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Current Evidence for Postoperative Monitoring of Microvascular Free Flaps

A Systematic Review

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Background: Despite a plethora of monitoring techniques reported in the literature, only a small number of studies directly address clinical relevant end points, such as the flap salvage rate and false-positive rate.

Method: We conducted a systematic review of current evidence regarding the postoperative monitoring of microvascular free-tissue transfer via extensive electronic and manual search and perusing databases, such as PubMed, Cochrane, American College of Physicians (ACP) Journal Club, Cumulative Index of Nursing and Allied Health Literature (CINAHL), Excerpta Medica Database (EMBASE), and Ovid MEDLINE. The included literature (n = 184 publications) was critically appraised using March 2009 Oxford Centre for Evidence-Based Medicine definitions, focusing on the evidence for the efficacy of each technique in improving the flap salvage rate of compromised flaps.

Result: There is a paucity of outcome-based studies, with only implanted Doppler probes, near-infrared spectroscopy, laser Doppler flowmetry, quantitative fluorimetry, and digital photography assessment using smartphones having been demonstrated in comparative studies to improve flap salvage rate. Currently, the implantable Doppler probe is the technique with the largest number of comparative studies and case series to demonstrate its effectiveness compared with clinical monitoring.

Conclusions: Future studies need to evaluate the most promising monitoring techniques further with a focus on assessing clinically relevant outcomes, such as the flap salvage rate and the false-positive rate, and not simple clinical series reporting patient and physician satisfaction.

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Aided by surgical and technical advancements, success rates for microsurgical flap procedures are generally reported to be 95% or greater.[1–4] Preoperative assessment of the flap vasculature aids in flap territory selection and may contribute to improvement in flap outcomes,[5–7] whereas intraoperative evaluation of pedicle and flap perfusion has allowed for greater confidence in the viability of larger free flaps.[8] Moreover, evidence suggests that correction of an intraoperative flow problem is associated with decreased risk of postoperative vascular complications.[9,10]

There remains, however, a small but significant flap failure rate, even in the hands of the most experienced surgeons. The use of clinical monitoring has been shown to salvage some of these threatened flaps, with some experienced groups showing that salvage of approximately 70% to 80% of compromised free flaps is possible.[11–14]

Flap failures may be attributed to arterial or venous occlusion arising from thrombosis, external compression, vessel kinking, or hematoma. Available evidence and expert opinions both indicate that timely detection of flap compromise and subsequent reexploration significantly increases the rate of flap salvage.[15–18] This need for early diagnosis and management of vascular complications in free flaps has led to a plethora of monitoring techniques being studied and assessed clinically.

A broad range of different technologies has been described for this role, but few studies use a significant clinical outcome as the primary end point of the trial. As such, there is little substantial evidence for any particular technique. Surveys of plastic surgical units show substantial differences in the selected methods and implementation of monitoring after free-tissue transfer,[19–21] suggesting that there is no currently established standard method for monitoring free flaps.

The purpose of flap monitoring is to rapidly identify circulatory compromise. It has been known for many years that flap ischemia becomes irreversible after a short period.[22–24] The no-reflow phenomenon described in 1978,[25] was a significant confirmation that reversibility was closely related to the ischemic time, with the hope of flap salvage eliminated after only a few hours of microvascular thrombosis and tissue ischemia.

Creech and Miller outlined essential criteria for free-flap monitoring,[26] stating that an ideal monitoring technique should be:

– Harmless to the patient and free flap.
– Rapid, repeatable, reliable, recordable, and rapidly responsive.
– Accurate and inexpensive.
– Objective and applicable to all kinds of flaps.
– Equipped with a simple display that could alert relatively inexperienced personnel to the development of circulatory impairment.

There have been several descriptions in the literature of the optimal comparative measures for evaluating adjunctive monitoring techniques.[26–28] The optimal test for monitoring efficacy is the salvage rate, which is the ability of a monitoring technique to allow early intervention and salvage of a truly compromised flap. This measure encompasses both the sensitivity of the method as well as its clinical importance. The other major measure of efficacy is the false-positive rate, which is a measure of the rate of precipitating needless take backs to the operating theater.[27,28] The use of these outcome measures can then enable assessment of a technique against the use of no monitor at all.

At this time, only a small number of studies show any technique to be better than basic clinical monitoring in terms of reexplorative

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outcome.[28–37] There are many anecdotal reports that claim that some devices managed to determine flap compromise earlier than clinical monitoring,[38–44] but this apparent performance was not associated with improved flap salvage or other measureable outcomes.[37–43] Comparisons of large studies using different monitoring techniques reveal similar flap success rates (97%-99%) and salvage rates (up to 80%), regardless of the monitoring system used.[1,3,5,10,32–47]

This review has been undertaken to clarify the currently available evidence related to postoperative flap monitoring.

METHODS

We performed a systematic review to evaluate the current evidence regarding postoperative monitoring of microvascular free flap transfer with an electronic and manual search, using the search string "flap AND monitoring." The inclusion criteria was simple: any publication directly studying or commenting on the use of free flap monitoring techniques of any kind were included in this review. We perused the following electronic databases: PubMed, PubMed Central, Cochrane Database of Systematic Reviews, American College of Physicians Journal Club, Database of Abstracts of Reviews of Effects, Cochrane Central Register of Controlled Trials, Cochrane Methodology Register, Allied and Complementary Medicine, Cumulative Index of Nursing and Allied Health Literature, Excerpta Medica Database, Ovid MEDLINE in-process, and other non-indexed citations. To avoid the language bias, we included articles in English, Italian, French, Spanish, and German. Secondary references found through bibliographic linkage were also retrieved. The literature identified was critically evaluated based on the March 2009 Oxford Centre for Evidence-Based Medicine (CEBM) definitions.[48]

