Institution: University of Sussex

Unit of Assessment: 12 – Engineering

Title of case study: Improving cancer and kidney stone treatment with quantitative texture analysis of medical images

Period when the underpinning research was undertaken: 2000 – 2012

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:
Chris Chatwin	Professor in Engineering	1995 – present
Rupert Young	Reader in Engineering	1995 – present

Period when the claimed impact occurred: 2014 – 2020

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

1. Summary of the impact

Thousands of hospital patients across the world have received improved care and treatment for cancer, kidney stones, and other conditions, using technology based on the work of the Industrial Informatics and Signal Processing Research Group at the University of Sussex. The image texture analysis software for diagnostic radiological and MRI scans enables images to be assessed with unprecedented detail. By helping clinicians to distinguish tumours from normal background tissue, and to characterise kidney stones, the technology facilitates better decision-making about prognosis and treatment. The product is installed in over sixty leading medical centres across Europe, North America, Asia and Australasia.

2. Underpinning research

Originally developed to detect and track vehicles against different backgrounds, the research distinguishes weak structured signals within cluttered images. Specifically, it tracks objects using modified Wiener type filters, optimised by including the statistics of the clutter-noise within the filter **[R1]**.

The process represented a background by parametrically estimating the average of a large number of different cluttered backgrounds, within which the object could be expected to be found. The results demonstrate excellent sensitivity **[R2]**.

In 2004, the research was applied to medical applications, to detect variations in the texture of organs and tissues. Young and Chatwin began a collaboration with Professor Kenneth A. Miles at Brighton and Sussex Medical School (BSMS) to detect such tissue heterogeneity associated with cancer. In this case, the images analysed are generated by computerised tomography (CT) or, with contrast material present, perfusion CT. Using the previously described approach, modified Wiener Filters **[R3]** identified and quantified variations in texture to generate quantitative heterogeneity biomarkers.

In 2007, analysis of 28 colorectal cancer patients' historical CT data **[R3]** demonstrated a relationship between liver texture and blood-flow. This showed the research could analyse liver-texture as a way to screen patients for colorectal cancer. Texture analysis at different image spatial frequencies correlate with disease severity and progression. Similarly, liver blood-flow variations, reflected as subtle coarse texture changes, can be used to identify colorectal cancer patients with an apparently normal liver appearance **[R4]**. In 2009, an historical study of 48 patients with colorectal cancer **[R5]** suggested that texture analysis on portal phase CT images was a better predictor of survival than hepatic perfusion CT **[R5]**.

A further study, which has been cited more than 200 times, assessed the diagnostic value of the texture analysis in three groups of colorectoral cancer patients **[R6]**. This project showed that relative texture analysis of unenhanced hepatic CT scans can reveal changes in apparently disease-free areas of the liver, which previously required more complex perfusion measurements for detection. The technology therefore reduces costs, radiation burden, and risk.

As a result of international clinical trials conducted by customers using TexRAD technology, over 120 refereed journal and conference papers have been published by third parties. These include outputs in leading journals such as *Radiology* and *Clinical Cancer Research***.** The effect of these findings is to validate the use of the algorithms in the prediction of the survival and treatment response of patients with squamous cell carcinoma of the head and neck, non-small-cell lung cancer, renal cancer, oesophageal cancer, prostate cancer and colorectal cancer. In addition, numerous papers have explored the value of TexRAD texture analysis in guiding the diagnosis and treatment of conditions ranging from kidney stones to Alzheimer's disease.

3. References to the research

R1 Tan, S., Young, R.C.D., Budget, D.M., Richardson, J.D. and Chatwin, C.R. (2000) 'Performance comparison of a linear parametric noise estimation Wiener filter and non-linear joint transform correlator for realistic clutter backgrounds', *Optics Communications*, 182(1-3): 83-90. https://doi.org/10.1016/S0030-4018(00)00796-3

R2 Birch, P., Tan, S., Young, R.C.D., Koukoulas, T., Claret-Tournier, F., Budgett, D., Chatwin, C.R. (2001), 'Experimental implementation of a Wiener filter in a hybrid digital–optical correlator', *Optics Letters*, 26(8): 494-496. https://doi.org/10.1364/OL.26.000494

R3 Ganeshan, B., Miles, K.A., Young, R.C.D. and Chatwin, C.R. (2007) 'In search of biologic correlates for liver texture on portal-phase CT', *Academic Radiology*, 14(9): 1058–68. https://doi.org/10.1016/j.acra.2007.05.023

