

Tools and methodologies for generating digital twins in medical research

An overview of the latest advances of the use of CAE technologies in the medical field

By **Marco Evangelos Biancolini¹**, **Ubaldo Cella¹**, **Corrado Groth²**, **Stefano Porziani²**

1. Università di Roma Tor Vergata - 2. RBF Morph

The pervasive use of engineering simulation during the design phase and for virtual testing, thus eliminating the need for multiple prototypes prior to product launch, is well established today. The continuously growing availability of computing power and simultaneous algorithmic improvements now make high-fidelity numerical resolution of complex problems possible, integrating methodologies that are becoming established procedures in many fields of engineering. Clinical research has benefitted from these advances. Furthermore, the advent of technologies such as big data management, augmented reality, automated computer-aided engineering (CAE) processing in high performance computing (HPC) environments, and additive manufacturing are changing the way healthcare is delivered with implications for the skills required by the next generation of healthcare professionals and academic researchers. The use of numerical simulation to address clinical problems has been consolidated in Europe through several research activities that also involved non-medical institutions specialized in engineering technologies. This article provides a non-exhaustive overview of some of the latest advances in the adoption of CAE technologies in the medical field by citing some ongoing EU research programs.

The need for numerical simulations capable of accurately predicting the behavior of a device or prosthesis is constantly increasing [1] [2]. Furthermore, in the era of in-silico medicine, the combination of computer simulations with big data is mandatory. Engineering simulations generate tremendous amounts of data to be processed and that must be rapidly integrated and correlated with patient data. Such data-intensive research can be adequately supported by creating dedicated cyber-infrastructure that integrate data, tools, and research protocols in a unified and easily accessible environment: this is the Digital Twin concept. Healthcare is rapidly embracing this technology. The goal of this trend is to provide personalized data-driven medicine.

Digital twins are built on computer-based, or in-silico, models powered by individual and population data. They have been applied to complex systems in different fields of engineering. As a virtual representation of a physical object or system across its life cycle, digital twins aim to model systems computationally to develop and test them more quickly and economically than is possible in a real-life context. Ideally, in medicine, the concept of the digital twin can be translated to patients to improve diagnostics or treatment, and to accelerate medical innovation and regulatory approval using an ideal replica of a human body showing the

physiological and pathological results in the present and future. From this perspective, digital twins provide a safe environment to test the impact of changes on the performance of a healthcare system, improving the selection of optimal solutions and reducing the risk of harm to patients.

Despite the efforts in research, the extensive use of scientific computing tools in medical practice is still in its infancy. Bringing innovation to the healthcare sector is a long and costly process that requires clinical evaluation and regulatory approval. The validation of numerical simulations through clinical studies therefore remains challenging and scarce, or limited to small cohorts. The European Union is improving innovation by funding several programs focused on the role of digital twins in medical research. The heterogeneous know-how involved in the development of such technologies promotes the generation of a new class of consortia in which several highly specialized non-medical competences work side by side in a novel and extraordinarily stimulating environment. In this scenario, the “Tor Vergata” University of Rome is playing an important role by sharing engineering technologies, joining research partnerships and leading international networking training programs. Here is an overview of some of the EU research on this topic and relevant examples of where different CAE numerical technologies have been adopted to generate digital twins able to model the physics involved in clinical problems.

Digital twin technologies

A wide range of technologies can be adopted for the generation of a digital twin. Similar to many biological mechanisms, which require modelling by combining different numerical environments, digital twins can be based on CAE tools with different levels of “fidelity” combined together to model complex multi-physical phenomena. A common example is the fluid structure interaction (FSI) mechanism, typical of the dynamics of most biological fluid flows. The numerical tools involved in such models include computational fluid dynamics (CFD), finite element method (FEM) and coupling procedures that are efficiently implemented by adopting radial basis function (RBF)-based mesh morphing technologies. When the model response must be as fast as possible and when accuracy requirements can be relaxed, the adoption of reduced order models (ROM) offers the possibility to limit the computational burden and to provide a powerful and viable medical digital twin [3] generally able to interact in real time. Additive manufacturing is another technology that offers new opportunities in medical research. The combination of personalized digital twins and 3D printing techniques to create custom models and in-vitro testing are opening new frontiers in the development of tomorrow’s prosthetic devices.

RBF mesh morphing

Mesh morphing consists of adapting a computational grid commonly used for CAE. The solid or shell mesh of a structural part ready to be processed by a finite element analysis (FEA)

