Institution: AECC University College

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

Title of case study: Dynamic biomechanical imaging assessment of spinal joints

Period when the underpinning research was undertaken: 1 Jan 2002- 31 Dec 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:**
Alan Breen	Professor of Musculoskeletal Health Care	1986-present
Alexander Breen	Senior Research Fellow	2010-present
Fiona Mellor	Senior Lecturer	2002-4, 2009-14, 2019-present
Alister du Rose	Senior Lecturer	2012-15, 2020-present

Period when the claimed impact occurred: 1 August 2013 to 31 December 2020

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

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

This case study describes the development, validation, dissemination, engagement activity and commercialisation of quantitative fluoroscopy (QF) - a technology based on fluoroscopy and image processing - for performing biomechanical examinations of the spine for the clinical assessment of treatment resistant spinal pain. Through multiple international collaborative partnerships, the researchers have contributed a number of resources that have been used by spine clinicians, imaging services and the international medical devices and spine research communities. These are based on methodologies for the use of key measurement indices and their normative values and reliability as human phenotypes and biomarkers in nonspecific spinal pain.

2. Underpinning research (indicative maximum 500 words)

In 2002, **BREEN A** obtained a grant from the NHS New and Emerging Application of Technology programme for the development of a prototype QF system in collaboration with the Radiology Department and Spinal Treatment Centre at Salisbury District General Hospital. Following completion of this project, the AECC University College (AECC UC) obtained a contract with Zimmer Spine Ltd and collaborated with radiologists and surgeons at the Royal Hampshire County Hospital in a study of a flexible spinal implant. AECC UC purchased a Siemens Avantic C-arm fluoroscope in 2008, whereupon **BREEN Ax**, a medical physicist, joined the team to support clinical research and commercialisation, investigating normative values for intervertebral motion and relationships between this and back pain. The following studies have provided the first evidence of these. In all, they have received more than 8000 downloads.

From 2014 to 2020, **BREEN A, BREEN Ax** and **MELLOR** conducted studies that were the first to show that uneven motion sharing between vertebrae during recumbent passive motion is an objective biomarker for nonspecific low back pain (1). They replicated these results in three

further studies (e,g, 2). **BREEN A** and **BREEN Ax** also demonstrated the kinds of spinal surgery that have the greatest associations with aberrant spinal mechanics and showed that excessive intervertebral translation and laxity have little relationship to nonspecific back pain. They published these findings in leading journals and discovered a further biomarker based on upright active motion (3). They also established normative values, repeatability and other biomarkers (4) in collaboration with Cardiff University, CMCC in Canada and UCO in London, providing a basis for use in longitudinal studies.

In 2015, AECC UC purchased a 3T open upright MRI scanner and used it with QF to investigate relationships between disc degeneration and back pain. Having already discovered that disc degeneration is present with back pain only if the sharing of motion between vertebrae is abnormally unevenly distributed. (1), the team went on to disprove the longstanding theory that early to moderate disc degeneration is associated with spinal instability (5) (Radiological Research Trust grant). A subsequent study included **DUROSE** and added electromyography during motion, confirming the theory that muscle activity during bending stabilises the spinal segments, supporting the use of back strengthening exercises and bracing during lifting (6). These outputs have been highly accessed, leading to considerable debate in the back pain research community worldwide.

The researchers concurrently entered into a number of collaborations with other groups interested in the QF technology and conducted studies into relationships between intervertebral motion and spine loading with colleagues at the universities of Exeter (UK), (CRC grant) Koblenz-Landau (Germany) and KU Leuven (Belgium), as well as extending the motion investigations to the cervical spine in further collaborations with colleagues in the Faculty of Health and Social Care at Bournemouth University and in the Department of Health Science and Technology at Aalborg University (Denmark). These studies quantitatively described the normal kinematic control of the neck at segmental level for comparison with injured patients, patients who received neck surgery and people with whiplash-associated disorders.

