Institution: University of Nottingham		
Unit of Assessment: 12		
Title of case study: Improving burns assessment and treatment decisions for children using a faster laser doppler blood flow imaging device		
Period when the underpinning research was undertaken: 2000-2013		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s): Barrie Hayes Gill Steve Morgan Yiqun Zhu John Crowe	**Role(s) (e.g. job title):** Professor Professor Assistant Professor Professor	**Period(s) employed by submitting HEI:** 04/1986 - Present 03/1996 – Present 09/2004 - Present 09/1987 – 07/2020
Period when the claimed impact occurred: 08/2013 to 12/2020		
Is this case study continued from a case study submitted in 2014? N		

1. Summary of the impact

Fast and accurate assessment of burns is essential to reducing pain and unnecessary surgery. Research in the Faculty of Engineering has enabled the development of a fast, commercially available burns assessment device- the CE marked and FDA approved moorLDLS-BI. The device produces scans in just 4s (30 times faster than other methods), overcoming issues of unusable images due to movement of distressed, agitated and wriggly children during longer scans. The device is used by specialist burns centres worldwide to assess severe burns and scalds in children. In the REF period its use has increased the accuracy of prognostic assessments, decreased skin grafts (including associated scarring and pain) by 17%, reduced the time it takes for surgical decisions to be made by 2.7 days.

2. Underpinning research

Laser Doppler Imaging (LDI) is used routinely to image blood flow to wounds to determine healing potential and treatment options. Conventional methods of LDI are slow, requiring the scanning of one pixel at a time to build up an image point by point. This can result in issues of motion artefact (including blurred and unusable images) if the patient being imaged is not kept completely still. This is a particular problem when imaging the burns of young children. Research at the University of Nottingham (UoN) has enabled the development of a new faster technique for acquiring blood flow images of burns. This technique speeds up the imaging process from 120s to just 4s thus reducing instances of motion artefact in children.

In 2003, the UoN team, led by Prof Morgan of the Optics and Photonics Group, began working with Moor Instruments Ltd (a UK based, leading global specialist in products for tissue blood flow and oxygen assessment) to help them develop a faster LDI burns imager. Moor Instruments were already producing a conventional, single point scanning device (moorLDI2-BI) and were keen to investigate methods of providing more rapid image acquisition. The UoN team recognised the potential of incorporating complementary metal-oxide-semiconductor (CMOS) imaging sensor technology as it is ideally suited to the high frequency (up to 20KHz), low modulation depth (approximately 1%) signals found in LDI.

Since 2000, UoN research had created new CMOS camera chips for a range of applications, including metrology and healthcare. These bespoke CMOS sensor integrated circuits, pioneered by the UoN research team [2], comprised a photodiode array with signal processing electronics on the same chip [8]. They could extract high frequency modulated light signals at each pixel and could therefore image when conventional cameras did not possess sufficient speed or dynamic range. This is important because many real-world signals, such as those in laser Doppler blood flow imaging, are rapidly fluctuating small signals on a large static background. Development of these sensors by the UoN team was a considerable engineering challenge requiring expertise in optical design, electronic instrumentation, microelectronics and signal processing to ensure that all opto-electronics could be implemented on the same integrated circuit [2]. To enable optimisation of the signal processing and electronics, a development platform was created based on a photodiode array and a field programmable gate array (FPGA) [1]. This was ultimately incorporated into the moorLDLS-BI, to provide rapid data processing.

Recognising the potential application of the above research, between 2003 and 2013, the UoN team collaborated with Moor Instruments to explore the creation of CMOS integrated circuits for LDI. This was initially via small scale arrays (16x1, 4x4 pixels) [5, 6] and culminated in a fully integrated CMOS 64x64 pixel array [7]. By increasing the number of pixels, the image could be acquired much faster, with 4,096 image points acquired simultaneously [7, 9]. However, this is challenging as data is acquired rapidly and simultaneously, which creates a bottleneck. To accelerate commercialisation of the technology, the UoN team collaborated with Moor Instruments Ltd and clinical experts on an Innovate UK funded project (2006 to 2010) [10]. The aim was to reduce image acquisition times compared to Moor Instrument's existing commercially available LDI: the moorLDI2-BI. The new device created from this project involved scanning a line of light over the tissue (rather than point by point) and projecting this back onto a 64x1 photodiode array to form an image. The UoN team made fast image acquisition possible by implementing more powerful hardware and more efficient signal processing. This involved the integration of an FPGA [3] and associated signal processing (developed at UoN) [4], with a commercially available photodetector array, enabling the data to be acquired and processed fast enough to eliminate the bottleneck. This greatly reduced image acquisition times to 4s (from a typical 120s), thus virtually eliminating motion artefacts.

