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ADVANTAGE

SPECIAL ISSUE 2018

PERSONALIZING HEALTHCARE

By **Thierry Marchal**
Global Industry Director
Healthcare
ANSYS

The current one-size-fits-all approach to healthcare fails to recognize significant differences in the physical size, shape and behavior of different patients. This creates inefficiencies and cost overruns in both new medical equipment design and patient treatment systems and, more significantly, affects the quality of care provided. By personalizing a specific treatment to each patient, efficiencies will make healthcare more affordable for patients and more profitable for providers. Personalized healthcare still requires a significant paradigm shift for those in the healthcare business, as well as a new technology toolkit to collect data via devices and wearables so that treatments can be customized. While this medical digital twin concept might seem like science fiction, advanced technology is poised to improve quality of life for people around the world.

Applying big (medical) data to P4 medicine (participatory, personalized, predictive and preventive) is expected to save millions of lives in the near future and improve billions of others through early diagnosis and continuous monitoring of vital signs. Healthcare suppliers expect that this medical Internet of Things (IoT) revolution will not be possible without a technology shift. This shift must include the adoption of engineering simulation, also known as *in silico* healthcare. Designing and obtaining approval for new wearables employed by those willing to continuously monitor their health is greatly accelerated through simulation. Predicting the evolution of a pathology for a given patient and adjusting the treatment to achieve a better outcome (outcome-based medicine) requires predictive simulation tools (see the article "A Healthy Future").

Wearables

The proliferation of safe and reliable wearable electronics is crucial to personalized healthcare and to make patients more autonomous. The medical IoT is leveraging the emergence of 5G wireless communication and its increased bandwidth to safely and reliably transmit medical data to healthcare professionals. The impact is already being felt. Oticon, a leading hearing aid supplier, increases patient comfort by employing multiphysics simulation that takes into account the individual's head and torso shape (personalization) to improve directional performance of the hearing aid (read the article "Hearing Gain"). Personalized medicine has also reached the veterinary field in the form of an IoT-enabled halter that communicates with horse owners when colic strikes. The halter could mean the difference between life and death for horses (view "Horse Sense").

Medical Digital Twin

In the future, a medical digital twin comprising a computer model for each of us will gather the big data collected by wearables. The first implementations of medical digital twins already combine patient-specific geometry with patient-realistic material properties and operating conditions/ pathologies. Sim&Cure uses a localized digital twin to help surgeons treat patients suffering from cerebral aneurysms (see "Brain Trust for Aneurysm Treatment"). CBBL at Oklahoma State University leverages a human digital twin to assist the pharmaceutical industry in more efficiently targeting cancerous lung tumors (read the article "Targeting a Tumor").

Additive Manufacturing

As medicine and orthopedic surgery become personalized, the one-size-fits-all orthopedic implant will no longer satisfy the patient and the clinical staff. To preserve patient bone capital while extracting a tumor or fixing a major trauma, surgeons must customize the implant to each patient. OMX uses a combination of simulation and additive manufacturing to more quickly design and test implants for maxillofacial surgery (see "Personalized Implants Restore Smiles").

Patient Adjusted Surgery

Staying abreast of progress in engineering simulation, innovative surgeons are eager to collaborate closely with local engineering groups. The University of Shanghai works with local hospitals to assess pediatric and newborn heart surgery scenarios. Using accurate simulation in conjunction with skilled surgery will increase the effectiveness of these procedures and provide the young patients with better quality of life (read the article 'Hearts Content").

Customized Medicine

As the healthcare world begins to collaborate on personalized medicine, the pharmaceutical industry must adjust to reduce medication and personalize drug doses. The drug manufacturing process is often modified to cost-effectively produce smaller quantities of a drug or to design single-use equipment. A manufacturer of single-use biopharmaceutical mixing equipment leveraged simulation to save hundreds of thousands of dollars by significantly reducing the need to build and test prototypes (view "The Right Mix" article).

Leveraging simulation for healthcare can improve treatment, reduce costs and improve the well-being of people worldwide. The stories in this special issue of *ANSYS Advantage* reveal just a small part of what entrepreneurs, hospitals, clinicians, and medical device and pharmaceutical companies are doing to incorporate simulation into their product development plans to save time, money and — most importantly — lives.

ANSYS ADVANTAGE

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The Best of Healthcare

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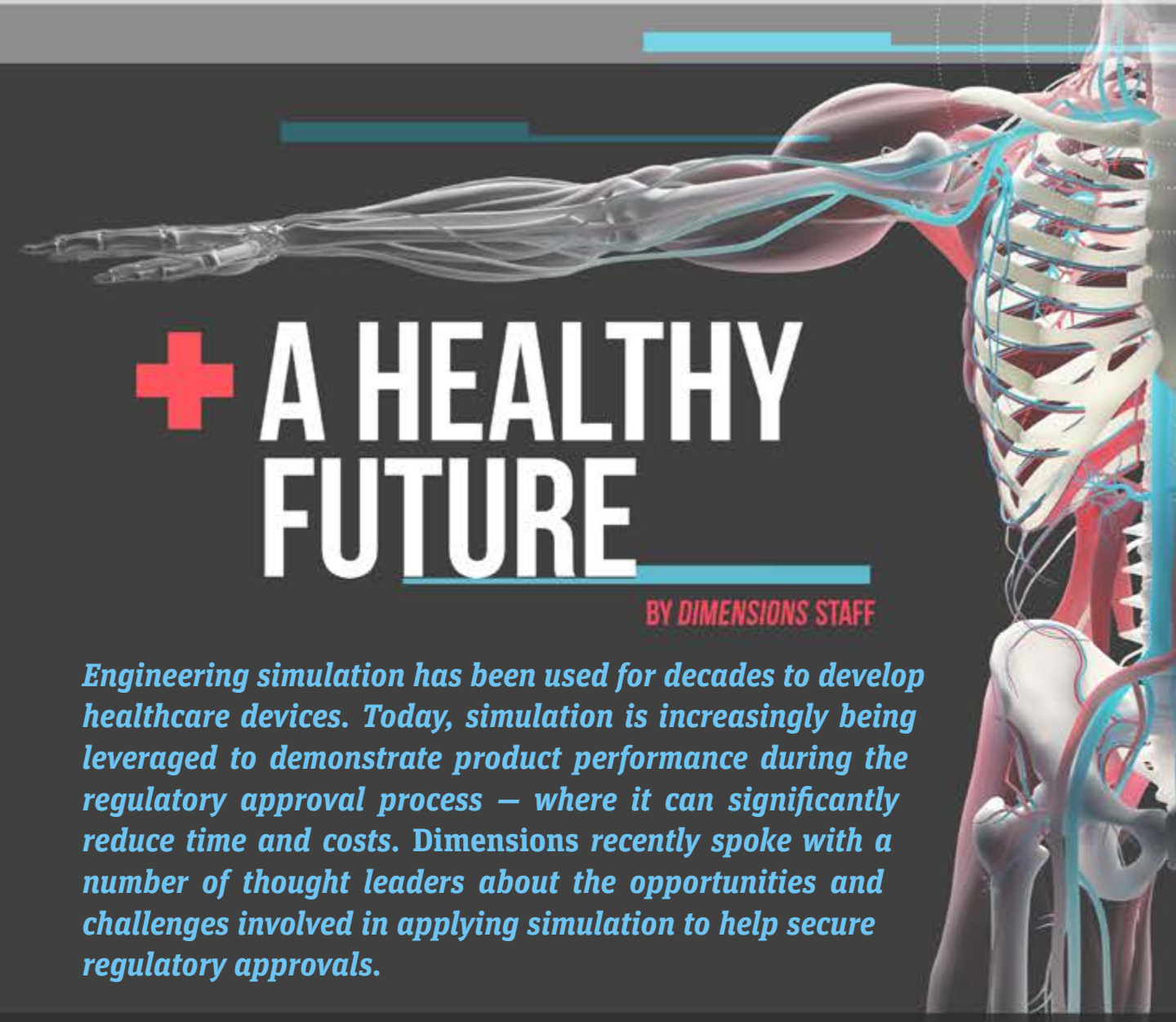


A HEALTHY FUTURE

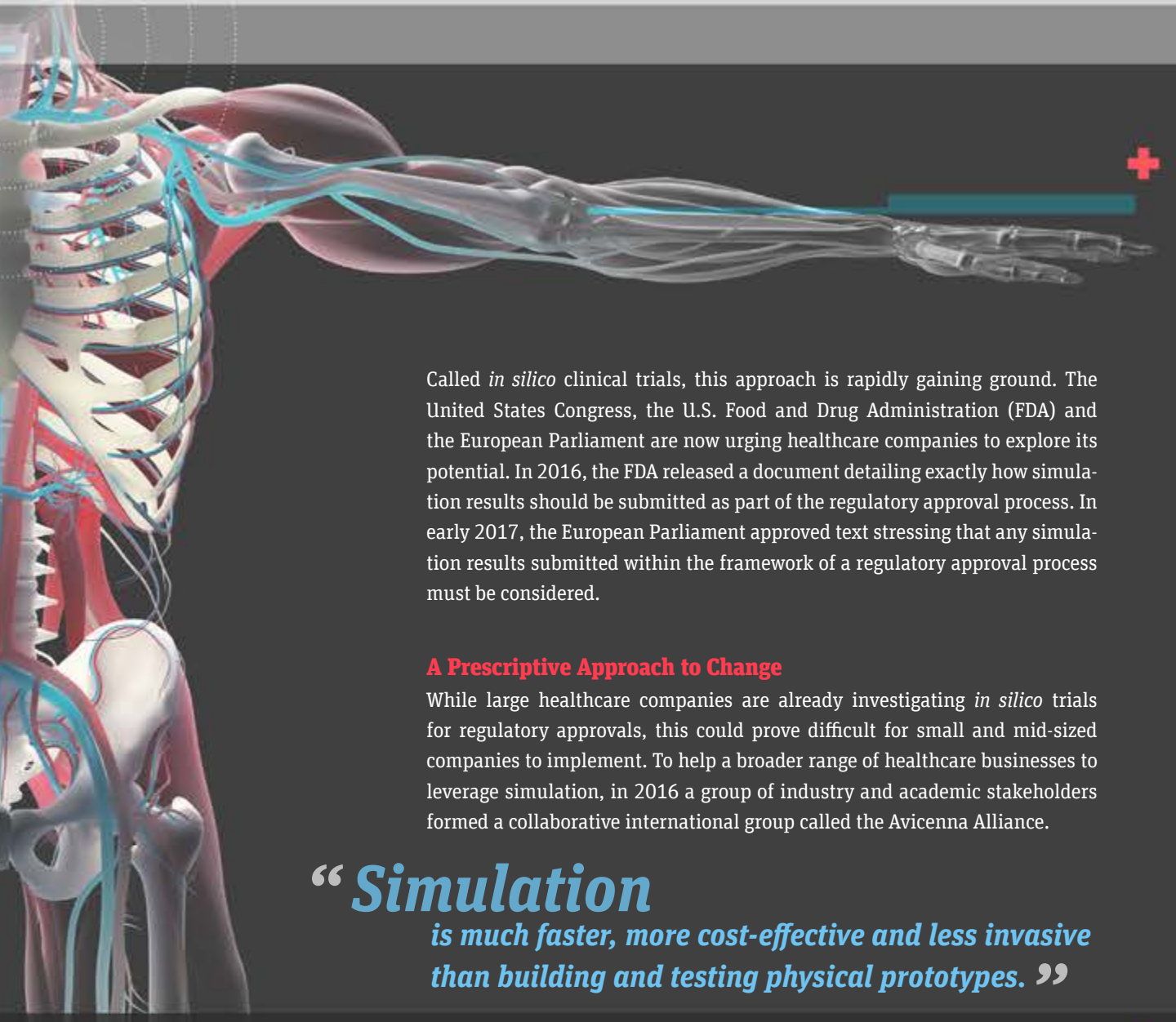
BY DIMENSIONS STAFF

Engineering simulation has been used for decades to develop healthcare devices. Today, simulation is increasingly being leveraged to demonstrate product performance during the regulatory approval process — where it can significantly reduce time and costs.* Dimensions *recently spoke with a number of thought leaders about the opportunities and challenges involved in applying simulation to help secure regulatory approvals.

While all product development processes are rigorous, time-consuming and resource-intensive, this is especially true in the healthcare industry — where devices have the potential to impact the well-being of millions of patients. For decades, engineering simulation has helped reduce the time, cost and risk involved in designing these devices. By engineering and testing patient solutions in a virtual design space, healthcare companies can propel products to the launch phase much faster, and with a higher degree of confidence that they will perform as expected in the real world.

By building 3D models of products and the human body in a virtual design environment, healthcare product developers can test and verify performance, using simulation and digital exploration to make modifications quickly and easily. Simulation is much faster, more cost-effective and less invasive than building and testing physical prototypes.

However, product development is only the first step in launching innovative healthcare devices — which must next undergo a lengthy process to secure regulatory approvals from government agencies. Historically, simulation has been largely ignored during this phase. However, healthcare companies and regulatory agencies alike are now recognizing that, because it can replicate and demonstrate the way devices will actually perform under real-world conditions, simulation is critical to support the regulatory approval process.



Called *in silico* clinical trials, this approach is rapidly gaining ground. The United States Congress, the U.S. Food and Drug Administration (FDA) and the European Parliament are now urging healthcare companies to explore its potential. In 2016, the FDA released a document detailing exactly how simulation results should be submitted as part of the regulatory approval process. In early 2017, the European Parliament approved text stressing that any simulation results submitted within the framework of a regulatory approval process must be considered.

A Prescriptive Approach to Change

While large healthcare companies are already investigating *in silico* trials for regulatory approvals, this could prove difficult for small and mid-sized companies to implement. To help a broader range of healthcare businesses to leverage simulation, in 2016 a group of industry and academic stakeholders formed a collaborative international group called the Avicenna Alliance.

> *"Simulation is much faster, more cost-effective and less invasive than building and testing physical prototypes."*

Named for the Persian philosopher and scientist who is often considered the founder of modern medicine, the Avicenna Alliance was created by four founding members: ANSYS, a developer of simulation software; medical device manufacturer Medtronic; consulting group Rohde Public Policy (RPP); and the Virtual Physiological Human (VPH) Institute, a European initiative that aims to enable collaborative investigation of the human body as a single complex system. Today the Alliance has incorporated other healthcare stakeholders, including private companies, lobbyists, consultants and medical experts who are committed to the use of simulation for regulatory approvals.

Adriano Henney, secretary general for the partnership, holds a Ph.D. in medicine and worked for years in pharmaceutical and biological research before helping to form the Avicenna Alliance. He first became passionate about modeling devices and the human body while working for AstraZeneca, establishing one of the first Systems Biology departments in the industry. He subsequently led a collaborative, government-funded study on liver

dysfunction. "Modeling a healthcare device inside the human body, and looking at interactions in a simulated environment, just makes sense," notes Henney. "It reduces costs, it saves time and it minimizes the impact on human patients. The potential benefits of using this process over traditional clinical trials are enormous."

"The only problem is that this idea is so new," Henney continues. "Private companies, researchers, government regulators — we're all working to understand how *in silico* trials can be implemented consistently on a global basis. That's why we formed the Avicenna Alliance, to create a bridge between all the stakeholders, inform policy decisions and begin to articulate a structure for leveraging simulation that everyone can agree will produce the highest-quality results."

A Prescriptive Approach to Change

One of the Avicenna Alliance's most critical activities is working with policymakers around the world to educate them about the benefits of *in silico* medicine, so they can make informed decisions as they draft new regulatory guidelines. James Kennedy is associate director with Rohde Public Policy Group, which serves as the secretariat of the Alliance and leads this effort.

"It's very unusual for a consultancy to invest heavily in a scientific topic," points out Kennedy. "But if we can take the same technology that Formula 1 carmakers use to develop fuel injection systems — and apply it to optimize blood flows inside the human body — why wouldn't we want to do that? Advanced modeling technology opens up so many doors and holds the potential to improve the health and well-being of millions of people."

Kennedy regularly meets with both government regulators and healthcare executives to promote the need for practical guidelines for the use of *in silico* clinical trials. "The policy structure we have today simply can't take the weight of all these new *in silico* approaches," states Kennedy. "Policy needs to evolve along with technology."

Henney notes that legislators and regulators are extremely enthusiastic about healthcare simulation, which supports the general trend toward patient-specific treatments and personalized medicine. "I think everyone realizes that customized treatment approaches represent the future of the healthcare industry," he says. "If we can use simulation and modeling to verify not just that a device works, but that it works for a specific individual, we are now taking product safety and confidence to a new level. We can design devices aimed at a specific patient. This represents a quantum leap in quality of care, which can reduce overall treatment and insurance costs significantly."

Diagnosing and Meeting Technology Needs

In addition to supporting the development of clear legislation and regulatory guidelines, the Avicenna Alliance is working to ensure that user-friendly simulation technology is available to a new group of healthcare customers. As a founding member of the Alliance and an industry leader in simulation software, ANSYS is spearheading this effort.

"Simulation is a standard practice in developing healthcare products," says Thierry Marchal, industry director for healthcare at ANSYS. "To begin employing simulation as part of the regulatory process, most businesses simply need to bring their simulation experts together with their regulatory experts — and investigate how their efforts can be combined."

In Silico Trials: Getting Started

To help small and mid-sized healthcare companies capitalize on the benefits of* in silico *trials, Adriano Henney and James Kennedy of the Avicenna Alliance offer these practical guidelines:

- Identify the simulation experts within your company. "Chances are, someone in your product development organization is already using engineering simulation to model products," Henney says. "Find out who they are, and discuss integrating the existing results into your existing regulatory approval process."

- Explore opportunities for collaboration beyond your own organization. "By partnering with companies who are further along in the *in silico* journey, you can make faster progress and benefit from the lessons they've learned," notes Henney.

- Open a dialogue with local regulatory officials. "Many businesses view government agencies as adversaries, when in fact they can be valuable partners," Kennedy states. "Because simulation is still a relatively new topic for regulators, they are eager to learn — and to partner with healthcare companies to advance this practice."

ANSYS partners with technology startups like Promeditec to develop specialized apps and portals that help integrate simulation into accepted clinical trial workflows (see sidebar, "Promeditec: Facilitating *In Silico* Trials"). "By identifying and collaborating with innovative companies like Promeditec, ANSYS simulation software is placed into the hands of healthcare specialists who already require regulatory approvals," explains Marchal.

"We're not suggesting that *in silico* trials will completely replace traditional clinical trials in the short term," Marchal adds. "But, to remain competitive and begin to accelerate the approval process, healthcare companies must define new practices for sharing simulation data and establishing simulation expertise outside of the product development function."

While the Avicenna Alliance was founded in 2016, this collaborative effort is already making great strides in promoting the use of simulation for regulatory approvals. This could mean significantly reduced healthcare costs, more personalized medical treatment and improved well-being for patients worldwide.

Promeditec: Facilitating In Silico Trials

Based in Milan, Italy, Promeditec is a technology startup that supports healthcare companies in executing clinical trials — including the management of data, processes and workflows, and documentation for regulatory compliance. To add value, Promeditec has partnered with ANSYS, the industry leader in simulation software, to support its customers' use of *in silico* trials for regulatory compliance via an interactive website called inSilicoTrials.com.

"inSilicoTrials.com represents a new concept for the small and mid-sized companies we serve," explains Luca Emili, CEO of Promeditec. "Our goal in collaborating with ANSYS is to create an easy, cost-effective tool that enables them to capitalize on simulation technology and model their healthcare products in a low-cost, risk-free virtual environment."

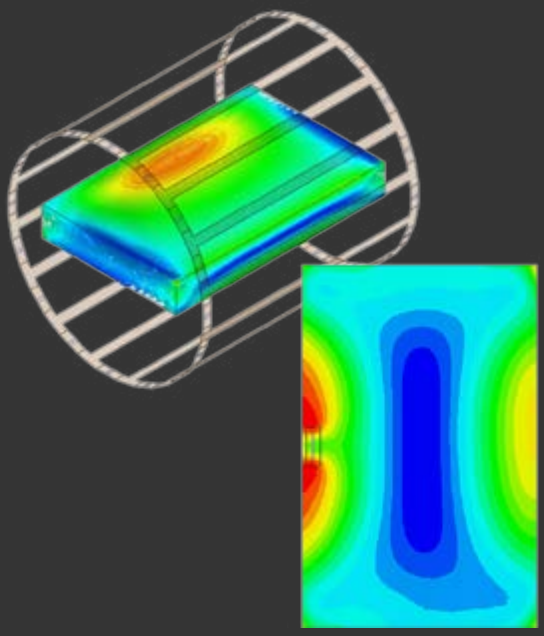
Promeditec hosts ANSYS software in the cloud, and has also devised an extremely user-friendly app that gives customers easy access to the power of simulation — while also offering compatibility with the company's apps for data management and other functions.

Already, Promeditec customers have begun realizing the benefits of *in silico* modeling to support their regulatory approval processes. For example, the first application publicly available on inSilicoTrials.com is a tool for magnetic resonance imaging (MRI) safety analysis for implanted metal stents. The simulation, developed by the U.S. Food and Drug Administration (FDA) as part of a joint five-year collaborative agreement with Promeditec, is accessible through a user-friendly web interface and runs in the cloud. This tool will provide users with a report that follows FDA guidelines and is suitable to be submitted for regulatory approval.

