

# **Laser Doppler Imaging – The Role of Poor Burn Perfusion in Predicting Healing Time and Guiding Operative Management**

Shahab Shahid.	MBBS, BSc(Hons), PgCert, MRCS 1
Marco Correia Duarte.	MBBS, PGCE (Clin. Ed.), MSc, MRCS 1
Jufen Zhang.	PhD 2
Daniel Markeson.	MBBS, BSc (Hons) Neurosci, MD (Res), FRCS (Plast) 1
David Barnes.	FRCS(Plast) 1

- 1) St Andrew's centre for Plastic Surgery and Burns, Broomfield Hospital, Chelmsford, UK
- 2) School of Medicine, Anglia Ruskin University, Chelmsford, UK

Corresponding author:	Shahab Shahid
Email:	Shahab_shahid@outlook.com
Address-	St Andrew's Centre for Plastic Surgery & Burns Broomfield Hospital Chelmsford, UK CM1 7ET

Declaration of interest:	None
--------------------------	------

Funding:	None
----------	------

Keywords:	Burns; Burn perfusion; Laser Doppler Imaging; Intermediate depth burns; Healing time
-----------	---

## **Abstract:**

**Aim:** To identify if the proportion of poor blood flow (blue) within an LDI (Laser doppler Imaging) image of a burn independently correlates with healing time.

**Methods:** Patient age, gender, burn type, and burn surface area were collected from the IBID (International Burn Injury Database). All LDI images were copied from the MoorLDI2-BI- Laser Doppler (MLDI) Scanner, onto Adobe Photoshop® version 2020 for pixel counting analysis and calculation of % TBSA (Total Body Surface Area) blue. Multiple linear regression analysis determined if there was a proportional relationship of each parameter (age, gender, % TBSA Blue and comorbidities) with healing time.

**Results:** 110 patients with 197 burns were scanned with MLDI. Median age was 5 years (IQR 1-6). Median burn surface area was 1.5% (IQR 1-2.4). 56.4% of patients were male and patients were scanned an average of 2.68 days (SD±1.37) following burn injury. Number of physical comorbidities and age were found to have a statistically significant relationship with healing time ( $p=0.03$ ,  $p=0.002$ ). Gender and %TBSA blue did not have a statistically significant relationship with healing time ( $p=0.07$  and  $p=0.058$  respectively). There was a statistically significant difference in the mean healing time between burns with and without blue (3.43 weeks vs. 2.80 weeks,  $p=0.0001$ ). % TBSA Blue was more than four times higher in the operated group (0.48% vs. 0.11%) and was shown to have a statistically significant relationship with decision to operate ( $p=0.027$ ). Positive predictive value for the presence of blue on operative rate was 71.6%. Age, gender and number of comorbidities did not have a statistically significant influence on operative rate ( $p=0.07$ ,  $p=0.50$  and  $p=0.49$ ).

**Conclusion:** % TBSA blue was not found to be a reliable individual indicator of burn healing time, but the presence of blue within an LDI image, advanced patient age and increased number of comorbidities did have a statistically significant relationship with healing time. This suggests their standardised inclusion into management decisions regarding intermediate depth burns is warranted.

## **Manuscript:**

### **Introduction:**

Laser doppler imaging (LDI) is an important part of the recommendations by the National Institute for Health and Care Excellence (NICE) for use 'in the assessment of intermediate burn depth, where doubt about the depth exists after assessment by an experienced clinician [1].' The Moor LDI2- BI Laser doppler (MLDI) scanner is associated with 97% accuracy in the determination of burn depth compared to 71.4% by experienced clinician examination alone [2,3]. The scanner indirectly measures burn depth by measuring burn perfusion; a reliable surrogate for burn depth [4,5]. LDI is non-invasive and mobile but despite these advantages, the device is large and cumbersome to move between clinical areas. Furthermore, it has an upfront cost of £53,942 and £8,301 for yearly maintenance [1].

