Uncertainty Quantification of the Optimal Stimulation Area in an Electro-Stimulative Hip Revision System

Christian Schmidt, Ulf Zimmermann, and Ursula van Rienen

***Abstract*— Electro-stimulative hip revision systems accelerate the bone growth around the implant and are capable of reducing the number of side effects such as aseptic implant loosening. A computational model was developed to determine the optimal electrode arrangement for such a system, which is currently under development. The optimization process depends on the electrical properties of bone material and the used bone substitute, which are subject to uncertainty in literature and its production process, respectively. To quantify the influence of these uncertain parameters on the optimal stimulation ratio (OSR), the computationally effective non-intrusive polynomial chaos technique was applied. The results indicate that the conductivity of bone substitute is most sensitive to the OSR, while its uncertainty was comparatively small compared to that of the uncertain parameters.**

I. INTRODUCTION

Since the 1990s the number of total hip athroplasty revisions increased substantially, which is predicted to grow by 137 % between 2005 and 2030 [1]. According to Springer et. al [2], about one out of three total hip athroplasty revisions have to be revised due to aseptic implant loosening. This loosening is a result of mechanical instability at the implant-bone-interface, which is facilitated by bone necrosis. In 1974, Basset et al. [3] showed that electro-stimulation accelerates the healing of fractures and bone defects, which results in a decrease of bone necrosis and an enhance of bone recovery. Therefore, combining a hip revision system with a system for electro-stimulation could result in an improved mechanical stability and durability of the implant.

A prototype of such an electro-stimulative hip revision system is currently developed by the orthopedic clinic at the University Medicine of Rostock. The prototype consists of an inductively coupled system to induce an electric field distribution of a certain intensity in an area around the implant, which is considered to be beneficial for bone growth and bone recovery. To provide the optimal positioning of the stimulation electrodes, a computational model of the hip revision system, comprising the implant as well as a model of a pelvic bone, was developed and applied to a multi-objective optimization algorithm [4]. Besides the geometry of the implant and the pelvic bone, which are controllable parameters in the considered hip revision system [5], the material properties of bone tissue and bone substitute, which is used to fixate the implant, are subject to uncertainty in literature [6], [7]. This uncertainty results from the heterogeneity and composition of the materials as well as from deviations in the measurements of biological tissue, *in vivo* and *ex vivo* [8].

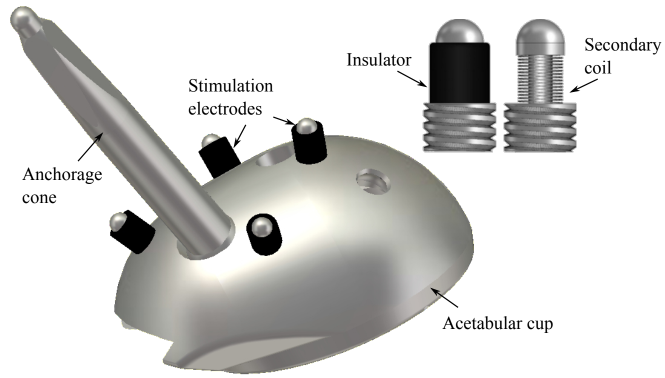

Fig. 1. Model of the acetabular cup including anchorage cone and four stimulation electrodes.

The quantification of the influence of this uncertainty on the optimization of the electro-stimulative hip revision system can be carried by stochastical methods, such as Monte Carlo simulation (MCS), but require typically a large number of realizations of the deterministic model to provide a sufficient accuracy of the statistics. Therefore, MCS is not applicable to a computationally expensive models such as the one presented here. To reduce the computational burden of the uncertainty quantification, the polynomial chaos technique (PCT) can be used. The PCT approximates the statistics of the quantity of interest by an expansion in multivariate orthogonal polynomials, for which only the evaluation of the coefficients require the realization of the deterministic model.

For the uncertainty quantification of the optimal electrode arrangement an in-house implementation of a non-intrusive version of the PCT is used, which was already successfully applied in the field of neural engineering [9]. A global sensitivity analysis based on Sobol' indices is performed to investigate the influence of each of the uncertain material properties in the computational model as well as their interaction [13].