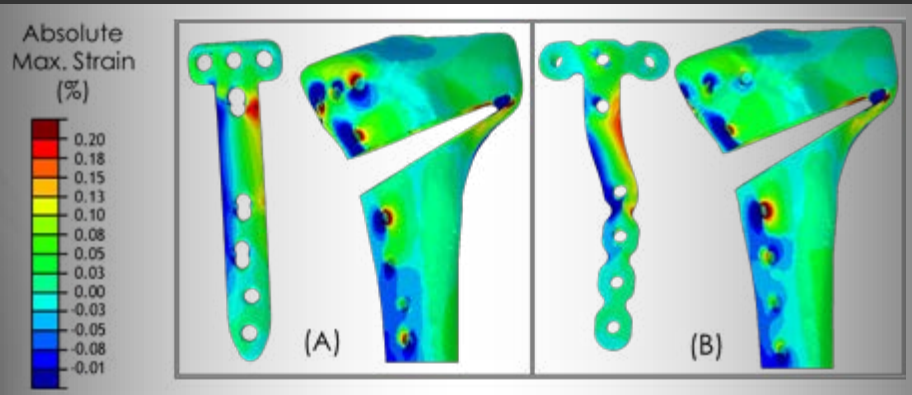
Another example is a specific web process developed for the simulation of a novel, patient-specific orthopedic device for treating early stage osteoarthritis of the knee. The aim of the *in silico* trial is to evaluate the safety equivalence between a well-established existing generic device and the novel patient-specific device, ToKa, which was designed by a collaboration between the University of Bath, the Royal Devon and Exeter Hospital, and 3D Metal Printing Ltd.

Based on the 3D anatomy of a cohort of 30 patients, a multi-objective robust design optimization and multi-criteria decision analysis was implemented, while the computational time required was reduced. The simulation report will be part of the regulatory submission package for the new medical device.

This could mean significantly reduced healthcare costs, more personalized medical treatment and improved well-being for patients worldwide.



MRI safety simulation for implanted metal stents



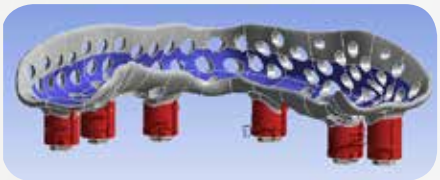
Simulation of the original device for treating osteoarthritis of the knee (A) and patient-specific device (B).

Personalized Implants Restore Smiles

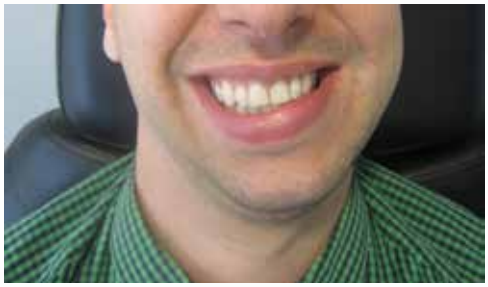
By **Sarah Fink**,
Design Engineer and
Aaron Atkinson,
Design Engineer,
OMX Solutions,
Melbourne, Australia

When people are missing multiple teeth and large sections of their oral bone structure, they are not good candidates for standard dental implants. The usual treatment for this condition is bone grafting, which requires multiple staged surgeries that usually take a year or more to complete. With the help of ANSYS Mechanical, OMX Solutions uses additive manufacturing to produce implants that fit the jaw and match facial contours and require only a single surgery. Those affected can have their appearance properly restored and can eat immediately after surgery.

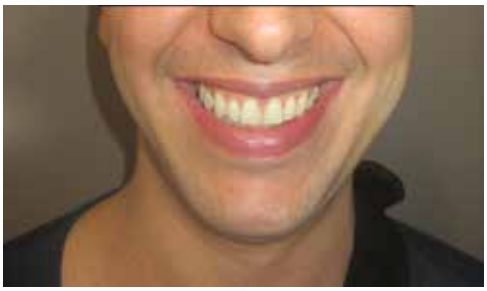
Dental procedures can be trying for many people. A filling, an implant or even a root canal are minor compared to the replacement of multiple teeth and large sections of bone that is required when trauma, fractures, tumors, degenerative bone disease and other issues occur. Severe bone loss is usually treated by harvesting bone from the patient's rib or fibula (in the leg), which requires at least three traumatic surgeries over 12 to 18 months. These same problems, as well as osteoarthritis and other conditions, may necessitate the replacement of the temporomandibular joint (TMJ), commonly known as the jaw joint. The jaw joint may be replaced with off-the-shelf components that often leave patients with a poor fit and reduced functionality. OMX Solutions, a world leader in digital solutions for surgical challenges, has developed improved solutions by using digital design and additive manufacturing to produce custom implants that fit the



CAD model of Osseo-Frame



Before



After

> **"Simulation identifies potential *problems* with the *interactions between components* and gives an indication of potential points of *failure*."**

patient's existing bone perfectly. OMX Solutions uses ANSYS Mechanical to simulate the bone and implant as a unit, which, when confirmed with physical testing, ensures that these implants can withstand forces associated with mastication. The result is made-to-order facial and jaw implants that improve surgical outcomes, enhance quality of life, significantly reduce the number of surgeries required and eliminate donor site pain and morbidity.

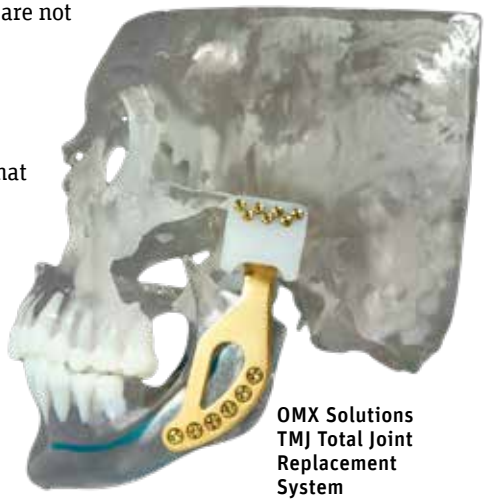
LIMITATIONS OF CONVENTIONAL IMPLANTS

When a large amount of bone and multiple teeth are missing, conventional dental implants do not provide enough stability to resist bite forces. Another option is a temporary removable denture, which can be uncomfortable and unstable. To remedy this, surgeons usually perform one procedure to remove a bone from the donor site and implant it into the jaw. Additional surgeries are required to implant teeth. The patient requires considerable time for recovery between surgeries, and the total time to complete the repair can be a year or more. Because the bone-grafting process is complex, it is difficult to match the patient's facial contour, so patients are often left with an unbalanced look. Pain and donor site infection are also common.

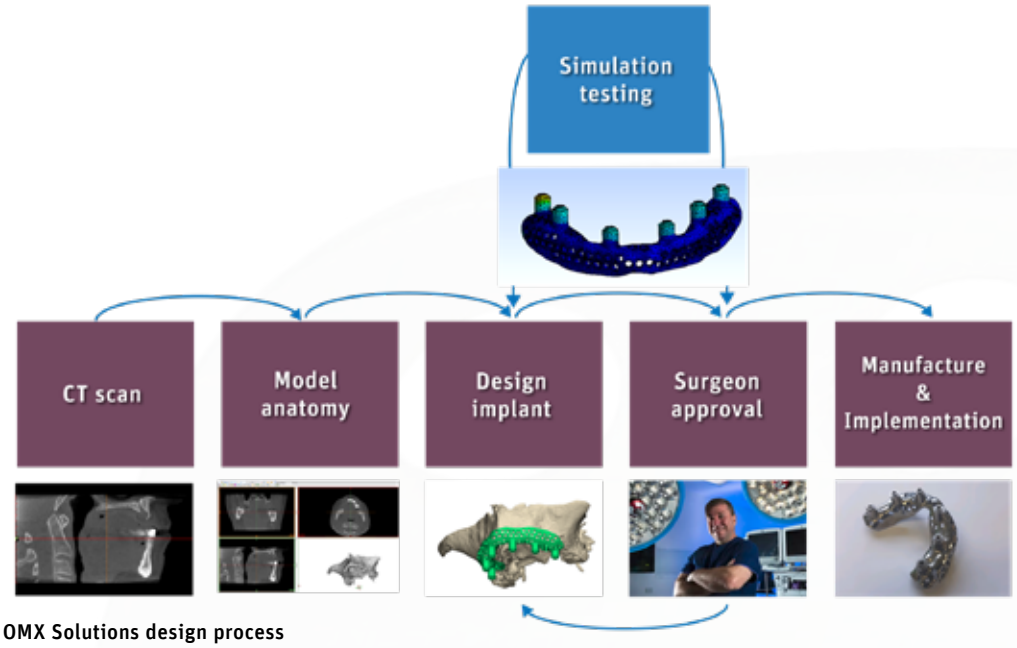
When TMJ replacement is required, the limited number of standard TMJ implant sizes available does not conform to the wide range of jaw and bone-loss configurations that are encountered in clinical practice. If there has been major bone loss, patients may be left with deformities and poor TMJ function because the stock implants are not fully compatible with the patient's condition and morphology.

NEW APPROACH USES ADDITIVE MANUFACTURING

OMX Solutions has developed solutions to address these conditions. The OMX Solutions Osseo-Frame is a jaw implant that provides a secure, rigid bone replacement and mounting point for dental prostheses. It eliminates the need for bone grafts when the native bone site is not suitable for conventional dental implants. The implant is digitally designed and 3D printed to match the patient's alveolar bone ridge, which ensures that the device perfectly fits to the natural bone without the need for bone modification. The microscrews and baseplate provide primary stability, so that the implant (and artificial teeth) can immediately be loaded without a protracted healing period.



OMX Solutions TMJ Total Joint Replacement System



OMX Solutions design process

The OMX Solutions TMJ Total Joint Replacement completely replaces the patient's temporo-mandibular joint. The 3D-printed titanium mandibular component is digitally sized and adjusted to fit each individual patient's bone structure using the patient's computed tomography (CT) data. The polyethylene fossa is also digitally sized and customized using computer numerical control (CNC) machining. The two then work together as a custom-fitted ball (condyle) and socket (fossa) joint.

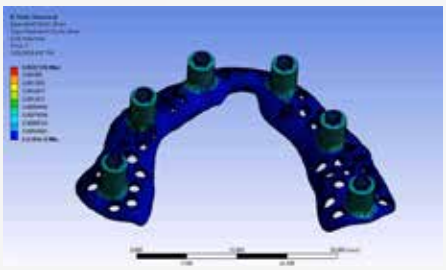
Both systems can be supplied with cutting, drilling and positioning guides to improve surgical precision.

DESIGN PROCESS FOR CUSTOM IMPLANTS

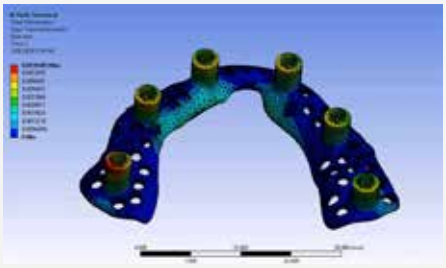
The first step in customizing these devices to the bone contours of the individual patient is to perform a CT scan that accurately shows the geometry of the patient's existing bone structure. OMX Solutions production engineers then use Materialise Mimics® software to convert the CT scan output to a digital model of the patient's bone and Materialise 3-matic® software to design the implant to closely match the patient's 3D skeletal anatomy.

In designing custom implants, OMX Solutions production engineers must ensure that the entire assembly, including bone, attachments and implant components, will not fail. Without simulation, it would be necessary to print each implant and conduct physical tests on them. If it did not pass, it would be necessary to redesign, remanufacture and retest, which is expensive in both time and money. Moreover, conducting physical tests on the entire implant–bone assembly for every patient is not possible.

Patient-specific simulation is the only way for OMX Solutions to cost-effectively ensure the integrity of each implant.



Display of equivalent strain experienced in an Osseo-Frame



Display of total deformation occurring in an Osseo-Frame

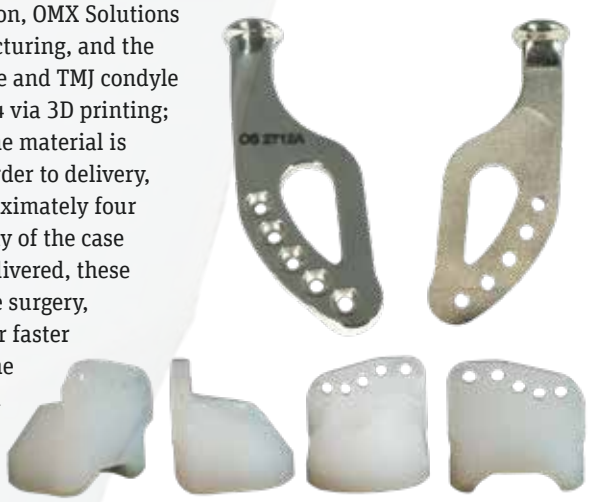
ANSYS MECHANICAL SIMULATION

OMX Solutions selected ANSYS because of its intuitive user interface. The company's production engineers first simulate the device alone using the average bite force as found in the literature. This is typically the average bite force of a 25-year-old male, although the average patient for OMX products is older and has reduced muscle strength. As such, they have a less powerful bite, so this approach provides a comfortable margin of safety. Once they are confident with the device integrity, the engineers then simulate a full mock-up, including a multimaterial model of the bone derived from the CT scan and the screws attaching the implant to the bone. All materials are treated as nonlinear. This model includes frictional contacts between the bone, screws and the implant. Contact detection is used to register the contacts that occur between each face of each screw in the bone model and to identify any potential separation that may occur during use, such as the frame coming off the bone. The run time of this simulation is typically two to five hours on a 4-core personal computer.

"OMX Solutions has developed improved implant solutions by using *digital design and additive manufacturing* to produce custom jaw implants that fit the patient's existing bone perfectly."

This simulation identifies potential problems with the interactions between components and gives an indication of potential points of failure. For example, it may show where the screw may cause bone fracture due to high levels of stress that are induced locally or where the screws are not capable of securely fastening the implant. When OMX Solutions production engineers are confident that the assembly is secure, they provide the design to the surgeon for review. The surgeon sometimes suggests changes based upon clinical feasibility and usability, in which case another round of simulation may be required.

Once they have approval from the surgeon, OMX Solutions transfers the digital design files to manufacturing, and the components are produced. The Osseo-Frame and TMJ condyle components are produced from titanium-64 via 3D printing; the fossa component is CNC machined as the material is currently not able to be 3D printed. From order to delivery, a custom implant can be produced in approximately four to eight weeks, depending on the complexity of the case and the experience of the surgeon. Once delivered, these devices are ready for installation in a single surgery, providing a permanent solution up to a year faster than traditional methods, at a fraction of the total surgical cost and significant reduction in pain and morbidity for the patient.



TMJ Total Joint Replacement Systems components include mandibular (top) and fossa (bottom).

Those with bone loss and reduced jaw function can find it difficult to enjoy food and eat a healthy diet. They may also have reduced self-esteem because of their appearance. OMX Solutions implants help these people rapidly recover their previous dental function and smile without undergoing a long series of operations. Patients who could not move their jaw in the past without pain can now eat and talk comfortably. People who had difficulty chewing and were not candidates for conventional implants can now eat normally. Patients whose faces had a sunken or lopsided look due to bone loss can be restored to their previous appearance. OMX Solutions custom implants restore a patient's ability to eat, speak and smile with renewed self-confidence and peace of mind.

BONING UP

ANSYS software simulates the stress and strain on bones of individual patients to study a new hip-implantation method.

Increasing numbers of patients are suffering from pain, stiffness or difficulty in moving due to osteoarthritis in their hips. Doctors typically recommend hip replacement surgery for patients with pain so severe that it limits everyday activities or reduces their range of motion. In hip replacement surgery, a damaged hip joint is surgically replaced with an artificial implant. The surgeon removes the head of the femur with a saw and then attaches a ball that is anchored by a shaft extending into the femur. A mating cup is attached to the pelvis. Most hip replacement patients, after recovering from surgery, experience higher levels of functionality and greatly reduced pain.

By **Tim Weber**, Mechanical Engineer; **Simon Gross**, Mechanical Engineer; and **Sebastian Dendorfer**, Biomedical Engineer, OTH Regensburg, Laboratory for Biomechanics, Regensburg, Germany

Even though hip replacement has been proven to be a safe procedure, failures sometimes occur. A recent study showed that nearly 25 percent of hip replacements required additional surgery [1]. Malpositioning of the ball and cup is believed to be one of the major causes of hip replacement failures. It may reduce the patient's range of motion and could also lead to impingement, which refers to implant-to-implant contact, bone-to-bone contact or bone-to-implant contact. Impingement is one of the major causes of postoperative pain, dislocation and implant breakage. Malpositioning also may increase wear rates and the risk of dislocation of the implant.

> "Hip ***replacement failures*** are common."

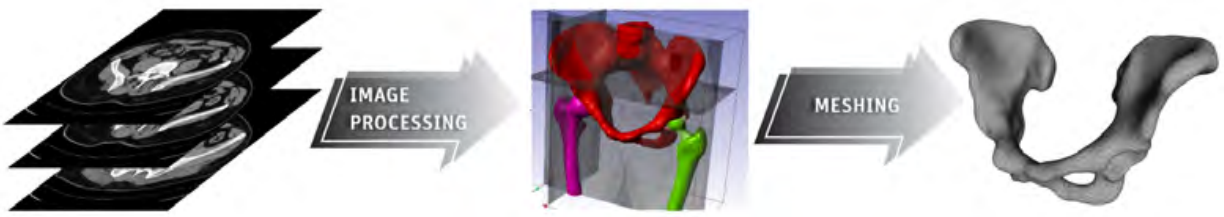
Researchers at the OTH Regensburg Laboratory for Biomechanics are studying computer-assisted surgery as an alternative to traditional hip replacement surgery to reduce misalignment problems. The researchers are in the midst of a new study that compares computer-assisted surgery with the traditional approach. The investigation compares both methods using a gait study that measures anatomical markers while walking, as well as the reaction forces applied to the ground. Then musculoskeletal modeling software is used to extrapolate forces applied by muscles to the bones and the reaction forces at the hip. Finally, ANSYS Mechanical finite element analysis software is em-

ployed to calculate stresses and strains in the pelvis and femur of the patients six months after the surgery to determine which method of surgery was more effective.

NEW SURGICAL ALTERNATIVE

In traditional surgery, the position of the ball, shaft and cup are manually determined by the surgeon, who must position the implant to provide the best range of motion, minimize the potential for impingement and achieve stable cup containment. The OTH Regensburg researchers are comparing this approach with a new method that uses an algorithm to optimize component positioning.

The new method begins with the insertion of the shaft into the femur. Using imageless motion capture techniques and patient-specific anatomy, an algorithm determines the position of the ball based on the shaft and then calculates an optimal position for the cup that addresses range of motion, impingement and containment. Reference pins are inserted into the femur and pelvis during surgery



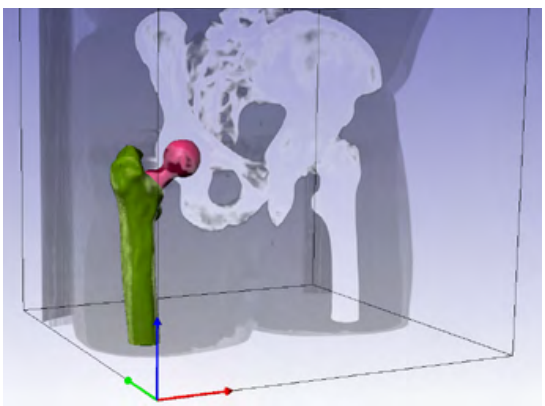
^ Patient-specific volume meshes from CT scans (left) and patient-specific muscle forces from musculoskeletal modeling (center) were used as inputs to finite element analysis (right).

so that the computer-assisted surgery software can determine their positions and guide the surgeon to place the cup in the optimal location. After the operation, computed tomography (CT) scans are used to produce a 3-D reconstruction of the femur and pelvis.

The researchers are conducting the first patient- and observer-blinded, randomized, controlled trial to compare the manual and computer-assisted surgery methods. The study is designed to determine whether or not computer-assisted surgery can reduce hip replacement failures by improving the range of motion, reducing the occurrence of impingement and providing other benefits. The trial consists of 60 patients, 32 of whom received conventional surgery and 28 who received computer-assisted surgery.

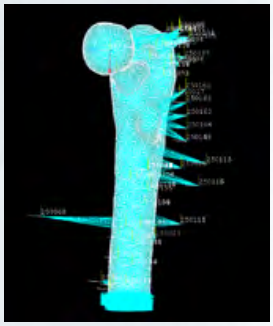
DETERMINING MUSCULOSKELETAL LOADING

The researchers set out to determine the musculoskeletal loading of the patients to better understand the differences in functionality between the two operating methods. The traditional approach is to use instrumented implants to measure the reaction forces. This method is regarded as the gold standard, since it is the only way to physically measure forces; however, it has several disadvantages. It is highly invasive, which limits its use to very small sample sizes, and it provides measurements at only a few discrete points.



^ Volume mesh shows grayscale coding used to assign material properties to bone.

Instead, researchers used computer modeling to predict joint reaction forces [2]. Each patient in the study was instrumented with 27 reflective markers on anatomical landmarks. The patients then walked across a 10-meter walkway. Video cameras recorded the position of the markers while ground reaction forces were recorded with force plates. The measured ground reaction forces and the trajectory of the markers were used as inputs for the musculoskeletal model.



Muscle forces were used as boundary conditions.

The inverse dynamics software AnyBody Modeling System™ was then used to simulate muscle and joint forces in the entire body. A generic model of the human body was scaled to fit to the individual patient using advanced morphing methods. In that way the patient-specific motion was coupled with the individual anatomy, which allows computing of the biomechanics on a very detailed level, including hundreds of muscle forces.

