

# Semi-Permanent Use of Indocyanine Green Latex Phantom for Fluorescence Emission

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## Abstract

**Introduction:** Testing the fluorescence emission of the vascular circulation status of the indocyanine green (ICG) fluorescence contrast agent to validate the system performance is crucial. Hence, the development of an ICG phantom is imperative, and this study proposes a method for manufacturing an ICG phantom.

**Method:** The ICG with an initial concentration was subjected to 0.2 cc sampling through syringe(x), and an ICG (0.2 cc) is diluted with silicon (Si) latex lubber (10 mL) during the manufactured the phantom. The brightest fluorescence expression state is 30  $\mu$ M, and if it exceeded 50  $\mu$ M, fluorescence fading occurred and changed to a dark color.

**Results:** The liquid (ICG) of the concentration range is 0.003 mM to 0.24 mM, and the maximum fluorescence expression range is 0.005 to 0.006 mM when the phantom is irradiated using a 780-nm (800 mW) LED. In addition, the fluorescence emission is reduced to 0.24 mM, and the fluorescence expression concentration is 10  $\mu$ M, 30  $\mu$ M, and 50  $\mu$ M, respectively. The decreasing of the fluorescence emission is beginning to 50  $\mu$ M.

**Conclusions:** In this study, the proposed phantom with ICG fluorescence emission using latex lubber is proposed. In this works, the proposed phantom is improved the performance for ICG fluorescence emission. In the manufactured phantom, the phantom is used for gelatin, and the advance of phantom has easy manufacturing and long-life fluorescence emission (semipermanent) due to incorrodible material (latex lubber). To experimental results of a phantom, the ICG fluorescent contrast medium (0.055 mM) is same to 30  $\mu$ M. Then, the 0.055 mM and 30  $\mu$ M have high resolution and fluorescence emission status. Thus, the results are in good agreement.

## Keywords

indocyanine green (ICG), phantom, blood flow, fluorescence emission, LED irradiation

## Introduction

The malignant tumors are distributed in numerous blood vessels. Malignant tumors and blood vessels are similar in color.<sup>1</sup> Hence, after removing the tumor, the state of blood circulation is observed through external light source investigation and external monitoring using indocyanine green (ICG) as a fluorescent contrast agent to validate the damaged state of the vascular.<sup>2</sup> The development of a fluorescence microscope for surgery to suit the use of the operator is in progress.<sup>3,4</sup> Moreover, the animal tests and clinical trials have to conducted validate the microscope for development. However, many tested must be performed during the system development process to conduct animal experiments and clinical trials. Currently, the phantoms are essential for animal and clinical testing processes are uneconomical and time-consuming.<sup>5</sup> Although the ultrasonic phantom has been developed,<sup>6,7</sup> and the phantom development of fluorescent ICG contrast medium for blood circulation are limited. In most cases,

the developed fluorescence ICG contrast agent phantom is in the liquid form.<sup>5</sup> The liquid form has a service life of less than 18 h. Therefore, the development of a phantom

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that is durable is crucial. This study proposes the production of a phantom in the form of gelatin that can be reused continually. The manufactured phantom is an ICG-only phantom that can be used to develop the system.

## Analysis of the Correlation Between Phantom and Animal Experiment

Analysis of phantom production needs: To develop a fluorescence microscope for surgery, a clinical trial is conducted after approval of the medical device through animal testing, as shown in Figure 1. From the figure, a phantom should be used when testing is required for validation during the system development process. When the phantom is irradiated with an external light source, fluorescence is expressed in the phantom, and fluorescence staining and expression conditions can be observed using a camera.

Such as a phantom must be produced in a gelatin form, and a fluorescent tank agent should be injected into the gelatin material for fluorescence expression. The fluorescent phantom should be reusable and resistant to corrosion.

