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Reconstructive

The Direct Observation of Lymphaticovenular Anastomosis Patency with Photoacoustic Lymphangiography

Yushi Suzuki, MD*
Hiroki Kajita, MD*
Hikaru Kono, MD*
Keisuke Okabe, MD, PhD*
Hisashi Sakuma, MD, PhD†
Nobuaki Imanishi, MD, PhD‡
Sadakazu Aiso, MD, PhD‡
Kazuo Kishi, MD, PhD*

Summary: It is difficult to evaluate the postoperative patency of lymphaticovenular anastomosis, but this evaluation is essential for determining surgical results. When using the current standard modality, near-infrared fluorescent lymphography, it is difficult to observe patency if the anastomotic point is veiled by dermal backflow. In this study, we used a new photoacoustic imaging device, PAI-05, to check the patency of anastomosis. We performed photoacoustic lymphangiography after lymphaticovenular anastomosis surgery. By digitally subtracting the superficial area, we can examine an area deeper than the dermal backflow, which is not visible by near-infrared fluorescent lymphography. The connection between the lymphatic vessel and the venule observed in the image is an indication of the patency of anastomosis. However, in a non-patent anastomosed site, the lymphatic vessel has a gap that separates it from the venule at the anastomosed site. Although photoacoustic lymphangiography cannot be used to visualize the lymphatic vessels that are not contrasted by indocyanine green, the resulting high-resolution images and clear anastomosis evaluation afforded by it will contribute to the development of future lymphedema treatments. *(Plast Reconstr Surg Glob Open 2021;9:e3348; doi: 10.1097/GOX.0000000000003348; Published online 28 January 2021.)*

INTRODUCTION

Lymphaticovenular anastomosis (LVA) is a surgical treatment whereby the lymphatic vessels and veins are connected to relieve symptoms of lymphedema caused by congestion of lymphatic flow. The patency of the anastomosis needs to be assessed in a postoperative evaluation. However, with the current standard for evaluation via near-infrared fluorescence (NIRF) lymphography,[1–6] the fluorescence diffuses in the deep subcutaneous fat and results in a blurry image. In addition, it is exceedingly difficult to assess the patency of anastomosis beneath the dermal backflow (DBF), especially if the DBF spreads rapidly. The photoacoustic imaging (PAI) system PAI-05 allows for clearer observations at a similar depth as that of NIRF lymphography. In addition, this new imaging system can process DBF images, allowing for clear visualization of the anastomosis.[7] Here, we present 2 cases where patent anastomoses were observed by photoacoustic lymphangiography (PAL), and discuss the usefulness of this device in assessing the anastomosis patency of LVA.

PATENCY OBSERVATION TECHNIQUE

We used PAL, which is a new imaging technique for observing lymphatic vessels using PAI,[8–10] to evaluate the patency of anastomoses. We used the high-resolution PAI device PAI-05 to determine the patency of the anastomosis. By irradiating 2 types of laser wavelengths, PAI can be used to differentiate between lymphatic vessels and veins by utilizing the differences in the light absorption characteristics of the contrast agent and hemoglobin.

*From the *Department of Plastic and Reconstructive Surgery, Keio University School of Medicine, Tokyo, Japan; †Department of Plastic and Reconstructive Surgery, Tokyo Dental College Ichikawa General Hospital, Chiba, Japan; and ‡Department of Anatomy, Keio University School of Medicine, Tokyo, Japan.*

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Indocyanine green (ICG) (Diagnogreen 0.5%; Daiichi Sankyo Pharmaceutical, Tokyo, Japan; 5.0 mg/mL) is typically used as the contrast agent in PAL. In this study, ICG was dissolved in a 5% glucose solution, and 0.2 mL injections of ICG were administered into the subcutaneous tissue.

After injection, PAL images were taken and subsequently analyzed using the Kyoto University Rapid and Universal MIP Imager, a 3-dimensional image viewer suitable for viewing photoacoustic images.[11] NIRF lymphography was performed simultaneously using PDE-neo (Hamamatsu Photonics, Hamamatsu, Japan) for comparison.

RESULT

The patency of the anastomosis was successfully determined by PAL in 2 cases.

