

Summary: Appropriate Use Criteria for Lymphoscintigraphy in Sentinel Node Mapping and Lymphedema/Lipedema

Kevin J. Donohoe¹, Brett J. Carroll², David K. V. Chung³, Elizabeth H. Dibble^{1,4}, Emilia Diego⁵, Francesco Giammarile⁶, Frederick D. Grant¹, Stephen Y. Lai⁷, Hannah Linden⁸, Megan E. Miller⁹, Neeta Pandit-Taskar^{1,10}, Nicholas E. Tawa, Jr.¹¹, and Sergi Vidal-Sicart⁶

¹*Society of Nuclear Medicine and Molecular Imaging, Reston, Virginia;* ²*Society for Vascular Medicine, East Dundee, Illinois;* ³*Australia and New Zealand Society of Nuclear Medicine, Vermont South, Australia;* ⁴*American College of Radiology, Reston, Virginia;* ⁵*Society of Surgical Oncology, Rosemont, Illinois;* ⁶*European Association of Nuclear Medicine, Vienna, Austria;* ⁷*American Head and Neck Society, Los Angeles, California;* ⁸*American Society of Clinical Oncology, Alexandria, Virginia;* ⁹*American Society of Breast Surgeons, Columbia, Maryland;* ¹⁰*American College of Nuclear Medicine, Reston, Virginia;* and ¹¹*American College of Surgeons, Chicago, Illinois*

Expert representatives from 11 professional societies, as part of an autonomous work group, researched and developed appropriate use criteria (AUC) for lymphoscintigraphy in sentinel lymph node mapping and lymphedema. The complete findings and discussions of the work group, including example clinical scenarios, were published on October 8, 2022, and are available at <https://www.snmmi.org/ClinicalPractice/content.aspx?ItemNumber=42021>. The complete AUC document includes clinical scenarios for scintigraphy in patients with breast, cutaneous, and other cancers, as well as for mapping lymphatic flow in lymphedema. Pediatric considerations are addressed. These AUC are intended to assist health care practitioners considering lymphoscintigraphy. Presented here is a brief overview of the AUC, including the rationale and methodology behind development of the document. For detailed findings of the work group, the reader should refer to the complete AUC document online.

Key Words: lymphoscintigraphy; lymphedema/lipedema; appropriate use; sentinel node mapping

J Nucl Med 2023; 64:525–528
DOI: 10.2967/jnumed.123.265560

Since the introduction of the “sentinel lymph node” (SLN) concept more than 40 y ago the use of lymphoscintigraphy for mapping the lymphatic system and localizing sentinel nodes has evolved with improvements in imaging technology and in the expanding clinical use of lymphatic mapping. To better define current recommendations for the use of lymphoscintigraphy, expert representatives from 11 professional societies, as part of an autonomous work group, researched and developed appropriate use criteria (AUC) to describe the use of lymphoscintigraphy in SLN mapping and lymphedema. This process was performed in accordance with the Protecting Access to Medicare Act of 2014, which requires that all referring physicians consult AUC by using a

clinical decision support mechanism before ordering advanced diagnostic imaging services. The result of the literature review and workgroup discussions was published on the Society of Nuclear Medicine and Molecular Imaging (SNMMI) website on October 8, 2022, and is available at <https://www.snmmi.org/ClinicalPractice/content.aspx?ItemNumber=42021>. Here we present a brief report on and summary of these AUC.

The full AUC include several possible clinical scenarios for which lymphoscintigraphy may be considered. Once these clinical scenarios were collected, the expert panel considered and graded them for appropriateness based on available literature as well as expert opinion. The most common current clinical use of lymphoscintigraphy is for SLN detection of breast and cutaneous malignancies; therefore, these indications are covered in more detail. However, the value of lymphoscintigraphy is recognized for SLN detection in other malignancies, as well as for mapping lymphatic flow in lymphedema. The work group prepared the AUC to assist health care practitioners who may be considering lymphoscintigraphy for their patients. Because each patient is unique, the appropriateness recommendations should not replace clinical judgment.

