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Advances and current concepts in reconstructive surgery for breast cancer ☆

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ABSTRACT

In this article, we report on recent advancements in reconstructive care of the breast cancer patient. New developments in sensate breast reconstruction to help address the problem of numbness after mastectomy have emerged and show promise. Methods to restore lymphatic physiologic flow after axillary lymphadenectomy using supermicrosurgical techniques have begun to show benefit by reducing the short-term incidence of breast cancer related lymphedema (BRCL). Breast implant safety has received significant recent attention and we explore the emergence of BIA-ALCL (Breast Implant Associated Anaplastic Large Cell Lymphoma) and its implications for the breast cancer patient and their multidisciplinary care team.

Introduction

Reconstructive care of the breast cancer patient has emphasized restoring breast form following mastectomy, and significant success has been achieved in this regard through refinement in technique and enhanced collaboration with breast surgery teams. Recent advancements in reconstruction, however, are increasingly focused on preservation and restoration of function after cancer extirpation. Mastectomy can produce long term disability and affect quality of life by causing chest wall numbness. Axillary dissection increases the risk of lymphedema development. New techniques in nerve and lymphatic reconstruction have been developed to restore anatomy and physiologic function at the time of cancer excision. Recently, increased attention has been directed to breast implant safety. In this review, we also discuss the emergence of Breast Implant Associated Anaplastic Large Cell Lymphoma (BIA-ALCL) and its current implications for breast cancer patients and their providers.

Restoring sensation after mastectomy

A 2017 New York Times article, "After Mastectomies, an Unexpected Blow: Numb New Breasts," [1] highlighted the impact of hypoesthesia after mastectomy. In many ways this served as call to action within the breast surgery community to enhance preoperative education about postoperative numbness, and further, reignited interest in finding functional solutions.

Intercostal nerve branch transection during mastectomy results in breast skin and chest wall numbness. Neurotization of the reconstructed breast is a technique which reconstitutes the nerve gap resulting from this surgical injury. Coapting a cutaneous nerve(s) from an autologous tissue flap (DIEP/TRAM, etc.) divided during harvest to a transected chest wall cutaneous intercostal nerve branch has been shown to increase sensitivity in the reconstructed breast over time through targeted reinnervation (Fig. 1).[2] This, however, requires additional dissection and disruption of normal anatomy in order to gain sufficient length to approximate the nerve ends. The introduction of decellularized nerve allograft technology has allowed for the development of more efficient and less destructive new techniques for reinnervating the autologous breast reconstruction.[2,3] Novel means of restoring sensation to the nipple areolar complex by employing nerve grafting techniques during implant-based approaches also show promise (Fig. 2).[4,5]

☆ No prior or upcoming presentation of abstracts at meetings regarding this research.

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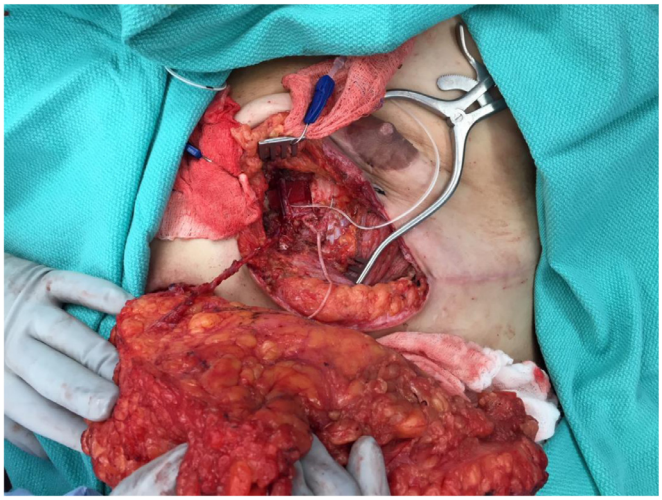

Fig. 1. Intraoperative photograph of a patient undergoing delayed autologous breast reconstruction with deep inferior epigastric artery perforator (DIEP) flaps; note the preservation of a medial cutaneous nerve branch with subsequent coaptation using decellularized nerve allograft to an intercostal nerve branch for sensory restoration.

