Platform for the Modeling of In Vivo Effects Relevant to Implant EM Exposure Safety

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***Abstract*—The safety assessment of implant EM exposure is typically performed by numerically or experimentally evaluating field strengths in (frequently strongly simplified) phantoms or anatomical models. Determining quantities more closely related to the effect of concern can aid in detecting insufficient safety margins, reducing the necessity for overly conservative limits, and increasing the understanding of the mechanisms. SIM4LIFE is a multiphysics simulation platform optimized for computational life sciences with strong support for image based modeling and simulations involving complex anatomical models, offering solvers optimized for the modeling of living tissue, including biological and physiological processes. In the context of implant EM exposure safety, particularly under MR imaging, the platform offers powerful functionality for the modeling of the exposure, but also for the investigation of the induced effects. Tools to study induced heating (considering perfusion and thermoregulation), thermal dose, tissue damage estimation, and EM induced neuronal dynamics are presented here.**

Keywords—EM exposure safety; MRI; multiphysics modeling; induced heating; thermal dose; tissue damage; neuronal dynamics

I. INTRODUCTION

When investigating safety in the presence of implants under EM exposure, typically the EM-field enhancement and SAR are determined, for example using EM simulations involving anatomical models or strongly simplified phantom models. If measurements of SAR and temperature increase are performed, this generally requires the use of homogeneous, tissue simulating media-filled phantoms.

For questions of safety it can, however, be relevant i) to assess quantities more closely related to unintended biological or physiological effects, and ii) to do so in setups resembling the human body to the greatest possible extent. Examples of effect related quantities of interest include induced in-vivo heating, thermal dose, tissue damage, and neuronal activity.

SIM4LIFE, a computational life sciences platform, has been developed for the modeling of interactions between physical stimuli and the human body and for the modeling of processes in the human body. It has been applied to a wide variety of, primarily EM-related, medtech problems. Here, the platform will be introduced and approaches to investigating implant MR safety relevant effects will be discussed.

II. SIMULATION PLATFORM

The multi-physics simulation platform SIM4LIFE has been developed to specifically address needs from the computational life sciences field [1]:

- the ability to perform simulations based on medical image data (for geometry, material parameter and boundary condition information),
- the ability to model setups involving complex and realistic anatomical models,
- the ability of visualizing measurement data, simulation results and image data together,
- the availability of solvers specifically modeling the physics, biology and physiology of living tissue.

The SIM4LIFE platform includes a wide range of physics solvers (EM, flow, acoustics, temperature, mechanics, convection-reaction-diffusion) that have been optimized for the modeling of living tissue (e.g., inclusion of advanced perfusion models in the thermal solver). High performance computing support is available for these solvers (parallelization of FEM solvers based on PETSc [2] and GPU acceleration of FDTD solvers) In addition, there are specific solvers for biological processes, some of which will be discussed in more detail below.

A segmentation tool integrated into SIM4LIFE allows the generation of whole-body or regional anatomical models from medical image data. As an alternative, preprocessed anatomical models have been generated (Virtual Population http://www.itis.ethz.ch/vip [3]) that can be used, e.g., to investigate device safety across different anatomies in order to capture inter-person variations. The posture of the models can be interactively modified and morphing functionality is available to further parameterize the anatomy and increase population coverage.

The platform offers support for Python scripting, vtk-based visualization [4], and an own GUI SDK.

III. MR EXPOSURE MODELING

Both FDTD (finite-differences time-domain) and multiple electro- and magneto-quasi-static low frequency EM solvers are available. They work on non-uniform, rectilinear meshes, for which a gridder and a voxeler are available. Special functionality allows to construct and tune birdcage and gradient coil models for MRI related exposure studies.

For the modeling of birdcage coils, typically broadband simulations are used to help tuning the coil to the correct resonance mode. Subsequently, harmonic simulations are used. When high resolution is required in the vicinity of the implant, a total-field/scattered-field approach (Huygens' box [5]) can be used to significantly increase the resolution and accuracy, without generating overly large and slow simulations.

