

# Functional and Psychosocial Outcomes following Innervated Breast Reconstruction: A Systematic Review

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**Background:** With the incidence of breast cancer, breast cancer survival rates, and prophylactic mastectomies all increasing, efforts to optimize breast reconstruction and improve quality of life are becoming increasingly important. Nerve coaptation has been investigated for its potential to remedy the clinical and psychosocial deficits in newly reconstructed breasts. The purpose of this review is to gauge the efficacy of nerve coaptation during breast reconstruction in creating worthwhile benefits in both objective and subjective dimensions of sensation.

**Methods:** A Prospero registered systematic review was conducted. Databases including PubMed, SCOPUS, and ScienceDirect were screened using search terms “innervation,” “breast reconstruction,” and “neurotization” and relevant inclusion criteria.

**Results:** Twenty-three studies were found that met parameters for inclusion. We identified studies that assessed DIEP-based reconstruction (7), TRAM-based reconstruction (9), implant-based reconstruction (2), and five studies that looked at a variety of reconstructive modalities. Monofilament testing was the most common modality used to assess sensation, while pain, temperature, and pressure thresholds were assessed more infrequently. Various tools were used to measure psychosocial impacts, including the BREAST-Q. While the methods for evaluation of both aspects of sensation were heterogenous, there was a trend towards improved outcomes with neurotization.

**Conclusions:** The results of this review show promising improvements in clinical and psychosocial outcomes in innervated breasts compared to non-innervated breasts. However, the heterogeneity of studies in the literature indicates that more multicenter studies with standardized methodology including the BREAST-Q, sensory testing and complication analysis are needed to adequately demonstrate the value of neurotization in breast reconstruction. (*Plast Reconstr Surg Glob Open* 2022;10:e4559; doi: [10.1097/GOX.0000000000004559](https://doi.org/10.1097/GOX.0000000000004559); Published online 28 September 2022.)

## INTRODUCTION

The incidence of breast cancer rose from 10.8% of women in 1990, to 15.2% in 2010, while the lifetime risk of death fell from 4.5% to 3.8% in that same time period.<sup>1</sup> Additionally, there is an increasing trend toward prophylactic contralateral mastectomy procedures in women receiving mastectomy for breast cancer.<sup>2</sup> With the

incidence of breast cancer, breast cancer survival rates, and prophylactic mastectomies all on the rise, efforts to optimize breast reconstruction and improve quality of life are becoming increasingly important.

While breast reconstruction has come a long way in the past 20 years, a large deficit is still appreciable for patients. Despite advancements in the construction of an aesthetically pleasing breast mound, the lack of sensory ability in newly constructed breasts can become a constant unwanted reminder of patients' cancer and procedure. Additionally, a completely insensate breast mound presents a potential long-term health liability as pain and protective sensation are no longer present in the soft tissue.<sup>3</sup>

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In addition to objectively measured sensation and protective function, often measured via monofilament test, there is an emotional dimension to sensory return as well. Studies describe erogenous sensation, feelings of femininity and that the reconstructed breast is the “patient’s own” as determinants of overall satisfaction in the reconstructed breast and quality of life.<sup>3,4</sup> The BREAST-Q is a tool used to measure patient self-reported outcomes and quality of life following breast surgery, and has different domains, including patient satisfaction and physical, psychosocial, and sexual well-being. This tool allows physicians to understand and quantify the more subjective facets of sensory return with an objective, evidence-based methodology.

While some sensation has been shown to return to the breast after reconstruction, the amount and quality is extremely variable between patients and therefore unpredictable.<sup>5</sup> Further, stress on breast sensation has led surgeons to develop new reinnervation techniques, signaling a shift in the goals of reconstructive breast surgery from largely aesthetic, to functional. New neurotization techniques have shown some improvement in breast sensation; however, there is still a long way to go and no current consensus regarding an evidence-based best method.

This systematic review aims to evaluate the literature surrounding the current state of breast reconstruction reinnervation in women over the last 20 years and gauge the efficacy of nerve coaptation during breast reconstruction in creating worthwhile clinical benefits in both objective and subjective dimensions of sensation.

## METHODS

### Review of Literature

A Prospero registered systematic review was conducted. Databases including PubMed, SCOPUS, and ScienceDirect were screened using search terms “inner-ner-ation,” “breast reconstruction,” and “neurotization.” We included primary research involving human subjects published within the last 30 years that addressed the question in this review. The screening process can be seen in Figure 1.

Using these included studies, data were extrapolated into tables. Multiple parameters were analyzed, including various modalities of sensory testing, methods of neurotization, type of breast reconstruction, and other important secondary factors.

