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Explant analysis and implant registries are both needed to further improve patient safety

M M Morlock[1], E Gomez-Barrena[2], D C Wirtz[3], A Hart[4] and J P Kretzer[5]

[1]Institute of Biomechanics, TUHH Hamburg University of Technology, Hamburg, Germany
[2]Department of Orthopaedic Surgery and Traumatology, Universidad Autónoma de Madrid, Madrid, Spain
[3]Department of Orthopaedics and Traumatology, University Hospital Bonn, Bonn, Germany
[4]London Implant Retrieval Centre, Royal National Orthopaedic Hospital, Stanmore, UK
[5]Department of Orthopaedic Surgery, Heidelberg University Hospital, Heidelberg, Germany

Correspondence should be addressed to M M Morlock
Email
morlock@tuhh.de

- In the early days of total joint replacement, implant fracture, material problems and wear presented major problems for the long-term success of the operation.
- Today, failures directly related to the implant comprise only 2–3% of the reasons for revision surgeries, which is a result of the material and design improvements in combination with the standardization of pre-clinical testing methods and the post-market surveillance required by the legal regulation.
- Arthroplasty registers are very effective tools to document the long-term clinical performance of implants and implantation techniques such as fixation methods in combination with patient characteristics.
- Revisions due to implant failure are initially not reflected by the registries due to their small number.
- Explant analysis including patient, clinical and imaging documentation is crucial to identify failure mechanisms early enough to prevent massive failures detectable in the registries.
- In the past, early reaction was not always successful, since explant analysis studies have either been performed late or the results did not trigger preventive measures until clinical failures affected a substantial number of patients.
- The identification of implant-related problems is only possible if all failures are reported and related to the number of implantations.
- A system that analyses all explants from revisions attributed to implant failure is mandatory to reduce failures, allowing improvement of risk assessment in the regulatory process.

Keywords

- implant failure
- risk assessment
- explant analysis

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History

Arthroplasty became popular in the second half of the 20th century and has developed since then into one of the most successful fields in orthopaedics (1). This development was not free from problems and failures. The reduction of polyethylene (PE) wear debris was initially the main focus of implant research (Fig. 1). A satisfactory solution was finally achieved by the introduction of modern cross-linked and oxidation-stabilized PEs (2, 3). Some product developments and innovations failed systemically during their clinical use. These failures included corrosion-induced loosening of cemented titanium stems (4), mechanical breakdown of a polymethylmethacrylat (PMMA) bone cement due to problems with the glass transition temperature (5), wear problems with highly crystalline phase-modified polyethylene (6) and toxicological surface contamination on porous-coated sockets (7). Innovative procedures such as hip resurfacing and large metal-on-metal hip joint bearings (8) (Fig. 2), dual-taper modular primary hip stems (9, 10) (Fig. 3) or titanium alloys with reduced material stiffness (11) worked well clinically as long as they were used in the inventor's hands but showed insufficient robustness for the wider use by the orthopaedic community, frequently resulting in discontinuation.

All the above-mentioned products failed despite intensive laboratory testing and the approval of regulatory competent authorities either in the US or in Europe. Failures despite fulfilling all requirements result in harm to the patient and detriment of the medical device company due to recourse claims from the patients and in the midterm to a loss of confidence among surgeons. How can it happen that fully approved and tested implants fail? The key aspect in this context

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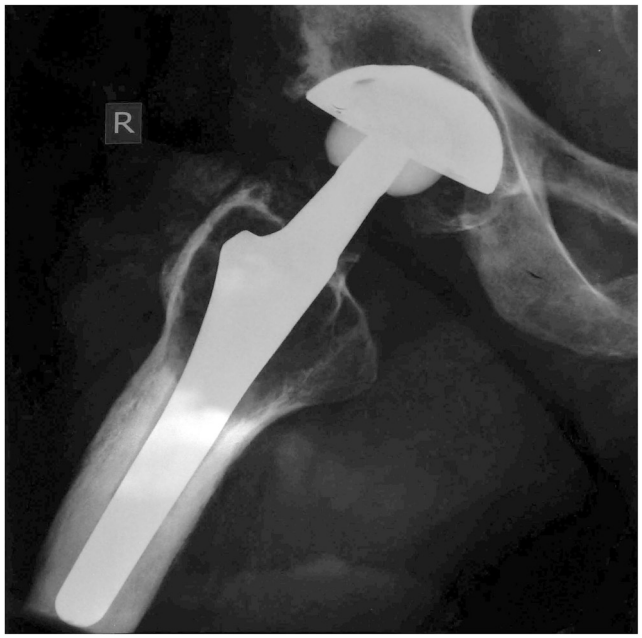

Figure 1
Massive osteolysis around the acetabular cup and the femoral stem of an uncemented total hip arthroplasty due to PE wear 7 years after implantation.

is the 'risk assessment' based on a worst-case scenario, which forms the basis for the required pre-clinical testing and the approval of a product. If the risks are not really predictable as with completely new implant designs, the only solution is a well-defined clinical evaluation investigating the safety and functionality of the product. This aspect is now regulated by the Medical Device Regulation (MDR) (12), which took effect in 2021 and replaced the Medical Device Directive issued in 1993. The MDR requires post-market surveillance of all class IIb and III products by the manufacturers, who have to demonstrate the clinical safety of their products on a yearly basis. This will provide a substantially higher level of safety for most orthopaedic bone and joint implants that belong to these classes.