II. METHODS

A. Hip Revision System and Optimal Electrode Arrangement

The electro-stimulative hip revision system consists of an acetabular and a femoral component, at which surface the

The work was supported by the DFG (German Science Foundation) Research Training Group 1505 "welisa".

Asterisk indicates corresponding author.
*C. Schmidt, U. Zimmermann, and U. van Rienen are with the Institute of General Electrical Engineering, University of Rostock, 18059 Rostock, Germany.
E-mail: christian.schmidt6 at uni-rostock.de

stimulation electrodes are attached (Fig. 1). A primary coil around the patient's hip provides a time-harmonic magnetic field at a frequency of 20 Hz, which induces a location-dependent current in the secondary coils of the stimulation electrodes, resulting in an electric potential distribution in the area around the implant. An effective stimulation depends substantially on the electrode arrangement. Therefore, an optimization of this arrangement would allow for an optimal stimulation in future designs. Due to the damage of the primary implant, the bone shows generally defects in the femoral and acetabular area. The defects in the acetabular area, which comprises cavities and discontinuities, are treated by the use of a larger acetabular cup and replenishment with bone substitute.

Since the design of the femoral component is limited by mechanical requirements of the system, the optimization is only carried out for the acetabular component. Based on the work of Kraus [10] and clinical advice, an electric field of $5-70\,\mathrm{Vm}^{-1}$ in the proximity of the implant and $35-70\,\mathrm{Vm}^{-1}$ in the defective area, which both forms the area of interest, is considered to be optimal. These requirements constitute the primary and secondary optimization goals, respectively. The optimization is carried out for an arrangement of four electrodes, because of practical reasons considering the attachment of the electrodes during surgery.

B. Computational Model and Optimization Algorithm

The computational model comprises a layered CAD model of the pelvic bone, which is derived from computer tomography scans and altered manually to emulate a defective bone by inserting a cavity filled with bone substitute, and the acetabular cup (Fig. 2). The model geometry is updated for each electrode arrangement given by the optimization process. Since the electrical properties are linear, the principle of superposition can be applied to obtain the electric field for any possible electrode arrangement out of the electric field distributions generated by each electrode. These basis distributions are computed with the Finite-Integration-Technique using CST EM Studio® by subsequently applying a stimulation amplitude of $1\,\mathrm{V}$ at one electrode at each possible position. This approach enables the optimization process to be carried out in post-processing and, therefore, reduces substantially its computational expense. The optimization process uses the multi-objective, evolutionary algorithm NSGA II to obtain out of a randomly chosen set of electrode arrangements a new generation [11]. After a sufficient amount of generations a stable state is reached, which gives a good approximation of the set of Pareto optimal arrangements [5].

C. Uncertainty Quantification Using Polynomial Chaos

Uncertainty quantification is applied to the computational model to investigate the sensitivity and robustness of the optimal stimulated area in the proximity of the implant regarding the uncertain conductivity of cancellous bone κ_c and bone substitute κ_s for the previously computed optimal electrode arrangement.

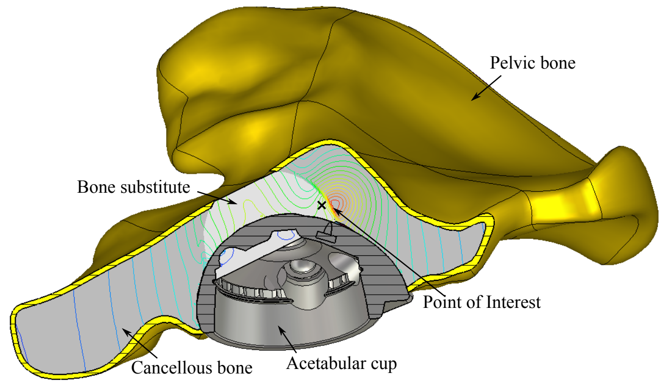

Fig. 2. Acetabular cup fixated in the model of the pelvic bone with the defect filled up with bone substitute. The electric field norm is shown exemplary in the cut-plane.