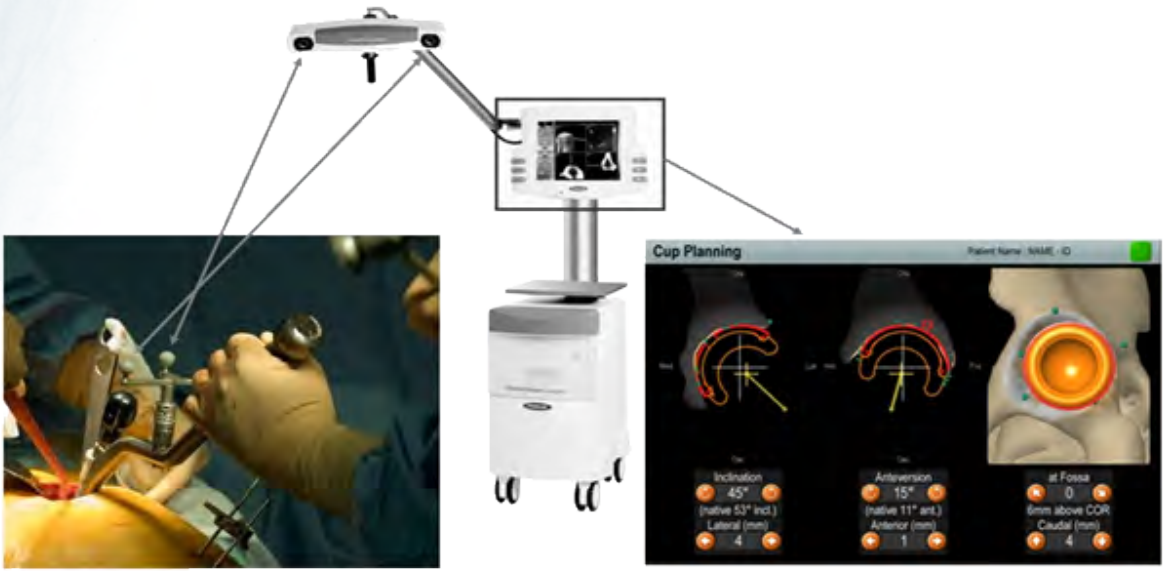
FINITE ELEMENT ANALYSIS

After computing the reaction forces and muscle forces, the researchers needed to determine whether or not computer-assisted surgery would provide more equally distributed stress at the interface of the bone and the implant. This information, obviously, could not be obtained from physical measurements, so they turned to computer simulation with ANSYS Mechanical software.

> **"At the six-month point the walking ability of the *computer-assisted surgery* group was superior."**

Simpleware software (Simpleware Ltd., Exeter, UK) was used to convert CT scans performed on all patients at six months after surgery into an ANSYS Mechanical input file. Since the bone is a naturally grown material, its properties vary from person to person. To take this into consideration, researchers created 12 different material models for the cortical bone as well as for the cancellous bone of each subject. These materials were linked to certain grayscale values of the CT scans. After this step, the team exported the 3-D models into the structural software, including the grayscale based material properties.

AnyBody software exported muscle forces in ANSYS Mechanical format, which were used as boundary conditions in the FEA simulation. The model was fixed at the lower end of the femur. ANSYS Mechanical calculated stress and strain in the bones of each patient. The results revealed no significant difference between the stress and strain distribution in the



Computer-assisted hip replacement surgery

computer-assisted and manual surgery even though the loads were different. One possible explanation for this is that the bone has already adapted to balance the stresses and strains. The different load scenarios may therefore be advantageous for the implant system, but may not impact the bone.

Significant improvements were seen in other parameters in patients who were treated with computer-assisted surgery. The typical hip reaction forces 12 months after the operation were practically the same as for a young and healthy adult, in contrast to 23 percent lower hip reaction forces for the conventional surgery group. In particular, the orientation of the hip reaction forces was within 10 percent of optimum for the computer-assisted surgery group of patients at six months post-operative. Decreased asymmetries were also seen in the gait pattern of the computer-assisted surgery group relative to the control group, but there were no significant differences between the groups. This indicates that at the six-month point the walking ability of the computer-assisted surgery group was superior [3]. An ongoing study will determine if the computer-assisted group is also superior in terms of wear. A

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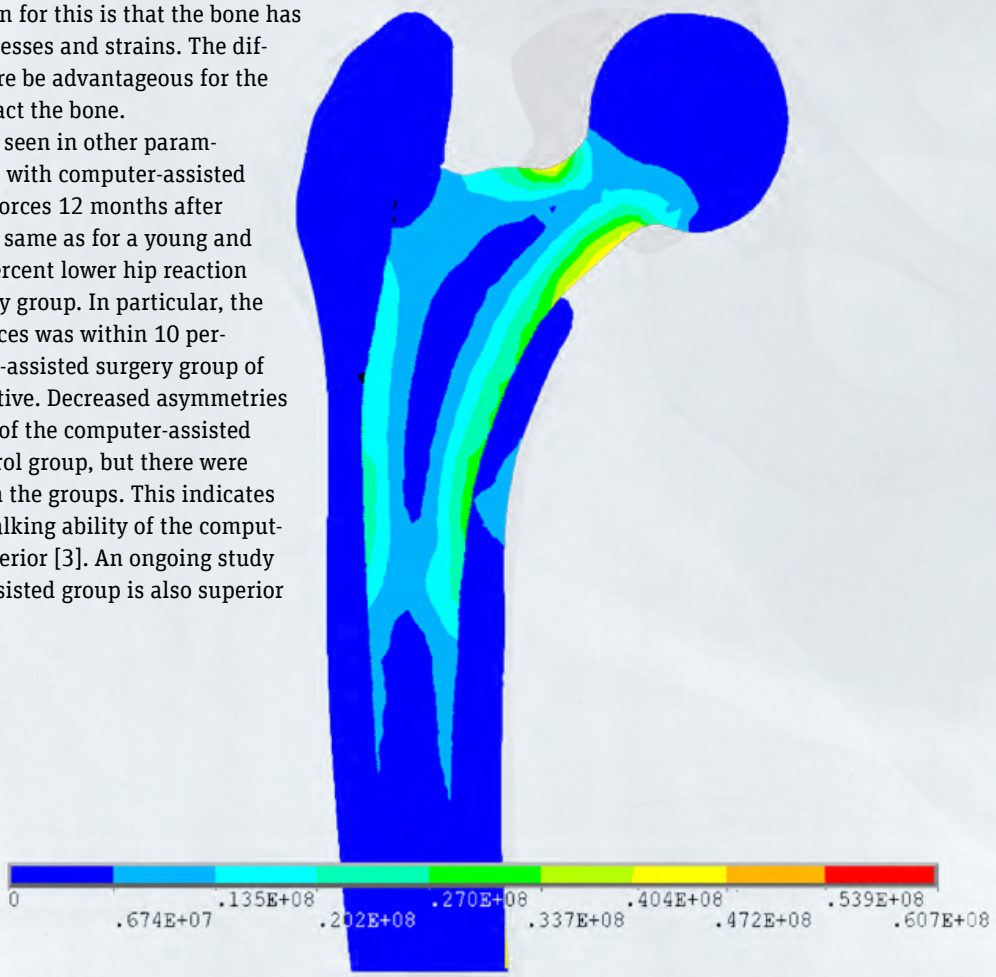

^ Von-Mises stress results. Blue indicates lower stress and yellow shows higher stress.

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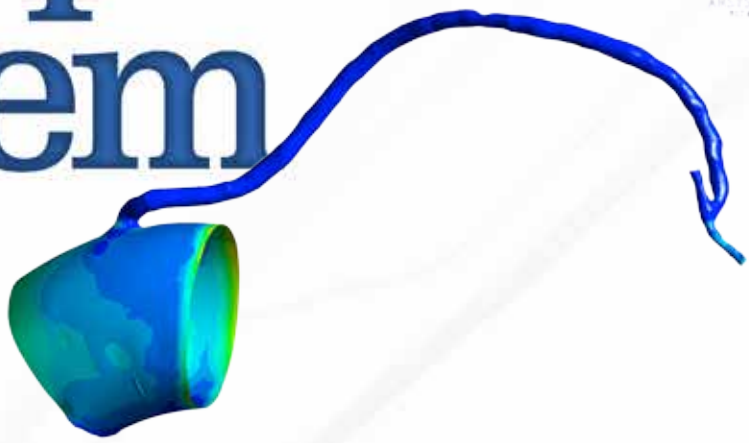
Support System



Each year, more than 2 million patients worldwide undergo a procedure called coronary artery bypass grafting (CABG). Used to treat blocked arteries and restore normal blood flow to the heart, CABG involves grafting a blood vessel — typically taken from the leg — around the diseased area, re-establishing blood flow to the heart tissue.

Veins used for CABG offer an inadequately durable solution to coronary artery disease, with a long-term outlook that is not promising. Within 18 months, 25 percent of the implanted veins fail — and, after five years, that failure rate increases to 40 percent.

"The blood vessels in the leg are relatively large and easy to harvest and implant, but unfortunately they are not built for the high flow rates and pressures near the heart," explains Mohammed El-Kurdi, co-founder and director of research at Neograft, a startup headquartered in Taunton, U.S.A. "Over time, these grafted veins begin to dilate and eventually become blocked, necessitating another surgery."

A mechanical engineer by training, El-Kurdi focused his doctoral work at the University of Pittsburgh on designing a structural support system that would improve the durability of arterial vein grafts. In 2009, he co-founded Neograft, and Jon McGrath, a seasoned health care entrepreneur, became the company's chief executive officer. Neograft markets a patented product called Angioshield that is designed to increase success rates for CABG procedures.

"Through a novel process called electrospinning, our Angioshield technology creates a 'scaffold' of polymer material around the vein prior to implant. This scaffold improves both the vein's strength and its geometric uniformity," says El-Kurdi.

According to El-Kurdi, Neograft's proprietary advanced material is key to the success of Angioshield. "Our polymer sheath shapes itself to the vein without deforming it," he notes. "And, because the material is porous, it allows nutrients and new cells to migrate to the tissue. Over time, this results in the growth of stronger and healthier graft tissue."

Because of the difficulty associated with visualizing and manipulating structures inside the human body, El-Kurdi began relying on the power of engineering simulation while still in the Ph.D. program at Pitt. Today, Neograft engineers use simulation to model different blood flows inside implanted veins, as well as to understand diverse mechanical forces that act on vein grafts, such as the motion associated with a beating heart. Product developers can then change the physical properties of the polymer scaffold as they increase their understanding of vein graft mechanics.

An external stent for the grafted vein, Angioshield is deposited directly onto the outer surface of the vein via a novel electrospinning process. Neograft's product development team has used ANSYS finite element analysis (FEA) software to ensure the structural strength of the stent, and has leveraged ANSYS computational fluid dynamics (CFD) software to study and optimize blood flows inside the grafted vein. Fluid–structure interaction analysis is planned for the future, as Neograft expands its use of ANSYS solutions.

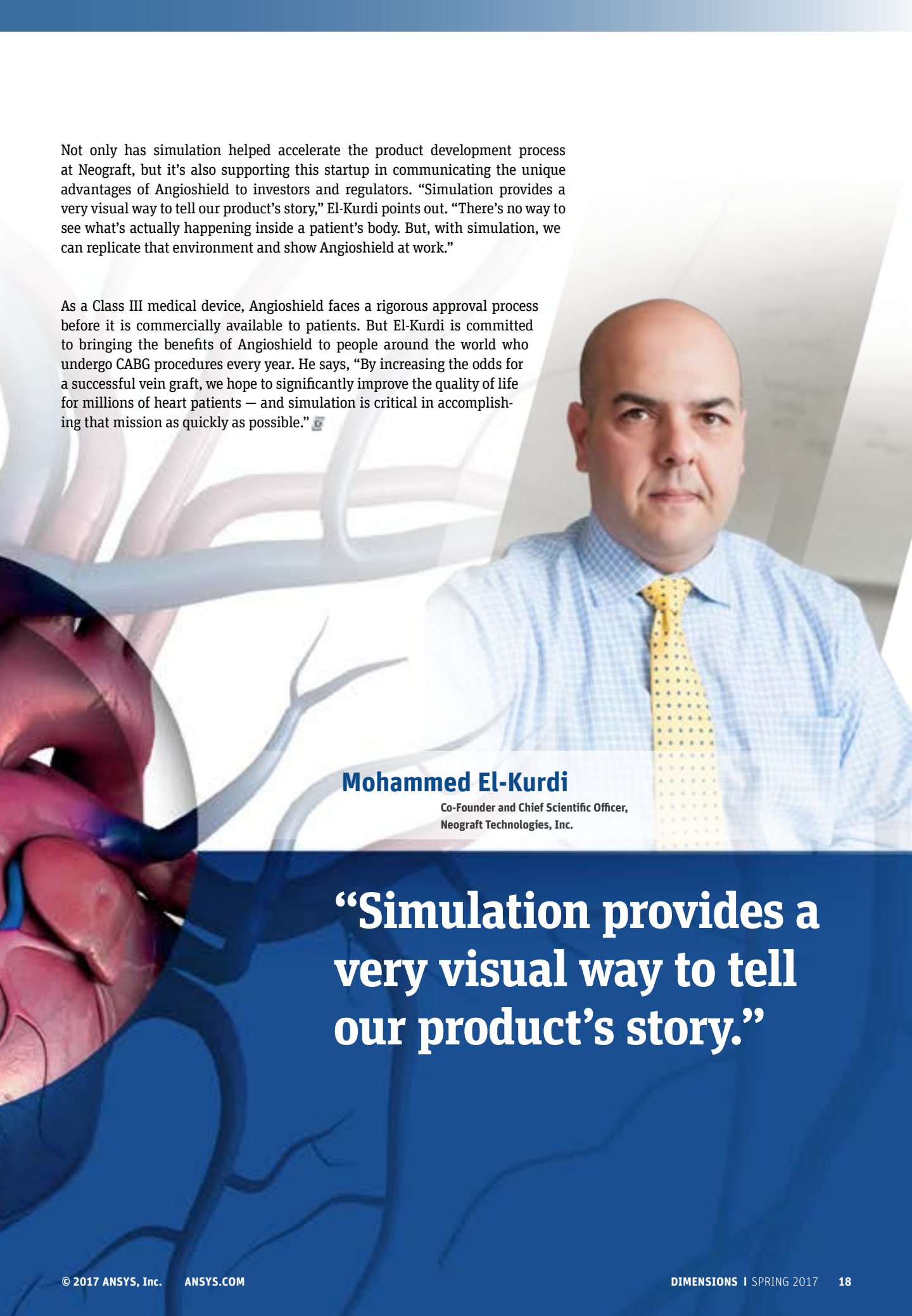
"Perfecting the Angioshield material is an iterative process, during which we apply different material configurations, then test the treated vein's resulting strength and durability," states El-Kurdi. "It would be impossible to move so quickly, and conduct so many studies, without working in a risk-free virtual design environment. By the time we moved to animal and clinical trials, we had a deep foundation of knowledge that allowed us to predict outcomes very accurately. And we continue to add to that knowledge base every day."

Today, as Angioshield is tested in patients, computerized tomography angiography (CTA) generates images of the implanted vein. These images are fed back into ANSYS software to generate 3-D models of Angioshield inside an actual human body. "We're currently using simulation as an investigative tool to understand patient-specific behaviors of treated veins," says El-Kurdi. "Our studies will enable the Neograft engineering team to build better predictive models and continually improve the product."

"It would be impossible to move so quickly, and conduct so many studies, without working in a risk-free virtual design environment."

Not only has simulation helped accelerate the product development process at Neograft, but it's also supporting this startup in communicating the unique advantages of Angioshield to investors and regulators. "Simulation provides a very visual way to tell our product's story," El-Kurdi points out. "There's no way to see what's actually happening inside a patient's body. But, with simulation, we can replicate that environment and show Angioshield at work."

As a Class III medical device, Angioshield faces a rigorous approval process before it is commercially available to patients. But El-Kurdi is committed to bringing the benefits of Angioshield to people around the world who undergo CABG procedures every year. He says, "By increasing the odds for a successful vein graft, we hope to significantly improve the quality of life for millions of heart patients — and simulation is critical in accomplishing that mission as quickly as possible."



Mohammed El-Kurdi

Co-Founder and Chief Scientific Officer, Neograft Technologies, Inc.

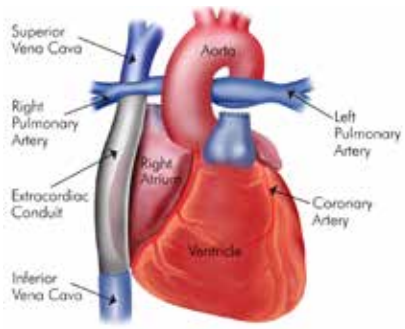
"Simulation provides a very visual way to tell our product's story."

"Using accurate simulation in conjunction with skilled surgery will increase the effectiveness of these procedures and provide the young patients with better quality of life."

Hearts Content

The long-term prognosis for babies born with single-ventricle heart defects can depend on the location of vascular connections made during corrective surgery. **Shanghai Children's Medical Center** uses simulation to individualize this surgery. Researchers employ computational fluid dynamics to determine the optimal connection points based on the patient's cardiovascular anatomy, improving surgical effectiveness and resulting in a better quality of life for these children.

By **Liu Jinlong**,
Associate Professor,
Department of Cardiothoracic Surgery,
Shanghai Children's Medical Center, Shanghai, China



^ Heart after correction with Glenn and TCPC surgical procedures

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In a normal heart, the left ventricle pumps oxygenated blood to the body and the right ventricle pumps deoxygenated blood to the lungs. But about two out of every 1,000 babies are born with only a single ventricle. The oxygenated and the deoxygenated blood blend in the ventricle, and the mixture is pumped throughout the body, causing symptoms that include shortness of breath, low energy and a blue color in the extremities. This condition places such a heavy burden on the single ventricle that, without surgical correction, most children born with this disorder will die from heart failure within one year.

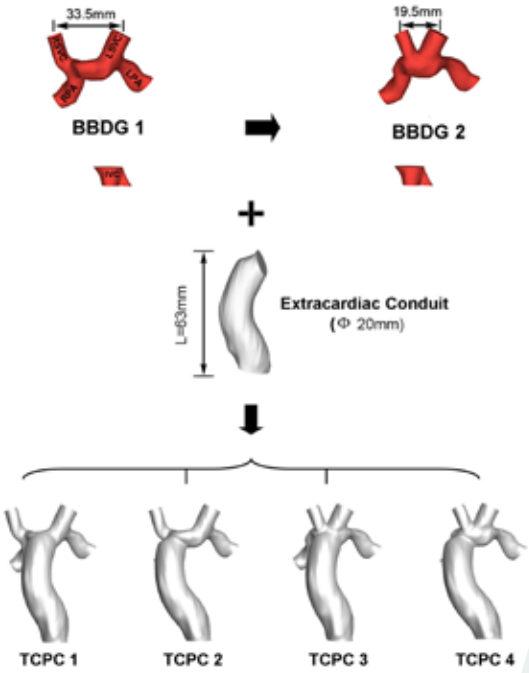
Correcting single ventricle defects normally involves reconfiguring the circulatory system to ease the burden on the ventricle. The ventricle still pumps blood to the body, but the blood returning from the body travels directly to the lungs via blood vessel connections for reoxygenation, before reaching the malformed heart's single pumping chamber.

The surgery is performed in a staged approach. The first stage, required in most but not all babies born with this defect, balances the blood flow so that an equal amount of blood travels to the body and lungs (Norwood procedure). In the second stage, called a bidirectional Glenn procedure, the vessels that drain blood from the head and upper body — the left and right superior vena cava (LSVC and RSVC) — are disconnected from the heart and sutured directly to the pulmonary artery (PA), which provides blood to the lungs. This removes some of the work done by the single ventricle. In the third stage, called the total cavopulmonary connection (TCPC) or Fontan procedure, the vessel returning blood from the lower half of the body — the inferior vena cava (IVC) — is disconnected from the heart and connected directly to the PA.

Clinical studies have found a wide variation in the long-term survival rate and post-operative quality of life of patients receiving these procedures. One reason for this disparity is that surgeons have the flexibility to connect the LSVC, RSVC and IVC to different points on the PAs. Which connection point will work best for a particular patient depends on the patient's heart structure and other variables that affect flow patterns in the veins. These flow patterns, in turn, have a major impact on the efficiency of the pulmonary system and the burden that is placed on the single ventricle.

TAKING PATIENTS' INDIVIDUAL ANATOMY INTO ACCOUNT

Until recently, surgeons have not had a method to determine the effects of different connection points on the patient's long-term health. Researchers at Shanghai Children's Medical Center use computational fluid dynamics (CFD) to perform virtual operations that take each patient's unique heart and blood vessels into account while evaluating



^ Connection points from the large veins to the pulmonary artery were varied in the four different models developed for this study (front view shown on top and back view on bottom).

different sites to connect vessels to the PA. Researchers can then compare power losses and energy efficiency across the flow domain to determine the configuration that will maximize energy efficiency for that specific patient. To calculate energy efficiency, clinicians divide the total energy leaving the flow domain across the two outlets by the sum of energy entering the system across the three inlets.

In a recent example, researchers performed magnetic resonance imaging (MRI) on a five-year-old boy who had been born with a single ventricle, and had already undergone the Glenn procedure, and whose doctors were planning to perform a TCPC. His MRI images were imported into Materialise Mimics® software for 3-D reconstruction of his vascular anatomy, which was used to perform virtual operations based on these configurations. First, a second Glenn procedure was performed virtually by moving the connection sites of the LSVC and RSVC vessels closer to the PA. Then two different virtual TCPC operations were performed on each of these two models with different connection points for the IVC. The result was four different geometrical models, each based on different attachment alternatives, for the Glenn and TCPC surgeries.

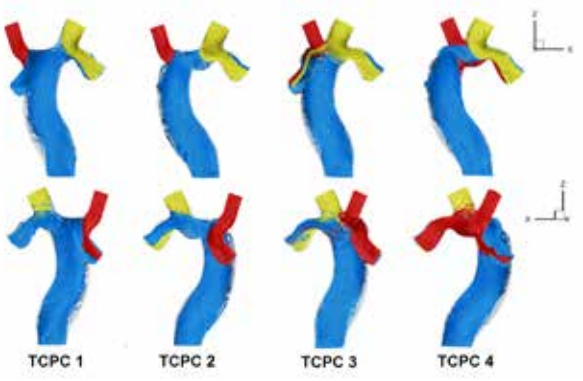
The researchers exported the four models as STL files that they then imported into ANSYS Workbench. A tetrahedral mesh was generated in the central connection area, and five boundary-fitted prism layers were created at the near-wall regions to improve the resolution with which fluid motion could be determined in this critical area.

