Institution: Middlesex University		
Unit of Assessment: 11		
Title of case study: Electrical Impedance Tomography		
Period when the underpinning research was undertaken: 2014 and ongoing		
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:**
Prof Richard Bayford	Professor of Biophysics and Engineering	1986 to date
Dr Andrew Tizzard	Associate Professor in Bioengineering	1986 to date
Dr Andy Bardill	Associate Professor in Product Design	1994 to date
Period when the claimed impact occurred: 2014 to date		
Is this case study continued from a case study submitted in 2014? Y		

1. Summary of the impact (indicative maximum 100 words)

Middlesex University has pioneered the use of Electrical Impedance Tomography (EIT)

Key impacts:

- Provision of imaging algorithms and clinical analysis impacting on clinical software (4.1).
- Creation of the largest clinical data store for EIT clinical data in the world (> 50TBytes) for use by clinicians and industrial/academic researchers (4.2).
- New wearable hardware for application on patents impacting on clinical usability of EIT (4.3).
- Used successfully to monitor preterm neonates in the largest clinical study undertaken to date and identifying key parameters for the clinical management of neonates with respiratory conditions impacting on clinical practices (4.4).

2. Underpinning research (indicative maximum 500 words)

What is EIT?: EIT provides impedance changes arising from injection of small electrical currents into an electrode array placed on the subject and the measurement of the subsequent voltages. It can be used to image organ function in real time (100 images a second). Compared with existing technology it is highly portable, inexpensive and lends itself readily to remote imaging in order to save lives. The impact described here evolved from a series of specific developments employing Electrical Impedance Tomography. EIT requires the solution to an inverse problem to create the image of organ function in real time. This requires an accurate geometric finite element (FE) model, known as the forward model.

*First 2D images **(1996 –2003)***

Prior to REF2014 Prof Bayford pioneered software resulting in successful generation of the first 2D images of impedance change inside the human head using EIT. This led to a range of applications, including neuronal activity, stroke, visual evoked response and localising epileptic activity [1].

*Automatically generating subject-specific FE models **(2003 –2007)***

The 2D image work led to development of a method of automatically generating subject-specific FE models through elastic deformation from electrode position data for brain function [2]. In collaboration with Great Ormond Street Hospital, this work subsequently resulted in the application of EIT for monitoring lung development in pre-term neonates [3].

*Further algorithm development **(2008 to present)***

Prof Bayford developed a wavelet algebraic multigrid and estimated boundary form [4]. With an international team of colleagues, he instigated and developed a Graz consensus Reconstruction algorithm for EIT (GREIT). This could then be used as a benchmark for evaluating the effectiveness of future development of EIT algorithms for enhanced monitoring of lung function [5].

This was an award-winning article in *Physiological Measurement* with significant contribution by the research group at Middlesex comprising accurate forward models of adult male and female thorax, but more specifically of an infant's thorax. These significant developments of EIT led to four significant grants that ultimately allowed this work to be applied in a clinical setting. The first from EPSRC in 2008, resulted in the contribution to the Electrical Impedance and Diffuse Optical Reconstruction Software project (EIDORS). This is a freely available website that provides software algorithms for forward and inverse modelling for EIT and Diffusion based Optical Tomography in medical and industrial settings. This site is also used worldwide to share data and promote collaboration between groups working in this area (over 2000 downloads and cited on over 100 published papers).

Clinical translation and hardware development ***(2016 onwards)***

The research described above allowed the team to develop algorithms and hardware for image reconstruction, parameter measurement and boundary form generation [6]. This culminated in the first large scale study monitoring the lung function of 200 neonates (preterm, high risk) for 72 hours each. As a result of this work the team at Middlesex University led a successful EU funding application (Horizon 2020) for €5M in 2016 for a project entitled "Continuous Regional Analysis Device for Neonate Lung (CRADL)" leading to a clinical system for use in neonatal intensive care units. Dr Bardill joined the project in 2016 to progress hardware development, create a new wearable device and continues to be part of the team with Prof Bayford and Dr Tizzard going forward. The work continues with follow-on funding (£1.8M) in early 2020 from EPSRC – "Preterm Neonate/neonatal Embedded Universal Microelectronic wearable, Acquisition for Cardiorespiratory Intensive Therapy" (PNEUMACRIT, EP/T001240). This project further develops clinical hardware for bedside monitoring of lung gestation of pre-term neonates. The research continues to flourish and diversify with the recent award of £700K from UKRI in 2020 to repurpose the hardware and techniques for monitoring Covid19 pneumonia in adult ITUs: COVID Regional Lung Electrical Impedance Tomography (CoRLEIT, EP/V044036).

3. References to the research (indicative maximum of six references)

[1] Bayford RH, Gibson A, Tizzard A, Tidswell AT and Holder DS, (2001) Solving the forward problem for the human head using IDEAS (Integrated Design Engineering Analysis Software) a finite element modelling tool. Physiological Measurements (Institute of Physics), Vol. 22 No 1. pages 55-63. 0967-3334/01/010055.