R4 Ganeshan, B., Miles, K.A., Young, R.C.D. and Chatwin, C.R. (2007) 'Hepatic enhancement in colorectal cancer: texture analysis correlates with hepatic hemodynamics and patient survival', *Academic Radiology,* 14(12): 1520–30. https://doi.org/10.1016/j.acra.2007.06.028

R5 Ganeshan, B., Miles, K.A., Young, R.C.D. and Chatwin, C.R. (2009) 'Texture analysis in non-contrast enhanced CT: impact of malignancy on texture in apparently disease-free areas of the liver', *European Journal of Radiology*, 70(1): 101–10. https://doi.org/10.1016/j.ejrad.2007.12.005

R6 Miles, K.A., Ganeshan, B., Griffiths, M.R., Young, R.C.D. and Chatwin, C.R. (2009) 'Colorectal cancer: texture analysis of portal phase hepatic CT images as a potential marker of survival', *Radiology*, 250(2): 444–52 https://doi.org/10.1148/radiol.2502071879

4. Details of the impact

The research described in section 2 led to an initial patent (filed in 2007, patent GB0705223.6 **[S1]**.) Further improvements in algorithms and software performance over the next four years then allowed the research team to launch a commercial product TexRAD. This is an advanced image texture analysis software tool that analyses routinely acquired diagnostic medical images (for example CT and MRI scans) to reveal features not always evident to the human eye. The software also includes a novel data-mining tool to statistically analyse results and identify parameters associated with patient outcome.

Following further commercial development supported by the Regional Development Agency and the University's Enterprise Development Fund, a spin-out company, TexRAD Ltd, was launched in 2011 as a joint venture between the University of Sussex, Imaging Equipment Ltd, Cambridge Computed Imaging Ltd, and Miles Medical. The Scientific Director and subsequently CEO of TexRAD since its foundation is Dr Balaji Ganeshan, who had been supported by the University's Enterprise Development Fund; and the clinical founding director is Prof Kenneth A. Miles (who was employed by Brighton and Sussex Medical School until 2011).

In 2014, TexRAD merged with Feedback plc. Sales of the TexRAD software has increased the income for Feedback plc (which currently has a market value of £11.74 million (18/11/2020 LSE)), and CE approval, granted in 2017 **[S2]**, led to a lucrative licensing and distribution agreement with General Electrical Healthcare (GEHC) **[S3]**. Feedback plc's 2020 annual report (for year end May 2020) confirms that: *"to date, TexRAD has been deployed in more than 60 research centres around the world, each one looking to find a link between texture changes and disease."* **[S4a]**

The software has been licensed to numerous hospitals in the UK, North America, Europe, Asia and Australasia, where it is used to produce information critical for clinical trials and medical

studies. Eight hospitals in the UK use TexRAD, including King's College Hospital, University College London Hospital and the Cambridge University Hospitals. Internationally, users include:

- **North America:** Johns Hopkins University Medical School, Georgetown University Hospital, University of Mississippi Medical Centre, Massachusetts General Hospital, Scottsdale Clinical Research Institute, University of Wisconsin, University of Pittsburgh School of Medicine **[S4b]**, Indiana University, St Jude Childrens's Research Hospital, Sunnybrook Health Sciences Center (McGill University) Canada.
- **Europe:** Aarhus University Hospital, European Institute of Oncology, Oslo University Hospitals, University of Rome Sapienza, Universitatsspital Basel, Centre Hospitalier Universitaire de Reims, Evangelische Lungen Klinik, Haukeland University Hospital, Gustave Roussy Cancer Centre, University, Centre Hospitalier Universitaire De Grenoble, University of Brescia **[S4c]**, Turku University Hospital.
- **Rest of world:** Tata Medical Centre, India; Peking Union Medical College Hospital, China; International University of Health and Welfare, Japan **[S4d];** Seoul National University Bundang Hospital, Korea; Princess Alexandra Hospital, Australia.

For example, in 2018 researchers at the Princess Alexandra Hospital (Australia) published an 18-month prospective observational study in *Academic Radiology*, for which it provided the TexRAD software to five radiology and nuclear medicine specialists as a tool to quantify texture parameters in lung tumours. Among other results, the study observed *"significant differences in survival… for patients categorized using the two reported CTTA values*" **[S4e]**. Feedback plc announced that these findings "*suggest that there is a huge potential for the implementation of quantitative imaging in the assessment of tumour heterogeneity and engagement from radiologists is key to its success*." **[S4e]**

One client, Andrea Laghi, Professor of Radiology at the Sapienza University of Rome, says: "*TexRAD deeply helps my research team in exploiting medical images in oncologic patients."* He adds: *"Data mining is critical in current oncologic research. It is complex and takes time. TexRAD is a user-friendly platform which makes our data analysis semi-automatic and thus easier and quicker than other manual approaches."* **[S4f]**

