Lymphoscintigraphy

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9.1 Clinical Indications [1, 2]

- Sentinel lymph node (SLN) localization in malignancies, more common in children with diagnosis of melanoma and soft tissue sarcoma
  Assessment of lymphedema.

9.2 Pre-exam Information

- *For SLN detection*
  - Type and location of the malignancy.
  - History or planning of the surgical resection of the tumor.
- *For lymphedema and lymphatic malformations*
  - Site of extremity edema.
  - History of surgery or trauma that could affect lymphatic drainage.
  - Suspected chyloascites or chylothorax.
  - Suspected developmental anomalies of the lymphatic system such as abdominal or thoracic lymphangiectasia.

Study Protocol for Lymphoscintigraphy [3]

Patient preparation

- The skin at the injection site should be cleaned with antiseptics.
- Anesthetic cream should be applied on the skin 30–60 min before injection.
- Despite the local anesthetic, the patient must be warned that temporary stinging pain might be experienced during tracer injection.

Study scheduling:

- *For SLN mapping and biopsy*
  - Number and type of injections depend on tumor type and whether it has been excised.
  - Coordination of lymphoscintigraphy and surgical excision of SLN is required.
- *For lymphedema or lymphatic malformation*

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- The procedure may take several hours, depending on the speed of the lymphatic transit.
- Scheduling the study in the morning is advised, given the potential duration of the study.

Radiopharmaceutical, Administrated activity, Mode of delivery

Radiopharmaceutical

- [^{99m}Tc] labelled colloidal nanoparticles.

Activity

- 18.5–37 MBq (0.5–1.0 mCi) total dose for all ages.

Delivery

- The tracer activity is split into 2–4 separate syringes.
- The injected volume in each syringe should be limited to 0.1–0.3 ml and should contain at least 10–15 MBq (0.1 mCi).
- The tracer is injected intradermally for most indications.
- The location and number of injections depend on the study indication and involved region.

For SLN mapping and biopsy

- For soft tissue sarcomas of the limbs, this may involve peritumoral or intramuscular injections adjacent to the tumor.
- For cutaneous tumors of the extremities, the protocol requires two injections proximal to the margin of the lesion or the scar, or four injections in opposite directions around the lesion or surgical scar.
- For cutaneous tumors of the head, neck, torso, and upper thighs, 2–4 injections around the tumor or site of surgical resection are essential because lymphatic drainage from these locations is unpredictable.

For lymphedema or lymphatic malformation

- The tracer is usually injected intradermally in the interdigital web space between the first and second digits, with one injection in each foot or hand.
- Some centers employ intradermal injections in the dorsum of the feet or hands just proximal to the toes. Injections are easier to administer in these sites and may cause less discomfort to the patient.

Acquisition protocol

For SLN mapping and biopsy [4, 5]:

- Collimator: High-resolution, parallel hole.
- Acquisition begins with dynamic images, 10 seconds/frame for 2–3 min.
- Static images are acquired following the dynamic study for 3–5 min/view.
- The time interval between static images is variable and depends on the rate of tracer transit from the injection sites. Typically, the patient remains on the imaging bed and images are acquired every few minutes.
- The SLN is often visualized within 15–60 min post-injection, occasionally earlier in younger children.
- The field of view (FOV) should include the injection site and the expected lymph drainage basins where the SLN is likely to be present.
  - For tumors in the limbs and head and neck, the FOV should include the adjacent torso.

  - For tumors located in the torso, the entire torso should be imaged.
- When the first lymph node (LN), the SLN, is visualized, the overlying skin should be marked with a surgical pen marker.
- Lateral or oblique views improve the localization of the sentinel node.
- SPECT/CT, when available, is the best method for accurate localization of the SLN prior to surgical excision.
- Marking the overlying skin in two planes can be useful for planning the excision of the sentinel node, providing more insight into the depth of the node.
- If images show lymph transit to more than one drainage basin, the SLN in each basin should be identified and marked.