RESULTS

Clinical Monitoring

Clinical bedside monitoring is the current standard for flap monitoring, used by almost all microsurgical units.[19–21] It involves using the flap color, temperature, capillary refill, skin turgor, hand-held Doppler findings, and pinprick as measures of adequate perfusion of the flap. Regular monitoring during the first few days postoperatively has enabled some units to produce flap salvage rates of up to 80% and overall success rates of up to 99%.[1,14] Reviews of multiple large case series shows that salvage rates range from 40% to 80% and overall success rates range from 94% to 99%,[1,4,14,49–55] but these case series are not necessarily monitored in a standard way, or monitored at all. The only large series of clinically monitored cases published are those by Disa et al and Chubb et al. The study of Disa et al[14] comprised a retrospective review of 750 cases and emphasized the importance of clinical monitoring through the observation that there was 0% salvage rate of all unmonitored buried free flaps with a compromised microcirculation, clearing showing the need for effective clinical monitoring. Chubb et al reviewed 1140 cases and showed that venous thrombosis has a significantly greater salvage prognosis than arterial, and that the recipient site for the free flap has implications on the false-positive rate for clinical monitoring, with flaps used on extremities more likely to be inadvisably reexplored.[54]

One of the significant limitations of the standard clinical monitoring techniques is the inability to examine flaps that are buried or located in difficult to access areas. In the literature, investigators have bypassed this issue by creating a distal skin paddle,[56–59] a chimeric flap,[60–62] or an exteriorized flap,[63–66] on which the usual clinical examinations can be performed. Such "monitoring flaps" provide an indirect indication about the perfusion status of the flap of interest. However, any derivation must be carefully interpreted caused by the potential risk of a false-positive or -negative result arising from vascular complications specific to the "monitoring flap."[62]

Clinical monitoring provides a standard against which adjunctive and alternative monitoring techniques must be compared. To date, only a few techniques have been shown to improve flap salvage rates in comparison to clinical monitoring, and all of these case series have based their analysis on small numbers of failing flaps.[29–38]

The Cook-Swartz Implantable Doppler Probe

An implantable Doppler probe was first used in free flap monitoring in 1984,[67] and the Cook-Swartz probe was first developed in 1988 specifically for use in free flap operations.[68] A Cook-Swartz implantable Doppler probe directly measures the blood flow in the pedicle and consists of a silicone cuff approximately 5 mm in width containing a 20-MHz piezoelectric crystal. The cuff is secured around the venous pedicle using microclips,[69] sutures,[70] a fibrin sealant,[71] or an elongated silicone cuff.[72,73] Earlier studies placed the probe around arterial pedicle, but subsequent studies demonstrated that it is more sensitive when placed on the venous anastomosis.[73] A venous Doppler signal immediately detects both venous and arterial blood flow obstruction. In contrast, an arterial Doppler signal can detect arterial compromise instantaneously, but venous occlusion would only be identifiable after 3 to 4 hours.[73] The probe's proximal end exits the surgical wound as a thin wire and is connected to a transportable monitor at the bedside. The wire is usually sutured to the patient in order to prevent accidental pulling leading to false-negative results. At 5 to 10 days postoperatively, depending on the length of direct vessel monitoring required by the surgeon, the electrode can be pulled free from the cuff when a tension of 50 g is applied.

There have been 6 comparative studies of the implanted Doppler probe in free flap monitoring.[29–32,46,74] In 4 studies, the implanted Doppler probe has demonstrated an increase in the flap salvage rate compared to standard clinical monitoring.[29–32] All of these studies have small numbers of flap salvage attempts (n = 20, 10, 35, 33), and statistical significance is only achieved in one of them.[30] However, a meta-analysis of 547 consecutive patients from the first 3 studies by Rozen et al[30] produced a statistically significant improvement in the salvage rate (80% vs 66%). In addition, Frost et al.[73] have prospectively compared the Cook-Swartz Doppler probe, microdialysis, and clinical monitoring, and demonstrated that both devices indicate vascular compromise statistically earlier than clinical signs, but the study was not sufficiently powered to demonstrate an improvement in the flap salvage rate using this technique.[74] Um et al[46] have compared the effectiveness of the implanted probe to the Synovis Flow Coupler in 220 free flaps (Synovis Life Technologies, Inc., Minneapolis, MN). The latter is a device that combines an end-to-end anastomotic coupler with a removable 20 MHz Doppler probe enabling the vascular anastomosis and the probe installation to be performed simultaneously and, thus, saving intraoperative time.[47,75,76] The authors demonstrate no statistically significant difference between the Cook-Swartz Doppler probe and the Synovis Flow Coupler in the false-positive rate (0.9% vs 1.8%, respectively) and the flap salvage rate (82% vs 80%, respectively). The authors did not demonstrate whether these high flap salvage rates represent an improvement from the standard clinical monitoring.

