Editorial Commentary

How best to regulate new implants in the market—is radiostereometric analysis enough?

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Introduction

The demands of the modern patient, both in terms of what a hip replacement will allow them to do as well as for how long it will last, mean that pre-market testing and close surveillance should be robust to avoid the problems of previous implants. Implants that fail in the short-term are relatively easy to detect. Implants that fail in the medium to long-term, but sooner or in more damaging modes than their peers, are much more difficult to identify. What would be the optimal strategy to evaluate a new implant prior to release if time and resource was unlimited? Would the new implant only be released to all surgeons after careful introduction in a small cohort with detailed assessment and extended follow-up? How long is sufficient follow-up?

We do not live in an "ideal" world with unlimited time and resource, and if we did, it still remains unknown how best to evaluate an implant. Pragmatism, whilst addressing safety, cost effectiveness, and robust clinical outcomes is necessary. But how best to implement such an approach?

Pre-clinical study

When designing a new implant, even if based on a previously successful design, there are certain processes to which adherence is mandatory. Orthopaedic history is littered with examples of new "improved" designs that failed catastrophically, even when based closely on a very well performing implant (1,2). Subtle modifications that aim to improve implant properties can be extremely detrimental to implant performance. Furthermore, many of these adverse modifications have resulted in implant failure in a manner that could have been detected by stringent pre-clinical testing. The International Organisation for Standardisation (ISO) have well documented guidelines on mechanical testing of new hip implants (3). Their guidelines cover all feasible failure modes of an implant, from fatigue testing of the metallurgy to wear of the bearing surfaces. It therefore appears clear how mechanical testing of a new implant should be performed. However, this presents the first dilemma. Mechanical testing is expensive and time consuming. Do you test the whole inventory of available sizes? Are smaller implant sizes more or less likely to wear abnormally? Over what range do you test acetabular component orientation (4)? Only perfect inclination and version as described in the operative technique guide or do you allow for surgical inexactitude and test extremes of position? With the increase in computational power it is now more reasonable to test implants extensively using techniques such as finite element analysis. This method should highlight areas of concern, such as edge loading in certain orientations or stem fracture risk under high loads. The expensive, time consuming mechanical testing can then be focused on situations or orientations that are most at risk of poor performance.

Further pre-clinical testing should utilise dry-bone testing of both the implants and instruments. Good instrumentation is vitally important to allow reliable, reproducible implantation of a given prosthesis. A thorough test of all the instruments by a series of surgeons will allow modifications to the design and ensure they are fit for purpose. This process can be completed on cadaveric specimens to ensure the most beautifully designed instrument is not foiled by the presence of soft tissue. Even the best implants will have an unnecessarily high failure rate

if the method of implantation is suboptimal.

Clinical release

Most implant companies adopt a safe approach to clinical release, starting with designer surgeon cohorts or high volume centres. This allows the assessment of an implant in closely controlled conditions and in well-defined patient cohorts (5). It may also allow collection of enhanced outcomes measures, such as radiostereometric analysis (RSA), gait analysis, and cross-sectional imaging such as computerised tomography.

RSA is able to identify implants at increased risk of failure in the medium-term (6). Adverse implant migration or wear patterns on RSA maybe evident well before the implant fails clinically, identified through clinical follow-up or registry data. However, RSA can be time-consuming and labour-intensive, and originally it could only be performed using modified implants. For these reasons RSA was not widely used to evaluate implant performance. Traditionally, most studies came from centres in Europe, where RSA was an integral part of that institution's research programme. This trend has changed in the last decade with the development of model based RSA that allows non-modified implants to be tested with faster analysis platforms (7). But RSA remains expensive and requires considerable time and resource from implant companies, surgeons, and institutions, especially outside of established research centres with expertise in this field. RSA allows accurate assessment of implant performance, but in the quest for faster and more inexpensive methods, it is important that accuracy remains adequate to provide meaningful data. Furthermore, RSA studies must adhere to the recommended standards for a robust investigation (8). At present there is significant variation in the quality of published RSA studies. Although, RSA is a powerful tool for detecting implant loosening and migration (9), and bearing surface wear (10,11), there are many other modes of failure. An RSA study of an implant showing excellent fixation or minimal wear should not be taken as the only evidence of good long-term performance.