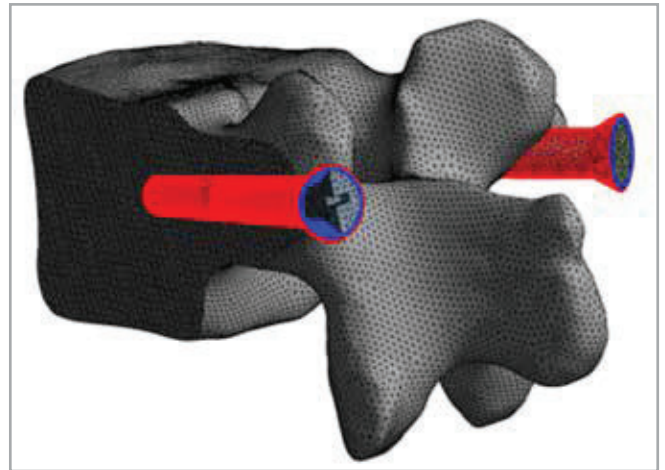


Fig. 1 – Example of RBF Morph design technology in a study of surgical screws in a vertebra (courtesy SPINNER)

solver, or a volume mesh complete with boundary conditions for a CFD solver, can be adapted to a new shape by simply updating the nodal positions. This means that the topology of the mesh (node count, cell count, connectivity) remains unchanged. Only the x,y,z coordinates of the nodes in the part of the model whose shape is being modified are updated. Mesh morphing can be used for different purposes: to create shape parameters (i.e. to modify a length, an angle or a thickness), to switch to a new known shape (i.e. to obtain the geometry as manufactured, or designed by CAD), to switch to a shape provided by the CAE solution (automatic shape optimization with adjoint or biological growth method (BGM)), and/or to support Multiphysics (to move the CFD mesh according to the evolution of the one connected to the FEM, enabling erosion/deposition).

Usually mesh morphing is faster than remeshing for a number of reasons: it avoids the “remeshing noise” (having the same mesh adjusted means that the effect of a parameter is not confused with the effect of a new mesh structure), so the variation effects can be evaluated even with a coarser mesh; the CAE model can be updated in the background keeping all the original settings (boundary conditions); and updating the nodal positions usually requires less computational effort than a complete mesh regeneration. Creating shape parameters with mesh morphing is generally faster than creating a parametric CAD model.

One of the most efficient mathematical frameworks to address the problem of mesh morphing is recognized as radial basis functions (RBF) [4]. RBFs are mathematical tools capable of interpolating known fields on a cloud of points. Mesh morphing defines a displacement field on a cloud of source points (usually some of the surfaces/curves of the CAE mesh) and then propagates it over a cloud of target points (usually the volume/surface mesh nodes of the CAE model being adapted). The method is well-suited to the needs of mesh morphing: its meshless nature allows you to easily manage partitioned meshes used for HPC parallel computing while its node-based nature allows you to have full control of specific areas. The computing cost of RBF can be very high, so specific algorithms (fast radial basis functions) are necessary to reap these benefit for industrial applications.

Fluid structure interaction analysis

Many physiological systems require the ability to explain the structural deformation induced by fluid flow. For this class of simulations, an FSI study based on numerical environments that combine structural solutions and fluid dynamics solvers is mandatory. Several approaches are possible to solve the problem, ranging from the uni-directional dependence of the fluid dynamics

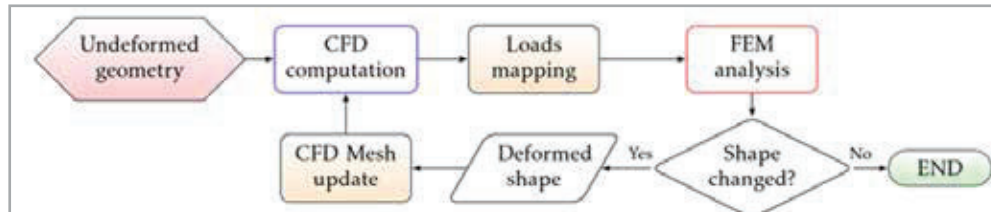


Fig. 2 – Workflow of an RBF-based two-way FSI analysis procedure

domain on the structural response [5] to a complete coupling of the two in an iterative cycle (the so-called two-way procedure) [6]. RBF-based tools are excellent candidates to implement the bidirectional link between structural and fluid dynamics solvers. The workflow of a steady two-way FSI analysis is summarized in Fig. 2.

The process begins with the CFD analysis of the rigid model in the desired condition. A mapping procedure is then applied to transfer the fluid loads into an FEM model of the object under investigation. The structural analysis solution, in terms of wet surface displacement, is used as a target for the morphing action of the meshes in order to update the fluid dynamics domain based on the estimated deformed shape.

The CFD calculation is restarted on the new configuration and the cycle continues until a final deformed shape (for a steady condition) is reached.

Reduced order models

As their name suggests, reduced order models (ROM) are simplified numerical models of complex systems (fluid, structure, or other physics) capable of operating very quickly (usually in real time). They are defined by applying data compression algorithms to many different instances (also known as snapshots) of the model to be reduced. ROMs are key enablers of the digital twin: the original system is modelled using high fidelity CAE methods (such as CFD and FEA) taking into account multiple configurations (different shapes, different boundary conditions or modifying any input to the model) that are screened using a large amount of computing resources (ROM creation); the compression stage allows the model to be compressed into a lighter and more portable piece of software. The ROM obtained can then be used as part of a complex simulation workflow or embedded in a physical resource to enable the digital twin. Mesh morphing is an excellent companion to ROM, as a constant mesh topology is required for

ROM creation; this is related to the nature of the compression methods that extract the ROM.

