Reconstruction of different tissue defects by means of various flaps in plastic surgery

Ph.D. Thesis

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LIST OF PUBLICATIONS

List of full papers related to the subject of the dissertation

I. Szolnoky G, **Mohos G**, Dobozy A, Kemény L: Manual lymph drainage reduces trapdoor effect in subcutaneous island pedicle flaps. International Journal of Dermatology 2006; 45:1468-1470. **IF: 0.998**

II. **Mohos G**, Szabad G, Szolnoky G, Varga E, Kemény L: Lábszáron elhelyezkedő kiterjedt laphámrák kezelése izomlebeny és bőrtranszplantáció kombinációjával. Magyar Traumatológia, Ortopédia, Kézsebészet, Plasztikai Sebészet 2006; 49(4):378-381.

III. Varga J, Pintér S, **Mohos G**, Kis E, Kocsis Á, Nagy K, Kemény L: Kutyaharapás után kialakult felső ajak hiány rekonstrukciója Kazanjian lebennyel. Bőrgyógyászati és Venerológiai Szemle 2009; 85(2):83-85.

IV. **Mohos G**, Vass G, Kemény L, Jóri J, Iván L: Extended lower trapezius myocutaneous flap to cover a deep lateral neck defect on irradiated skin: A new application. Journal of Plastic Surgery and Hand Surgery 2013; 47:70-72. **IF: 0.521**

V. Varga J, **Mohos G***, Varga Á, Erős G, Bende B, Németh IB, Kocsis Á: A possible technique for the complex reconstruction of exposed breast implant: applicability and microcirculation of the capsule flap. Journal of Investigative Surgery 2018; doi:10.1080/08941939.2018.1442532 **IF: 1.122**
*: Varga J and Mohos G contributed equally to the work

List of other full papers

I. Sera T, **Mohos G**, Papos M, Osvay M, Varga J, Lazar M, Kiss E, Kapitany K, Dobozy A, Csernay L, Pavics L: Sentinel node detection in malignant melanoma patients: radiation safety considerations. Dermatologic Surgery 2003; 29(2):141-145. **IF: 1.806**

II. Bajory Z, **Mohos G**, Rosecker A, Bordás N, Pajor L: Surgical solutions for the complications of the Vaseline self-injection of the penis. Journal of Sexual Medicine 2013; 10(4):1170-1177. **IF: 3.150**

III. Vass G, **Mohos G**, Paczona R, Varga J, Iván L, Rovó L: Ajtószárny lebenyek speciális felhasználási lehetőségei fej-nyaki tumoros beteganyagunkon. Magyar Traumatológia, Ortopédia, Kézsebészet, Plasztikai Sebészet 2015; 58(4):257-265.

IV. Vass G, **Mohos G**, Bere Z, Iván L, Varga J, Piffko J, Rovo L: Secondary correction of nasal deformities in cleft lip and palate patients: surgical technique and outcome evaluation. Head & Face Medicine 2016; 12:34. **IF: 1.370**

V. Korponyai C, Szél E, Behány Z, Varga E, **Mohos G**, Dura Á, Dikstein S, Kemény L, Erős G: Effects of locally applied glycerol and xylitol on the hydration, barrier function and morphological parameters of the skin. Acta Dermato-Venereologica 2017; 97(2):182-187. **IF: 3.127**

VI. **Mohos G**, Kocsis Á***,** Erős G, Korponyai C, Varga Á, Bende B, Varga J: Reconstructionof alar-perialar defects with a combined subcutaneous and cutaneous pedicled rotation-advancement nasolabial flap. Journal of Investigative Surgery 2019; doi: 10.1080/08941939.2018.1538397 **IF: 1.122**

*: Mohos G and Kocsis Á contributed equally to the work

1. ABBREVIATIONS

25p	25th percentile
75p	75th percentile
ADM	Acellular dermal matrix
Caps.	Capsulotomy
CF	Capsule flap
Fix. of the flap	Fixation of the flap
FNA	Fine needle aspiration
H&E	Hematoxylin-eosin
Inc.	Incision
LDMF	Latissimus dorsi myocutaneous flap
LTMF	Lower trapezius myocutaneous flap
M	Median value
MLD	Manual lymph drainage
NMSC	Non-melanoma skin cancer
PET	Positron emission tomography
Prep. of the flap	Preparation of the flap
TRAM flap	Transverse rectus abdominis myocutaneous flap
VAS	Visual analog scale

2. INTRODUCTION

2.1. Background

It is the cornerstone of reconstructive surgery to provide a safe coverage for tissue defects of different origin and to restore original shape and function. For these goals, careful defect analysis, clear definition of surgical goals, thorough consideration of surgical options, precise performance and appropriate post-operative follow-up are required. Several various techniques are available for reconstruction and in many cases it may be difficult to choose the best method. In the last decades, the "reconstructive ladder" was a widely accepted guide for surgical decision making. In this concept, the complexity of the technique is considered and the simplest method appropriate for the given wound is suggested (**Mathes & Nahai, 1982**). Accordingly, the first stage of the reconstructive ladder is the direct wound closure. If direct closure is not possible, skin graft can be applied as the next level. In case of more complex wounds, local flaps can be chosen and microvascular tissue transplantation means the last resort of the reconstructive ladder (**Mathes & Nahai, 1997**).

However, many advances have been achieved in the last years (e.g. evolution of flaps, tissue expansion and microsurgery) that led to a new paradigm. It is now suggested to make surgical decision on the basis of quality instead of simplicity. More complex techniques may produce better results in terms of shape and function and are not necessarily accompanied by an increased rate of complications. Thus, the new paradigm, the "reconstructive triangle" is an integrated approach for the selection of the best treatment modality (which can be a complex method, as well) considering the surgeon's experience and his/her familiarity with the various methods (**Mathes & Nahai, 1997**). Different techniques are often combined in order to provide individualized treatment for specific defects. **Table 1** summarizes the essentials of reconstructive ladder and reconstructive triangle.

Table 1. Reconstructive ladder and reconstructive triangle

Reconstructive ladder	Reconstructive triangle
Distant flap	Flaps
Local flap	
Skin grafts	Microsurgery
Direct closure	Tissue expansion

Different types of tumors and their excision may lead to large tissue defect which often requires reconstructive intervention. Non-melanoma skin cancers (NMSC) localized to the tibial region can be treated with several methods. Curettage or cryosurgery can be the method of choice, if the tumor is small and superficial (**Housman et al., 2003; Kuflik, 2004**). If an NMSC with a diameter under 1 cm is excised, primary wound closure is possible. NMSC of medium size (10-35 mm) may require coverage with flap or skin transplantation (**Dixon & Dixon, 2004**). However, surgical management of large NMSC in this region is problematic. The tighter skin, the higher age and the potential comorbidities may result in decreased blood supply that leads to impaired wound healing.

Similarly, treatment of tissue loss in the region of head and neck raises special questions. In reconstruction of soft tissue lesions in the neck, the primary goal is to appropriately cover the exposed vital organs with well-vascularized tissue harvested from a distant donor site (**Ndayishimiye et al., 2009**). Thorough defect analysis, evaluation of the patient's general condition and the anatomy of the defect site shall support the surgical decision on the applied method (**Papadas et al., 2005; Datta et al., 2009**). The extended lower trapezius myocutaneous flap (LTMF) and latissimus dorsi myocutaneous flap (LDMF) seem to provide good solution since these muscle compartments can be transferred on a reliable vascular pedicle to the dorsal, suprascapular and neck regions. The flap shall be selected after consideration of their anatomy, their way rotation and an analysis of the size, extension and site of the defect (**Datta et al., 2009**).

