications, No. of harvested LN 등의 결과를 확인하고 이를 서술적으로 기술하고자 하였으며, oncologic outcome (2-year local recurrence free survival, 5-year survival)은 Kaplan-Meier survival curve를 통해 결과를 도출하고자 계획됨. (단, Pilot 연구로 통계적 방법을 이용한 결과 분석은 시행하지 않음)

- 본 연구는 보다 안전하게 피험자를 보호하기 위해 전체 12 case중 3 case씩 수술이 진행되는 단계 (3-6-9-12)에서, intra-operative and immediate postoperative complication 발생을 지속적으로 점검하여 위의 중간평가 단계에서 중대한 합병증 (수술 후 1개월 이상의 입원기간 연장 또는 퇴원 후 재입원 또는 재수술이 필요한 경우) 발생률이 기존의 직장암 수술 후 발생 가능한 20%를 넘는 경우 이를 IRB에 보고하고, 수술 방법의 문제점을 다시 점검하고, 수술 방법을 변경하여 진행하도록 계획하였음.

- 연구 결과 전체 12명의 환자 중 1명을 제외한 11례(91.7%)에서 complete or near complete TME quality를 확인할 수 있었음. 또한 distal resection margin과 circumferential resection margin은 각각  $2.6\pm 2.4\text{cm}$  과  $9.5\pm 0.4\text{mm}$  이었으며, Mean number of harvested lymph nodes는  $15.8\pm 4.0$  로서 early outcome에서 oncologic safety를 확인할 수 있었음.

- 다음 과제로서는 본 pilot study 결과를 토대로 phase I or II trial을 계획할 수 있으며, TEM platform과 soft platform의 차이를 확인하는 연구도 필요할 것으로 판단됨.

- 또한 본 연구결과를 바탕으로 operation procedure를 standardization하여 추 후 다기관 연구 등을 위한 education과 training program 개발이 필요하며, 이와 함께 registration system도 구축이 필요함. 현재 진행하고 있는 international NOTES-TME registration을 함께 이용하는 것도 고려할 수 있음.



### 3) Development of NOTES platform & instruments

- 제작된 LED-TEM을 이용한 임상시험을 위해 KFDA 허가를 얻어야 함; 허가 규정이 까다롭게 변경되어 자체 제작된 시제품으로는 허가받기 힘들어짐
- LED-TEM의 KFDA허가를 위한 공인된 기관에서의 water proof test & sterilization test를 계획하였으나, KFDA 허가 규정이 변경에 따라 연구 계획을 일부 수정함 ==> 기존 제작된 시제품의 문제점을 추가 분석하여 개선된 시제품을 제작하는데 주력하였으며, 경항문 접근을 통한 NOTES 기술을 위해 NOTES platform (Robot system) 제작을 함께 진행함.
- TEM 장비의 구성 요소 중에서 기구 삽입구 위치는 지나치게 좁을 경우 시술 시 수술 도구들 간의 간섭 및 부딪힘 현상이 발생하며, 지나치게 넓을 경우 특정 방향으로의 시술이 불가능해지는 문제가 있음. 따라서, 국립암센터에서 TEM 기술을 실제 집도하는 임상의를 대상으로 자문 의뢰하여 두 개의 기구 삽입구들의 위치를 중앙선 상의 중심점을 기준으로 좌우 10 mm 위치에 있는 것으로 고정하였음.
- 기존 TEM 장비들의 설계 치수를 고려하여 틀 및 기구 삽입부의 전체 길이는 60 mm 로 고정하였으며, 경통부의 두께는 사용되는 재료의 강성을 고려하여 1 mm 로 고정하였음.
- 실제 각 관절에 모터를 사용한 다굴절형 platform을 제작해 본 결과 원하는 방향으로 platform의 진행은 가능하였으나, 관절이 많아짐에 따라 기구 자체의 무게를 견딜 수 있는 모터와 기어 시스템이 필요함을 확인함.
- 현재 사용 가능한 소형 모터 범위에서 최대한의 토크를 얻을 수 있도록 설계가 필요하며, 기존의 내시경의 삽입이 가능하도록 5mm 이상의 working channel을 마련하는 것도 필수적임.
- 모터와 기어 자체가 체내 삽입됨으로서 발생 가능한 문제 등에 대해서는 기존의 유사한 로봇 의료기기 시스템의 문제점 등에 대해 문헌 고찰 및 리뷰가 필요함.
- 본 시스템의 동물실험과 카테바 실험을 위해서 특수 제작된 얇은 고무튜브를 사용하였으나, 반복 실험시 고무 파열이 일어남을 확인함. 기존 내시경 피복 재료를 사용할 수 있는지에 대해서도 추가적인 검토 필요함.
- 본 기기의 성능테스트를 위한 반복적인 실험을 위해서는 동물실험보다는 3D 프린터를 이용한 인체 골반강 모형을 제작하여 사용하는 것도 바람직할 것으로 보임.
- Platform의 설계와 함께 수술시 사용 가능한 end effector에 대해서도 미리 생각하여 platform에 적용 가능하도록 설계시 함께 고려하는 것이 필요함.

