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Failure analysis of the cement mantle in total hip arthroplasty with an efficient probabilistic method

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Abstract

Accurate prediction of long-term behaviour of cemented hip implants is very important not only for patient comfort but also for elimination of any revision operation due to failure of implants. Therefore, a more realistic computer model was generated and then used for both deterministic and probabilistic analyses of the hip implant in this study. The deterministic failure analysis was carried out for the most common failure states of the cement mantle. On the other hand, most of the design parameters of the cemented hip are inherently uncertain quantities. Therefore, the probabilistic failure analysis was also carried out considering the fatigue failure of the cement mantle since it is the most critical failure state. However, the probabilistic analysis generally requires large amount of time; thus, a response surface method proposed in this study was used to reduce the computation time for the analysis of the cemented hip implant. The results demonstrate that using an efficient probabilistic approach can significantly reduce the computation time for the failure probability of the cement from several hours to minutes. The results also show that even the deterministic failure analyses do not indicate any failure of the cement mantle with high safety factors, the probabilistic analysis predicts the failure probability of the cement mantle as 8%, which must be considered during the evaluation of the success of the cemented hip implants.

Keywords

Cemented hip prosthesis, failure of cement mantle, probabilistic modelling, response surface method

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Introduction

Computational simulations, such as finite element analysis (FEA), are widely accepted and used in orthopaedic biomechanics to develop better performing implants. These methods are naturally deterministic, for instance, stresses in an orthopaedic part are determined using fixed values of parameters such as loads that the orthopaedic parts are subjected to or material properties of the orthopaedic parts. However, there may be significant uncertainties in the response of the orthopaedic organs due to the inherent variability of the parameters. The traditional way of dealing with uncertainties is to use a safety factor, which sets conservative limits for design values. On the other hand, a more appropriate approach to deal with uncertainties can be the utilization of probabilistic methods in which uncertain variables are treated by means of their statistical distribution.

Probabilistic approaches have been introduced recently in orthopaedic applications. Nicolella et al.[1] developed a three-dimensional (3D) model of a cemented hip prosthesis where uncertainties in material properties and loadings were taken into account to predict the probability of failure. Bah and Browne[2] studied possible failure modes of the cement mantle in the hip implants by considering geometry, material properties and loadings as random variables. More recently, an optimum shape of the hip prosthesis has been studied

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by taking into account the variability of the design parameters.[3,4]

Although probabilistic analysis can provide significant information on the possible outcomes of the implant behaviour, there are some drawbacks of the application of this method for implant designs. One of the main disadvantages of probabilistic approach is the computational cost since carrying out the probabilistic analysis of the cemented hip implant requires many more trials. Kayabasi and Ekici,[4] for instance, spent 48 h for the computation of the failure probability. Similarly, Easley et al.[5] spent approximately 17 h to carry out 1000 Monte Carlo trials. Dopico-Gonzalez et al.[6] completed the failure analysis of an uncemented total hip replacement in 3 days, for which they utilized Latin hypercube sampling (LHS; with a sample size of 10,000). Therefore, making some simplifications in the model is a common approach for the probabilistic analysis, such as the use of a linear elastic, isotropic material model, describing a perfect bond at the interface between cement and prosthesis.[7] These simplifications are almost inevitable to get a solution in a reasonable computation time since both optimization and probabilistic methods require multiple iteration steps of the time-consuming FEA. Rather than using a simplified model during the probabilistic analysis, meta-modelling techniques can be used to generate a surrogate model in place of time-consuming analysis.[8,9] On the other hand, Laz and Browne[10] pointed out that one of the main disadvantages of using a surrogate model is to approximate entire sample space, which yields less accuracy mainly for nonlinear functions. The size and quality of the initial training dataset are critical requirement for realistic predictions of the implant behaviour.[8] Therefore, to have a better surrogate model, more training points are needed. This has been realized by some of the researchers such as Bah and Browne[9] and Galibarov et al.[8] However, they either used a model, which was a simplified version of the cemented hip prosthesis, or they did not use specific training points developed especially for the probabilistic analysis.

Accordingly, the objective of this research is to introduce an approach by which the computation time of the probabilistic analysis for the cemented hip prosthesis can be significantly reduced by using one of the meta-modelling techniques specifically developed for the probabilistic analysis. It requires much less computation time, and thus, analyses of the orthopaedic implants can be carried out in a manageable time. It also enables us to use a more realistic model during the analysis of orthopaedic implants. To realize this objective, a MATLAB[11]-based program has been developed. The 3D model of the cemented hip prosthesis was generated and exported to a FE program to carry out stress analyses required by the probabilistic analysis. A deterministic failure analysis was performed for the most common failure states of the cement mantle. As the results indicate that the fatigue failure of the cement mantle is the most critical failure state, the probabilistic failure analysis was carried out considering the fatigue failure of the cement mantle. Since the probabilistic analysis required large amount of time, the response surface methods (RSMs) specifically developed were used to replace time-consuming FEA. In addition, to benchmark the results obtained from the approximation methods, the failure probability of the cement mantle was also computed using a Monte Carlo simulation (MCS)[12] method.