Mass flow rates measured by the MRI on each vessel entering the PA were imposed as boundary conditions. They set a static pressure boundary condition at the outlet of the left pulmonary artery (LPA) and set five different static pressures at the outlet of the right pulmonary artery (RPA) to vary the relative flow rates between the LPA and the RPA. The flow rates were varied (40:60, 45:55, 50:50, 55:45 and 60:40) because different levels of vascular resistance of the LPA and RPA lead to this degree of disparity in patients. The team calculated the power loss in each simulation based on the static pressure, velocity and flow rate on the cross-sections of each of the five vessels.

DETERMINING THE IDEAL SURGERY

The results showed that the power loss was the lowest and the energy efficiency the highest in the TCPC 2 configuration, while TCPC 4 provided the largest power loss and the lowest energy efficiency. TCPC 1 and TCPC 3 fell in between. The variation in the relative pulmonary flow rates (LPA:RPA) did not affect the relative ranking of the different TCPC surgical options; however, it did significantly affect the relative differences between these options. For example, the value power loss reached its lowest level at an LPA:RPA flow ratio of 50:50 in TCPC 1 and TCPC 3. However, in TCPC 2 and TCPC 4, the flow domain power loss kept decreasing as the RPA flow ratio increased.

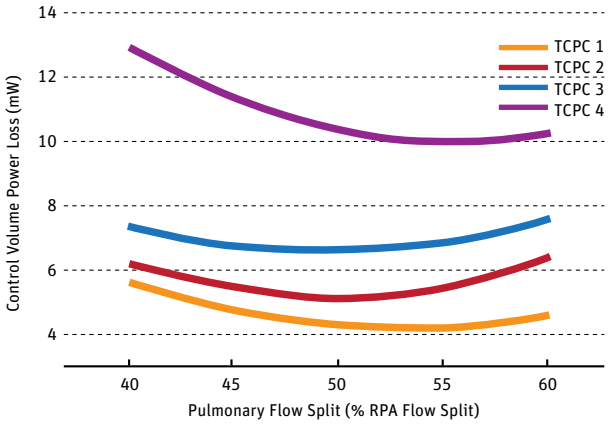
The flow pattern results helped explain why the different designs performed as they did. For example, the results



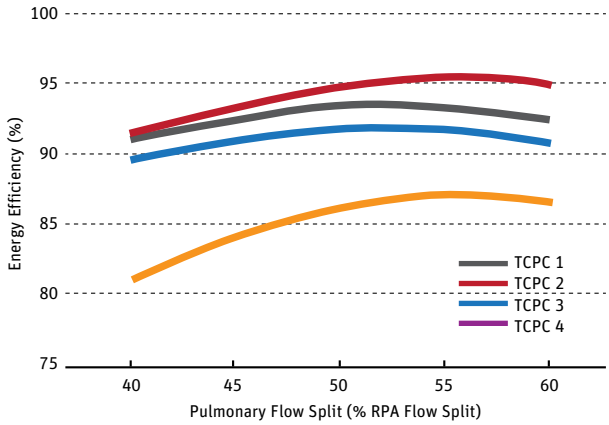
Velocity flow streamlines for the four different models (front view shown on top and back view on bottom) showing direction of flow. Each inlet is represented by a different color.

showed that the particular connections used in TCPC 1 caused interaction between the IVC and LSVC streams, producing turbulence that wasted power. However, when the connection was moved in TCPC 2, there was no turbulence in this area. Researchers concluded that the streams from the LSVC and RSVC should not interact with the IVC in order to avoid turbulence and resulting power loss.

Based on the simulation results, Shanghai Children's Medical Center researchers recommended that the TCPC 2 surgical configuration be performed on the patient. Once researchers optimized the surgical procedure, they printed a



Power loss for the different geometries and flow splits

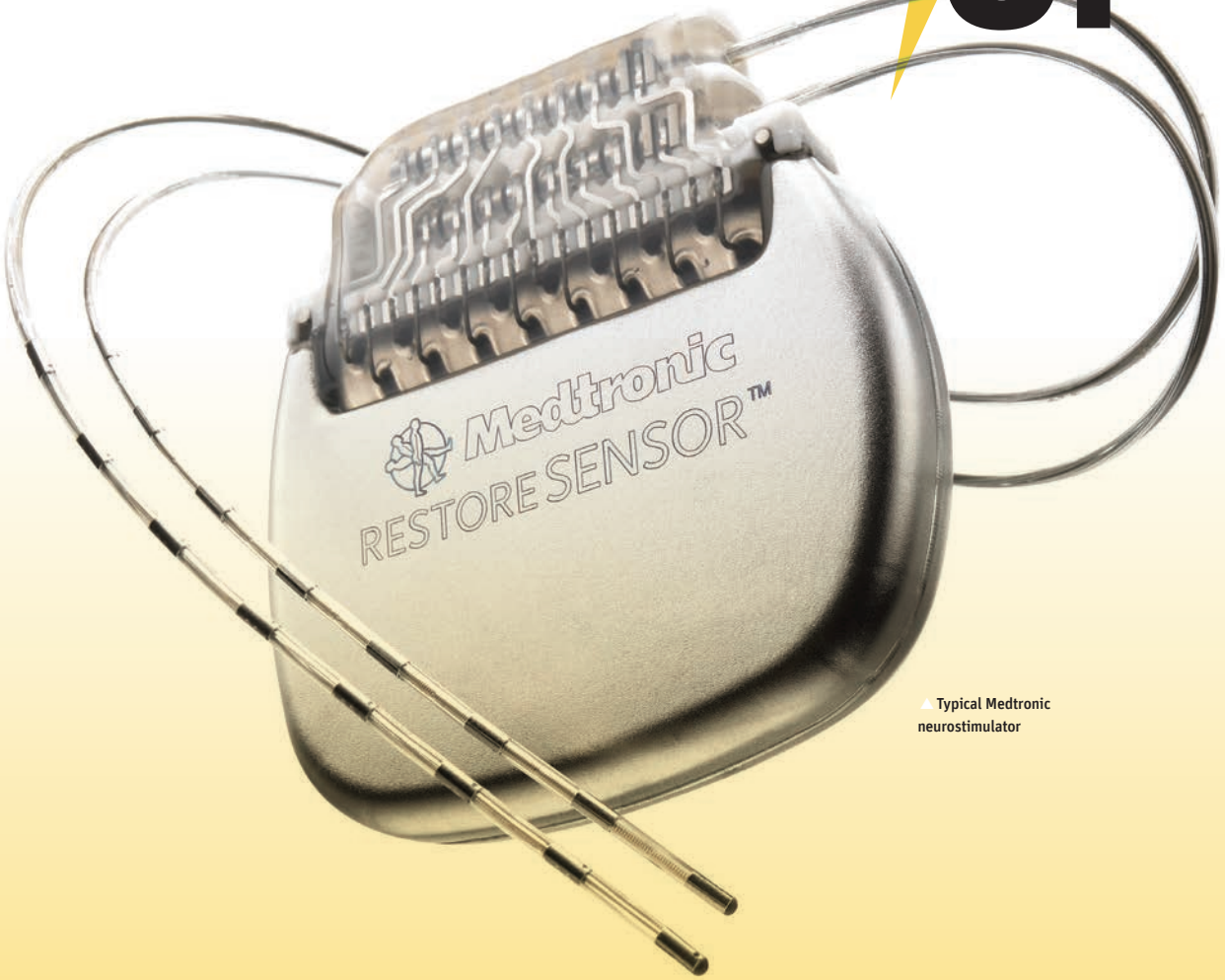


Energy efficiency for the different geometries and flow splits

3-D model of the recommended surgical geometry as a guide for the surgeon. At the patient's 5-year and 10-year follow-ups, he showed no signs of cardiac failure and displayed normal physical capacity. The latest echocardiogram showed no obstructions in the reconfigured areas of the circulatory system and normal cardiac function. Both sides of the branch pulmonary arteries were well developed. While it is not yet practical to perform simulation on every patient, one of the goals of the research team is to reduce the time and effort required for simulation in order to make this possible in the future. Another goal is improving the accuracy of the simulation by using a transient simulation with boundary conditions controlled by a user-defined function (UDF) to model the variations in inlet flow and velocity during the pulmonary cycle.

It is hoped that using accurate simulation in conjunction with skilled surgery will increase the effectiveness of these procedures and provide these young patients with better quality of life.

CHARGED UP



Typical Medtronic neurostimulator

Medtronic ensures the safety of recharging subcutaneous medical devices through simulation.

By Venkat Gaddam, Senior Electrical Engineer, Medtronic, Minneapolis, U.S.A.

Neurostimulators that are placed under the patient's skin deliver mild electrical signals to provide pain relief by blocking pain messages before they reach the brain. Unlike oral medications that circulate through the patient's body, the neurostimulator targets the precise area where pain is experienced. Patients can try a neurostimulator to see if it relieves their pain before committing to long-term therapy; the device can be surgically removed later if the patient decides to pursue a different treatment. The batteries of rechargeable neurostimulators are recharged by

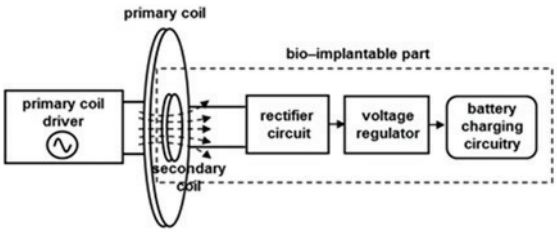
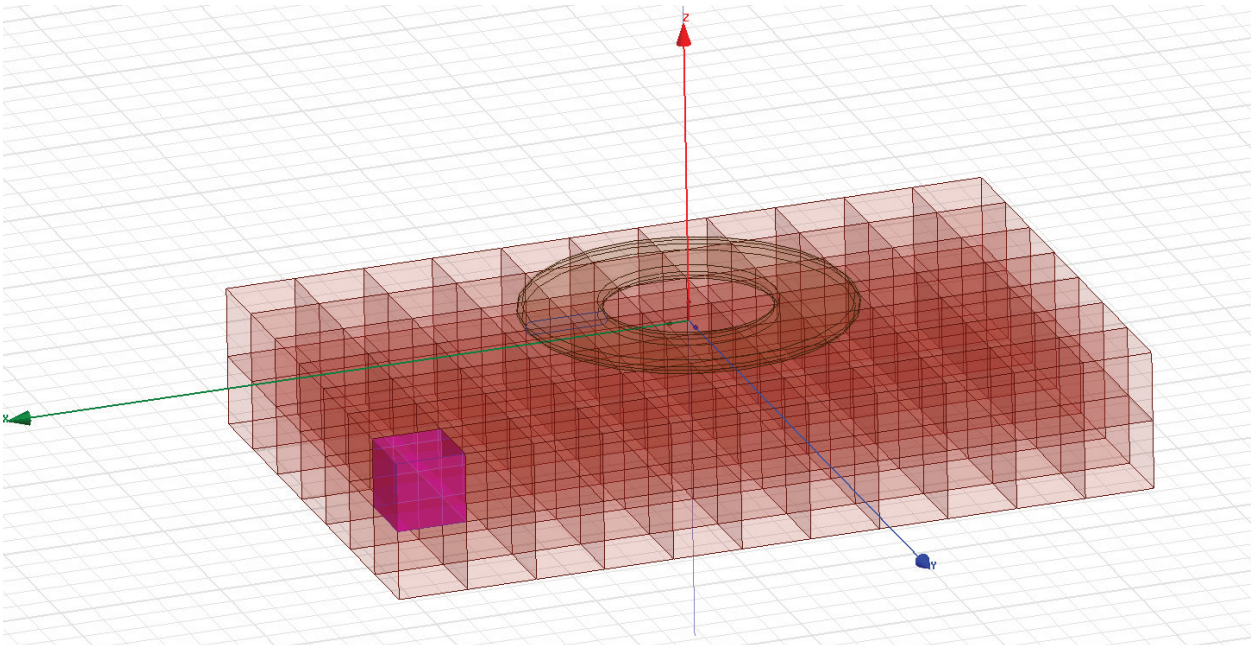


Diagram of recharger and neurostimulator



▲ 10-gram tissue model in ANSYS Maxwell with recharger coil

low-frequency inductive energy transfer using a recharger that is attached to the patient's belt. The recharger emits a non-radiating magnetic field ranging from 3 kHz to 300 kHz that penetrates human tissue and the implanted device's sealed metal enclosure for communication and recharging.

Depending upon the operating configuration, wireless power transfer devices operating at frequencies above 9 kHz are subject to Part 15 and/or Part 18 of Federal Communications Commission (FCC) rules. Medical device manufacturers routinely file Office of Engineering and Technology Laboratory Division Knowledge Database (KDB) inquiries with the FCC to obtain further guidance for wireless power transfer compliance evaluations. As a result of one such inquiry, Medtronic — the world's largest medical technology company — was asked to demonstrate radio frequency (RF) exposure compliance for a wireless power transmitter.

The cost and time required to build a test rig capable of measuring specific absorption rate (SAR) — the rate at which energy is absorbed by the human body when exposed to an RF electromagnetic field — from the recharger is quite high. Medtronic was able to avoid these costs and delays in developing its neurostimulators by using ANSYS Maxwell electromagnetic field simulation software to simulate the operation of the recharger and predict SAR in local body tissues. Simulation showed that SAR generated by the recharger was far below existing FCC limits; the FCC accepted the simulation results for certification of the neurostimulator recharger.

MEDTRONIC AND ANSYS
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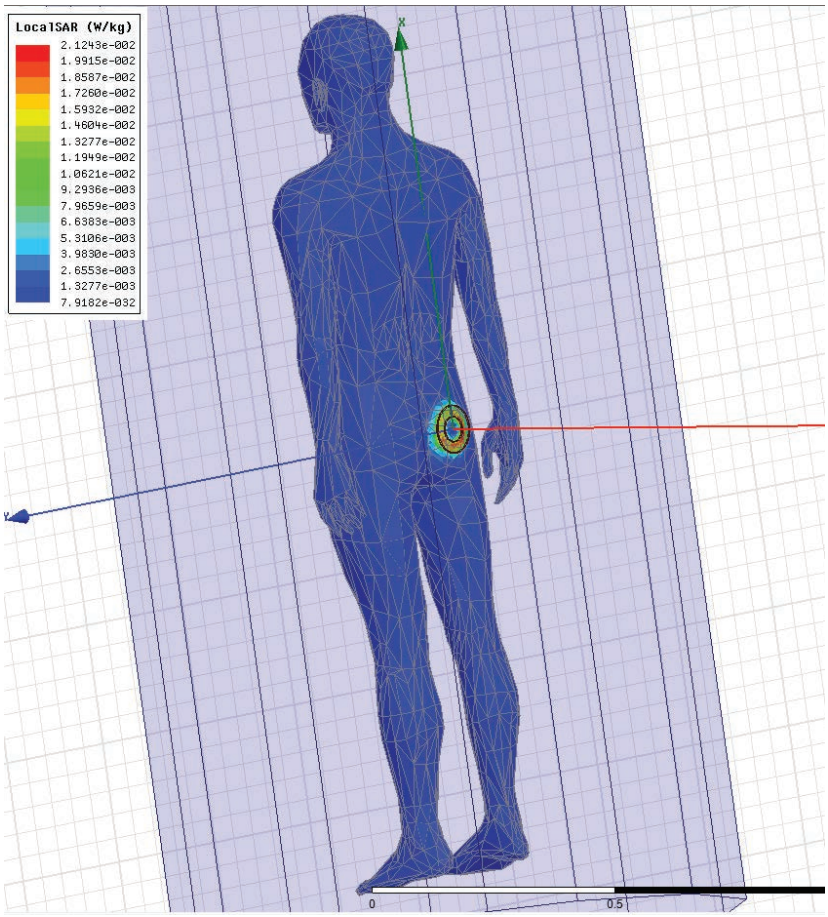
TRANSCUTANEOUS RECHARGE INDUCED SAR

The existing FCC RF exposure requirement prescribed by §2.1093(d)(2) requires a SAR exposure limit of 0.08 W/kg as averaged over the whole body, and a spatial peak SAR not exceeding 1.6 W/kg as averaged over any 1 gram of cube-shaped tissue. SAR is the variable typically used to quantify the effects on tissue exposure to RF signals (defined as the time derivative of the incremental energy absorbed by an incremental mass contained in a volume of given density). Spatial peak SAR is determined by calculating the SAR values in the neighborhood of the electromagnetic source. The domain is then divided into cubes of a given size, and the average SAR value in each cube is evaluated. The peak spatial-averaged SAR is determined by the cube with the highest average SAR value.

Medtronic engineers were confident that their recharging system produced low levels of exposure but needed to measure these levels to obtain approval for a new product. There are a number

Medtronic was able to avoid costs and delays in developing its neurostimulators by using ANSYS Maxwell to simulate the operation of the recharger and predict SAR in local body tissues.

Engineers were confident that the recharging system produced levels of exposure far below the limit specified in the regulation but needed to measure these levels to submit a new product.



▲ Coil positioning in ANSYS human body model

of FCC-certified testing organizations that perform SAR measurements on a contract basis, but Medtronic engineers soon learned that these organizations were not set up to run tests at frequencies as low as those used by the neurostimulator recharger.

ESTIMATING SAR WITH ANSYS MAXWELL

Medtronic engineers used ANSYS Maxwell to estimate the SAR values generated by the recharger coil, with the expectation that the FCC would accept accurate, validated simulation results in lieu of physical testing. They selected Maxwell because the tool makes it easy to set up the model and mesh, and solution times are relatively short. Medtronic engineers employed human tissue models that are available with Maxwell, including muscle sectioned into 10-gram cubes and muscle sectioned into 1-gram cubes. They also used a section tissue model containing skin, fat, fascia and muscle layers. The engineers specified the strength and geometry of the magnetic field generated by the charger. Maxwell adaptively

Model Type	Mass for averaging (g)	Peak spatial averaged SAR (mW/kg)	Peak local SAR (no averaging) (mW/kg)
Muscle	10	9.953	24.877
Muscle	1	15.63	24.965
Muscle (swept cube)	1	15.68	25.09

▲ SAR values based on the simulation results

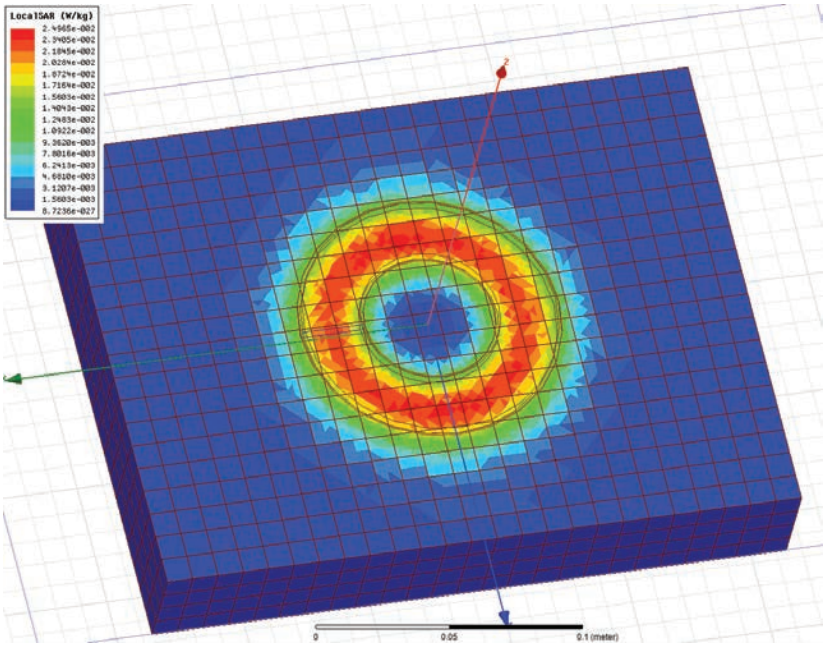
generated an appropriate mesh for solving the problem and used the finite element method to calculate the quasi-static electromagnetic field throughout the solution domain.

Medtronic engineers worked with ANSYS support engineers to create a simple Visual Basic script that calculated SAR values based on the results of the simulation. To calculate the peak spatially averaged SAR, the script calculated the SAR at every element in a 0.25-meter by 0.19-meter by 0.04-meter tissue section. Each 10-gram cube had 2.15-centimeter edges. The peak SAR values as predicted by Maxwell simulation were much lower than the current FCC limits.

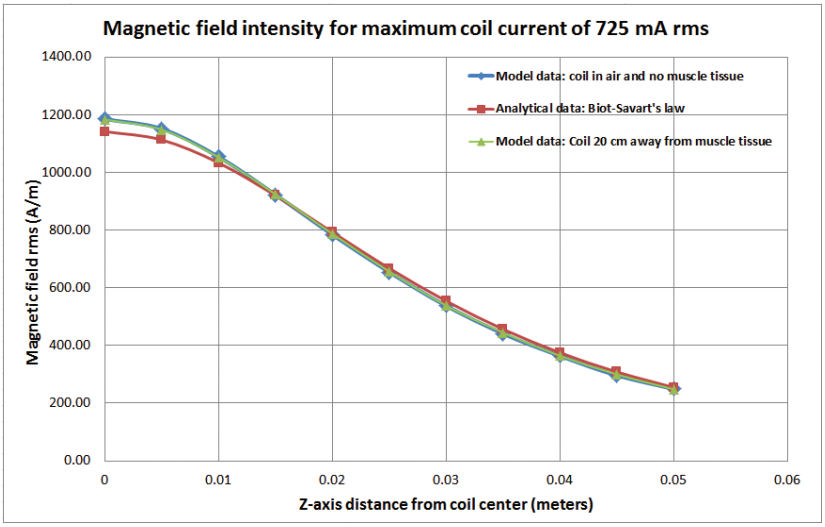
VALIDATING THE SIMULATION

Medtronic engineers used three different methods to validate the accuracy of Maxwell's predictions. First, they created a very simple model and hand-calculated the magnetic field with the Biot–Savart equation — which relates the magnetic field to the magnitude, direction, length and proximity of the electric current — and at the same time performed the calculation with Maxwell software. Second, they set up a simple physical test using a NARDA Safety Test Solutions® electric and magnetic field probe analyzer to measure the magnetic fields generated by the recharger, and then compared these measurements to a Maxwell simulation. Finally, engineers used ANSYS HFSS 3-D full-wave electromagnetic field simulator to simulate peak 10-gram–averaged and peak 1-gram–averaged SAR values. The Maxwell simulations generated results within a few percent of those produced by each of the validation methods.

