Journal of Plastic, Reconstructive & Aesthetic Surgery (2008) **61**, 282–288

JPRAS
An International Journal of Surgical Reconstruction
www.JPRASurg.com

A study of perfusion of the distal free-TRAM flap using laser Doppler flowmetry

Darren I. Booi*, Iris B.J.G. Debats, Willy D. Boeckx, Rene R.W.J. van der Hulst

Maastricht University Hospital, Department of Plastic, Reconstructive and Hand Surgery, P.O. Box 5800, 6202 AZ Maastricht, The Netherlands

Received 12 July 2006; accepted 24 July 2007

KEYWORDS
Free TRAM flap;
Microcirculation;
Laser Doppler flowmetry;
Choke vessels

Summary The aim of this study was to characterise microcirculatory changes in the distal part of a flap and to evaluate whether measurement of the microcirculation may predict flap complications (FC).

In this prospective study, 30 patients undergoing a delayed breast reconstruction were included. Perioperative data were recorded and with the laser Doppler flowmetry (LDF; Perimed®) blood flow was recorded in the central part (zone I) and the distal part (zone IV) of the flap.

A lower blood flow was observed in zone IV of patients with flap complications compared to patients without flap complications ($P = 0.013$). In addition, LDF demonstrated different flow trends in zone I compared to zone IV indicating a delayed opening of the choke vessels connecting the angiosomes in the distal part of the flap.

The LDF has proven to be a useful investigative tool to monitor microcirculatory changes. In future studies it will be used to evaluate interventions aimed at decreasing distal ischaemia and reducing flap complications.

Necrosis of skin flaps, either partial or complete, is a major complication in reconstructive surgery. Increased knowledge of anatomy, physiology and improved surgical technique have changed flap surgery.[1–4] Due to these advances, success rates of microsurgical reconstruction are now well above 90%. However, despite careful trimming of a free flap in order to exclude a questionable part of the flap with poor blood flow (usually minor), complications with flap viability after free tissue transfer can still occur. These complications occur despite successful anastomosis and therefore must be a result of poor blood flow within the flap itself. In addition, random pattern flaps are still widely and regularly used in many (plastic-) surgical procedures such as abdominoplasty, mammaplasty and skin flaps after mastectomy. All these procedures may be complicated by

* Corresponding author. Tel.: +31 43 3875496; fax: +31 43 3875485.
E-mail address: darrenbooi@gmail.com (D.I. Booi).

1748-6815/$ - see front matter © 2007 British Association of Plastic, Reconstructive and Aesthetic Surgeons. Published by Elsevier Ltd. All rights reserved.
doi:10.1016/j.bjps.2007.07.014

insufficient blood flow in the flaps.[5–9] The purpose of this study was to investigate the microcirculation changes in the peri- and postoperative period in the proximal as well as the distal part (zone IV) of the free flap.

In our experience the TRAM flap has a high rate of flap complications (FC) such as fat necrosis and partial flap loss (PFL) if zone IV is incorporated in the reconstructed breast. The low perfusion of zone IV and clinical experience has led some surgeons to systematically discard zone IV for reconstruction. However, recent studies still show the use of zone IV.[10,11] One reason for this might be to achieve adequate volume and projection.

Inevitable changes in blood supply to the free flap are due to changes in vascularisation, denervation and ischaemia-reperfusion injury. This leads to complex interactive changes in vascular reactivity which occur at a neural, humoral, physical and metabolic level during flap harvest, transfer and in the post transfer period.[12]

Macroscopic changes in the blood flow in recipient and donor vessels that occur after free flaps have shown that there is an increase in postoperative flow.[13–15] In addition, arterial flow does not appear to be dependent on the chosen recipient vessel, but mainly on the vascular resistance in the flap.[15,16]

The vascular resistance in the flap is controlled by the smaller vessels within the flap itself (arterioles). However, little data are available on the microcirculatory changes in the various parts of the flap during surgery and especially in the following acclimatisation period. Some centres have used measurement of microcirculation with variable success to monitor the free flap postoperatively. In these studies only the (central) proximal part of the flap was monitored.[17–19] In two previous studies by Tuominen et al.[20] and Hallock[21] microcirculation was assessed during the operation. The studies revealed the deep inferior epigastric artery as the dominant source of blood supply of the TRAM flap over the superior inferior epigastric artery and the superficial epigastric artery. In both studies the differences in microcirculation during surgery in the proximal (zone I) and the distal part (zone IV) have been measured. However, the expected adaptations of the microcirculation in the days after surgery have not yet been investigated. The purpose of this study was to monitor the microcirculation in the peri- and postoperative period in the proximal part (zone I) and the distal part (zone IV) of the free TRAM flap.

