Institution: University of Essex

Unit of Assessment: 26 – Sport and Exercise Sciences, Leisure and Tourism

Title of case study: Developing optical measurements of muscle physiology

1. Summary of the impact

Research at Essex underpinned the development and application of near infrared muscle oxygen spectroscopy (NIRS) devices that have had medical and sporting applications in three areas:

1) Research on second derivative spectroscopy underpinned the concept of the **Hutchinson Technology InSpectra™** tissue spectrometers, and later Essex publications validated the technology. The current device is used for muscle research worldwide, including in sports and exercise science. It has US Food and Drug Administration approval and has been sold for use in many US hospitals with improved clinical outcomes and economic benefits.
2) Applied research, undertaken at Essex, made first use of the **Artinis Inc. Portamon™** portable NIRS device in elite athletes (UK short track speed skaters). Subsequently this technology has been used to assist the training of a number of sports teams including [text removed for publication] and the Team GB hockey team.
3) This work was also used to **engage the public in sports science research** both nationally (e.g. Edinburgh and Cheltenham Science Festivals 2010-2013) and internationally (Abu Dhabi Science Festival 2011-2013).

2. Underpinning research

Research at Essex over the last 15-20 years has played a key role in developing new ways of using light to measure oxygen delivery and metabolism in human tissue non-invasively. The methods make use of near infrared spectroscopy (NIRS). This technique uses wavelengths of light – invisible to the naked eye – that can penetrate deep into tissue. Once in the tissue, different wavelengths are absorbed by the blood protein haemoglobin, as well as the cellular proteins myoglobin and mitochondrial cytochrome *c* oxidase. Haemoglobin and myoglobin transport oxygen to the mitochondrion inside the cell, where the cytochrome oxidase consumes it. These methods of oxygen delivery and utilisation are responsible for over 95% of the oxygen consumed by the body, and hence the vast majority of the energy requirements that drive all cellular processes.

NIRS has been known for over 30 years as a safe and non-invasive means of reporting on human biology and medicine with widespread potential for on-going applications in sport and exercise sciences. However, a major problem with the development of this technology is that near infrared light is multiply scattered by tissue. This makes it difficult to convert the amount of light reaching the detector into the quantifiable concentration of haemoglobin and cytochrome oxidase necessary for meaningful physiological and biological interpretation of the data. Research at Essex has used interdisciplinary methods to approach this problem, combining the complementary expertise of sports scientists, psychologists, physiologists, clinicians, physicists and biochemists to develop new methods to analyse and interpret data. Important developments have been made in both brain and muscle research, but this impact case study focuses on the muscle work. The key underpinning research at Essex has been in **two areas:**

1) The discovery of the use of second derivative spectroscopy of deoxyhaemoglobin to eliminate artefacts from light scattering in tissue near infrared spectroscopy (Cooper et al., 1998; Myers et al., 2005). This method enables absolute concentrations of tissue chromophores to be determined, in particular deoxyhaemoglobin (the form of haemoglobin that has released its oxygen to tissue), hence informing on oxygen extraction. This work was carried out by Professor Chris Cooper (exemplar publication: Cooper et al., 1998) and the idea was developed by researchers at Hutchinson Technology Inc. (US). Hutchinson applied the second derivative technique to a wider wavelength range that also incorporates the oxyhaemoglobin chromophore. This meant that the ratio of the oxyhaemoglobin and deoxyhaemoglobin concentration in muscle could be determined. This ratio is defined as tissue oxygen saturation (StO2) – an important clinical and biological parameter. The key piece of original peer-reviewed research that validated this technology was undertaken in 2005 by the company in collaboration with Cooper, who advised on the details of methodology and analysis (Myers et al., 2005).

2) The application of portable NIRS as a means of measuring real time muscle oxygen delivery and utilisation that can inform training programs (see: Hesford et al., 2012; 2013a; 2013b). As part of a 2007 EPSRC 'Achieving Gold in 2012' project grant, medical engineers at UCL and Essex researchers (biochemists, clinicians, physiologists and coaches) were funded to: **(i)** develop a new portable muscle optics device; and **(ii)** determine the benefits of such a device as a tool to optimise sports performance. The Essex team consisted of Cooper (Professor and Project Lead), Beneke (Professor and co-applicant, now employed as Professor of Sports Medicine in Marburg, Germany), Angus (Lecturer in Exercise Physiology, who left Essex in 2011) and Parry (Triathlon coach at the time of the study, now Lecturer and Human Performance Unit Director at Essex).