## Method of the Phantom Manufacturing

The normal saline (NS) of 10 cc is injected into the ICG(F) powder (M:25 mg) when the manufacture the phantom which is shows the Figure 2 and equations (1) to (3), and the initial concentration ( $C_1$ ) is also be 2.5 mg/mL. At this time, the constant (MC) of ICG mass per mol is 774.98 g/mL.

$$C_1 = \frac{M}{NS} \quad (1)$$

$$C_2 = \frac{C_1}{NS} \quad (2)$$

$$x = 10 \times 10^{-6} \left( \frac{V}{C_2} \right) \quad (3)$$

The ICG with an initial concentration is subjected to 0.2 cc (sampling) through syringe (x), and an ICG of 0.2 cc is diluted with silicon ( $S_i$ ) latex lubber (10 mL). Consequently, the concentration of the diluted latex lubber ( $C_2$ ) is 3.23 mol. The concentrated latex lubber

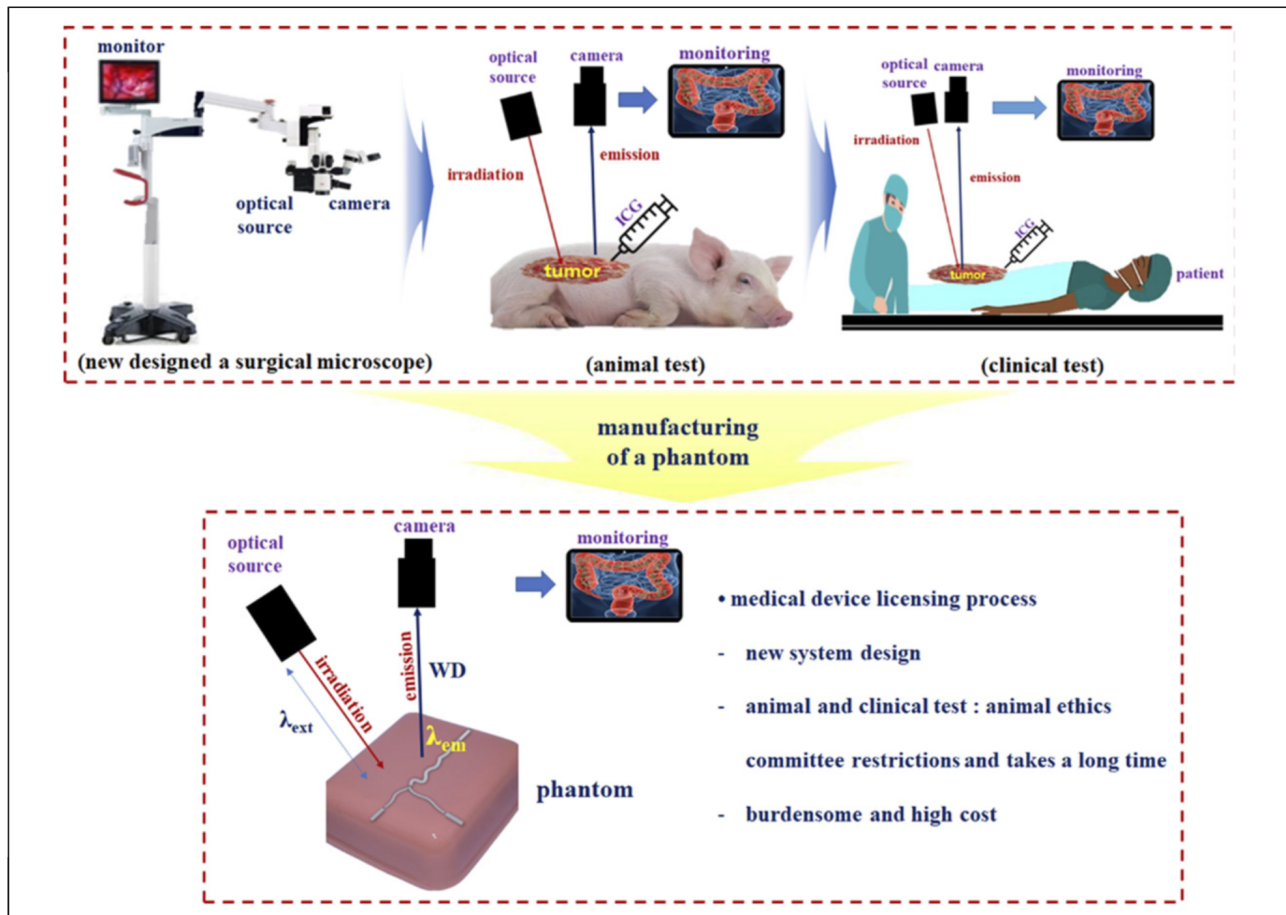


Figure 1. Progress of the phantom manufacturing.

