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Negative pressure-induced hyperemia, a new modality in the monitoring of skin paddle containing free flaps

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Summary *Background:* In free tissue transfer, monitoring is paramount to timely detect vascular complications. Although various technical methods have been introduced, clinical flap monitoring and, particularly, capillary refill test (CRT) remain the gold standard. In pale flaps, CRT is challenging as it relies on the color difference between blanched and perfused skin. We proposed a new method of negative pressure-induced hyperemia (NPIH) using handheld electrical negative pressure devices to improve flap monitoring.
Methods: Forty consecutive patients who received 42 free flaps in our institution were included in the study. Postoperatively, digital photographs were taken during CRT and NPIH, and the color difference (ΔE) was calculated based on the images. Additionally, three surgeons and three nurses evaluated the ease of assessment of capillary refill and NPIH on each flap using five grades.
Results: NPIH yielded a significantly higher color difference than CRT with a mean ΔE of 10.3 ± 3.3 versus 6.8 ± 4.2. Although for CRT, ΔE of 14 flaps was <5 and of seven flaps <3, all flaps had a ΔE of >5 for NPIH.
Subjectively, both surgeons and nurses found NPIH in all flaps to be easier to assess with a mean score of 1.1 ± 0.3 versus 1.8 ± 1.1 for CRT. However, some flaps were found to be challenging or not assessable by CRT.

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Conclusion: NPIH represents a safe, easily applicable, and cheap addition to the established clinical and technical examination methods and may offer advantages over conventional CRT in detecting arterial complications in pale flaps.

Introduction

In reconstructive surgery, free tissue transfer with microsurgical vessel anastomosis has become a standard technique since its introduction in the 1950s and is widely applied from breast to all kinds of tissue reconstruction.

Despite immense progress being made in the operative technique and the microcirculatory understanding of free-tissue transfer, flap revision rates remain as high as 16% and flap loss rates around 5% for high-risk flaps like in lower extremity or head and neck reconstruction in high-volume centers.[1,2]

It is widely accepted that timing is key in the detection of vascular complications and directly predicts salvage rates.[3]

Therefore, the monitoring of tissue perfusion is paramount. Creech and Miller outlined the ideal criteria for free-flap monitoring in 1975[4]:

- Simple and harmless to the patient and flap
- Rapid, repeatable, reliable, recordable, and rapidly responsive
- Accurate and inexpensive
- Objective and applicable to all kinds of flaps
- Equipped with simple displays that could alert relatively inexperienced personnel

Over the past, multiple technical methods, such as metabolic measurements,[5,6] implantable Doppler,[7] video-based applications,[8] fluorescence angiography,[9] near-infrared spectroscopy,[6] or contrast-enhanced duplex,[10] have been used to improve monitoring. However, clinical examination remains the gold standard and the most widely used method.[11,12] Chubb et al. reported a take-back rate of 8.2% with a salvage rate of 62.8% in 1140 flaps using clinical monitoring only.[13]

Upon clinical monitoring, the judgment of capillary refill test (CRT) is arguably the most important single criterion next to color, turgor, edema, temperature, and bleeding characteristics.

Capillary refill test is usually performed by applying mechanical pressure to the tissue followed by observing the capillary refill of the blanched skin. Hence, it relies on the visibility of the color difference between the blanched skin and perfused skin.

Depending on the type and origin of the flap, the native skin tone of the patient, and general circulatory factors, such as blood pressure or hemoglobin level, the occurring color difference can vary, and detecting arterial complications in pale flaps represents a challenge in the clinical judgment of capillary refill.

