Use of Computational Simulation of Medical Technology

by
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Introduction

Medical devices continue to provide a crucial component in the diagnosis, prevention, monitoring, and treatment for diseases. Unlike drugs or biologics, a medical device can vary from the simple, which poses little or no risk to the user such as a tongue depressor or toothbrush, to the life-sustaining such as a pacemaker or medical imaging equipment. Traditionally, assessment of the safety, reliability and effectiveness of medical devices has relied on laboratory based in vitro testing of physical prototypes and subsequent in vivo testing in animals and/or humans. While physical testing can provide valuable information, it is slow, expensive and can only examine a limited number of variables. In vivo testing presents further difficulties in measuring any device performance: the inability to look at variations quickly and systematically, and ethical considerations associated with conducting extensive in vivo tests.

Here we will present a series of Blogs that will describe the application of Physics-based Computer Modeling and Simulation to a range of activities associated with the development of medical devices and technology.

1. **Background**

Physics-based Computer Modeling and Simulation (PCM&S) can provide an alternative approach to examine the limitations of initial design concepts and explore the use of novel technology without the need for physical prototype development and testing. While PCM&S has typically been used in the early design and development of devices, it is also being increasingly applied to study performance under envisaged operating conditions. In parallel, the U.S. Food and Drug Administration (FDA) is actively encouraging the use of PCM&S to support patient safety and technology innovation in medical devices.

Developers of medical technology are consistently under pressure to develop and extend the use of life-saving therapies, while simultaneously meeting safety standards, obtaining regulatory approval and reducing the time and cost for increasingly complex technology to reach the patient. Computational simulation is becoming increasingly important in overcoming these obstacles and expediting the development and implementation of life-saving medical technology. Current uses for simulation range from physical medical devices, pharmaceutical development, manufacturing technology and replacement of human trials to name but a few.

Developers can build predictive simulation models of devices to calculate the behavior of a device under a wide range of conditions. Adjustments can be made quickly to assess the response of different designs and operating conditions, allowing a large number of scenarios to be investigated in a relatively short period of time. These in silico tests will

not replace traditional in vitro and in vivo tests but are designed to complement them by reducing the reliance on bench, animal and human testing. In this way, it is expected that the use of PCM&S for development of medical devices will reduce the time and cost of the development process and enhance confidence in future application.

With the increasing complexity of new medical devices, the technology and design can rely on any combination of mechanical, electronic, software or chemical/biochemical action to achieve their purpose. For many years, PCM&S studies have been used to support device design/development and reported in submissions for authorization of medical device use. Traditionally these studies have covered the simulation of fluid dynamics to evaluate flow phenomena in ventricular assist devices; solid mechanics to assess stresses in hip implants; electromagnetics for radiofrequency safety; optics for spectroscopy devices; ultrasound propagation in body tissue; and heat transfer from devices into body tissue. With the increasing sophistication and capability of computational simulation, and in particular simulation of multiple physical phenomena, the utility of computational simulation for advancing medical technology is crucial. Some examples of medical technologies that have used simulation in their development are shown in Figure 1.1.

Figure 1.1: Examples of medical technology developed using computational simulation.

Developers of innovative medical technology face a number of pressures among which are:

- The complexity in the response of the human body, coupled with the inherent variability encountered across the billions of potential human subjects, makes it impossible to investigate performance using experimental approaches.
- Increased levels of miniaturization and functional integration allow medical devices to be developed to address an increasing number of potential applications across the broad field of biotechnology. The complexity of the new device operation can no longer be represented by traditional build and test approaches.
- Gaining support for new device development increasingly requires early demonstration of performance to meet targeted therapeutic needs. The pressure to demonstrate feasibility as early as possible helps minimize the need for continued redesign and additional prototype development and testing.
- With the increased complexity of device functionality, device design needs to be optimized as soon as possible in the development cycle to minimize delays in

getting functioning prototypes to the market. This can only be done by having a more detailed understanding of the device operation and what may be limiting achievement of defined performance criteria.
- In a competitive market, alternative devices will be available such that the window for successful development, demonstration and implementation of new therapies may vanish quickly.
- In vitro testing and in vivo trials can be both expensive and time consuming. While they cannot be eliminated, in silico simulations can be used to identify critical cases for physical testing and support demonstrations of efficacy of new treatments thereby potentially reducing obstacles for regulatory approval.

In the past decade, major changes have taken place that have played a significant role in stimulating the use of computational simulation in the development of novel medical technology, namely:

1. Successful application of medical devices typically requires the integration of multiple physics within any operation. Computational simulation software is now available that can provide integrated simulation of multiple physical phenomena. The algorithms that represent the mathematical description of the physical phenomena of interest have greatly expanded over recent years and the improved accuracy and efficiency of solving the equations has allowed solutions to previously intractable problems to be achieved.
2. Regulatory bodies have become increasingly aware of how and when simulation can provide value and benefit. They are now accepting, and in some cases, actively promoting the inclusion of simulation in device submissions.
3. Improvements in computer hardware and its availability at relatively low cost has allowed widespread use across the scientific and engineering community, providing support and competition to conventional build and test development approaches.

In the remainder of this article, we will look at some examples where computational simulation has been successfully used in the development of a medical technology from the initial proof of concept to application in the design of patient therapies. We will conclude the article with a look at some emerging trends in computational simulation that may be important for expanded use in the medical industry.

