"Intra-operative tissue perfusion measurement by Laser Speckle Imaging (LSI): a potential aid for reducing post-operative complications in free flap breast reconstructions."

Introduction

Non-invasive imaging of tissue perfusion in free flap breast reconstruction has potential to aid intra-operative decisions and reduce perfusion-related post-operative complications; these include: complete flap failure (2%[1]); fat necrosis (17% depending on flap type[2]); skin necrosis in free-flaps (14%[3]) and skin sparing mastectomy (SSM) skin (3%[4]). Intra-operative and post-operative complication rates for breast reconstruction are approximately 45% for mixed study cohorts[5,6] and between 20% and 100% in others[7]. These complications can result in further surgery, delayed recovery, prolonged hospital stay, poor cosmetic outcome and cause distress to patients and carers[1,8].

Currently, the assessment of intra-operative tissue perfusion and its viability relies mainly on clinical judgement and experience based on anatomy[5,9-11]. Skin colour, turgidity and temperature, capillary refill time and dermal bleeding are commonly assessed but can be unreliable[12-15].

Intra-operative knowledge of tissue perfusion has been shown to aid surgical decisions and reduce complications using the indocyanine green fluorescence (ICG) technique[5,6,9,12,13,16-21]. ICG requires injection of potentially anaphylactic dye; the dye has a transit time of 60 to 90 seconds[18,22]; it is a non-continuous technique[21] that has a delay of 10 to 15 minutes[18] for re-imaging (ICG plasma half-life is 3 to 4 minutes[23,24]). The ICG also comes at a high cost [25-28] (USD76,700–250,000 for equipment; and USD105–275 for ICG per case for dye[27,28]). The total cost of use for SPY Elite may be as high as USD650 per case when other factors are considered[27].

In comparison to ICG, an imaging technique that is dye-free, continuous and at lower recurrent cost, could be an alternative for assessing tissue perfusion during surgery. One example is the Laser Speckle Imaging (LSI) technique[29]. Application of LSI use has been previously reported in neurosurgery[30-32], dermatology[33], ophthalmology[34] and following excision of head and neck tumours[35]. It is a non-contact technique at lower cost (USD80,000 for equipment, USD60 for sterile cover). We have assessed the potential of using LSI in free flap breast reconstruction with the objectives to assess: (i) feasibility of using LSI intra-operatively during free flap breast reconstruction, (ii) ability of the LSI to quantify perfusion across Holm's zonal classifications and (iii) the potential of LSI to inform intra-operative surgical decision making.

Patients and Methods

This single centre observational study was performed at the Royal Devon and Exeter NHS Foundation Trust, Exeter, UK (Ethics approval: 13/SW/0289). All adult patients (≥18 years) scheduled to receive free flap breast reconstruction were invited and written consent obtained.

Laser Speckle Imaging technique

Tissue perfusion images were obtained intra-operatively by use of the non-invasive, non-contact, diverging infrared laser technique of a full-field LSI (50mW laser, wavelength 785nm; moorFLPI-2, Moor Instruments Ltd, Axminster, UK). The LSI technique is sensitive to perfusion no deeper than the dermis (i.e. only the microvasculature). A 6-colour palette was used for the tissue perfusion range 0 to 400 Perfusion Units (PU, a diffusion-based unit); blue indicates low tissue perfusion and red indicates high perfusion (figure 1) (see Video, Supplemental Digital Content 1, which demonstrates the setup of real-time blood flow imaging in surgery).

Scanning protocol of intra-operative LSI

Scan times included: (i) abdominal area and breast(s) before incision, (ii) native breast skin envelope post mastectomy (immediate reconstructions), (iii) abdominal flap isolated on pedicle, (iv) flap after anastomosis, (v) flap skin paddle and native breast skin after flap inset and (vi) post closure.

LSI images were recorded continuously for approximately ten seconds with the LSI scan-head positioned 25cm above the skin; i.e. two scans, 15cm x 20cm, were required for the abdomen (left and right, overlapping; figure 1).

Data analysis

Data analysis was performed (using moorFLPI V4 software, Moor Instruments Ltd.) to compare: (i) tissue perfusion in the four zones (Holm's) of each abdominal flap when isolated on the deep inferior epigastric pedicle and (ii) the proportions of zonal areas with perfusion below an arbitrary threshold (as a proof of concept to assess potential clinical relevance regarding tissue viability). The arbitrary threshold was set at 200PU, close to the average flap perfusion level. Representative images were prepared by averaging 50 frames (two seconds) from a stable section of each LSI image sequence. Regions of interest were drawn corresponding to the 4 zones (figure 1). Analysis of Variance (ANOVA) and non-parametric pair-wise Wilcoxon tests (IBM SPSS Statistics for Windows, Version 24, Armonk, NY, USA) were used for data analysis. Statistical significance was set at $p \leq 0.05$. All tissue perfusion data are expressed as median (range) unless stated otherwise.