The quantification of color differences can be typically achieved as point measure colorimetric analyses. Analysis on digital photography has been shown to generate similar effective results when appropriate protocols are used.[14]

ΔE represents the difference between two colors and can be calculated based on digital images after converting them to the standardized CIELAB format and then using a calculation formula, the most recent being the CIEDE2000.[14,15]

Higher ΔE values represent larger differences in color, a ΔE of 1 or smaller is described as not perceivable by the human eye. A study describing color changes in the skin found a ΔE of 3 being the minimum to reliably distinguish two colors in this setting.[16] This technique has been applied to examine the success of port-wine stain treatment[17] or evaluate scar color.[18]

Negative pressure has been applied to the skin in the form of cupping therapy for millennia in ancient medicine, predominantly in Asia.[19] It is known that negative pressure leads to shear stress in the underlying tissue, causing vasodilatation and increasing the blood flow.[20] As a repeated measure, it has also been shown in more recent studies that negative pressure can lead to proangiogenic changes.[21]

The idea for this study was to use negative pressure-induced hyperemia (NPIH) to improve the clinical monitoring of free flaps. Although there are multiple ways to apply negative pressure to the skin, we decided to use commercially available electrical handheld pore-cleansing devices that use adjustable negative pressure over a nozzle, intended to remove sebum and other skin waste material, given their ease of application.

Materials and methods

The study was approved by the local ethics committee (approval number 18-6440-BR) and was conducted according to the Declaration of Helsinki. Written consent was obtained from patients included in the study.

Forty consecutive patients who had received musculocutaneous, fasciocutaneous, or adipocutaneous free-flap transplantation were included in the study.

For every flap, at 1–6 h postoperatively on the day of surgery, representative photos and videos were taken during the testing of capillary refill using the handle of a pair of scissors (Figure 2a and b). Immediately afterward, a pore suction device (Pore Cleanser®, Klean Cosmetics, Switzerland, Figure 1) was used for NPIH. For this purpose, the second lowest intensity setting (330 mmHG according to the manufacturer) was selected, and the device was held with the nozzle directed to the skin of the flap and removed after 2 s (Figure 2c and d). The induced hyperemia and the capillary refill caused by the rim of the nozzle were noted as signs of perfusion. Photographs and videos of the process and hyperemia were again taken. The whole process of NPIH testing normally took less than 5 s.

Figure 1 Handheld negative pressure device used in this study (Pore Cleanser®, Klean Cosmetics, Switzerland).

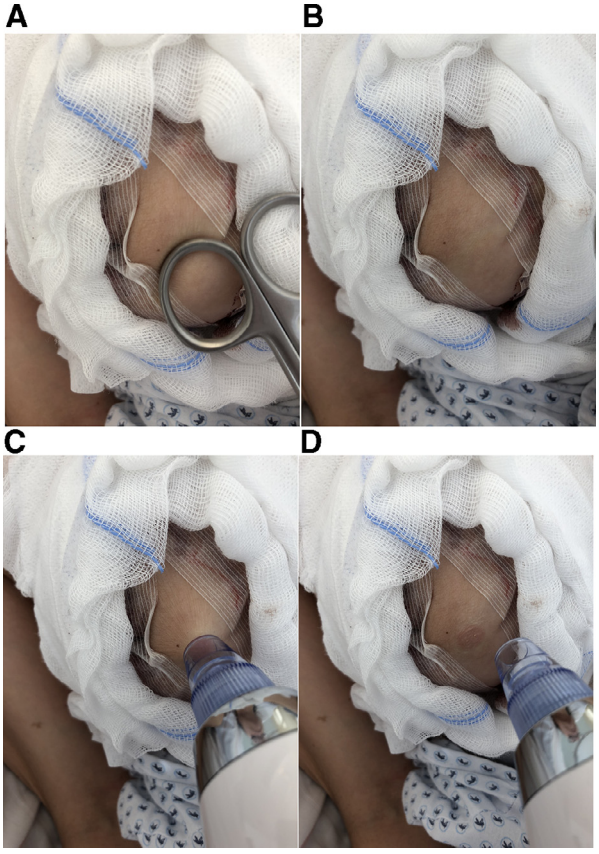

Figure 2 (a–d) Capillary refill test (CRT, a and b) and negative pressure-induced hyperemia (NPIH, c and d) on a PAP-flap for breast reconstruction (ΔE CRT = 5.9, ΔE NPIH = 14.6).

