Real-time localization of the parathyroid gland in surgical field using Raspberry Pi during thyroidectomy: a preliminary report

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Abstract: We created an auto-para viewer, an autofluorescence imaging device, to localize the parathyroid glands during thyroidectomy using an inexpensive Raspberry Pi. A special emission filter in the auto-para viewer was designed to pass 1/100 of visible light and nearly all infrared light longer than 808 nm. With this emission filter, we simultaneously acquired an autofluorescence image of the parathyroid and a visible light image of the surrounding surgical field. The auto-para viewer displayed four times brighter autofluorescence of the parathyroid glands compared to the background tissues without operating room light. Additionally, it showed two times brighter autofluorescence than the background tissues simultaneously showing the surgical field illuminated by the visible light from the operating room light. The NOIR camera, using the auto-para viewer, could reduce the camera's exposure time so the parathyroid glands to be viewed in real-time, which is expected to prevent unintentional damage to the parathyroid gland during thyroidectomy.

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1. Introduction

Preservation of normal tissues during surgery is important. In particular, the parathyroid glands can cause low parathyroid hormone levels and hypocalcemia if damaged; therefore, they must be carefully preserved during a thyroidectomy [1]. However, it is difficult for surgeons to distinguish parathyroid glands with the naked eyes. The typical parathyroid size is as small as 2–4 mm. Their characteristics are similar to fat or connective tissue, and they are usually buried in surrounding tissues. Actually, not only beginners but also relatively experienced surgeons could unintentionally remove the parathyroid glands by as much as 14.25% [2–4]. Although various procedures have been introduced to preserve the parathyroid glands, they have not been widely applied because they are what to be gained from the long experience [4–6]. After surgery, 46% of patients experience temporary discomfort due to the previous reason, and 6% of patients undergo further treatment with permanent impairment [3, 4, 7].

Recent advances in biomedical technology have introduced techniques for identifying the parathyroid glands using the near-infrared autofluorescence phenomena. The technique began with the theory that the parathyroid glands emit light at longer near infrared wavelengths when they receive light from a near infrared wavelength without exogenous fluorescent dye. Currently, imaging research of the parathyroid is actively under way [8–12]. These studies intuitively show the location of the parathyroid glands in the actual surgical area. There is a marked clinical significance because they overcome the limitations of previous experience-dependent procedures and showed objective methods through visual images.

Previous methods using image autofluorescence of the parathyroid gland have some disadvantage. The intensity of autofluorescence is very weak compared to the fluorescence intensity when using an exogenous contrast agent. This requires the surgical room to be dark throughout the time of shooting. Accordingly, the surgeon had to turn off both the room light and the surgical light to reduce background noise for confirmation of the autofluorescence of the parathyroid gland. Therefore, the method required at least two images to match the parathyroid gland in the surrounding surgical field; one without the room light, the other with the room light. Other disadvantages are that an expensive, bulky infrared camera has been used to obtain autofluorescence images. It is inconvenient to find a very small parathyroid gland in a narrow surgical area with such a camera [9, 10, 12].

The goals of this study are (1) to develop a way to overcome the drawback of turning off the lights for autofluorescence imaging and (2) to develop a real-time imaging technology while using a cheap camera. We developed the so-called “auto-para viewer” for real-time
imaging of autofluorescence. We investigated the parathyroid/background ratio according to the presence or absence of the room light and examined the possibility of applying it during the actual surgery.

2. Materials and methods

2.1 Intraoperative equipment set-up for near-infrared autofluorescence imaging

The lab-made equipment was used for parathyroid autofluorescence imaging experiments. Experiments were performed using a Raspberry Pi camera (NOIR Camera board V2, Premier Farnell, Leeds, UK) for image acquisition with a 785 nm diode laser (WSLS-785-002-H, Wavespectrum Laser Inc., Beijing, China) as an excitation source, and with a Raspberry Pi development board (Raspberry Pi 2 Model B, Premier Farnell, Leeds, UK) for image generation in a display. (Fig. 1) An excitation filter (84105, Edmund Optics, NJ, USA) was attached in front of the diode laser to limit the wavelengths for exciting intrinsic fluorophores in the parathyroid glands. Emission filters (Di02-R785 + LP02-808RU, Semrock, NY, USA) were attached in front of the camera lens to selectively detect the infrared light (> 808 nm) emitted from the parathyroid glands and the visible light reflected from the surrounding surgical field with a ratio of 1:0.01. The light of excitation laser was limited to the OD8 level so that the autofluorescence image could not be affected. (Fig. 1B) Each part was put into a plastic case to make one instrument, which was named as the auto-para viewer.