### Included Articles

Our included articles have been broken down into reconstruction methods and further investigated by the outcome measures they included. Below are tables that outline the methods in each article. Supplemental Digital Content 1 includes methods from DIEP reconstruction articles.<sup>3,5-10</sup> (See table 1, Supplemental Digital Content 1, which displays DIEP article methods. <http://links.lww.com/PRSGO/C172>.) Supplemental Digital Content 2 includes TRAM reconstruction studies.<sup>11-19</sup> (See table 2, Supplemental Digital Content 2, which displays TRAM

## Takeaways

**Question:** Are nerve repair techniques during breast reconstruction able to meaningfully improve postoperative sensory return?

**Findings:** Based on the 23 articles included in this systematic review, we have found that nerve coaptation yields promising results so far, but there is no definitive conclusion on its efficacy, in part because of substantial heterogeneity of methods and procedures.

**Meaning:** Nerve repair during breast reconstruction is a promising avenue for addressing sensory deficits and improving long-term satisfaction and quality of life following mastectomy, but further investigation with standardized methodology is needed.

article methods. <http://links.lww.com/PRSGO/C173>.) Supplemental Digital Content 3 is implant-based articles (See table 3, Supplemental Digital Content 3, which displays implant-based article methods. <http://links.lww.com/PRSGO/C174>)<sup>20,21</sup> and Supplemental Digital Content 4 is other included studies.<sup>22-26</sup> (See table 4, Supplemental Digital Content 4, which displays other article methods. <http://links.lww.com/PRSGO/C175>.)

## RESULTS

Twenty-three studies were found that met parameters for inclusion into this review. Of the studies included, seven looked primarily at DIEP flaps,<sup>3,5-10</sup> nine looked primarily at TRAM flaps,<sup>11-19</sup> two studies were novel implant-based studies,<sup>20,21</sup> and the remaining five studies dealt with other reconstructive modalities, including some where a technique was not specified.<sup>22-26</sup>

### DIEP Studies

The seven studies identified throughout the literature that looked specifically at DIEP flaps included a total of 263 innervated DIEP flaps and 218 non-innervated flaps across 361 patients. The most common modality of sensory testing was Semmes-Weinstein monofilament (SWMF) testing to assess perception of static touch. Additionally, two studies included pressure perception via a device other than SWMF,<sup>9,10</sup> and only one tested temperature sensation.<sup>5</sup> Average age for patients included in DIEP studies was 42.7 years. The findings of each study are summarized in Supplemental Digital Content 5. (See table 5, Supplemental Digital Content 5, which displays DIEP article results. <http://links.lww.com/PRSGO/C176>.) Six out of seven studies had favorable conclusions regarding the utility of nerve coaptation,<sup>3,5-8,10</sup> while one found inconclusive results.<sup>9</sup> Three out of seven studies<sup>3,5,9</sup> assessed subjective, patient-reported outcomes. Magarakis et al found no significant differences between groups, with most patients denying the return of erogenous sensation. Blondeel et al found that there was high patient satisfaction in all patient groups, but that 30% of patients in the innervated DIEP group reported a return of erogenous sensation, compared with 8% for non-innervated DIEP and 4% with

non-innervated TRAM. Cornelissen et al found an appreciable, but statistically insignificant trend toward higher scores on BREAST-Q physical well-being of chest domain with innervation.

**TRAM Studies**

Nine studies were identified that looked specifically at innervation during TRAM reconstruction.<sup>11-19</sup> Among these studies, there were 172 innervated TRAM flaps and 91 non-innervated TRAM flaps across a combined total of 251 patients. The most common modality for sensory testing was again SWMF. Several included studies also tested pressure, temperature, and pain sensation as well. Average age of included patients was 51.4 years. The detailed results of the TRAM-specific studies are included in Supplemental Digital Content 2. (See table 2, Supplemental Digital Content 2, <http://links.lww.com/PRSGO/C173>.) Overall, seven studies concluded that neurotization was a worthwhile addition to breast

reconstruction,<sup>11-17</sup> whereas the other two deemed their results inconclusive.<sup>18,19</sup> Five studies assessed subjective, patient-reported outcomes, with two reporting that no patients achieved a return of sexual sensation.<sup>14,17</sup> Puonti et al found no significant differences between groups, with high satisfaction in all patients. Slezak et al also found no significant differences and found that all patients reported some sensation in their reconstructed breast even if there was no objectively measurable sensation. Finally, Temple et al assessed patient-reported outcomes via several questionnaires, which are summarized in Supplemental Digital Content 6. (See table 6, Supplemental Digital Content 6, which displays TRAM article results. <http://links.lww.com/PRSGO/C177>.)