In the presence of active implants featuring long leads, it is often possible to separate the modeling of the coupling of energy into the lead and the simulation of the translation into local energy deposition at critical locations (e.g., lead tip). In such a case, the characterization of the lead can be performed independently from the simulation of the incident field, accelerating for example the investigation of a large number of possible lead trajectories.

For parallel transmit coils, it is possible to calculate the E-fields from different channels separately and construct interference matrices [6]. These matrices allow rapid evaluation of field conditions for any set of coil steering parameters.

IV. INDUCED EFFECT MODELING

A. Induced Heating

The EM energy deposition (SAR) results in heating of the tissue. When determining the degree of heating, it is important to consider the following effects: thermal conductivity (especially relevant near sharp/small implant features such as pace-maker fixation helices), perfusion cooling (by large vessels and microvasculature), thermoregulation (local and sometimes whole-body), and convective heat removal (especially near flowing blood, internal air, or at the body surface).

A thermal solver has been developed that can account for blood flow on multiple levels: a Pennes Bioheat equation-like term [7] allows to consider the impact of microvasculature and vascular bleed-off. By allowing for tensorial effective thermal conductivity, the directivity of blood flow can be considered. Coupling of the 3D thermal simulation with a pseudo-1D simulation of vascular trees permits accounting for the local effect of discrete vasculature and heat transport. Finally, it is possible to use flow velocity field computed using computational fluid dynamics to consider the complex convective impact of large vessels.

Local thermoregulation can be considered using temperature dependent perfusion and metabolic heat generation rates. Body-core heating due to prolonged EM exposure is accounted for in a similar manner as in [8].Special thin structure models allow the accurate and rapid simulation of implanted metallic wires and actively cooled catheters. The overestimation of surface effects such as convective cooling due to stair-casing errors is compensated using a novel conformal correction scheme.

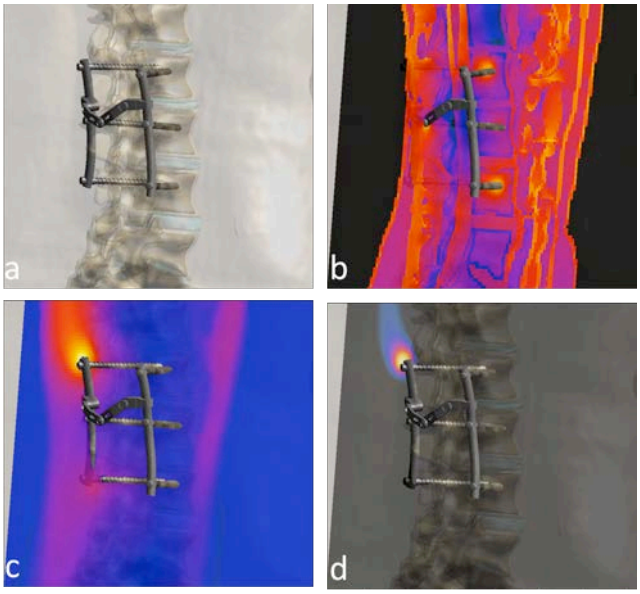

Fig. 1. a) Spinal stabilization implant model. b) SAR distribution as a result of MR exposure. c) Induced temperature increase distribution. d) Accumulated thermal dose distribution.

B. Thermal Dose and Tissue Damage

While temperature is already more directly related to the assessment of safety and damage than deposited energy, it still fails to consider the exposure duration, the varying sensitivity of different tissues, and the transient nature of the heating process. Therefore, two methods for the estimation of thermal effect and damage have been implemented:

- The CEM43 (cumulative equivalent minutes at 43ºC, [9]) dose concept allows to translate transient temperature development at a specific location into a dose value that states how many minutes of heating at 43ºC would result in a similar effect. Threshold values for different tissues have been suggested [10].
- Alternatively, the tissue damage can be calculated directly, based on the Arrhenius tissue damage model, which is derived from first order reaction kinetics. This model directly accounts for the amount of damage to be expected provided two tissue- and effect of interest-specific parameters have been determined. Selected values can be found in [11].

