Institution: Aberystwyth University

Unit of Assessment: 11: Computer Science and Informatics

Title of case study: Improving patient outcomes and developing commercial benefits via medical image analysis

Period when the underpinning research was undertaken: 2006-2020

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 Reyer Zwiggelaar	Senior Lecturer; Professor	1 August 2004 – 31 May 2009; 1 June 2009 - present
Dr Chuan Lu	Lecturer	1 May 2012 – present
Dr Yonghuai Liu	Lecturer; Senior Lecturer	3 September 2001 – 30 September 2011; 1 October 2011 – 16 September 2018

Period when the claimed impact occurred: 2014-2020

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

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

The research on medical image analysis within the Vision Graphics & Visualisation (VGV) research group at Aberystwyth has led to a wide range of impact. It has enabled developments in healthcare informatics, especially around commercial orthopaedics' segmentation software, international deep endometriosis standard, MS/stroke segmentation and stroke rehabilitation, and retinal disease treatment. Such impact has positively affected populations of different sizes, ranging from individual patients to a group of hospitals. It has resulted in changing practices with newly introduced international standard in the relevant healthcare sector, and in benefiting the commercial sector with improved tools that in turn enhance patient outcomes.

2. Underpinning research (indicative maximum 500 words)

A key focus of the VGV group is the conduct of research in medical image analysis and healthcare informatics. Such research has been supported by a range of externally funded facilities, including developments such as the Research Institute of Visual Computing, Advanced Medical Imaging and Visualization Unit [3.7], Supercomputing Wales, and a UKRI CDT in Artificial Intelligence, Machine Learning & Advanced Computing [3.8].

Much of our ultrasound (US) related work since 2012 has been delivered with a series of international multi-centre studies on the development and evaluation of Transvaginal Sonography (TVS) techniques for diagnosis and management of endometriosis, which has included collaborators at the University of Sydney and Liverpool Public Hospital [3.1]. Our work on preoperative real-time dynamic TVS evaluation has established means of determining whether the pouch of Douglas is obliterated, with a high degree of certainty. In particular, a preoperative Ultrasound-Based Endometriosis Staging System (UBESS) has been developed to predict the level of complexity of laparoscopic surgery for endometriosis [3.2]. The most recent developments in this area are exploring advanced deep learning techniques for the interpretation of US data.

Our work on segmentation techniques in medical image analysis has been used extensively in the development of computer-aided diagnosis (CAD) techniques [3.3]. Over the years this has had a strong emphasis on mammographic and prostate-based applications, where the

segmentation techniques formed the essential pre-processing step before further analysis/classification and clinical recommendation might be possible. Such pre-processing steps enable the establishment of novel mechanisms that can exploit texture and intensity topology natures of image data. This research has resulted in, and subsequently benefitted from, extensive academic collaboration with international research groups including the University of Girona, University of Pennsylvania and Manchester Metropolitan University.

During 2010 the VGV group's research extended the then mainly breast/prostate research into the area of brain segmentation, with an emphasis on MS lesions segmentation in MRI/PET data [3.4]. In parallel with these developments, we collaborated with X. Llado from the University of Girona, from 2015 to 2020, as a main contributor to two significant MS lesion-driven projects (DPI2017-86696-R). The pre-processing techniques established by us [3.4] form a key foundation of these projects. As a direct result of these projects a spin-out company (Tensormedical) was created which is providing transversal and longitudinal lesion analysis in clinical environments. In recognition of this research, AU has received significant grants on extending it to dealing with the rehabilitation problems of stroke patients from NHS Wales and Health and Care Research Wales.

The original retinal work is based on Retinex research developed within the VGV group. Through exploiting novel 2-D / 3-D symmetric filters, the process of detecting vascular and other structures is automated, helping understand the mechanism, diagnosis, and treatment of many vascular pathologies. This research has been conducted in close collaboration with a group of clinical end-users (including Peking University Third Hospital and Royal Liverpool University Hospital), tackling a range of retinal specific clinical challenges, which include lesion and vascular segmentation/classification [3.5]. The work on retinal images is directly based on our earlier investigation into linear structures in medical images [3.6], in collaboration with the University of Manchester.

