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DIEP flap perfusion assessment using microdialysis versus Doppler ultrasonography: A comparative study

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Abstract

Background: The increasing number of buried free-tissue transfer procedures and the need for an objective method to evaluate vascular complications of free flaps has led to the development of new technologies. Microdialysis has been used to monitor free flaps using interstitial biological markers. Previous uses mainly focused on muscular flaps. Our aim is to compare external Doppler ultrasonography (EDU) evaluation versus microdialysis in the early follow-up of adipocutaneous flaps, and propose an efficient postoperative monitoring protocol.

Methods: We retrospectively assessed 68 consecutive DIEP flaps (50 patients) performed between January 2019 and March 2021. All flaps received standardized post-operative monitoring using clinical signs, EDU and microdialysis. Glucose and lactate concentrations were assessed using glucose <1 mmol/L and lactate >6 mmol/L as ischemic trend thresholds. We calculated Glucose/Lactate ratio as a new parameter for the assessment of flap viability.

Results: Among all the 68 flaps, two flaps returned to the operative theater when a combination of unsatisfactory microdialysis values and clinical/EDU signs identified vascular impairment; only one developed total flap necrosis. Reoperation rate was 2.94% with an overall flap success rate of 98.53%. External Doppler ultrasonography had 100% sensitivity and 82% specificity, while microdialysis had 100% sensitivity and 100% specificity.

Conclusions: Microdialysis values proved flap viability sooner than external Doppler ultrasonography, making it an excellent tool for post-operative monitoring. With the appropriate thresholds for glucose and lactate concentrations, and glucose/lactate ratio used as a new parameter, it can help potentially avoiding unnecessary re-explorations, and reducing flap ischemia times.

1 | INTRODUCTION

Free flap failure is a catastrophic event both the patient and the surgeon and it increases patient morbidity, length of hospital stay, and healthcare costs (Setälä et al., 2009). It occurs in 1%–15% of cases, with an average of 5% overall. (Bui et al., 2007; Kwok & Agarwal, 2017; Yu et al., 2009) Failure risk reaches its peek during the first 12–24 h, then decreases during the following 24–72 h, becoming minimal after 72 h. (Chao et al., 2013; Chao & Lamp, 2014; Cusano & Fernandes, 2010; Kroll et al., 1996; Wax & Rosenthal, 2007) Its incidence can be significantly reduced with an accurate preoperative evaluation, meticulous surgical technique and careful postoperative monitoring (Santanelli Di Pompeo et al., 2014). Early recognition of vascular distress greatly increases the likelihood of flap salvage. (Chen et al., 2007; Gillani et al., 2012; Khalil et al., 2006) In fact, performing rapid re-exploration with revision of the anastomosis is possible when a monitoring protocol has been established, with valid, effective, and reproducible methods, carried out by well-trained medical and nursing staff. To date, the hand-held external Doppler ultrasonography (EDU) is the most used method for postoperative flap monitoring (Hosein et al., 2016). Its sensitivity and specificity is evaluator- and flap-specific, with reports of either false positives which can lead to unnecessary reintervention, (Cervenka & Bewley, 2015; Jackson et al., 2009) or false negatives which prolong time of ischemia before vascular impairment can be recognized (Freed et al., 1979). Countless novel monitoring methods and devices have been implemented in clinical practice to detect flap compromise as early as possible, including implantable Doppler probes, laser Doppler flowmetry, tissue oximetry, intravenous fluorescein, infrared skin temperature measurement, tissue pH measurement, electromagnetic flowmetry, transcutaneous/tissue pO2 measurement, photoplethysmography and lastly, microdialysis. (Chang et al., 2013; Delgado et al., 1972; Keller, 2007; Koshima et al., 1993; Siemionow & Arslan, 2004; Ungerstedt & Pycock, 1974; Yang et al., 2014) The latter is a minimally invasive post-operative monitoring technique based on the assessment of tissue metabolism of the microsurgical flap (Jyränki et al., 2006). It reliably measures ischemia-related metabolic markers such as glucose, lactate, pyruvate and glycerol contained in the flap's interstitial fluids. Microdialysis is especially useful for flaps that are difficult to monitor, that is, buried flaps or flaps with a small sentinel skin paddle (Laporta et al., 2015). Microdialysis has been successfully described in muscular flaps, with metabolic marker thresholds described for these flap. Use in adipocutaneous flaps for breast reconstruction is still lacking and requires further assessment.

