Institution: Newcastle University

Unit of Assessment: 12 Aeronautical, Mechanical, Chemical and Manufacturing Engineering

Title of case study: Supporting national and international policy development on the use of metal-on-metal hip implants

1. Summary of the impact

The high failure rate of metal-on-metal hip implants led to worldwide concern. Collaborative research between Newcastle University and University Hospital of North Tees identified design features that are considered to have contributed to the failure. The research helped to inform policy makers both nationally, such as the Medicines and Healthcare products Regulatory Agency (MHRA), and internationally, such as the US Food and Drug Administration (FDA). The final outcome was a worldwide withdrawal of one design of implant (the DePuy ASR) and a ban in several countries of a set of implants sharing common features (large head metal-on-metal total hip replacements). The research has reduced the risk of harm to patients who will now receive products with a significantly lower failure rate, and will have financial implications for implant manufacturers and healthcare providers.

2. Underpinning research

Metal-on-metal (MoM) hip replacements were originally introduced in the 1950s as an alternative to the original metal-on-polyethylene designs. They were further developed through the 1980s and early 1990s, both as a replacement and a resurfacing (where only the bearing surfaces of the hip are replaced), with the aim of providing a longer lasting product for the increasing number of younger people who required hip replacement. However, concerns started to be raised from 2006 onwards about their performance.

Research at Newcastle has covered two main areas:

(i) Identifying the reasons for failure of a specific MoM hip resurfacing (the DePuy Articular Surface Replacement, ASR).

(ii) Investigation of generic design features that affected several different types of large-diameter head MoM total hip replacements.

Initial exploratory research in 2007 by Joyce at Newcastle University in collaboration with Langton and Nargol at the University Hospital of North Tees, investigated possible causes of abnormal wear in the ASR hip. Radiography was used to determine the orientation of the cup component of the implant within the patient, and blood samples were taken to determine levels of cobalt (Co) and chromium (Cr) metal ions. This initial work (P1, as listed in section 3) found that metal ion concentration was associated with orientation of the ASR cup, and was the first to demonstrate that the ASR cup was particularly vulnerable to sub-optimal placement. Publication of this and subsequent research was in the Journal of Bone and Joint Surgery, which was selected as it is widely read by the orthopaedic surgeons who decide which implants to use in their patients. Awarded as a consequence of P1, grant G1 allowed this collaborative work to continue, increasing the number of hips studied and providing a comparison to the Birmingham Hip Resurfacing (BHR) and Conserve Plus (C+); two similar, well-established, implants. Two grants (G2 and G3) supported further work (P2-P4, published between 2008 and 2011) that revealed two aspects: firstly, that ASR hips had a significantly higher Co concentration than BHR hips, and secondly that the ASR cup was sensitive to sub-optimal positioning due to the shallow nature of the cup (P2). In 2010, 418 ASR and 155 BHR patients were investigated (P3) for adverse reaction to metal debris. This paper found that all patients with such an adverse reaction had ASR hips, whereas no adverse reaction was seen in BHR patients. The largest study of hip resurfacings at the time of publication (P4) was carried out in 2011, analysing over 4200 ASR, BHR and C+ hips. ASR

patients had a significantly higher risk of revision (where the implant requires replacement) than those with BHR or C+, as a consequence of an adverse reaction to metal debris. The ASR was confirmed as the most vulnerable to positioning of the cup, a critical factor since consistency of placement during surgery cannot currently be guaranteed.

The second area of research was into failure of large-head MoM total hip replacements. Starting in 2009, Joyce, Lord, Langton and Nargol quantified wear in failed total hip replacements (P5) using a co-ordinate measuring machine funded by G1. It was found that material was lost from both the articulating surfaces and from the junction of the head and neck of the implant. Further research led to the first paper in the field (P6) to quantify loss from this junction, which was proposed to be a result of two design elements common to most large-head (≥36mm) MoM total hip replacements: the reduction in the size of the taper connection and the increase in diameter of the femoral head.

The key researchers at Newcastle University have been:

- **Joyce**: Lecturer in Bioengineering 2007-2009; Senior Lecturer in Bioengineering 2009-2010; Reader in Biotribology 2010-12; Professor of Orthopaedic Engineering, 2012 to date.
- **Langton**: Research Fellow, 2008-2010 (and also research registrar at the University Hospital of North Tees from 2007-2008).
- **Lord**: PhD Student, 2008-2011.