The scanner works by directing a low power laser beam at the burn wound by reflecting off a mirror. The laser light directed at the burned tissue is scattered when it encounters red blood cells. It undergoes a doppler frequency shift, which is directly proportional to the speed of the underlying blood cells. The subsequent photocurrent is displayed as a colour-coded image [6]. The original colour pallet for MLDI had 16 separate colours to indicate burn perfusion but, in order to improve the clinical application of MLDI, a 6-section colour code to indicate relative levels of perfusion within a burn was later devised and validated (Table A) [6–8]. The authors determined that dark blue areas within a burn had a 96% chance of taking longer than 21 days to heal, and those with light blue a 74.4% change of taking longer than 21 days to heal [7]. Therefore we aimed to determine if % TBSA Blue (percentage total body surface area blue), proportion of blue within a burn, or whether the presence of blue alone was associated with poorer healing potential, and therefore longer healing time.

## Methods:

Patient age, gender, burn type, and burn surface area were collected from the IBID (International Burn Injury Database). Patient comorbidities were collected from the electronic patient record system (Lorenzo). Healing times were collected from the Burns Outpatient clinic notes. Completion of epithelialisation was determined by complete healing of the burn wound as assessed by the burns nurses in the burns outpatient clinic. Reviewing the burns in The Shapiro Wilk test was applied to assess for normal distribution. Multiple linear regression analysis was used to determine if there was a proportional relationship of each parameter (age, gender, % TBSA Blue and number of comorbidities) with healing time. When calculating p values between categorical variables, the Chi squared test was used, and when between continuous variables, the paired t test was used.

All burns that had LDI in 2019 at our institution were stored within the hard drive of the MLDI scanner, and retrospectively collected. These images were copied onto Adobe Photoshop® version 2020 for further analysis. Adobe Photoshop has an inbuilt colour pallet that has a range from 0 to 255 for each colour. Colour code 255 is the purest version of the colour (in this case blue), and 1 is identified as black. First, the colour code for each of the two shades of blue within the scanner's colour range was identified by utilising the colour pallet built into the software, outputting two number codes: 64 for dark blue and 255 for light blue [9].

The polygonal lasso tool was used to trace each burn wound (Figure 3), thus calculating the total number of pixels within the burned area. The blue filter on the histogram was visualised for the selected burn, and the total number of pixels within the highlighted burn that contributed to each of the two blue peaks was recorded (Figures 4 & 5). By multiplying the proportion of blue pixels within each burn with the total body surface area (TBSA%) of each burn, the % TBSA blue for each burn was determined. A similar method has been used for quantification of immunological markers from tissues samples in previous studies [10,11].

For the purposes of this study, we focused in the light blue and dark blue part of the colour pallet, <200 perfusion units and <140 perfusion units respectively (Table A) [7,8]. The colour code developed by Pape et

al is built into the MLDI scanner, where healing potential is displayed as a <14 days, 14-21 days and >21 days [7,8].

**Theory/Calculation:**

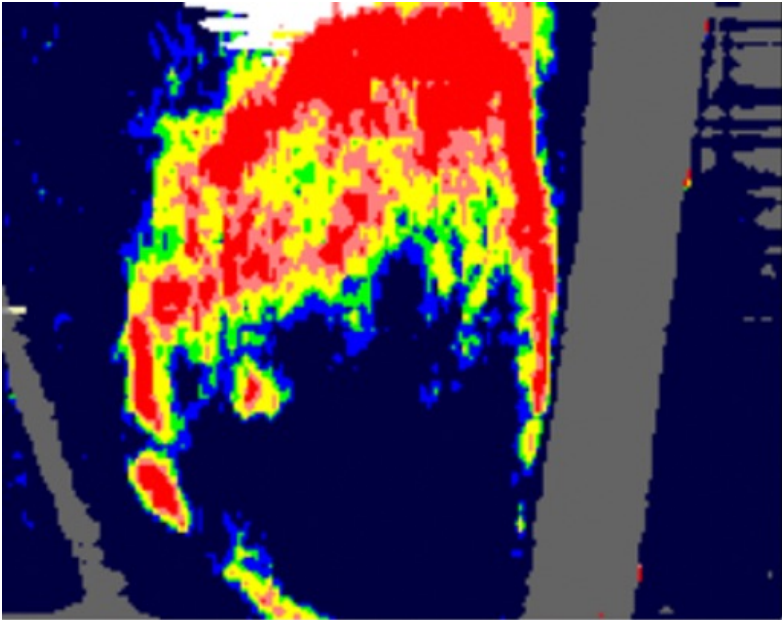


Figure 1- LDI Image of patient's left knee.