Proof-of-Concept: In the Beginning There Was...

Innovative product concepts and technologies invariably need to provide some level of Proof of Concept before an organization or agency will commit significant investment in money and/or resources to support continued development and commercialization. PCM&S is being increasingly used during the proof-of-concept phase to demonstrate technical feasibility, identify critical technical blocks and define the critical path for future success.

Consider the development of technology for the treatment of benign or malignant tumors: it is important to ablate undesirable tissue in a controlled and focused manner without affecting adjacent healthy tissue. Over the years, a number of minimally invasive techniques have been developed to selectively destroy tumors as an alternative to more invasive surgery. Each technique has specific advantages and disadvantages depending on the nature of the tumor and its location. A brief summary of currently available approaches is given below:

1. Chemical ablation: chemical agents are injected into the undesirable tissue. Unfortunately, the affected area cannot be controlled because of the local blood flow and transport of the chemical species beyond the targeted tumor.
2. Thermal ablation:
    - Cryosurgery: a low temperature minimally invasive technique in which tissue is frozen on contact with a cryogenically cooled probe inserted into the undesirable tissue.
    - Focused ultrasound: tissue is heated to coagulation using high-intensity ultrasound beams focused on the undesirable tissue.
    - Radiofrequency (RF) ablation: an active electrode is introduced into the undesirable area and a high frequency alternating current is used to heat the tissue to coagulation.
    - Interstitial laser coagulation: tumors are slowly heated to temperatures exceeding the threshold of protein denaturation using low power lasers delivered through optical fibers.
3. Irreversible electroporation: a well-defined radiofrequency pulsed electric field irreversibly opens the cell membrane, thermal damage associated with the electric field distribution may also be superimposed, and tissue necrosis ensues.

High temperature thermal therapies have the advantage of ease of application but the disadvantage that the extent of the treated area is difficult to control because blood circulation strongly affects the temperature field developed in the tissue.

As developers try to minimize the spread of thermal or electroporation damage beyond the target volumes, they are turning to increasingly complex control systems and device designs. Consider the case of a balloon catheterization technology, Figure 2.1.

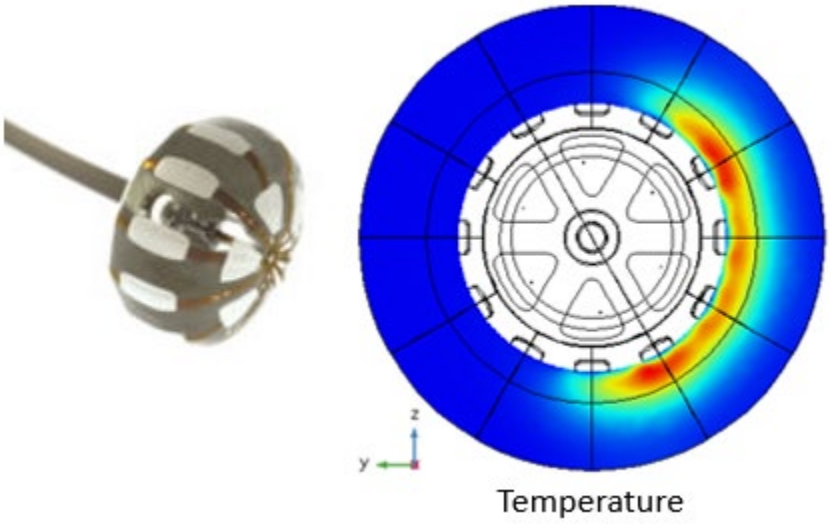

Figure 2.1: Simulation of temperature distribution associated with selected excitation.

Here, controlled local electrical and thermal transient histories of selected tissue volumes can be developed by simultaneously selecting patches that can be independently heated and cooled. Heating of selected patches is achieved by electrically exciting conductive patches while simultaneous cooling specified volumes by controlled fluid flow. This problem represents a highly coupled electrical-thermal-fluid multiphysics problem of the type that could not realistically be addressed without simulation. The large number of

potential combinations of heated and cooled patches available with this approach is such that testing the large number of possible combinations would be impossible using conventional testing approaches.

To provide demonstration of the effectiveness of the technology to produce tissue necrosis with achievable operating conditions, a coupled electrical-thermal-fluid multiphysics simulation can be integrated with available mathematical methods for calculating tissue necrosis. There are a number of mathematical methods for calculating when cell death occurs due to thermal exposure. Among the most recognized are:

1. A damage integral based on the Arrhenius equation provides the most general formulation.
2. An Arrhenius rate approach in which the Cumulative Equivalent Minutes (CEM) at a specified temperature is calculated; for the case of tissue the temperature is usually taken as 43° The amount of time to produce the required damage for the tissue of interest is measured and used for comparison.
3. A threshold temperature method is used when hyperthermic conditions are maintained for a short period of time. A target temperature is specified which, once exceeded, causes tissue necrosis. This binary approach is preferred for its simplicity, but may not provide a sufficient level of differentiation in regions of high thermal gradients.

Simulation provides a useful tool for assessing the temperature-time history of tissue subjected to a heat source; the calculations of tissue necrosis can be done directly based on the simulation output.

