Lymphoscintigraphy for the diagnosis of extremity lymphedema: Current controversies regarding protocol, interpretation, and clinical application

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Abstract
Appropriate diagnosis, staging and a further selection of the best treatment are fundamental for the management of patients with extremity lymphedema. Several clinical and imaging tools have been described for these purposes. Lymphoscintigraphy is still considered the gold standard imaging modality for diagnosing lymphedema. However, protocol variability and poor image resolution can make the interpretation challenging. Here, we reviewed technical aspects of lymphoscintigraphy, interpretation of the lymphoscintigraphy findings, staging, and its clinical application.

KEYWORDS
extremity lymphedema, lymphatic microsurgery, lymphedema diagnosis, Lymphedema Grading System, lymphoscintigraphy

Lymphedema is a chronic debilitating disease that can produce adverse health impact on quality-of-life and psychosocial well-being in that it brings great physical and visual discomfort. Lymphedema consists on an abnormal accumulation of protein-rich interstitial fluid within the tissues of the body, adipose deposition and progressive fibrosis with thickening of the skin, secondary to either a structural distortion of lymphatic ducts (primary lymphedema) or a mechanical disruption and blockage (secondary lymphedema).1 This disruption in lymphatic flow results in swelling of the affected limb.

Approximately 1/1000 people in the United States and 200 million worldwide are affected by lymphedema and is considered a common and one of the most devastating sequelae of cancer care.2-4 Upper limb lymphedema, affecting 10%-50% of the breast cancer patients, is the most common site of lymphedema in the United States.5-7 On the other hand, lower extremity lymphedema affects 10%-49% of patients after gynecological cancer treatment.8-10 Risk factors of lymphedema include the number of axillary or pelvic lymph nodes removed and radiotherapy.9-13

Primary lymphedema is a less common condition with a prevalence of 1.2 per 100 000 patients in the pediatric population.14 Accurate diagnosis and appropriate management are fundamental to successful treatment of patients with extremity lymphedema. A limb overgrowth can result from different conditions requiring different treatment.15-18 Although most of these conditions can be differentiated by history and physical examination,19 correct diagnoses can be a challenge for the physician in an attempt to find the cause and start an effective treatment.20

Lymphoscintigraphy has been widely considered for many years the primary investigation to confirm the lymphedema diagnosis visualizing the functional status of the lymphatic system and for a further strategy of management in some centers.21-24 This imaging modality is a noninvasive test available at most centers, easy to perform, involving an intradermal or subcutaneous injection of particulate radiotracer attached to technetium-99m (99mTc) in the distal aspect of the swollen limb with subsequent imaging of the lymphatic vasculature.25 Apart from the central role in the diagnosis, lymphoscintigraphy could be used to assess the severity of lymphedema distinguishing between partial and total obstruction and may help to guide the treatment. However, it is difficult to compare the findings across the