Handheld projective imaging device for near-infrared fluorescence imaging and intraoperative guidance of sentinel lymph node resection

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Abstract. We propose a handheld projective imaging device for orthotopic projection of near-infrared fluorescence images onto target biological tissue at visible wavelengths without any additional visual aid. The device integrates a laser diode light source module, a camera module, a projector, an ultrasonic distance sensor, a Raspberry Pi single-board computer, and a battery module in a rugged handheld unit. It is calibrated at the detected working distance for seamless coregistration between fluorescence emission and projective imaging at the target tissue site. The proposed device is able to achieve a projection resolution higher than 314 μm and a planar projection bias less than 1 mm at a projection field of view of 58 × 108 mm² and a working distance of 27 cm. Technical feasibility for projective imaging is verified in an ex vivo model of chicken breast tissue using indocyanine green as a fluorescence agent. Clinical utility for image-guided surgery is demonstrated in a clinical trial where sentinel lymph nodes in breast cancer patients are identified and resected under the guidance of projective imaging. Our ex vivo and in vivo experiments imply the clinical utility of deploying the proposed device for image-guided surgical interventions in resource-limited settings.

Keywords: handheld; near-infrared fluorescence imaging; projective imaging; surgical navigation; sentinel lymph node.

Sentinel lymph node biopsy (SLNB) has become a widely accepted method of nodal staging for patients with clinically lymph-node-negative breast cancer. Compared with axillary lymphadenectomy, SLNB significantly decreases the rate of postoperative complications, reduces the cost of patient care, and improves patients’ quality of life after surgery. The National Comprehensive Cancer Network (NCCN) guidelines on breast cancer have recommended SLNB after preoperative systemic therapy for patients with surgical axillary stages I and II.

Near-infrared fluorescence (NIRF) imaging of indocyanine green (ICG) is an established technique for medical imaging and image-guided interventions. In the recent years, various NIRF imaging systems have been developed and clinically validated for sentinel lymph node (SLN) mapping in breast cancer patients. These systems rely on either screen display or in-situ projection of NIRF images. The screen display method requires an additional screen that challenges the already limited space in an operating room (OR). In addition, it distracts the surgeons by switching their fields of view between the screen and the surgical site. The in-situ projection method enables SLN mapping in a natural mode of visual perception. However, previously reported projective imagers are bulky and require manual calibration at the specific working distance for coregistration between fluorescence emission and projective imaging.

In this letter, we report a projective imaging device that integrates NIRF acquisition, visible image projection, and working distance detection in a handheld unit. The device uses a single-board computer for data acquisition and processing, a laser diode (LD) array as the excitation light source, and an ultrasonic sensor for working distance detection. Fluorescence emission from the surgical site is acquired by the device, calibrated based on the detected working distance, and projected back to the surgical site for surgical guidance. Technical feasibility of projective imaging is validated in an ex vivo tissue model. Clinical utility of image-guided SLN resection is demonstrated in breast cancer patients. To the best of our knowledge, this is the first report of SLN resection surgery guided by a handheld projective imaging device with automatic working distance detection and calibration.

Figures 1(a) and 1(b) show the engineering design and the working prototype of the proposed projective imaging device. The overall size of the device is 200 mm × 140 mm × 140 mm, incorporating an excitation light source module, a detection module, a projection module, a single-board computer, and a 3D-printed cover. The light source module consists of five 200 mW LDs at a central wavelength of 780 nm. An ED1-C20-MD engineered diffuser (Thorlabs Inc., New Jersey) is placed at the output window of the light source, providing a uniform excitation illumination. The detection module consists of a 0.3-megapixel EO-0413M CMOS camera (Edmund Optics, Mainz, Germany) coupled with a 0814MM lens system (AZURE Photonics Co., Fujian, China) and two FF01-832/37-25 optical filters (Semrock Inc., New York). These filters are placed in front of and behind the lens, with their angles of incidence and cutoff wavelengths carefully designed to ensure appropriate fluorescence detection in the desired field of view (FOV). A URM37 V4.0 ultrasonic proximity sensor is used to detect the working distance between the device and the surgical site. The projection module is a miniprojector (Philips, Amsterdam, Netherlands) with its optical axis aligned in parallel with the camera. A Raspberry Pi 3b single-board...
computer (Raspberry Pi Foundation, United Kingdom) performs the parallel tasks of fluorescence image acquisition, working distance detection, system calibration, image processing, and visible image projection in multiple threads at an average latency of 593 ms. Based on our clinical observation, this latency does not induce significant motion blurring during an SLNB procedure. The latency can be shortened by using field-programmable gate array and by optimizing the imaging algorithms.

