Institution: University of Ulster

Unit of Assessment: Engineering (12)

Title of case study: Healthcare Sensor Systems and Health Technology Solutions to Address Global Challenges

Period when the underpinning research was undertaken: 1 January 2000 to 31 December 2020

Details of staff conducting the underpinning research from the submitting unit:

Name(s):	Role(s) (e.g., job title):	Period(s) employed by submitting HEI:
Professor James McLaughlin	Professor of Advanced Functional Materials	1990 - present
Professor John Anderson (d.2012)	Professor of Medical Electronics	1994 - 2007
Professor Dewar Finlay	Professor of Electronic Systems	2001 - present
Professor Omar Escalona	Professor of Advanced Cardiovascular Research	2007 - present
Dr Daniel Guldenring	Lecturer in Electronic Engineering	2014 - 2018
Dr Patrick Lemoine	Lecturer in Engineering	2002 - present
Dr Raymond Bond	Reader in Computer Science	2010 - present

Period when the claimed impact occurred: 1 August 2013 to 31 December 2020

Is this case study continued from a case study submitted in 2014? N

1. Summary of the impact

The development of globally relevant healthcare technologies for the benefit of patients and the economy is a core theme in the Ulster Engineering research portfolio. Our research is intricately linked with international partners in both the commercial and clinical spheres. It has impacted local government policy through our **leadership in forums that include MATRIX** and **Innovate UK/Health KTN**. We have also witnessed global impact through our representation in international scientific forums such as **Computing in Cardiology** and the **International Society for Computerised Electrocardiology,** and our **ECG signal processing algorithms have been adopted by the United States Food and Drug Administration (FDA)**. Collectively, this activity has resulted in the growth of the GBP9,300,000 industry-focused Connected Health Innovation Centre (CHIC) established at Ulster, the EUR8,400,000 Eastern Corridor Medical Engineering Centre (ECME), the GBP7,300,000 industry-focused Biodevices Rapid Prototyping Laboratory and the showcasing of our **research on the global stage through our team's 3rd place success in the XPRIZE Tricoder competition**. Our research has recently resulted in the sale of the successful Ulster spin-out company **Intelesens to Ultralinq for [redacted] (2017).** The commercialisation of this cardiovascular monitoring technology has had beneficial impact on health costs and patients' lives on a global scale over the past seven years.

2. Underpinning research

Ulster has an extensive record in the development of healthcare sensor systems and is unique in its ability to deliver on the entire technology stack required in the **development of end-to-end, 'sensor-to-diagnosis', healthcare technology devices**. These activities range from the design, development, and fabrication of physical sensing electrodes to the development of software algorithms for highly accurate automated diagnosis and decision support. A key specific theme in Nanotechnology and Integrated Bioengineering Centre's (NIBEC) record of accomplishment over the past 25 years has been major advancements in the **acquisition and analysis of cardiac bio-signals**.

ECG Electrode System Development - Early work during this period in the development of flexible multi sensor arrays **[R1] (Lemoine, McLaughlin, Anderson, 2000)** and novel low impedance Agr/AgCl colloid inks **[R2] (McLaughlin, 2002)** resulted in state-of-the-art dry electrode systems for ECG measurement. A major novelty of this work was the focus on reducing electrode impedance, through Ag/AgCl plasma surface modification, and accommodation for body motion artefacts using a mixture of advanced micro-fabrication techniques with a high-volume manufacturing focus. This electrode research was the catalyst for the formation of Intelesens Ltd by McLaughlin, Anderson, and McAdams in 2001. Even though the technology had taken on a commercial development route, the focus remained on pursuing innovation through research. One of the critical avenues for innovation advantage was the early adoption of data analytics and data science techniques to help address challenges in improving the signal quality in mobile cardiac monitoring systems. This work included the analysis of large datasets to identify patterns that helped to identify the best recording site/electrode positions for recording ECGs in the context of various cardiac abnormalities **[R3] (Finlay, 2010)**. Importantly, this has included optimised ECG electrode locations for detecting general ventricular arrhythmias **[R4](Finlay, 2013)** as well as accurately diagnosing atrial fibrillation **[R5] (Finlay, Guldenring, Bond, McLaughlin, 2016)**.