The research described above was licensed to Moor Instruments Ltd in 2011 and incorporated into a new high-speed line scanning device for burn wound assessment, the moorLDLS-BI.

3. References to the research (Authors affiliated to UoN highlighted in **bold**)

[1] **Pui, B. H., Hayes-Gill, B., Clark, M., Somekh, M., See, C., Piéri, J. F., S.P. Morgan, & Ng, A.** (2002). The design and characterisation of an optical VLSI processor for real time centroid detection. *Analog integrated circuits and signal processing*, *32*(1), 67-75. https://doi.org/10.1023/A:1016075825331

[2] **Pui, B. H., Hayes-Gill, B., Clark, M., Somekh, M. G., See, C. W., Morgan, S.P., & Ng, A.** (2004). Integration of a photodiode array and centroid processing on a single CMOS chip for a real-time Shack-Hartmann wavefront sensor. *IEEE Sensors Journal, 4*(6), 787-794. doi: https://doi.org/10.1109/JSEN.2004.837494

[3] **Nguyen, H. C., Hayes-Gill, B. R., Morgan, S. P., Zhu, Y.,** Boggett, D., Huang, X., & Potter, M. (2010). A field-programmable gate array based system for high frame rate laser Doppler blood flow imaging. *Journal of medical engineering & technology, 34*(5-6), 306-315. https://doi.org/10.3109/03091902.2010.481032

[4] **Nguyen, H. C., Hayes-Gill, B. R., Zhu, Y., Crowe, J. A., He, D., & Morgan, S. P**. (2011). Low resource processing algorithms for laser Doppler blood flow imaging. *Medical engineering & physics, 33*(6), 720-729. https://doi.org/10.1016/j.medengphy.2011.01.009

[5] **Kongsavatsak, C., He, D., Hayes-Gill, B. R., Crowe, J. A., & Morgan, S. P.** (2008). Complementary metal-oxide-semiconductor imaging array with laser Doppler blood flow processing. *Optical Engineering, 47*(10), 104401. https://doi.org/10.1117/1.2993318

[6] **Gu, Q., Hayes-Gill, B. R., & Morgan, S. P.** (2008). Laser Doppler blood flow complementary metal oxide semiconductor imaging sensor with analog on-chip processing. *Applied optics, 47*(12), 2061-2069. https://doi.org/10.1364/AO.47.002061

[7] **He, D., Nguyen, H. C., Hayes-Gill, B. R., Zhu, Y., Crowe, J. A.,** Gill, C., Clough, G.F., **Morgan, S. P.** (2013). Laser doppler blood flow imaging using a cmos imaging sensor with on-chip signal processing. *Sensors, 13*(9), 12632-12647. https://doi.org/10.3390/s130912632

Grants

[8] UoN PI: Prof Stephen Morgan; **Full field laser Doppler flowmetry**; 2002-2005; Paul Instrument Fund, Royal Society; Total grant (all to UoN): GPB41,607

[9] UoN PI: Prof Stephen Morgan; **Video rate laser Doppler blood flowmetry;** 2005-2010; Department of Health; NEAT (Project ID E060); (GPB224,995 in total).

[10] UoN PI: Prof Stephen Morgan; **Blood Vessel Imaging for Phlebotomy and Surgery;** 2005-2009; Innovate UK (DTI/TSB) (Project ID 100306); https://gtr.ukri.org/projects?ref=100306 , (GPB170,583 in total).