#### 4. 연구성과 및 목표달성도

##### (1) 연구성과

가. 국내 및 국제 전문학술지 논문 게재 및 신청

논문명	저자 (저자구분 <sup>1)</sup> )	저널명(I.F.)	Year; Vol(No):Page	구분 <sup>2)</sup>	지원과제번호 <sup>3)</sup>
Safety and Efficacy of Single-Port Colectomy for Sigmoid Colon Cancer:A Phase II Clinical Trial	손대경 (공동)	Journal of laparoendoscopic and advanced surgical techniques (1.066)	2013; 23(9):745-750	국외 SCIE	1210170
Transanal natural orifice transluminal endoscopic surgery total mesorectal excision in animal models: endoscopic inferior mesenteric artery dissection made easier by a retroperitoneal approach	손대경 (교신)	Annals of Surgical Treatment and Research (0.616)	2014; 87:1-4	국내 SCIE	1210170
Randomized Clinical Trial Comparing Reduced-Volume Oral Picosulfate and a Prepackaged Low-Residue Diet With 4-Liter PEG Solution for Bowel Preparation	손대경 (교신)	Diseases of the Colon & Rectum (3.198)	2014; 57(4):522-528	국외 SCI	1210170
A novel semi-automatic snake robot for natural orifice transluminal endoscopic surgery: preclinical tests in animal and human cadaver models (with video)	손대경 (교신)	Surgical Endoscopy (3.313)	2014 Oct 8. [Epub ahead of print]	국외 SCI	1210170
Transanal Rectosigmoidectomy Using a Single Port in a Swine Model	손대경 (교신)	Surgical Innovation (1.537)	2013; 20(3):225-229	국외 SCIE	0910520 (NOTES-1)
Analysis of the Anatomical Characteristics of the Pelvis in Koreans to Aid in Development of a NOTES Platform	손대경 (교신)	Surgical Innovation (1.537)	2013; 20(2):134-141	국외 SCIE	0910520 & NRF-2011-0 004496
Factors associated with complete local excision of small rectal carcinoid tumor	손대경 (교신)	International journal of colorectal disease (2.238)	2013; 28(1):57-61	국외 SCIE	0910520 (NOTES-1)
Predictors for lymph node metastasis in T1 colorectal cancer	손대경 (공동)	Endoscopy (5.210)	2012; 44(6):590-595	국외 SCI	없음
Transanal rectosigmoid resection via natural orifice transluminal endoscopic surgery (NOTES) with total mesorectal excision in a large human cadaver series.	손대경 (공동)	Surgical Endoscopy (3.427)	2013; 27(1):74-80	국외 SCI	없음
Clinicopathological characteristics of T1 colorectal cancer without background adenoma	손대경 (공동)	Colorectal Disease (2.081)	2013; 15(3):124-9	국외 SCI	없음

1) 저자구분 : 교신, 제1, 공동

2) 구분 : 국내, 국내 SCI, 국내 SCIE, 국외, 국외SCI, 국외SCIE 등

3) 지원과제번호(Acknowledgement)

