Institution: Ulster University

Unit of Assessment: Computer Science and Informatics (11)

Title of case study: ICS5 Computational Cardiology Impacting on Medical Devices, Safer Drug Trials, Medical Training and Technical Standards

Period when the underpinning research was undertaken: 2011 - 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:
Dr Raymond Bond	Reader in Data Analytics	2010 - present
Prof. Chris Nugent	Professor of Biomedical Engineering	1998 - present
Dr Mark Donnelly	Senior Lecturer in Computer Science	2009 - present
Prof. Dewar Finlay	Professor of Electronic Systems	2001 - present
Dr Daniel Guldenring	Lecturer in Electronic Engineering	2013 - 2018

Period when the claimed impact occurred: August 2013 - December 2020

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

1. Summary of the impact

Ulster research on electrocardiography (ECG), which is used to detect cardiovascular disease (leading cause of death worldwide) resulted in the following impacts:

I1 – an ECG algorithm that has been used by the FDA [redacted] to monitor the risk of drug-induced abnormal heart rhythms,

I2 – an interactive ECG recording simulator that was integrated into a medical textbook selling [redacted], 2014-2019)

I3/I4 – research on automated cardiac defibrillation resulted in the [redacted] and the approval of a new AED which has been used to save lives. Informing working standards/reports (IEC 80601-2-86, IEEE P7003).

2. Underpinning research

The research is described in 4 strands associated with research **[R1-R6],** linked to impacts **[I1-I4]** and evidenced in **[C1-C10].**

R1 – ECG algorithm for computing biomarkers
The electrocardiogram (ECG) is a diagnostic tool for detecting cardiovascular disease (the most common cause of death worldwide). Ulster developed an algorithm in 2012 to transform the ECG into a 3D model to compute spatial ECG features (QRS-T angle) that are important for predicting mortality/morbidity. This work was in collaboration with the U.S. Food and Drug Administration (FDA) but was led by Ulster academics (Guldenring, Finlay, Bond). In collaboration with the FDA Ulster demonstrated that Ulster's algorithm was more accurate than the state-of-the-art **[R1]**. This work was selected as an invited talk at the International Society for Computerized Electrocardiology. This algorithm has been adopted by the FDA and is used for computing biomarkers in drug trials. The FDA described and cited Ulster's algorithm in a draft

standard document and associated reports (IEC 80601-2-86).

R2-R4 – ECG recording errors and a computer simulator
Many professionals are not aware of the effects of ECG recording errors and that electrode misplacement is a common error. Using ECG signals recorded from the entire torso, Bond et al. developed a simulator **[R2]** to allow users to see the effects of recording errors on signals and diagnoses **[R3]**. A paper describing the simulator was published in 2011 (Journal of Electrocardiography) but was also described alongside a detailed use case experiment in the Methods of Information in Medicine Journal **[R2]**. Research funded by the Higher Education Academy (Bond, Nugent, Finlay) demonstrated that the simulator improved the training of physiologists **[C3]**. This simulator was then integrated into a medical textbook (12th ed., Marriot's Practical Electrocardiology).

Ulster (Bond et al., 2012) used the simulator to research the effects of electrode misplacement **[R3]** and showed that there can be a 24% chance of a misdiagnosis. This research was identified by a company (eNNOVEA Medical) to progress the validation of their product (Cardio-Quick Patch) for reducing electrode misplacement errors. Ulster (Bond, Finlay) worked with this company to validate this product showing that it reduces electrode misplacement. This work also won best poster award in 2016 at the International Society for Computerized Electrocardiology.

R5 – User interface validation of a cardiac defibrillator
HeartSine technologies (1997 Ulster spinout company) and Ulster carried out a study in 2016 to validate the efficacy of a novel automated defibrillator **[R5]**. Our study found that embedded computer programs in AEDs can provide automated audio-visual feedback that can assist users and improve their chest compression rates whilst maintaining a high chest compression fraction which is advocated by resuscitation guidelines. The work was published in IEEE Human Machine Systems Journal **[R5]**.

R6 – Automation bias in ECG interpretation
Ulster (Bond, Finlay) conducted studies in 2017/2018 to measure automation bias amongst doctors (when users naïvely over-trust algorithms). This was presented as an invited talk at the International Society for Computerised Electrocardiology and published in the International Journal of Medical Informatics and the Journal of Electrocardiology **[R6]**. Bond et al demonstrated that the doctor's accuracy in reading ECGs can drop from 86.38% to 27.43% when the algorithm provides unreliable advice.