Through the use of multiphysics simulations, a large number of potential combinations of heating/cooling can be simulated to demonstrate the ability to control local temperature distribution in tissue, and thus tissue necrosis, as well as provide a platform for the development of patient specific treatment protocols based on an individual patient's condition.

Getting to Market: Product Design and Development

After providing proof of concept for a new medical technology, device or development of second-generation devices, the next step is finalizing the product design. This is one of the most important stages in the development of a successful medical device since a flawed design may lead to it being ineffective or unsafe. Simulation can play an important role in the efficient development of safe and effective product designs.

As an example, let's consider the case of a device to provide controlled drug delivery to the lungs. To efficiently pass through the respiratory tract and reach the lungs, aerosol droplets must contain a specific size distribution and provide a sufficient dose to be clinically effective. To efficiently enter the respiratory tract, the aerosol must be integrated with an inhaler mask that can ensure controlled entry over a range of breathing regimes, Figure 3.1.

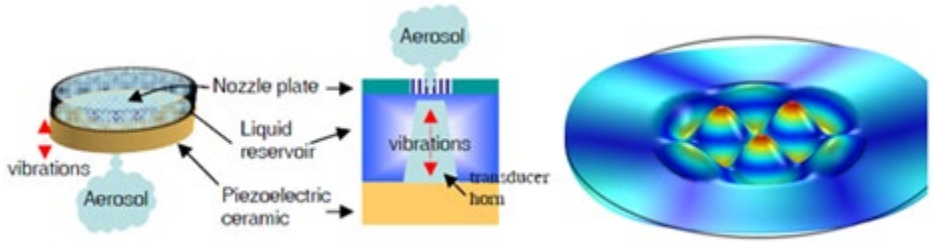

Figure 3.1: Droplet production through vibrating mesh.

In this particular product, a piezoelectric plate is excited in a controlled manner. The piezoelectric plate causes vibration of a mesh that interacts with a liquid reservoir to produce aerosol droplets having a characteristic distribution of droplet size that can be controlled by the displacement of the mesh during excitation.

Simulations of the PZT ceramic predicted the vibration behavior of the mesh and, when coupled with analyses of two-phase fluid flow, predicted the resulting aerosol volume and droplet size distribution. While the simulations enable identification of the operating conditions to produce the appropriate aerosol properties, successful development of the product requires that the aerosol droplets be integrated with the flow conditions associated with an inhaler mask to facilitate transport of the active species to the lungs. Design of the inhaler mask has to work for a range of breathing conditions and physical positions, while simultaneously ensuring passage of maximum doses of critical species into the lungs, Figure 3.2.

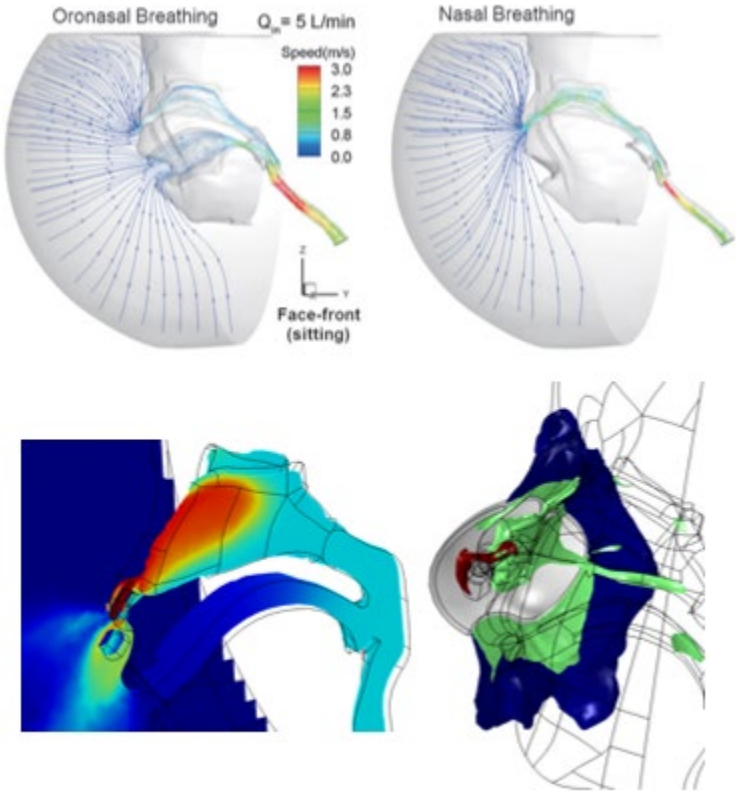

Figure 3.2: Breathing pattern and associated flow distribution.

Simulations of the multiphase fluid flow behavior of the combination of droplets and gas provide an understanding of the multiphase flow within the mask to ensure delivery of the vapor to the respiratory tract. The simulations investigated the flow behavior for a range of breathing modes, i.e. combinations of mouth and nose, and physical positions of the head and respiratory tract. The simulations can be extended to investigate the influence of alternative mask designs and operating conditions to provide optimization of the flow characteristics with effective droplet transport to the lungs. Integration of the flow behavior with geometric models of infant respiratory tracts predict passage of the droplets and delivery of critical drug species to the lungs. In this way, the most effective design and operating conditions can be identified without the need to build and test a range of physical prototypes.