[2] Tizzard A and Bayford RH. (2007) Improving the Finite Element Forward Model of the Human Head by Warping using Elastic Deformation. Physiol. Meas. *Meas.* 28 S163-S182 doi:10.1088/0967-3334/28/7/S13.

[3] Joo Moy Khor, Andrew Tizzard, Andreas Demosthenous and Richard Bayford. (2014) Wearable sensors for patient-specific boundary shape estimation to improve the forward model for electrical impedance tomography (EIT) of neonatal lung function doi:10.1088/0967-3334/35/6/1149.

[4] Bayford RH, Kantartzis P, Tizzard A, Yerworth R, Liatsis P and Demosthenous A. (2008) Development of a neonate lung reconstruction algorithm using a wavelet AMG and estimated boundary form *Physiol. Meas.* 29 S125-S138 doi: 10.1088/0967-3334/29/6/S11.

[5] A Adler, JH Arnold, R Bayford, A Borsic, B Brown, P Dixon, TJC Faes, I Frerichs, H Gagnon, Y Gärber, B Grychtol, G Hahn, WRB Lionheart, A Malik, RP Patterson, J Stocks, A Tizzard, N Weiler, GK Wolf. (2009) "GREIT: a unified approach to 2D linear EIT reconstruction of lung images", Physiol Meas, 30:S35-S55,. (**Awarded IPEM's Martin Black prices for best paper**)

[6] Sven Nordebo, Mariana Dalarsson, Davood Khodadad, Beat M□uller, Andreas Waldman, Tobias Becher, Inez Frerichs, Louiza Sophocleous, Daniel Sjoberg ,Nima Seifnaraghi , Richard Bayford. (2018) A parametric model for the changes in the complex valued conductivity of a lung during tidal breathing in Journal of Physics D Applied PhysicsDOI: 10.1088/1361-6463/aabc04.

4. Details of the impact (indicative maximum 750 words)

Software and data impact:

(4.1) The GREIT algorithm with new forward models is being adopted by a manufacturer of EIT systems (Swisstom/SenTec)[1,] which will represent a significant improvement for commercial medical EIT systems in product development for EIT-based monitoring of neonate patient respiration and regional air content within patient's lungs at the bedside. (2018) (5.1) It has also been adopted by Emergex to extend EIT for other applications including cancer detection. We have also provided new models for these applications (See 4.2)

The models generated have also been used extensively by other groups internationally that focus on the development of imaging solutions. For example, Bayford and Tizzard, working with Dartmouth College and Florida State University in the USA, have been developing EIT and optical tomography imaging of both adult and neonate human heads and extensive use is being made of the public domain tool (eidors3d.sourceforge.net/) in this work.

Further work on the automatic generation of subject-specific forward models, namely the warping algorithm (2007), and with Prof. Janet Stocks, Great Ormond St. Hospital (2007 – 2009) which formed the basis of extending the process in the current REF period to imaging lung function specifically in neonates in collaboration with Prof. Andreas Demosthenous, Dept. Electronic and Electrical Engineering, UCL. This initial impact led to the CRADL project in 2016 (5.2).

(4.2) The creation of the largest data store for EIT clinical data in the world at Middlesex University (over 50TBytes). This resource is in use for ongoing clinical studies (5.4, 5.5 and 5.6). This resource is also being used by SenTec to improve their user interface and test their system.
The work improved breast tumour imaging in collaboration with Dr Andrea Borsic and Prof. Ryan Halter, Dartmouth College, NHR (2010), and is based on using elastic deformation to warp standard or idealised geometry – all of which provided extensions of the public domain toolset.

Hardware impact:

(4.3) In addition to its clinical use, the group obtained a patent that describes a flexible wearable device to extract boundary information for the warping algorithm. The system dynamically generates and modifies subject specific forward models in real time. This work addresses the urgent need for objective, non-invasive measures of lung maturity and development, oxygen requirements and lung function, suitable for use in small, unsedated infants, to define the nature and severity. This led to the following:
We have signed an NDA with Swisstom (now Sentec) to develop the wearable device [(H2020 cradlproject.org)(5.3,5.3)] and have a patent in place (Filed in 2015, WO2015025113A1, European patent number 3035846 2020). A new wearable device was developed with PEL during CRADL and are submitting a patent before arranging a licensing agreement.
The group is also working with Emergex to extend the application of EIT for the detection of cancer. A joint patent (WO/2010/052503, Detection of Cancer) is in place with this company. This work is also subject to an NDA, which limits the information we are allowed to disclose in this document. However, the system is presently being developed to locate new COVID vaccines in animal models in the USA.

Clinical Practice impact:

(4.4) Our models have been used successfully to monitor preterm neonates in two clinical studies using the CRADL system with the University of Oulu and Oulu University Hospital, Finland, and the Department of Neonatology, Emma Children's Hospital, Amsterdam. The group's electrical impedance tomography system has been used to detect ventilation distribution, end-expiratory lung impedance (EELZ) and tidal impedance variation during monitoring of preterm neonates requiring invasive ventilation and repeated surfactant treatment. This study demonstrated a significant effect of surfactant treatment on lung function (5.4, 5.6). This has enabled the use of EIT in new studies for adopting into larger clinical use.

