

# Routine Intraoperative Ultrasound for the Detection of Liver Metastases during Resection of Primary Colorectal Cancer – A Systematic Review

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## ABSTRACT

During the discovery of ColoRectal Cancer (CRC), 20% to 30% of patients have synchronous liver metastases. Ten to 30% of patients have non-evidence of Liver Metastases (LM) following preoperative imaging such as Contrast-Enhanced Ultrasound (CE-US), multi-slice Contrast-Enhanced Computed Tomography (CE-CT), Contrast-Enhanced Magnetic Resonance Imaging (CE-MRI), and Positron Emission Tomography-Computed Tomography (PET-CT). Today, IntraOperative UltraSound (IOUS) in open surgery and Laparoscopic UltraSound (LUS) in laparoscopic or robotic surgery are considered the “gold standard” for detecting liver metastases. The object of this review is to demonstrate the higher sensitivity and specificity of IOUS and LUS in the detection rate of liver metastases.

**Keywords:** IntraOperative UltraSound (IOUS), Contrast-Enhanced IntraOperative UltraSound (CE-IOUS), Laparoscopic UltraSound (LUS), Contrast-Enhanced Laparoscopic UltraSound (CE-LUS), ColoRectal Cancer (CRC), Liver Metastases (LM), staging.

## INTRODUCTION

Colorectal cancer (CRC) represents one of the most common solid tumours. Studies demonstrated that, during the discovery and course of CRC, almost 15% to 25% of patients have synchronous liver metastases (SLM), other 50% will develop them, while 10-30% will have unrecognized preoperative hepatic metastases despite the use of preoperative contrast-enhanced ultrasound (CE-US), multi-slice contrast-enhanced computed to-

graphy (CE-CT), contrast-enhanced magnetic resonance imaging (CE-MRI) and positron emission tomography-computed tomography (PET-CT). Hepatic resection offers by far the best opportunity for cure from CLM. Early detection improves the chances of life-prolonging treatment. Intraoperative ultrasound (IOUS) in open surgery and laparoscopic ultrasound (LUS) in laparoscopic or robotic surgery are considered the “gold standard” for detecting liver metastases at early stage. Their use seems to reduce the number of patients with

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unrecognized preoperative hepatic metastases, especially <1 cm liver metastases, giving the possibility of a major accuracy in staging the disease (1-3).

### Aim

The aim of our study was to assess the ability of IOUS, CE-IOUS, LUS, CE-LUS to detect additional liver lesions/metastases at primary CRC surgery using PubMed review articles published between 2000 and 2020, in order to demonstrate the more accurate detection of unrecognized liver metastases in patients during surgery for primary colorectal cancer.

### METHODS

A systematic electronic literature search was conducted through PubMed using the following key words: intraoperative ultrasound (IOUS), laparoscopic ultrasound (LUS), contrast-enhanced intraoperative ultrasound (CE-IOUS), contrast-enhanced laparoscopic ultrasound (CE-LUS), colon cancer, rectum cancer, liver metastasis, staging. Of the 90 studies found by using the above-mentioned search terms and object of each study, only 39 were included, the remaining 51 being excluded due to non-relevance to the topics.

The following inclusion criteria were used: English language articles, primary resection for CRC, preoperative use of CT-scan or MR or PET-CT, detection of intraoperative liver metastases not seen during preoperative imaging and change in initial treatment strategy. A total of 90 publications were identified, but only 39 proved to be potentially relevant and were thus retrieved for detailed evaluation and assessment of their reference list according to our inclusion criteria, while the rest of 51 did not meet our inclusion criteria. Both authors (DC and SL) have independently selected the studies.

### Current status of knowledge

When compared to preoperative CE-CT scan and US, IOUS detected a higher number of additional patients with liver metastases from 5% up to 14%. The use of LUS found more than 13% additional metastases compared to preoperative CE-CT (2, 3). Ferrero *et al* noted intraoperative changes in 26.4% of 140 patients (4-6). Hata *et al* saw that 25.6% of subjects had new lesions on intraopera-

tive exploration and hepatectomy strategy was altered in 18.5% of patients (7-10). Ankur J. Shah performed a single-centre prospective pilot study on IOUS and CE-IOUS. They found that up to 25% of patients had previously undetected hepatic lesions when intraoperative ultrasound (IOUS) of the liver was used during CRC resection, and CE-IOUS altered the diagnosis of non-enhanced IOUS in 19% of patients. IOUS and LUS showed an increased detection rate in liver metastases, including those <10 mm (11-13).

Also, CE-IOUS and CE-LUS had a higher sensitivity and specificity for detecting liver metastases compared to non-enhanced IOUS and LUS (1). Some studies have reported that IOUS had a 90-96% sensitivity for detecting liver lesions greater than 10 mm (14-16). Several surgical series (5-9) have reported that the superiority of IOUS to stage hepatic disease in CRLMs compared to various imaging modalities improvements over the years represented a challenge for the current role of IOUS. As expected, the rate of new CRLMs found by IOUS remains noteworthy (ranging from 8% to 21%). IOUS detects lesions not identified by preoperative imaging in up to 40% of patients and alters the surgical strategy in 25% to 50% of cases undergoing resection for CRLM (17, 18). In 38% of patients, IOUS differed from preoperative CT scan (20). Wiering *et al* analyzed the accuracy of CT and FDG-PET compared to IOUS. Both PET and CT were sensitive for detecting lesions of 2 cm in size. However, sensitivity declined rapidly when lesions were < 2 cm. Only 16% of lesions < 1 cm were detected preoperatively. They found that the sensitivity of PET/CT alone was 63% versus 93% when PET/CT was combined with IOUS. In 35% of cases, IOUS changed the surgical plan (6). CE-IOUS altered the diagnosis of non-enhanced IOUS in 19% of patients compared to preoperative CT positron emission tomography (PET) and MRI (11, 20). In contrast to these studies, some authors concluded that, with adequate preoperative staging, finding additional lesions during surgery had a very low rate (8, 21). Wagnetz *et al* found a change in surgical management attributable to IOUS in only 2.7% of cases (21). Bartosz Ryzdzewski *et al* used FDG-PET and noted that the positive predictive value for FDG PET was 93% with a change of only 2% when using IOUS (21). Although the use of IOUS or CE-IOUS is safe and efficient, this procedure is uncommon during colorectal resection owing to the need for addi-

tional operating time and specialist equipment as a result of non-availability of ultrasound training for colorectal surgeons (21). An accurate description of intraoperative findings by the colorectal surgeon is important for liver resection (LR) at the time of primary CRC resection and when considering cases for future LR (11).

## CONCLUSIONS

Intraoperative US is a safe and inexpensive procedure, which allows for the detection and characterization of nodules, locates vascular and biliary structures and makes the execution of anatomic or non-anatomic liver resection more

precise (25). The routine use of intraoperative ultrasound (IOUS) of the liver during primary CRC surgery is effective for detecting additional lesions from 2% to 20% of cases as well as for liver resection at the time of primary CRC resection and when considering cases for future liver resection (11, 26). Although the importance in changing strategy of IOUS/CE-IOUS, LUS/CE-LUS, this procedure continues to be uncommon during colorectal resection because the need for additional operating time and specialist equipment, both of which being explained by a lack of ultrasound training for colorectal surgeons (27). □

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