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Superficial and Functional Lymphatic Anatomy of the Upper Extremity

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Background: Knowledge of detailed lymphatic anatomy in humans is limited, as the small size of lymphatic channels makes it difficult to image. Most current knowledge of the superficial lymphatic system has been obtained from cadaveric dissections.

Methods: Indocyanine green lymphography was performed preoperatively to map the functional arm lymphatics in breast cancer patients without clinical or objective evidence of lymphedema. A retrospective review was performed to extract demographic, indocyanine green imaging, and surgical data.

Results: Three main functional forearm channels with variable connections to two upper arm pathways were identified. The median forearm channel predominantly courses in the volar forearm (99 percent). The ulnar forearm channel courses in the volar forearm in the majority of patients (66 percent). The radial forearm channel courses in the dorsal forearm in the majority of patients (92 percent). Median (100 percent), radial (91 percent), and ulnar (96 percent) channels almost universally connect to the medial upper arm channel. In contrast, connections to the lateral upper arm channel occur less frequently from the radial (40 percent) and ulnar (31 percent) channels.

Conclusions: This study details the anatomy of three forearm lymphatic channels and their connections to the upper arm in living adults without lymphatic disease. Knowledge of these pathways and variations is relevant to any individual performing procedures on the upper extremities, as injury to the superficial lymphatic system can predispose patients to the development of lymphedema. (*Plast. Reconstr. Surg.* 150: 900, 2022.)

of normal lymphatic anatomy is limited. The small size of lymphatics limits the imaging and mapping of this organ system. For example, whereas the largest artery (aorta) and vein (vena cava) in the human body are 2 to 3 cm in diameter, the largest lymphatic (thoracic duct) is only 2 mm in diameter. Historically, detailed imaging of the lymphatic system was possible using lymphangiography, but it was primarily used in the study of the lymphatic system in patients with a diagnosis of lymphedema. Moreover, routine use has fallen out of favor given its invasive nature. Although lymphoscintigraphy has become the standard of lymphatic imaging in the workup of lymphedema,

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it cannot be used for fine anatomical mapping, as its main utility is demonstrating lymphatic function. Current knowledge of normal lymphatic anatomy in humans comes almost exclusively from cadaveric studies. However, even in cadavers, the small size of the lymphatic channels necessitates specialized injections and months of dissection for a single extremity, limiting understanding of functional anatomy, including its variations in vivo. The anatomy of the superficial lymphatic system and its variations are pertinent to any practitioner who performs procedures on the upper extremity, as division of lymphatics, even outside a nodal basin, can predispose patients to lymphedema.

Cadaveric studies have provided a fundamental understanding of lymphatic anatomy, dating back to the eighteenth and nineteenth centuries when Mascagni and Sappey, respectively, first published the results of their dissections.^{6,7} In a landmark article from 1993 of 300 cadaveric dissections (90

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percent fetal), Leduc et al. laboriously described the lymphatic pathways of the upper extremity and provided their nomenclature.8 Suami et al., using a similar method of cadaveric dissection, described these channels but, rather than naming them individually, divided the extremity into lymphosomes, or lymphatic territories that drain to a particular node or nodal basin.^{4,9} Although the findings from these cadaveric dissections have been central to our current understanding of lymphatic anatomy, a critical limitation is their lack of characterization of functional lymphatic anatomy. All vascular systems in the body are dynamic, and cadaveric studies do not allow us to understand how these pathways function in relation to one another. A relatively newer imaging modality, indocyanine green lymphography, allows for realtime visualization of functional lymphatic channels. We have previously noted that the lymphatic system would preferentially drain to certain pathways even when other pathways were present. 10 To date, indocyanine green lymphography has been used primarily for the clinical staging and evaluation of patients with lymphedema and not for further elucidation of normal functional anatomy.

