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Breast Cancer-Related Lymphedema: Magnetic Resonance Imaging Evidence of Sparing Centered Along the Cephalic Vein

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Abstract:

Background A distinct pattern of edema distribution is seen in breast cancer-related lymphedema. The area of edema sparing has not been characterized in relation to anatomy. Specifically, alternate lymphatic pathways are known to travel adjacent to the cephalic vein. Our study aims to define the location of edema sparing in the arm relative to the cephalic vein.

Methods A retrospective review of patients who underwent magnetic resonance imaging (MRI) between March 2017 and September 2018 was performed. Variables including patient demographics, arm volumes, and MRI data were extracted. MRIs were reviewed to define the amount of sparing, or angle of sparing, and the deviation between the center of sparing and the cephalic vein, or angle of deviation.

Results A total of 34 consecutive patients were included in the analysis. Five patients demonstrated circumferential edema (no sparing) and 29 patients demonstrated areas of edema sparing. Advanced age (69.7 vs. 57.6 years) and greater excess arm volume (40.4 vs. 20.8%) correlated with having circumferential edema without sparing ($p = 0.003$). In 29 patients with areas of edema sparing, the upper arm demonstrated the greatest angle of sparing (183.2 degrees) and the narrowest in the forearm (99.9 degrees; $p = 0.0032$). The mean angle of deviation to the cephalic vein measured 3.2, −0.1, and −5.2 degrees at the upper arm, elbow, and forearm, respectively.

Conclusion Our study found that the area of edema sparing, when present, is centered around the cephalic vein. This may be explained by the presence of the Mascagni-Sappey (M-S) pathway as it is located alongside the cephalic vein. Our findings represent a key springboard for additional research to better elucidate any trends between the presence of the M-S pathway, areas of sparing, and severity of lymphedema.

Keywords
- ► lymphedema
- ► BCRL
- ► anatomy
- ► M-S pathway

The patterns of edema distribution in breast cancer-related lymphedema (BCRL) have not been well characterized. A recent magnetic resonance imaging (MRI) study of BCRL patients demonstrated a distinct pattern of edema in the affected arm.[1] Our study aims to characterize the areas that are spared. Specifically, we have noted that areas without edema correlate closely with the path of the cephalic vein. This observation is potentially important as an alternate lymphatic pathway travels alongside the cephalic vein. Being able to better define the areas of sparing, and potentially why they are spared, may be useful in planning lymphatic operations.

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While the predominant drainage pathway of the upper extremity terminates in the axilla, an alternative pathway, termed the Mascagni-Sappey (M-S) pathway, is variably present and courses along the cephalic vein.[2,3] Notably, the M-S pathway is presumably spared after an axillary lymph node dissection (ALND) as it traditionally avoids the axilla,[4] which may explain why certain patients never develop lymphedema despite ALND.[5–8] We retrospectively reviewed MRIs for BCRL patients with the aim of mapping the areas without edema and analyzing their relationship to the cephalic vein.

Methods

Patient Selection

Patients presenting to our lymphatic center who were diagnosed with BCRL and underwent MRI between March 2017 and September 2018 were included. Patient demographics, volume measurements, and MRI data were obtained. Compression garments were removed 48 hours prior to volumetry and MRI. This retrospective study was approved by our institutional review board (IRB 2018P000085).

Volume Evaluation

A perometer (Perometer 1000 NT, Pero-System Messgeräte GmbH, Wuppertal, Germany) was utilized to measure limb volumes.[9] All measurements were obtained by two certified lymphedema therapists.

Magnetic Resonance Imaging Technique

Dedicated upper extremity MRIs were performed on a single 1.5 T scanner, the Siemens Magnetom Aera, (Siemens Healthcare, Erlangen, Germany) by using two 13-channel body array coils. Patients were positioned supine, with arms at the sides and palms facing medially. Axial short-tau inversion recovery (slice thickness 6 mm, in-plane resolution 1.5–1.7 mm, TR: 7,000–7,500 ms, TE: 50–60 ms) sequences were acquired from shoulder to elbow and then forearm to hand. The imaged unaffected limb served as a control.

Magnetic Resonance Imaging Analysis

Two radiology residents and a board-certified radiologist analyzed MRI images using McKesson PACS. The angle of sparing and angle of deviation were measured (►**Fig. 1**).

