



L. F. Gonzalez-Ciccarelli¹ · P. Quadri¹ · D. Daskalaki¹ · L. Milone² · A. Gangemi¹ · P. C. Giulianotti¹

¹ Division of General, Minimally Invasive and Robotic Surgery, Department of Surgery, University of Illinois Hospital and Health Sciences System, Chicago, USA

² Brooklyn Hospital Center, Brooklyn, USA

Robotic approach to hepatobiliary surgery

Introduction

Minimally invasive surgery began in the 1980s with laparoscopy [1–3]. The first laparoscopic cholecystectomy was performed by Professor Erich Mühle in 1985 [4–6]. Even though laparoscopic surgery has been adopted by almost all surgical specialties, it presents several disadvantages such as limited mobility of straight instruments, unstable camera platform, two-dimensional imaging, and poor ergonomics for the surgeon [1, 2, 7]. The robotic surgical system was created to overcome these surgical limitations [7]. Robotic surgical platforms have been available since the late 1990s [2] and the first successful robotic procedure was reported in 1997 by Drs. Cadriere and Himpens in Brussels, who performed a cholecystectomy using a da Vinci[®] prototype [7–10]. The use of robots to assist in performing surgical tasks has been developing over the past 20 years and currently is widely utilized in various surgical specialties [11]. These novel engineered systems improve surgeons' performance when completing complex tasks [11]. The robotic system used in surgery is fully controlled by the surgeons at the console [11]. Robotic technology has improved many aspects of minimally invasive surgery including: stable camera platform, elimination of physiologic tremor, three-dimensional imaging, simulation of the movement of a surgeon's wrist, enhanced dexterity, increased precision, and a comfortable

and ergonomically optimal operating position [1–4, 7, 8, 12, 13].

The routine application of robotic technology in surgery was slow [11]. It started with cardiac surgery; however, urologists truly adopted this new system in its application in prostate surgery [3, 11, 12]. In the following years, robotic surgery was used increasingly in gynecology and urology and has slowly penetrated different areas of general surgery [3, 11, 14]. Giulianotti et al. [10] reported one of the first experiences in robotics in general surgery in 2003. They reported 193 patients, who were operated using minimally invasive robotic technology, between October 2000 and November 2002. Within this experience, they reported the first robotic Whipple and the first hepatic segmentectomies.

One of the main issues concerning robotic technology are its high costs [2, 11]. Currently only one company produces and sells the robotic system and the da Vinci[®] surgical system is the only United States Food and Drug Administration (FDA) approved robotic platform [4]. Many hospitals cannot afford this new technology because the acquisition of the robot, coupled with the maintenance, is very expensive [11]. However, some authors, depending on how costs are analyzed, have reported lower surgical costs for the robotic approach [15].

Since the advent of robotic technology, the choice between a robotic or laparoscopic approach for different procedures has been controversial [8]. To date, robotic technology has demonstrated to be safe and effective for several different procedures (hysterectomy, cholecys-

tectomy, nephrectomy, fundoplication, and prostatectomy) [8, 16]. However, specific advantages for patients and surgeons are not well defined in most cases [8]. Robotic technology has provided the possibility of extending the use of minimally invasive surgery to procedures that are generally performed with the open technique, which enabled surgeons who were not comfortable with standard laparoscopy to perform minimally invasive surgery without the increased risk of complications associated with the initial learning curve [3, 8]. The robot could be the bridge between open and minimally invasive surgery for surgeons who struggle with laparoscopy, even for simple procedures with lower conversion rates [17]. Robotic surgery has emerged as a very important component of modern minimally invasive surgery and the development of new robotic systems and decrease in costs will facilitate a broader adoption of this new technology [12].

Robotic approach to the liver

Since the Louisville Consensus Conference in 2008, the number of minimally invasive liver resections has increased worldwide. Their recommendations towards laparoscopic major hepatectomies and extended hepatectomies (biliary reconstruction is needed) were limited, especially when the lesions were in close proximity to the hepatic hilum or major vessels [18]. Moreover, in the last consensus presented in Morioka in 2014, they still described that, with a small number of studies on robotic liver resection reported in the literature, the outcomes

The German version of this article can be found under doi:10.1007/s00104-016-0249-3.

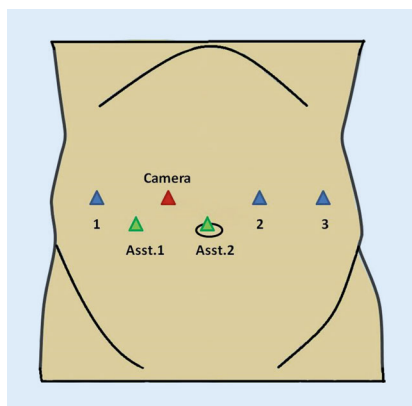


Fig. 1 ▲ Right hepatectomy robotic port setting

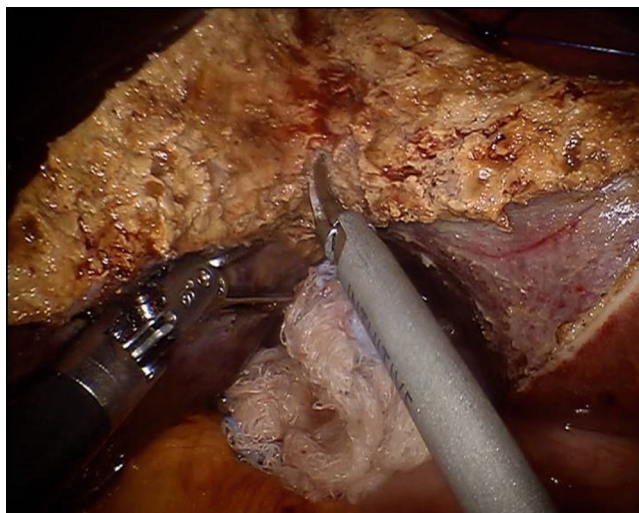


Fig. 2 ◀ Parenchymal liver transection

were superior and not inferior when compared to other techniques [19]. There were no specific recommendations or indications due to lack of evidence from previous and present experience to draw new guidelines. However, the overall conclusion from the studies is that robotic liver surgery is a feasible and safe procedure when the indications for surgery are respected and performed by experienced surgeons in highly specialized centers.

Major and minor resections were defined using the classical definition described by Couinaud. The removal of three or more liver segments is considered a major resection and the removal of two or less hepatic segments is considered a minor resection [19]. Most of the authors followed this definition [20–25]. Tsung et al. [26] considered the resection of 4 or more liver segments as being a major hepatectomy.

Major robotic hepatectomies

Major hepatectomy is a complex procedure, regardless of the approach, that requires a high level of expertise, advanced surgical skills and perfect knowledge of the anatomy, which is probably why the total number of procedures reported is still low: 63 right hepatectomies and 41 left hepatectomies. The port setting for right hepatectomy is shown in **Fig. 1**.