Mapping of sentinel node location should be performed for each patient undergoing SLN sampling. SLN mapping can be done with optical agents, such as isosulfan or methylene blue, as well as with radiotracers and fluorescent tracers or a combination of techniques. SLN localization with these techniques in individual patients has allowed a more accurate localization of nodes draining a primary tumor site. Histopathologic evaluation of the sentinel node allows patients to avoid the risk of the morbidity and mortality associated with complete node bed dissection if there is no evidence of metastatic disease in the sentinel node. The full AUC document discusses the challenges with the variety of lymphoscintigraphy tracers in use around the world. In the United States, only 2 tracers are generally available for clinical use: ^{99m}Tc-sulfur colloid and ^{99m}Tc-tilmanocept. Those tracers were the primary radiopharmaceuticals considered in the writing of the AUC document.

METHODOLOGY

Expert Work Group

Experts in this AUC work group were convened by SNMMI to represent a multidisciplinary panel of health care providers with substantive knowledge about the use of nuclear medicine in

Received Feb. 3, 2023; revision accepted Feb. 3, 2023.
For correspondence or reprints, contact Kevin J. Donohoe (kjd@bidmc.harvard.edu).
Published online Mar. 23, 2023.
COPYRIGHT © 2023 by the Society of Nuclear Medicine and Molecular Imaging.

lymphoscintigraphy. In addition to SNMMI members, representatives from the Society for Vascular Medicine, Australia and New Zealand Society of Nuclear Medicine, American College of Radiology, Society of Surgical Radiology, European Association of Nuclear Medicine, American Head and Neck Society, American Society of Clinical Oncology, American Society of Breast Surgeons, American College of Nuclear Medicine, and American College of Surgeons were included in the work group. Thirteen physician members were ultimately selected to participate and contribute to the AUC. A complete list of work group participants and external reviewers can be found in Appendix A in the online version of the AUC, where additional appendices provide term definitions and acronyms, author disclosures, and the process used to engage public commentary. Also included are qualifying statements and evidence limitations.

AUC Development

The process for AUC development was modeled after the RAND/UCLA Appropriateness Method and included identification of relevant clinical scenarios in which lymphoscintigraphy may be used, a systematic review of evidence related to these clinical scenarios, and a systematic synthesis of available evidence, followed by grading of each of the clinical scenarios using a modified Delphi process. In addition, the work group followed Institute of Medicine standards for developing trustworthy clinical guidance. The final document was drafted based on group ratings and discussions. A total of 32 relevant clinical scenarios were identified, with resulting AUC based on evidence and expert opinion regarding diagnostic accuracy and effects on clinical outcomes and clinical decision making. Other factors affecting the AUC recommendations were potential harm (including long-term harm, which may be difficult to

capture), costs, availability, and patient preferences. An extensive systematic review of the relevant literature was conducted by the Pacific Northwest Evidence-Based Practice Center at the Oregon Health and Science University under the direction of Roger Chou, MD, guided by key questions from the work group about lymphoscintigraphy in nodal staging and lymphatic dysfunction. Inclusion criteria, search parameters, and databases searched are included in the full AUC document, as well as data extraction, evidence weighting, rating, and scoring procedures. The work group met several times online via audiovisual conference to analyze results and contribute clinical expertise to derive final consensus scores for each clinical indication/scenario. Final appropriate use ratings were summarized in a format similar to the RAND/UCLA Appropriateness Method. Each clinical scenario was scored on a scale from 1 to 9; a score of 7–9 indicates that the procedure is appropriate for the specific clinical indication and is generally considered acceptable; a score of 4–6 indicates that the procedure may be appropriate for the specific indication and may imply that more evidence is needed to definitively classify the indication; and a score of 1–3 indicates that the procedure is rarely appropriate for the specific indication. Division of scores into 3 general levels of appropriateness is partially arbitrary, and numeric designations should be viewed as a continuum. When work group members could not agree on a common score, those indications were given “may be appropriate” ratings to indicate a lack of definitive literature and lack of work group consensus, indicating the need for additional research.