(3.23 mol) is mixed with a 40-mL (latex lubber) to match the injection volume of 50 mL. The liquid (V) of 50 mL with latex lubber is injected into a silver cell dish and heated for 6 hours through induction, and the liquid heated in the cell dish turned into a gelatinous phantom. Notably, when volume of the dilute latex lubber that was mixed with an additional concentrated latex lubber ( $C_2$ : 3.23 mol) ranged from 10 to 100 mL, the mole value of the fluorescence expression state changed from 10 to 50  $\mu\text{M}$ . At this time, the largest fluorescence expression state was 30  $\mu\text{M}$ , and if it exceeded 50  $\mu\text{M}$ , fluorescence fading occurred and changed to a dark color.

## Experimental Result

**Figure 3** shows the manufactured phantom, experimental methods, and experimental results, respectively. A comparative evaluation is performed by combining a liquid obtained to mixing ICG and normal saline in a range of 1/50 to 1/1000 and the manufactured phantom. The LED module, a phantom, and a NIR camera (Lt225M-NIR-SCI) were used for the experiment. The camera and LED module are included the working distance of 7 cm from the phantom while the phantom is irradiated using a LED (780 nm @ power of 800 mW). Furthermore, the fluorescence is emitted through

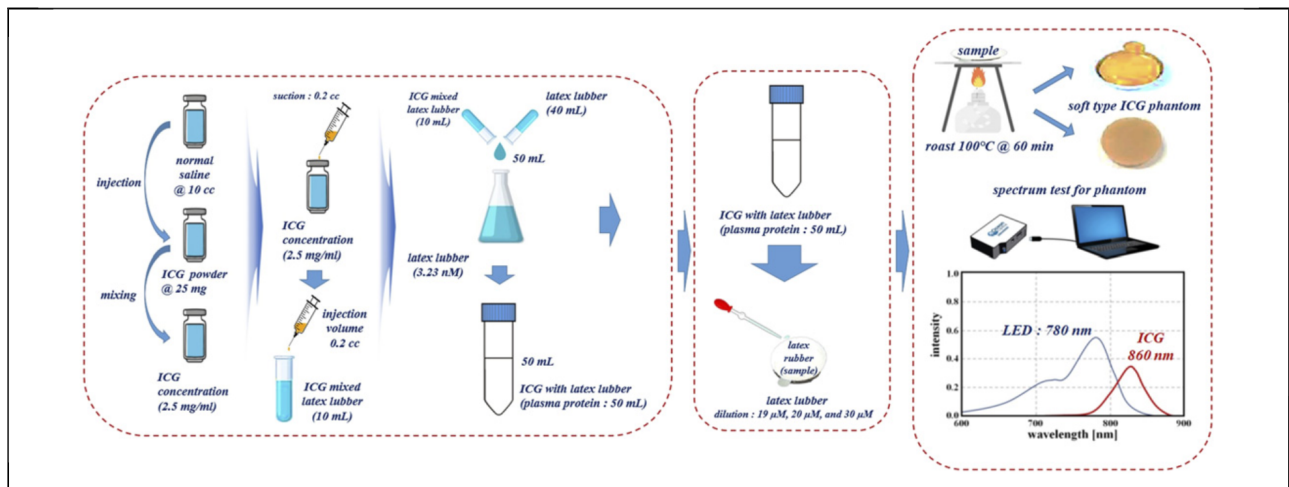