Patients and methods

We prospectively evaluated 30 patients in this clinical study. The institutional ethical committee of the Maastricht University Hospital approved the study protocol. Written informed consent was obtained from all patients. Exclusion criteria were a lower vertical laparotomy scar and a disproportional abdominal mass compared to the volume needed for breast reconstruction. These patients were excluded because the blood flow measurement location was expected to be discarded (medial border of zone IV). In addition only patients with a secondary breast reconstruction with no surplus of skin at the recipient site were included. Trimming of the flap started with removal of zone IV beyond the measurement site of zone IV. If not needed distal parts to the location of the perforator vessels of zones III, II and I were also discarded. These steps ensured the use of the skin tissue of the flap and preservation of the measurement sites in zone I and the medial border of zone IV. As a result all patients who were included in the study had both measurement sites intact for the duration of the study (Fig. 1). Flap blood flow zones were named in accordance with our own clinical experience and recent literature with zones I and II on the ipsilateral side of donor vessels and zones III and IV on the contralateral side.[22]

Operations were performed by experienced plastic surgeons. The muscle-sparing free TRAM flap was used in all patients for breast reconstruction; with this procedure a small medial part of the rectus abdominis was harvested along with several lateral (two to three) and medial (one to two) perforators.[23] In all patients the internal mammary vessels were used for the anastomosis.

Relative risk factors were not considered as exclusion criteria. Incidence of various risk factors included in the study was: smoking (8/30; 27%), obesity defined as a BMI equal to or greater than 28 (9/30; 30%), chest wall irradiations (12/30; 40%) and chemotherapy (23/30; 77%). Flap characteristics, e.g. flap weight, reconstructed breast weight and ischaemia period were also recorded. In addition, influencing factors on blood flow such as haemodynamics, room, patient and flap temperature were analysed. Fluid management and haematocrit levels were analysed, due to the possible effect of haemodilution on blood viscosity and blood flow. Flap complications (FC) were carefully recorded according to the definition used (Table 1).

Cutaneous microcirculatory blood flow was measured using the Periflux 5000 system (Perimed®). This is a reliable

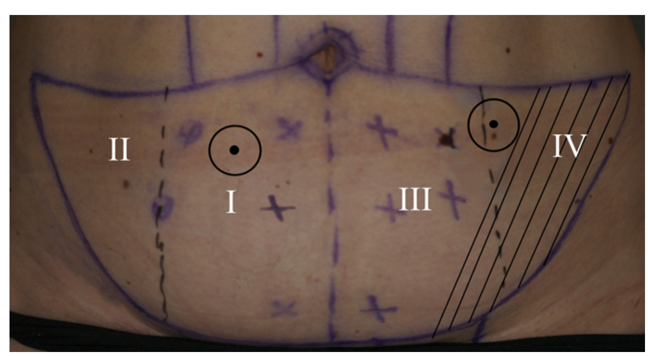

Figure 1 Zone classification and LDF measurement sites. I–IV = Blood flow zones. ⊙ = Laser Doppler flowmetry sites. Black dots in the centre of the circle represent the blood flow measurement sites in zones I and IV. Ipsilateral to the vascular pedicle, the LDF probe holder in zone I is sutured between the medial and lateral row of the perforators, whereas the second holder is sutured at the medial border in zone IV. The shaded area represents the part of the flap (zones III and IV) which is usually discarded. If needed, distal parts to the perforator vessels were also discarded in zone II and zone I. This method ensured a measurement location in zone I and zone IV.

Table 1 Definition and abbreviations used for flap complications

1	Fat necrosis (FN)	A palpable hard mass in the reconstructed breast without loss of cutaneous tissue.
2	PFL < 5% (PFL < 5)	Loss of a cutaneous portion of the flap with or without fat necrosis. Skin necrosis is less than 5% of the skin surface used in the reconstructed breast. Can be treated conservatively without adverse outcome.
3	PFL 5–10% (PFL 5–10)	Same as PFL < 5 but with 5–10% loss of skin surface. Surgical intervention was necessary for a good aesthetic outcome.
4	PFL > 10% (PFL > 10)	Same as PFL < 5 but with more than 10% loss of skin surface. Surgical intervention with significant reduction in reconstructed breast and contralateral breast in order to achieve a good aesthetic outcome.
5	Flap complications (FC)	Flap complications (FC). All the above with either FN and/or a degree of PFL.

