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Technical Note

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Technical tips for indocyanine green-guided minimally invasive anatomical liver resection

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Abstract
Minimally invasive anatomical liver resection is increasingly feasible due to the improved availability of preoperative 3-dimensional (3D) reconstruction of the liver as well as endoscopic cameras with near-infrared indocyanine green fluorescence overlay visualization. In this article, we share our experience and perceived benefits of anatomical liver resection with preoperative 3D liver reconstruction, provide technical tips to improve success at pedicle isolation and address common pitfalls that may be encountered by adopters early on their learning curve.

Keywords: Anatomic resection, indocyanine green, negative-staining, minimally invasive hepatectomy

INTRODUCTION
Anatomical liver resection (ALR) has been defined by an international expert committee at the Precision Anatomy for Minimally Invasive Hepatobiliary Pancreatic Surgery Consensus in 2021 as the complete removal of the liver parenchyma confined within the responsible portal territory[1]. The preference for ALR is still guided largely by the location and size of the tumor. Often, the learning curve required to reliably and consistently secure the inflow pedicle for true anatomical resection in minimally invasive surgery (MIS) is daunting and may deter surgeons from pursuing this technique routinely. However, the ability to perform anatomical resections as part of a minimally invasive liver surgeon's armamentarium is especially beneficial

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for deep lesions so as to avoid significant residual ischemic parenchyma, which has been associated with increased complications, prolonged hospitalization, and poorer overall survival in hepatocellular carcinoma (HCC)[2]. ALR has also been shown to have oncological benefits in HCC with microvascular invasion[3].

In our practice, we have also found benefits in ALR for lesions that are poorly defined on sonography. With improved quality of cross-sectional imaging and surveillance regimens, lesions may be radiologically detected for their arterial enhancement pattern but poorly visualized during intraoperative sonography, especially in cirrhotic nodular livers or in cases of viable disease post-thermal ablation. In addition, while hypothesized in literature to be oncologically beneficial for HCC, colorectal liver metastases that have shown significant response post-neoadjuvant intent chemotherapy may also be sonographically challenging to detect. As such, select patients with colorectal liver metastases may also require ALR for complete excision.

With the availability of preoperative 3-dimensional (3D) reconstruction of the liver and the improved technology of indocyanine green (ICG) fluorescence guidance with overlay visualization, MIS ALRs such as segmentectomies and subsegmentectomies as described by Tokyo 2020 terminology are also more feasible in spite of complex or curvy-linear resection lines[1]. Surgeons can opt for resections with improved parenchymal preservation as opposed to more conventionally selected resection lines of sectionectomies.

This article aims to provide surgeons with technical tips for negative staining ICG-guided ALR and address commonly encountered pitfalls in its early adoption.

TOOLS TO FACILITATE ALR

High-quality triphasic CT with pre-op 3D reconstruction

With the availability of high-quality computer tomography (CT) images, a 3D reconstruction of the liver, including its portal venous (PV) and hepatic venous (HV) branches, can be readily generated. In our practice, we import axial PV 3 mm CT cuts into a software - Liver Analysis Synapse 3D (Fujifilm, Tokyo, Japan). We rely on the reconstruction of the PV, HV, and inferior vena cava branching pattern alone in our preoperative planning, omitting the arterial reconstruction, as we prefer the Glissonean approach for the inflow pedicle. PV branches beyond the third-order division are also more consistently visualized on CT due to their larger caliber and, therefore, more reliably reconstituted, although on occasion, may require manual input for accurate 3D reconstruction - particularly if the planned resection is a subsegment or single cone unit. With the additional projection of the tumor into the 3D model, the 3D reconstruction serves as a useful visual tool for appropriate preoperative selection of the inflow pedicles necessary to encompass the lesion with appropriate surgical margins. [Figure 1].

We find the 3D reconstruction software additionally useful for the reasons listed below.

1. Segmental resections or sub-segmental resections

Selection of the inflow pedicle of interest allows the software to generate a simulated boundary, which will then facilitate decision-making process for suitability of isolated segmental or subsegmental resections, to maximize parenchymal preservation without compromising oncological margins.