**Figure 2.** Phantom production process and Mole test result.

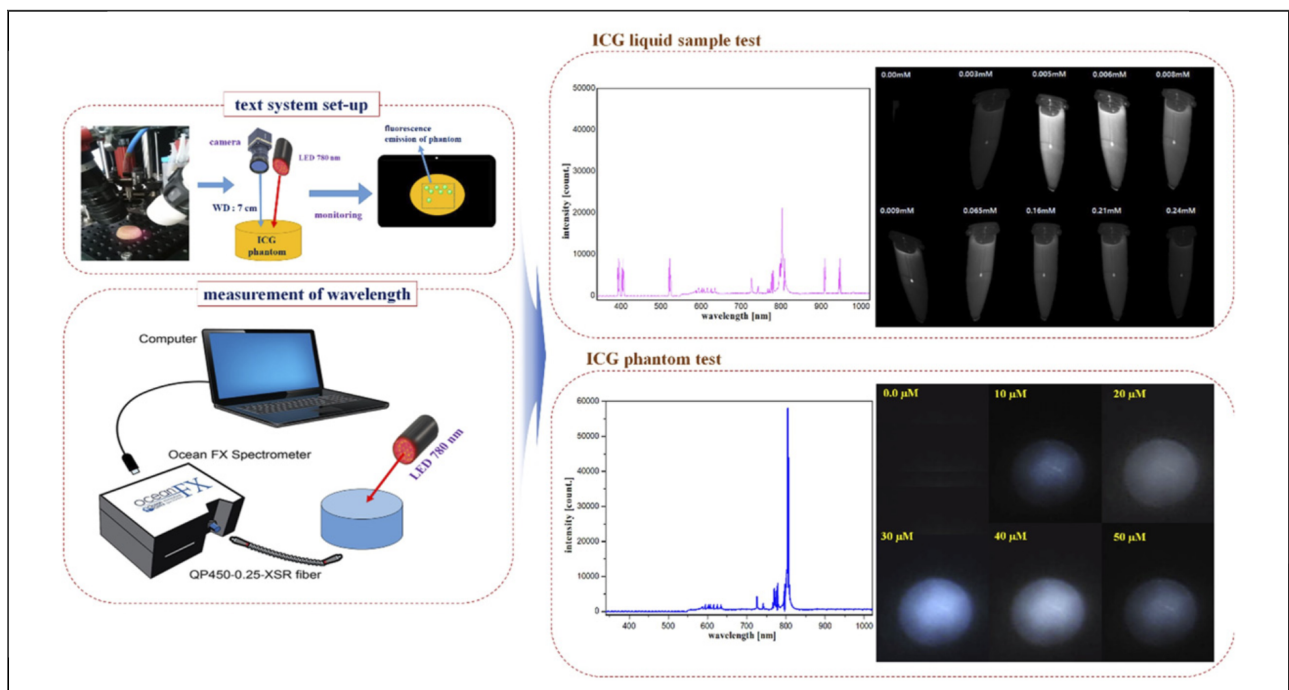


**Figure 3.** ICG phantom test and results.

a chemical change in the phantom, and a wavelength of fluorescence emission is 860 nm which is measured to the spectrometer. Then, the concentration range of fluorescence emission is the 0.003 mM to 0.24 mM in the ICG liquid, and the maximum fluorescence emission range has 0.005 to 0.006 mM. The 0.24 mM is reduced to fluorescence emission. Then, the phenomenon of fluorescence emission is finished. The concentration of the maximum fluorescence emission in the manufactured phantom is 10  $\mu$ M, 30  $\mu$ M, and 50  $\mu$ M, respectively which is finished the fluorescence emission at the 50  $\mu$ M.

## Conclusion

The proposed phantom has simple manufacturing method and semipermanent material. The proposed phantom can be used for simple test instead of animal and clinical test using surgical microscopes, and it can be applied to early reliability test of performance to development of surgical microscope.

## Declaration of Conflicting Interests

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## Supplemental Material

Supplementary material for this article is available online.

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