At our institution, all breast cancer patients who are deemed high risk for developing lymphedema undergo preoperative indocyanine green lymphography to map their lymphatic system according to our standard of care. Of significant note, none of these patients has lymphedema or a history of lymphedema before imaging. These indocyanine green lymphographs, therefore, provide a unique view of the in vivo superficial and functional lymphatic anatomy of the upper extremity. In this study, we describe the anatomy of the main superficial lymphatic channels that arise in the hand and forearm and drain to the torso by means of the upper arm.

METHODS

Indocyanine Green Lymphography

Under sterile conditions, 0.1 cc of stock (2.5 mg/cc) indocyanine green solution (Akorn Inc., Lake Forest, Ill.) with albumin was injected intradermally at three anatomical locations: 1 cm proximal to the first and fourth web spaces on the dorsum of the hand and 1 cm proximal to the wrist crease in the volar forearm. The locations of these injections were based on the lymphosome concept described by Suami et al.⁴ By injecting each lymphosome, the major lymphatic drainage pathways of the hand and

forearm are represented.⁴ A near-infrared imaging device, the PDE-Neo II (Hamamatsu Photonics KK, Hamamatsu, Japan) was used to visualize the superficial lymphatic channels of the extremity. All indocyanine green lymphographs were obtained by one of two members of the lymphatic surgery team (E.T. or D.S.), and final interpretation was performed by a single lymphatic surgeon (D.S.) for all studies.

Three major superficial lymphatic pathways arising from the hand and forearm were consistently described and recorded in real time immediately following injection. The median channel was defined as the channel arising from the volar forearm injection. The radial channel was identified as that arising from the first web space injection. Finally, the ulnar channel was defined as the pathway arising from the fourth web space injection. Continuation of these pathways into the upper arm were labeled as medial and/or lateral channels. Lateral upper arm channels were defined as those coursing along the cephalic vein (identified using ultrasonography before injection) in the lateral upper arm. Medial upper arm channels were those that coursed along the basilic vein in the medial upper arm.

Retrospective Review

A retrospective review of our lymphatic surgery Research Electronic Data Capture database was performed. Institutional review board approval was obtained (protocol number 2020P000274). Consecutive patients with a diagnosis of nodepositive breast cancer undergoing ipsilateral preoperative indocyanine green lymphography were identified. Patient demographics and cancer characteristics were extracted for analysis. Exclusion criteria included (1) any subjective or objective evidence of lymphedema before indocyanine green imaging and/or (2) any surgical history involving the extremity. Our objective criteria for lymphedema included a volume differential of greater than 10 percent or an L-Dex (ImpediMed, Inc., Carlsbad, Calif.) score greater than 10.

RESULTS

Patient Demographics and Cancer Characteristics

One hundred four consecutive indocyanine green lymphographs from November of 2018 to October of 2020 were analyzed. Average age at the time of axillary surgery was 55 ± 12 years, and body mass index was 28.2 ± 6 kg/m². Most patients were female (98 percent). Most patients completed

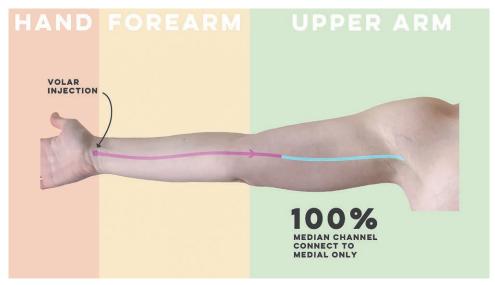


Fig. 1. Schematic depiction of the anatomical course of the median forearm channel.

neoadjuvant chemotherapy (62 percent) at the time of imaging. All patients had node-positive disease, established by fine-needle aspiration (13 percent), core needle biopsy (39 percent), or sentinel lymph node biopsy (48 percent). The median number of nodes removed during sentinel lymph node biopsy was three (interquartile range, two to four). Following indocyanine green lymphography, the median number of nodes removed during axillary lymph node dissection was 15 (interquartile range, 10.75 to 22) and the median number of nodes demonstrating metastatic disease was one (interquartile range, zero to three).