The PCT allows for the quantification of the influence of a number of uncertain parameters $X_1, \ldots, X_M$ on the quantity of interest Y by approximating the statistics of the quantity of interest Y by an expansion in a truncated series of multi-variate orthogonal polynomial basis functions $\psi_i(\boldsymbol{\xi})$, where the stochastically independent random variables $\boldsymbol{\xi} = (\xi_1, \ldots, \xi_M)$ are modelled to be uniformly distributed in the interval $[-1, 1]$. The basis functions $\psi_i(\boldsymbol{\xi})$ can then be written as product of uni-variate basis functions. Considering the uniformly distributed random variables $\boldsymbol{\xi}$, the $p-$th order Legendre polynomials $L_p(x) \in [-1, 1]$ constitute an optimal choice [12]. By defining a bijective mapping

$$k := \boldsymbol{\alpha}^{(k)} = (\alpha_1^{(k)}, \ldots, \alpha_M^{(k)}) \tag{1}$$

with the uni-variate orders $0 \leq \alpha_i^{(k)} \leq p$, the multi-variate expansion of order p is given by

$$Y \approx \sum_{k=0}^{P_{out}} c_k \psi_k(\boldsymbol{\xi}) \tag{2}$$

where the expansion coefficients c_k are determined by projecting (2) on each basis function $\psi_i(\boldsymbol{\xi})$ and exploiting its orthogonality. The resulting integral is evaluated numerically by using nested tensor grids $TG(L, M)$ with grid level $L = p$, where the one-dimensional nodes $n(L)$ are given by the Clenshaw-Curtis rule with exponential growth given by $n(L) = 2^L + 1$. The Sobol' indices $S(i, \ldots, j)$ determine the relative influence of each uncertain parameter as well as their interactions and is determined by an analysis of variance (ANOVA) decomposition of Y [13]

$$S(i, \ldots, j) = \frac{\mathbb{V}(i, \ldots, j)}{\mathbb{V}} \tag{3}$$

where the conditional variances $\mathbb{V}(i, \ldots, j)$ for the uncertain parameters $X_i, \ldots, X_j$ can be computed out of the expansion coefficients c_k and $\mathbb{V}$ is the total variance [15].

D. Modeling of the Material Properties

Bone substitute is an artificial material, which composition comprises parts of disintegrated parts cancellous bone. Therefore, its electrical properties depend substantially on

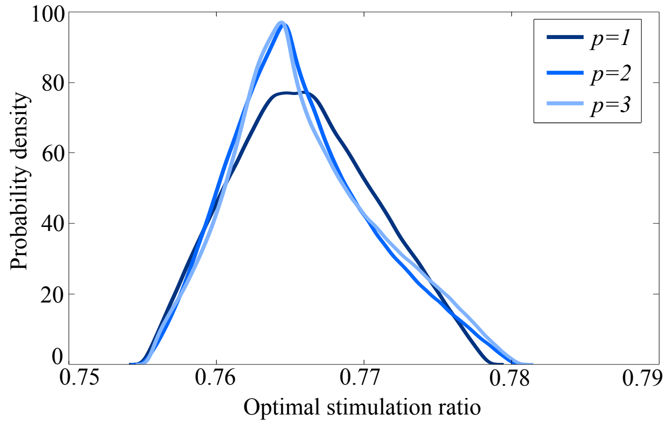

Fig. 3. Estimated probability density of the optimal stimulation ratio (OSR) for different expansion orders p.

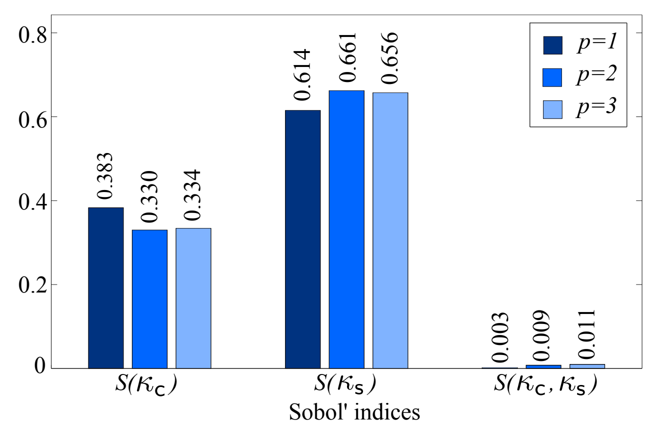

Fig. 4. Derived Sobol' indices S of the OSR for the conductivity of cancellous bone κ_c and bone substitute κ_s.

