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PII: S1743-9191(20)30453-2

DOI: https://doi.org/10.1016/j.ijsu.2020.05.070

Reference: IJSU 5545

To appear in: *International Journal of Surgery*

Received Date: 28 February 2020

Revised Date: 7 April 2020

Accepted Date: 20 May 2020

Please cite this article as: Di Benedetto F, Petrowsky H, Magistri P, Halazun KJ, Robotic liver resection: hurdles and beyond, *International Journal of Surgery*, https://doi.org/10.1016/j.ijsu.2020.05.070.

Robotic liver resection: hurdles and beyond

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None

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Please specify the contribution of each author to the paper, e.g. study design, data collections, data analysis, writing. Others, who have contributed in other ways should be listed as contributors.

Fabrizio Di Benedetto : study design, manuscript drafting and critical review
Henrik Petrwosky : manuscript drafting and critical review
Paolo Magistri : data collection and analysis, manuscript drafting
Karim J Halazun : manuscript drafting and critical review

Guarantor

The Guarantor is the one or more people who accept full responsibility for the work and/or the conduct of the study, had access to the data, and controlled the decision to publish. Please note that providing a guarantor is compulsory.

Fabrizio Di Benedetto

Abstract:

Laparoscopy is currently considered the standard of care for certain procedures such as left-lateral sectionectomies and wedge resections of anterior segments. The role of robotic liver surgery is still under debate, especially with regards to oncological outcomes. The purpose of this review is to describe how the field of robotic liver surgery has expanded, and to identify current limitations and future perspectives of the technology. Available evidences suggest that oncologic results after robotic liver resection are comparable to open and laparoscopic approaches for hepatocellular carcinoma and colorectal liver metastases, with identifiable advantages for cirrhotic patients and patients undergoing repeat resections. Excellent outcomes and optimal patient safety can be only achieved with specific hepato-biliary and general minimally invasive training to overcome the learning curve.

Keywords:

HCC; CRLM; cirrhosis; cholangiocarcinoma; learning curve; LDLT; ICG

1. Introduction

The benefits of minimally invasive (MIS) approaches to the liver for both primary and metastatic tumors have been clearly demonstrated over the last two decades (1). The introduction of robotic technology in the field of liver surgery may make technically difficult MIS approaches to the liver more feasible. Such resections include posterior sectionectomies and tumors located in superior segments 4a and 8 (2). Although robotic surgery is rapidly growing and expanding in several surgical fields, with favorable peri-operative outcomes, there are still concerns with regards to mid- and long-term oncological outcomes, especially in complex hepatobiliary surgery (3)(4). The aim of this study is to describe how the field of robotic liver surgery has expanded, identifying current limitations and future directions for the robotic platform through the analysis of significant technical considerations, with particular attention to oncological outcomes for both primary and metastatic liver tumors.

2. Technical considerations

2.1 Patient positioning

For liver resections, patients are usually positioned supine, in a range of 20° to 35° reverse-Trendelemburg ,and can be slightly rotated to the left. A “bump” can be placed under the right shoulder to allow an easier access to right and posterior segments by increasing the rotation. For posterior lesions in segment 6/7, a left-sided position (left lateral decubitus) may be preferable for easy access. With the Si DaVinci platform, a double docking is required for combined liver and colonic resections, while using the novel Xi platform that allows multi-quadrant surgery in a single docking will be sufficient. This is also possible due to the integrated table motion that couples the robotic cart with the operating table allowing variations of table rotation and inclination during surgery.

2.2 Port placement

Exploratory laparoscopy is recommended before docking the patient cart in order to assess the resectability and safe insertion of trocars. The position of the trocars will differ according to the robotic platform used. As a general rule, trocars should be positioned very high in the subcostal and lateral line for the posterior superior segments and closer to the transverse umbilical line for the anterior segments, shifting toward the left or right depending on the location of the lesion, to create an adequate triangulation with enough space between the ports (6 to 10 cm on average, depending on patient conformation) (5,6). The fourth robotic arm is generally positioned on the left side to retract the liver and expose the transection plane. In major liver resections and bisegmentectomies, a holding stich can be applied to the opposite surface of the transection plane, which applies retraction inside the abdomen or percutaneously to further improve exposure. Figure 1 shows an example of trocar placement with Si platform in case of right hepatectomy and left lobectomy.

2.3 Parenchymal transection

One of the most common limitations of robotic liver surgery is that the system does not integrate a Ultrasonic Aspirator (UA) for parenchymal transection. This limitation is probably the main factor preventing smoother transition from open/laparoscopic to robotic liver surgery. Therefore, surgeons have to create in between novel strategies to achieve safe parenchymal transection. Despite missing device angulation and reduced motion, the daVinci® Harmonic ACE™ (Ethicon, Somerville, NJ, USA) remains the most appropriate tool for parenchymal transection, together with a meticulous vascular and biliary dissection assisted by bipolar forceps. However, some robotic surgeons might prefer the assistance of bed-side laparoscopic UA transection as long as no comparable robotic transection device is available.