ROM are commonly used and successfully applied in different fields of classical mechanics for highly complex systems, in order to replace the complete model with a low degree-of-freedom one so as to drastically reduce the overall computing cost. Contrary to classical mechanics, however, the implementation of ROM in the field of biomechanics is very recent and limited to a few works [7][8]. In generating digital twins for medical applications, ROMs are a promising solution that offer the possibility to interactively predict the consequences of the change of state in a biological system from healthy to pathological.

Additive manufacturing

Additive manufacturing is a technology whose role over the last decade has evolved from that of a tool for prototype generation to a manufacturing approach to be fully integrated into the production process. One great potential of this technology is the significant flexibility it offers in generating complex components by circumventing many of the limitations imposed by more traditional manufacturing approaches. 3D printing technologies

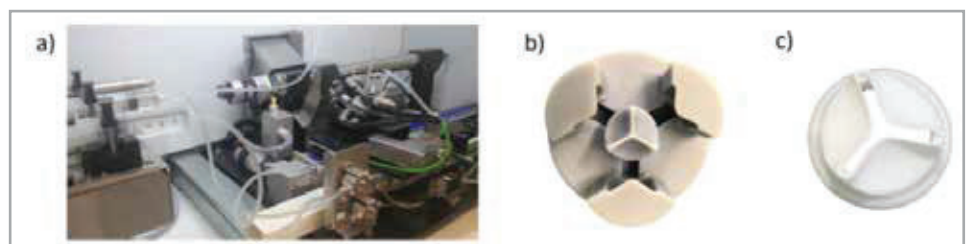


Fig. 3 – Spray machine (a) for additive manufacturing, custom mold/modular outer mold system (b) and final valve (c)

offer a cost-effective option not only as a fast prototyping tool but also for small- and medium-scale production, revolutionizing the manufacturing and design process.

Complex shapes can be easily produced for greater design flexibility and new geometries can be reshaped directly from the physics without having to consider rigid manufacturing constraints. In medical applications, 3D printing techniques could allow the creation of personalized models for each patient.

Various technologies are available for additive manufacturing. Fig. 3 shows, for example, the spray deposition technique used to manufacture a polymer aortic valve.

Examples of medical digital twins

Below is a non-exhaustive selection of examples where the technologies introduced above have been used to generate digital twins for biomedical research. RBF-based mesh morphing is the

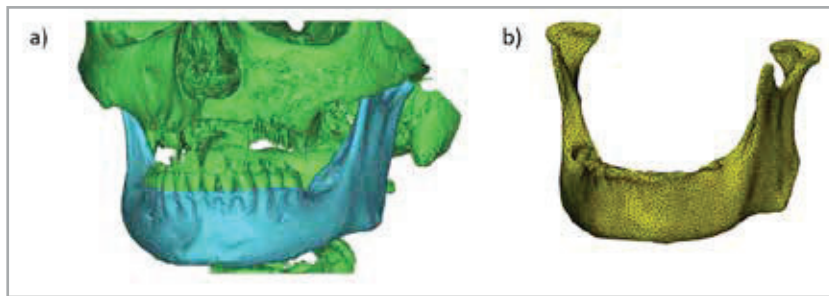


Fig. 4 – Mandible model from CT scan (a) and the generated mesh (b)

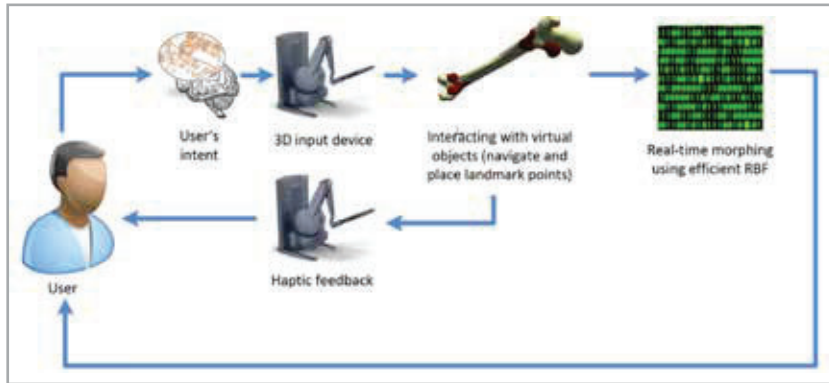


Fig. 5 – Schematic diagram of the methodology integrating the haptic device with force feedback and the RBF mesh morphing algorithms

protagonist of the methodologies implemented and allows the parameterization of the shapes used to build the whole numerical framework.

Parametric model of the mandibular (jaw) bone

Parametric modelling is useful in biomechanics to create patient-specific models based on a limited set of measurements (from the patient or x-rays). In this example, the RBF mesh morphing technique was used to generate a parametric model of the jaw bone. The aim was to create a tool for the creation of patient-specific morphologies as an alternative to CT scans (not always available for the definition of bone morphology).

The procedure consisted of generating a database of CT scans of mandibular bones from patients of different ages and genders. The images were segmented using a threshold filter (HU) to retain only bone tissue (Fig. 4). A subsequent remeshing process removed inaccuracies due to the process and reduced the number of nodes. All jaw models had to share an iso-topical mesh so that Principal Component Analysis (PCA), which is a statistical technique in which an orthogonal transformation is used to convert a set of observations of possibly related variables (called principal components) into a set of linearly unrelated variables, could be applied. Given a tolerated approximation range, PCA allows the number of principal coordinates to be reduced. In this case, eight principal components were sufficient to explain the 85% variability in the original set of mandibles. The next step was the generation of a template mesh that was parameterized using an RBF morphing algorithm, based on the morphing modes, to match all other mandibles. A morphing mode is a set of nodal displacements that defines the transition from the average shape to another shape.