Materials and methods

FE model of the cemented hip prosthesis

First of all, a 3D FE model of the cemented hip prosthesis was generated and then used in both deterministic and probabilistic analyses. The computer-aided design (CAD) model of a standardized femur was obtained from Biomed Town[13] depository and transferred to Pro/ENGINEER[14] to create a solid CAD model of the femur. A well-known Charnley prosthesis (Figure 1(a)) was modelled, from which the cement mantle (Figure 1(b)) was generated using the outer surface of the prosthesis by giving 2 mm in thickness. The final femur CAD model was obtained by extracting the assembly of the prosthesis and the cement from the femur model (Figure 1(c)). Before exporting the model to the ANSYS FE package,[15] the prosthesis, cement and femur were assembled to form the cemented hip prosthesis (Figure 1(d)).

In order to obtain the FE model, an element having 3D 10-node tetrahedral structural solid with a quadratic displacement behaviour, which is suitable to model irregular meshes such as the model used in this study, was selected.

To determine an appropriate mesh size, a convergence study has been carried out, in which the mesh size was reduced gradually from 9 to 2 mm with the decreasing rate of 0.5 mm. The variation of the stress results is graphically shown in Figure 2.

As the results presented in Figure 2 indicate, the stresses do not change significantly, depending on the mesh size. However, if the mesh size is below 2.5 mm, the stress values start jumping to higher values since the uneven geometry of the cortical bone causes stress singularity. The whole model was then meshed, considering the element size of 5 mm (Figure 3(a)). Thus, the femur, prosthesis and cement were meshed with 23,997 nodes and 14,417 elements, 7945 nodes and 4964 elements and 5214 nodes and 2606 elements, respectively.

In the assembly model (Figure 3(b)), there are three boundary conditions applied: (1) the load applied to the femoral head, (2) the load applied to the proximal area of the greater trochanter by abductor muscle loads and (3) the femur completely constrained at the distal end. These boundary conditions represent the magnitude of a person with 70 kg.

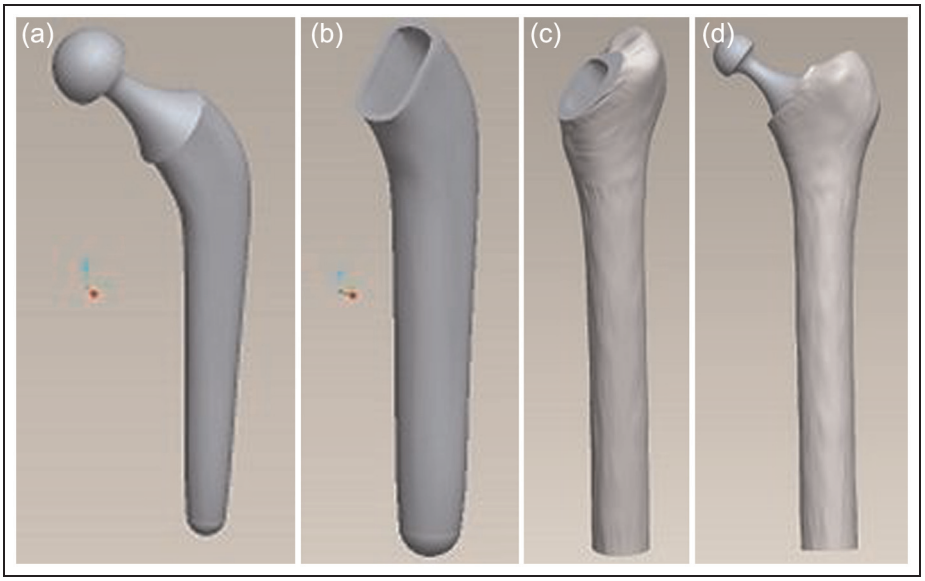

Figure 1. (a) Charnley prosthesis, (b) cement mantle, (c) osteotomized femur, and (d) assembly model of the prosthesis, cement and femur.

