

Peer Review File

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Reviewer A

This is a well written and comprehensive review of the current state of LYMPHA/ILR, including current outcomes data and future directions for investigation. However, the discussion should be streamlined and reformatted to improve the flow and readability of information. My suggestions are as follows:

Comment 1: Outcomes data should be represented as a table including year, sample size, level of evidence/study design, patient characteristics, surgical technique, length of follow up, and lymphedema incidence, etc. This will allow the reader to easily synthesize the information presented.

Reply 1: The main goal of this review article is to highlight important studies supporting the efficacy of ILR in reducing the risk of BCRL for the reader. To have a table with a complete list of all reported data is outside the scope of a review article, and more consistent with a systematic review and/or meta-analysis. The reader may refer to recent systematic reviews for this information, which are summarized in the Outcomes section on page 11.

Comment 2: Please include the following references: -

https://journals.lww.com/plasreconsurg/Abstract/9900/A_Four_Year_Institutional_Experience_of_Immediate.1634.aspx

https://journals.lww.com/plasreconsurg/Citation/2023/02000/Lymphatic_Microsurgical_Preventive_Healing.36.aspx

Comment 2: The two references above have been added in the Outcomes section (page 10).

Comment 3: Would add a Limitations section specifically dedicated to limitations before future directions, discussing the current limitations of available studies, and would move the information in "Improved Quality of Outcomes Research" into this section.

Reply 3: A Limitations section has been added to the Discussion (pages 12-13).

Comment 4: Future Directions should be reorganized to improve flow of information in a logical manner - would start with patient selection criteria > surgical technique > adjunct therapies.

Reply 4: The Future Directions section has been reorganized as suggested (pages 13-14).

Reviewer B

This is a great review about LYMPHA that I enjoyed reading. However, I thought it is short, incomplete and not enough to learn about ILR. The paper can benefit from a major revision.

Comment 1: ILR includes different types of surgery: 1) ARM, 2) LYMPHA and 3) S-LYMPHA. When I read the title, I thought I will read a general review on ILR including the different methods etc.. . However, you focussed only on LYMPHA. Even so, you have not presented any information on the success rate, the clinical outcome (any meta-analysis published etc..), how often LYMPHA could not be performed (some suggest 25%), due to inability to find the right vein, use vein grafts from other areas (Singhal group) etc...., that there is a phase III trial in progress at MSKCC. I think the readers will appreciate including all this.

Reply 1: Thank you for your comment. We previously did mention ARM and S-LYMPHA but have expanded on these topics more (see below in the responses to questions 2 and 3).

For your comments on LYMPHA, we believe we have already addressed much of your questions. Success rate and outcomes are mentioned in the Outcomes section (pages 9-11). How often LYMPHA could not be performed is mentioned in the last paragraph of Technical Tips and Potential Pitfalls (page 9, paragraph 2). RCTs including the phase III trial at MSKCC are mentioned in the last paragraph of the Limitations section (page 12, paragraph 3).

Comment 2: Using only ARM and the ALLIANCE trial by Klimberg. May be description of this method, with some figures and pictures as well as some clinical data from metaanalysis or others etc..

Reply 2: We have mentioned the Alliance A221702 trial by Klimberg in the section on ARM in the Historical Background on page 6, paragraph 1. However, we did not expand upon this trial, as it does not involve ILR.

Comment 3: S-LYMPHA or simplified LYMPHA with the work from Ozmen et al, and the difference with the standard LYMPHA etc.... There is data about that.

Reply 3: We have expanded on S-LYMPHA in the Outcomes section (page 10, paragraph 2).

Comment 4: The Pro's and Con's of each method. The short FU in the literature, the accuracy of the methodology to measure lymphedema, which lymphedema definition

the authors used etc..

Reply 4: We believe these comments were previously addressed in the Outcomes and Limitations sections.

Comment 5: Is there any impact of radiation on the area of anastomosis?

Reply 5: The effects of radiation on long term patency rates of LYMPHA are unknown.

Comment 6: Would like more figures and pictures for the non-plastic surgeons to understand and appreciate (an ICG for a patient, diagram of each method for general MD's who are not familiar with these methods.

Reply 6: As this paper is solely about LYMPHA, we do not have any specific images of ICG. However, our images do show the anatomy of the lymphovenous anastomosis performed in this surgery.