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INTRODUCTION

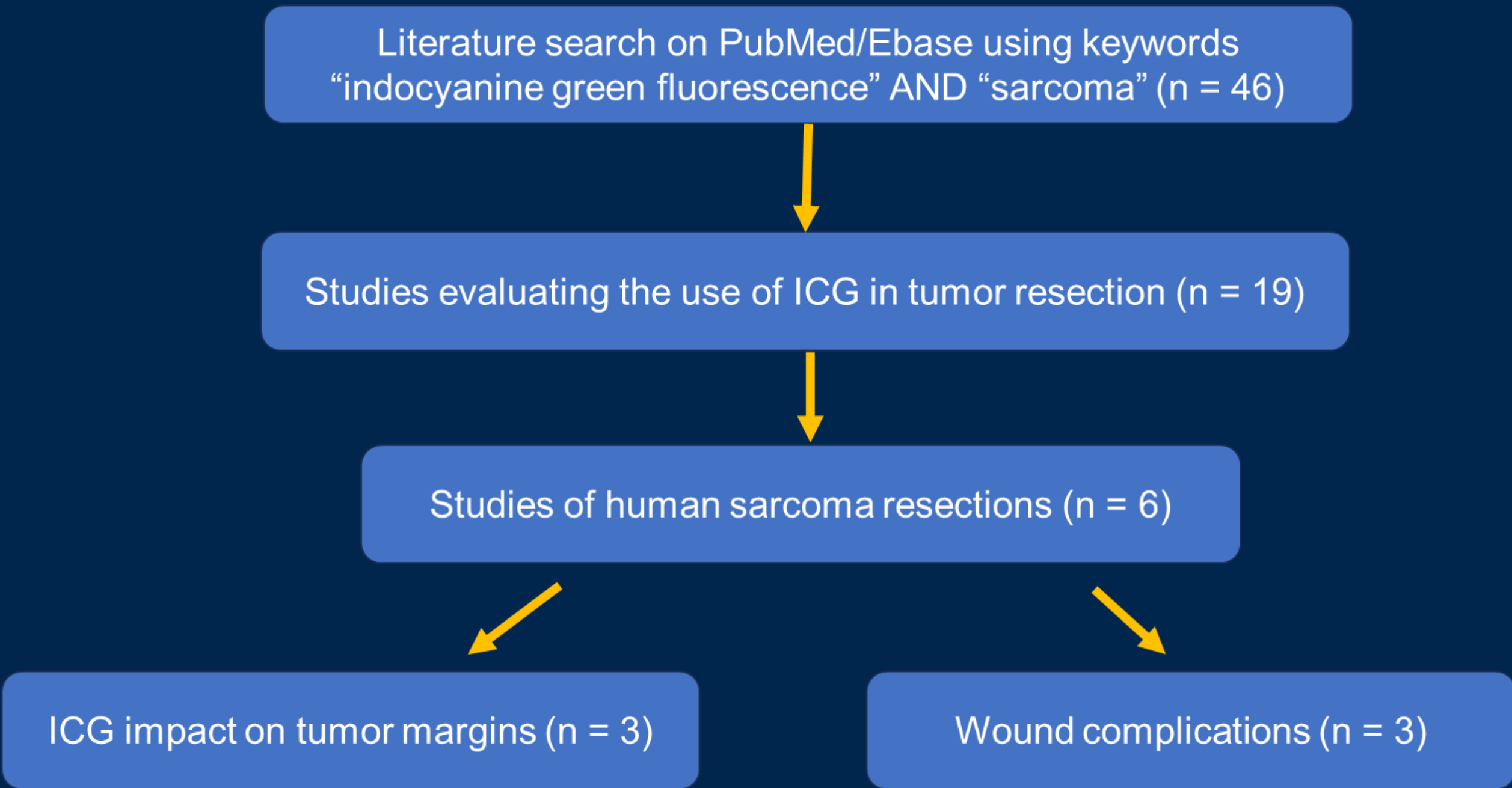
Sarcomas, a group of malignant tumors, are particularly prone to high rates of local recurrence. Achieving negative surgical margins in sarcoma resections is critical for reducing local recurrence and improving overall patient outcomes. While intraoperative navigation is now well established for bone sarcomas, there is currently no technology available for intraoperative tumor identification in soft tissue sarcomas. Indocyanine green (ICG) fluorescence imaging is currently used intraoperatively for the visualization of blood vessels, as well as in various tumor entities such as gastrointestinal tumors, sentinel lymph nodes, and hepatobiliary malignancies. Although ICG is a non-tissue-specific contrast agent, it accumulates in sarcomas through two main mechanisms: 1) Increased uptake via upregulated clathrin-mediated endocytosis in tumor cells¹ 2) Enhanced permeability and retention (EPR effect) due to leaky vasculature and impaired lymphatic drainage²⁻⁴. To evaluate vascularity after tumor resection, a small intravenous dose of ICG is administered. This allows clear differentiation between well-perfused and poorly perfused areas.

AIM

Our aim was to evaluate whether intraoperative ICG fluorescence imaging actually improves surgical margins and reduces postoperative complications compared to traditional techniques in sarcoma surgery.

METHODS

In February 2025, a systematic literature search was performed using the keywords “indocyanine green fluorescence” and “sarcoma.” Studies not conducted in humans or without data on resection margins or wound complications were excluded. Three studies fulfilled the inclusion criteria.



RESULTS

TUMOR MARGINS

A total of 90 patients with bone and soft tissue sarcomas were included. Neoadjuvant therapy was applied in 25% of cases with variable dosing and timing. No fluorescence was detected intraoperatively in 5 tumors. Surgeons reported intraoperative ICG fluorescence as helpful in 36% of cases, and R0 resection was achieved in 94%. Compared to a control group without ICG guidance⁷, significantly more R1 resections occurred when ICG was not used.