**Implant-based Studies**

Two studies were identified that investigated a relatively novel concept of using nerve preservation during mastectomy and allografting to specifically innervate

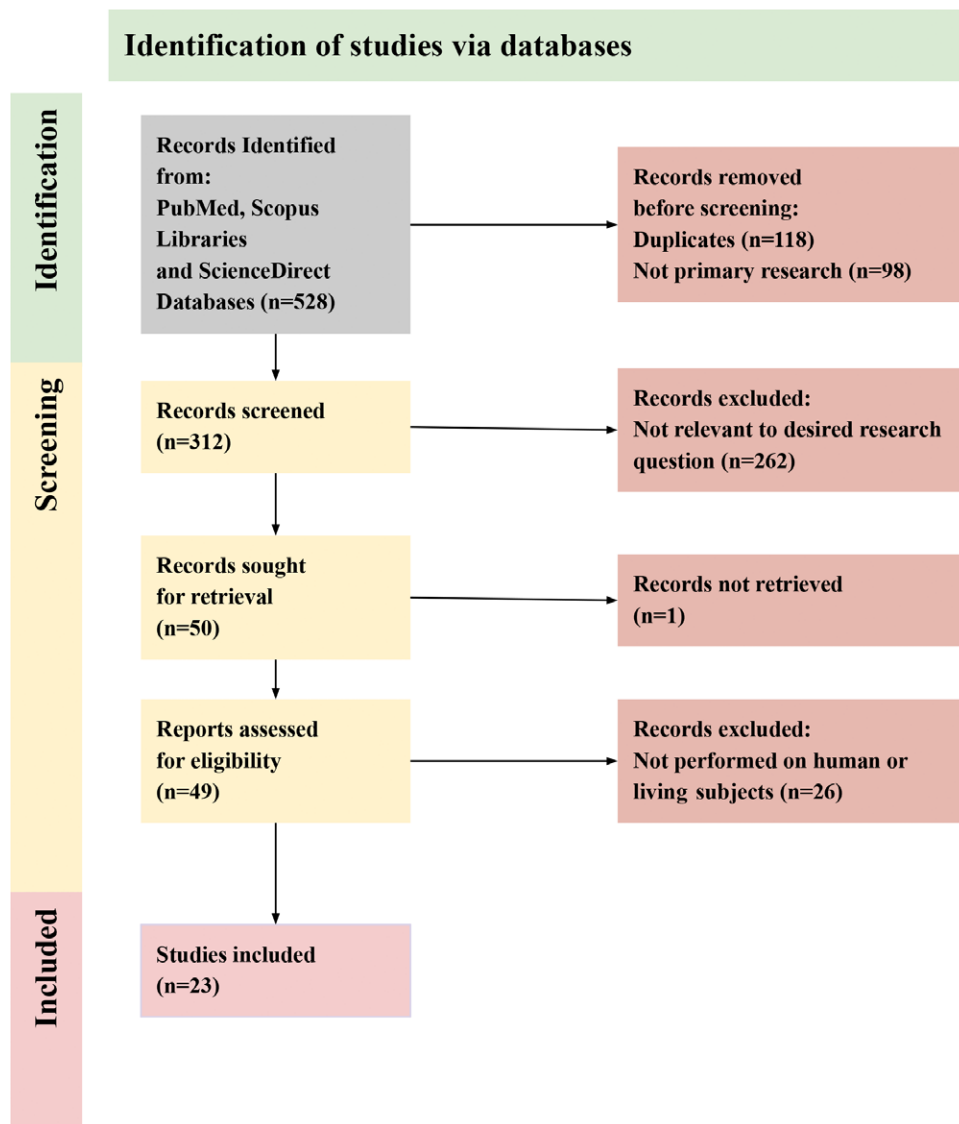


Figure 1. PRISMA diagram.

the nipple-areola complex (NAC) during implant-based reconstruction.<sup>20,21</sup> These studies included 46 reconstructed breasts between 24 total patients. Average age of included patients was 38 years. Their results are summarized in Supplemental Digital Content 7. (See table 7, Supplemental Digital Content 7, which displays implant-based article results. <http://links.lww.com/PRSGO/C178>.)

