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Medical **R**eview **Laparoscopic Liver Resection as a Less Invasive Treatment Option for Hepatocellular Carcinoma**

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Laparoscopic Liver Resection as a Less Invasive Treatment Option for Hepatocellular Carcinoma

Improving the Safety of Laparoscopic Surgical Procedures with Intraoperative Contrast-Enhanced Ultrasound and Puncture Guides

The clinical application of laparoscopic partial liver resection (including marginal liver resection) has been expanding in Japan since it was included in the list of therapeutic procedures covered by the Japanese national health insurance system. In parallel with the growing clinical acceptance of relatively less invasive radical surgical therapy for hepatocellular carcinoma, there has been steady improvement in the performance capabilities of diagnostic ultrasound systems, which are indispensable for ensuring the quality and safety of laparoscopic surgical procedures.

An ultrasound transducer designed for laparoscopic surgery known as the PET-805LA has recently been released in the market. This transducer is remarkable for its light weight and easy one-handed operation. It can acquire clear high-contrast

images for precise navigation during laparoscopic surgical procedures such as liver tumor resection. In addition, slots for holding and guiding puncture needles are provided at five locations on the head of the transducer, making it easier to accurately position the needle during puncture procedures. A center marker is also provided to clearly indicate the center of the image.

In this special edition, we have invited Dr. Satoru Seo, Department of Surgery from the Graduate School of Medicine, Kyoto University, to share his clinical impressions of the PET-805LA transducer used in combination with the Aplio™ Platinum Series diagnostic ultrasound system and to discuss the clinical usefulness of intraoperative contrast-enhanced ultrasound.

Introduction

In the treatment guidelines for hepatocellular carcinoma,¹⁾ liver resection by laparotomy or laparoscopic surgery is only recommended for patients with liver damage classification A or B and with 3 tumors or fewer. Ablation may also be an option for tumors measuring 3 cm or less. However, the issue of distant metastasis following liver resection or tumor ablation has not yet been fully clarified, and a multicenter study (the SURF trial) is currently underway to investigate the usefulness of resection and radiofrequency ablation for the initial treatment of hepatocellular carcinoma in patients with 3 tumors or fewer that measure 3 cm or less.

The number of laparoscopic liver resection (LLR) procedures for hepatocellular carcinoma has been rapidly increasing since it was included in the list of partial liver resection procedures covered by the Japanese national health insurance system in April 2010. According to the 12th Nationwide Survey of Endoscopic Surgery in Japan,²⁾ the number of laparoscopic surgical procedures performed for liver diseases at 1380 facilities across Japan between 1990 and 2013 (survey response rate: 48.4%) was 10,524, with 6059 (58%) of these

procedures performed for hepatocellular carcinoma, 2108 (20%) for metastatic tumors, and 1495 (14%) for liver cysts. With regard to surgical procedures, the largest number was 7415 (63%) for liver resection, of which 70% were performed in 2010 or later. The number of adverse events, such as cases in which laparotomy was required in order to control bleeding or in which other organs were injured during the procedure, was 206, and laparotomy was required during the procedure in 187 cases. The number of postsurgical complications, such as bile leak, wound infection, peritonitis, or abscess at the liver stump, was 523, and laparotomy was required after the procedure in 35 cases.

On the other hand, from the end of 2014, following a series of reports concerning fatalities in difficult LLR procedures, Japanese laparoscopic societies issued warnings regarding compliance when performing new surgical procedures not covered by the national health insurance system and also initiated fact-finding investigations. It is widely recognized that the degree of difficulty of LLR depends on the size of the tumor, the presence of major vessels in the vicinity, the amount of liver tissue to be resected, and the patient's liver function status.