Results

The study was performed in 20 patients (mean age 50, range: 32–68 years). 23 flaps were included (3 bilateral), 10 immediate and 13 delayed breast reconstructions; 17 were muscle-sparing transverse rectus abdominis myocutaneous (MS-TRAM) flaps; 6 were deep inferior epigastric perforators (DIEP) flaps (see Table, Supplemental Digital Content 2, which shows patient characteristics and reconstruction type).

Zonal perfusion and zonal area with perfusion below an arbitrary threshold

For abdominal flaps isolated on pedicle (Figure 1), LSI perfusion in Zone IV (125 [102-220]PU) was significantly lower than in Zone I (238 [187–313]PU; $p<0.001$), Zone II (222 [120–265]PU; $p<0.001$) and Zone III (206 [120–265]PU; $p<0.001$) (see Figure, Supplemental Digital Content 3, which shows averaged LSI tissue perfusions for Zones I, II, III and IV (Holm's)). When comparing the proportion of each zone below the arbitrary perfusion, Zone IV (99 [25–100]%) had the highest proportion of tissue area below the arbitrary perfusion threshold compared with Zone I (20 [0.3–75]%; $p<0.001$), Zone II (41 [3–99]%; $p<0.001$) and Zone III (49 [9–97]%; $p<0.001$) (see Figure, Supplemental Digital Content

4, which shows proportion of zonal area (%; Holm’s) with tissue perfusion below an arbitrary perfusion threshold).

Case report

A 42-year old woman presented with mastectomy native breast skin necrosis postoperatively. Retrospective data analysis of LSI images revealed that the lower medial quadrant of the left breast envelope, after skin-sparing mastectomy contained an area of low tissue perfusion, as indicated by blue on the LSI images (Figures 2 middle and right) (see Table, Supplemental Digital Content 5, which shows perfusion related post-operative complications for the 23 breast reconstructions). This ischemia was not detected clinically intra-operatively and subsequently became necrotic requiring excision on day 23.

Discussion

The wide ranges of tissue perfusion in all zones indicate the large variability of flap perfusion in the study population. Our analysis has confirmed the ability of LSI to quantify perfusion across Holm’s zonal classifications. Furthermore, the case report illustrated the intra-operative potential of LSI to avoid further surgery by identifying an area at risk of developing post-operative complications.

Conclusions

LSI was found to be feasible, quick, safe and easy to use intra-operatively. Results of zonal perfusion analyses aligned with Holm’s classification and indicated the ability of LSI to quantify tissue viability intra-operatively. The case presented is one example showing potential for LSI to aid intra-operative decision making.

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Conflicts of interest statement

RG is employed by Moor Instruments Limited, the company responsible for the development of the LSI system loaned for use in this study. No other authors have any conflicts of interests to declare.

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Figure legends

Figure 1 Intra-operative LSI tissue perfusion; black dotted lines indicate zonal regions of interest, for both sides of the flap when raised on pedicle for a breast reconstruction using a muscle-sparing free TRAM flap. The regions of interest illustrate the analysis area of averaged zonal perfusion.

Figures 2 Mastectomy native breast skin with subsequent post-operative complication. Breast skin envelope (photo, left) and corresponding LSI tissue perfusion (middle); and LSI post closure (right). Note the area of low perfusion (LSI blue) on the skin envelope persisted following closure (right; red circular area corresponds to the skin paddle of the abdominal flap).

Supplemental Digital Content legends

Video, Supplemental Digital Content 1, Setup of real-time blood flow imaging in surgery.

Table, Supplemental Digital Content 2, Patient characteristics and reconstruction type.

Figure, Supplemental Digital Content 3, Averaged LSI tissue perfusions for Zones I, II, III and IV (Holm's). The wide ranges of median tissue perfusion in 20 patients are illustrated in box plots which show median, range and 25th and 75th percentiles.

Figure, Supplemental Digital Content 4, Proportion of zonal area (%; Holm's) with tissue perfusion below an arbitrary perfusion threshold in 20 abdominal flaps isolated on pedicle; box plots show median, range and 25th and 75th percentiles.

Table, Supplemental Digital Content 5, Perfusion related post-operative complications for the 23 breast reconstructions.