![Image](image_url)

**Fig. 1.** (A) Main components of the auto-para viewer, a Raspberry Pi development board and a Raspberry Pi camera. (B) Specification of the emission filter used in the experiment.

2.2 Patient selection and imaging procedure

The study was performed on six parathyroid glands in three patients who underwent thyroidectomy for papillary thyroid cancer (Table 1). All patients underwent unilateral lobectomy and prophylactic cervical lymphadenectomy on the ipsilateral side. The surgeries were performed by one skilled surgeon as follows. The thyroid was exposed. The thyroid gland was pulled medially with a pair of forceps to expose the posterior surface and the fatty tissue near to the airway. An image of the surgical area was taken by the auto-para viewer when the suspected parathyroid tissue was visible. (Fig. 2) Photographs were taken in three steps to compare the normal photographs in visible light, autofluorescence in near infrared light, and autofluorescence in visible and near infrared light. First, when the suspected parathyroid gland was found with the naked eye, the operation area was photographed to acquire the reference image with a general digital camera. (Fig. 3(A)) Second, autofluorescence images of the parathyroid gland were photographed with the auto-para viewer by illuminating the near-infrared exciting light in the surgical site without the surgical light and the room light to minimize effects from other wavelengths. (Fig. 3(B)) Finally, only the room light was turned on, and the near infrared auto fluorescence image was taken once
again with the auto-para viewer. (Fig. 3(C)) This was to examine the effect of the room light on the autofluorescence and background image.

**Table 1. Patient demographic data**

| Patient Number | Age | Gender | Diagnosis | Operation Extent | Number of Parathyroid Glands | Confidence Level of Surgeon |
|----------------|-----|--------|-----------|-----------------|-----------------------------|---------------------------|
| 1              | 38  | F      | PTC       | Hemithyroidectomy right, CCND | 2                           | high                      |
| 2              | 42  | F      | PTC       | Hemithyroidectomy right, CCND | 2                           | high                      |
| 3              | 41  | F      | PTC       | Hemithyroidectomy right, CCND | 2                           | high                      |

*PTC*, papillary thyroid carcinoma; *CCND*, central compartment neck dissection

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**Fig. 2.** Intraoperative equipment set-up for NIR imaging. Upon the suspected area of the exposed parathyroid gland, the auto-para viewer took autofluorescence image while the region of interest was illuminated by a diode laser.

**Fig. 3.** Three steps were used to take pictures in the experiment. (A) The reference images were taken with a normal DSLR camera with the room light. (B) Autofluorescence images were taken with the auto-para viewer with the room light turned off and a diode laser with a wavelength of 785 nm illuminated. (C) After the room lights were turned back on, the auto-para viewer captured the autofluorescence images.

All equipment for parathyroid imaging was ready for operation prior to surgery. The general digital camera and the auto-para viewer were placed at a distance of about 30 cm near the operating table when shooting. The general digital camera photographed the operation area using dedicated illumination. The auto-para viewer photographed an area of approximately 5x5 cm², including both the tissue expected to be the parathyroid and the surrounding area, with a 785 nm diode laser. Simultaneously, both the surgical lights and the room lights were turned off. The exposure time for autofluorescence was 2 seconds to obtain a sufficient intensity of parathyroid image in a still image. The auto-para viewer could
provide video in addition to the still image in real-time via the preview mode. In addition, the autofluorescence image was taken when using the room lights turned on to compare the effect of the room light on the image. The total time spent in the experiment was about 1-2 minutes and did not affect the overall operation time.

This study was approved by the Institutional Review Board of Kosin University Hospital and was performed after all patients were informed and consent was obtained.