2. Preoperative recognition of anatomical variants

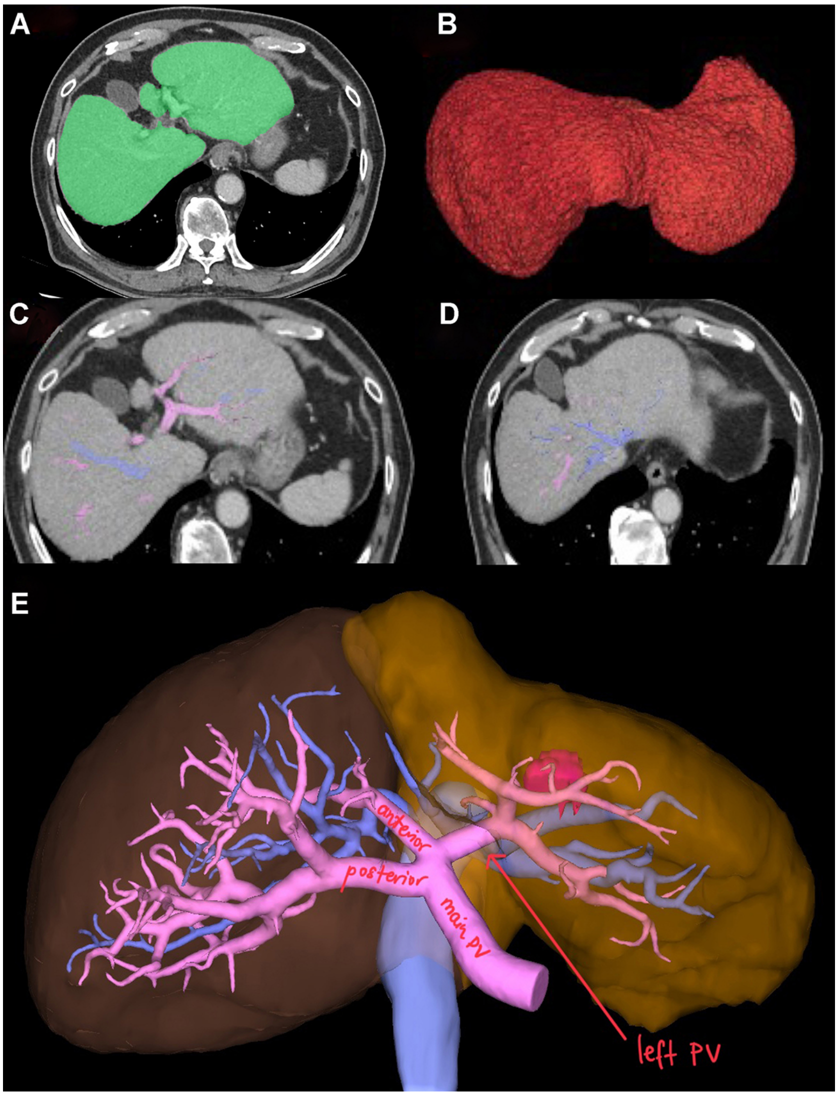

Figure 1. (A) The Synapse 3D software isolates the liver from each available axial cut of the CT. This can be manually fine-tuned where necessary, as the spleen may occasionally be misidentified as liver, especially when the lateral segments come into close contact with the spleen; (B) A 3D image of the liver is constructed, allowing the surgeon to visualize the surface contours of the liver; (C and D) The portal vein inflow branches are highlighted in pink and the hepatic vein branches are highlighted in blue; (E) A 3D view of the liver is then reconstructed, which can be rotated in any direction to provide the surgeon with spacial clarity. In this image, the left inflow is selected to demonstrate its corresponding simulated boundary. Notably, the posterior sectoral PV arises directly off the main PV, and the anterior PV and left PV bifurcate thereafter. 3D: 3-dimensional; CT: computer tomography; PV: portal venous.

While the left inflow is fairly consistent, the right anterior and posterior sections often have variations. Posterior segments may have duplication inflow pedicles that supply the anterior sector, and similarly, a duplication branch may arise from the anterior sector that supplies the posterior segment[4]. If unrecognized preoperatively, systemic ICG administration will result in a demarcation line that does not completely negatively stain the area of interest. Preoperative 3D reconstruction addresses this concern as the simulated resection boundary will highlight the variation accordingly.