Perioral defects may originate in malignancies, traumas and congenital disorders. Reconstruction of the upper lip is a difficult surgical problem because of its prominent location, elegant form and important functions. If small and full-thickness defects affect only one-fourth to one-third of the lip (the width does not exceed 2 cm), primary wound closure is possible. Larger lip defects require application of flaps. In such cases, local flaps shall be chosen because they minimize donor site morbidity and these provide the best functional and esthetic outcome (**Coppit at al., 2004; Anvar et al. 2007**). If the defect involves 1/3-2/3 of the lip, the following methods can be chosen for reconstruction. Cross-lip flaps e.g. *Abbé* or *Estlander* flaps (**Krunic et al., 2005; Anvar et al., 2007**), circular-rotational flaps as described by *Karapandzic* or *Gillies* (**McCarn & Park 2005; Anvar et al., 2007**), the nasolabial flap (**Pinar et al., 2005**) and *Kazanjian* reverse flap (**Kazanjian & Roopenian, 1954**) are the appropriate techniques. If reconstruction is performed in more steps, combined local flaps are applied. In the first step, the oral sphincter is reconstructed e.g. with the extended *Karapandzic* flap or the *Kazanjian* (**Karapandzic, 1974; Anvar et al., 2007;**

Ethunandan et al., 2007). Subsequently, the volume and symmetry of the upper and lower lips are restored with the cross-lip flap (**Ethunandan et al., 2007**). Furthermore, distant free flaps with microvascular technique (microvascular flap) can also be applied as well as advancement myocutaneous flaps. Radial forearm flap is frequently chosen and is often transplanted with the tendon of long palmar muscle in order to support the lip (**Kushima et al., 1997; Anvar et al., 2007**). Since its nerve (lateral antebrachial cutaneous nerve) can be reconnected to the mental nerve or to the inferior alveolar nerve hereby providing the sensory function, this flap can be considered as a sensory flap and is an ideal choice for reconstruction of total and subtotal lip defects. Moreover, alternative free flaps can be applied e.g. gracilis muscle free flap (**Lengelé et al., 2004**) and free temporal scalp flap (hair-free outer side and mucosa on the inner side) (**Chang et al., 2003**). Nevertheless, total reconstruction of large lip defect is a significant challenge.

Various types of breast cancer belong to the most frequent malignancies. Hence, restoration of breast shape after tumor surgery is a pivotal question. Immediate one-stage breast reconstruction is becoming a widely-accepted and preferred method. Implants should be covered with tissue of appropriate thickness and viability especially if patients receive post-mastectomy radiation therapy. It is known that radiotherapy may be accompanied by a number of complications (**Behranwala et al., 2006**) including impaired wound healing, wound separation, infection and fistula (**Forman et al., 1998; Abramo et al., 1999; Ariyan, 2006**). These factors may lead to a considerable contraction of the capsule around the implant. This shrinking makes the surface of the implant irregular which therefore exerts uneven pressure on the overlying skin. According to a hypothesis, the increased pressure affecting such areas may impair the microcirculation of the covering tissue layer potentially resulting in necrosis and exposure of the implant (**Abramo et al., 1999**). Inappropriate surgical technique may also cause insufficient local blood supply leading to necrosis and implant protrusion. Accompanying infection may contribute to this process. Although exposed implants are traditionally treated by insertion of a new one, many authors have reported successful salvage of implant (**Forman et al., 1998; Ariyan, 2006; Behranwala et al., 2006**) or alternative therapeutic strategies (**Weber & Hentz, 1986; Planas et al., 1995; Abramo et al., 1999; Spear et al., 2004; Persichetti et al., 2014**). However, these interventions may fail in case of previous radiotherapy or where tissue is injured or thin, necessitating implant removal. For such cases, capsuloplasty seems to be an appropriate technique. The capsule appearing around the implant is a reaction to foreign material (**Bassetto et al., 2010; Persichetti et al., 2014**). It consists of fibroblasts and collagen fibers, has own blood supply and previous radiotherapy

contributes to its development (**Behranwala et al., 2006**). *Bengston* and coworkers described the application of capsule flap decades ago. According to their animal experiments, capsule flaps are viable and their vascular system is sufficient for the nutrition of the overlying skin graft (**Bengston et al., 1993**). In human, several areas of capsule flap were reported e.g. prevention of implant wrinkling (**Hobman & Sharpe, 2008; Persichetti et al., 2014**), pharyngeal reconstruction (**Persichetti et al., 2010**), shaping of inframammary fold (**Persichetti et al., 2013**) and cover for exposed implants (**Weber & Hentz, 1986; Planas et al., 1995; Spear et al., 2004; Persichetti et al., 2014**). However, the blood flow in capsule flaps has not yet been quantitatively determined *in vivo*.

In addition to reconstruction, it is also important to provide appropriate post-operative treatment in order to avoid different complications. After application of flaps, trapdoor effect is a possible complication. The trapdoor effect is the bulging elevation of the tissues within the confines of a semicircular or circular scar and is common with subcutaneous pedicle flaps. *Mustarde* described it as a pincushion scar which usually starts 3 weeks after the intervention (**Mustarde, 1991**), but its appearance may be delayed for 6-8 months (**Koranda & Webster, 1985**) and cause cosmetologic disability (**Clodius, 2002**). The causes and successful treatment modalities have not been clarified. Lymphatic and venous obstruction, scar hypertrophy, excessive fatty redundant tissue, beveled wound edges and contracture of the scar are considered to be involved in its development (**Koranda & Webster, 1985**). *Clodius* defined it as a lymphatic consequence of the reconstruction of face defects with flaps (**Clodius, 2002**). The formation of blood vessel anastomoses precedes that of lymphatic anastomoses therefore an overload of the post-capillary venules and increasing capillary filtration will usually occur. The scar formation further hampers the development of the vascular and lymphatic network (**Van Duyn, 1969**).Multiple, small Z-plasties around the periphery of the flap appear to cause some reconstruction to the shape (**Koranda & Webster, 1985**). Another successful method has been performed with triamcinolone acetonid injections (**Koranda & Webster, 1985**), but continuous compression with silicone does not provide a satisfactory solution. The combination of scar excision, compression and immobilization (interdental wiring) can improve appearance, although it is sometimes rather exhausting for the patients (**Clodius, 2002**).

These special surgical problems and questions let us design individual treatment modalities and assess their applicability and efficacy for reconstruction and for sustaining the results of surgical intervention.

2.2. Aims

Our primary aim was to find appropriate solutions for injuries which are difficult to cover due to their size and/or anatomical localization. For this goal, special flaps were designed, performed and the healing of the patients were monitored. Moreover, a new therapeutic approach was tested in order to retain the esthetic result achieved by the flaps and to decrease trap door deformity. The study comprises 5 parts with different objectives. The detailed aims are listed below:

- to cover a large defect in the anterior tibial region, which affected the cortical region of the bone, with application of a muscle flap and skin graft (Part 1),
- to find an optimal solution for the reconstruction of a deep tissue loss in the cervical region, which was exposed to irradiation and an earlier flap reconstruction has failed, utilizing myocutaneous flap (Part 2),
- to reconstruct a large upper lip defect due to dog bite by using combined flaps (Part 3),
- to treat exposed breast implants with capsule flap (Part 4), and
- to reduce trapdoor effect in subcutaneous island pedicle flaps with manual lymph drainage (MLD) (Part 5).

3. METHODS

3.1. Reconstruction of a defect on the tibia using tibialis anterior turnover flap combined with skin graft

A 58-year-old male patient was admitted to our department with an ulcerating lesion on the anterior part of the right tibia. The lesion was covered with discharge, its diameter was measured to be 14 cm (**Figure 1**). Inguinal lymph nodes were not palpable. Prior to the intervention, biopsy was taken and histological examination has described squamous cell carcinoma.