SUMMARY RECOMMENDATIONS FROM THE WORK GROUP

Breast Cancer (Table 1)

The use of radiopharmaceuticals for SLN mapping in breast cancer is appropriate for patients <70 y old after initial diagnosis

TABLE 1
Appropriateness Ratings for Clinical Scenarios for Lymphoscintigraphy in Breast Cancer

Scenario no.	Description	Appropriateness	Score
1	Invasive breast cancer of any histologic type without evidence of axillary or distant metastases and without evidence of skin or chest wall invasion	Appropriate	9
2	Invasive breast cancer of any histologic type with pathologic evidence of axillary metastases and no evidence of skin or local chest wall invasion or distant metastases	May be appropriate	5
3	Invasive breast cancer of any histologic type with evidence of distant metastases	May be appropriate	5
4	Ductal carcinoma in situ (DCIS) without suspicious features and DCIS or pleomorphic lobular carcinoma in situ (LCIS) without planned mastectomy or other surgery affecting lymphatic drainage	Rarely appropriate	2
5	DCIS with suspicious features and DCIS or pleomorphic LCIS with planned mastectomy or other surgery affecting lymphatic drainage	Appropriate	8
6	Planned reduction mammoplasty or risk-reducing mastectomy in patients without a known breast cancer diagnosis	Rarely appropriate	1
7	In-breast recurrence or de novo ipsilateral breast cancer without evidence of axillary or distant metastases and without evidence of skin or chest wall invasion	Appropriate	9
8	Inflammatory breast cancer or breast cancer with evidence of skin or local chest wall invasion	Rarely appropriate	1
9	Phyllodes tumor	Rarely appropriate	1
10	Paget disease of the breast, cancer not identified before surgery	May be appropriate	6

TABLE 2
Appropriateness Ratings for Clinical Scenarios for Lymphoscintigraphy in Skin Cancer

Scenario no.	Description	Appropriateness	Score
11	Primary cutaneous melanoma of appropriate stage without clinical evidence of metastasis	Appropriate	9
12	Cutaneous melanoma after a local-regional recurrence	May be appropriate	6
13	Pigmented lesions of uncertain metastatic potential	May be appropriate	6
14	Primary melanoma of the anus or vagina without clinical evidence of metastasis	Appropriate	7
15	Cutaneous and mucosal (penile, vulvar) squamous cell carcinoma (SCC) or basal cell carcinoma without clinical evidence of metastasis	Appropriate	8
16	Merkel cell carcinoma without clinical evidence of metastasis	Appropriate	9
17	Malignant adnexal cutaneous tumors (eccrine, sweat gland, SCC with eccrine dedifferentiation) without clinical evidence of metastasis	May be appropriate	6
18	Selected sarcoma subtypes (synovial, epithelioid, rhabdomyosarcoma, angiosarcoma, clear cell sarcoma) without evidence of metastasis	May be appropriate	6

of invasive breast cancer of any histologic type if there is no clinical or imaging-based evidence of axillary or distant metastasis, either in the de novo setting or in the setting of an in-breast recurrence. In patients with evidence of local or distant metastatic disease, however, the benefit of SLN mapping is less apparent.

SLN biopsy (SLNB) may be appropriate in patients ≥ 70 -y-old if the results will impact adjuvant treatment. SLN mapping may also be considered appropriate in patients with ductal carcinoma in situ or pleomorphic lobular carcinoma in situ for whom a mastectomy is planned or in the setting of breast-conserving surgery where the procedure may affect the option for future lymphatic mapping or where suspicion for invasive disease is present.