For lymphedema or lymphatic malformations [6–9]:

- Following tracer injection, serial static images of the extremities and subsequently (as transit progresses) images of the pelvis, abdomen, and chest are obtained for up to 100 K counts.
- Continuous body sweeps for 120 seconds /bed position can be also performed. They may show a composite image of the tracer location in the body.

9.3 Study Interpretation

For SLN mapping and biopsy [4, 5, 10, 11]:

- Check for the site of injections
- Identify the site of SLN and look for potentially more than one SLN

For lymphedema or lymphatic malformations [7, 8, 12, 13]:

- Tracer transit from the injection site proximally through the lymphatic channels of the lower or upper limbs should be symmetrical.
- The normal transit rate depends on the size of the particles and may vary from one commercial preparation to the other.
- As a general reference, tracer should be seen in:
  - Inguinal LNs within 45 min after foot injections.
  - Axillary LNs within 30 min after hand injections.
  - Liver within 4 h post-injection.
- Delayed transit of tracer is suggested when:
  - There is a delayed appearance of LNs
  - Lymphatic channels appear dilated.
  - Collateral lymphatic channels have been identified.
  - Diffuse tracer activity is seen in the superficial soft tissues (dermal backflow).
  - There is a paucity of tracer localization in inguinal and pelvic LNs.
- Diffuse tracer activity in the pleural or abdominal cavities suggests:
  - Chylous pleural effusion and/or chylous ascites.
  - Intestinal lymphangiectasia or pulmonary lymphangiomatosis.
- Findings for lymphatic insufficiency include: delay or absence of lymphatic transport from the injection site, asymmetric or absent visualization of regional lymph nodes, and the presence of radiotracer uptake in dermal lymphatics called dermal backflow.
- In cases of a postsurgical leak from the thoracic duct:
  - Tracer injection in the feet or left arm will show tracer accumulation in the pleural cavity.
  - Tracer injection in the right arm will show normal transit into the systemic circulation and normal liver accumulation.

9.4 Correlative Imaging [9, 14]

- Lymphoscintigraphy has replaced lymphangiography, direct injection of contrast agents into lymphatic channels, being highly sensitive and easier to perform and carrying fewer risks of complications.
- If available correlate lymphoscintigraphy with MR lymphangiography.

9.5 Red Flags [15–17]

- Injection of the entire dose should be ensured to avoid false negative results.
- A potential second deep injection is performed selectively in some centers when superficial injection may have failed to be diagnostic.
- Despite the noninvasive nature of the study, significant pain is experienced for a short while at the injection sites.
- For SLN detection:
  - Particle size differs among various commercial preparations. This can affect the velocity of tracer transit and the time required to detect the SLN.
  - In cases with tumors of the torso transit from the injection site is less predictable and could include more than one drainage basin.
  - External radionuclide markers to outline the body surface or a superimposed ^{57}Co flood source transmission image helps localize the sites of tracer activity.
  - Care should be taken not to miss a SLN if it may be located adjacent to the injection site and therefore masked by the high tracer activity. In these cases, use SPECT/CT whenever possible.
- In cases of lymphedema:
  - The study provides functional information on lymph transit. However, it may be limited in discerning the etiology of the abnormality and associated morphological findings.
  - The injections into each limb should be performed in rapid succession to ensure that differences in the rate of tracer transit in the limbs are not related to a delay in the timing of the second injection.
  - Continuous body sweeps and the resulting composite image of the tracer location in the body are easier for orientation.
  - When there is slow tracer transit from the feet, limb movement should be encouraged between the imaging sets to stimulate lymphatic transit. Furthermore, depending on the findings and clinical questions, repeated imaging may be required for several hours.
  - Delayed transit may be due to obstruction of the lymphatic pathways or abnormal development of lymphatic channels.

