

Clinical Application of Indocyanine Green Fluorescence Imaging for Detection of Sentinel Node in Gastric Cancer Surgery

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Abstract: The indocyanine green fluorescence imaging is a promising technique for sentinel node biopsy with advantages of dye-guided method, which is potentially safer, more convenient, and more cost-effective compared with the radio-guided one. It could simplify the dye-guided method in both open and laparoscopic gastric cancer surgery, and possibly shortens the learning curve, which is one of the most crucial factors in the clinical application of SN concept.

Keywords: ICG fluorescence imaging, gastric cancer, sentinel node biopsy, laparoscopic surgery

INTRODUCTION

Regional lymphadenectomy is indicated for patients with gastric cancer who have clinically suspicious lymph node metastases. A major controversy exists regarding this procedure for patients with T1 gastric cancer because most of these patients are without nodal metastases.

THE CONCEPT OF SENTINEL NODE IN GASTRIC CANCER SURGERY

The sentinel node (SN) is defined as a lymph node that directly drains a specific cancer. The concept of SN is based on the notion that non-sentinel nodes are unlikely to contain cancer cells if the sentinel node is cancer cell-free. To avoid unnecessary lymphadenectomy, the SN technique has been clinically applied to the management of a variety of cancers such as melanoma and breast cancer [1, 2].

Our group was the first to use SN biopsy with indocyanine green (ICG) in open gastric cancer surgery with a high success rate, and reported that the SN status can predict the lymph node status with high degree of accuracy [3]. The injected ICG, as a tracer for SN biopsy, binds rapidly to albumin and is carried more specifically through the lymphatic vessels compared with indigo carmine and Evans blue [4]. The ICG-related allergic reactions are fewer than those of blue dyes such as isosulfan blue [5]. Compared with the radioactive probe-guided method subjected to the limitation of legal considerations and costs in general hospitals, the dye-guided method is safe, convenient, and cost-effective [6]. However, the dye-guided method has certain limitations, such as loss of visibility in dense fat and rapid transit of the dye, and thus adequate training is required [7-9]. A multicenter phase II trial, Japan Clinical Oncology Group (JCOG) 0302, pressed the point of the technical learning curve for SN biopsy (unpublished data). The accuracy of SN biopsy depends on the individual

surgeon, meaning that convenient but reliable methods are in great demand for clinical application of this technique.

INDOCYANINE GREEN FLUORESCENCE IMAGING FOR DETECTION OF SENTINEL NODE

Kitai *et al.* [10] were the first group to report the use of SN biopsy guided by ICG fluorescence imaging in breast cancer surgery. We applied the novel detection technique in gastric cancer surgery and reported the results of our preliminary clinical exploration/feasibility study [11]. In that study [11], the ICG fluorescence imaging system allowed easy visualization of the lymphatic vessels draining from the primary gastric tumor toward the lymph nodes, although some lymph vessels and nodes were hardly recognized by ICG green color or infrared imaging, e.g., infrared ray electronic endoscopy (IREE) [12]. Indeed, detection by absorption spectroscopy is more sensitive than color perception, but the sensitivity of fluorescence spectroscopy is much greater than that of absorption spectroscopy [10]. In a preliminary study using phantoms, fluorescence images could be obtained for ICG solutions embedded 10 mm deep in a material with optical properties similar to that of human tissue, whereas detection by infrared imaging videoscope was limited to a depth of 3 mm only in fatty tissues [10, 13]. The difference in the degree of penetration between the two techniques could be critical in SN detection in obese patients (Fig. 1) [13].

At about the same time of our report [11], Kusano *et al.* reported their series of 22 patients with gastric cancer [14]. In their study, the detection rate was 91%, but the accuracy and false-negative rates were 89 and 33%, respectively, in patients with T1 cancer, and 70 and 60%, respectively, in all patients, representing impractical and a disappointing outcome. More recently, the same group reported another series of 37 patients with clinically T1 gastric cancer [15]. In this series, the accuracy was 97% and false-negative rate was 14%, allowing them to conclude that ICG fluorescence imaging provides accurate and highly sensitive image-guided intraoperative SN mapping. They commented that preoperative injection of ICG was associated with a higher accuracy compared with intraoperative ICG injection. Based

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on our experience [11], one advantage of preoperative tracer injection is that it eliminates the time-consuming intraoperative endoscopy, but has the disadvantage of loss of real-time tracing.