The FOV of the projector varies from 32.5 mm × 60 mm to 86 mm × 160 mm within the range of working distance \( H \) from 15 to 40 cm. Structural design of the handheld device ensures that the optical axes of the camera and the projector overlap in the horizontal direction. However, there is an angular difference between two optical axes in the vertical direction, leading to the vertical bias between the projected and the actual images of fluorescence emission. Therefore, calibration in the vertical axis is needed to ensure accurate mapping. The image processing algorithm also crops the nonoverlapped FOVs between the camera and the projector so that fluorescence emission can be projected to the surgical site with high fidelity.

Figure 1(c) shows the generation of the positional bias between the projected image and the actual field of surgery in the vertical direction. Let us denote \( L \) as the width of the overlapped area between surgical FOV and projective imaging; \( p \) as the number of the projected pixels within \( L \); \( m \) as the number of the camera pixels within \( L \); \( h_0 \) as the current working distance. \( k_1h_0 \) and \( k_2h_0 \) are pixel sizes for the camera and the projector, respectively, at the current working distance, where \( k_1 \) and \( k_2 \) are constants related to the camera and the projector. Thus, \( m \) can be derived as

\[
m = \frac{k_2h_0p}{k_1h_0} = \frac{k_2p}{k_1}.
\]

Since \( p \) remains as a constant within the working distance range, the number of pixels for the width overlap between the camera and the projector \( m \) is a constant. For an arbitrary working distance \( h \), the projection bias \( \Delta l \) is linearly correlated with the working distance:

\[
\Delta l = \Delta h(\sin \theta - \sin \alpha) = (h - h_0)(\sin \theta - \sin \alpha).
\]

Let us denote \( n \) as the number of pixels in width \( \Delta l \):

\[
n = \frac{(h - h_0)(\sin \theta - \sin \alpha)}{k_1h_0} = \frac{a}{h_0} - b,
\]

where \( a \) and \( b \) are constants.

To calibrate the projective device, 10 sampling points are acquired at different working distances from 20 to 30 cm, and the images are adjusted to the desired sizes coincident with the actual scene. The values of the cropping parameter \( n \) are acquired at 10 different working distances \( h_0 \) and fit into Eq. (3) in order to obtain the calibration factors \( a \) and \( b \). To verify the calibration accuracy, 10 testing points in the working distance range from 20 to 30 cm are selected, and the calibration factors are applied based on their actual working distances. According to Fig. 1(d), the planar projection bias is controlled within 1 mm through the working distance ranges from 20 to 30 cm.

The achievable spatial resolutions for fluorescence imaging and projective imaging are characterized by a 1951 USAF resolution target, as shown in Figs. 2(a) and 2(b). Top images are the acquired and the projected images of the target. Limits of resolving power are determined by the largest group of the element pairs where the spacing pattern is no longer discernible. The 1951 USAF target test shows that the projective imaging device is able to achieve the spatial resolutions of 140 and 314 μm for fluorescence imaging and projective imaging, respectively.

To test the fluorescence imaging sensitivity of the proposed device, we dilute ICG in water at concentrations of 10, 7.5, 5, 3, 1, 0.75, 0.5, 0.25, 0.125, 0.0625, 0.05, 0.005, 0.001, 0.0005, and 0 μM, respectively. Figure 2(c) shows the fluorescence images
Views of the tissue sample show complete removal of fluorescence sensitivity at an ICG concentration of around 5 nM.6

Fig. 2(d), our device is able to detect fluorescence emission with the accuracy of our device in SLN localization.10 Five to 10 min exposure time, the projective navigation device is able to detect ICG concentrations around 5 nM. Technical feasibility of the device is verified in a chicken breast tissue model ex vivo. Clinical utility of the device is demonstrated by SLN resection surgery in breast cancer patients. Our ex vivo and in vivo experiment results imply the clinical potential of the proposed device for imaging-guided SLNB and for many other medical interventions where intraoperative guidance is necessary.

Disclosures
The authors have no relevant financial interests in this letter and no potential conflicts of interest relevant to disclose.

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