All photographs were taken by the same examiner with the same camera under a standardized ambient temperature of 22 °C. The environment depended on the location of the patient (e.g., intensive care unit); therefore, lighting conditions differed slightly between the patients. Different techniques were performed for each patient and documented immediately one after the other using identical lighting conditions and distance.

A supplementary video of the testing under different circumstances can be found in the online section of this article.

The difference of the colors of blanched skin and surrounding skin for capillary refill and hyperemic skin with the surrounding blanched skin for NPIH was measured using the Delta-*E* technique. For this purpose, the eyedropper tool with a sample size of 5 × 5 pixels (Photoshop CS5 for Mac, Adobe, USA) was utilized to assess L^*a^*b-values of different color tones on the digital images. ΔE calculation was then performed using the CIEDE2000 formula.[15]

Additionally, CRT and NPIH testing on each flap were performed bedside by three different members of the surgical staff and three different members of the trained nursing staff. Each examiner was asked to evaluate the ease of assessment using 5 grades: 1 = very easy to assess, 2 = easy to assess, 3 = assessable with moderate effort, 4 = challenging to assess, and 5 = not assessable/unsafe. The clinical progress of patients, including vascular complications, need for revision, and result of revision, was recorded.

As an additional intraoperative examination, during free-flap harvest of 3 anterolateral thigh (ALT) flaps, after clipping and cutting the pedicle, NPIH was induced repeatedly using a sterile suction adjusted to 330 mmHG. Simultaneously, capillary refill was tested using the handle of a pair of scissors, and the time was measured until each phenomenon was no longer inducible.

Continuous variables were expressed as mean ± SD and categorical data as frequencies and percentages. Normality was tested by the Kolmogorov-Smirnov test. Statistical analyses were performed using Student's *t*-test or paired *t*-test when appropriate to compare means in parametric data. The Wilcoxon signed-rank test was performed to compare medians in nonparametric data. All the tests were 2-sided, with $p < 0.05$ considered as statistically significant. Prevalence-adjusted and bias-adjusted kappa (PABAK) was calculated to analyze inter-rater reliability.

Results

Forty patients were included in the study with a median age of 56 years, which comprised 15 male and 25 female patients. Of these, 21 received an adipo- or fasciocutaneous

Table 1 Study population.

	Total patients ($n=40$)/total flaps ($n=42$)
Age	
<30 years	4
30-60 years	22
>60 years	14
Sex	
Male	15
Female	25
Flap type	
ALT	21
DIEP	10
PAP	2
MLD	6
Parascapular	1
SCIP	2
Anatomical region	
Head/neck	1
Trunk (excluding breast reconstruction)	3
Breast reconstruction	11
Upper extremity	9
Lower extremity	18

ALT-flap, six patients received a myocutaneous latissimus dorsi-flap, two patients a superficial circumflex iliac artery perforator (SCIP)-flap, one patient a parascapular flap, two patients a profunda artery perforator (PAP)-flap, six patients received a single deep inferior epigastric perforator (DIEP)-flap, and two patients a bilateral DIEP-flap.

Most flaps ($n=18$) were transferred for lower extremity soft-tissue reconstruction, whereas other indications were soft-tissue reconstruction of the upper extremity ($n=9$), of the breast ($n=11$), of the trunk ($n=3$), and of the head and neck region ($n=1$). Characteristics of the study population are presented in Table 1.

The documented monitoring was performed 1-6 h postoperatively on all patients.

Measuring the color difference between blanched skin and surrounding skin during CRT and between hyperemic skin and surrounding blanched skin during NPIH showed a significantly higher color difference for NPIH, representing easier visual detectability ($p < 0.001$, Figure 3). CRT resulted in a mean ΔE of 6.8 ± 4.2. Fourteen of the 42 flaps had a ΔE below five during CRT and seven flaps had a ΔE below three. At the same time, NPIH resulted in a ΔE of over 5 in all flaps with a mean value of 10.3 ± 3.3.

Analogously, examiner evaluation of both surgical and nursing staff revealed significantly higher ease of assessment.