ECG Algorithm Developments – NIBEC's expertise in the ECG data analytics has been **recognized by scientists from the US Food and Drug Administration (FDA)** via a request for assistance in the development of an algorithm to transform data from one ECG recording format to another to determine the potential cardiac risk of newly developed drugs. Ulster published this work in **collaboration with the FDA** and our algorithm was shown to be more accurate than the existing state of the art methods **[R6] (Finlay, Guldenring, Bond, McLaughlin, 2015)**. In recognition of the importance of these developments, we received an invite (Guldenring) to present this work at the prestigious International Society for Computerized Electrocardiology (ISCE) Annual Conference in 2017. As a result of this activity, **Ulster's algorithm has now been fully adopted by the FDA** and used for computing ECG biomarkers in drug trials. The FDA has also described **our algorithm in the current draft standard and associated reports (IEC 80601-2-86)**.

Contributions to the International Health Technology Knowledge Base - Over and above published scientific outputs, Ulster's researchers have made a significant contribution via strategic/international Scientific Committees and Boards: McLaughlin in MATRIX NI and Innovate UK; KTN Healthcare Technology Board in 2015; Finlay in Computing in Cardiology Board of Directors Appointment (2012-2020) and International Society for Computerised Electrocardiology (2014-2017). Most recently, McLaughlin was appointed to the UK Rapid Test Consortium (UK-RTC) which has directed the development and manufacture of the approved COVID-19 Point of Care lateral flow tests as part of the Government's five pillar national testing strategy for SARS-CoV-2.

3. References to the research

Outputs can be provided by Ulster University on request.

[**R1**] Lemoine, P., Mailley, P., Hyland, M., McLaughlin, J.M., McAdams, E., Anderson, J.M.C.C., Lynch, A., Diamond, D. and Leader, M., 2000. Swelling and delamination of multi-electrode sensor arrays studied by variable-pressure scanning electron microscopy. *Journal of Biomedical Materials Research: An Official Journal of The Society for Biomaterials, The Japanese Society*

for Biomaterials, and The Australian Society for Biomaterials and the Korean Society for Biomaterials, *50*(3), pp.313-321.
[R2] Escoffier, C., Maguire, P.D., Mahony, C., Graham, W.G., McAdams, E.T. and McLaughlin, J.A., 2002. Plasma Chloriding of Thin-Film Silver: A Novel Process in Silver-Silver Chloride Reference Electrode Fabrication. *Journal of The Electrochemical Society*, *149*(4), pp.H98-H102.
[**R3**] Finlay, D.D., Nugent, C.D., Donnelly, M.P. and Lux, R.L., 2010. Eigenleads: ECG leads for maximizing information capture and improving SNR. *IEEE transactions on information technology in biomedicine*, *14*(1), pp.69-78.
[**R4**] Daly, M.J., Finlay, D.D., Scott, P.J., Nugent, C.D., Adgey, A.A.J. and Harbinson, M.T., 2013. Pre-hospital body surface potential mapping improves early diagnosis of acute coronary artery occlusion in patients with ventricular fibrillation and cardiac arrest. *Resuscitation*, *84*(1), pp.37-41.
[**R5**] Kennedy, A., Finlay, D.D., Guldenring, D., Bond, R.R. and McLaughlin, J., 2016. Detecting the elusive P-wave: a new ECG lead to improve the recording of atrial activity. *IEEE Transactions on Biomedical Engineering*, *63*(2), pp.243-249.
[**R6**] Guldenring, D., Finlay, D.D., Bond, R.R., Kennedy, A., McLaughlin, J., Galeotti, L. and Strauss, D.G., 2015. The derivation of the spatial QRS-T angle and the spatial ventricular gradient using the Mason–Likar 12-lead electrocardiogram. *Journal of Electrocardiology*, *48*(6), pp.1045-1052.

The above journal articles have been subject to blind peer review practice by internationally based editorial boards

Relevant Grant Awards:
G1: Anderson, McLaughlin, Turner
MATCH-Multi Disciplinary Assessment of Technology Centre for Healthcare.
EPSRC-GR/529874/01
01/10/2003 - 02/11/2009
GBP821,984

G2: Mclaughlin, Finlay, Guldenring, Escalona
The Biodevices Rapid Prototyping Laboratory
InvestNI
01/10/2015-31/12/2020
GBP3,704,039

G3: McLaughlin, Finlay
CHIC-The Connected Health Innovation Centre
InvestNI-Competence Centres
01/05/2011-31/12/2023
GBP7,979,657