9.6 Take Home Messages

- Lymphoscintigraphy has an important role in identifying SLNs and planning their surgical excision.
- Meticulous technique is required when performing lymphoscintigraphy and for marking the SLN.
- Initial dynamic images are important to visualize the lymphatic collectors or tracts and for the detection of the first LN visualized (the SLN).
- Good communication with surgeons is essential for the correct localization and excision of the SLN.
- Gamma probes are utilized during surgery to detect the SLN, often in conjunction with blue dye lymphatic mapping.
- Marking an SLN on the skin can help in planning surgery and therefore the patients should be in the same position as they will be during surgery. If an arm, for example, is stretched out to one side during surgery, it should be in the same position during imaging and marking.
- In cases with lymphedema, normal, and timely visualization of the liver indicates that there is normal lymph drainage into the systemic circulation via the thoracic duct or right lymphatic duct.

- Dermal backflow refers to a phenomenon in which lymphatic fluid leaks and accumulates in the skin and soft tissues by regurgitating the lymphatic flow because of increased pressure caused by occluded lymphatic vessels.

9.7 Representative Case Examples

Case 9.1 Normal Lymphatic Transit (Fig. 9.1)

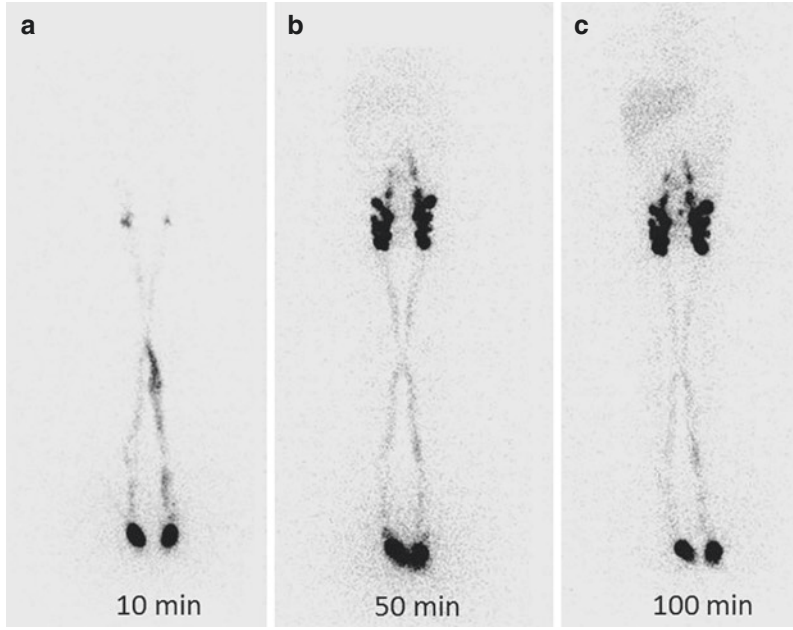

Fig. 9.1 History: An 8-year-old boy with a history of prematurity, short bowel syndrome due to necrotizing enterocolitis, and multi-organ transplantation of bowel, liver, and pancreas presented with lower limb edema. Study report: Anterior whole-body sweeps were obtained at various time points following intradermal injections of Tc-filtered sulfur colloid in the interdigital web space between the first and second digits in both feet. Rapid ascent of tracer from the injection sites is noted. At 10 min post-injection, (**a**) tracer is seen in the major lymphatic channels of the lower extremities as well as initial accumulation in the inguinal nodes. At 50 min post-injection (**b**) there is symmetrical tracer accumulation in inguinal and iliac nodes. Faint activity is noted in the liver suggesting initial drainage of lymphatic fluid into the systemic circulation. At 100 min (**c**) liver uptake is more obvious. Impression: Normal symmetric tracer transit through the lymphatic system with no evidence of obstruction or abnormal development of lymphatic channels

Case 9.2 Lymphatic Obstruction (Fig. 9.2)