non-invasive method for evaluating microcirculatory blood flow and has been described previously.[17–20,24,25] Laser Doppler flow measurements were performed intermittently for 5 days simultaneously in zones I and IV with the Periflux 5000 system (Table 2). Room temperature was standardised during the first 24 h of the study (operating theatre and recovery room). All measurements were performed at absolute rest and for a period of 3 min. Probe holders were sutured to the flap to ensure identical measurement sites during the study. The probe of zone I was placed between the lateral and medial row of perforators, whereas the second probe was placed at the medial border in zone IV (Fig. 1). Laser Doppler flowmetry (LDF) was first measured during surgery with the flap on its pedicle. This was performed after the muscle-sparing TRAM flap was completely dissected and solely connected to the vascular pedicle (with a standard acclimatisation period of 10 min). At this point the entire flap is supplied by the deep inferior epigastric vessels which lead to the categorisation of the flap zone (I–IV). After successful transplantation, LDF was measured hourly up to 5 hours after reperfusion. From the first to the fourth postoperative day LDF was measured three times a day (Table 2).

All data are presented as mean values ± SD. The SPSS program was used for statistical analysis. Repeated measures ANOVA was used for analysis of all the repeated measurements. Mann-Whitney U test was used for analysis of the quantitative parameters. Fisher's exact test was used for categorical data. A P value < 0.05 (two-tailed) was considered statistically significant.

Table 2 Materials and methods

	0–24 h (day 0)		Day +1	Day +2	Day +3	Day +4
	Surgery	Recovery				
Blood pressure	Every 15 min	Hourly	–	–	–	–
Heart rate	Every 15 min	Hourly	–	–	–	–
Temperature (patient)	Every 15 min	Hourly	Hourly	Every other hour	–	–
Temperature(flap)	–	Hourly	Hourly	Every other hour	–	–
Temperature (environment)	Controlled (21 °C)	Controlled (21 °C)	Not controlled	Not controlled	Not controlled	Not controlled
Standard controls[a]	–	Hourly	Hourly	Every other hour	Every 4 h	Four times a day
Laser Doppler flowmetry	FOP,[b] ischaemia and 1 h after reperfusion	At 2, 3, 4 and 5 h after reperfusion	Three times a day (at 8:00, 12:00, 17:00)[c]	Three times a day (at 8:00, 12:00, 17:00)[c]	Three times a day (at 8:00, 12:00, 17:00)[c]	Three times a day (at 8:00, 12:00, 17:00)[c]
Vasoactive medication	Similar use	Not used	Not used	Not used	Not used	Not used

[a] Standard controls include: Ultrasound Doppler of perforators within the flap, skin colour and capillary refill.
[b] FOP = LDF measurement prior to division of the vascular pedicle. At this point the entire flap is supplied by the deep inferior epigastric vessels which lead to the categorisation of the flap zone (I–IV).
[c] Statistical analysis was performed with these separate measurements. In graphs mean daily values are shown in order to facilitate the data overview.

Results

Mean age at the time of operation was 47.7 (± 7.7) years and mean BMI was 26.1 (± 3.4) (Table 2). After adaptation of the abdominal flap, the mean weight of flap used for breast reconstruction was 800 (± 221) g. The measurement location of both measurement sites remained in the reconstructed breast in all patients. An average of 85% (± 14%) of the original abdominal flap weight was used for breast reconstruction. One hundred per cent of the flap was used for reconstruction in five cases (two of these patients experienced PFL). Mean flap ischaemia time was 54 (± 22) min (Table 3). The number of perforators included in the muscle-sparing free TRAM flap ranged from two to four. Muscle lateral to the lateral perforators was left intact.

Out of 30 patients 11 experienced FC all of which were located in zones III/ IV (11/30; 37%). Two patients had PFL > 10% (in zone III and IV) and four patients had PFL 5–10% (only zone IV) (Table 4). These patients were planned for acute debridement and symmetrisation shortly after the first procedure. One of the patients with PFL > 10% needed a split skin graft (SSG) in order to close the partial defect and was considered to have a poor result. Five patients had PFL< 5% (in zone IV) and were treated conservatively and were planned, with the other patients without FC, to undergo the symmetrisation procedures ± 3 months after the breast reconstruction. A final good aesthetic result was obtained in all but the one patient who required the SSG to cover the partial defect (96%). Procedures performed to achieve final satisfactory aesthetic results were predominantly ptosis correction of the contralateral breast and if needed scar revision of the reconstructed breast in some patients.