The aim of this study is to compare EDU evaluation versus microdialysis in the early post-operative follow-up of Deep Inferior Epigastric Artery Perforator (DIEP) flaps used for breast reconstruction, and propose an efficient postoperative monitoring protocol.

2 | PATIENTS AND METHODS

Between January 2019 and March 2021, we prospectively enrolled 50 consecutive patients who received DIEP flap-based BR, for a total of 68 flaps. Inclusion criteria were women with confirmed breast cancer diagnosis or cancer-predisposing condition for which they underwent a mastectomy, who were eligible for microsurgical BR using the DIEP flap, and who received post-operative free flap monitoring using clinical assessment, EDU and microdialysis. Eligibility for microsurgical BR was assessed individually for each patient, according to American Society of Anesthesiologists (ASA) Physical Status score, availability of abdominal donor tissues and patient desires. Age was not considered a contraindication. (Cordova et al., 2021; Laporta, Sorotos, et al., 2017) Frail patients with an ASA score above III and/or with a contraindication for abdominal free flaps (i.e., previous abdominal surgeries, low body mass index [BMI], insufficient donor tissues) received different reconstructive options and were excluded from the study.

The following patient data were collected: age, BMI, laterality (unilateral/bilateral), type of mastectomy (nipple-sparing [NSM], skin-sparing [SSM] or modified radical [MRM]), timing of reconstruction (immediate/delayed), smoking history. None of the included patients had diabetes mellitus. The following surgery-related data was also collected: operative times, complications, reoperations and postoperative monitoring data. Average follow-up period was 30.7 months (range 13.3–38.9). Flap complications were recorded, and patients who underwent emergency reoperation for suspicion of vascular compromise were included in a "reoperation" category. Any return to the operating room for reasons other than perfusion problems were excluded from this category.

2.1 | DIEP flap monitoring protocol

All patients received the same post-operative monitoring protocol, which consisted in the assessment of clinical signs of perfusion impairment and EDU to detect vascular flow, as per standard practice by the nursing staff, under medical supervision. The nursing staff received training on the use of the technology, with instructions on every step of the flap monitoring flowchart described in Figure 1, and the threshold values warranting attention (Figure 1).

In addition, microdialysis was used to calculate the concentration of ischemia-related metabolites. EDU was performed using a portable mini-Doppler probe (Minidop ES-100VX with 8 MHz probe, Hadeco Inc., Kawasaki, Japan), while the analysis of biochemical markers concentration was carried out using the ISCUS^{flex} microdialysis analyzer. The flap was monitored every hour for the first 30 h from surgery, then every 2 h from 30 to 48 h, every 3 h from 48 to 96 h, then every 8 h from 96 h onwards. Free flap features used during post-operative assessment are described according to type of monitoring technique and perfusion status (vascularized, congested or ischemic flap) in Table 1 (Table 1). During the first 24 h, the surgeon reviewed data from the nurses' free flap monitoring every 4–6 h. If the nursing or medical staff detected microdialysis parameters which suggested an *ischemic trend*, the following measures were set in place: (1) re-evaluation of the flap's vascular status using clinical assessment and EDU; (2) correction of the patient's position and blood pressure; (3) replacement of micro-vials for repeat analysis 30 min after the last

