Institution: Ulster University

Unit of Assessment: Computer Science and Informatics (11)

Title of case study: ICS2 Guiding life changing operations and rehabilitating stroke survivors through the Northern Ireland Functional Brain Mapping (NIFBM) facility – A unique facility for neuroscience across the island of Ireland

Period when the underpinning research was undertaken: 2005 - 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:
Prof Damien Coyle	Professor of Neurotechnology	2005 – Present
Prof Girijesh Prasad	Professor of Intelligent Systems	1999 – Present

Period when the claimed impact occurred: 2016 - 2020

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

1. Summary of the impact

Ulster has impacted epilepsy and stroke patients, across the island of Ireland, via the Northern Ireland Functional Brain Mapping Facility. Impacts include:

I1 – Epilepsy patients have been scanned and presurgical evaluation reports informed successful life-changing operations involving surgical brain resection at Beaumont Hospital, Dublin, Ireland.

I2 – Change of clinical practice for presurgical evaluation of patients with refractory epilepsy in Northern Ireland and the Republic of Ireland (taking an all-island approach to Epilepsy Care and Treatment).

I3 – Chronic post-stroke patients have achieved significant upper limb motor function recovery following brain-computer interface-driven hand exoskeleton rehab therapy over multiple sessions.

2. Underpinning research

Since 2002 Ulster's Intelligent Systems Research Centre (ISRC) (formerly Intelligent Systems Engineering Lab) has been undertaking research in neuroscience and neurophysiology and building sustained expertise and infrastructure for brain research, beginning with a brain-computer interface (BCI) lab with electroencephalography (EEG) equipment (GBP140,000) in 2004, then establishing a computational neuroscience research team (GBP1,540,000) in 2009, followed by the Northern Ireland Functional Brain Mapping (NIFBM) Facility (GBP5,300,000) in 2014 and, more recently, the Spatial Computing and Neurotechnology Innovation Hub (GBP360,000), building a strong track-record in computational and cognitive neuroscience, neuroimaging and neurotechnology R&D. The case for investment in these facilities within a Computer Science and Informatics Unit was strongly evidenced by the interdisciplinary underpinning research across a range of neuroimaging modalities – EEG, magnetoencephalography (MEG), functional magnetic resonance imaging (fMRI), diffusion tensor imaging (DTI), and functional near infrared spectroscopy (fNIRS) by ISRC researchers. Developing this underpinning research and infrastructure, coupled with the associated competency and expertise, has enabled research that has had lasting impact on patients with stroke, and life-changing impact on patients with epilepsy – and has given medical practitioners confidence to engage the NIFBM as a facility for the assessment of patients and one which can inform patient care and treatment as evidenced in **[C1-C6]**. Significant research advances that

underpins the above impacts, clustered in two main topics and mapped to references [**R1-R6**] and the specific impacts (**I1-I3**) are:

R1-R3 – Presurgical evaluation of epilepsy patients [I1, I2]: Magnetic source imaging (MSI), combining MEG and structural cerebral MRI, is increasingly being used for presurgical evaluation of patients with focal epilepsy, particularly when: (a) there are undetermined, or multiple epileptic foci; and (b) there are no identifiable lesions. Ulster and UPMC Paris's collaborative research led by Prof. Coyle in 2009-10 **[R1, R2],** which presents novel methods for (f)MRI structural/functional analysis, has enabled advanced analysis of patient MRI scans supplied by clinical collaborators prior to patients having MEG scans at the NIFBM. Furthermore, a highly advanced method for estimating brain functional connectivity has been developed by NIFBM researchers led by Prof. Prasad **[R3]** during 2015-17. Thus, the team has developed methodology and acquired advanced level expertise necessary for MEG-based presurgical evaluation of epilepsy patients.