Anatomical Analysis

Two patients were found to have nonlinear (e.g., diseased) lymphatic channels and thus were excluded from the anatomical analysis. The course of the three main lymphatic pathways of the hand and forearm of the remaining 102 patients are detailed below, including their variable connections to the upper arm.

Median Channel (Dermal Injection of the Volar Forearm)

A schematic depiction of the anatomical variants of the median channel is available in Figure 1. The median channel continues in the volar forearm 99 percent of the time (n = 101). In one patient, the median channel transitioned to the dorsal forearm over the radial side of the forearm. All median channels connected to only the medial upper arm channel (100 percent).

Radial Channel (Dermal Injection 1 cm Proximal to the First Web Space)

A schematic depiction of the anatomical variants of the radial channel is available in Figure 2. The radial channel courses in the dorsal forearm 92 percent (n = 94) of the time. These dorsal forearm channels continued to connect to only the medial upper arm pathway in 56 percent (n = 53), only the lateral upper arm pathway in 16 percent (n = 15), and both the medial and lateral pathways in 28 percent (n = 26). A branch off the dorsal radial forearm channel was identified in 30 percent of cases (n = 28). All branches off the dorsal radial forearm channel transitioned to the volar forearm and connected to the medial upper arm channel.

The radial channel did not continue in the dorsal forearm, transitioning to the volar forearm 8 percent (n = 8) of the time. All these channels connected to the medial upper arm channel only. Including all 102 patients described, the radial forearm channel connected to only the medial upper arm pathway in 60 percent (n = 61), only the lateral pathway in 9 percent (n = 9), and both in 31 percent (n = 32).

Ulnar Channel (Dermal Injection 1 cm Proximal to the Fourth Web Space)

A schematic depiction of the anatomical variants of the ulnar forearm channel is available in Figure 3. The ulnar channel courses in the dorsal forearm 34 percent (n = 35) of the time. These dorsal ulnar forearm channels continued to connect to only the medial upper arm pathway in 11 percent (n = 4), only the lateral pathway in 66

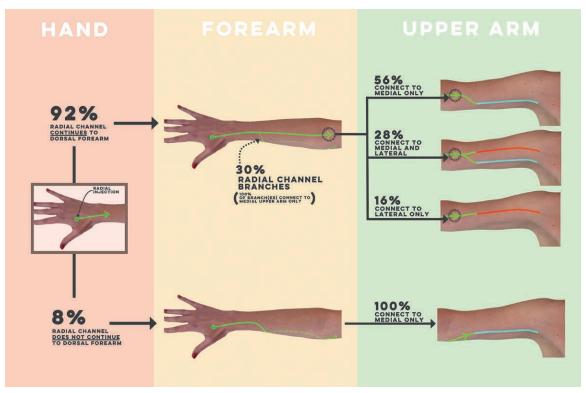


Fig. 2. Schematic depiction of the anatomical course of the radial forearm channel.

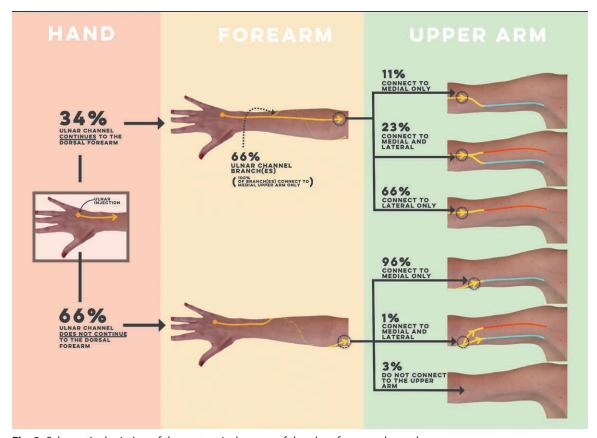


Fig. 3. Schematic depiction of the anatomical course of the ulnar forearm channel.

percent (n = 23), and both the medial and lateral pathways in 23 percent (n = 8). A branch off the dorsal ulnar forearm channel was identified in 66 percent of patients (n = 23).