Creation of the largest data store for EIT clinical data (> 50TBytes). This is an available resource for ongoing clinical studies (5.9) including Dartmouth and Florida use of EIDORS. It has been used successfully to monitor preterm neonates in four large-scale clinical studies (5.3). The following organisations have benefited from these resources:

- Consultant Paediatric Cardiologists and clinical researchers in the PEDEGO Research Unit, University of Oulu and Oulu University Hospital, Finland (2015 - on-going) (5.4)
- The Department of Neonatology, Emma Children's Hospital Amsterdam undertook the clinical study of CRADL (5.6)
- Dr Karaoli Nicosia General Hospital (NGH), Cyprus also undertook the clinical study.

Consultant Neonatologists and clinical researchers at the Royal Hospital for Children, Glasgow, Scotland are working with the group on a new clinical study related to the PNEUMACRIT[5] project which has been enabled through CRADL (5.5).

More clinical groups are using EIT as a result of the work at Middlesex and are identifying outcomes for imaging neonate lung function. The work has led to the recognition that EIT can address the urgent need to improve ventilation strategies in children. It is been clinically used to monitor lung function in neonates and adult patients (see link to Draeger/Sentec below) using some of the developments created for neonate imaging (5.8).

Industry impact:

(4.5) We are also working with PEL (Printed Electronics Limited)[7] a UK based technology company providing advanced research and development, concept development and production capability for printed electronics and related functional material structures and systems, to develop print on flexible printed circuits for the EIT neonate system. They are members of the EU Graphene Flagship. PEL has worked with us on the CRADL, PNEUMACRIT and new CoRLEIT projects. PEL 3D printing are working with their commercial abilities to augment those in the Middlesex teams and concurrently we are enabling the company to get new markets and new business opportunities in the future (5.7)

Cost saving:

(4.6) EIT estimated cost saving of 928 to 10,705 euros per patient in the Dutch setting or 1,124 to 8,496 euros in the German setting. (5.10)

5. Sources to corroborate the impact (indicative maximum of 10 references)

1. https://www.sentec.com/products/eit/lms/lms-n/ and https://www.sentec.com/products/eit/lm-disposables/ (web links to SenTec showing the products produced from the Cradl project lead by Middlesex University.
2. https://cordis.europa.eu/project/id/668259 EU project link for CRADL showing all the partners in the project showing that EIT is impacting on many organisation who had not previously

been involved with it use. This includes Cyprus who had not previously been using EIT for clinical practice, hence increasing the user base of this technology.

3. Web site (cradlproject.org) showing the device used in Hospitals (see video on website). Middlesex led the development of the CRADL project and coordinated it, along with key contributions in hardware (new belt designs) and software. This shows its impact on all areas, software, hardware and clinical practice. The industry partner was able to disseminate the use of EIT to a wider clinical group at conferences and major trade shows (Full list in evidence appendix)
4. Consultants in the Pediatric Cardiologyand Intensive Carein the PEDEGO Research Unit, University of Oulu and Oulu University Hospital were invited as associate partners in the CRADL project which enabled them to adopt EIT in clinical practice. They are using EIT in Finland to develop new clinical management methods (See Oulu support letter)
5. Consultant Neonatologists and clinical researchers at the Royal Hospital for Children, Glasgow are working with us on PNEUMACRIT to extend the technology and impact on clinical practices for a multi sensor system on neonates along with PEL (See Glasgow support Letter).
6. Consultants from the Department of Neonatology, Emma Children's Hospital, Amsterdam have used the CRADL system in clinical studies (See Amsterdam support letter) They are using EIT to identify apnoea in infants among other conditions.
7. PEL (Printed Electronics Limited) (printedelectronics.com), helped in the development of the EIT belt and is involved in adapting it for COVID-19 use. (See PEL support letter) PEL is a UK based technology company providing advanced research and development, concept development and production capability for printed electronics and related functional material structures and systems. They are members of the EU Graphene Flagship. We developed with them flexible circuitry in the form of belts made from a soft fabric material that provide unintrusive patient interfaces for impedance spectroscopy in Covid patients and neonates. They contribute expertise and support on print on flexible printed circuits and access to their facilities (See support letter, and NDA would be needed with external partners).
8. https://www.3sat.de/wissen/nano/201016-sendung-nano-102.html (Interview for German TV Nano Science program on CRADL (15mins into programme). Impacting on the visibility of EIT for clinicians, patients and general public. (web pages in support letter).
9. The CRADL data is available on request subject to a number of ethical and GDPR requirements. It includes images of infants. The data is being used in studies to improve clinical management of patients. We can provide access to the data if the REF panel request it subject to the required conditions.
10. CRADL implementation in NICU's can lead to substantial medical cost savings especially in hospitalization and complication cost, while leading to improved health outcomes. The health economic analysis predicts the technology to be cost-effective in terms of ICER per deaths avoided and ICER per BPD cases avoided in the German and Dutch setting. (Cost benefit analyses undertaken by Panaxea, (isabelle.nefkens@panaxea.eu)(report available on request).