Medtronic included the Maxwell simulations as part of its new product submission to the FCC. Medtronic engineers were further able to demonstrate that the SAR value would not have been any larger if the tissue geometry in the model had been divided into a different set of cubes. This was addressed by moving a cube around the tissue geometry in discrete step sizes and calculating the average SAR value at each possible position for the cube. Sweeping the cubic volume determined the average SAR value of every possible cube within the tissue volume of interest. The results showed that the maximum possible peak average SAR value for a 1-gram cube is 15.68 mW/kg, less than 1 percent higher than the value in the model that was arbitrarily partitioned.



▲ 1-gram muscle tissue Maxwell model



▲ Validating the model against analytical and physical testing results

Engineers used three different methods to validate the accuracy of Maxwell's predictions.

Medtronic determined that ANSYS Maxwell provides a fast and relatively simple method of measuring 10-gram and 1-gram peak spatially averaged SAR as required to comply with FCC regulations for recharging devices. The FCC accepted the simulation results, saving the company a considerable amount of time and money that would have been required to obtain the same data using physical testing.

HEARING GAIN

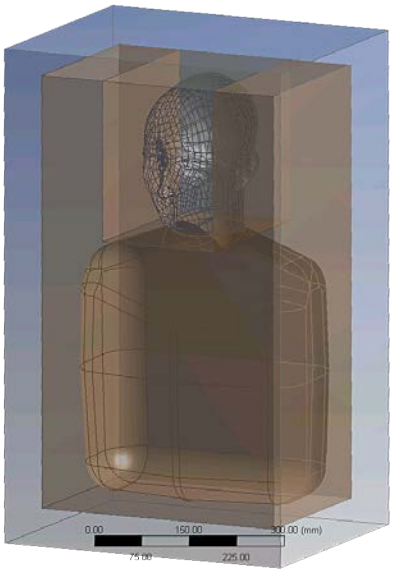
Hearing aid directional filters are normally designed to provide optimal performance on an average head. However, directional performance actually depends on the individual's head and torso shape. Oticon uses multiphysics simulation to advance the personalization of hearing aid performance.

By Martin Larsen, R&D Engineer, Oticon, Copenhagen, Denmark
Stine Harder, Postdoctoral Student, Technical University of Denmark, Copenhagen, Denmark

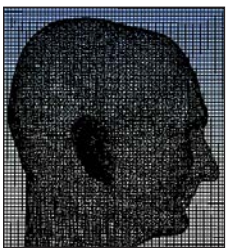
To suppress sounds coming from any direction other than in front of the wearer, hearing aids typically use a software-based digital filter. Because the wearer normally looks in the direction of the person who is speaking, or toward some other sound they want to hear, designers engineer the devices to target sound originating from the front. Designed only once for each model type, engineers develop these digital filters by fitting a physical model of a head and torso with a specially instrumented hearing aid and taking measurements from a surrounding array of speakers. However, research has shown that the directional performance of a hearing aid depends on the specific geometry of each human head and torso, and that people whose head size and shape is different from the norm often obtain less benefit from a directional microphone.

It would be ideal to design a custom digital filter for each hearing aid wearer. However, the physical approach described above is much too expensive and cumbersome to be used in a clinical practice. Oticon has developed a new approach in which an accurate 3-D model of the individual's head and torso is used to perform simulations of this clinical setup to optimize the directional filter for the wearer's head and torso geometry. Simulation makes it possible to quickly determine personalized settings for the hearing aid to reduce background noise and allow the hearing aid wearer to focus on more relevant sounds.

Simulation makes it possible to quickly determine personalized settings for the hearing aid to reduce background noise and allow the hearing aid wearer to focus on more relevant sounds.



▲ Empty space surrounding head and torso used for acoustic simulation



▲ Mesh for the air surrounding the head

MEASURING DIRECTIONAL PERFORMANCE

Typical hearing aids contain a front and a rear microphone; the digital filter subtracts a time-delayed version of the rear microphone's output from the front microphone sound. The directional microphone performance of a hearing aid is measured by the directivity index (DI), which describes the sensitivity to sounds arriving from the front relative to sounds arriving from all directions. The directional filter performance is usually evaluated using head-related transfer functions (HRTFs) measured on a physical model of a head and torso. An HRTF describes how a sound from a specific point will be affected as it travels through the air to the outer end of the auditory canal. Research has shown a large range of benefits provided by directional microphones, and has proven that many people could benefit from a directional filter that is optimized specifically for their head and torso.

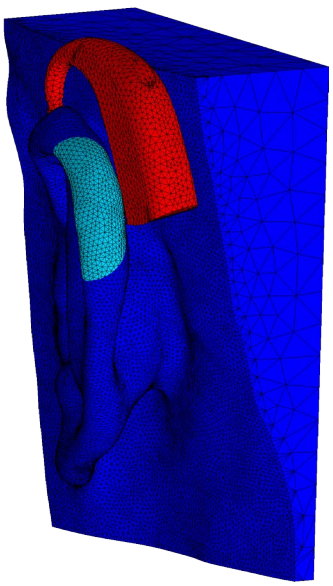
Oticon recently engaged in a joint research project with the Technical University of Denmark to determine whether it was possible to simulate the physical test setup described above to accurately simulate HRTFs based on an individual's head and torso shape. The goal was to develop a personal digital filter optimized for the wearer. The advantage of this approach is that a 3-D model can be obtained in much less time and at a lower cost than would be required to perform physical testing. Oticon selected ANSYS simulation tools because of their multiphysics capabilities, which made it possible to perform the mechanical and acoustical simulations in the same environment with minimal data handling.

The Technical University of Denmark researcher used ANSYS Mechanical to simulate ear deflection when the hearing aid is worn, and to calculate the HRTFs generated in the ear from a speaker array based on a common test setup. The personalized model of the human head and torso used in the simulation was obtained via 3-D scanning of the individual undergoing HRTF testing. This made it possible for the simulation results to be adjusted to the participant's physical measurements.

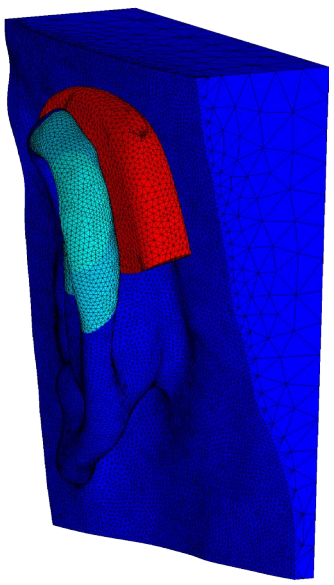
MULTIPHYSICS SIMULATION

The researcher generated a mesh for the ear deflection simulation with 25,580 nodes for the ear and 4,754 nodes for the hearing aid, and then simulated the event by applying a displacement to the hearing aid. The displacement was then released and the hearing aid moved to its final position. The deformed mesh of the ear and hearing aid was substituted for the natural ear geometry to create a full system model of the hearing aid in position. The new simulated head model was then placed inside a box with dimensions of 420 mm by 700 mm by 250 mm. The model was subtracted from the box,

Optimizing the directional filter for the individual user provides an improvement that can make the difference between understanding and not understanding a sentence.



▲ Initial position of ear deflection simulation



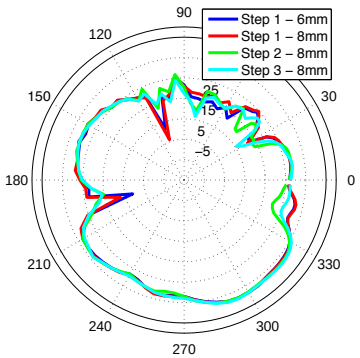
▲ Final position of ear deflection simulation

Researchers concluded that current simulation accuracy levels are sufficient to optimize hearing aid directional performance for individual users.

leaving empty air space surrounding the model.

Sound reaches the ear through pressure changes in the air-filled space. The air surrounding the simulated head was meshed with first-order acoustic elements. To reduce computational times, one mesh was created for frequencies below 7.5 kHz and another for frequencies below 10 kHz. Considerably larger elements can be used in the lower frequency mesh, which greatly reduces computational times. The low-frequency mesh was used for rapid evaluation of alternative cases, while the higher-frequency mesh was used for validation purposes.

Acoustic measurements are performed in a semi-anechoic room with special internal surfaces that eliminate reflections off the walls, ceiling and floor that would otherwise interfere with sound measurements. In the simulation, a similar effect was achieved by adding a 40 mm perfectly matched layer (PML) to the outside of the simulation model. The non-reflective PML absorbs all sound waves traveling outward from the bounded domain, and is also used to calculate sound pressure in the far field outside the box. The key advantage of using a PML is that it requires only a fraction of the computational resources that would otherwise be required to model the far field. Engineers took advantage of the acoustical principle of reciprocity, which states that the speaker and microphone positions can be swapped with each other without affecting HRTFs, to reduce the number of simulations needed. Placing the speakers in the subject's ear in the simulation and positioning several microphones around the subject made it possible to measure the HRTFs for all speakers used in the physical tests in a single simulation run.

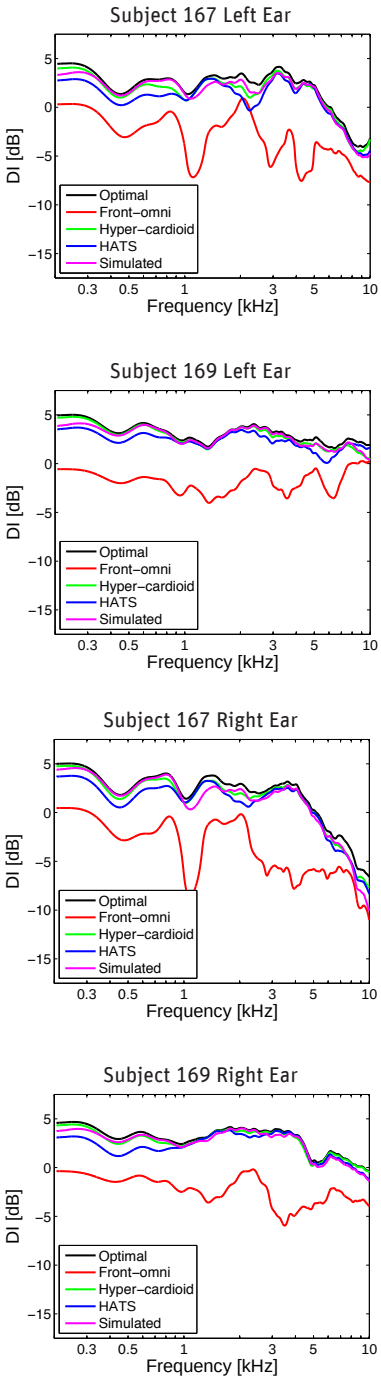


▲ The polar plots show the directionality at a specific frequency. A perfect circle means that sounds coming from all directions are weighted equally. The plots show how the head and torso create a directional pattern, where sounds from some angles are suppressed. Acoustic simulation results are shown for three different cases and two different element sizes. Step 1: Head model only; Step 2: Head and half of torso; Step 3: Head and full torso.

VALIDATION WITH PHYSICAL MEASUREMENTS

The HRTF simulation results were compared with HRTF measurements obtained with an instrumented hearing aid. Engineers concluded that simulations and physical experiments exhibited similar overall trends. Oticon engineers optimized the directional filter based on the simulation results. Additional measurements showed that the resulting directional microphone performs almost as well as a directional microphone optimized using physical testing. Researchers concluded that current simulation accuracy levels are sufficient to optimize hearing aid directional performance for individual users.

Optimizing the directional filter for the individual user provides an improvement in directionality of up to 2 dB to 3 dB, which in many cases can make the difference between understanding and not understanding a sentence. Performing this optimization using physical testing would require the patient to travel to one of only a few suitably equipped facilities in the world for tests that would cost at least $500. The current goal is to gain more insight into individualized hearing directionality using simulation. At some point in the future, it may become possible for a customer to visit a clinic, be scanned and then have a custom directional filter designed through simulation.



▲ Direction filter optimized with simulation (red line) shows 2 dB to 3 dB improvement over standard directional filter (blue line).

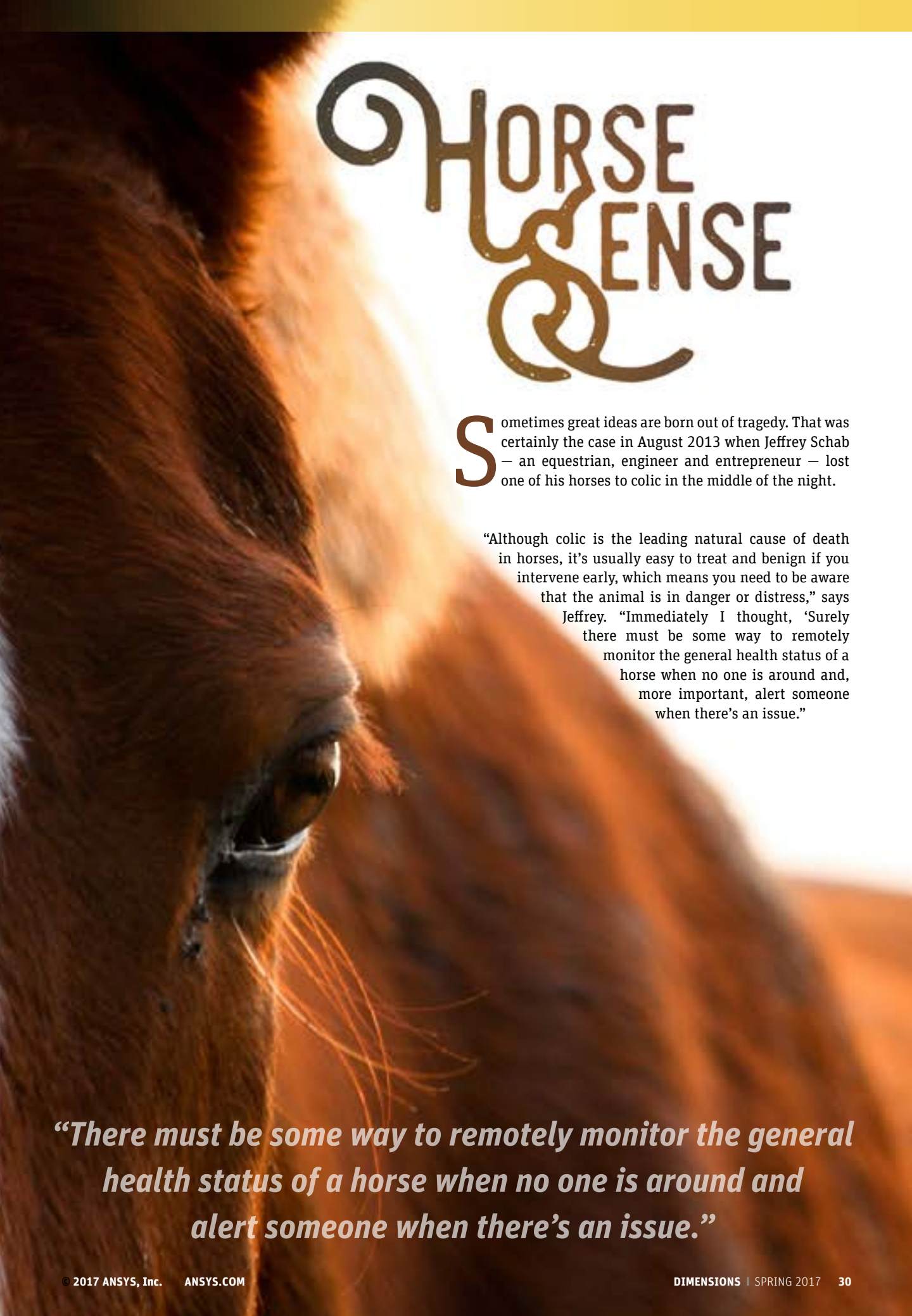
HARMONIC VIBRATIONS AND ACOUSTICS — ARTICLE
ansys.com/acoustics101

Oticon integrates simulation into the product development process

In addition to cutting-edge research, Oticon has also tightly integrated ANSYS simulation tools throughout the product development process. Confronted with increasing product complexity and the need to stay competitive in a fast-paced and highly regulated market, the company made the strategic choice to democratize the use of simulation across its organization. Oticon is taking advantage of ANSYS ACT, a development tool that leverages a common language to configure and customize the simulation user interface, simulation workflow and solver extensions. The company has made advanced simulation technology accessible to designers not traditionally exposed to simulation by integrating the company's product development best practices directly into the ANSYS user interface.

Oticon analysts have developed simulation models of critical hearing aid components, such as the receiver suspensions and microphone inlets, that are used extensively for validating designs prior to the final prototyping/testing phase. As a result, up to 75 percent of the work traditionally done by experts is now delegated to designers, freeing time for engineers to quickly create more innovative and reliable products. The successful deployment of simulation to a broader user base was a significant step forward for Oticon, extending its capabilities to innovate while delivering the highest quality products in the shortest possible time. The company has gained insight into the design of its products, eliminated trial-and-error design loops, and reduced troubleshooting in the later stages of the product development process.

Up to 75 percent of the work traditionally done by experts is now delegated to designers, freeing time for engineers to quickly create more innovative and reliable products.



Horse Sense

Sometimes great ideas are born out of tragedy. That was certainly the case in August 2013 when Jeffrey Schab — an equestrian, engineer and entrepreneur — lost one of his horses to colic in the middle of the night.

"Although colic is the leading natural cause of death in horses, it's usually easy to treat and benign if you intervene early, which means you need to be aware that the animal is in danger or distress," says Jeffrey. "Immediately I thought, 'Surely there must be some way to remotely monitor the general health status of a horse when no one is around and, more important, alert someone when there's an issue."

"There must be some way to remotely monitor the general health status of a horse when no one is around and alert someone when there's an issue."

As a world-class equestrian, biomedical engineer and co-founder of a successful network of healthcare marketing companies, Jeffrey knew he had both the passion and the expertise to invent and commercialize a remote monitoring solution for horses. So he formed a new company, Protequus LLC — which combines the word "protection" with *equus,* the Latin word for horse — to answer this market need.

However, Jeffrey faced one major challenge. He needed someone to design and fabricate the necessary software and hardware to make his vision a reality. Fortunately, he didn't have to look far. His brother, Michael Schab, is also an established engineer and entrepreneur — as well as owner and co-founder of a technology consulting firm, NRGXP LLC, which specializes in Internet of Things (IoT) solutions.

Although Protequus is headquartered in Austin, Texas, and NRGXP is based in Rochester, New York, the brothers' close relationship has bridged the physical distance and resulted in a successful business partnership. "My initial vision and product idea came solely from an emotional place, and the fact that I had witnessed a market need firsthand," notes Jeffrey. "Michael brought the expertise, bench strength and conviction needed to engineer the best possible solution."

The resulting IoT-enabled product, NIGHTWATCH®, is the world's first smart halter — or optional safety collar — that can save a horse's life through early intervention in the event of danger or distress. By continuously monitoring real-time data on a horse's heart rate and respiratory rate, as well as its behaviors, motions and posture, NIGHTWATCH identifies abnormal patterns. The device then automatically alerts a caretaker via text, phone or email.

"NIGHTWATCH is like a home security system for your horse's health. The system is designed to automatically alert you to a problem, any time of the day or night, so you don't have to worry or stay up monitoring an app or video camera yourself," says Jeffrey. "Since horses spend about half their time unsupervised, whether in a pasture or a barn, NIGHTWATCH is there when you can't be."