2.4 Indocyanine green fluorescence

In liver surgery, indocyanine green (ICG) fluoroscopy can improve the visualization of the biliary tree anatomy and offers a useful method to distinguish between tumor and normal liver parenchyma. In particular, it has been reported that ICG demarcation facilitates performing true anatomical resections with minimally invasive approach, with help of selective occlusion of the specific Glissionian pedicles (7). For biliary tree visualization we have standardized the administration in the OR of 1 mg ICG before induction. ICG infusion might be also used for direct lesion identification where tumors are usually hypo-fluorescent with no ICG uptake (8). Long-term comparative results in terms of oncological benefit are still pending (9).

2.5 Learning curve

Learning robotic liver resection is generally considered easier compared to standard laparoscopy, thanks to the flexibility and stability of the instruments. However, gaining proficiency in a novel surgical technique brings potential harm to patients at the beginning of the surgeons learning curve. This is the reason why every first attempt to use the robot for surgical procedures should be preceded by extensive simulation and wet lab training. It is advisable to start the robotic program with the help of a proctor to increase the safety of the procedure. In terms of outcomes, Chen et al. demonstrated that for major hepatectomies, the robotic learning curve can be divided into three phases: initial (phase 1, 15 patients), intermediate (phase 2, 25 patients), and mature (phase 3, 52 patients) (10). The literature shows that lengths of surgery and hospital stay are improved after overcoming the initial phase, while the intermediate phase was required to reduce the overall blood loss (310 mL during phase 2 *vs* 109 mL during phase 3, p=0.003). Similarly, even in the context of an experienced HPB high-volume center, Magistri et al. showed that at least 30 cases of robotic liver resection are required to reduce operative time, blood loss, and hospital stay (11).

3 Oncological outcomes

4.1 Primary liver tumors

In the setting of cirrhotic patients, minimally invasive liver surgery is associated with a great benefit in terms of reducing the risks of liver decompensation and related complications (12). A recent literature review including ten studies on robotic liver resection for HCC with a total of 302 patients reported ranges of disease-free (DFS) and overall survival (OS) at 2 years of 72%-84% and 94%-98%, respectively (13). Table 1 provides data from studies with at least 20 cases of robotic HCC. It has been proposed that a robotic approach may also improve the access to the abdomen in cases of tumor recurrence with potential requirement of a liver transplant in the future, opening to the possibility of its adoption for both down-staging and bridging strategies (14).

A recent review from China reported 4 studies on the use of robotic approach for hilar cholangiocarcinoma (15). Among those, two studies presented case series of at least 10 patients (3,16), while the other two were case reports (17,18). In the study by Xu and colleagues, outcomes were not favorable, resulting in a longer operative time, higher post-operative morbidity and shorter recurrence-free survival (RFS) compared to open surgery (16). Notably, in the larger series published by Liu et al., only 3 patients underwent a formal anatomical left hepatectomy, while the others were treated with tumor resection and biliary reconstruction or drainage. Moreover, 1 case of port-site metastasis was reported (3). The experience with hilar cholangiocarcinoma is too limited so far to draw conclusions on its feasibility, and should be reserved to highly experienced centers.

Finally, few data are available on robotic liver resection for intra-hepatic cholangiocarcinoma, and no significant data on oncological outcomes are currently available (16,19,20).

4.2 Secondary liver tumors

In patients with liver metastases, several studies already demonstrated the non-inferiority of minimally invasive surgery versus classical open approach. A recent multi-institutional study from high-volume centers in the United States reported a propensity-matched comparison between laparoscopic and robotic liver resection for metastatic colorectal cancer (20). No statistically significant differences were found in terms of perioperative death, overall and high-grade complications, surgical margin status, and need for readmission or reintervention. After a median follow-up of almost 3 years, there were no statistically significant differences in OS and DFS between the robotic and laparoscopic group (61% versus 60% p=0.78, and 38% versus 44% p=0.62, respectively). Table 2 presents data from studies with at least 20 cases of robotic resections for colorectal liver metastasis (CRLM). It has been also reported that minimally invasive liver surgery allows a parenchymal-sparing approach with the possibility to easily access the liver in case of recurrence and consequently facilitates repeated liver resection (21,22). This is of particular importance in the natural history of CRLM. From a technical point of view, combined colorectal and liver surgery in case of synchronous CRLM may require a double docking when using the Si platform, which may be relevant for the length of surgery.

4 Robotic procurement for living donation

Robotic liver procurement for living donor liver transplant is currently less developed compared to kidney procurement and transplantation for living donation, currently the standard of care in kidney procurements. (21–23). Laparoscopic donor hepatectomy, either pure or hybrid, has been successfully applied to both left and right procurement from living donors. It has been proven safe and effective and is associated with fast recovery to daily activities in expert centers (24–26). In 2016, Chen et al. reported a series of 13 patients who underwent living donor robotic right hepatectomy for liver transplantation (27). In this study, robotic surgery resulted in better pain control and enabled a faster return to work without affecting liver transplant outcomes and with similar outcomes to laparoscopic approaches, when compared with the traditional open approach.

