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REVIEW PAPER / META-ANALYSIS

The application of ICG in surgical fields of medicine – a short narrative review

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Abstract

Background: Intraoperative near-infrared imaging using indocyanine green (ICG) has been increasingly used in procedural medical fields in recent years. The purpose of our work is to provide a general overview of the use of indocyanine green in procedural medical fields. We reviewed publications posted in PubMed, whose authors used ICG in their research, but also daily surgical practice. Many large studies have demonstrated the usefulness of this method. Currently, new directions for the use of this dye are being sought. In the future, the use of ICG in near-infrared (NIR) imaging may become a standard used in daily medical practice.
Material and methods: A review of the available literature was conducted using the PubMed. The search terms 'ICG', ''indocyanine green', 'indocyanine green fluorescence', and 'NIR' were used.
Results: We analyzed several dozen articles from the large database available in PubMed. ICG is currently used in many different fields of medicine. Below we list the applications found in this review.
Conclusions: Indocyanine green has demonstrated utility across various surgical disciplines within the medical field. A growing body of research has elucidated the multiple advantages conferred by this dye, thereby propelling its increased adoption by researchers and practitioners. Despite these advances, there remains a need for extensive research before ICG can be integrated into routine clinical applications.
Keywords: ICG, indocyanine green, fluorescence, near-infrared (NIR) imaging, intraoperative imaging

Introduction

The origins of indocyanine green (ICG) use in medicine date back to the 1960s, when it was approved for clinical use in the USA by the FDA (Food and Drug Administration). It was originally used mainly in ophthalmology

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[1,2]. Since its introduction, it has been the most widely used fluorescent dye. ICG is a tricarbocyanine dye with very high water hydrophilic properties. Depending on the indication, and the pathology one wants to detect, it can be administered intravenously (usually a dose of 5 mg) or topically, even submucosally (usually a dose of 5–6.25 mg) [3–5].

The fluorophore remains confined in the intravascular compartment until it is eliminated. In due course after excitation, it provides tissue perfusion information [6]. The imaging technique using ICG is based on the use of a medical CCD (charge-coupled device) camera to capture the near-infrared light that is emitted when the indocyanine green molecule binds to α1 lipoprotein in the blood, thus allowing visualization of tissues in the living body [7].

Initially, only a handheld NIR camera was developed to assess blood flow by detecting intravascular ICG fluorescence. Today, a laparoscopic camera is more commonly used, making ICG angiography available for use in minimally invasive surgery, both laparoscopic and robotic. The cameras used in laparoscopic and robotic surgery are designed to operate in both conventional white-light mode but are then activated in NIR mode after ICG is applied [8]. The excitation wavelength of ICG is in the near-infrared wavelength range between 750 and 810 nm, and the maximum fluorescence wavelength in plasma is 845 nm enabling distinguishing structures about 1 cm deep in the tissue [9,10]. The test is based on the administration of ICG into the body and stimulation with infrared light. Infrared fluorescence is then generated, which is then recorded with a photodynamic eye (PDE) and observed using contrast [4]. The procedure using indocyanine green is readily available, inexpensive to use, and, most importantly, non-toxic to the patient [3,7]. ICG has found wide application in the surgical fields of medicine. It is used both in elective procedures and for vital indications, providing intraoperative information on tissue, and organ perfusion, and thus having a significant impact on decision-making [11].

This short narrative review aims to provide the audience with possible-applicationsofICG fluorescence in everyday clinical practice.

Methods

A review of the available literature was conducted using the PubMed. The search terms 'ICG', 'indocyanine green', 'indocyanine green fluorescence', and 'NIR' were used.

Results

We analyzed several dozen articles from the large database available in PubMed. ICG is currently used in many different fields of medicine. Below we list the applications found in this review.

Pancreatic Surgery

In a study by Newton and colleagues, during pancreatectomy, dye reliably accumulated within malignant pancreatic tumors, thus showing very accurate tumor borders, which is invaluable for intraoperative assessment of margins and extent of disease [12].

Biliary Tract Surgery

Currently, ICG plays a significant role in identifying the cystic duct and common bile duct. The study, which was conducted by Broderick and colleagues, compared surgery time, conversion rate to open surgery, and hospitalization time, in patients who used ICG to visualize the bile ducts and without using ICG visualization. The results of this study are promising; in the group of patients who used indocyanine green imaging, leading to improved patient outcomes concerning operative times, decreased conversion to open procedures, and shorter length of hospitalization. However, there was no significant difference at 30 days after surgery in the two groups. Similar findings were presented in their review paper by Serban and colleagues. In conclusion, the use of ICG is considered a promising tool to increase the safety of biliary identification [13,14].