2.3 Experiment principle and image analysis

Autofluorescence is a light that naturally radiates when a biological structure absorbs light of a particular wavelength. This term is used to distinguish itself from an artificial fluorescence from an exogenous fluorescent dye, such as indocyanine green [13]. The technique of revealing the parathyroid using autofluorescence is the latest research field. In general, autofluorescence has been known to occur in the visible light region by absorbing ultraviolet light. Paras et al. [14] first introduced the fact that the parathyroid gland emits light at a wavelength of 820 nm when it absorbs near-infrared light at a wavelength of 785 nm in 2011. The researchers also reported that the surrounding tissues such as fat, muscles, blood vessels, nerves, and trachea could be visually discriminated from the parathyroid glands because they did not have autofluorescence [14]. Although the principle of autofluorescence has not yet been elucidated, the calcium-sensing receptors were found in the chief cell of the parathyroid glands, more than in the thyroid glands, and were not distributed in other tissues of the neck. This receptor was presumed to be the cause of autofluorescence [15].

The laser light source irradiated the light of the center wavelength of 785 nm through the excitation filter (769 nm center wavelength, 41 nm bandwidth, and OD >6) to the surgical region predicted to be the parathyroid gland. The parathyroid glands immediately emitted light of a longer wavelength than the excitation light when they absorbed the excitation light. This light was called autofluorescence. The emitted autofluorescence light with information of the parathyroid location was transmitted through a 785 nm long pass filter and an 808 nm long pass filter inside the auto-para viewer to eliminate the illuminated light for excitation. Finally, it entered the NOIR camera. (Fig. 4) The information input to the camera was output to the monitor as an image that could be observed in real time. Intraoperatively, the images were checked in real-time by the monitor. The bright portion compared to the surrounding tissue was considered to be the potential parathyroid gland. The operation was performed by applying the parathyroid gland conservation technique using information taken by the auto-para viewer.

Fig. 4. Schematic of the system. Diode laser emits light at a wavelength of 785 nm through the excitation filter onto the parathyroid glands. The autofluorescent light creates an image by the auto-para viewer with the emission filter.
Additionally, this study used ImageJ software for quantitative analysis of the images. This is a verifiable software for the intensity of each pixel in the image. The location of thyroid, parathyroid, and background tissue in the images taken during surgery were designated. ImageJ was used to select approximately 300 pixels from the center of the designated location. Quantitative evaluation was carried out by measuring the mean value and standard deviation value of the selected area. The ratios of the intensities of the background tissues to the parathyroid gland were compared.

3. Results

Experiments were carried out according to the protocol to obtain a visible image, an autofluorescence image, and an autofluorescence image with visible light. (Fig. 5) The parathyroid glands were small in size and similar in color to the surrounding tissue, as shown in Fig. 5(A). The photograph from a general digital camera with a flash showed that it was difficult for the surgeon to distinguish between the parathyroid gland and surrounding tissues with a naked eye. The image of autofluorescence made it easier to distinguish the parathyroid gland because it was brighter than the surrounding tissues. (Fig. 5(B)) The autofluorescence image, which was illuminated by the room light, was weaker than before, but could still distinguish the parathyroid gland sufficiently. Furthermore, this showed the surrounding tissues with identifiable brightness and color. (Fig. 5(C)) This allowed the surgeon to locate the parathyroid glands in the actual surgical area without great difficulty.

Fig. 5. Images of the three-step experiment. (A) A visible image by a normal DSLR. The superior parathyroid gland was presumed (arrowhead). (B) Near-infrared image taken with the auto-para viewer when the room light was off. The autofluorescence of the parathyroid gland was strong (arrowhead). (C) Dual wavelength image by auto-para viewer with the room light. The entire surgical field was visualized in its original form because part of the visible light entered the camera sensor.

The quantitative data from ImageJ were normalized to facilitate comparison. The mean intensity values of thyroid and the surrounding tissues were divided by the mean intensity value of parathyroid. The normalized values were shown in Fig. 6. When the room light was off, the parathyroid gland was about four times brighter than the surrounding tissues. When the room light was on, it was about two times brighter. This result showed lower contrast than the second step, but still twice as bright. In addition, the parathyroid gland was 206% brighter in the second step and 169% brighter in the third step than the thyroid gland. It is sufficiently distinguishable.
4. Discussion

The first step was to confirm the location of the organ during surgery for the preservation of the parathyroid glands. Several methods have been introduced to identify the parathyroid glands intraoperatively. Intraoperative ultrasound, frozen section parathyroid, and a sestamibi scan have been used. These methods have limitations in that they are difficult to apply or are potentially damaging to normal parathyroid glands. In addition, these have the disadvantage of increasing the operation time because it takes time to obtain the results [16, 17]. Recently, methods of using exogenous fluorescent dye and using the autofluorescence property of the parathyroid gland have been introduced. Methylene blue, aminolevulinic acid, and other substances were introduced as external fluorescent substances, but there are limitations such as complications. Recently, indocyanine green (ICG) has taken a spotlight because it is stable and has few side effects. On the other hand, the methods using autofluorescence of the parathyroid glands are fundamentally advantageous in that there are no side effects, such as complications, since there is no injection of external substances.