The advantage of the robotic platform is that it holds the potential to overcome the technical limitations of laparoscopy.

The robot allows complex hilum preparations and hepatocaval dissections, as well as parenchymal transections with minimal blood loss (**Fig. 2**). The endowristed instruments allow for better control of the vasculature, thus, decreasing the risk of bleeding. The platform stability and the use of the 4th arm aids in the retraction of the liver for better visualization, selective control, dissection, and handling during the different steps of the procedure that require better exposure of the anatomy.

The addition of fluorescence with indocyanine green (ICG) to the robotic platform provides the surgeon with direct real-time visualization of the biliary tree anatomy, recognition of vascular anatomy, discrimination of anatomical variants, evaluation of organ and tissue perfusion, lymph node identification and, foremost, the distinction between normal liver parenchyma and tumor cells. Tumor cells are usually hypofluorescent lesions with no ICG uptake ([27]; **Fig. 3**).

» Use of indocyanine green allows for direct real-time visualization

Indications for major robotic hepatectomies included malignant and benign liver lesions. Malignancy was the indication for resection in 60–100 % of the cases and it most frequently included hepatocellular carcinoma (HCC) [22, 24, 25] and colorectal metastasis (CRM) [20, 21,

26]. Mean operative time ranged from 229–621 min. Similar operative times were described by Giulianotti et al. [20], Tsung et al. [26], and Ji et al. [25] (313, 330, and 338 min, respectively), although there is a difference in the number of cases (27, 21, and 9, respectively). Estimated blood loss ranged from 200–478 ml. Ji et al. [25] described a reduced estimated blood loss (EBL) with the robotic approach in his series compared to laparoscopic, and open approach (280, 350, and 470 ml, respectively). Giulianotti et al. [20] reported a higher EBL in cirrhotic patients who had liver resections. The transfusion rate ranged from 6–44 %. Tsung et al. [26], in his series comparing robot vs. open approaches, reported a significant difference in EBL (200 vs. 500 ml) and transfusion rates (1 vs. 6). Conversion to open rate ranged from 0–47 %. The reasons for conversion were mainly due to difficulty in bleeding control, failure to respect oncologic margins, especially when the tumor was located in the posterior surface of the liver or adjacent to major vessels. The hospital length of stay ranged from 5–15 days.

» Shorter length of stay with robotic approach compared to the open approach

A shorter length of stay was described by Tsung et al. (5 vs. 8 days) in his series when compared to the open approach [26]. The overall complication rate was

19 %, ranging from 7–40 %. The most common complications reported in the literature were bile leak and intrabdominal fluid collections [23]. Zero mortality was reported in all of the studies.

The resection margins were zero in most cases. Lai et al. [24] described R1 resection in 7 % ($n = 3$) of cases. From the 3 patients, 2 patients had colorectal metastases that were treated with radiofrequency ablation without local recurrence.

Robotic extended liver resections have also been reported in the literature. Giulianotti et al. were the first to describe this resection in a series in 2010. The author described 3 cases in 2 different publications. The first case described was an extended right hepatectomy with biliary reconstruction for a hilar cholangiocarcinoma [28] and 2 cases of right trisectionectomy in a later report [20]. Ji et al. [25] described one case of left hemihepatectomy with caudate lobe resection and Spampinato et al. [21] included a case of extended right hemihepatectomy in his series. A case report published by Chen et al. [29] reported a left hemihepatectomy with revision hepaticojejunostomy. A left extended hepatectomy converted to open due to bleeding after biliary reconstruction was described by Quijano et al. [30]. The results of the most important series of major hepatectomies are summarized in **Table 1**.

Minor robotic hepatectomies

Minor hepatectomy is one of the most performed liver procedures worldwide. The most commonly reported procedures include wedge resections, bisegmentectomy, segmentectomy, and left lateral segmentectomy. Minor robotic hepatectomies resection included malignant and benign liver lesions. Malignant tumor resection ranged between 54 and 100 %. CRM [26, 31, 32] and HCC [20, 22, 24, 33] pathology were most frequent resected.

The mean operative time ranged from 142–403 min with a tendency towards an increased operative time observed in series that had a smaller number of cases. Estimated blood loss ranged from 30–415 ml. Giulianotti et al.

Chirurg 2017 · 88 (Suppl 1):S19–S28 DOI 10.1007/s00104-016-0223-0
© Springer-Verlag Berlin Heidelberg (outside the USA) 2016

L. F. Gonzalez-Ciccarelli · P. Quadri · D. Daskalaki · L. Milone · A. Gangemi · P. C. Giulianotti

Robotic approach to hepatobiliary surgery

Abstract

Robot-assisted hepatobiliary surgery has been steadily growing in recent years. It represents an alternative to the open and laparoscopic approaches in selected patients. Endowristed instruments and enhanced visualization provide important advantages in terms of selective bleeding control, microsuturing, and dissection. Cholecystectomies and minor hepatectomies are being performed with comparable results to open and laparoscopic surgery. Even complex procedures, such as major and extended hepatectomies, can have excellent outcomes, in expert hands. The addition of

indocyanine green fluorescence provides an additional advantage for recognition of the vascular and biliary anatomy. Future innovations will allow for expanding its use and indications. Robotic surgery has become a very important component of modern minimally invasive surgery and the development of new robotic technology will facilitate a broader adoption of this technique.

Keywords

Robotic surgical procedures · Hepatobiliary surgery · Liver surgery · Biliary surgery · Indocyanine green fluorescence

Roboterassistierte hepatobiliäre Chirurgie

Zusammenfassung

Die roboterassistierte hepatobiliäre Chirurgie ist in den letzten Jahren stetig gewachsen. Sie stellt bei ausgewählten Patienten eine Alternative zu den offenen und laparoskopischen Verfahren dar. Die Endowrist-Instrumente und die verbesserte Visualisierung bieten einen wichtigen Vorteil bezüglich Blutungskontrolle, Mikronähten und Dissektion. Cholezystektomien und kleinere Hepatektomien werden mit vergleichbaren Ergebnissen durchgeführt wie offene und laparoskopische Operationen. Auch komplexe Verfahren, wie z. B. schwere und erweiterte Hepatektomien zeigen exzellente Ergebnisse, sofern sie von Experten durchgeführt werden. Der zusätzlich verwendete fluoreszierende Farbstoff

Indozyaningrün bietet einen weiteren Vorteil zur Erkennung der vaskulären und biliären Anatomie. Zukünftige Innovationen werden es ermöglichen, die Anwendung und Indikationsgebiete für dieses Verfahren zu erweitern. Die roboterassistierte Operation ist zu einem sehr wichtigen Teil der modernen minimal-invasiven Chirurgie geworden, und die Entwicklung neuer Robotertechnologien werden eine breitere Anwendung dieser Technik fördern.

