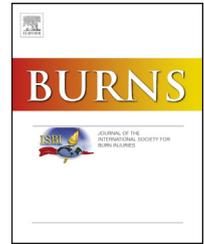


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Interobserver reliability of laser speckle contrast imaging in the assessment of burns

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ABSTRACT

Objectives: Laser speckle contrast imaging (LSCI) is an emerging technique for the assessment of burns in humans and interobserver differences have not been studied. The aim of this study was to compare assessments of perfusion images by different professional groups regarding (i) perfusion values and (ii) burn depth assessment.

Methods: Twelve observers without LSCI experience were included. The observers were evenly recruited from three professional groups: plastic surgeons with experience in assessing burns, nurses with experience in treating burns, and junior doctors with limited experience of burns. Ten cases were included. Each case consisted of one digital photo of the burn with a pre-marked region of interest (ROI) and two unmarked perfusion images of the same area. The first and the second perfusion image was from 24 h and 72–96 h after injury, respectively. The perfusion values from both perfusion images were used to generate a LSCI recommendation based on the perfusion trend (the derivative between the two perfusion values). As a last step, each observer was asked to estimate the burn depth using their clinical experience and all available information. Intraclass correlation (ICC) was calculated between the different professional groups and among all observers.

Results: Perfusion values and perfusion trends between all observers had an ICC of 0.96 (95% CI 0.91–0.99). Burn depth assessment by all observers yielded an ICC of 0.53 (95% CI: 0.31–0.80) and an accuracy of 0.53 (weighted kappa). LSCI recommendations generated by all observers had an ICC of 0.95 (95% CI: 0.90–0.99).

Conclusion: Observers can reliably identify the same ROI, which results in observer-independent perfusion measurements, irrespective of burn experience. Extensive burn experience did not further improve burn depth assessment. The LSCI recommendation was more accurate in all professional groups. Introducing LSCI measurements would be likely improve early assessment of burns.

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1. Introduction

To assess partial-thickness burns successfully is difficult, even for someone experienced in the treatment of burns [1]. The accuracy of clinical assessment alone in injuries 0-5 days old is reported to vary between 60% and 70% among experienced surgeons [2-4]. The depth of the burn is estimated clinically by investigating time taken for capillaries to refill, sensitivity, and the appearance of the wound [5,6]. These factors are weighted together and evaluated subjectively, often without using an established standard. The accuracy therefore rests largely on the experience of the surgeon. This often causes a delay in surgical decision-making because clinical demarcation is often not apparent until at least eight days after the injury [4]. Early excision and grafting have been shown to improve

clinical outcome and reduce the risk of hypertrophic scarring [7,8]. Accurate and early assessment of the true depth of the burn is therefore vital to facilitate early excision and split-thickness skin grafting when appropriate.

Perfusion is an objective measure, which is a reliable predictor of the healing capacity of the wound [2]. So far, laser Doppler imaging (LDI) has been the leading non-invasive measurement of perfusion in burns [3]. Several studies have shown that it is more accurate than clinical assessment alone during the first week after injury [4,9-18]. That LDI is so successful in early assessment of burns lends credence to the idea of perfusion as an excellent objective method of assessment.

Even though LDI has been extensively validated, it has gained only limited approval and there might be several reasons for this. One reason for this could be that most LDI