4. Details of the impact

A new, commercialised high-speed line scanning device for burn wound assessment, the moorLDLS-BI, was developed from UoN research described in section 2. The device, used in specialist burns centres worldwide [a], received FDA approval in January 2014 [b]. It has extended laser doppler imaging (LDI) blood flow assessment of burns to children, improving treatment decisions and health outcomes. The device has also been a commercial success for Moor Instruments Ltd.

The Senior Application Scientist at Moor Instruments Ltd wrote, "*The unrivalled expertise offered by [UoN] Optics and Photonics group was extremely attractive to Moor Instruments and was critical in helping us overcome technological research barriers previously restricting the development of such a device.*

The moorLDLS-BI maintains the high accuracy of burn wound assessment as the original moorLDI2-BI but, due to line scanning mechanism and the inclusion of a FPGA, reduces image acquisition time helping to greatly reduce motion artefact issues, especially in paediatric patients. This has significantly improved clinician and patient satisfaction and enabled the benefits of LDI to be extended to many more paediatric patients." [c]

Full details of the impacts to clinicians and patients are described below:

<u>Improved burns assessment and treatment for children</u>

Burns and scalds are the fourth most common injury to children. The most serious burns are treated at specialist burns centres which are equipped with the most up to date technology to ensure optimal patient outcomes. Around the world, there are only a relatively small number of such centres (e.g. 10 in the UK). The moorLDLS-BI is now used in many of these centres in the UK, Australia, U.S, Europe, and Canada [c]. 66% of the sales have occurred since August 2013 [a] and estimates from clinical practitioners indicate that it is currently used on 3,700 children per year [d].

Recommended by both the National Institute for Health and Care Excellence (NICE) and the European Burns Association (p120), LDI provides important information (without causing pain) about the depth of the burn and blood flow to the wound. It has an accuracy rate of 97%, compared to 60-80% using clinical observation alone. This information is used to determine the healing potential of the affected tissue and to decide on the most appropriate burn management to optimise scarring and functional outcome. However, its application to distressed children was problematic, as any excess motion by the patient during the scan made it impossible to obtain a useable image.

The UoN research [1-7] optimised signal processing and electronics, resulting in a new, rapid method of image acquisition using line rather than point scanning. This technology was licenced to Moor instruments in March 2011 and incorporated into the moorLDLS-BI, which was sold from 2009 and received FDA approval in 2014. This significantly improved scan times compared to the moorLDI2-BI point scanner (4s vs typical 120s), whilst providing comparable accuracy (95% vs 97% for the moorLDI2-BI) [e]. The extremely short scan time eliminates the image quality issues arising from movement during longer scans, thus making it possible to extend the clinical benefits of LDI to children. These benefits, outlined in a NICE guidance document [f], include:

- 17% reduction of skin graft operations (resulting in less scarring and subsequent pain of donor sites)

- Reduction of 2.7 days in the time it takes for surgical decisions to be made
- 2-day reduction in the length of hospital stay

A consultant burns and plastic surgeon from University Hospital Birmingham described the benefits of the moorLDLS-BI:

"Since 2014, we have used the moorLDLS-BI every week, mostly for children. We find this technology is preferable for children, who may wriggle, as the scan times are quicker. The significant benefit of the moorLDLS-BI is its ability to image blood flow at the site of the burn. This allows me to determine whether burns will heal without my intervention. Consequently, it has stopped me from needlessly skin grafting patients who, upon clinical observation, looked like they had deep burns. This saves the patients from having painful and unnecessary skin-graft procedures, which can lead to further scarring and slower healing times, of mixed-depth. The use of the moorLDLS also allows me to specifically target which areas within a burn need grafting, rather than the whole area. This again limits the size of the graft required." [g]