In order to ensure that an LLR procedure can be performed safely, it is necessary to conduct a thorough preoperative evaluation of the patient as well as a detailed assessment of the technique and experience of the operator. In addition, researchers have been working to establish a scoring system for estimating the difficulty of LLR beforehand.³⁾ LLR should be performed only in patients who would be able to tolerate the equivalent abdominal surgical procedure and who have no obvious ascites or bleeding tendency.⁴⁾ It is considered that LLR is indicated for the treatment of single nodular tumors with clearly defined borders measuring 4 cm or less (larger for protruding superficial tumors) localized to the surface or rim of the lower or outer regions of the liver (segment 2 or 3) and with no invasion into surrounding structures (such as the main hepatic veins, portal vein, or diaphragm), with no severe compression or displacement, and with no embolization.

Improving patient's quality of life

In general, good short-term outcomes have been reported for LLR. At Kyoto University Hospital, nearly 30% of liver resections (approximately 100 cases per year, excluding partial liver resection for living donor liver transplantation) are now performed as laparoscopic procedures. The abdominal:laparoscopic surgery ratio is 7:3, which reflects the situation at university hospitals, which tend to treat patients with more severe disease. There is also a trend for the abdominal:laparoscopic surgery ratio to gradually reverse at general hospitals, and LLR is gaining wider acceptance as a less invasive treatment option.

Dr. Seo notes that the most important advantage of LLR is that it avoids the need to make a large surgical incision in the abdominal wall, allowing the patient to resume his or her normal activities more quickly and also improving the patient's overall quality of life. In liver surgery, an inverted T incision is made, cutting through the rectus abdominis muscle and the external oblique muscle. In the past, the idea "Great Surgeon, Big Incision" was widely accepted because a large incision makes it easier to deal with unexpected bleeding. However, it is now increasingly recognized that the surgical incision has significant effects on the patient's quality of life.

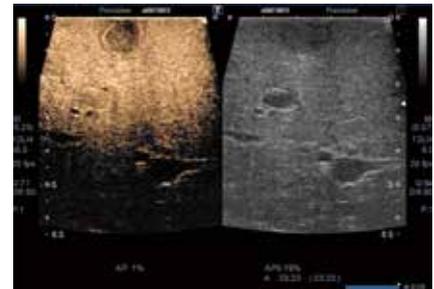
Based on the results of an anonymous questionnaire survey of living donors, the most frequently reported postoperative symptoms were a sensation of tightness and a loss of skin sensation, and these symptoms had not resolved in 18% of the donors even 1 year after the procedure.⁵ Patients with hepatocellular carcinoma face great physical and mental challenges, particularly due to the high recurrence rate and the frequent need for repeat treatment. Therefore, in addition to improving survival rates, it is important to develop less invasive curative treatments that allow patients to continue working and also enjoy leisure activities.

Dr. Seo and his group have conducted a comparative study involving 69 patients with liver metastasis of colorectal carcinoma who had undergone partial liver resection or partial marginal liver

resection. The 24 patients in the laparoscopic surgery group were compared against the 45 patients in the abdominal surgery group. The results showed that the total hospital stay (12.1 days vs. 18.7 days, $p=0.02$, t-test) and the postoperative interval before the start of chemotherapy (34.5 days vs. 51.8 days, $p=0.0028$, t-test) were both significantly shorter in the laparoscopic surgery group than in the abdominal surgery group. Dr. Seo also observes that the application of a less invasive approach such as LLR may help to improve patient outcomes in a multidisciplinary treatment setting. We have now reached the point where the 5-year

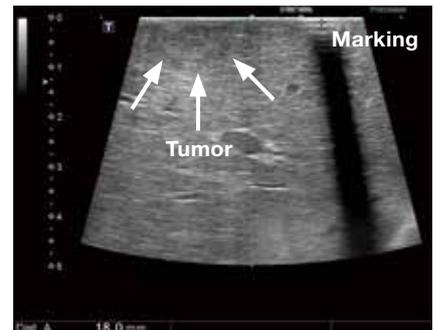
recurrence-free survival rate after LLR can be evaluated, allowing us to assess LLR as a therapeutic option for liver cancer that is by no means inferior to abdominal surgery in terms of the long-term cure rate and quality of life. It would be very desirable to establish a framework for conducting nationwide multicenter studies.