Figure 2 - Burn Image of patient's left knee.

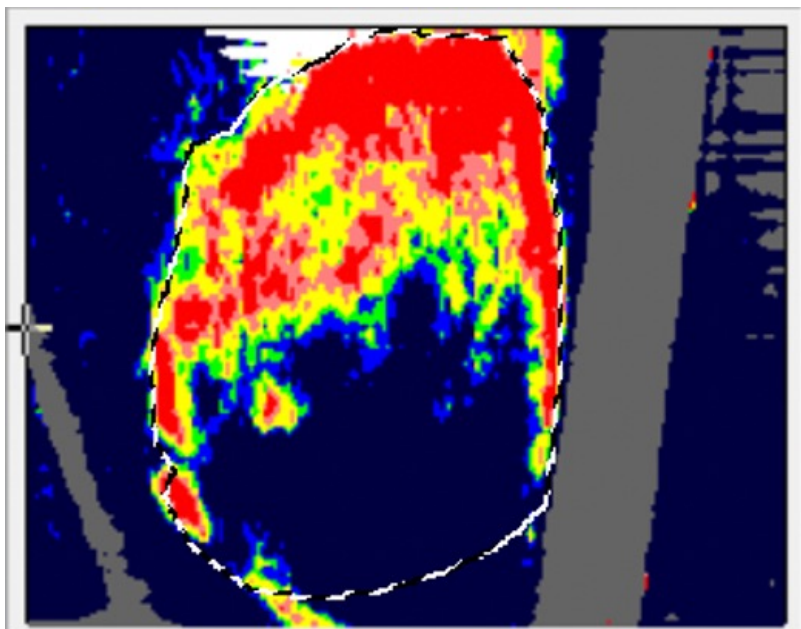


Figure 3 - Polygonal lasso tool to draw around the burned area.

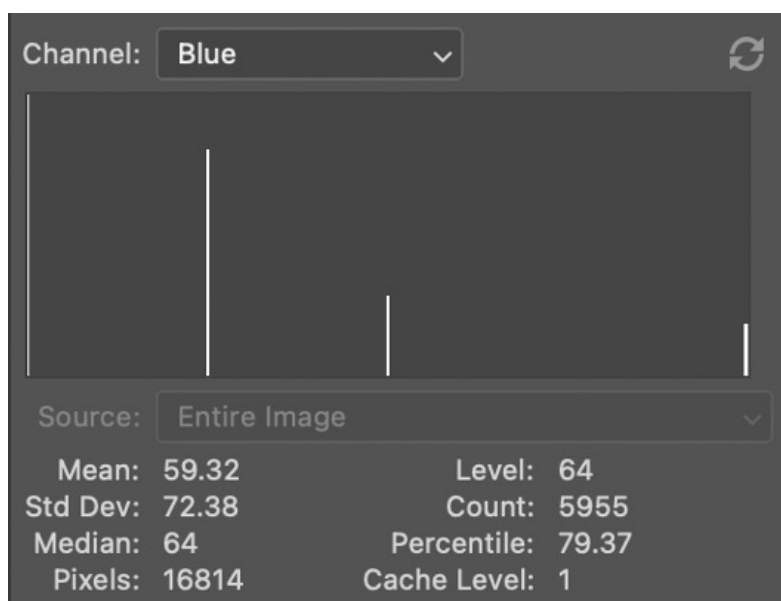


Figure 4 - Dark blue peak (64), pixel count of 5955, total pixel count for burned area 16814.