this composition. To investigate the sensitivity and uncertainty in the optimal electrode arrangement in dependence of the conductivity of cancellous bone κ_c and bone substitute κ_s, both parameters were modelled to be uniformly distributed random variables in $\mathcal{U}[a,b]$, where the lower boundary $a = 0.08\,\mathrm{Sm}^{-1}$ and the upper boundary $b = 0.15\,\mathrm{Sm}^{-1}$ are based on literature data [6], [7]. The resulting magnitude of uncertainty in the random model parameters, determined by the relative standard deviation $\sigma_\mathsf{r} = \sigma/\mu$ with the mean μ and the standard deviation σ, is approximately $18\,\%$. Since the random parameters X_i are uniformly distributed, the mapping on the random variables $\boldsymbol{\xi}$, which is required in (2), can be carried out by a linear transformation. The optimal electrode arrangement, which was required for the uncertainty quantification of the optimal stimulated area, was computed for the conductivity of cancellous bone and bone substitute set to the values of the lower boundary and the mean, respectively.

III. Results

The investigated quantity of interest was the optimal stimulation ratio (OSR), which is defined as the ratio between the area of optimal stimulation provided by the Pareto set of optimal electrode arrangements and the area of interest. In addition, the norm of the electric field at a point of interest (POI) in the defective area close to the material boundary of cancellous bone was investigated (Fig. 2). To provide an accurate approximation of the statistics of the quantity of interest, the relative error of its variance $\mathbb{V}(OSR)$ and its mean $\mathbb{E}(OSR)$ was controlled for increasing expansion orders p. An increase of the expansion order from $p = 3$ to $p = 4$ resulted in a relative error of $\epsilon_{\mathbb{E}(\mathsf{OSR})} < 0.2\,\%$ and $\epsilon_{\mathbb{V}(\mathsf{OSR})} < 1.6\,\%$, respectively. The average error in the mean of the electric field norm was below $4 \cdot 10^{-7}\,\%$ and below $3 \cdot 10^{-6}\,\%$ for its variance. The estimated probability density of the OSR showed a slightly asymmetric distribution with a peak at relatively small ratios (Fig. 3). The estimation of the probability densities was carried out by applying MCS to the computed PCT expansion with a number of $1 \cdot 10^6$ random samples, which ensured a sufficiently accurate estimation.

TABLE I

Statistic measures of the model parameters, the electric field norm $||\boldsymbol{E}||_2$ at the point of interest (POI), and the optimal stimulation ratio (OSR).

	μ	σ	σ_r
$\kappa_\mathsf{s}, \kappa_\mathsf{c}$	$0.11\,\mathrm{Sm}^{-1}$	$0.02\,\mathrm{Sm}^{-1}$	$17.9\,\%$
$\|\|\boldsymbol{E}_\mathsf{POI}\|\|_2$	$70.6\,\mathrm{Vm}^{-1}$	$8.3\,\mathrm{Vm}^{-1}$	$11.7\,\%$
OSR	0.766	0.005	$0.65\,\%$

An investigation of the Sobol' indices indicate that the uncertainty in the OSR is most sensitive to the uncertainty in the conductivity of bone substitute κ_s, with an influence ratio of approximately two-thirds compared to the uncertainty in the conductivity of cancellous bone κ_c (Fig. 4). The influence of the interaction of both uncertain parameters was negligible. The investigation of the statistic measures of the OSR suggested that in average $76.6 \pm 0.5\,\%$ of the area of interest are optimal stimulated, which resulted in an uncertainty in the OSR of $0.65\,\%$. The uncertainty in the electric field norm at the POI was with a value of approximately $12\,\%$ substantially larger than the uncertainty in the OSR (Table I). The mean area of optimal stimulation is enclosed by areas of over-stimulation in the proximity of the stimulation electrodes and areas of under-stimulation at the exterior boundaries of the acetabular cup (Fig. 5). The largest optimal stimulation area is situated around the leftmost electrode, which is the position of the defective area.