- 과제번호를 연차 표시(-1, -2, -3 등)를 생략하고 7자리로 기재하고, 과제와 관련성은 있으나



불가피하게 Acknowledgement가 누락된 경우에는 '없음'으로 기재

나. 국내 및 국제 학술대회 논문 발표

논문명	저자	학술대회명	지역 <sup>1)</sup>	지원과제번호
A Novel Semi-Automatic Robotic NOTES System	손대경 (교신)	SAGES 2013 (Society of American Gastrointestinal Endoscopic Surgeon)	국외	1210170
A Semi-automatic operation Robotic NOTES System using snake algorithm	손대경 (교신)	CARS 2013 (Computer-assisted Radiology & Surgery)	국외	1210170

1) 지역 : 국내, 국외

다. 산업재산권

구분 <sup>1)</sup>	특허명	출원인	출원국	출원번호
발명특허	다목적용 의료 영상 표지자 및 이의 제 조방법	국립암센터 (손대경 외)	대한민국	10-2014-0043485
발명특허	내시경용 주사장치	국립암센터 (손대경 외)	대한민국	10-2013-0123509
발명특허	내시경용 주사장치	국립암센터 (손대경 외)	대한민국	10-2014-0136540
발명특허	내시경용 주사장치 (10-2013-0123509 & 10-2014-0136540)	국립암센터 (손대경 외)	PCT출원	PCT/KR2014/009562
발명특허	의료용 수술 기구	국립암센터 (손대경 외)	대한민국	10-2012-0115882
발명특허	선형 삽입깊이 측정장치	국립암센터 (김광기 외)	대한민국	10-2012-0108485

1) 구분 : 발명특허, 실용신안, 의장등록 등

라. 저 서

저서명	저자	발행기관(발행국, 도시)	쪽수	Chapter 제목, 쪽수 (공저일 경우)

마. 연구성과의 정부정책 기여

보고서명	정부정책	기여내용

바. 기타연구성과

(2) 목표달성도

가. 연구목표의 달성도

최종목표	연차별목표		달성내용	달성도(%)	
				연차	최종
자연개구부무흉터내시경수술법(NOTES)의 개발 및 임상 적용	1차년도	NOTES 전임상실험 + 임상시험 준비	NOTES rectosigmoidectomy 전임상 실험	90	90
			LED-TEM 임상 시험 준비		
	2차년도	NOTES 전임상시험 + 임상시험	NOTES rectosigmoidectomy 임상 시험	100	100
			NOTES platform 설계 및 제작		
	3차년도	NOTES 전임상시험 + 임상시험	NOTES rectosigmoidectomy 임상 시험	100	100
			NOTES platform 개선 및 overtube 설계		

나. 평가의 착안점에 따른 목표달성도에 대한 자체평가

평가의 착안점	자 체 평 가
NOTES 전임상실험	임상시험을 위한 human cadaver 실험 완료 및 pure NOTES 수술법 개발을 위한 동물실험 완료
NOTES 임상시험	임상시험 IRB 승인 및 Clinicaltrial.gov 등록. 연구기간 내 계획한 임상시험 완료
NOTES 기기 개발 (LED-TEM)	1차 시제품 평가를 통한 개선된 2차 시제품 제작 및 동물 실험을 통한 검증 완료. 하지만 의료기기 임상시험을 위한 KFDA 승인을 얻기 위해서는 기술이전이 우선적으로 필요함을 확인하고, 기술이전 추진으로 연구 계획 변경
NOTES 기기 개발 (Platform 등)	1차 시제품 설계 제작 및 문제점 확인 후 2차 시제품 제작 완료. pig model 3회, human cadaver model 2회 전임상 실험 완료

## 5. 연구결과의 활용계획

### (1) 연구종료 2년후 예상 연구성과

구 분	건 수	비 고
학술지 논문 게재	2	Surgical Endoscopy (3.3) - 임상시험 및 Platform 개발 결과 발표
산업재산권 등록	2	대한민국 (내시경용 주사장치, 다목적용 의료 영상 표지자 및 이의 제조방법)
기 타		후속 연구 시행에 따른 임상 시험