Intraoperative localization of the parathyroid using autofluorescence was first introduced in 2013 by McWade et al. This study showed a high parathyroid detection rate, but showed only a parathyroid on the image. It made difficult for surgeons to confirm the exact location among peripheral structures, such as the thyroid gland. Although it is possible to confirm the position using two images taken by the visible light camera and the near infrared camera, the two image synthesis steps can cause disadvantages, such as a delayed operation time [8]. In our previous study, a near-infrared imaging method was proposed to overcome their shortcomings. The method additionally provided broadband near-infrared light, allowing the simultaneous taking of the peripheral structures without image processing. The time required to acquire the image was about 2-3 minutes, which did not affect the overall operation time [11].

This study was carried out by using Raspberry Pi for autofluorescence NIR imaging of the parathyroid glands. This aimed to localize the parathyroid intraoperatively. The autofluorescent light incident of the camera was sufficient. Enough light intensity could reduce the camera's exposure time required for shooting. This made it possible to use the video method as well as the existing photographic method. The emission filters also transmitted a portion of the light in the visible light region unlike the conventional method. The incident visible light allowed the surgeon to observe the surgical area at a glance. The surgeon could easily find the parathyroid gland that was hard to see with the naked eye during surgery. In addition, the discrimination could be improved by turning off the room light when the position of the parathyroid gland was not clear.
On the other hand, the limitations of this study are as follows. The near infrared light has the advantage of penetrating tissue, but its depth is only several millimeters. Therefore, the auto-para viewer can be used to confirm when the predicted site of the parathyroid gland is exposed, as in the conventional studies. Next, the image is affected by the room light. The image looks green, entirely unlike the first step, which uses an additional camera flash. The image was dominated by 540 nm because the operating room light strongly illuminated at 540 nm. On the other hand, the entire image can be seen as white when the surgical area is taken in a surgical light. Surgical light is an indispensable element during surgery, allowing the operator to see the surgical field without any difference in contrast. It has a relatively high energy and an even spectrum distribution compared to a room light. The images are saturated and appear white because the energy of the light passing through the filter inside the auto-para viewer is too strong to distinguish between the parathyroid gland and surrounding tissues. Another limitation is that the auto-para viewer is not able to monitor the blood flow of the parathyroid gland. The blood flow of the parathyroid gland is an evidence of the function of the parathyroid gland to be normal. In other words, though the auto-para viewer contributes to the preservation of the parathyroid gland, it does not determine if its function is normal. Improvement of this technique remains for future work to be resolved via ongoing research.

Another purpose of this study was to develop a device specialized for parathyroid autofluorescence imaging to be widely used in practice. The Raspberry Pi and infrared cameras are priced at a reasonable price of $80 in this study. It showed the possibility of real-time confirmation of the parathyroid gland at the laboratory stage; although, there was a disadvantage that the image quality was not excellent. This study demonstrates the possibility of developing a device capable of real-time localization of the parathyroid gland in the future.

5. Conclusion

We demonstrated that the auto-para viewer described in this study was suitable for the detection of autofluorescence of the parathyroid glands. To the best of our knowledge, this is the first real-time autofluorescence imaging method that uses only an optical method to confirm the surgical area instantly without image processing. The instrument selectively detected 1/100 of visible light and nearly all infrared light (>808 nm) by the purposely designed emission filters. The autofluorescence of the parathyroid gland was about four times brighter than the background tissues without the room light and two times brighter with the room light. Real-time imaging was possible due to the sufficient incident light to the camera. Therefore, the surgeon could localize the parathyroid glands intraoperatively in real time. The low-cost infrared camera used for dissemination is expected to be complemented during further development progresses for clinical use, although the current resolution is low due to the limited number of pixels.

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Disclosures

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