1. Evaluation of the main tumor, detection of intrahepatic metastases



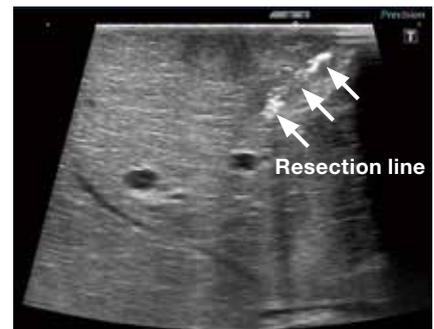
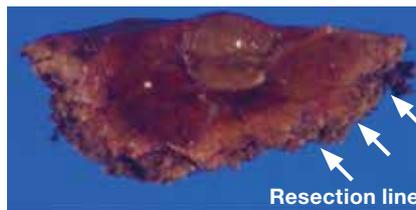
The borders between the tumor and the vessels to be conserved are more clearly visualized in contrast-enhanced ultrasound images.

2. Determination of the resection line, marking



The operator can operate the transducer with the non-dominant hand and perform marking with the dominant hand while observing the B-mode image.

3. Confirmation of the incision line and stump



The operator applies the forceps to the 2-cm protruding superficial hepatocellular carcinoma localized to segment 8, confirms the resection line in the B-mode image, exposes the vessels, controls bleeding, and resects the target lesion.

Figure 1. Role of intraoperative contrast-enhanced ultrasound (Data courtesy of Dr. Satoru Seo)

Ultrasound is indispensable for tumor localization and tumor resection.

In laparoscopic partial liver resection procedures, a 2-cm to 4-cm paraumbilical incision is made, the laparoscope is introduced, the abdominal cavity is insufflated, additional 5-mm to 1-cm incisions are made at three or four locations, and surgical trocars are inserted. In addition, the abdominal cavity is observed using a transducer connected to a diagnostic ultrasound system. According to Dr. Seo, "Intraoperative contrast-enhanced ultrasound serves three main roles: <1> confirmation of tumor localization, <2> determination and marking of the resection line, and <3> confirmation of the incision line and the stump." (Fig. 1). Contrast enhancement using Sonazoid is performed during the procedure in all patients, permitting the visualization of structures that cannot be depicted by B-mode scanning. In addition, small tumors measuring 5 mm or less in the liver that are undetectable by preoperative contrast-enhanced MRI or B-mode scanning can be identified, permitting final determination of the number of tumors.

Clinical experience with the PET-805LA

A laparoscopic surgical procedure using the PET-805LA was performed for a female patient in her 60's. Two protruding superficial tumors measuring 5 mm or less were found in segment 8 by preoperative contrast-enhanced MRI. For such protruding superficial tumors, LLR is the treatment of choice because ablation procedures are associated with a higher risk that the tumor capsule may rupture, resulting in the spread of malignant cells. In intraoperative contrast-enhanced ultrasound images, the tumors appear white during the arterial phase immediately after the injection of Sonazoid and are not visualized (appear black) during the Kupffer phase, which follows the vascular phase (Fig. 1-1). Ideally, a tumor can be resected as a circular region with a sufficient margin around the entire circumference of the tumor. However, segment 8 is located in a relatively inaccessible part of the liver, and the plane of resection should therefore be viewed obliquely from above, which makes it difficult to achieve the desired angle. Taking this issue into consideration, compared to the margin on the rear surface, the margin on the front surface was increased by a factor of 1.5 times (to 1.5 cm). On the other hand, although the tumor was not visualized during the Kupffer phase (which is suggestive of malignancy), this finding was not observed for the sub-lesion. Therefore, only the main lesion was resected (Fig. 1-3).

Ultrasound imaging and tumor marking can both be performed by a single operator.