### (2) 연구성과의 활용계획

- NOTES 연구를 통해 다양한 수술 기기의 개발이 가능해짐
  - ; 내시경을 통한 봉합 기기/자동문합기기 개발
  - ; 내시경을 통한 다굴절 또는 다관절 기기 개발
  - ; 로봇틱 수술을 위한 새로운 복강내 진입로의 개발 등
- 또한, NOTES 수술법은 임상적으로 다음과 같은 암연구 분야에 활용 가능할 것을 기대됨.
  - ; 조기위암 및 조기 대장암에 대한 내시경적 전층 절제 및 봉합
  - ; 위암에 대한 감시리프절 생검 및 조직검사
  - ; 주변 장기 침습을 보이지 않는 직장암의 수술
  - ; 진행성 암에서의 진단적 복강내시경 검사 등

### 1) 연구의 기대 효과

- 본 연구에서 개발 및 적용하고자 하는 NOTES 수술법은 현재 각광받고 있는 최소침습수술 분야 중에서도 최첨단 기술로써 받아들여지고 있으며, 미국 및 유럽 등의 의료선진국가에서도 대규모의 연구비 지원을 통해 개발하고자 노력 중인 분야임. NOTES수술법의 개발은 실질적인 무흉터수술(Scarless surgery)을 가능하게 함으로써 수술적 치료를 요하는 환자들의 삶의 질 향상에 크게 기여할 것으로 기대됨.
- 또한 NOTES에 대한 연구는 향후 진행될 로봇틱 수술 등의 새로운 수술 기기 개발에도 커다란 영향을 미칠 것으로 예상되고 있으며, 향후 조기암 등에 대한 소화기내시경 치료의 영역에서도 치료 기기 및 술기의 발달에 크게 영향을 미칠 것으로 사료됨.

## 2) 연구 결과의 활용방안

- NOTES 수술법의 연구를 통해 다양한 기기의 개발이 가능해짐
  - ; 내시경을 통한 봉합 기기/자동문합기기 개발
  - ; 내시경을 통한 다굴절 또는 다관절 기기 개발
  - ; 로봇틱 수술을 위한 새로운 복강내 진입로의 개발 등
- 또한, NOTES 수술법은 임상적으로 다음과 같은 암연구 분야에 활용 가능할 것을 기대됨.
  - ; 조기위암 및 조기 대장암에 대한 내시경적 전층 절제 및 봉합
  - ; 위암에 대한 감시립프절 생검 및 조직검사
  - ; 주변 장기 침습을 보이지 않는 직장암의 수술
  - ; 진행성 암에서의 진단적 복강내시경 검사 등

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## 7. 첨부서류

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DYNAMIC MANUSCRIPT

# A novel semi-automatic snake robot for natural orifice transluminal endoscopic surgery: preclinical tests in animal and human cadaver models (with video)

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### Abstract

**Background and study aims** Natural orifice transluminal endoscopic surgery (NOTES) is an emerging surgical technique. We aimed to design, create, and evaluate a new semi-automatic snake robot for NOTES.

**Materials and methods** The snake robot employs the characteristics of both a manual endoscope and a multi-segment snake robot. This robot is inserted and retracted manually, like a classical endoscope, while its shape is controlled using embedded robot technology. The feasibility of a prototype robot for NOTES was evaluated in animals and human cadavers.

**Results** The transverse stiffness and maneuverability of the snake robot appeared satisfactory. It could be advanced through the anus as far as the peritoneal cavity without any injury to adjacent organs. Preclinical tests showed that the device could navigate the peritoneal cavity.

**Conclusions** The snake robot has advantages of high transverse force and intuitive control. This new robot may be clinically superior to conventional tools for transanal NOTES.

**Keywords** Natural orifice transluminal endoscopic surgery · Medical device · Semi-automatic · Surgical robot

**Electronic supplementary material** The online version of this article (doi:10.1007/s00464-014-3854-6) contains supplementary material, which is available to authorized users.

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Conventional endoscopes show limited functionality in the complex tasks of natural orifice transluminal endoscopic surgery (NOTES). However, NOTES has been performed using endoscopes since no satisfactory NOTES-specific tool is available. Detailed requirements for NOTES have been formulated by the Natural Orifice Surgery Consortium for Assessment and Research (NOSCAR) [1]. The flexibility of endoscopes is a disadvantage in NOTES, since surgery often requires the ability to apply push and pull forces to tissue. A specialized robotic NOTES tool, with both rigid and flexible characteristics, is therefore needed. This is a challenging requirement, as a device cannot be both rigid and flexible at the same time.