Statistical Analysis

A one-way ANOVA test was performed to evaluate (1) the relationship between extent of edema involvement versus patient demographics and arm volumes, and (2) the angle of sparing at three anatomic locations. A Fisher's exact test was performed to evaluate the relationship between the extent of edema involvement and cancer treatments.

Results

In total, 35 consecutive women with unilateral BCRL underwent MRI during the study period. It should be noted that the MRIs were obtained as part of a comprehensive evaluation, including lymphoscintigraphy and indocyanine green (ICG) lymphangiography. One patient demonstrated no edema on MRI and was excluded. Of the remaining 34 patients, five patients (15%) demonstrated circumferential edema (no sparing) while 29 patients (85%) demonstrated areas of sparing. Patient demographics are summarized in ►**Table 1**. Advanced age correlated ($p = 0.003$) with having circumferential edema. In these five patients, the average volume differential between the affected and unaffected arm was 40.4% compared to 20.8% in patients with evidence of sparing ($p = 0.003$; ►**Fig. 2**).

In the 29 patients with evidence of edema sparing, the upper arm demonstrated the greatest angle of sparing (183.2 degrees) and the forearm demonstrated the narrowest (99.9 degrees; $p = 0.0032$). The cephalic vein's angle of deviation from the center of sparing was 3.2, –0.1, and –5.2 degrees at the upper arm, elbow, and forearm, respectively ($p > 0.5$; ►**Fig. 3**).

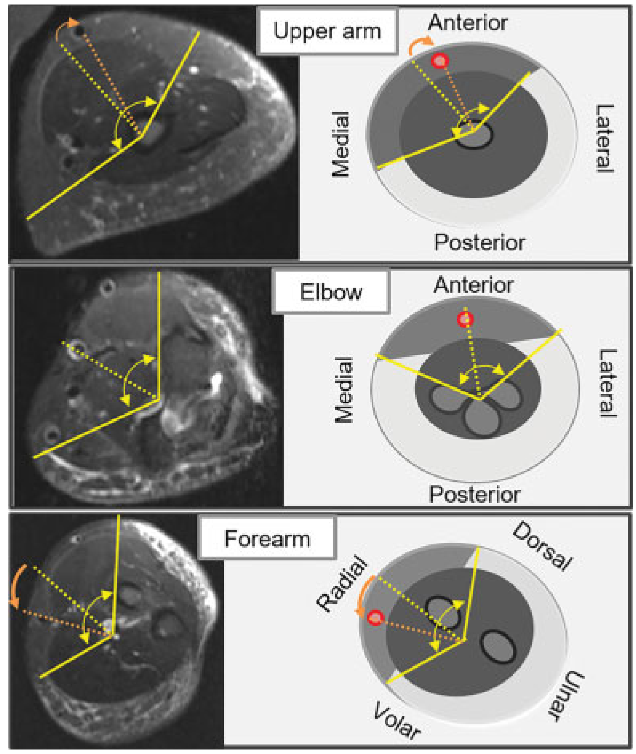

Fig. 1 Calculating the angle of sparing and angle of deviation. In this representative case, the arm was evaluated at three anatomic locations: (upper arm) 5 cm cephalad to the humeral epicondyle, (elbow) at the humeral epicondyle, and (forearm) 5 cm caudal to the epicondyle. The cephalic vein was identified by tracing the medial superficial branch from the subclavian vein. The most medial and lateral edges of edema were identified (solid yellow lines) and the angle of sparing between the edges was measured. This angle was then bisected to mark the center (dotted yellow line), and the angle of deviation between the center and the cephalic vein (dotted orange line) was calculated. For analysis, positive angle measurement denotes lateral deviation of the true location of the cephalic vein relative to the expected location at the middle of the area of sparing.