5 Costs and financial burden

Several analyses on costs of robotic surgery have been reported so far, with controversial results about the balance between costs and benefits (28). A recent analysis demonstrated that robotic surgery performs better as compared to laparoscopic and open liver resections in terms of costs, hospital stay, and risk of readmission (29). Such uncertainty may be related to the difficulty to compare overall costs, in particular among different healthcare systems and regulations worldwide. A paper comparing costs of robotic and laparoscopic left lateral sectionectomy showed no differences in terms of the total surgical supply ($5'130 vs. $4'408, p=0.401) (30). Notably, this analysis was performed without indirect costs for robotic surgery excluding initial purchase and maintenance, that significantly increase the costs of robotic procedure. Taken together, data in literature are too heterogeneous so far to clearly solve the issue of costs comparison between robotic surgery and other techniques.

6 Discussion

On February 2019 the US Food and Drug Administration (FDA) released a safety communication about the use of robotic-assisted surgical systems for every surgical specialty (31). This warning was mainly related to the use of robotic surgery for hysterectomy, and cited the outcomes of a clinical trial published on November 2018 in the New England Journal of Medicine (32). This study analyzed radical hysterectomy for various uterine and cervical malignancies and showed inferior DFS and OS for the minimally invasive (laparoscopic and robotic) compared to the open group. This observation initiated an intense debate in the gynecologic community in the setting of already widespread acceptance of minimally invasive approaches for gynecological neoplasia. However, these inferior results appear to be related to the learning curve rather than the used instrumentation approach. Improved credentialing protocols are needed to guarantee the best results for safety and oncological outcomes (33).

Several studies focused on the comparison between laparoscopic and robotic surgery, failing to identify clear advantages on one over another approach (34). It should be taken into account that robotic surgery offers a different approach from standard laparoscopy, tending to an overall increased control of the surgical field and, therefore, improved safety in the correct hands. Beside being aware of the existence of other robotic platforms, it should be clarified that all available evidences herein analyzed are referred to *da Vinci* platforms (Intuitive, Sunnyvale, CA, US). The use of robotic surgery should be reserved to highly specialized centers in order to maximize the opportunities to offer radically curative treatment without compromising safety. This statement is also consistent with the latest definition of robotic liver surgery at the Morioka conference, where robotic surgery was proposed to be in the development phase of the IDEAL grading system (Idea, Development, Exploration, Assessment and Long Term Follow Up Collaboration) (35,36). Despite some reservations towards robotic liver surgery, even advanced procedures such as major vascular reconstructions and Associating Liver Partition and Portal vein ligation for Staged hepatectomy (ALPPS) have been successfully performed with a partial (37) or full robotic approach (38-40) in advanced minimally invasive centers. ALPPS is well known to be technically demanding even with a traditional open approach (41-43), however, minimally invasive approaches, especially at stage one, may reduce the incidence of inter-stage complications and facilitate better tolerability of the inter-stage course (44).

With regards to instrumentation, the lack of an efficient robotic transection device as the UA is the most important limitation of robotic liver surgery. There are current difficulties in product development, which clearly delay the introduction of a fully compatible robotic UA device. In addition, there is an ongoing debate of whether the use of laparoscopic UA by the bedside surgeon may be the solution, challenging the efficiency of the robotic approach in terms of loss of control by the console surgeon during parenchymal transection. Another limitation of this set-up is that significant resources that will be required, since two experienced surgeons will be needed to perform the procedure, one console surgeon and one bedside surgeon using the UA. This demand of experienced manpower might be a hurdle for many centers to implement this technology. Many robotic liver surgeons consider their parenchymal transection technique a return to the classical open approach of parenchymal crush (45), in a finer, magnified, and precise fashion (Figure 3). However, such approach may not be widely applicable, and instrumentation still represents a barrier, for example, to robotic living donor hepatectomy. While growing, experiences in this field remain sparse with little data available.

The spatial distance between the operating and robotic platform and its considerable size remain an important obstacle, making undocking and gaining access to the patient potentially difficult in emergency scenarios. (46,47). Due to the improved agility in narrow spaces and tremor filtration, the robot may provide an easier dissection of the hilum, which is crucial in this setting. Robotic approaches for liver malignancies are becoming more common, with a growing number of reports being published. While reasonable data on DFS and OS are available for HCC and CRLM, little is known on intrahepatic cholangiocarcinoma, but this might be related in parts to the lower prevalence of this disease. Only few cases are reported for hilar cholangiocarcinoma (15,17), although biliary reconstruction is feasible and reproducible as demonstrated in the experiences with robotic pancreatico-duodenectomies. Furthermore, the requirements for extensive resections and vascular reconstructions make these hilar tumors difficult to treat with the robotic approach. In addition, the absence of haptic feedback, which is still important in the evaluation of perihilar tumor spread in open surgery, may contribute to inferior outcomes. There is general agreement that these advanced robotic procedures require a dedicated learning curve, which may be longer than that for standard robotic resections of intrahepatic tumors (10,11).

Another limiting factor of robotic surgery is the operative time, that is in the majority longer compared to other approaches. From a practical point of view, robotic cart docking has been considered the most time-consuming part of robotic surgery. Nowadays, this step is usually fast and comparable to laparoscopic trocar placement due to the advancement of the robotic technology. However, robotic surgery is still slower than standard laparoscopy for two main reasons. First, the operating surgeon controls camera and instruments, therefore camera adjustments require stopping of instrument motion even if for few seconds. Second, the exchange of operating instruments requires disconnections, which takes longer compared to classic laparoscopic or open surgery.

