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Special Issue

Sensory reinnervation of free flaps in reconstruction of the breast and the upper and lower extremities☆

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Abstract
There is long-standing debate about sensate *versus* non-sensate free microvascular flaps among microsurgeons. The principle of connecting not only the vascular supply, but also sensitive nerves, in free tissue transfer is attractive. However, increased operating time and partial spontaneous innervation led to the common decision to restrict microsurgical tissue transfer to the vascular anastomosis and to leave the nerves “untreated”. Nevertheless, in special cases such as breast reconstruction or extremity reconstruction, the question about sensory nerve coaptation of the flaps remains open. We present our experience with free microvascular tissue transfer for breast and extremity reconstruction and compare the data with previous literature and conclude that most free flap surgeries do not benefit from nerve coaptation.

Key Words
free tissue flap; mammaplasty; dermatoplasty; free tissue transfer flap; free microvascular tissue transfer; breast reconstruction; extremity reconstruction; sensate flap; non-sensate flap

Research Highlights
(1) This study focused on regeneration of sensation postoperatively in free flaps with or without sensory microsurgical reconstruction using nerve coaptation.
(2) The data presented do not support the hypothesis that nerve coaptation in free flaps leads to increased sensation.

Abbreviations
DIEP, deep inferior epigastric artery perforator; ALT, free anterolateral thigh

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INTRODUCTION

Reconstructive microsurgery has developed tremendously in the last several decades. Due to new techniques, improved instruments and microscopic magnification, sophisticated surgical procedures can be performed and these have improved plastic surgery beyond the filling of tissue defects without regard for function and aesthetics[1]. Although soft tissue reconstruction using local or pedicled flaps provides safe tissue transfer, in selected cases the introduction of free flaps is an important tool to treat larger defects or cases in which pedicled flaps are not possible.

The success of reconstructive microsurgery is now measured not only by free flap survival and defect coverage but also by providing aesthetically pleasing tissue and keeping donor site morbidity to a minimum combined with good functional outcomes[2].

A rational consequence to this evolution is to perform free functional muscle transfer and provide free flaps with sensory improves long term stability and recovery of load, prevents plantar ulcerations, decreases potential wound breakdown and positively influences overall patient satisfaction[3-4].

The coaptation of sensory nerves in soft tissue reconstruction with free flaps is being used more and more often. However, the spontaneous return of sensation in free tissue transfer without sensory nerve coaptation has been reported by a number of authors[5-8].

The aim of this study was to determine if there is a significant benefit to the coaptation of sensory nerves, justifying additional surgical work, longer operation time and eventually higher donor site morbidity. Additionally, we compared sensory nerve repair in breast and extremity reconstruction in our patient population to the published literature.

RESULTS

There is a lack of studies on flaps and sensory reconstruction involving large numbers of patients. Many papers report single cases or a small number of patients/flaps (< 10), so significance is inconclusive.

Major complications occurred in 7% of our patients and included flap necrosis or flap loss, bleeding or hematoma, infection, local skin breakdown or wound dehiscence. Thermal injury due to lack of sensate reinnervation of the deep inferior epigastric artery perforator (DIEP) flap tissue in the left reconstructed breast occurred after 6 months in one female patient (Figure 1).

Figure 1 2nd degree burn injury with hot water after breast reconstruction using a deep inferior epigastric artery perforator flap.

Reulceration of the foot occurred in two patients. We point out that in reconstruction of the hand or plantar surface of the foot, sensate local flaps were our preferred method of reconstruction (dorsalis pedis artery flap, interosseous artery flap, *etc*).

Due to the retrospective design of our study, there was no reliable follow-up protocol for the measurement of sensory reinnervation after breast reconstruction in our patients. However, 89.3% of the female patients in our population receiving autologous breast reconstruction reported sensory reinnervation in the medial as well as in the lateral part of their reconstructed breast after a mean period of 6.5 months. In those without sensation, spontaneous regeneration did not develop if it did not occur within the first six months. This has clinical relevance in the need for local anesthesia in the case of nipple reconstruction or reconstruction of the areola by surgical pigmentation of the areola as a second stage procedure in breast reconstruction. None of the female patients complained of reduced sensation once sensation was achieved.