3. Dynamic liver remnant volumetry calculation

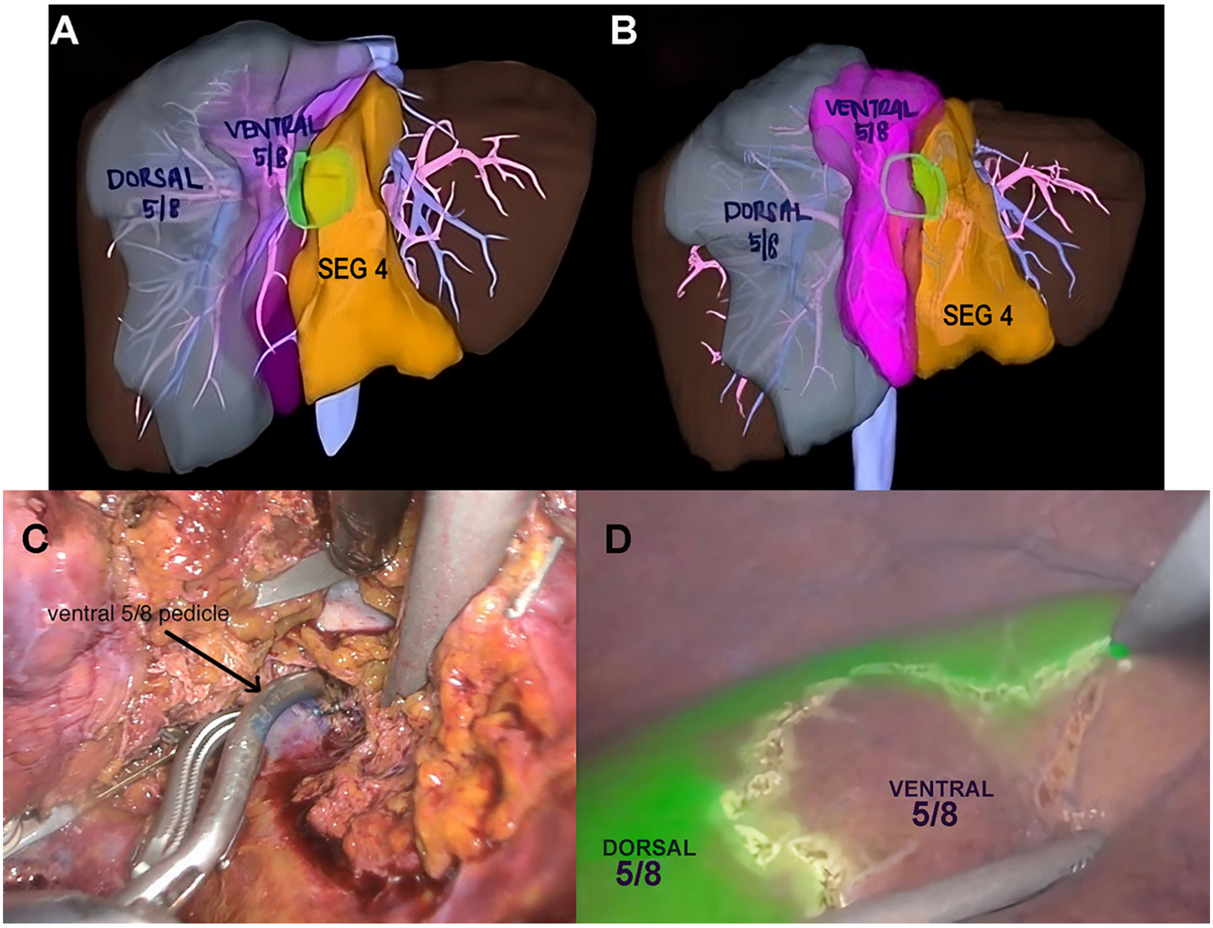

Figure 2. (A and B) The tumor outlined in green straddles segment 4 and segments 5/8. This patient has a dominant dorsal segment 5/8 of 512 mL and a smaller ventral segment 5/8 of 178 mL. In order to preserve volumetry, a central hepatectomy sparing dorsal segment 5/8 is performed. 27.2% of the liver is spared; (C) This demonstrates the clamping of the inflow pedicle of the ventral segment 5/8 pedicle. The ischemic line is then visualized on the surface of the liver and the pedicle is thereafter ligated definitively, followed by systemic intra-venous ICG administration; (D) The negatively staining ICG on the liver capsule along the lateral border of ventral segment 5/8 correlates well with the simulated boundary obtained by the 3D reconstruction in (B). As is often noted, the anatomical boundary is not a linear line. The cut line is marked with diathermy, respecting the true anatomical boundary to guide dissection in the anatomical plane. # Seg 4: 166 mL (8.8%); # Dorsal anterior section: 512 mL (27.2%); # Ventral anterior section: 178 mL (9.4%). ICG: Indocyanine green; 3D: 3-dimensional.

In patients where parenchymal preservation is critical, volumetry calculation is readily available simply by varying the selection of inflow pedicle that results in modification of the simulated resection boundary. [Figure 2A and B].

4. Intraoperative comparison and guidance

Real-time comparison of the intraoperatively detected Glissonean branching patterns with the preoperatively derived 3D image is a useful guide to ensure accurate identification of the inflow pedicle. Upon clamping the pedicle, the ischemic line visualized on the liver capsule surface also has a useful correlation with the simulated boundary obtained in the simulation. This provides additional confirmation prior to the administration of systemic intravenous ICG. [Figure 2C and D].