Although these are both pilot studies that serve primarily to introduce the concept, they achieved good sensory recovery results that may serve a particularly strong role in the psychosocial dimension, as the NAC is particularly important for erogenous sensation and sexual feeling in the breast.<sup>5</sup> Peled et al surveyed patients and found that all had strong satisfaction with their sensory recovery, and 67% of patients reported similar NAC preoperative and postoperative sensation, although the authors did not survey the return of erogenous sensation specifically.

### Other Studies

We included an additional five studies that included other reconstructive modalities and techniques.<sup>22–26</sup> Some studies included the gold standard abdominal based flaps in addition to others such as the lateral thigh perforator flap, latissimus dorsi flap, and gracilis flap, the details of which are elaborated in the Methods. In other studies, no exact technique was specified. Average age of included patients was 46.3 years. The results of these studies that investigated outcomes following a miscellanea of different modalities are summarized in Supplemental Digital Content 8. (See table 8, Supplemental Digital Content 8, which displays other article results. <http://links.lww.com/PRSGO/C179>.) All studies but one<sup>26</sup> found nerve coaptation to be useful for sensory recovery. Only Sinis et al assessed patient-reported outcomes and found no benefit with nerve coaptation.

## DISCUSSION

Despite evidence of benefits, some hesitancy exists surrounding neurotization due to increased risk of postoperative complications and longer operating time; however, one included study showed that when patient comorbidities and operative characteristics are adjusted for, neurotization did not significantly impact their 30-day complication rates.<sup>27</sup> Additionally, the vast majority of included studies reported an increase in surgical time no greater than 30 minutes with nerve coaptation. Thus, these concerns have largely been addressed.

Breast reconstruction post mastectomy has been shown to increase the quality of life in women for many years.<sup>3,28</sup> While this has made great strides in plastic surgery, what it lacks is ability to provide a sensitized breast. Sensation in the newly formed breast is important for many reasons including protective tactile sense and avoidance of noxious stimuli, emotional weight of “feeling like one’s breast is not their own” as well as effects on body image and for sensual connectedness to one’s partner. There are multiple methods for breast

reconstruction, including free tissue flaps with deep inferior epigastric perforator flaps (DIEP) and TRAM being popular and also implant-based reconstructions. On top of this, there are various techniques for nerve coaptation perioperatively.

Sensation to the natural breast is typically supplied anteriorly by the anterior cutaneous branches of the first through sixth intercostal nerves and laterally by the lateral cutaneous branches of the second through sixth intercostal nerves as well as superior sensation from the supraclavicular nerve.<sup>6</sup> For DIEP flaps, included studies showed use of the anterior cutaneous branch of the second, third, or fourth intercostal nerve as the recipient nerve and the tenth through twelfth intercostal nerves as the donor nerves from the flap under a microsurgical microscope with epineural stitches.<sup>3</sup> The anterior cutaneous branches are frequently used because mastectomies tend to cause damage to the lateral branches. Furthermore, the fourth intercostal nerve is most commonly used due to its original function in giving sensation to the nipple-areola complex, an important area for re-sensitization.<sup>6</sup> The best nerve for coaptation is generally decided based on its vicinity to the perforator vessels and its ability to create a tensionless connection while also considering equal diameters of both recipient and donor nerves.<sup>7</sup>

The effects of perioperative radio/chemotherapy on the return of breast sensation indicate that these treatments likely do not have a significant effect on the return of sensation following mastectomy and reconstruction. Several studies assessing various proposed factors affecting sensory recovery have shown that on univariate and multivariate analysis, previous radiation and chemotherapy is not significantly associated with post-reconstruction sensation.<sup>6,29,30</sup> This is somewhat perplexing, given the findings of Magarakis et al, which found that, in the non-irradiated group, skin overlying implants had better sensation compared with DIEP flap skin, whereas DIEP flap skin had better sensation in the irradiated group. Additionally, innervated DIEP flaps had better sensation than non-innervated flaps for non-irradiated breasts, but neurotized breasts actually had poorer sensation than non-neurotized breasts when looking at previously irradiated breasts. The authors noted, however, that they did not have a large enough sample size to independently evaluate the effects of neurotization on sensory return. While the current literature suggests that sensory return is within reach regardless of chemo or radiotherapy status, the body of work on this subject is thin, and more studies must be conducted to evaluate the interplay between these therapies, as well as other potentially neuropathic processes such as diabetes, and sensory return in reconstructed breasts, especially in the setting of operative nerve coaptation.

