Institution: University of Southampton

Unit of Assessment: 15 General Engineering

Title of case study: 15-12 Design of a new total knee replacement

1. Summary of the impact

Each year an estimated 1,324,000 artificial knee joints (total knee replacements - TKR) are implanted worldwide; an estimated third of these utilise an implant manufactured by DePuy International. Underlying computer-based research performed by the Bioengineering Sciences Research Group has played a central role during the development of a new design of TKR for DePuy. The design programme, the biggest in DePuy's history, had a budget in excess of US$10 million and aimed to replace the existing TKR system, which had annual sales of approximately US$100 million.

Between 2007-2010, DePuy adopted the computational techniques developed by the group as screening tools to (i) assess polyethylene wear and (ii) account for the effects of surgical variability during the early design phases. DePuy states "*This research allowed us to choose the most robust solution when proceeding to mechanical testing and saved years in the design cycle. Patients also benefit from increased confidence in an implant that is able to withstand the rigors of use*".

2. Underpinning research

In a total knee replacement (TKR), the damaged surfaces of the knee joint are replaced by a metal component articulating against a polyethylene component. It is the wear of the polyethylene component that constitutes one of the main factors limiting the longevity of total knee (and hip) replacements as it can lead to loosening, necessitating reimplantation, or "revision". According to the National Joint Register for England and Wales, 6.2% of all knee replacements were revision procedures in 2010. Pre-clinical experimental wear testing of TKR components is an invaluable tool for evaluating new implant designs and materials. However, this can be a lengthy and expensive process, and hence parametric studies evaluating the effects of geometric, loading, or alignment perturbations may at times be cost-prohibitive. Also, experimental wear testing can only be performed late in the design process, when physical parts exist.

Experimental studies in the academic literature had suggested that multi directional movements, or "cross shear" of the metal on the polyethylene component may lead to increased wear. Therefore, in an effort to provide efficient implant wear evaluation, particularly in the early design phases when only a CAD geometry exists, the Bioengineering Group developed numerical techniques to simulate wear of total knee replacements that incorporated cross shear; at the time there were only one or two groups in the world attempting to computationally simulate this. In order to achieve this, it was first necessary to be able model the variation in movement and contact pressure distribution at the knee during typical daily activity [3.1].

Initial work [3.2] implemented a simple Archard's wear law (with wear simply being a function of contact pressure and sliding distance) and achieved reasonable corroboration with experimental data for a specific implant design. However, it was found that when this applied to a wide range of implant designs and movement inputs, the law was found to be implant specific, so the predictive power was low [3.3]. This led to the development of a 2nd generation of wear algorithms, which also included a cross-shear term. In a corroboration study of multiple implant designs, subjected to a range of kinematic inputs, the 2nd generation wear algorithms had a significant predictive capability for all implants [3.3]. These 2nd generation wear algorithms were subsequently used in the design screening phase of the new DePuy total knee replacement.

In parallel, research was being performed to develop efficient methods for assessing the impact of patient and surgical variability on the performance of total knee replacement. The vast majority of published research in this field performs either deterministic analyses or simple one variable parametric studies. However, the in vivo kinematics, contact pressure distribution and subsequent wear of total knee replacement are highly variable and are likely to be a result of a complex interaction of patient and surgery related parameters. To address these issues, we applied probabilistic modelling techniques (Monte Carlo analysis and response surface methods) in combination with computationally efficient models (multibody dynamic analysis rather than the traditional finite element modelling techniques) to explore the combined impact of patient and surgical variability [3.4, 3.5]. Analysis of such a wide patient cohort, together with their associated pathologies, had not been attempted before; thus the implant was designed to cater for extremes of patient size/weight. Again, these techniques were implemented by DePuy Inc to assess the robustness of the new implant design.

This research was carried out between 2000 to 2010 and involved Professor Mark Taylor (Head of group throughout the research period - left December 2011) and Prof Martin Browne (Current Head of Group) in supervisory roles and Professor David Barrett (consultant orthopaedic registrar throughout the research period) as clinical advisor. A team of PhD researchers were responsible for several key areas of investigation: Ms Anne Celine Godest (PhD student 2000-2003) developed the underlying force driven finite element model that enabled knee kinematics and stresses to be reproduced. Ms Lucy Knight (PhD student 2003-2007) [6] developed the preliminary (1st generation) and cross shear (2nd generation) models. Mr Anthony Strickland (PhD student 2006-2009 and post-doctoral researcher 2009-2010) developed the probabilistic techniques that were applied to the cross shear models to understand the effect of surgical variability [3.6].

3. References to the research (the best 3 are starred)

3.1 Godest, A.C., Beaugonin, M., Haug, E., Taylor, M. and Gregson, P. J., Simulation of a knee joint replacement during a gait cycle using explicit finite element analysis. Journal of Biomechanics, 2002. 35(2): p. 267-276.

3.2* Knight, L.A., Pal, S., Coleman, J. C., Bronson, F., Haider, H., Levine, D. L., Taylor, M. and Rullkoetter, P. J., Comparison of long-term numerical and experimental total knee replacement wear during simulated gait loading. Journal of Biomechanics, 2007. 39: p. 1550-1558.

3.3* Strickland, M.A. and M. Taylor, In-silico Wear Prediction for Knee Replacements - Methodology and Corroboration. Journal of Biomechanics, 2009. 42: p. 1469–1474.