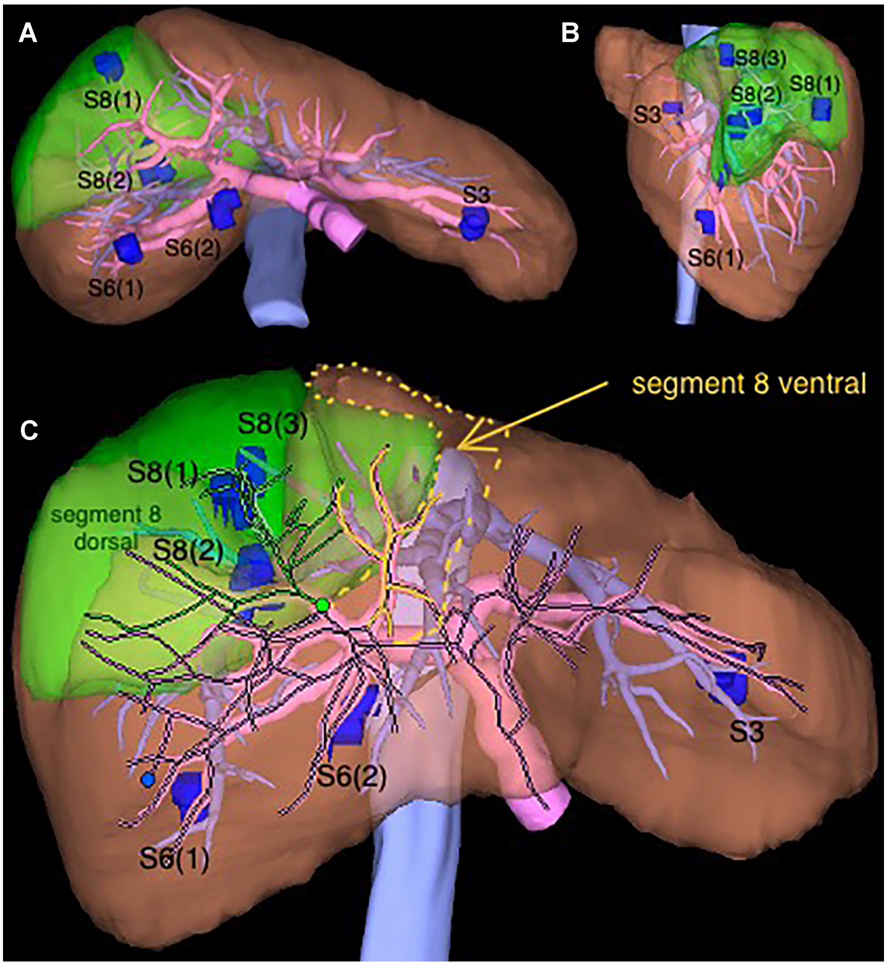

Figure 3. A case of colorectal metastases that have responded to neoadjuvant chemotherapy. The original location of the tumors is input manually into the 3D simulation to facilitate appropriate preoperative surgical planning. (A) There is a subcapsular lesion in segment 3 (labeled s3) and two subcapsular lesions in segment 6 [labeled s6 (1) and s6 (2)]. These lesions are easily accessible with a wedge resection; (B) This view demonstrates three lesions that are located in dorsal segment 8 [labeled s8 (1), s8 (2), s8 (3)], of which s8(1) and s8 (3) are subcapsular but s8 (2) is located deep; (C) S8 (2) is noted to be deep and close to the dorsal segment 8 inflow pedicle that is highlighted in green - when the dorsal segment 8 inflow is selected, its boundary is noted to encompass all three segment 8 lesions (demarcated in green in A-C). The decision is made to perform anatomical dorsal segment 8 resection, sparing the ventral segment 8 (outlined in yellow). 3D: 3-dimensional.

5. Facilitates tailored approach to pedicle of interest

A 3D portrayal of the branching pattern of the segmental inflow pedicles also facilitates decision making as to the optimal approach to inflow pedicle isolation - be it an extra-hepatic hilar approach, an intra-parenchymal Glissonean approach, or a combination approach. A tailored strategy for pedicle isolation should be adopted for reliable isolation of the inflow-pedicle[5]. The extra-hepatic Glissonean approach following Sugioka's "gate" theory is often feasible for second-order and third-order pedicle isolation between Laennec's capsule and the Glissonean sheath at the hilum[6]. Subsegmental pedicles tend to arise deep in the liver parenchyma, making a hilar approach challenging, especially in an attempt to isolate dorsal branches. In select cases, a combination approach may be beneficial - initial clamping of the section inflow pedicle followed by hepatotomy along the ischemic line to identify the segmental pedicle deep in the parenchyma. Alternatively, hepatotomy using anatomical landmarks guided by the 3D reconstruction together with intraoperative ultrasound (IOUS) guidance to isolate pedicles intra-parenchymally can be