IV. Discussion

Focus of this study was the investigation of the uncertainty in the OSR for an optimal electrode arrangement of an electro-stimulative hip revision system in dependence of the uncertain conductivity of cancellous bone and bone substitute. With a value of approximately $0.7\,\%$, the uncertainty in the OSR was substantially smaller than in the model parameters, which showed an uncertainty value of approximately $18\,\%$ (Table I). The uncertainty in the POI

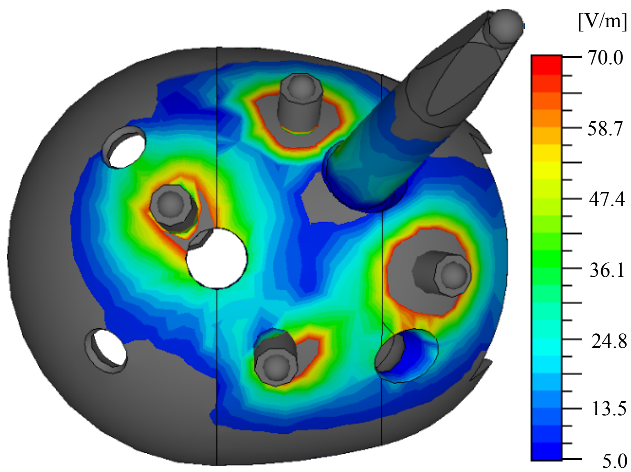

Fig. 5. Optimal stimulation area regarding the first optimization goal for the mean OSR. Areas of over-stimulation are situated in the proximity of the stimulation electrodes.

was substantially larger as in the OSR. Since the POI was chosen to be close to a stimulation electrode as well as the boundary between bone substitute and cancellous bone (Fig. 2), the larger uncertainty in the POI is presumably a result of the sensitivity of the electric field to the electrical properties at a material boundary. This result points out that in local areas larger uncertainties may occur despite an overall small uncertainty in the OSR, which can result in over- or under-stimulation in these areas depending on the material properties of the used bone substitute. Knowledge about possible areas of over- and under-stimulation is crucial, since they may result in death of bone cells or the absence of the beneficial electro-stimulative effect, respectively.

The investigation of the Sobol' indices revealed a larger influence of the uncertainty in bone substitute than in cancellous bone and negligible influence of their interaction on the uncertainty in the OSR (Fig. 4). This finding can be attributed to a stricter requirement on the optimal stimulation effect in the defective area, which was filled with bone substitute. This stricter requirement formed by the second optimization goal resulted in a larger optimal stimulation area at the defect, which is situated around the leftmost stimulation electrode in Fig. 5.

An expansion order of $p = 3$, resulting in 81 integration nodes, was found to approximate the statistics of the quantities of interest with a sufficient accuracy given by relative errors below $1.6\,\%$. However, to provide the estimate of the relative error, 208 additional realizations of the deterministic model had to be computed. Tensor grid integration is limited by an substantial growth of the required integration nodes with grid level and dimension. Therefore, the used non-intrusive PCT is only applicable for a small number of uncertain model parameters compared to MCS, which is dimension-independent. In addition, the convergence of the PCT depends on the quantity of interest being sufficiently smooth in the integration domain [14]. Comparing the approximation errors for the electric field norm at the POI and for the OSR shows larger errors for the OSR, which could be a result of additional functional dependencies arising from the computation of the OSR out of the given electric field. The investigation of the response surfaces of the OSR with respect to the model parameters confirmed this assumption by parts by showing small discontinuities in the integration domain. Therefore, an improvement of the deterministic model accuracy may improve the convergence of PCT as well.