Making it Work: Manufacturing Technology

Once a functional product design has demonstrated the ability to meet the technical and market needs, developers must turn their attention to manufacturing the product with the required degree of precision, reliability and cost.

Simulation of all or part of the manufacturing process can be both informative as well as lead to quantifiable actions. For example, if thermal processes are used during fabrication does the local heat flow affect critical components? Are residual stresses developed that affect product performance and operating lifetime? Does the selected manufacturing process lead to material failure? Simulation of the manufacturing technology can then be used to modify the set up and operation of the manufacturing process to avoid any potentially catastrophic problems.

Among the typical manufacturing processes that can be simulated are:

- **Material fabrication**
  - Casting
  - Injection molding
  - Additive manufacturing
  - Powder sintering
  - Composite fabrication
- **Joining technology**
  - Thermal welding
  - Friction welding
  - Adhesive bonding
- **Product shaping**
  - Metal forming
  - Cutting
  - Rolling
  - Extrusion
  - Forging
- **Heat treatment**
  - Material property development
  - Relief of residual stresses
  - Surface conditioning
  - Distortion

As an example of the use of PCM&S for the manufacture of medical devices, consider the manufacture of a tissue cutting tool using metal forming operations. As part of the

manufacturing process the cutting component has to be formed to a specific radius without fracturing the cutter while simultaneously storing sufficient elastic energy to ensure rapid penetration through the selected tissue mass.

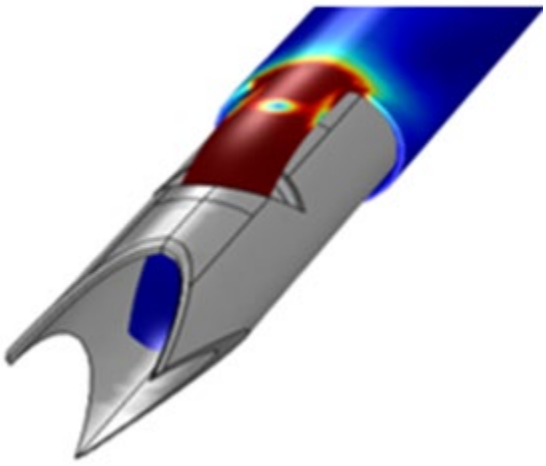

Figure 4.1: Stress distribution due to forming.

Simulation of the forming operation can address a wide range of issues such as the design of the forming tools, material selection, forming load evaluation, friction effects, forming stresses, material spring-back, etc.

In addition to simulating the response for a single output parameter, e.g, temperature, stress, flow velocity etc, one of the powerful aspects of simulation is the ability to isolate individual parameters that cannot be separated in experimentally based approaches and identify their significance for the manufacturing technology and product performance. By integrating the results of simulations with statistically significant systematic changes in input parameters, it is possible to identify what level of variance in device operation or design will lead to conditions where the device does not function correctly or the manufacturing technology would be expected to operate outside acceptable limits.

Further, information of this type can lead to identification of conditions where it may not be possible to maintain the required level of tolerance with the proposed manufacturing technology or can identify certain components that require monitoring to a specific level of accuracy to maintain product performance. When simulations are interfaced with commonly used statistical evaluation methodologies a powerful bridge is created that links product design, manufacturing technology and quality control.

Operating Safely: Patient Well-being

The safe and effective operation of medical devices, instrumentation and related technologies are critical to ensuring satisfactory patient outcomes and maintaining healthcare worker safety through the product life cycle. To reduce the impact of potential risks associated with the use of any new medical device or technology, regulatory bodies such as the FDA require the collation of copious amounts of supporting information. PCM&S is not only being used to ensure the initial device operation has high levels of safety and reliability but is also being used to help identify which critical cases need to be tested experimentally to provide acceptable information for regulatory submission.

Use of PCM&S for simulation of fluid flow in devices such as pumps, catheters and valves has been used to assess the propensity for damage to the blood that could lead to an increased risk of clotting and potential organ failure. Typically, there are no standards for identifying conditions for hemolysis and consequently qualitative assessments have been made based on observations of low or stagnated flow. In contrast, assessment of thermal damage to tissue has been the subject of more extensive development of quantitative approaches to defining tissue necrosis, more information will be provided on this topic in a later section of this series of blogs.

As an example of the use of PCM&S in identifying conditions under which tissue necrosis may occur, let's consider the effect of electromagnetic fields on passive and active implanted devices, Figure 5.1.