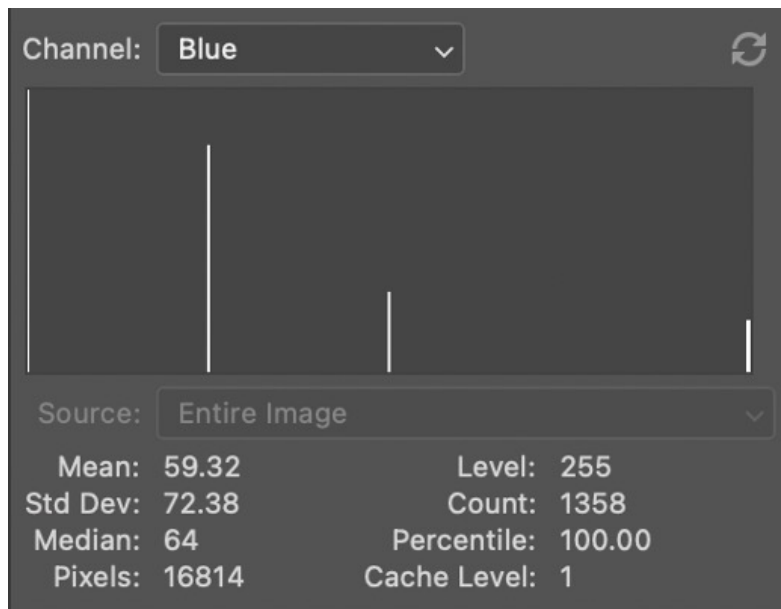


Figure 5 - Light blue peak (255), pixel count 1358, total pixel count for burned area 16814.

#### Calculation of % TBSA Blue using above image as an example

$$\begin{aligned}
 \%TBSA \text{ blue} &= (\text{light blue pixel count} + \text{dark blue pixel count} / \text{total pixel count}) \times (\text{burns surface area}) \\
 &= (5955 + 1358 / 16814) \times (1.5\%) \\
 &= (7313 / 16814) \times 1.5 \\
 &= 0.65\%
 \end{aligned}$$

The clinical notes and electronic patient records were used to collect a range of variables including the healing time of each burn, the presence or absence of medical comorbidities, age, gender and whether operative or conservative treatment was instigated.

## Results:

During 2019, 110 patients had a MLDI scan resulting in 197 burn wound images. Eight burns were excluded from the analysis due to image distortion; 3 of these were due to tattoos and 5 were due to image distortion occurring in the process of storing onto the scanner hard drive. This cohort of 110 scanned patients were from a total number of 495 patients assessed with intermediate depth burns seen at our burns centre in 2019 (23.7%). In this cohort of patients, neither age nor burn surface area was normally distributed. Median age was 5 years (IQR 1-6), with an age range of 2 days to 85.6 years. Median burn surface area was 1.5% (IQR 1-2.4). 58.6% of burns were between 1-5% TBSA (Table 2). 56.4% of patients were male and patients were scanned an average of 2.68 days (SD±1.37) following burn injury. Scalds were the cause of burn injury in 74.5% of patients.

<b>Dark blue</b>	<140
<b>Light Blue</b>	<200
<b>Green</b>	200-260
<b>Yellow</b>	260- 440
<b>Pink</b>	440-600
<b>Red</b>	>600

Table A: 6 colour pallet for burn perfusion, reproduced from Pape et al [7,8].

<b>Scald water</b>	68.2	(75/110)
<b>Flame</b>	18.2	(18/110)
<b>Scald oil/food</b>	6.4	(7/110)
<b>Contact</b>	6.4	(7/110)
<b>Chemical</b>	2.7	(3/110)
<b>Total</b>	110	

Table 1: Burn mechanism

<b>&lt;1</b>	10.7	(21/197)
<b>1</b>	27.4	(54/197)
<b>1-5</b>	58.4	(115/197)
<b>&gt;5</b>	3.5	(7/197)
<b>Total</b>	197	

Table 2: Burn Surface area



## Healing Time Data

<b>Age (years)</b>	0.01	(0.005 to 0.02)	3.09
<b>Sex</b>	-0.28	(-0.58 to 0.03)	-1.79
<b>% TBSA-blue</b>	0.77	(-0.02 to 1.56)	1.90
<b>Comorbidities</b>	-0.47	(-0.90 to -0.04)	-2.12
			0.002
			0.07
			0.058**
			0.03