In conclusion, robotic surgery has become an important tool in the armamentarium of liver surgeons. Currently only major vascular resection and advanced hilar cholangiocarcinoma are considered relative contraindications for a robotic approach to the liver. Robotic surgery does not replace laparoscopy, but it has great potential for future technological developments including real-time navigation and augmented reality in a single expansible platform (Figure 4). Robotic hepatobiliary surgery should not be approached without specific training in hepatobiliary and general minimally invasive surgery in order to overcome the steep learning curve. In addition, it requires a profound knowledge of the machine, since well-trained robotic surgeons need to know the mechanisms of this tool and the principles of troubleshooting. Moreover, different skill sets are required and should be taught when compared to standard surgical training in order to gain robotic competence. Indications can be pushed in experienced centers to better define outcomes and technical principles, which should finally translate in improved safety and better surgical as well oncological outcomes.

Provenance and peer review

Commissioned, externally peer-reviewed

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Figure 1: Trocar disposition

a) Right hepatectomy with DaVinci Si robotic platform
b) Left lateral sectionectomy with DaVinci Si robotic platform

Figure 2: Use of ICG fluorescence:

a) ICG (“Firefly Technology”) During Left Hepatectomy showing biliary bifurcation
b) ICG with lack of enhancement of neuroendocrine tumor during robotic hepatectomy
c) Demonstration of biliary trifurcation with low take off of right posterior duct during robotic right hepatectomy

Figure 3: Robotic approach to the liver

a) Hilar dissection: left hepatic artery
b) Hilar dissection: left portal vein
c) Right hepatic vein dissection
d) Parenchymal transection: use of Maryland bipolar forceps

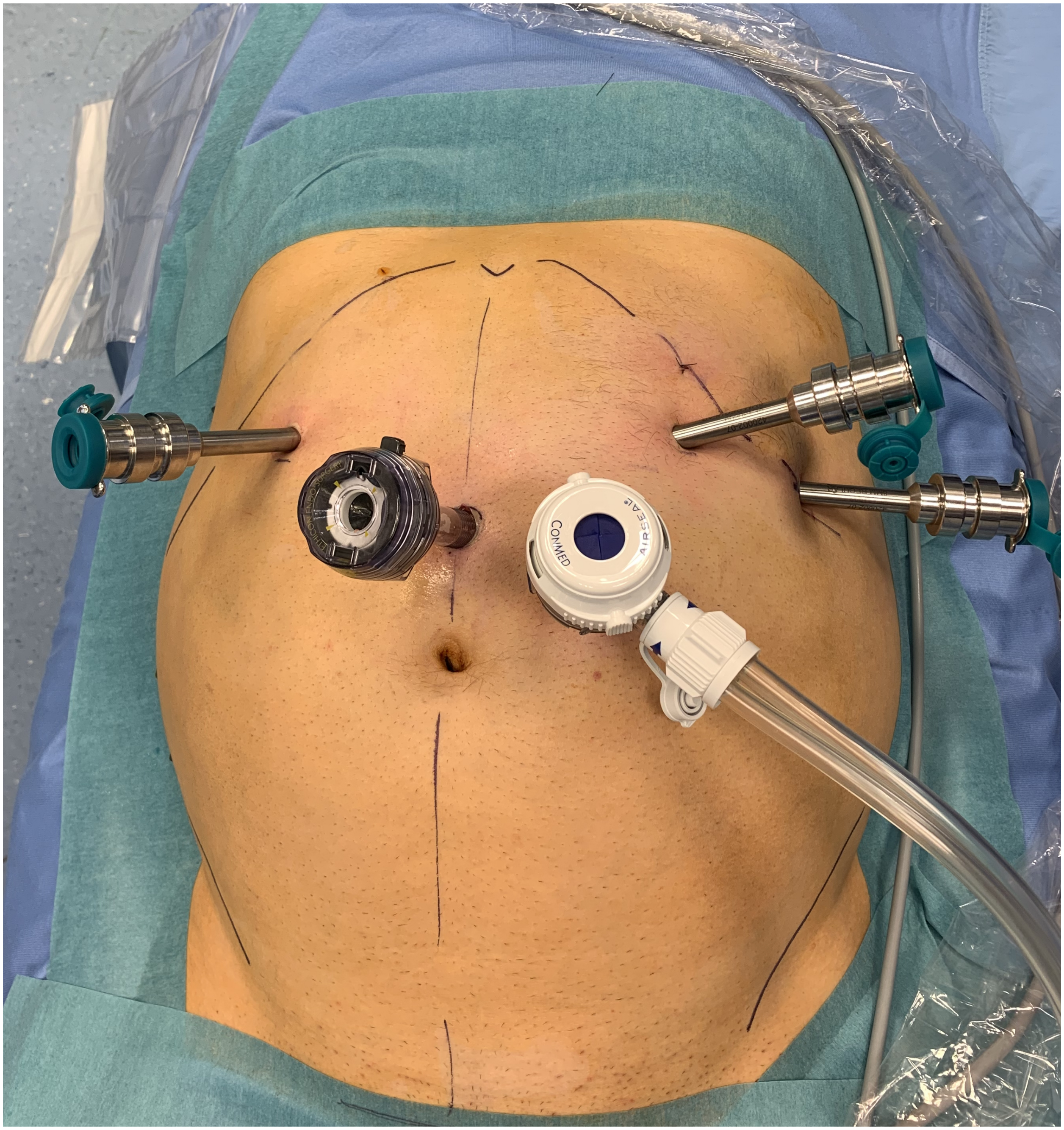
Figure 4: An example of 3D model for pre-operative surgical planning for HCC

