Institution: University of Leeds

Unit of Assessment: 12

Title of case study 2: Lower wearing, longer lasting joint replacements in the hip and knee

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

This UoA has developed the largest independent simulation laboratory in the world for pre-clinical evaluation of the wear of artificial joints, which has been used to develop and commercialise novel pre-clinical simulation systems for joint replacements, in partnership with Simulation Solutions Ltd. Simulation Solutions Ltd is now the market leader of joint simulation systems outside North America.

We have also co-developed lower wearing ceramic-on-ceramic and ceramic-on-metal bearings for hip joints, and have worked with DePuy Orthopaedics Inc to define lower wearing tribological solutions for polyethylene knees. This work has benefited hundreds of thousands of patients worldwide during the REF period.

2. Underpinning research (indicative maximum 500 words)

This case study is underpinned by research led by Professor J. **Fisher** in this UoA and Professor E. Ingham of UoA 5 at the University of Leeds. **Fisher** is Principal Investigator on the grants [i]-[xii] listed in Section 3.

The need to develop lower wearing bearings for total joint replacements for younger, more active patients emerged during the 1990s. Laboratory joint simulators were developed to undertake research, support new product development and conduct pre-clinical testing.

In 1997, this UoA initiated a partnership with Prosim (now Simulation Solutions Ltd) with the aim of developing joint simulation systems that could be used for their own research, by other research laboratories and by implant manufacturers. The partnership, which has lasted over 15 years, has brought together the University's research expertise in joint replacement, biomechanics and tribology with the company's expertise in control systems, robotics and commercialisation.

The initial collaborative research project with Simulation Solutions [grant i] led to the development of a ten-station hip simulator, which was used in studies of polyethylene wear in acetabular cups. The University's tribological research defined new input wave forms for the simulator that were subsequently adopted by the ISO Standard in 2000. The research validated the simulator design and generated reference data for standard polyethylene cups [1] and extended the simulation methods to replicate a wider range of clinical conditions [2].

The researchers expanded their collaborative research with Simulation Solutions [ii, iii] to develop the first knee joint simulator that enabled control of the AP axis and IR axis in either force or displacement mode [3]. This system was used to investigate the effect of kinematics and design on polyethylene wear in the knee [4]. A fifth active axis, an abduction adduction torque, was subsequently added, which generated femoral condylar lift off motion and resulted in an increase in wear [5].

The simulation systems have been applied in collaborative tribological research with industry to develop lower wearing, longer lasting hip joints [grants v, vi] between 2000 and 2008. The researchers were the first to show that alumina ceramic bearings produced stripe wear when subjected to edge loading and showed that ceramic-matrix-composite ceramic-on-ceramic bearings had lower wear under these adverse conditions than alumina ceramic-on-ceramic bearings [2] in 2003. The researchers developed and patented the novel differential-hardness ceramic-on-metal bearing, which had lower wear compared to metal-on-metal bearings [6] in 2001.

In the knee, the researchers defined, in collaboration with DePuy, the mechanism of reduced polyethylene wear in the rotating-platform knee design, resulting from the decoupling of motions and reduction in cross shear [4] in 2005. In fixed bearing knees, the team's tribological research [viii, x] has shown that polyethylene wear is dependent on surface area and demonstrated a

reduction in wear in low-conforming knees.

The excellence of this research has resulted in Fisher's Presidential guest lectures at the American Hip Society and American Knee Society, and the Queen's Anniversary Prize for Higher and Further Education in 2011 to the University of Leeds.

Research Team

Professor J. **Fisher**, 1990-present.
Dr L. **Jennings**, Research Fellow, 2001-2004, Senior Research Fellow, 2004-2012 Assoc, Prof.
Dr T. **Stewart**, Research Fellow, 1997-2006, Lecturer, 2006-2009, Senior Lecturer, 2009-present.
Dr J. **Tipper**, Research Fellow, 2001-2009, Senior Lecturer, 2009-present.
Professor E. Ingham (UoA 5), 1990-present.