As more patients inquire about restoring sensation after mastectomy, surgeons will have to align patient goals pertaining to breast form with functional expectations based on reconstructive technique. Through shared decision making, plastic surgeons should help guide selection of reconstructive modality while considering technical aspects associated with reconstructive success for a wide variety of donor sites.[6,7] To date, the majority of studies in sensate breast reconstruction have utilized the 3rd to 7th anterior or lateral cutaneous branches of the intercostal nerves as the breast donor nerve.[8,9] The lateral cutaneous intercostal nerve branch has not been utilized as frequently in recent literature, perhaps due to difficulty locating the nerve. Thus, the anterior cutaneous intercostal nerve is more commonly utilized, as this nerve is easily identified in the microsurgical field when preparing internal mammary recipient vessels and does not require additional dissection. The fourth intercostal nerve is primarily responsible for supplying sensation to the nipple areolar complex and central breast. Our group recently published a cadaveric study characterizing the location of the lateral intercostal nerve at the lateral 4th intercostal space to allow for ease of dissection.[10] When utilizing the lateral intercostal nerve for sensory reinnervation of tissue flap reconstruction, long lengths of the donor flap sensory nerve are required for direct coaptation, and surgical exposure at the chest wall can be challenging. Identification and length preservation of the lateral 4th intercostal nerve at the time of mastectomy allows for ease of coaptation can be achieved through collaborative breast and plastic surgical planning. The recent use of allograft nerve conduits as interposition grafts have greatly facilitated breast reinnervation from both anterior and lateral intercostal nerve branches. Early results are encouraging,[3] however, long term follow-up is required to assess the functional impact and effect on pateints' health-related quality of life.

Immediate lymphatic reconstruction

While there has been a trend to reduce axillary surgery in the breast cancer patient, axillary lymph node dissection (ALND) remains a critical component in the management of selected patients. Despite advances in the diagnosis and treatment of breast cancer, there have been very few modifications in the surgical approach for ALND since its original description by Halsted.[11] Lymphedema is a well-recognized complication following lymphadenectomy that is associated with both acute and chronic disability.[12,13] Multiple risk factors exist for development of breast cancer related lymphedema (BRCL), major contributors among them include the number of nodes removed and radiation therapy to the nodal basin.[14] While BRCL is generally thought to occur in approximately thirty percent of breast cancer patients, a recent meta-analysis of patients who underwent ALND for breast cancer demonstrated a variable rate of lymphedema ranging from 7% to 77%.[15] Prevention strategies, when implemented, have focused on education, early detection, compression and physiotherapy. Surgical strategies have emerged to reestablish physiologic lymphatic flow after axillary surgery.[16–24]