Under general anesthesia, the tumor was excised. Since it has reached the periosteum of the tibia, the periosteum with a thin cortical layer was removed for the safe elimination of the tumor (**Figure 2**).

Figure 1. Ulcerating lesion in the proximal anterior part of the right tibial region. Preoperative status.

Figure 2. The wound after removal of the tumor, the periosteum and a thin cortical layer of the tibia

In order to cover the wound, the anterior tibial muscle flap was applied. The lateral part of the muscle was used which was pedicled from the proximal direction thereby retaining the blood supply. The flap was partially rotated onto the bone surface (**Figure 3**).
This flap was an appropriate basis onto which a split-thickness meshed skin graft (ratio 1:1.5) was placed. The donor site of the skin graft was the region of the right thigh.

Figure 3. Tibialis anterior turnover flap

3.2. A new application of the extended lower trapezius myocutaneous flap (LTMF)

In 2003, a 49-year-old male patient was admitted to our head and neck surgery department with a diagnosis of squamous cell carcinoma in the right tonsillar region and the soft palate (T2N0M0). The tumor was excised by means of a transoral carbon dioxide laser device. Histopathological examination showed tumor-free resection margins. Postoperative radiotherapy was given (total dose 66 Gy). A late metastasis was found in the right submandibular region 4 years later and it was verified with fine needle aspiration (FNA). Modified radical neck dissection was performed and the patient received 4 cycles of postoperative chemotherapy. During the next 2 years, solitary metastases appeared which were verified by both PET scanning and FNA in 2 occasions from the deep compartments of the neck. These metastases were removed. Histopathological examination revealed tumor-free margins for each specimen. Furthermore, irradiation (32 Gy) and cetuximab was applied postoperatively, as well. Despite the complex therapy the tumor spread aggressively and in November 2009 another late metastasis was found below the mastoid region that infiltrated the skin, the subcutaneous tissue, the deep neck muscles and the carotid artery. The tumor was removed as radically as possible. Even the X cranial nerve and the external branch of the carotid artery were excised. Histological examination revealed tumor-free margins and scar tissue. The large and deep tissue defect (5x12x3 cm) required extensive coverage. Thus, a latissimus dorsi myocutaneous flap (LDMF) was made from the same side that seemed to be

able to fill the defect. However, the LDMF slowly necrotized. Since this flap failed, another solution was sought for the remaining defect (**Figure 4**).

Figure 4. The large defect (5x12x3 cm) on the neck after necrosis of the LDMF

For this aim, the extended LTMF was chosen which is also safe, has sufficient blood supply from the dorsal scapular artery and its size seems to be appropriate to cover a dorsocervical defect as an alternative flap.

The trapezius and the rhomboid muscles and the contour of the scapula were marked on the skin. The rotation point was marked next to the medial-superior edge of the scapula where the supplying vessels enter the muscle. Finally, above the end of the trapezius muscle a skin island – equivalent in size to the defect (5x12 cm) – was determined (**Figure 5**).

Figure 5. Operative planning. The black arrow shows the rotation point of the flap while the white arrow points at the skin island.

After excision, the muscle pedicle of the flap was dissected up to the rotation point at the medial-superior edge of the scapula (**Figure 6**). On the lower surface of the pedicle, the supplying vessels were identified (**Figure 7**). The recipient site was prepared for the new flap:

the carotid artery was freed of scar tissue and the remnants of the LDMF pedicle were removed. The tunnel of the pedicle was drained. The extended LTMF was rotated laterally into the defect and the donor site was closed free of tension after mobilization of the wound edges (**Figure 8 A,B**).

Figure 6. Preparation of the myocutaneous flap with the skin island

Figure 7. The forceps is pointing on to the supplying dorsal scapular artery

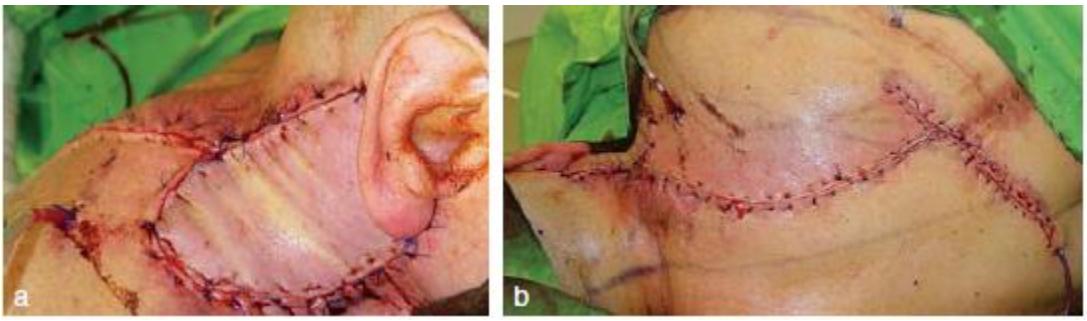


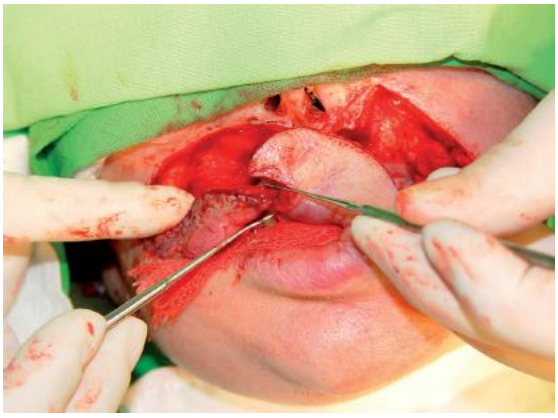
Figure 8. A: Viable skin island sutured into the defect; **B:** Primary closure of the donor site

3.3. Reconstruction of a large upper lip defect due to dog bite by Kazanjian flaps

A 57-year-old female patient was attacked by her dog in her home. The patient suffered serious scalp and facial injuries. She required cardiopulmonary resuscitation in the field. The patient was admitted to the intensive care unit of the University of Szeged, and after 42 days of treatment, she was transferred to our department for the reconstruction of the upper lip (**Figure 9**). In the first phase of reconstruction, the skull was covered by a microvascular flap of the greater omentum and a right facial artery-retromandibular vein end-to-end anastomosis was prepared. Due to the injuries, approximately 70% of the upper lip was missing. Adhesions were found in the lateral sides, the upper denture was exposed and the oral mucosa was dry and painful. Further, the patient's ability for nutrition and speech was limited. The tracheostoma prepared during the period of intensive care healed well. The patient also had a jejunostomy, prepared as part of the emergency management procedures. This was maintained during the period of the inpatient treatment.

Figure 9. The patient before the upper lip reconstruction

For reconstruction, a *Kazanjian* flap was rotated from the left lower lip area to repair the upper lip defect. An incision was made parallel to the mentolabial and nasolabial lines. The skin and the subcutaneous tissue were harvested and care was taken that the nerves and vessels at the lateral edges were preserved. The fibers of the orbicular oris muscle were then identified, the adhesion was separated and the fibers of the muscle were reconnected in the original position. The defect was closed layer-by-layer. The repaired upper lips made it possible to close the mouth and provided coverage for the teeth (**Figure 10**).



