

Expanding the Role of Interventional Oncology in the Lymphatic System: Emerging Opportunities

Mayura P. Umapathy, BS¹; Mina S. Makary, MD²

¹The Ohio State University College of Medicine, Columbus, OH

²Division of Interventional Radiology, The Ohio State University Wexner Medical Center, Columbus, OH 43210

Introduction

- The lymphatic system plays a critical role in cancer defense and progression as well as immune modulation.
- Current interventional approaches targeting the lymphatic network have been largely limited to non-oncologic procedures (e.g. lymphangiography, thoracic duct embolization).
- However, the growing emphasis on precision oncology, immunotherapy, and targeted drug delivery provides an opportunity to expand image-guided lymphatic approaches within oncology.

Current Lymphatic IO Techniques

1. Image-Guided Nodal Ablation

Image-guided minimally invasive ablation (RFA & MWA) are routinely used for metastatic lymph nodes in thyroid cancer

- High technical success and significant nodal shrinkage across studies
- Complete disappearance rates range from 63–90%
- Major complication rates are low

2. IR-Assisted Sentinel Node Localization (SLN)

In select settings, IO provides minimally invasive SLN localization via image-guided tracer delivery and advanced imaging techniques, particularly in breast and bladder cancer

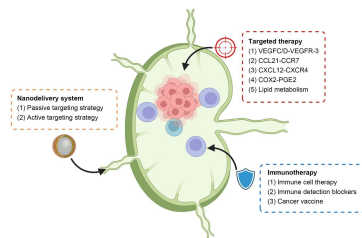
Localization methods include:

- Contrast-enhanced ultrasound with microbubble and ¹²⁵I seed placement enabled precise SLN marking in breast cancer.
- Hybrid SPECT/CT + hybrid tracer indocyanine green mapping in bladder cancer allowed preoperative SLN localization and intraoperative confirmation.
- Near-infrared fluorescence imaging with indocyanine green achieved >95% SLN detection in breast cancer.

Emerging applications of IO in the lymphatic system

1. Targeted Drug Delivery to Lymph Node Metastases

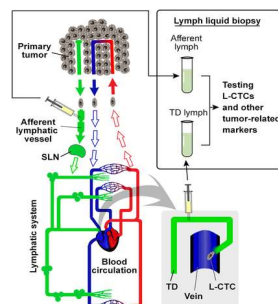
- Many cancers metastasize first to lymph nodes. Local drug delivery may treat micrometastases before systemic spread
- Animal models using lymphatic cisplatin delivery show improved survival and disease control.
- Still preclinical; clinical trials and optimized delivery systems are needed



Ji, H., Hu, C., Yang, X. et al. Lymph node metastasis in cancer progression: molecular mechanisms, clinical significance and therapeutic interventions. *Sig Transduct Target Ther* 8, 367 (2023). <https://doi.org/10.1038/s41392-023-01576-4>

2. Lymph Fluid Sampling for disease monitoring

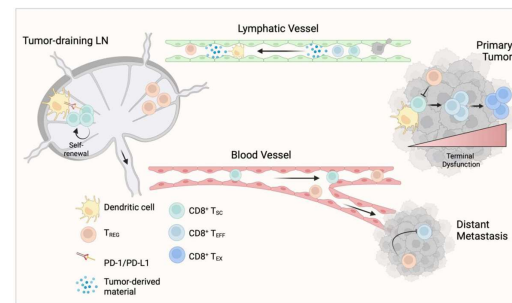
- Lymph fluid may contain earlier, more specific biomarkers than blood.
- In murine melanoma, stem-like tumor cells appeared in lymph before blood.
- Tumor-draining lymph nodes (TDLNs) show immune profiles predictive of immunotherapy response
- Clinical NSCLC and melanoma studies found PD-1+ T cells and immune activation markers in TDLNs predictive of treatment response
- Techniques lack standardization; clinical validation needed for integration.



Han M, Watts JA, Jamshidi-Parsian A, Nadeem U, Siegel ER, Zharov VP, Galanzha EI. Lymph Liquid Biopsy for Detection of Cancer Stem Cells. *Cytometry A*. 2021 May;99(5):496–502. doi: 10.1002/cyto.a.24221. Epub 2020 Sep 18. PMID: 32869909; PMCID: PMC9237844.

3. Intranasal Immunotherapy Delivery

- Lymph nodes are ideal for immune activation. A Phase I/II trial used ultrasound-guided dendritic cell vaccine injections in metastatic melanoma (n = 15).
- Safe and feasible: mild flu-like symptoms and injection site reactions reported
- All patients responded to KLH (a standard immune control), confirming vaccine delivery; 14% showed tumor-specific T cell responses.
- Among 8 evaluable metastatic patients: 1 mixed response, 2 stable disease (~2 years), 5 progressive disease
- Limited immunogenicity; further optimization and larger trials needed.



Delclaux I, Ventre KS, Jones D, Lund AW. The tumor-draining lymph node as a reservoir for systemic immune surveillance. *Trends Cancer*. 2024 Jan;10(1):28–37. doi: 10.1016/j.trecan.2023.09.006. Epub 2023 Oct 18. PMID: 37863720; PMCID: PMC10843040.