There are also 4 series of reexplorations (n = 9, 19, 18, 77) associated with the use of the implanted Doppler probe showing salvage rates of 83, 94, 61, and 56%, respectively.[10,46,77,78] Interestingly, only 2 of the studies demonstrate rates better than literature values for clinical monitoring.[46,77] However, the other 2 studies report reasonable sensitivity (67% and 87%, respectively) and high specificity (95% and 99%, respectively) of the technique, and it can be concluded that the implanted Doppler probes are still accurate and effective.[10,77] Furthermore, the implanted Doppler probes are especially beneficial in monitoring buried free flaps or cutaneous flaps that are located in poorly accessible areas. Schmulder et al[32] reported that the difference in the flap salvage rate between the implanted Doppler probe and clinical monitoring is even greater in buried flaps (94% vs 40%).[32]

The implantable Doppler probes are also the most cost-effective postoperative free flap monitoring technique.[78] Implantable Doppler probes are financially more advantageous if the rate of flap failure before reexploration is 6% to 10% or greater.[79]

The Cook-Swartz probe is associated with a small false-positive rate,[29,79,80] and initial studies reported a low rate of probe malfunction, which was thought to be due to a learning curve for the surgeons in placing the probe around the venous pedicle.[45,61,68,73,81,82] Later studies have not reported this problem, and recently published reports indicate that the device can be easily and reliably secured.[69] Interestingly, Kim et al[81] describe a novel technique in a small case series where the probe is placed on a chimeric flap to yield a surrogate measure of flow, preventing excessive tension on the anastomosis.[83] However, this method introduces an additional operative time by raising a chimeric flap and potentially increases the donor site morbidity. More clinical studies will be required to validate this technique. Recent studies by Paydar et al[76] and Schmulder et al[32] report that a small number of false-positive cases can still arise because of the subjective interpretation of the Doppler signal by an inexperienced healthcare professional.

The optimal use of the Cook-Swartz Doppler probe requires adequately trained health care personnel and reliable application on the venous pedicle. It should be used to replace the clinical examinations in buried and poorly accessible flaps and, when in doubt, needs to be complemented by clinical monitoring and handheld Doppler.[78,81]

Microdialysis

First described in the setting of free flap monitoring by Udesen et al,[84] microdialysis consists of a double-lumen catheter with a semipermeable membrane at the end, which is placed within the flap to be monitored, and a small amount of fluid is pumped through the catheter. As this fluid passes through the semipermeable membrane, small molecules may pass into the dialysate, which can then be analyzed. The level of certain metabolites within the transferred tissue can be used to ascertain its metabolic state. Typical metabolites used for this technique are lactate, glucose, glycerol, and pyruvate.[84–86] Several other molecules, such as complement 3a and thromboxane A2, have been mooted as candidates for further study.[87,88] Udesen et al used a similar catheter placed elsewhere in the body for a reference comparison, whereas some later studies have simply compared results to reference values or used increasing lactate/pyruvate ratios as a measure of ischemia. In a recent animal study, Kristensen et al[89] demonstrated that using lactate and glucose levels, lactate-to-glucose ratio, and glucose challenge test, they could differentiate between ischemic and non-ischemic flaps, and identify hematoma. In a large retrospective analysis of 268 free flaps, Setala and Gudaviciene[89] concluded that high lactate:glucose ratio can be used to predict total or partial flap necrosis requiring reexploration.[90]

Major advantages associated with microdialysis are that it provides an accurate, objective measure of the flap metabolism in ischemia and produces a timely and sensitive indication of flap failure.[91,92] Similar to the implantable Doppler probes, it is potentially useful in buried flaps and cutaneous flaps that are difficult to examine.[93,94] Edsander-Nord et al[84] have illustrated the sensitivity of this technique by showing that microdialysis can detect a difference in metabolism between free and pedicled transverse rectus abdominis myocutaneous flaps, and between zones I and II of the same group of flaps.[85] Sorensen[95] successfully used microdialysis in buried free jejunal transfers to identify flap compromise early and salvage 2 such flaps. Mourouzis et al[96] published a case report where they used microdialysis to monitor a bone-only free flap in which no compromise occurred. Jyranki et al[97] reported a case series of free flaps, and found in 2 cases that metabolic changes can be detected before the clinical signs, although both of these flaps failed after reexploration. Several other authors have concluded that microdialysis is a method that can give early warning of flap failure.[84,98]

There have been 2 trials comparing microdialysis to other monitoring techniques.[74,86] Whitaker et al[86] performed a retrospective analysis and showed no benefit for either implanted Doppler or microdialysis over each other or clinical monitoring, although it did show a significant increase in the false-positive rate when microdialysis was used as a sole method of monitoring. In a prospective cohort study, Frost et al[74] demonstrated that both microdialysis and the Cook-Swartz Doppler probes detect flap compromise statistically earlier than the standard clinical monitoring. Of note, microdialysis showed a superior detection rate in comparison to the implantable probe (number needed to diagnose: 1.00 vs 1.05) and a higher specificity rate (100% vs 67%). Both studies are not sufficiently powered to show flap salvage rate advantages. Interestingly, Whitaker et al reported a high false-positive rate of 8.5%, while Frost et al recorded 0%.

Major limitations of microdialysis are associated with its high cost (USD 597 per flap) and its relatively high false-positive rate. Nielsen et al reported that false-positive cases only occurred during the early learning phase and are associated with technical issues that are significantly reduced with the development of a decision algorithm to standardize the process and the operator experience.[90,92]

Oximetry

Pulse oximetry is a simple, noninvasive technique that assesses the oxygen saturation of arterial hemoglobin (SaO_2) in real-time. Decrease in oxygen saturation occurs significantly earlier than changes in clinical signs after both venous and arterial occlusion.[99] Hence, several studies have attempted to use SaO_2 as a measure of perfusion in free flaps. Initial animal studies in 1979 showed oximetry to be a potential predictor of flap survival.[100,101] Successful use of transcutaneous SaO_2 was tested in 1981,[102] and since then, numerous studies of similar topics, including the use of implanted oximetry probes and transflectance probes, have been published.[103–106] Although there are anecdotal reports of flap compromise detected by implanted SaO_2,[103–106] and other studies showing successful use of implanted SaO_2 probes,[105] no studies have adequately demonstrated oximetry as having clear advantages over clinical monitoring on the basis of flap salvage rate.