The PET-805LA (Fig. 2) can be used with a standard trocar measuring 12 mm in diameter. The field width of this transducer is 45 mm, the rotation angle is 130 degrees or more, and trapezoidal scanning is supported. Based on Dr. Seo's clinical experience, "The PET-805LA has a number of advantages compared to a conventional transducer: <1> it is extremely light and has excellent operability, <2> one-handed operation is possible, allowing a single operator to both manipulate the transducer and perform marking of the tumor, <3> the balance between stiffness and flexibility of the bending section is ideal, allowing the transducer to be easily applied to the rounded surface of the liver for stable image acquisition." In addition, it should be noted that special care is required when examining high-risk livers with severe fibrosis or patients with coagulation disorders. Dr. Seo notes, "The PET-805LA is judged to be very 'liver-friendly' because the stability of the tip of the transducer makes it easier to avoid applying excessive force to the liver."

With regard to image quality and tumor detectability, "Contrast-enhancement mode improves visualization of the borders of tumors and vessels, making it very useful for determining the resection line. The image quality and sensitivity are quite good in deeper regions in B-mode images." In this patient, a tumor located 2 cm below the surface of the liver was

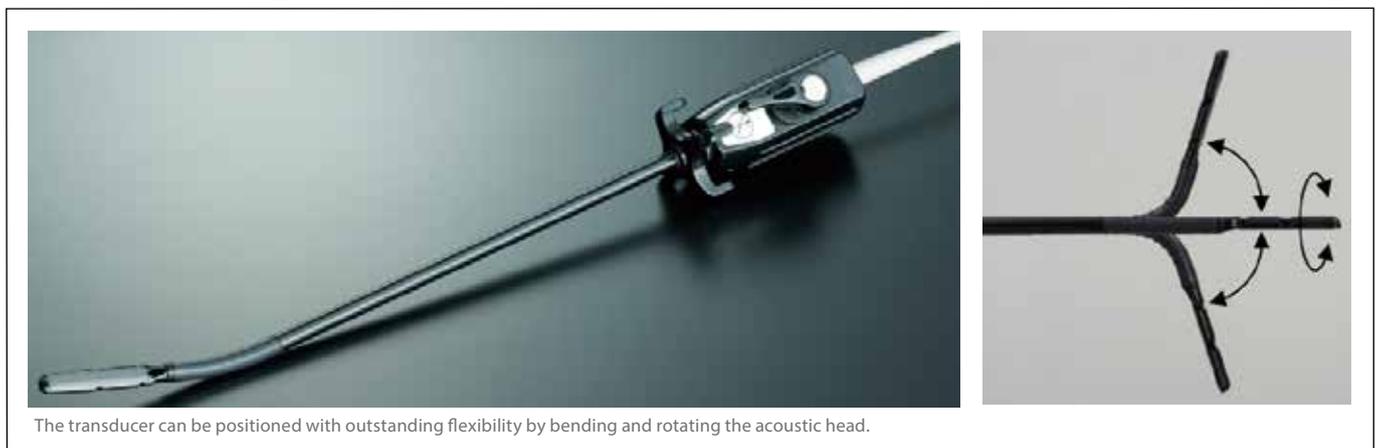


Figure 2. Ultrasound transducer for laparoscopic surgery PET-805LA (Data courtesy of TOSHIBA MEDICAL SYSTEMS CORPORATION)

resected with a margin of 1 cm to 1.5 cm. With the focal depth set to 1.5 cm in B-mode, acceptable image quality was maintained to a depth of approximately 3 cm, but an obvious deterioration in image quality was observed at approximately 3.5 cm or more. In contrast-enhancement mode, small tumors measuring 5 mm or less can be detected, and higher cure rates can therefore be expected.

If small tumors are detected in the deeper regions of the liver (not found in this patient), laparoscopic radiofrequency ablation can be performed during the same session. The PET-805LA allows the operator to perform puncture procedures while holding the transducer and needle in one hand, with slots to hold and guide puncture needles (puncture position guide grooves) provided at five locations on the head of the transducer (one at the tip and the other four on the sides). A guide mark on the rear of the transducer (one at the tip and the other four on the sides). A guide mark on the rear of the transducer head is displayed at the top of the ultrasound image, making it easy for the operator to determine the orientation of the transducer. In addition, a center marker is displayed, allowing the position of the needle to be precisely observed when the needle is inserted along one

of the slots provided on the sides of the transducer (Fig. 3). Dr. Seo also notes, "The needles used for radiofrequency ablation are 20 cm to 25 cm in length, so they tend to bend easily and may deviate from the target. The PET-805LA allows puncture procedures to be performed with the needle perpendicular to the target, which reduces the risk of needle deviation."