Liver surgery

It is also an indispensable part of liver surgery. It allows the detection of intrahepatic bile leakage after liver resection. In addition, liver tumors are imaged with ICG, which also provides the opportunity to identify well-differentiated hepatocellular carcinoma tumors [15]. Intraoperative ICG staining is considered important in minimally invasive liver resection. In Fujiyama's study, when ICG was observed through a camera system, a clear ICG border appeared on the liver surface between fluorescent areas, with the liver preserved, and non-fluorescent areas, with the liver resected. Significant in this study was the presence of a demarcation line both on the liver surface and within the parenchyma. The key role of intraoperative staining with indocyanine green was demonstrated in this study [16].

Mainly, two staining methods are currently in use: positive staining, where ICG is injected into the portal vein to stain the liver segment to be resected, and negative staining, where ICG is injected intravenously, staining the liver except for the segment with clamped inflow [17]. The need for standardization and further validation of oncologic outcomes of proposed methods can be a drawback, and this applies in all fields of use. Securing the surgical margin, intraoperative cholangiography, and detection of subcapsular hepatic tumors also reinforce the arsenal of the hepato-pancreato-biliary surgeon [18].

Colorectal surgery

ICG facilitates imaging of organs at risk of intraoperative damage, e.g.: ureters during rectal cancer surgery. When the tumor is located in a difficult area, fluorescence provides real-time angiography of the vascularization of the tumor area for vascular dissection, and thus safe intervention and greater oncologic purity [19]. It plays a very important role in assessing the perfusion of the rectal stump, which is important in assessing the risk of anastomotic leakage [20]. Fluorescence imaging with indocyanine green has been proven in many studies to be an effective tool for assessing anastomotic perfusion [21,22]. A regimen of administering the dye 2 times during each surgical procedure has been developed. First, ICG was injected intravenously after transection of the mesentery and central vessels along the planned transection line, but before the anastomosis was performed. Then, after the anastomosis is performed, another bolus is injected to confirm the perfusion of the anastomosis [19]. A study by Son and colleagues showed a decrease from 10% to 1–2% in complications related to intestinal anastomotic leaks [8].

Urology and Gynecology

ICG also has applications in urology and gynecology. It has been shown to provide high-precision imaging of anemic structures, identifying key anatomical elements and pathological structures, significantly improving surgical outcomes. In the detection of the sentinel node in surgical protocols of gynecologic oncology a 95–98% success rate is estimated, and in the case of vulvar cancer SNL (sentinel node) detection is at 100% [23–26].

Head and neck surgery

This dye is very important in determining the exact location of tumor lesions, its margin, and visualization of surrounding structures located within the head and neck, allowing for better perioperative results, better “oncologic purity,” and longer progression-free time [27]. Auspicious results have been observed especially in pituitary tumors, the use of indocyanine green allows the removal of lesions within the healthy margin, while safely preserving the healthy gland, without excessive resection [28–30].

Microsurgery

In microneurosurgery, ICG has emerged as a very promising tool to reduce the risk of perioperative vascular damage during ventriculostomy, the standard treatment for hydrocephalus [31].

Adrenal gland surgery

It has also been shown to be very useful in adrenal surgery, the primary usefulness of ICG fluorescence in adrenal surgery is to help delineate adrenal resection margins, allowing for more precise resection. This is especially true for patients with bilateral adrenal disease or hereditary disease associated with a high risk of recurrence [32].

Vascular surgery

It also appears to be very helpful in assessing the geometry of aneurysms in the brain, as well as surrounding vessels. A study evaluating 16 patients surgically treated for unruptured cerebral aneurysms demonstrated the usefulness of using indocyanine green for endoscopic and microscopic angiography. Endoscopic and microscopic angiography were compared, with ICG playing a major role in both. Better brain vessel imaging results were obtained with endoscopic imaging. It is expected that the introduction of this type of imaging into daily practice will be possible shortly [33].

Breast surgery

In breast surgery, ICG is used to identify sentinel nodes in breast cancer patients. In a study by Guo and colleagues, the percentage of detecting sentinel nodes in women with early breast cancer was higher than using methylene blue. The difference was almost 10% in favor of indocyanine green. However, the best results were shown with a combination of the two methods, with an efficiency of almost 100% [34]. The use of ICG has been investigated for the assessment of mastectomy skin flap ischemia. Indocyanine green angiography can assist in locating poorly perfused areas intra-operatively. With high intraoperative accuracy, it can predict postoperative outcomes [35].