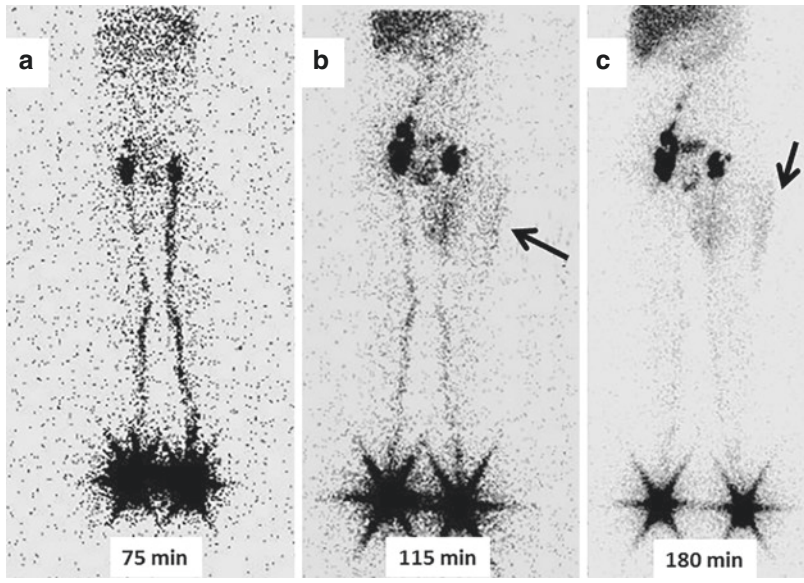

Fig. 9.2 History: A 6-year-old boy presented with lymphedema of the left thigh and buttock that developed 6 months after surgery for a left inguinal hernia. Lymphoscintigraphy was performed following two intradermal injections of Tc-filtered sulfur colloid administered in the interdigital web space between the first and second digits of the feet. Study report: Selected anterior whole-body sweeps starting at 75 min after tracer administration (**a**) show a symmetrical ascent of tracer from the injection sites through the major lymphatic channels of the lower extremities up to the groin levels. Activity is also noted in the liver, indicating physiologic lymphatic drainage into the systemic circulation. Images obtained at 115 (**b**) and 180 min (**c**) post-injection show a relative paucity of tracer accumulation in left inguinal lymph nodes and a lack of tracer accumulation in the left iliac nodes. Diffuse tracer activity is noted in the superficial soft tissues in the lateral (arrows) and medial aspects of the proximal left thigh, suggesting "dermal backflow." Impression: The findings suggest lymphatic obstruction at the level of the left groin

Case 9.3 Gastrointestinal Tract Lymphangiectasia (Fig. 9.3)