Risk factors included in the analysis were obesity (defined as BMI > 28), smoking, radiotherapy, chemotherapy, and high flap weight (Table 3). Confirming previous reports, smoking was found to be a significant risk factor for the development of FC ($P = 0.028$). Flap weight was somewhat higher in patients with FC, although not significant. Analysis of BMI and percentage of the abdominal flap (FWU) used for reconstruction revealed no significant differences. Analysis of the other possible influencing risk factors on the occurrence of FC revealed no statistical difference in this study (Table 4).

No significant differences were noted in the haemodynamics (blood pressure and heart rate) and room temperature (measured every 15 min) during the first 24 h after surgery when comparing patients with FC compared to those without FC (data not shown). After reconstruction, the flaps with FC seemed to have a lower skin flap temperature (Fig. 2; $P = 0.151$).

LDF measurements prior to division of the pedicle revealed higher blood flow in zone I compared to zone IV ($P < 0.000$). Our study revealed different microcirculatory blood flow patterns in the first postoperative days when comparing zone I to zone IV. Near ischaemia LDF values were measured in zone IV during the first 48 h. Only during the second and third day of the study these values increased steeply to near zone I blood flow values (Fig. 3). In some patients LDF values in zone IV even surpassed those measured in zone I in the latter part of the study (data not shown).

LDF measurements prior to division of the pedicle showed a lower blood flow in both measurement sites when comparing patients with FC to patients without FC, however, this was not statistically significant (Figs. 4 and 5). During the initial 5 hours after reperfusion the mean LDF measurements in the flaps with FC demonstrated a lower increase of blood flow in zone IV (Fig. 5).

In addition, LDF was particularly accurate in detecting arterial occlusion at a very early stage. In two patients, LDF showed ischaemic values in zone I (three to four arbitrary units) at 1 h after reperfusion. Patients were still in the operating theatre and the anastomosis was re-evaluated and revealed in both cases a twist of the artery. After repositioning the artery, the blood flow was restored and there was no need to revise the anastomosis in both cases.

Discussion

The LDF is presented as a valuable and non-invasive research tool to investigate ischaemia-related changes that occur in the distal part of the flap in a clinical setting.

A significant lower blood flow was measured in zone IV during the first 5 hours after reperfusion in patients with FC (Fig. 5). The patients with FC also appeared to have a lower flap temperature compared to those without (Fig. 2). This slightly lower skin flap temperature is probably a consequence of the lower perfusion which was measured with LDF. At this stage (first 5 h after reperfusion) clinical signs were not visible at the measurement sites.

Table 3 Preoperative risk factors and patient demographics

	All patients ($n = 30$)	FC ($n = 11$)	No FC ($n = 19$)	P value
Smoking[a]	8 (27%)	6 (55%)	2 (11%)	0.028
Radiation[a]	12 (40%)	7 (37%)	5 (45%)	0.119
Chemotherapy[a]	23 (70%)	9(82%)	14 (74%)	1.000
Age (years)[b,c]	47 (±8)	47 (±8)	47 (±8)	0.914
BMI[b,c]	26.1 (±3.4)	27.0 (±2.4)	25.8 (±3.8)	0.349
Obesity[a,d]	9 (30%)	3 (27%)	6 (32%)	1.000
Length of stay (days)[b,c]	5.8 (±1.2)	6.4 (±1.7)	5.5 (±0.6)	0.196

[a] Statistical analysis was performed with the Fisher's exact test.
[b] Mean ± SD.
[c] Mann-Whitney U test (all P values are 2-tailed).
[d] BMI greater than 28 was defined as obese.

Table 4 Flap datasheet (means ± SD)

	All patients ($n = 30$)	FC ($n = 11$)	No FC ($n = 19$)	*P* value
Flap weight (g)[a,b]	801 ± 241	905 ± 246	741 ± 222	0.081
FWU (%)[b,c]	86 ± 14	86 ± 15	86 ± 13	0.892
Medial border of zone IV	intact	intact	intact	—
Use of abdominal flap (> 95%)[d]	8 (27%)	3 (10%)	5 (17%)	1.000
Ischaemia period (min)[b]	54 ± 22	50 ± 16	57 ± 24	0.485

[a] Flap weight used for breast reconstruction.
[b] Mann-Whitney U test was used for statistical analysis.
[c] FWU, percentage of abdominal flap weight used for reconstruction.
[d] Fisher exact test used (all *P* values are 2-tailed).

