INTRODUCTION
Fluorescence-guided surgery (FGS) is a technique that has gained popularity in recent years due to its ability to provide better visibility of anatomical structures and real-time perception of organ perfusion during surgery.\(^1\) Indocyanine green (ICG) has been widely used since its Food and Drug Administration approval in 1954. In recent years, ICG Fluorescence Imaging (ICG-FI) has been used in various surgical procedures such as monitoring lymph nodes, testing blood supply during coronary artery bypass grafting, and cleavage of cerebral aneurysms.\(^2\) The use of ICG-FI for visualization of hepatobiliary structures during hepato-pancreato-biliary (HPB) surgery was first reported by Japanese surgeons in the late 2000s.\(^3\) The technique enables Real-Time Visualization of complex fluorescent structures that cannot be seen under traditional white light. It helps highlight extrahepatic bile duct anatomy, hepatic tumors, and hepatic segments based on the fluorescence properties of ICG and its biliary excretion. The real-time visualization and location of hepatic tumours can help surgeons perform therapeutic liver resections with reduced post-operative complications.

Fluorescence cholangiography is used to obtain fluorescence images of bile ducts after intrabiliary or intravenous injection of ICG.\(^4\) However, the limitation of fluorescence imaging is its low tissue penetration ability, which makes it challenging to visualize lesions deeper than 10mm from the liver surface.\(^5\) Despite this limitation, ICG-FI is relatively low-cost and widely available, and innovations in imaging systems are likely to increase its use in various surgical specialties. The fluorescence imaging method can provide the surgeon with real-time identification of a specific structure.

**Keywords:** fluorescence imaging, indocyanine green, hepatobiliary surgery, pancreatic surgery, real-time surgery, hepatocellular carcinoma
without using ionizing radiation, thus reducing the surgical procedure’s invasiveness and complications while preserving tumour-free tissues. In addition, several studies have validated the use of ICG-FI for precise liver tumour recognition and localization, supporting its potential clinical application in liver resection surgery. ICG-FI can provide a high yield of valuable data by visualizing the anatomical structures, delineating the tumour boundaries, displaying the vascular and biliary systems, and monitoring the hepatic function during hepatectomy.

The ICG-FI technique has recently gained attention in numerous areas of medicine, including hepatobiliary, pancreatic, colorectal, and breast cancer surgeries. It has the potential to change the paradigm of surgical navigation, mapping, and delineation, particularly in HPB surgery. This comprehensive review was done to understand better its potential applications in other surgical specialties.

**METHODS**

The present study utilized a systematic approach to gather information on the use ICG fluorescence in hepatobiliary surgery. A comprehensive literature search was conducted using several electronic databases, including PubMed/Medline, Embase, Cochrane, and Google Scholar. An expert in the field was also consulted to identify any missed articles or studies. The search was performed by using a combination of relevant keywords such as “ICG”, “Fluorescence”, “Real-Time Surgery”, “Hepatectomy”, “Hepatocellular Carcinoma”, “Liver Metastases”, “Extra-hepatic bile duct”, and “Cholangiocarcinoma”. The inclusion and exclusion criteria were established to ensure that only relevant studies were included in the review.

The studies that were included in this review had to meet the following criteria: (1) the study had to report on the use of ICG fluorescence in HPB surgery, including hepatocellular carcinoma, liver metastases, and extra-hepatic bile duct and cholangiocarcinoma, (2) the study had to be published in English, (3) the study had to be full-text articles, and (4) the study had to be either randomized or non-randomized clinical trials, observational studies, or case reports. Conversely, manuscripts that focused on the use of ICG fluorescence in other surgical fields were excluded from this review. After screening the studies by title and abstract, the full-text articles were reviewed.

The selected studies were then analyzed, and the relevant information was extracted. This systematic approach allowed us to understand comprehensively the importance of ICG fluorescence in HPB surgery. By utilizing the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) framework, we ensured our study was conducted with high rigour and transparency. The PRISMA methodology is a widely recognized and rigorous evidence-based approach to conducting systematic reviews, which identified 105 potential studies that met the inclusion criteria. Following initial screening and assessment for eligibility, 33 studies that were specific to the use of ICG fluorescence-guided resections in hepatobiliary surgery were included.

The final analysis included studies on the safety, feasibility, diagnostic accuracy, and prognostic value of ICG fluorescence-guided HPB surgery. The information gathered provides crucial insights into the current and potential use of ICG fluorescence imaging in HPB surgery, paving the way for further research and advancements in this emerging area of surgical navigation.