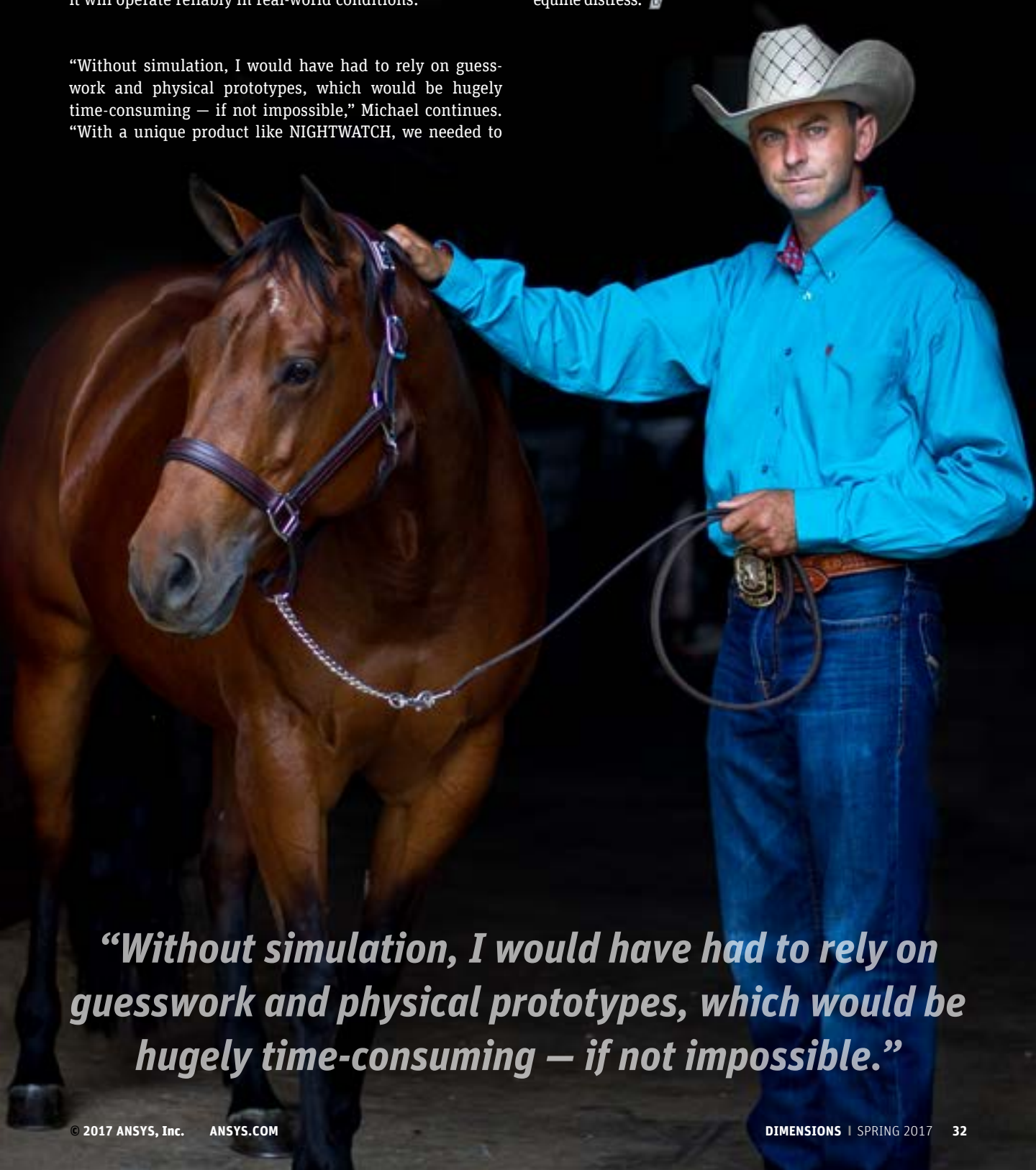
Having earned a degree in electrical and computer engineering, Michael understands the power and value of engineering simulation, especially when combined with design of experiments (DOE) methodologies. Throughout the NIGHTWATCH development program, ANSYS HFSS was utilized exclusively to understand and identify the driving factors affecting the reliable performance of the halter's onboard ultra-wideband impulse radar (UWB-IR) antenna.

Simulation enabled the Protequus team to study a wide range of factors that could impact antenna performance, while high-performance computing allowed numerically large computations to be run in parallel extremely quickly.

"The halter has a novel antenna system that uses UWB-IR to measure biometrics, which are often the first sign of pain and distress in these animals," Michael explains. "ANSYS HFSS has served as a kind of 'tuning fork' to help perfect the signaling capabilities of NIGHTWATCH and ensure that it will operate reliably in real-world conditions."

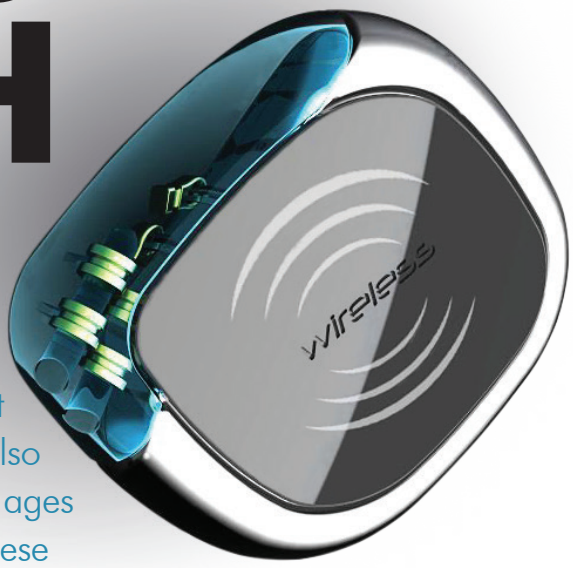
"Without simulation, I would have had to rely on guesswork and physical prototypes, which would be hugely time-consuming — if not impossible," Michael continues. "With a unique product like NIGHTWATCH, we needed to have complete confidence in signal integrity, while moving quickly to make this lifesaving device available to as many horses as possible."

"Each day, more than 100 horses in the United States alone will die of colic, and that's what keeps us up at night," states Jeffrey. "We're literally on the cusp of not only saving horses' lives, but also revolutionizing how insurance companies assess risk, how veterinarians practice telemedicine, and how researchers use real-world data to study and prevent colic and other forms of equine distress."



"Without simulation, I would have had to rely on guesswork and physical prototypes, which would be hugely time-consuming — if not impossible."

WIRED INTO HEALTH



The Internet of Things for healthcare requires antennas in implantable medical devices to operate safely within the human body, over longer distances than before and at more than one frequency. These devices must also be reliable in the wide range of body types and ages that comprise the human population. To take these many factors into account, Cambridge Consultants uses ANSYS software to model body variations and simulate antenna performance.

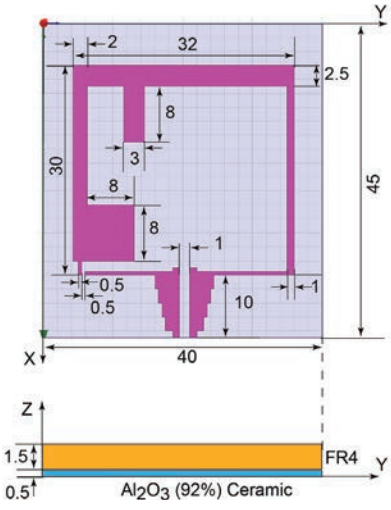
By **Arun Venkatasubramanian**, Associate Director,
Cambridge Consultants, Boston, USA

Wireless technology adds a new dimension to medical implants, allowing remote monitoring and treatment optimization. However, to design a successful wireless implant, designers must address many different use cases and regulatory requirements, each of which poses its own unique challenges.

Typically, a smart medical implant must communicate wirelessly with an external handheld device in at least three different environments:

- The operating room, where the implant is programmed before being inserted into the patient.
- The medical office, where a clinician needs to carry out follow-up monitoring by wirelessly communicating with the implant using the external programmer device.
- The home, often using a bedside wireless box that talks to the implant to relay diagnostic information, as well as any alarm conditions, immediately to the doctor/caregiver.

Body tissue affects wireless radio performance by causing reflections and absorbing some of the wireless signal, as well as affecting the operating frequency and bandwidth of the antenna. The patient's body type has a significant effect on the communication distance between the implant and the external device. In recent years, Bluetooth® Smart communication to smartphones has emerged as a popular choice for connectivity. Implantable device manufacturers will no doubt want to explore this option. Bluetooth operates at much higher frequencies than current wireless technologies used in medical devices,

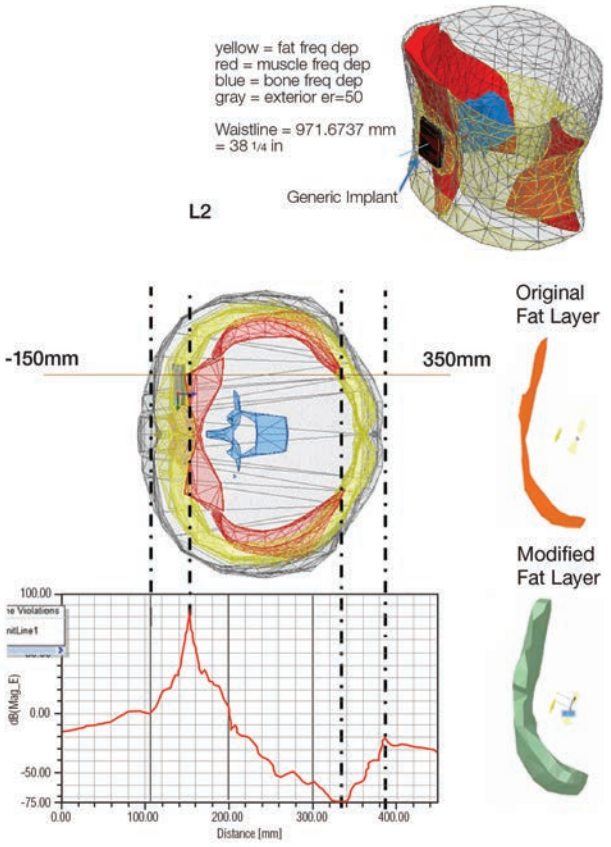


Model of the antenna for an implantable device

> "Engineering simulation tools from ANSYS enable Cambridge Consultants to design innovative medical devices faster."

which means that the body absorbs an even higher proportion of this energy, making the range problem even more difficult. The antenna may need tuning from time to time to accommodate patient physiology changes — for example, if the patient gains or loses weight. Finally, regulatory bodies place stringent restrictions on the radiated power, the specific absorption rate, and the rate and amount of data that can be transmitted over the air.

Cambridge Consultants, a world-class supplier of innovative product development engineering and technology consulting, uses ANSYS simulation tools to overcome these challenges. Simulation allows engineers to optimize the design of implanted device antennas to increase their range, enable them to operate at desired frequencies, and validate their performance in advance for a wide range of body types.



^ The ANSYS HFSS human body model was modified with ANSYS SpaceClaim Direct Modeler to represent different body types. ANSYS SpaceClaim can easily change the geometry of an object.

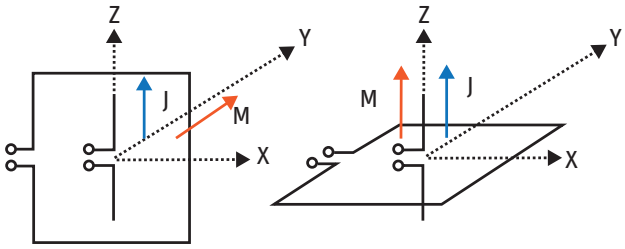
DESIGNING AN IMPLANTABLE ANTENNA

Cambridge Consultants' engineers recently designed a small antenna that works on both the 402 to 405 MHz (medical implant communications service [MICS]) and 2.4 to 2.5 GHz (industrial, scientific and medical [ISM]) bands, and enables wireless communication at a range of 2 meters or more so that it can be used outside the sterile zone in the operating room. The capacitive nature of human tissue, along with the large capacitive reactance of traditional electric dipole antennas, produces a residual negative reactance that must be compensated with a lumped inductive load to match the microchip impedance. So engineers used a relatively new antenna design approach — a compound field antenna that employs both magnetic loop radiators and co-located electric field radiators. This approach provides an intrinsic inductive reactance that enables engineers to match impedance to the implanted electronics much more easily, and better supports miniaturization and biocompatibility.

Fat, muscle, various types of bone, skin and blood all have different dielectric properties. The dielectric properties of the surrounding tissue strongly affect the behavior of the antenna, for example, lowering the resonant frequency compared with the free-space performance of an antenna with the same dimensions. But the effect of the body on the antenna differs depending on the location of the antenna in the body and on the patient's body type. Nearly all engineers who design antennas for implantable devices perform electromagnetic simulation using a human body model with elements designed to match the relative permittivity and conductivity of various body materials such as skin, fat, compact bone, spongy bone, muscle and blood. The problem with many of these models is that they are difficult to change to match different body types. So engineers usually optimize the antenna for one average body type, which often leads to antenna performance issues when the device is implanted into a patient with an atypical body type.

Internet of Things: Wearables and Medical Devices
ansys.com/wearables

> "Cambridge Consultants' engineers use ANSYS SpaceClaim Direct Modeler software to rapidly modify the ANSYS HFSS human body model to represent changes in body morphology."



Cambridge Consultants developed a compound field antenna that uses both magnetic loop radiators and co-located electric field radiators.

ANTENNA PERFORMANCE AND BODY WEIGHT CHANGE

Cambridge Consultants designs its antennas by simulating performance using ANSYS HFSS electromagnetic software with the HFSS human body model to represent the antenna's use environment. Recognizing the critical importance of developing an antenna design that is robust to changing body morphology (weight), Cambridge Consultants' engineers use ANSYS SpaceClaim Direct Modeler software to rapidly modify the HFSS human body model to represent changes in body morphology.

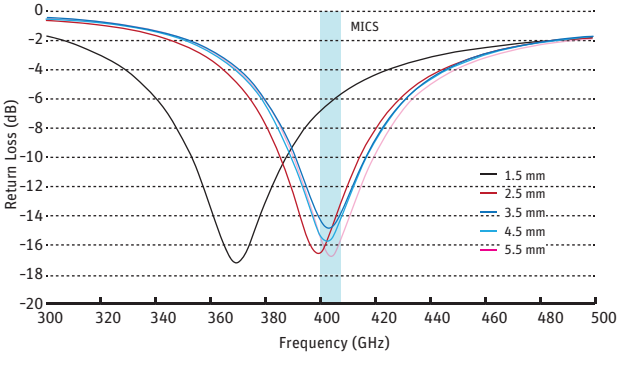
SpaceClaim enables users to create, edit and repair geometry without worrying about underlying technology, thereby speeding up time to analysis. Users can pull, move, fill and combine features of a model to, for example, create rounds, move a feature to another face or change the size of a face. If they prefer, users can enter explicit body dimensions.

This allows Cambridge Consultants to alter fat layer thickness and surrounding skin and muscle layer contours to scale a single body model. This capability is currently not available in other software packages in which a family of body types is provided rather than a single scalable body model.

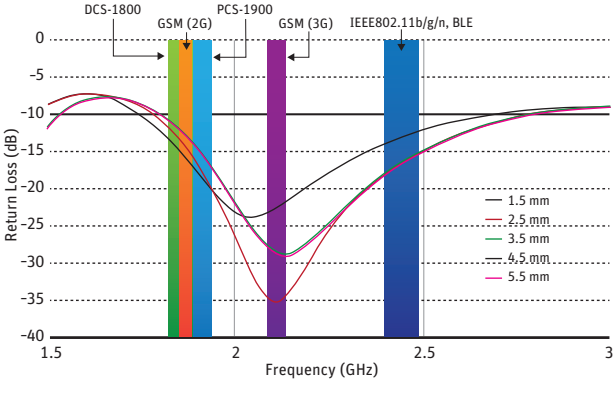
OPERATING IN TWO FREQUENCY BANDS

Nearly all modern wireless implants operate in the MICS band, but recently manufacturers are interested in developing devices that can operate in the ISM band. Using the ISM band can enable devices to communicate with smartphones, eliminating the need for a custom external communications component, and making it possible to take advantage of the powerful capabilities of smartphone technology. Cambridge Consultants engineers designed a new antenna from the ground up to work with both bands.

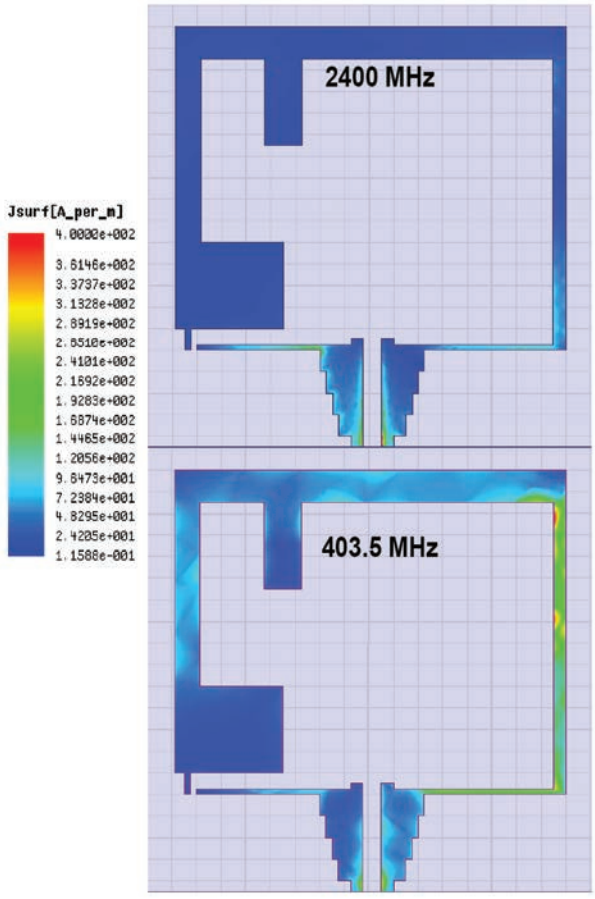
The dual band compound antenna topology was simulated on a 1.5 mm FR4 (glass-reinforced epoxy laminate printed circuit board) substrate with a 0.5 mm Al_2O_3 (aluminum oxide) substrate backing. The fat thickness in the HFSS human body model was varied between 1.5 mm and 5.5 mm in 0.5 mm steps. The antenna return loss was



Frequency response of antenna in MICS band for different amounts of body fat



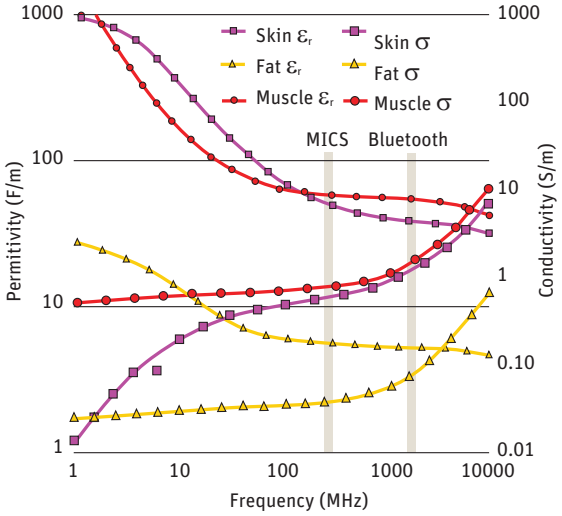
Frequency response of antenna in ISM band for different amounts of body fat



Surface current density for 2.4 GHz and 403.5 MHz, two of the bands in which the antenna must operate

optimized for both frequency bands. The surface current density for the antenna structure was plotted for excitations at the two center design frequencies. The antenna demonstrated a peak gain of –11.42 dBi in the ISM band and –14.62 dBi in the MICS band.

The coupled electric and magnetic dipole antenna provides sufficient gain, radiation efficiency and broadband response in both the 402 to 405 MHz and 2.4 to 2.5 GHz bands in a wide range of body types and dimensions to enable the external communications component to operate outside the sterilized zone. The single planar structure is easily fabricated on a single 40 mm by 45 mm bilayer substrate (FR4/Al_2O_3). This antenna and others developed using similar simulation methods will help to improve healthcare by enabling the design of a new generation of medical devices that operate at a longer range to collect patient data for many body types.

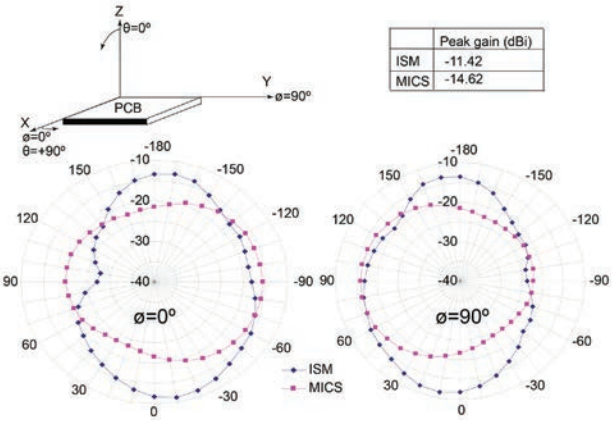


Dielectric properties of fat, muscle and skin

DELIVERING INNOVATION FASTER

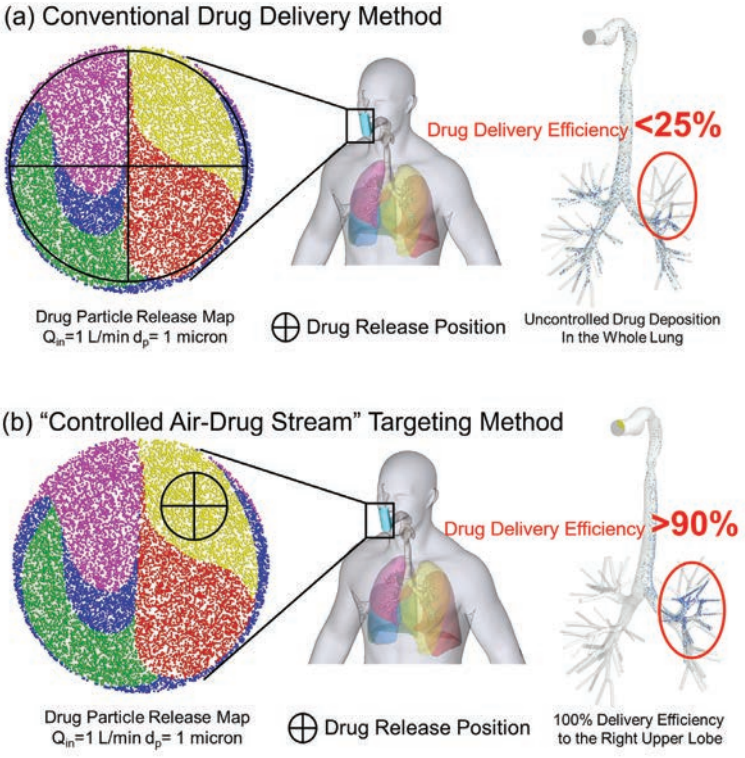
Modern implantable devices are very complex and require engineers to balance performance, safety, reliability, cost and time-to-market constraints. Engineering simulation tools from ANSYS enable Cambridge Consultants to design innovative medical devices faster.

Developing a scalable human body model helps Cambridge Consultant engineers to perform regression analysis on antenna designs right from the beginning of



Antenna radiation patterns showing gain vs. radiation angle

the design process. This halves the number of iterations needed and reduces the design time by 25 percent. The company has been able to increase the radio range for its novel antenna designs by 45 percent compared with traditional PIFA and loop antennas. Field data shows a very close correlation between the simulated and finished product results.