CASE PRESENTATION

Case 1

We assessed the right lower extremity of a 69-year-old woman with secondary lymphedema. Lymphaticovenular anastomosis superior to the knee joint and lower extremity was performed. End-to-end anastomosis was performed at the knee area, and side-to-end anastomosis was performed at the lower extremity area. To determine the patency, an examination was performed postoperatively at 1.5 years. By PDE-neo, we were not able to evaluate the anastomotic patency at the knee area of the lower extremities (Fig. 1). However, we were able to evaluate the patency of the anastomosis at the knee area via PAL but not in the lower extremity area (Figs. 2–4). (**See Video [online]**, which shows the animation of the photoacoustic lymphangiography images showing the continuity of the anastomosis.) (**See figure 1, Supplemental Digital Content 1,** which displays (a): a microscopic view of a side-to-end anastomotic site during operation; (b): the view of the anastomotic site in photoacoustic lymphangiography. The vein could not be located, possibly due to obstruction of the vessel. http://links.lww.com/PRSGO/B538.)

Case 2

We assessed the left lower extremity of a 44-year-old woman with secondary lymphedema. Lymphaticovenular anastomosis at the dorsal area was performed. The evaluation was performed 3 months after the surgery. Both PDE and PAL showed that the anastomosis was patent (**See figure 2, Supplemental Digital Content 2,** which displays the left lower extremity of a 44-year-old woman with secondary lymphedema. Photoacoustic lymphangiography was performed postoperatively at 3 months. Continuity of the lymphatic vessel and venule suggests that the anastomosis was patent. http://links.lww.com/PRSGO/B537).

DISCUSSION

An important surgical treatment for lymphedema is LVA, for which there are many options for postoperative evaluation. In general, changes in the circumference and volume of the affected limb are evaluated using the lower extremity lymphedema index and water displacement method,[12–14] and questionnaires are used to determine whether the patient's quality of life has improved.[15] However, the volume of the extremity is easily affected by compression therapy, and quality of life cannot be evaluated objectively.

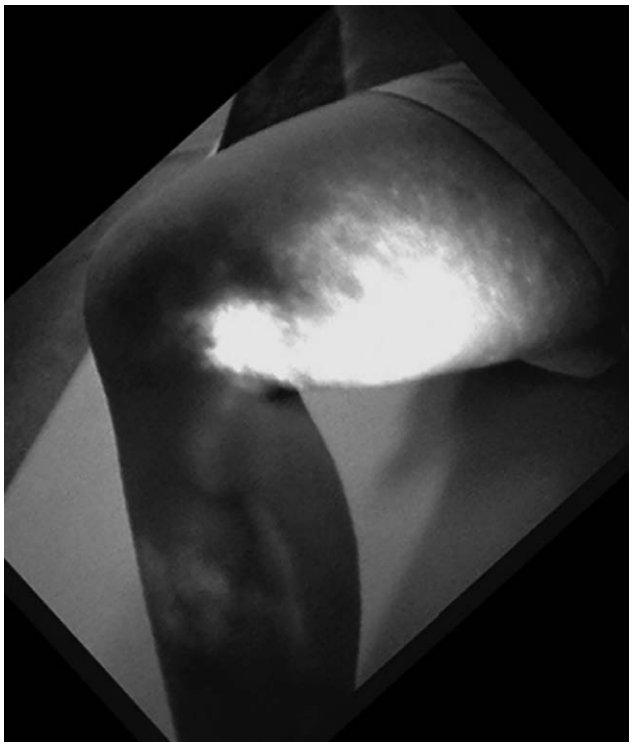

Fig. 1. The right lower extremity of a 69-year-old woman with secondary lymphedema. Lymphaticovenular anastomosis superior to the knee joint was performed. We were unable to evaluate the anastomotic site by PDE-neo due to dermal backflow.

In LVA surgery, lymphatic vessels and venules are connected, thereby releasing the congested lymphatic fluid into the peripheral blood vessels. Therefore, the patency of the anastomosis is an important surgical outcome. Of course, the main goal is to address the patients' symptoms and decrease the diameter of the patients' extremity. However, to achieve this result, anastomosis is patient is premise. If all anastomoses were obstructed, the patient's edema would never improve.

However, it is difficult to evaluate anastomoses by the modalities commonly used previously. For example, lymphoscintigraphy can be used to determine patency at the anastomotic site through changes in the DBF pattern,[12,14,16] but it is difficult to evaluate local anastomotic sites, especially if many anastomoses are performed in 1 operation. Thus, to evaluate the patency of the anastomosis one by one, NIRF lymphography is used.