C. Neuron Stimulation

Particularly at low frequencies, e.g., due to gradient field switching, stimulation of (peripheral) nerve stimulation, or alternative interferences with neuronal dynamics, can occur. The presence of implants often produces locally enhanced fields, such that these effects are exacerbated.

A special low-frequency EM solver capable of considering the anisotropy of the neural tissue conductivity has been

developed. SIM4LIFE offers the possibility of coupling calculated EM-fields to neuronal dynamics simulations based on NEURON using its external potential mechanism. An implementation of the SENN model [12], commonly employed for the derivation of the basis of low frequency safety standards, has been realized. In addition, the SENN model has been extended to allow considering the impact of local temperature on neuronal dynamics (e.g., tissue heating due to RF-coil, s. above) based on the temperature dependence of the underlying Frankenhauser-Huxley model. Stimulus pulse shape and neuron trajectory can be flexibly defined and existing detailed neuron models from the ModelDB [13] can be imported.

The coupled EM-neuronal dynamics modeling allows determining stimulation thresholds (using an automated titration procedure), locations of high risk, and interaction mechanisms.

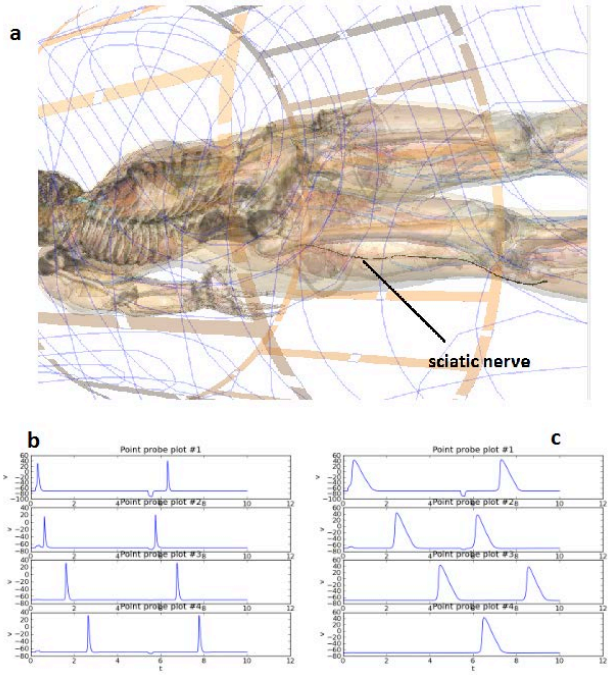

Fig. 2. a) Anatomical model placed inside an RF body coil and a gradient coil. The sciatic nerve is highlighted. b) Simulated gradient coil switching induced neuronal dynamics in the sciatic nerve using the SENN model and considering the impact of temperature (incl. RF induced heating). c) Same as b), but neglecting the impact of temperature.

V. Discussion & Conclusions

When ascertaining the safety of implants under EM exposure (e.g., during MR imaging), assessment is often limited to investigating whether threshold values from guidelines are not exceeded. However, it can be important to directly investigate the resulting effects because: i) thresholds can under some conditions be insufficiently conservative (e.g., novel imaging technology such as parallel transmit coils lead to completely different local energy deposition distributions [6]), ii) making them conservative can lead to a need for high safety margin when the limited quantity is not strongly related to the safety related quantity of interest (e.g., using thermal dose based limits can potentially lead to less stringent restrictions on MR imaging), and iii) investigation of the induced effects yields insight into the mechanisms and enhances understanding.

The SIM4LIFE platform has been developed with the needs of computational life sciences in mind. It offers (high performance computing enabled) solvers optimized for the modeling of living tissue, as well as biology/physiology specific solvers. It can handle complex, realistic anatomical models and inherently supports image data.