Several approaches have been investigated to meet this demand. One approach uses a specially designed insertion tube, with mechanical stiffness that can switch between rigidity and flexibility [2, 3]. However, the shape of this tube cannot be fully controlled, and it may be difficult to place such a tube at the desired position and in the desired shape within a human body. Another approach attempts to increase dexterity by adding a robotic manipulator to the tip of an existing endoscope [4, 5], but this system lacks the required rigidity because the tube is still that of the endoscope. A more interesting approach is to replace the entire flexible endoscopic structure with multi-segment robots that resemble snakes. However, the actuation of multi-segment robots has been a significant barrier for its application to NOTES, since the number of actuators must equal the number of degrees of freedom (DOF), the size of the system is too large for use in a human body, or the system requires a huge attached control box at the proximal end of the robot body [6, 7].

In this study, we developed a novel semi-automatic snake robot system for NOTES, which employs the characteristics of both a manual endoscope and a multi-segment



## Transanal natural orifice transluminal endoscopic surgery total mesorectal excision in animal models: endoscopic inferior mesenteric artery dissection made easier by a retroperitoneal approach

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**Purpose:** We report the performance of natural orifice transluminal endoscopic surgery (NOTES) low anterior resection in animals using transanal total mesorectal excision (TME) with laparoscopic assistance and endoscopic inferior mesenteric artery (IMA) dissection.

**Methods:** Four pigs weighing 45 kg each, and one dog weighing 25 kg, underwent surgery via a transanal approach. The rectum was occluded transanally using a purse-string suture, approximately 3–4 cm from the anal verge. The rectal mucosa was incised circumferentially just distal to the purse-string. A SILS or GelPOINT port was inserted transanally. Transanal TME was assisted by laparoscopy and proceeded up to the peritoneal reflection. More proximal dissection, including IMA dissection, was performed along the retroperitoneal avascular plane by endoscopy alone and facilitated by CO<sub>2</sub> insufflation. The IMA was clipped and divided endoscopically. The mobilized rectosigmoid were exteriorized transanally and transected. A colorectal anastomosis was performed using a circular stapler with a single stapling technique.

**Results:** Endoscopic dissection of the IMA was successful in all five animals. The mean operation time was 125 minutes (range, 90–170 minutes). There were no intraoperative complications or hemodynamic instability. The mean length of the resected specimen was 14.4 cm (range, 12–16 cm).

**Conclusion:** A NOTES retroperitoneal approach to the IMA with CO<sub>2</sub> insufflation and intact peritoneal covering overcame the difficulties of retraction and exposure of endoscopic dissection in animals.

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**Key Words:** Natural orifice transluminal endoscopic surgery, Retroperitoneal approach, Total mesorectal excision, Inferior mesenteric artery

### INTRODUCTION

Natural orifice transluminal endoscopic surgery (NOTES) is a new method of using a natural orifice to access the intra-

abdominal space. Despite experimental and clinical studies, however, NOTES has encountered many complex obstacles and technical limitations associated with endoscopic surgery, including limitations in endoscopic tools, less precise move-

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## Safety and Efficacy of Single-Port Colectomy for Sigmoid Colon Cancer: A Phase II Clinical Trial

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### Abstract

**Background:** Recently, single-port surgery for colon cancer has been increasingly attempted. However, prospective studies investigating the efficacy of single-port colectomy for colon cancer are lacking. The aim of this study is to determine whether single-port colectomy for sigmoid colon cancer is a safe and effective surgical option.

**Subjects and Methods:** Forty-eight patients were enrolled for this prospective single-arm Phase II trial. All patients underwent single-port laparoscopic-assisted sigmoidectomy through the umbilicus. The primary outcome was the number of retrieved lymph nodes. Secondary measures included the conversion rate, postoperative morbidities, mortalities, and short-term clinical outcomes.

