Section A

Institution: Durham University

Unit of Assessment: UoA 10: Mathematical Sciences

Title of case study: Bayesian approaches to X-ray imaging for material inference, dose reduction and improved image quality

Period when the underpinning research was undertaken: 2007 – 2019

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:**
Camila Caiado	Associate Professor	2011 – present
Michael Goldstein	Professor	1990 – present
Ben Lopez	PDRA	2018 – 2019
Ian Vernon	Associate Professor	2006 – present

Period when the claimed impact occurred: 2014 – 2020

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

Section B

1. Summary of the impact

IBEX Innovations is an X-ray imaging technology firm "dedicated to developing innovative X-ray imaging solutions since 2014". Durham University collaborated with IBEX Innovations to develop methods to extend their technology portfolio and underpin their software only solutions 'Trueview®' and their patented multi-absorption-plate (MAP) technology. The project showed tangible benefits in several applications which enabled IBEX to develop products in quality control, security and, most importantly, medical markets. They have raised GBP6,000,000 in funding for product development and have secured 14 Jobs in the North East of England. Their technology is now incorporated into CurveBeam, is being incorporated into Planmed products and further agreements with other Original Equipment Manufacturers (OEMs) are in development.

2. Underpinning research

Bayesian statistics is a powerful tool to produce novel technology in industry. In this project, a number of approaches developed at Durham University were used for applications in the X-ray industry. The methods used are best split into two areas of Durham's research: i) Bayes linear methods [**R1**], which were used to extract material information from IBEX's patented multi absorption plate (MAP) technology and develop an anomaly detection algorithm, and ii) their application to the analysis of complex computer models [**R2-R5**], which were used to a) build fast approximations (emulators) of an expensive simulator, b) solve the inverse problem of finding a patient's material composition from an X-ray image and c) make inferences in the real world using complex computer models to improve image quality and infer a patient's material composition.

It is often of interest to make inferences about the material composition (thickness and alloy) of an object being examined using X-ray imaging technology. In conventional X-ray imaging approaches, two different materials can look identical in the X-ray image. For example, a thick piece of aluminium can look identical to a thin piece of lead, meaning the problem of material inference is ill-posed. The MAP, developed by IBEX, helps resolve this problem by adding multi-spectral information into the X-ray image. Durham University, in collaboration with IBEX, developed novel approaches which in conjunction with Durham research into Bayes linear statistics [**R1**] and second order exchangeability [**R6**] resulted in the contaminant detection method. This method enabled different materials (and alloys of two materials) to be differentiated at any thickness, greatly enhancing the applicability of the MAP by IBEX [**E9**].

When X-rays travel through an object, they can either i) traverse the object unperturbed, ii) be absorbed or iii) scatter. Scatter is considered a form of spatially correlated noise which adds a deformed projection of the object onto the image, degrading image quality. To reduce scatter in clinical X-ray images, an anti-scatter-grid (ASG) is added. This engineering solution preferentially attenuates scattered photons reducing the scatter in an image. However, some unperturbed photons are also blocked meaning the dose to the patient is increased to compensate. A method, termed the scatter reassignment method (SRM), to mathematically remove scatter was developed using i) Bayes Linear emulation [**R3-R5**], to match a simulation of an X-ray image to an actual real world X-ray image. The simulator used by IBEX took days to run. In contrast, our Bayes linear emulator approximates the simulator and enabled IBEX to make this process much faster, taking around 6 seconds to run. ii) Bayesian inverse problem solving [**R3-R5**] which uses history matching using implausibility to say whether the simulated X-ray image matches the actual X-ray image. iii) Reified Bayesian analysis [**R2**]. A simulator is only a model of the real world and there is always a difference between the simulator and the system it purports to represent. Reified Bayesian analysis is a method of coherently i) analysing this difference between a simulator and the real world, ii) reducing that difference and iii) including knowledge of how large any remaining difference is in the analysis. This was a big advantage for SRM as other companies using simulators to remove scatter do not consider the difference between the simulator and the real world at all. In less statistical terms, i) it enables the simulator to get much closer to the real world, ii) provides a measure of confidence in the accuracy of the approach and iii) we know when the match is good enough that there is no point searching for a better one. There were two key outputs from SRM: i) improved image quality over that of an ASG and ii) we showed that it was possible to make inferences about material composition using scattered photons. This means that better image quality can be returned and, in some cases, at a lower dose to the patient. X-ray images are used to calculate diagnostics measures, for example, areal-Bone-Mineral-Density (aBMD). This measure is used to assess whether a patient has osteoporosis. In current practice, patients at risk of osteoporosis are sent for a specialised scan. We showed that, by considering scatter rather than removing it with an ASG, it was possible to estimate aBMD using standard X-ray examination equipment. Expert opinion was that the problem was ill-posed and for that reason it could not be solved. When scatter was considered, the problem was not in the Bayesian sense ill-posed and, therefore, aBMD could be estimated.