One point measurement analysis during surgery (LDF prior to division of its pedicle and 1 h after reperfusion) revealed no significant differences between patients with FC compared to those without FC. Therefore the LDF can be used as an investigative tool and not as a tool to assist in the trimming of questionable parts of a flap during surgery. The probable reason for this is that the flap is still in its acclimatisation process during the course of the surgery. Nevertheless, the LDF proved to be a valuable method for monitoring the flap postoperatively for arterial occlusion due to the instant drop in LDF values, as was shown in two cases in this study.

In an investigative setting the LDF was a valuable and non-invasive tool to investigate ischaemia-related changes that occurred in zones I and IV. Compared to zone I the slow initial increase in microcirculatory blood flow in zone IV was followed by the steep increase on the second/third day (Fig. 4).

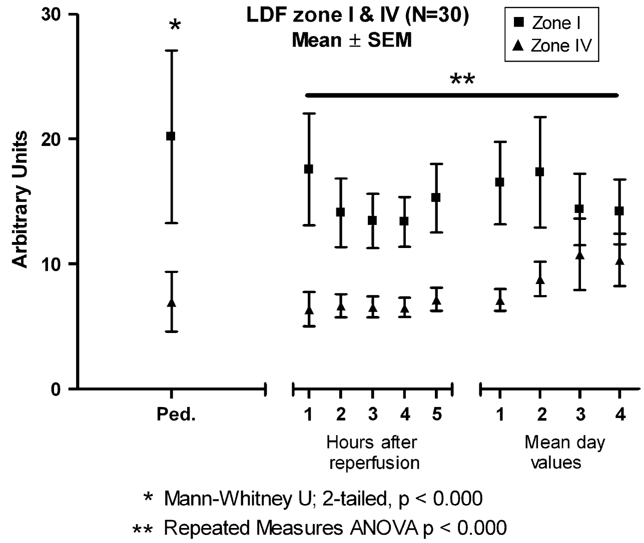

Figure 3 Blood flow trends in zones I and III/ IV. A higher blood flow was seen in zone I during the course of the study. In zone III/IV a slow increase was observed from ischaemia values. A steep increase in blood flow was seen in almost all patients on days 2–3.

The low blood flow values in zone IV during the first measurements can be explained by Heitmann's[26] fresh cadaver perfusion study where little or no staining of zone IV was found. Clinical perfusion studies by Holm et al.[22] also confirmed the poor perfusion of zone IV during the operation. Both studies demonstrated poor arterial blood flow of zone IV through the deep inferior epigastric artery. An even larger obstacle may be the insufficient venous drainage of zone IV.[27] These studies explain why survival of the zone IV portion of such flaps is so variable and unpredictable. The probable reason for this is that with the TRAM or DIEP flap with zone IV more than one adjacent angiosome

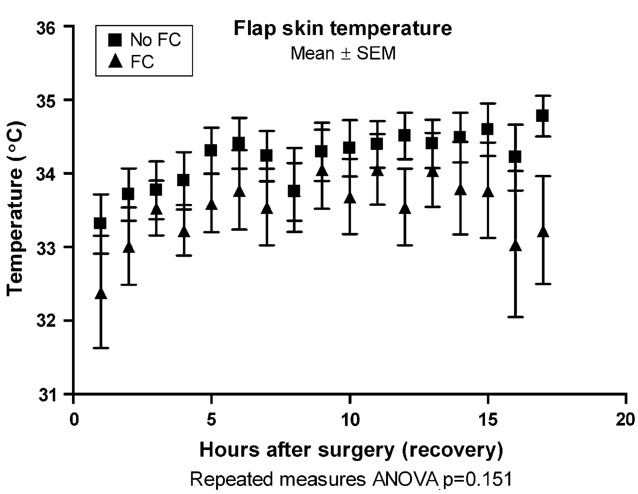

Figure 2 Flap skin temperature. After reconstruction, the flaps with FC seemed to have a lower skin flap temperature (not significant; $P = 0.151$). This slightly lower skin flap temperature is probably due to a lower perfusion which is correlated with LDF measurements and flap complications.