R4-R6 – Feasibility trials with stroke patients [I3]
Mental practice (MP) in conjunction with physical practice of goal-directed rehabilitation tasks, enhances functional recovery of paralyzed limbs among stroke sufferers. BCI supported motor imagery practice with (gamified) visual feedback can support this type of rehab therapy. Ulster researchers led by Prof. Prasad **[R4]** reported the first such results from a pilot trial conducted in 2007-08, involving five people with chronic stroke, showing clinically important effects on upper limb function (patent submitted: 0821877.8). This was a precursor to **[I3]** and the Ulster and Indian Institute of Technology Kanpur (IITK) collaborative research led by Prof. Prasad in 2014-17 **[R5, R6],** which transitioned from using a visual feedback of sensorimotor response to physical feedback through a hand exoskeleton actuated by the BCI response (Indian patent: 84996) and, subsequently, understanding the influence of the rehab therapy on brain function through combined EEG and MEG (supported by three (GBP144,557, GBP45,200 and GBP144,546 UK-India Education and Research Initiative (UKIERI) funded projects in collaboration with IITK, 2008-2020). The most recent findings demonstrate a significant and lasting effect of the therapy.

3. References to the research Outputs can be provided by Ulster University on request.

R1 – X. Li, D. Coyle, L. Maguire, T. M. McGinnity, D. R. Watson, and H. Benali, "A least angle regression method for fMRI activation detection in phase-encoded experimental designs," Neuroimage, vol. 52, no. 4, pp. 1390–1400, 2010.

R2 – X. Li, D. Coyle, L. Maguire, D. R. Watson, and T. M. McGinnity, "Gray matter concentration and effective connectivity changes in Alzheimer's disease: A longitudinal structural MRI study," Neuroradiology, vol. 53, no. 10, pp. 733–748, 2011.

R3 – J. M. Sanchez Bornot, K. F. Wong-Lin, A. L. Ahmad, and G. Prasad, "Robust EEG/MEG Based Functional Connectivity with the Envelope of the Imaginary Coherence: Sensor Space Analysis," Brain Topography, vol. 31, no. 6, pp. 895–916, 2018.

R4 – G. Prasad, P. Herman, D. Coyle, S. McDonough, and J. Crosbie, "Applying a brain-computer interface to support motor imagery practice in people with stroke for upper limb recovery: a feasibility study," BMC Journal of NeuroEngineering and Rehabilitation, *7*(60), 1-17, 2010.

R5 – Chowdhury, A., Meena, Y. K., Haider, R., Bhushan, B., Uttam, A. K., Pandey, N.,Prasad, G. (2018). Active physical practice followed by mental practice using BCI-driven hand exoskeleton: a pilot trial for clinical effectiveness and usability. *IEEE journal of biomedical and health informatics*, *22*(6), 1786-1795.

R6 – Rathee, D., Chowdhury, A., Meena, Y., Dutta, A., McDonough, S., & Prasad, G. (2019). Brain-Machine Interface Driven Post-Stroke Upper-limb Functional Recovery

Correlates with Beta-band Mediated Cortical Networks. *IEEE Transactions on Neural Systems and Rehabilitation Engineering*, *27*(5), 1020-1031.

Comment on Research Publications: All outputs have been peer reviewed by the internationally-based editorial boards of the journals. Research in [**R1-R2**] was undertaken as part of the establishment of a Computational Neuroscience Research Team funded by the Department of Learning as a Cross Border Initiative in collaboration with Trinity College Dublin (GBP1,540,000) and involved other international collaborators (Benali). Research in [**R3 – R6**] were performed under the NIFBM facility development funding (GBP5,300,000) as well as international collaborations through three (GBP144,457, GBP45,200 and GBP144,546) UK-India Education and Research Initiative (UKIERI)-funded projects in collaboration with IIT Kanpur, India between 2008 and 2020.

- McGinnity, Coyle, Prasad and Maguire.
  Computational Neuroscience Research Team.
  All-island Cross-Border R&D Programme.
  03/11/2008 - 31/03/2011. GBP1,535,807.

- Prasad, Bjourson, Cecotti, Wong-Lin, Coyle, Maguire, Coleman and McGinnity.
  NI Functional Brain Mapping Facility. Invest NI, Grant for R&D – Capital Project.
  01/04/2013 - 15/03/2020. GBP2,607,301. (Total Value ~GBP5,300,000 - 50% provided by Invest NI).