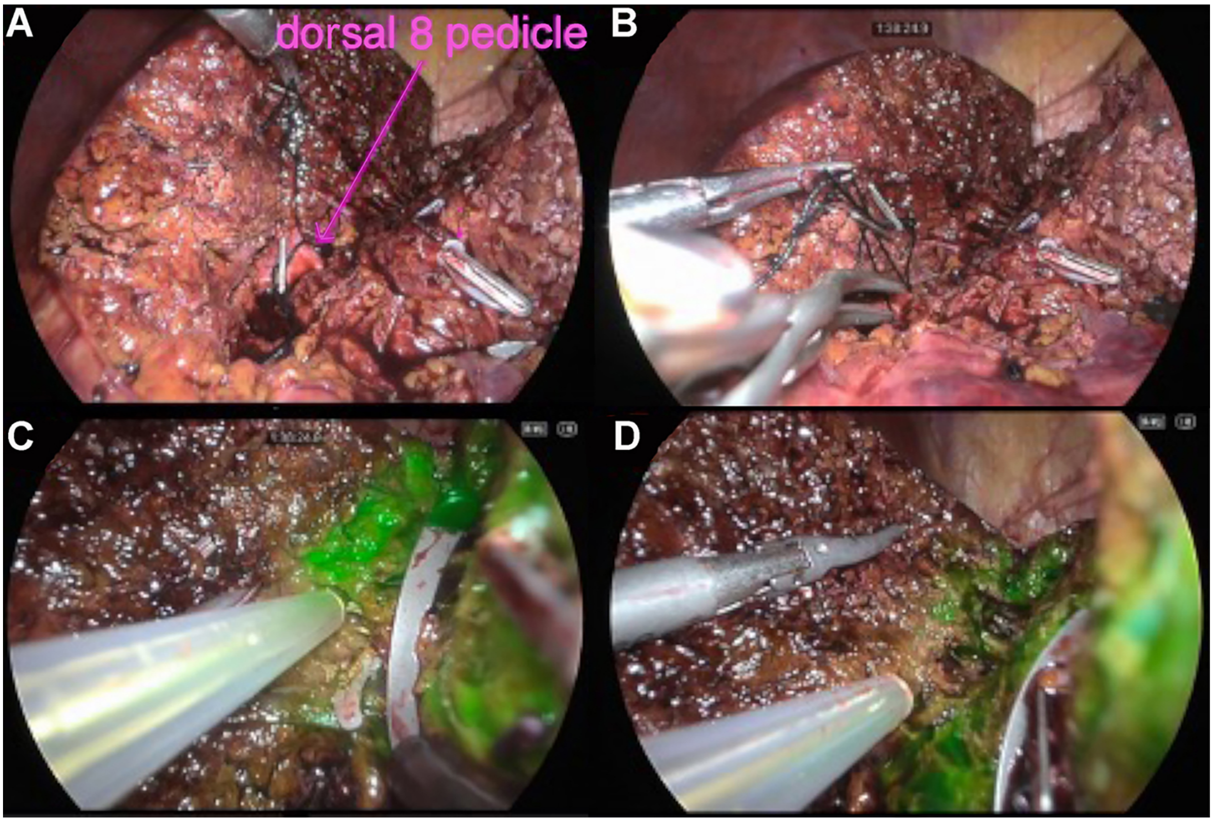

Figure 4. These images demonstrate the intraoperative hepatectomy views. (A) As there is the intention to preserve ventral segment 8, the decision is made to approach the dorsal pedicle via a hepatotomy rather than from the hilum. Hepatotomy is performed along the anterior fissure vein of the middle hepatic vein that has been identified with IOUS and with help from the 3D reconstruction. The dorsal segment 8 inflow pedicle is identified deep in the parenchyma and slung with a silk tie (marked with an arrow); (B) The dorsal segment 8 inflow pedicle is test clamped with a laparoscopic bulldog to confirm the ischemic demarcation and thereafter formally occluded with a Hem-o-lok; (C and D) Intravenous ICG is then administered for negative staining and the deep parenchymal transection proceeds with ICG-fluorescence overlay guidance in the anatomical plane. The ventral segment 8 does not stain with ICG as its inflow has been occluded. 3D: 3-dimensional; IOUS: intraoperative ultrasound; ICG: indocyanine green.

performed. [Figures 3-5].

ICG fluorescence guidance with overlay visualization

With the introduction of endoscopic camera systems with improved near infra-red sensitivity and overlay function, deep parenchymal transection for segmental and subsegmental resections with ICG fluorescence guidance is much more feasible in spite of the often curvilinear resection planes. Similar to Fujiyama *et al.*'s experience, we have found negative ICG staining less technically challenging than positive ICG staining[7]. However, in our early experience, we identified pitfalls of the negative ICG staining procedure and have since developed a more standardized approach to improve the success of anatomical ICG staining.