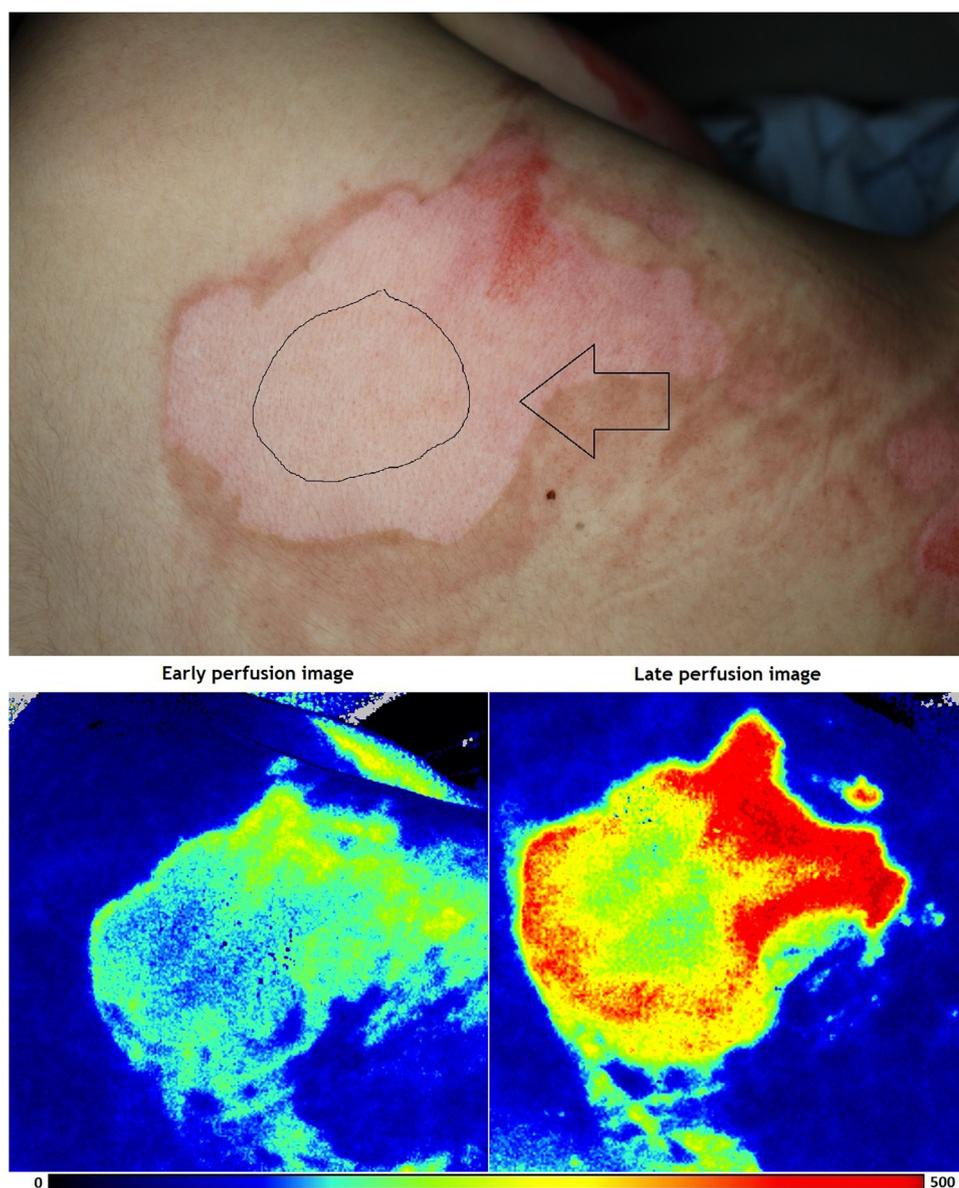


Fig. 1 – A typical case (case 3). Each observer was presented with a pre-marked (black line) normal digital photograph of the scald (upper part of the figure). They then had to find the corresponding area in both perfusion images and outline the ROI. The perfusion values from both images were then put into an Excel file, which calculated the LSCI recommendation and presented it to the observer. Based on all available information, the observer was asked to predict the outcome of the burn.

systems are cumbersome and require a relatively long time to make the measurement, even when line-scanners are used. Another reason could be problems with movement artifacts, particularly in children [19]. Full-field LDI systems are still being developed and there are promising reports of their usefulness [20], but these systems have yet to be proved clinically.

Laser speckle contrast imaging (LSCI) is a method for measurement of perfusion that works in a slightly different way from LDI [21]. Both systems produce a color-coded map of the investigated area with "red" indicating high perfusion and "blue" low perfusion [21]. Perfusion is measured using arbitrary perfusion units (PU), and calibrations in a standard assay ensure consistency between systems and over time [21-23]. It uses a divergent laser beam to illuminate the tissue and a typical measurement area is 20 × 20cm. The entire image is captured simultaneously without any scanning. The speckle pattern arises within the measurement area because of constructive and destructive interference in the laser light [22,23]. Light scattered by moving red blood cells causes spatial and temporal fluctuations in the speckle pattern, which causes blurring during the image integration time [22,23]. The degree of blurring is quantified and is proportional to the perfusion in the tissue. These images are recorded at roughly 10-40Hz, with the option to average the images to trade temporal for spatial resolution [23]. For high quality images of burns, this translates to an acquisition time of 200-1000ms.

For the perfusion images to be useful, they must be interpreted correctly. Classically, both LDI and LSCI images have been evaluated by subjective assessment of which color is the most prominent within the area being investigated [4,21,19]. A color cut-off is then used to indicate when operation is recommended [4,19]. Another way to do this is to outline the region of interest (ROI) and calculate its mean perfusion [24,25,26]. This may allow for a more objective assessment. Regardless of method, the interobserver reliability of LSCI assessments have not yet been established. How LSCI images and perfusion information will assist in clinical burn practice is also unknown.

LSCI has previously been used in several studies investigating burn depth in both animal models and in humans [24-29]. We have previously reported that LSCI has a 100% sensitivity and specificity in predicting the need for operation when a "double measurement" approach is used, at 0-24 and 72-96h after injury [26]. In the same study, all ROI were outlined

by the first author (RM) and the interobserver reliability could not be studied. The primary aim of the present study, therefore, was to investigate the interobserver reliability in the assessment of burns using LSCI. We hypothesized that there would be high correlation in mean perfusion values among observers. We also hypothesized that knowledge of perfusion values would lead to high interobserver reliability in surgical decisions made early.

2. Methods

2.1. Observers and task description

The observers, who had no previous experience of the assessment of burns with LSCI, were divided into three groups. The first consisted of plastic surgeons with experience of treating burns, the second of nurses experienced with burns, and the third of junior doctors with little or no experience of burns. They had an oral introduction to the subject aided by a PowerPoint presentation beforehand. In addition, they were also given written instructions, which they could keep for the duration of the trial. The observers could ask questions about the presence of optical artifacts in the images.

The task consisted of creating a ROI in each of 20 perfusion images from 10 patients according to a pre-marked normal digital photograph, which was from either the early or the late measurement. An example image is shown in Fig. 1. Each digital photograph was marked with how many hours/days had passed since the injury, and this was clearly presented to all observers. In each perfusion image, the observer outlined one ROI in accordance with the pre-marked ROI in the digital photograph from roughly the same angle. This was done for both an early and a late LSCI measurement, 0-24 and 72-96h after injury, respectively, which yielded two perfusion values for each case and observer. These two values were then incorporated in a mathematical formula to calculate the perfusion change between the measurements, and generated a dichotomous LSCI recommendation, "surgery" or "spontaneous healing". We have described this formula in a previous study which investigated the sensitivity and specificity of assessment of the depth of a burn using LSCI [26]. After each observer had received their LSCI recommendation, they were asked to predict the outcome of the burn using all the available information and their clinical experience by making a choice between the following categories:

Table 1 – Descriptive data of the cases shown to the observers.

| Patients No. | Type of burn | Time to heal | Correct prediction | Time after injury of pre-marked digital photograph |
|--------------|--------------|--------------|---------------------------|--|
| 1 | Scald | Surgery | Surgery | 4 days |
| 2 | Scald | 7 days | Spontaneous healing | 4 days |
| 3 | Scald | 12 days | Spontaneous healing | 17 h |
| 4 | Scald | 8 days | Spontaneous healing | 18 h |
| 5 | Scald | 21 days | Maybe spontaneous healing | 24 h |
| 6 | Scald | Surgery | Surgery | 23 h |
| 7 | Scald | 9 days | Spontaneous healing | 3 h |
| 8 | Scald | 8 days | Spontaneous healing | 17 h |
| 9 | Contact burn | Surgery | Surgery | 19 h |
| 10 | Scald | 11 days | Spontaneous healing | 4 days |

“spontaneous healing/0”, “maybe spontaneous healing/0.33”, “maybe surgery/0.67”, and “surgery/1”.

2.2. Cases

The cases presented consisted of nine scalds and one contact burn. Details for each case are shown in Table 1. Three of the cases went through excision and split-thickness skin grafting after a 14-day observation window of “no healing”. One of the cases consisted of a small ROI of 1 × 2 cm that required 21 days to heal; in this case “maybe spontaneous healing” was deemed the most reasonable assessment. The remaining six cases consisted of scalds that healed between 1–2 weeks. The pre-marked normal digital photographs were captured during the early measurement in seven of the cases (cases 3–9) and during the late measurement in the remainder (cases 1, 2, and 10).

Contact burns often generate anomalous results when our formula for perfusion change is applied, giving a false recommendation, even when the observer has marked the ROI correctly. However, these are easily identified by the experienced LSCI observer because of their low perfusion and clinical appearance. One of the selected surgical cases (case 9), therefore was of a contact burn to find out if the observers with extensive experience in burns would be able to avoid this pitfall.

2.3. Equipment

The perfusion images in the ten cases were previously collected in children treated as outpatients or admitted to the intensive burn care unit at Linköping University Hospital. The same LSCI system (Pericam PSI, Perimed AB, Järfälla, Sweden) was used to collect all perfusion images in the material. The system uses a divergent laser with a wavelength of 785 nm and fluctuations in the arising speckle pattern is used to calculate the perfusion of the tissue. We have previously described the principles of LSCI in detail [25] and methodological aspects when using LSCI for perfusion measurements in the skin [30].

Image size was set to 18 × 18 cm and the distance between the camera and the burn wound was kept between 18 to 27 cm. Perfusion was recorded with 21 images per second and the final image presented to the observers was the average of 42 images. The spatial resolution was roughly 0.2 mm/pixel in the final image. The system was regularly calibrated according to the recommendation of the manufacturer.

The digital photos were captured using a separate digital camera (Canon EOS 600D, Canon Inc., Tokyo, Japan). This camera was also equipped with a cross polarization system, which removes the reflection from fluids present in burn wounds considerably improving the image quality compared to a standard camera system. These images were recorded at roughly 18–27 cm and from the same angle as the perfusion images if possible.

Since the room must be dark for the TiVi-system to work, the digital photos were not always collected at each wound dressing. For this reason, we decided to only present one of potentially two digital photos to the observers from either 24 h or 72–96 h after injury. In cases where two digital photos existed; similarities in angle and distance from the skin compared to the two perfusion images were used as selection criteria.

2.4. Statistical analysis

All correlation analyses were made using intraclass correlation (ICC) testing for absolute agreement, with a two-way random model for the variable being measured. All ICC values are reported as single measurements.

Kappa values were calculated to measure the accuracy of the assessments made by the different observers compared with the actual outcome. All kappa values were calculated using a weighted kappa with a weight equal to 1 for each increasing ordinal level of disagreement. Kappa statistics were selected because random chance agreement is considered, and therefore better capture the probabilistic nature of assessments. Weights were applied as the test variables were ordinal.

Descriptive statistics are reported as mean (SD). A one-way ANOVA with multiple comparisons was done using Fisher’s exact test to assess the significance of differences between the groups of observers.

All statistical analyses were made with the aid of GraphPad Prism version 5.02 for Windows (GraphPad Software, San Diego California USA, www.graphpad.com), SPSS version 25 (IBM, Armonk NY, USA, www.ibm.com) and Excel 2016 (Microsoft, Redmond Washington USA, www.microsoft.com).

3. Results

Each observer outlined a total of 20 ROI in 10 patients on both early and late perfusion images (0–24 and 72–96 h after injury). In Table 2, the degree of agreement is shown for all

Table 2 – The absolute agreement using ICC is shown between the groups of observers with the 95% CI in brackets. Perfusion units (PU) in early/late measurement refers to the ICC of perfusion values from the first/second perfusion image. Perfusion trends use the values from both measurements to calculate perfusion change. The “Burn assessment” category is the observers’ final judgment, taking all factors into account. LSCI recommendation shows the agreement of the recommendations produced by the observers’ perfusion values.

