

## Peer Review File

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COMMENT#1: This manuscript covers an important and relevant topic. However, I have severe concerns about the methodological quality and contents, and find the structure suboptimal.

RESPONSE#1: Thank you for your comment. We have addressed the concerns from the reviewer.

COMMENT#2: Regarding methodology:

The methodology of this review does not fit the purpose. To review neurotization outcomes and techniques, a systematic review is of higher methodological quality and is already done by several other authors. I therefore question the novelty, and more importantly the added value of this work.

RESPONSE#2: Thank you for your comment. If a appropriately conducted, a systematic reviews usually tend to answer a hypothesis that the authors want to test. Therefore, most systematic reviews are limited to answer a specific research question.

There are a limited number of reviews evaluating the surgical outcomes of innervated breast reconstruction. Additionally, new articles have been published that were not previously summarized in other reviews. With our review, we offer an extensive description of the state-of-the-art in breast neurotization, we provide a diligent organization of then information presented in different studies using a rigorous citation technique, and provide one of the largest reviews in the topic.

COMMENT#3: Regarding contents:

While a narrative review is inferior to a systematic review in quality and level of evidence, it does present the opportunity to paint a more complete picture as it is less strictly limited to certain outcomes. A good narrative review should therefore at least be meticulous, comprehensive, and needs to give a complete overview of the subject. This review however, is incomplete and the amount of included studies seems limited.

RESPONSE#3: Thank you for your comment. We have included most of the manuscript we found on breast innervation. Including papers from 2023.

COMMENT#4: In the introduction I miss several important references; first innervated breast reconstruction, first innervated DIEP flap, refinement of the technique to use the third anterior intercostal nerve.

RESPONSE#4: Thank you for your comment. We added the information requested by the reviewer.

COMMENT#5: In the results section (which lacks a clear heading) the authors omitted to describe the relevant anatomy. The innervation of the breast, and anatomy of suitable donor and recipient nerves (also regarding non-abdominal flaps) are of critical importance. The technique of the nerve harvest is not described. This needs to be more

precise and include anatomical planes and references, and course of the nerve including motor branches that need to be spared.

RESPONSE#5: Thank you for your comment. The information and data requested by the reviewer was added.

COMMENT#6: When the authors describe E-S neurotization, they do not mention their references. This would be interesting, since it is not often used in breast reconstruction where you usually have a suitable transected recipient nerve. The authors state that E-S neurotization can be done '[..] to preserve the original function of the donor's nerve.' (129-130) This is incorrect and needs to be corrected.

RESPONSE#6: Thank you for your comment. We added the necessary references. Also, we corrected the mistake highlighted by the reviewer.

COMMENT#7: When describing nerve grafts, the authors do not specify whether these are allografts or autografts. A distinction should be made in this regard. (143-154)

RESPONSE#7: Thank you for your comment. We added the brand and type of graft.

COMMENT#8: When describing the testing methods, the authors merely present which are used. A critical reflection is lacking. This is important, since reliability of testing methods is often debated. (196-215)

RESPONSE#8: Thank you for your comment. We added the information requested by the reviewer. Please, see the modifications in red.

COMMENT#9: As the authors sum up the results of other authors regarding sensory recovery, they do not mention what kind of flap this concerns. (238-256)

RESPONSE#9: Thank you for your comment. The type of flaps were added.

COMMENT#10: I am pleased to see that the authors addressed QoL. However, a few important studies that investigated QoL after innervated breast reconstruction with the BREAST-Q, are missing. Consider a more thorough literature search on this. Also, the BREAST-Q Sensation needs to be mentioned as it is a promising means to address QoL after neurotization. (313-333)

RESPONSE#10: Thank you for your comment. We addressed this question to the best of our abilities. As we mentioned, the tools to evaluate this parameter are extremely heterogeneous. We added the information the reviewer requested.

COMMENT#11: In the 'Conclusion' the authors mention sensation to pain and temperature (337), which is interesting as they did not address these aspects of sensation in their results. In their conclusions the authors also acknowledge that sensory recovery of innervated breasts still does not reach 'normal' sensation (364/365). I miss some reflection on why, how this can be improved, and a brief discussion of fundamental knowledge about sensation and sensory recovery.

Altogether, the reader would expect, based on the title of this manuscript, to receive a more complete overview than is actually given.

RESPONSE#11: Thank you for your comment. We added the information requested by the reviewer. We added several segments: “Many studies have reported higher sensitivity, or decreased sensory threshold for pressure, vibration, temperature discrimination, and pain in innervated breasts with direct coaptation for neurotization than non-innervated breast reconstruction.”

“For instance, while Mori et al. reported that non-innervated flaps showed worst recovery of touch and pain sensations than innervated flaps when a conventional mastectomy was performed, comparisons between the non-innervated and innervated groups showed no significant difference when nipple-sparing or skin-sparing mastectomies were used”

“Overall, the majority of the questions inquired about pain, numbness, abnormal sensation, hypersensitivity, breast skin feeling natural, cosmetic outcomes, and patient satisfaction. Other studies have simply used subjective open-ended questions about the patients’ experience and overall sensation satisfaction after breast reconstruction”

“Initial reports indicated that the innervated TRAM flaps provided better quality of life,(13) temperature differentiation ( $p = 0.02$ ), and sensitivity to fine touch in the flap skin ( $p = 0.003$ ) and in the non-flap skin (mastectomy flap;  $p = 0.037$ ) compared with non-innervated TRAM flaps ( $p < .001$ ).”

COMMENT#12: Regarding structure:

The order of the ‘introduction’ is illogical. Consider to shorten and move forward the general background information that is given in paragraph 2.

RESPONSE#12: Thank you for your comment. We reduced the first paragraph. We believe it is important to provide a background on peripheral nerve surgery, as these techniques will be reviewed in the manuscript

COMMENT#13: The structure of the ‘Results’ section is unclear. The authors chose to first describe the methods that are used in the literature, and later on present the outcomes. However, it would be easier to read and more logical if the outcomes are presented immediately after the method that is used.

RESPONSE#13: Thank you for your comment. We re-structured the manuscript.

COMMENT#14 A final comment is related to the writing style of the results section. The main body of the manuscript consists of many sum-ups of other author's findings, which is unpleasant to read. Two examples: 155-163 presents a sum-up of several nerve lengths that authors have found; and 164-171 presents a sum-up of several sutures that have been used. The same accounts for the sensory testing methods. To improve readability, consider summarizing these instead of mentioning each author separately. The overview of the literature can be a lot more clear and concise.

RESPONSE#14: Thank you for your comment. We re-structured the manuscript.

COMMENT#15: Altogether, the readability of the manuscript is affected by suboptimal (and sometimes illogical) structure of the manuscript.

RESPONSE#15: Thank you for your comment. We modified the structure of the

manuscript. We hope the modifications performed to this review can improve its quality.