Schlüsselwörter

Roboterassistierte Chirurgie · Hepatobiliäre Chirurgie · Leberchirurgie · Gallenchirurgie · Indozyaningrün

[20] reported a lower EBL in these set of patients when compared with major hepatectomies (150 vs. 300 ml), although the transfusion rates were similar between the two procedures (21 vs. 22 %). Among the 9 transfusions performed, 5 were for cirrhotic patients and 4 for noncirrhotic patients. Tsung et al. demonstrated a significant decrease in operative time, EBL and LOS with increased experience. Authors compared initial with later experience, but did not specify between major and minor procedures [26]. The transfusion rate ranged from 0–21 %. Authors that compared robotic to open hepatectomies

have also confirmed a significant reduction in intraoperative blood loss and length of hospital stay in the robotic groups [34, 35]. Conversion to open rate ranged from 0–20 %, with bleeding being the most common cause [31, 36]. The hospital length of stay ranged between 4 and 11 days. Morbidity rate ranged from 0–50 %. Biliary leak [31] and intrabdominal fluid collection [23, 35] were the most commonly described complications in the studies [31, 34, 36]. Mortality was reported in two studies ($n = 3$) [35, 37].

Robot-assisted liver resections allow for complex reconstructions of vascular

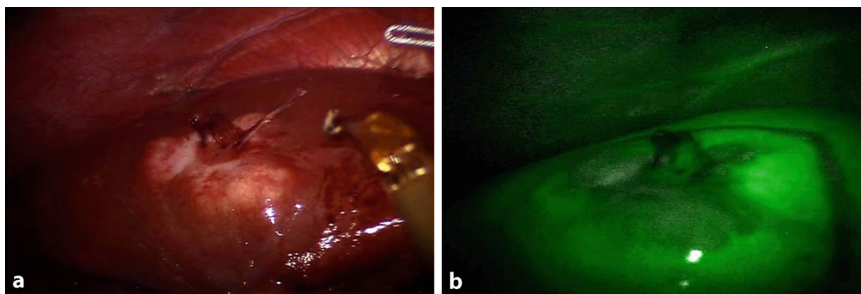


Fig. 3 ▲ Intraoperative view of a liver colorectal metastasis (a) and fluorescence pattern of the lesion (b)

and biliary anastomosis and will aid to preserve liver parenchyma in lesions located in the posterior–superior segments, avoiding the lesions to be treated with a major hepatectomy [31]. Minor robotic liver resections are reported in the literature in other smaller series [25, 38, 39]. Their outcomes are similar with the studies mentioned in this review. The outcomes of the most important series of minor hepatectomies are summarized in **Table 1**.

Current literature scarcely describes long-term follow up for minor and mayor hepatectomies. Lai et al. [24] described a median follow-up of 14 months. Only 6 patients had a recurrence with the two different approaches. Only 1 patient from the robot cohort developed recurrence of HCC after surgery. With a median follow-up of 24 months, Troisi et al. [31] described a 37 % recurrence rate for the robotic experience. CRM disease-free patients at 1 and 3 years were 79 and 62 % with a mean follow-up of 9.6 months. Choi et al. [23] experienced no HCC recurrences at the 11-month follow-up, with 1 patient who developed CRM recurrence at the 5-month follow-up. Felli et al. [32] reported no liver-related postoperative complications with zero day mortality at the 11.3-month follow-up.

Learning curve of minimally invasive liver resection

The learning curve for laparoscopic liver resection is long and steep, although the surgical technique has improved in recent years, making it feasible and safe in expert hands. Several authors [40–43] have described the learning curve for laparoscopic liver resections. For minor and major resections, the learning curve

has been reported at 22 cases [40] and between 45 and 75 cases [41], respectively. For both resections, a total of 60 cases were described to overcome the learning curve [42]. In order to improve the perioperative outcomes in major complex resections, a minimum of 10 cases were required [43].

Although there is no specific learning curve established for robotic liver surgery, Tsung et al. [26] compared his early experience with 13 patients to 44 patients performed in his later phase. The authors reported a significant decrease in EBL (300 vs. 100 ml), operative time (381 vs. 232 min), overall room time (466 vs. 314.5 min) and length of stay (5 vs. 4 days). The authors concluded that these improvements are due to the increased experience of the surgeon with the robot platform. Choi et al. [23] analyzed the operative time on 10 consecutive left hepatectomies. The authors reported that parenchymal transection was the most time-consuming step. The console time and overall operative time decreased after the seventh case. The robotic approach might have a lower learning curve as surgeons become more experienced with the technique and more familiar with the platform. Moreover, because robotic surgery and open surgery share the same set of skill principles, the learning curve at the console will most likely be shorter even for inexperienced minimally invasive surgeons [10].

Robotic approach to the gallbladder

More than 1 million cholecystectomies are performed annually in the United States [14]. Cholecystectomy has un-

dergone considerable changes over the past 25 years [17]. Initially, the laparoscopic approach was faced with skepticism from societies and was ignored for several years [4]. Currently, laparoscopic cholecystectomy is considered the gold standard for benign gallbladder pathology and has shown well-characterized benefits compared to open surgery [4, 6, 13, 17, 44], with more than 90 % of cholecystectomies performed laparoscopically in the United States [5, 14]. Laparoscopic single-site surgery was first introduced in an effort to improve cosmetic outcomes, but no clinical advantages were demonstrated over standard laparoscopy [4]. Parallel to this new development, robotic technology appeared to improve precision and dexterity, and was also able to expand into the field of single-site surgery [4]. Robotic-assisted cholecystectomy was first introduced by Himpen in 1997 [7–9]. Since then it has gained popularity in general surgery as more surgeons become familiar with this new technology [14]. Although cholecystectomy remains one of the most frequently performed procedures in general surgery, there are few studies that compare robotic and laparoscopic cholecystectomies [45].