Clinical follow up of the sensory-augmented free flaps for extremity reconstruction did not demonstrate any significant difference compared to the non-sensate flaps according to the chosen tests (pin-prick, ulceration, hyperkeratosis, wound breakdown and lacerations). Thirteen of 14 cases demonstrated a variable, but measurable, pin-prick sensation over the center of the flap, which was also found in the non-sensate flaps. In one case, where a free anterolateral thigh (ALT) flap was harvested and transplanted to the lower leg with coaptation of the cutaneous femoral nerve to a branch of the sural nerve, the pin-prick test was better than in the non-sensate flaps in the sensitive area, which sometimes included the complete flap (Figures 2A–C).

DISCUSSION

While functional free muscle transfer is commonly used in reconstruction of the facial nerve or in brachial plexus lesions, the coaptation of sensory nerves in reconstructive microsurgery is controversial in the literature[2, 4, 8]. There is a lack of clinical studies including large numbers of patients, revealing that sensory reconstruction in free flaps is not routinely performed. One reason for this may be the development of spontaneous reinnervation after free flap reconstruction causing surgeons to choose faster procedures using free flap transfer without nerve coaptation.

However, sensory nerve coaptation in free flaps is described in the literature only for breast reconstruction or extremity repair; other methods of constructing sensate flaps are used for reconstruction in the facial

area and for genital reconstructions.

The restoration of sensation in breast reconstruction is inconsistent[9]. In many cases, a breast was considered to have restored sensation if even a small area had regained a certain level of sensation[5-7, 10-11]. The measurement of reinnervation varies widely depending on the time of reconstruction (*e.g.* primary, early or late secondary), the surgical technique for mastectomy and the technique used for reconstruction[2].

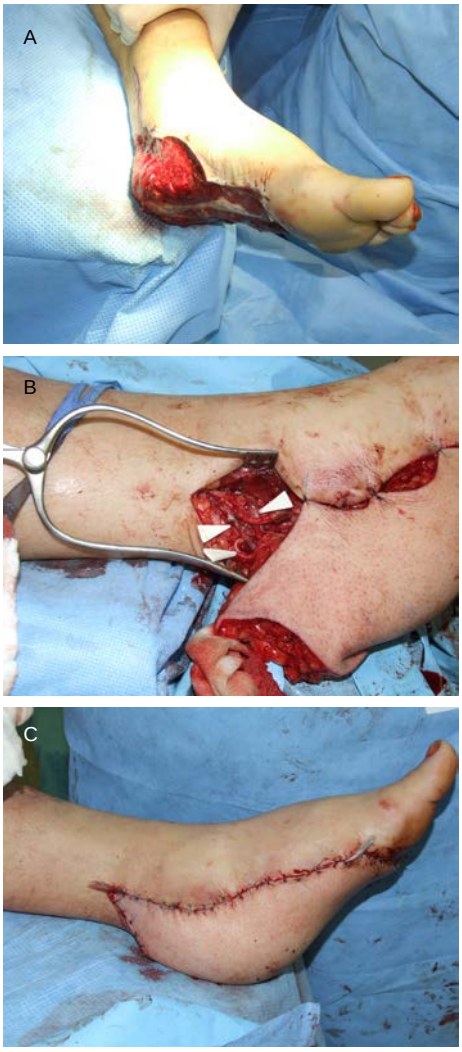

Figure 2 Soft tissue defect of the leg.

(A) Defect of the calcaneal area.

(B) Connection of the vascular supply to the posterior tibial vessels (one artery and two veins) and the sural nerve branch (left lower white triangle indicates the coaptation site to the sural nerve). The upper two white triangles indicate the venous anastomosis. The end-to-site anastomosis to the posterior tibial artery is not marked.

(C) Early postoperative result.