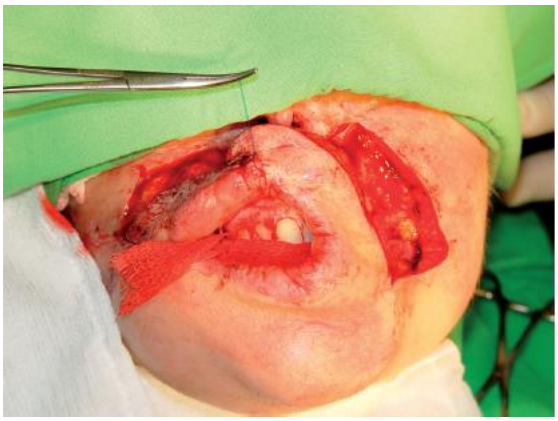


Figure 10. Tailoring of the flap and uniting of different layers

In the second stage of the lip reconstruction, a cross-lip flap (*Abbe*) was used in order to restore the symmetry and volume of the upper and lower lips (**Figure 11**). During the treatment, microstoma developed, which was corrected by commisurotomy and mucosa plasty of the series of operations. Neither venous circulation defect, nor wound healing problems and other complications appeared.

Figure 11. Application of the cross-lip flap (Abbe)

3.4. Reconstruction of exposed breast implant with capsule flap

3.4.1. Patients

Capsuloplasty was performed in 19 females between January 2016 and November 2017. These patients underwent earlier mastectomy and immediate breast reconstruction. The average age was 47.6 years (range: 33-72 years). The right side was affected in 10 cases and the left side in 9 cases. 4 patients underwent bilateral mastectomy. Bilateral capsuloplasty was performed in 3 of these 4 patients, the remaining 1 female underwent unilateral capsuloplasty (right side). **Table 2** demonstrates the localization of the defects indicating the operation. None of these patients received radiotherapy except 1 patient who underwent irradiation 1 year before mastectomy.

Table 2. Localization of the defects indication the operation

Localization of the tissue defect	**Side**	
	Left	**Right**
Wound separation in the scar of mastectomy	3	3
In the borderline of the inferior quadrants	2	4
In the inferior lateral quadrant	0	2
In the inferior medial quadrant	2	2
In the superior lateral quadrant	1	0

3.4.2. Surgical procedures

Each intervention was preceded by careful consideration of the following parameters: quality and thickness of the breast skin, presence of inflammation, discharge and fistula, previous radiotherapy, localization of tissue damage, patient requirements and the extension of necrosis and wound separation. The patients were carefully observed in order to detect visible signs of inflammation (erythema, edema). Moreover, leukocyte number, C-reactive protein and procalcitonin levels were also measured in each patient and samples were taken for microbiological examination. Signs of serious inflammation and large tissue defect were considered exclusion criteria. However, in case of the involved patients the mentioned

parameters did not display elevation and pathogenic bacteria were not found. (If capsule flap is not feasible, the implant is to be removed and delayed reconstruction with a flap e.g., latissimus flap or abdominal TRAM flap shall be performed.) **Figure 12 A** demonstrates a patient chosen for capsuloplasty. A pivotal point was the timing: the intervention should not be performed sooner than an appropriate capsule is formed around the implant. The tissue defect in our patients appeared 8-13 weeks after the mastectomy (median interval: 9 weeks). By this time, the capsule around the implant was well-developed therefore it was appropriate to be used for reconstruction. When the complication was recognized, the patients started to be prepared for the reconstruction which was performed within 3-5 days. During this period, the defect was covered with sterile dressing. Perioperative antibiotic therapy was launched that involved daily 1000 mg cefuroxime (2x500 mg) administered orally. This therapy lasted 10-14 days. Another important issue was the determination of the area from which capsule can be gained for reconstruction. In 3 cases, an attempt was made to close the wound primarily after removal of the necrotic tissue. The operation involved the following steps: after opening the wound the necrotic parts were excised, the implant was removed and capsulotomy was performed, the base of the flap remained intact, the planned flap was dissected free (**Figure 12 B**). After that, the implant was positioned and covered with the capsule flap (**Figure 12 C**). Mentor's Cohesive III implant with anatomical shape and textured surface was applied. In most cases, new implants were used. In a minority of the cases, when the risk of infection and inflammation seemed to be low, the same old implants were applied. If the wound was able to be closed tension free after application of the capsule flap, the implant size was not reduced. If the tension free wound closure seemed to have difficulties, a smaller implant was chosen. The wound was closed with sutures (**Figure 12 D**). Drainage was applied when necessary. Various capsule flaps were applied: anterior-superior medial, anterior-superior lateral, in 1 case divided flap, and also posterior flaps from the chest wall. In 3 cases, thoraco-epigastrial fasciocutaneous flaps were used together with capsule flap in order to complete the reconstruction due to a large defect. Patients were discharged on 3^{rd}-5^{th} postoperative day. An examination was performed 1 week after the surgery. The second examination and removal of the stitches were 1 week later. Following this, the patients were examined monthly once (inspection and palpation of the operated site and the above mentioned laboratory examinations were performed, too). Ultrasound imaging was performed in every 3 months (presence of capsular contracture and peri-implant fluid).

3.4.3. Laser Doppler flowmetry

Microcirculation of the flaps was monitored by means of the PeriFlux System 5000 (Perimed, Järfälla, Sweden). This equipment transmits low power laser light (780 nm) to the tissue via a fiber optic probe. The returning light is processed and the relative number and velocity of the blood cells in the tissue are calculated and presented as blood perfusion. The sensor was fixed to the tissue with a sterile adhesive strip provided by the manufacturer. Measurements were performed at 4 different time points: before the incision of the intact capsule (baseline), after capsulotomy, after preparation of the capsule flap and after fixation of the flap. At each time point, recordings were made for 5 minutes. Perisoft for Windows software was used for data collection, storage and analysis. The data are presented as perfusion unit (P.U.).

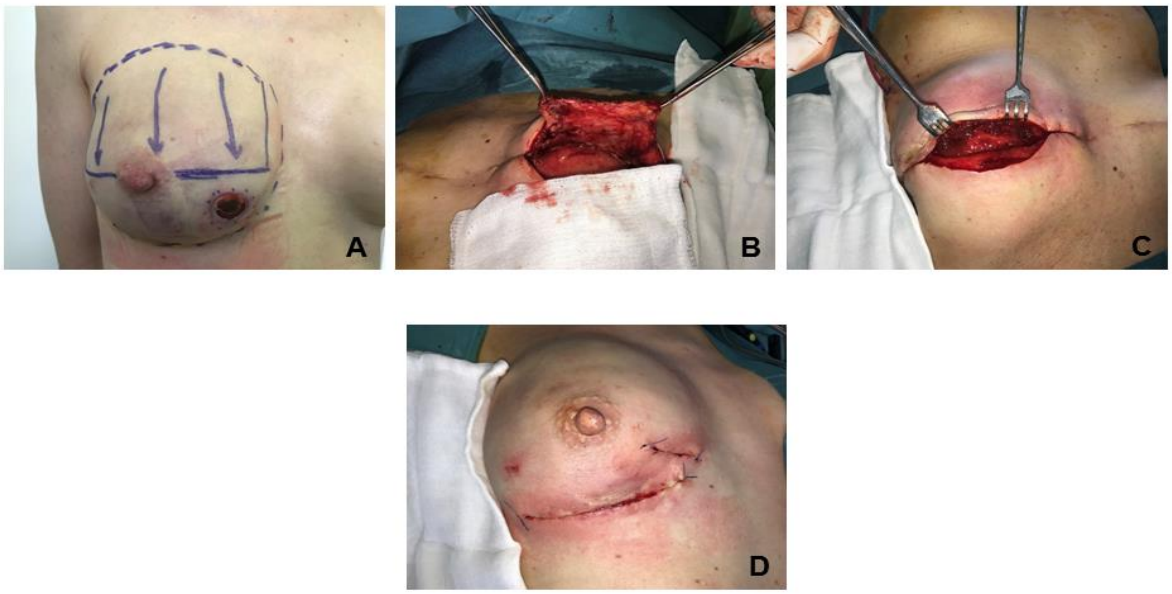


Figure 12. Photo documentation of the surgical intervention. A: a patient selected for capsulotomy; B: the dissected capsule flap; C: the implant after positioning and covering with the capsule flap; D: the closed wound.