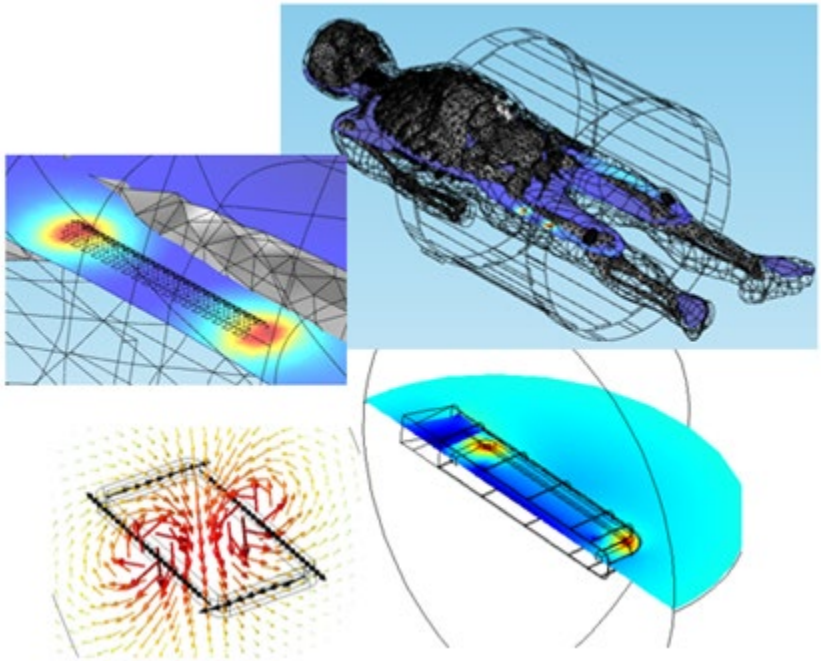

Figure 5.1: EM field exposure of implanted medical devices.

The main ways in which the interaction of EM fields with implanted medical devices are most likely to occur are:

1. Implants in patients who undergo imaging modalities such as MRI technology, where the patient is exposed to a global EM field that can be simultaneously static and dynamic
2. Remote charging of devices such as pacemakers using EM coils external to the body
3. Excitation of an external coil whose EM field interacts with an implant to heat a local volume of tissue and deliberately cause tissue necrosis of tumors

In these applications the presence of the device or implant can perturb the distribution of the EM field or lead to induced fields, both of which can cause local heating around the device or hinder correct operation.

The strong EM fields associated with MRI operation can also place additional constraints on device designs that must be satisfied to achieve regulatory approval. For devices with potential exposure to an MRI field, any passive implanted device has to provide MRI

safety labeling; there are a few exceptions, but the requirement for safety labeling is expanding not shrinking. At the moment the major focus of the MRI safety requirement is centered on vascular devices, orthopedic implants and gastrointestinal devices.

The main areas that must be addressed for MRI safety compatibility are:

1. Heating due to exposure to the EM field developed by the RF coil
2. Displacements/Forces on the device from the EM fields to ensure the device does not move from its prescribed location
3. Disruption to the image quality

The most significant of these is RF induced heating associated with excitation from the RF coil of an MRI. These generally operate at either 64 MHz for a 1.5T machine or 128 MHz for a 3T machine, and currently safety approval requires the manufacturer to provide standardized test results for the devices under consideration.

Thus, depending on the type of product, development of acceptable information may result in the need for many hours of time consuming and expensive physical testing. An orthopedic spinal stabilization system may contain large numbers of rods, connectors, screws and nuts, each combination of which may have to be tested and the limiting temperature rise verified. Alternatively, for an implanted stent there may be fewer numbers of products but there would still be a requirement to perform extensive testing of the range of different lengths of the product.

The mismatch in properties between the implantable medical device and the surrounding tissue perturbs the local distribution of the externally imposed EM field. This perturbation results in local heating at specific locations along the device; for a simple geometry in the shape of a straight wire, maximum heating will be observed at the ends of the device, for more complex geometries this simplified thermal distribution will be dependent on geometric complexity and material inhomogeneity.

PCM&S can be used to accurately predict the interaction between the EM field developed by the RF coil of an MRI machine and an implanted medical device. For example, one specific geometric arrangement, or length of stent, will provide maximum heating. But this value is dependent on the MRI field strength, and the length of stent providing maximum heating will be different for a 1.5T machine compared to a 3T machine, Figure 5.2.

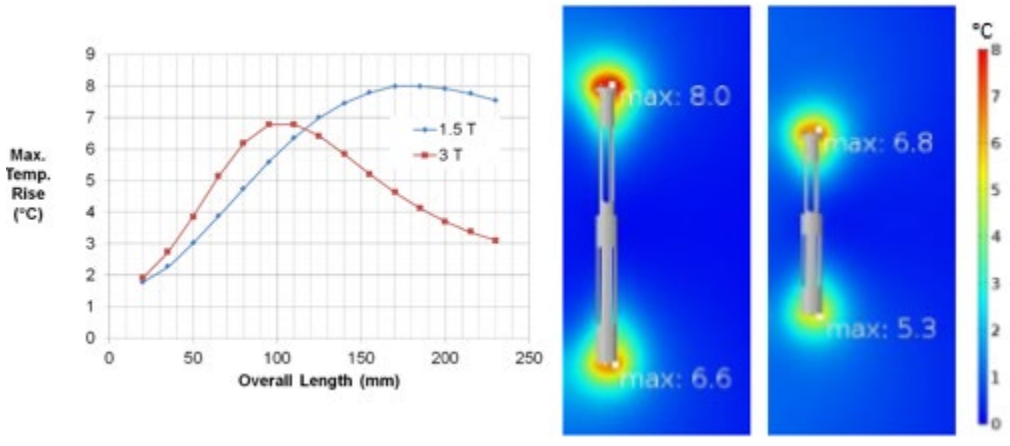

Figure 5.2: Temperature rise for stent exposed to EM field of RF coil in 1/5T and 3T MRI.

The 3T machine shows a lower peak temperature than the 1.5T machine and also a shorter length at which the peak temperature is observed.