Blondeel *et al* [2] evaluated the influence of sensory nerve coaptation of pure sensory nerves originally innervating the rectus abdominis muscle at the level of the 4th intercostal nerve in breast reconstruction with DIEP flaps with nerve repair ($DIEP^+$) and DIEP flaps ($DIEP^-$) and free transverse rectus abdominis muscle (TRAM) flaps without nerve coaptation[8]. The assessment included determination of the pressure threshold using Semmes-Weinstein monofilaments, hot and cold recognition and high- and low-frequency vibratory sensation. Patients who underwent reconstruction after skin-sparing mastectomy were tested in the exposed skin island of the flap and on the remaining mastectomy skin. Although sensation in the reconstructed tissue with DIEP flaps and nerve coaptation was significantly less than in normal breast tissue, in 75% of the $DIEP^+$ flaps at least protective sensation was present in all five segments of the breast. All $DIEP^-$ flaps had at least one segment that was sensitive to one of the monofilaments, confirming that spontaneous return of sensation can occur. Tindholdt *et al* [8] investigated the spontaneous reinnervation of DIEP flaps after secondary breast reconstruction following radical mastectomy in 29 women (30 flaps). This study also used Semmes-Weinstein monofilaments for evaluating the pressure thresholds of the skin island. Thirty percent of the flaps were categorized as having normal or diminished light touch sensation at one or more testing points[8]. Sensitivity to pressure was better in the medial and inferior part of the skin island than in the lateral and superior part, which suggests nerve ingrowth from the sides, especially from the inferomedial part of the flap. Thermal sensation is statistically significantly better in re-innervated reconstructions.

Our experience confirms the high potential of spontaneous reinnervation in the breast area. This is the main reason why we do not routinely perform sensory nerve coaptation in cases of autologous breast reconstruction. A second reason is the high incidence of neuroma formation and chronic pain syndrome (intercostal neuralgia) after dissection of the intercostal nerves for coaptation[12-14]. Also, in our experience and that of other authors, the main reason why the patients asked for autologous breast reconstruction was a problem with the implant (either in the form of capsular fibrosis or a foreign body sensation) and the wish for symmetry of the breast and no loss of sensation[6, 15-16]. Nevertheless, we observed one patient who suffered thermal injury to the reconstructed breast due to reduced sensation (Figure 1). In our hands, the main problem after breast reconstruction is reduced sensation in the abdominal area when using DIEP or TRAM flaps. Several weeks following abdominoplasty to close the donor site, seven patients developed

ulceration (chronic irritation of the trouser button) or thermal injuries (use of a hot water bag) in the infraumblical area. Nearly all patients complained of sensitivity disorders on the trunk after harvesting the flap, which disappeared spontaneously in 64 percent of affected patients. Sensate abdominoplasty for defect closure, if feasible, overcomes this problem because the terminal branches of the intercostal nerves (proximal nerve stump) are preserved and marked during flap dissection (Figure 3A). Later, during mobilization of the cranial abdominal skin, the cutaneous branches are dissected immediately above the muscular fascia (distal nerve stump) and marked for the subsequent coaptation (Figure 3B).

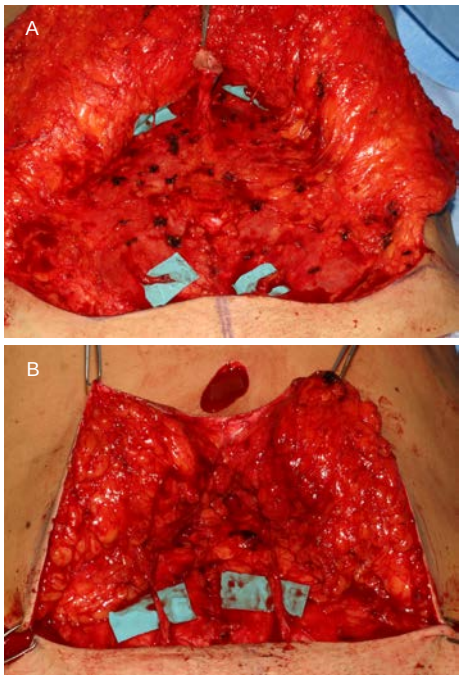

Figure 3 The intercostal branches to the supraumbilical skin are cranial to the umbilicus.