Table 3 – Healing time association with Age, sex, % TBSA Blue and comorbidities (\*\*percentage tbsa-blue

was significantly associated with the healing time in the simple linear regression model. In addition, the p-

value=0.048 if an outlier (percentage\_tbsa\_blue>1) was excluded using the multiple models.) Multiple

linear regression, R-squared =0.26, \*Based on 1000 bootstrap replicates

<b>No Blue</b>	32	19.60	±3.50	18.34 to 20.90
<b>Blue</b>	24	24.00	±4.34	22.20 to 25.90
<b>Combined</b>	56	21.50	±4.41	20.30 to 22.70
<b>Difference</b>	-	-4.40	-	-6.50 to 2.30

Table 4 - Healing times (days) for Burns with blue vs. burns without blue. P value generated using two-

sample t test, p= 0.0001

<b>Number of burns</b>	41	15
<b>Mean days?</b>	20.3	43.4
<b>Median</b>	16.0	42.0
<b>25<sup>th</sup> Centile</b>	12.0	24.0
<b>50<sup>th</sup> Centile</b>	16.0	42.0
<b>75<sup>th</sup> Centile</b>	25.0	60.0
<b>Standard deviation</b>	±11.0	±22.5
<b>Minimum</b>	8.0	10
<b>Maximum</b>	53.0	70

Table 5. Healing time (days) of adult vs paediatric burns - A: <16 years old at time of burn, B: >= 16

years old at time of burn. P values calculated using multiple linear regression model, p=0.002

<b>Hand</b>	10	19.4	±12.3	12.0	16.0	18.0	11.0	53.0
<b>Foot</b>	9	26.4	±16.3	15.0	28.0	28.0	9.0	60.0

Forearm	7	17.7	±5.0	14.0	16.0	24.0	11.0	24.0
Thigh	6	35.3	±29.4	10.0	26.5	70.0	9.0	70.0
Shoulder	4	25.8	±11.6	18.0	24.5	33.5	13.0	41.0
Leg	4	17.3	±14.6	9.0	11.0	25.5	8.0	39.0
Abdomen	4	36.3	±25.4	17.0	31.0	55.5	13.0	70.0
Chest	4	15.3	±7.5	10.0	12.5	20.5	10.0	26.0
Knee	3	58.7	±1.2	58.0	58.0	60.0	58.0	60.0
Upper arm	2	18.5	±4.9	15.0	18.5	22.0	15.0	22.0
Abdomen + Chest	1	46.0	-	46.0	46.0	46.0	46.0	46.0
Calf	1	42.0	-	42.0	42.0	42.0	42.0	42.0
Face	1	35.0	-	35.0	35.0	35.0	35.0	35.0

Table 6. Healing time (days) by burn location

### Operative Data

Not operated (56)			
Mean	15.8	0.08	0.11
25 <sup>th</sup> Centile	1.0	0	0
Median	4.5	0	0
75 <sup>th</sup> Centile	21.0	0.12	0.19
Standard deviation	±21.9	±0.14	±0.20
Minimum	0	0	0
Maximum	65.0	0.60	1.10
Operated (102)			
Mean	19.6	0.24	0.48
25 <sup>th</sup> Centile	1.0	0	0
Median	2.5	0.09	0.17
75 <sup>th</sup> Centile	38.0	0.34	0.67
Standard deviation	±24.2	±0.32	±0.75
Minimum	0	0	0
Maximum	85.0	1.04	4.0

Table 7 – Operated vs Non operated: Age, % blue of burn and %TBSA Blue for burn. (158/197 fully reported)

Paediatric	59.4 (60/101)	40.6 (41/101)	0.07
Adult	73.7 (42/57)	26.3 (15/57)	
Combined	64.6 (102/158)	35.4 (56/158)	

Table 8 - Operative Rates for Paediatric vs Adult burns. P value calculated using Chi squared test , 158/197 fully reported

<b>Operated</b>	62.0 (44/71)	67.0 (59/88)	0.50
<b>Not Operated</b>	38.0 (27/71)	33.0 (29/88)	

Table 9 - Operative rates for Male vs Female patients. P value generated using Chi squared test, 159/197

fully reported

<b>Nil</b>	63.0 (68/108)	37.0 (40/108)	0.49
<b>Present</b>	68.6 (35/51)	31.4 (16/51)	