Conclusion

What is necessary to firmly establish the effectiveness of laparoscopic surgery? Dr. Seo explains, "One of the main safety concerns related to laparoscopic surgery is whether it is possible to deal with unexpected bleeding. In patients who are candidates for LLR, it is our objective to ensure that the safety and cure rates of LLR are comparable to those of abdominal surgery. The quality of life of every patient can be improved only if this objective is achieved. It is becoming ever more important in clinical practice to ensure the effectiveness of team-based medical care and techniques along with progress in gathering clinical evidence and developing medical devices. Laparoscopic surgery allows all medical staff,

including medical students and student nurses, to share a real-time view of the surgical field by observing the monitor. This not only promotes transparency and information-sharing in medical care, but can also be expected to be very useful for medical education."

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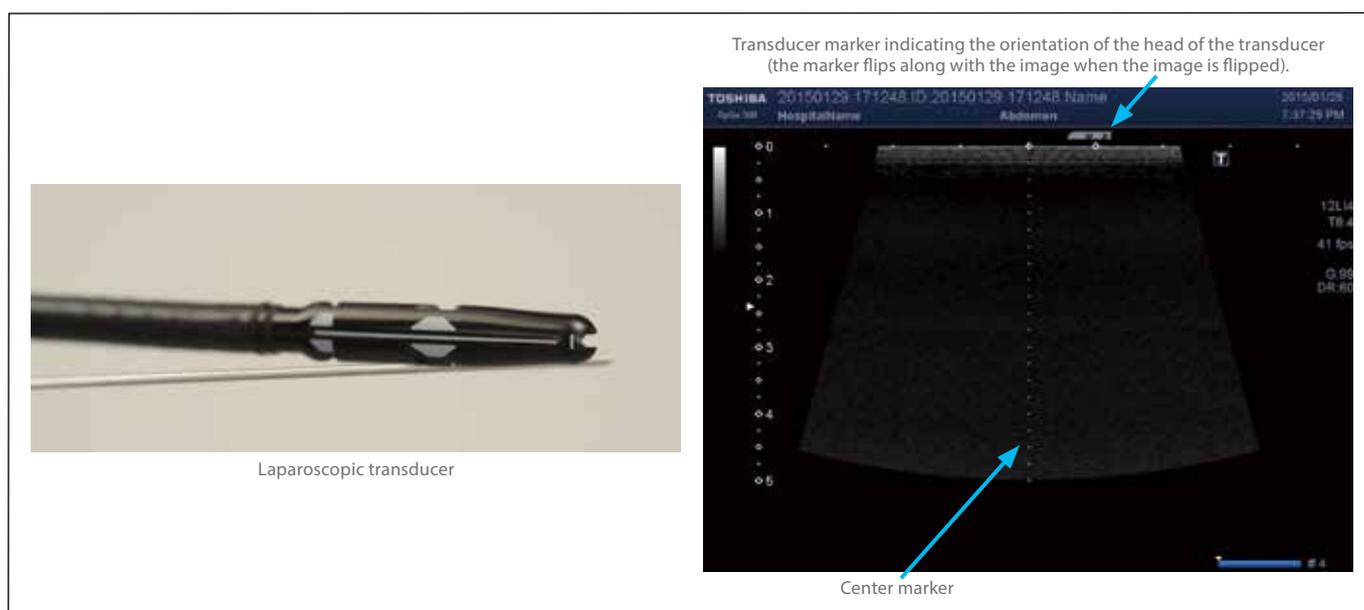


Figure 3. Needle positioning guide functions during puncture procedures (Data courtesy of TOSHIBA MEDICAL SYSTEMS CORPORATION)

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