Targeting the upper right lobe of the lung using the human digital twin prototype: (a) conventional drug inhalation therapy (efficiency less than 25 percent) (b) the controlled air-drug stream delivery method (efficiency greater than 90 percent)

TARGETING A TUMOR

By devising a new computational method that tracks the flow of therapeutic drug particles in an aerosol from the lips to the lungs, researchers can deposit a drug on a targeted lung tumor with 90 percent efficiency. This is a major improvement over the 20 percent efficiency of conventional aerosol treatment methods. One key to the success of this new computational method is the development of a human digital twin that can be made patient-specific using the real geometry of the patient's lungs.

By **Yu Feng**, Assistant Professor
School of Chemical Engineering
Oklahoma State University
Stillwater, USA

Personalized medicine is starting to replace the current "one size fits all" approach to medical treatment. One goal is to deliver the right dose of the right drug, at the right time and location, to the specified patient. Researchers at Oklahoma State University used ANSYS computational fluid dynamics (CFD) simulations to devise a computational fluid–particle dynamics (CFPD) method for comprehensive analysis of inhaled drug particulate matter dynamics. CFPD is designed to answer the questions: "How can we determine where a given drug particle in an inhaled aerosol stream ends up in the lung?" and "How can we change the properties of the aerosol to target a specific location in the lung?"

Through an academic partnership with ANSYS, university researchers at the Computational Biofluidics and Biomechanics Laboratory (CBBL) apply ANSYS CFD to study the precision delivery by an inhaler device of cancer-destroying drugs to tumor-only locations in the lungs (healthy tissue is not exposed). CFPD is also capable of subject-specific health risk assessment for in silico occupational exposure studies,

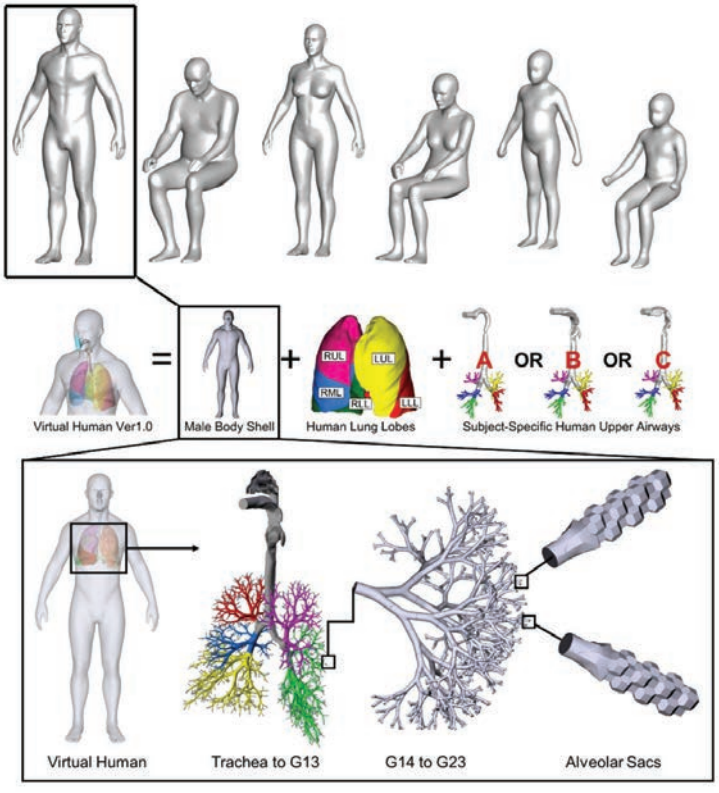
"By increasing the *accuracy* of delivering a chemotherapeutic drug to a lung tumor to *90 percent*, versus 20 percent by conventional aerosol methods, they have *potentially improved* the prognosis for many cancer patients."

including simulations of real-time ventilation, skin absorption and lung deposition.

COMPUTATIONAL FLUID PARTICLE DYNAMICS

In the conventional drug delivery method for inhaled aerosol medications, the drug is distributed evenly throughout the volume of the aerosol. Upon reaching the lungs, the drug reaches its target — for example, a tumor in the upper lobe of the right lung — with 20 percent accuracy. The remaining drug falls on healthy tissue. In addition to drug loss, side effects can occur and healthy lung tissue can be damaged.

To improve on this result, CBBL researchers ran CFPD simulations to provide comprehensive analysis of the flow path of particulate matter in inhaled drugs. The goal was to determine whether 100 percent of the nano-in-micro drug particles can be directed to the localized lung tumor sites by restricting the injection area of the active drug particles to a smaller region during inhalation. By varying drug particle diameters, particle density inhalation flow rate and the initial location of the drug particles in the aerosol stream, the researchers were able to simulate drug particle movement in the aerosol through an adult upper airway configuration from the mouth to the lungs. The final mesh contained approximately 10 million dense, hybrid tetrahedral/pentahedral elements. Using Euler-Euler and Euler-Lagrange models, as well as the dense discrete phase model (DDPM) with discrete element method (DEM), the researchers confirmed that, when the drug is restricted to a smaller region of the aerosol at the point of inhalation, the delivery efficiency can reach values greater than 90 percent. This controlled-air drug stream method is clearly more efficient than the conventional aerosol delivery method.



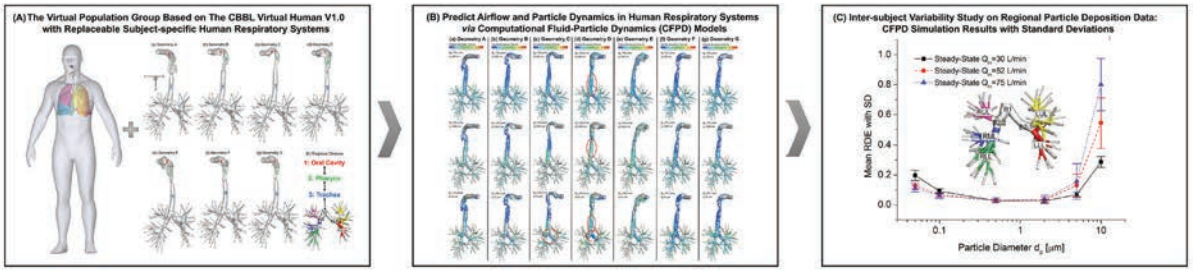
The CBBL virtual human system version 2.0 with a representative human respiratory system for computational fluid-particle dynamics (CFPD) simulations covering the entire conducting and respiratory zones

HUMAN DIGITAL TWINS

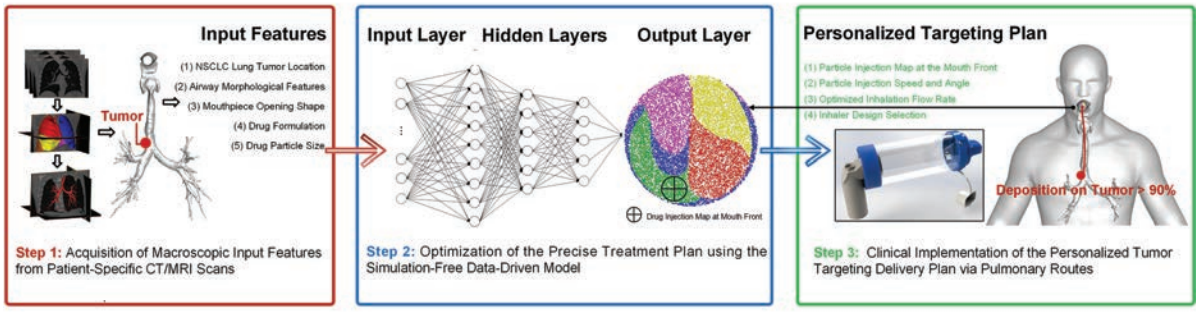
A key to the success of these simulations is the development of a "virtual human system" — an individualized digital twin. Version 2.0 of the human digital twin comprises six models: an adult male, an adult female and a child, each in sitting and standing positions. Each digital twin models a high-resolution human respiratory system covering the entire conducting and respiratory zones, lung lobes and body shell. The CBBL virtual humans are CFPD-ready. The human digital twins can be made patient-specific by performing a CT/MRI scan of the patient and importing the geometry of the lungs into the shell of the digital twin.

THE CBBL VIRTUAL POPULATION GROUP

Taking the simulations a step further, the CBBL researchers have created a large group of human



The CBBL virtual population group version 1.0 and the in silico intersubject variability investigation framework



Flowchart of the personalized, targeted pulmonary drug delivery planner

digital twins for better statistical analysis — the researchers refer to this as "CFPD simulation results with error bars." The virtual population group (VPG) is a set of detailed, high-resolution anatomical models created from CT/MRI data of human subjects. The VPG makes it newly possible to analyze variations in the general population or within specific subpopulation groups, increasing the statistical robustness of numerical studies.

However, as these analyses consider individual anatomical differences, they are computationally expensive. Using a reduced-order model (ROM) to accelerate the computation, future work will include the compilation of precomputed lung aerosol dynamics libraries to train the ROM and simplify the in silico, personalized, pulmonary drug delivery planning process.

THE MULTISCALE CFPD-PBPK/TK MODELING FRAMEWORK

The deposition of drugs in the lung is not the endpoint of the cancer treatment. Toxicologists, pharmacists and clinicians are more interested in the after-deposition dynamics, i.e., the time course of therapeutic or toxic species in plasma and different organs throughout the whole human body. CBBL has combined the CFPD model with a physiology-based pharmacokinetic/toxicokinetic (PBPK/TK) model to predict the systemic translocation of nicotine and acrolein (initial examples) in the human body after the deposition in the respiratory system. With this multiscale CFPD-PBPK/TK modeling framework, it is now possible to run simulations of extremely complex, lung–aerosol dynamics phenomena and whole-body translocation mechanisms at unprecedented levels of detail. This method can be easily modified to fit in other pulmonary research areas, such as drug delivery and occupational exposure risk assessment.

THE FUTURE: PERSONALIZED PULMONARY HEALTHCARE PLANNER APP

CBBL researchers are now working on an app using ANSYS ACT that would automate patient-specific analyses, as shown in the flowchart of personalized lung disease treatment. Clinicians could use the app to design a treatment plan. With a few morphological parameters based on the patient-specific CT/MRI data of the human respiratory system, as well as the coordinates of known lesions, the personalized pulmonary healthcare planner could provide an integrated solution to target localized lung sites based on a pre-computed database connected with a reliable machine-learning model. This fast, noninvasive, reliable, easy-to-use app is also patient-specific, and would prescribe treatment based on a personal digital twin.

"The human *digital twin* can be made patient-specific by *performing* a CT/MRI scan of the patient and importing the geometry of the lungs into the shell of the *digital twin*."

Researchers at the Computational Biofluidics and Biomechanics Laboratory at Oklahoma State University used ANSYS CFD to develop a unique simulation method that will advance the field of personalized medicine. By increasing the accuracy of delivering a chemotherapeutic drug to a lung tumor to 90 percent, versus 20 percent by conventional aerosol methods, they have potentially improved the prognosis for many cancer patients. The advancement of patient-specific, or personalized, medicine will continue to be dependent on the work of innovative researchers and the development of new simulation techniques to eradicate disease.

ACKNOWLEDGMENTS

The use of ANSYS software as part of the ANSYS-OSU academic partnership agreement is gratefully acknowledged. Some of the computing for this project was performed at the OSU High Performance Computing Center at Oklahoma State University (Dr. Dana Brunson, Director, and Dr. Evan Linde, Research Cyberinfrastructure Analyst).

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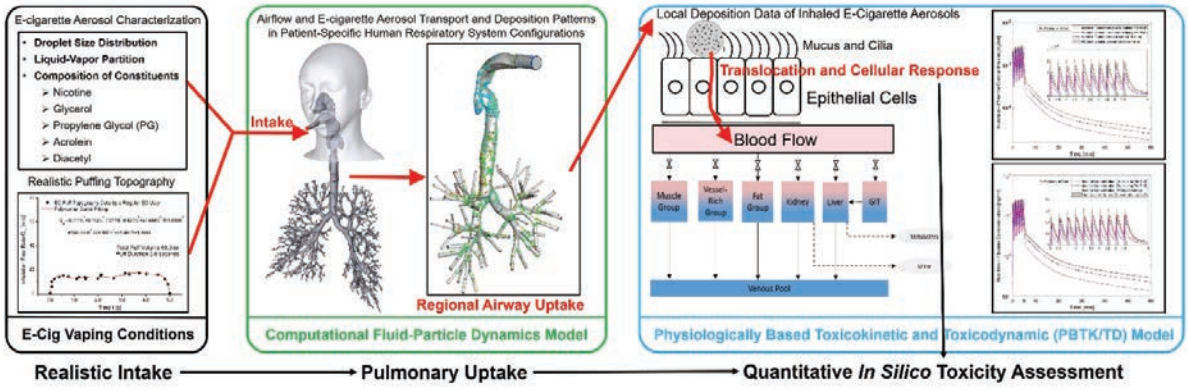


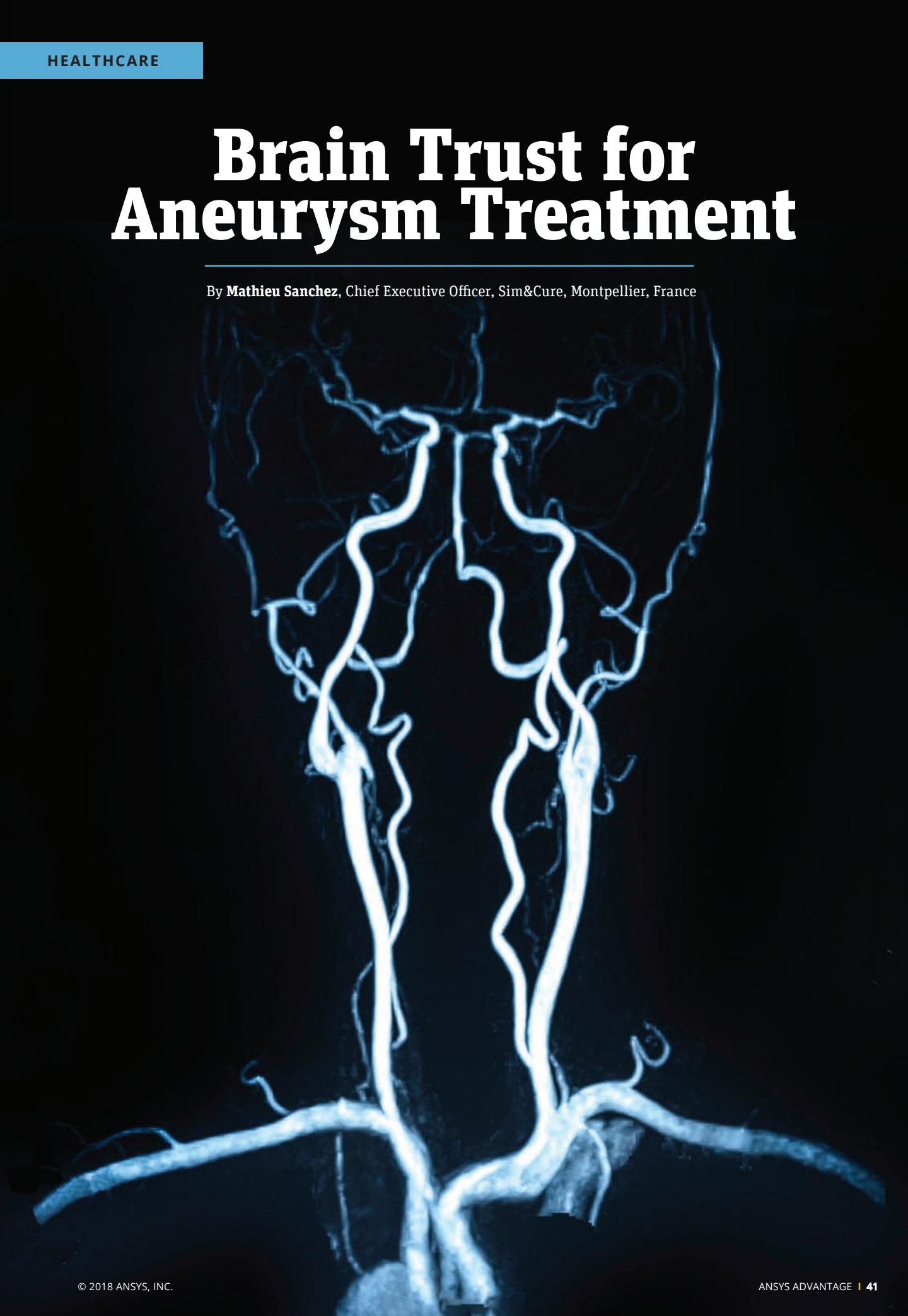
The multiscale computational fluid-particle dynamics (CFPD) plus physiological-based toxicokinetic (PBTK) modeling framework

ABOUT DR. YU FENG

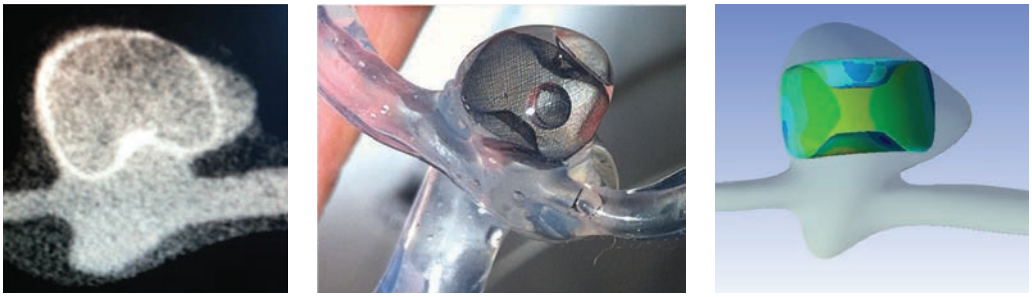
Dr. Yu Feng is an assistant professor in the School of Chemical Engineering at Oklahoma State University, and a center investigator in the Oklahoma Center for Respiratory and Infectious Diseases (OCRID). He founded the Computational Biofluidics and Biomechanics Laboratory (CBBL) at Oklahoma State University, which focuses on developing and applying advanced CFPD models toward multiple applications associated with pulmonary healthcare. He has over 10 years of experience in modeling lung-aerosol dynamics on ANSYS CFX and Fluent platforms, and is published in more than 20 top-ranked journals of fluid dynamics and aerosol science.

Brain Trust for Aneurysm Treatment

By **Mathieu Sanchez**, Chief Executive Officer, Sim&Cure, Montpellier, France



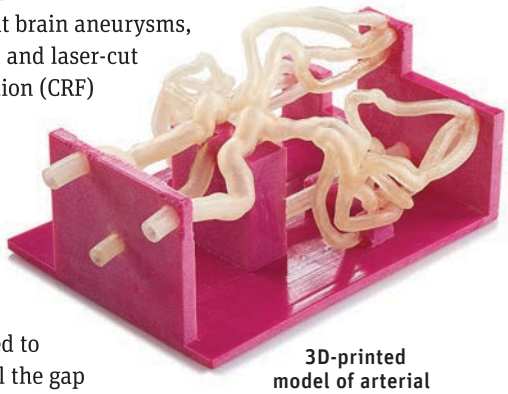
TO PROVIDE EFFECTIVE TREATMENT FOR BRAIN ANEURYSMS, a pioneering healthcare company has developed a digital twin to help physicians place implant devices during surgery. Incorporating ANSYS structural mechanics solutions, the surgeon can simulate the deployment of the implant and determine its optimal sizing and positioning to decrease the risk of failure and reduce operating times.



Medical devices can be tested using three methods — within the body (in vivo, left), outside the body (in vitro, center) and within a computer (in silico, right).

Approximately 2 percent of the population has a brain aneurysm, an enlarged section of an artery caused by a weakening of the arterial wall. Although most show no symptoms or have no health problems, about 1 percent of these aneurysms rupture every year, and about 30 percent of ruptures result in death. Small aneurysms with a low probability of causing damage are often managed simply by tracking their size. One way to treat larger aneurysms is to surgically open the brain, remove the diseased section of artery and clip the remaining ends together. Retrospective analyses have found that surgical options are associated with a higher risk of bad outcomes, longer hospital stays and longer recovery times compared with endovascular procedures. In an endovascular procedure, a catheter is inserted into an artery of the leg near the groin. Aided by medical imaging, the surgeon guides the catheter, which carries the implant, to the aneurysm. Once the device is in position, the surgeon expands the implant and removes the catheter.

Several types of endovascular implants are used to treat brain aneurysms, including flow diverters (FDs), intrasaccular devices (IDs) and laser-cut stents. According to the Cardiovascular Research Foundation (CRF) and the National Center for Biotechnology Information (NCBI), selecting an implant with the right diameter, length and expansion to closely fit the cross section and length of the aneurysm is of paramount importance in achieving the best outcome for the patient. Papers published by the NCBI indicate that up to 65 percent of endoscopic procedures are characterized by various types of geographic miss. For example, if an ID implant designed to deploy inside the aneurysm sac is too small, blood can fill the gap and apply pressure on the aneurysm. Oversizing of the implant could lead to the creation of a clot and an ischemic stroke.



3D-printed model of arterial network in brain

Sim&Cure's solution to this involves the generation of a digital twin. While the patient is under anesthesia, the surgeon runs software that incorporates a model of the structure and behavior of the patient's damaged blood vessel. The software quickly and accurately helps physicians to define the optimal size of the implant and where it should be positioned to give the best results.

In Vivo, In Vitro, In Silico!
ansys.com/in-vivo

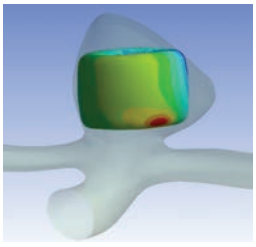
Current Methods for Implant Sizing

Physicians have traditionally used one of two methods to size and position the implant. One approach is to perform measurements on 2D scans captured as part of 3D rotational angiography, or measurements of the 3D scans themselves, just before surgery. This takes at least 10 minutes, so it lengthens the time the patient must be under anesthesia, increasing the risk of complications. These measurements do not account for the deformation and movement of the implant during the procedure, so effective deployment depends upon the skill, experience and intuition of the individual physician.