In the last decade, near-infrared spectroscopy (NIRS) has been tested with promising results experimentally and clinically.[107] The NIRS has additional advantages over oximetry in that it can determine tissue hemoglobin content, which may allow for clinical differentiation between arterial and venous occlusion.[108] Tissue oxygen saturation measured by NIRS is reliable because it is not affected by external factors, such as supplemental oxygen and blood pressure, and flap-specific variables, such as the perforator size and number.[109] Follow-up trials show that detection of compromise often occurs before the clinical suspicion of thrombosis.[38,110–112] Furthermore, NIRS can eliminate the need for a specialized intensive nursing care and, thus can reduce the cost.[113] There have been 3 comparative studies evaluating the combination of NIRS and clinical monitoring against clinical monitoring alone.[33,34,39] All 3 studies reported high flap salvage rates (94%, 100%, and 100%, respectively), but only 2 trials showed statistical significance.[33,34] The other study by Lohman et al[37] included too few flap salvage attempts (n = 5) to satisfy statistical analysis. The same authors report that NIRS detects vascular compromise earlier and more reliably than other adjunctive monitoring methods, such as the handheld Doppler and implanted Doppler probes.[37]

Visible Light Spectroscope

In comparison to NIRS, visible light spectroscopy (VLS) is a real-time, localized method that utilizes visible light to measure the hemoglobin saturation at capillary level. Because visible light is absorbed by hemoglobin 100 times more than infrared light, VLS is theoretically more sensitive to alterations in tissue oxygenation than NIRS. Cornejo et al[38] first reported the application of VLS in free flap monitoring.[39] The authors noted that VLS detected flap ischemia earlier than the implantable Doppler probe and clinical examination. However, the only patient in the study was considered too unstable for reexploration, and subsequent flap loss made it difficult to ascertain if early detection could have resulted in flap salvage. There is only 1 comparative study reported in the literature.[40] These authors report that VLS detected flap compromise 50 minutes before clinical assessment. The authors did not report an impact on the flap salvage rate.

Mulitspectural Imaging

Multispectral spatial frequency domain imaging (SFDI) is a new oxygenation imaging technique that enables visualization of oxygenation over a large area of tissue. The SFDI detects alteration in oxygen saturation secondary to partial blood flow obstruction earlier than visual cutaneous changes.[41] In animal studies, SFDI demonstrated accuracy within 10% of Food and Drug Administration–approved oxygen saturation probes.[114,115] The first pilot study in a human patient confirmed its safety and feasibility.[114]

Luminescence ratiometric oxygen imaging (LROI) is a new technique that measures relative transdermal oxygen consumption for quantitative assessment of perfusion.[116] The LROI consists of a fluorescent oxygen sensory foil covering the cutaneous surface of a flap and a handheld fluorescence microscope. The sensory foil contains a reservoir of oxygen, which is consumed by the tissue. In a prospective analysis of 52 free flaps, Meier et al concluded that relative transdermal oxygen consumption of less than 0.3 indicates a well-perfused flap and greater than 0.3 a poorly perfused flap.[116] Mueller et al[117] performed a prospective study of 15 osseocutaneous flaps showing that using both LROI and contrast-enhanced ultrasound (CEUS) can complement each other where the CEUS assesses the deep tissues, such as bone, and LROI evaluates the skin.

CO_2 Monitoring

In addition to monitoring SaO_2, Hashimoto et al[118] proposed the use of CO_2 monitoring as a better method of detecting flap compromise, but no follow-up study has been performed. Similarly, Jonas et al[119] used a polarographic sensor to monitor the partial pressure of oxygen and produced a salvage rate of 59%. This technique is invasive, however, and has not gained wide acceptability.

There is good evidence that the use of SaO_2 and/or $SaCO_2$ could be beneficial, but further studies involving a randomized clinical trial is needed to demonstrate definitive clinical benefit of these various techniques.

Laser Doppler Flowmetry

Laser Doppler flowmetry is a simple, noninvasive technique in which the Doppler shift of a laser shone into a free flap is used to derive the speed at which blood flows in the flap and give a measure of the tissue perfusion. It is used in many experiments that require comparative measurements of skin blood flow.[119–126] The main advantages of this method are that it can be used to monitor buried flaps and to provide an immediate qualitative measure of the tissue blood flow. Anecdotally, it provides a warning of flap compromise up to several hours before the onset of clinical signs[127] and has a low false-positive and -negative rates.[128] Possible causes of error that may arise using laser Doppler flowmetry include the assumption that speed and velocity are similar and the ignorance of random interstitial cell movement.[129] A major limitation of this technique is its depth of penetration (8 mm), restricting its utility in monitoring buried flaps.

Some retrospective studies of units using this device show similar flap salvage rates to units using clinical monitoring alone,[130] whereas 1 study has shown an increase of salvage rate from 50% to 85% in a group of 12 complicated flaps.[35] This study represents CEBM level 2b evidence, the highest level of evidence available for laser Doppler.

Recent investigations using this technique have turned to a tissue oxygen analysis system, called Oxygen to See (O2C, Lea Medizintechnik, Giessen, Germany), combining the laser Doppler with white light spectrophotometry. The white light can additionally determine oxygenation and the relative amount of hemoglobin. A significant advantage associated with O2C is that it enables differentiation between venous congestion and arterial occlusion.[108,131] In a prospective study of 34 patients and 5 reexploration attempts, O2C produced 80% salvage rate, which is favorable to the standard clinical monitoring.[132] Recently, a prospective study by Mucke et al[133] demonstrated that using O2C that during early stages of the free flap integration, different parameters contribute at different times. In the immediate postoperative period, both superficial and deep blood flow and velocity decrease below the baseline. However, from the second postoperative day, a downward trend of these parameters suggests a need for reexploration. The investigators further demonstrated that oxygen saturation is not associated with ultimate flap failure. Further studies with large numbers are needed to prove that this method can alter flap salvage rates.