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

3.1 Tompsett, J., Leonardi, M., Gerges, B., **Lu, C.**, Reid, S., Espada, M., Condous, G. Ultrasound-based endometriosis staging system: validation study to predict complexity of laparoscopic surgery. Journal of Minimally Invasive Gynecology 26 (3), 477-483 (2019). DOI: 10.1016/j.jmig.2018.05.022

3.2 Reid, S., **Lu, C.**, Hardy, N., Casikar, I., Reid, G., Cario, G., Chou, D., Almashat, D., Condous, G. Office gel sonovaginography for the prediction of posterior deep infiltrating endometriosis: a multicenter prospective observational study. Ultrasound in Obstetrics and Gynecology 44: 710–718 (2014). DOI: 10.1002/uog.13422

3.3 He, W., Hogg, P., Juette, A., Denton, E.R.E., **Zwiggelaar, R**. Breast image pre-processing for mammographic tissue segmentation. Computers in Biology and Medicine 67, 61-73 (2015). DOI: 10.1016/j.compbiomed.2015.10.002

3.4 Z. Zeng, J. Wang, B. Tiddeman, **R. Zwiggelaar**. Unsupervised tumour segmentation in PET using local and global intensity-fitting active surface and alpha matting. Computers in Biology and Medicine 43 (10), 1530-1544 (2013). DOI: 10.1016/j.compbiomed.2013.07.027

3.5 Zhao, Y., Zheng, Y., **Liu, Y.**, Zhao, Y., Luo, L., Yang, S., Na, T., Wang, Y., Liu, J. Automatic 2-D/3-D vessel enhancement in multiple modality images using a weighted symmetry filter, IEEE Transactions on Medical Imaging 37 (2), 438-450 (2018). DOI: 10.1109/TMI.2017.2756073

3.6 **Zwiggelaar, R.**, Astley, S.M., Boggis, C.R.M., Taylor, C.J. Linear structures in mammographic images: detection and classification. IEEE Transactions on Medical Imaging 23 (9), 1077-1086 (2004). DOI: 10.1109/TMI.2004.828675

Research Grants

3.7 **Zwiggelaar, R.;** BRU - The Advanced Medical Image Analysis and Visualisation Unit; Nat Institute for Social Care & Health Research (NISCHR); 1 October 2011 – 31 May 2015; GBP270,736

3.8 **Zwiggelaar, R.;** UKRI Centre for Doctoral Training in Artificial Intelligence, Machine Learning and Advanced Computing; Engineering & Physical Sciences Research Council; 1 April 2019 - 30 September 2027; GBP795,594

3.9 **Lu, C.;** Predictive modelling for diagnosis of early pregnancy complications & endometriosis: The collaborative link development; OMNI Gynaecological Care; 1 July 2012 – 30 June 2013; GBP2,000

3.10 **Liu, Y**.; Learning to Annotate Consumer 3D scans; Innovate UK; 1 December 2015 – 30 November 2016; GBP44,999

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

International Deep Endometriosis Standard

Endometriosis affects an estimated 1 in 10 women during their reproductive years, which is approximately 176,000,000 women world-wide and costs the UK economy GBP8,200,000,000 a year in specific treatment, loss of work and daily healthcare The methodologies [3.2] developed from this line of clinical studies have been included as the major sonographic steps for endometriosis diagnosis, published as a consensus opinion by the International Deep Endometriosis Analysis Consensus Group [5.1.1][3.1]. This Group is part of International Society of Ultrasound in Obstetrics and Gynaecology (ISUOG), with over 15,700 practicing members worldwide [5.1.2]. This has a major implication for clinical practice in endometriosis, for example, a preoperative scoring system has been developed by the University Hospital of Poissy Saint-Germain en Laye (France) based on UBESS for accurate prediction of rectosigmoid involvement in patients with endometriosis. These studies also provided underlying evidence for the National Institute for Health and Care Excellence (NICE) guideline on the standard of using ultrasound imaging as cost-effective tools for endometriosis (nice.org.uk/guidance/ng73) [5.1.3]. Aberystwyth's research:

> *"…has substantially contributed to our development and field application of a novel TVS technique and of a preoperative ultrasound-based endometriosis staging system (UBESS), for predicting the level of complexity of laparoscopic surgery for endometriosis. This has helped to significantly improve our diagnostic procedures, especially in minimising our laparoscopic investigations while reducing the considerable chronic pain endured by patients." [5.1.2].*