Kamiński et al. [14] compared laparoscopic ($n = 733,929$) and robotic ($n = 1,608$) approaches and reported essentially no differences in intraoperative and postoperative complications and length of hospitalization. Our institution also performed a retrospective study comparing 147 laparoscopic vs. 179 robotic cholecystectomies [45]. There were no statistical differences in operative time, blood loss, length of hospitalization, or major complications. Thus, it was concluded that both approaches were safe and feasible and that the robotic approach could also potentially have a role in biliary ducts injury management [45]. Moreover, another advantage to robotic technology is the fluorescent equipment [46]. This is a novel and emergent technology that can be useful to help guide the surgeon during the procedure and is not available in all laparoscopic cameras [46, 47]. To our knowledge, our group has published the largest series of ICG fluorescent cholangiography with 184 patients [46, 47]. Outcomes showed high

Table 1 Important series of major and minor hepatectomies described in the literature												
Author	Cases (n)	Mean age (years)	Type of procedure	Mean operative time (min)	EBL (ml)	Transfusion rate (%)	Conversion to open rate (%)	Morbidity rate (%)	Mortality rate (%)	Mean LOS (days)	Malignant (%)	Resection margins (R0)
<i>Major hepatectomies</i>												
Giulianotti et al. (2011) [20]	27	57 ^a	RH (20) LH (5) RT (2)	313 ^b	300 ^b	22	4	30	0	8 ^b	74	100 %
Spampinato et al. (2014) [21]	25	63 ^b	RH (16) LH (7) ERH (1) LLS + S6 (1)	430 ^b	250 ^b	44	4	16	0	8 ^b	68	100 %
Tsung et al. (2014) [26]	21	60	NR	330 ^b	200 ^b	6	19	24	0	5 ^b	71	100 %
Wu et al. (2014) ^a [22]	20	61	RH (12) LH (6) Three S (1) LLS + S5, 6 (1)	380	325	NR	5	8	0	8	100	NR
Choi et al. (2012) [23]	20	52 ^a	RH (6) LH (14)	621	478	15	10	40	0	15	70 ^a	100 % ^a
Lai et al. (2013) ^a [24]	10	61	RH (7) LH (3)	229	413	7 ^a	9 ^a	7 ^a	0	6	100	93 %
Ji et al. (2013) ^a [25]	9	NR	RH (2) LH (6) LH + CS + RnYH (1)	338	280	0	0	8	0	7	62	100 %
<i>Minor hepatectomies</i>												
Kingham et al. (2016) ^a [35]	65	64	S (26) BIS (7) W (22) LLS (10)	163 ^b	100 ^b	1.6	6.3	11	2	4	78	98 %
Giulianotti et al. (2011) [20]	43	57 ^a	S (16) BIS (10) W (8) LLS (9)	198	150	21	7	16	0	6 ^b	51	100 %
Troisi et al. (2013) ^c [31]	40	65	S (7) BIS (8) W (15) LLS (2) NAS (6)	271	330	NR	20	13	0	6	70	93 %

rates of cystic duct (97.8 %), common hepatic duct (94 %), and common bile duct (96.1 %) visualization which were reduced, but still high (91.6, 79.1, and 79.1 %, respectively), in cases of acute cholecystitis [46]. No biliary injuries or major biliary complications were registered [46]. **Table 2** summarizes the largest series of robotic cholecystectomy recently reported [12, 14, 45, 46, 48].

Even if outcomes of laparoscopic and robotic cholecystectomy are comparable, the application of the robot in general surgery has always been a point of discussion, with costs often being at the center of the discussion [17]. Rosemurgy et al. [17] reported that variable costs for robotic cholecystectomy were \$250

over the laparoscopic approach and that hospital charges for robotic cholecystectomy were US\$ 8000, significantly higher than laparoscopy. Including the amortized cost of the robot, an analysis of 20 different robot-assisted procedures found that the robot added a 13 % cost to procedures (about US\$ 3200 higher).

Kamiński et al. [14] also reported significantly higher total costs for robotic cholecystectomy compared to laparoscopic cholecystectomy. Probably, the increased expenses of the robot are related to the acquisition of the system, the steep learning curve, the prolonged operating time and the surgical instruments which have limited number of uses. As the surgeon gains experience, the op-

erating time is reduced and becomes less deciding in cost determination. Despite these reports, more prospective randomized studies are needed to assess real costs of robotic surgery in different procedures [49].

Cholecystectomy is one of the simplest procedures in general surgery, so this operation can be used to gain experience with the robot and with lower conversion and morbidity rates [17]. Many agree that it is beneficial to start with a procedure that the trainee is comfortable with and may be repeated at short intervals so that the surgeon can focus on becoming familiar with the console and docking [44]. Robotic surgery may require some different skills than tra-

Table 1 Important series of major and minor hepatectomies described in the literature (Continued)

Author	Cases (n)	Mean age (years)	Type of procedure	Mean operative time (min)	EBL (ml)	Transfusion rate (%)	Conversion to open rate (%)	Morbidity rate (%)	Mortality rate (%)	Mean LOS (days)	Malignant (%)	Resection margins (R0)
Tsung et al. (2014) [26]	36	60	NR	198 ^b	285 ^b	3	0	17	0	4 ^b	69	93 %
Montalti et al. (2016) ^c [37]	36	62	S (6) BI (6) W (15) M (9)	306	415	NR	13.9	19	1	6	69	69.4 %
Lai et al. (2013) [24]	33	61	S (7) BIS (4) W (10) LLS (12)	203	373	7 ^a	9 ^a	3	0	6 ^a	100	93 %
Wu et al. (2014) ^a [22]	32	61	S (8) BIS (24)	380	325	NR	5	8	0	8	100	NR
Tranchart et al. (2014) [36]	26	67	S (7) BIS (1) W (13) LLS (5)	210	200	14	14	36	0	6	54	–
Felli et al. (2015) ^a [32]	18	65	S (10) W (4) LLS (4)	142	50	5	0	20	0	5.7	75	84 %
Quijano et al. (2016) [30]	13	59 ^a	S (3) BIS (2) W (8)	207	119 ^a	0	0	8	0	11	65 ^a	100 % ^a
Packiam et al. (2012) [40]	11	57	NR	175	30	0	0	27	0	4	55	NR
Yu et al. (2014) [33]	10	50	LLS (10)	292 ^a	389 ^a	0	0	0	0	8	77	NR
Choi et al. (2012) [23]	10	52 ^a	S (2) W (4) LLS (4)	403	184	10	0	50	0	8	70 ^a	100 % ^a

EBL estimated blood loss, LOS length of hospital stay, RH right hepatectomy, LH left hepatectomy, RT right trisegmentectomy, ERH extended right hepatectomy, LLS left lateral segmentectomy, S segmentectomy, BIS bisegmentectomy, W wedge resection, NAS non-adjacent segmentectomies, SS subsegmentectomies, CS caudate segmentectomy, RnYH Roux-en-Y hepaticojejunostomy

^aAuthors include both major and minor hepatectomy results

^bValues are expressed as median

^cCases may overlap between the studies

ditional laparoscopic surgery [12]. Vidovszky et al. [13] analyzed the learning curve for robotic cholecystectomy where they found around 20–30 cases are needed to gain experience in this procedure. They divided the learning curve in three stages, 15 cases each, and reported a significant reduction in operative time between the first and third stage, this corresponded mainly to a reduction in the docking time rather than the robotic time. Moreover, robotic cholecystectomy is an effective model for teaching residents [12]. Significant and reproducible improvement can be gained with low risk of adverse outcomes for patients [12].

