

The Principle of ICG Fluorescence Method

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Abstract: Intraoperative angiography or lymphography with an Indocyanine Green (ICG) fluorescence imaging technique is becoming popular clinical tool. Since 2003, it started to use for Breast Cancer Sentinel Lymph Node Navigation, the applications increased rapidly to other fields such as plastic and reconstruction surgery, brain surgery, Gastroenterological Surgery, and so on. Thus the ICG fluorescence method is a very powerful device for intraoperative navigator and also it's expected some improvement for the real diagnostic tool. We will explain the principle of ICG fluorescence method and the subjects to be improved.

Keywords: ICG fluorescence imaging, instrumentation, optical property of ICG, near infrared.

INTRODUCTION

Interest in near-infrared optical imaging by using the fluorescence of Indocyanine Green (ICG) as contrast agent has increased in recent years as clinical tool. This technique, called "ICG fluorescence method", has several advantages which are safe (radiation free), compact and relatively inexpensive instrumentation, real time monitoring, easy operation, no requirement of radiation controlled area, and so on. Since ICG fluorescence method applied to the breast cancer sentinel lymph node navigation in 2003 [1], its clinical applications spread widely and rapidly to other field, such as detecting cerebral vessels, coronary arteries bypass grafting, biliary trees, marking tumor location, and detecting small HCC, etc.

INDOCYANINE GREEN (ICG)

ICG (774.96 molecular weight) is a widely used diagnostic reagent which is clinically approved for use in the examination of hepatic function and liver blood flow diagnostic. Molecular formula is shown in Fig. (1).

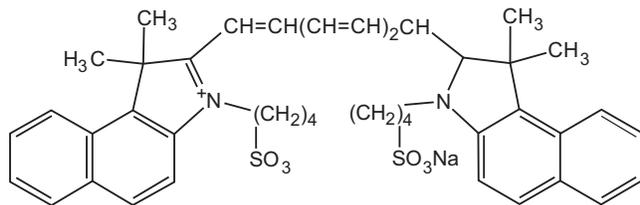


Fig. (1). Molecular formula of ICG.

It's also well known as optical contrast agent. When ICG is injected in a human body, it rapidly bound to plasma protein, mainly high-density lipoprotein [2], and generates fluorescence in near-infrared (845nm center wavelength) with illuminating the light between 750-800nm wavelength as excite light (Fig. 2) [3]. These optical characteristics are

very important for tissue measurement. In a human tissue, the major optical absorbers are hemoglobin and water. The absorbance of hemoglobin and water according to wavelength are shown in Fig. (2). The visible light below 650nm wavelength will be absorbed by hemoglobin strongly. Above 900nm infrared light will be also absorbed by water. The near infrared wavelength between 650nm and 900nm, so called optical window, are relatively "transparent" due to the low optical absorption of the hemoglobin and water. This is the reason why ICG fluorescence method is able to observe the deep (about 10mm) image from the surface of skin.

ICG toxicity is low but it contains sodium iodide. So it should be used with caution in patients who have a history of allergy to iodides [3].

ICG in aqueous solution is unstable. The strong fluorescence can be observed from "fresh" ICG solution mixed with blood plasma. But if the ICG solution is "old", the fluorescence will be decreased. According to our in-vitro experiment, the fluorescence intensity from one day old ICG solution will be a half of the fresh one. The fresh ICG solution should be used for efficient trials.

INSTRUMENTATION

Fig. (3) shows the external view of ICG fluorescence imaging system (Photo Dynamic Eye "PDE", Hamamatsu Photonics) [4]. The system consists of Camera Unit, Remote controller and Main Unit. The Camera Unit built in 760nm wavelength light emitting diode (LED) as excite light for ICG, high sensitive CCD camera in near infrared wavelength region, imaging lens and optical filter which can passing through only fluorescence image. The remote controller has the functions for adjusting the gain and offset of video signal and adjusting LED intensity so that the fluorescence image can be observed clearly. The main unit supplies the power for CCD and LED, and incorporated with a video processor. The video signal from main unit will be connected with TV monitor and display the fluorescence image in real time. The video can be recorded on a DVD simultaneously. The PDE system is compact size and light weight, so it's suitable as intra-operative diagnostic medical tool.