3.4.4. Histology and immunohistochemistry

During operation, biopsies were taken from the capsule. Tissue samples were fixed in a buffered solution of formaldehyde (4%), embedded in paraffin and 4-μm thick sections were taken. In addition to routine hematoxylin-eosin staining, sections were processed for immunohistochemical localization to highlight CD34 positive vessel density. Primary antibody to CD34 (clone QBEN/10 M7165; DAKO Glostrup, Denmark) was used at 1:200 (20 min). Antigen retrieval was performed by Bond Epitope Retrieval solution 2 at pH=9 by BOND MAX Autostainer (Leica Biosystems, Newcastle Ltd., UK). Immunosections were counterstained with conventional hematoxylin.

3.4.5. Statistical analysis

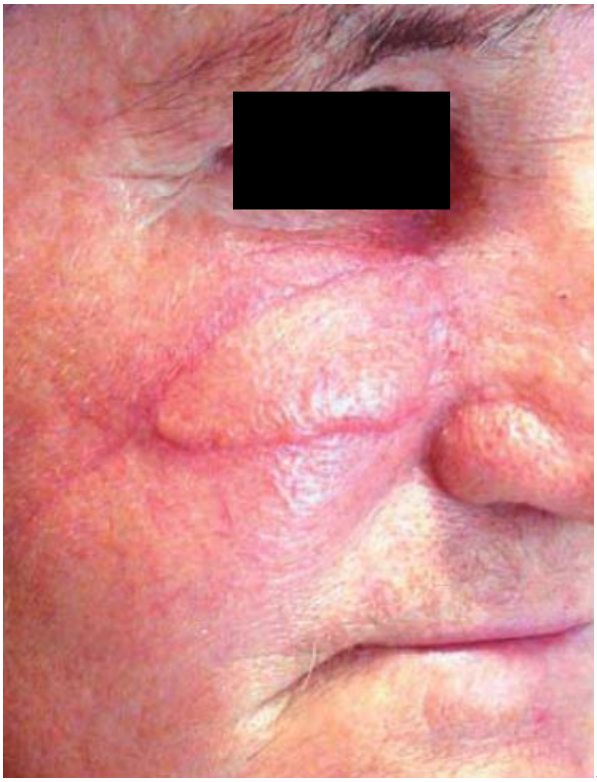
Data analysis was performed with SigmaStat for Windows (Jandel Scientific, Erkrath, Germany). Since the normality test (Shapiro-Wilk) failed in few cases, nonparametric test was chosen. Friedman repeated-measures analysis of variance on ranks was applied. In the Figure and Results, median values (M) with 25^{th} and 75^{th} percentiles (25p and 75p, respectively) are given, $p<0.05$ was considered statistically significant.

3.5. MLD for reduction of trapdoor effect in subcutaneous island pedicle flaps

This part of the study involved 2 patients. The first patient was a 54-year-old woman, who underwent an excision of a nominal 11x6 mm basal cell carcinoma on the left cheek. The skin defect was covered with a subcutaneous island pedicle flap from the lateral side, as described elsewhere (**Gardner & Goldberg, 2002**). After 2 months the trapdoor deformity developed, which was initially treated with a silicon compression for 1 month, but without success; it was further treated by MLD.

The second patient was a 58-year-old woman who developed a nominal 22x24 mm basal cell carcinoma on the right cheek. It was surgically removed and the defect was reconstructed with a subcutaneous pedicle flap. The patient noticed swelling of the reconstruction 3 weeks post-operatively. **Figure 13 A** and **B** demonstrates the trapdoor phenomenon.

Both patients were treated with a daily 30-min MLD 3 times / week for a 1-month period after written informed consent approved by the Institutional Review Board of the University of Szeged. The MLD consisted of drainage of the neck region followed by the stimulation of the lymph nodes of the corresponding area (**Földi & Kubik, 2000**). The drainage of the flap included standing circles around the scar and superficial linear manual drainage parallel to the lymph collectors. The patients were followed up over the preceding 4 months. The efficacy was photographically assessed by a visual analog scale (VAS) (**Klassen et al., 1996**) from day 0 to the end of treatment and follow up.


A


B

Figure 13. Trapdoor phenomenon (A and B)

4. RESULTS

4.1. Successful reconstruction of the defect on the anterior part of tibia

2 days after surgery, the viability of the skin graft placed onto the anterior tibial muscle flap was visible (**Figure 14**). The entire operation site was found to be healed 2 months later and the cosmetic result was good (**Figure 15**). The histological analysis revealed an ulcerated squamous cell carcinoma which infiltrated also the deeper dermal layers. In a few areas, keratinization was observed and the tumor cell islands were well-differentiated (**Figure 16**). Other parts of the tumor displayed more expressed pleomorphism, dyskeratotic cells and atypical mitoses were seen. The margins were found to be tumor-free.

Figure 14. The anterior tibial turnover flap covered with skin graft on the 2nd postoperative day

Figure 15. Reconstructed tibial region, 2nd postoperative month

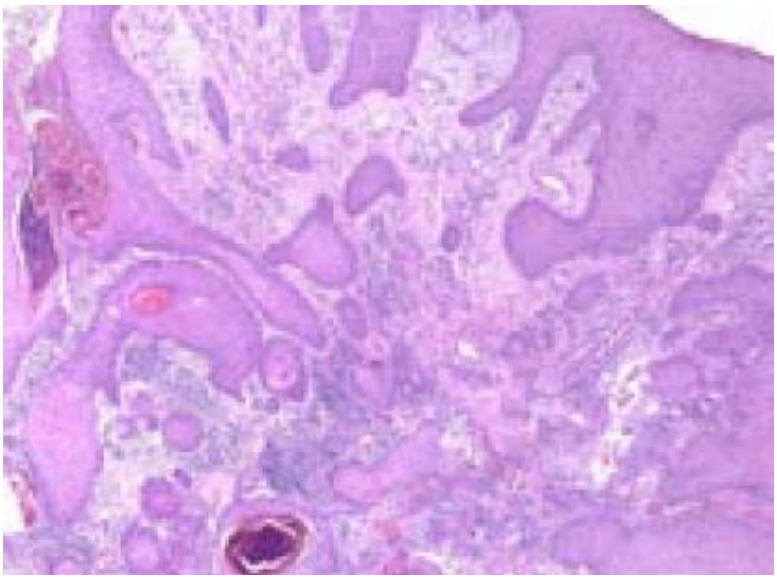


Figure 16. A well-differentiated part of the tumor. Tumor cell islands infiltrate the dermis. Keratinization and keratin pearls can be seen. In the stroma, chronic inflammatory reaction and focal bleedings were found.

4.2. Reconstruction of the deep neck defect

The operation was successful, the flap remained viable and the wound healed primarily (**Figure 17**).

Figure 17. 5 weeks after the operation, the skin island is vital and wound healing undisturbed

4.3. Restored upper lips with the Kazanjian flap

In the operation site, the sensory function returned in 3 months. After 6 months, the movements of the lip were intact. The patient was able to pucker the lips, open the mouth and to eat. The intervention led to both functionally and esthetically satisfactory results (**Figure 18**).