Table 10 - Operative rates for patients with and without comorbidities. P value generated using Chi squared

test, 158/197 fully reported

<b>Nil</b>	55.6 (40/72)	44.4 (32/72)	0.027
<b>Present</b>	72.4 (63/87)	27.6 (24/87)	
<b>Combined</b>	64.8 (103/159)	35.2 (56/159)	

Table 11 - Operative rates for patients with Blue vs without Blue. P values generated using Chi Squared test,

159/197 fully reported

## Discussion:

Number of physical comorbidities and age were shown to have a statistically significant relationship with healing time ( $p=0.03$  and  $p=0.002$  respectively). This is in concordance with other studies, where wound healing has been demonstrated to be influenced by patient age and comorbidities [12,13]. Gender and % TBSA blue did not have a statistically significant relationship with healing time ( $p=0.07$  and  $p=0.058$ , respectively) (Table 3). Although Pape et al identified that light and dark blue were associated with an increased chance of burns taking longer than 21 days to heal (and therefore more likely to heal with hypertrophic scarring), they also stated that green and yellow areas of LDI images have a 49.2% and 10.1% chance of taking >21 days to heal [7,8]. As a result of these mixed depth burns without significant amounts of blue and with variable healing potential, %TBSA blue was not found to be an accurate isolated predictor of wound healing potential.

We compared mean healing times for burns with blue to burns without any blue, and found a statistically significant difference (3.43 weeks vs. 2.80 weeks,  $p=0.0001$ ). This supports the use of blue within a burn as a factor for operative decision making (Table 3). % TBSA Blue was more than four times higher in the operated group vs the non-operated group (0.48% vs. 0.11%). This demonstrates % TBSA blue was a reliable adjunct to clinical assessment, as the patients treated with surgery were also identified with the scanner. We are already using LDI as an adjunct to clinical assessment for operative decision making as per NICE guidelines [1].

However 31.4% (32/102) of patients with a %TBSA blue of 0, still received an operation. Factors including clinical status of the patient, number of comorbidities and patient preference have a crucial role in deciding whether to operate, and were assessed alongside LDI images in order to determine the final management plan.

Age and gender were not found to have a statistically significant influence on operative rate ( $p=0.07$ , Table 7,  $p=0.50$ , Table 8). However we found that age had a directly proportional effect on healing time ( $p=0.002$ , Table 3). Number of comorbidities was not shown to independently correlate with our decision to operate ( $p=0.49$ , Table 9), despite this study determining that patients with comorbidities had a statistically significant

and proportionally longer healing time than those without. However only 28.6% (10/35) of patients with comorbidities were children, hence healing times for comorbid patients will have been influenced by their higher median age (Table 10).

%TBSA blue was shown to have a statistically significant relationship with decision to operate and the positive predictive value for the presence of blue on operative rate was 71.6%. This demonstrates that the MLDI scanner has a direct correlation with burn severity, and an influence on our decision to operate. This is consistent with NICE guidelines for the utilisation of the scanner as an adjunct to clinical assessment ‘where doubt about burn depth exists [1].’

A Systematic review of LDI, comprising of 14 studies and 1818 patients, found overall LDI sensitivity for detection of burn depth to be 91%, and similar results have been reported in numerous studies [14–17]. However technical factors influence this accuracy and include the stillness of the patient, the angle of the scanner (which has been demonstrated to be more accurate when close to 90 degrees), debris over the burn, reflection off the burn surface, surface creams and treatments and obscuring factors such as tattoos [5].

A 92 burn, 34 patient study found that clinical assessment and LDI had a diagnostic accuracy of 81.52% vs 90.21% respectively. The sensitivity of clinical assessment was 81% and of LDI 92.75%, whereas the specificity was 82% for both [18]. The diagnostic accuracy of clinical assessment alone to determine intermediate burn depth, has been reported to be as low as 65% [19].

Accuracy of LDI in determining burn depth improves with time, with a 100% accuracy at 8 days [3]. Stetinsky et al demonstrated that duration between burn injury and scan should be used to determine cut-off perfusion scores for decision to operate. This is due to the dynamic nature of burn wounds, and linear healing that occurs with time [20]. We scanned patients at an average of 2.68 days post burn injury, as early excision and closure of deep wounds has been associated with reduced morbidity and mortality [21,22].