3. References to the research

Publications:

P1. D J Langton, S S Jameson, T J Joyce, J Webb, A V F Nargol (2008). The effect of component size and orientation on the concentrations of metal ions after resurfacing arthroplasty of the hip. Journal of Bone and Joint Surgery (JBJS). **90B** (9): 1143-51. DOI:10.1302/0301-620X.90B9.20785.
***Key paper**: the first paper in the field to identify the specific vulnerability of the DePuy ASR that led to high blood metal ion concentrations. The Journal of Bone and Joint surgery is a leading journal in orthopaedics, widely read by orthopaedic surgeons.*

P2. D J Langton, A P Sprowson, T J Joyce, M Reed, I Carluke, P Partington, A V F Nargol (2009). Blood metal ion concentrations after hip resurfacing arthroplasty: a comparative study of ASR and BHR arthroplasties. JBJS **91B** (10): 1287-95. DOI: 10.1302/0301-620X.91B10.22308.

P3. D J Langton, S S Jameson, T J Joyce, N J Hallab, S Natu, and A V F Nargol (2010). Early failure of metal-on-metal bearings in hip resurfacing and large-diameter total hip replacement: a consequence of excess wear. JBJS **92B**, 38-46. DOI: 10.1302/0301-620X.92B1.22770.

P4. D J Langton, T J Joyce, S S Jameson, J Lord, M Van Orsouw, J P Holland, A V F Nargol, K D De Smet (2011). Adverse reaction to metal debris following hip resurfacing: the influence of component type, orientation and volumetric wear. JBJS **93B**, 164-171. DOI: 10.1302/0301-620X.93B2.25099. DOI: 10.1302/0301-620X.93B8.26040.
***Key paper**: the largest study, outwith a national register, of the performance of metal-on-metal hip resurfacings.*

P5. D J Langton, S S Jameson, T J Joyce, J N Gandi, R Sidaginamale, P Mereddy, J Lord, A V F Nargol (2011). Accelerating failure rate of the ASR total hip replacement. JBJS **93B** (8): 1011-1016. DOI: 10.1302/0301-620X.93B8.26040.

P6. D J Langton, R Sidaginamale, J Lord, A V F Nargol, T J Joyce (2012). Taper junction failure in large-diameter metal-on-metal bearings. Bone and Joint Research **1** (4): 56-63. DOI: 10.1302/2046-3758.14.2000047.
***Key paper**: the largest study of failed taper junctions in large head metal-on-metal total hip replacements.*

Key Research Grants:

G1. Joyce and McCaskie. Ex vivo analysis of failed resurfacing hip prostheses. £143,282. British Orthopaedic Association, April 2009-October 2010.

G2. Joyce. Service for the investigation of failed lower limb arthroplasties. £29,318. Newcastle University EPSRC Knowledge Transfer Account. November 2010-September 2012.

G3. Joyce. When technology fails patients: engaging with stakeholders about the case of the ASR™ hip joint failures. £30,000. Newcastle University EPSRC Impact Award. July 2011 - June 2012.

4. Details of the impact

The impact of the research has been in three areas; (i) policy changes implemented by government agencies, which in turn led to (ii) prevention of harm to future patients, and (iii) financial implications for implant manufacturers and healthcare providers. This impact was the result of research carried out at Newcastle University (NU) and University Hospital North Tees (NT) into (a) abnormally high levels of metal ions in patients with the ASR hip, and (b) failure of all large-head MoM total hip replacements. NU has led the engineering research, such as the analysis and characterisation of wear and roughness of the implants, whilst NT led the clinical research, including the radiographic analysis of implant orientation and blood ion levels.

The first change in policy relates to the use of ASR hip implants, in both the resurfacing and total hip replacement form. Although the withdrawal of the ASR was voluntary, international healthcare bodies changed their policy in the light of the growing body of evidence of the poor performance of the ASR, for example calling for patients to be monitored for the life of the implant (S1). The second change in worldwide policy concerned the use of large-head metal-on-metal (MoM) implants, of which approximately a million have been implanted worldwide. Regulatory bodies, including the FDA began to issue new policies and guidance and in early 2012 guidance was issued by the MHRA (Medicines and Healthcare products Regulatory Agency) (S2), the Danish Orthopaedic Associations (S3) and Health Canada (S4) recommending against the use of large-head MoM implants until further evidence was available.

