

# Improving Quality of Life After Breast Cancer: Can Surgeons Do Better?

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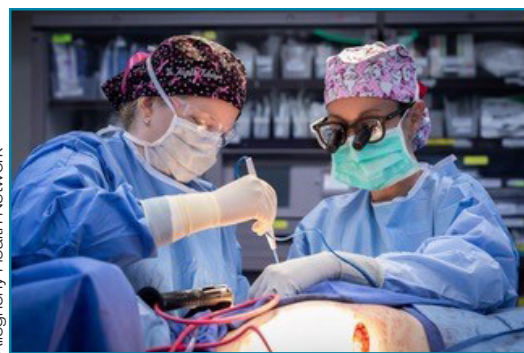
**B**reast cancer is a complex disease that can affect all aspects of a woman's life. When receiving a diagnosis of breast cancer, there is much to take in—fears and concerns to overcome, treatment options to decide, and outcomes to consider (*Breast Care, Treatment and Reconstruction QMP*: Saint Louis-Missouri, 2011). Fortunately, with advancements and innovations in breast cancer treatment, patients are recovering well and living longer. Nevertheless, now they face new challenges triggered by the long-term effects of the cancer treatment in their quality of life (*Breast Sensations Research Report* Inspired Health, October 2020; *Breast Cancer* 2018; doi: 10.1007/s12282-018-0862-8).

After a mastectomy, one of the undesirable consequences experienced by women is the loss of sensation to the breast skin and nipple. Lack of sensation of the reconstructed breast may be a minor problem for some patients, but a fundamental one for others, leading to a negative impact on their lives (*J Plast Reconstr Aesthet Surg* 2021; doi: 10.1016/j.bjps.2020.11.021).

## Explaining Post-Mastectomy Numbness

When a mastectomy is performed and breast tissue is removed, nerves that provide sensation to the breast and the overlying skin are removed as well. Once cut, nerves are unable to carry signals back and forth leaving a woman's chest anywhere from partially to completely numb.

This loss can be devastating in unexpected ways and can impact quality of life, intimacy, and body image (*Breast Sensations Research Report* Inspired Health, October 2020; *J Plast Reconstr Aesthet Surg* 2021; doi: 10.1016/j.bjps.2020.11.021). Sensation loss can lead to diminished sexual arousal, negatively impact self-esteem, and potentially



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lead to physical harm or injury. Women may be unable to feel changes in temperature, increasing their risk for accidental burns due to sun exposure, flat irons and curling irons, or kitchen accidents (*Aesthet*

*Surg J* 2021;41(7):NP773-NP779). Some women mention the sadness of realizing they can't feel their partner or their children's hugs and kisses, or a head on their chest because of the loss of sensory awareness.

Studies have shown that only 30–60 percent of women spontaneously recover some sensation after a mastectomy. However, this happens randomly, and many women do not recover sensation at all (*J Plast Reconstr Aesthet Surg* 2021; doi: 10.1016/j.bjps.2020.11.021).

## Understanding Choices for Reconstruction

Breast reconstruction is the act of rebuilding a breast after a full or partial mastectomy. This can be confusing, however, as it is not recreating the same breasts or the physical purpose of the breast (such as milk-producing tissue) again. Instead, it is an aesthetic procedure that many women choose to recreate the look of the breast (*Breast Care, Treatment and Reconstruction QMP*: Saint Louis-Missouri, 2011).

The decision to consider breast reconstruction after mastectomy is fully personal. Women might seek reconstruction to improve their



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sense of femininity, self-confidence, and sexual attractiveness. Other women might choose breast reconstruction as a means to restore their body image and feel more whole after the cancer experience (*Breast Care, Treatment and Reconstruction QMP*: Saint Louis-Missouri, 2011; *J Plast Reconstr Aesthet Surg* 2021; doi: 10.1016/j.bjps.2020.11.021; *Breast Cancer Res Treat* 2018; <https://doi.org/10.1007/s10549-017-4547-3>).

