Institution: Edinburgh Napier University

Unit of Assessment: 13 – Electrical and Electronic Engineering, Metallurgy and Materials

Title of case study: Signal Analysis Solutions for the Medical Device Industry

1. Summary of the impact

Translational research created new techniques for medical biosignal analysis in both the ECG and Pulse Oximetry areas. CardioDigital, a university spin-out company, was incorporated in 2001 to commercialise the research and became a world leader in the development and supply of signal analysis solutions for the medical device industry. The technology has been applied to defibrillation techniques to improve survival rates following sudden cardiac arrest, with a range of closely linked pulse oximetry based technologies applicable for general ward use. The technologies provide both enhanced and extended performance of the pulse oximeter leading to improved patient care and hospital workflows.

2. Underpinning research

The initial research was derived from an EPSRC funded study - *Wavelet Transforms for Low Strain Integrity Testing of Foundation Piles* (*Aug 1998 – Jul 2000*) undertaken by Dr Paul Addison, senior lecturer in fluid mechanics, subsequently professor (2002 until 2008), to develop wavelet based techniques to decompose non-destructive stress wave signals taken from *in situ* piled foundations in order to better facilitate their interpretation. The results indicated that low oscillation complex wavelets were optimal in highlighting anomalies within structural elements. In addition, new signal de-noising methods were developed specifically for the sonic echo traces based on wavelet modulus maxima techniques.

The wavelet transform's unique ability to decouple non-stationary, aperiodic signal components also made it ideal for developing enhanced signal processing algorithms for medical devices. Prof Addison and his team demonstrated that the wavelet transform could extract extremely subtle physiological information, 'unseen' by traditional temporal or Fourier methods [ref 1].The results were brought to the attention of a Norwegian company *Laerdal Medical*, a specialist manufacturer of resuscitation equipment. Funding was provided for a pilot study to establish whether the de-noising software could be applied to ECG signals recorded during ventricular fibrillation which hitherto was thought to represent disorganized and unstructured electrical activity of the heart. The research developed a new signal analysis technique which revealed previously unreported structure within the ECG tracing. These findings provided the first evidence linking this structure to unexpected mechanical phenomena occurring in the heart [ref 2,3]. A patent GB9910019 was filed on the 1st May 1999 and a company CardioDigital Ltd was spun out from the University in 2001 to commercialise the research findings.

A parallel stage of research commenced in collaboration with a US company, *Nellcor Puritan Bennett*, which specialised in pulse oximetry monitoring. This resulted in a novel time–frequency method for the measurement of oxygen saturation using the signals from a standard pulse oximeter machine. The method utilised the time–frequency transformation of these red and infrared signals to derive a novel 3D Lissajous figure. By selecting the optimal Lissajous, the method provided an inherently robust basis for the determination of oxygen saturation as regions of the time–frequency plane where high and low frequency signal artefacts are to be found were automatically avoided. A patent GB200115284 was filed on the 22nd June 2001 and the findings published in 2004 [ref 4]. Under the guidance of Professor Addison, co-founder and CEO, the company acquired a suite of adjacent blood pressure technologies from Canadian company, VSM Medtech, in 2007. During the same year CardioDigital Inc., a US subsidiary of CardioDigital Ltd, was incorporated in Portland, Oregon. It was through this company that CardioDigital sold its suite of oximetry technologies to Covidien, one of the world's largest healthcare providers, in May 2008.

Over the 7 years between 2001 and 2008, Professor Addison continued his research at Edinburgh Napier University publishing over 150 technical papers including 40 journal publications while further developing and implementing novel technology algorithms for the next generation of medical devices [refs 5,6].

