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Sentinel Lymph Node Detection in Cutaneous Melanoma Using Indocyanine Green-Based Near-Infrared Fluorescence Imaging: A Systematic Review and Meta-Analysis

Marcus Wölffer, Rémy Liechti, Mihai Constantinescu, Ioana Lese, Cédric Zubler

Department of Plastic and Hand Surgery, Inselspital, University Hospital Bern, University of Bern

Objectives

The standard of care approach to identify sentinel lymph nodes (SLN) in clinically non-metastatic cutaneous melanoma patients is Technetium (Tc)-based lymphoscintigraphy (LS), a costly and radioactive method with limited availability. Indocyanine green (ICG)-based near-infrared fluorescence imaging (NIRFI) offers a potential alternative proven safe and effective in breast cancer surgery. This systematic review and meta-analysis investigate the diagnostic accuracy of ICG-only and Tc-only approaches in identifying cutaneous melanoma SLNs, metastatic SLNs, and metastatic patients, with special regard to the false-negative rate (FNR).

Methods

A systematic review and a meta-analysis were conducted according to the PRISMA 2020 guidelines. In December 2023, MEDLINE via PubMed, Embase, and the Cochrane Library databases were systematically searched. Studies with a different outcome than the diagnostic accuracy of ICG and Tc in cutaneous melanoma, using of a hybrid tracer or other dyes were excluded. Seven studies were methodologically assessed using the MINORS criteria. FNR of ICG and Tc was the primary outcome. We defined a false negative event as a recurrence in a previously sampled, negative SLN basin during follow-up or a positive SLN identified only by the other method. Four studies were included in the FNR meta-analysis and seven studies in the meta-analysis for number of SLNs and metastatic patients identified. Review Manager (RevMan, version 5.3.5) was used for analyses, with p-value below 0.05 considered statistically significant.

Results (continued)

FNR for ICG was higher or equal as compared to Tc with a meta-FNR of 13% for ICG and 10% for Tc. Tc identified a significantly higher number of SLNs and of metastatic SLNs out of all metastatic SLNs only in prospective studies (p = 0.001, p = 0.02, respectively). No significant difference was found for the number of identified metastatic SLNs out of all SLNs, metastatic patients, or FNR. More metastatic patients, SLNs, and metastatic SLNs were identified by Tc than by ICG, this difference was however disproportionately high for SLNs.

Discussion

SLN identification with Tc is limited by old age, head and neck location and the shine-through effect. Limiting factors of ICG include a high body mass index and axillary lymph node fields, likely due to a transcutaneous visibility of only 2 cm. Tc may have identified a higher number of SLNs and metastatic SLNs in prospective studies due to study design or the impact of one study on this sample size. They did not translate into a higher number of identified metastatic SLNs out of all SLNs or patients, potentially due to uncertainties regarding the radioactive counting rate threshold. While the excision of multiple SLNs might lead to lower FNRs, it also contributes to morbidity. No significant difference was found for the number of identified metastatic patients and the FNR, crucial for initiation of adjuvant therapy. Introduction of ICG in practice is obstructed by costs, staff training and regulatory requirements. Furthermore, its accuracy might be overestimated, as most studies localize SLNs with Tc and merely confirm these basins with ICG. Higher transcutaneous detection rates than the reported 79.4% would optimize SLN identification and dissection, and will determine whether ICG becomes a viable alternative.

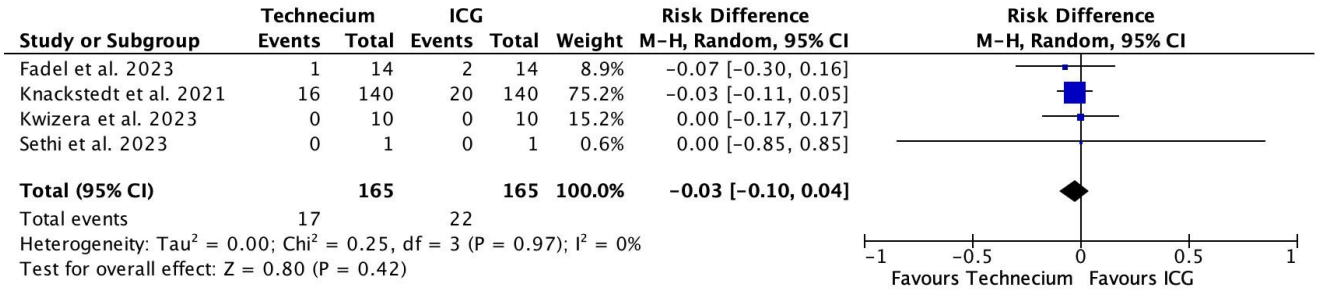

Figure 1: Forest plot depicting effect estimates regarding the number of false-negative patients missed by Tc or ICG out of the total number of true-positive and false-negative patients with corresponding risk differences.

Results

Out of 319 studies reviewed, 7 monocentric cohort studies remained, including 3 prospective studies. A total of 941 patients were included.

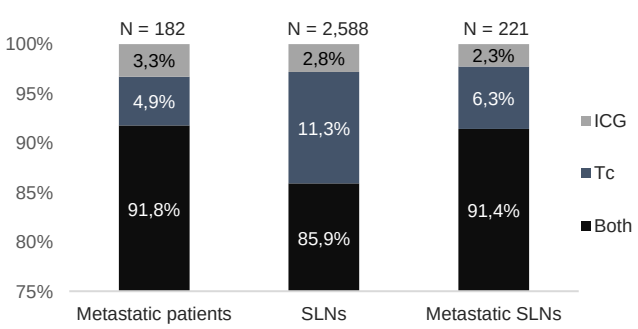

Figure 2: Relative identification of metastatic patients, SLNs and metastatic SLNs by both methods, Tc only and ICG only respectively.

Conclusions

While neither method performs optimal during SLNB, no significant differences were found for the identification of metastatic patients and FNRs. ICG may be a non-inferior alternative to Tc in cutaneous melanoma SLNB in the context of an advantageous adverse events profile, cost considerations, and limited availability of Tc. Randomized controlled, multicenter trials with a large cohort size and adequate follow-up period are needed.

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