In an article by Prasad et al. [50], more than 80 % of the iatrogenic bile duct injuries occur following cholecystectomy. Risk factors for biliary duct injuries are variable biliary and vascular anatomy, inappropriate exposure, ag-

gressive attempts at hemostasis and the surgeon's experience. This complication could have devastating consequences on patients' quality of life. Depending on the type of lesion, a resection of the duct might be necessary, followed by a Roux-en-Y hepaticojejunostomy reconstruction. Although many centers have reported favorable results with laparoscopic Roux-en-Y hepaticojejunostomy [50], this procedure is technically demanding and advanced laparoscopic skills like suturing and intracorporeal knot techniques are needed [51, 52]. The robotic system has allowed for improved precision, accuracy, and safety by reproducing the surgeon's natural movements with a stable camera and reduced tremor [50–53]. The benefits of the robotic approach can be seen in the fine dissection of dense adhesions, the suturing of the hepaticojejunostomy and

the jejunojunctionostomy anastomosis [50, 51] with comparable operative times to laparoscopy [51]. The robotic system has also been successfully applied in pediatric choledochal cysts [53]. Alizai et al. [53] have reported 27 cases of robotic-assisted resections of choledochal cysts and hepaticojejunostomies in pediatric patients with an 81 % of success (22 of 27 cases). They concluded that the robotic approach was safe [52, 53] and patients had a rapid recovery, low complication rate, and good cosmetic outcomes [53].

Robotic cholecystectomy is a safe and feasible procedure [13] that is growing in the United States [14]. There are no clear clinical benefits of the robotic approach over laparoscopy [13, 14, 46] but robotic technology still has higher costs than laparoscopy, although they are decreasing [12–14, 46].

Table 2 Most important series of robotic cholecystectomies described in the literature										
Author	Cases (n)	Mean age (years)	Mean BMI (kg/m ²)	Type of surgery	Mean operative time (min)	Conversion to open rate (%)	Morbidity rate (%)	Biliary duct injury rate (%)	Mortality rate (%)	Mean LOS (days)
<i>Multiport robotic cholecystectomy</i>										
Kamiński et al. (2014) [14]	2010: 524, 2011: 1084	53.3, 55.8	15.2 ^d , 17.5 ^d	RC, RC	–	0, 1.66	Intraoperative: 4.5, 4	–	–	3.63, 4.59
Baek et al. (2015) [48]	925	41.1	25.5	RC	49.8	0.1	0.9	0.1	0	1.2
Ayloo et al. (2014) [45]	179	40.2	32.9	RC	95.7	1.1	3.3	0	0	0.9
Nelson et al. (2012) [12]	160	46.0	93 ^c	RC	104.4	1.3	1.9	0	0	–
Daskalaki et al. (2014) [46]	112	42.4 ^b	32.1 ^b	RC	85.5 ^b	0	3.2 ^b	0	0	72 % out-patient ^b , 28 % 3.7 ^b
<i>Single incision robotic cholecystectomy</i>										
Gonzalez A et al. (2015) [6]	465	48 ^f	25 to <30 ^f	SIRC	52 ^f	2.2 ^a	2.6	0	–	16.3 ^{e,f}
Kubat et al. (2016) [59]	150	E 57.6, U 50.4, U 74)	E 25.7, U 28.2	SIRC	83.3	0.7	E 5.2, U 12.2	0.7	0	1
Bibi et al. (2015) [62]	102	51	28.26	SIRC	110	3.9 ^a	4	0	–	1.97
Pietrabissa A et al. (2012) [63]	100	53.4	24.4	SIRC	71	2	0	0	0	–
Vidovszky et al. (2014) [60]	95	45.2	30.1	SIRC	88.63	1.1, 6.3 ^a	Readmissions 6.3, Reoperations 1.1	0	0	88.4 % out-patient
Morel et al. (2014) [64]	82	48.74	26.33	SIRC	91.05	1.2, 2.4 ^a	4.88	0	–	2.4
Daskalaki et al. (2014) [46, 65]	72	37.5	32.1 ^b	SIRC	84	0	0	0	0	72 % out-patient ^b , 28 % 3.7 ^b
Chung et al. (2015) [61]	70	40.3	29.5	SIRC	111.5	1.4	Readmissions 2.8	0	0	1.5

RC robotic cholecystectomy, SIRC single-incision robotic cholecystectomy, E elective, U urgent, BMI body mass index, LOS length of hospital stay
^aAdditional port or conversion to laparoscopy
^bMean values including both single-incision and multiport cholecystectomy
^cMean weights in kilograms
^dObesity rate (%)
^eTime expressed in hours
^fValues are expressed as median

Single-incision robotic cholecystectomy

The first single-incision laparoscopic cholecystectomy was published in 1997 [6, 54]. It is a challenging operation with a prolonged surgical time and learning curve; some of the challenges surgeons must face are limited visualization, lack of triangulation, and internal/external collisions [6]. Single-incision robotic

cholecystectomy was introduced in 2011 [5, 14] with the first experiences being described by Kroh and Wren [5, 55]. Robotic technology tried to reproduce advantages of the single-incision approach with the same principles of multiport laparoscopic cholecystectomy [5]. The advantages of the robotic approach are the high definition stereoscopic three dimensional visualization, the single-site port with four openings

(one for the camera, two for the surgeon and one for assistant), the reassignment of the instruments (since they cross the fascia preventing any confusion from the surgeon sitting at the console) and the curved trocars that cross the fascia and re-approximate at the target reproducing the triangulation necessary for laparoscopy [5].

Outcomes on robotic single-incision cholecystectomy vary between studies

but most agree on longer operative time and no significant differences in length of hospitalization and complication rates compared to the laparoscopic approach [6, 44, 56].

Gonzalez et al. [6] performed a multicenter study with 465 patients (66.4 % obese or overweight, 65.2 % with surgical indication of symptomatic cholelithiasis or biliary colic, 48.6 % with previous abdominal surgery and 18 % with ASA 3–4). Single-incision robotic cholecystectomy was successfully completed in 455 (97.8 %) of the patients. The mean operative time and length of hospitalization were 52 min and 16.3 hs, respectively. Male gender, obesity, and primary indication other than biliary dyskinesia were independent predictors of extended surgical time. Failure was reported to occur in 10 patients (2.2 %): 2 with diagnosis of cholecystitis and 8 biliary colic, and 7 of them were men. Complication rate was 2.6 % with 2 (0.4 %) biliary leaks, 7 (1.5 %) surgical site infections, 2 (0.4 %) organ/gall bladder fascia infections, and 2 (0.4 %) wound disruptions. These rates were comparable to other publications on laparoscopic single-incision and open cholecystectomy, which report biliary duct injury rates of 0.72 % and 0.4 %, respectively [6, 57].

Antoniou et al. [58] performed a systematic review that included 29 studies and a total of 1166 patients who underwent a single-incision laparoscopic cholecystectomy and reported a 90.7 % success rate and 6.1 % complication rate. Acute cholecystitis was a factor predisposed to failure (success rate 59.9 vs. 93 %, $p < 0.0001$). The mean operative time was 70.2 min and the mean hospital stay 1.4 days. They also reported a prolonged operative time in obese patients and patients with diagnosis of cholecystitis.