The whole procedure was tested on two mandibles that did not belong to the PCA database. The accuracy of the reconstruction ranged from 0.025 to 3.235mm with an average accuracy of less than 1mm. The largest errors were observed in the lateral alveolar parts. The test was repeated on a mandible with a significantly different shape from the other mandibles. The maximum error in this case was 2.587mm with the most critical areas being located on the lateral alveolar parts, the central alveolar part, and the chin area.

Interactive sculpting of a human femur

Mesh morphing can be effectively used in predictive medicine workflows where a patient-specific numerical model is taken as a reference to understand the physics of interest using simulation-driven techniques. The example of Fig. 5 proposes a methodology for interactive geometric remodeling of the human femur with a force-feedback device, which is used to guide the morphing of an FEA template model onto the patient's geometry by

positioning a series of landmark points. A first morphing action allows the solid model to be warped according to the RBF deformation field produced by the landmarks points, performing a final projection onto the target surface to complete the task [9]. The complete configuration involves four main steps: three interactive steps (Fig. 6) and one batch run. The initial step (Step 0) consists of positioning the landmark points on the target geometry; the user is guided through the sequential definition of the positions of the landmarks in correspondence with the predefined positions already present on the template shape. Once the landmarks are positioned, the first RBF-based step (Step 1) can be enabled. The RBF field is defined using the landmarks. The landmarks on the template geometry are used as sources and their corresponding real scalar values are obtained by subtracting the landmark point in the target destination from those in the template. The displacement field is applied to all the points on the tessellated surface mesh representing the original shape. The last interactive step (Step 2) concerns the definition of a second RBF

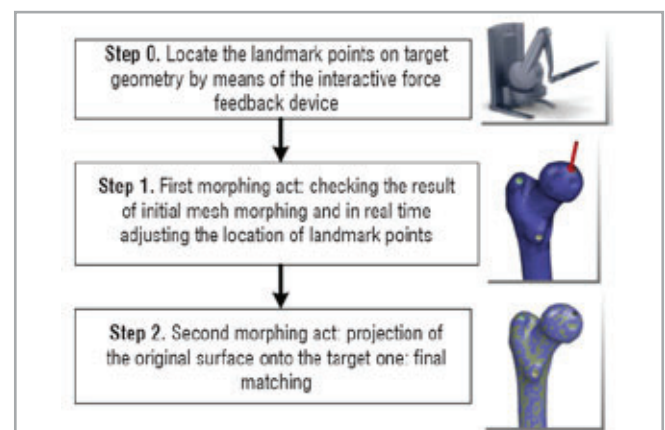


Fig. 6 – Interactive mesh morphing workflow

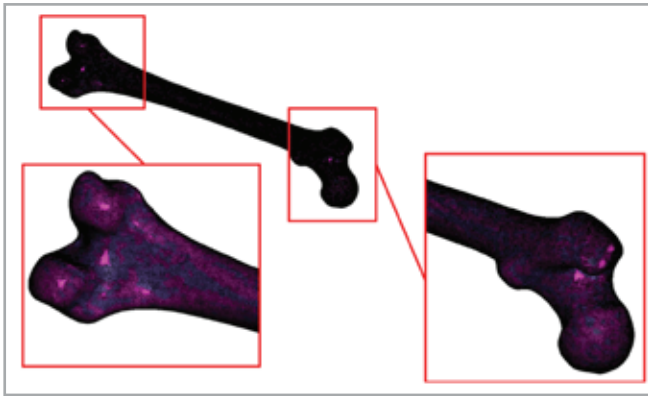


Fig. 7 – Final morphed mesh (Step 3) superimposed on the target (initial) CAD geometry

field capable of projecting the calculated approximate shape obtained at the end of the Step 1 onto the target entity. The final step (Step 3, performed in a batch) involves a sequential application of the two morphing fields generated for the final update of the FEA volume mesh.

The approach proved to be fast, effective, and ergonomic thanks to the haptic device and the high level of interactivity. New patient-specific CAE models were generated in a very short time, preserving the excellent quality of the computational mesh and the coherence with the input CAD model (Fig.7).

