

# The Impact of Obesity on the Perioperative, Clinico-pathologic, and Oncologic Outcomes of Robot Assisted Total Mesorectal Excision for Rectal Cancer

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## ABSTRACT:

**Purpose:** To analyze the feasibility and outcomes of robotic rectal cancer surgery in obese patients.

**Methods:** From 2005 to 2012, 101 consecutive rectal cancers operated robotically were enrolled in a prospective database. Patients were stratified into obese ( $BMI \geq 30 \text{ kg/m}^2$ ) and non-obese ( $BMI < 30 \text{ kg/m}^2$ ) groups. Operative, perioperative parameters, and pathologic outcomes were compared. Data was analyzed using SPSS 22.0, while statistical significance was defined as a p value  $\leq .05$ .

**Results:** There were 33 obese patients (mean  $BMI 33.8 \text{ kg/m}^2$ ). Patients were comparable regarding gender, T stage, and type of operation. Operative time and blood loss were higher in the obese group; only operative time was statistically significant. The conversion rate, length of stay, and anastomotic leak rates were similar. Circumferential margin positivity and lymph node yield were comparable. Disease free and overall survivals at 3 years were 75.8% versus 80.9% and 84.8% versus 92.6%, respectively for obese and non-obese subgroups.

**Conclusions:** Robotic surgery for curative treatment of rectal cancer in the obese is safe and feasible. BMI does not influence conversion rates, length of stay, postoperative complications, and quality of the specimen or survival when the robotic platform is used.

## KEYWORDS:

obesity, Rectal cancer, Robotic surgery, Body mass index, Total Mesorectal Excision

## INTRODUCTION

Obesity, defined by the World Health Organization as a body mass index (BMI)  $> 30 \text{ kg/m}^2$ , is a rapidly growing epidemic in the developed world with an estimated 36% of the American population being obese. Similar increases over the past few decades in other parts of the world are reported. The age-adjusted prevalence of obesity was 35.5% (95% CI 31.9–39.2%) among adult men and 35.8% (95% CI 34.0–37.7%) among adult women in the 2009–2010 National Health and Nutrition Examination Survey (NHANES) [1].

Obesity is a risk factor for colorectal cancers and diverticular disease and increasingly the ‘normal’ patient presenting to the surgeon with these diseases is obese or overweight. The impact of obesity is well known through its associations with diabetes mellitus, cardiovascular disease, stroke, and premature death. Obese patients are also at increased risk of cardiovascular, pulmonary and thromboembolic complications after major surgery [2].

Surgery for rectal cancer is the mainstay of treatment and is a technically demanding operation especially in an obese patient. Two commonly cited studies reported lower sphincter preservation rates and higher local recurrence rates in obese patients with low rectal cancer [3,4]. However, these studies were conducted before the era of neoadjuvant chemoradiotherapy, which could limit the applicability of their findings in today’s age where the majority of patients are operated after preoperative treatment [3,4].

While the laparoscopic approach to colon and rectal cancers has been extensively validated in large multicenter randomized trials, obese patients have been excluded in many of these stud-

ies due to the negative connotations and perception of technical difficulty in such individuals [5,6,7]. The literature is divided as regards the outcomes of laparoscopic rectal surgery in the obese with few studies specifically looking at short-term and long-term outcomes in the subgroup with rectal cancers.

While experienced colorectal surgeons from major centers report equivalent oncologic outcomes for rectal cancer surgery in the obese when performed laparoscopically, it still remains the bastion of a select few [8,9,10]. The majority of surgeons favor the open approach in this subgroup.

The robot with its high definition three dimensional optics, stable retraction and articulating instruments provides an advantage in the narrow pelvic confines, which define rectal surgery. We previously published our experience on the potential advantage of robotic assistance in the obese patient with rectal cancer and recently the long-term outcomes of robot assisted total mesorectal excision (RTME) in our institution; and we sought to expand this premise by looking at perioperative, clinico-pathologic, and oncologic outcomes in a group of rectal cancer patients stratified by BMI to determine whether the robotic platform was able to level the playing field, in essence enabling the same quality of surgery and similar outcomes irrespective of BMI [11,12].

## METHODS

Between August 2005 and October 2012, 101 patients with rectal adenocarcinoma underwent robotic rectal resection.