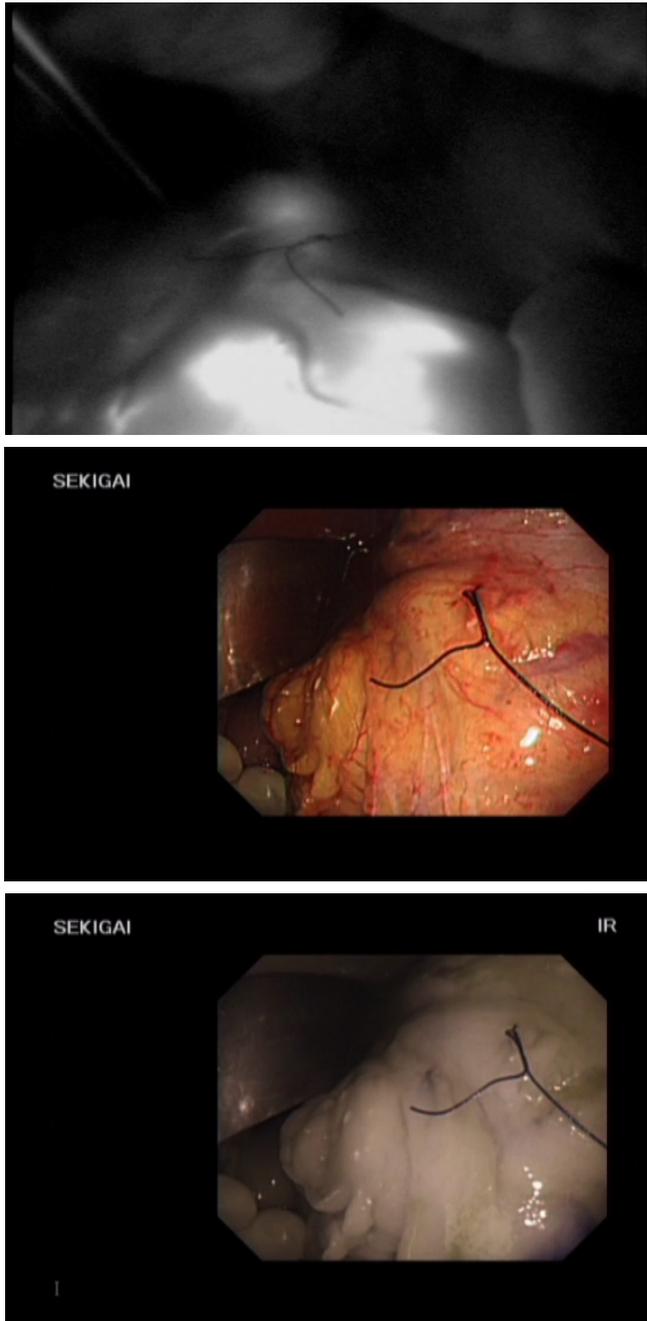


Fig. (1). A lymph node hardly recognized by the green color only (middle) or infrared imaging (lower) were easier to identify through dense fat by fluorescent imaging (upper).

INDOCYANINE GREEN FLUORESCENCE IMAGING IN LAPAROSCOPIC SURGERY

To date, laparoscopic SN biopsy, either by radioactive probe or dye-guided technique, has not been widely accepted [16]. The shine-through effect from the injection site seriously restricts the use of laparoscopic gamma probe [17]. Several limitations of the dye-guided method, such as loss of visibility in dense fat and rapid transit of the dye, are more

critical in laparoscopic surgery. Due to technical difficulties, there has been no practically suitable laparoscopic ICG fluorescence imaging system until quite recently. Recently, we have completed a preliminary study using a newly developed prototype laparoscopic ICG fluorescence imaging system [18], which overcomes the limitations of the dye-guided SN biopsy. A new report on its use in laparoscopic surgery has been submitted for publication.

CONCLUSIONS

The ICG fluorescence imaging is a promising technique for SN biopsy with advantages of dye-guided method, which is potentially safer, more convenient, and more cost-effective compared with the radio-guided one. It could simplify the dye-guided method in both open and laparoscopic gastric cancer surgery, and possibly shortens the learning curve, which is one of the most crucial factors in the clinical application of SN concept.

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