| | Plastic surgeons | Nurses | Junior doctors | All groups |
|-------------------------|------------------|------------------|------------------|------------------|
| PU in early measurement | 0.99 (0.97–1.00) | 0.95 (0.89–0.99) | 1.00 (0.99–1.00) | 0.98 (0.95–0.99) |
| PU in late measurement | 0.99 (0.97–1.00) | 0.87 (0.72–0.96) | 1.00 (0.99–1.00) | 0.95 (0.90–0.99) |
| Perfusion trend | 0.98 (0.95–0.99) | 0.84 (0.65–0.95) | 0.99 (0.98–1.00) | 0.94 (0.87–0.98) |
| Burn assessment | 0.30 (0.04–0.67) | 0.51 (0.21–0.81) | 0.75 (0.50–0.92) | 0.53 (0.31–0.80) |
| LSCI recommendation | 1.00 (n/a) | 1.00 (n/a) | 0.87 (0.71–0.96) | 0.95 (0.90–0.99) |

measurements for each subgroup and as a pooled value. The pooled ICC of all groups was 0.98 (95% CI 0.95-0.99) in the early perfusion images, 0.95 (95% CI 0.90-0.99) in the late perfusion images, and 0.94 (95% CI 0.87-0.98) for calculation of perfusion change. Figs. 2 and 3 are scatter plots showing the contributions of each observer to each case.

The ICC of assessment of the depth of the burn was 0.30 (95% CI 0.04-0.67) in the group of plastic surgeons, 0.51 (95% CI 0.21-0.81) among the nurses, and 0.75 (95% CI 0.50-0.92) for the junior doctors. Pooled LSCI recommendations for all groups showed an ICC of 0.95 (95% CI 0.90-0.99).

The accuracy of the different observers compared with the actual outcome was measured using weighted kappa (Table 3). The kappa value was 0.38 among the plastic surgeons, 0.62 among the nurses, and 0.60 among the junior doctors. The accuracy of the LSCI recommendation was 0.74 for the plastic surgeons, 0.74 for the nurses, and 0.80 for the junior doctors.

Table 4 shows the descriptive statistics of the observers. None of the differences between the groups were significant except for age; the junior doctors were significantly younger than both the plastic surgeons (p=0.001) and the nurses (p=0.024).

4. Discussion

Our main finding was that all the observers marked ROI with similar perfusion values, and this was not influenced by previous experience in the treatment of burns. Additionally, when we used the formula for perfusion change, the results

were reproducible among observers, which resulted in nearly identical LSCI recommendations. However, observers often decided to trust their clinical experience over the perfusion values that they produced using the images. This suggests that clinicians must develop a level of confidence towards the information in the perfusion images, particularly the generated perfusion values, before they are comfortable to use it as a tool in clinical practice.

Previous experience in the treatment of burns does not seem to facilitate better assessment of the depth of a burn when combined with LSCI assessment. On the contrary, extensive experience might sometimes make the observer over-confident, despite the limited information in one digital image. Strangely enough, this was not the case among nurses with extensive experience in burns, whose results did not differ from those of the junior doctors with limited experience. The improvement in the accuracy of assessment, had the LSCI recommendations been followed to the letter, was 0.36 among the plastic surgeons, 0.11 among the nurses, and 0.20 among the junior doctors using the mean difference in weighted kappa. It seems therefore that extensive burn experience has limited added value when the observer is new to using LSCI for assessment of the depth of a burn. However, the value of extensive clinical experience among observers who are also experienced in LSCI is still unknown.

As we expected, one of the more complicated cases was case 9 (Fig. 4), with a contact burn that generally produced erroneous LSCI recommendations. In this case the observers produced 11 erroneous and 1 correct LSCI recommendations. One of the four plastic surgeons suggested surgery, while three

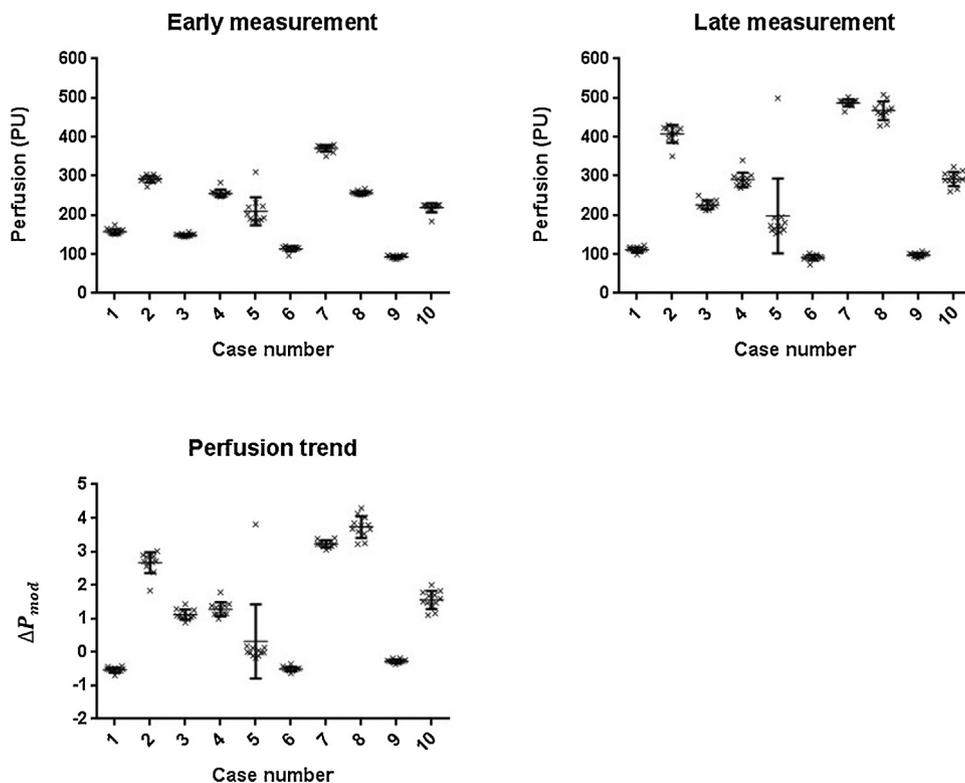


Fig. 2 – Scatter plots of each observers’ recorded perfusion values and perfusion trend values. Horizontal bars show the mean value and vertical error bars the SD. Case number is given on the x-axis and either perfusion or perfusion change (ΔP_{mod}) on the Y axis. Perfusion trends were obtained by using perfusion values from both the early and the late measurements.