Conclusions

- Interventional oncology in the lymphatic system offers minimally invasive opportunities for cancer diagnosis, treatment, and symptom management.
- Further research is needed to define its role in improving clinical outcomes.

References

- Upadhyaya A, Upadhyaya SA, Chang L, Li Y, Wei X. Ultrasound-guided Percutaneous Radiofrequency and Microwave Ablation for Cervical Lymph Node Metastasis from Papillary Thyroid Carcinoma: A Systematic Review and Meta-analysis of Clinical Efficacy and Safety. *Acad Radiol*. 2025 May;32(5):2533–2544. doi: 10.1016/j.acra.2024.12.064. Epub 2025 Jan 11. PMID: 39800601.
- Wu J, Wei Y, Zhao ZL, Cao SL, Li Y, Peng LL, Li SQ, Yu MA. A clinical study of microwave ablation for cervical lymph node metastasis from papillary thyroid cancer. *Front Endocrinol (Lausanne)*. 2025 Apr 25;16:1580765. doi: 10.3389/fendo.2025.1580765. PMID: 40352454; PMCID: PMC12061701.
- Dou, J., Han, Z., Che, Y. et al. Thermal ablation for radioactive iodine refractory cervical lymph node metastasis in differentiated thyroid cancer. *Eur Radiol* (2025). <https://doi.org/10.1007/s00330-025-11823-7>
- Barentsz MW, Verkooijen HM, Pijnappel RM, Fernandez MA, van Diest PJ, van der Pol CC, Witkamp AJ, Hobbink MG, Sever AR, van der Bosch MA. Sentinel lymph node localization with contrast-enhanced ultrasound and an I-125 seed: an ideal prospective development study. *Int J Surg*. 2015 Feb;14:1–6. doi: 10.1016/j.ijsu.2014.12.019. Epub 2015 Jan 2. PMID: 25560747.
- van Gennep EJ, Pisano G, Kleinjan GH, Rietbergen DDD, Hendricksen K, Mertens LS, Vd Kamp MW, Wit EMK, van Montfort ML, Donswijk M, van Rhijn BWG, van Leeuwen FWB, van der Poel HG. Prospective clinical study of sentinel node detection in bladder cancer using a hybrid tracer - Towards replacement of pelvic lymph node dissection in cases with sentinel node visualization on SPECT/CT? *Eur J Nucl Med Mol Imaging*. 2025 Aug;52(10):3653–3661. doi: 10.1007/s00259-025-07240-z. Epub 2025 Apr 4. PMID: 40183956; PMCID: PMC12316797.
- Verbeek FP, Troyan SL, Miegog JS, Liefers GJ, Moffitt LA, Rosenberg M, Hirshfield-Bartek J, Gioux S, van de Velde CJ, Vahrmeijer AL, Frangioni JV. Near-infrared fluorescence sentinel lymph node mapping in breast cancer: a multicenter experience. *Breast Cancer Res Treat*. 2014 Jan;143(2):333–42. doi: 10.1007/s10549-013-2802-9. Epub 2013 Dec 13. PMID: 24337507; PMCID: PMC3899688.
- Tada A, Horie S, Mori S, Kodama T. Therapeutic effect of cisplatin given with a lymphatic drug delivery system on false-negative metastatic lymph nodes. *Cancer Sci*. 2017 Nov;108(11):2115–2121. doi: 10.1111/cas.13387. Epub 2017 Sep 15. PMID: 28846190; PMCID: PMC5666029.
- Han M, Watts JA, Jamshidi-Parsian A, Nadeem U, Siegel ER, Zharov VP, Galanzha EI. Lymph Liquid Biopsy for Detection of Cancer Stem Cells. *Cytometry A*. 2021 May;99(5):496–502. doi: 10.1002/cyto.a.24221. Epub 2020 Sep 18. PMID: 32869909; PMCID: PMC9237844.
- Goode EF, Roussos Torres ET, Irshad S. Lymph Node Immune Profiles as Predictive Biomarkers for Immune Checkpoint Inhibitor Response. *Front Mol Biosci*. 2021 May 24;8:674558. doi: 10.3389/fmolb.2021.674558. PMID: 34141724; PMCID: PMC8205515.
- Bol KF, Figdor CG, Aarntzen EH, Welzen ME, van Rossum MM, Blokx WA, van de Rakt MW, Scharenborg NM, de Boer AJ, Pots JM, Olde Nordkamp MA, van Oorschot TG, Mus RD, Croockewit SA, Jacobs JF, Schuler G, Neyns B, Austyn JM, Punt CJ, Schreiber G, de Vries JJ. Intranasal vaccination with mRNA-optimized dendritic cells in metastatic melanoma patients. *Oncoimmunology*. 2015 Apr 1;4(8):e1019197. doi: 10.1080/2162402X.2015.1019197. PMID: 26405571; PMCID: PMC4570143.