**Results:** The mean number of retrieved lymph nodes was 21.1 (95% confidence interval, 18.1–23.99). The conversion rate was 14.6% (open conversion, 4.2%), and the overall proportion of morbidity was 31.2%. The majority of complications involved wound problems (18.8%); the mortality rate was 0%. The median postoperative hospital stay was 8 days (range, 7–12 days), and the median time from surgery until the first episode of flatus was 3 days (range, 1–5 days).

**Conclusions:** Single-port colectomy for sigmoid colon cancer is safe and oncologically feasible in selected patients. Considering the relatively high conversion rates, improvement of the instruments for single-port colectomy is needed.

### Introduction

MINIMALLY INVASIVE SURGERY has been widely applied in the field of colorectal cancer. As a minimally invasive approach, laparoscopic colectomy was approved as one of the standard procedures for colon cancer after its long-term safety was indicated by randomized clinical trials.<sup>1–3</sup> Laparoscopic colectomy has short-term benefits in terms of bowel movement, postoperative pain, and hospital stay.<sup>3–5</sup> Recently, single-incision laparoscopic surgery through the umbilicus was introduced.<sup>6</sup> As an embryonic natural orifice, the umbilicus can be used as an intraabdominal access channel. The umbilical incision can lead to improved cosmesis because it can easily be concealed. Based on these characteristics, single-port colectomy has been introduced

and increasingly attempted.<sup>7</sup> However, prospective studies investigating the efficacy of single-port colectomy for colon cancer are lacking. The aim of this study is to determine whether single-port colectomy for sigmoid colon cancer is a safe and effective surgical option.

### Subjects and Methods

#### Study design

We designed a single-arm Phase II trial of single-port colectomy for sigmoid colon cancer. The study was conducted in the Center for Colorectal Cancer of the National Cancer Center Hospital, Goyang, Korea. The trial was conducted from January 2011 through August 2011. The study was reviewed and approved by the Institutional Review Board of

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## Factors associated with complete local excision of small rectal carcinoid tumor

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### Abstract

**Purpose** Although small rectal carcinoid tumors can be treated using local excision, complete resection can be difficult because tumors are located in the submucosal layer. We evaluate the factors associated with pathologically complete local resection of rectal carcinoid tumors.

**Methods** Data were analyzed of 161 patients with 166 rectal carcinoid tumors who underwent local excision with curative intent from January 2001 to December 2010. A pathologically complete resection (P-CR) was defined as an en bloc resection with tumor-free lateral and deep margins. The study classified treatments into three categories for analysis: conventional polypectomy (including strip biopsy, snare polypectomy, and hot biopsy), advanced endoscopic techniques (including endoscopic mucosal resection with cap and endoscopic submucosal dissection), and surgical local excision (including transanal excision and transanal endoscopic microsurgery). We evaluated the P-CR rate according to treatment method, tumor size, initial endoscopic impression and the use of endoscopic ultrasound (EUS) or transrectal ultrasound (TRUS).

**Results** The mean tumor size was  $5.51 \pm 2.43$  mm (range 2–18 mm) and all lesions were confined to the submucosal layer. The P-CR rates were 30.9, 72.0, and 81.8 % for conventional polypectomy, advanced endoscopic techniques, and surgical local excision, respectively. Univariate analysis showed that P-CR was associated with treatment

method, use of EUS or TRUS, and initial endoscopic impression. Multivariate analysis showed that only treatment method was associated with P-CR.

**Conclusion** Pathologically complete resection of small rectal carcinoid tumors was more likely to be achieved when using advanced endoscopic techniques or surgical local excision rather than conventional polypectomy.

**Keywords** Rectal carcinoid tumor · Pathologically complete resection

### Introduction

The number of cases of neuroendocrine tumors has increased over time, most likely due to increased awareness among physicians and greater use of endoscopy [1, 2]. Endoscopic screening has not only increased the number of rectal carcinoid tumor cases, but has also led to earlier detection [2].