3. References to the research

[R1] Guldenring D, Finlay DD, Bond RR, Kennedy A, McLaughlin J, Galeotti L, Strauss DG. The derivation of the spatial QRS-T angle and the spatial ventricular gradient using the Mason–Likar 12-lead electrocardiogram. *Journal of Electrocardiology*. 2015 Nov 1;48(6):1045-52, DOI: 10.1016/j.jelectrocard.2015.08.009

[R2] Bond R, Finlay D, Guldenring D, Breen C. Data driven computer simulation to analyse an ECG limb lead system used in connected health environments. *Methods of information in medicine*. 2016 Apr 20;55(3):258-65. DOI: 10.3414/ME15-01-0120

[R3] Bond RR, Finlay DD, Nugent CD, Breen C, Guldenring D, Daly MJ. The effects of electrode misplacement on clinicians' interpretation of the standard 12-lead electrocardiogram. *European Journal of Internal Medicine*. 2012 Oct 1;23(7):610-5, DOI: 10.1016/j.ejim.2012.03.011

[R4] Bond RR, Finlay DD, McLaughlin J, Guldenring D, Cairns A, Kennedy A, Deans R, Waldo AL, Peace A. Human factors analysis of the CardioQuick Patch®: A novel engineering solution to the problem of electrode misplacement during 12-lead electrocardiogram acquisition. *Journal of Electrocardiology*. 2016 Nov 1;49(6):911-8. DOI: 10.1016/j.jelectrocard.2016.08.009

[R5] Torney, H, O'Hare, P, Davis, L, Delafont, B, Bond, R, McReynolds, H, McLister, A, McCartney, B, Di Maio, R and McEneaney, D, 2016. A usability study of a critical man–machine interface: Can layperson responders perform optimal compression rates when using a public access defibrillator with automated real-time feedback during cardiopulmonary resuscitation? *IEEE Transactions on Human-Machine Systems*, 46(5), 749-754, DOI: 10.1109/THMS.2016.2561267

[R6] Bond RR, Novotny T, Andrsova I, Koc L, Sisakova M, Finlay D, Guldenring D, McLaughlin J, Peace A, McGilligan V, Leslie SJ. Automation bias in medicine: The influence of automated diagnoses on interpreter accuracy and uncertainty when reading electrocardiograms. *Journal of Electrocardiology*. 2018 Aug 10, DOI: https://doi.org/10.1016/j.jelectrocard.2018.08.007

Indicators of research quality

The above journal articles have been subject to blind peer review practice by internationally based editorial boards. **[R4]** was associated with research presented at the 41st Annual Conference of the International Society for Computerised Electrocardiography where it won best poster presentation prize (awarded to Bond in 2016). **[R5]** relates to AED data analysis research involving Bond and Torney which later received the 2019 Paul Dudley White International Scholar award at the Resuscitation Science Symposium in 2019 to recognise Torney et al.'s research as the highest ranked research that was submitted from the UK.
The following grants supported or followed the research presented in R1-R6:

- Awarded to: Nugent (PI), Finlay. Grant title: Cross-border Centre for Intelligent Point-of-Care Sensors. Sponsor: NI-Department of Employment and Learning. Period: 2008-2011. Value: GBP1,991,283

- Awarded to: Bond (PI), Grant title: Eye Tracking Technology during Clinical 12-lead ECG Interpretation: Where do Expert Cardiologists look? Sponsor: Royal Irish Academy. Period: 2013. Value: GBP1,760

- Awarded to: Finlay (PI), Bond, Nugent, Breen and Moore. Grant title: Improving Clinical Practice with the Introduction of Modern Teaching Tools for an Old Science. Sponsor: Higher Education Academy. Period: 2011-2012. Value: GBP2,500

- Awarded to: Bjourson (PI), Coates, Maguire, Wong-Lin, Prasad, Bond, Mc Clean, Mc Gilligan, Coyle. Grant title: Centre for Personalised Medicine: Clinical Decision Making and Patient Safety (CPM). Sponsor: EU INTERREG VA. Period: 2017-2022. Value: Overall Grant £7,343,563.45 - Ulster apportionment GBP3,642,928. *Note: This is the most recent grant that supported the research on automation bias.* The work was carried out in the cardiovascular research cluster which is one of a number of clusters funded by this large grant.

4. Details of the impact

I1 – ECG algorithm for computing biomarkers
This impact directly follows from **[R1]**. The algorithm has now been fully adopted since our final 2015 publication and is being used to compute ECG biomarkers in drug trials **[C1]**. The algorithm is being used to compute features such as the J-T peak and the QRS-T angle which are regarded as important for predicting mortality/morbidity and adverse side-effects in drug trials. According to the FDA, Ulster's 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. While FDA regulatory constraints place an embargo upon the surrounding specific drug trials, we are able to clearly demonstrate that Ulster's research has impacted upon the practice of a large regulatory organization (FDA) which has adopted Ulster's algorithm for routine use.