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

1. Barbour PSM, Stone MH, **Fisher** J. A hip joint simulator study using new and physiologically scratched femoral heads with ultra-high molecular weight polyethylene acetabular cups. Proceedings of the Institute of Mechanical Engineers. Journal of Engineering in Medicine, 214H; 569-576 (2000), DOI: 10.1243/0954411001535598.
2. **Stewart** TD, **Tipper** JL, Insley G, Streicher RM, Ingham E, **Fisher** J. Long-term wear of ceramic matrix composite materials for hip prostheses under severe swing phase micro separation. Journal of Biomedical Materials Research, Applied Biomaterials, 66B; 567-573 (2003), DOI: 10.1002/jbm.b.10035.
3. Barnett PI, McEwen HMJ, Auger DD, Stone MH, Ingham E, **Fisher** J. Investigation of wear of knee prostheses in a new displacement/force-controlled simulator. Proceedings of the Institute of Mechanical Engineers. Journal of Engineering in Medicine, 216H; 51-61 (2002), DOI: 10.1243/0954411021536289.
4. McEwen HMJ, Barnett PI, Bell CJ, Farrar R, Auger DD, Stone MH, **Fisher** J. The influence of design, materials and kinematics on the in vitro wear of total knee replacements. Journal of Biomechanics, 38; 357-365, (2005), DOI: 10.1016/j.jbiomech.2004.02.015.
5. **Jennings** LM, Bell CJ, Ingham E, Komistek RD, Stone MH, **Fisher** J. The influence of femoral condylar lift-off on the wear of artificial knee joints. Proceedings of the Institution of Mechanical Engineers. Journal of Engineering in Medicine, 221H; 305-314 (2007), DOI: 10.1243/09544119JEIM215.
6. Firkins PJ, **Tipper** JL, Ingham E, Stone MH, Farrar R, **Fisher** J. A novel low wearing differential hardness, ceramic-on-metal hip joint prostheses. Journal of Biomechanics 34; 1291-1298 (2001), DOI: 10.1016/S0021-9290(01)00096-3.

Note: All of the above journals are internationally recognised with rigorous review processes and international editorial boards. The quality of the underpinning research being at least 2* is demonstrated by references 2, 4 and 5.

Underpinning Research Grants (with Fisher as PI)

i) Fisher & Ingham.. A ten station hip simulator for study of wear and wear debris in acetabular cups, EPSRC GRL 28715, 1997-2000; £50K.
ii) Fisher, Ingham & Stone. JREI; A five station knee joint simulator; EPSRC GRL 84995, 1998-2001; £62K.
iii) Fisher, Ingham & Stone. A six station knee joint simulator, EPSRC GR92096; 2000-2003; £72K.
iv) Fisher, Ingham & Stone, Tribology, wear debris and biological reactions to metal on metal and ceramic on metal bearings; EPSRC GRK 9742401, 1997-2001; £146K.
v) Fisher & Ingham, Functional biocompatibility and osteolytic potential in orthopaedic implants; EPSRC GRM 94274, 2000-2003; £400K.
vi) Fisher & Ingham Portfolio Partnership Tissue replacement and regeneration; EPSRC GRS63891, 2003-2008; £2.2M.
vii) Fisher, Ingham *et al.* Furlong Research Charitable Foundation; Wear of meta-on-metal and ceramic-on-ceramic hips. 01/07/07-30/06/10; £286K.
viii) Fisher, Ingham *et al*. Platform Grant, Functional Tissue replacement and Substitution: EPSRC EPF04387201, 1/10/08-30/09/13; £817K.
ix) Fisher. NIHR Senior Investigator award; 01/06/08-30/05/16; £105K.

x) Fisher, Ingham *et al.* WELMEC Centre of Excellence in Medical Engineering; Wellcome Trust and EPSRC, WT088908/z/09/z, 01/10/09-30/09/2014; £11.2M.
xi) Fisher, Willams,Tipper. DePuy Technology Partnership. 01/01/2001-01/01/2014; £4M.
xii) Fisher & Jennings, Mathys; Tribology of ceramic hips, 01/01/2008-01/01/2013; £200K.

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

Reference letters refer to sources of impact in section 5, reference numbers to research papers in section 3.

Source [A] and statement [B] confirm that the research [1,3] has supported Simulation Solutions in the development and commercialisation of novel hip and knee joint simulators. Specifically it has:

- Supported the design and co-development of the simulation systems;
- Commissioned, evaluated and validated new simulation systems;
- Produced control and reference data over 5 billion cycles of reference data.
- Provided training and standard operating procedures for users and customers
- Published journal papers on the simulation systems company web site.

The simulation facility established in this UoA has over eighty stations offering full-joint simulation in Class 2 clean rooms and is believed to be the largest academic facility in the world [1,2,3,4]. These simulators have been used to support product development, to assess performance and evaluate safety and reliability of joint replacements.

We have worked in partnership with industry to research, invent and develop novel lower wearing bearings for the hip. The ceramic-on-metal hip [6] developed with DePuy [C,D] and the tougher and lower wearing [2] ceramic-matrix-composite bearings [E] developed with DePuy and Mathys were both major strides in this area. In the knee, the research [4] has supported the development and adoption of the DePuy Sigma rotating-platform knee [F] and a new low-conforming partial knee [G].

The advanced hip simulation systems have also been used to quantify the increase in wear in larger diameter metal-on-metal hip replacement systems due to edge loading [H]. This provided evidence that informed the subsequent decision to discontinue their clinical use.