When considering the value and impacts of innervation, we must first consider whether or not there is “demand” for a sensate breast to begin with. While some authors point out issues with loss of protective sensation in the reconstructed breast,<sup>31</sup> others report that they

actually receive more patient complaints due to sensory issues in the donor abdominal region.<sup>26</sup> Furthermore, despite authors such as Cornelissen et al asserting the importance of sensation for satisfaction in the reconstructed breast, there is already strong patient satisfaction with insensate DIEP flaps<sup>32</sup> and considerable potential for spontaneous reinnervation<sup>33</sup> reported throughout the literature.

The conflicting information in the literature regarding both the demand for sensate breast flaps and the outcomes following innervated breast reconstruction points to a fundamental limitation. It must be recognized that the heterogeneity of the methods used throughout the included studies makes it difficult to directly compare them in any sort of meaningful, empirical way. Despite the fact that most studies conducted had favorable conclusions regarding neurotization in breast reconstruction, there was a lack of consistency in the outcomes being measured, the tools used to measure said outcomes, and the techniques used for both breast reconstruction and nerve coaptation. This variety ultimately precludes a meta-analysis of the data. Additionally, the small sample size and retrospective nature of many of the included studies call their generalizability into question. Despite these limitations, we feel that the favorable results of neurotization in most of the included studies indicate that this addition to breast reconstruction is worth further trial and investigation. However, future investigations must develop and adopt a standardized methodology, including the reconstruction modality, neurotization technique, sensory assessment, and validated psychosocial outcomes tool used. Furthermore, more prospective, multi-center studies with sufficient sample size and power are necessary. Without these adjustments, the data will continue to have the aforementioned limitations and our understanding of the true value of nerve coaptation will be lacking.

### LIMITATIONS

This review was limited mainly by the wide array of methods used throughout the available literature. These discrepancies made a meta-analysis not attainable for this work.

In analysis of the included studies, the GRADE tool was implemented to assess the quality of evidence in each study.<sup>34</sup> In Figure 2, the number of articles that fit into each GRADE category can be seen.

While the average GRADE rating was between low and moderate, this is mostly due to the nature of the research not allowing itself very well to be included in randomized trials. However, the large number of included studies and patients per study leads to a higher evidence-based conclusion. As with all research, there are also important biases to consider. With decreased ability to randomize and blind data pertaining to breast reconstruction, some studies are open to response bias of women knowing they had reinnervated versus non-reinnervated breasts. Another vulnerability of this data lies in measurement bias as the wide array of outcome measures become difficult to compare.

### CONCLUSIONS

The results of this review show promising improvements in clinical and psychosocial outcomes in neurotized breasts compared to insensate breasts. Ultimately, direct synthesis of each of the included studies' results would represent an "apples to oranges" comparison, given the variability between studies. The heterogeneity of studies in the literature indicates that more multi-center studies with standardized methodology, including the BREAST-Q, sensory testing, time to follow-up, and complication analysis, are needed to adequately demonstrate the value of neurotization in breast reconstruction and determine if this is the path to better long-term outcomes following mastectomy and reconstruction.

GRADE Ratings of Included Studies

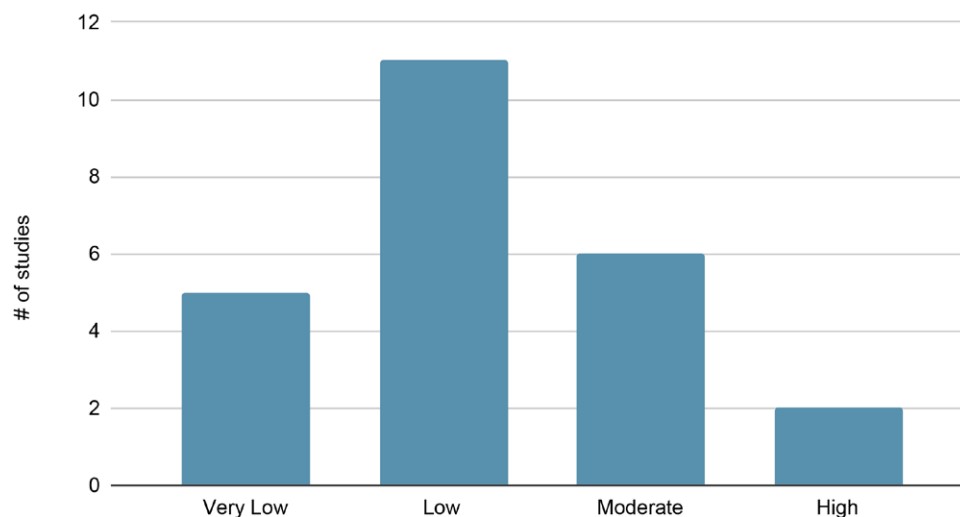


Figure 2. GRADE scale.

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