Pancreatic fluorescence using continuous indocyanine green infusion

Domenech Asbun  
*Miami Cancer Institute*, Domenech.Asbun@baptisthealth.net

Filipe Kunzler de Oliveira Maia  
*Miami Cancer Institute*, FilipeK@baptisthealth.net

Horacio Asbun  
*Miami Cancer Institute*, horacioa@baptisthealth.net

Follow this and additional works at: https://scholarlycommons.baptisthealth.net/se-all-publications

Citation  
Journal of Surgical Oncology (2022) 126(7):1215-1218

This Article – Open Access is brought to you for free and open access by Scholarly Commons @ Baptist Health South Florida. It has been accepted for inclusion in All Publications by an authorized administrator of Scholarly Commons @ Baptist Health South Florida. For more information, please contact Carrief@baptisthealth.net.
HOW I DO IT

Pancreatic fluorescence using continuous indocyanine green infusion

Domenech Asbun MD1 | Filipe Kunzler MD1 | Rebecca Marin BS2 | Horacio J. Asbun MD, FACS1

1Hepato-Biliary and Pancreas Surgery, Miami Cancer Institute, Miami, Florida, USA
2Herbert Wertheim College of Medicine, Florida International University, Miami, Florida, USA

Correspondence: Domenech Asbun, MD, Hepato-Biliary and Pancreas Surgery, Miami Cancer Institute, 8900 N Kendall Dr, Miami, FL 33176, USA.
Email: domenechasbun@gmail.com

KEYWORDS
fluorescent imaging, indocyanine green, pancreatic surgery

Disclosure: Horacio J. Asbun—Boston Scientific: honorarium, consultant/panelist; Stryker: honorarium, speaker; Olympus: honorarium, consultant/panelist; and Johnson and Johnson: honorarium, consultant. Other authors: No disclosures.

INTRODUCTION

Fluorescence imaging (FI) technology with indocyanine green (ICG) has become an important adjunct to multiple surgical procedures. Among other uses, FI helps surgeons visualize the biliary tree, assess perfusion to alimentary tract anastomoses, localize hepatic neoplasms, identify the ureters, and assess lymphatic drainage territories. In these cases, ICG is traditionally administered as a bolus of reconstituted solution. This is most commonly an intravenous (IV) injection, although sometimes it is injected directly into a target organ.

Despite the increasingly widespread adoption of FI in abdominal surgery, there has not been a significant increase of its use in pancreatic surgery. Applications of FI for pancreatic surgeons are experimental and largely center around the use of fluorescence-tagged particles with affinity to specific molecular targets in pancreatic cancer (e.g., near-infrared labeled epidermal growth factor receptor [EGFR] peptides). Other investigations focus on identifying lymphatic drainage patterns around the pancreas. Many of these applications are still in early experimental phases, and the utility of their use remains unclear.

The above examples do not focus on enhancing the visualization of pancreatic parenchyma. The authors present a novel approach to using FI during pancreatic surgery, in which ICG is given as a continuous IV infusion to accentuate pancreatic parenchyma. This ongoing infusion results in steady uptake of ICG by the pancreas without significant interference from surrounding tissue.

METHODS

An intraoperative near-infrared FI system is used, with the choice of manufacturer left to the surgeon’s preference. The authors preferentially perform pancreatic resections laparoscopically, and thus have the most experience using laparoscopic FI systems.

2.1 ICG dosage and infusion rate

The ICG solution is mixed by reconstituting 25 mg of powder ICG into a 100-ml bag of injectable saline, for a concentration of 0.25 mg/ml. The solution is photosensitive and thus the bag must be kept covered from light.

The ICG is infused at 0.4 mg per minute. Infusion is generally started 10 min before the anticipated need to visualize pancreatic parenchyma. The exact timing depends on the operation being performed and when fluorescence of the pancreas is deemed most useful (Table 1).

2.2 Intraoperative technique

FI view is toggled as needed throughout the case, but is usually not constantly activated. Visualization with an "overlay" mode is often...
the most useful, as it allows for white light visualization of tissue in combination with an image overlay of the fluorescent ICG-impregnated pancreatic parenchyma (Figure 1). The fluorescence gain is adjusted as needed depending on the degree of ICG uptake and the distance of the camera from the pancreas. The camera held too close or too far from the pancreas can make proper visualization difficult, regardless of gain adjustments. Supporting Information: Video 1 shows continuous ICG use for a difficult uncinate process dissection during pancreaticoduodenectomy in a patient with a history of pancreatitis. ICG infusion can be stopped when differentiation of pancreatic parenchyma from surrounding tissue is less critical, such as during the reconstruction phase of a pancreaticoduodenectomy.

3 | RESULTS/DISCUSSION

To our knowledge, this is the first report of continuous ICG infusion for pancreatic fluorescent visualization. The result of using an infusion settles issues we had previously faced when using IV ICG boluses. Specifically, IV bolus administration lead to a temporary peak in pancreatic fluorescence that was associated with hyper-fluorescence of nearby organs and surrounding tissue. The pancreatic fluorescence would subsequently washout, necessitating additional ICG boluses. This made ongoing differentiation of pancreatic parenchyma difficult and thus subtracted from the utility of FI.

