VARIABLES AFFECTING POSTOPERATIVE TISSUE PERFUSION MONITORING IN FREE FLAP BREAST RECONSTRUCTION

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Postoperative flap monitoring is a key component for successful free tissue transfer. Tissue oxygen saturation measurement (TOx) with near-infrared spectrophotometry (NIRS) is a method used for this purpose. The aim of this study was to identify external variables that can affect TOx. Patients who had breast reconstruction with free flaps were monitored prospectively and intra-operative details were recorded. Flap TOx was recorded with NIRS pre-extubation, postextubation, and then every four hours for 36 hours. At each of these time points, blood oxygen saturation (SO2), amount of supplemental oxygen, and blood pressure were recorded. Thirty flaps were monitored. Initially, a significant trend over time was detected such that for every increase of 24 hours, TOx decreased on average by 2.1% ($P = 0.025$). However, when accounting for SO2 levels, this decrease was no longer significant ($P = 0.19$). An increase by 1% in SO2 produced an increase in TOx reading of 0.36 ($P = 0.007$). The amount of supplemental O2, systolic blood pressure, and diastolic blood pressure did not have a significant impact on TOx ($P > 0.05$). The TOx values were highest in the free TRAM flaps and were lower in decreasing order in the muscle-sparing TRAM, DIEP, and SIEA flaps ($P > 0.05$). The TOx values did not significantly correlate with vessel size, perforator number, or perforator row. Postoperative flap TOx was found to correlate with SO2 and was not significantly dependent on blood pressure, supplemental O2, or surgical variables. Careful interpretation of oximetry values is essential in decision making during postoperative flap monitoring. © 2014 Wiley Periodicals, Inc. Microsurgery 00:000–000, 2014.

Because of advances in microsurgical techniques, free tissue transfer for reconstruction of various defects has become increasingly utilized. In recent large studies, free flap survival rate has been reported in the range of 94.3–99.3%.[1–5] Although overall success rate is high, flap compromise does occur and early detection of perfusion problems is directly correlated with increased flap salvage.[1,3,5–7]

During the early era of microsurgery, the mainstay of postoperative flap monitoring was clinical observation. However, this method is highly subjective, and it is impossible for the surgeon to observe the flap continuously. Therefore, several adjunctive devices have been developed to help detect early disturbances in flap perfusion before clinical signs are evident. These include, but are not limited to, implantable and surface Doppler monitoring, thermometry, laser Doppler flowmetry, quantitative fluorescence, near-infrared spectrophotometry (NIRS), visible light spectroscopy, transcutaneous oxygen measurements, thermography, and microdialysis.[8–14] Although an ideal monitoring device is yet to be determined, continuous measurement of tissue oxygenation (TOx) has proven to be reliable in detecting circulatory compromise.[6,10,11,15–18] While most studies focus on TOx changes with flap compromise, reports describing the factors and variables that might impact the tissue oxygenation measurements are scarce.

The contribution of local factors (i.e. skin thickness and density of capillary network) to tissue perfusion is known[19–22] and possible contribution of systemic factors to perfusion has been anecdotally mentioned.[17,19,23] The time-based changes in oxygenation and blood flow dynamics of free flaps have also been a point of interest and studied repeatedly, however, reports are contradictory.[6,7,14,17,23–31]. The purpose of this study was to investigate the time-based flap oximetry trends and elucidate the contribution of external factors to a free flap's tissue oxygen saturation. We hypothesized that a patient's systemic oxygenation, blood pressure, and the size and number of recipient and/or flap vessels are potential confounders to TOx readings.

PATIENTS AND METHODS

Patients who were scheduled to undergo breast reconstruction using free abdominal tissue were enrolled in this prospective study. Active smokers who did not quit smoking more than 4 weeks prior to the operation were excluded from enrollment. Patients who had complications during the monitoring period were excluded in an effort to focus on effect of other variables besides flap compromise. Patients' age, race, and body mass index were recorded. During the operative procedure, the following details were recorded: (1) flap type, (2) size, number, and location of recipient vessels, (3) size and number of flap vessels, and (4) perforator number and

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Table 1. Fixed Effects Estimates for Flap TOx by Time Model

	Slope (%)	95% Confidence interval	*P*-value
Time (24 hours)	−2.12	(−3.97, −0.27)	0.025
Time (24 hours)[a]	−1.31	(−3.24, 0.62)	0.19

The combined table is made up of the results of separate models.
[a]The time trend was no longer significant after adjusting for sO_2.

row for perforator flaps. Measurements were obtained using a caliper prior to anastomosis and prior to dilation of vessels, without application of any local vasodilator agents.