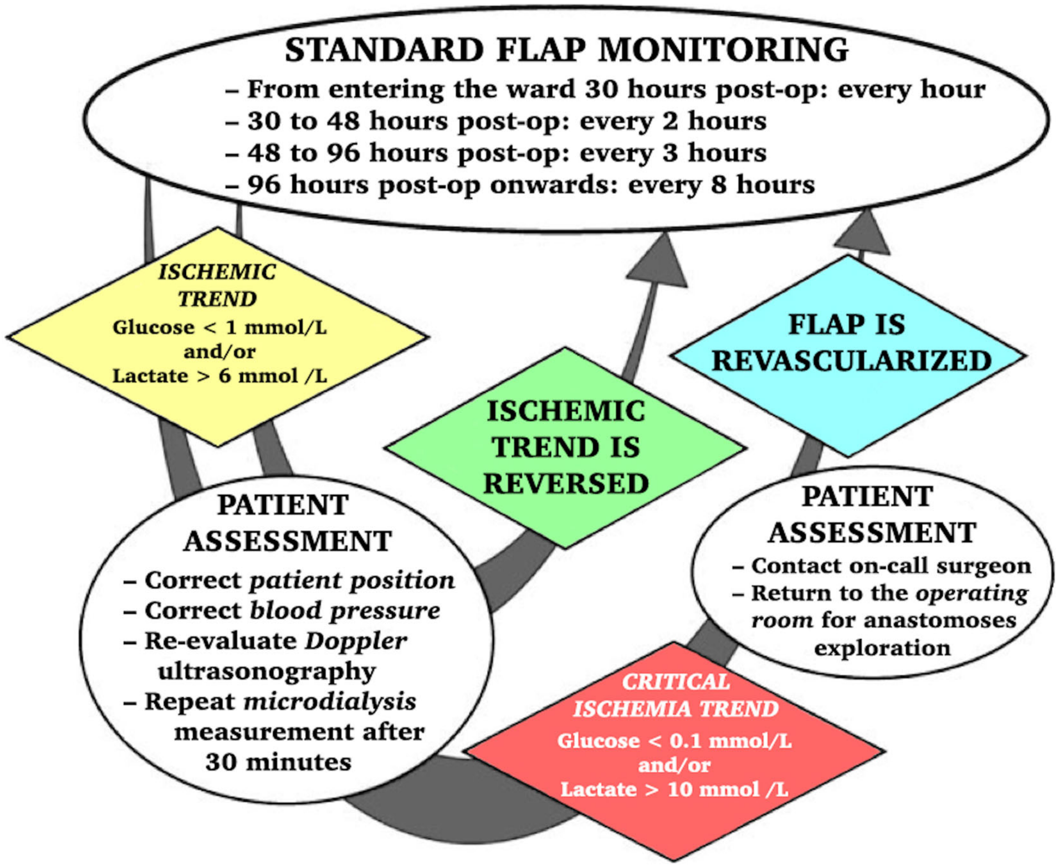

FIGURE 1 Flowchart representation of the Sant'Andrea operative protocol for microsurgical flap monitoring.

TABLE 1 Free flap features during post-operative assessment according to type of monitoring technique. Characteristics are listed in normal conditions for a well-vascularized flap (a), and in flaps with vascular impairment, due to venous congestion (b) or ischemia (c).

A	Vascularized flap
Doppler ultrasonography	Doppler: presence of arterial and venous signal
Microdialysis	Glucose >1 mmol/L, Lactate <6 mmol/L
Clinical Inspection	Color: pink Flap temperature: warm Capillary refill time: normal (∼2 s)
B	Flap with venous congestion
Doppler ultrasonography	Doppler: Absence of venous signal, arterial signal may be present
Microdialysis	Glucose < 0.1 mmol/L, Lactate > 15 mmol/L
Clinical Inspection	Color: Dark blue, starting from the edges Flap Temperature: Warm Capillary refill time: Fast (<2 s)
C	Ischemic Flap
Doppler ultrasonography	Doppler: Absence of arterial and venous signal
Microdialysis	Glucose < 0.1 mmol/L, Lactate > 15 mmol/L
Clinical Inspection	Color: White Flap temperature: Cold Capillary refill time: Absent

measurement. If the values returned within normal range, nursing staff was allowed to return to the standard monitoring protocol. If glucose concentration decreased below 0.1 mmol/L and/or lactate concentration roses above 10 mmol/L, this classified as *critical ischemia trend*. If the repeated measurement's data set was abnormal, the patient was taken to the operating room for emergent exploration of anastomoses. Overall, take-back surgery was considered when microdialysis values remained within range of ischemic or critical ischemia consistently for over 30 min, or if clinical signs and EDU assessment corroborated microdialysis findings.