Pediatric surgery

In pediatric surgery, ICG is used in hepatoportoenterostomy (HPE) with the Kasai procedure, which is the treatment of choice for biliary atresia (BA). Hirayama and colleagues suggested that the use of an ICG cholangiogram can better visualize the biliary flow of the hepatic duct at the porta hepatis before dissecting the fibrous cone, thus a more appropriate level and extent of dissection can be determined. It can also be used to evaluate biliary excretion post-operatively by observing the fluorescence of the feces and comparing it to the pre-operative value [36]. Indocyanine green is increasingly applied in pediatric surgical oncology. Esposito and colleagues used ICG in 18 patients undergoing open surgery for head, neck and chest tumors. Histopathology reports confirmed complete mass excision in all the cases. They assessed that ICG may be useful in pediatric surgery [37].

Bariatric Surgery

Staple line leaks remain a profound complication after bariatric surgical procedures. Kalmar and colleagues conducted a retrospective cohort study of all bariatric patients undergoing Roux-en-Y gastric bypass or sleeve gastrectomy procedures performed by one attending surgeon at a tertiary care facility designated as a bariatric surgical center of excellence. "Indocyanine green leak testing had a sensitivity of 100.00% and specificity of 98.28%." [38:4194]. In their study showed indocyanine green is an alternative for intraoperative detection leaks in the staple during bariatric surgical procedures with comparable specificity to intraoperative gastroscopy [38]. Mongelli and colleagues in their study evaluate the usefulness of indocyanine green angiography during conversional or revisional bariatric surgery in patients qualified for re-operation. In their study, postoperative complications, operative time, and length of hospital stay were similar in groups that use ICG and without ICG. It was assessed that indocyanine green was not useful in assessing the blood supply to the gastric pouch [39].

Future applications

The technology of the NIR visualization also changes with time. In their study van Oosterom et al. introduce a novel Click-On fluorescence-based sensing technology for existing robotic surgical instruments, effectively transforming standard forceps into molecular sensing apparatuses. This sensing modality demonstrated the capacity to detect ICG in tissue consistently throughout various stages of surgical procedures, irrespective of the fluorescence laparoscope model and its configurations [40].

Frontier research groups provide promising data in the field of contrast-based targeted therapy for cancer. ICG-conjugated gemcitabine showed less toxicity to normal cells and superior anti-tumor action compared to gemcitabine alone in a subcutaneous tumor xenograft model. This suggests that ICG conjugation can provide a novel fluorescent drug delivery system for the treatment of liver cancer, offering a method that can be used for both diagnosis and treatment of HCC [41].

The utilization of ICG fluorescence, particularly when integrated with sophisticated advanced artificial intelligence, holds the potential for enhancing surgical training. This combination could offer surgeons a data-driven roadmap and facilitate a more individualized decision-making process in the operating theater.

Conclusions

Indocyanine green has demonstrated utility across various surgical disciplines within the medical field. A growing body of research has elucidated the multiple advantages conferred by this dye, thereby propelling its increased adoption by researchers and practitioners. Despite these advances, there remains a need for extensive research before ICG can be integrated into routine clinical applications.

Our experiences with ICG

In our daily work, we have used indocyanine green in cholecystectomy many times. Below there are photos of several of our procedures (Figure 1–4).