Patients who had advanced T4 disease after chemoradiation or were unfit for a minimally invasive approach, were excluded. During the same period, 108 other patients underwent an open, laparoscopic or hybrid hand-assisted approach, wherein the total mesorectal excision was performed open through a small Pfannenstiel incision, and the vascular control and lymphadenectomy and the colon mobilization were completed laparoscopically. A total of 209 patients with rectal cancer thus underwent surgery during the study period. A board-certified colorectal surgeon evaluated all patients with colonoscopy and endorectal ultrasound [ERUS]; imaging by computerized tomography of the chest, abdomen and pelvis was mandatory for staging. In patients with tumors, which were bulky, not accessible or impassable with ERUS, a magnetic resonance imaging [MRI] was performed. The hospital Institutional review board approved the study.

All patients were discussed in a multidisciplinary tumor board and patients with mesorectal infiltration or mesorectal lymphadenopathy were treated with preoperative concurrent long-course chemoradiotherapy. Surgery was performed on average 8-10 weeks after neoadjuvant therapy.

## SURGICAL APPROACH

The da Vinci system [Intuitive surgical, Sunnyvale, CA, USA] was used for the resections. All patients received bowel preparation and prophylactic antibiotics. The vascular control, lymphadenectomy and colonic mobilization from splenic flexure to pelvic brim were performed either robotically or laparoscopically [hybrid approach]. The total mesorectal excision was always performed robotically. Specimen extraction and anastomosis was through a 5-6 cm Pfannenstiel incision except in abdominoperineal resections [APR] where extraction was performed through the perineum. For APR the prone jack-knife position was most often used for the perineal dissection. The APR was performed via the extralevelator approach. In restorative cases an anastomosis was created by a double-stapled technique in distal lower third of the rectum and by a single stapled technique at mid rectal level. For ultralow anterior resections restitutio was by a coloanal anastomosis. End to side anastomoses, colonic J-pouch and coloplasty were all used at the discretion of the operating surgeon. Diversion by ileostomy was used in all radiated patients and with anastomosis below the peritoneal reflection [palpable on rectal exam].

## FOLLOW-UP

Patients had cancer-specific follow-up as per National Comprehensive Cancer Network (NCCN) guidelines. For the first 2 years, they were seen every 3-4 months and for the next 3 years semiannually for clinical examination, fecal occult blood test, and carcinoembryonic antigen assay. Annual colonoscopy and computerized tomography (CT) surveillance of the abdomen, pelvis, and thorax were also performed. Survival was calculated from the time of surgery to the last follow-up or the time of death. Postoperative mortality was defined as death within 30 days from surgery or as in-hospital mortality.

**Tab. I.** Patient demographics, tumor characteristics, and operative outcomes

VARIABLE	NON-OBESE N= 68	OBESE N=33	P VALUE
Age (years), mean $\pm$ SD	63,4 $\pm$ 10,5	57,7 $\pm$ 11,3	0,014*
Sex, n (%)			
Male	45 (66,2)	18 (54,5)	
Female	23 (33,8)	15 (45,5)	0,258
BMI (kg/m <sup>2</sup> )	25,2 $\pm$ 3,2	33,8 $\pm$ 3,4	<0,001**
ASA class, n (%)			
1	5 (7,5)	4 (12,1)	
2	47 (70,1)	24 (72,7)	
3	15 (22,4)	5 (15,2)	0,568
Tumor location (from anal verge), n (%)			
Upper (10,1-15 cm)	22 (32,4)	4 (12,1)	
Mid (5,1-10 cm)	29 (42,6)	17 (51,5)	
Lower (0-5 cm)	17 (25,0)	12 (36,4)	0,086
Preoperative chemoradiation, n (%)	46 (67,6)	29 (87,9)	0,029*
Operation type, n (%)			
APR	14 (20,6)	8 (24,2)	
LAR /uLAR	54 (79,4)	25 (75,8)	0,676
<b>OPERATIVE &amp; PERIOPERATIVE MEASURES</b>			
Total operative time (min), mean $\pm$ SD	335 $\pm$ 84	367 $\pm$ 58	0,048*
Robotic docking time (min), mean $\pm$ SD	10 $\pm$ 5	12 $\pm$ 6	0,178
Robotic TME time (min), mean $\pm$ SD	95 $\pm$ 40	110 $\pm$ 35	0,096
EBL (mL), mean $\pm$ SD	175 $\pm$ 111	220 $\pm$ 154	0,102
LOS (days), mean $\pm$ SD	6,8 $\pm$ 5,2	6,4 $\pm$ 2,4	0,689
Time to clear liquids, mean $\pm$ SD	1,7 $\pm$ 2	2,1 $\pm$ 2	0,360
Time to flatus/ostomy function, mean $\pm$ SD	2,8 $\pm$ 1,9	2,7 $\pm$ 1,1	0,840
Diverting ileostomy, n (%)	41 (60,3)	22 (66,7)	0,535
Conversions, n (%)	3 (4,4)	1 (3,0)	1,000

