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PICTORIAL REVIEW

Pearls and pitfalls of radionuclide imaging of the lymphatic system. Part 2: evaluation of extremity lymphoedema

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ABSTRACT. This is the second of two pictorial essays on radionuclide imaging of the lymphatic system and will focus on evaluation of extremity lymphoedema using lymphoscintigraphy. Lymphoedema results from anatomical or functional obstruction of the lymphatic system. Lymphoscintigraphy is the imaging modality of choice for assessing lymphoedema. The technique plays a pivotal role in determining the aetiology of extremity swelling and helps guide treatment. The diagnostic utility of radionuclide imaging in lymphoedema depends upon careful technical performance and accurate image interpretation. We present a pictorial review emphasising the technical and interpretative pearls and pitfalls of radionuclide evaluation of lymphoedema.

Extremity lymphoedema results from impaired lymphatic drainage due to various aetiologies including congenital lymphatic anomaly, infection and lymphatic injury. It is frequently misdiagnosed [1]. Lymphoscintigraphy is a sensitive method to distinguish lymphatic causes of limb swelling from other disorders such as obesity, venous disease and hypoalbuminaemia [2]. Some forms of lymphoedema are more likely to respond to treatment and lymphoscintigraphy can help identify these cases [3].

Lymphoedema can be classified as primary or secondary. Primary lymphoedema is uncommon and usually manifests before the age of 35 years. The condition results from lymphatic deficiency (hypoplasia or aplasia) and may be genetically inherited (e.g. Milroy disease) or be non-familial. Typically there is spontaneous limb swelling with no precipitant.

By contrast, secondary lymphoedema is more common and has a multitude of causes. In the developed world the most common antecedent is cancer therapy, particularly axillary or pelvic lymph node dissection and/or radiotherapy [1]. In the developing world, filariasis and other infections are the most common causes. Other aetiologies include chronic venous disease, cellulitis, traumatic lymphatic damage and malignant infiltration [1]. The condition usually develops insidiously, over months or years, after the initial insult. Often the underlying cause of lymphoedema is complex and it may develop due to a secondary cause superimposed on sub-clinical primary lymphatic deficiency.

The clinical utility of lymphoscintigraphy depends upon scrupulous technique and careful image evaluation. We present a pictorial review of radionuclide imaging of lymphoedema with an emphasis on key interpretative pearls and pitfalls.

Technical performance of lymphoscintigraphy

Radionuclide imaging of the lymphatic system was first described over 50 years ago [4]. Technetium (99Tc) labelled tracers such as sulphur colloid, microaggregated albumin and antimony sulphide are the most commonly used agents [1]. In our institution 99Tc-albumin-nanocolloid is used for radionuclide evaluation of the lymphatic system.

The radiotracer can be given via subcutaneous, intradermal or subfascial injection. Intradermal administration is associated with rapid lymphatic transport and better tracer kinetics than the other two methods [5] and is the optimal technique for sentinel node lymphoscintigraphy. Subcutaneous injections have been shown to produce more reliable results in lymphoedema patients when compared with intradermal injections [6]. Sub-fascial injection is restricted to analysis of the deep lymphatic system [1].

In lymphoedema assessment, a small volume of tracer (~0.2 ml) is injected subcutaneously into the first to third web spaces on each hand or foot. Both limbs are examined, even if one appears normal, to detect subclinical abnormalities, provide internal comparison and monitor injection and camera technique. Images are acquired using a high-resolution, parallel hole, collimator. The arrival of tracer at the knees and groin (or elbows and axillae) is timed. A transmission scan using a flood source may be useful for anatomical localization. Quantitative parameters derived from tracer clearance...
data can be used to detect incipient lymphoedema but we do not routinely perform this in our institution. After 30 min if no groin (or axillary) activity is demonstrated the patient is encouraged to mobilize/stress their limbs briefly. Lower extremity stress manoeuvres include walking, limb massage or bicycle exercise. For upper limb stressing, repetitive squeezing of a rubber ball, use of a hand-grip or massage can be used. In our institution we find stress lymphoscintigraphy to be highly valuable and routinely mobilize patients if no activity is demonstrated after 30 min. They are then re-imaged to see if the proximal lymphatic system has been demonstrated. If there is still no activity, patients are encouraged to mobilize for several hours and delayed imaging is performed after 3–4 h [7].

**Interpretative pearls and pitfalls of lymphoscintigraphy**

In patients with normal lymphatic anatomy and function there should be symmetrical transport of the radiotracer through discrete lymph vessels (3–5 vessels per calf, 1–2 vessels per thigh) and uptake within proximal lymph nodes bilaterally within 30 min (Figure 1). Occasionally one or more popliteal nodes may be visualized (Figure 2a) and

![Figure 1. Normal lower extremity lymphoscintigraphy. Frontal images showing normal (a) calf, (b) popliteal and (c) thigh lymphatic vessels and (d) inguinal nodal uptake.](image_url)
Figure 2. Normal variants. (a) Frontal image showing left sided popliteal nodal uptake (arrow). (b) Frontal image showing normal iliac and para-aortic nodal and hepatic tracer uptake.

Figure 3. Primary lymphoedema – absent lymphatic vessels. Frontal image from a lymphoscintigram (thigh level) showing normal right and absent left sided lymphatic vessels in a patient with left sided primary lymphoedema.