Fluorimetry

Initially used in 1940s to determine the viability of areas of pedicled flaps, early studies showed that this method accurately predicted the survival of areas of pedicled flaps. Fluorimetry measures the ultraviolet-induced fluorescence of fluorscein dye in tissue following intravenous injection (arterial phase) and renal excretion (venous phase). In tissue with a single artery and vein. These measurements assess arterial and venous patency respectively.[134] This technique was later easily adapted for use in monitoring free flaps. The introduction of fiberoptic fluorimetry by Silverman et al[133,134] allowed for the monitoring of elimination as well as perfusion with fluorescein.[135–137] Subsequently, other studies showed that using oral fluorescein was possible.[138,139] Fiberoptic measurement of fluorescein permitted use of small dye doses and frequent reexaminations. Monitoring 200 free flaps, Whitney et al[28] demonstrated a sensitivity of 91% and an increase in flap salvage rate from 55% (with clinical monitoring) to 85%, with the control being free flaps performed before the introduction of fluorimetry to the unit.[28] This study was particularly important because it is one of the earliest studies in the literature directly comparing an adjunctive monitoring technique to clinical monitoring.

Issing and Naumann[136] showed that fluorimetry was a more specific indicator of flap survival than either pH monitoring or surface temperature monitoring.[138] This technique is extremely sensitive and is able to detect areas of flap necrosis as well as thrombosis within the pedicle.[138] However, monitoring requires expertise and the injection of fluorescein has the potential for adverse effects, including anaphazis.

The use of indocyanide green (ICG) may be safer than fluorescein, and initial results are promising.[139–142] Mothes et al[143] studied the use of ICG fluorescence angiography (ICG-FA) both intraoperatively and postoperatively and concluded that this technique was useful intraoperatively but no better than clinical monitoring postoperatively. Furthermore, anaphylactic reaction to the ICG has been reported in the literature, and it is contraindicated in patients with iodine allergy.[144] In recent times, ICG-FA has been used more frequently for intraoperative assessment of microvascular circulation in free flap operations.[145,146]

Fluorimetry is one of the few techniques in the current literature to provide CEBM level 2 evidence for an adjunctive monitoring technique. Reasons for its limited applicability include adverse reactions, nursing work demands, and its inefficacy with muscle tissue and pigmented skin.[28]

Temperature Measurement

Temperature measurement was first discussed in a review by Harrison et al[147] in 1981. This technique is one of the oldest and the simplest adjunctive monitor methods. In 1983, May et al[148] used an implanted temperature probe on the vascular pedicle to monitor flaps. This idea showed promise, but there have been no subsequent studies to determine the effectiveness of this technique. Issing and Naumann[138] showed that temperature changes were significant, only after 15 hours of flap ischemia, a period far too long for a flap to be successfully revascularized.

One of the major problems with surface temperature monitoring is the difficulty in properly controlling results. Skin surface temperature fluctuates by as much as 8°C in normal subjects, depending on clothing, humidity, core temperature, room temperature, and many other factors. Khouri and Shaw[149] showed in a retrospective analysis that a properly controlled comparison of flap skin temperature to a control temperature yielded 98% sensitivity and 75% specificity for anastomotic blockage. Chiu et al[150] suggested using adhesive temperature strips as an inexpensive adjunct, but not a replacement, to the standard clinical monitoring. Recently, Kannan[151] reported a modified technique using a standard digital thermometer where a decrease in the skin surface temperature in the center of the flap compared to the surrounding skin was significant for an arterial occlusion. Their findings would need to be reproduced in large clinical studies and require statistical support.

In place of the traditional thermometers, some investigators report their use of the infrared thermometers,[152–155] a noncontact technique that is more sensitive than the implantable and the surface contact thermometers. Anecdotal reports demonstrate that flap areas with lower temperature are associated with areas of later necrosis.[152,153] In a retrospective analysis, Papillion et al[154] reported using an infrared thermometer, and that the flap surface temperature starts to decrease 8 hours postoperatively with a mean reduction of 2°C is observed in failed free flaps. Their findings are supported by a clinical trial where the free flap temperature measured by a digital infrared thermometer correlated with alteration in the capillary blood flow and hemoglobin oxygenation measured by O2C (Lea Medizintechnik, Giessen, Germany).[155] The authors concluded that a decrease greater than 3°C in the flap skin temperature compared to the surrounding skin is significant for an arterial, but not venous, thrombosis. Furthermore, a reduction of 3°C in the center of the flap indicated arterial occlusion and a reduction of 1°C to 2°C venous compromise. The current consensus is that infrared thermometers are a simple, inexpensive, reliable adjunctive method in postoperative monitoring of free flaps; this would need to be supported in the setting of a larger clinical trial.

Glucose and Lactate Measurement

Measuring the flap glucose level and lactate is a cheap, simple, and rapid method of predicting microvascular complications in free flaps. In a multicenter clinical trial, Henault et al[42] used flap glucose levels of less than 3.85 mmol/L and lactate levels greater than 6.4 mmol/L to indicate pedicle compromise. This technique yielded sensitivity of 98.5% and specificity of 99.5%. Changes in glucose and lactate level occurred in average 5.7 hours before the onset of clinical signs. Hara et al[156,157] reported high sensitivity and specificity when only flap glucose level was used to detect venous thrombosis. Di Lorenzo et al[158] calculated a ratio of flap glucose to systemic glucose level and demonstrated its accuracy in identifying both arterial and venous occlusions requiring reanastomosis. It is yet unclear why flap glucose level drops as a result of pedicle compromise.[159,160] It is hypothesized that a reduction of blood supply to a compromised flap leads to a shortage of tissue glucose supply.[161]