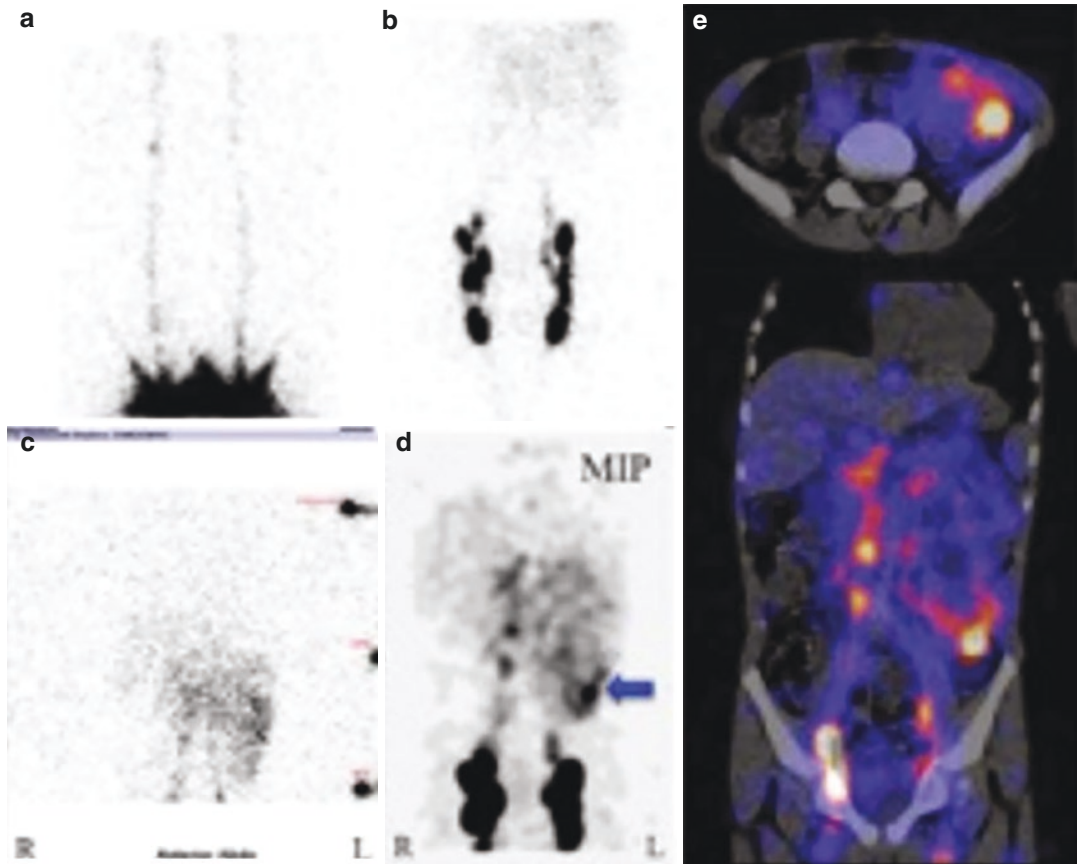

Fig. 9.3 History: An 8-year-old boy was investigated for protein-losing enteropathy with hypoalbuminemia and lymphocytopenia. Lymphoscintigraphy was performed following two dorsal pedal intradermal injections of Tc-antimony sulfide colloid. Study report: The initial dynamic images (**a**, **b**) show normal lymphatic collectors in the legs and activity in femoral and inguinal lymph nodes bilaterally. Delayed images at 1 h (**c**) show a diffuse increase in tracer activity in the left mid-abdomen and only faint accumulation of tracer in the liver. Abdominopelvic SPECT MIP (**d**) and SPECT/CT (**e**, upper-transaxial, lower–coronal slices) demonstrate tracer activity in the gastrointestinal tract, specifically in a bowel loop located in the left lower abdominal quadrant. Impression: The study suggests diffuse gastrointestinal lymphangiectasia, predominantly involving the small bowel, further confirmed by capsule endoscopy

Case 9.4 Sentinel Lymph Node in a Patient with Melanoma (Fig. 9.4)