Another customer is Imaging Endpoints, a major US clinical imaging company that employs 40 radiologists. Ronald L Korn, the company's CEO, said:

> *"TexRAD is a very powerful software analytical tool that allows for in-depth evaluation of solid tumours for predictive, prognostic and treatment response categorization. We have used it in our Core Imaging lab on multiple occasions to help accelerate drug development for our pharmaceutical clients. It truly offers advanced information unlike any other technology in the field!"* **[S4g]**

In January 2020, Imaging Endpoints announced it had been issued a patent for a "*breakthrough radiomic evaluation tool [that] allows for rapid diagnosis of the nature of a patient's breast abnormalities from standard mammography images*", enabled by TexRAD technology. Commenting on this technology – which the company anticipates "*could provide patients and physicians the advantage of faster, less invasive information that is critical to treatment decisions and patient outcomes*" – Korn states:

> *"A reliable imaging signature for differentiating between malignant and non-malignant BI-RADS 4 mammographic lesions has remained elusive until now. The Imaging Endpoints invention provides a biomarker signature for determining whether a lesion identified in a breast image is malignant. The signature is derived from processing mammography data using a Quantitative Textural Analysis™ platform (TexRAD); generating respective histograms and related quantitative metrics, and performing logistical regression to yield a model predictive signature. Imaging Endpoints believes that its technology offers a real-time advantage with rapid results."* **[S4h]**

New orders for TexRAD have also been received from France, Italy, Belgium, and Portugal, expanding the customer base in Europe **[S5].** Feedback have also signed an exclusive marketing and distribution agreement with Korea Computer Motion ISG **[S6a],** who have access

to a large number of medical imaging customers. Samsung Medical Centre purchased TexRAD in September 2018 **[S6b,c]**, as a part of the new PET-CT scanner installed by Siemens at Seoul National University Bundang Hospital (SNUBH) for use by the Nuclear Medicine department. Research, facilitated by TexRAD, will be conducted there on cancer and other diseases, to inform clinical decision-making in the diagnosis and management of patients.

Dr. Ho-Young Lee, Assistant Professor in the Department of Nuclear Medicine, Seoul National University, comments:

> *"We are very excited with the prospects of using the TexRAD imaging research software platform in conjunction with the new PET-CT scanner being installed at our institution, further reinforcing our vision and reputation of being early adopters of new technologies, particularly in the fascinating area of quantitative imaging and its applications in cancer care"* **[S6c].**

TexRAD has also had significant impact in the treatment of kidney stones. Licensed as StoneChecker, the software helps to distinguish those patients who would respond best to lithotripsy — treatment which breaks up kidney stones using sound waves — from those for whom surgery might be more appropriate. Lithotripsy is less invasive and, for kidney stones smaller than 20mm, it is cheaper than surgery (including minimally invasive options such as percutaneous nephrolitholapaxy) **[S7a]**. Nevertheless, each treatment costs around £1,200 in the UK **[S7a]** and over $13,000 in the USA. Further, lithrotripsy fails and surgery is required for around a third of patients. The technology therefore supports a key decision about treatment. In addition, the technology supports clinical decision-making by helping to estimate the number of sound-wave shocks that will be needed for successful treatment.

Markets in Europe, the USA and Korea were opened by the granting of regulatory approval to StoneChecker software in 2017 (CE approval **[S8a]**), 2019 (FDA approval **[S8b,c]**) and 2020 (KFDA approval **[S9a,b]**) respectively.

In 2019, the UK National Institute for Health and Care Excellence (NICE) published a briefing on StoneChecker that concluded*: "CT texture analysis using StoneChecker can differentiate uric acid from non-uric stones… This may make it possible to predict the number of shocks needed to treat kidney stones."* It also recorded experts' comments that StoneChecker *"could help clinical decision making about treatment choice", especially for patients at high risk of lithotripsy failure, or those with no symptoms but with large or multiple stones."* **[S7b].** This briefing is highlighted in the flowchart designed by NICE to support those in the NHS considering using or commissioning new technologies for the treatment of Renal and Ureteric Stones **[S7c],** embedding the reach of StoneChecker across all hospitals in England.

StoneChecker software has already guided the treatment of more than 1,000 patients in the USA, European Union, China and South Korea **[S10]**. Kidney stones affect around 300,000 million adults around the world, and the substantial investment in the technology by hospitals globally indicates that many thousands of patients will benefit in the near future.