- Coyle and McCreadie.
  The Spatial Computing and Neurotechnology Innovation Hub (SCANi-hub).
  Department for Economy and Ulster University, Higher Education Capital Funding.
  02/01/2019 - 31/12/2020. GBP266,227.

- Prasad, Coyle and McGinnity.
  Innovations in Intelligent Assistive Robotics.
  UK-India Education and Research Initiative (UKIERI), DST - UKIERI call 2007.
  01/01/2008 - 31/12/2011. GBP144,557.

- Prasad, McDonough and Dutta.
  A BCI Operated Hand Exoskeleton-based Neurorehabilitation System for Movement Restoration in Paralysis.
  UK-India Education and Research Initiative (UKIERI), DST - UKIERI call 2013.
  15/04/2014 - 31/05/2017. GBP45,200.

- Prasad, McDonough and Dutta.
  Advancing MEG-based Brain-Computer Interface Supported Upper Limb Post-Stroke Rehabilitation.
  UK-India Education and Research Initiative (UKIERI), DST - UKIERI call 2016.
  01/04/2017 - 31/12/2020. GBP144,546.

4. Details of the impact

The NIFBM facility houses the only magnetoencephalography (MEG) laboratory on the island of Ireland (and, to our knowledge, the only one housed in a computer science research facility in the UK, perhaps the world). NIFBM has a focus on clinical research and applied clinical applications – positioning the facility uniquely to facilitate neuroimaging, brain dynamics analysis, interdisciplinary knowledge and expertise that inform life-changing operations and interventions. Impacts include:

I1: Presurgical evaluation of epilepsy patients using advanced Magnetic Source Imaging

Refractory epilepsy is characterized by frequent recurrent seizures that are resistant to medication. A systematic review and meta-analysis (2015) found that surgery offers patients with refractory epilepsy an improved quality of life and a better chance of becoming seizure-free. In January 2015 Consultant Neurologist/Neurophysiologist at Beaumont Hospital Dublin, Ireland, and Clinical Lead of the National Epilepsy Programme in Ireland **[C1]**, contacted the NIFBM facility to discuss the clinical application of MEG for pre-surgical evaluation of refractory epilepsy patients, particularly when there is an undetermined location of seizure-onset.
To date, the NIFBM facility, underpinned by methods and knowledge presented in **[R1-R3],** has completed a presurgical evaluation for seven patients under the care of the Consultant Neurologist, 3 of whom are detailed in **[C1, C3] "** *…MEG* has a well-defined role in the identification of epileptiform dipole, deep to the sensitivity of surface EEG and immune to the characteristics of skull breach, highlighted well in [patient A's] case…*" and *"…MEG* provided critical understanding of the location of the seizure onset zone within the large region of dysplasia. In addition motor evoked potentials, identified the primary motor regions, which were adjacent, but distinct from the seizure onset zone. In this case MEG served a critical role in operative planning, and [patient R] underwent a focal palliative resection, dissecting out the bulk of the peri-sylvian dysplasia, with particular attention to the epileptiform region as highlighted by MEG study and sparing similarly recognised Motor Regions within the MRI imaging abnormality. He is now employed, leading an active professional and social life, and has been free of seizure with associated alteration of awareness and generalised convulsion since 2016". and "MEG study identified independent bi-hemispheric epileptiform foci… and provided accurate informative information with regard to the currently active source for seizures in [patient R's] case, and we hope to incorporate repeat study when future therapeutic options are available".*
All reports added clinical value, aiding in decision-making processes that led to improved outcomes for all patients.
**(in the letter meaning our MEG imaging and analysis)*

I2: Change of practice for presurgical planning of epilepsy patients on the island of Ireland using clinical MEG