Smartphone Applications and Telecommunication

In the era of readily accessible Internet and ubiquitous smartphones with camera functionality,[162,163] digital photography represents an opportunity for surgeons to monitor free flaps remotely, enable rapid communication between nursing and medical staff, and potentially

TABLE 1. Factors Affecting Types of Monitoring Techniques Used

Method	Cost	Availability	Ease of Application	Time to Diagnosis
Clinical	+++	+++	+++	Medium
Implanted ultrasound (Cook-Swartz probe)	+	++	++	Short
Microdialysis	+	+	+	Medium
Implanted pO_2	++	+	+	Short
NIRS	+	++	++	Short
VLS	+	++	++	Short
SFDI	+	+	+	Short
LROI	++	+	++	Short
Laser Doppler	++	++	++	Short
Fluorimetry	++	+	+	Long
Implanted temperature	++	+	+	Long
Surface temperature	+++	+++	+++	Long
Glucose & lactate	+++	+++	+++	Short
Smartphones	++	+++	+++	Short
PPG	++	+	++	Short
Handheld Doppler	++	++	+	Medium
Color Doppler	+	+	+++	Medium
CEUS	+	+	+	Medium
Impedance plethysmography	++	+	+	Short
SDFI	+	+	++	Short
Confocal microscopy	+	+	+	Medium
Orthogonal polarized light	+	+	+	Short
Scintigraphy	+	++	+	Long
PET	+	+	+	Long
pH	++	+	+	Medium
Hydrogen clearance	+	+	++	Short

pO_2 indicates partial pressure of oxygen.

reduce the response time to reexploration.[42] There have been 2 comparative studies.[36,164] Hwang and Mun[36] compared the clinical outcome before and after their unit adopted an instantaneous Internet messaging service to share digital photos of postoperative free flaps. The flap salvage rate improved (100% vs 50%) and the response time to reexploration reduced significantly (1.4 hours vs 4.0 hours). These elements translated to a higher rate of overall flap survival (100% vs 96.2%). A prospective study by Engel et al[161] who also reported a significant decrease in the response time using remote digital photography over "in-person examination" (8 minutes vs 180 minutes).[164] Recently, Kiranantawat et al[165] have developed a smartphone application that analyzes digital photos for color difference and demonstrated high sensitivity (94%) and specificity (98%) in detecting vascular compromise.

As the integration of smartphone and telemedicine becomes commonplace in plastic surgery, Gardiner and Hartzell[166] suggest that despite 96% of publications from their literature review displaying its benefit, a significant 51% documented adverse effects, such as technical issues, cost, misdiagnosis, and learning curve for a new technology. Furthermore, with the storage of clinical photography and other potentially patient-identifiable information in personal electronic devices, there may arise legal issues associated with privacy and security requiring resolution before a wide adoption of this technology.

Photoplethysmography

Similar to SaO_2 monitoring, photoplethysmography (PPG) uses reflected spectrographic means (either green or infrared light) to determine real-time perfusion. However, PPG directly measures the flux of red blood cells, rather than a mathematical derivative of SaO_2 flux, which is the technique used by NIRS. Recent development of a custom-made photoplethysmographic and pulse oximetry optical and fiber-optical probe and the processing system has enabled direct continuous monitoring of arterial oxygen saturation in real time.[167,168] The PPG demonstrates much higher correlations to radioactive microsphere measurements than laser Doppler flowmetry and is, hence, very accurate.[169] Clinical testing has shown high sensitivity and specificity in a blinded clinical trial.[170] Anecdotal reports show that this device may be able to reliably determine successful tissue perfusion in situations when both clinical and duplex Doppler assessment could not rule out flap compromise.[171,172] It appears that this extremely sensitive device holds promise, but further clinical trials are required to demonstrate its efficacy.

Ultrasound

Handheld Doppler ultrasound probes are the most commonly used adjunct to the clinical examination in assessing pedicle flow,[173] but it has not been evaluated as a stand-alone technique apart from its application in the implantable Cook-Swartz Doppler probe. One of the major disadvantages associated with the handheld Doppler devices is that it is difficult to differentiate between the pedicle and the adjacent vessels in the recipient site, and also, between arterial and venous flow. These issues are compounded by the presence of anastomotic couplers and in buried flaps. Color Doppler ultrasound can be advantageous. It is a noninvasive bedside technique that can accurately demonstrate flow and flap viability.[174] Furthermore, it can provide objective assessment of perfusion in buried flaps.[175] In addition, color Doppler probes can be used to estimate the resistance to flow and produce a pulsatility index, which is a widely accepted alternative to measuring flow.[176] The authors reported that venous compromise is associated with a significantly high pulsatility index.

TABLE 2. Characteristics of Monitoring Techniques

Method	Sensitivity	Detect Arterial or Venous Compromise	Differentiate Arterial Versus Venous Compromise	Differentiate Territorial Versus Pedicle Compromise
Clinical	High	Venous > arterial	Yes	Yes
Implanted ultrasound (Cook-Swartz probe)	High	Both	No	Yes
Microdialysis	High	Both	Yes	No
Implanted pO_2	Medium	Both	No	No
NIRS	High	Both	Yes	Yes
VLS	High	Both	No	No
SFDI	High	Both	Unknown	No
LROI	High	Both	No	Yes
Laser Doppler	High	Both	Yes	Yes
Fluorimetry	High	Both	Yes	Yes
Implanted temperature	Medium	Arterial > venous	No	No
Surface temperature	Medium	Arterial > venous	No	No
Glucose & lactate	High	Both	Unknown	No
Smartphones	High	Venous > arterial	Yes	Yes
PPG	High	Both	Yes	Yes
Handheld Doppler	Medium	Arterial > venous	No	No
Color Doppler	High	Both	Yes	Yes
CEUS	High	Both	Yes	Yes
Impedance plethysmography	High	Both	Yes	No
SDFI	High	Both	Unknown	No
Confocal microscopy	High	Both	Yes	Yes
Orthogonal polarized light	High	Unknown	Unknown	Yes
Scintigraphy	High	Both	No	Yes
PET	High	Both	No	No
pH	High	Both	No	No
Hydrogen clearance	High	Both	Yes	No