3. References to the research

R1. Goldstein, M., & Wooff, D. (2007). Bayes linear statistics: Theory and methods (Vol. 716). John Wiley & Sons. [https://doi.org/10.1002/pst.328]
Comment: The original research contained in **R1** was supported by a number of EPSRC grants, all of which were highly graded in final review.
R2. Goldstein, M., & Rougier, J. (2009). Reified Bayesian modelling and inference for physical systems. Journal of Statistical Planning and Inference, 139(3), 1221-1239. [DOI: 10.1016/j.jspi.2008.07.019]
Comment: This was chosen as the first ever discussion paper in this journal.
R3. Goldstein, M., & Rougier, J. (2006). Bayes linear calibrated prediction for complex systems. Journal of the American Statistical Association, 101(475), 1132-1143. [https://doi.org/10.1198/016214506000000203]
R4. Vernon, I., Goldstein, M., & Bower, R. G. (2010). Galaxy formation: a Bayesian uncertainty analysis. Bayesian analysis, 5(4), 619-669. [DOI:10.1214/10-BA524]
Comment: This paper extended history matching techniques for general heavy simulators in multiple directions and demonstrated these improvements on a large and complex model of Galaxy formation. Awarded the major worldwide prize in Bayesian statistics: the Mitchell Prize jointly awarded by the American Statistical Association and the International Society for Bayesian Analysis.
R5. Caiado, C. C. S., & Goldstein, M. (2015). Bayesian uncertainty analysis for complex physical systems modelled by computer simulators with applications to tipping points. Communications in Nonlinear Science and Numerical Simulation, 26(1-3), 123-136. [*http://dx.doi.org/10.1016/j.cnsns.2015.02.006*]
R6. Rougier, J., Goldtstein, M. & House, L. (2013) Second-Order Exchangeability Analysis for Multimodel Ensembles, Journal of the American Statistical Association, 108:503, 852-863, [https://doi.org/10.1080/01621459.2013.802963]

4. Details of the impact

IBEX Innovations Limited was created in 2010 to develop and commercialise an innovative X-ray detector technology. It has been collaborating with Durham since 2015 on Bayesian approaches to improving X-ray imaging [**E3**]. The collaboration has greatly enhanced the commercial capability of the patented technology and '*allowed a small North East company to compete on a world stage*' [**E3, E4, E5**]. Specifically, Durham research underpins their patented multi absorption plate (MAP) technology and their Trueview® product which uses the Scatter Reassignment Method (SRM) [**E9**]. IBEX has raised almost GBP6,000,000 in funds for product development and to secure international customers [**E2**], securing a total of 14 Jobs in the North East of England (gross value added for full time equivalent jobs to the North East is GBP662,144) [**E3, E4**].

The MAP technology developed by IBEX in collaboration with Durham University enabled inferences, not possible with standard X-ray methods, about the material composition of an object being imaged with the MAP equipped detector [**E3**]. A core technology at IBEX, it is at the base of a number of their products as outlined below.

1. The first product developed was for security, which enabled portable X-ray examination equipment capable of extracting accurate information about the materials being imaged. Portable X-ray examination systems are key for safety when objects being examined cannot be moved. For example, one may want to X-ray image a suspicious bag in an airport without moving it. IBEX signed a Joint Development Agreement (JDA) with 3DX-ray, (the main trading subsidiary of Image Scan Holdings plc), to incorporate IBEX technology into 3DX-ray's next product on an Innovate UK assisted project. [**E1b, E3**]. JDAs give a route to market for IBEX's technology and increase their revenues.

2. IBEX are also combining the MAP technology with their food inspection products. Recently, chocolate bar manufacturers have had to recall bars due to possible plastic contamination, therefore, an accurate plastic contamination system could save chocolate manufacturers the cost of recalling products and the negative media publicity associated with it. IBEX signed a JDA with Mettler-Toledo, a manufacturer of precision instruments, to develop a methodology for i) plastic contamination detection and ii) bone in chicken breast detection, on an Innovate UK assisted project (IBEX GBP109,163, Mettler-Toledo GBP24,775) [**E6**]. IBEX expect this product to generate revenues of GBP1,000,000 per annum and the JDA has already secured 3 jobs within the company [**E4**].

In addition to the research related to the MAP, our research supported the development of the SRM which is core IP at IBEX and forms the basis of their software patented product 'Trueview®' [**E3**]. SRM offers benefits of i) "really good image detail", ii) with "no additional equipment to reduce scatter, reducing the number of radiographs taken" (Nicola Hind, Consultant Radiographer, Royal Victoria Infirmary, Newcastle) [**E1**] and iii) improved diagnostic measures in medical X-ray images. IBEX obtained a software patent to protect the novel approaches developed in collaboration with Durham University (WO2016051212A1, GB2563115A) [**E5**]. The proof-of-concept helped IBEX receive numerous grants and venture capital funding to market their technology [**E1-E4, E6, E7**]. Current impact around Trueview® includes:

1. The Trueview® software has undergone clinical trial at The James Cook University Hospital in Middlesbrough [**E8**]. It measures a patient's bone health from a standard X-ray and initial trial results indicate that it provides an accurate early warning of osteoporosis, and therefore a patient's risk of potentially fatal fragility fractures. The study which was led by the orthopaedic research team, collaborating with colleagues in radiology and rheumatology, "compared images from the new software to results from 130 patients who had attended appointments for a DEXA bone scan at James Cook with positive results" [**E8**]. IBEX Trueview® offers early detection, early intervention and better outcomes. Poor bone health represents a substantial global healthcare challenge. In the UK, the NHS spends around £1bn per annum on the diagnosis and treatment of hip fractures, but sadly it remains the largest single cause of accident-related death. IBEX Trueview® provides opportunistic early screening for bone health of all patients referred for a Digital Radiography scan, enabling timely detection of early stage osteoporosis before debilitating hip fractures occur.
2. IBEX have signed an agreement with CurveBeam to integrate the Trueview® product into their products [**E2, E3**]. Leading cone-beam computed tomography systems (CBCT) manufacturer, CurveBeam LLC have chosen Trueview® to deliver unrivalled image quality for their weight-bearing CT products, including the new flagship HiRise system. CurveBeam President, Arun Singh, says that it produces "the best bilateral foot renders I have ever seen" [**E10a**]. CurveBeam specialises in weight bearing CT imaging **[E10b]**. The Curvebeam HiRise system has attained FDA approval with Trueview® incorporated so will be on sale shortly. Two HiRise systems were installed for investigational studies prior to FDA clearance at University of Iowa Carver School of Medicine's Department of Orthopedics and Rehabilitation in Iowa City, IA and at Tennessee Orthopaedic Clinics (TOC) in Knoxville, TN. Researchers at the University of Iowa have used HiRise for multiple research studies, including examining hip dysplasia infunctional position and evaluating wrist injuries in gymnasts. "The HiRise promises to revolutionize our biomechanical understanding of the entire lower extremity the same way previous generations of CurveBeam's weight bearing CT systems enabled better investigation into the foot, ankle

and knee," said Dr. Cesar de Cesar Netto, MD, PhD, Assistant Professor of Orthopedics and Rehabilitation at University of Iowa [**E10c**].

3. IBEX have signed a licensing agreement to integrate Trueview® into Planmed's Clarity 2D, Clarity 3D and Clarity S mammography systems [**E2, E7**]. The company is part of Finnish Planmeca Group, a well-known company in the medical and dental field which provides tools for healthcare professionals in over 80 countries worldwide. The target release for this product has been delayed by Covid-19. Trueview® enables better image quality, improved workflow and better patient outcomes. It has been demonstrated to give better contrast in 2D and 3D mammograms – with up to 50% lower patient dose and up to 25% less breast compression [**E7**]. Of the collaboration Mr Jan Moed, Managing director of Planmed says "We are constantly listening to our customers and developing our product lines accordingly. We feel that this collaboration will bring added value, not only for the users but ultimately for the patients which is what really matters," [**E7**].
4. A grant has been obtained by IBEX to see how Trueview® can improve AI algorithms. This resulted in one new hire. The grant number is 44808 and the award was for GBP288,136 and a continuity grant 74463 was obtained for GBP100,000. [**E6**].

In summary, Durham research underpins the technology that is enabling IBEX to grow as a company, receive funding and take products to market [**E3, E4**]. Ian Wilson, who leads Mercia's team in the North East of England, which provided funding via the North East Venture Fund to IBEX, says: "IBEX is the only one in the market that can achieve this quality of images. The company continues to make progress in both developing new products and new commercial relationships. Mercia is delighted to support IBEX once again and help roll out this new system which will be an important step forward in breast cancer detection.'' [**E2**].

5. Sources to corroborate the impact

[E1] A. collection of IBEX announcements B. Image Scan Holdings - https://www.research-tree.com/newsfeed/ArticleOffset?articleSeoTitle=preliminary-results-608859&page=3
[E2] Medical technology firm IBEX brings in more than GBP500,000 of new investment - https://www.business-live.co.uk/technology/medical-technology-firm-ibex-brings-18256755
[E3] Letter from Chief Technical Officer IBEX Innovations
[E4] Letter from Chief Scientific Officer IBEX Innovations
[E5] IBEX's MAP technology is covered by UK patents: GB2498615, GB2532634, GB2532897, GB2533233, GB2563115A, WO2016051212A1.
[E6] List of Ibex grants
[E7] Planmed and IBEX Innovations sign a collaboration agreement - https://www.planmed.com/press/news-main-page/planmed-and-ibex-innovations-sign-a-collaboration-agreement/
[E8] A. Talking point, Autumn 2020 discussing Trueview clinical trial success - https://www.southtees.nhs.uk/content/uploads/Talking-Point-Autumn-2020-web-3.pdf B. Details on the clinical trial results - https://www.ibexmedical.co.uk/wp-content/uploads/2020/07/IBEX-Trueview-Bone-Health-July-2020.pdf
[E9] IBEX white paper, pages 22 and 30 show acknowledgements to Durham University collaboration
[E10] A. The New Standard For CBCT - https://www.ibexmedical.co.uk/1817-2/ and B. Curvebeam website - https://curvebeam.com/about/curvebeam/ and C. FDA 510(K) clearance (https://curvebeam.com/news/curvebeam-announces-fda-510k-clearance-for-hirise-weight-bearing-ct-system-for-the-entire-lower-extremity/)