

## Peer Review File

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### **Reviewer #1**

The authors present thorough review of the impact of radiation in the setting of nipple sparing mastectomies. Given the increasing prevalence of this approach as well as the documented aesthetic benefits to preserving the nipple areolar complex, this is a very important issue to address in which we can increase the preservation of the NAC in patients undergoing treatment for breast cancer.

**Comment 1:** Can the authors provide any data on their own experience? They are high volume surgeons with tremendous experience in both oncologic mastectomy and reconstruction. Have they had patients who have had NSM and radiation in any setting? What is their experience? If the authors have some photos of patients they have treated, this would certainly enhance the manuscript.

Reply 1: It's a pity that our hospital has not conducted relevant research yet, and maybe it will be conducted based on this review in the future. Some photos of patients treated in NSM and intraoperative radiation is attached. These photos are from the First Affiliated Hospital, Guangzhou Medical University.

**Comment 2:** Is there any data on radiation and implant reconstruction and ADM? There are claims that ADM may prevent capsular contracture in device based reconstruction. Do textured implants have an impact on contractures and complications? Given the fear with BIA-ALCL, has this impact the surgeon's practice?

Reply 2 : Thank you for the advice and we researched radiation and implant reconstruction and ADM. According to the study of Salzberg[1], reported a low capsular contracture rate (1.9%) when ADM was used in one-stage partial subpectoral implant-based breast reconstruction, and this lower capsular contracture rate persisted after postmastectomy radiation therapy. But researches relevant to this aspect are limited so that in this review we would not discuss radiation and implant reconstruction and ADM. Thank you for your advice and we would do more research on it.

**Comment 3:** There are some minor grammatical errors that should be corrected.

Reply 3: Thank you for your advice and we corrected some grammar errors.

### **Reviewer #2**

The authors present a review article addressing the issue of radiotherapy in nipple sparing mastectomy. They nicely summarize the literature and discuss the various time points of radio therapy along with a discussion of indications for XRT.

**Comment 1:** While the literature review appears to be comprehensive in nature, it would be advantageous if the authors would include their search strategy for identifying the studies which date ultimately included in their analysis. This would strengthen the manuscript considerably.  
Several additional corrections seem warranted.

Reply 1: search strategy :

A literature search on PubMed was done using a combination of the keywords: “reconstruction”, “breast cancer”, “nipple-areola complex-sparing mastectomy”, “preoperative radiotherapy”, “intraoperative radiotherapy”. and “postoperative radiotherapy”.

All types of articles were included. Articles that were not in English, where abstracts only were available were excluded. The search was performed in June 2020 and there was no prior time limit set for inclusion of data.

**Comment 2:** The last sentence of the first paragraph "SSM and NSM are often called conservative mastectomies, which is the development of oncoplastic surgery" should be revised. The authors' notion, as presented, of the connection between SSM & NSM with oncoplastic surgery is questionable.

Reply 2: Thank you for this advice and this sentence should be removed, with our careful consideration.

**Comment 3:** Line 43: The work “artificial” preceding NAC reconstruction should be removed. Perhaps the authors can use the word “secondary” instead. Also, the connection between NAC reconstruction with oncoplastic breast surgery is unclear. Sentence revision strongly suggested.

Reply 3: The work “artificial” should be replaced by the word “secondary”.

**Comment 4:** Line 48: Radiotherapy treatment (RT) - Remove treatment as it is redundant. Line 66: Trials is misspelled.

Reply 4: Radiotherapy treatment (RT) – Remove “treatment”.

**Comment 5:** Manuscript should be edited for grammar, syntax, and spelling.

Reply 5: Thank you for your advice and we had polished this review.

Major changes are listed as follows:

Line 80 : “artificial” is replaced by the word “secondary”

Line 81 to 87 is changed into “ Compared with post-mastectomy breast reconstruction, NSM can not only preserve the integrity of the NAC in the surgery and optimize cosmetic outcomes, but also reduce patient morbidity while providing an oncologically-safe surgical procedure (6, 7). In the treatment of NSM, surgeons have not yet reached a consensus about some key points of safety, such as whether the

local recurrence rate of NSM is acceptable and whether NSM should be performed solely or combined with local radiotherapy.”

Line 88: Radiotherapy treatment (RT) – Remove “treatment”.

Line 117: “Most” is changed into “many”

Line 253: “It is the first time to report the feasibility” has been changed into “It is the first study reporting the feasibility “

Line 323 to 347 has been changed into “Nipple-sparing mastectomy has significantly increased in prevalence in recent years. There is abundant evidence in the literature that nipple-sparing mastectomy provides better appearance and quality-of-life for patients. Meanwhile, it reduces the need for additional nipple reconstruction and provides an acceptable level of oncologic safety. Based on the treatment principle of NSM, the selection of patients and the quality control of operation are the key to the whole treatment. The application of pre-, intra-, and/or postoperative RT is still a grey zone in the literature as regards the specific impact of RT on the NAC. Considering of the limited number of cases in each study and the short follow-up time, a larger sample randomized controlled study and further follow-up are needed to evaluate the long-term efficacy. More clinical studies and data are needed to explain whether combined radiotherapy should be performed and what kind of radiotherapy and how much the dose should be used. ”