SD: Standard Deviation; BMI: Body Mass Index; ASA: American Society of Anesthesiologists; APR: Abdominoperineal Resection; LAR: Low Anterior Resection; uLAR: Ultralow Anterior Resection; TME: Total Mesorectal Excision; EBL: Estimated Blood Loss; LOS: Length of Stay; \*p < .05; \*\*p < .001

## STATISTICAL ANALYSIS

Descriptive statistics including means  $\pm$  standard deviations are reported for all continuous data, while numbers (%) are reported for all categorical data. To compare the outcomes of the two BMI groups, Student's t-tests were performed for the continuous data and Chi-squared or Fisher's exact tests were performed for the categorical data. Kaplan-Meier curves and 95% confidence intervals were calculated for overall survival and disease-free survival at 3 years. To compare the survival rates between the groups, Log Rank (Mantel-Cox) tests were performed. A two-tailed p value of  $\leq$  .05 was considered statistically significant for all analyses. All data was analyzed using SPSS for Windows, Version 22 (SPSS, Chicago IL).

## RESULTS

### 1. Patient demographics

While the BMI groups were comparable regarding gender, with the majority of patients being male in both groups, patients in the non-obese group were statistically older (63,4 vs. 57,7 years,

$p = .014$ ). The mean BMI for the non-obese group was  $25.2 \pm 3.2 \text{ kg/m}^2$  and  $33.8 \pm 3.4 \text{ kg/m}^2$  in the obese group. Similar distributions of tumors at each location (upper, middle and lower rectum) were noted. The numbers of patients receiving preoperative chemoradiation were 87.9% and 67.6% in the obese and non-obese groups respectively ( $p = .029$ ). Other parameters are outlined in Table 1.

## 2. Perioperative outcomes

The totally robotic operation was performed in 24 cases and hybrid operation in 77 patients. There were 80 sphincter-saving operations (ultralow - uLAR and low anterior - LAR resections) and 21 abdominoperineal resections (APR). The proportion of patients receiving sphincter-saving operations were 75.8% and 79.5% respectively in the obese and non-obese groups ( $p = .676$ ). The mean total operating time was  $345 \pm 78$  minutes and robotic TME time  $100 \pm 39$  min. The mean operative time was higher in the obese group ( $367 \pm 58$  min) compared to the non-obese ( $335 \pm 84$  min,  $p = .048$ ), while there was no difference in the robotic TME time. While the mean estimated blood loss was higher (as expected) in the obese cohort, the difference was not statistically significant (220 vs. 175 ml,  $p = .102$ ). No differences regarding other operative measures were found. The mean time to clear liquid diet was  $1.7 \pm 2$  days for the non-obese and  $2.1 \pm 2$  days for the obese ( $p = .360$ ) and for passage of flatus/ostomy function was  $2.8 \pm 1.9$  days and  $2.7 \pm 1.1$  days for obese and non-obese patients respectively ( $p = .840$ ). Length of stay was  $6.7 \pm 4.5$  days overall,  $6.8 \pm 5.2$  days in the non-obese, and  $6.4 \pm 2.4$  days in the obese ( $p = .689$ ) (Table 1). Four patients needed non-emergent conversion, for more extensive disease than detected preoperatively; the mean BMI of converted patients was  $31.2 \pm 5.4 \text{ kg/m}^2$ .