2.2 | Surgical technique and microdialysis implementation

The device consisted in a sterile double lumen catheter with a semi-permeable dialysis membrane at its far end, connected to an infusion pump (CMA 106 microdialysis pump, Microdialysis Company, Stockholm, Sweden). The surgeon inserted the double-lumen catheter percutaneously into the subcutaneous adipose tissue of the flap, then anchored it to the skin using 4-0 Nylon sutures to prevent its dislocation. The device pumped sterile isotonic Ringer's solution through the catheter at a 0.3 μL/minute flow rate from one lumen, and collected

TABLE 2 Patient demographics and surgical details from study population.

	Patients	Breasts
Number (No.)	50	68
Age	52.46 (range: 30–72)	–
BMI (kg/m^2)	26.26 (range: 19.6–38.1)	–
Reconstruction laterality		
Unilateral	32 (64.0%)	32 (47.1%)
Bilateral	18 (36.0%)	36 (52.9%)
Reconstruction timing		
Immediate	43 (86.0%)	61 (89.7%)
Delayed	7 (14.0%)	7 (10.3%)
Type of mastectomy		
NSM	–	11 (16.2%)
SSM	–	30 (44.1%)
MRM	–	20 (29.4%)
Smoking		
Yes	11 (22.0%)	15 (22.1%)
No	39 (78.0%)	53 (77.9%)

TABLE 3 Free flap operative characteristics, complication rates and post-operative monitoring details using external Doppler ultrasonography.

Number	68
Operative time (min)	306.9 (212–480)
Unilateral	259.9 (212–480)
Bilateral	390.6 (230–480)
Flap weight (grams)	598.7 (130–1610)
Unilateral	627.8 (235–1330)
Bilateral	572.9 (130–1610)
No early Doppler signal	19 (27.94%)
Doppler + after 1 h	0 (0%)
Doppler + after 2 h	1 (1.5%)
Doppler + after 3 h	2 (2.9%)
Doppler + after 4 h	1 (1.5%)
Doppler + after 5 h	3 (4.4%)
Doppler + after 6 h	5 (7.4%)
Doppler + after 7 h	1 (1.5%)
Consistently absent Doppler signal	6 (8.82%)
Reoperation	2 (2.94%)
Complication	3 (4.41%)
Fat necrosis	1 (1.47%)
Partial flap necrosis	1 (1.47%)
Total flap necrosis	1 (1.47%)

extracellular fluid from the other. The semipermeable membrane allowed low-molecular-weight substances (<20 KDa) to spread according to concentration gradients between interstitial fluid and dialysate. The latter was collected into micro-vials (holding up to 200 μL) in a minimum span of 20 min, and its composition was analyzed using the ISCUS^{flex} Microdialysis Analyzer (Microdialysis Company, Stockholm, Sweden) in under 1 min. The contents of the micro-vials reflected the composition of the interstitial fluid and specific concentrations of glucose and lactate were used to monitor the free flap (Supporting information S1).

2.3 | Statistical analysis

Postoperative monitoring data were classified as true positives, true negatives, false positives and false negatives, according to whether the reported findings concurred with perfusion status. The data obtained were analyzed by means of a statistical analysis program (SPSS for Mac OS, 27.0, SPSS Inc., IBM Corporation, Chicago, IL) using descriptive statistics, analysis of variance (ANOVA) and expressed as means, minimum and maximum values, and standard deviations when appropriate.