As medical professionals, it is our responsibility to make sure every breast cancer patient understands her options, so she can make informed decisions to help support long-term quality of life. Unfortunately, sensation loss after mastectomy is common, but isn't consistently discussed between a woman and her care team. Physicians are generally taught that loss of sensation after a mastectomy is a given, and that there is very little they can do to improve it. Literature on sensory recovery is also variable, so physicians avoid presenting the subject to their patients.

## Advancements in Neurotization

As we continue to push breast reconstructive surgery forward, patient expectations have also evolved. They are looking for more than the creation of a breast mound and seeking the restoration of breast functionality. The nipple-areolar complex is the signature element of the breast and its preservation is associated with superior psychological outcomes in breast reconstruction. Nipple sparing mastectomy has been widely adopted for immediate breast reconstruction patients due to better aesthetic results without significantly affecting local recurrence or survival rates relative to skin sparing or conventional mastectomy (*Breast Cancer* 2018; doi: 10.1007/s12282-018-0862-8).

The question we should try to answer is: Does your reconstructed breast feel like your own? It is questionable whether this goal can be achieved by the reconstruction of a mound of soft tissue alone. Although aesthetically pleasing, active effort is required to restore sensation to the breast (*J Plast Reconstr Aesthet Surg* 2021; doi: 10.1016/j.bjps.2020.11.021). Thanks to advancements in breast neurotization (reconnecting nerves cut during a mastectomy), we can now help our patients look and feel more like themselves again (*Breast Sensations Research Report* Inspired Health, October 2020).

We work together as a team, each involved in the surgical treatment of our patients. During the reconstruction, we perform Resensation, a surgical technique that uses a nerve allograft to reconnect nerves cut during a mastectomy (*Breast J* 2019; doi: 10.1111/tbj.13420). Over time, the allograft guides regrowth of nerve fibers and can lead to restored sensation to the breast tissue.

When discussing this technique with our patients, we explain to them that we are still learning and evaluating outcomes of the procedure. However, we know that we are on the right path and that restoring breast sensation can be impactful.

In a recent study, women reported that regaining breast sensation helped them recover and move on from their experience with

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manually determine the frequency and timing of cardiovascular disease (CVD) event-related post-marketing warnings in anticancer drugs and biologics awarded new drug applications by the FDA between 1998 and 2018.

CVD events associated with cancer therapies can include heart failure, hypertension, coronary disease, myocardial infarction, stroke, thromboembolic disease, arrhythmia or abnormal electrocardiographic changes, and sudden cardiac death. Communications included withdrawals, black box warnings, drug warnings, and precautions.

The team assessed characteristics related to approval, including drug class, therapeutic area, orphan drug status, priority review status, accelerated approval status, regulatory review times, near-regulatory deadline approval status, and the presence or absence of preceding early-phase trial reports of cardiotoxic effects. Moreover, the researchers evaluated drug characteristics associated with the need for and timing of safety communications with multivariable stepwise backward-selection logistic regression.

Although more than 25 percent of contemporary FDA-approved cancer therapies required CVD warnings, post-marketing issuance of the warnings trailed clinical approval and other safety communications almost 5 years.

The researchers identified 125 therapies that were approved over the evaluated period, among which 82 were biologics, targeted, or immune-based therapies. They also noted 411 postmarketing safety communications were issued, including 33 black box warnings, 7 withdrawals, 24 dose-adjustment warnings, and 347 general warnings or precautions.

According to the findings, although more than 25 percent of contemporary FDA-approved cancer therapies required CVD warnings, post-marketing issuance of the cardiotoxicity warnings trailed clinical approval and other safety communications almost 5 years after a drug's approval—40 percent longer than it took to issue non-cardiac warnings.