Figure 18. The reconstructed lips (6 months after surgery)

4.4. Breast implantation salvage with capsule flap

Attempts at the primary closure of wounds after removal of necrotic tissue failed in the above mentioned 3 cases: the implants were exposed again. However, application of capsule flaps led to the healing of these patients without complication. Postoperative follow-up (ranging from 2 months to 19 months) showed that capsule flaps survived in each case. No signs of inflammation, infection, hematoma, wound separation and implant protrusion were found. Slight erythema was detected in 2 cases. In few cases, uneven surface and wrinkling were detected. However, our examinations excluded the capsular contracture and all of these signs ceased within 3 months. **Figure 19** shows a patient in the 3rd postoperative month, a complete healing can be seen.

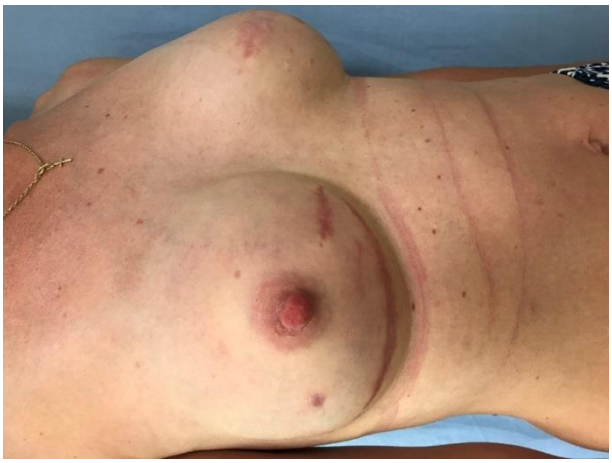


Figure 19. The healed wound 3 months after the operation

As concerns microcirculation of the flaps, the baseline median value in capsule flaps was 98.97 P.U. (25p=73.56, 75p=124.09). The perfusion in the capsule did not change after the capsulotomy (M=106.96%, 25p=62.82, 75p=157.07) as referred to the baseline values. Although a slight decrease was measured after preparation of the capsule (M=64.08%, 25p=33.36, 75p=135.99) and fixation of the flap (M=51.41%, 25p=32.7, 75p=96.99), this change was not statistically significant (**Figure 20 A**).

The baseline values of the thoraco-epigastrial fasciocutaneous flaps: M=14.87 P.U., 25p=10.37, 75p=32.15. No decrease was found in their blood flow after incision (M=95.56%, 25p=48.14, 75p=127.44), after preparation of the flap (M=120.27%, 25p=45.32, 75p=173.77) or after fixation of the flap (M=62.52%, 25p=31.58, 75p=108.59) (**Figure 20 B**).

Histological analysis revealed that capsules were well-vascularized and several vessels were present in the connective tissue which may provide sufficient blood supply for the capsule (**Figure 21 A**). Immunohistochemistry confirmed this finding: the CD34-positive structures demonstrated angiogenesis in the capsule (**Figure 21 B**).

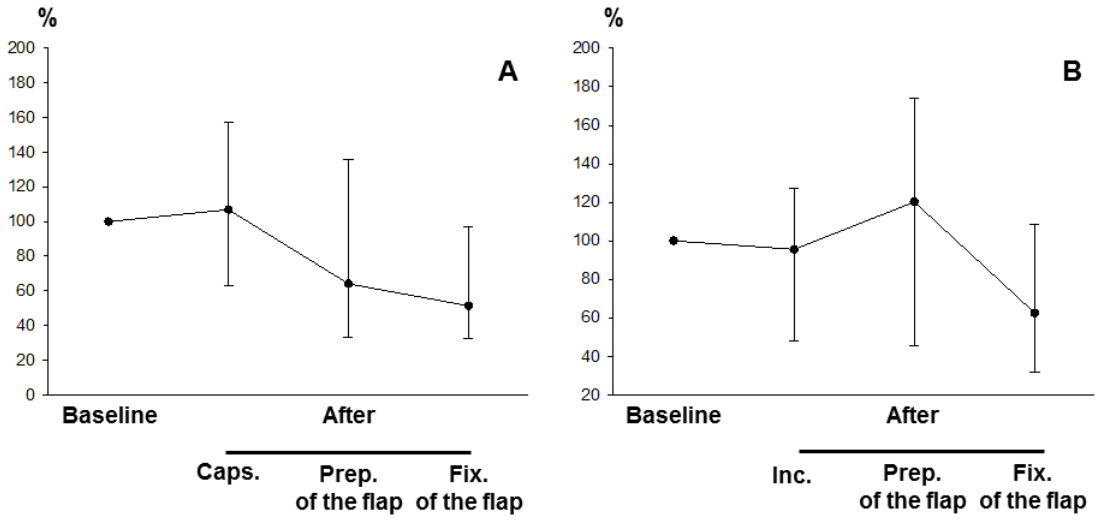


Figure 20. A: blood flow of capsule flaps and B: thoraco-epigastrial fasciocutaneous flaps in different stages of the operation. M values with 25p and 75p are demonstrated.

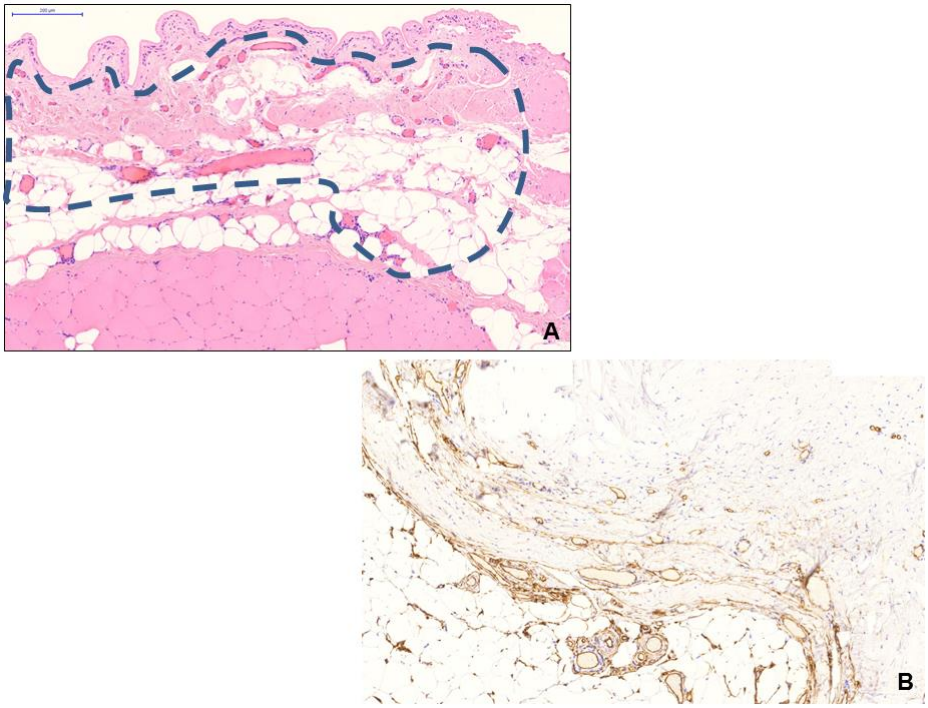


Figure 21. A: low power micrograph of the capsule (H&E staining, slide scanning, scale bar: 200 μm). Perforating vessels in the connective tissue between striated muscle and capsule (dashed line). B: CD34-positive structures (appearing brown).

4.5. Successful therapy of trapdoor effect

On completion of the MLD (**Figure 22 A, B**) and the follow-up period, the trapdoor deformity of 2 patients was effectively restored. The VAS showed a drastic improvement in both patients' quality of life (69-84-84 and 74-87-87, respectively).