Recent studies using ultrasound contrast media (SonoVue, Bracco, Italy) have shown that CEUS used to measure dermal microcirculation correlates highly with the results obtained from ICG-FA,[177] fluoride positron emission tomography (PET),[178] and contrast-enhanced magnetic resonance imaging.[179,180] The CEUS is quick and noninvasively monitors the anastomoses of a free flaps,[181] including bone flaps.[182] One of the major advantages of CEUS is that it provides both qualitative assessment of the capillary perfusion in different flap areas and quantitative analysis using parameters derived from a special perfusion software QONTRAST (Bracco, Italy), such as time to PEAK and regional blood volume.[183,184] Furthermore, Sharma et al[185] demonstrated that both qualitative and quantitative assessments by CEUS are associated with high sensitivity (100% and 100%, respectively) and specificity (86% and 100%) in predicting flap failure. In a recent retrospective analysis, Geis et al[186] demonstrated that vascular complications estimated by QONTRAST and CEUS produced a high flap salvage rate of 85%. Potential issues with CEUS include the repeated exposure to contrast media and the potentially long period of time between clinical suspicion of compromise and an ultrasound examination of a flap. Until they are tested in large clinical trials, all ultrasound techniques currently remain best used as an adjunct to clinical assessment and for reassurance in borderline cases.

Impedance Plethysmography

The assessment of thoracic blood flow by electrical impedance is an established research technique. In an application of this technique, a small electrode array has been developed in which an alternating electric current is passed through a cutaneous free flap and the induced voltage across a small volume measured. A graphical display of this changing voltage illustrates the pulsatile flow through the flap, allowing continuous assessment of perfusion. According to the original articles describing this technique, it is accurate, easily interpreted, and usable by inexperienced staff.[187,188] Studies in animals showed that analysis of results by an investigator blinded to the status of the pedicle could quickly determine pedicle obstruction and accurately determine venous or arterial blockage in 100% of cases.[189] However, the technique is invasive, and no comparative clinical study has yet been reported.

Sidestream Dark Field Imaging

Sidestream Dark Field Imaging (SDFI) is a new noninvasive technique that evaluates end-capillary microcirculation at the cellular level. A central light guide is surrounded by concentrically placed stroboscopic light-emitting diodes to provide sidestream dark field illumination. It produces a real-time visualization of the red blood cells, independent of their oxygenation status, and all other cells found in the blood stream.[190] The main advantages of SDFI are that it provides a direct measure of blood flow to the flap and requires minimal training. To date, its use in postoperative free flap monitoring has only been demonstrated in animal studies[191] and a case report.[192] The authors of the clinical report suggest that SDFI may be useful in patients with pigmented skin where clinical examination of skin capillary refill is difficult to assess accurately.[192]

TABLE 3. Currently Available Levels of Evidence for Monitoring Techniques

Method	Best Reported False-Positive Rate	Best Reported True-Positive Rate	Highest Level of Evidence Regarding Flap Salvage Rate	Highest Reported Flap Salvage Rate (No. Cases)
Clinical	NR	NR	Current standard	77% (57)
Implanted ultrasound (Cook-Swartz probe)	0.9%	100%	2a	100% (16)
Microdialysis	0%	100%	4	NR
Implanted pO_2	NR	NR	4	NR
NIRS	0%	100%	2b	100% (3)
VLS	NR	NR	4	NR
SFDI	NR	NR	5	NR
LROI	NR	NR	4	NR
Laser Doppler	0%	100%	2b	83% (12)
Fluorimetry	6%	91%	2b	86% (23)
Implanted temperature	NR	NR	4	NR
Surface temperature	25%	98%	2b	NR
Glucose & lactate	NR	NR	2b	NR
Smartphones	1%	NR	3	100% (4)
PPG	4%	95%	4	NR
Handheld Doppler	N/A	N/A	N/A	N/A
Color Doppler	NR	100%	4	NR
CEUS	NR	NR	4	NR
Impedance plethysmography	NR	100%	5	NR
SDFI	NR	NR	5	NR
Confocal microscopy	NR	NR	5	NR
Orthogonal polarized light	N/A	N/A	5	NR
Scintigraphy	NR	NR	5	NR
PET	NR	NR	4	NR
pH	NR	NR	4	NR
Hydrogen clearance	NR	NR	4	NR

NR indicates not reported; N/A, no relevant studies.

Confocal Microscopy

Confocal microscopy is a well-known laboratory technique that uses laser technology to create virtual sections of a tissue, an application of which is the evaluation of the capillary beds of free flaps. The evaluation of these capillaries postoperatively is a means of perfusion assessment, with both arterial and venous compromise potentially differentiated by this method. It has been shown that venous obstruction results in a significant dilatation of the capillaries and thickening of the epidermis caused by edema, and flow across the capillary beds is significantly reduced in both arterial venous compromise.[193] Currently, there are no clinical studies evaluating this technique in postoperative free flap monitoring.