(A) Caudal to the umbilicus, the recipient nerves (cutaneous branch from the lower abdomen) are isolated.

(B) Nerve coaptation for neurotization of the abdominoplasty.

Tension is reduced during closure of the defect by placing sutures between Scarpa's fascia and the muscular fascia and the microsurgical nerve coaptation is then performed using 10/0 epineural sutures. The preliminary results are promising but further studies are needed to validate this method. Based on our results, sensory reconstruction using an abdominal donor site instead of the breast seems a more reasonable procedure.

Reconstruction of sensation in extremity reconstruction is also a challenging field with particular difficulties compared to breast reconstruction. The need for sensation after free flap reconstruction in the upper and, especially, the lower extremity is of even higher significance[4, 17-19]. Despite this consideration, sensate free flaps are the second choice in reconstruction of hand and foot defects because local pedicled, sensate flaps (Foucher flap) are easy to dissect and therefore free flaps can sometimes be avoided[18]. However, one should bear in mind that there is a difference in nerve regeneration in the upper and lower extremities and one explanation may be the larger distances that the regenerating axons have to travel in the lower extremities.

Intact sensation constitutes an important protective mechanism for the plantar surface of the foot. Kalbermatten *et al* [4] hypothesized that improved sensate recovery after reconstruction of foot defects with a fasciocutaneous flap decreases potential wound breakdown. In this prospective study with 34 patients (5 excluded from the study), 15 underwent end-to-side neurorrhaphy of the lower lateral brachial cutaneous to the tibial nerve and 14 were controls who had a free lateral arm flap for reconstruction of defects of the lower leg and ankle without sensory reconstruction. The clinical follow up included static two-point discrimination, temperature, pain, vibration and the use of Semmes-Weinstein monofilaments for neurosensory testing and the evaluation of ulceration, hyperkeratosis, wound breakdown and lacerations. Comparison of the study and control groups did not reveal any difference in wound stability or occurrence of chronic wound problems, hyperkeratotic zones, or ulcerations. Despite better neurosensory test results, there was no difference in long-term stability and durability between the sensate and non-sensate flaps.

In contrast, Santanelli *et al* [17] showed that in the weight-bearing area of the foot, more ulcerations were found in non-sensate flaps. Eleven of twenty patients (six excluded or lost in follow up) underwent reconstruction of a plantar defect with a free forearm flap with surgical nerve repair in which the antebrachial nerve was coapted to branches of the sural nerve. The clinical investigation of sensory reinnervation of the flaps included static two-point discrimination, Semmes-Weinstein monofilament testing along with pain and thermal sensation. In the group with sensate reconstruction, a good level of protective sensation returned three months postoperatively and a statistically significant advantage was evident in the Semmes-Weinstein monofilament test and tests for pain and thermal sensation. Although the non-sensate flaps

showed signs of reinnervation at least six months after surgery, the quality of reinnervation was inferior.
The results in our patients showed that only a very small group of patients received sensate free flaps for extremity reconstruction. In these cases, the ALT was the most chosen procedure due to the ease of dissection of the cutaneous nerve, its long pedicle and low donor site morbidity[1, 19-20]. However, non-sensate free muscle flaps (*e.g*. gracilis-muscle-flap) are an alternative for reconstruction of the foot. The main requirement in foot (plantar) reconstruction is a non-relocatable tissue to avoid reulceration, which is achieved using the gracilis muscle as a free flap (Figures 4A–C) [19, 21].

Figure 4 Gracilis muscle as a free flap in foot (plantar) reconstruction.

(A) Defect of the plantar pedis.

(B) Coverage of the defect by free gracilis muscle transplantation and skin graft.

(C) Result after one year following free gracilis muscle transplantation.