Figure 22. Trapdoor phenomenon was efficiently reduced by the end of the treatment with MLD

5. DISCUSSION

Prior to direct restorative interventions, ablative procedures are often necessary to be performed in order to eliminate the underlying disease or injury. Complete ablative procedures are required for a successful reconstruction and the extension of tissue loss due to ablative intervention can be considered in advance when designing the method of restoration (**Wei & Mardini, 2009**). Different techniques can be used to eliminate tumors depending on their histological type and size. Cryosurgery is an accepted method for the treatment of small NMSC. (**Holt, 1988; Graham & Clark, 1990**). If tumor margins are difficult to be judged, the tumor infiltrates the deeper layers or its size does not allow curettage and cryosurgery, excision is necessary with appropriate coverage. In the tibial region, only minor NMSC can be treated by means of simple excision. Several cutaneous flaps with random blood supply have been developed in order to cover the defect originating in the removal of medium sized tumors (10-35 mm). For instance, the double V-Y advancement flap is suggested for the reconstruction of skin defects in the anterior lower leg (**Blair et al., 1993**). However, blood supply of the subcutaneously pedicled island flaps is not better than that of random flaps unless they have axial artery. The goal of random flaps is to decrease tension hereby reducing the skin necrosis in the flaps (**Dixon & Dixon, 2004**). In case of appropriate wound basis, skin transplantation is an accepted method for the coverage of large skin defects, but the

cosmetic result is not always satisfactory. Fasciocutaneous and musculocutaneous flaps are seldom applied for reconstruction after excision of NMSC because such tumors do not often infiltrate layers under the subcutaneous tissue.

In the present case, the periosteum and the cortical layer of the tibia had to be removed since the tumor reached the deeper layers. Thus, the wound basis was the bone which is not ideal for the survival of a skin graft and even if the graft survives, the increased risk of ulceration shall be considered. Accordingly, the partial transposition of the anterior tibialis muscle was chosen in order to provide a good basis for the skin graft and to cover the bone. In the *Mathes & Nahai* classification, tibialis anterior muscle flap belongs to type IV, i.e. it is characterized by segmental vascular pattern (**Wei & Mardini, 2009**). Utilization of the anterior tibialis muscle as a musculocutaneous flap results in a large defect and a serious loss of function. However, use of the muscle itself leads only to a moderate weakness in the movements of the ankle (**Sood et al., 2003**) and if the lateral or the medial part is applied alone, the function remains intact and the muscle part can freely be rotated (**Chang et al., 1997**).

Deep defects of the anterior lower leg (affecting the cortical layer of tibia), that may originate in e.g. burns and traumatic injuries, can be covered by partial rotation of the anterior tibialis muscle flap (**Chang et al., 1997**). This technique is safe, reliable, not difficult and is not accompanied by loss of function. The present case confirms that a deep defect after the removal of an extended tumor over the tibia can effectively be reconstructed with a combination of the anterior tibialis turnover flap and a skin graft.

It seemed to be a technically difficult problem to find an optimal covering option for the deep lesion in the cervical region, as well. Decades ago, the trapezius myocutaneous flap was described. This flap is characterized by intact transverse cervical artery and paraspinous attachment of the trapezius (**Demergasso & Piazza, 1979**). Moreover, the application of extended LTMF for reconstructing cutaneous defects and also for subcutaneous augmentation of the face has been reported (**Baek et al., 1980**). Useful data were then published on the vascular anatomy and clinical application of the extended LTMF based on the dorsal scapular arterial system (**Tan & Tan, 2000**) and it was suggested to use the extended vertical trapezius myocutaneous flap based solely on the transverse cervical artery in order to save failed previous flaps and recurrent tumors (**Ugurlu et al., 2004**).

The superior trapezius flap receives its blood supply from the occipital artery and its paraspinous perforators, while in case of the lateral and lower island trapezius myocutaneous flaps the branches of the transverse cervical artery play a pivotal role (**Tan & Tan, 2000;**

Chen et al., 2009). Lower trapezius myocutaneous flap shall not be used when there is suspicion of trauma to the descending branch of the transverse cervical artery (**Stillaert & Van Landuyt, 2009**). An extension of the flap is incorporated that runs obliquely from the tip of the scapula towards the midaxillary line (**Tan & Tan, 2000**). The cornerstone of this technique is the vascular supply from the dorsal scapular artery, which originates either directly from the subclavian artery as an independent branch or from the trunk of the transverse cervical artery (**Tan & Tan, 2000; Chen et al., 2009; Stillaert & Van Landuyt, 2009**).

As compared to the LDMF, it can be stated that the latissimus dorsi muscle offers a limited axis of rotation, its pedicle has an axillary origin and frequently there is a need for a split thickness skin graft at the donor site because it may be difficult to achieve a tension-free closure of the wound during the management of extensive defects (**Urken et al., 1991; Papadas et al., 2005; Datta et al., 2009; Stillaert & Van Landuyt, 2009**).

The extended LTMF flaps are characterized by many advantages: the donor site can usually be closed easily, leading to a tension-free but rather long scar; the flap fills the defect created by the neck dissection and covers the cervical vessels, preventing damage of the vessels; and the long, thin musculocutaneous pedicle allows for easy transfer of the island flap, which can even be tunneled into a defect if necessary (**Urken et al., 1991; Ugurlu et al., 2004; Papadas et al., 2005; Stillaert & Van Landuyt, 2009**).

As concerns LDMF (which was our first solution), it was found that tunneling of the flap may be difficult. However, the supplying vessels of the trapezius muscle and the muscle itself remained intact therefore it was possible to use this flap for the secondary reconstruction (**Ugurlu et al., 2004**).

Another complex question was the reconstruction of the lips after a severe trauma. Lips play a pivotal role in the body image and have other important functions, as well. They are necessary for speech, non-verbal communication, and social interactions. Further, they also determine the esthetic appearance of the face. These complex functions require normal morphology (consisting of skin, musculature and mucous membrane), as well as intact motor- and sensory innervation. Thus, reconstruction of large injuries is a major challenge. Although direct closure is possible if one-third of the lip is missing, bigger defects need to be closed with local or distant flaps. The choice of method often depends on the extent of the defect. If the size of the defect is up to 70-80% of the lip, it can usually be repaired by using the remaining lip tissue. In case of larger defects additional tissue is required. Several methods are known for the reconstruction of upper lip defects. *Abbe*'s cross-lip flap, the *Estlander* and *Gilles* flaps

and their modifications, the Karapandzic flap, Kazanjian's lower facial flap are the best known methods for lip reconstruction (**Kazanjian & Roopenian, 1954; Karapandzic, 1974; Smith et al., 1982; McGregor & McGregor, 1986; Baker & Svanson, 1995**). When preparing cross-lip flaps, it is important to retain their nourishing arteries and hereby viability. The neurovascular myocutaneous flap described by *Kazanjian* is also a safe and accepted technique both for lower- and upper lip reconstruction. Contrary to other flaps, motor- and sensory innervation can be saved, and intersection of orbicular oris muscle can be avoided. Hence, sphincter denervation and atrophy is minimized, sensory- and motor functions are improved.

Moreover, this method is free of problems characterizing distant and microvascular flaps. *Kazanjian*'s flap harmonizes with the adjacent tissue and the new sphincter functions well. Combination of this technique with *Abbe*'s flap seems to be an excellent method to restore subtotal or total loss of lips.