Trained nursing staff and surgical staff evaluated capillary refill as "very easy" or "easy" to assess in 70.7% and 80.2% of examinations, respectively, and NPIH as very easy or easy to assess in 100% of examinations among both examiner groups. Overall, the change in the score was highly significant ($p < 0.001$, Figure 4).

On the flaps with a ΔE of below 3 during CRT, nursing and surgical staff evaluated CRT as challenging to assess with a mean score of 4 ± 0.8 and 3.3 ± 1, respectively, whereas NPIH was evaluated as very easy or easy to assess with a mean score of 1.3 ± 0.5 and 1.1 ± 0.3, respectively. The change was significant for each examiner group using the Wilcoxon signed-rank testing (Figure 5).

As the vast majority of flaps were rated as "very easy" to assess, PABAK was calculated instead of Fleiss-kappa to analyze inter-rater-reliability. Here, nursing staff had a fair level of agreement ($\kappa = 0.35$) and surgical staff a moderate level of agreement ($\kappa = 0.52$) in the assessment for CRT while both groups had a strong level of agreement for NPIH ($\kappa = 0.68$ and 0.81, respectively).

Two patients without inducible hyperemization and capillary refill were taken back to the operative room, where arterial thrombosis was detected in the anastomotic region with a patent venous anastomosis. After thrombectomy and reanastomosis, the patients presented inducible hyperemization and CRT. One patient had an uneventful further clinical course, whereas the other suffered partial flap loss and required skin grafting. Two patients who needed operative exploration for venous compromise only presented capillary refill during NPIH testing, while no further hyperemization of the already hyperemic skin could be achieved. Both flaps could be salvaged.

Intraoperative examinations revealed a mean time of 11 ± 8 min after pedicle clipping, in which NPIH was demonstrable and 16 ± 6 min after clipping, in which CRT remained demonstrable. In all tested patients, NPIH stopped being inducible before capillary refill.

Discussion

Our results show that NPIH is safe and easy to apply. The hyperemia is transient and the induced color difference is significantly higher and easier to detect when compared with conventional CRT.

The combination of the blanching caused during NPIH by the nozzle and the central hyperemia increases the color difference and ease of assessment (Figure 6).

In pale flaps without detectable capillary refill, NPIH may only visualize hyperemia. In our small sample size, we were able to show that this is a clinical phenomenon that can only be induced in perfused skin and shortly after the perfusion is stopped and vanished earlier than capillary refill, which is described to be inducible in resected pannus up to 75 min after extinguished inflow.[22]

In hyperemic and congested flaps, no further hyperemization was seen during NPIH, whereas capillary refill is easily displayed by both conventional testing and NPIH.

Subjectively, both surgical and nursing staff found NPIH significantly easier to detect, particularly in patients with low color difference during CRT ($\Delta E < 5$).

Among the 42 tested flaps, the conventional clinical assessment of capillary refill was not feasible in three pale flaps, whereas NPIH was able to prove perfusion as well as enable CRT on hyperemized skin.

Although ease of assessment of the capillary refill depended on individual flap and examiner, NPIH was evaluated as very easy to assess on every flap by every examiner.

It has been shown that the quality of flap monitoring strongly relies on the examiners' experience.[23] It is rarely