There are few direct comparisons between laparoscopic and robotic single-incision cholecystectomy. Gustafson et al. [44] compared 38 laparoscopic vs. 44 robotic single-incision cholecystectomies performed by a single surgeon between 2011 and 2013. No significant difference were found in the conversion rate, length of hospitalization, incidence of incisional hernia requiring repair, in-

traoperative and postoperative complications, wound complications, and readmissions related to the procedure [18].

Kubat et al. [59] reported the use of the robotic single-incision approach in elective and urgent cholecystectomy. Urgent robotic single-incision cholecystectomy presented with significantly longer operative time and length of hospitalization but with no significant differences in complication rates, 30 day mortality, and readmissions. Thus, they concluded that single-incision robotic cholecystectomy is safe and can be applied for elective or urgent surgery.

Table 2 summarizes the largest series of single-incision robotic cholecystectomy reported in the literature in recent years [6, 46, 59–65].

To conclude, single-site robotic cholecystectomy improved many of the disadvantages of the single-site laparoscopic approach with three dimensional vision, reassignment of the instruments and improved ergonomics [5]. It is safe and feasible in all patients with different gallbladder pathologies [5, 6, 44] and fluorescent cholangiogram available in the robotic console aids in augmenting its safety [5]. Costs are higher [5, 44] but the shorter learning curve allows for reduced operative times when compared to laparoscopy [5]. Cosmetic outcomes and patient satisfaction for the single-incision robotic approach are better than conventional laparoscopy [66].

Innovations and future applications

Several surgical innovations will be available in the future and will change the way hepatobiliary surgery is performed. Efforts towards bioartificial liver development and liver regeneration are being made [67, 68].

» Real-time cancer detection and fluorescent-guided surgery will soon be possible for patients

New fluorescent molecules with deeper tissue penetration and improved signal, as well as monoclonal antibodies conjugated to near-infrared fluorophores are

being developed [69, 70]. In vivo, real-time cancer detection and fluorescent-guided surgery will soon be possible in humans and not only in a lab setting [71, 72].

New technological advancements will also include better processing of images, new computer interfaces, more advanced robotic systems and surgical tools. All of which will eventually lead to the development of a “new operating room” concept that will allow for better overall patient treatment.

Conclusion

Robot-assisted hepatobiliary surgery has been steadily growing over recent years. Current literature has shown that even complex procedures, such as major and extended hepatectomies, can be performed with excellent results, in expert hands. Limitations include bulky lesions, resections in posterior–superior segments, and results that are not generalizable in nonexpert hands. Nevertheless, this is a promising technology that could expand the indications to minimally invasive hepatobiliary surgery.

Corresponding address

P. C. Giulianotti, MD, FACS
Division of General, Minimally Invasive and Robotic Surgery, Department of Surgery, University of Illinois Hospital and Health Sciences System
840 S Wood St, 60612 Chicago, IL, USA
piercg@uic.edu

Compliance with ethical guidelines

Conflict of interest. L. F. Gonzalez-Cicarelli, P. Quadri, D. Daskalaki, L. Milone and A. Gangemi have no conflicts of interest. P. C. Giulianotti is a consultant for Covidien LP and Ethicon, Inc.; he has a proctoring agreement and Grant support as Chief of the Division.

The accompanying manuscript does not include studies on humans or animals.

The supplement containing this article is not sponsored by industry.