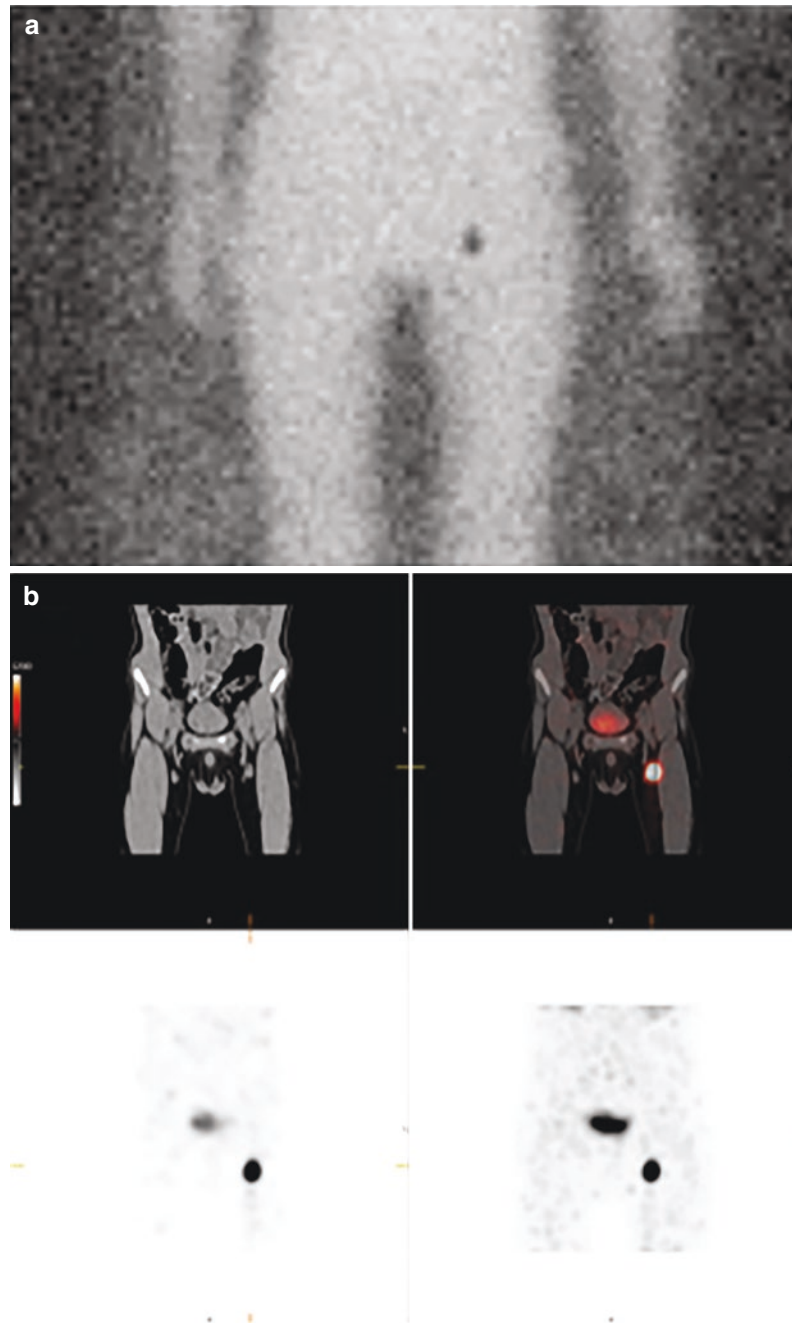

Fig. 9.4 History: A 5-year-old boy with melanoma in the left leg was evaluated prior to surgery. Study report: Planar scintigraphy of the abdominopelvic region and thighs superimposed on a ^{57}Co flood source transmission image (**a**) shows a focal area of uptake in the left inguinal region localized to a lymph node on SPECT and SPECT/CT coronal slices (**b**). Impression: The focus of uptake represents the sentinel lymph node located in the left inguinal region. At surgery, this lymph node was resected and found negative for melanoma

Case 9.5 Left Leg Swelling and Increasing Bilateral Leg Edema and Pleural Effusion (Fig. 9.5)