The role of national or international bodies

There is no consensus on how implants should be introduced to a market and different rules or requirements exist in different countries. In Europe, all implants must be CE marked (Conformité Européenne) (12), whereas in the USA implants must be approved by the FDA (Food and Drug Administration) (13). In the UK, there is also the MHRA (Medicines and Healthcare products Regulatory Agency) (14), which has its own requirements and the National Institute of Healthcare and Clinical Excellence (NICE) provides guidance on what implants should be used (15). The NICE guidelines arose because of two main factors. First, an enormous array of implants are used. In the UK, in 2018 there were 110 different acetabular components implanted in 96,887 primary hip arthroplasty procedures, with 32 different implants used fewer than ten times each (16). Second, there are several examples in the recent past of catastrophic implant failure with exceptionally high revision rates (17). In response to both these issues, NICE recommend that surgeons only implant hip replacements that have high-quality long-term data, with a minimum survival of 95% at 10 years (15). This approach, whilst correctly focusing fully on patient safety, risks stifling innovation and development. The Beyond Compliance system was developed in the UK in response to the NICE guidelines (18). The system is voluntary on the part of the implant manufacturers, but after the device has been registered and preclinical testing results submitted, the device is released clinically. This release is usually in a small number of selected centres that sign up to a research study or surveillance programme. Patients are enrolled into the programme and there is frequently collection of additional outcome measures to routine care, such as patient reported outcome measures and imaging studies. It requires additional clinical resource but provides valuable data for submission to regulatory bodies (19). The implant is then made available more widely, but each surgeon who wishes to use a newly introduced implant is invited to register as a Beyond Compliance surgeon. One of the greatest strengths of early surveillance across a cohort of patients from several centres is the quality and depth of the initial data. A report is prepared every 3 months summarising the numbers implanted and the revision rate. There is also an analysis comparing performance against National Joint Registry (NJR) data, both within the category of the implant (e.g., cementless stem) and against the category leader (e.g., best performing cementless stem at 10 years). The surgeon and manufacturer are given a numerical chance of the implant under investigation becoming an outlier in the future. Modes of failure or reasons for revision are also listed (e.g., periprosthetic fracture or aseptic loosening) which may assist surgeons on their learning curve. For example, if there are several early revisions for aseptic loosening there may be

an issue with undersizing a cementless stem. Alternatively, they may choose to use a different implant.

This regular feedback on implant performance is only possible due to the large dataset within the NJR, with data collection starting in 2003, and being compulsory since 2011 (20). Every joint replacement in the UK is registered with patient demographics and surgeon details, the indication for surgery and the implant details. The results of the Beyond Compliance surveillance then directly feeds in to the Orthopaedic Data Evaluation Panel (ODEP) (21) and the implant gains a rating based on survival at set time points. The standard time points are 3, 5, 7, 10 and 13 years, with and A*, A and B suffix to identify the quality of the follow-up data and the level of survival. For example, an implant with a rating of 7B has data to 7 years and has evidence of good survival in a moderately large cohort, whereas a rating of 10A* has data to 10 years, with a larger patient cohort and a survival of at least 95% at that time point. The ODEP rating system has already been adopted in several countries around the world. Strengths include its simplicity but rigorous evaluation of implant performance. It is also publicly available and patients are increasingly encouraged to discuss implant selection with their surgeon, both in terms of anticipated improvements in pain and function, but also anticipated implant longevity.

There are now implant registries in many countries and each offers unique insight into implant performance. Registries differ in the length of time they have been established, the data collected, and the analysis performed and reported output. The Scandinavian registers have been established for a long period of time and offer the longest-term data with particularly robust information on the performance of cemented implants (22-24). The Australian register also has long-term data and offers insight on the role of surgeon volume on revision rates (25). Annual reports often focus on specific topics, such as arthroplasty in the elderly or periprosthetic fractures. There have been attempts to establish national joint registries in other European countries and in North America. These registries would enhance our knowledge base and further enable the orthopaedic community to select implants that perform well.

Functional outcome measures

The importance of Patient Reported Outcome Measures (PROMs) is increasingly recognised given the goal of arthroplasty surgery is to improve pain and function. Registries are powerful tools for studying implant revision rates, but have less value in evaluating other outcomes. It is widely recognised that an implant that is challenging to revise will have a higher survival rate at any given time point when compared with an implant that is easier to revise. However, the two implants may be associated with different levels of pain and function, and the implant with the higher revision rate may provide better patient reported outcomes prior to revision. Implant studies should use outcome scores that have been validated in patient populations undergoing joint replacement, such as the Oxford Hip Score (26,27) or Harris Hip Score (28).

Summary

Implant manufacturers and surgeons must work together to introduce implants in a safe and reliable manner. Surgeons should only use implants that have a proven track record, or any implants that are new to the market should have robust pre-clinical and early clinical data. Patients should be appropriately consented and enrolled in surveillance programmes, ideally through an independent body to minimize bias. RSA can be used as part of this early clinical evaluation but should form part of multimodal outcome measures that include patient reported outcomes and revision rates. Encouragingly there appears to be significant progress in this field with engagement from both industry and clinicians to deliver safe surgery to patients worldwide.

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Footnote

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