References

1. Corcione F, Esposito C, Cuccurullo D, Settembre A, Miranda N, Amato F et al (2005) Advantages and limits of robot-assisted laparoscopic surgery: preliminary experience. *Surg Endosc* 19(1):117–119
2. Antoniou SA, Antoniou GA, Antoniou AI, Granderath FA (2015) Past, present, and future of minimally invasive abdominal surgery. *JLS* 19(3) doi:10.4293/JLS.2015.00052
3. Altieri MS, Yang J, Telem DA, Zhu J, Halbert C, Talamini M et al (2016) Robotic approaches may offer benefit in colorectal procedures, more controversial in other areas: a review of 168,248 cases. *Surg Endosc* 30(3):925–933
4. Romero-Talamas H, Kroh M (2014) Cholecystectomy by using a surgical robotic system. *J Hepatobiliary Pancreat Sci* 21(1):11–17
5. Escobar-Dominguez JE, Hernandez-Murcia C, Gonzalez AM (2015) Description of robotic single site cholecystectomy and a review of outcomes. *J Surg Oncol* 112(3):284–288
6. Gonzalez A, Murcia CH, Romero R, Escobar E, Garcia P, Walker G et al (2015) A multicenter study of initial experience with single-incision robotic cholecystectomies (SIRC) demonstrating a high success rate in 465 cases. *Surg Endosc* doi:10.1007/s00464-015-4583-1
7. Tomulescu V, Stanculea O, Balescu I, Vasile S, Tudor S, Gheorghe C et al (2009) First year experience of robotic-assisted laparoscopic surgery with 153 cases in a general surgery department: indications, technique and results. *Chirurgia (Bucur)* 104(2):141–150
8. Acquafresca PA, Palermo M, Rogula T, Duza GE, Serra E (2015) Most common robotic bariatric procedures: review and technical aspects. *Ann Surg Innov Res* 9(1):9 doi:10.1186/s13022-015-0019-9
9. Himpens J, Leman G, Cadiere GB (1998) Telesurgical laparoscopic cholecystectomy. *Surg Endosc* 12(8):1091
10. Giulianotti PC, Coratti A, Angelini M, Sbrana F, Cecconi S, Balestracci T et al (2003) Robotics in general surgery: personal experience in a large community hospital. *Arch Surg* 138(7):777–784
11. Szold A, Bergamaschi R, Broeders I, Dankelman J, Forgione A, Lango T et al (2015) European Association of Endoscopic Surgeons (EAES) consensus statement on the use of robotics in general surgery. *Surg Endosc* 29(2):253–288
12. Nelson EC, Gottlieb AH, Muller HG, Smith W, Ali MR, Vidovszky TJ (2014) Robotic cholecystectomy and resident education: the UC Davis experience. *Int J Med Robot* 10(2):218–222
13. Vidovszky TJ, Smith W, Ghosh J, Ali MR (2006) Robotic cholecystectomy: learning curve, advantages, and limitations. *J Surg Res* 136(2):172–178
14. Kaminski JP, Bueltmann KW, Rudnicki M (2014) Robotic versus laparoscopic cholecystectomy inpatient analysis: does the end justify the means? *J Gastrointest Surg* 18(12):2116–2122
15. Umer A, Ellner S (2015) Commentary: Robotic vs. standard Laparoscopic technique – what is better? *Front Surg* 2:38
16. Rosiek A, Leksowski K (2015) Technology advances in hospital practices: robotics in treatment of patients. *Technol Cancer Res Treat* 14(3):270–276
17. Rosemurgy A, Ryan C, Klein R, Sukharamwala P, Wood T, Ross S (2015) Does the cost of robotic cholecystectomy translate to a financial burden? *Surg Endosc* 29(8):2115–2120
18. Buell JF, Cherqui D, Geller DA, O'Rourke N, Iannitti D, Dagher I et al (2009) The international position on laparoscopic liver surgery: The Louisville Statement, 2008. *Ann Surg* 250(5):825–830
19. Wakabayashi G, Cherqui D, Geller DA, Buell JF, Kaneko H, Han HS et al (2015) Recommendations for laparoscopic liver resection: a report from the second international consensus conference held in Morioka. *Ann Surg* 261(4):619–629
20. Giulianotti PC, Coratti A, Sbrana F, Addeo P, Bianco FM, Buchs NC et al (2011) Robotic liver surgery: results for 70 resections. *Surgery* 149(1):29–39
21. Spampinato MG, Coratti A, Bianco L, Caniglia F, Laurenzi A, Puleo F et al (2014) Perioperative outcomes of laparoscopic and robot-assisted major hepatectomies: an Italian multi-institutional comparative study. *Surg Endosc* 28(10):2973–2979
22. Wu YM, Hu RH, Lai HS, Lee PH (2014) Robotic-assisted minimally invasive liver resection. *Asian J Surg* 37(2):53–57
23. Choi GH, Choi SH, Kim SH, Hwang HK, Kang CM, Choi JS et al (2012) Robotic liver resection: technique and results of 30 consecutive procedures. *Surg Endosc* 26(8):2247–2258
24. Lai EC, Yang GP, Tang CN (2013) Robot-assisted laparoscopic liver resection for hepatocellular carcinoma: short-term outcome. *Am J Surg* 205(6):697–702
25. Ji WB, Wang HG, Zhao ZM, Duan WD, Lu F, Dong JH (2011) Robotic-assisted laparoscopic anatomic hepatectomy in China: initial experience. *Ann Surg* 253(2):342–348
26. Tsung A, Geller DA, Sukato DC, Sabbaghian S, Tohme S, Steel J et al (2014) Robotic versus laparoscopic hepatectomy: a matched comparison. *Ann Surg* 259(3):549–555
27. Daskalaki D, Aguilera F, Patton K, Giulianotti PC (2015) Fluorescence in robotic surgery. *J Surg Oncol* 112(3):250–256
28. Giulianotti PC, Sbrana F, Bianco FM, Addeo P (2010) Robot-assisted laparoscopic extended right hepatectomy with biliary reconstruction. *J Laparoendosc Adv Surg Tech A* 20(2):159–163
29. Chen KH, Chen SD, Chen YD, Chang YJ, Lin TC, Siow TF et al (2014) Robotic left hepatectomy with revision of hepaticojejunostomy. *Asian J Surg* 37(2):106–109
30. Quijano Y, Vicente E, Ielpo B, Duran H, Diaz E, Fabra I et al (2016) Robotic liver surgery: early experience from a single surgical center. *Surg Laparosc Endosc Percutan Tech* 26(1):66–71
31. Troisi RI, Patrili A, Montalti R, Casciola L (2013) Robotic assistance in liver surgery: a real advantage over a fully laparoscopic approach? Results of a comparative bi-institutional analysis. *Int J Med Robot* 9(2):160–166
32. Felli E, Santoro R, Colasanti M, Vennarecci G, Lepiane P, Ettorre GM (2015) Robotic liver surgery: preliminary experience in a tertiary hepato-biliary unit. *Updates Surg* 67(1):27–32
33. Yu YD, Kim KH, Jung DH, Namkoong JM, Yoon SY, Jung SW et al (2014) Robotic versus laparoscopic liver resection: a comparative study from a single center. *Langenbecks Arch Surg* 399(8):1039–1045
34. Patrili A, Cipriani F, Ratti F, Bartoli A, Ceccarelli G, Casciola L et al (2014) Robot-assisted versus open liver resection in the right posterior section. *JLS* 18(3) doi:10.4293/jls.2014.00040
35. Kingham TP, Leung U, Kuk D, Gonen M, D'Angelica MI, Allen PJ et al (2016) Robotic liver resection: A case-matched comparison. *World J Surg* 40(6):1422–1428. doi:10.1007/s00268-016-3446-9
36. Tranchart H, Ceribelli C, Ferretti S, Dagher I, Patrili A (2014) Traditional versus robot-assisted full laparoscopic liver resection: a matched-pair comparative study. *World J Surg* 38(11):2904–2909
37. Montalti R, Scuderi V, Patrili A, Vivarelli M, Troisi RI (2016) Robotic versus laparoscopic resections of posterosuperior segments of the liver: a propensity score-matched comparison. *Surg Endosc* 30(3):1004–1013
38. Croner RS, Perrakis A, Brunner M, Matzel KE, Hohenberger W (2015) Pioneering robotic liver surgery in germany: first experiences with liver malignancies. *Front Surg* 2:18
39. Berber E, Akyildiz HY, Aucejo F, Gunasekaran G, Chalikhonda S, Fung J (2010) Robotic versus laparoscopic resection of liver tumours. *HPB (Oxford)* 12(8):583–586
40. Lin CW, Tsai TJ, Cheng TY, Wei HK, Hung CF, Chen YY et al (2015) The learning curve of laparoscopic liver resection after the Louisville statement 2008: Will it be more effective and smooth? *Surg Endosc* doi:10.1007/s00464-015-4575-1
41. Nomi T, Fuks D, Kawaguchi Y, Mal F, Nakajima Y, Gayet B (2015) Learning curve for laparoscopic major hepatectomy. *Br J Surg* 102(7):796–804
42. Viganò L, Laurent A, Tayar C, Tomatis M, Ponti A, Cherqui D (2009) The learning curve in laparoscopic liver resection: improved feasibility and reproducibility. *Ann Surg* 250(5):772–782
43. Spampinato MG, Arvanitakis M, Puleo F, Mandala L, Quarta G, Baldazzi G (2015) Assessing the learning curve for totally laparoscopic major-complex liver resections: a single hepatobiliary surgeon experience. *Surg Laparosc Endosc Percutan Tech* 25(2):e45–e50
44. Gustafson M, Lescouffair T, Kimball R, Daoud I (2015) A comparison of robotic single-incision and traditional single-incision laparoscopic cholecystectomy. *Surg Endosc* doi:10.1007/s00464-015-4223-9
45. Ayloo S, Roh Y, Choudhury N (2014) Laparoscopic versus robot-assisted cholecystectomy: a retrospective cohort study. *Int J Surg* 12(10):1077–1081
46. Daskalaki D, Fernandes E, Wang X, Bianco FM, Elli EF, Ayloo S et al (2014) Indocyanine green (ICG) fluorescent cholangiography during robotic cholecystectomy: results of 184 consecutive cases in a single institution. *Surg Innov* 21(6):615–621
47. Pesce A, Piccolo G, La Greca G, Puleo S (2015) Utility of fluorescent cholangiography during laparoscopic cholecystectomy: A systematic review. *World J Gastroenterol* 21(25):7877–7883
48. Baek NH, Li G, Kim JH, Hwang JC, Kim JH, Yoo BM et al (2015) Short-term surgical outcomes and experience with 925 patients undergoing robotic cholecystectomy during a 4-year period at a single institution. *Hepatogastroenterology* 62(139):573–576
49. Schwaitzberg SD (2015) Financial modeling of current surgical robotic system in outpatient laparoscopic cholecystectomy: how should we think about the expense? *Surg Endosc* 30(5):2082–2085. doi:10.1007/s00464-015-4457-6
50. Prasad A, De S, Mishra P, Tiwari A (2015) Robotic assisted Roux-en-Y hepaticojejunostomy in a post-cholecystectomy type E2 bile duct injury. *World J Gastroenterol* 21(6):1703–1706
51. Villegas L, Lagoo S, Schwartz T, Athar N, Greene R, Eubanks WS (2004) Robotically assisted laparoscopic Roux-en-Y hepaticojejunostomy. *JLS* 8(3):239–244
52. Lai EC, Tang CN, Yang GP, Li MK (2011) Approach to manage the complications of choledochodu-