Aortic heart valve

Heart valve disease is one of the leading causes of heart failure worldwide. In such pathologies, prosthetic heart valves are commonly used to address the increasing prevalence of the disease. An ideal prosthetic heart valve replacement would closely mimic the characteristics of a normal native heart valve. In-silico characterization plays a key role in the development of new aortic valve (AV) designs. In-silico evaluation of prosthetic heart valves can be addressed by structural simulations, simplifying the pressure loads without considering fluid flow or taking the FSI mechanism into account. The first approach is simpler, but usually leads to overestimation of the deformations since pressures are applied uniformly on the valve leaflet throughout the opening phase. The latter, on the other hand, is more accurate

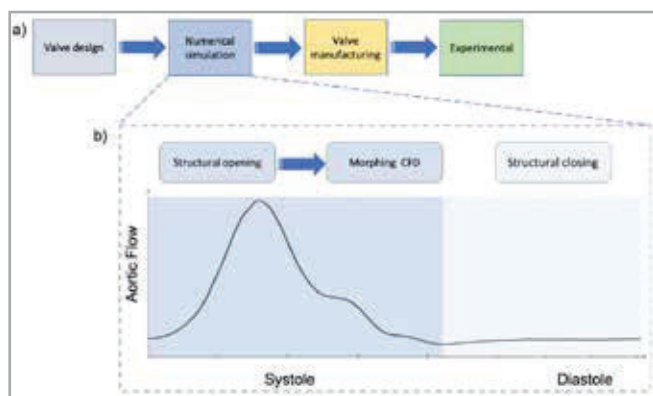


Fig. 8 – Overall study workflow (a) and schematic workflow of the numerical approach

but requires more computing resources and a more complex configuration. The study described in [10], sketched in Fig.8 and briefly reported here, concerned the design of a polymer AV for a surgical application addressed with an FSI analysis and its experimental verification. The geometric model of the tri-leaflet aortic valve prosthesis was generated in the closed position by elliptic hyperbolic surfaces. FEM analyses were conducted throughout the entire cardiac cycle by separately simulating the systolic (valve opening) and the diastolic (valve closing) phases. In the systolic phase, the system is affected by both static and dynamic pressures. In contrast, in the diastolic phase, fluid flow velocities have become negligible, so the system is only affected

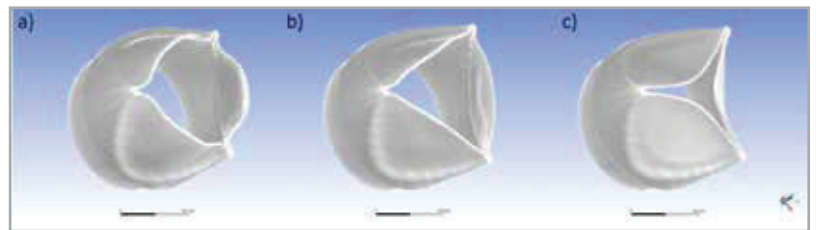


Fig. 9 – Morphing at three opening levels: maximum (a), mid (b), minimum (c)

by the static physiological transvalvular pressure.

The FSI analysis was performed for the systolic phase according to the following steps:

- A transient structural analysis was performed by applying the systolic physiological pressure to the valve leaflets as a load;
- The deformed structural shapes of the valve were used to configure the mesh morphing procedure (Fig. 9);
- An FSI simulation was conducted by imposing the adaptation of the fluid domain based on the position of the leaflets (Fig. 10).

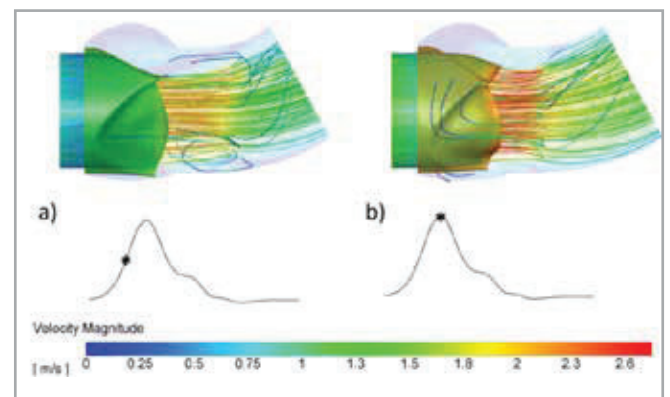


Fig. 10 – Flow velocity streamlines at two instances in the cardiac cycle

The diastolic simulation was performed with a structural transient analysis in which the surfaces of the leaflets were loaded with a pressure equal to the diastolic physiological transvalvular pressure (Fig. 11). Also in this case, the FEM mesh adaptation task required an RBF mesh morphing procedure.

The valve leaflets were manufactured using spray technology and an external modular custom 3D printed mold system (Fig. 3). The valve ring was manufactured using fused deposition technique and positioned on a tubular mold. The hydrodynamic performance of the

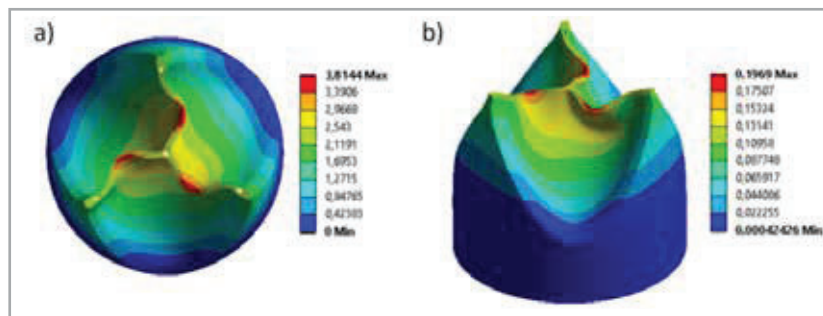


Fig. 11 – Radial displacement in mm (a) and equivalent strain (b) resulting from the FEM analysis in the diastolic phase