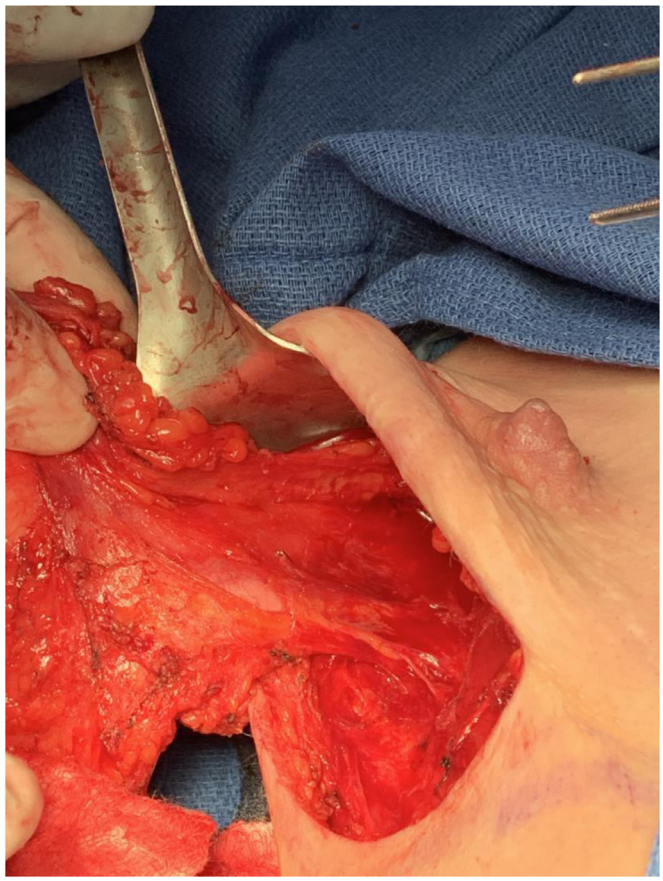

Fig. 2. Intraoperative photograph at the time of nipple-sparing mastectomy, demonstrating identification and preservation of an intercostal cutaneous nerve branch for eventual nerve coaptation and sensory restoration following implant-based breast reconstruction.

Lymphaticovenous bypass (LVB) has been shown to be viable treatment option to treat or prevent lymphedema. A recent meta-analysis identified 22 studies that reported on outcomes using therapeutic LVB. Pooled results demonstrated that 89% of patients reported a subjective improvement, 88% experienced a quantitative improvement, and 56% of patients were able to discontinue compression therapy.[25] The success of LVB is largely dependent on the ability of the surgeon to identify functional lymphatic channels that may decrease in caliber and visibility as the disease becomes more chronic.[26] LVB can also be performed at the time of mastectomy to prevent the development of lymphedema. This approach is termed immediate lymphatic reconstruction (a.k.a. LYMPHA), and can be aided with axillary reverse mapping (ARM) at the time of ALND to allow for identification and sparing of lymphatic vessels that drain the arm.[15,16]

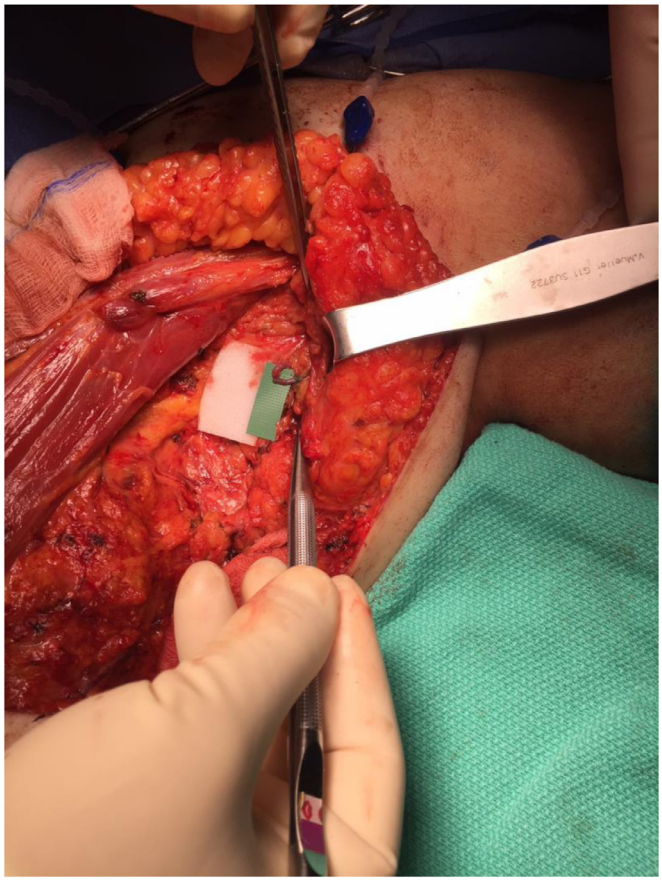

Fig. 3. Intraoperative photograph of a patient that elected to undergo immediate lymphatic reconstruction with axillary lymphaticovenous bypass (LVB) for lymphedema prevention at the time of mastectomy; note the single anastomosis demonstrated at the end of the micro forceps.

