Institution: Middlesex University

Unit of Assessment: 3 – Allied Health Professions, Dentistry, Nursing and Pharmacy

Title of case study: Biomedical Imaging

1. Summary of the impact

This case study describes how research in bio-imaging using Electrical Impedance Tomography (EIT) at Middlesex University stimulates collaborative development in EIT applications particularly in imaging brain function, lung function and tumour detection, and the development of Optical Tomography of brain function in neonates. The researchers have contributed a range of public domain, open source resources to the international industrial and research communities such as novel reconstruction algorithms, geometric models for generating accurate finite element and boundary element forward models and methods to generate subject-specific forward models in the belief that collaborative use of such resources is the most effective route to impact.

2. Underpinning research

The development of bio-imaging, commonly known as Electrical Impedance Tomography (EIT), is a low-cost, portable, non-invasive technique that does not use ionising radiation and allows the subject to move during the capture of image data. It is therefore ideal for clinical applications and the group has been developing this method for over 20 years. Measured conductivity can be presented as a 2D or 3D image for clinical evaluation and diagnosis of a range of conditions associated with gastric emptying, breast tumour localisation, lung function and brain function. As EIT is an inverse problem, the group has mainly focussed its work on demonstrating that a valid and viable forward model is required for successful implementation. Additional significant research findings have centred on the development of more accurate forward models, their associated algorithms and potential clinical application.

In collaboration with the Medical Physics group at University College, a significant outcome of this work was the generation of the first successful 2D images of impedance change inside the human head (Bayford et al, 1996). The main motivation of the work was to develop EIT for localising epileptic foci for possible surgical intervention. Since 1999, Dr Andrew Tizzard has been working on improving the forward models for the human head, one outcome being the generation of the underlying geometry and finite element (FE) models of adult and neonate heads enabling the progress of the algorithm development to imaging in 3D and, separately, the development of a method of automatically generating subject-specific FE models through elastic deformation from electrode position data (Tizzard and Bayford, 2007).

This led to the key finding that boundary form plays a major factor in reducing artefacts in the reconstructed image. The research produced the first image of epileptic focus in a human using EIT (Bagshaw et al, 2003). Bayford and Tizzard have developed this research further for monitoring neonate lung function using a wavelet AMG and estimated boundary form (Bayford et al. 2008). They also contributed significantly to an international collaboration for a consensus algorithm for EIT of lung function (Adler et al. 2009) and are extending the research to image rectal cancer. This key research on boundary form has provided the basis for improving this imaging technique.

An extensive international collaboration of a number of research groups, instigated by Bayford and colleagues, resulted in the work published by Adler et al (2009) which features a significant contribution by Tizzard for the accurate forward model of the adult thorax. It describes a consensus algorithm intended to be a benchmark for comparing future developments of EIT algorithms for monitoring lung function. The framework for the algorithm consists of: 1) detailed finite element models of a representative adult and neonatal thorax; 2) consensus on the performance figures of merit for EIT image reconstruction; and 3) a systematic approach to optimise a linear reconstruction matrix to desired performance measures.

Paper 6 (Adler et al, 2012) was also influenced by the work at Middlesex and resulted in the software contributed to the EIDORS project (eidors3d.sourceforge.net/). This has had over 1000 downloads and is now used collaboratively by clinicians and researchers in industry and research hospitals globally.

3. References to the research

The research was based on major, competitively funded peer reviewed research, led to two patents, and was published in peer reviewed journals of high repute as detailed below:

(1) **Bayford R.H.**, Boone K.G., Hanquan, Y. and Holder, D.S. (1996) Improvement of the positional accuracy of EIT images of the head using a Lagrange multiplier reconstruction algorithm with diametric excitation. *Physiol. Meas., 17(4),* A49-A57.

(2) **Tizzard A** and **Bayford RH**, (2007) Validations of Finite Element mesh warping for improving the forward model in EIT of brain function. In Hermann Scharfetter, Robert Merva (Eds.), ICEBI 2007, IFMBE Proceedings Volume 17, 368-371, Springer-Verlag Berlin Heidelberg.

(3) Bagshaw A.P., Liston A.D., **Bayford R.H., Tizzard A.**, Gibson A.P., Tidswell T., Sparkes M.K., Dehghani H. and Holder D.S. (2003) Validation of reconstruction algorithms for Electrical Impedance Tomography of human brain function. *Neuroimage, 20*, 752-764.

(4) **Bayford R.H.**, 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

(5) Adler A., Arnold J.H., **Bayford R**., Borsic A., Brown B., Dixon P., Faes T.J.C., Frerichs I., Gagnon H., Gärber Y., Grychtol B., Hahn G., Lionheart W.R.B., Malik A., Patterson R.P., Stocks J., **Tizzard A.**, Weiler N., Wolf G.K. (2009) GREIT: a unified approach to 2D linear EIT reconstruction of lung images. *Physiol. Meas., 30*, S35-S55. (Authors in alphabetic order) (Awarded IPEM's Martin Black prices for best paper)

(6) Adler A., Amato M.B., Arnold J.H., **Bayford R**., Bodenstein M., Böhm S.H., Brown B.H., Frerichs I., Stenqvist O., Weiler N., Wolf G.K. (2012) Whither lung EIT: where are we, where do we want to go and what do we need to get there? *Physiol Meas., 33(5)*, 679-94.
(IoP featured article) (Authors in alphabetic order)

Grants:

2009 EPSRC **EP/G061572/1** **New imaging methods for the detection of cancer biomarkers (£800K)** Total grant for all partners £1.7M

2007 EPSRC EP/E031633/1, A Novel Analogue Bio-impedance system-on-a-chip for monitoring of neonate lung function (£182466) Total for all partners 600K

Patents:
(WO/2010/052503) Detection of Cancer

(61/867,904 : US) "A flexible wearable device for the acquisition of data for EIT of lung function"

4. Details of the impact

Work by Bayford and Tizzard on the development of algorithms and the generation of geometrical finite element forward models, applied to imaging impedance changes inside the human brain, has led to impact in three areas. Firstly, the availability of the software has led to its adoption in commercial software. Secondly, work on neonate lung function monitoring has generated a patent. Thirdly, the software has been used by both industrial and academic research groups for the provision of further imaging solutions such as in improving breast tumour images. Some of this work is commercially confidential.

(i) The algorithm is in the process of undergoing adoption by commercial companies involved in product development research of EIT systems and has led to a significant improvement to the only existing commercial medical EIT system originally developed by Viasys. (now Carefusion). Dräger, a leading international company in the fields of medical and safety technology (http://campaigns.draeger.com/pulmovista500/en/) has also adopted the EIDORS software (Sources 1, 2, 6 and 7).

(ii) Work on neonate lung function monitoring by Middlesex and its collaborators at UCL and City University has led to a patent being filed that describes a flexible wearable device to extract boundary information for the warping algorithm to dynamically generate and modify 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 of lung dysfunction. We have signed an NDA with Swisstom to develop the wearable device [note: **this is commercially confidential information**] and have a provisional patent in place (61/867,904: US; Source 3).

Use of the research outcomes for imaging neonate lung function will significantly reduce the cost of patient care and mortality by allowing systematic monitoring of child lung function for time-critical intervention. There is an urgent need to improve ventilation strategies in children with acute lung injury (ALI), which has a high mortality (22%) compared with the overall mortality of paediatric intensive care unit patients. Disorders of lung growth, maturation and control of breathing are among the most important problems faced by the neonatologist. Although it is not yet used clinically to monitor lung function in neonates, EIT is being used for adult patients (see link to Dräger above) using some of the developments created for neonate imaging.

(iii) The models generated have also been used extensively internationally by other groups focused on the development of imaging solutions. For example, clinicians at Dartmouth College and Florida University in the USA are developing EIT and optical tomography imaging of both adult and neonate human heads, making extensive use of our algorithms downloaded from EIDORS (Source 7, eidors3d.sourceforge.net/). Further work on the automatic generation of subject-specific forward models, namely the warping algorithm, has formed the basis of extending the process to imaging lung function, specifically in neonates, in collaboration with Prof. Andreas Demosthenous, Dept. Electronic and Electrical Engineering, UCL, Prof. Panos Liatsis, City University and Prof. Janet Stocks, Great Ormond St. Hospital (2007 – 2009). At Dartmouth College, the work is also being used to improve breast tumour imaging in collaboration with Prof. Alex Hartov's team that includes Dr Andrea Borsic and Prof. Ryan Halter (2010 ongoing; Source 4). This work is based on using elastic deformation to warp standard or idealised geometry – all of which is intended to provide extensions of the public domain toolset.

(iv) We are also working with Midatech Ltd (source 5) to extend the application of EIT for the detection of cancer. The imaging method may be used to visualise primary lesions in cancers such as colon, prostate, breast and brain cancer, and in the early location of metastases and may also have an application as a mechanism killing tumour cells. Using EIT, especially MfEIT, has the advantage that the imaging technique does not emit potentially harmful ionising radiation like CT or X-Rays, and is highly portable and inexpensive. A joint patent (WO/2010/052503; Detection of Cancer) is in place with this company, which is led by Prof. Rademacher (Source 5). This work is also subject to an NDA, which limits the information we are allowed to disclose in this document.

5. Sources to corroborate the impact

S1. Andy Adler and William R.B. Lionheart (2006) Uses and abuses of EIDORS: An extensible software base for EIT. Physiological Measurement, 27. S25-S42 [Confirmation on the use of the EIDORS software]

S2. Prof. Andy Adler P.Eng. [manager of the EIDORS software at Sourceforge]. Systems and

Computer Engineering, Carleton University, Ottawa, Canada. Prof. Adler manages the EIDORS software repository, and will be able to confirm that we have contributed to it and that it can be used by industrial users.

S3. Paul Casbon, Lucas & Co., Chartered Patent Attorney; European Patent Attorney (re. 61/867,904: US). Can corroborate the filing of the provisional US patent.

S4. Prof. Alex Hartov, Professor of Engineering, Dartmouth College, Hanover, USA. Prof Hartov can confirm that we have been working on boundary shape for breast imaging with them and that we have modified the work on the lung to accommodate this.

S5. Prof. Rademacher (Chief Scientific Officer and Chairman), Midatech Ltd., Oxfordshire OX13 6BH, UK. Prof. Rademacher can confirm that we hold a joint patent in EIT and are working on the clinical application of EIT within the limits of the NDA agreement we have with him.

S6. Dräger (Drägerwerk AG & Co.):"Regional lung function monitoring - how EIT can help to guide ventilation therapy"; http://campaigns.draeger.com/pulmovista500/en/

S7. EIDORS: Electrical Impedance Tomography and Diffuse Optical Tomography Reconstruction Software; http://eidors3d.sourceforge.net/