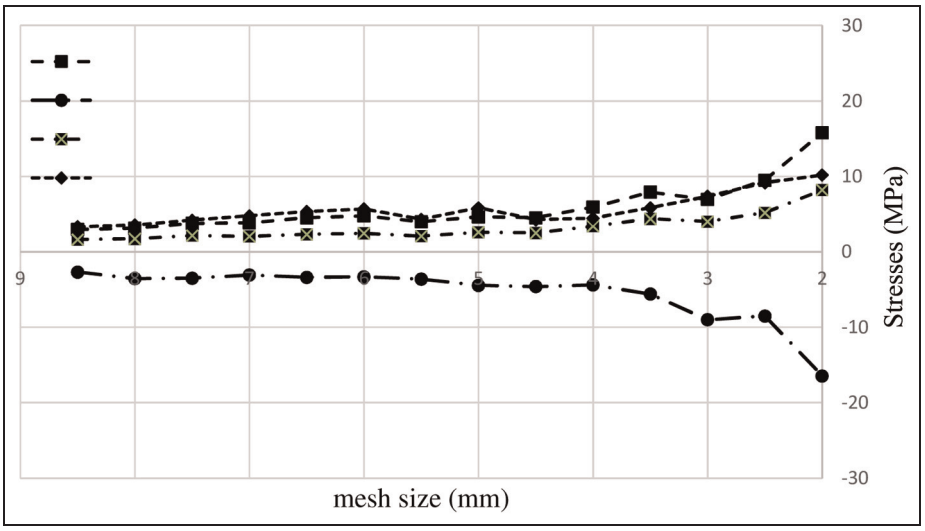

Figure 2. Variation of the stress values –σ_{VM}: von Mises stress; σ_{III}: minimum principal stress; σ_{Tr}: Tresca stress and σ_I: maximum principal stress.

Linear isotropic Ti-6Al-4V was chosen as the prosthesis material. Different material models were assigned to the inner and outer parts of the femur (cancellous bone and cortical bone) to truly evaluate its effect in the prosthesis. The cement material was considered as linear isotropic. The material properties of the prosthesis, femur and cement (Table 1) were obtained from the literature.[3]

Probabilistic analysis of the cemented hip prosthesis

For the probabilistic analysis of the cemented hip prosthesis, 10 random variables were considered in this study, similar to the previous works published,[3,4] which are the applied loads and material properties of the bone and cement. Besides, the fatigue limit of the cement, which is taken into account in describing the failure mode of the cemented hip prosthesis, was also taken as a random variable (Table 1). These random variables are the most important parameters affecting the performance of the cemented hip prosthesis, as indicated in the literature.[9]

In a probabilistic analysis, the probability of failure can be represented by describing a performance function, which is a function of random variables. Thus, the formulation of an appropriate performance function is needed to evaluate the failure of the cemented hip prosthesis. In the literature, both the bulk cement mantle

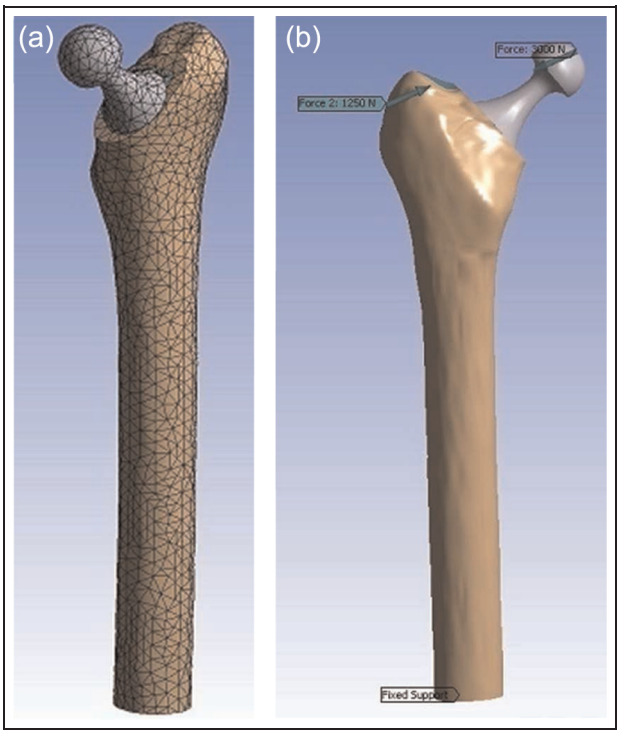

Figure 3. (a) FE model of the cemented hip prosthesis and (b) the boundary conditions applied.

and the prosthesis–cement interface[3] were taken into account since the cemented hip prosthesis is often associated with the failure of the cement mantle or debonding of prosthesis–cement interface.[16,17] However, only the failure of the bulk cement was considered in this work. A performance function, which describes cement failure due to fatigue, for the cemented hip prosthesis was used in this study since it is most likely when compared to other failure types.[3] In addition, the deterministic analysis carried out in this study indicates the lowest safety factor for the fatigue failure among other failure modes. Thus, the performance function describing the failure of the cement mantle can be written as

$$g_1(x) = R_{FL} - S_{\sigma_1}(X) \leqslant 0 \quad (1)$$

where R_{FL} is the random variable describing the cement fatigue limit and $S_{\sigma_1}(X)$ denotes the maximum principal stress.