Table 1. Robotic resection for HCC in literature

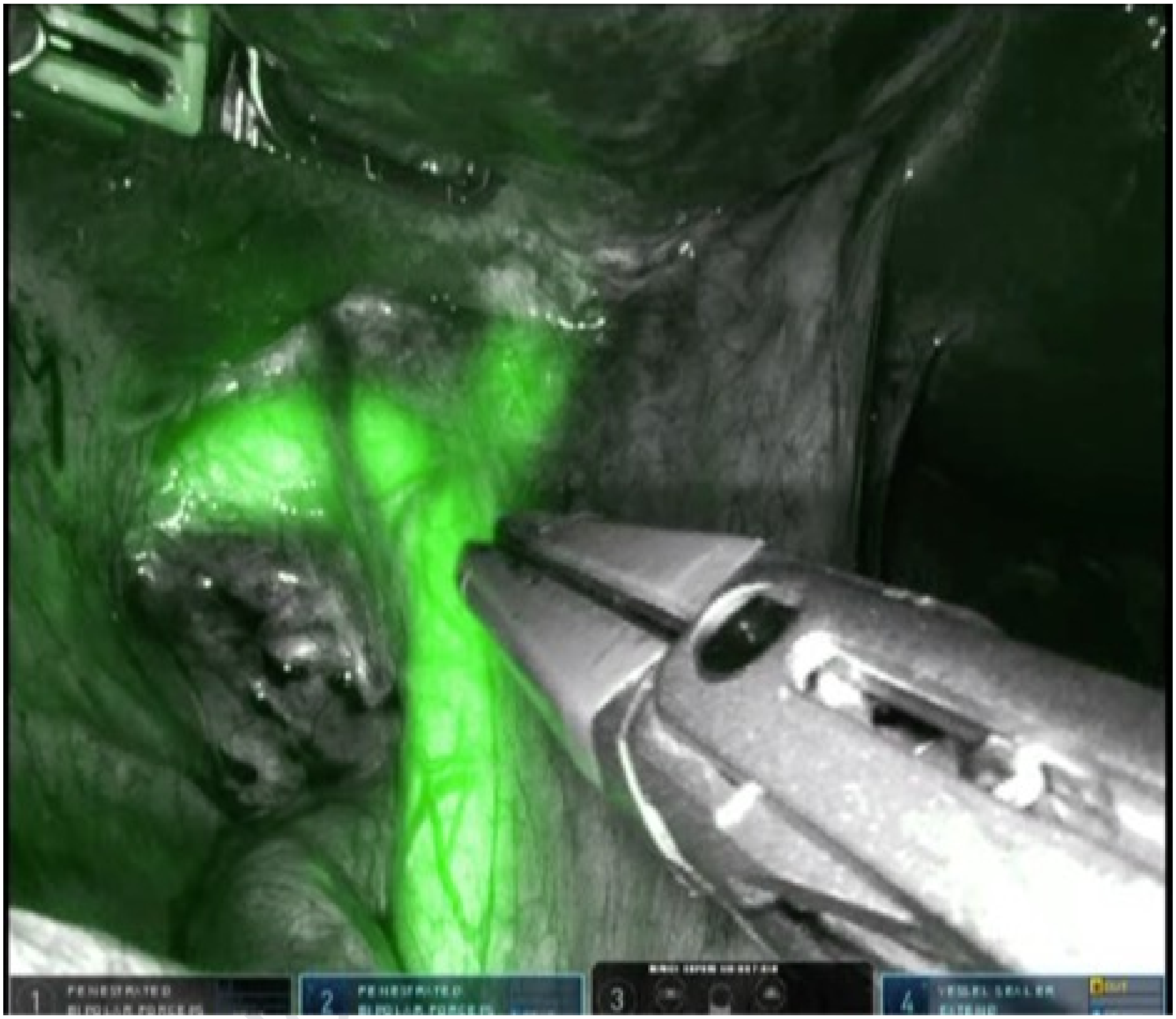
Author	Year	No. of HCC patients	Minor/major resections	Complications rate	Hospital stay	Oncologic follow-up data
Lai et al. (48)	2013	42	32/10	3 (7.1%)	6.2 (days, mean)	n.a.
Wu et al. (49)	2014	38	n.a.	3 (8%)	7.9 (days, mean)	n.a.
Chen et al. (50)	2017	81	47/34	4 (4.9%)	7.5 (days, median)	3-years DFS 72.2% OS 92.6 %
Magistri et al. (51)	2017	22	20/2	2 (9.1%)	5.1 (days, mean)	n.a.
Wang et al. (52)	2018	63	63/0	7 (11.1%)	6.2 (days, mean)	3-years DFS 71.9% OS 97.7%
Khan et al. (53)	2018	34	23/11	12 (35.2%)	4 (days, median)	During a F-U of 75 months 44% patients had recurrence of which the majority (n=10) recurred in the liver