3 | RESULTS

Study population featured 50 patients with a mean age of 52.46 years (range: 30–72), and a BMI of 26.26 kg/m^2 (range: 19.6–38.1). Demographics and surgical characteristics are further summarized in Table 2. Mean operating time for unilateral procedures was 259.9 min (range: 212–320), while for bilateral procedures was 390.6 min (range: 230–480). The mean flap weight was 627.8 g (range: 235–1330) for unilateral reconstruction and 572.9 g (range: 130–1610) for bilateral reconstruction. Patients were discharged after an average of 3.89 postoperative days (range: 3–6). One flap developed minimal fat necrosis (1.47%) which could be detected by ultrasound during a routine follow-up visit. One flap developed marginal necrosis (1.47%), which required only outpatient dressings. Two flaps returned to the operative theater for unsatisfactory microdialysis values associated with clinical signs of vascular impairment, with a reoperation rate of 2.94% (2 of 68 flaps). Out of these two flaps, one developed arterial thrombosis but was salvaged, while the other developed a venous congestion which could not be salvaged despite takeback surgery for anastomosis revision during the postoperative monitoring window, and thus caused total necrosis (1.47%). Two cases required a return to the operating room for management of complications other than vascular compromise of the flap (i.e. axillary hematoma). Overall flaps success rate was 98.53%. Free flap operative characteristics, complication rates and post-operative monitoring details using EDU are summarized in Table 3.

Regarding EDU monitoring, there were 12 false positives, 0 false negatives, 2 true positives and 54 true negatives, resulting in 100% sensitivity and 82% specificity. With microdialysis monitoring, there

TABLE 4 Microdialysis measurement values.

Number of flaps	68	
Total measurements	3692	
Total measurements per patient	54.29 (8–82)	
GLU (G) average (mmol/L)	2.31 (0.03–4.23)	
LAT (L) average (mmol/L)	1.43 (0.29–11.25)	
PYR average (mmol/L)	77.45 (4.28–365.4)	
GLY average (mmol/L)	211.02 (52.42–579.90)	
G/L average	2.45 (0.02–6.63)	
GLU alarm measurements		
Total	712	19.28%
Per patient	10.47 (0–43)	
Glucose true positive	20	2.81%
Glucose false positive	692	97.19%
Glucose true negative	2980	100%
Glucose false negative	0	0%
LAT alarm measurements		
Total	27	0.73%
Per patient	0.40 (0–11)	

Abbreviations: GLU (G), glucose; GLY, glycogen; G/L, glucose-to-Lactate ratio; LAT (L), lactate; PYR, pyruvate.

TABLE 5 Glucose and Glucose-to-Lactate ratio thresholds according to flap outcome, with sensitivity, sensibility and predictive values in the ability to detect flap failure.

Glucose	Flap failure	Uneventful flap	Total
Positive (<1 mmol/L)	20	692	712
Negative (>1 mmol/L)	0	2980	2980
Total	20	3672	3692
Sensitivity	100.00%		
Specificity	81.15%		
Positive predictive value	2.81%		
Negative predictive value	100.00%		
***G/L* ratio**	**Flap failure**	**Uneventful flap**	**Total**
Positive (<0.15)	20	692	712
Negative (>0.15)	0	2980	2980
Total	20	3672	3692
Sensitivity	100.00%		
Specificity	81.15%		
Positive predictive value	2.81%		
Negative predictive value	100.00%		

were 0 false positives, 0 false negatives, 2 true positives and 66 true negatives, thus resulting in 100% sensitivity and 100% specificity.