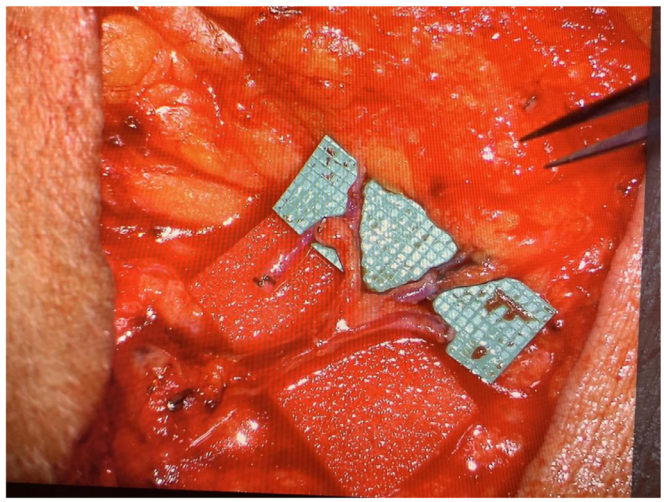

Fig. 4. Intraoperative photograph of another patient who elected to undergo lymphaticovenous bypass (LVB) surgery at the time of mastectomy for lymphedema prevention. Note that this photograph was obtained via the microscope, to demonstrate the surgeon's perspective, and depicts multiple anastomoses. For reference, 1 square on the green background equals 1mm.

To perform ARM and LVB at time of mastectomy, collaboration between the breast and reconstructive surgeon is required. Initially a dye tracer is in injected into the upper inner arm and ALND is performed using loupe magnification and minimal cautery dissection. Blue stained lymph nodes outside the axillary resection borders are preserved and unassociated lymphatic channels are left in-continuity. Veins and small tributaries are carefully preserved. After ALND, the lymphatic architecture is assessed. Transected, blue dye containing lymphatics are mobilized and target veins are identified and assessed for size match, proximity to lymphatic structures, excursion, and valvular competency. One or more lymphatic vessel to venous anastomoses are performed using supermicrosurgical technique (Figs. 3 & 4). If blue dye is visualized traversing the lymphaticovenous anastomosis, the connection is deemed patent. Indocyanine green dye lymphangiography of the upper extremity and axilla performed with a near infrared camera allows further confirmation of patency. Short term results are promising and demonstrate lymphedema rates similar to those associated with sentinel lymph node biopsy.[16–19] Additional follow-up is required to elucidate long-term efficacy and effects of axillary radiotherapy on the microsurgical bypass.

Breast implant associated - anaplastic large cell lymphoma

BIA-ALCL represents a subtype of non-Hodgkin's T-cell lymphoma that originates not within the breast parenchyma, but instead, within the fibrous periprosthetic capsule surrounding the implant itself.[27] Since the first report in 1997, 888 cases have been reported across the globe as of February 2020, including 33 deaths.[28,29] Patients may initially present with late-onset (approximately 2-8 years), asymmetric swelling consistent with seroma accumulation (Fig. 5).[30,31] Locally invasive disease has also been reported, and although patients may complain of pain, systemic symptoms such as fever, weight loss, and night sweats seem less common.[32] Given that over 1.8 million procedures involving breast implants were performed worldwide in 2018, and the millions of women already living with breast implants, BIA-ALCL represents an important consideration for plastic surgeons and patients when deciding upon the approach to reconstruction.[33] Although BIA-ALCL represents a growing concern amongst patients considering mastectomy with implant-based reconstruction, or presenting to the clinic after reconstruction, the precise pathophysiology remains to be definitively elucidated. Interestingly, no current, well-documented case exists in patients who have undergone implantation with smooth surface devices [29,34,35] and by contrast, the literature overwhelmingly demonstrates a relationship with textured devices.[36] Initial reports favored an etiology involving bacterial contamination of the implant with potential biofim formation in genetically susceptible patients,[34,35] however, recent theories implicate an exaggerated adaptive immune response to debris from the implant itself.[37] Theories and hypotheses aside, more information is urgently needed in order to arrive at a definitive, etiologic conclusion. In 2018, using data from a Dutch pathology database, the absolute lifetime risk amongst women with textured devices was estimated as 1/35,000 by age 50 to 1/7000 by age 75 (number needed to harm of over 6,920).[30] In the United States, by contrast, recent data now exists to support an overall risk as high as 1/355 amongst women with a history of textured devices following breast reconstruction.[38] Interestingly, post-mastectomy reconstruction has not demonstrated an increased risk versus aesthetic augmentation, nor has implant fill (silicone versus saline).