For a single device exposed to the EM field from the RF coil, heating of a stent is transient in nature. The maximum temperature rise is observed at the ends of the stent, Figure 5.3.

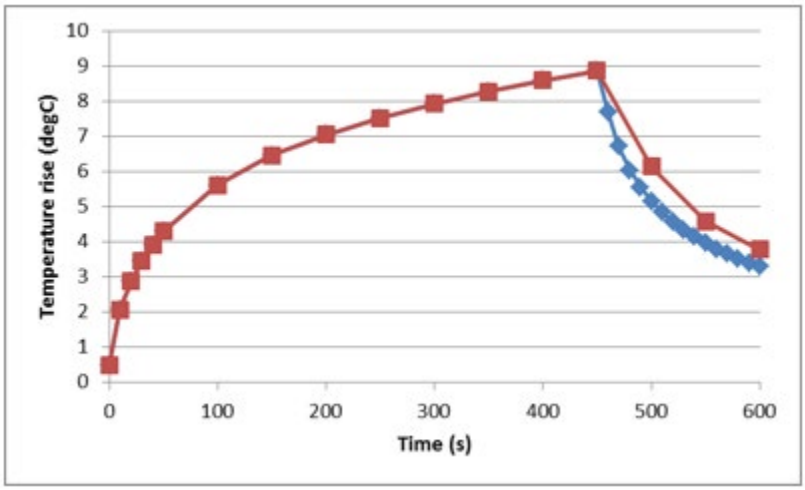

Figure 5.3: Transient heating of stent exposed to EM field of RF coil in an MRI.

Simulations of this type have been used to identify configurations of implanted devices that provide the highest temperature rise such that physical testing is then performed around that peak. This drastically limits the number of tests that need to be performed and the justification for a limited number of tests to support safety labeling requirements.

Because the thermal response of a device, due to exposure to the MRI field, can be simulated, the effect of the body's ability to dissipate heat can also be included. Practically, there are two main mechanisms by which thermal dissipation would be expected to occur: perfusion from the tissue around the stent and dissipation of heat due to flow of blood over a stent located in an artery or vein.

To investigate this response, simulations of RF induced heating of a stent with fluid arterial or vascular flow have been performed, Figure 5.4.

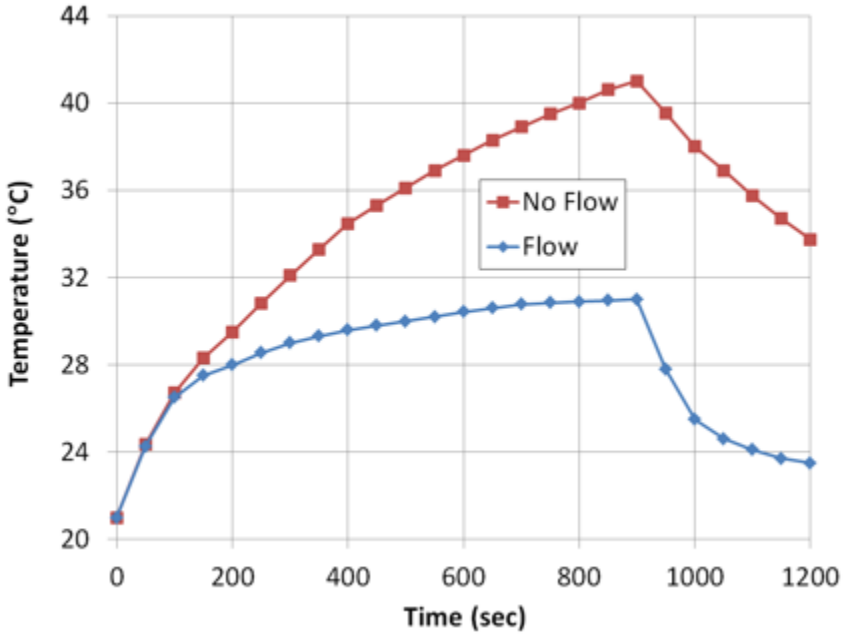

Figure 5.4: Effect of fluid flow in temperature rise of a stent exposed to EM field of an RF coil in an MRI.

As might be expected, blood flow significantly reduces the peak temperature as well as the rate at which the peak temperature is achieved. Further studies indicate that the temperature rise can also be affected by the rate, uniformity and pulsed nature of any fluid flow over the stent when exposed to an MRI field.

Although these analyses have been performed assuming material with uniform material properties around the stent, the effect of the body's structure and the associated inhomogeneities of material properties can also be simulated. The human body is a mixture of tissue, bone and organs all of which have different electrical and thermal properties. Given the inhomogeneity of the structure of the human body, questions arise about how this variation may affect heating of devices placed in locations that are typical of their intended use.

Scans of a human body can be imported into a simulation and material properties assigned to the various tissues, organs and skeletal structures. The Specific Absorption Rate (SAR) distribution, Figure 5.5, demonstrates how the inhomogeneity of tissue properties affects the absorption of RF power from an MRI.