A standardized treatment for small rectal carcinoid remains to be established. Small rectal carcinoid tumors without muscularis propria invasion can be treated using local excision since they rarely metastasize [3–6]. Following local excision, patients may need to undergo further treatment according to margin status, the size of the primary tumor, the depth of invasion, the presence of angiolymphatic invasion, and the mitotic rate. Achieving complete excision has a major bearing on the type of post-excision treatment. However, carcinoid tumors arise from the deep portion of the epithelial glands and then penetrate the muscularis mucosa into the submucosal layer where they form a nodular lesion. Those characteristics have made it difficult to achieve a tumor-free resection margin using conventional polypectomy and have led to the development of new

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# Randomized Clinical Trial Comparing Reduced-Volume Oral Picosulfate and a Prepackaged Low-Residue Diet With 4-Liter PEG Solution for Bowel Preparation

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**BACKGROUND:** Reduced-volume bowel preparation with a low-residue diet prior to colonoscopy would result in better patient compliance and sufficient bowel preparation.

**OBJECTIVE:** To compare the clinical efficacy of reduced-volume sodium picosulfate and a prepackaged low-residue diet with that of the standard bowel preparation using 4L of PEG solution.

**DESIGN:** Prospective, single center, single blind, active control, randomized study (NCCCTS-12-619, KCT0000470).

**SETTING:** Ambulatory outpatient clinic at the National Cancer Center, Republic of Korea.

**PATIENTS:** A total of 194 subjects were randomly assigned for this study, 97 in each group. After exclusions, 94 subjects in the Picolight group and 90 in the PEG group completed the study and were analyzed.

**INTERVENTIONS:** Sodium picosulfate with a prepackaged low-residue, one-day diet or 4-L PEG for bowel preparation.

**Funding/Support:** This study was supported by a grant from the National Cancer Center (NCC-1210170).

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Y. S. Kim, C. W. Hong, and B. C. Kim contributed equally to this study.

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**MAIN OUTCOME MEASURES:** Success rate of the bowel preparation, tolerability, adverse events, cecal intubation time, polyp detection rate and adenoma detection rate.

**RESULTS:** The bowel preparation success rate was significantly higher (91.5% vs. 81.1%,  $p = 0.04$ ) and the rates of adverse events, including abdominal distension, pain, nausea, vomiting and abdominal discomfort, were significantly lower in the picosulfate group than the PEG group. Cecal intubation times and the polyp and adenoma detection rates were similar in the 2 groups.

**LIMITATIONS:** Single center, limited population, all colonoscopies were performed in the morning.

**CONCLUSIONS:** Bowel preparation with low-volume oral picosulfate and a prepackaged low-residue diet enhances colon cleansing and is better tolerated than the standard bowel preparation.

**KEY WORDS:** XXX

Colorectal cancer is the third most common cancer in the Western world, and its incidence is rapidly increasing in Asian countries.<sup>1</sup> Although colonoscopy is the gold standard for detecting colorectal cancers and for preventing cancers by removing adenomatous polyps,<sup>2-4</sup> fecal occult blood tests are more frequently used in national screening programs in many countries,<sup>5</sup> including Korea. One of the main obstacles to colonoscopy is the need for bowel cleansing.

Adequate bowel preparation is essential for a successful examination of the colonic mucosa during colonoscopy.<sup>6</sup> Polyethylene glycol (PEG) solution, introduced in the 1980s,<sup>7</sup> is generally used for bowel preparation; however, PEG solution has an unpleasant taste and

## Transanal rectosigmoid resection via natural orifice transluminal endoscopic surgery (NOTES) with total mesorectal excision in a large human cadaver series

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### Abstract

**Background** The authors' group has previously described successful transanal rectosigmoid resection via natural orifice transluminal endoscopic surgery (NOTES) in both porcine and cadaveric models using the transanal endoscopic microsurgery platform. This report describes the largest cadaveric series to date as optimization of this approach for clinical application continues.

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**Methods** Between December 2008 and September 2011, NOTES transanal rectosigmoid resection with total mesorectal excision (TME) was successfully performed in 32 fresh human cadavers using transanal dissection alone ( $n = 19$ ), with transgastric endoscopic assistance ( $n = 5$ ), or with laparoscopic assistance ( $n = 8$ ). The variables recorded were gender, body mass index (BMI), operative time, length of the mobilized specimen, integrity of the mesorectum and the resected specimen, and complications. Univariate statistical analysis was performed.