A total of 3692 measurements were recording with microdialysis, for an average of 55 measurements per patient (ranging from 8 to 82). Mean glucose concentration was found to be 2.25 mmol/L. Mean values below 1 mmol/L were recorded in five flaps though only one of those outliers resulted in free flap failure. The highest mean value of glucose was 5.98, while the lowest mean value was 0.12 mmol/L. Mean value of lactate concentration was found to be 1.17 mmol/L, with the highest mean value of 4.6 and lowest mean value of 0.1 mmol/L. Mean pyruvate concentration was 77.63 mmol/L with the highest mean value 365.4 mmol/L and lowest mean value of 4.28 mmol/L. Mean glycerol concentration was 210.64 mmol/L with highest mean value 580 mmol/L and lowest mean value of 52.42 mmol/L. Mean value of the lactate-to-pyruvate ratio was 0.03 with the highest mean value of 0.46 and the lowest mean value of 0.01. Overall, 623 (18.3%) measurements recorded an ischemic trend, with values of glucose concentration < 1 mmol/L, though lactate concentrations were higher than the cut-off value of 6 mmol/L in only 27 measurements, and had a mean of value of 0.44 mmol/L. In 19 out of 68 flaps (27.94% of all flaps) EDU signal was initially absent while microdialysis suggested proper functioning of the flap. In our cohort, 41 flaps were classified as buried. In those cases, the skin island was very small, and Doppler signal could not always be identifiable in all cases, compared to microdialysis measurements which were unrelated to the skin island size. There were no cases of catheter displacement in our case series. All microdialysis measurement values are further detailed in Table 4. We analyzed *G*/*L* ratio, finding an average value of 2.45 (range 0.02–6.63). In all DIEP flaps with uneventful outcome, *G*/*L* was never lower than 0.15. We found this value to be lower in the failed flap, with a negative predictive value of 100% (Table 5).

4 | DISCUSSION

The high success rate of free flap reconstruction can be attributed to both proper surgical technique and adequate postoperative monitoring (Laporta, Longo, et al., 2017). In 1975, Creech and Miller described how an ideal monitoring technique should be simple, rapid, non-invasive, harmless to the patient and flap, accurate, reliable, repeatable, recordable, cheap, with continuous real-time measurements and suitable for all kinds of flaps (Creech & Miller, 1975). To this day, no monitoring system that meets all of these criteria. Microdialysis has been introduced into clinical practice in 1966 by Bito et al. (1966) for the detection of cerebral ischemia. Ròjdmark et al. (1998) later described its first application for free flap monitoring in 1998. We have experienced several advantages in its use. Firstly, the low operator-dependency, especially if compared to clinical examination and external EDU, make it objective and easily reproducible. Secondly, the simplicity of the apparatus made the learning curve short even for the inexperienced staff. Thirdly, this type of monitoring appeared to cause considerably less discomfort to patients as it did not require loud signals to function, nor did it require frequent wake-up periods during the monitoring period. Finally, we were able to confirm the use of this system in patients undergoing DIEP flap with a small sentinel skin paddle after NSM or SSM. This study is the first description of its kind where microdialysis has been used specifically for the assessment of adipo-cutaneous free flaps. Other recent uses include muscle flaps used for lower limbs in humans (Neubert et al., 2016), and pure muscle flaps to experimentally assess the methodology in a pig model (Rauff-Mortensen et al., 2020).

When comparing EDU to microdialysis, we found that out of the 68 free flaps monitored, 19 cases were negative to Doppler signal in the first 12 h, while microdialysis values were consistently reassuring within normalcy range during the same period. Despite negative Doppler signals, those 19 patients did not require surgical reintervention, and in fact, EDU alone would likely have resulted in many unnecessary takebacks. The Doppler signal anticipated reassuring values on microdialysis in only 1 instance, where values still reached reassuring levels 2 h later. It should also be noted that while 18.3% of microdialysis measurements recorded an ischemic trend and were abnormal, the abnormal trend persisted in only two instances which led to takeback surgery. This supports the efficacy of the monitoring protocol used in this series. Microdialysis was the more accurate than EDU, with equal sensitivity and higher specificity (100% compared to 82%). The benefits of a more accurate monitoring device include the potential reduction in unnecessary takeback surgeries for suspicion of perfusion compromise, and the possible reduction of ischemia time if flap complication is detected early, which potentially increases success rate of revascularization.