The bespoke portable device is still under development at UCL. However, the sports application ideas developed by the Essex researchers resulted in a number of sports science publications using a commercial NIRS spectrometer. Arising from this work, a new collaboration was developed between Cooper and Dr. Marco Cardinale, at the time Head of Sports Science and Research at the British Olympic Association. This funded a PhD student at the University of Essex, Catherine Hesford. The collaboration between 2009-2012 resulted in a series of peer-reviewed publications (see: Hesford et al., 2012; 2013a; 2013b) using a new commercial **portable** muscle spectrometer (Artinis Inc. Portamon™), which demonstrated clearly the potential benefits of the use of a NIRS device for monitoring elite athletes in the field. This research revealed aspects of the muscle physiology, measured in real time by wireless NIRS, that were challenged during the extreme stress of short track speed skating. This opened the possibility of testing for improvements in local muscle oxygen delivery and utilisation following training and/or nutritional interventions.

3. References to the research [can be supplied by HEI on request]

Cooper, C.E., D.T. Delpy and E.M. Nemoto (1998) The relationship of oxygen delivery to absolute haemoglobin oxygenation and mitochondrial cytochrome oxidase redox state in the adult brain: a near-infrared spectroscopy study. *Biochem. J.* 332, 627-632 (51 citations – Nov '13) Available at: http://www.biochemj.org/bj/332/0627/3320627.pdf [Accessed 13 Nov '13]

Myers, D.E., C.E. Cooper, G.J. Beilman, J.D. Mowlem, L.D. Anderson, R.P. Seifert and J.P. Ortner (2005) Noninvasive method for measuring local hemoglobin oxygen saturation in tissue using wide gap second derivative near-infrared spectroscopy. *J. Biomed. Opt.* 10(3), 034017 (116 citations – Nov '13) DOI:10.1117/1.1925250

Hesford, C.M., S.J. Laing, M. Cardinale and C.E. Cooper (2012) Asymmetry of quadriceps muscle oxygenation during elite short-track speed skating. *Med. Sci. Sports Exerc.* 44, 501-508. DOI:10.1249/MSS.0b013e31822f8942

Hesford, C.M., S.J. Laing, M. Cardinale and C.E. Cooper (2013a) Effect of race distance on muscle oxygenation in short-track speed skating. *Med. Sci. Sports Exerc.* 45, 83-92. DOI:10.1249/MSS.0b013e31826c58dd

Hesford, C.M., S.J. Laing and C.E. Cooper (2013b) Using portable NIRS to compare arm and leg muscle oxygenation during roller skiing in biathletes: A case study. *Adv. Exp. Med. Biol.* 789, 179-184. DOI:10.1007/978-1-4614-7411-1_25

Research funding:

Cooper, Griffin, *Can imaginary exercise be used to control and focus muscle blood flow changes?* Wellcome Trust Showcase Award, 2003-2006, £125k

Cooper, Beneke, Parry, *Non invasive measurements of muscle oxygenation in elite athletes in the field*, EPSRC, 2007-2008, £28k

Cooper, *Non-invasive measurement of muscle oxygenation in elite sport*, Olympic Medical Institute, 2008-2011, £46k

Cooper, *Quantifying the effects of adipose tissue thickness on muscle near infrared signals*, Artinis Inc., 2012-2013, £125k