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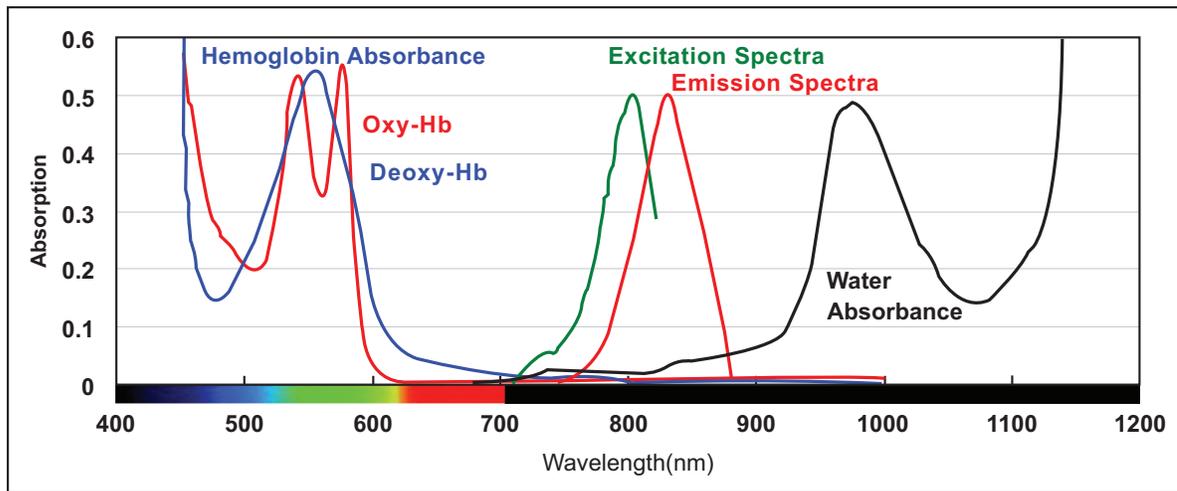


Fig. (2). Excitation and emission spectra of ICG (Excitation and Emission wavelength are drawn by yellow and red line respectively) and Hemoglobin (pink line), and water (black line) absorbance spectra.

SUBJECTS TO BE IMPROVED

ICG fluorescence method is very useful tool for medical applications. But there are several points to be improved.

Difficult Operation Under the Shadowless Light

Conventional shadowless light includes a lot of near infrared light which is the same wavelength as ICG fluorescence. Turn off the shadowless light is recommended during ICG fluorescence method is performed.

Penetration Depth

Limitation of penetration depth is the most biggest concern for optical tissue measurement. Near infrared technique can improve this problem but penetration depth is only 10~20mm from the surface. Mechanical improvements, stronger excite light illumination or adoption of high sensitive detector will be expected. And also the optimum condition of ICG solution such as the concentration, injection volume, injection location, etc will be necessary to consider.

Quantitative Analysis

So far, ICG fluorescence method is expected to monitor the lymphatic vessels or blood vessels inside of human tissue clearly. Recently, quantitative analysis of fluorescence image

is strongly desired. The intensity of fluorescence is depends on various condition, such as the distance between detector and subject to be measured, intensity of excite light, detector sensitivity, surrounding lighting condition (room light or sun light). These conditions have to be controlled sufficiently.

The “quenching effect” is necessary to consider. If the concentration of ICG is enough low, the relationship between intensity and concentration will be kept in proportion. But the concentration is beyond certain level, the fluorescence intensity and concentration does not keep the proportional condition anymore. This phenomenon is called “quenching”. The quenching is not controllable effect, so it’s better to keep low level concentration to avoid this problem.

CONCLUSION

ICG fluorescence method utilized near infrared fluorescence from ICG is expected as powerful medical diagnostic tool because of safe and cost effective technique. It’s becoming popular at the breast cancer sentinel lymph node navigation application in Japan. This technique is also started to clinically applied to various surgeries, such as Cardiovascular surgery, Neuro surgery, Fetal surgery, Gastroenterological surgery and Plastic and Reconstructive surgery [5].



Fig. (3). External View of ICG fluorescence Imaging System (PDE).

We hope that we can contribute to the improvement of patient's QOL and maintain the human's healthy life through ICG fluorescence method.

REFERENCES

- [1] Kitai T, Inomoto T, Miwa M, Shikayama T. Fluorescence navigation with indocyanine green for detecting sentinel lymph nodes in breast cancer. *Breast Cancer* 2005; 12: 211-5.
- [2] Yoneya S, Saito T, Komatsu Y, *et al.* Binding properties of indocyanine green in human blood. *Invest Ophthalmol Vis Sci* 1998; 39: 1286-90.
- [3] Cardio-Green Instruction manual. Becton Dickinson, April, 1981.
- [4] Hamamatsu Photonics Web sites. Available at : http://jp.hamamatsu.com/products/life-science/pd428/pde/index_ja.html
- [5] Kusano M, Ed. *A New Light for Minimally Invasive Surgery*. Intermedica, Tokyo Japan 2008.

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