SLN mapping is rarely appropriate in patients diagnosed with an inflammatory breast cancer or breast cancer with evidence of skin or local chest wall invasion, with Paget disease of the breast without evidence of an underlying invasive cancer identified before surgery, with Phyllodes tumors, or in the setting of a prophylactic mastectomy or reduction mammoplasty in women without a history of breast cancer.

Skin Cancer (Table 2)

SLNB has been shown to be helpful in the management of patients with melanoma and Merkel cell carcinoma. Preliminary evidence of SLNB with other cutaneous lesions suggests there may be some utility; however, more controlled studies are needed. At present, SLNB in rare tumors may be performed when the nodal status will affect management, when the possibility of nodal metastasis is believed to be significant, or when there is no other evidence of metastatic disease. As therapy for some cutaneous malignancies improves, the need for SLNB will change, particularly when sentinel node status no longer changes management or prognosis.

Cancers at Other Sites (Table 3)

The success of sentinel node localization in melanoma and breast cancer has led to the application of sentinel node scintigraphy to several other diseases, including gynecologic, gastrointestinal, urologic, bladder and renal, and thyroid cancers. Other than for cervical cancer and oral cavity cancers, the effectiveness of SLNB using radiotracers in these other malignancies is still under investigation.

TABLE 3
Appropriateness Ratings for Clinical Scenarios for Lymphoscintigraphy in Cancers at Other Sites

Scenario no.	Description	Appropriateness	Score
19	Prostate cancer (initial stage)	Appropriate	7
20	Cervical cancer (initial stage)	Appropriate	7
21	Endometrial cancer, low-risk patient	May be appropriate	5
22	Endometrial cancer, high-risk patient	May be appropriate	6
23	Ovarian cancer	Rarely appropriate	3
24	Vaginal squamous cell cancer	May be appropriate	6
25	Primary malignancy of the gastrointestinal tract without clinical evidence of metastasis	May be appropriate	5
26	Oral cavity cancer	Appropriate	9
27	Oropharyngeal cancer	May be appropriate	6

TABLE 4
 Appropriateness Ratings for Clinical Scenarios for Lymphoscintigraphy in Lymphedema and Lipedema

Scenario no.	Description	Appropriateness	Score
28	Clinical suspicion for primary lymphedema of the extremities	Appropriate	8
29	Clinical suspicion for secondary lymphedema of the extremities	Appropriate	7
30	Clinical suspicion for breast lymphedema	May be appropriate	4
31	Lipedema of the extremities	May be appropriate	6
32	Limb edema of unclear etiology	Appropriate	8

Lymphedema (Table 4)

Lymphoscintigraphy is an appropriate test for evaluation of primary lymphedema or limb edema of unclear etiology. Lymphoscintigraphy can also be appropriate for patients with suspicion for secondary lymphedema, particularly if the clinical history or exam is not definitive for the diagnosis of lymphedema. Lymphoscintigraphy can be helpful to confirm lymphatic dysfunction before lymphatic surgery. Lymphoscintigraphy may be appropriate in select patients with lipedema or breast lymphedema, although the value of lymphoscintigraphy in these populations is not widely published.

Pediatric Considerations

The pediatric indications for lymphoscintigraphy and SLNB are similar to those in adults, although the differing incidences and causes of lymphatic diseases in children should be considered.

It is uncommon for studies of the clinical utility of lymphoscintigraphy to focus solely on children, yet many published reports include children in their study populations. Lymphoscintigraphy has been reported to have a role in guiding the management and treatment of some pediatric cancers and in evaluation of lymphedema in children. The complete AUC document includes statements on lymphoscintigraphy in pediatric breast and skin cancers, as well as pediatric sarcoma and lymphedema.

SUMMARY

This report is a summary of the complete Appropriate Use Criteria for Lymphoscintigraphy in Sentinel Node Mapping and Lymphedema/Lipedema, available at <https://www.snmami.org/ClinicalPractice/content.aspx?ItemNumber=42021>.