Flap tissue oxygen saturation values were measured using NIRS technology (T.Ox™ Tissue Oximeter, ViOptix, Fremont, CA). This monitoring device had a probe that is externally applied to the area to be monitored and connected to a computer console that displays tissue oxygen saturation. At the end of the procedure, the probe was placed over the skin island of the flap on an area not directly overlying a perforator vessel. The probe was secured in place intra-operatively and remained attached at the same site. Special care was taken to avoid direct light (such as operating room lights) on the probe. The measurements were recorded in a temperature controlled environment (the step down flap unit of the hospital) with the patient in the same position (standard postoperative position with the head of the bed elevated 30°). TOx readings were recorded prior to extubation, after extubation, and every 4 hours for the next 36 hours. The following data were also recorded simultaneously: (1) patient's blood SO2 (pulse oximetry), (2) amount of supplemental O2 (lt/min), and (3) systolic and diastolic blood pressures. Additionally, hemoglobin, hematocrit, and blood gas levels were recorded whenever they were available. Institutional review board approval was obtained prior to initiation of this project.

Data Analysis

Continuous variables were summarized using means and standard deviations, while categorical variables were summarized using counts and percentages. Mixed effects models were used to model TOx measurements, accounting for correlations introduced by repeated measurements taken on flaps in the same patient. Correlations between observations over time given a patient and side were modeled using a first-order autoregressive structure. The estimates of the fixed effects were provided, and represent average effects. Models of pre-extubation TOx readings by surgical variables contain one level of hierarchy, since there are no longer repeated observations over time. All analyses were performed in R software (version 2.15.1, Vienna, Austria). A significance level of 0.05 was assumed for all testing.

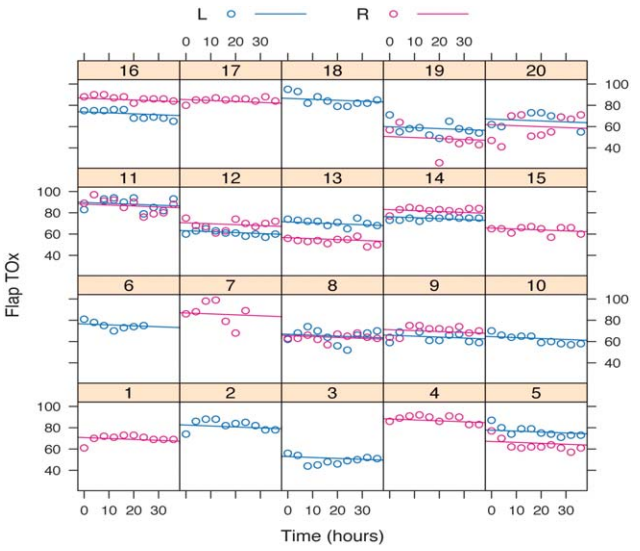


Figure 1. A plot of TOx over time for each flap, grouped by patient, is demonstrated. Superimposed on each panel is a line giving the estimated average TOx over time for each flap. (L: left, R: right, TOx: Tissue oximetry). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

RESULTS

Thirty flaps in 20 consecutive patients without complications were monitored for this study. The flap types were: deep inferior epigastric perforator (DIEP, $n = 24$, 80%), muscle sparing transverse rectus abdominis myocutaneous (Ms-TRAM, $n = 3$, 10%), superficial inferior epigastric artery (SIEA, $n = 2$, 6.7%), and transverse rectus abdominis myocutaneous (TRAM, $n = 1$, 3.3%). The internal mammary vessels were used in all cases as recipient vessels. Average age was 49.3 ± 7.4 and average BMI was 28.6 ± 3.5. Of 20 patients, 10 (50%) had undergone chemotherapy prior to the procedure. Of 30 recipient sites, 11 (36.7%) were radiated. In half of the cases (50%) reconstruction was immediate. No patient had cardiopulmonary comorbidities or peripheral vascular disease.

Tissue Oximetry Trend with Time

Initially, a significant trend over time was detected, such that for every increase of 24 hours, flap tissue oxygenation decreased on average by 2.1% ($P = 0.025$) (Table 1). After accounting for SO2 level, the average decrease in TOx was no longer significant ($P = 0.19$) (Table 1). Figure 1 illustrates a plot of TOx for each flap, grouped by patient. The superimposed line represents the estimated average TOx over time for each flap. The figure shows that while several patients displayed an initial increase in TOx over time followed by a decrease, this was not true for patients in general. Some patients displayed an initial decrease in TOx followed by an

Table 2. Results of Modelling Flap TOx by sO_2, O_2 and Blood Pressure after Adjusting for Time Trend

	Slope (%)	95% Confidence interval	*P-value*
SO2	0.36	(0.1, 0.62)	0.007
O2	−0.06	(−0.39, 0.27)	0.74
Systolic BP	0.04	(0, 0.08)	0.09
Diastolic BP	−0.002	(−0.08, 0.08)	0.96

The combined table is made up of the results of separate models.

