The London Implant Retrieval Centre
Alister Hart, on behalf of many colleagues, announces an exciting new initiative

On 12 November 2008 the London Implant Retrieval Centre was officially opened. This is the culmination of 3 years of collaborative work on metal ions and research into problems associated with metal on metal articulations, and heralds an exciting future for research and understanding in metal on metal articulations (MOM).

We had initially embarked on a research programme into metal ion measurement and their effects in patients after MOM hips. Subsequently a rare but persistent problem was identified of the cohort of patients with unexplained pain after MOM hips. We therefore identified a clinical need for a service that surgeons could rely on for advice, clinical assessment and analysis of tissue, blood samples for metal ion measurement and wear analysis of components.

The great strength of the unit is that we can analyse all of the above in the clinical context of patient symptoms and presentation and perform rigorous analysis and measurement of component position on radiographs and CT scans. We also realized that the service must be independent, with the support of Industry but without affiliation to any one company, run by surgeon clinicians and have at its core a strong research team with advanced skills in Chemical Analysis, Histopathology, Immunology, Tribology and tissue metal mapping and speciation. Our approach has always relied on assembling teams of experts to work with Orthopaedic Surgeons to analyse clinical observations and problems.

The funding model has been complex but it seemed clear that Industry should and would want to fund such a research project. To maintain independence Funds are provided by the ABHI (Association of British Healthcare Industries) as an umbrella organization for 8 companies (Stryker, Smith & Nephew, Corin, Finsbury, DePuy, Mathys, Biomet, JRI) and donated via the British Orthopaedic Association; in September 2008 a contract was signed to create a research and service collaboration between Imperial College London, the RNOH NHS Trust, the 8 companies, the Association of British Healthcare Industries (ABHI) and the British Orthopaedic Association. The LIRC is supported by the Medicines and Healthcare products Regulatory Authority (MHRA). The London Implant Retrieval Centre (LIRC) was founded in 2007. The aim of the centre is quite simply to investigate the mechanism of failure of metal on metal (MOM) hip replacements.

A higher early failure rate is reported for MOM hip resurfacings when compared to standard type hips. It is not clear whether this is due to a selection bias, with hip resurfacing being used more commonly in young and active patients or whether it is being used in older patients or patient groups for whom it may be inappropriate. In many cases the cause of failure is not explained by clinical tests prior to revision, i.e. unexplained pain. As it is relatively straightforward to revise a resurfacing arthroplasty, there may be a tendency to revise and explain all painful implants as an MOM problem. We believe that the cause should be investigated rigorously for all MOM explants and that a minimum dataset should be established. It seems essential to identify who will do well with MOM or HR and ideally those who should not have this procedure. All surgeons ultimately want the best for their patient.

**Sterile Inflammation**

A possible explanation for failure and unexplained pain is a sterile inflammatory response to the metal wear (nano)particles cobalt, chromium and molybdenum. This has been described as a vasculitis, delayed-type hypersensitivity or a granulomatous foreign-body reaction and termed Aseptic lymphocyte-dominated vasculitis associated lesions (ALVAL). Recent radiological and histopathological reports have identified abnormalities in tissues surrounding painful MOM hips. We do not know whether the adverse inflammatory response is dose related and if so, what are the factors that determine the dose (ie hip wear rate)? We also don’t know why it doesn’t happen in everyone so conversely who is most susceptible.

The MHRA, BHS, BOA have become interested in establishing the incidence of severe soft tissue reactions to MOM implants, characterized by soft tissue swellings, fluid collections and tissue necrosis. Currently, via the NJR, an analysis of causes of failure of MOM hips in 572 patients in a series of 59,785 recorded for both primary and revision procedure on the NJR, is underway. However it will be the detailed analysis of specimens from these cases in a multi-disciplinary retrieval centre such as this that will help unravel such problems at the clinical/cellular level.

**Service function of the LIRC**

The service function of the centre is to provide a report of the analysis of the material collected to the referring surgeon. With a full dataset of blood for metal ions, radiographs, metal artifact reduction MRI, low dose CT scan, the explanted components and capsular tissue from the revision operation, we can make some observations on what may have happened that may allow the surgeon and patient to move forward. The information will also be forwarded to the manufacturer who has an obligation in certain circumstances to inform the MHRA.

The centre has ethical and Human Tissue Act approvals for research on material from all UK hospitals and meets or exceeds all of the current UK and EEC regulations for storing and analyzing human tissue. In our first year of operation we received 79 failed implants with associated tissue and data from 20 UK hospitals. In the last two months we have received a further 20 explants.

**Use of technology for research**

We have pioneered the use of laser ablation mass spectrometry and microfocus spectroscopy from the Diamond Light Source to look at body tissue con-
Methods

Wear analysis of explanted hips
The Tribology department of Imperial College are leading the wear analysis. We are currently analyzing the surface texture and the wear. We will be seeking to develop the first international standards for these measurements as applied to explanted MOM hip joints. We recognize the sources of error in the wear measurement, specifically the accuracy required and the computation of the original form. So far we have found that some hips have been worn at a rate that is 70 times greater than that predicted by manufacturer’s tests in a laboratory.

Blood and synovial fluid metal ion analysis
This is performed at the Trace Element Laboratory at Charing Cross Hospital. This lab is a member of the Trace Element Quality Assurance Scheme (TEQAS) and the Supraregional Assay Service (SAS). We have validated our protocols through interlaboratory analysis with Jonathan Powell from the MRC HNR centre in Cambridge.

Analysis of wear data in clinical context
Interpretation of the mechanical wear data of the removed hips is enhanced through the use of the associated clinical, imaging (see figure), trace element and histopathological data. The more of this data provided by the surgeon, the more reliably we can determine the mode of failure.

Analysis of hip tissue
The hip capsule tissue is stored in the Human Biomaterials Resource Centre at Charing Cross Hospital. Further analysis of the tissue has taken place at the Diamond Light Source, the UK’s national synchrotron (a special type of particle accelerator) facility. We are the first group to use this facility for metal mapping spectroscopy experiments on human tissue and the first to perform these experiments on human tissue from live patients. This is in collaboration with Fred Moselemans and Paul Quinn of Diamond. We are applying for funding to study the tissue in more detail, specifically to more fully characterize the so-called Aseptic Lymphocyte Vasculitis Associated Lesion (ALVAL).

Dissemination of results
Contributing surgeons will receive a full report of the analysis. The centre is currently undergoing the rigorous development of standardised reporting following the development of validated methodologies (some of which have been the subject of our research for more than 3 years). We will be having a results and discussion meeting, open to any surgeon that has contributed to the centre, at 6pm on Thursday 22 January 2009. Some related data on painful MOM hips will be presented as 3 podium presentations and one poster at the 2009 AAOS in Las Vegas.

Founders and clinical leads: Alister Hart1 (Senior Lecturer and Consultant Orthopaedic Surgeon) and John Skinner2 (Consultant Orthopaedic Surgeon)

Steering committee: Prof Justin Cobb1 (Consultant Orthopaedic Surgeon); Miss Sarah Muirhead-Allwood2 (Consultant Orthopaedic Surgeon); Mr Martin Porter3 (Consultant Orthopaedic Surgeon)

Core scientific team: Dr Barry Sampson4 (Consultant Clinical Chemist); Dr Ann Sandison5 (Consultant Histopathologist); Dr Adam Mitchell6 (Consultant Radiologist); Dr Philippa Cann1 (Principal Researcher in Tribology); Mr Johann Henckel7 (Spr in Orthopaedics); Dr Richard Underwood1 (Engineering Research Assistant)

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