- denostomy: robot-assisted laparoscopic Roux-en-Y hepaticojejunostomy. *Surg Laparosc Endosc Percutan Tech* 21(5):e228–e231
53. Alizai NK, Dawrant MJ, Najmaldin AS (2014) Robot-assisted resection of choledochal cysts and hepaticojejunostomy in children. *Pediatr Surg Int* 30(3):291–294
 54. Navarra G, Pozza E, Occhionorelli S, Carcoforo P, Donini I (1997) One-wound laparoscopic cholecystectomy. *Br J Surg* 84(5):695
 55. Kroh M, El-Hayek K, Rosenblatt S, Chand B, Escobar P, Kaouk J et al (2011) First human surgery with a novel single-port robotic system: cholecystectomy using the da Vinci Single-Site platform. *Surg Endosc* 25(11):3566–3573
 56. Gonzalez AM, Rabaza JR, Donkor C, Romero RJ, Kosanovic R, Verdeja JC (2013) Single-incision cholecystectomy: a comparative study of standard laparoscopic, robotic, and SPIDER platforms. *Surg Endosc* 27(12):4524–4531
 57. Joseph M, Phillips MR, Farrell TM, Rupp CC (2012) Single incision laparoscopic cholecystectomy is associated with a higher bile duct injury rate: a review and a word of caution. *Ann Surg* 256(1):1–6
 58. Antoniou SA, Pointner R, Granderath FA (2011) Single-incision laparoscopic cholecystectomy: a systematic review. *Surg Endosc* 25(2):367–377
 59. Kubat E, Hansen N, Nguyen H, Wren SM, Eisenberg D (2016) Urgent and elective robotic single-site cholecystectomy: analysis and learning curve of 150 consecutive cases. *J Laparoendosc Adv Surg Tech A* 26(3):185–191
 60. Vidovszky TJ, Carr AD, Farinholt GN, Ho HS, Smith WH, Ali MR (2014) Single-site robotic cholecystectomy in a broadly inclusive patient population: a prospective study. *Ann Surg* 260(1):134–141
 61. Chung PJ, Huang R, Policastro L, Lee R, Schwartzman A, Alfonso A et al (2015) Single-site Robotic cholecystectomy at an inner-city academic center. *JSL* 19(3):e2015.00033 doi:10.4293/jsls.2015.00033
 62. Bibi S, Rahnama-Azar AA, Coralic J, Bayoumi M, Khorsand J, Farkas DT et al (2015) Single-site robotic cholecystectomy: the timeline of progress. *World J Surg* 39(10):2386–2391
 63. Pietrabissa A, Sbrana F, Morelli L, Badessi F, Pugliese L, Vinci A et al (2012) Overcoming the challenges of single-incision cholecystectomy with robotic single-site technology. *Arch Surg* 147(8):709–714
 64. Morel P, Buchs NC, Iranmanesh P, Pugin F, Buehler L, Azagury DE et al (2014) Robotic single-site cholecystectomy. *J Hepatobiliary Pancreat Sci* 21(1):18–25
 65. Daskalaki D, Masrur M, Patton K, Bianco FM, Giulianotti PC (2014) Single-site robotic cholecystectomy with Indocyanine green fluorescent cholangiography: 72 cases with no complications. SAGES 2014 Annual Meeting, Salt Lake City, Utah, 2014.
 66. Pietrabissa A, Pugliese L, Vinci A, Peri A, Tinozzi FP, Cavazzi E et al (2015) Short-term outcomes of single-site robotic cholecystectomy versus four-port laparoscopic cholecystectomy: a prospective, randomized, double-blind trial. *Surg Endosc* doi:10.1007/s00464-015-4601-3
 67. Dhar DK, Mohammad GH, Vyas S, Broering DC, Malago M (2015) A novel rat model of liver regeneration: possible role of cytokine induced neutrophil chemoattractant-1 in augmented liver regeneration. *Ann Surg Innov Res* 9:11
 68. Mazza G, Rombouts K, Rennie HA, Urbani L, Vinh LT, Al-Akkad W et al (2015) Decellularized human liver as a natural 3D-scaffold for liver bioengineering and transplantation. *Sci Rep* 5:13079 doi:10.1038/srep13079
 69. Gioux S, Mazhar A, Cuccia DJ, Durkin AJ, Tromberg BJ, Frangioni JV (2009) Three-dimensional surface profile intensity correction for spatially modulated imaging. *J Biomed Opt* 14(3):034045 doi:10.1117/1.3156840
 70. Themelis G, Yoo JS, Soh KS, Schulz R, Ntziachristos V (2009) Real-time intraoperative fluorescence imaging system using light-absorption correction. *J Biomed Opt* 14(6):064012
 71. Metildi CA, Kaushal S, Luiken GA, Hoffman RM, Bouvet M (2014) Advantages of fluorescence-guided laparoscopic surgery of pancreatic cancer labeled with fluorescent anti-carcinoembryonic antigen antibodies in an orthotopic mouse model. *J Am Coll Surg* 219(1):132–141
 72. Metildi CA, Kaushal S, Hardamon CR, Snyder CS, Pu M, Messer KS et al (2012) Fluorescence-guided surgery allows for more complete resection of pancreatic cancer, resulting in longer disease-free survival compared with standard surgery in orthotopic mouse models. *J Am Coll Surg* 215(1):126–135 (discussion 35–36)