When a patent anastomosis is achieved via end-to-end anastomosis, the lymphatic fluid can be directly observed using NIRF lymphography as it enters the venule. Further, in end-to-side anastomosis, patency is confirmed by 2 separate flows of the lymphatic fluid,

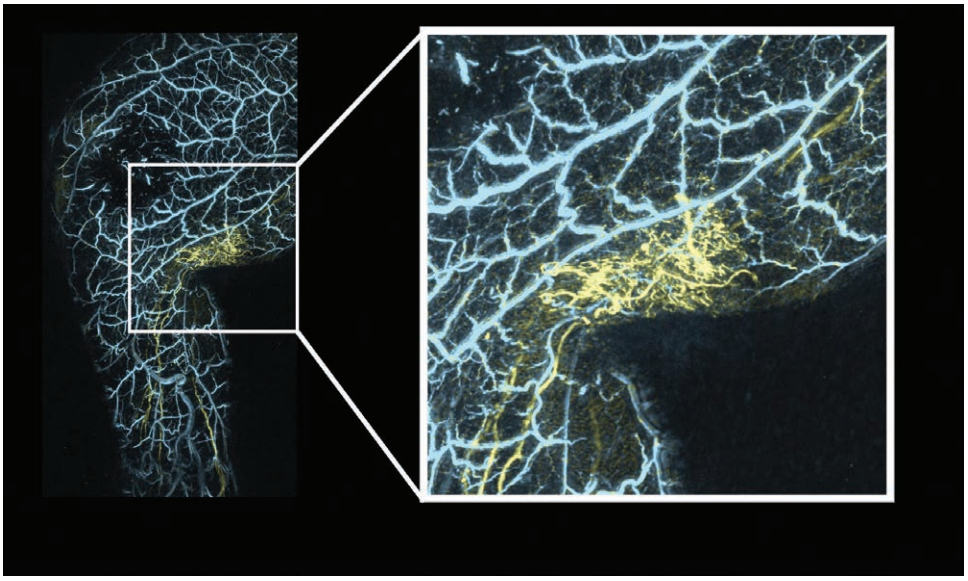

Fig. 2. Photoacoustic lymphangiography was performed postoperatively at 1.5 years. The anastomotic site was covered by dermal backflow; thus, the patency could not be assessed.

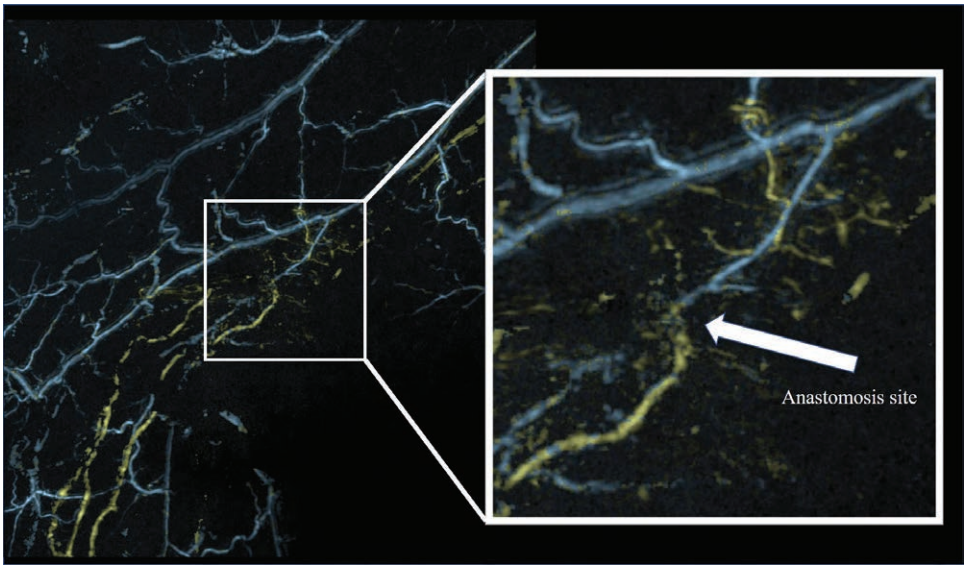

Fig. 3. A function of the Kyoto University Rapid and Universal MIP Imager viewer was used to digitally subtract the dermal backflow, allowing the continuity of the lymphatic vessel (yellow) and the venule (blue) to be observed.

and the vein is shown across the anastomotic point in NIRF lymphography. However, not all anastomoses can be evaluated using NIRF lymphography as they are in a deep subcutaneous area where the image obtained is blurrier, and in some cases, DBF covers the anastomosis area.[17–19] To solve this problem, we used a high-resolution PAI device, the PAI-05, to determine the patency of the anastomosis.