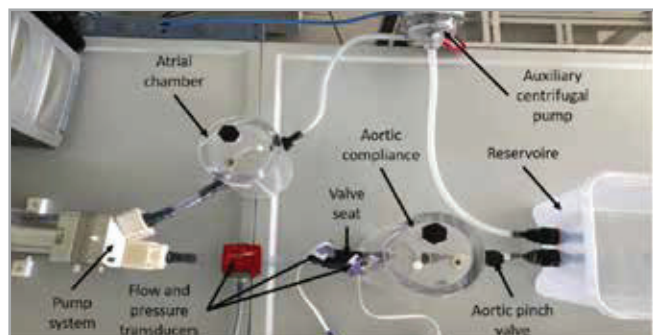


Fig. 12 – In-vitro experimental setup

valve was evaluated by in-vitro testing according to the ISO-5840 standard guidelines (Fig. 12). The experimental tests confirmed that the numerical solution correctly reproduced the AV kinematics. The advantage of adopting an RBF-based mesh morphing approach was demonstrated in [11] where this option was shown to provide a computational configuration that was about 16 times faster than a remeshing-based configuration. Furthermore, no significant differences were observed between the fluid dynamics solutions provided by the two numerical environments.

A video describing the study reported here was awarded the best simulation example at the 2019 Ansys Hall of Fame competition (<https://www.ansys.com/blog/ansys-hof-2020>).

Thoracic aorta hemodynamics

Among the victims of cardiovascular disease (CVD), the ascending thoracic aortic aneurysm (aTAA) is the 19th most common cause of human death. There is therefore a clear interest in the

development of digital twins in order to provide a structured, reproducible and predictive framework for the interpretation and integration of clinical data, thus paving the way for the development of personalized and preventive management strategies for CVDs. The rigid wall assumption, which could be a reasonable simplification in cases of high arterial stiffness, is not applicable for the numerical fluid dynamics solution of the aortic aneurysm.

The interaction mechanism of the fluid structure cannot be neglected in this case. However, the high-fidelity numerical solution of such a complex problem remains prohibitively expensive in many query and real-time contexts, both in terms of CPU time and memory demand. To overcome this limitation, many stochastic approaches have been proposed to provide answers in acceptable times for clinical

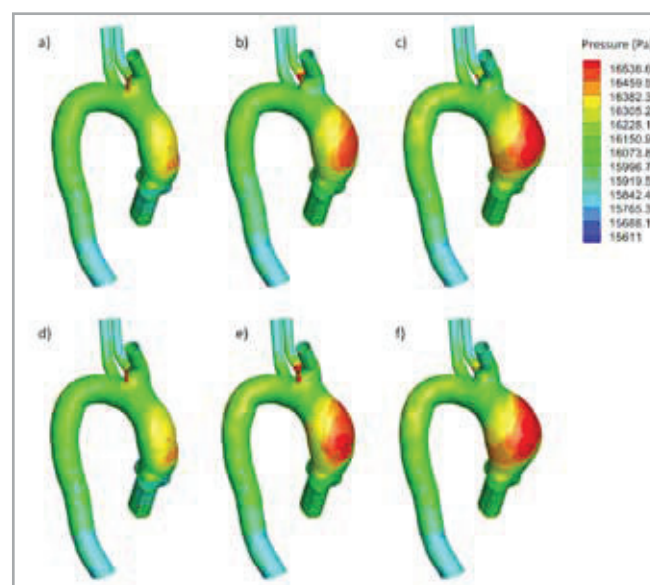


Fig. 14 – Comparison of the evaluation of the pressure contours between ROM (above) and CFD (bottom).

timing. Such techniques take into account material properties and geometrical variations, as well as a series of uncertainties that may affect finite element simulations. Recent advances in numerical tools to support computational analyses, such as reduced order models (ROM) can deepen the knowledge of complex phenomena related to clinical scenarios. Combined with efficient RBF mesh morphing techniques, ROMs enable a very powerful and practical medical digital twin that provides real time solutions.

The typical workflow for the generation of a ROM is divided in two main tasks: the generation of training data, which involves the generation of a database of high fidelity solutions, and the extraction of the ROM. The first step is the most time-consuming activity while the second step requires minimal user intervention and provides almost real-time solutions. Fig. 13 shows the ROM workflow in the Ansys