The optimal stimulation ratio was approximately $76.6 \pm 0.5\,\%$. A further increase of this ratio is limited by the presence of the anchorage cone, which have an adverse effect on the optimal stimulation area. In the optimization procedure, the used electrode arrangements try to counteract this effect, which also results in increased areas of over-stimulation in the proximity of the stimulation electrodes (Fig. 5). In future studies, this over-stimulation could be reduced by adding a third optimization goal.

References

[1] S. Kurtz, K. Ong, E. Lau, F. Mowat, and M. Halpern, Projections of Primary and Revision Hip and Knee Arthroplasty in the United States from 2005 to 2030, J. Bone Joint Surg. Am., vol. 89, Apr 2007, pp. 780-785.

[2] B. D. Springer, T. K. Fhering, W. L. Griffin, S. M. Odum, and J. L. Masonis, Why Revision Total Hip Arthtroplasty Fails, Clin. Orthop. Relat. Res., vol. 467, Jan 2009, pp. 166-173.

[3] C. A. L. Bassett, R. J. Pawluk, A. A. Pilla, Acceleration of fracture repair by electromagnetic fields. A surgically noninvasive method, Ann. NY Acad. Sci., vol. 238, Oct 1974, pp. 242-262.

[4] C. Potratz, D. Kluess, H. Ewald, and U. van Rienen, Multiobjective Optimization of an Electrostimulative Acetabular Revision System, IEEE Trans. Bio. Eng., vol. 57, Feb 2010, pp. 460-468.

[5] U. Zimmermann, and U. van Rienen, An Automatic Pareto Classifier for the Multiobjective Optimization of an Electrostimulative Acetabular Revision System, Proceedings of COMPUMAG 2013, Budapest, Hungary, PD1-18.

[6] S. Gabriel, R. W. Lau, and C. Gabriel, The dielectric properties of biological tissues: III Parametric models for the dielectric spectrum of tissues, Phys. Med. Biol., vol. 41, Nov. 1996, pp. 2271-2293.

[7] H. Ewald, R. Bader, D. Kluess, R. Souffrant, C. Potratz, U. van Rienen, and W. Mittelmeier, Untersuchungen der elektrischen und dielektrischen Eigenschaften von Hüftknochen für den Einsatz elektrostimulierender Implanate, 5th Symposium on Automatic Control, 2008, pp. 1847-1850.

[8] C. Gabriel, A. Peyman, E. H. Grant, Electrical conductivity of tissue at frequencies below 1 MHz, Phys. Med. Biol., vol. 54, Aug 2009, pp. 4863-4878.

[9] C. Schmidt, P. F. Grant, M. M. Lowery, and U. van Rienen, Influence of Uncertainties in the Material Properties of Brain Tissue on the Probabilistic Volume of Tissue Activated, IEEE T. Bio. Eng., vol. 60, May 2013, pp. 1378-1387.

[10] W. Kraus, Magnetfeldtherapie und magnetisch induzierte Elektrostimulation in der Orthopädie, Orthopädie, vol. 13, Apr 1984, pp. 78-92.

[11] K. Deb, A. Pratap, S. Agarwal, and T. Meyarivan, A Fast and Elitist Multiobjective Genetic Algorithm: NSGA-II, IEEE T. Evolut. Comput., vol. 6, Apr 2002, pp. 182-197.

[12] D. Xiu, Numerical Methods for Stochastic Computations: A Spectral Method Approach. Princeton: Princeton University Press, 2010.

[13] I. M. Sobol, Global sensitivity indices for nonlinear mathematical models and their Monte Carlo estimates, Ma. Comput. Sci. Eng., vol. 55, Feb. 2001, pp. 271-280.

[14] F. Nobile, R. Tempone, and C. G. Webster, A sparse grid stochastic collocation method for partial differential equations with random input data, SIAM J. Numer. Anal., vol. 46, May 2008, pp. 2309-2345.

[15] O. Moreau, K. Beddek, S. Clenet, and Y. Le Menach, Stochastic Nondestructive Testing Simulation: Sensitivity Analysis Applied to Material Properties in Clogging of Nuclear Powerplant Steam Generators, IEEE T. Magn., vol. 49, May 2013, pp. 1873-1876.