The complication profile in the 2 groups is documented in Table 2. There were 42 complications in 30 patients (29.7%), graded as mild, moderate, and severe as per the Accordion grading system. While more mild complications were noted in the obese group (8.8% vs. 24.2%), this difference was found to be statistically non-significant ( $p = 0.062$ ). No statistical differences were found regarding moderate and severe complications either ( $p = 1.000$  and  $.557$ , respectively). There were 5 (6.3%) anastomotic leaks, of which 2 occurred in the non-obese and 3 in the obese group ( $p = .327$ ).

## 3. Pathologic outcomes

The pathologic AJCC stages are reported in Table 3. The mean node yield was  $15 \pm 7$  nodes for all patients. The lymph node yield between the groups was similar. CRM positivity was seen in 5 patients (5 %) of which 2 were non-obese and 3 were obese ( $p = .327$ ).

## 4. Oncologic outcomes

With a median follow-up of 33 months [range 1-100 months] and a mean follow-up of  $34.9 \pm 18.4$  months, the 3-year overall survival (OS) was 90.1% [95% CI 84-96%] and 3-year disease-free survival (DFS) was 79.2% [95% CI 63.4-83%] for all patients. The DFS for the obese group was 75.8% [95% CI 60.9-92.2%] and 80.9% [95% CI 50.9-64.0%] for the non-obese group ( $p = .688$ ) (Figure 1). The OS was 84.8% [95% CI 76.7-97.5%] for the obese and 92.6% [95% CI 63.2-72.2%] for the non-obese cohorts ( $p = .355$ ) (Figure 2).

**Tab. II.** Postoperative complications

VARIABLE	NON-OBESE N=68	OBESE N=33	P VA- LUE
<b>Mild complications, n (%)</b>	<b>6 (8,8)</b>	<b>8 (24,2)</b>	<b>0,062</b>
Abdominal wound infection	1	1	
Perineal wound infection	0	2	
SBO (conserved)	1	2	
Fever	0	1	
Urinary retention	1	0	
Postop ileus	2	2	
Wound hematoma	1	0	
<b>Moderate complications, n (%)</b>	<b>8 (11,8)</b>	<b>4 (12,1)</b>	<b>1,000</b>
DVT (PICC line related)	0	1	
Postoperative peripheral neuropathy	1	2	
Cerebrovascular accident	1	0	
Aspiration pneumonia	3	0	
Atrial fibrillation	2	0	
Foot drop (post sacrectomy)	1	0	
Pulmonary embolism	0	1	
<b>Pulmonary embolism</b>	<b>9 (13,2)</b>	<b>6 (18,2)</b>	<b>0,557</b>
Anastomotic leaks	2	3	
C.difficile colitis	3	0	
Septic shock	1	0	
Gastric perforation	1	0	
Myocardial infarction	1	0	
Pulmonary edema needing reintubation	1	0	
Omental pedicle necrosis-reexplored	0	1	
Perineal wound bleed-reexplored	0	1	
Perineal wound necrosis-debrided	0	1	
30 day mortality, n (%)	(1,4)	0	

\*Data excludes abdominoperineal resection patients; SBO: Small Bowel Obstruction; DVT: Deep Vein Thrombosis; PICC: Peripherally Inserted Central Venous Catheter; SNS: Sacral Nerve Stimulator

Patients who were metastatic at presentation and then progressed after resection were excluded in order to calculate both local and distance recurrence rates. The cumulative incidence of local recurrence was 4% [95% CI 0-8%]. The cumulative incidence of systemic recurrence was 17% [95% CI 9-24%] for all stages combined. The local recurrence rate in the obese group was, 6.1% [95% CI 1.6-19.6%] compared to 2.9% [95% CI 0.8-10%] in the non-obese group ( $p = .668$ ). The systemic recurrence rates were 21.2% [95% CI 12.8-41%] for obese and 13.2% [95% CI 7.1-23.3%] for the non-obese patients ( $p = .741$ ).

Finally, gender comparisons of outcomes of robotic TME in obese patients are reported in Table 5. No statistically significant differences were reported between males and females regarding any of the studied outcomes ( $p > .05$ ).

## DISCUSSION:

Our study is the first to look specifically at outcomes of robotic rectal resections in relation to BMI. We recently presented our data on oncologic outcomes with longer follow-up and reported equivalent oncologic outcomes to open and laparoscopic surgery with 3-year follow-up, attesting that robotic TME is safe, feasible, and the robot is an important, albeit expensive tool for the surgeon dealing with rectal cancer [12].