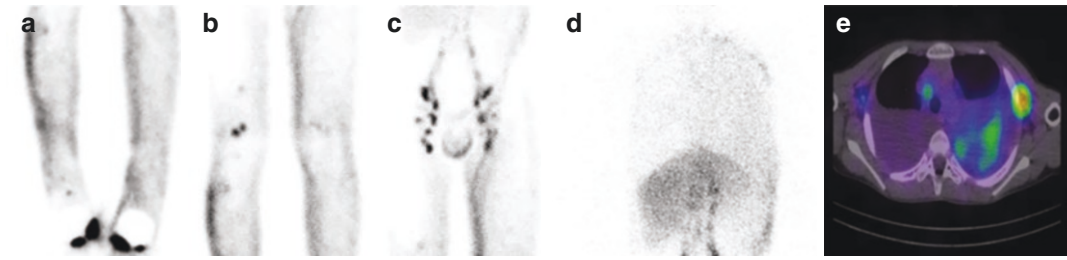

Fig. 9.5 History: A 9-year-old boy presented with left leg swelling, increasing bilateral leg edema, and pleural effusion. He had been previously treated for acute myeloblastic leukemia with total body external beam radiotherapy. Study report: Selected anterior whole-body sweeps starting at 75 min after tracer administration (**a**–**d**) show significant dermal backflow in the lower limbs, more pronounced on the left side (**a**–**c**) with adequate visualization of bilateral inguinal lymph nodes. There is a visualization of the liver with significant abdominal dermal backflow (**d**). SPECT/CT shows axillary and mediastinal lymph nodes with a chylous leak into the left hemithorax (**e**). Impression: Collateral aberrant lymphatic drainage with abdominal wall dermal backflow, axillary and mediastinal lymph nodes, and chylous leak into the left hemithorax

References

1. Grant FD, Maclellan RA, Greene AK. Lymphoscintigraphy. In: Treves ST, editor. Pediatric nuclear medicine and molecular imaging. New York, NY: Springer; 2014. p. 189–202.
2. Greene AK, Sudduth CL, Taghinia A. Lymphedema (Seminars in pediatric surgery). Semin Pediatr Surg. 2020;29(5):150972.
3. Howman-Giles R, Pascual T, Uren R. Lymphoscintigraphy in paediatric and adolescent patients. Clin Transl Imaging. 2016;4(2):103–17.
4. Neville HL, et al. Lymphatic mapping with sentinel node biopsy in pediatric patients. J Pediatr Surg. 2000;35(6):961–4.
5. Jeremiasse B, et al. Value of the sentinel node procedure in pediatric extremity rhabdomyosarcoma: a systematic review and retrospective cohort study. Ann Surg Oncol. 2021;28(13):9048–59.
6. Bellini C, et al. Lymphatic dysplasias in newborns and children: the role of lymphoscintigraphy. J Pediatr. 2008;152(4):587–9, 589.e1-3
7. Bellini C, et al. Lymphoscintigraphy patterns in newborns and children with congenital lymphatic dysplasia. Lymphology. 2014;47(1):28–39.
8. Baulieu F, et al. Contributions of SPECT/CT imaging to the lymphoscintigraphic investigations of the lower limb lymphedema. Lymphology. 2013;46(3):106–19.
9. Pieper CC, et al. MR lymphangiography of lymphatic abnormalities in children and adults with Noonan syndrome. Sci Rep. 2022;12(1):11164.
10. Toro J, et al. Sentinel lymph node biopsy in children and adolescents with malignant melanoma. J Pediatr Surg. 2003;38(7):1063–5.
11. Bay SB, Görgün Ö, Kebudi R. Children with malignant melanoma: a single center experience from Turkey. Turk Pediatri Ars. 2020;55(1):39–45.
12. Karaçavuş S, Yılmaz YK, Ekim H. Clinical significance of lymphoscintigraphy findings in the evaluation of lower extremity lymphedema. Mol Imaging Radionucl Ther. 2015;24(2):80–4.
13. Kwon HR, et al. Predictive role of lymphoscintigraphy undergoing lymphovenous anastomosis in patients with lower extremity lymphedema: a preliminary study. BMC Med Imaging. 2021;21(1):188.
14. Chavhan GB, et al. Magnetic resonance lymphangiography. Radiol Clin North Am. 2020;58(4):693–706.
15. Yang J, Codreanu I, Zhuang H. Minimal lymphatic leakage in an infant with chylothorax detected by lymphoscintigraphy SPECT/CT. Pediatrics. 2014;134(2):e606–10.
16. Hassanein AH, et al. Diagnostic accuracy of lymphoscintigraphy for lymphedema and analysis of false-negative tests. Plast Reconstr Surg Glob Open. 2017;5(7):e1396.
17. Turpin S, Lambert R. Lymphoscintigraphy of chylous anomalies: chylothorax, chyloperitoneum, chyluria, and lymphangiomatosis-15-year experience in a pediatric setting and review of the literature. J Nucl Med Technol. 2018;46(2):123–8.