Editorial Commentary

Nerve coaptation in deep inferior epigastric perforator (DIEP) flap breast reconstruction

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Breast cancer can be treated by different surgical techniques, including oncoplastic reduction mammoplasty, breast conserving surgery, and different types of mastectomies (1). Many women report the development of negative self-esteem and severe stress following these surgeries. Autologous reconstruction has shown to result in greater patient satisfaction and better quality of life compared to implant-based reconstruction, notably for respiratory functions (2-7).

The deep inferior epigastric perforator (DIEP) flap is the gold standard flap in autologous breast reconstruction (8). Along with the growing popularity of DIEP flap breast reconstruction, many studies have been performed to identify risk factors leading to worsened postoperative outcomes. Neither age nor body mass index (BMI) have been linked to worse outcomes in large meta-analysis, leading surgeons to broaden the range of patients eligible for this procedure (9,10).

The literature describes multiple recipient vessels, including the internal mammary artery, as well as vessels selected in the axilla, especially the circumflex scapular vessels, of which prospective evidence suggests increased safety and vessel size, as described by Santanelli *et al.* (11). As the flap is harvested, some cutaneous nerves innervating the skin paddle are sacrificed, which can result in impaired breast sensitivity. Not only does reduced sensibility affect the patient's quality of life, as thermoregulatory reflexes such as vasodilatation, sweating and other protective behaviours relying on skin sensibility, the reconstructed breast can be susceptible to substantial risk of thermal lesion, as was presented in the case series by Enajat *et al.*, where thermal injuries occurred in four patients between 2 and 18 months after reconstruction (12,13).

As microsurgical breast reconstruction techniques continue to advance, plastic surgeons are increasingly focused on methods that enhance both functional and psychosocial outcomes, including the restoration of breast sensation. In recent years, there has been a marked interest among patients and surgeons in the neurotization of breast flaps to attenuate the loss of sensation and numbness of the reconstructed breast, with many studies highlighting the benefits associated to such a reconstruction (14,15). Although many newer nerve repair techniques have been developed, end-to-end nerve coaptation is still considered the surgical gold standard (16-19). Efforts to improve sensation, with or without coaptation of free flaps has also been explored in lower limb reconstruction. Two studies from our group have shown that nerve coaptation in lower limb free flap reconstruction resulted in a partial and progressive sensory function recovery (20,21).

A recent meta-analysis by Shiah *et al.* demonstrated that the neurotization with direct nerve coaptation in

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breast reconstruction did not lead to significantly higher operative times, with reported operative times dedicated to the neurotization ranging from 8 to 38 minutes. However, the study highlighted several other challenges, including irretrievable recipient nerves, insufficient nerve lengths or inadequate flap orientation (19).

In a recent study by Bubberman *et al.*, the authors performed a double-blinded randomised controlled trial including 41 patients, corresponding to 29 innervated and 38 non-innervated reconstructed breasts. The surgeons coapted the flap donor nerve with the anterior cutaneous branch of the second or third intercostal nerve. Sensory testing was realised both preoperatively and postoperatively using Semmes-Weinstein monofilaments (SWM), Pressure Specified Sensory Device (PSSD), and a thermostimulator, for tactile and temperature thresholds. In this interim analysis, the authors noted that at 24 months follow-up, there was a significantly lower mean SWM evaluator size when testing innervated flaps compared to non-innervated flaps. Furthermore, touch threshold using PSSD was also significantly lower in the group in which nerve coaptation was performed, and heat pain was more often imperceptible in non-innervated flaps, albeit not significantly so. The authors also noted that there were no adverse events associated with sensory nerve coaptation (18).

Some elements from their study need to be addressed. While Bubberman *et al.* report that postoperative complications did not differ across groups, the authors disclose that 6 breast flaps were initially allocated to the innervated group and were crossed over to the non-innervated group for final analysis, because of sensory nerve coaptation failure, including one case where an initial nerve coaptation was performed but had to be sacrificed during surgical re-exploration. This is noteworthy, as 17.1% (6/35) attempts of nerve coaptation were unsuccessful, potentially tilting the complication rates reported in the innervated group, due to possibly additional dissection and longer operative times. Another element that limits the generalizability of Bubberman *et al.* results are differences in baseline characteristics in spite of the randomized nature of the study, including a higher average age and a higher proportion of patients having undergone radiation therapy in the non-innervated group, potentially biasing the comparison in complication rates. The type and timing of mastectomy performed, the distribution across groups, as well as the methods used for de-epithelization were not reported by the authors. These factors have been shown to affect nerve sprouting and would have been interesting aspects to investigate (22).

Moreover, in Bubberman *et al.*'s study, the subgroup analysis of immediate and delayed reconstructions was not realized due to insufficient data for reliable subgroup analysis. These findings are in contrast with results from a prospective study which documented 30 patients who received modified radical mastectomy, axillary node dissection, and immediate reconstruction with an adipocutaneous DIEP flap (23).

The result found in the prospective comparative study from Beugels *et al.* published in 2019 concur with the results of Bubberman *et al.* Beugels *et al.*'s study included 48 innervated flaps and 61 non-innervated flaps. The patients were tested at different follow-up time points, and the authors discovered that there was a significant association between nerve coaptation and lower SWM evaluator size, which decreased at every monthly follow-up. They concluded that nerve coaptation improved sensibility in both immediate and delayed breast reconstructions (17).

Among the limitations that Bubberman *et al.* have listed, the authors recognised the importance of patient-reported outcomes and shared their plan to include the BREAST-Q questionnaire results in the analysis of the completed randomised controlled trial. Bijkerk *et al.* conducted a study on the effects of sensory nerve coaptation in DIEP flap breast reconstruction using the BREAST-Q questionnaire to assess patient's satisfaction at a minimum of 12-month follow-up and found that patients reported better outcomes and better sensation if they had undergone an innervated breast reconstruction (15).

Regarding the use of SWM in the study of Bubberman *et al.*, a study by Lavery *et al.* evaluated the accuracy and effective service life of SWM with repeated loadings. Their research revealed that the monofilaments were neither precise nor accurate, with SWM plasticity increasing with repeated loadings, and the mean bending forces showing important variability both within and across monofilament brands (24). Furthermore, a study by Haloua *et al.* found that temperature and humidity were factors that could significantly change the monofilaments' buckling force, and thus, lead to potential misinterpretation from examiners (25).

In conclusion, Bubberman *et al.*'s interim analysis provides valuable insights into breast reconstruction using DIEP flaps with nerve coaptation. Postoperative breast sensibility is a critical factor for both patient safety and quality of life. However, there is a a paucity of randomized controlled trials evaluating the sensory benefits of nerve

coaptation in the literature. Research on breast sensory recovery following reconstruction is a complex field and additional fundamental and clinical studies would be greatly beneficial to enhance the understanding of this intervention. The complete results of Bubberman *et al.* are looked forward to.

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Footnote

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