Translating Medical Image Analysis Research to the Commercial Sector

Orthopaedic problems are significantly affecting people worldwide and liver disease is the third leading cause of premature death in the UK. Combined these two factors are affecting over 2,500,000people in the UK. The main impact in this area has been the translation of mammographic image analysis techniques (see for example [3.3]) to a range of applications in the commercial sector. Typical examples for this are the orthopaedic segmentation tools developed at Synopsys, a major software company [5.2.1,5.2.2], and the CT Liver analysis software developed at Toshiba Medical Systems [5.2.1,5.2.3] which are being extensively used in the clinical domain *"….the Auto Segmenter module has become a key offering in the Synopsys Simpleware portfolio and we expect it will continue to be a game changer for its end users for many years to come"* [5.2.1]. These commercial tools significantly contribute to clinical reporting and improving patient outcomes.

MS/Stroke Image Analysis and Stroke Rehabilitation

The prevalence of Multiple Sclerosis in the UK is estimated at 190 cases per 100,000 people, counting for more than 130,000 cases in total, with about 7,000 new cases each year. In addition, there are over 113,000 people suffering from stroke each year in the UK, and currently there are around 1,000,000 stroke survivors. Our international collaborative research (with the University of Girona) in this life-critical area has led to a spin-out company, Tensormedical [5.3.1,5.3.2]), which develops software specific for Multiple Sclerosis and stroke-related diseases. Such tools have been deployed within clinical environments (for example Hospital of Vall d'Hebron, Barcelona). This not only helps clinical experts but also contributes directly to patient well-being, especially in the case of longitudinal assessment of lesions.

Retinal Disease Treatment

Dry eye disease affects tens of millions of individuals around the world and is considered a major international health concern. In 2014 the cost of related prescription items to the NHS was over £27,000,000 and the expectation is that improved diagnosis will lead to more appropriate treatment and reduction of the associated costs. There are around 3,500,000 diabetic suffers in the UK (2019), which is expected to raise to 4,000,000 by 2025, and of these up to 50% might be affected by neuropathy. The incorporation of automated segmentation for the tortuosity of corneal nerve fibres [3.5] has provided a consistent approach to the assessment of dry eye disease and diabetic neuropathy. At the same time, it has significantly accelerated the processing time of the staging of patients, increasing the volume of patients being treated by 10%. This has meant that for a single hospital (Peking University Third Hospital) 200 more patients can be assessed and treated each year [5.4.1], with similar effects in the Royal Liverpool University Hospital. This also led to the recent development with Hywel Dda UHB where retinal scans are linked to neurological and mental health diseases [5.4.2].

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

5.1.1 Guerriero, S. et al. Systematic approach to sonographic evaluation of the pelvis in women with suspected endometriosis, including terms, definitions and measurements: a consensus opinion from the International Deep Endometriosis Analysis (IDEA) group. Ultrasound Obstet Gynecol 48: 318–332 (2016). DOI: 10.1002/uog.15955

5.1.2 Letter from Professor George Condous, Head of Discipline OBGYN, Assoc. Professor of Gynaecology, Sydney Medical School Nepean, University of Sydney

5.1.3 Endometriosis: diagnosis and management. NICE guideline [NG73] Published date: 06 September 2017. ISBN 978-1-4731-2661-9. www.nice.org.uk/guidance/ng73

5.2.1 Letter from Dr. Wenda He, R&D Engineer (Sr II), Synopsys

5.2.2 Synopsys Simpleware software www.synopsys.com/simpleware/software/auto-segmenter-modules.html

5.2.3 Toshiba Medical Systems CT Liver analysis software www.vitalimages.com/product-information/ct-liver-analysis/

5.3.1 Letter from Professor Xavier Llado, Computer Vision and Robotics Institute, University of Girona & CSO, Tensormedical

5.3.2 Tensormedical company website www.tensormedical.ai/

5.4.1 Letter from Professor Hong Qi, Senior Opthalmologist, Peking University Third Hospital

5.4.2 Letter from Eirini Skiadaresi MD, Consultant Ophthalmic Surgeon, Hywel Dda UHB