Diagnosis is confirmed following seroma aspiration or open biopsy, with immunohistochemistry and/or flow cytometry revealing CD30-positive and ALK-negative T lymphocytes, among other cell-surface proteins.[39,40] Following confirmation, staging proceeds with PET scanning. For now, expert opinion does not support routine screening for BIA-ALCL in asymptomatic women with breast implants or a history of breast implants regardless of surface texture. Standard periodic examination by a board-certified plastic

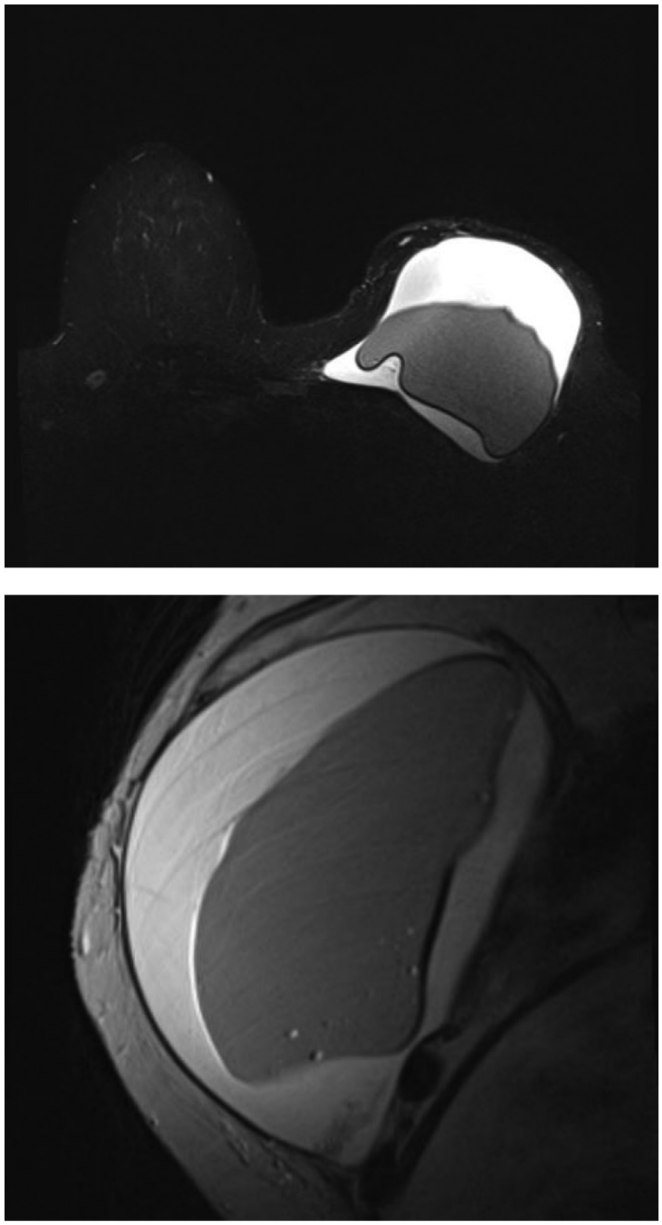

Fig. 5. Axial (superior) and sagittal (inferior) T2-weighted MRI images of the left breast, demonstrating a large peri-prosthetic seroma, in a middle-aged patient that originally underwent immediate breast reconstruction with sub-pectoral tissue expander placement and subsequent exchange to a textured, permanent silicone implant. At the time of device removal, approximately 7 years following her index operation, seroma fluid was sent for cytology and confirmed BIA-ALCL.