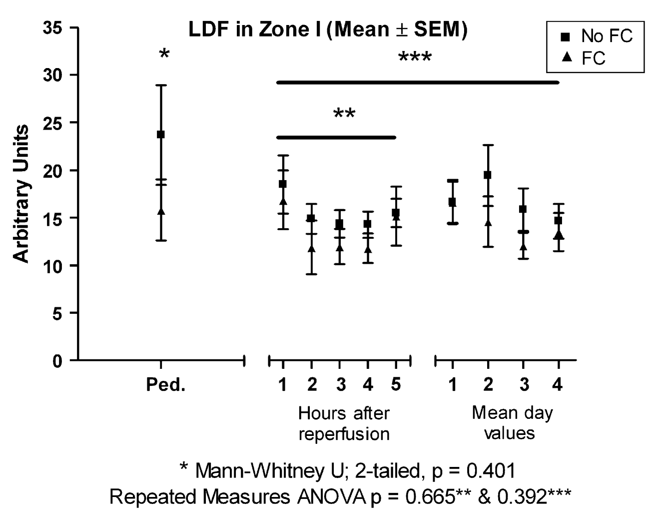

Figure 4 Blood flow in zone I. A lower blood flow was seen in zone I of patients with FC compared to those without FC. However, this was not significant ($P = 0.401$). The following measurements in zone I revealed no differences.

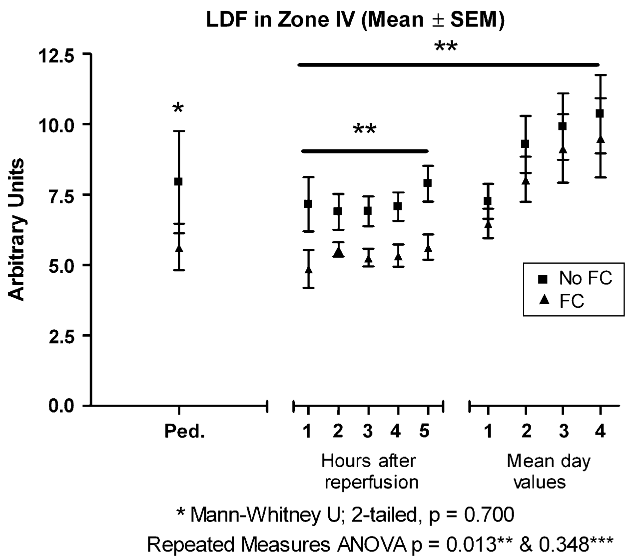

Figure 5 Lower blood flow 1–5 h after reperfusion precedes FC. In zone IV a lower blood flow was measured during the first 5 hours after reperfusion ($P = 0.013$). This lower blood flow was measured before FC was clinically evident. The increase in blood flow on the second to third day was observed only in zone IV. This indicates a delayed opening of choke vessels.

of the selected deep inferior epigastric artery is included. Experimental and clinical studies have shown that when a flap is based on one artery, the anatomic territory of the adjacent artery can safely be included and that necrosis tends to occur if tissue is included beyond this territory.[28,29] Blood flow in distal part of a flap, such as zone IV in the free TRAM flap, becomes dependent on connecting arterial and vein branches between the angiosomes.

Our study shows poor perfusion of zone IV demonstrated by the low-ischaemic LDF values measured in zone IV during surgery (Fig. 5). However all patients, with the exception of one with FC > 10%, showed an increase in blood flow through zone IV with the steepest increase on the second to third day (Fig. 3). This phenomenon cannot be explained by angiogenesis due to the short time elapse. It can only be explained by a dilatation or opening of existing (choke) vessels within the flap itself.[30,31] This confirms the results of animal studies in which the progressive dilatation was shown, which was seen maximally at the level of the choke vessels. An accelerated rate of choke vessel dilatation was consistently seen between 48 and 72 h after surgery in these studies.[30,32]

Therefore the viability of zone IV depends on the number and dilatation time of the choke vessels. The dilatation of these choke vessels may be a target for possible interventions.[31] Stimulating nitric oxide (a potent vasodilatator) availability has been shown to increase flap survival.[33–35] Another possible mechanism may be to protect the tissue at risk until blood flow in the flap is sufficient to sustain viability.[36] However, clinical studies have not been performed so far.

The clinical relevance of these findings is that zone IV may be included in reconstructive surgery; however, patients' risk factors such as smoking should be noted. Smoking may impair the dilatation of the choke vessels, and proved to be a significant risk factor in this study (Table 4). Recent studies show that zone IV can be included to a reliable degree in selected patients.[10,11] This shows that in selected (slim) patients the whole lower abdomen may be used and therefore keeping autologous reconstruction with sufficient volume safely possible.