The role of registries and regulatory bodies

During the early days of arthroplasty, many of the observed problems were directly related to the design and the material of the endoprostheses (13). Joint arthroplasty registries were established to identify problematic designs and materials, to remove these from the market step by step and to improve the quality of joint replacement surgeries (14). In part, as a result, today endoprostheses for hip and knee replacement show very good results after 10 and 20 years (15, 16).

The problem with hip resurfacing and large head metal-on-metal (MoM) articulations in total hip replacement (THR) is an example from the past which hopefully would not repeat today with new innovative designs. The regulatory bodies finally intervened but it took quite long until measures were taken. In April 2010, the Medicines and Healthcare products Regulatory Agency in the UK issued the Medical Device Alert MDA/2010/033 informing all people involved in the management of patients with joint replacement about revisions of MoM hip replacements associated with soft tissue reactions. Systems had to be put in place for the follow-up of patients implanted with MoM implants including blood metal ion measurements and cross-sectional imaging, as appropriate. In September 2010, the ASR design was recalled (MDA/2010/069). This design had already been recalled in Australia by the Therapeutic Goods Administration in December 2009. Publications based on clinical studies and explant analysis pointing out different problematic issues such as a more difficult surgical technique, femoral neck fractures, tissue reactions, wear sensitivity and design-specific issues with hip resurfacing and large-diameter MoM THRs had started around 2005 (17). From then on, it took about 5 years until these problems were widely recognized and appropriate measures were initiated, resulting in a rapid decline in the use of these implants. The manufacturers and the regulatory system 'learn' from such scenarios, adapting requirements and standards, hopefully preventing

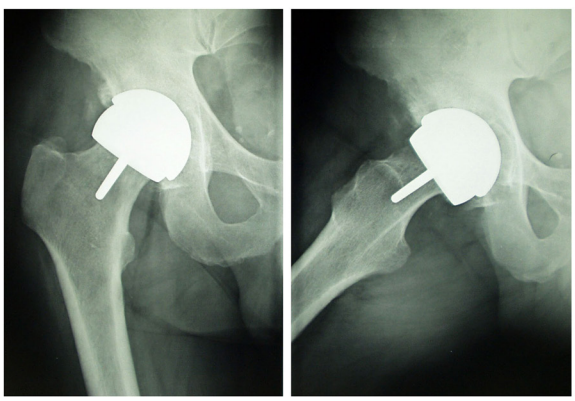

Figure 2
Excessive wear of a hip resurfacing couple due to edge loading caused by misalignment of the cup resulting in ARMD (left: post-OP X-rays, right: wear maps for cup and head showing the deviation to pristine components).

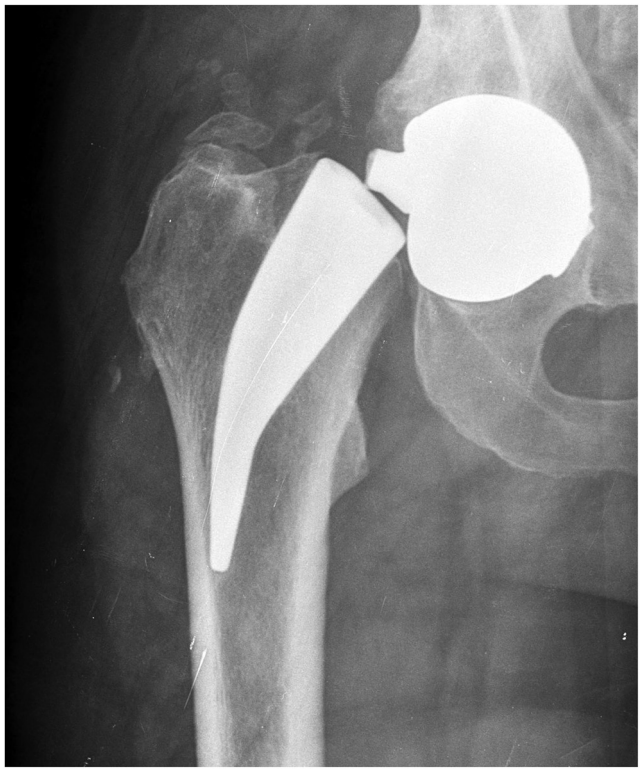

Figure 3
Fracture of the neck piece of a bi-modular hip stem.

future failure. In 2005, total hip, knee and shoulder joint replacements were reclassified from Class IIb to III (2005/50/EC) in the European Union, with a transition period between 2007 and 2009.

Today, revisions due to implant failure are not clearly reflected in the joint arthroplasty registries due to their small number. Revision surgeries directly related to an implant failure comprise today only 2–3% of all revision surgeries (18, 19), which is a result of the material and design improvements in combination with the standardized mandatory pre-clinical testing methods.