Our patient has lost approximately 75% of the total volume of the upper lip due to the above described injury. In this sense, this case was surgically more challenging than larger injuries (like complete degloving) without significant tissue loss (**Catunda et al., 2012**). Although the reconstruction resulted in a slight decrease in the size of the orifice, the subsequent mucosa plasty led to a functionally and esthetically acceptable size. Oral movements, liprounding, speaking, eating and use of cutlery were fully possible. No complication in wound healing was observed during the postoperative period. The satisfactory cosmetic results allowed the patient's social reintegration. Lip reconstruction may be very difficult when patients underwent serious injuries of this region. For such cases, application of combined flaps may be considered because it seems to be a good choice which can have functionally and esthetically acceptable outcome.

Salvage of exposed implant is a great challenge in reconstructive surgery. Different factors may lead to implant protrusion e.g. errors in planning, thermal and mechanic injuries as surgical complications, smoking in the patient's history or previous radiotherapy. In our Institution, the ration of local complications after immediate breast reconstruction with implant comes to 11.6% of the cases. Traditional therapeutic approaches involve antibiotics, drainage, rinsing, capsulotomy, change of the device and primary closing of the wound after excision of the necrotic tissue (**Weber & Hentz, 1986; Planas et al., 1995; Persichetti et al., 2014**). However, they may also fail in cases of decreased tissue viability and irradiation. Implant protrusion is a gradual process and its later stages require a more invasive surgical intervention (**Fodor et al., 2003**). Several techniques are used for the covering of implants

e.g. deepithelialized skin (**Hammond et al., 2002; Ibrahim et al., 2012**), abdominal fascial flaps (**Isken et al., 2009**), acellular dermal matrix (ADM) (**Breunig & Colwell 2007; Nahabedian, 2009; Salzberg et al., 2011; Sbitany & Langstein, 2011**), autologous dermal graft (**Hudson et al., 2012**) and polyglycol mesh (**Mofid et al., 2012**). If signs of inflammation are not detected, latissimus dorsi flaps or local perforator flap can be applied (**Unal et al., 2011; Cagli et al., 2012**). In case of inflammation, the implant should be removed and later reconstruction or implantation of autologous fat can be chosen (**Spear et al., 2004**). However, these procedures may have disadvantages. ADM is expensive (**Jansen & Macadam, 2011**) and its application can be accompanied by seroma and infection (**Parks et al., 2012; Persichetti et al., 2014**). Furthermore, patients often refuse more radical surgical therapies (e.g. different flap techniques) due to the esthetic and functional damage to the donor site and they prefer less radical methods.

Capsule flaps provide a less invasive and cost-effective solution. In animal experiments, capsules were used to support the survival of transplanted dermal grafts (**Heymans et al., 1993**) as random (**Bengston et al., 1993**) or axial flaps (**Cariou et al., 1991; Schuringa et al., 2007**). It has also been shown that capsule flaps are suitable for the correction of postimplant breast rippling (**Massiha, 2002**) and contour deformities of the breast (**Persichetti et al., 2014**). Capsule flap can be obtained from the anterior surface and also from the tissue layer adjacent to the chest wall. Subject to localization of the defect and viability of the tissue, superior, inferior, medial or lateral flaps can be applied (**Cariou et al., 1991; Bengston et al., 1993; Heymans et al., 1993; Schuringa et al., 2007**).

Since sufficient blood supply is a cornerstone of tissue survival, several investigations have focused on the vascularity of capsule flaps. Some evidence has already indicated the appropriate blood supply of the capsule flap. According to clinical observation, bleeding of the edges when tailoring the flap indicates a good vascularization (**Persichetti et al., 2014**). Moreover, a histological examination found angiogenesis in non-expanded capsules from the 4^{th} postoperative week on, and the peak of this process was achieved by the 8^{th} week (**Thomson, 1973**). It is a further question whether expansion of the flap influences the vascularization and perfusion of the tissue. In expanded flaps, vessels of higher volume were found as compared to primer flaps, but no statistically significant difference was detected in terms of vessel density (**Bengston et al., 1993**). In another study, the radioactive microsphere technique did not reveal difference between the blood flow of expanded and non-expanded flaps (**Sasaki & Pang, 1984**).

Our results, in accordance with findings in the literature, show that capsule flaps provide a well-vascularized layer which prevents protrusion of the implant and decreases tension, thereby promoting wound healing and reduced risk of inflammation and superinfection. An important novel aspect of our study is the *in vivo* determination of microcirculatory status during the operation. Laser Doppler flowmetry was chosen for the measurements since it is an accurate and reliable method for assessing microcirculatory function (**Swiontkowski, 1991**).
Our in vivo finding has confirmed that surgical stress does not decrease the blood supply of flaps which then provided an optimal ground for the healing process.
Thus, the capsule flap seems to be appropriate for salvage of exposed implants and for enhancement of implant cover in case of thin and injured tissue. Capsule flaps are reliable, not difficult to prepare, have good circulation and may therefore play an important role in reconstructive surgery of the breast. On the other hand, capsule flaps shall not be applied in case of serious inflammation and larger tissue defect. Moreover, the number of published cases of breast reconstruction with capsule flaps is relatively low (**Persichetti et al., 2014**). Hence, more experience with the technique may be needed before widespread adaptation.
After reconstructive interactions, it is an important question how to retain the achieved esthetic results and to avoid complications. Subcutaneous pedicle flaps often develop trapdoor type deformity, with several possible causes (**Clodius, 2002**). Any excessive subcutaneous fat might not play a role, as defatting did not lead to improvement. Owing to its rarity, hypertrophy of the scar might not cause trapdoor deformity (**Clodius, 2002**). Contracture of the scar contributes to impaired microcirculation: Invasive methods to decrease scar contracture may cause a noticeable improvement (**Clodius, 2002**). Tissue undermining may prevent trapdoor formation in transposition flaps in animal models (**Kaufman et al., 1993**). The MLD is a method of choice to treat head and neck swellings (**Einfeldt et al., 1986**) and causes cosmetologic improvement (**Földi & Kubik, 2000**). Furthermore, MLD improves microcirculation and tissue perfusion, reduces lymph stasis, increases protein resorption and softens fibrosis and scars. Nevertheless, optimal choice of surgical technique may also contribute to the prevention of trapdoor deformity. Our working group has described a combined subcutaneous and cutaneous pedicled advancement nasolabial flap which allows safe and esthetically correct reconstruction of alar- and perialar defects with very low complication rate. (The manuscript describing the technique has been submitted for publication.)
In conclusion, careful defect analysis and thorough preoperative design provide possibility for a reconstruction which is esthetically and functionally satisfactory. In several cases,

combination of different techniques and individualized therapy seem to be necessary for a good result. The continuous evolution of flap techniques may broaden the toolbox of treatment strategies and hereby contribute to a better healing of complicated tissue defects.

6. SUMMARY AND NEW FINDINGS

Our study was focused on the treatment of various difficult-to-heal injuries by means of special flaps. Furthermore, the efficacy of MLD in trapdoor deformity was examined. We have demonstrated that such carefully designed, individual therapeutic approaches result in satisfactory healing.

- We have shown that the tibialis anterior turnover flap together with skin graft can be successfully used for the coverage of extended lesions in the anterior tibial region even if they affect the cortical layer of the bone.
- LTMF is a useful possibility for the reconstruction of deep lateral neck defects and can be used when other flaps fail.
- *Kazanjian*'s flap in combination with *Abbe*'s flap can be an excellent method to restore subtotal or total loss of lips.
- According to our results, capsule flaps are well-vascularized and have sufficient perfusion therefore they are appropriate for the salvage of exposed breast implants and for enhancement of implant cover in the case of thin and injured tissue.
- MLD leads to a significant cosmetologic improvement in case of trapdoor deformity.

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APPENDIX