Some studies have assessed differences between flap monitoring methods (Chae et al., 2015). Whitaker et al. (Whitaker et al., 2010) conducted a multicentric retrospective study which did not have a homogenous population as it evaluated different flaps such as DIEP, Superficial Inferior Epigastric Artery (SIEA) and Superior Gluteal Artery Perforator (SGAP) flaps. The flaps were monitored with each center's own specific criteria and protocol. Moreover, each center only used a single monitoring method, and the cohorts presented significant differences in terms of participants (Clinical assessment, $n = 235$, Cook-Swartz implantable Doppler probe $n = 121$, microdialysis $n = 42$). This is different from our study which was conducted prospectively, as our patient cohort was highly homogeneous: all patients received the same type of flap and underwent the same type of monitoring protocol based on clinical assessment, EDU and microdialysis, thus reducing the risk of bias.

Published cut-off points for the detection of ischemia with microdialysis are a glucose concentration < 1.0 mmol/L and lactate concentration > 6 mmol/L (Kristensen et al., 2013; Setala & Gudaviciene, 2013). The analysis of the values obtained by the microdialysis monitoring provided some unexpected results. We found our measured lactate values to be consistently lower than those published in literature (<6 mmol/L) (Setala & Gudaviciene, 2013). We can speculate that this might have occurred because all our monitored flaps were adipo-cutaneous or adipose-only. In fact, this threshold was determined for muscular free flaps, where myocytes are rich in mitochondria and have a high metabolic rate, heavily relying on glucose and Krebs cycle to generate energy (Birke-Sørensen et al., 2010). Lactate is generated by muscle tissue through the Cori cycle during anaerobic glycolysis, or by conversion from pyruvate through lactate dehydrogenase enzyme when the tissue is poorly oxygenated (Constantin-Teodosiu & Greenhaff, 1999; Yang et al., 2020). Conversely, adipose tissue mainly constituted by white adipocytes has fewer mitochondria, is characterized by a slower metabolic rate and mainly relies on fatty acids to generate energy (Frayn et al., 2006), which might explain the lower lactate measures. Of note, we even found lactate values to remain consistently below ischemic threshold even in the single case with ischemic trend that later evolved to total flap failure. In summary, no case with reassuring microdialysis measurements concealed an underlying vascular compromise which later led to flap failure. Glucose values proved to be very reliable when within normalcy range, with a sensitivity and negative predictive value of 100%. Conversely, lactate values were less reliable in the ranges previously described in literature (Jackson et al., 2009). Nevertheless, while the ranges taken alone might be misleading, we observed that the concentrations of glucose and lactate often fluctuated in a directly proportional fashion. The glucose-to-lactate ratio (G/L) seemed to be the most reliable parameter, alongside glucose levels alone. In fact, we found that when glucose and G/L measurements were reassuring despite negative Doppler signals, no reintervention was needed because the free flap was viable. The cut-off of 0.15 was selected based on the fact that in all viable DIEP flaps where outcome was uneventful, G/L ratio was never lower than said value. Unfortunately, the limited data in our hand did not allow us to perform regression analysis in order to demonstrate the superiority of this observation.

A major drawback to our study was the limited sample of only 68 flaps, as well as the limited event number of ischemic flaps which was only two. The concern is that with such low ratios it would be difficult to establish true comparative efficacy, false positive, false negative, sensitivity and specificity of different treatment modalities. Nevertheless, findings were found to be statistically significant despite our concerns. Other limitations to microdialysis monitoring include the fact that the system is more labor-intensive, requiring more nursing time with hourly measurements from a trained staff, and has high costs. Specifically, Setala et al. (2009) found that the incremental cost for monitoring one free flap with microdialysis was approximately 535 €, which can be subdivided into two types of expenses: the cost for the initial investment (monitoring apparatus) and for the single-use supplies per patient. However, Setala et al. concluded that if one or two flaps were to be saved through early detection made by microdialysis in a year, then this would cover the additional expenses for its use. In our experience, 68 free flaps were monitored which accounts for $535 \times 68 = 36{,}380$ € in flap monitoring costs. Microdialysis monitoring allowed us to identify two instances in which early reoperation was necessary, however salvage was successful only in one of the two instances. The strength of microdialysis lies in the fact that it saves costs by being more specific than other monitoring systems, since it identifies the cases that do not require reoperation, rather than those which do. Furthermore, the superiority of microdialysis to classical physical examination lies in the time it takes for complications to be identified. Clear and visible signs of vascular compromise are usually recognized several hours after onset has begun, which is even more difficult to notice in buried flaps. In our two instances of vascular compromise, the microdialysis identified them the earliest.