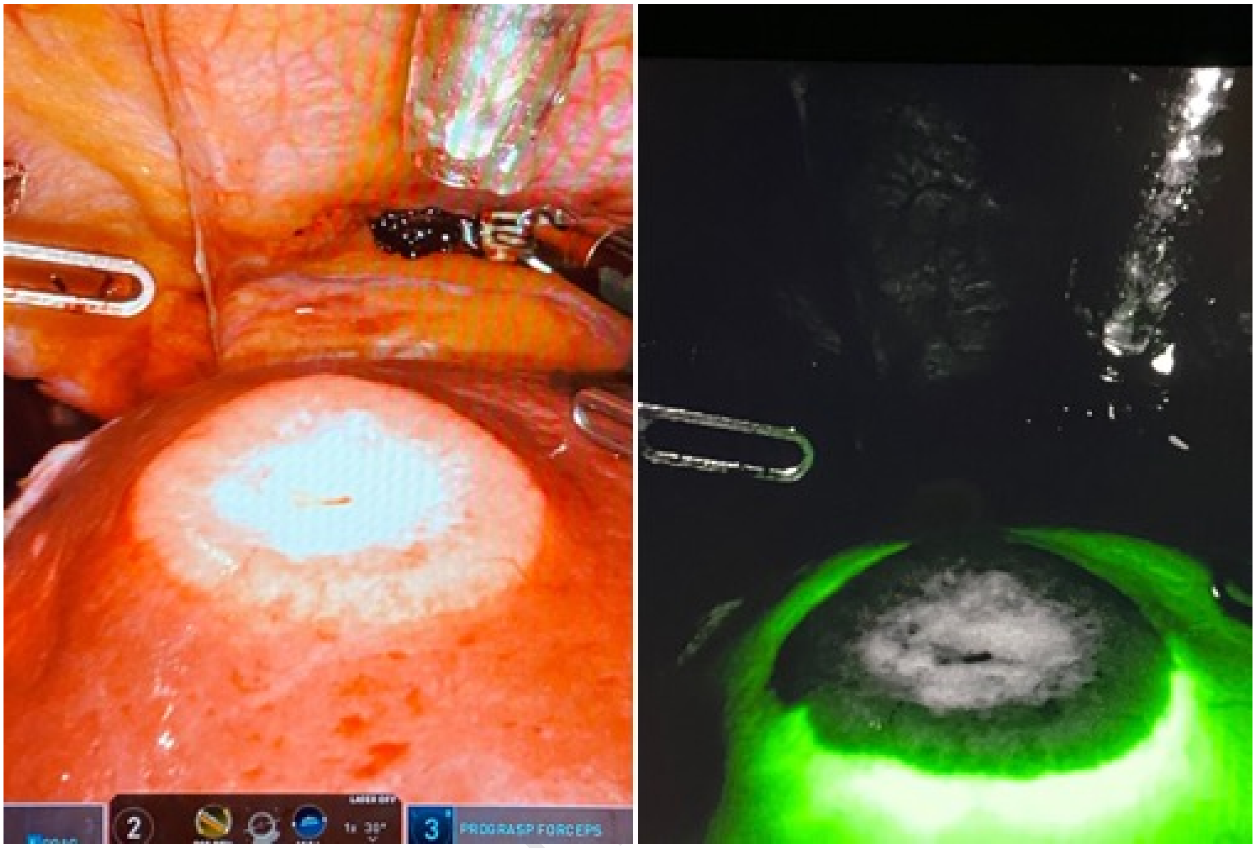
Table 2. Robotic resection for CRLM in literature