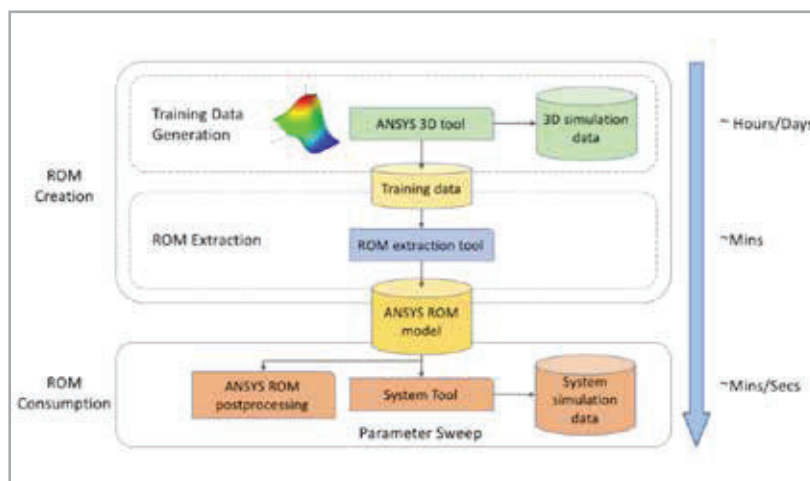


Fig. 13 – ROM generation workflow in the Ansys framework environment



Fig. 15 – A patient-specific high-fidelity FEA model representing one vertebra and two prosthetic screws was created; mesh morphing allows the diameter and length of the screw to be updated to optimize individual patient treatment

framework environment. The key concept of the ROM workflow is its integration with the response surface (RS) technique. Using RS, outer parameter values are obtained as a function of the input parameters at the design points defined in the configuration of the design of experiments. Finally, interpolation methods are used to construct the entire model.

In order to verify the ROM strategy in this new hemodynamic context, both reduced and not reduced i.e. the complete system of differential equations describing the CFD case were compared using a single geometric parameter that gradually morphs the healthy aorta into an aneurysmatic one, monitoring the difference in the main quantities of interest. In Fig. 14, the ROM and CFD simulations were compared at three stages of accretion ranging from healthy, (a) for ROM and (d) for CFD, to a fully developed aneurysm, (c) for ROM and (f) for CFD. The images (b) and (e) refer to the ROM and CFD evaluations for the medium developed shape, respectively. The differences between the two solutions are negligible from a practical point of view.

ROM-assisted spinal surgery

Back pain is an extremely common problem with more limited solutions than limb joints. The number of patients requiring

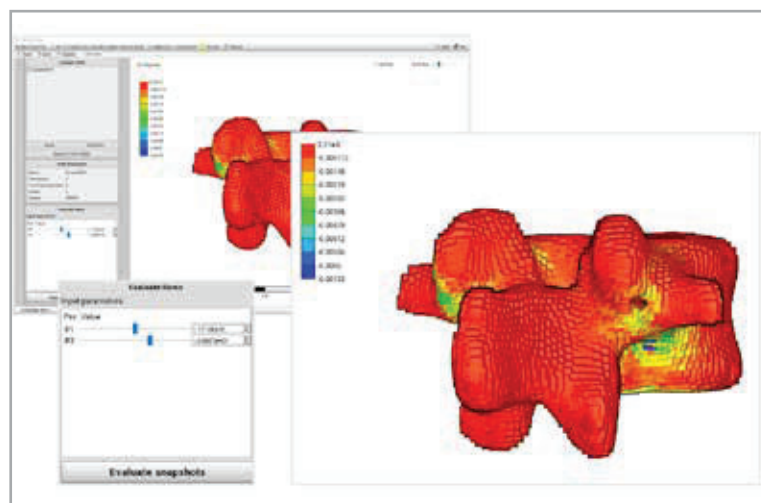


Fig. 16 – The Twin Builder Viewer, powered by a mesh-less and solver-independent rendering tool, allows interaction with the Digital Twin of the vertebra. The P1 and P2 sliders allow you to update the diameter and length of the screw in real time and to see how the minimum principal strain varies

complex spinal surgery is rapidly increasing and the biomedical engineering industry needs properly trained innovators to produce cost-effective solutions to support the healthy ageing of Europe's population. The European Spinner project (spinner-eid.eu) was created to study the use of medical digital twins for spinal surgery applications.

A high-fidelity FEA model was defined by using the geometry of the real patient's vertebra with the prosthetic screws positioned so that an assessment of the stress on the prosthetic part and on the patient's bone tissue was possible (Fig. 15).

The image data made it possible to define an accurate structural model that matched the patient's shape and the actual bone density distribution. Then an offset of the screw placement and size was introduced by mesh morphing.

Two parameters enabled the possible screw sizes (length and diameter) to be navigated and four parameters were used to modify the positioning (vertical and lateral adjustment for both vertebrae). The parametric shape with six degrees of freedom was then evaluated for 200 configurations using HPC.

ROM technology was then used to compress the simulation results into the digital twin, resulting in a portable tool for real-time inspection that is easily available to the medical doctor and his staff (Fig. 16).

The environment of EU-funded research programs

The "Mario Lucertini" Enterprise Engineering department of the "Tor Vergata" University of Rome has substantial experience in developing CAE-based numerical analysis tools for mechanical applications.

The company RBF Morph, developers of the homonymous mesh morphing technology based on radial basis functions and an Ansys advanced solution partner, is active in several research projects concerning biomedical engineering. Recently, two Marie Skłodowska-Curie Innovative Training Network (ITN) programs, involving the RBF Morph technology, have been activated: MeDiTATe, which aims to develop digital twins for the treatment of aneurysms, and SPINNER, which studies materials and techniques for spinal surgery.

MeDiTATe

MeDiTATe ("The Medical Digital Twin for Aneurysm Prevention and Treatment") will provide a comprehensive framework of simulation and imaging technologies aimed at industrial and clinical translation to accelerate the process of personalized cardiovascular medical procedures, validated through an integrated experimental program to ultimately improve patient care.