Incidence of hypertrophic scarring is low if burns heal within 14 days in children and 21 days in adults [8,23]. We have found that burns without blue had a mean healing time of 19.6 days, vs 24 days for those with blue.

However 11 of the 32 conservatively managed burns without blue, still took longer than 21 days to heal. This supports the growing body of evidence that LDI and presence of blue alone, should not determine operative management. Sample size for this study was limited to one year. Burn surface area was also the result of visual estimation at time of assessment, hence was not an exact measure. Despite these limitations, the findings of this study have provided a context for MLDI to be utilised for the assessment and management of intermediate depth burns.

**Conclusion:**

MLDI was found to be a reliable adjunct for the assessment of intermediate depth burns. However, %TBSA blue was not a reliable individual indicator of burn healing potential. That said, the presence of blue within LDI images, along with patient age and number of comorbidities had a statistically significant relationship with healing time of burns. Our operative management was influenced by the presence of blue within LDI images, but was not influenced by number of comorbidities or age of the patient. Both number of comorbidities and patient age were found to have a statistically significant effect on healing times, suggesting there standardised inclusion into management decisions regarding intermediate depth burns is warranted. Further research is required to confirm our initial findings.

## References:

- [1] NICE. moorLDI2-BI: a laser doppler blood flow imager for burn wound assessment. Guidance and guidelines. <https://www.nice.org.uk/Guidance/Mtg2/Chapter/1-Recommendations> n.d. Accessed 07/09/2021
- [2] Axminster: Moor Instruments. Moor Instruments. Laser Doppler Line Scanner. Rapid laser Doppler blood flow imaging. Scan times from 4 seconds. <https://gb.moor.co.uk/Product/MoorLDLs2-Laser-Doppler-Line-Scanner/10> 2017. Accessed 09/09/2021
- [3] Hoeksema H, van de Sijpe K, Tondut T, Hamdi M, van Landuyt K, Blondeel P, et al. Accuracy of early burn depth assessment by laser Doppler imaging on different days post burn. *Burns* 2009;35(1): 36-45. <https://doi.org/10.1016/j.burns.2008.08.011>.
- [4] Pape SA, Skouras CA, Byrne PO. An audit of the use of laser Doppler imaging (LDI) in the assessment of burns of intermediate depth. *Burns* 2001;27(3): 233-239. [https://doi.org/10.1016/S0305-4179\(00\)00118-2](https://doi.org/10.1016/S0305-4179(00)00118-2).
- [5] Droog EJ, Steenbergen W, Sjöberg F. Measurement of depth of burns by laser Doppler perfusion imaging. *Burns* 2001;27(6): 561-568. [https://doi.org/10.1016/S0305-4179\(01\)00021-3](https://doi.org/10.1016/S0305-4179(01)00021-3).
- [6] Niazi ZBM, Essex TJH, Papini R, Scott D, McLean NR, Black MJM. New laser doppler scanner, a valuable adjunct in burn depth assessment. *Burns* 1993;19(6): 485-489. [https://doi.org/10.1016/0305-4179\(93\)90004-R](https://doi.org/10.1016/0305-4179(93)90004-R).
- [7] Pape SA, Baker RD, Wilson D, Hoeksema H, Jeng JC, Spence RJ, et al. Burn wound healing time assessed by laser Doppler imaging (LDI). Part 1: Derivation of a dedicated colour code for image interpretation. *Burns* 2012;38(2): 187-194. <https://doi.org/10.1016/j.burns.2010.11.009>.
- [8] Monstrey SM, Hoeksema H, Baker RD, Jeng J, Spence RS, Wilson D, et al. Reprint of: Burn wound healing time assessed by laser Doppler imaging. Part 2: Validation of a dedicated colour code for image interpretation. *Burns* 2012;38(2): 195-202. <https://doi.org/10.1016/j.burns.2012.01.008>.
- [9] Adobe. About Histograms. <https://helpx.adobe.com/Photoshop/Using/Viewing-Histograms-Pixel-Values.html> 2020. Accessed 01/09/2021.
- [10] Burkhardt D, Hwa S-Y, Ghosh P. A novel microassay for the quantitation of the sulfated glycosaminoglycan content of histological sections: its application to determine the effects of Diacerhein on cartilage in an ovine model of osteoarthritis. *Osteoarthritis and Cartilage* 2001;9(3): 238-247. <https://doi.org/10.1053/joca.2000.0381>.
- [11] Duplancic R, Kero D. Novel approach for quantification of multiple immunofluorescent signals using histograms and 2D plot profiling of whole-section panoramic images. *Scientific Reports* 2021;11(1): 8619. <https://doi.org/10.1038/s41598-021-88101-1>.
- [12] Hermans MH. A general overview of burn care. *International Wound Journal* 2005;2(3): 206-220. <https://doi.org/10.1111/j.1742-4801.2005.00129.x>.
- [13] Tiwari VK. Burn wound: How it differs from other wounds? *Indian Journal of Plastic Surgery* 2012;45(2): 364-373. <https://doi.org/10.4103/0970-0358.101319>.
- [14] Wang R, Zhao J, Zhang Z, Cao C, Zhang Y, Mao Y. Diagnostic Accuracy of Laser Doppler Imaging for the Assessment of Burn Depth: A Meta-analysis and Systematic Review. *Journal of Burn Care & Research* 2020;41(3): 619-625. <https://doi.org/10.1093/jbcr/irz203>.
- [15] Venclauskiene A, Basevicius A, Zacharevskij E, Vaicekauskas V, Rimdeika R, Lukosevicius S. Laser Doppler imaging as a tool in the burn wound treatment protocol. *Videosurgery and Other Miniinvasive Techniques* 2014;9(1): 24-30. <https://doi.org/10.5114/wiitm.2014.40273>.
- [16] Peeters W, Anthonissen M, Deliaert A, van der Hulst R, van den Kerckhove E. A comparison between laser-doppler imaging and colorimetry in the assessment of scarring: “a pilot study.” *Skin Research and Technology* 2012;18(2): 188-191. <https://doi.org/10.1111/j.1600-0846.2011.00552.x>.
- [17] Stewart TL, Ball B, Schembri PJ, Hori K, Ding J, Shankowsky HA, et al. The Use of Laser Doppler Imaging as a Predictor of Burn Depth and Hypertrophic Scar Postburn Injury. *Journal of Burn Care & Research* 2012;33(6): 764-771. <https://doi.org/10.1097/BCR.0b013e318257db36>.



