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Commentary regarding evolving applications of fluorescence guided surgery in pediatric surgical oncology: A practical guide for surgeons

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ABSTRACT

This is an invited commentary on the manuscript by Goldstein S, Heaton T, Bondoc A, et al., titled Evolving Applications of Fluorescence Guided Surgery in Pediatric Surgical Oncology: A Practical Guide for Surgeons.

Invited Commentary: A Treatise on the Many "Exciting" Applications of Fluorescence-Guided Surgery in Pediatric Surgical Oncology.

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The authors present a well-researched and thorough overview of an important topic: the emerging use of fluorescence guidance in pediatric surgical oncology. Although the technology continues to be refined and its full potential has yet to be fully understood, surgeons are already using it in myriad ways to help children with cancer achieve more complete primary resection, better staging information, potentially improved survival, and in many cases, a better quality of life. Such an erudite and even-handed review is a welcome addition to the literature and a useful introduction to practices that until recently might have been considered fanciful or investigational.

Pediatric surgeons play a pivotal role in the care of children with solid tumors and metastatic cancer along the entire spectrum of their treatment. This might include being asked to perform a diagnostic biopsy or staging procedure, to establish reliable central venous access, or simply to provide an experienced and reassuring voice while an individualized treatment strategy is being formulated. For most children with solid tumors, this also entails getting the patient to a point whereby the tumor is safely resectable – preferably with a margin of normal tissue – or for metastases to be amenable to a minimally invasive biopsy or complete resection with curative intent. Traditionally, surgeons have had to rely primarily on their skill and experience to accomplish these objectives and for the vast majority of patients, this is more than sufficient to ensure an excellent outcome. But for a small but significant minority of patients, whose extent of tumor for example might defy being easily defined by palpation or imaging, or whose metastases are especially difficult to localize in the operating room without an extensive and potentially morbid dissection, help in the form of a relatively easy-to-master set of techniques based on a safe and actually rather elegant physiologic principle is a welcome addition to the surgeon's skill set.

The basis for the techniques outlined in this paper is the clinical use of indocyanine green (ICG), a chemical that fluoresces brightly when exposed to near-infrared (NIR) light. This phenomenon is produced in the operating room using specialized NIR emitters that are commercially available through several biomedical equipment suppliers and designed specifically to be used in open and/or endoscopic procedures. ICG is a chemical that might seem almost too good to be true. Relatively inexpensive and widely available, it has been shown after decades of clinical use in humans to be extremely safe and well-tolerated, and displays chemical properties and metabolism that can be exploited in certain specific situations to the benefit of the surgeon and patient. And, although the uses described herein are technically off-label, the drug was approved by the FDA for use in patients more than 50 years ago. It can be injected intravenously, where it is highly protein-bound, rapidly hepatically cleared, and highly concentrated in the bile (and hepatocytes), or into the skin or soft tissues where it is rapidly and visibly cleared through lymphatics and lymph nodes. It is especially useful for work with neoplasms, which by virtue of their increased vascular permeability and impaired lymphatic drainage tend to concentrate and retain ICG. It has been used extensively for many years to assess the perfusion of skin flaps and bowel ends prior to anastomosis, highlight biliary structures to avoid injury during complex hepatobiliary procedures, and to map out lymphatic channels and lymph nodes during sentinel lymph node biopsy, where its bright green fluorescence can often be seen through the skin. Although the NIR emitters necessitate a

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significant upfront capital expenditure, the potential benefits and numerous conceivable applications of the equipment suggest it might be considered a sound investment at some centers.

This paper describes the various potential uses of the technology specifically in the care of children with cancer. Although no original data are presented, the authors collectively speak from a vast personal experience and nicely review the literature with a dispassionate tone that could easily have veered into salesmanship or hyperbole. They admit that there remains a great deal to be learned about the benefits and the limitations of the technique, and that surgeons who undertake to use it in their practice are well-advised to plan ahead, become well-versed in its proper use, and consider employing it as part of a well-thought-out institutional program or approved local or multi-institutional trial.

Upon learning about these techniques in this review, I suspect most experienced pediatric surgical oncologists will realize that this could help them provide better care for their patients, and that in the near future it is likely to become, at least in certain circumstances, the new standard of care.

The most promising applications, I believe, include:

1. Helping to localize and define safe resection margins of hepatic primary tumors, which have a special affinity for ICG. Achieving negative margins and identifying every tumor in the case of multifocal disease within the liver is critical to the survival of patients with hepatoblastoma or hepatocellular carcinoma.
2. Mapping the biliary tree (and ruling out bile leaks!) during difficult hepatobiliary dissections. This can be done after intravenous injection or by direct injection into the gallbladder or biliary ducts and can be utilized during open or laparoscopic procedures depending on the availability of the specialized systems required.
3. Visualizing lymphatic routes of spread or leaks, and as an adjunct to $^{[99]}$technetium scan for sentinel lymph node biopsy.
4. Localizing lung nodules to allow safer and more complete metastasectomy by, depending on the circumstances, either thoracotomy or thoracoscopy.
5. Assessment of perfusion of musculocutaneous flaps and bowel prior to anastomosis after an extensive and possibly fraught dissection.

The authors have done a nice job describing these and other potential uses for ICG-based fluorescence guidance, including possible other uses in the future, and potential pitfalls and limitations of the techniques in a way that is both edifying and useful. Pediatric oncologic surgeons who are dedicated to their craft will find that this timely monograph provides practical advice and many helpful hints about an intriguing and emerging technology for which many will find useful applications in their own practice moving forward.