surgeon is recommended as is adherence to FDA imaging recommendations for surveillance of silicone filled implants. Treatment consists of complete surgical resection (e.g., implant removal with capsulectomy), which is often curative (Fig. 6).[39,41] In cases of advanced, incompletely excised, or recurrent BIA-ALCL, the current National Comprehensive Cancer Network guidelines recommend a multi-disciplinary approach involving adjuvant chemotherapy (CHOP, CHOEP, or EPOCH as first line treatment with consideration of Brentuximab Vedotin as second line treatment), and radiotherapy in instances of non-resectable disease or recurrence.[39] Long term outcomes are pending and the optimal approach requires further study.

Appropriately identifying and managing patients presenting with BIA-ALCL as a mass lesion remains crucial. Thirty three percent of patients may initially present in this fashion, and the mere presence of a mass corresponds with an aggressive clinical course requiring expanded treatment algorithms, and increased mortality.[42–47] Diagnosis requires a high degree of suspicion on the part of providers caring for patients with a breast implant. Prompt referral and coordination and amongst surgeons, breast radiologists and pathologists is critical for achieving rapid confirmation and instituting the appropriate treatment plan. Multiple aspiration attempts, in patients with persistent or late onset seromas, could impair the likelihood of pathologic confirmation of BIA-ALCL secondary to insufficient anaplastic cells within the aspirated fluid.[48] Consequently, we recommend that in patients presenting with late-onset seroma with clinical history or exam suspicious for BIA-ALCL, appropriate referral to a specialized center prior to invasive diagnostic testing remains paramount. This will continue to ensure collaboration, efficiency, accuracy, and availability of multidisciplinary experts. Furthermore, we now routinely discuss BIA-ALCL with all patients undergoing implant-based breast reconstruction or breast augmentation surgery. Breast oncologists, radiologists, primarily care providers and those involved in multidisciplinary breast cancer team survivorship efforts need to be increasingly aware of this entity and should have a low threshold to refer patients for plastic surgery evaluation.

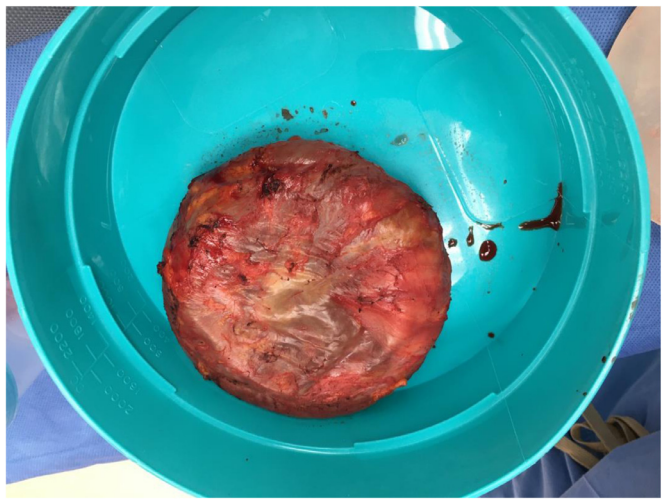

Fig. 6. Intraoperative photograph of a complete capsulectomy specimen, removed en bloc along with the intact breast implant, in a patient with concern for BIA-ALCL that elected to undergo removal.

Conclusion

Exciting advances in reconstructive care of the breast cancer patient focus on function, namely sensory restoration and preservation of lymphatic flow dynamics. Emerging techniques show promising early results and require long term follow-up. Interdisciplinary collaboration remains paramount throughout the breast cancer patient's continuum of care in order to maximize oncologic and surgical outcomes, ongoing patient safety and health related quality of life.

Declarations of Competing Interest

None.

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