This worldwide impact was a consequence of the increase in understanding of the vulnerabilities of the ASR and all large head MoM. The importance of the work has been recognised in several ways. Both P1 and P3 are included within the FDA's Executive Summary published in June 2012 (S5). An article by authors from the National Joint Registry for England and Wales and the MHRA (S6) stated that "*Data critical of the performance of the ASR were presented at numerous scientific meetings in 2008 and onward to the time of this writing, particularly at meetings of the British Hip Society (BHS) and the British Orthopaedic Association (BOA). This factor, rather than the MHRA alert in July 2010, almost certainly led to the subsequent drop in sales of that implant*". Newcastle University researchers starting presenting their data on the performance of the ASR at meetings in 2008, with one presented at the British Hip Society meeting in February 2008, and two at the BOA Annual Congress in Liverpool in September 2008. The advisory document produced by the BOA in March 2011 refers to the research performed at NT (S7). In recognition of his expert status, Joyce spoke at the House of Commons Select Committee in May 2012, a session dedicated to discussing medical implant regulation and several recommendations put forward by Joyce were accepted in the Committee's final report (S8). For example, recommendation 16: "The Government should ensure that raw data from the National Joint Registry (NJR) is published where possible. In addition, explanted joints should be analysed, and subsequent data generated should be reported to the NJR and published."

The withdrawal of both the ASR and large-head metal-on-metal hips from the market reduces the

harm and prevents risk of injury to future patients that may have been eligible for these implants. On the basis that 1 million hips per annum are implanted (S9) and that, in the US, 35% were metal-on-metal (S10) then 350,000 potential patients per year have been protected from the adverse effects of metal-on-metal hips. The financial impact for health providers is also significant. In the UK the cost of replacing a failed artificial joint with a new implant in a 'revision' operation can be up to £25,000 per patient. With the latest Australian data showing a 44% revision rate for the ASR hip, and almost 100,000 implanted worldwide, the costs of revision are projected to exceed £1 billion. Redress is also being sought in courts in a number of countries. In the first ASR case to come to trial in the USA, the litigant was awarded $8.3 million. There are currently 11,000 ASR litigants in the US alone, with class actions due to commence in that country in late 2013.

5. Sources to corroborate the impact

S1 MHRA Medical Device Alert MDA/2010/069. "DePuy ASR Hip Replacements," 7th Sept. 2010.

S2 MHRA Medical Device Alert MDA/2012/008. "All metal-on-metal (MoM) hip replacements." 28 Feb 2012.

S3 Danica Societas Orthopaedica, "Metal on Metal Hip Prosthesis" (www.ortopaedi.dk/index.php?id=351; in Danish, English translation available).

S4 Health Canada, "Metal-on-Metal Hip Implants - Information for Orthopaedic Surgeons Regarding Patient Management Following Surgery - For Health Professionals" (http://www.healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2012/15835a-eng.php).

S5 FDA Executive Summary Memorandum, "Metal-on-Metal Hip Implant Systems" (www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/OrthopaedicandRehabilitationDevicesPanel/UCM309302.pdf)

S6 Tucker *et al*., (2011). Monitoring the Introduction and Performance of a Joint Replacement: The United Kingdom Metal-on-Metal Alert. JBJS 93 Suppl 3 (E): 37-42.

S7 British Hip Society joint statement with the British Orthopaedic Association, "Large Diameter Metal on Metal Bearing Total Hip Replacements" (www.britishhipsociety.com/pdfs/BHS_MOM_THR.pdf).

S8 House of Commons Science and Technology Committee 5th Report on Medical Device Regulation in the EU and UK. (available from http://www.parliament.uk/business/committees/committees-a-z/commons-select/science-and-technology-committee/inquiries/parliament-2010/regulation-of-medical-implants1/).

S9 Pivec et al., (2012). Hip arthroplasty. The Lancet, 380, 1768-1777.

S10 Bozic et al., (2009). The Epidemiology of Bearing Surface Usage in Total Hip Arthroplasty in the United States. JBJS, 91, 7, 1614-20.