Discussion

In this study, we characterized the areas without evidence of edema on dedicated upper extremity MRIs of patients with BCRL. Areas without any edema centered around the cephalic

Table 1 Patient demographics

All patients with edema on MRI ($n = 34$)			
Patients with circumferential edema (no sparing) ($n = 5$)		Patients without circumferential edema (sparing) ($n = 29$)	*p*-Value
Age, mean (SD)	69.7 (3.3)	57.6 (9.4)	0.008
BMI in kg/m^2, mean (SD)	25.8 (3.6)	31.0 (6.1)	0.08
Symptom duration in years, mean (SD)	4.9 (2.9)	5.5 (4.4)	0.77
Type of breast surgery, *n* (%)			
Mastectomy	4 (80)	23 (79)	0.60
Lumpectomy	1 (20)	6 (21)	
Type of axillary surgery, *n* (%)			
SLNbx	0 (0)	2 (7)	1.0
ALND	5 (100)	27 (93)	
Chemotherapy, *n* (%)	5 (100)	27 (93)	1.0
Regional lymph node radiation, *n* (%)	5 (100)	26 (90)	0.55

Abbreviations: ALND, axillary lymph node dissection; BMI, body mass index; MRI, magnetic resonance imaging; SD, standard deviation; SLNbx, sentinel lymph node biopsy.

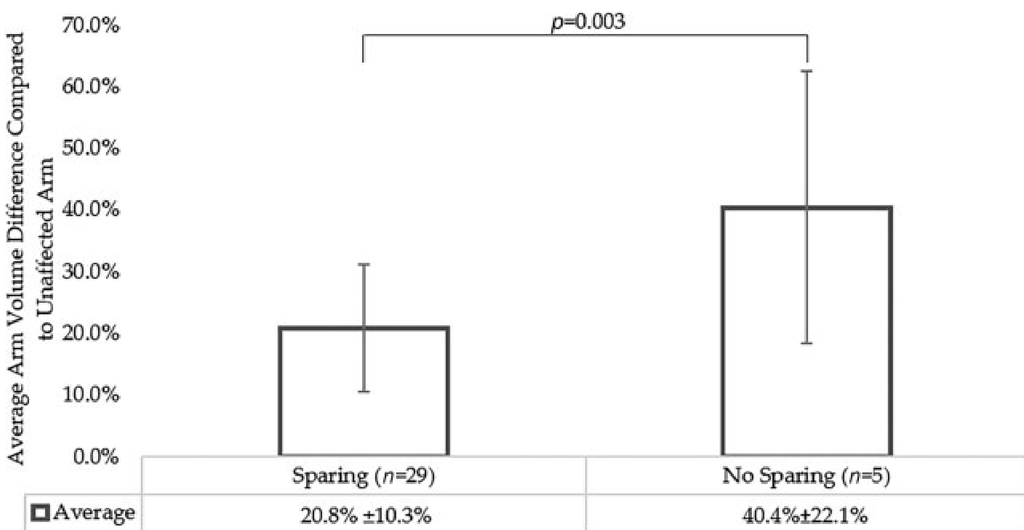

Fig. 2 Differences in arm volume in patients with and without sparing. In our study, the average difference in arm volume was measured by using perometry in patients without circumferential edema (with sparing) and patients with circumferential edema (without sparing), and their respective standard deviations (± standard deviation).

vein. The tissue in the forearm demonstrated less sparing than in the upper arm ($p = 0.003$). We found that patients with circumferential edema (without sparing) were older ($p = 0.008$) and demonstrated larger volume differences than those with evidence of sparing ($p = 0.003$).

A key finding of this study is that areas without edema are centered around the cephalic vein. A plausible explanation is that the M-S pathway, which travels adjacent to the cephalic vein, is effectively clearing the lymphatic fluid in that lymphosome.[8,10] If true, this would have implications for lymphatic operations. Debulking procedures may preferentially avoid this lymphosome so as not to inadvertently damage any functioning channels. This information could also be useful in the preoperative planning of physiologic lymphatic procedures.

We found that the edema was more diffuse at the forearm than the upper arm. The finding of worsening disease in the distal arm is consistent with prior reports and thought to be related to dependency.[1,11,12] If lymph node transplants works as a "sump pump," our finding would provide credence to transferring lymph nodes distally.[12–14] Moreover, as the edema is most concentrated away from the cephalic vein, transplants based on the ulnar system may be more effective than those based radially.