After describing the performance function for the cemented hip prosthesis, the next step is to choose a method to evaluate the performance function. In this regard, there are several approaches that can be utilized, among which are simulation-based methods such as MCS, importance sampling[18] and LHS.[19] Although these methods can closely estimate the exact result, if sufficient simulation trials are employed, a great number of calls to the performance function is required, which usually takes a great deal of time especially for the problems for which an explicit performance function cannot be formulated. This is common for the failure evaluation of hip implants, which yields significant computation time as indicated in the literature. Bah and Browne,[9] for instance, have reported that using direct MCS to compute the failure of the cemented hip prosthesis, even though an idealized model of the hip cemented stem was used, 10,000 FE runs required 350 h of central processing unit (CPU) time. The computation time can be reduced by using a simplified model or eliminating insignificant random variables. A similar burden has been reported by Dopico-Gonzalez et al.,[6] for which the computation of the failure probability of an uncemented hip replacement by using LHS took 3 days. Therefore, conducting probabilistic analysis in a reasonable time is very important not only to carry out analyses requiring extensive computation time but also to use a much more realistic model in the analyses. One of the approaches to reduce the computation time is to use an approximation model in place of a time-consuming analysis. Since the approximation model is used as a surrogate for the original code, it is often referred to as a surrogate model, approximation model or metamodel which is a 'model of a model'.[20] Several methods exist to obtain the metamodel, such as the RSM,[21] Neural Networks,[22] Inductive Learning[23] and Kriging.[24] The RSM, the most widely used in most of the biomechanical applications, has been developed especially for deterministic analyses to generate an

Table 1. Random variables and their distribution.

Random variables	Mean	Standard deviation	Distribution type
Cortical bone modulus (GPa)	20.3	2.3	Lognormal
Cancellous bone modulus (GPa)	2.13	0.12	Lognormal
Bone cement modulus (GPa)	1.95	0.15	Lognormal
Joint load, X-direction (N)	1492.0	237.23	Lognormal
Joint load, Y-direction (N)	915.0	408.09	Lognormal
Joint load, Z-direction (N)	2925.0	731.25	Lognormal
Muscle load, X-direction (N)	1342.0	335.5	Lognormal
Muscle load, Y-direction (N)	832.0	208.0	Lognormal
Muscle load, Z-direction (N)	2055.0	513.75	Lognormal
Bone cement fatigue limit (MPa)	10.81	4.47	Lognormal

Table 2. Most common failure states of the cement mantle.

Failure functions	Mean value of the strength (MPa)	Maximum stresses (MPa)	Safety factor
Interface shear failure: $R_{I\tau} - \sigma_{VM}$	33	4.63	7.12
Compressive failure: $R_{UCS} - \sigma_{III}$	81.4	4.44	18.33
Shear failure: $R_{\tau} - \sigma_{Tr}$	30	2.60	11.53
Fatigue failure: $R_{FL} - \sigma_{I}$	10.81	5.84	1.85

$R_{I\tau}$: interface shear strength; R_{UCS}: ultimate compressive strength; R_{τ}: shear strength; R_{FL}: fatigue limit strength; σ_{VM}: von Mises stress; σ_{III}: minimum principal stress; σ_{Tr}: Tresca stress; σ_{I}: maximum principal stress.

approximate model. On the other hand, it should be noted that this approach is not always suited to the probabilistic analysis of the implants. Some points in the formation of the approximate model for a probabilistic analysis need special attention such as approximating the region, which contributes most significantly to the probability of failure, better than other regions, and using criteria to assess the goodness of the approximate model. Therefore, the RSM was modified in order to better fit for applications of the probabilistic analysis. In this regard, Bucher[25] first applied a modified version of the traditional RSM to the reliability problems. Then several new approaches have been proposed, which can better estimate unknown responses from the probabilistic analysis.[26]

The application of the RSM has been recently realized for biomechanical design and analyses.[27,28] Moreover, some commercial FE software such as ANSYS has been recently added a new capability of carrying out the probabilistic analysis, thus researchers can easily assess the probability of failure of the model concerned. However, not only the works mentioned but also some commercial software utilize traditional RSM, thus the approximate model is generated for responses such as the equivalent stress of the hip joint prosthesis. This approach requires taking into account the whole design space, rather than concentrating on the region which contributes most significantly to the probability of failure. Therefore, to have a better approximation model, more training points are needed than applying the RSM developed specifically for probabilistic analysis.