However, in a patient with risk factors, a smaller reconstructive breast size with removal of zone IV in combination with breast reduction to the contralateral side is the best method to reduce complications and morbidity. In addition, in our experience with DIEP flaps, recently introduced in our clinic, even more careful trimming of the flap is necessary to avoid complications. As a result zone IV in DIEP flaps is systematically discarded at our institution. Even when zone IV is completely removed small complications such as PFL and FN can still occur at the distal part of the flap.

Although distal ischaemia and subsequent partial flap loss are mainly described in the breast reconstruction studies (using either TRAM or DIEP flaps), they may also occur in other free flap types regardless of tissue type or in local transposition flaps (axial or random pattern). The increased knowledge of regional blood supply has significantly improved flap design and flap choice which we use in a clinical setting. However, despite the optimised flap design and high success rates, distal ischaemia will always occur to some extent in either free or pedicled flaps. This is caused by factors that are inevitable due to flap surgery. This article is yet another piece in the understanding of flap physiology. Nevertheless, further basic research in improving the distal blood flow and even further improving the outcome is necessary. Our objective must not merely be survival rates of >95% of (free) flaps, but also to increase the blood flow in the whole flap and thereby further reduce complications with flap surgery such as PFL or FN.

References

1. Kerrigan CL. Skin flap failure: pathophysiology. *Plast Reconstr Surg* 1983;**72**:766–77.
2. Kerrigan CL, Wizman P, Hjortdal VE, et al. Global flap ischemia: a comparison of arterial versus venous etiology. *Plast Reconstr Surg* 1994;**93**:1485–95 [discussion 1496–7].
3. Myers MB, Cherry G. Causes of necrosis in pedicle flaps. *Plast Reconstr Surg* 1968;**42**:43–50.
4. Taylor GI, Palmer JH. The vascular territories (angiosomes) of the body: experimental study and clinical applications. *Br J Plast Surg* 1987;**40**:113–41.
5. Chang RR, Mehrara BJ, Hu QY, et al. Reconstruction of complex oncologic chest wall defects: a 10-year experience. *Ann Plast Surg* 2004;**52**:471–9 [discussion 479].
6. Mansour KA, Thourani VH, Losken A, et al. Chest wall resections and reconstruction: a 25-year experience. *Ann Thorac Surg* 2002;**73**:1720–5 [discussion 1725–6].
7. Atterhem H, Holmner S, Janson PE. Reduction mammaplasty: symptoms, complications, and late results. A retrospective study on 242 patients. *Scand J Plast Reconstr Surg Hand Surg* 1998;**32**:281–6.
8. Cardenas-Camarena L. Aesthetic surgery of the thoracoabdominal area combining abdominoplasty and circumferential lipoplasty: 7 years' experience. *Plast Reconstr Surg* 2005;**116**: 881–90 [discussion 891–2].
9. Rainsbury RM. Skin-sparing mastectomy. *Br J Surg* 2006;**93**: 276–81.