I2 – Medical training
This impact directly followed **[R2]** and **[R3]**. Having developed a simulator that allows users to see the effects of ECG recording errors, it was shown to be a useful educational tool **[C3]**, and was hence integrated into a medical textbook (12th edition Marriott's Practical Electrocardiography, first established in 1954) and [redacted] **[C2]** resulting in gross revenue of [redacted] (2014 to 2019). Also, one educator created an online video using the simulator receiving approximately *7,828* views since August 2018 **[C4]**.

I3 – Validated medical devices
This impact directly follows **[R2-R5]**. Ulster's work in **[R5]** with HeartSine involved validating the user performance of a novel defibrillator inbuilt with automated audio-visual feedback. From this work, HeartSine went on to gain regulatory approval for a first-of-kind medical device (AED) that uses advanced feedback technology to guide users to perform CPR. This device is now available on the market, and has been approved [redacted]. According to HeartSine, sales of these devices have [redacted] since the study involving Ulster. Feedback from a paramedic who recently used the device to save a life said that: *"I have been a Paramedic for 30 years.… I recommend this AED daily to anyone that asks"* **[C7]**.

Ulster's research in **[R2]** and **[R3]** on the effects of ECG electrode misplacement errors on ECG signals was highlighted by the U.S. Department of Health **[C5]** and identified by a medical company (eNNOVEA Medical) **[C6]**. Ulster collaborated with eNNOVEA Medical and helped demonstrate that its device (CardioQuick Patch) reduces electrode placement errors **[R4]** as well as improving ECG reproducibility (since patients often require multiple recordings). The solution (CardioQuick Patch) is available on the market: Quote from [redacted] at eNNOVEA Medical: *"it was this time last year that we kicked off the … CardioQuick Patch®: … study. Since its presentation as a poster at ISCE and publication in the Journal of Electrocardiology we have engaged over 15 new hospitals including prestigious institutions such as UPMC and University Hospitals Cleveland Medical Centre as well as private industry such as Eli Lilly Pharmaceuticals. In addition, we have entered into negotiations with a major ECG instrument manufacturer to have us OEM the CardioQuick Patch for sale by their field force. Much of this would not have happened so rapidly if it were not for the research, manuscript development and presentation you and the university were part of. In the 30 years of device development and new product launches, I can say that working with you… was the most fruitful and delightful experience I have had. …."*

I4 – Informing standards
This directly follows **[R1]** and **[R6]**. Ulster's ECG algorithm as adopted by the FDA has informed a draft standard and associated technical reports in 2018 **[C1]**, namely IEC 80601-2-86 (medical electrical equipment). The FDA has included a description of Ulster's algorithm in these documents **[C1]**. Ulster's work on [**R6**] regarding automation bias of ECG algorithms has been cited and used to inform the working IEEE standard (P7003) on algorithmic bias in 2018 **[C8]**. Our work on ECG data structures informed the development of PDF-ECG **[C9, C10]** in collaboration with companies such as AMPS, Phillips Medical, Mortara Instrument and GE Healthcare. PDF-ECG is a novel electronic solution that preserves the raw data as well as presenting an image of the ECG. PDF-ECG was used as a proof of concept at Fondazione Poliambulanza Hospital (Brescia, Italy).

5. Sources to corroborate the impact

C1 – Statement of fact in the form of an official letter from the [redacted], US FDA.

C2 – Statement of fact in the form of an official letter from the book publisher, [redacted], Wolters Kluwer. The letter also confirms that the publisher has used the simulator to create educational videos to illustrate the effects of electrode misplacement.

C3 – Report evidencing use of the simulator within Ulster University along with quantified evidence of its impact on student learning (note: this is a 2012 document and is used to demonstrate 2012 impact but evidences the initiation of the simulator which impacted on a textbook).

C4 – Medical training video using Ulster's simulator created by an instructor of Basic Life Support and Advanced by American Heart Association.

C5 – US Department of Health's Patient Safety Network logging the research on ECG electrode misplacement errors.

C6 – Electronic communication from [redacted] at eNNOVEA Medical.

C7 – Statement of fact in the form of a letter from the [redacted] at HeartSine Technologies Ltd (now acquired by Stryker).

C8 – Official Letter from the [redacted] IEEE P7003 standard Algorithmic Bias and Considerations working group.

C9 – Publication of PDF-ECG in clinical practice: A model for long-term preservation of digital 12-lead ECG data.

C10 – Official letter from the [redacted], an international medical company providing ECG analysis software tools.