All branches transitioned to the volar forearm and connected to the medial upper arm pathway. The ulnar channel transitioned to the volar forearm 66 percent (n = 67) of the time. Of these, 96 percent (n = 64) connected to only the medial upper arm pathway, and 1 percent (n = 1) connected to both the medial and lateral upper arm pathways. Two ulnar channels on the volar forearm did not connect to any upper arm pathways (3 percent). Including all 102 patients described, the ulnar forearm channel connected to only the medial upper arm pathway in 67 percent (n = 68), only the lateral pathway in 4 percent (n = 4), the medial and lateral pathways in 27 percent (n =28), and did not connect to the upper arm in 2 percent (n = 2).

DISCUSSION

In this article, we describe the in vivo superficial and functional anatomy of the superficial lymphatic system of the upper extremity in patients without evidence of lymphedema. Of note, although the channels appear as single pathways on indocyanine green imaging, they represent the convergence of small tributaries in a particular lymphosome and therefore are composed of many individual lymphatic channels. Moreover, based on the lymphosome concept, these visualized channels are representative of the course of the other nonvisualized lymphatics within the given lymphosome. We tracked the course of three main pathways from the hand and forearm (median, radial, and ulnar) and their connections to two pathways in the upper arm (medial

and lateral). Specifically, the median forearm channel predominantly traveled in the volar forearm (99 percent) (Fig. 4). We found that the radial channel coursed in the dorsal forearm in the majority of patients (92 percent). In contrast, the ulnar forearm channel coursed in the volar forearm in the majority of patients (66 percent) (Fig. 5). Regarding connections to the upper arm, the median channel was the most consistent, with 100 percent connecting to the medial upper arm channel. In contrast, for radial and ulnar forearm channels, the type of upper arm connection correlated with the course of the channel in the forearm. Specifically, regardless of injection site, if the pathway transitioned from the dorsal to the volar forearm, it almost universally connected to the medial upper arm (Fig. 6). However, if the pathway coursed in the dorsal forearm, a contribution to the lateral upper arm pathway was more likely (Fig. 7).

There is considerable variation in the anatomical course of the radial channel. The radial channel usually courses along the dorsal forearm (92 percent) as it progresses toward the upper arm. When traveling dorsally in the forearm, this channel demonstrates variability in its connections to the upper arm, with a predominance of medial upper arm connections (84 percent) versus lateral upper arm connections (44 percent). In contrast, when the radial channel transitions to the volar forearm, or a branch off a dorsal radial channel transitions to the volar forearm, these ultimately connect to the medial upper arm only.

The ulnar channel also demonstrates significant variability. The ulnar forearm channel transitions to the volar forearm in the majority of patients (66 percent), unlike the radial channel, and predominantly connects to only the medial upper arm. When the ulnar channel travels in the

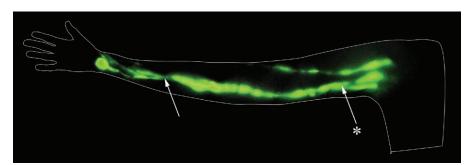


Fig. 4. Indocyanine green lymphography imaging of the median forearm channel of a right arm with the palm supinated. The median forearm channel is identified on the volar aspect of the forearm (*arrow*). It connects to the medial upper arm pathway (*). This image was created from still images taken from a video captured with the PDE-Neo II. Still images were captured from the video and stitched together, and no other alterations were made.