Results

The failure analysis of the cement mantle is assessed using both deterministic and probabilistic approaches, and the results from both the analyses are summarized in the following.

Results from the deterministic analysis

In order to find out the effect of the variability in the parameters on the performance of the cemented hip prosthesis, first a deterministic stress analysis was carried out, taking the mean values of the random variables (Table 1) as the value of the design parameters of the cemented hip implant in the FEA.

Several failure states for the cement have been proposed in the literature,[3] and the most important failure states (Table 2) are considered in this study. In order to compute the safety factors, the deterministic stress analyses were carried out considering the FE model presented (Figure 3).

The results from these deterministic analyses are presented (Figure 4) for the von Mises stress, Tresca stress,

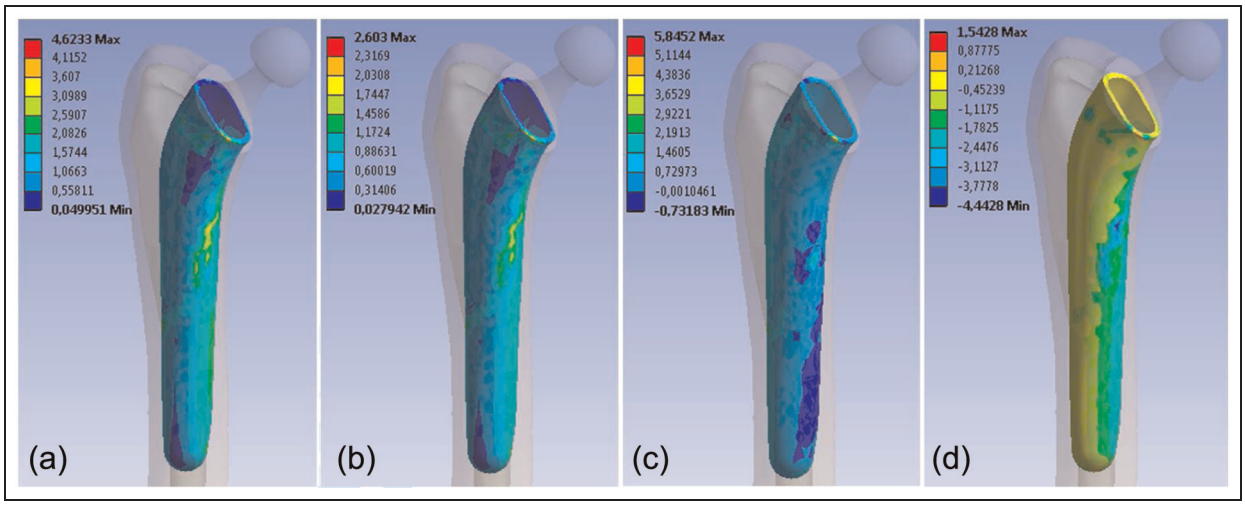

Figure 4. Stress results from the deterministic analysis: (a) von Mises, (b) Tresca, (c) maximum principal and (d) minimum principal.

Table 3. Results from the probabilistic analysis.

Methods applied	No. of FE runs	Probability of failure
Importance sampling	1000	8.00%
The FORM	71	5.92%
Bucher RSM	42	7.85%
Kriging RSM	50	8.011%

FE: finite element; FORM: first-order reliability method; RSM: response surface method.

maximum principal stress and minimum principal stress since these are the mostly used responses that describe the failure states of the cemented hip prosthesis. The mean value of the strength of the cement material[3] was taken into account during the computation of the safety factor (Table 2) for each failure state. The fatigue failure is the most critical failure mode since its safety factor is well below that of the other failure modes. However, all these safety factors indicate that the cement mantle is deterministically safe.

Results from the probabilistic analysis

The probabilistic analysis of the cemented hip prosthesis was carried out considering the fatigue failure state specified in equation (1) since it has the lowest safety factor among the other failure modes.

To have a benchmark result with which the probabilistic results from the RSM can be compared, importance sampling simulation with 1000 samples was carried out to compute the probability failure of the cemented hip prosthesis, which was directly performed on the FE model of the cemented hip prosthesis. Importance sampling gives the probability of failure as 0.08, which can be regarded as the exact result.

Two types of meta-modelling techniques were used in this work. In Bucher's RSM, the coefficient of a quadratic function was obtained using 42 training points whose values were specifically determined for the probabilistic analysis. As a second method, the Kriging was performed to get the approximation function for which LHS with 50 samples was selected as training points. Table 3 presents the failure probability of the cement mantle computed using the both approaches.