3. References to the research

1) ***The Illustrated Wavelet Transform Handbook: Applications in Science, Engineering, Medicine and Finance***
P.S. Addison, *Taylor and Francis*, 2002. (Published in Japanese in 2005.)
ISBN 0-7503-0692-0
Cited by 889

2) **Wavelet transforms and the ECG: a review**
PS Addison - Physiological Measurement, IOP Science, Volume 26, Number 5, R155, (2005)
DOI 10.1088/0967-3334/26/5/R01.
Cited by 276

3) ***Evaluating arrhythmias in ECG signals using wavelet transforms***
PS Addison, JN Watson, GR Clegg, *Engineering in Medicine and Biology Magazine, IEEE*
Volume 19, Issue 5, pp 104-109 (2000) DOI 10.1109/51.870237
Cited by 83

4) ***A novel time–frequency-based 3D Lissajous figure method and its application to the determination of oxygen saturation from the photoplethysmogram***
PS Addison, JN Watson - *Measurement Science and Technology*, IOP Science Volume 15, Number 11, L 15-18 (2004) DOI 10.1088/0957-0233/15/11/L01
Cited by 72

5) ***Heart rate variability measurements and the prediction of ventricular arrhythmias***
MJ Reed, CE Robertson PS Addison – *Quarterly Journal of Medicine*, Oxford Univ Press
Volume 98, Issue 2, pp 87-95 (2005) DOI 10.1093/qjmed/hci018
Cited by 68

6) **Improved prediction of defibrillation success for out-of-hospital VF cardiac arrest using wavelet transform methods.**
JN Watson, N Uchaipichat, PS Addison, GR Clegg, - Resuscitation, Elsevier, Volume 63, Issue 3, pp 269-275, (2004) DOI 10.1016/j.resuscitation.2004.06.012
Cited by 46

Early grants in support of the research and development at ENU are as follows:

1. **EPSRC Grant No. GR/M21881; Value: £79K (Oct 98)** *" Wavelet transforms for low strain integrity testing of foundation piles"* Grantholders: P S Addison & A Sibbald

2. **Laerdal Medical Foundation Grant No 1831; Value £6K; (Feb 1999) "***Wavelet Analysis of the Human Electrocardiogram during Ventricular Fibrillation (VF)".* Grantholder: P S Addison

3. **MRC Grant No. G/0001060; Value: £47K (Feb 2001)** "*Wavelet Transform* Based Prediction of Shock Outcomes in Ventricular Fibrillation" Grantholder: P.S. Addison

4. **Scottish Executive SMART Award: £45K (March 2001):** *'Wavelet Analysis of Electrocardiograph Signals and the Next Generation of Heart Defibrillators.'* Grantholder: P.S. Addison

5. **Wellcome Trust Development Fund Award: £582K (December 2002):** *'Novel Signal Analysis Tools for Pulse Oximeters and Defibrillators'.* Grantholder: P.S. Addison

6. **Scottish Executive SPUR+ Award: £341K (January 2003):** *Matched funding by the Scottish Executive in respect of the Equity Investment by the Wellcome Trust above.* Grantholder: P.S. Addison

7. **Scottish Enterprise Business Support Awards: £48K (June 2004 to April 2005):** *To assess the market opportunity of the technologies in the USA and the restructuring costs associated with the setting up of CardioDigital Inc.* Grantholder: P.S. Addison

8. **Wellcome Trust Strategic Translation Award: £18K (May 2005):** *Contribution towards market opportunity analysis of CardioDigital's pulse oximeter and atrial fibrillation technologies carried out by Wood Mackenzie - used to inform the business strategy.* Grantholder: P.S. Addison

9. **Wellcome Trust: £435K (November 2006):** *Convertible loan for the development of AF technologies including large scale multi-centre clinical trials.* Grantholder: P.S. Addison

10. **Laerdal Medical: £64K (March 2007).** *Collaboration deal to develop wavelet methods for CPAP, ventilator products and sleep diagnostic devices.* Grantholder: P.S. Addison

4. Details of the impact

Economic Impact:

As indicated in the summary, CardioDigital Ltd, was spun out from the University in 2001 to commercialise the research and has now become a world leader in the development and supply of signal analysis solutions for the medical device industry. The Company, which is led by Professor Addison as CEO, is located at the Roslin Biocentre, one of the UK's leading commercial centres for life science research.