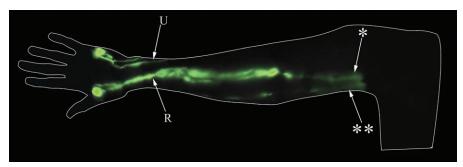


Fig. 5. Indocyanine green lymphography imaging illustrating the radial and ulnar forearm channels of a right arm with the palm pronated. The radial forearm channel in the dorsal forearm (*R*), connects to the lateral upper arm pathway (*). The ulnar forearm channel does not continue to the dorsal forearm, transitioning to the volar forearm (*U*). The ulnar channel connects to the medial upper arm pathway (**). This image was created from still images taken from a video captured with the PDE-Neo II. Still images were captured from the video and stitched together, and only zoom was altered to create contiguous channels of similar size. All arms were reflected to standardize anatomical landmarks. No other postproduction alteration was conducted, including changes in contrast.



Fig. 6. Indocyanine green lymphography imaging illustrating the radial forearm channel of a right arm with the palm pronated. The radial forearm channel does not continue in the dorsal forearm, but rather transitions to the volar forearm (*arrow*). It connects to the medial upper arm pathway (*). This image was created from still images taken from a video captured with the PDE-Neo II. Still images were captured from the video and stitched together, and no other alterations were made.

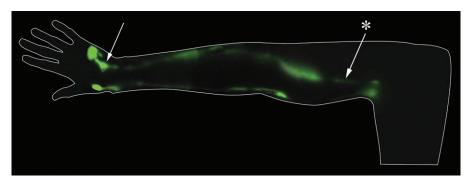


Fig. 7. Indocyanine green lymphography imaging illustrating the radial and ulnar forearm channels of a right arm with the palm pronated. The ulnar forearm channel continues in the dorsal forearm (*arrow*). It connects to the lateral upper arm pathway (*). The radial channel also remains in the dorsal forearm but connects to the medial upper arm channel. This image was created from still images taken from a video captured with the PDE-Neo II. Still images were captured from the video and stitched together, and no other alterations were made.

dorsal forearm (34 percent), connections to the lateral upper arm (89 percent) are most likely versus those to the medial upper arm (34 percent). Interestingly, in two patients, the ulnar channel abruptly discontinued at the antecubital fossa. We believe that this is because of the pathway diving deeper into the extremity, perhaps connecting to the deep lymphatic system. 9,12

The above findings are commensurate with reports by Suami et al.^{4,9} Specifically, using the lymphosome concept, Suami et al. noted that the majority of the lymphatic pathways from the hand and forearm flowed into the medial upper arm and into a sentinel lymph node in the axillary region. Moreover, Suami et al. noted that pathways that passed along the dorsal aspect of the arm may bypass the main sentinel node in the axilla and reach smaller "sentry" nodes. 4 Previously, we demonstrated that the lateral upper arm pathway, often referred to as the Mascagni-Sappey pathway, most often bypasses the main lymph nodes of the axillary basin.¹³ Similarly, we also demonstrated that the lymphatic pathways of the medial upper arm, overlying the basilic vein, universally drained into the axillary basin. 13 Our current study provides further granularity in the mapping of the functional lymphatic pathways of the upper extremity and how their specific anatomical course affects their connections to the medial versus lateral upper arm and, subsequently, their draining nodal basins. This anatomical understanding has significant clinical implications as, if both the medial and lateral pathways are present, they can act as a "backup" pathway for each other in the event of injury, as has been previously postulated.¹⁴