G4: McLaughlin, Finlay, Bond
Eastern Corridor Medical Engineering Centre (ECME)
EU INTERREG VA
01/04/2017-31/03/2022
GBP2,447,924

4. Details of the impact

I1 - Medical Device Commercialisation Underpinned by High Quality Research - Intelesens Ltd, under the leadership of McLaughlin as CTO, developed and commercialised a product portfolio of miniaturised chest-worn medical devices that allow for real-time monitoring for cardiac arrhythmias and related events. These commercially available devices, all of which have undergone rigorous regulatory approval (FDA approval and CE marking) **(C1)**, allow recording and transmission of ECG, impedance-based respiration and movement/accelerometery data to the cloud.
The device platform is based on a sensor system which relies on Ulster's early research on electrode technology **(R1-R2)**. Indeed, aside from utilisation in Intelesens' own monitoring

solution, this electrode technology has emerged as a significant revenue stream for Intelesens through supply of electrodes to third-party device manufacturers (**C2**).
Intelesens devices are highly configurable allowing different recording and transmission options depending on the clinical need. A particular aspect of this is the positioning of recording electrodes to optimise recording in particular disease scenarios. Ulster's extensive research on selecting ECG record sites and electrode positions has fed directly into Intelesens device development and configuration (**R3-R5**).
Intelesens devices use novel intelligent algorithms for the detection of cardiac arrhythmias from ECG recordings. If necessary, these events are immediately transmitted to clinical monitoring centres for urgent intervention. This functionality relies on highly accurate automated algorithms for event detection. Intelesens has relied significantly on Ulster research (**R4+R5**) in understanding the mechanisms of lethal cardiac arrythmias in the development of their critical algorithms, which are all regulated (FDA/CE) to the highest standards expected in medical device technology.

I2 - Innovations Leading to Economic Impact and Global Recognition for NI - After entering a strategic partnership with GE Healthcare in 2011, Intelesens was able to grow to approximately [redacted] employees by 2017 (**C2**). In 2014, following a series of regional and national heats, Intelesens was honoured with a "Best for Innovation" award by the British Private Equity and Venture Capital Association in recognition of the achievements of the management team with McLaughlin as CTO driving innovation (**C3**). Based on its rapidly growing commercial success, the company **was acquired by New York-based UltraLinq Healthcare for** [redacted] in 2017 (**C4**). At the time of the sale, the CEO of UltraLinq recognised the contribution of Ulster University citing: *"When you combine that level of engineering quality and skill with the **technology support that Intelesens has enjoyed from Ulster University** and a supportive development agency like Invest NI, Belfast becomes an obvious choice for continued corporate development."* (**C5**) **(R1-R5).**

Ulster's Engineering researchers, in partnership with Intelesens, further developed their innovative diagnostic sensor **(R1-R2)** and associated data science technology **(R3-R4)** as an entry to "The Qualcomm Tricorder XPRIZE Global Competition" (2015-2017). The USD10,000,000 global competition was designed to incentivise the development of innovative technologies capable of accurately diagnosing a set of 13 medical conditions independent of a healthcare professional or facility with the ability to continuously measure 5 vital signs, while delivering a positive consumer experience. Of the 300 official entries to the competition, the **Ulster/Intelesens led team finished in joint third position** having been shortlisted to a pool of 7 finalists (**C6**). The contribution to the competition has led to the early-stage formation of a **new start-up (Pulse-AI)** in AI based ECG analysis with Finlay, McLaughlin, Bond and Guldenring as Scientific Advisors (**C7).** This activity is being supported by the [redacted] of research income that has been secured in relation to the XPRIZE competition performance.

I3 - Adoption of ECG algorithms by Medical Device Regulators - Work conducted by Ulster's researchers has had direct impact on the process of regulation of new drugs in respect to their assessment for cardiac toxicity. Specifically, our algorithms **(R6)** have been adopted by the US Food and Drug Administration (FDA) to compute ECG biomarkers in FDA drug trials **(C8)**. The algorithm computes features such as the J-T peak and the QRS-T angle which are important for predicting mortality and morbidity and for detecting adverse side-effects in drug trials. According to the FDA, the Ulster algorithm is being used to predict "*the risk of drug-induced abnormal heart rhythms*." To date, the **FDA has used Ulster's algorithm** [redacted] to detect adverse cardiac side-effects ensuring patient safety and drug quality. For regulatory ethical purposes, the FDA cannot fully disclose the particulars of this impact on specific drug trials. Nevertheless, the information disclosed clearly shows that Ulster's research has had **impact by changing the practice of the US FDA** and that they have adopted our methodology for routine use. In addition, Ulster's ECG algorithm, as adopted by the FDA, has informed a draft standard and associated technical reports in 2018, namely IEC 80601-2-86 (medical electrical equipment). The FDA has included a description of Ulster's algorithm in these documents **(C8)**.