Figure 4. Primary lymphoedema – paucity of lymphatic vessels. Frontal image showing absent right and attenuated left calf lymphatics with dermal backflow in the right foot and left upper calf (arrows).
the liver may be visualized due to systemic circulation of the tracer on later images (Figure 2b). Early hepatic tracer uptake suggests partial intravascular injection.

In patients with primary lymphoedema there is typically delayed or absent radiotracer transport, absence (Figure 3) or paucity of lymph vessels (Figure 4), poorly visualized or absent regional lymph nodes (Figure 5) and occasionally there may be dermal backflow on early images (Figure 6). This constellation of appearances is diagnostic in the absence of a clinical history suggesting a secondary cause.

Lymphoscintigrams in patients with secondary lymphoedema are more likely to show prominent lymphatic vessels or lymphangectasia (Figure 7), collateral vessels (Figure 8), delayed transport of tracer and dermal backflow on delayed images (Figure 10). If there is no uptake in the regional nodes after 30 min, re-imaging following mobilization may demonstrate regional nodal uptake (Figure 11) representing a lesser degree of lymphatic dysfunction. Late phase imaging may demonstrate a lymphatic leak (Figure 12). Clinical history may be helpful when trying to distinguish between localized dermal backflow and extravasation; previous surgery and trauma are more commonly associated with the latter.

There may be a mixed aetiology of the lymphoedema, e.g. a secondary cause decompensating subclinical lymphatic hypoplasia. These cases often demonstrate the scintigraphic appearances of both primary and secondary lymphoedema.

A summary of the key interpretative pearls and pitfalls is detailed in Table 1.

**Treatment of extremity lymphoedema**

The main treatment goals are symptom relief, prevention of disease progression and reduction of limb size. Conservative, pharmacological and surgical therapies are available [8]. In mild cases limb elevation and compression stockings may be successful. Other conservative measures include massage and special exercises to enhance lymphatic drainage. A combination of these measures is usually employed in the first instance and is referred to as combined physical therapy. Pharmacological agents such as micronized purified flavonoid fraction and benzopyrones have been successful in lymphoedema treatment, but at present are not widely available [8]. Surgery is usually reserved for refractory cases. Prompt, aggressive antibiotic therapy is required for any limb infection to prevent further lymphatic obliteration.

**Conclusion**

Radionuclide imaging of suspected extremity lymphoedema is a simple and accurate technique. It can help distinguish between swelling of venous and lymphatic origin, may demonstrate the underlying cause and help guide therapy. Careful attention to technical performance and image evaluation is essential to maximize the clinical utility of the investigation. We have described the key interpretative pearls and pitfalls of the technique.
Figure 7. Secondary lymphoedema – lymphangectasia. (a) Frontal image showing dilated right thigh lymphatics in a patient with right leg oedema due to right sided pelvic lymphatic obstruction by a large ovarian tumour (not shown). (b) Frontal images showing bilateral calf megalymphatics and (c) partial right thigh lymphangectasia in a patient with bilateral lymphoedema. Note also the dermal backflow around the left knee and collateral vessels in the mid left thigh (arrows). The aetiology was felt to be due to chronic bilateral lower limb cellulitis.
Figure 8. Secondary lymphoedema – collateral vessels. Frontal image showing prominent right calf collateral vessels in a patient with right leg lymphoedema.

Figure 9. Secondary lymphoedema – disruption of lymphatic vessels. Frontal images from two separate patients showing tracer extravasation into the right calf and lymphatic disruption (a, b). Both patients had developed lymphoedema following varicose vein surgery.

Figure 10. Secondary lymphoedema – late dermal backflow. Frontal image obtained 3 h after injection showing prominent left sided dermal backflow in the left thigh of a patient with lymphatic obstruction of uncertain aetiology.
Figure 11. Importance of patient mobilization. (a) Frontal image showing bilateral complete absence of lower extremity lymphatic tracer uptake on early image (30 min). (b) Later frontal image showing normal bilateral inguinal nodal uptake, immediately following 15 min of walking in the same patient.

Figure 12. Importance of delayed imaging. Frontal image obtained 3 h following injection showing extravasation of tracer within the left calf and associated dermal backflow. This was not present on early imaging and was due to lymphatic damage during varicose vein surgery.

Table 1. Pearls and pitfalls of the lymphoscintographic evaluation of lymphoedema

<table>
<thead>
<tr>
<th>Interpretative pearls</th>
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<tbody>
<tr>
<td>A) Primary lymphoedema</td>
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<tr>
<td>Delayed or absent radiotracer transport</td>
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<tr>
<td>Paucity of lymphatic vessels and nodes</td>
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<tr>
<td>(Dermal backflow on early images)</td>
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<tr>
<td>B) Secondary lymphoedema</td>
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<tr>
<td>Prominent or dilated lymphatics</td>
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<td>Collateral vessels</td>
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<td>Dermal backflow on late images</td>
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<td>(Tracer leak/extravasation at operative site)</td>
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<td>C) Complex/mixed picture</td>
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<td>Combination of both</td>
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<th>Interpretative pitfalls</th>
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<tr>
<td>No regional nodal uptake on 30 min image</td>
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<td>→ Patient mobilization and re-image</td>
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<tr>
<td>If symmetrical regional nodal uptake</td>
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<tr>
<td>= borderline normal lymphatic function</td>
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<tr>
<td>If asymmetrical or absent uptake</td>
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<tr>
<td>= abnormal lymphatic function</td>
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<tr>
<td>Delayed or absent tracer transport: Re-image after 3–4 h to</td>
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<td>identify dermal backflow</td>
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References