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RESULTS

ICG fluorescence-guided surgery during hepatectomy has shown promising outcomes in real-time monitoring of intraoperative liver function remnant. Several studies have investigated the use of ICG injection after arterial and portal vein clamping of the affected liver, providing real-time assessment of the function of the non-affected liver and reducing the risk of post-

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ICG, IndoCyanine Green; HCC, hepatocellular carcinoma

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hepatectomy liver failure. This technique has been employed both before and after hepatectomy to simulate the post-resection situation and control the non-resected liver. The administration of an intravenous injection of ICG at a dose of 0.25 mg/kg body weight has been utilized in these measurements. A study conducted in Japan demonstrated that ICG near-infrared fluorescence imaging enables visualization of hepatocellular carcinoma (HCC), hepatic perfusion, tumour perfusion, and the demarcation line after clamping, thereby aiding in the navigation of laparoscopic surgery. Surgeons introduced 2.5 mg of ICG following clamping or closure of the proximal Glissonean pedicles, which clearly delineated the fluorescent parenchyma from non-fluorescent areas and facilitated visualization of the resection line. In a Chinese study, the use of ICG observed with PhotoDynamic Eye allowed for the evaluation of the boundaries of HCC lesions and revealed small HCC tumours that were not visualized preoperatively in 50 patients. This method was considered a simple and safe tool that provides real-time imaging of HCC, aiding in liver resection and margin guidance, with high sensitivity for detecting new small HCC.

The initial application of near-infrared/ICG fluorescence for liver tumour identification was reported by Ishizawa et al. in 2009. This series expanded to include 170 subjects and 276 HCCs by 2013, with a false-positive rate reduced to 1%. Near-infrared fluorescence identified 273 out of 276 lesions (99%), including 21 grossly unidentifiable lesions. Morita et al. further evaluated ICG fluorescence imaging and demonstrated that ICG fluorography identified 73 out of 76 (96%) preoperatively diagnosed HCC lesions. Overall, near-infrared fluorescence sensitivity for HCCs was 96%, with a positive predictive value of 71.5%. Kudo et al. developed a technique for laparoscopic ICG fluorescence imaging and evaluated its efficacy in identifying subcapsular liver cancers during laparoscopic hepatectomy. This technique enables real-time identification of subcapsular liver cancers, facilitating the estimation of the necessary extent of hepatic mobilization and determining the appropriate hepatic transection line. Aoki et al. reported an intraoperative technique for identifying liver segments and subsegments using high-sensitivity near-infrared fluorescence imaging for anatomical hepatic resection.

In 33 out of 35 patients, stained subsegments and segments of the liver were identifiable (94.3%). Alternatively, Uchiyama et al. proposed combining a fluorescence navigation system using ICG and contrast-enhanced intraoperative ultrasound with Sonazoid for the detection of liver sections and segments. This combined approach has proven to be a useful and safe tool for performing liver resection. Recent studies have demonstrated that ICG fluorescence imaging accurately identifies primary and metastatic liver tumours. In a study involving 37 patients with hepatocellular carcinoma (HCC) and 12 patients with colorectal carcinoma (CRC) metastasis undergoing liver resection ICG-fluorescent imaging, following routine liver function tests, we successfully identified all microscopically confirmed HCCs (n = 63) and CRC metastases (n = 28) in the surgical specimens.

**DISCUSSION**

ICG fluorescence-guided real-time surgery is a promising technique in liver surgery, but certain limitations and biases must be considered when its effectiveness is evaluated. ICG fluorescence-guided real-time surgery provides critical real-time information for surgeons during liver surgery, including differentiation between abnormal and normal tissue and preservation of vital blood vessels. ICG fluorescence can also assist in monitoring liver function and identifying small hepatic lesions, making it a versatile tool in intraoperative imaging. Fluorescence cholangiography with intrabiliary injection of ICG is an effective method for identifying biliary lesions during surgery. However, its publication bias and variable injection timing impact the effectiveness of ICG fluorescence-guided real-time surgery. Studies that report positive outcomes preferentially may overestimate the effectiveness of ICG fluorescence-guided real-time surgery. Surgeons with limited exposure to the technique may achieve less favourable outcomes than those with extensive experience. ICG injection timing requires careful consideration based on the patient’s liver function and...
can be influenced by subjective factors, requiring standardized protocols to minimize bias and ensure consistency. While ICG fluorescence is valuable during surgery, it should not replace preoperative imaging and clinical evaluation. Cost may also be a limiting factor in adopting ICG fluorescence-guided real-time surgery in some healthcare settings.\textsuperscript{17-21}

**Conclusion**

In summary, using ICG-FI as an intraoperative navigation technology holds great promise for hepatic resection and clinical exploration in colorectal liver metastases, HCC, tumour boundaries, liver function testing, and the study of the extra and intra-hepatic biliary tree. The real-time high sensitivity of ICG-FI in identifying both minute and grossly unidentifiable liver cancer tumours enhances the precision of liver resection and the accuracy of operative cancer staging. However, it is important to acknowledge that the technique does have certain limitations. These limitations include limited tissue penetration and modest specificity, which can be mitigated by incorporating the gold standard of intraoperative ultrasound for the detection of deeper tumors. Further clinical studies are necessary to evaluate the sensitivity and specificity of ICG-FI in the context of hepatobiliary surgery.

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**Author Contributions**

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**Conflict of Interest**

The authors declare no conflicts of interest.

**Ethical Approval**

This is a review work. Ethical approval was not necessary.

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IndoCyanine Green fluorescence guided resections of hepatobiliary system