A single FEA of the cemented hip joint takes approximately 26 s using a computer of Intel i7 CPU 920 at 2.66 GHz with 8 GB of RAM. It took approximately 7 h and 13 min to complete the simulation with 1000 samples. However, utilizing Bucher's RSM took only 18 min to compute the probability of failure of the cemented hip prosthesis, while the Kriging method required 21 min to complete the probabilistic analysis. These results, when compared to the results obtained from the direct simulation, indicate that using an RSM can not only reduce the computation time significantly but also give a reasonable prediction on the failure of the bulk cement when compared to the results in the literature.

Discussion

The main aim of this work is to show that using a RSM that was specifically developed for the probabilistic analysis could significantly reduce the computation time of the probabilistic analysis of the cemented hip prosthesis. Compared to the FE model of the cemented hip prosthesis given in the literature,[9] the model used in this work is a more realistic one. The CAD model, especially for the femur bone, is much more complex, thus meshing and specifying the contact properties need special attention during the FEA. In addition, the computation time of such a model is much higher. However, as pointed out earlier, the time required to complete the probabilistic analysis can be dramatically reduced if an RSM is utilized without considering any further simplification such as reducing the number of the random variables or using a simplified geometry for the femur bone.

The probabilistic sensitivity factors were also computed to indicate the effect of each random variable on the probabilistic results of the cemented hip prosthesis. To find out whether the effect of each random variable can be determined by using the RSMs, the results (Figure 5) were presented for two types of the RSMs utilized in this work along with the sensitivity factors computed from the simulation directly applied to the FE model of the cemented hip prosthesis since it serves as the exact solution. The sensitivity factors computed from the RSMs show similar trend when compared to that of the simulation. As outlined in the literature, the loadings and the fatigue limit strength of the bone cement[3] are among the most important parameters affecting the probabilistic results. However, the sensitivity results from this work also indicate that the cortical bone young modulus and bone cement young modulus have also important effects on the failure probability of the cemented hip prosthesis. This result is different from that presented in the literature in which the bone and cement young moduli are considered as insignificant variables during the probabilistic sensitivity analysis.[3,9] This difference might arise from the model used in this work since its geometry is much more complex than that given in the literature. Thus, the interfaces between the cement and cortical and cancellous bone are not smooth, which affects the stress distributions at the interface.

The simulation-based probabilistic analysis is considered as the reference method in the literature. However, a reasonable estimate for the failure probability requires having a sufficient number of simulation, in most cases more than 1000 or even more for computing low probabilities as pointed out by Dopico-Gonzalez et al.[28] For such applications requiring extremely high computation time, the RSM plays an important role in computing the failure probability in a reasonable time. In this work, though a relatively low number of simulation was considered, the calculation of the failure probability took more than 7 h when the

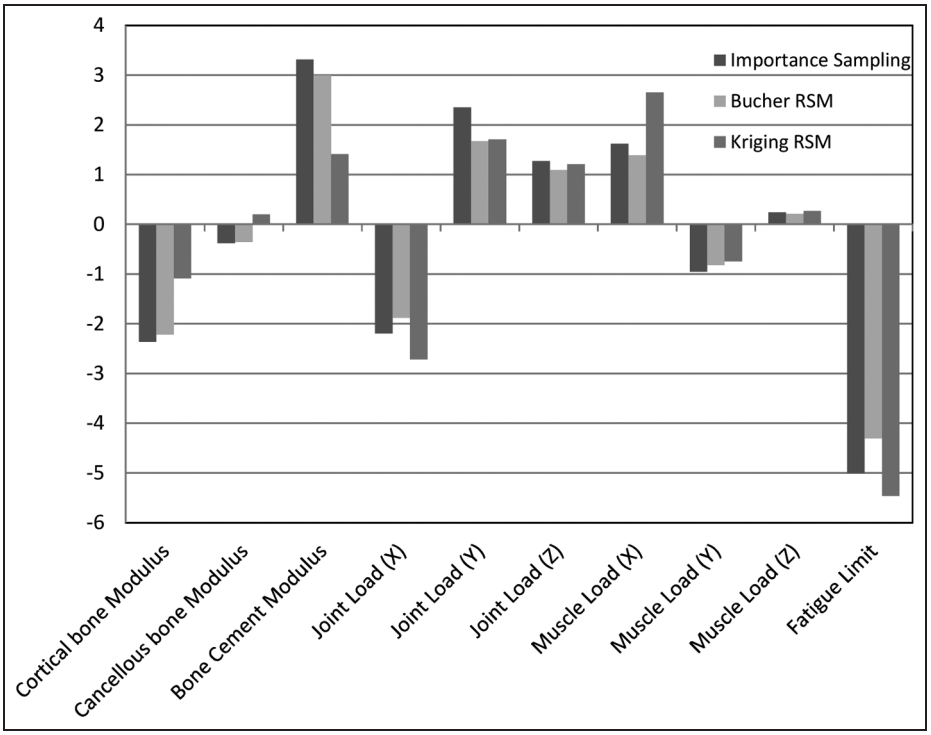

Figure 5. Sensitivity analysis of the cemented hip prosthesis for the fatigue cement failure.
RSM: response surface method.