The nature of the negative ICG staining technique is that there is only one opportunity to administer intravenous ICG after clamping of the inflow pedicle, as thereafter, the perfused liver parenchyma will retain the contrast for an extended duration of time. As such, we recommend the following sequence prior to the administration of systemic ICG.

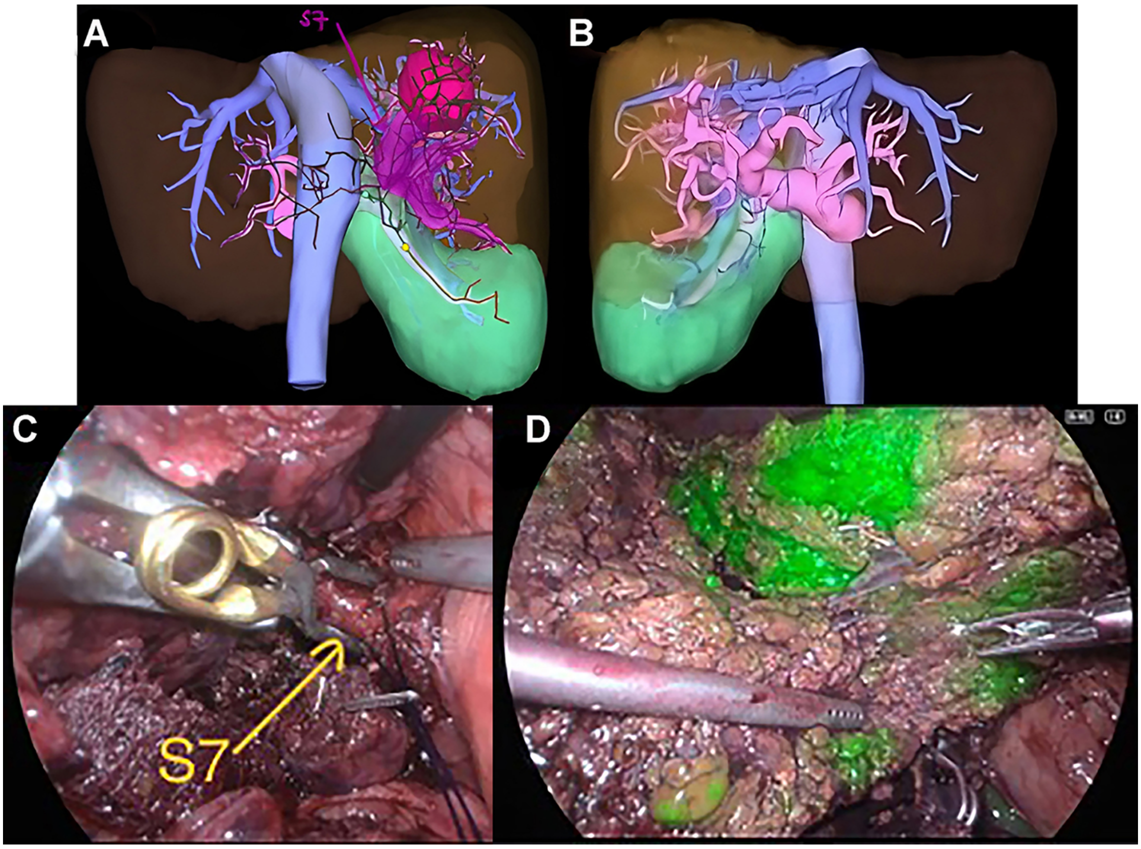

Figure 5. These images demonstrate the preoperative planning for a segment 7 resection and intraoperative hepatectomy views. (A) This image is a posterior view of the liver that demonstrates the location of the tumor (colored pink) and the segment 7 inflow pedicle highlighted in purple that branches; (B) This is an anterior view, whereby the segment 7 pedicle is poorly visualized due to its posterior and deep take-off. The segment 7 boundary is highlighted brown, and the segment 6 boundary is highlighted green. A segment 7 resection is deemed feasible for surgical margins. The segment 7 pedicle, in this case, is best accessed via a hepatotomy rather than from the hilum due to its posterior and deep take-off; (C) A hepatotomy is performed along the posterior surface of the liver adjacent to the inferior vena cava for intra-parenchymal isolation of the segment 7 inflow pedicle. The pedicle is doubly clamped to confirm the ischemic demarcation; (D) Systemic ICG is then administered for negative staining of segment 7. Liver parenchyma transection then proceeds along the demarcation line with ICG-overlay guidance. ICG: Indocyanine green.