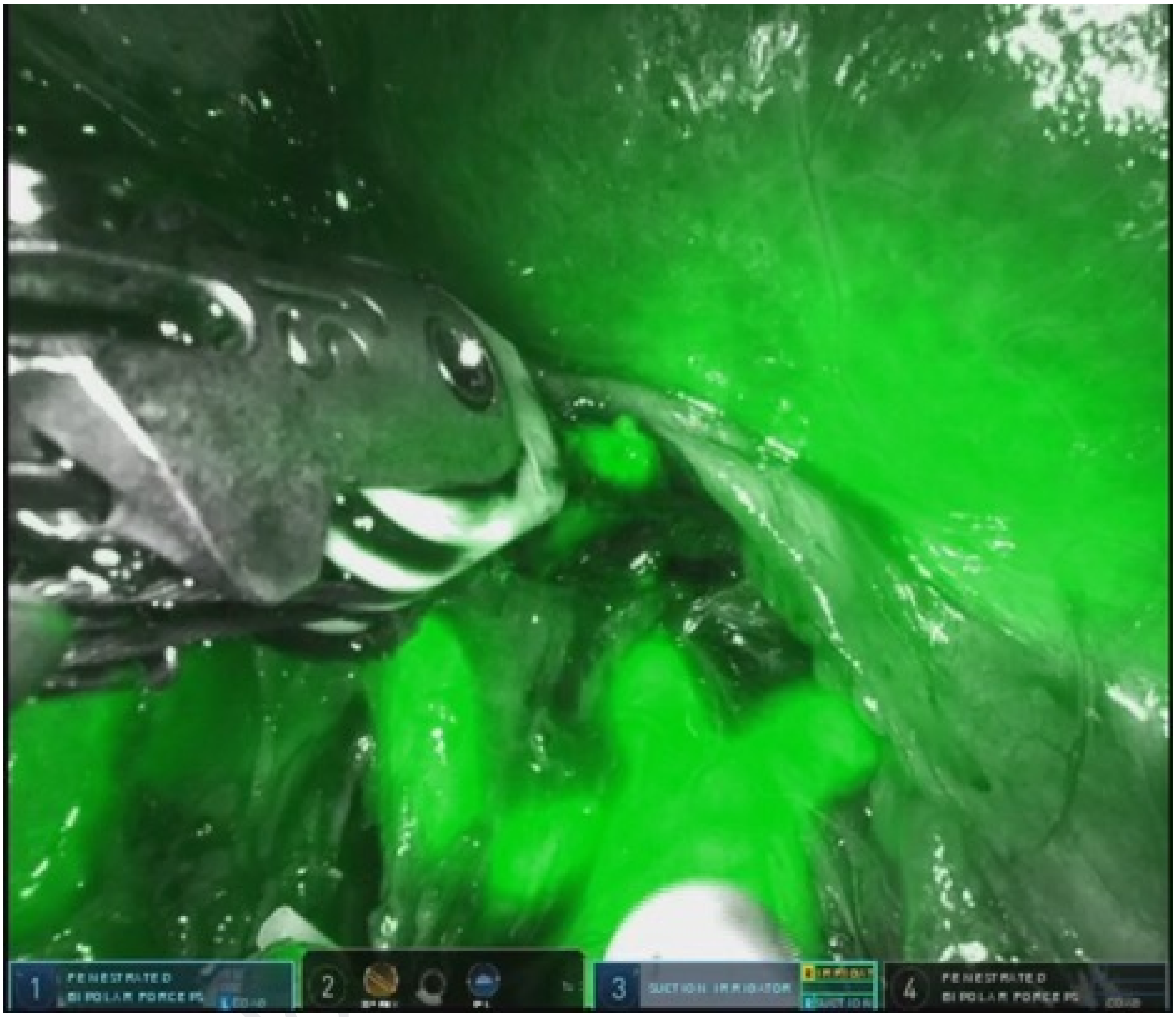
Author	Year	No. of patients	Minor/major resections	Complications rate	Length of hospital stay	Survival
Beard et al. (20)	2019	115	97/18	36 (31.3%)	5 (days, median)	5-years OS 61%, DFS 38%
Guerra et al. (54)	2019	59	78/4	16 (27%)	6.7 (days, mean)	3-years OS 66.1%