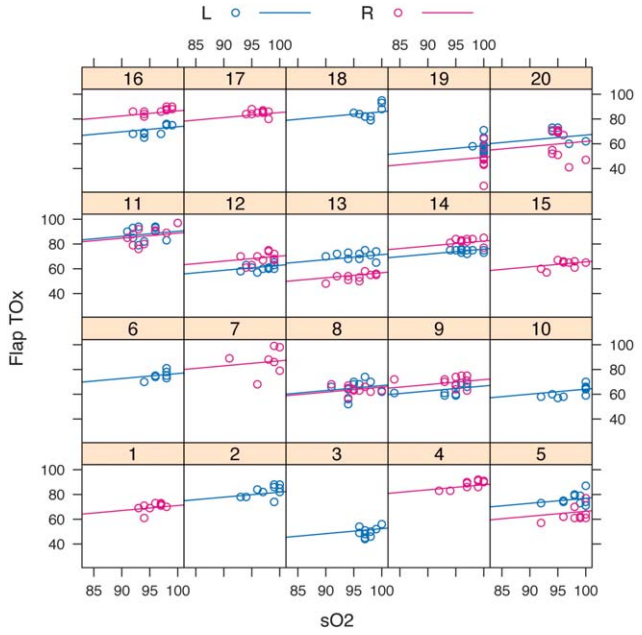


Figure 2. A plot of the relation between sO_2 and flap TOx is shown, grouped by patient. (L: left, R: right, TOx: Tissue oximetry, sO_2: Saturation measured by pulse-oximetry). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

increase, while others had fluctuations in time. Variations were observed not only between patients but between flaps in the same individual as well (Fig. 1).

Analysis of the Effect of Systemic Factors on TOx

Table 2 demonstrates the fixed effects estimate for models of flap tissue oxygenation by SO2, O2, and blood pressure accounting for the trend in TOx over time. There was a significant effect for SO2, such that at a fixed time point, every increase by 1% in SO2 produced an average increase in TOx of 0.36% ($P = 0.007$) (Fig. 2). Similarly, at a fixed time point, it was estimated that for each increase by 1 unit in systolic BP, the average TOx increases by 0.04% ($P = 0.09$). Although trending toward significance, the association between systolic blood pressure and NIRS readings did not achieve a level of statistical significance, after adjusting for the time trend. Neither the amount of supplemental O2, nor diastolic blood pressure, had a statistically significant impact on TOx after accounting for the TOx trend over time ($P = 0.74$, 0.96, respectively).

Table 3. Fixed Effects Estimates from Model of Pre-Extubation TOx by Surgical Characteristics

	Slope (%)	95% Confidence interval	*P*-value
Recipient artery size	−2.48	(−16.92, 11.96)	0.69
Recipient vein size	−2.48	(−16.92, 11.96)	0.69
Flap artery size	4.24	(−5.22, 13.7)	0.34
Flap vein size	4.04	(−12.79, 20.87)	0.58
Perforator number			0.46
2 vs 1	−2.17	(−18.72, 14.38)	
3 vs 1	−11.31	(−31.27, 8.65)	
Perforator row (medial vs lateral)	−2.4	(−15.23, 10.43)	0.63

The combined table is made up of the results of separate models.

Analysis of the Effect of Surgical Factors on TOx

The baseline (pre-extubation) TOx values were correlated to flap type. Though not statistically significant, it was found that on average, free TRAM and MS-TRAM flaps had baseline TOx measurements higher than DIEP flaps [higher by 11.2% (−11.7%, 34.2%) and 7.3% (−7.3%, 21.8%), respectively], SIEA flaps had baseline TOx measurements significantly lower than DIEP flaps, by 16.7% (−33%, −0.4%). No statistically significant associations were found between TOx values and recipient vessel size, flap vessel size, perforator number, or perforator row (Table 3).

DISCUSSION

The overall free flap failure rate is low because of advanced technology and continually improving surgical techniques.[1–3,32,33] When vascular compromise threatens the viability of free flaps, timely intervention is critical for flap salvage.[1,3,5–7,30,34] In current practice, surgeons often utilize an objective tool in addition to clinical observation for postoperative flap monitoring.