We believe that this anatomy is of utmost relevance to any surgeon operating on the upper extremity. Specifically, knowledge of the functional lymphatic pathways would support longitudinal incisions that would be least likely to damage the pathways that travel axially. Moreover, general knowledge of the location of the functional lymphatic pathways could inform surgeons of anatomical regions where extirpative procedures may be at high risk of causing lymphedema (e.g., in areas where the medial and lateral upper arm pathways may both be compromised). In cases where patients may have had prior compromise to one of the two upper arm pathways (e.g., a history of axillary surgery or a lateral upper arm skin cancer excision), further caution would be warranted before potentially compromising the remaining pathway providing drainage for the entire arm.¹⁴ In such cases, preoperative indocyanine green lymphography may provide appropriate mapping of the

pathways at risk and prophylactic rerouting of the functional lymphatic system could be considered. For lymphatic surgeons, the anatomical patterns described in this study may better inform the location of lymphovenous bypasses and lymph node transplantation. Specifically, in a patient with breast cancer-related lymphedema after an axillary lymph node dissection, the radial aspect of the forearm is slightly more likely to have drainage to the lateral upper arm pathway and therefore be able to bypass the axilla than the ulnar aspect of the forearm. In fact, magnetic resonance imaging studies from our institution have noted the edema of breast cancerrelated lymphedema patients to be significantly more notable at the ulnar aspect of the forearm.¹⁵ Therefore, lymphatic interventions may be more effective when performed at the ulnar aspect of the arm for breast cancer-related lymphedema.

Of note, two patients included in our study cohort had nonlinear (diseased) channels, or abnormal lymphatic anatomy. Although excluded from the above anatomical analysis, further commentary on their clinical scenarios is warranted. Specifically, one patient had undergone sentinel lymph node biopsy 6 months before in which seven nodes were removed, of which six were positive. This case is interesting, as it may indicate that lymphatic changes can occur very rapidly following a surgical insult. The second patient with nonlinear channels received steroid injections 21 months previously for ulnar wrist pain, overlapping the location of the nonlinear pattern visualized. Although patients with prior operations of the operative extremity were excluded from analysis, we did not exclude patients with histories of injections to the extremity. This case underscores the importance of delineating normal lymphatic anatomy to better understand and describe changes that routine intervention on the upper extremity may have on lymphatic anatomy and function.

This study has limitations. First, the study population had breast cancer with demonstrated axillary nodal metastases at the time of imaging. Therefore, an argument may be made that our findings may not represent the general population. However, we believe the anatomy described likely represents physiologic anatomy and is applicable to healthy patients, as most patients in this cohort did not have any significant axillary burden (median of one positive node from axillary lymph node dissection). Moreover, it has been previously noted that the arm and breast sentinel nodes do not overlap 96 percent of the time. Therefore, the likelihood of an axilla with low disease burden significantly impacting the functional lymphatic mapping of the upper

extremity is unlikely. We are currently undertaking a multiyear study in healthy volunteers to repeat the reported study in patients without cancer or any other interventions of the arm. We hope this work will corroborate that our findings in this article are a good representation of normal lymphatic anatomy and its variation. Second, although indocyanine green lymphography has many advantages as described, one disadvantage is its shallow depth of penetration (1, 2, and 4 cm), and therefore we were only able to describe the superficial lymphatic anatomy.¹⁷ In the two patients in whom the ulnar channel was no longer visible at the antecubital fossa, we can only hypothesize that the channels coursed deep, out of range of our indocyanine green imaging. The inability to concurrently describe the deep lymphatic system is an additional limitation of this study. Finally, although we did include patients of both biological sexes, our results are likely more relevant to women because of their overwhelming majority in our cohort (98 percent). Lymphatic anatomical variation between sexes is unknown.

CONCLUSIONS

We describe the in vivo superficial and functional lymphatic anatomy of the upper extremity. We consistently noted three main forearm channels (median, radial, and ulnar) and two main upper arm channels (medial and lateral), and their variable interconnections. Although historic cadaveric data describe other channels in the upper extremity, our data suggest that these are the most functionally active. To minimize iatrogenic disruption of the superficial lymphatic anatomy, we believe all practitioners who perform operations on the upper extremity should be aware of its anatomy. In the future, we hope to be able to corroborate these findings with highfrequency ultrasound, and correlate anatomical variants with the development of lymphatic dysfunction, to better guide all practitioners on the surgical and procedural planning of the upper extremity.

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