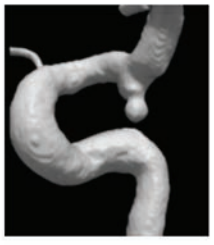
Another approach is to employ 3D rotational angiography to produce a computer-aided design (CAD) of the blood vessels. Then a 3D printer slowly builds a physical model of the blood vessels, which is used to test different device sizes and deployment factors. But the drugs used during the procedure significantly alter the size and shape of the artery, so the model builders must try to estimate these effects. Actual conditions may vary from the physical model that was used to size the implant.

Simulation Software Provides a More Accurate Solution

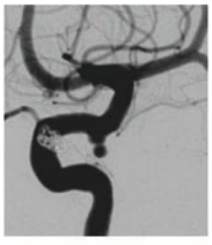
In Sim&Cure's new method, 3D rotational angiography is used to produce a 3D model of the aneurysm and surrounding blood vessels after the patient is prepped for surgery. Sim&Cure's software imports the model of the artery and presents it to the surgeon, who selects points on the artery that define the ideal final position and deployed size of the implant.



"Sim&Cure is the first company to be cleared to market a patient-based digital twin incorporating simulation for aneurysm treatment that includes expansion and deployment of implants based on the patient's unique arterial geometry."



Arterial system with aneurysm viewed with 3D rotational angiography



Arterial system with aneurysm (circular protrusion from artery) viewed with 2D axial angiography

Sim&Cure's IDsize® software simulates intrasaccular device implants incorporating models of a wide range of sizes of the available implant devices so the surgeon can select the specific implant that he or she wishes to simulate. Sim&Cure combines the model of the patient's arteries with a model of the selected device and produces an ANSYS Mechanical input file. ANSYS Mechanical analyzes the deformation of the device and arteries, along with their interaction with each other, and provides a 3D model of the device deployed in the patient's artery that shows the implant and the aneurysm superimposed on each other.

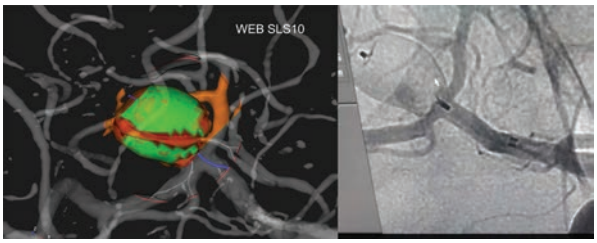
The physician can translate, rotate and zoom the image to fully understand the relationship between the implant and the aneurysm. Color coding can be used to show the exact area where the implant touches the embolism (blockage). A cross-sectional profile indicates any gaps between the implant and the artery. Each simulation takes only 10 to 25 seconds, depending on the device that is selected. The surgeon can easily select and simulate additional devices and sizes for analysis in order to determine which one will provide the best results. In less than five minutes, the surgeon can complete the simulation process, select the optimal device and begin the operation.

Clinical Trial Results are Positive

Normally, about 10 percent of endovascular treatments require follow-up surgery, usually because of issues with the sizing or positioning of the implant. But in more than 500 surgeries conducted in three clinical trials with Sim&Cure's software, follow-up surgery has never been required for a single patient.

In many aneurysm surgeries, a second or even a third implant may be required, usually because the one that was originally selected turns out to be the wrong size when inserted into the patient. This results in a longer surgery and increases the risk of complications to the patient. Doctors who used Sim&Cure software have reduced the number of devices used per surgery from 1.35 in the past to only 1.05 now. Besides reducing the risk to the patient, this saves 3,000 euros (approximately US$3,600) per operation. The trials also show that Sim&Cure reduces the time required to perform surgery by about 30 minutes, which further reduces the risk of complications and provides additional cost savings.

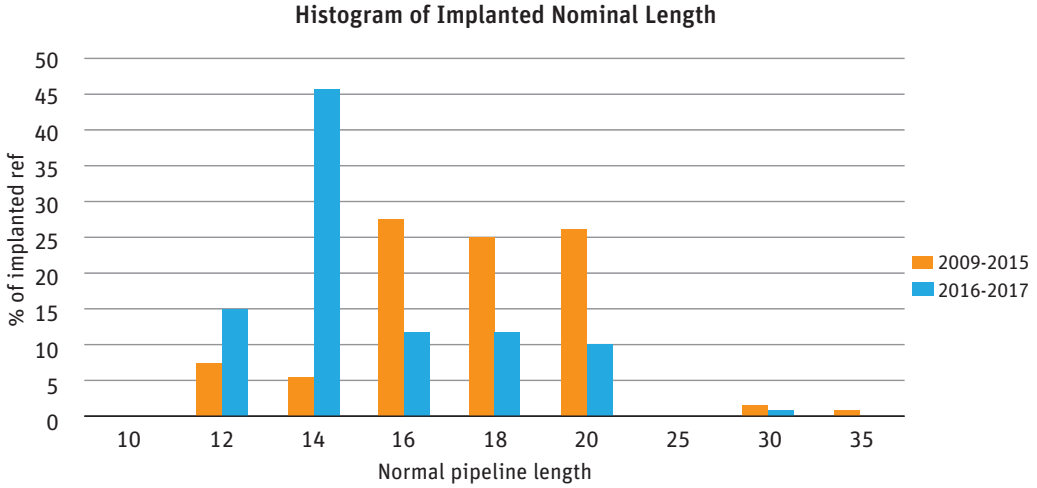
"ANSYS Mechanical analyzes the deformation of the device and arteries, along with their interaction with each other, and provides a 3D model of the device deployed in the patient's artery."



ANSYS Mechanical simulation of implant deployed in aneurysm (left). The surface of aneurysm that abuts the implant is shown in green. Simulation results accurately predicted implant deployment, resulting in successful intervention.

Sim&Cure engineers selected ANSYS Mechanical for this application for several reasons. They wanted to avoid the time and resources that would be required to develop their own finite element analysis software, and they wanted the package with the highest level of accuracy and the strongest reputation in the medical field. ANSYS Mechanical filled both requirements. The ANSYS customer excellence team in Europe worked closely with Sim&Cure engineers to help ensure a fast and seamless integration.

Sim&Cure is the first company to be cleared to market a patient-based digital twin incorporating simulation for aneurysm treatment that includes expansion and deployment of implants based on the patient's unique arterial geometry. Clinical trials conducted in three European hospitals have shown a significant reduction in follow-up surgeries and in surgery duration. Sim&Cure's solution is now being used in 17 different countries with expectations that it will be used in more than 2,000 surgeries by the end of this year.



Histogram shows how use of Sim&Cure software in 2016–2017 made it possible to use smaller implants than were employed previously, reducing risk of complications.

THE RIGHT MIX

CFD simulation saves time and money by validating the ability of a single-use mixer design to scale to 5,000 liters.

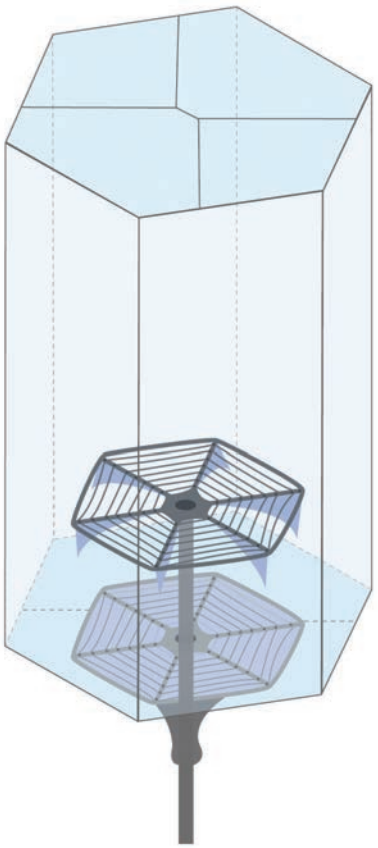
By Rudolf Pavlik, Director, Product Development, ASI, Millersburg, U.S.A.
Szymon Buhajczuk, Principal CFD Engineer (Canada), and
Mark Goodin, CFD Consulting Engineer (U.S.A.), SimuTech Group Inc., Toronto, Canada

▲ imPULSE single-use mixer

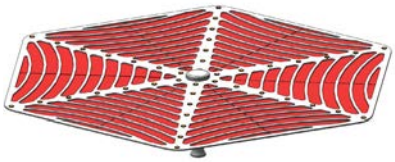
ASI faces the challenge of providing different sizes of its products for various stages of the therapeutic development process.

Biopharmaceutical manufacturers continually need to scale up production as they move from small pilot studies to progressively larger clinical trials, then finally into large-scale production as the drug reaches the market. As a provider of single-use systems and bioprocess equipment utilized in biopharmaceutical manufacturing, ASI regularly faces the challenge of providing different sizes of its products for these various stages of the therapeutic development process. Until recently, biopharmaceutical manufacturing facilities relied solely on hard-piped systems, such as stainless steel bioreactors, tanks and piping. ASI has pioneered development of single-use equipment, designed to be employed once and then disposed of. These systems drastically reduce the need for harsh and lengthy cleaning requirements while improving production speed due to quick changeover between batches.

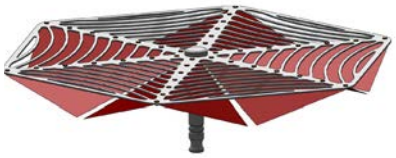
ASI is a leading global provider of advanced single-use systems for the healthcare and life sciences industries. The company's imPULSE single-use mixing series is a unique system that consists of a stainless steel hexagonal mixing vessel and a matching single-use mixing bag. Together, the system can be



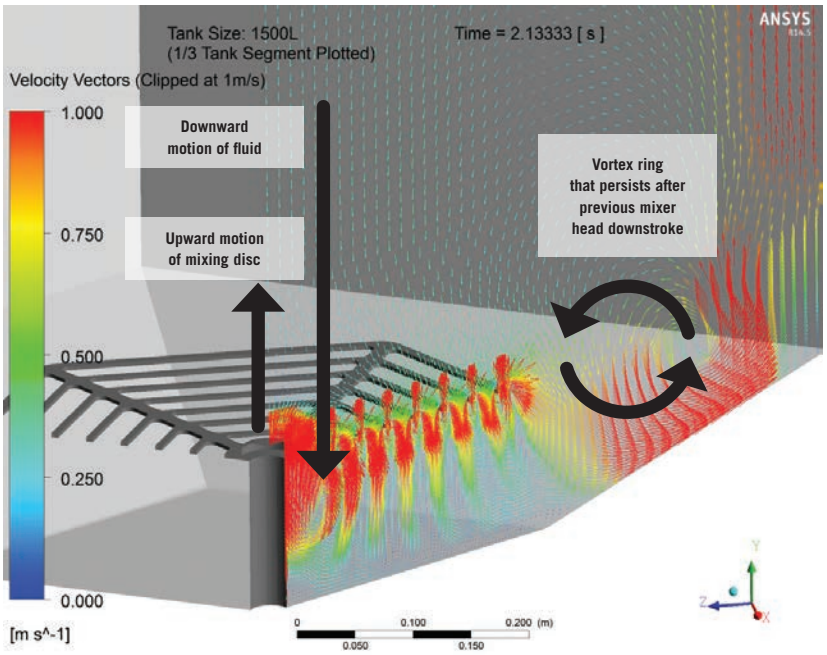
▲ Reusable mixing bag



▲ Flow during mixing downstroke



▲ Flow during mixing upstroke



▲ Velocity vectors show mixing motion.

configured for a variety of end-user mixing applications. The disposable polymer mixing bag is engineered with an integrated mixing disc that consists of multiple slots and film flaps. The flaps open and close as the mixing disc moves up and down within the mixing bag. On the downstroke, the flaps close, and energy is directed to the bottom of the mixing bag and up the sidewalls. On the upstroke, the flaps open, allowing the fluid to flow through the slots, thus producing one-way flow and very effective mixing. Simulation with ANSYS Fluent helped ASI to eliminate the cost and lead time of prototyping, demonstrating that ASI's design could be scaled up to an industry-leading 5,000-liter size while providing the same mixing performance as smaller mixers.

ASI first developed the imPULSE design in a 250-liter (L) size and expanded the portfolio to include sizes from 30 L to 1,500 L. As customers further scaled up their batch sizes, they demanded larger mixers. Although it was not difficult to scale up the mixer, it was a challenge to maintain mixing efficiencies and patterns. The time required to achieve a certain level of homogeneity is critical to the efficiency of biopharmaceutical manufacturing. To sell the larger mixers, ASI needed to prove that mixing time would be consistent in both larger and smaller mixers. The lead time and cost required to build a prototype of the new 5,000-liter mixer was quite high. So ASI investigated the potential for using computational fluid dynamics (CFD) simulation to validate the design of the larger mixer. Besides being faster and less expensive than building and testing a prototype mixer, CFD provides more diagnostic information, such as flow velocities throughout the tank along with shear rate, all of which are useful in diagnosing and improving a mixer design.

Besides being faster and less expensive than building and testing a prototype mixer, CFD provides more diagnostic information.

ASI contracted with consultants from ANSYS channel partner SimuTech Group, a supplier of engineering simulation software, support, training, consulting and testing services. The team used ANSYS Fluent to simulate the motion of the mixer discs. Fluent's dynamic layering method

CUTTING DESIGN COSTS: HOW INDUSTRY LEADERS BENEFIT FROM FAST AND RELIABLE CFD
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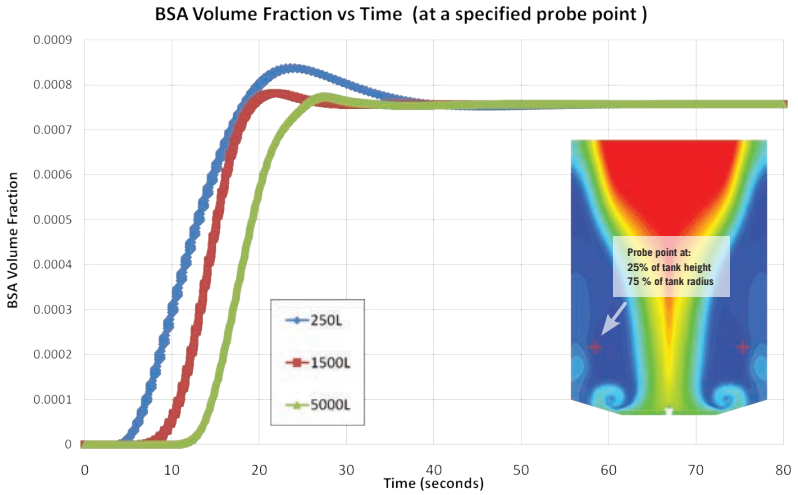


▲ BSA volume fraction versus time for different tank size

250 L

1,500 L

5,000 L

▲ Flow circulation patterns for different tank sizes

CFD simulation saved hundreds of thousands of dollars, providing characterizations that apply to the overall scalability of ASI's products and significantly reducing the need for building and testing prototypes.

adds or removes layers of cells adjacent to a moving boundary based on the height of the layer bordering the moving surface, which enables simulation of devices with complex moving parts. The dynamic layering method allows users to specify an ideal layer height on each moving boundary. The layer of cells neighboring the moving boundary is split or merged with the layer of cells next to it based on the height of cells in the adjacent layer. This unique approach to simulating a moving boundary eliminates accuracy problems, which are caused by cell shape deformation.

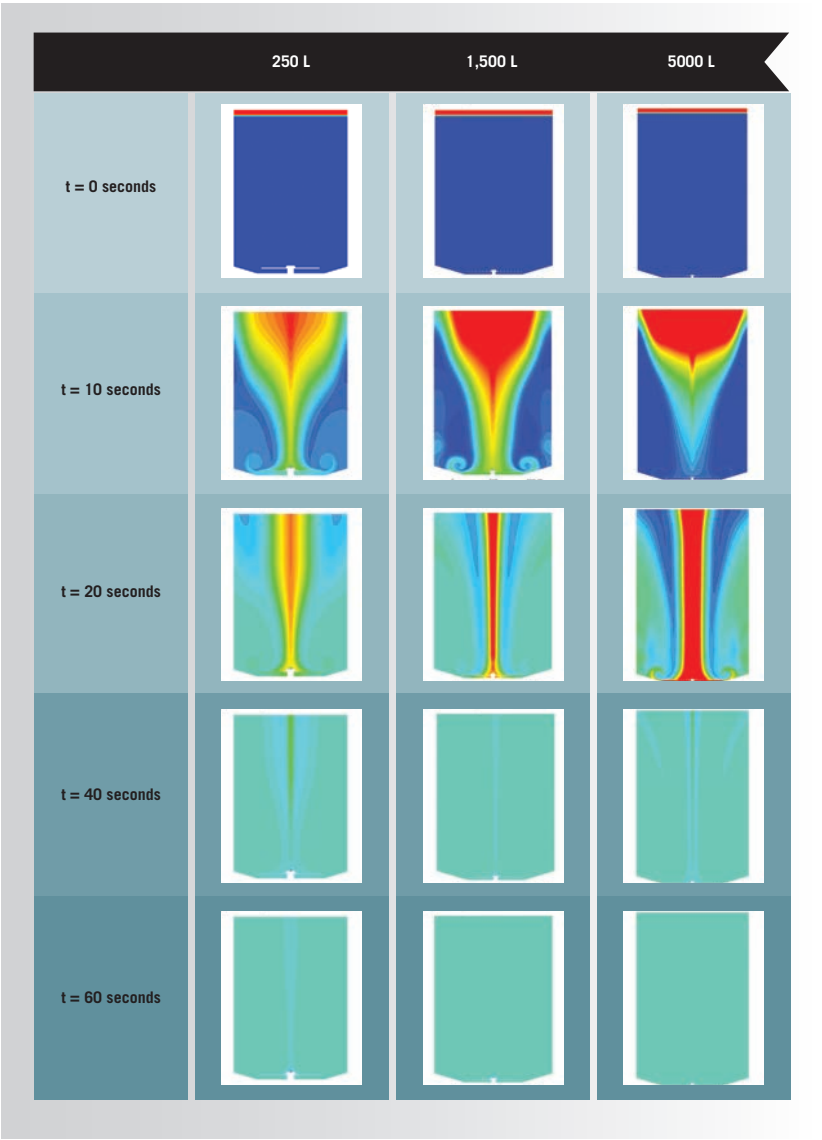
SimuTech engineers simulated performance of the bag in mixing two different particles: salt and bovine serum albumin (BSA). The software enabled engineers to customize material properties to model the properties of each particle type. The simulation showed that the flow traveled up along the outer walls, crossed over at the top of the tank, and returned in a downward moving column. This was expected since the mixing disc, located in the center of the bag, was designed to push the fluid on the downstroke, but not on the upstroke due to the opening of the membrane film flaps. The result is that during the downstroke bulk flow is accelerated, but on the upstroke a more complicated local mixing flow pattern is formed around the mixing disc. A complicated local mixing flow pattern is evidence of the random and aggressive mixing patterns this disc creates. The aggressive behavior creates a turbulence that generates random patterns, which provide additional paths for the solutions and bulk flow to conjoin.

The simulation showed that localized flow near the mixing disc changes significantly depending on its position in the stroke cycle. On the downstroke, with the membranes closed, the flow is pushed outward toward the tank walls at a high velocity. A vortex ring forms around the periphery of the mixing disc, which is beneficial to mixing and persists even after the mixing disc starts to move up again. The vortex generally follows

the bulk flow, so the circulation pattern migrates toward the walls. When the mixing disc is moving up, the bulk of the fluid in the center column continues to move down, but now the mixing disc opposes this motion. With the membranes/holes open, the flow is free to bypass the mixing disc by moving through these holes, which further agitates flow. The localized vortices illustrated in the CFD results generate turbulence with the ability to mix even difficult powder/liquid solutions at a rate that will enhance conjoining the bulk fluid and powder/liquid product solution. The localized vortices near the disc show that air is not being entrained or pulled in; only unmixed product is pulled in through the submerged disc.

To compare and predict scalability across various sizes, SimuTech engineers compared flow patterns of three different-sized mixers — 250 liters, 1,500 liters and 5,000 liters — to determine whether or not the tanks behave similarly. The results showed that flow patterns were largely unchanged in the larger devices as compared to the 250-liter baseline. Within a few seconds, all the tanks establish the pattern of flow moving up along the outer walls and down through the center column.

CFD simulations saved ASI hundreds of thousands of dollars.



▲ BSA particle mixing patterns for different tank sizes

The mixing patterns were observed directly through multiphase simulations with salt and BSA particles present in the tank. These results showed that at 6 seconds all three mixers had significantly suspended salt into the fluid. For the smallest equipment size, significant concentrations of salt were present at the top of the tank; even for the largest sizes, significant concentrations were present two-thirds of the way up the height of the tank. The near-neutrally buoyant BSA particles, which started in a thin layer at the top of the bag, were drawn down in the center column of descending fluid, then agitated by the mixing disc and eventually dispersed throughout the entire tank. The simulations showed that within 60 seconds, the concentrations throughout the tank were relatively uniform.

To quantify the mixing of BSA particles over a longer period of time, researchers created a monitor point in the three tanks. This point was placed 25 percent of the way up the height of the tank at a radial position of 75 percent. The results showed that the smaller tanks mixed faster than the larger tanks, but within practical limits, all tanks mixed very quickly. Within 60 seconds, the volume fractions in all of the tanks stabilized at about the same level. Overall, while slight differences were present in time scales in the different tanks, the tanks all scaled well, since they all mixed in less than a minute and displayed similar mixing patterns for the specific CFD testing conditions.

Because ASI engineers confirmed the simulation predictions with actual data in three sizes, they can draw a correlation between the actual and simulated data for application across the company's entire portfolio of mixing products. Overall, CFD simulation saved hundreds of thousands of dollars, providing characterizations that apply to the overall scalability of ASI's products and significantly reducing the need for building and testing prototypes.