Overall, CVD was the most common reason for any black box warning (37.2%), with sudden death triggering 11.6 percent of black box warnings. Immune-based or targeted therapies, and those within classes with prior reported cardiotoxic events, were significantly more likely to have black box warnings (odds ratio, 1.99;  $P=.047$ ). Moreover, 24 therapies (21.6%) had multiple cardiovascular toxic effects warnings. Myocarditis was associated with only two therapies. After arrhythmias (23.5%), uncontrolled hypertension (12%), heart failure (11.4%), and sudden death (3.2%) were the most common reasons for CVD warnings. Thirty-two cancer therapies (25.6%) had postmarketing cardiac safety communications, including seven (33.3%) with new black box warnings.

Addison and colleagues also noted that CVD-related warnings took longer to be issued (median, 1,670 days) compared with the issuance of non-cardiac warnings (median, 1,120 days;  $P=.03$ ). The authors also discovered the average time to FDA warning issuance by CVD type varied greatly by event type. FDA warning issuance regarding heart failure or hypertension, for example, appeared approximately 1,200 days after a drug approval. However, it took approximately 2,200 days for warnings regarding arrhythmias to be issued.

Daniel Addison, MD, Assistant Professor of Medicine and Director of the Cardio-Oncology program at The Ohio State University Comprehensive Cancer Center, provided additional thoughts on cardiotoxic risk communications for patients with cancer.

**Oncology Times:** *What do the findings of this study mean for cancer patients?*

**Addison:** “Our findings suggest that patients should be aware of the long-term risk of heart disease with modern, initially lifesaving, cancer therapies.”

**Oncology Times:** *What are the current guidelines to help assist practitioners who have cancer patients with, or at risk, of cardiotoxicity?*

**Addison:** “Current guidelines vary but have increasingly been released by the American Heart Association, American College of Cardiology, International Cardio-Oncology Society, and American Society of Clinical Oncology societies, depending on the type of heart disease manifestations. Generally, providers should have a low threshold to consider the potential risk of heart issues for patients treated with cancer therapies. Providers may use tests such as echocardiography and cardiac MRI to help identify changes and impending toxicity earlier. If there is any significant concern, an early threshold to refer the patient to cardio-oncology or cardiologist is advised.”

**Oncology Times:** *Why has there been this significant lag in cardiotoxicity warnings compared to other types of warnings issued by the FDA for cancer therapies?*

**Addison:** “Often there is historic focus on life-saving cancer control and lab-based toxicities. Unfortunately, cardiotoxicity is often not clear until the drugs are tested in patients. There is also a tendency to consider any heart issues as due to ‘traditional cardiovascular risk factors alone.’ This leads to delay in recognition of the potential that a cancer drug may actually be affecting the heart and contributing to the heart events.”

**Oncology Times:** *In your opinion, what are possible strategies to enhance post-marketing regulation?*

**Addison:** “Including more incorporation of review of reporting rates and threshold in real-world reporting registries would improve capture. Additionally, increased emphasis on dose-range toxicity analysis would improve capture and recognition.” **OT**

*Dibash Kumar Das is a contributing writer.*

- believe that restoring breast sensation should become standard of care for breast reconstruction.

## Moving Forward

Now that this type of groundbreaking technology is widely available, we believe that sensation loss after mastectomy needs to be discussed much earlier in the patient pathway. As surgeons, we must do more to educate women about why mastectomy can lead to chest numbness and inform them about the technology available that may restore sensation during reconstruction.

With advanced neurotization techniques paving the way, we have even more options available for helping to restore some normalcy for our patients. The opportunity to not face the rest of their life with an unexpectedly numb chest is a huge step in the right direction. By communicating openly about this issue from the start, we can help patients look—and feel—like themselves again. **OT**

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cancer, the mastectomy, and the reconstruction process (*Breast Care, Treatment and Reconstruction* QMP: Saint Louis-Missouri, 2011). They also stated that regaining sensation helped them feel more normal and more like their old selves. In fact, 97 percent of women interviewed for this study who underwent the procedure:

- would recommend that a friend or family member explore neurotization options;
- noted potential rewards in terms of physical and emotional impact and quality of life outweighed potential risk of the procedure not being successful; and