Additionally, we believe that our findings further support the previously held observations of heterogeneous presentation of patients with lymphedema as well as the fact that lymphedema occurs in a subset of patients who have undergone breast cancer treatments. Surgically, our finding has important implications as debulking procedure may need to

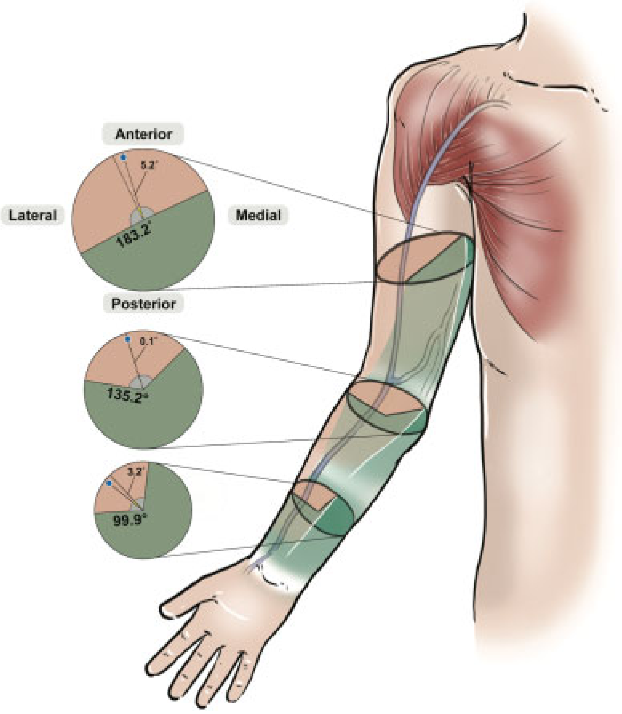

Fig. 3 Schematic of an upper extremity demonstrating areas with sparing and their relationship to the cephalic vein. In this schematic of the whole arm, you can see areas without circumferential edema and their relationship to the cephalic angle at the upper arm, elbow, and forearm. The blue circle represents the cephalic vein. The areas without circumferential edema are indicated by green shading. Average angle of sparing from cephalic vein and the SD at three anatomic locations, upper arm, elbow, and forearm are 183.2 ± 109.4, 135.2 ± 80.9, and 99.9 ± 104.9 degrees ($p = 0.0032$ between upper arm and forearm). Average angle of deviation from cephalic vein and the SD at the same three anatomic locations, upper arm, elbow, and forearm are 3.2 ± 27.3, −0.1 ± 27.2, and −5.2 ± 24.6 degrees ($p > 0.5$). The angles of deviations are expressed in absolute values and their direction are depicted in the figure. SD, standard deviation.

be planned in advance to avoid this area if this sparing is seen on MRI as not to damage the alternate pathway, and perhaps utilize the MS pathway for a lymphovenous bypass or lymph node transplant.

Finally, we noted that patients with circumferential edema (no sparing) were significantly older and had larger affected arms. Age has been previously correlated with worsening lymphatic function, though future research is needed to establish a causal relationship.[15] With regard to arm size, if the area of sparing is ultimately found to correlate with the M-S pathway, this finding would imply that a functioning alternate lymphatic pathway results in less severe lymphedema.[16] Recently, it was found that the M-S pathway can be reliably identified using a refined ICG technique.[17] Further studies evaluating the anatomy and function of the M-S pathway using the new ICG technique and imaging protocol described are needed.

Our study has several limitations. The study was conducted at a single institution at a single time point. Moreover, our study did not aim to visualize the lymphatics and instead used the cephalic vein as a marker for the M-S pathway. Consideration of other imaging modalities used in lymphedema evaluation must be discussed. While lymphoscintigraphy was also performed in these patients, this imaging modality lacks the ability to differentiate dermal backflow overlying the cephalic vein (or MS pathway). Similarly, while ICG lymphography was also obtained in these patients, the technique to visualize the MS pathway had not been developed at the time at the time of the MRI exams. In fact, we regard our imaging finding as a proof of concept and additional credence to the existence of MS pathway and its possible function.

Further research is needed to corroborate our MRI findings with ICG lymphography findings detailing the simultaneous course of the M-S pathway and function.

Conclusion

We found most patients with BCRL demonstrate areas spared of edema centered around the cephalic vein which may be explained by the presence of the M-S pathway. The distal arm is more affected than the proximal arm. Patients with circumferential edema, that is with no sparing, were older and demonstrated larger arms.

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Conflict of Interest
L.L.T. is a consultant for Agile Devices, Inc., Boston, MA, with a founding equity stake. This relationship has no direct impact or influence on the manuscript. The other authors declare no conflict of interest.

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