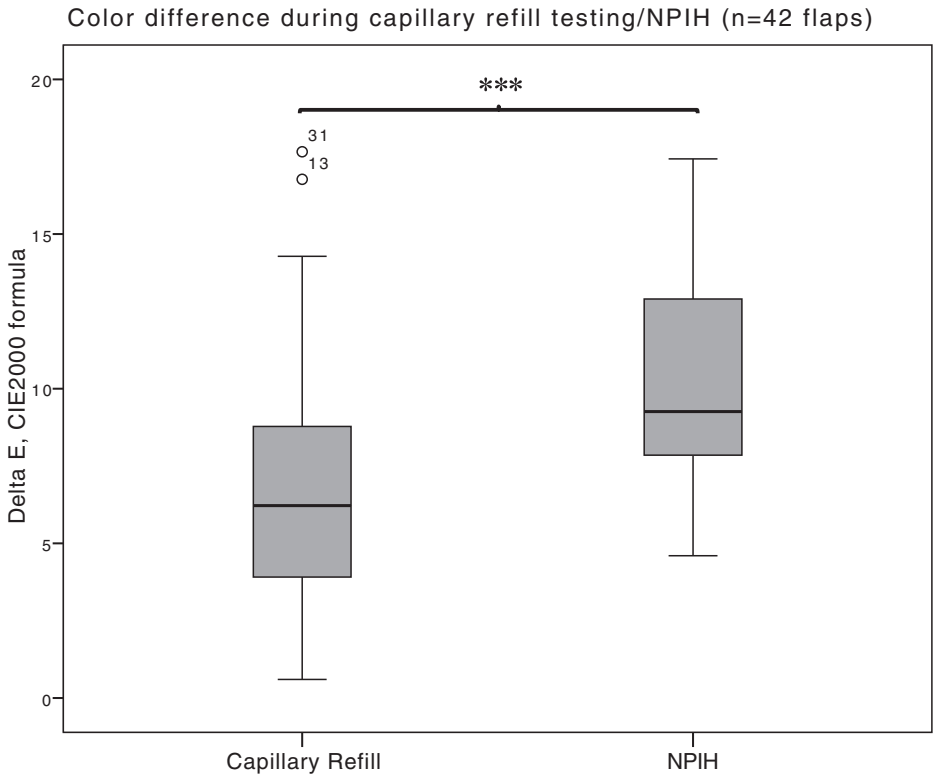

Figure 3 Color difference ΔE measured on digital photographs of the capillary refill test (mean 6.8 ± 4.2) and negative pressure-induced hyperemia (mean 10.3 ± 3.3) of 42 flaps. NPIH yielded a significantly higher color difference. $^{***}p < 0.001$ (paired *t*-test).

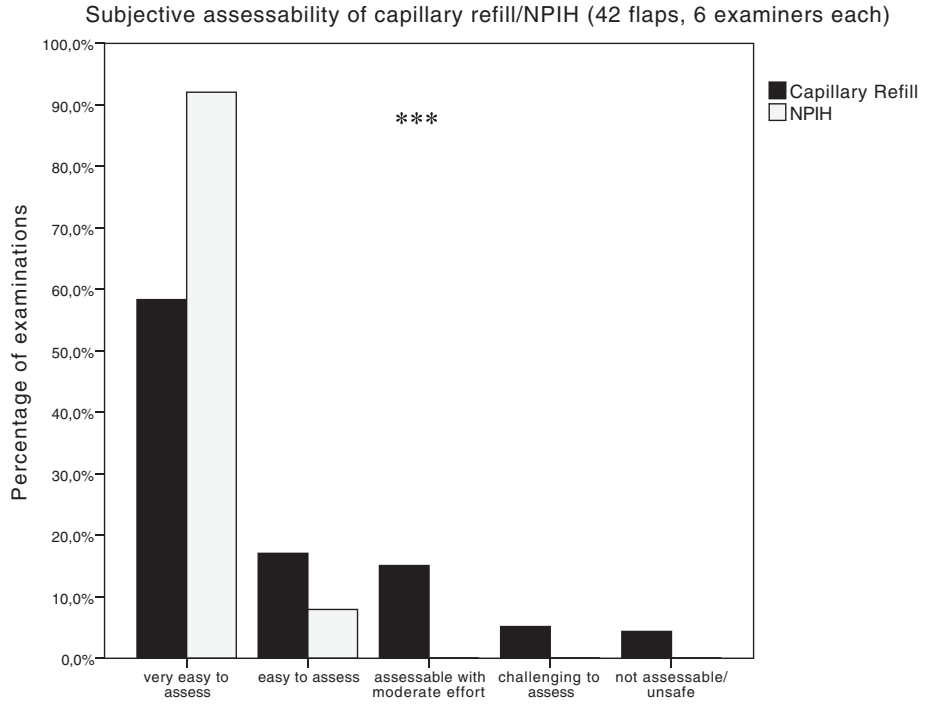

Figure 4 The percentage of subjective evaluations of the assessability of capillary refill test and negative pressure-induced hyperemia by three members of the nursing staff and surgical staff each for 42 flaps. NPIH was significantly easier to assess. $^{***}p < 0.001$ (Wilcoxon signed-rank test).