In the context of implant EM exposure safety assessment, particularly under MR imaging, the platform offers powerful functionality for the modeling of the exposure, but also for the investigation of the induced effects. The aspects that have been discussed here are the modeling of induced heating (considering for example perfusion and thermoregulation), the calculation of thermal dose (CEM43) and tissue damage, as well as the simulation of EM induced neuronal dynamics (also considering the impact of simultaneous tissue heating).

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References

[1] E. Neufeld, D. Szczerba, N. Chavannes, and Niels Kuster, "A novel medical image data-based multi-physics simulation platform for computational life sciences, " Interface Focus, vol. 3, no. 2, 2013.

[2] S. Balay, J. Brown, K. Buschelman, V. Eijkhout, W. Gropp, D. Kaushik, M. Knepley, L. Curfman McInnes, B. Smith, and H. Zhang, "PETSc: portable, extensible toolkit for scientific computation," see http://www.mcs.anl.gov/petsc/petsc-as/, 2010.

[3] M-C. Gosselin, E. Neufeld, H. Moser, F. Di Gennaro, E. Huber, S. Farcito, I. Hilber, L. Gerber, W. Kainz and N. Kuster, "Development of the next generation of high-resolution anatomic al models: the Virtual Population 3.0," 4th International Workshop on Computational Phantoms for Radiation Protection, Imaging and Radiotherapy (CP 2013), Zurich, May 2013.

[4] W. Schroeder, K. Martin, B. Lorensen, The visualization toolkit. Clifton Park, NY: Kitware Inc., see http://www.vtk.org, 2003.

[5] S. Benkler, N. Chavannes, and N. Kuster, "Novel FDTD Huygens source enables highly complex simulation scenarios on ordinary PCs," Digests IEEE Antennas and Propagation Society International Symposium, USA, pp. 1-4, 2009.

[6] E. Neufeld, M-C. Gosselin, M. Murbach, A. Christ, E. Cabot, and N. Kuster. "Analysis of the local worst-case SAR exposure caused by an MRI multi-transmit body coil in anatomical models of the human body," Physics in Medicine and Biology, vol. 56, no. 15, p. 4649, 2011.

[7] H.H. Pennes, "Analysis of tissue and arterial blood temperature in the resting human forearm," J. Appl. Physiol., vol. 1, pp. 93–122, 1948.

[8] A. Hirata, H. Sugiyama, M. Kojima, H. Kawai, Y. Yamashiro, O. Fujiwara, S. Watanabe, and K. Sasaki, "Computational model for calculating body-core temperature elevation in rabbits due to whole-body exposure at 2.45 GHz" Physics in Medicine and Biology, vol. 53, no. 12, p. 3391, 2008.

[9] S. A. Sapareto, and W. C. Dewey, "Thermal dose determination in cancer therapy," International Journal of Radiation Oncology* Biology* Physics, vol. 10, no. 6, pp. 787-800, 1984.

[10] G. C. van Rhoon, T. Samaras, P. S. Yarmolenko, M. W. Dewhirst, E. Neufeld, and N. Kuster, "CEM43° C thermal dose thresholds: a potential guide for magnetic resonance radiofrequency exposure levels?," European radiology, pp. 1-3, 2013.

[11] X. He, and J. C. Bischof, "Quantification of temperature and injury response in thermal therapy and cryosurgery," Critical Reviews in Biomedical Engineering, vol. 31, pp. 355-422, 2003.

[12] J. P. Reilly, and A. M. Diamant, Electrostimulation: Theory, Applications and Computational Model. Artech House, 2011.

[13] M. L. Hines, T. Morse, M. Migliore, N. T. Carnevale, and G. M. Shepherd, "ModelDB: a database to support computational neuroscience," Journal of Computational Neuroscience, vol. 17, no. 1, pp. 7-11, 2004.