

Peer Review File

Article information: <http://dx.doi.org/10.21037/abs-20-108>

Reviewer A

Comment 1: The authors are to be commended for contributing an insightful analysis of the positive effects of NAC reinnervation in multiple approaches to breast reconstruction.

Response 1: Thank you Reviewer A for your consideration of our manuscript. We are pleased to see that our original article successfully communicates the positive effects of NAC reinnervation in the field of breast reconstruction.

Reviewer B

Comment 1: Very interesting study, with an adequate methodology. The authors have to give sex/gender of patients. It is supposed that they are women but it is never assessed.

Response 1: Thank you Reviewer B for your comments. We have included more clarity on gender in our methods section. We clarify that we have both transmasculine and female patients in our study. Line 117 and line 121.

Reviewer C

Comment 1: Mammalian nipple-areola complex (NAC) is involved in sexual arousal and pleasurable sexual responses. To ensure these functions the nipple is supplied with somatosensory nerves that convey pressure, light touch, temperature and nociceptive stimulus to the central nervous system. Although it is generally accepted that functional roles of the nipple are related to a dense sensory innervation, and has been considered that nerve fiber density of the nipple exceeds most other skin areas, most of these conclusions came from the assessment of sensory detection thresholds from clinical assays. The present study represents a notable and interesting contribution in the field of breast innervation, especially NAC innervation patients undergoing mastectomy for both gender-affirmation and oncologic indications.

The manuscript is very well written, and it is easy to follow and understand. The methods are well detailed and allow to be replicated. The results are well exposed and illustrated. Discussion is dynamic and non-speculative. However, I would like to know the authors' opinion on the fact that if NAC is an important area in sexual arousal and pleasurable sexual responses, why is their sensitive innervation so scarce? (see doi: 10.1016/j.aanat.2019.151456)

Response 1: Thank you Reviewer C for your thoughtful commentary. We greatly appreciate the reference you provided as it raises an important point of discussion. We have introduced this histologic study into our paper's discussion. While our methodology is unable to further elucidate the complex neural structure of the NAC, we believe the sensory function must lie within

the deep dermal structures. This is the site where our nerve coaptation is performed and also the site of greatest density of sensory elements as demonstrated by Gutierrez-Villanueva et al. (Discussion Lines 279-287).

Reviewer D

Comment 1: When performing gender affirming surgeries, I would include operative times for the control and reinnervation the neurotization groups. The study is underpowered, but I would also inquire if there were significant differences between the patients that had one nerve computation in comparison to 3. As neurotization and advanced nerve procedures are becoming more popular, it is would be prudent to elucidate that information, even in small case series.

Were there any differences in "zones" of the breast. You comment on mastectomy skin, areola, and the nipple, but many new studies are looking at quadrants of the breast skin, aureola, and nipple, as sensation doesn't return uniformly with some of the modern nerve procedures.

Response 1: Thank you Review D for your comments. In this study we performed 1 coaptation per NAC and we are unable to make a comparison to cases of multiple neurotization. Our present-study focuses on the innervation of the NAC and 2cm of the surrounding breast skin. Our methodology differs from other studies that look to the different quadrants of the breast skin. We have included these limitations in our discussion. (Discussion Lines 301-303).

Reviewer E: Thank you for this very interesting and important manuscript. The concept of NAC sensation in the setting of cancer is only now being fully appreciated and introduction of this concept in the transgender patient is particularly novel. There are a couple of suggestions that I believe would make this manuscript even stronger:

Comment 1: Could the authors provide more details about how the nerve allograft is incorporated into the final construct? I assume the subcostal nerve harvested with the flap is coapted to the recipient nerve emerging from the pectoralis. However, I remain uncertain as to how the nerve allograft which is ultimately coapted to the subareolar tissues is then connected to the flap neural constructs. Is it coapted end-to side to the sub-costal nerve?

Response 1: Thank you Reviewer E for your comments. We have clarified in our methods that the coaptation of the donor nerve stump to the allograft is in an end-to-end fashion. The nerve allograft is then tunneled through the flap to the NAC, where it is coapted. (Methods Line 141-143).

Comment 2: When more than one neurotization was performed in the setting of oncologic reconstruction, were two separate allografts used?

Response 2: 1-2 nerve-allograft coaptations were performed in this study. We have clarified our methodology section (Methods Line 132-135). The

procedure takes approximately 20-30 minutes to perform.

Comment 3: Was peripheral breast skin sensation measured in all four quadrants of the breast?

Response 3: Peripheral breast skin sensation was limited to a region 2cm around the NAC. We have included in our limitation section that we did not fully assess all mastectomy skin quadrants in our methodology. (Discussion Lines 301-303).

Comment 4: Were sensory measurements performed at more than one time point post-operatively?

Response 4: Sensory measurements were performed 1-4 time points in the post-operative period. We waited for >8 months to allow for new nerve growth through the nerve allograft which we have noted in our methods section. (Methods Lines 156-157).

Comment 5: I feel as if the paragraph on the Bionic Breast is a bit of a non sequitur and could be removed.

Response 5: We have removed this section from the manuscript.