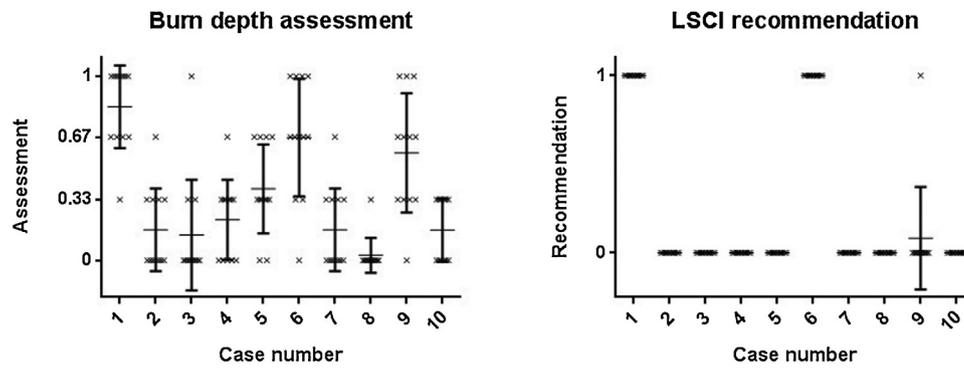


Fig. 3 – Scatter plots of each observers’ assessment and the LSCI recommendations that they were given. Horizontal bars show the mean value, and vertical error bars the SD. Case numbers are shown on the x-axis, and the assessment made by each observer together with the LSCI recommendation on the y-axis. 0=“spontaneous healing”, 0.33=“maybe spontaneous healing”, 0.67=“maybe surgery”, 1=“surgery”.

Table 3 – The accuracy of the assessments of the depth of the burn in the groups of observers expressed as a weighted kappa value. Recommendation, also calculated as a weighted kappa value, shows the accuracy of the LSCI recommendation they received. Improvement shows the gain in accuracy had all observers followed the LSCI recommendation.

| | Plastic surgeons | Nurses | Junior doctors | All groups |
|----------------|------------------|--------|----------------|------------|
| Accuracy | 0.38 | 0.62 | 0.60 | 0.53 |
| Recommendation | 0.74 | 0.74 | 0.80 | 0.76 |
| Improvement | 0.36 | 0.11 | 0.20 | 0.22 |

Table 4 – Descriptive statistics of the observers included in the study expressed as mean (SD). Age was significantly lower among the junior doctors compared with the plastic surgeons ($p=0.001$) and the nurses ($p=0.024$). For the variables: “Computer experience”, “Level of difficulty”, and “Confidence in assessment”, each observer was asked to respond with a value ranging from 0 to 10, where 0 was equivalent to “very limited” and 10 to “very extensive”.

| | Plastic surgeons | Nurses | Junior doctors | All groups |
|--------------------------|------------------|-------------|----------------|-------------|
| Age (years) | 41.8 (4.5) | 49.0 (14.7) | 26.5 (3.1) | 39.1 (11.5) |
| Computer experience | 6.8 (1.3) | 7.0 (2.4) | 8.5 (1.3) | 7.4 (0.9) |
| Level of difficulty | 5.0 (1.4) | 5.3 (2.2) | 6.3 (1.3) | 5.5 (0.7) |
| Confidence in assessment | 5.0 (0.0) | 6.3 (1.3) | 3.8 (1.7) | 5.0 (1.3) |
| Time (minutes) | 40.8 (12.6) | 55.3 (15.4) | 42.5 (7.0) | 46.2 (7.9) |
| Number of sessions | 1.5 (0.6) | 1.0 (0.0) | 1.3 (0.5) | 1.3 (0.3) |

of the four nurses, and three of the four junior doctors did. This indicates that extensive experience did not necessarily prove beneficial to the observers.

We included case 9 to test our hypothesis that experienced observers would be able to recognize the false LSCI recommendation. One of the junior doctors, however, managed to get a correct LSCI recommendation by marking only the very central aspects of the burn; this produced perfusion values with a decrease of 5 and 4 PU in the early and late measurements, respectively, compared with the mean of the other observers. Many of the participants did comment on the low perfusion values in both the early and the late images, and often compared these to perfusion values from previous cases. The general whiteness of the wound in the digital photograph also alerted several observers. These different factors caused many of the observers to disregard the LSCI recommendation because of a perceived difference from other cases, but extensive experience in the treatment of burns did not seem to

influence this decision. The inability of observers with extensive experience to classify case 9 reliably as a surgical case might also reflect the difficulty in assessment of the depth of a burn using digital photographs alone, often with the observer being unaware of the disadvantage.

As case 9 was a contact burn, and therefore generally generated a false LSCI recommendation, we wanted to investigate what kind of impact this case had on our results. All ICC analyses and kappa statistics were therefore done a second time, with case 9 excluded. The change in ICC values related to perfusion were smaller than the rounding difference. ICC values of the burn depth assessment improved slightly among observers, which caused a pooled change from 0.53 to 0.55. The weighted kappa value, which describes the accuracy of the burn depth assessment compared to the actual outcome, was improved from 0.53 to 0.56.