1. Test-clamp the pedicle of interest with a laparoscopic bulldog.

2. Assess for the ischemic line on the liver capsule that correlates with the simulated boundary obtained from the preoperative 3D reconstruction. This may, on occasion, be challenging to visualize in cirrhotic livers where the ischemic demarcation is not easily discerned.

3. IOUS to ensure that the pedicles leading to the tumor have no detectable flow on Doppler, and that the rest of the liver segments in that section of the liver have preserved perfusion.

4. Ideally apply a Hem-o-lok clip across the pedicle prior to ICG administration. Alternatively, apply two laparoscopic bulldog clamps if the pedicle is difficult to encircle without deeper parenchymal transection. Cross-contamination of the ICG demarcation line may occur if the clamp on the pedicle is not completely occlusive, and the initially sharp demarcation line visualized will gradually be lost.

Pedicle isolation under Pringle's maneuver is preferred as the collapsed pedicles are often easier to encircle. In addition, if a Pringle's snare is exteriorized inferiorly for the maneuver, tightening the snare provides countertraction on the hepatoduodenal ligament to facilitate hilar plate dissection for entry at the "gates".

Modern endoscopic camera systems have improved near-infrared sensitivity. As ICG uptake in the perfused liver intensifies gradually with time, it is advisable to administer intravenous ICG at a low starting dose. We routinely utilize 0.25 mg/body, and have found that occasionally, a top-up to a total of 0.5 mg/body is required. A top-up may be required in cirrhotic patients, whereby the initial ICG staining is noted to be slow, and as such, the demarcation line is initially poorly visualized. If technology is available, surgeons can adjust the intensity of the fluorescence by adjusting the near-infrared gain - starting with high gain and decreasing to medium or low gain as the case progresses to reduce the glare from the positively stained parenchyma as it gradually intensifies with time. The ICG overlay function enables recognition of the ICG demarcation line in the deep parenchymal transection plane. As such, parenchymal transection proceeds rapidly as no pedicle branches are encountered in the anatomical plane, only hepatic vein branches.

Liver retraction for optimal exposure to facilitate deep parenchymal transection

We also routinely utilize a modified version of the Pulley Maneuver for liver traction to facilitate plane dissection. Initially described by Kim *et al.*, we use a similar method of applying Stratafix Symmetric (15 cm, Ethicon Inc., Somerville, NJ, USA) to the liver and to the peritoneum of the diaphragm to gradually increase traction as the parenchymal transection deepens[8]. We modify the method by retaining the needle intra-abdominally for the duration of the liver resection such that we are able to change the location of the pulley on the diaphragm - with gentle retrograde retraction, the barbed suture can be withdrawn from the first peritoneal anchor point, and re-stitched to the next suitable location. This is atraumatic to the diaphragm as long as care is taken not to include muscle fibers in the initial bite through the peritoneum. We have since switched to this traction technique and prefer this technique to a previously described rubber-band traction technique by Choi *et al.*, as it eliminates the need for extracorporeal exteriorization of the suture and also enables retraction in directions that are above the costal margin[9]. The modification is especially useful as the parenchymal transection progresses and there is a need to change the angle of retraction, and also reduces the need for multiple lengths of suture. The Stratafix Symmetric is durable such that its barbs retain their form in spite of being pulled retrograde through the peritoneum, and are able to maintain traction on the new pulley site. [Figure 6].

Maximizing the benefit of ICG-guided resection to assess for bile leak

Lastly, at the end of the resection, we use gauze to check the cut surface of the liver as well as the hilar dissection area for bile leak. With the use of ICG overlay function, bile leak can be easily detected, as there will be fluorescence staining on the gauze as ICG dye has now entered the biliary system - if necessary, the pedicle can be reinforced with a suture or sealant glue. This is rarely required if the resection was performed in the true anatomical plane.

CONCLUSION

A conceptual understanding of Glissonean pedicle isolation is a prerequisite for successful ALR. With the availability of 3D reconstruction of the liver and improved ICG fluorescence overlay endoscopic functions, minimally invasive ALR is much more feasible. We hope that the abovementioned technical tips will serve as a useful guide for surgeons on their learning curve. As ALR increases in adoption, more high-quality data will be available in the future to conclusively determine the oncological benefits of anatomical resections for liver tumors to further support its use.