10. Cheng MH, Robles JA, Gozel Ulusal B, et al. Reliability of zone IV in the deep inferior epigastric perforator flap: A single center's experience with 74 cases. *Breast* 2006;**15**:158—66.
11. Ulusal BG, Cheng MH, Wei FC, et al. Breast reconstruction using the entire transverse abdominal adipocutaneous flap based on unilateral superficial or deep inferior epigastric vessels. *Plast Reconstr Surg* 2006;**117**:1395—403 [discussion 1404—6].
12. Blondeel PN, Morris SF, Hallock GG, et al. *Perforator Flaps: Anatomy, Technique & Clinical Applications*. Chapter 5. 1st ed. USA: Quality Medical Publishing; 2005. p. 69—89.
13. Lorenzetti F, Ahovuo J, Suominen S, et al. Colour Doppler ultrasound evaluation of haemodynamic changes in free tram flaps and their donor sites. *Scand J Plast Reconstr Surg Hand Surg* 2002;**36**:202—6.
14. Lorenzetti F, Salmi A, Ahovuo J, et al. Postoperative changes in blood flow in free muscle flaps: a prospective study. *Microsurgery* 1999;**19**:196—9.
15. Lorenzetti F, Suominen S, Tukiainen E, et al. Evaluation of blood flow in free microvascular flaps. *J Reconstr Microsurg* 2001;**17**:163—7.
16. Lorenzetti F, Kuokkanen H, von Smitten K, et al. Intraoperative evaluation of blood flow in the internal mammary or thoracodorsal artery as a recipient vessel for a free TRAM flap. *Ann Plast Surg* 2001;**46**:590—3.
17. Heller L, Levin LS, Klitzman B. Laser Doppler flowmeter monitoring of free-tissue transfers: blood flow in normal and complicated cases. *Plast Reconstr Surg* 2001;**107**:1739—45.
18. Yuen JC, Feng Z. Monitoring free flaps using the laser Doppler flowmeter: five-year experience. *Plast Reconstr Surg* 2000; **105**:55—61.
19. Hovius SE, van Adrichem LN, Mulder HD, et al. The predictive value of the laser Doppler flowmeter for postoperative microvascular monitoring. *Ann Plast Surg* 1993;**31**:307—12.
20. Tuominen HP, Asko-Seljavaara S, Svartling NE. Cutaneous blood flow in the free TRAM flap. *Br J Plast Surg* 1993;**46**:665—9.
21. Hallock GG. Physiological studies using laser Doppler flowmetry to compare blood flow to the zones of the free TRAM flap. *Ann Plast Surg* 2001;**47**:229—33.
22. Holm C, Mayr M, Hofter E, et al. Perfusion zones of the DIEP flap revisited: a clinical study. *Plast Reconstr Surg* 2006;**117**:37—43.
23. Nahabedian MY, Tsangaris T, Momen B. Breast reconstruction with the DIEP flap or the muscle-sparing (MS-2) free TRAM flap: is there a difference? *Plast Reconstr Surg* 2005;**115**: 436—44 [discussion 445—6].
24. Place MJ, Witt P, Hendricks D. Cutaneous blood-flow patterns in free flaps determined by laser Doppler flowmetry. *J Reconstr Microsurg* 1996;**12**:355—8.
25. Svensson H, Holmberg J, Svedman P. Interpreting laser Doppler recordings from free flaps. *Scand J Plast Reconstr Surg Hand Surg* 1993;**27**:81—7.
26. Heitmann C, Felmerer G, Durmus C, et al. Anatomical features of perforator blood vessels in the deep inferior epigastric perforator flap. *Br J Plast Surg* 2000;**53**:205—8.
27. Blondeel PN, Arnstein M, Verstraete K, et al. Venous congestion and blood flow in free transverse rectus abdominis myocutaneous and deep inferior epigastric perforator flaps. *Plast Reconstr Surg* 2000;**106**:1295—9.
28. Callegari PR, Taylor GI, Caddy CM, et al. An anatomic review of the delay phenomenon: I. Experimental studies. *Plast Reconstr Surg* 1992;**89**:397—407 [discussion 417—8].
29. Taylor GI, Corlett RJ, Caddy CM, et al. An anatomic review of the delay phenomenon: II. Clinical applications. *Plast Reconstr Surg* 1992;**89**:408—16 [discussion 417—8].
30. Dhar SC, Taylor GI. The delay phenomenon: the story unfolds. *Plast Reconstr Surg* 1999;**104**:2079—91.
31. Pang CY, Forrest CR, Morris SF. Pharmacological augmentation of skin flap viability: a hypothesis to mimic the surgical delay phenomenon or a wishful thought. *Ann Plast Surg* 1989;**22**: 293—306.
32. Aydin MA, Mavili ME. Examining microcirculation improves the angiosome theory in explaining the delay phenomenon in a rabbit model. *J Reconstr Microsurg* 2003;**19**:187—94.
33. Cordeiro PG, Santamaria E, Hu QY. Use of a nitric oxide precursor to protect pig myocutaneous flaps from ischemia-reperfusion injury. *Plast Reconstr Surg* 1998;**102**:2040—8 [discussion 2049—51].
34. McDonald WS, Lo Jr TP, Thurmond M, et al. Role of nitric oxide in skin flap delay. *Plast Reconstr Surg* 2004;**113**:927—31.
35. Mittermayr R, Valentini D, Fitzal F, et al. Protective effect of a novel NO-donor on ischemia/reperfusion injury in a rat epigastric flap model. *Wound Repair Regen* 2003;**11**:3—10.
36. Harder Y, Contaldo C, Klenk J, et al. Improved skin flap survival after local heat preconditioning in pigs. *J Surg Res* 2004;**119**: 100—5.