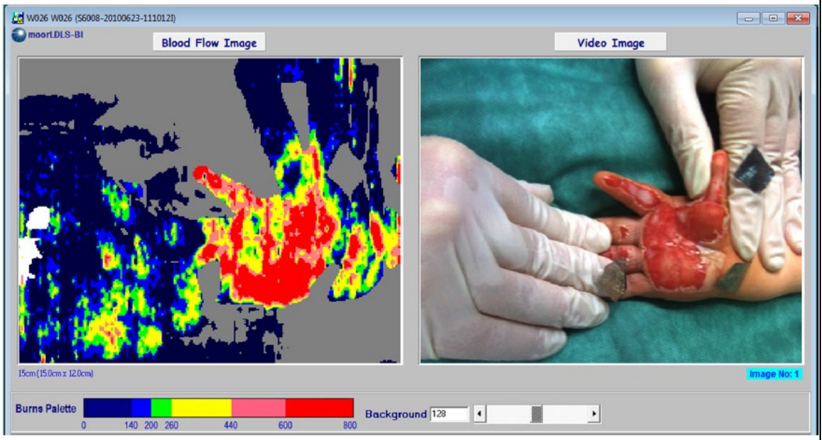

Fig 1 [i] *Contact burn of right forearm, 42 h post injury. The left side shows the laser doppler image in which regions of low blood flow (green/blue) across the burn would require a skin graft, whereas regions of high blood flow would heal without grafting. These are difficult to differentiate using visual inspection alone*

A Professor of Paediatric Surgery, Sydney Medical School, Australia [h] commented on the benefits of using the moorLDLS-BI:

"The moorLDLS-BI has been an invaluable addition to our LDI scanning capabilities and, since 1st August 2013, has been in regular use approximately 10 times per month to assess burns in our paediatric patients. We have experienced numerous beneficial impacts since using the moorLDLS-BI including:

- *Quicker examinations: These have reduced from 2 minutes to 4 seconds. A faster scan minimises the time a patient must remain still which is a significant advantage when working with distressed children. It also allows for the wound to be covered quicker to prevent infection*
- *Prioritising surgeries: We have found the moorLDLS-BI to be a very useful tool in prioritising patients for surgery and planning their elective procedures, consequently aiding in streamlining our flow of patients*
- *Objective assessment: The ability to objectively assess a burn wound is extremely helpful when subsequently assessing the need for and results of surgery"*

A 2014, an independent clinical trial, including 102 adults and 102 children [i], noted the 'significant advantages' of the moorLDLS-BI device in comparison to the leading alternative - the original moorLDI2-BI. These included:

- faster scan times when scanning burns of fractious infants
- less sedation needed to keep infants still
- LDLS is smaller and therefore easy to manoeuvre, enabling scanning during admission or in the outpatient clinic, and manipulated around the patient's bed
- battery power avoids the inconvenience of trailing leads

In summary, this case study describes how UoN research enabled the development of a burns assessment device (moorLDLS-BI), which received FDA approval in January 2014. The moorLDLS-BI can image burns 30 times faster than conventional Laser Doppler Imaging, extending the benefits of the burn scanning technique to children. Clinicians have provided testimonials on the benefits of using the moorLDLS-BI, indicating the significantly faster scans as a key factor to providing improved clinical interventions, and therefore outcomes, to an estimated 3700 paediatric patients per year.

5. Sources to corroborate the impact

[a] UoN information detailing licencing revenues

[b] FDA approval documentation

[c] Letter from Moor Instruments Ltd

[d] Estimate of usage by clinical practitioners

[e] Hoeksema, H., Baker, R. D., Holland, A. J., Perry, T., Jeffery, S. L., Verbelen, J., & Monstrey, S. (2014). A new, fast LDI for assessment of burns: A multi-centre clinical evaluation. *Burns*, *40*(7), 1274-1282. https://doi.org/10.1016/j.burns.2014.04.024

[f] NICE guidance document outlining LDI benefits

[g] Letter from the Consultant Burns and Plastic Surgeon, University Hospitals Birmingham NHS Foundation Trust

[h] Letter from Professor of Paediatric Surgery, Sydney Medical School, The University of Sydney, Australia

[i] Holland, A. J. A., Ward, D., La Hei, E. R., & Harvey, J. G. (2014). Laser doppler line scan burn imager (LDLS-BI): sideways move or a step ahead?. *Burns*, *40*(1), 113-119. https://doi.org/10.1016/j.burns.2013.05.008