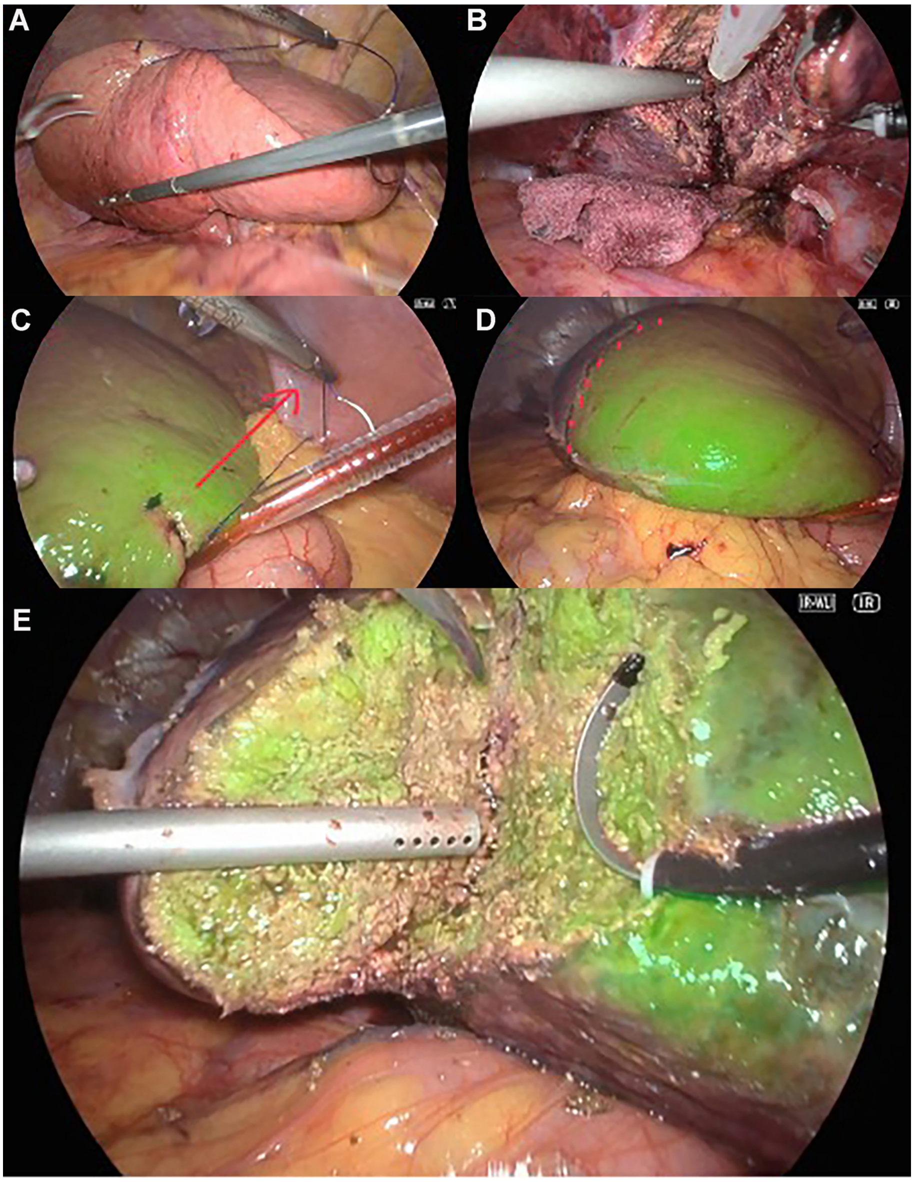

Figure 6. These images demonstrate the modified Pulley Maneuver using Stratafix Symmetric 3/0 for a segment 7 resection. (A) The Stratafix is sutured to the lateral liver edge and anchored to the anterior abdominal wall's peritoneum close to the midline (well above the costal margin), to provide superior and medial traction. The needle is retained intracorporeal for the duration of surgery; (B) The liver remains suspended due to the traction by the Stratafix pulley system. Only one assistant port is required to provide retraction whilst the hepatotomy deepens along the posterior surface of the liver, adjacent to the inferior vena cava, to isolate the segment 7 inflow pedicle; (C) Once the pedicle is isolated and clamped, ICG is administered systemically and segment 7 is negatively stained. The right triangular ligament is released to mobilize the liver, and the Stratafix needle is pulled in a gentle retrograde direction off from the prior peritoneal anchor point and now sutured to a new pulley site, the left lateral diaphragmatic surface. The left lateral retraction is further enhanced by tilting the patient's bed position, to maximize the effects of gravity; (D) The ICG demarcation line between the negatively stained segment 7 and segment 6 is now medialized (demarcated by the dotted line); (E) Parenchymal transection can now proceed with ICG-overlay guidance in the anatomical plane. ICG: Indocyanine green.

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Authors' contributions

Made substantial contributions to the conception, design, and drafting of this manuscript: Thiruchelvam N, Ong SY, Kim JH
Made substantial contributions to material support: Thiruchelvam N, Ong SY, Kim JH
Made substantive contributions to the revision of this manuscript: Thiruchelvam N, Chiow AKH, Tan HJ

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All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

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