5. Sources to corroborate the impact

S1 Patent applications, including UK patent application No.GB0705223.6 19/03/2007; international patent application under the PCT system PCT/GB2008/000977 19/03/2008; Canadian patent number CA2682267 granted 22/01/2013; US, Europe, Japan patent pending.

S2 Feedback Plc news via Regulatory News Service (RNS), the company news service from the London Stock Exchange. **a) "**First CE marked release of TexRAD® technology", 20/11/17, USA, RNS Number: 9059W **b) "**Distribution agreement with GE Healthcare", 25/04/2015, RNS Number: 0082M.

S3 Feedback Plc news via RNS. **a)** "First GE Healthcare order for TexRAD® medical imaging software", 15/08/2018 RNS Number: 8142X **b) "**Drug Trial and Trading Update", 29/5/15, USA, RNS Number: 5975L.

S4 Statements from: **a)** Feedback plc Annual Report of the Directors and Consolidated Financial Statements (for the year ended 31 May 2020) p11. From https://fbkmed.com/wp-content/uploads/2020/10/Feedback-plc-End-Results-13Oct2020-final.pdf.pdf **b)** Dr Amir

Borhani – Assistant Professor; Chief of Body CT, University of Pittsburgh, School of Medicine, USA. User since 2017; **c)** Professor Roberto Maroldi, Head of Department of Radiology, University of Brescia, Italy. User since 2014; **d)** Professor Shigeru Kiryu, Department of Radiology, International University of Health and Welfare, Japan. User since 2015; **e)** Feedback plc News: 'Academic Radiology publishes study on potential for clinical implementation of TexRAD analysis in lung cancer' (14/02/18) from: https://fbkmed.com/academic-radiology-publishes-study-on-potential-for-clinical-implementation-of-texrad-analysis-in-lung-cancer/ including URL to *Academic Radiology* paper (2018): https://doi.org/10.1016/j.acra.2017.11.019 **f)** Professor Andrea Laghi, Professor of Radiology, Sapienza University of Rome, Italy. User since 2014 **g)** Ronald L Korn, CEO and Founder of Imaging Endpoints Core Lab, an Arizona-based laboratory working on Phase I-III drug trials. User since before 2014; **h)** Imaging Endpoints, 'Breakthrough Radiomic Technology Patent Issued to Imaging Endpoints' 13/01/2020, from: https://imagingendpoints.com/breakthrough-radiomic-technology-patent-issued-to-imaging-endpoints/

S5 Feedback Plc news: **"**Feedback expands its European customer base with new orders for TexRAD® from prestigious European university hospitals" London Stock Exchange: Reach Report 22/10/2018; RNS number: 6860E.

S6 Feedback Plc news: **a) "**Feedback (FDBK) subsidiary Cambridge Computed Imaging announces exclusive distributor arrangement with Korea Computer Motion ISG". BRAND UK LTD, 08/06/17; **b)** "TexRAD® ordered by Samsung Medical Centre in South Korea", 10/09/18, RNS number: 1878A; **c) "**First sale of TexRAD in South Korea", 27/05/15, KOREA, RNS Number: 3371L.

S7 National Institute for Health and Care Excellence (NICE): **a)** Medtech innovation briefing [MIB 138] 26/01/2018. Minimally invasive percutaneous nephrolitholapaxy medium (MIP-M) for removing kidney stones — page 5, from: https://www.nice.org.uk/advice/mib138/resources/minimally-invasive-percutaneous-nephrolitholapaxy-medium-mipm-for-removing-kidney-stones-pdf-2285963402416837 ; **b)** Medtech innovation briefing [MIB171] 01/02/2019, "StoneChecker for Kidney stone evaluation", ISBN: 978-1-4731-3258-0; **c)** Pathways – "Renal and ureteric stones overview", page 3, from: https://pathways.nice.org.uk/pathways/renal-and-ureteric-stones#content=view-node%3Anodes-diagnostic-imaging

S8 IQ-AI Ltd news: **a)** "StoneChecker software gets CE mark", Stock Market Wire, 11/12/2017; **b)** "IQ-AI Shares Higher On US FDA Marketing Clearance For StoneChecker", Alliance News Limited, 27/09/19; **c)** "IQ-AI Limited FDA Clearance to Market for StoneChecker Software", ADVFN Financial News, 27/09/19 RNS Number: 9198N.

S9 IQ-AI Ltd news: **a) "**KFDA Clearance for StoneChecker Software", InvestEgate, 20/01/20, RNS Number: 2389A; **b)** "IQ-AI receives first commercial order for StoneChecker", Proactive 16/11/18.

S10 Statement from Dr B Ganeshan, Director, Stone Checker Software Ltd (19/10/20).

All items can also be supplied as PDF files.