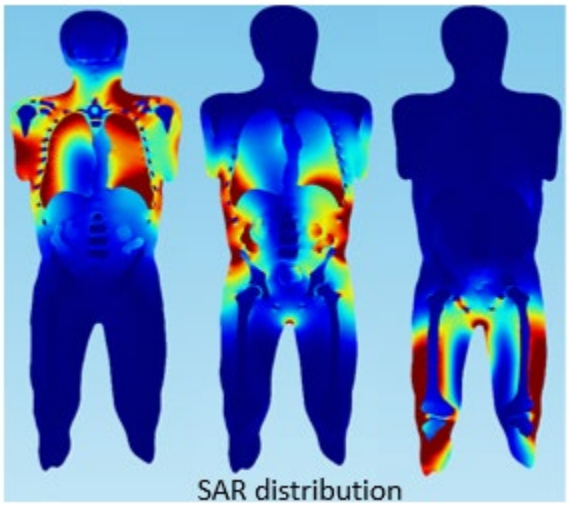

Figure 5.5: SAR distribution of human torso exposed to MRI EM field.

Precise calculation of SAR is mathematically complex and related to factors such as field strength, RF power, tissue properties, and body size among others. While not directly related to heating of implanted devices, SAR does show inhomogeneity in the distribution of RF power in the human body and thus that you might expect the location of a device in the body to affect the extent of heating. In simulations, medical devices can be placed in specific locations in the body in which they would typically be used and the influence of local body structure on SAR distribution and any device heating evaluated.

In Figure 5.6, a knee replacement has been imported into a simulation of RF heating and located in a typical area of use. Subsequent simulations of the effect of exposure to the EM field of the RF coil and the resulting temperature rise indicate that a maximum T rise of just under 5 degrees may be expected.

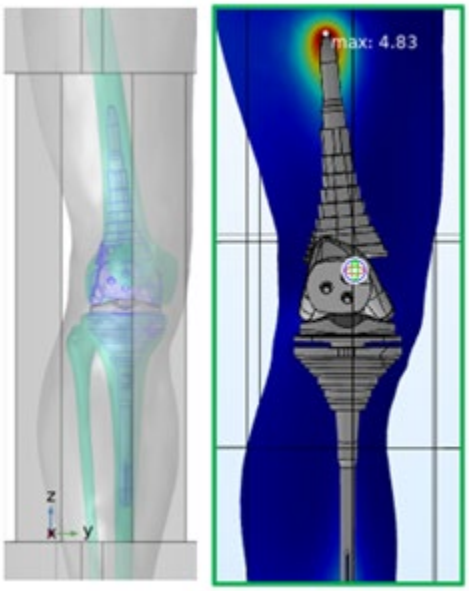

Figure 5.6: Knee implant in RF heating simulation.

Overall, we see that device heating due to exposure to the RF field of an MRI is a complex phenomenon, but by careful use of simulation we can identify the influence of

device design, guide the use of testing for safety labeling and provide an understanding of the role of the human body in affecting the exposure to RF power and dissipating heat generated in the vicinity of any implanted device.

Hopefully this has provided some examples of where simulation can help in the various stages of development and use of medical devices. This is a rapidly developing field as the ability to integrate predictive physics with the complexity associated with the variability in the human body increases.

Emerging Trends: Where Could PCM&S Go?

As the use of simulation continues to expand, there are a few areas emerging as topics that may become increasingly significant in extending the implementation of simulation driven design and manufacturing. A selection of a few of these areas is provided in the remainder of this article.

6.1: Regulatory viewpoint

The FDA is actively encouraging the use of PCM&S to support the development and use of medical products and technology for public health benefits. In parallel, the Senate Appropriations Committee is openly encouraging the FDA to "…. explore greater use, where appropriate, of in silico trials for advancing new devices and drug therapy applications". Aspects of in vitro and in vivo trials are now being actively replaced by in silico trials using computational simulations as a critical component in the development of new devices and patient therapies. With the increased insight into the operation and limitations of the effectiveness of medical device technology, a greater understanding of the increasingly complex behavior and interactions of medical device technology with human anatomy and physiology is being obtained, thus limiting potential risk to the public.

In addition, the development of life-saving medical technology can be made increasingly effective while simultaneously cutting the time and cost of the development process. Some Federal studies suggest that technology development using PCM&S can reduce development time by up to 90% and concurrently reduce the cost for development by up to 50%. Assessment of the benefits of PCM&S for a medical device development has documented device release up to 2 years earlier than scheduled with a resulting increase in the number of patients receiving benefit of up to 10,000. Reductions in the number of patients required to participate in the clinical trial led to overall cost savings approaching $10 million.

6.2: Human anatomy and physiology effects

In general, PCM&S has the advantage that a causal relation between model input and output can be established, whereas animal testing and human clinical trials can only provide a statistical correlation. Through the creation of virtual patient anatomies that account for variability in anatomy and physiology or in the use condition and/or product performance, virtual equivalents of in vivo clinical trials can be constructed. The use of such individualized computer simulations in the development or regulatory evaluation of a medicinal product, device, or intervention can allow simulated clinical trials. While assessment of all necessary endpoints is not feasible with the current understanding of biology, in silico clinical trials have successfully been used to reduce the complexity, size and duration of in vivo clinical trials.