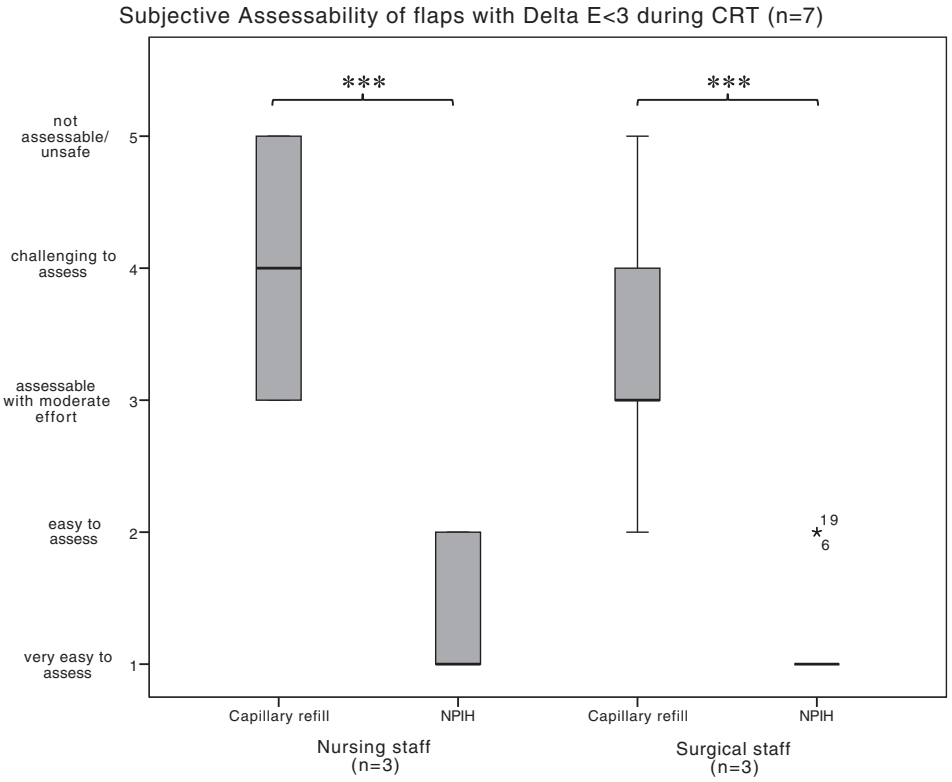

Figure 5 The subjective evaluation of the assessability of capillary refill test and negative pressure-induced hyperemia on subpopulation of flaps with $\Delta E < 3$ in the digital photography analysis of capillary refill test (CRT). NPIH was significantly easier to assess by both the examiner groups. $^{***}p < 0.001$ (Wilcoxon signed-rank test).

possible that the experienced surgeon performing the operation is the person in charge of continuous flap monitoring, so this task may be delegated to residents, nursing staff, and other members of the team. For this reason, Creech and Miller advocated that the flap-monitoring procedure should be simple and contain displays that could alert relatively inexperienced personnel back in 1975.[4]

NPIH testing with handheld negative pressure devices is easy to perform and reproducible, as it reliably uses constant negative pressure unlike the variable mechanical force applied during classical CRT. The technique requires only a small area of flap skin, making it also suitable for monitoring buried flaps with small monitor islands. In flaps with a good Doppler location, where the signal is specific and unmistakable, handheld Doppler is a highly valuable tool for flap monitoring. But, depending on the flap, vascular anatomy, and examiner, false positive or false negative assessment can result. The benefit of NPIH is the immediate tissue response as evidence of perfusion and its ease of use as an additional monitoring tool.