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

1. **BREEN A., BREEN AX.** (2017) Uneven intervertebral motion sharing is related to disc degeneration and is greater in patients with chronic, non-specific low back pain. An in-vivo, cross-sectional cohort comparison of intervertebral dynamics using quantitative fluoroscopy. European Spine Journal 27:145–153. https://doi.org/10.1007/s00586-017-5155-y

2. **BREEN AX, MELLOR F., BREEN A.** (2018) Aberrant intervertebral motion in patients with treatment-resistant nonspecific low back pain: a retrospective cohort study and control comparison. European Spine Journal 27:2831–2839. https://doi.org/10.1007/s00586-018-5666-1

3. **BREEN AX, BREEN A.** (2020) Dynamic interactions between lumbar intervertebral motion segments during forward bending. Journal of Biomechanics (invited paper) 102:26. https://doi.org/10.1016/j.jbiomech.2020.109603

4. **BREEN AX**, HEMMING R, MELLOR FE, **BREEN A**. (2018) Intra-subject repeatability of in vivo intervertebral motion parameters using quantitative fluoroscopy. European Spine Journal 28:450-460. http://link.springer.com/article/10.1007/s00586-018-5849-9

5. **BREEN A, MELLOR F**., MORRIS A, **BREEN AX.** (2020) An in-vivo study exploring correlations between early-to-moderate disc degeneration and flexion mobility in the lumbar spine. European Spine Journal 29:2619–2627. https://doi.org/10.1007/s00586-020-06526-0

6. **DU ROSE A, BREEN AX, BREEN A.** (2018) Relationships between muscle electrical activity and the control of intervertebral motion during a forward bending task. Journal of Electromyography and Kinesiology 43:48-54. https://doi.org/10.1016/j.jelekin.2018.08.004

Grants

Radiological Research Trust – MRI studies of the relationships between disc degeneration and intervertebral motion. F Mellor 2015-17 £3000

Chiropractic Research Charity (CRC) - Estimation of in vivo inter-vertebral loading during motion using fluoroscopic and MRI informed finite element models A Breen, J Meakin 2015-2017 £40,344

European Space Agency: Testing the Mk VI microgravity countermeasure 'Skinsuit' Ground-based Study A. Breen, Ax Breen, P Carvil 2017-19 £41,716

Patents

European Patent Office – Method for Imaging the Relative Motion of Skeletal Segments - EP 1 519 681 B1, published 29/11/2006.

US Patent Office - Method for Imaging the Relative Motion of Skeletal Segments - USP 7,502,641, published 3/10/2009

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US Patent Office - Devices, Systems and Methods for Measuring and Evaluating the Motion and Function of Joint Structures and Associated Muscles, Determining Suitability for Orthopedic Intervention, and Evaluating the Efficacy of Orthopedic Intervention – US 11/734,623, published 04/12/2007

FDA clearance
DEVICE: THE KINEGRAPH VMA (VERTEBRAL MOTION ANALYZER) SOFTWARE VERSION 2.2, THE MOTION NORMALIZER PATIENT HANDLING AND DATA ORTHO KINEMATICS, INC. 510(k) NO: K133875(SPECIAL) ATTN: JOHN J SMITH PHONE NO : 202 637 3638 555 13TH STREET, NW SE DECISION MADE: 17-JAN-14 WASHINGTON DC 20004 510(k) SUMMARY AVAILABLE FROM FDA
http://google2.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/510kClearances/ucm384648.htm

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

Services and Impacts where the beneficiaries may include businesses and services (new or established, private or NHS).

In 2001, **BREEN A** received a grant from the New and Applied Application of Technologies (NEAT) initiative (NHS R&D) to develop and validate QF for research and clinical use (No. B020) in collaboration with the Duke of Cornwall Spinal Unit in Salisbury **(S1**). The technology was patented internationally (see Patents) and a US start up medical devices company (Ortho Kinematics) was given an exclusive commercial licence. This attracted over $10m of start-up funding and established over 40 US imaging centres plus a central processing facility. The service was used by spinal surgeons for the presurgical assessment of over 10,000 patients **(S2)**. In 2011, AECC UC obtained research contracts from Ortho Kinematics to validate the technology in support of FDA clearance (see FDA clearance) allowing reimbursement of investigations for spinal surgery in the USA.

In 2003, the technology entered research and clinical use at the Institute of Orthopaedics in the Robert Jones and Agnes Hunt Orthopaedic Hospital in Oswestry. From 2004 to 2019, **BREEN A**

collaborated with spinal surgery departments in Oswestry, Salisbury, Winchester and Poole hospitals in the assessment of problem spinal patients, while refining the technology and further validating it. In 2008, AECC UC purchased a C-arm fluoroscope, motion standardisation equipment and computing hardware and software to progress the research **(S3**). Ninety-six patient referrals were received from musculoskeletal practitioners as far away as Norway, as well as from the Spinal Multidisciplinary Diagnostic Team at Poole Hospital **(S4)**.

In 2011 a PhD study in neck pain patients enabled us to give advice to the Chair of the House of Commons Transport Select Committee on the mechanics of whiplash associated disorder.

Evidence of debate among practitioners, leading to developments in attitudes or behaviours.