	N	Neoadjuvant therapy	Dose	Timing before surgery	No fluorescens	Intraoperative guidance	R0- Margin
Nicoli ⁵	11	0 (0%)	75mg	16-24h	2 (18%)	3/11 (27.3%)	9 (81%)
Brookes ⁶	39	2 (5%)	25-100mg	16-24h	2 (5%)	11/39 (28.2%)	37 (95%)
Huang ⁷	40	21 (30%)	0.5mg/kg KG	1-3h	3 (7.5%)	19/40 (47.5%)	39 (97.5%)
Total	90				5 (5.5%)	33 (36.6%)	85 (94.4%)

WOUND COMPLICATION

Three studies evaluated the role of ICG fluorescence in predicting and potentially reducing wound complications after sarcoma surgery. Most patients had received neoadjuvant radiotherapy. In two studies⁸⁻⁹, ICG fluorescence was performed after tumor resection and wound closure to document skin perfusion. The surgical plan was not modified. Wound complications occurred in 38% of patients. Sensitivity for predicting complications ranged from 50–100%, with specificity of 77–79%. In the third study¹⁰, 17 patients underwent ICG-guided wound closure, where poorly perfused areas were resected or soft tissue coverage was adapted. Compared to a control group of 71 patients, wound complications were significantly lower in the ICG group (11% vs. 42%).

	N	Type of closure	Neoadjuvant radiotherapy	Wound complication	Predicted wound complication with ICG
Lazarides ⁸	14	Direct	100%	6 (43%)	Sensitivity: 100% Specificity: 77.4%
Wilke ⁹	20	Direct: 43% Local flap: 39% Free flap: 9%	91%	7 (35%)	Sensitivity: 50% Specificity: 79%
Total	34			13 (38%)	
Wilke ¹⁰	17/ 71	Direct, local flap, free flap	88%	2 (11.8%) vs. 30 (42.3%)	

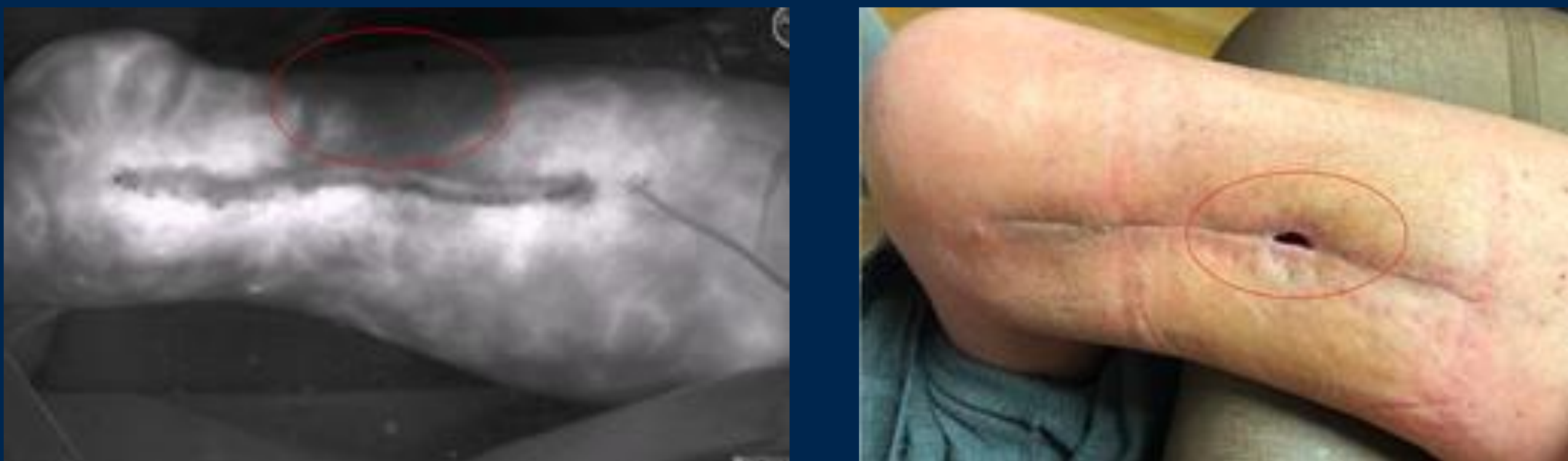


Figure 1. Intraoperative ICG fluorescence imaging. Left panels show reduced skin perfusion indicated by diminished ICG signal. This predicted a wound complication, which subsequently manifested as wound dehiscence. (Clinical example published by Lazarides et al.⁸)

CONCLUSION

ICG fluorescence is a promising adjunct in sarcoma surgery. It may support surgeons in achieving negative margins and has shown potential to reduce wound complications, particularly when used to guide soft tissue management. However, current evidence is limited to small, heterogeneous studies. Larger prospective trials are needed to validate its clinical impact.

1 Bunschoten, A. Biomaterials 2012, 33,867-875
2 Maeda H. Adv. Enzym. Regul. 2001;41:189-207
3 Maeda H. Adv. Drug Deliv. Rev. 2013
4 Madajewski B, Clin. Cancer Res. Off. J.Am. Assoc. Cancer Res. 2012
5 Nicoli F, Ann Surg. 2021 Feb.

6 Brookes MJ. Cancers (Basel). 2021 Dec.
7 Huang H, J Surg Oncol. 2023 Sep.
8 Lazarides AL. J Orthop Res. 2022 Oct.
9 Wilke BK. J Am Acad Orthop Surg. 2021 May
10 Wilke BK. J Am Acad Orthop Surg Glob Res Rev. 2021