Looking only at the impact of obesity as a disease in patients undergoing colorectal cancer surgery, it is now well established from large prospective series, systematic reviews and retrospective analyses that oncologic outcomes are not compromised [9,13,14].

In the absence of significant data on the outcomes of RTME in the obese, we reviewed the literature on the results of laparoscopy in this group. Most of the data on laparoscopic colorectal resections for cancer is heavily skewed towards colon resections and this data cannot be reliably extrapolated to rectal resections. The narrow confines of the pelvis especially in a male patient, the need for identification and preservation of the nerves, and the technical difficulties involved in secure division below the tumor and low pelvic anastomosis make it vastly different from the difficulties encountered in colon surgery. However, it is important to note that all robotic operations involve either laparoscopic mobilization of the left colon (hybrid approach) or robotic assistance for the same purpose; this is difficult in the obese and often the part of the operation where the surgeon may have to convert. In a study of nearly 6000 colon resections, Scheidbach et al. [15], concluded that obesity increases the operative time, influences conversion and has a higher rate of intra-abdominal complications. This is in concordance with data reported by Tekkis et al. [16] from the Cleveland Clinic and over 11 years, which revealed a linear increase in conversion rates with increasing BMI in laparoscopic colorectal surgery.

Conversion to open surgery is higher in laparoscopic series' than that in robotic series' varying from 7.3% to 34% [5, 17-19]. Conversion is associated with higher perioperative complication rates, increased cost and longer hospital stay, and with worse long-term oncological outcome irrespective of surgeon experience [6,17,20]. Conversion rates as high as 44% have been reported for laparoscopic TME in the obese subgroup and it is well accepted that after extensive disease, obesity is the major factor leading to conversion in laparoscopic rectal surgery [5,9,21].

Two studies have specifically looked at the relation of BMI to outcomes in laparoscopic rectal surgery. Bege et al. [8] found that when looking at short-term outcomes, obesity alters the feasibility (conversion rates and operative time) but not the complication rates or oncologic outcomes for laparoscopic TME. These findings were corroborated by Denost et al. [10], who found that BMI influenced the risk of conversion in laparoscopic rectal cancer resections but did not affect morbidity, quality of the operation or survival.

Regarding conversions in robotic TME for rectal cancer, Hellen et al. [22] reported one conversion to open procedure in a patient with a BMI of  $44 \text{ kg/m}^2$ ; Pigazzi et al. [23] reported 7 conversions of which 4 were due to obesity (4.9%) and the mean BMI of patients with conversion to open procedures was  $31.9 \text{ kg/m}^2$  (range, 25.8–44). An earlier report from our group documented 2 conversions in 44 patients (4.5%), both on account of obesity (mean BMI of converted patients was  $41.5 \text{ kg/m}^2$ ) [11]. In the present series, the mean BMI of converted patients in the non-obese group was  $28.7 \text{ kg/m}^2$  and the BMI of the lone conversion in the obese sub group was  $39 \text{ kg/m}^2$ ; increased BMI continues to influence conversion but its impact appears lessened in the robotic arena.

**Tab. III.** Pathologic outcomes

VARIABLE	TOTAL N=101	NON-OBESE N=68	OBESE N=33	P VALUE
<b>Pathologic AJCC stage, n (%)</b>				
Stage 0 (pCR)	19 (18,8)	15 (22,1)	4 (12,1)	
Stage I	32 (31,7)	21 (30,9)	11 (33,3)	
Stage II	18 (17,8)	13 (19,1)	5 (15,2)	
Stage III	23 (22,8)	12 (17,6)	11 (33,3)	
Stage IV	9 (8,9)	7 (10,3)	2 (6,1)	0,517
Lymph node yield, n (%)	$15 \pm 7,4$	$14,5 \pm 7,5$	$15,9 \pm 7,2$	0,378
<b>Margins</b>				
CRM (cm), mean $\pm$ SD	$1,8 \pm 1,6$	$2 \pm 1,8$	$1,4 \pm 1,3$	0,129
CRM positive ( $\leq 1 \text{ mm}$ ), n (%)	5 (5)	2 (2,9)	3 (9,1)	0,327
DRM (cm), mean $\pm$ SD	$3,5 \pm 2,7$	$3,6 \pm 2,8$	$3,1 \pm 2,4$	0,438
DRM positive, n (%)	2 (2)	2 (2,9)	0	1,000
<b>Tumor differentiation and histology, n (%)</b>				
Well differentiated adenocarcinoma	25 (24,8)	15 (22,1)	10 (30,3)	
Moderately differentiated adenocarcinoma	65 (64,4)	47 (69,1)	18 (54,5)	
Poorly differentiated adenocarcinoma	11 (10,9)	6 (8,8)	5 (15,2)	0,340
<b>Mesorectal grade, n (%)</b>				
Grade I	1 (1)	0	0	
Grade II	2 (2)	2 (2,9)	0	0,100
Grade III	98 (97)	66 (97,5)	33 (100)	