Orthogonal Polarized Light

This relatively new technique involves the use of polarized light to determine the state of the microcirculation in the skin. Polarized green (548 nm) light is shone onto the skin, and a certain proportion of this light is reflected back toward the source. A beam splitter directs the light through a second polarizer placed at 90° to the original polarization of the light. As a result, only light that has undergone a change in its polarization caused by Rayleigh scattering by hemoglobin can be visualized. It is estimated that the light must undergo 10 or more scattering events before it can be depolarized enough to pass through the second filter,[194] and so the depolarized light is assumed to have penetrated relatively deeply. This use of cross-polarization allows for high-contrast viewing of the microvasculature in skin, and for analyses of perfusion to be performed. Animal studies have shown this technique to accurately predict flap necrosis, and several investigators postulate this technique's usefulness in flap monitoring. However, no clinical studies on free flap monitoring have been performed utilising this modality.[195–197]

Nuclear Medicine

Radioactive isotopes can be used as direct measures of tissue perfusion. The injection of an isotope can be later measured by scintigraphy or PET, with the assumption that the isotope is metabolically inactive and that it diffuses freely in the tissues being monitored. One advantage of this technique is that scintigraphy images can show areas of partial flap hypoperfusion. Several different isotopes have been studied,[147,198–201] including ^{85}Kr, ^{133}Xe, ^{22}Na, and ^{99m}Tc. Aygit and Sarikaya[200] demonstrated that this technique was useful in determining flap viability, but note was made of several problems with this technique, making it ultimately unlikely to be useful in monitoring of flaps. Aside from issues related to access to nuclear medicine laboratories, the technique also requires a reasonable amount of time between the injection of radioactive agent and scintigraphy to allow isotope diffusion. This substantial time delay is likely to reduce its clinical benefit and unlikely to improve flap salvage rates.

Positron emission tomography imaging is a sensitive technique, which uses radiolabeled glucose to derive metabolic state of a tissue. As a postoperative monitoring technique in free flap reconstructions, radioactive water can be injected, instead, to quantify blood flow.[202,203] In a prospective study, Schrey et al[202] calculated the blood flow in a radial forearm free flap and the muscle on the contralateral forearm. They demonstrate that a low flap-to-muscle blood flow ratio predicts poor success of the entire flap. In a later study,[203] the same authors suggest that PET imaging is a useful adjunct where the flap is difficult to access for adequate clinical assessment and other monitoring methods, such as tissue oximetry probes, and where the indication to reexplore is equivocal. Similar to scintigraphy, practical application of PET in the immediate postoperative period is limited by its cost, access to a PET scan, and a potential time delay to reexploration. Furthermore, PET introduces exposure to radiation. Positron emission tomography may have a greater role for flap monitoring in the late postoperative setting.[204]

pH Measurement

In 1983, Raskin et al[205] first introduced the use of an implanted removable pH monitor. They showed in animal experiments that pH values decrease shortly after the onset of arterial occlusion. Dickson and Sharpe[206] showed that there was a similar decrease in pH during venous occlusion, again in animal studies. Dunn et al[207] conducted a small clinical study, in which pH monitoring pre-empted both clinical monitoring and Doppler ultrasound. Issing and Naumann[138] showed that this method was not as precise as fluorescein injection to demonstrate flap viability, but pH monitoring had several other advantages. It is fast, inexpensive, and can be used as a continuous monitor. There is no evidence that this technique changes flap salvage rates, and further studies are needed to demonstrate clinical efficacy.

Hydrogen Clearance

This technique uses the changing impedance of the body because of H_2 concentration within tissues. The decay of H_2 concentration in the tissue of interest is registered by electrodes. Mathematical analysis of clearance allows quantitative expression of blood flow values in milliliters per minute per 100 g of tissue. This technique is of interest because it is relatively simple, safe, can provide instantaneous results at many points in time, can measure perfusion within a buried flap, and is also a direct measure of tissue perfusion. There has been only 1 clinical study evaluating this technique, which although small (n = 9), demonstrated that hydrogen clearance measurement detected changes in blood flow earlier than clinical monitoring and was able to distinguish between arterial and venous outflow blockage.[208] This technique remains a potentially useful method, but more studies are required to demonstrate that it may influence clinical outcomes.

DISCUSSION

Only 5 monitoring techniques have shown any evidence for improvement of flap salvage rates. In limited studies, the Cook-Swartz implantable Doppler, NIRS, laser Doppler flowmetry, quantitative fluorimetry, and digital smartphone assessments have demonstrated either comparative or historical flap salvage improvement compared to clinical monitoring. None of these studies, however, has reached a level of evidence or a configuration of results leading to widespread clinical use.

There have been a plethora of objective and subjective methods for flap monitoring, with each having unique advantages. When deriving an objective comparison between the monitoring techniques and utilizing an adapted version of the criteria that Creech and Miller[26] suggested, several key findings are noted. Tables 1 and 2 display individual characteristics of each technique that may be particularly useful to an individual microsurgical unit. Table 1 reflects the cost and ease of use in general terms, whereas Table 2 identifies the intrinsic properties of the different types of monitoring techniques. The benefits of adjunctive monitoring methods lie in their ability to improve outcomes, compared to clinical monitoring alone. In Table 3, the evidence in the available literature is provided that supports each technique. The best available statistics for each technique is provided and the “level of evidence” for different methods in Table 3 refer to the Oxford CEBM Levels of Evidence (March 2009). This specifically describes the highest level of evidence available that a particular technique changes the flap salvage rate.

Of note, most of available literature on flap monitoring does not provide objective evaluation of the monitoring techniques. Despite the fact that flap salvage rate is a significant attribute of a technique that indicates its usefulness, it is evident from Table 3 that flap salvage rate is the characteristic that received the least attention. Furthermore, most of the currently available studies do not use clinical relevant end points to determine successes of their monitoring techniques.[27] Future studies must report clinically relevant parameters, such as the flap salvage rate and the false-positive rate, which enables objective comparison between different monitoring techniques.

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