Another issue we encountered during microdialysis monitoring was the frequent appearance of erroneous alarms on the screen due to incomplete filling of the microvials. Nevertheless, it was easy to distinguish from real vascular compromise, since all values fell to zero. Some previous studies suggested that in the event of an arterial thrombosis, microdialysis values would change faster than in the event of a venous thrombosis (Frost et al., 2015). In fact, in the event of an arterial thrombosis, clinical assessment of the flap becomes difficult yet microdialysis monitoring shows elevated sensitivity, thus becoming particularly useful. Conversely, venous thrombosis is considerably easier to assess by a clinical standpoint, whereas microdialysis monitoring is supposedly less efficient and requires more time to show critical ischemia. This is particularly relevant in the hypothesis of a takeback situation, since flaps with venous compromise are the most difficult to salvage (Boissiere et al., 2021). In one instance, we found microdialysis measurements to be within normalcy range, yet regular follow-up displayed partial flap necrosis affecting Holm's abdominal perfusion zone III (Holm et al., 2006). This because it only assesses the metabolic state of a small portion of the flap in direct vicinity to the catheter, thereby neglecting more peripheral areas. Therefore, a catheter placed in a partial, spotted non-perfused flap area with microdialysis might provide misleading perfusion data despite an overall well-vascularized flap. We, therefore, recommend the catheter to be placed in Holm's zones I or II where perfusion is more representative of the anastomoses patency.

Finally, the microdialysis catheter presents a risk of accidentally being placed within a previously developed hematoma, or the catheter itself might cause a hematoma in the surrounding tissues. Both instances cause a distortion of the results (Keller, 2007; Kristensen et al., 2013). To date, we have not experienced any of said issues with catheter insertion.

5 | CONCLUSIONS

To the best of our knowledge, this is the largest study analyzing the use of microdialysis in post-operative monitoring over a highly homogeneous cohort of patients who received the same type of free flap, including buried flaps, for BR. Microdialysis, which was previously used for muscular flaps has been validated for adipocutaneous flaps as well. The combination of measures described in the flap monitoring protocol of our report allowed us to keep vascular compromise complications low. The high success rate of BR with DIEP flap stems from the combination of surgical technique, management, and postoperative monitoring.

In our experience, the specificity and sensitivity of microdialysis is higher than that of EDU evaluation, representing an excellent tool that can be implemented in standard clinical practice. The use of microdialysis may reduce stress to both patients and surgeons and avoid unnecessary re-explorations. The operative protocol for free flap monitoring that we present successfully predicts flaps at risk, reducing times of ischemia and increasing success of revascularization rates.

CONFLICT OF INTEREST STATEMENT

"Fabio Santanelli di Pompeo" and "Michail Sorotos" are Editorial Board members of Microsurgery and co-authors of this article. To minimize bias, they were excluded from all editorial decision-making related to the acceptance of this article for publication. We, hereby certify, that to the best of our knowledge no financial support or benefits have been received by author or any co-author, by any member of our immediate family or any individual or entity with whom or with which we have a significant relationship from any commercial source which is related directly or indirectly to the scientific work which is reported on in the article.

DATA AVAILABILITY STATEMENT

Data available upon request.

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SUPPORTING INFORMATION

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