Yet, problems related to the implant itself still pose a serious concern in the European society, heralded by inadequate media interpretation of problems with new implants and medical devices, even though they involve only a very small percentage of surgical revisions.

Risk assessment

A weak spot of the current system for the introduction of new implants into the market and for the post-market surveillance of existing implants is the risk assessment. The risk assessment substantiates the whole approval process. It is executed by the manufacturer and approved by the notified body. In order to improve the risk assessment (and thus the requirements for the pre-clinical testing) in an implant category, every revision of an implant that occurs during clinical use and in which the implant plays a causative role has to be identified. Only then it is possible to decide whether the observed failure mode is a singular one or the beginning of a series. This will determine whether it is necessary to withdraw the implant from the market and to extend the pre-clinical testing for this implant category to evaluate the observed failure mechanism. However, this action mode would require that failed implants are preserved by the revising surgeon, a system to be available to identify relevant failures, and the required explant analysis to be provided. Such a system would help to identify 'new' unknown failure mechanisms earlier and would increase the trust of the patients in the implants and surgeons.

Explant analysis

The documentation of explant analyses in the literature had started in the 1980's. A search in the Pubmed database with the search terms 'retrieval', 'explant', 'analysis', 'hip' and 'knee' and the MESH term '[All Fields]' excluding the results from computer models and the term 'therapy', revealed 468 relevant publications. This rather low number could be due to the fact that the many explant analyses are published as case studies, which are rarely listed in Pubmed.

Current initiative on retrieved implants collection and analysis

In 2020, the European Federation of Orthopaedics and Traumatology (EFORT) launched an Implant & Patient Safety Initiative addressing the introduction of innovation, the off-label use and mix and match of arthroplasty components and the collection and analysis of implants retrieved during revision surgery. A pilot study in the latter topic was started in early 2022 to directly document, in a transparent way, implant or material-related problems leading to revision. The aim is to get a better understanding of the clinical situation related to implant failure. Fifteen selected hospitals with a large volume of revision surgeries were asked to provide implants from cases in which the reason for revision was suspected to be directly related to a mechanical failure or wear of the implant if the implant was implanted less than 5 years. Implants are only included if previously reported to the responsible regulatory body (BfArM) and to the manufacturer, as required by the German law. The documentation to include a case in the study requires the patient consent, radiographs both after implant surgery and pre-revision, the surgical reports of the index and the revision surgery, and finally the suspected reason for revision. Each explant is screened

free of charge by one of the four participating University laboratories (Hamburg, Heidelberg, Munich and Rostock), whose research is focused on Biomechanics and Implant Development. Based on the individual experience, each laboratory decides whether further explant analysis is indicated or if the reason for failure can be sufficiently assessed through the screening including only simple analysis and relevant literature and registry review. The hospital performing the revision surgery receives a short report within 4 weeks. In case of any significant finding, the national regulator BfArM, the manufacturer and the hospital are immediately informed.

The analysis is interposed into the standard process guided by the BfArM and designed to give a quick first independent result to the submitting hospital. In the past long response times, insufficient transparency and inconclusive reports from the manufacturers, who are legally mandated to analyse their failed implants, have resulted in little interest by the surgeons to report cases and submit explants for analysis. This has to be changed. In the first 3 months of the study, seven explants of which six were fractured revision implants (two revision knees hinge mechanism, one revision knee stem, two modular hip revision stem and one proximal femur) were received. None of the failure mechanisms observed were novel.

Conclusion

The regulatory requirements to introduce a new arthroplasty product to the market and the requirements to keep it there have been greatly extended over the last 30 years with the new MDR comprising the most recent step. Many manufacturers had to remove implants from the market since they could not demonstrate their clinical success, especially in the case of low-volume designs infrequently used. In order to be approved according to the MDR, a class III implant has had to demonstrate successful passing of all required pre-clinical tests. Furthermore, it has had to demonstrate its clinical safety in a clinical study. Despite this process, failures do and will occur, since variability in the patient and the surgical procedure is highly complex. Implant monitoring by the arthroplasty registries guarantees that underperforming implants will be identified and measures will be taken. But this process is rather slow and bears the risk that a large number of patients have already been treated. Another risk is that small numbers of implant-related failures will not bring attention if the overall implant success in the registries is satisfactory. Screening all explants, which are deemed to be responsible for their revision by independent experts, will help to early identify failure mechanisms eventually not included in the risk assessment for an implant category. It will also allow to improve the risk assessment for this implant category. In order to achieve this goal and organize the process, national systems need to be established. A first pilot study has been initiated in Germany based on the EFORT initiative.

ICMJE Conflict of Interest Statement

M M has been a consultant and received grants and lecture fees from DePuy Synthes. This is outside the submitted work; A H reports receiving funding from Nuvasive and Medacta; J P K reports being a consultant for Ceramtec and has received grants and/or lecture fees from DePuy Synthes, Implantcast, Mathys, Permedica, Questmed, Spineserv, Endolab, Endocon, Sintx, Implantec, IMA; E G B and D C W have no interests to declare.

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