The only measures that were notably changed were the agreement of the LSCI recommendation among observers, and the improvement in accuracy if the LSCI recommendations

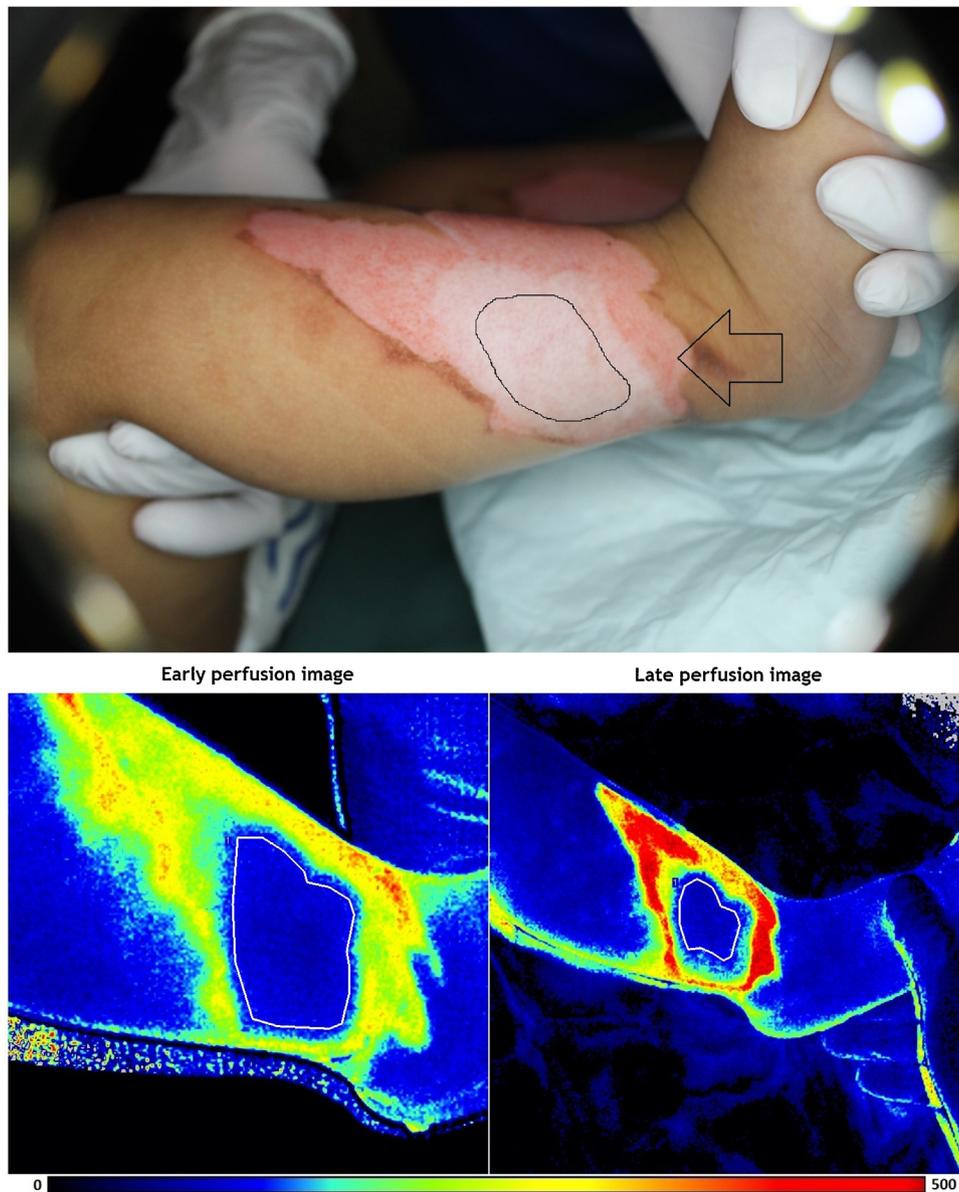


Fig. 4 – Case 9 was a contact burn, which often behave anomalously when perfusion dynamics are measured, possibly because there is a clear demarcation of the damaged tissue from the start. This prevent contact burns from going through the same degree of burn wound conversion, otherwise so commonly observed in scalds. The low perfusion values combined with a whitish to red speckled color pattern make this a clear-cut case for skin grafting in the eyes of the experienced LSCI observer. The ROI in the images are marked by the first author (RM) and produced a perfusion of 93 and 93 PU in the early and late measurements, respectively. The digital image was captured 19h after injury and surgery was required to achieve healing. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

had been followed to the letter. The agreement in LSCI recommendations changed from an ICC of 0.95 to 1.00, and the improvement in accuracy changed from a weighted kappa of 0.76 to 1.00. It therefore seems safe to say that the inclusion of this case had no significant effects on the results of the study, apart from the agreement and accuracy of the LSCI recommendations. However, if the LSCI would be used for measuring the depth of contact burns, different perfusion cut-off values would have to be used. Based on our limited experience with LSCI measurements in contact burns, an early value would

probably be able to provide an accurate assessment and could therefore be used instead of a double measurement.

One of the limitations of this study was that we did not have a completely standardized briefing before the trial, meaning that the observers might have each had slightly different information. The same PowerPoint presentation was used for all participants, and each slide was accompanied by the same commentary. However, each observer was allowed an unlimited number of questions, and those who asked questions may have had a better understanding than those who did not.