importance sampling was used, whereas the probability of failure computation was completed only in minutes when an RSM is utilized. Furthermore, the results obtained from both RSMs (Table 3) are within the acceptable limit. It should be noted that the FEA carried out for the performance function of the cemented hip prosthesis is a linear static analysis. In a case where nonlinear analyses are required, the computation time sometimes may take days as reported in the literature.[28] Therefore, using an RSM is almost inevitable to probabilistically assess the performance of implant designs.

It should be noted that some researchers suggested using numerical probabilistic methods such as advanced mean value (AMV), the first-order reliability method (FORM), in place of any simulation method in order to reduce the computation time. Therefore, in this work, the failure probability of the cemented hip prosthesis was also calculated using the FORM and found to be 5.92%, which is not as close to the exact result as that obtained from the RSMs. This difference can be explained such that the performance function is linearized in the FORM or approximated by a quadratic function in the second-order reliability method (SORM). Thus, for nonlinear performance functions, such approximations could give different results than that of the simulation, even for some applications may suffer from convergence problem.[29] In addition, the computation time is not less than that of the RSMs, which took approximately 30 min.

For the reasons mentioned above, the RSM has been recently applied to the probabilistic analysis of orthopaedic implants. Some of commercial FE software such as ANSYS have a capability of carrying out a probabilistic analysis utilizing an RSM for which central composite design (CCD) or optimal space filling design are used to generate the training points. To construct an approximate model using CCD by using such software for the probabilistic analysis of the cemented hip prosthesis studied in this work would require 149 FE analyses. However, the RSM in these applications is applied to the response variable of the FEA such as getting an approximate function for the maximum von Mises stress value without considering the region identified by the performance function. In this way, the goodness of such an approximate model is assessed considering the whole design space. On the other hand, any approximate model to be used in place of a performance function should be better fitted to a region where the most of the probability value is computed.[26] Therefore, the RSM in this work was applied to the performance function described in equation (1). Hence, the training points were selected from a design that was specifically developed for the probabilistic analysis, which results in a more accurate approximate model to be used in place of the performance function. This was confirmed by the results presented in this article.

Conclusion

In this study, it has been shown that the RSM specifically developed for the probabilistic analysis can serve as a powerful method to reduce the computation time

required to obtain the failure probability of the cemented hip prosthesis. The approximate model formed can be used in place of the performance function describing the fatigue failure of the cemented hip prosthesis. Hence, this approximate model used in the probabilistic analysis has enabled us not only to use a more realistic 3D model of the cemented hip prosthesis but also to get results in a reasonable time when compared to direct simulation or other numerical methods. This approach could resolve some problems of the probabilistic evaluation of the biomechanical applications such as simplification of FE model due to high computational cost, which is stated in most of the works in the literature,[5] or using a simpler model and method in reliability-based design optimization.[3,4]

It should be noted that the model used in this study needs further improvements. The material properties of the both cancellous and cortical bones, for instance, could be more realistically defined by considering a relationship between Young's modulus and the density which can be determined from the grey value in the computed tomography (CT) scan.[30] Thus, rather than having two layers to model both cancellous and cortical bones as used in this work, the material properties can be assigned to the individual elements of a femur based on this relationship.

Another improvement can be made on the definition of bone cement–prosthesis interface, which was defined as fully bonded in this study. On the other hand, a more realistic definition must include a frictional-type bonding at the interfaces.

Therefore, future work will focus on improving the model used in this study by considering the above remarks.

Declaration of conflicting interests

The authors declare that there is no conflict of interest.