I4 – Informing the Health Technology Knowledge Base and Supporting Industry Innovation

The recognition of Ulster for undertaking world leading research in Connected Health has allowed for impactful outcomes via establishment of the NI Connected Health Innovation Centre (CHIC) in 2012 to support business-led collaborative projects. The funding model is competence centre based and CHIC was the first approved NI centre of its type and is the only centre focused on healthcare. During the reporting period CHIC has now grown to include a team of over 12 researchers who provide R&D support to approximately 40 partner companies both local and international. Engagement with Ulster through CHIC has led to benefits to companies across a range of healthcare technology sub-disciplines. Examples include:

- Work in collaboration with Randox Laboratories on a project that has demonstrated **a framework to reduce hospital admissions due to Acute Myocardial Infarction (AMI) by 36%**. This was achieved by combining in depth knowledge of point-of-care sensing systems with novel data science techniques to eliminate false positives in the diagnosis of AMI (**C9**). This has informed the approach to risk stratification of patients resulting more efficient use of resources within the healthcare system.
- Work in collaboration with CIGA Healthcare on the development of a platform for biomarker analysis using a mobile phone app that connects to an automated handheld lateral flow reader. This work has led to CIGA Healthcare developing its own in-house testing capabilities (**C10)**.

In the case of the latter, the partnership has now been extended with both Ulster (McLaughlin) and CIGA Healthcare representatives joining the UK Rapid Test Consortium (UK-RTC) in July 2020. This consortium has overseen the **development and introduction of the Government's COVID-19 rapid testing strategy**. Ulster input, in the form of expertise in development of point-of-care sensors, validation of tests and lateral flow technology has been integral to these developments. (**C10**)

5. Sources to corroborate the impact

[**C1**] Press article relating to Intelesens device FDA approval: https://www.mobihealthnews.com/47424/fda-clears-intelesenss-zensor-a-wearable-vitals-monitor

[**C2**] Operations Director – Intelesens/Ultralinq, to provide account of impact of Ulster research in development of monitoring solution and subsequent impact on company growth/revenue streams.

[**C3**] Summer 2014 issue of the "The British Private Equity & Venture Capital Association (**BVCA**)" Journal listing Intelesens as winner of "Best for Innovation" award https://www.bvca.co.uk/Portals/0/library/documents/Journals/BVCA%20Journal%20Summer%202014.pdf

[**C4**] Press article in BBC announcing UltraLinq's acquisition of Intelesens in 2017: https://www.bbc.com/news/uk-northern-ireland-40817009

[**C5**] Press article relating to comments by the COO of UltraLinq, on recognising role of Ulster University in decision to acquire Intelesens Ltd. https://www.belfasttelegraph.co.uk/business/northern-ireland/medical-tech-firm-intelesens-sets-sights-on-growth-after-us-buyout-35998405.html

[**C6**] Press article acknowledging Ulster team's 3rd place in Tricorder XPRIZE competition. https://www.siliconrepublic.com/machines/ulster-university-tricorder-prize

[**C7**] CEO and Founder of PulseAI (https://www.pulse-ai.co.uk/), Recent University related start-up, to provide details of Ulster support and collaboration in start-up.

[**C8**] Official letter from the US FDA, outlining the collaboration between Ulster and the FDA.

[**C9**] Navarro-Paredes, C., Kurth, M.J., Lamont, J.V., Menown, I.B., Ruddock, M.W., Fitzgerald, S.P. and McLaughlin, J., 2018. Diagnostic Performance of a Combination Biomarker Algorithm for Rule-Out of Acute Myocardial Infarction at Time of Presentation to the Emergency Department, Using Heart-Type Fatty Acid-Binding Protein and High-Sensitivity Troponin T tests. *Journal of Clinical and Experimental Cardiology*, *9*(8), pp.1-9.

[**C10**] CEO/Founder of CIGA Heathcare Ltd and UK-RTC consortium member, to provide account of Ulster's impact in the development of Lateral Flow technology for Ciga healthcare and Ulster's input to the UK-RTC.