To promote the assessment of the effect of human anatomy and physiology on the operation and safety of medical devices and technology, the FDA has collaborated with European organizations to develop “The Virtual Family”: a set of four highly detailed, anatomically correct whole-body models of an adult male, an adult female, and two children (1). In parallel, Duke University has developed 54 adult models (male and female) of varying body types and ages as well as 58 pediatric models from 2 to 18 years of age (2). The four models are based on high-resolution magnetic resonance imaging (MRI) data of healthy volunteers. Organs and tissues of are represented by three-dimensional, highly detailed CAD. Currently, The Virtual Family models have been used for electromagnetic, thermal, acoustic and computational fluid dynamics (CFD) simulations.

Electromagnetic and thermal simulations have been performed to assess the safety of active and passive implanted devices on whole-body MRI coils (3). Electromagnetic and CFD simulations have calculated the magneto-hemodynamic effect as a biomarker for cardiac output (4). Acoustic simulations have been performed to assess the impact of the human anatomy on the propagation ultrasound waves (5). At the end of 2014, The Virtual Family was used to support over 120 medical device submissions to FDA.

6.3: Quantifying uncertainty

Uncertainty quantification (UQ) is the science of quantitative characterization and reduction of uncertainties in both computational and real-world applications. It tries to determine how likely certain outcomes are if some aspects of the system are not exactly known. This replaces traditional deterministic approaches with probabilistic solutions that can quantify the degree of risk that may be present. For example, physical data may be missing or unavailable. We may traditionally assume that material failure occurs at a single value of load, in practice there is a statistical distribution of failure loads. Physical testing may introduce errors due to variations and uncertainty in measurements. Uncertainty may also be introduced by approximations made in setting up the simulation from sources such as physical simulation errors due to inaccuracies in the mathematical representation of the phenomenon, errors in representing the precise geometry of the system, discretization and solution errors, and numerical round off errors.

Quantification of levels of uncertainty is now available and can influence how the results of simulation can be best interpreted and how to best use approaches for simulation in any subsequent attempt to develop optimal solutions and inverse problem solving.

6.4: Developing optimal solutions

One of the most valuable aspects of simulation is the ability to characterize the response of arbitrarily complex stochastic systems. Once a system has been successfully simulated, the simulations provide information about the response to select input conditions. Simulations in which parameters of interest are swept over a range of interest to the user while other parameters remain constant, allow the effect of the parameters on the performance objective to be calculated. While informative, this approach is a time-consuming method and may provide limited understanding and only partially improves the performance. To obtain an optimal solution with minimum computation and time, the problem must be solved iteratively where in each iteration the solution moves closer to the optimum solution.

In contrast, optimization processes select the best possible decision for a given set of circumstances without having to enumerate all of the possibilities. Simulation-based optimization methods are generally performed by two different techniques: Derivative-Free and Gradient-Based Optimization. Derivative-Free Optimization (DFO) is useful when the objective functions and constraints may be discontinuous and do not have analytic derivatives and have the advantage of simplicity. DFO requires less user interaction to set up but, due to the computational costs, are most effective when the number of design variables is around 10 or less.

Gradient Based Optimization (GBO) approaches looks for the local minimum of a desired objective function. The advantage of the gradient-based method is that it can address problems involving hundreds, or even thousands, of design variables with very low increase in computational cost as the number of design variables increases.

Optimization methods can be further classified by the types of variables being optimized: Dimension, Shape, and Topology.

- Dimensional optimization involves defining design variables and is usually used as the last step in the design process. It is performed once the design is more or less fixed in terms of the overall shape and typically incorporates DFO methods
- Shape optimization typically occurs earlier in the design process, and involves a more free-form alteration of the object. More care is usually required for choosing the design variables, as the objective is to improve the shape without over-constraining the design. For shape optimization the gradient-based method is preferred if an analytic objective function can be found.
- Topology optimization is used very early in the design process, typically in the conceptual stage. Topology optimization treats the distribution of material as a design variable and inserts or removes structures to improve the objective function. Due to the high number of design variables, GBO approaches are incorporated.

6.5: Expanding the use of simulation

Historically, simulation has required the use of experienced personnel, powerful software and dedicated hardware. Recent developments have moved in the direction of putting dedicated simulation tools in the hands of scientists and engineers who have no direct experience or knowledge of simulation. These SimApps essentially take the underlying computational simulation file but provide an easy-to-use GUI through which the inexperienced user controls predefined inputs. These are used to automatically perform the required simulation and display critical results. While SimApps are generally for solutions to a highly focused set of predefined problems, the range of potential applications covers the full range of physics and use of medical devices.

Currently Sim Apps are being adopted by a range of companies to study product design and manufacturing processing. However, most recently SimApps are being developed to support adoption of new therapies for cancer treatment. These SimApps are designed to be used by practicing clinicians to develop patient specific treatment protocols. In this way, new therapies can be brought to the patient application effectively and quickly.

Conclusion

- PCM&S is being widely used to aid the demonstration, development and manufacture of medical products.
- Increased adoption is driven by the increase in the number of different physical phenomena that can now be included in a simulation and the ability to include human body responses and structure into simulations.
- Simulation can provide significant reductions in expense and time for product development compared to traditional testing and evaluation approaches, with reported benefits showing up to a 90% reduction in time and simultaneously a 50% reduction in cost.
- Regulatory bodies are accepting the use of simulation data to support approval for use of new devices and, in some cases, actively requiring the use of simulation in supporting documentation.

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