Another limitation was that each observer had access to only one digital photograph and two perfusion images of each case, making it impossible to make a proper clinical assessment. Having only one digital photograph prevented the observers from evaluating the normal visual aspects of the burn wound progression they are used to investigating. In seven of the ten cases, the digital photo was captured 0-24h after injury, which potentially added further difficulty to clinical assessment of the burn depth. However, when the average accuracy of the burn assessment was calculated for these seven cases, it generated a weighted kappa value of 0.48 compared to 0.53 for all ten cases. This small difference is unlikely to have caused any larger bias.

There was often a discrepancy in angle and distance measured between the perfusion images and the pre-marked

digital photograph because the inbuilt documentation camera in the LSCI had poor resolution, which added an unnecessary difficulty. This might have generated several errors, particularly in case 5 (Fig. 5), in which there was a substantial discrepancy in the angle between the pre-marked digital photograph and the perfusion images. Much of the extensive clinical experience of the plastic surgeons might therefore not have been put to good use. However, case 5 which also had a large discrepancy in angles and distances proved to be the easiest case, where all observers correctly identified the burn wound as suitable for conservative treatment (Fig. 6).

It has been reported that assessment of a burn using a digital photograph has less accuracy than clinical assessment when used for the evaluation of partial-thickness burns [31]. Our results might therefore have been different if the

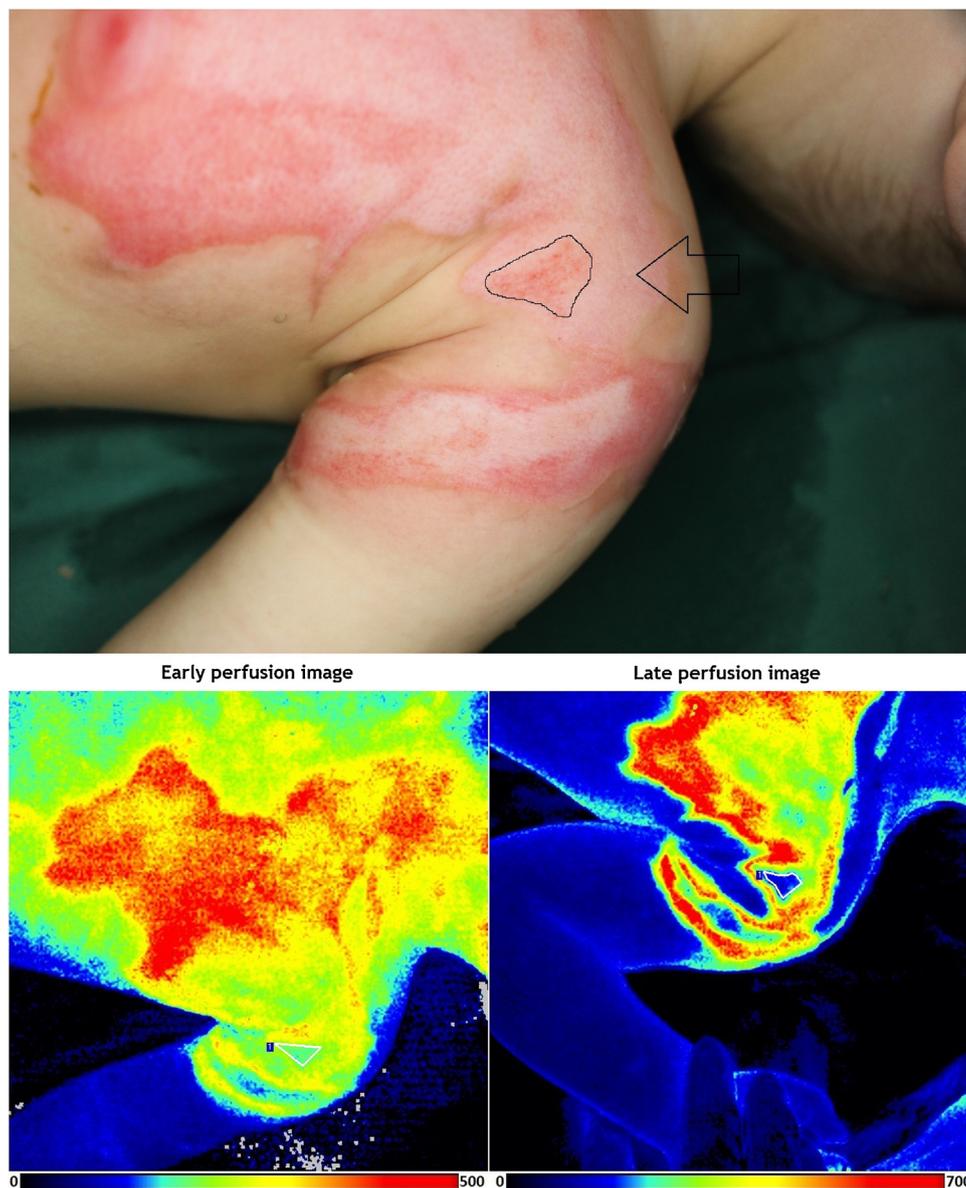


Fig. 5 – Case 5, where the main challenge was to find the proper placement of the ROI because of the angular difference between the LSCI images and the digital photograph. ROI in the images are marked by RM and produced a perfusion of 191 and 162 PU in the early and late measurements, respectively. The digital image was captured 24h after injury and the marked area in the photo required 21 days to heal and “maybe spontaneous healing” was deemed as an appropriate assessment.