4. Details of the impact

Impacts arising from the manufacture of biomedical equipment: Cooper's academic research on second derivative spectroscopy (Cooper et al., 1998; Myers et al., 2005) informed the development of the Inspectra™ StO2 near infrared spectrometers produced by Hutchinson Technology Inc. A letter of support from Hutchinson [see corroborating source 1] explains how: "Prof. Cooper's research underpinned the development of these systems in two ways". Firstly, the letter describes how development of the devices drew upon Cooper's original research, which

showed it was possible to make an absolute measurement of tissue deoxyhemoglobin concentration using second derivative optical spectroscopy (Cooper et al., 1998). The letter details how this research "informed the ideas that led to […] Hutchinson's modification of this method to measure absolute tissue oxygen saturation". Secondly, the letter notes how Cooper's research also contributed to device validation, outlining how the 2005 collaborative study (Myers et al., 2005) is "widely cited by users of the StO2 system to justify the use of the device in physiology and medicine". In the REF2014 impact period, the Inspectra™ StO2 series of NIRS devices has subsequently led to extensive **impact in three areas:**

Commercial impact: As a global technology manufacturer, Hutchinson employs 2,000 staff in two divisions. One of these, the BioMeasurement Division, designs, manufactures and sells a single product type – the Inspectra™ StO2 NIRS system. Over the five-year period 2008-12, the BioMeasurement Division reported net Inspectra™ sales of $9.04M [2] [3].

Clinical impact: The main clinical use of the current technology has centred on measurements of the thenar (thumb) muscle saturation as an indicator of peripheral oxygen delivery to tissue. Typical patient groups include: a) Blood Loss (trauma, post-surgical gastrointestinal bleed); b) Elderly (clinical signs confounded by medication, co-morbidities, infection or early sepsis); and c) Critical Care Patients (non-alarming clinical signs, difficult to diagnose, heart dysfunction). Two devices are used. Firstly, the *InSpectra™ StO2 Spot Check*, which is a small portable device used to quickly and cost-effectively identify patients at risk for circulatory distress. Once identified to have low StO2 (tissue oxygen saturation), patients are then continuously monitored with the *InSpectra™ StO2 Monitor*. These devices both received 510(k) clearance from the US Food and Drug Administration in 2011 and 2010 respectively, enabling them to be legally used in hospital emergency and critical care environments as cost-effective tools to help rapidly assess tissue perfusion and shock. There have been over 200 clinical studies on this technology, many of which cite the original Essex research. Illustrating a number of significant points, these studies show that, for instance, a low oxygen saturation can be associated with worse outcomes in critically ill patients (Lima et al., *Crit Care*. 2009; 13(Suppl 5):S13). It is also demonstrated that using saturation to guide patient treatment (Miner et al., *Crit Care Med*. 2010; 38(12):S86) can result in significant economic benefits in the form of shorter hospital stays (down from 11.4 to 8.9 days).

Applied sports impact: Hutchinson spectrometers have been applied extensively to examine muscle oxygen biology in applied sport and exercise science. A number of published articles report on such use of Hutchinson devices. Most notably, these include studies on: muscle oxygenation in handball players (*Int. J. Sports Physiol. Perform*. 2008; 3:251-26); sailors (*Int. J. Sports Med*. 2008; 29:11-15); high-altitude climbers (*Crit Care*. 2009; 13(Suppl 5):S7); and exercise in patients with symptomatic peripheral arterial disease (*Clin Sci (Lond*). 2009; 117:405-413) and intermittent claudication (*PM&R*. 2009; 1:932-940).

Impacts of muscle optics on elite sports performance: The more applied aspects of Cooper's academic research (see: Hesford et al., 2012; 2013a; 2013b), undertaken in collaboration with the British Olympic Association (BOA), demonstrated the potential for using real time wireless portable NIRS to enhance elite sports performance. It revealed asymmetry in muscle oxygenation due to the nature of the demands of high-speed cornering constricting blood flow to the right leg in speed skaters. These research findings were then used to test the efficacy of new equipment and nutritional supplementation strategies. For example, NIRS research demonstrated that nitrate-rich beetroot juice would both enhance performance and reduce the muscle oxygen asymmetry. The Head of Sports Science and Research at the BOA [4] notes that "this research made an outstanding contribution to the preparation of our winter sports athletes for the Winter Olympic Games in Vancouver in 2010 and is making an impact for the preparation of the Winter Olympic Games in Sochi in 2014...In particular, the research work improved the understanding of the physiological demands of speed skating and allowed the coaching team to develop a new approach to train single limbs with specific technical drills". He adds that "as a consequence of this work, there has been an increasing demand in the British sporting community and abroad for the use of NIRS in athletic populations".