This work has been elicited engagement at a number of levels. Additional collaborations have begun in low back studies with 1. the Institut für Sportwissenschaft,at the University of Koblenz-Landau in Germany for measuring ligament stresses in the spines of patients, 2. at the Catholic University of Leuven in Belgium and 3. at the Memorial University of Newfoundland to determine the accuracy of surface motion capture against QF as a gold standard for measuring vertebral motion. Since 2019, QF has been cited as the gold standard measure of spinal motion in patients **(S5)**. A Centre for Intelligent Spinal Biomechanics Research has been established at Bournemouth University in co-operation with AECC UC to utilise AI techniques for image registration and tracking.

This research has also had media coverage, notably the discovery of back pain biomarkers (S6) and evidence supporting avoidance of static radiographs for measuring instability **(S7)**. The research and its normative values and biomarkers have been reported in keynote papers and debated at international conferences, including the International Workshop on Spine Loading and Deformation in Berlin (2019), the North American Spine Society in 2015 and 2017 and two World Conferences on Low Back and Pelvic Pain in Singapore in 2017 and Antwerp in 2019. These led to a UK Society for Back Pain Research (SBPR) conference hosted by **BREEN A** titled “Biological factors in back pain” in 2015. Subsequently, the International Forum on Low Back and Neck Pain in Oslo in 2017 resolved that “Mechanisms” should be the next priority for back pain research. This was also SBPR’s theme for its subsequent meeting in Groningen in the Netherlands. **BREEN A** then co-authored an article published in the Journal of Orthopaedic and Sports Physical Therapy in 2019 as an international point-counterpoint debate **(S8)**. This concluded that biomechanics is useful in back pain diagnosis, but not as the sole factor. Some other research centres have adopted the fluoroscopic image tracking methods used in our studies over the past 10 years (Pittsburgh, Zurich, Harvard universities) using 3-D methods. Through public engagement **(S9)**, it has been a vehicle for improving the understanding of back pain.

From 2017-19 the researchers were contracted by the European Space Agency. In collaboration with the Centre of Aerospace and Physiological Sciences at Kings College London to study the effects of an astronaut microgravity countermeasure skinsuit used prior to return to earth. The aim was to reverse intervertebral disc swelling due to prolonged unloading in space. This is known to be associated with back pain and disc herniation on return to terrestrial gravity and is a barrier to longer space missions. The results have provided evidence that this countermeasure is effective and is under consideration by the ESA **(S10)**.

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

S1. The former Consultant Radiologist who participated in our research partnership with the Clinical Radiology Department at Salisbury District General Hospital can corroborate the research collaboration undertaken under the NHS NEAT project.

S2 The former Clinical Director of Ortho Kinematics can corroborate the activity of the first commercial partner, Ortho Kinematics.

S3 A publicly viewable video shows the imaging protocol used for QF in the European Space Agency studies.
https://www.youtube.com/playlist?list=PLc2dt6-8xH2jyKyu_VKqpdDfT9tLSBZ8P

S4 A patient whose QF investigation in 2018 enabled the avoidance of a third and unnecessary spinal surgery can corroborate the personal impact of the investigation.

S5 An article by Zwambag, D.P., et al., (Distinguishing between typical and atypical motion patterns amongst healthy individuals during a constrained spine flexion task) Journal of Biomechanics, 2019. 86: (introduction) confirms that QF is regarded as a gold standard fo measuring spine motion. https://doi.org/10.1016/j.jbiomech.2019.01.047

S6 Orthopaedics Weekly featured our discovery of the first biomarker for nonspecific low back pain in 2018 https://ryortho.com/breaking/new-insights-into-causes-of-back-pain/

S7. RAD Magazine featured our research which showed that QF assessment is superior to end of range radiographs for detecting spine instability in 2020.
https://www.radmagazine.co.uk/aecc-university-college-provides-insights-into-spine-instability/

S8 An international expert debate on the usefulness of spine biomechanics research in patient care was informed by our work and was published in the Journal of Orthopaedic and Sports Physical Therapy in 2019 (BREEN) www.jospt.org/doi/abs/10.2519/jospt.2019.8825

S9 A public engagement lecture to the Bournemouth Natural Science Society in August 2020 described the role of QF under “New Approaches to Understanding Back Pain”.
https://www.youtube.com/watch?v=eyffnwLgKno

S10 The HealthTec Cluster Manager at the Business and Innovation Directorate, Science and Technology Facilities Council, UK Research and Innovation can corroborate our collaboration with the Centre of Aerospace and Physiological Sciences at Kings College London that investigated the effectiveness of the ESA’s microgravity countermeasure skinsuit.