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References

1. Nicolella DP, Thacker BH, Katoozian H, et al. Probabilistic risk analysis of a cemented hip implant. *J Math Model Sci Comput* 2001; 13: 98–108.
2. Bah MT and Browne M. Failure of the cement mantle in hip implants: a probabilistic approach. In: *Transactions of the 50th annual meeting of the Orthopaedic Research Society*, San Francisco, CA, 7–10 March 2004. San Francisco, CA: Orthopaedic Research Society.
3. Nicolella DP, Thacker BH, Katoozian H, et al. The effect of three-dimensional shape optimization on the probabilistic response of a cemented femoral hip prosthesis. *J Biomech* 2006; 39(7): 1265–1278.
4. Kayabasi O and Ekici B. Probabilistic design of a newly designed cemented hip prosthesis using finite element method. *Mater Des* 2008; 29(5): 963–971.
5. Easley SK, Pal S, Tomaszewski PR, et al. Finite element-based probabilistic analysis tool for orthopaedic applications. *Comput Methods Programs Biomed* 2007; 85(1): 32–40.
6. Dopico-Gonzalez C, New AMR and Browne M. Probabilistic analysis of an uncemented total hip replacement. In: *European Society of Biomechanics workshop 2007: finite element modelling in biomechanics and mechanobiology*, Dublin, 26–28 August 2007.
7. Dopico-Gonzalez C, New AMR and Browne M. Probabilistic analysis of an uncemented total hip replacement. *Med Eng Phys* 2009; 31(4): 470–476.
8. Galibarov PE, Prendergast PJ and Lennon AB. A probabilistic modelling scheme for analysis of long-term failure of cemented femoral joint replacements. *Proc IMechE, Part H: J Engineering in Medicine* 2012; 226(12): 927–938.
9. Bah MT and Browne M. Effect of geometrical uncertainty on cemented hip implant structural integrity. *J Biomech Eng* 2009; 131: 054501 (5 pp.).
10. Laz PJ and Browne M. A review of probabilistic analysis in orthopaedic biomechanics. *Proc IMechE, Part H: J Engineering in Medicine* 2010; 224(8): 927–943.
11. MathWorks, Inc. *MATLAB* (MATLAB guide). Natick, MA: MathWorks, Inc., 2007.
12. Ditlevsen O and Madsen HO. *Structural reliability methods*. Chichester: John Wiley & Sons, 1996.
13. Biomed Town.http://www.biomedtown.org (2007).
14. Pro/ENGINEER. WildFire 5.0.Waltham, MA: Parametric Technologies Corporation, 2010.
15. ANSYS, Inc. *Theory reference manual* (release 12.0). Canonsberg, PA: ANSYS, Inc., 2010.
16. Jasty M, Maloney WJ, Bragdon CR, et al. The initiation of failure in cemented femoral components of hip arthroplasties. *J Bone Joint Surg Br* 1991; 73(4): 551–558.
17. Maloney WJ, Schmalzried T and Harris WH. Analysis of long term cemented total hip arthroplasty retrievals. *Clin Orthop Relat Res* 2002; 405: 70–78.
18. Melchers RE. Search-based importance sampling. *Struct Saf* 1990; 9(2): 117–128.
19. Olsson A and Sandberg G. Latin hypercube sampling for stochastic finite element analysis. *J Eng Mech* 2002; 128(1): 121–125.
20. Simpson TW, Booker AJ, Ghosh D, et al. Approximation methods in multidisciplinary analysis and optimization: a panel discussion. *Struct Multidiscip O* 2004; 27(5): 302–313.
21. Myers RH and Montgomery DC. *Response surface methodology: process and product optimization using designed experiments*. New York: John Wiley & Sons, 1995.
22. Hajela P and Berke L. Neural networks in structural analysis and design: an overview. *Comput Syst Eng* 1992; 3(1–4): 525–538.
23. Simpson TW, Poplinski JD, Koch PN, et al. Metamodels for computer-based engineering design: survey and recommendations. *Eng Comput* 2001; 17(2): 129–150.
24. Kaymaz I. Application of Kriging method to structural reliability problems. *Struct Saf* 2005; 27(2): 133–151.
25. Bucher CG. A fast and efficient response surface approach for structural reliability problems. *Struct Saf* 1990; 7: 57–66.

26. Kaymaz I and McMahon CA. A response surface method based on weighted regression for structural reliability analysis. *Probabilist Eng Mech* 2005; 20(1): 11–17.
27. Chang PB, Williams BJ, Bhalla KSB, et al. Design and analysis of robust total joint replacements: finite element model experiments with environmental variables. *J Biomech Eng* 2001; 123(3): 239–246.
28. Dopico-Gonzalez C, New AMR and Browne M. A computational tool for the probabilistic finite element analysis of an uncemented total hip replacement considering variability in bone-implant version angle. *Comput Methods Biomech Biomed Engin* 2010; 13(1): 1–9.
29. Wang L and Grandhi RV. Safety index calculation using intervening variables for structural reliability analysis. *Comput Struct* 1996; 59(4): 1139–1148.
30. Laz PJ, Stowe JQ, Baldwin MA, et al. Incorporating uncertainty in mechanical properties for finite element-based evaluation of bone mechanics. *J Biomech* 2007; 40(13): 2831–2836.