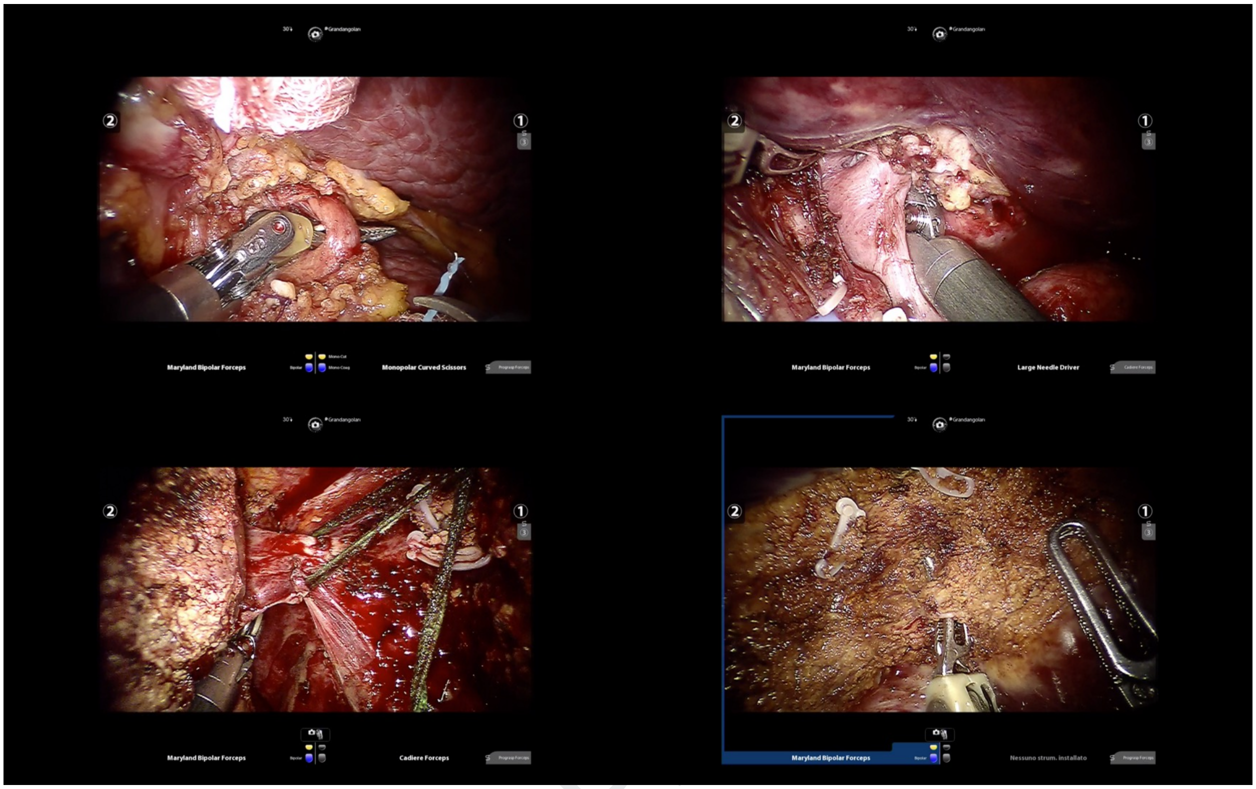

CONMED

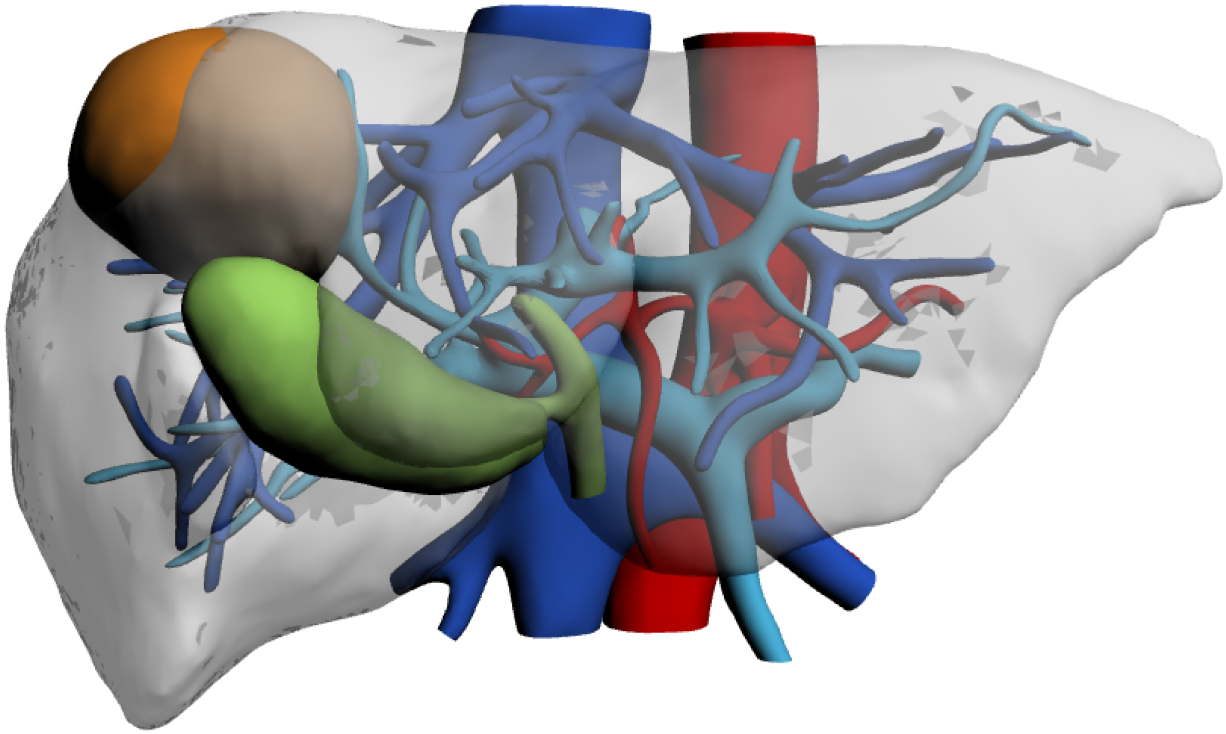

AIRSEAL




2
3
PROGRASP FORCEPS


1
FENESTRATED
BIPOLAR FORCEPS
2
3
SUCTION IRRIGATOR
4
FENESTRATED
BIPOLAR FORCEPS


Maryland Bipolar Forceps
Monopolar Curved Scissors
Maryland Bipolar Forceps
Large Needle Driver
Maryland Bipolar Forceps
Cadiere Forceps
Maryland Bipolar Forceps
Nessuno strum. installato



Highlights:

- Robotic surgery is an important tool in the armamentarium of liver surgeons
- Outcomes of robotic liver resection for hepatocellular carcinoma and colorectal liver metastases are comparable to laparoscopy and open
- Advanced procedure can be safely performed in expert centers
- Robotic surgery has great potential for further future technological developments

Data are available for sharing upon request to the corresponding author

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