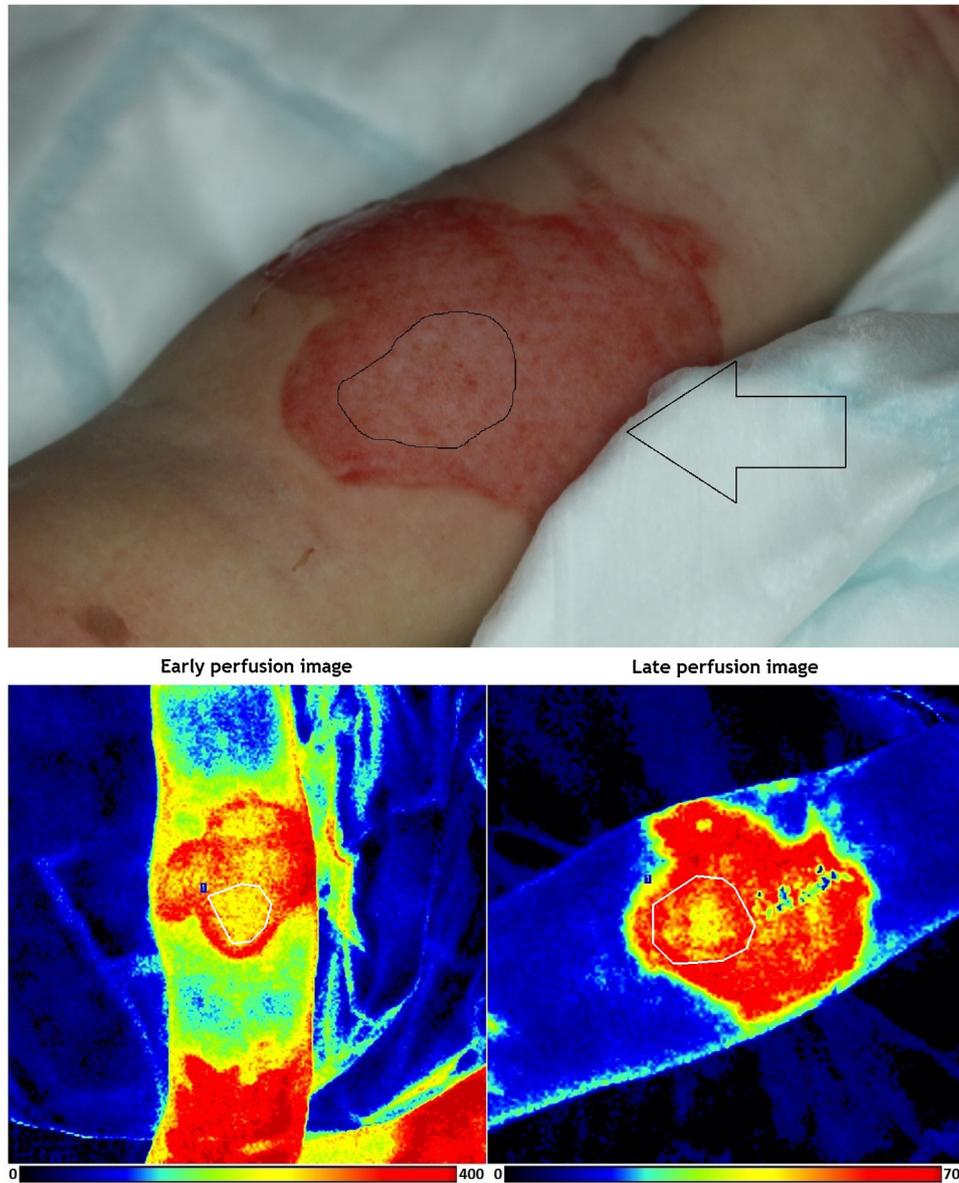


Fig. 6 – Case 8, which proved to be the easiest case. Perfusion values were similar among all observers, and it was almost exclusively assessed as “spontaneous healing”. The ROI in the images are marked by RM and produced a perfusion of 254 and 508 PU in the early and late measurements, respectively. The digital image was captured 17 h after injury and the scald had healed eight days after injury.

observers had had access to the actual wound instead of a digital image. However, making the observations on actual burn patients would have added a logistic challenge to the study, and made dressing changes unreasonably slow, potentially being hazardous to patients who are generally sedated during these procedures. Another way would have been to reduce the number of observers, but that would also have made the data less reliable.

Yet another limitation is the preselection of the ROI. In practice this means that different observers might not be interested in the same regions when LSCI is used clinically, which introduces a problem of interobserver reliability related to the different areas being investigated. However, it can be

said that this is already the case whenever assessments of the depth of a burn are made, regardless of method, and therefore not a problem inherent in LSCI.

The participants' most common reason for selecting a category different from that of the LSCI recommendation was uncertainty about the true meaning of the perfusion values that they were using. This highlights the need for experience with LSCI before it can be expected to produce good results, since each observer must build up a clinical reference table in their mind to feel comfortable with LSCI-aided assessments.

It has previously been shown that assessment of a burn that relies on LSCI predictions is accurate [26]. We can now for the first time show that interobserver reliability of perfusion

measurements using LSCI is high among observers regardless of professional group. Observers can reliably identify the same ROI, which results in observer-independent perfusion measurements irrespective of experience in burns. LSCI can therefore be expected to produce precise early assessments of the depth of a burn, and to be a reliable and objective method of measurement.

5. Conclusion

Observers with limited LSCI training can reliably outline ROI in perfusion images and arrive at perfusion values with a high degree of correlation, which results in observer-independent measurements of perfusion. Estimation of perfusion change over time also correlates well, which lends credibility to the accuracy of double measurements. LSCI recommendations yielded better accuracy than the observers' assessments. This highlights the need for clinicians to have a more thorough understanding of LSCI measurements before being able to use this powerful clinical tool to its fullest extent.

Conflict of interest

The authors declare that they have no conflict of interest.

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