- [18] Jan SN, Khan FA, Bashir MM, Nasir M, Ansari HH, Shami HB, et al. Comparison of Laser Doppler Imaging (LDI) and clinical assessment in differentiating between superficial and deep partial thickness burn wounds. *Burns* 2018;44(2): 405-413. <https://doi.org/10.1016/j.burns.2017.08.020>.
- [19] Watts AMI, Tyler MPH, Perry ME, Roberts AHN, McGrouther DA. Burn depth and its histological measurement. *Burns* 2001;27(2): 154-160. [https://doi.org/10.1016/S0305-4179\(00\)00079-6](https://doi.org/10.1016/S0305-4179(00)00079-6).
- [20] Štětinský J, Klosová H, Kolářová H, Šalounová D, Bryjová I, Hledík S. The time factor in the LDI (Laser Doppler Imaging) diagnosis of burns. *Lasers in Surgery and Medicine* 2015;47(2): 196-202. <https://doi.org/10.1002/lsm.22291>.
- [21] Sheridan RL. Burns. *Critical Care Medicine* 2002;30(11 Suppl): S500-S514. <https://doi.org/10.1097/00003246-200211001-00015>.
- [22] ENGRAV LH, HEIMBACH DM, REUS JL, HARNAR TJ, MARVIN JA. Early Excision and Grafting vs. Nonoperative Treatment of Burns of Indeterminant Depth. *The Journal of Trauma: Injury, Infection, and Critical Care* 1983;23(11): 1001-1004. <https://doi.org/10.1097/00005373-198311000-00007>.
- [23] Cubison TCS, Pape SA, Parkhouse N. Evidence for the link between healing time and the development of hypertrophic scars (HTS) in paediatric burns due to scald injury. *Burns* 2006;32(8): 992-999. <https://doi.org/10.1016/j.burns.2006.02.007>.