SD: Standard Deviation; pCR: Pathologic Complete Response; CRM: Circumferential Resection Margin; DRM: Distal Resection Margin

**Tab. IV.** Gender comparisons of outcomes of robotic TME in obese patients

VARIABLE	MALE N=18	FEMALE N=15	P VALUE
BMI ( $\text{kg}/\text{m}^2$ ), mean $\pm$ SD	$34,1 \pm 3,3$	$33,3 \pm 3,5$	0,495
EBL (mL), mean $\pm$ SD	$227,8 \pm 148,7$	$210 \pm 163,9$	0,746
Robotic TME time (min), mean $\pm$ SD	$110,2 \pm 30,6$	$109,3 \pm 40,5$	0,947
LOS (days), mean $\pm$ SD	$6,1 \pm 2,4$	$6,7 \pm 2,5$	0,471
Conversion, n (%)	1 (5,6)	0	1,000
CRM positivity, n (%)	3 (16,7)	0	0,233
Node yield, mean $\pm$ SD	$14,4 \pm 4,9$	$17,9 \pm 9,1$	0,233

BMI: Body Mass Index; EBL: Estimated Blood Loss; TME: Total Mesorectal Excision; LOS: Length of Stay; CRM: Circumferential Resection Margin

The mesorectum in the obese is friable, bleeds easily and is difficult to handle and further reduces the confines of the pelvis and makes laparoscopic surgery particularly challenging [11]. In addition, the peritoneum is fragile and difficult to grip and there is increase in fat under the endopelvic fascia, and increased presacral tissue all of which further impinge on the pelvic working space. In the obese subgroup of patients, the improved vision and ergonomics provided by the robotic approach makes a successful operation more likely, which is borne out by our 4% conversion rate despite 33% of our cohort being obese with a mean BMI of  $33,8 \pm 3,4 \text{ kg/m}^2$ .

The ability to obtain a negative circumferential resection margin (CRM) is the Holy Grail of rectal cancer surgery and the fact that robotic surgery produces a good quality specimen with a lower CRM positivity is well known [24]. There was no difference in the CRM positivity in relation to the BMI in the present study.

We did not find any difference in the length of stay, time to resumption of bowel function, or complication rates between the groups. Specifically, there was no increase in the wound infection rates. The complications in our series are stratified as per the Accordion grading system (Table 2) and the complication rate was approximately 30%.

One important consideration is that BMI is a crude measure of obesity. The waist to hip ratio or CT scan assessment of visceral obesity (Visceral Adipose Assessment-VAA) as done by Japanese surgeons is considered more reliable and may correlate better with outcomes in future studies. Ishii et al. [25] reported a better correlation of complication rates after laparoscopic colorectal surgery using VAA > 100 cm<sup>2</sup> as the parameter to separate the obese from non-obese.

The limitations of our study include the fact that this is a single-institution experience and the number of patients in each arm is small. Therefore, larger studies utilizing prospective study designs and being conducted at multiple centers are needed before firm conclusions are reached. Our data, however suggest that robotic surgery for rectal cancers in the obese can be completed safely with complication rates, perioperative pathologic and mid-term oncologic outcomes similar to those in a non-obese population.

## CONCLUSIONS

RTME is a safe operation even in the obese patient and while associated with longer operative times and blood loss, offers comparable clinico-pathologic outcomes, disease-free and overall survival as those in the non-obese. The low conversion rates as compared to laparoscopy in high-BMI individuals is a particularly important advantage which needs to be validated in prospective randomized multicenter trials. At present, it may be the preferred option in obese patients among surgeons experienced with laparoscopic and robotic platforms.

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