3.1 | Additional tips and recommendations

A continuous infusion of ICG has resulted in a more reliable visualization of the pancreas. However, the appropriate timing of ICG infusion is still important and case-specific. For example, in distal pancreatectomies, we find it most useful to start infusion soon after abdominal entry. The lesser sac is entered and exposed soon afterward, at which time it is useful to delineate the course of the pancreas through the left-sided retroperitoneum. We find visualization of pancreatic parenchyma helpful throughout the case.

When performing pancreaticoduodenectomies, the excretion of circulating ICG through the biliary tree is more relevant. ICG is excreted from the liver in less than 30 min in patients with normal hepatic function,8 and ICG subsequently empties into the duodenum. ICG in the duodenum can produce a significant amount of background fluorescence that may interfere with pancreas visualization. It is thus recommended that ICG infusion is started only after the bile duct has been clamped during pancreaticoduodenectomies. We have found visualization of pancreatic parenchyma helpful when creating a retropancreatic tunnel before transection, and especially helpful during the uncinate process dissection.

ICG boluses can be administered intravenously to help localize vascular structures throughout a case, although this will lead to a temporary hyper-fluorescence of the pancreas. This is particularly useful during pancreaticoduodenectomies, during which early identification and control of adjacent arteries and veins are important for safe dissection (Supporting Information: Video 2). We give small boluses with particular attention to timing of administration (Figure 2). The dose of these boluses is 1.25 mg, equivalent to 0.5 ml of the standard 25 mg vial diluted in 10 ml of saline.

<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>Recommended timing, dosage, and method of administration of indocyanine green based on operative details</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Timing</strong></td>
<td><strong>Method of administration</strong></td>
</tr>
<tr>
<td>Pancreatoduodenectomy</td>
<td>After clamping bile duct</td>
</tr>
<tr>
<td>Distal pancreatectomy</td>
<td>At start of procedure</td>
</tr>
<tr>
<td>Enucleation</td>
<td>At start of procedure</td>
</tr>
<tr>
<td>Arterial visualization</td>
<td>When assessing arterial flow</td>
</tr>
<tr>
<td>Venous visualization</td>
<td>When assessing venous flow</td>
</tr>
</tbody>
</table>

FIGURE 1 Overlay mode during fluorescence imaging of ICG-impregnated pancreatic parenchyma. Pancreatic uncinate process (left) appears green compared to the surrounding tissue. ICG, Indocyanine green.
3.2 | FI in pancreatic surgery

Other ongoing investigations related to FI in pancreatic surgery involve fluorescence-tagged molecular targets, such as antibodies conjugated with dye that bind EGFR, vascular endothelial growth factor, or carcinoembryonic antigen.3–5 Furthermore, pancreatic neuroendocrine tumors have also demonstrated increased uptake of ICG compared to surrounding pancreatic tissue, and thus intravenously administered ICG has been reported useful in identifying and delineating these lesions.9–11 FI with ICG has also been used to assess peripancreatic lymphatic drainage, and has been suggested as an adjunct for adequate lymph node harvest.6,7,12 In this last example, ICG is usually injected directly into pancreatic parenchyma.

Although the above uses are interesting and have the potential to significantly impact pancreatic surgery, the use of continuous ICG infusion presents a different set of benefits. It allows for continuous visualization of pancreatic parenchyma in general and not only neoplastic tissue. This makes infusion useful during any part of a pancreatic dissection and resection. ICG is readily available and can be administered during an operation without elaborate preoperative planning, which increases ease of use and accessibility to surgeons. Furthermore, the low dose of infusion (0.4 mg/min) allows for ongoing infusion throughout an operation without fear of nearing the maximum safe dose (up to 2 mg/kg).13,14

3.3 | Limitations

There are shortcomings to the use of ICG as a continuous infusion. Unfortunately, not all patients exhibit the same degree of ICG uptake in the pancreatic parenchyma. Patients with a history of chronic pancreatitis and those with high amounts of pancreatic/peripancreatic fat seem to exhibit decreased fluorescence. Sometimes increasing the rate of ICG infusion can compensate for weak fluorescence, but at times the visualization remains poor. The technique is also less useful in patients with significant pancreatic atrophy, as is expected. Finally, the authors note that their experience with ICG infusion is limited to minimally invasive operations, although technology is available for fluorescent imaging during surgery.

Further investigations may focus on optimizing the timing and dosage of ICG, which may be patient-specific. It would likewise be useful to search for other fluorescent dyes which may have better and more specific affinity for pancreatic parenchyma. Finally, the use of continuous ICG infusion may be helpful to visualize other abdominal organs. For example, the authors have used a similar technique to visualize the adrenal glands and adrenal lesions. This has been useful when an adrenal parenchymal preserving procedure is being considered during a bilateral adrenalectomy.

4 | CONCLUSION

Continuous IV infusion of ICG during pancreatic surgery aids in pancreatic visualization and dissection. The technique is easy to use and overcomes problems previously encountered with intravenous bolus injection. ICG infusion can be used in conjunction with other FI techniques.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no data sets were generated or analyzed during the current study.

ORCID

Domenech Asbun http://orcid.org/0000-0002-5032-3970

REFERENCES


SUPPORTING INFORMATION
Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Asbun D, Kunzler F, Marin R, Asbun HJ. Pancreatic fluorescence using continuous indocyanine green infusion. J Surg Oncol. 2022;126:1215-1218. doi:10.1002/jso.27055