Professor Addison also runs the Covidien R&D facility based at the Technopole Science Centre in Edinburgh, where over the past five years he has developed this facility creating high value PhD level jobs. Close links are maintained with Covidien in Boulder, Colorado where the respiratory and monitoring solutions division is headquartered. Covidien is a global medical device manufacturer with an annual turnover of $12B, a presence in over 150 countries and a workforce of 44,000 worldwide and, as such, has the global reach and commercial muscle to maximise the impact of the acquired technologies. The investment by Covidien in Scotland is seen as a significant economic impact.

CardioDigital Inc., a subsidiary of CardioDigital Ltd, was set up to commercialise the technologies in the large US market and was the point of sale for the Covidien deal in 2008. The technologies sold to Covidien at that time included methods for determining respiration rate and blood pressure from a pulse oximeter signal. Professor Addison became an employee of Covidien at the time of the sale. Since 2008, Edinburgh Napier University, as a key shareholder in the company, has benefited from a series of dividends resulting from that sale.These payments have been triggered by the meeting of milestones agreed between Covidien and CardioDigital as part of the sale agreement.

Health Impact:

The technology has been applied to defibrillation techniques to improve survival rates following sudden cardiac arrest, with a range of closely linked pulse oximetry based technologies applicable for general ward use. The technologies provide both enhanced and extended performance of the pulse oximeter leading to improved patient care and hospital workflows.

Continuous monitoring of respiration rate is especially important for adult patients receiving

medication for post-operative pain management, who are at increased risk for respiratory complications. New conclusions and recommendations from the US Anaesthesia Patient Safety Foundation (APSF) suggest continuous electronic monitoring of oxygenation and ventilation for these patients to reduce the risk of unrecognised, clinically significant respiratory complications.

The Chief Medical Officer of Respiratory and Monitoring Solutions at Covidien stated, 28 Nov 2011, "Despite its clinical importance, current methods of respiration rate monitoring are not always adequate. The addition of Respiration Rate to the Covidien Nellcor Respiratory Function portfolio provides a more holistic monitoring solution using a single, integrated sensor. Instead of merely knowing a patient's blood oxygen levels, we can now look at aspects of ventilation, or the passing of air into and out of the body. This gives healthcare professionals a more complete picture of a patient's respiratory status, so they can provide effective treatment and maintain patient safety."

In 2011 the U.S. Food and Drug Administration (FDA) granted 510(k) clearance to Covidien to market the Nellcor™ Respiration Rate Version 1.0 software and the Adult Respiratory Sensor. In the same year the respiratory monitoring platform obtained a CE Mark to allow it to market it throughout the European Economic Area. Market release of the product commenced in 2012.

In 2011, Professor Addison gained an Early Stage Innovator Award from Covidien and won Inventor of the Year award in 2012 for Covidien R&D projects.

Professor Addison, as inventor, has been granted over 30 US patents and a further 90 patents have been applied for. All but three of these have been written in the past 5 years whilst at Covidien. All concern novel methods for biomedical devices. The majority concern signal processing in a wide variety of medical signals. These speak directly to the impact of his work over the period and also the expected impact over future years.

5. Sources to corroborate the impact

1. **The Wellcome Trust** through its Catalyst Biomedica scheme supported both the proof-of-concept research and business development stage including clinical trials related to both pulse oximetry and defibrillation. (Named contacts supplied separately).

2. **The Royal Infirmary of Edinburgh**, Department of Accident and Emergency, was involved from a very early stage in providing data for analysis and during the clinical trials of the medical equipment. (Named contact supplied separately).

3. **Covidien Respiratory and Monitoring Solutions** have been involved in the research and development of the pulse oximetry equipment, both through their purchase of CardioDigital Inc and subsequently through the work of the Covidien Biosignal R&D Group in Scotland. (Named contact supplied separately).

4. **President and CEO, Brien Holden Vision diagnostics, Inc.**
   CEO of CardioDigital Inc in the US, was instrumental in negotiating the Covidien deal in 2008. (Named contact supplied separately).