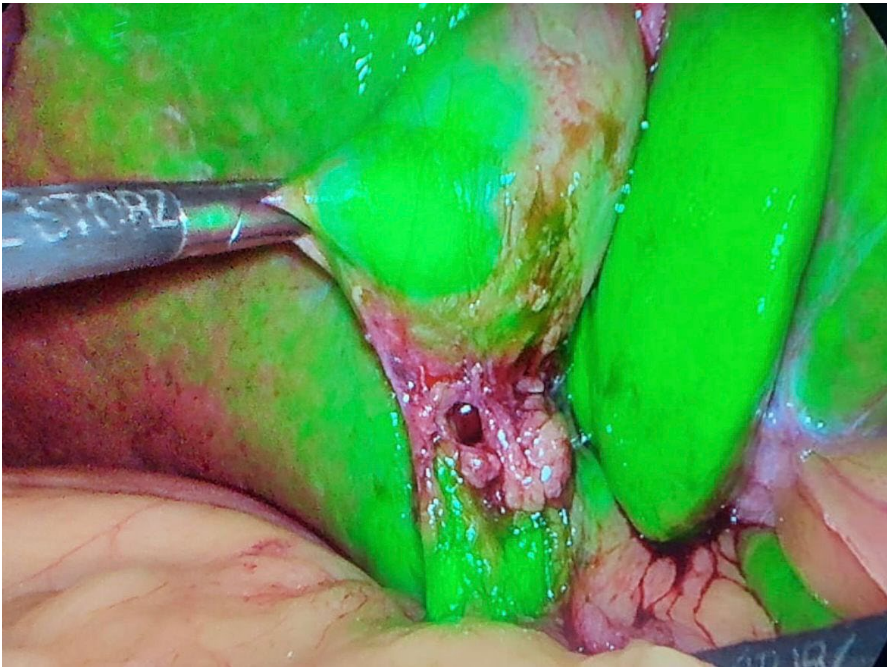

Figure 1. Gallbladder with chronic inflammation in NIR. Photo courtessy prof. Andrzej Komorowski.

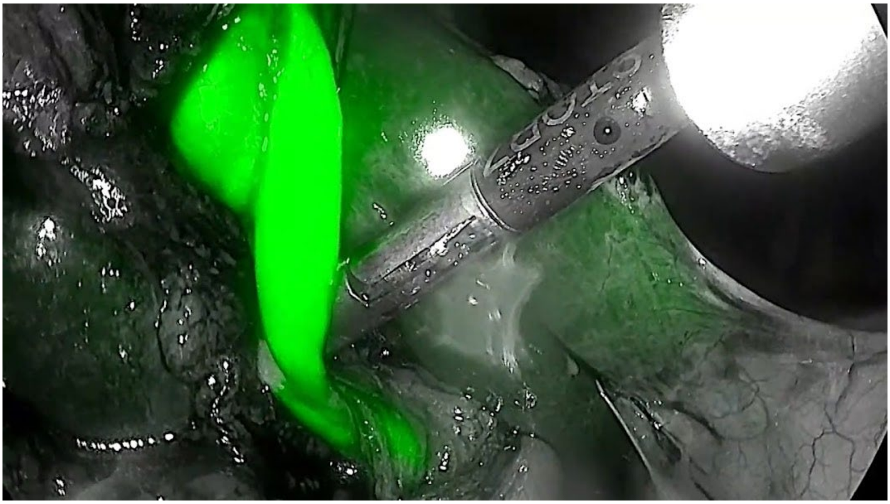

Figure 2. Cystic duct dissection. Photo by Oleksii Potapov.

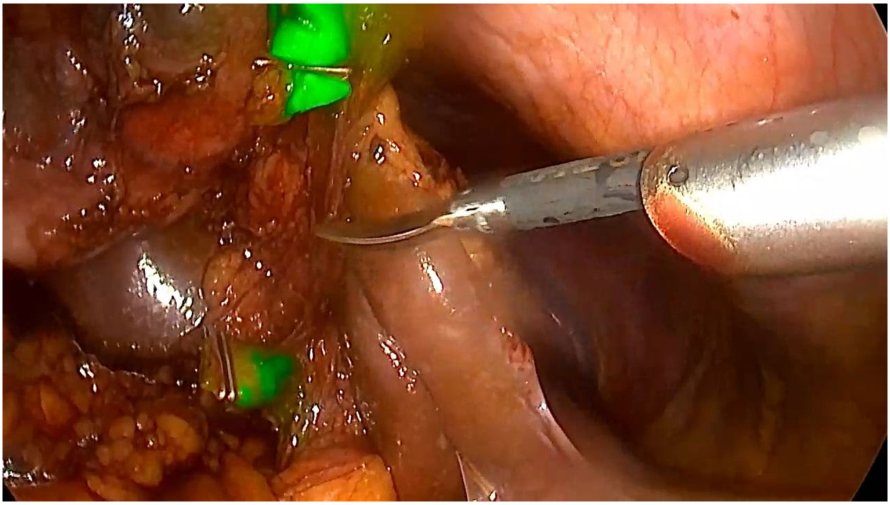

Figure 3. Remnant signal in a stump of the cystic duct. Photo by Oleksii Potapov.

Figure 4. View of the specimen using an external NIR camera. Photo by Magdalena Wąsik.

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