Economic impact

Demand for pre-clinical joint simulation systems has increased substantially since 2007, following the reclassification of joint replacements as Class 3 devices. The regulatory environment now requires most hip and knee joint replacements to undergo pre-clinical tribological simulation testing before entering clinical use.

Statement [B] confirms that: Simulation Solutions have increased their annual turnover to £2M/year and now employ 20 people to develop and manufacture hip joint simulation systems; the company's joint simulation systems are sold around the world, in China, India, Australia and Europe and the company is the market leader outside of North America.

Economic impact has been made through support for Simulation Solutions customers in the use of the technology. This is delivered through the licensing of standard operating procedures and a training-support package from the University to customers. One example is an agreement between the University of Leeds, Simulation Solutions and the Chinese Food & Drug Administration (CFDA) that has led to the installation of Simulation Solution simulators in CFDA laboratories in Tianjin [I].

Economic impact has also been delivered through the University's ISO-accredited research laboratory. This facility has supplied contract research services to industry and supported companies in developing products to meet new regulations. Not all implant manufacturers have joint simulation systems. This is particularly true of small- to medium-sized enterprises. The University has supported new product development in orthopaedic companies including Mathys, JRI, Ceramtec, Ceramconcept, and Corin. Collaboration with Mathys has supported the development of the new ceramic–matrix-composite ceramic-on-ceramic hip for clinical use [J].

The 12-year-long strategic research partnership with DePuy [K] has supported the development of improved bearings with lower wear. Statement [L] confirms that this has helped DePuy protect its market share and meet the expectations of high-demand patients [L]. Some figures describing the extent of the impact of the research at Leeds are:

- Approximately 10,000 ceramic-on-metal hips implanted worldwide. There has been a 97% success rate at five years for 1,500 hips in the UK registry
- Over 300,000 ceramic femoral heads sold and implanted outside of the USA since 2008, for which the University of Leeds has received a royalty payment from DePuy [M]

Statement [L] from DePuy confirms that our advanced research methods have been adopted by industry and that 15 DePuy R&D staff have been trained in Leeds. The adverse hip simulation methods and edge loading of the head on the rim of cup and advanced knee simulation methods are used in DePuy company testing laboratories in the UK and USA.

Health impact

Young, active and high-demand patients with improved lower wearing prostheses benefit from extended active working lives. The reduction in wear-related failures and revision operations provide benefits to healthcare providers. The research has led to the collaborative development of improved prostheses [C,D,E,F,G], following clinical trials [D], this has resulted in lower wearing joint replacements used by hundreds of thousands of patients worldwide.

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

A. Company web site (accessed December 2012) www.prosim.co.uk or www.simsol.co.uk
B. Simulation Solutions Letter supporting evidence from Managing Director.
C. Fisher J & Farrar R. Combination of material for joint prosthesis. UK Patent. PCT/GB00/03428 2001.
D. *Williams S, Schepers A, Isaac G, Hardaker C, Ingham E, van der Jagt D, Breckon A, Fisher J.* The 2007 Otto Aufranc Award. Ceramic-on-metal hip arthroplasties: a comparative in vitro and in vivo study. Clinical Orthopaedics & Related Research, 465; 23-32 (2007).
E. Al-Hajjar M, Leslie IJ, Tipper J, Williams S, Fisher J, Jennings LM. Effect of cup inclination angle during microseparation and rim loading on the wear of BIOLOX® delta ceramic-on-ceramic total hip replacement. Journal of Biomedical Materials Research Applied Biomaterials 95, 263-268 (2010)
F. Fisher J, McEwen HMJ, Jennings LM, Farrar R, Stone MH, Ingham E. Wear-simulation analysis of rotating-platform mobile-bearing knees. Orthopaedics, 29; 36-41 (2006).
G. Brockett CL, Jennings LM, Fisher J. The wear of fixed and mobile bearing unicompartmental knee replacements. Proceedings of the Institution of Mechanical Engineers, Part H, Journal of Engineering in Medicine 225H; 511-519 (2011).
H. Leslie IJ, Williams S, Isaac G, Ingham E, Fisher J. High Cup Angle and Microseparation Increase the Wear of Hip Surface Replacements. Clin Orthop Relat Res, 467-9, 2259-2265, (2009).
I. Licence agreement for standard operating procedure and training 2012, University of Leeds commercial contract.
J. Research contracts with Mathys. University of Leeds research contract.
K. Strategic research partnership agreement with DePuy University of Leeds contract.
L. DePuy Company Letter of supporting evidence from DePuy from Distinguished fellow and from worldwide tribology manager.
M. Royalty agreement DePuy 2008 University of Leeds commercial contract.