The Clinical Lead of the National Epilepsy Programme in the Republic of Ireland [**C1**] has made progress in joining forces with colleagues in Belfast to establish an all-island Epilepsy Surgical Programme for adults and paediatrics. This has been promoted and supported by a Consultant Radiologist, who has worked with the Clinical Lead of the National Epilepsy Programme and the NIFBM to establish a clinical programme via the NIFBM. The Consultant Radiologist was instrumental in promoting the use of NIFBM for epilepsy care in Ireland stating **[C2] "…***Arising from the development of NIFBM and the successful presurgical evaluation of epilepsy patients going for life changing surgery for epilepsy treatment in 2018 we have made significant progress towards establishing clinically applied MEG services in Ireland – specifically the launching of an all-Ireland epilepsy programme, and the progression of MEG as diagnostic tool for traumatic brain injury (TBI)...".* Following the success of the impacts highlighted in **[I1]** it has been recommended by the Clinical Lead of the National Epilepsy Programme that clinical care for patients with refractory epilepsy will involve a presurgical evaluation using MEG, given the added clinical value MEG brings to the presurgical evaluation procedure "…*repeated study and incorporation in our clinical decision process, will allow for the further development of MEG at NIFBM, and has the potential to lead patients with otherwise life limiting Epilepsy towards the prospect of seizure freedom..."* The NIFBM facility, as the only MEG in Ireland and given the expertise available at the facility **[R1-R3]**, will be engaged to undertake these evaluations when the facility is fully established for clinical care. Currently approximately 60,000 people across the Rep. of Ireland and Northern Ireland suffer from epilepsy. Refractory epilepsy (resistant to medication) can occur in 20% to 40% of cases, having a debilitating impact on the patient – loss of self-confidence, livelihood, adverse effects on education and relationships, increased risk of memory deficits (particularly long-term, which includes autobiographical memory), and increased risk of depression and anxiety disorders. Thus, the change in patient care stimulated by the impacts **[I1]** not only frees more patients from recurring and frequent seizures, but significantly improves patients' quality of life and their clinical outcomes relating to these secondary impacts as evidenced on **[C1, C2]**.

I3: Brain-computer Interface supported post-stroke neurorehabilitation
A novel BCI-driven hand exoskeleton supported rehab therapy has undergone phase-2 trials **[R5]**. Pilot clinical trials on post-stroke participants have been conducted in two phases. The first phase involved ten healthy individuals and ten chronic stroke patients participating in a feasibility study followed by the participation of four chronic stroke patients in a longitudinal pilot trial in India during Aug-Sept 2016. In the 2nd phase during Apr-May 2017 at Ulster, five post-stroke patients undertook up to twelve sessions of rehab therapy and underwent weekly resting state MEG scanning to assess recovery related cortical changes **[R6]**.
A standard hand functional recovery measurement, the action-research arm test (ARAT), revealed that all the chronic stroke participants that underwent ten or more therapy sessions in the clinical trial achieved clinically important improvement in their hand function **[R5, R6]** and all reported transformative change in their quality of life because of the recovery of upper limb functional use and in improvement of overall mental health. A testimony from a patient as a video interview as well as a handwritten letter **[C4]** highlights multiple impacts this improvement in function has had e.g., *"…more coordination of my hand picking things up… like a button… I can touch back of my head… hold my umbrella steady… tie my shoe laces… I feel more confident when I go out… to restaurant, using knife + fork... [looking forward] to upcoming wedding",* which were earlier not possible. A report from the occupational therapist details the improvement in patient outcomes following engagement with the technology developed at the NIFBM facility, *"…having undergone the pilot trials the stroke participants have reported transformative change in their quality of life, particularly in the recovery of upper hand motor functions. This is clearly evident from the video interview I conducted with at least one of the patients"* **[C5, C6]**.

5. Sources to corroborate the impact

C1 – Letter from a Consultant Neurologist/Neurophysiologist at Beaumont Hospital Dublin, Rep. of Ireland.
C2 – Letter from a Consultant Radiologist at Health Service Executive, Rep. of Ireland.
C3 – Presurgical reports presented for 3 patients.
C4 – Testimonials from a stroke patient.
C5 – Letter from a Senior Occupational Therapist, Altnagelvin Hospital, Derry-Londonderry, who helped in clinical trials, detailing improvements observed in stroke patients.
C6 – A video interview with a stroke patient.