Although clinically detecting venous congestion is easier due to the capillary filling, the detection of arterial complications poses more challenges. Particularly in pale flaps, NPIH may be of great help to visualize hyperemia or capillary refill as the clinical signs of intact perfusion, avoiding invasive measures such as flap scoring or puncturing with associated risks. There are various ways of applying negative pressure to the skin, and cupping devices with manual pumps, modified syringes, or negative pressure drains may be functional for NPIH. However, commercially available electrical handheld pore cleansing devices of any manufacturer with an ideally large nozzle represent the most practical and reliable method in our opinion.

Although recent systematic reviews of implantable Doppler probes and near-infrared spectroscopy show encouraging results suggesting increased sensitivity compared to clinical monitoring alone, the cost and availability limit their broad application.[24,25] As clinical assessment still represents the cornerstone and gold standard of flap monitoring,[11,12] NPIH can become an adjunct to improve its quality.

Limitations

The environment of the photographs and the lighting was approximated but not standardized between different patients. However, this represents the clinical demand that flaps have to be monitored in different environments under various lighting conditions. Most importantly, standardization of measuring conditions was performed for different methods of monitoring within each patient.

We are aware that color changes during CRT cannot always be documented by digital photography, and CRT might be clinically assessable despite a color difference not being detectable on the photographs by our used methods. To overcome this flaw, the subjective evaluation of bedside assessment by both surgical and nurse examiners has been performed.

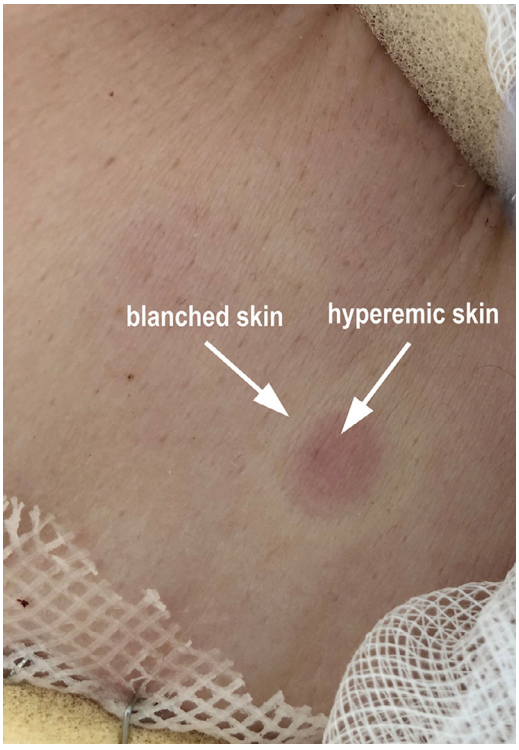

Figure 6 Typical configuration of negative pressure-induced hyperemia demonstrated on a myocutaneous latissimus dorsi flap. Note the annular blanching of the skin by the rim of the nozzle and the central hyperemic skin.

Limitations have to be made due to the small sample size of the study and the potential bias by the examiners, knowing they are testing a new method. In addition, CRT can be improved beyond the described static method by dynamic scraping or stroking of the skin.

This study, neither by design nor by sample size, was intended to compare different methods of flap monitoring based on the outcome and provide statements about sensitivity and specificity. However, it introduces a new method of clinical perfusion visualization as a proof of concept study and provides evidence for easier visual detectability in comparison with conventional CRT.

Conclusion

We believe that NPIH represents a safe, easily applicable, and cheap addition to the established clinical and technical flap examination methods. Although most flaps containing a skin paddle can be assessed easily by CRT, NPIH may offer advantages in the monitoring of pale flaps.

The technique can be broadly applied and may be particularly helpful for monitoring by less experienced personnel; however, long-term data and validation of the method are still needed.

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Ethics

The study was conducted according to the Declaration of Helsinki and approved by the ethics committee of the Ruhr-University in Bochum (approval number 18-6440-BR). The STARD guidelines were adhered to where applicable.

Declaration of Competing Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.bjps.2019.09.008.

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