Tissue oximetry via NIRS provides continuous and noninvasive measurements of flap perfusion based on optical technology. A probe, which emits near-infrared light, is used to investigate the flap. The reflected light is measured by the sensor, and interpreted by the attached computer to calculate the percentage of oxygenated hemoglobin using spectrophotometric principles.[35–38] Changes in the percentage of oxygenated hemoglobin closely correlate with vascular perfusion.[37–41] When using NIRS, there often is considerable variation in tissue oxygenation between individuals, between flaps, and even between different areas on the same flap. Therefore, it is generally accepted that observing a flap's unique

oximetry trend is more important than looking for an absolute value.[18,26] Many reports have established NIRS's high specifity and sensititivity in predicting flap failure as evidenced by a drop in the TOx value.[15–18,24,26,31,42] On the other hand, other factors affecting a flaps' oxygenation have been less studied.

Previous reports of time-based trends in postoperative flap oximetry and blood flow are contradictory. Several authors have shown a postoperative decrease in flap oxygen saturation[7,29–31] or a transient increase,[6,14,23,27,28,43] while others have found stable flap oxygenation.[17,24–26] The increase in TOx has been explained by vasodilation (because of autonomic denervation, increased inflammatory reaction and ischemia) and by progressive dissolution of microthrombi.[6,25,27,43,44] On the other hand, any decrease has been explained by the time lapse required to establish microcirculation and higher oxygen consumption of the newly transplanted tissue.[7,30] In the cited studies, monitoring duration, flap type, recipient site, and monitoring technology are variable and inconsistent, and thus may explain the conflicting findings. In our study, we initially detected a trend of decrease in TOx with time. However, after adjusting for patients' SO2, this was no longer statistically significant. We suggest that observed time-based trends in flap oxygenation may be attributed to a patient's hemodynamic status, rather than any changes in actual flap perfusion over time. Our research failed to show a significant "time-associated" flap TOx trend.

The contribution of systemic variables to skin perfusion and flap circulation has been mentioned by only a few authors.[17,19,23] Wolff et al. have proposed that various factors such as age, cardiovascular diseases, and nicotine consumption may influence oxygenation of the skin.[19] Keller has suggested that nasal oxygen can cause an elevation of the TOx by 5–10%, but this comment was based on his clinical observations rather than actual data comparison.[17] On the other hand, Kyle et al. showed that high inspired O2 concentrations had only a relatively small effect on TOx, as measured on the thenar eminence of healthy volunteers.[45] To the best of our knowledge, there exist no studies that provide objective data on the influence of systemic variables on flap perfusion. In our study, we have attempted to identify factors that may confound free flap oximetry readings. We found that only SO2 significantly correlated with flap TOx. However, the small change in TOx reading with SO2 is not overly marked, and in clinical practice the SO2 would not be knowingly allowed to drop so low that the corresponding drop in TOx would be meaningful. Similarly, a trend of increase in TOx with increased blood pressure was observed. If blood pressure were allowed to fluctuate widely, this may potentially affect the TOx values. However, such variations were not observed as we managed to control blood pressure within physiologic limits. Given the limited number of time points and patients in which hematocrit and arterial blood gas O2 were recorded, no strong conclusions could be reached regarding their effect on TOx (data not shown).

Tissue perfusion shows variation between individuals, males and females, and different flap types.[19,23,26,31,45–47] The variations may stem from differences in surgical technique (i.e. perforator flaps), anatomy, tissue thickness, and / or the density of capillary vessels.[19,30,47–49] Blood flow in perforator flaps is believed to be less robust by some authors,[50,51] while others propose that it is actually enhanced.[48,49] There are also publications reporting that as the flap is based on fewer and smaller-caliber vessels, complication rates increase because of diminished perfusion.[4,52] To date, there is not any clear evidence that quantifies the differences in perfusion between the variations of abdominal based free flaps. Our data showed decreasing baseline TOx measurements between the free TRAM, MS TRAM, DIEP, and SIEA flaps, respectively. However, a majority of flaps were of the DIEP type and while there is some evidence here that a difference between flap types exists, a definitive conclusion could not be reached. Our findings did not show any correlation of TOx values with recipient vessel size, flap vessel size, perforator number, or perforator row.

The current study has a number of limitations that need to be considered. We did not employ TOx measurement prior to flap elevation and this precluded us from comparing pre-anastomosis and postanastomosis perfusion of the flaps. Although the postoperative measurements were obtained in a temperature controlled flap unit, the patient's actual body temperature was not a data collection point, which could potentially confound perfusion readings. Furthermore, because of the sole usage of internal mammary vessels in the cases, a comparison of different recipient vessels was not possible. Finally, studies with larger sample sizes are required to further elucidate any correlation between surgical variables and perfusion.

CONCLUSION

Free flap monitoring using tissue oximetry provides the investigator with valuable information about postoperative flap perfusion. The flap TOx was found to significantly correlate with a patient's SO2. No significant relationship was found between TOx readings and blood pressure, supplemental O2, flap type, perforator number, or vessel caliber. Careful interpretation of oximetry values is essential in decision making during postoperative flap monitoring.

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