**Results** Of the 32 cadavers, 22 were male with a mean BMI of  $24 \text{ kg/m}^2$  (range  $16.3\text{--}37 \text{ kg/m}^2$ ). The mean operative time was 5.1 h (range 3–8 h), and the mean specimen length was 53 cm (range 15–91.5 cm). After the first five cadavers, specimen length significantly improved, and a trend toward decreased operative time was demonstrated. The mesorectum was intact in 100 % of the specimens. In nine cadavers, endoscopic dissection was complicated by organ injury. Evaluation by the operative approach demonstrated a significantly longer specimen with laparoscopic assistance (67.7 cm) than with transgastric assistance (45.4 cm) or transanal dissection alone (49.2 cm) ( $p = 0.013$ ). Comparison of the technique used for inferior mesenteric pedicle division demonstrated both significantly decreased operative time (4.8 vs 6 h;  $p = 0.024$ ) and increased specimen length (57.7 vs 39.6 cm;  $p = 0.025$ ) when a stapler was used in lieu of a bipolar cautery device.

**Conclusion** Transanal NOTES rectosigmoid resection with TME is feasible and demonstrates improvement in specimen length and operative time with experience. Transitioning to clinical application requires laparoscopic assistance to overcome limitations related to NOTES instrumentation, as well as procedural training with fresh human cadavers.

# Transanal Rectosigmoidectomy Using a Single Port in a Swine Model

Surgical Innovation  
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## Abstract

**Background.** Natural orifice transluminal endoscopic surgery (NOTES) and single access surgery are emerging techniques that reduce surgical invasiveness. This study was performed to evaluate the feasibility of NOTES transanal rectosigmoidectomy using a single port in a swine model. **Methods.** Ten male pigs were used to conduct 2 studies, 4 for a nonsurvival study and 6 for a survival study. After anesthesia, the rectum was occluded transanally with a purse-string suture, and then a single port was placed. CO<sub>2</sub> gas was insufflated, and full-thickness rectal dissection was extended using laparoscopic instruments as far cephalad as possible. A 5-mm trocar was placed on the abdominal wall for transabdominal laparoscopic view, and then further colonic mobilization was performed using the endoscope through the anus. When the dissection was completed, the specimen was exteriorized and colorectal anastomosis was performed using a circular stapler. In the survival study, necropsies were performed on postoperative day 7. **Results.** Full-thickness circumferential rectosigmoid mobilization was achieved in all cases. The mean length of resected colon was 10 cm (range = 8–15 cm). No anastomotic defects were noted. All resected rectosigmoid specimens were grossly intact. No mortality or significant postoperative complications was observed in the survival group. On necropsy, a small abscess in the pelvic cavity was noted in 1 case and bladder distention was noted in 3 cases. **Conclusions.** NOTES transanal rectosigmoidectomy using the single port is feasible and safe. Further experimental studies are warranted, especially in human cadaver model.

## Keywords

NOTES, single port, colorectal surgery, transanal surgery

## Introduction

Laparoscopic colorectal surgery has become a mainstream procedure over the past 2 decades. The advantages of laparoscopic surgery over conventional open procedures include a smaller wound size and faster recovery.

Recently, natural orifice transluminal endoscopic surgery (NOTES) has been introduced. This approach further reduces surgical invasiveness. Whiteford et al<sup>1</sup> have reported on transrectal rectosigmoid resection using the transanal endoscopic microsurgery (TEM) platform on human cadaver model. Sylla et al<sup>2</sup> evaluated the feasibility of NOTES for rectosigmoidectomy using TEM with or without transgastric endoscopic assistance in swine nonsurvival and survival models.<sup>3</sup> In addition, Sylla et al<sup>4</sup> have reported on the first clinical case of a NOTES transanal resection for rectal cancer using TEM and laparoscopic assistance.

Single access surgery is another emerging technique that can reduce surgical invasiveness.<sup>5</sup> This approach has

been facilitated by the development of new single ports. Atallah et al<sup>6</sup> reported that transanal minimally invasive surgery can be effective for resection of both malignant and benign lesions of the rectum using a single-incision laparoscopic surgery port (SILS port, Covidien, Mansfield, MA). The port is introduced into the anal canal by applying steady manual pressure with standard laparoscopic instruments, including graspers, thermal energy devices, and needle drives.

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