Intraoperative Use of a Portable Large Field of View Gamma Camera and Handheld Gamma Detection Probe for Radioguided Localization and Prediction of Complete Surgical Resection of Gastrinoma: Proof of Concept

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BACKGROUND: Surgical management of Zollinger-Ellison syndrome (ZES) relies on localization and resection of all tumor foci. We describe the benefit of combined intraoperative use of a portable large field of view gamma camera (LFOVGC) and a handheld gamma detection probe (HGDP) for indium-111 (^{111}In)-pentetreotide radioguided localization and confirmation of gastrinoma resection in ZES.

STUDY DESIGN: Five patients (6 cases) with ^{111}In-pentetreotide-avid ZES were evaluated. Patients were injected with ^{111}In-pentetreotide for diagnostic imaging the day before surgery. Intraoperatively, an HGDP and LFOVGC were used to localize ^{111}In-pentetreotide-avid lesions, guide resection, assess specimens for ^{111}In-pentetreotide activity, and to verify lack of abnormal post-resection surgical field activity.

RESULTS: Large field of view gamma camera imaging and HGDP-assisted detection were helpful for localization and guided resection of tumor and removal of ^{111}In-pentetreotide-avid tumor foci in all cases. In 3 of 5 patients (3 of 6 cases), these techniques led to detection and resection of additional tumor foci beyond those detected by standard surgical techniques. The ^{111}In-pentetreotide—positive or—negative specimens correlated with neuroendocrine tumors or benign pathology, respectively. In one patient with mild residual focal activity on post-resection portable LFOVGC imaging, thought to be artifact, had recurrence of disease in the same area 5 months after surgery.

CONCLUSIONS: Real-time LFOVGC imaging and HGDP use for surgical management of gastrinoma improve success of localizing and resecting all neuroendocrine tumor—positive tumor foci, providing instantaneous navigational feedback. This approach holds potential for improving long-term patient outcomes in patients with ZES. (J Am Coll Surg 2015;221:300—308. © 2015 by the American College of Surgeons)

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Abbreviations and Acronyms

HGDP = handheld gamma detection probe
^{111}In = indium-111
LFOVGC = large field of view gamma camera
NET = neuroendocrine tumor
SPECT = single-photon emission CT
ZES = Zollinger-Ellison syndrome

Zollinger-Ellison syndrome (ZES) was first described in 1955 at The Ohio State University.[1] Zollinger-Ellison syndrome is a rare cause of peptic ulcer disease, and has an estimated annual incidence of approximately 1 case per million in the population. It is characterized by severe peptic ulcer disease caused by gastrin-secreting neuroendocrine tumors (NET) of the gastrointestinal tract, which are located predominately in the duodenum and pancreas.[2] Most gastrinomas occur sporadically, and 25% occur in association with multiple endocrine neoplasia syndromes. Approximately 60% to 90% of gastrinomas are considered malignant.[2] Due to the vague and nonspecific symptoms associated with ZES, the diagnosis is often delayed, with an approximate time from symptom onset to diagnosis of approximately 6 years.[2]

Early on, the mainstay of management of patients with gastrinomas was surgery.[2] However, with the development of H2-antagonist and proton pump inhibitor medications, medical management of symptoms has become more prevalent.[2,3] Regardless, surgical management, in appropriately selected patients, affords the only chance for cure. Surgery for gastrinoma now focuses on eradication of primary disease, treating refractory disease, and attempting to afford prolonged survival.[4] In fact, resection increases the disease-related survival, with postoperative cure rates of 60% and 34% at 5 and 10 years, respectively.[5,6]

The biology of gastrinomas is itself a confounding factor for achieving successful and complete surgical resection of all possible sites of disease. The tumors and their metastatic foci of disease are frequently small in size; difficult to palpate; multiple in number; and lie in variable locations, usually adjacent to vital structures, making these lesions difficult to identify and completely remove during surgery. As a result, resection of the entire tumor burden is challenging, and surgical management frequently fails to meet the desired expectations. In addition, during the past several decades, there have been very few notable advancements in the surgical management of ZES.

The successful surgical management of ZES requires that all gastrinoma lesions be localized and extirpated, which is best done at the time of the first operation. Fortunately, most gastrinomas express somatostatin receptors, specifically subtypes 2 and 5. As a result, long-acting somatostatin analogs, such as octreotide, have been developed to target these receptors.[7,8] By radiolabeling octreotide with indium-111 (^{111}In), those gastrinomas can be identified.[9-11] Among all conventional imaging modalities, somatostatin receptor scintigraphy with ^{111}In-pentetreotide, has the highest sensitivity in detecting gastrinomas. Unfortunately, it still identifies only 70% to 80% of lesions.[2,10]

During the past 20 years, various groups have reported improved intraoperative detection of NETs using a handheld gamma detector probe (HGDP) during surgery after the administration of various radiolabeled somatostatin analogs.[2,10,12-18] When an HGDP is used to attempt to successfully identify small tumors within the confines of the large surface area and irregular contours of the abdominal surgical field, a high degree of technical proficiency is required by the surgeon.[19-21] To assure successful identification of all possible sites of disease, it is prudent for the surgeon to have some form of preoperative diagnostic imaging verification of the general locations of the sites of disease, to obtain good surgical exposure, and to perform the HGDP survey of the abdominal surgical field in a methodical and systematic fashion. Yet, the reliance on preoperative diagnostic imaging alone for verification of the general locations of the sites of disease at the time of surgery limits the surgeon's ability to actively incorporate these static preoperative diagnostic imaging findings into the real-time localization approach provided by the HGDP. The ability to incorporate real-time imaging into the operating room during attempted intraoperative tumor localization with the HGDP provides the surgeon with instantaneous navigational feedback for optimizing the identification and resection of all possible sites of disease. Therefore, imaging technology that can be incorporated into intraoperative radioguided detection schema can be useful for improving complete resection rates, including specimen imaging. A portable large field of view gamma camera (LFOVGC) (Ergo; Digirad Corporation), capable of detecting gamma photon emissions in the 50 to 350 keV range, is capable of providing the surgeon with this real-time intraoperative imaging and navigational assistance.

Our institution has long been on the forefront of radioguided surgery technology[22-33] and ZES.[1,2] In the current report, we bring these two together as a proof of concept, describing the use of a LFOVGC and HGDP for real-time intraoperative identification and verification of complete removal of all site of disease in 5 patients (6 cases) presenting with symptomatic ZES.