Although detecting patency using PAL is equally difficult, an advantage of PAL over NIRF lymphography is that even if the anastomosis area is obscured by DBF, this obstruction can be removed in PAL via the Kyoto University Rapid and Universal MIP Imager viewer. Therefore, the connection of the lymphatic vessel and the venule at the site of anastomosis can be clearly depicted.

In Figures 2 and 3, the colors of the lymphatic vessel and vein are different, and the connection between them is observed only at the anastomotic site, thus revealing the patency of the anastomosis. Moreover, because the image can be freely rotated by 360 degrees, the anastomotic site can be confirmed from a cross-sectional point of view. Later, the lymphatic vessel, anastomotic site, and venule can all be drawn in one figure under the DBF (Fig. 4). To show this, we have created an animation by combining the slices of the images obtained. In this video, the yellow lymphatic vessels connected to the blue veins beyond

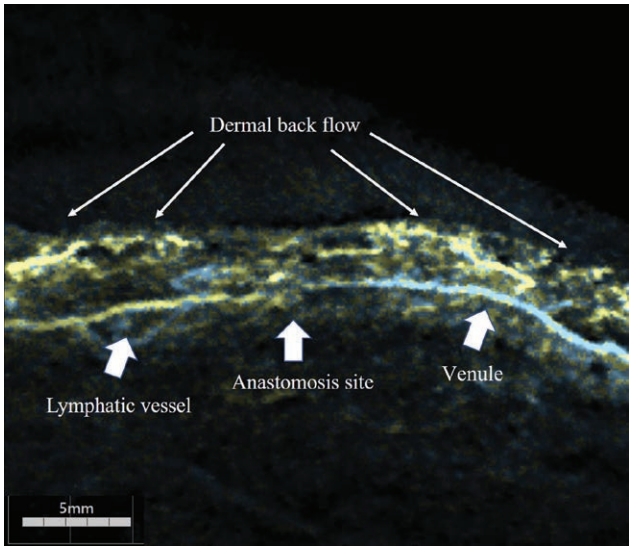

Fig. 4. A cross-sectional view of the anastomotic point; the anastomotic site was visualized beneath the dermal backflow. The lymphatic vessel is indicated in yellow, and the vein in blue.

the anastomotic site can be clearly observed. (**See Video [online]**, which shows the animation of the photoacoustic lymphangiography images showing the continuity of the anastomosis.)

However, if the anastomotic site is not covered by DBF, we can directly evaluate anastomotic patency by directly visualizing the connection between the lymphatic vessel and the vein. (see **Supplemental Figure 2**, which displays the left lower extremity of a 44-year-old woman with secondary lymphedema. Photoacoustic lymphangiography was performed postoperatively at 3 months. Continuity of the lymphatic vessel and venule suggests that the anastomosis was patent. http://links.lww.com/PRSGO/B538.)

Conversely, the image in which the lymphatic vessel was not connected to the venule at the anastomotic site indicated a non-patent anastomosis (see Figure in Supplemental Digital Content 3). We hypothesize that when the anastomosis is patent, the veins are visible due to the presence of hemoglobin. However, occlusion by thrombosis and the resulting blood clot results in a loss of the appropriate light absorber, which leads to a loss of the photoacoustic signal.

One of the limitations of PAL is that it cannot be used to visualize lymphatic vessels that do not take up the ICG. In addition, not all anastomotic sites can be observed due to a limitation of the photographic range. Thus, it is still not possible to evaluate the patency of all anastomotic sites by PAL. However, we believe that this technique can provide useful information toward the development of future treatments for lymphedema at anastomotic sites that could not be evaluated by NIFR lymphography.

CONCLUSIONS

This is the first report documenting the confirmation of anastomotic patency using PAL, which, to date, has not been established by other imaging modalities. We believe that PAL may be a good option for evaluating postoperative patency of LVA.

Yushi Suzuki, MD
Department of Plastic and Reconstructive Surgery
Keio University School of Medicine
35 Shinanomachi, Shinjuku-ku
Tokyo 160-8582
Japan
E-mail: yushisuzuki-kei@umin.ac.jp

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