The Indocyanine Green Fluorescence Navigation May be Useful to Personalize Lymph Nodes Dissection

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Abstract: The indocyanine green (ICG) fluorescence imaging is a tool to detect sentinel nodes and the associated lymphatic network including para-sentinel nodes. According to recent experiences in breast cancer treatment, a real-time lymphatic mapping with ICG fluorescence may provide a possibility of being able to personalize lymph node dissection. This novel concept needs to be investigated in various types of diseases.

Keywords: ICG fluorescence imaging, lymphatic mapping, personalization of lymph node dissection, breast cancer.

In most of solid cancers, dissection of regional lymph nodes is conducted with radical resection of the tumor-bearing tissue. It is widely accepted that this surgical concept contributes to improve local control. It is reasonable to remove and examine the regional lymph nodes where cancer metastasis occurs initially [1-4]. Nodal status provides information about the presence or absence of metastasis as well as the degree of metastasis, i.e. the number of involved nodes, which plays a role in predicting prognosis. In addition, this prediction helps to determine the treatments such as radiation therapy and systemic therapy with anticancer agents. Therefore, lymph node dissection results not only in reducing local recurrence but also in mimicking systemic relapse.

However, it is also known that full lymph node dissection often causes functional disorders and cosmetic problems. Dissection of regional lymph nodes is unnecessary for the patients without node metastasis essentially. To avoid this problem, approximately 10–15 years ago, a concept with sentinel node (SN) was engaged in the surgical treatment of cancers, such as breast cancer and skin cancer [5]. Identification of the absence of metastasis, using radioisotope and/or blue dye, allows us to avoid full dissection of the regional nodes because of the low frequency of metastasis in the remaining non-sentinel nodes. For instance, full axillary lymph node dissection is merely indicated for primary breast cancer patients having a SN-negative status. The clinical application of SN biopsy to breast cancer practice certainly contributes to preserve axilla and improve quality of life of the patients.

On the other hand, full axillary dissection is still often performed for breast cancer patients having a SN-positive status. It should be unavoidable for the patients with extensive metastases, however it might be possible to optimize the dissection area for the patients with minimal metastasis such as just SN+ but no other metastasis. A difficulty on this issue could be due to an uncertainty in identification of para-SNs. Although there are various attempts to predict a presence of metastasis in the para-SNs, still it is under investigation [6].

A novel methodology with indocyanine green (ICG) fluorescence imaging has been recently developed to identify SNs [7]. This method does not require a radioisotope facility, and therefore, it is now being extensively used to identify SNs in various types of cancers, not only breast cancer but also other types of cancers particularly in Japan. Although confirmatory studies are needed, our preliminary studies indicate high detection rate of SNs with the ICG method [8].

In addition, ICG fluorescence imaging enables lymphatic mapping that includes SNs, para-SNs and the associated lymphatic ducts during the operation in real-time. Although little is known about the precise mechanism of the attachment or affinity of ICG conjugates with lipoprotein in lymphatic vessels and nodes, this technology is sensitive and can help to identify SNs and para-SNs as lymphoscintigraphy. Thus, the visualized lymphatic mapping during surgery enables to conduct lymph node removal from SNs to additional para-SNs in the anatomical order. Depending on the extent of lymph node metastasis, appropriate resection of the axilla can be performed for each case. Therefore, it will be possible to realize the personalization of lymph node dissection with this type of mapping technique as a hypothesis.

Since this methodology is still new, much work is needed in order to demonstrate its efficacy and clinical usefulness. As already described, in addition to mechanism analysis, in-depth studies concerning the site of injection, the volume of injection and timing of imaging are necessary. According to our preliminary experiences, it seems that control of lymphatic flow by surgical hands during surgery may be important for successful lymphatic mapping. Comparative studies between ICG fluorescence and conventional methodologies, such as the radioisotope method, are required in various types of diseases. Furthermore, quantitative measurement of ICG fluorescence is also required.

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ICG fluorescence imaging is a new tool to detect SNs and the associated lymphatic network. A lymphatic mapping with ICG fluorescence may help to personalize the surgical dissection of lymph nodes.

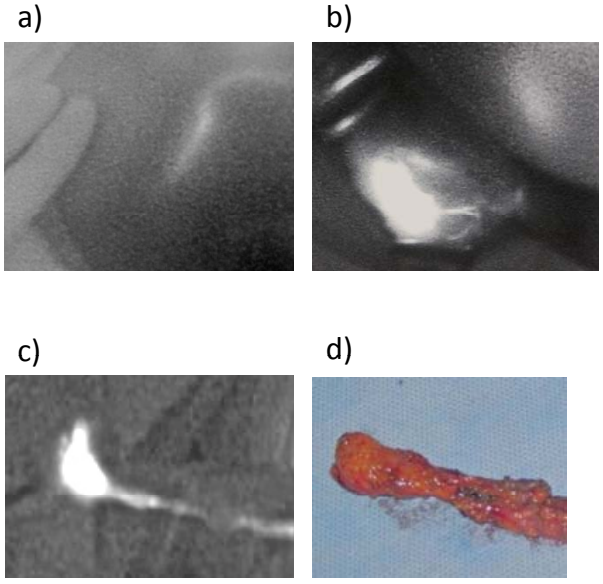

Fig. (1). Lymphatic mapping with an indocyanine green fluorescence navigation method. **a**) After injection of indocyanine green (ICG), fluorescence signal comes up immediately. ICG was injected periareola in this case. **b**) The lymphatic duct and sentinel lymph nodes are visualized during the operation in real time. **c**) ICG fluorescence is able to navigate other associated node and lymphatics. **d**) Macroscopic view of the resected specimen by eyes.

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