Our experience as well as that of other authors demonstrates that there is an excellent possibility of spontaneous reinnervation in skin grafts over free muscle flaps[17, 21]. However, our data are based on the pin-prick test, which makes it difficult to compare to previous studies. Interestingly, Bayramicli *et al* [22] reported in an animal study, that reinnervation of the skin is significantly better in animals with reinnervated free muscles than in those with non-innervated muscle flaps. He also discussed that activity in skin appendages indicating nerve regeneration may imply only gross sensation and, in the absence of any myelinated nerve fibre transmission, finer sensation did not occur in any of the study groups.The selection of the ideal flap for coverage of such defects follows different algorithms. Since older patients have increased risks with long operation times, we use the free gracilis muscle flap because harvesting the flap is quick and easy to perform. In younger patients, long operation times are less of a concern and we use perforator flaps, since there are no known anatomic variations of the perforators that extend the operation time. Additionally, in elderly patients, nerve regeneration after nerve coaptation is limited due to age, small vessel disease or polyneuropathy in the diabetic patient, for example. Therefore, young patients can receive free fasciocutaneous perforator flaps, sensate if possible, while elderly patients benefit more from the non-sensate gracilis muscle flap.
In conclusion, a sensate free flap is an amazing tool in the armamentarium of the plastic surgeon[23]. Due to the high incidence of spontaneous reinnervation after free flap transfer and the longer operation times, we do not routinely perform microsurgical nerve coaptation for sensate reconstruction in free flap surgery of the breast or the extremities. In our departments, we use cutaneous nerves found near the pedicles in order to augment the quality of sensation. However, whether this operative step contributes to better sensation is unknown since our data are limited and the literature cites few case numbers. Therefore, if the neighboring structures do not provide potentially transferrable nerves, no time is spent exploring to identify candidate tissue for sensitive augmentation of the flaps.

MATERIALS AND METHODS

We performed an online search reviewing the current literature using PubMed with a search for sensate flaps and sensory reinnervation in free flaps. 303 papers were found and we excluded case reports or descriptions not related to reconstruction of the breast

or extremities. Using the same search criteria, we reviewed fifteen abstracts describing free flap reconstruction with sensate flaps. Finally, we reviewed the papers and compared the results with our clinical experience and results.

We retrospectively analyzed all free flaps performed in the Department of Hand Surgery, Microsurgery and Reconstructive Surgery of the Breast, at Marien Hospital, Stuttgart, Germany, as well as in the Department of Plastic-, Hand- and Reconstructive Microsurgery, at St. Marien Krankenhaus, Berlin, Germany, over the last two years. We assessed the following factors: flap type, indications, age of patient, complications and postoperative outcomes and included 364 free flaps in the study. Surgery occurred between January 2010 and December 2011. Of the 364 flaps, we included 321 that occurred in reconstruction of the breast or upper and lower extremity. The average age of the patients was 52.1 years (range, 15–96 years). Indications for the application of the free flaps were breast reconstruction after breast cancer in 259 cases, and defects of the upper and lower extremities in 62 patients. In the breast reconstructions, there were 201 DIEP flaps, 4 superior gluteal artery perforator flaps and 54 transverse musculocutaneous gracilis flaps. None of the free flaps for breast reconstruction achieved re-innervation and sensation.

The following flaps were used for extremity reconstruction: 20 ALT-flaps, 6 latissimus-flaps, 1 radial forearm flap, 33 Gracilis-flaps, one serratus anterior flap and one free musculus gastrocnemius flap (the pedicle was lacerated during flap harvesting, so we switched from a pedicle-based to a free flap). In total, 14 of 62 flaps for reconstruction of the extremity were performed, including sensory reconstruction. In these 14 cases, 13 ALT flaps and 1 serratus anterior muscle flap were performed with sensory nerve coaptation. The donor site nerves were the lateral cutaneous nerve of the leg in the case of the ALT flaps and one branch of the long thoracic nerve in the serratus flap.

All patients included in this retrospective analysis had postoperative courses longer than 24 months. Since the two-point discrimination and other examinations based on different devices are not feasible and reasonable in all cases and flaps, the only criteria for measurement of flap re-innervation in our cases was the pin-prick analysis. The mean postoperative time of analysis was 17.2 months (range, 5–23 months).

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Author contributions: All authors participated in the study concept and design. Nektarios Sinis, Frank Werdin, and Thomas Schoeller were in charge of study implementation. Androniki Lamia and Helml Gudrun collected the data and made the review of the literature.

Conflicts of interest: None declared.

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