3.4 Strickland, M.A., M. Browne, and M. Taylor, Could passive knee laxity be related to active gait mechanics? An exploratory computational biomechanical study using probabilistic methods. Computer Methods in Biomechanics and Biomedical Engineering, 2009. 12(6): p. 709 - 720.

3.5* Strickland, M.A., Dressler, M. R., Render, T., Browne, M. and Taylor, M., Targeted computational probabilistic corroboration of experimental knee, Medical Engineering and Physics, 2011. 33(3): p. 295-301.

3.6 This work was supported by an EPSRC PhD studentship (Strickland), Arthritis Research Campaign grant (Reference: T0527) and DePuy International, and resulted in PhD theses (Knight, 2009; Strickland 2009). Total funds provided by DePuy as part of a University Technology Partnership since 1999 ~ £1.9M

4. Details of the impact

The UK hip and knee registry details the number and types of knee implants being utilised in knee operations in the UK; the data reflects the general trends observed worldwide [5.1]. The 2011 register shows that 81,979 knee replacements were implanted in 2010 in the UK alone; the predecessor DePuy knee design, the PFC sigma, was noted as the market leader between 2003-2010, being used in 36% of these procedures [5.2].

Historically, the development of new orthopaedic devices has relied on accumulated knowledge from clinical practice and limited empirical testing (either numerical or experimental). Pre-clinical evaluation has typically occurred late in the process when design is close to being fixed and when physical parts existed. The advances in numerical modelling conducted at Southampton (to assess polyethylene wear and account for the influence of surgical variability) has meant that screening of potential designs can be performed much earlier in the design phase before physical prototypes exist.

Since 2000, DePuy have been involved in a technology partnership with the University of Southampton, with the objective of developing numerical tools to help assess the performance of total joint replacements. Based on the maturity of the developed techniques, in 2007 DePuy took the decision to integrate Southampton's tools into the design process of a new total knee joint replacement [5.3].

This work was carried out solely within the Bioengineering Group at Southampton. The design phase was split into two distinct parts, an initial screening of potential designs followed by refining of candidate designs. In the initial phase, between 2008-2009, the wear simulation tool was used to assess DePuy's existing products as well as those of competitors. These data acted as a bench mark and informed the direction of design process for DePuy.

A range of parameters thought to control both the kinematics and wear of the new design were then investigated; this was the first time that DePuy had exploited numerical modelling to this extent. As a result of using this tool, a much larger number of design variants could be explored, and a greater understanding of the effect of design changes on the performance of the implant was realised. In addition, a significant reduction of time in the design cycle was achieved.

In the second phase, between 2009-2010, Southampton's probabilistic modelling techniques were used to assess the robustness of existing designs and potential new designs to surgical variability.

The research was used by DePuy to show that that the final design was more robust to surgical variability than their existing designs and those of their competitors [5.3].

The information gained was also used to inform the design of the instrumentation required to implant the new design. Knee development team leader at DePuy US states "*The techniques that were employed in collaboration with Southampton allowed us to first of all evaluate analytically our component design against various options in manners that we would never have been able to mechanically test in any reasonable amount of time. For example, the wear modeller was used to assess a variety of testing conditions to challenge the robustness of the design variants and allow us to choose the most robust solution to progress to full mechanical testing. To have performed the same work mechanically would have added years to the development program*." [5.3]

There have been pre-launch implantations of the new device which was launched to a wider audience of users in Q2 of 2013. DePuy states: "*The new knee will be DePuy's flagship brand for the future and as such is a critical component of our business. More than half of the DePuy Joint Reconstruction sales are from total knees and so clearly it is an important part of our business since the new knee will represent more than 80% of that within 5 years' time*". [5.3]

The new knee implant is central to DePuy's business in the UK and abroad. DePuy states: "*The techniques developed at Southampton for analysis were central in the design evaluation process allowing us to distinguish between designs and be selective about features to ensure a good robust design solution. The product will ultimately become a major part of our sales generating multiple millions of dollars of revenue and returning even greater value to the patients who receive the product since they will have the confidence in the design and its robustness to withstand the rigors of use. The company has invested 10's of millions of dollars in developing the new product and will invest 10 times that again in deploying the product over the next several years and then we will invest millions again in further developing and completing the product line so that our customers will have a full line solution to all the challenges they face in surgery for total knees. The product we hope will return us to the lead position in the marketplace ahead of our main competitors.*" [5.3]

5. Sources to corroborate the impact

5.1 A summary of the number of total knee replacement procedures carried out worldwide (split between regions and countries including the UK) is presented in: Steven M. Kurtz, Kevin L. Ong, Edmund Lau, Marcel Widmer, Milka Maravic, Enrique Gómez-Barrena, Maria de Fátima de Pina, Valerio Manno, Marina Torre, William L. Walter, Richard de Steiger, Rudolph G. T. Geesink, Mikko Peltola and Christoph Röder, International survey of primary and revision total knee replacement, International Orthopaedics (SICOT) (2011) 35:1783–1789.

5.2 Knee replacement numbers by implant type in England and Wales can be verified in the 8th National Joint Register at www.njrcentre.org.uk

5.3 Knee R&D team member, DePuy Orthopaedics Inc, Warsaw, Indiania, USA

This contact was a leading figure in the project management and development of the new knee replacement design with DePuy Inc.