An example of this increasing demand is that Essex was commissioned to assist in the training of [text removed for publication] and the British hockey team. [text removed for publication] [5] explains that: "The technique suggested that our intended training goal of improving oxygen

consumption at the level of the muscle was realised in the majority of the players tested, helping to inform their future training direction […] this project illustrates that the muscle optics research of Professor Cooper has useful application in the real world elite sporting environment as a non invasive measure of muscle function". The Senior Strength and Conditioning Coach of the Great Britain and England Hockey Team states [6] that: "Chris Cooper's groups at the University of Essex are leading the way in the use of NIRS and proved invaluable for GB Hockey in a recent training study […] the NIRS device proved to be an excellent non-invasive assessment tool that has helped quantify performance changes and further our knowledge around oxygen kinetics and adaptation rates in muscle tissue following a training intervention".

Impacts from public engagement: Significant public engagement activity has been undertaken by Essex staff, describing their latest research in muscle NIRS. As well as national and international coverage via broadcast and print media (including international magazines such as *Wired*) sports performance research has been used to engage the public directly. Most notably this has been at the Edinburgh International Science Festival (EISF). In 2010, Cooper was involved in developing *Blood Bar*, a workshop and show supported in part by a grant from EPSRC. Blood Bar featured discussions of the colour of blood and its use in health and sport monitoring, including examples of Essex optics research. Blood Bar returned to the festival in 2011, 2012 and 2013 and has become one of its most popular events. The workshop has also toured to Cheltenham Science Festival (2011) and to the Abu Dhabi Science Festival (2011, 2012 and 2013). In 2011, Cooper organised a live scientific research study adjacent to the Blood Bar – "Shining Light on Exercise" – looking at the effect of age and gender on muscle oxygenation during high-intensity exercise (Wingate Test). Cooper also gave public lectures in 2010 and 2011 as part of the festival program.

In 2012, EISF staged *InMotion*, a major interactive exhibition on the science of human movement, which demonstrated the latest research in this area. Cooper advised on experiments and provided optics research equipment for an interactive demonstration on heart rate and oxygen saturation. InMotion appeared at the National Museum of Scotland in 2012, toured to Abu Dhabi later that year and then returned to be part of the 2013 EISF. The exhibition will go to the Glasgow Science Centre for six months starting at Easter 2014, to mark the Commonwealth Games. Details of all the public engagement activities undertaken by Cooper and others are included in a letter of support from the Director of the Edinburgh International Science Festival [7].

Evaluation reports show that the Blood Bar filled to capacity each year (1,740 children, average age 9.3); the Cheltenham (2,000 visitors) and Abu Dhabi (2,400 visitors) events had a similar age spread. InMotion had 35,000 visitors at the Museum in 2012, 3,500 at the Ocean Terminal Mall (Edinburgh) in 2013 and 5,000 in Abu Dhabi [8] [9] [10]. In his letter, the EISF Director, notes that; "We have had a highly productive partnership with you and your group over the last four years which has contributed to some of the most successful events EISF has staged" [7].

5. Sources to corroborate the impact [All sources saved on file with HEI, available on request]

[1] Development Manager, BioMeasurement Division, Hutchinson Technology Incorporated
[2] 10-K; Hutchinson Technology Inc. Annual Report Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934 For the Fiscal Year Ended September 30, 2012. Available from: http://thomson.mobular.net/thomson/7/3323/4687/document_0/HTCH%202012%2010-K%20-%20reduced.pdf [Accessed 8 October 2013]
[3] 10-K; Hutchinson Technology Inc. Annual Report Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934 For the Fiscal Year Ended September 27, 2009. Available from: http://phx.corporate-ir.net/phoenix.zhtml?c=61195&p=irol-reportsannual [Accessed 8 October 2013]
[4] Head of Sports Science and Research, British Olympic Association
[5] [text removed for publication]
[6] Senior Strength and Conditioning Coach Great Britain and England Hockey Team, English Institute of Sport
[7] Director, Edinburgh International Science Festival
[8] Blood Bar Evaluation Report
[9] Blood Bar and InMotion data
[10] Final EISF Evaluation report, May 2012