The main idea of MeDiTATe is therefore to develop a digital twin and make it available as a "service" for everyone in

academic, hospital and industrial settings. To achieve these objectives, the following techniques are integrated:

- Clinical and imaging data;
- Computer-aided engineering (CAE) Multiphysics simulation with radial basis function (RBF) mesh morphing, finite element method (FEM), computational fluid dynamics (CFD), fluid-structure interaction (FSI), inverse FEM;
- Real-time interaction with the digital twin via augmented reality, haptic devices, and reduced order models (ROM);
- High performance computing (HPC) tools, including graphic processing units (GPUs) and cloud-based paradigms for fast, automated CAE processing of clinical databases;
- Big data management for the patient population's imaging data and high-fidelity CAE twins;
- Additive manufacturing of physical mock-ups for surgical planning and training.

The MeDiTATe project is led by the "Tor Vergata" University of Rome.

SPINNER

SPINNER (SPINe: Numerical and Experimental Repair strategies) is a doctoral training program aimed at early stage bioengineering researchers, to train bioengineers in the design of next-generation repair materials and techniques for spinal surgery. SPINNER brings together partners from the biomaterials, implantable devices, and computational modelling industries with orthopedic clinicians and academic experts in cell, tissue and organ scale biomaterials and medical device testing. The project covers topics such as biomaterials, clinical biomechanics, in-vitro testing and in-silico biomechanics. An inter-disciplinary training program between academia and industry is planned.

The SPINNER project is led by the University of Sheffield.

Conclusions

The basic concept of a digital twin is that a computer model can predict the specific functioning of an individual's body. It is well known that the patient-specific computational model can provide additional information by extrapolating data that is not clinically available. In this context, numerical simulations can help identify patients prone to adverse outcomes by providing detailed information on hemodynamic factors. In addition, numerical models can support clinicians by virtually simulating different interventional strategies.

This article provided an overview of the tools and methodologies adopted for the generation of digital twins in medical research along with a brief description of the methods that represent the key components in the development of numerical modelling as well as a series of examples of where digital twins have provided reliable models of biological phenomena.

The roles of the "Tor Vergata" University of Rome and its partner RBF Morph were highlighted within the framework of the EU research programs on medical research.

References

- [1] Morrison T. M., Pathmanathan P., Adwan M. and Margerrison E., "Review of numerical methods for simulation of mechanical heart valves and the potential for blood clotting", *Frontiers in medicine*, 5, (2018).
- [2] Zakaria, M. S., Ismail, F., Tamagawa, M., Aziz, A. F. A., Wiriadidjaja, S., Basri, A. A., Ahmad, K. A., "Review of numerical methods for simulation of mechanical heart valves and the potential for blood clotting", *Medical & biological engineering & computing* 55(9), 1519-1548 (2017).
- [3] Ballarin F., Faggiano E., Ippolito S., Manzoni A., Quarteroni A., Rozza G. and Scrofani R., "Fast simulations of patient-specific haemodynamics of coronary artery bypass grafts based on a POD-Galerkin method and a vascular shape parametrization". *Journal of Computational Physics*, 315, pp. 609-628, (2016).
- [4] Stefan Jakobsson and Olivier Amoignon, "Mesh deformation using radial basis functions for gradient-based aerodynamic shape optimization", *Computers & Fluids*, 36(6), pp. 1119-1136, (2007).
- [5] Capellini, K., Cella U., Costa E., Gasparotti E., Fanni B.M., Biancolini, M. Celi, S. "A coupled CFD and RBF mesh morphing technique as surrogate for one-way FSI study", In *Proceedings VIII Meeting Italian Chapter of the European Society of Biomechanics (ESB-ITA 2018)*, (2018).
- [6] K. Czechowicz, J. Badur and K. Narkiewicz, "Two-way FSI modelling of blood flow through CCA accounting on-line medical diagnostics in hypertension", *Journal of Physics: Conference Series*, Volume 530, XXI Fluid Mechanics Conference 15-18 June 2014, AGH-UST, Krakow, Poland.
- [7] Manzoni, A., Quarteroni, A., and Rozza, G., "Model reduction techniques for fast blood flow simulation in parametrized geometries", *International journal for numerical methods in biomedical engineering*, 28(6-7), pp. 604-625 (2012).
- [8] Niroomandi, S., Alfaro, I., Gonzalez, D., Cueto, E. and Chinesta, F. "Real-time simulation of surgery by reduced-order modeling and x-fem techniques". *International Journal for Numerical Methods in Biomedical Engineering*, 28(5), pp. 574-588.
- [9] Biancolini, M.E., Valentini, P.P., "Virtual human bone modelling by interactive sculpting, mesh morphing and force-feedback", *International Journal on Interactive Design and Manufacturing (IJDeM)*, Vol. 12, pp. 1223-1234 (2018).
- [10] E. Gasparotti, U. Cella, E. Vignali, E. Costa, G. Soldani, A. Cavallo, P. Losi, M. E. Biancolini and S. Celi, "A combined approach of numerical simulation and additive manufacturing technique for in-silico and in-vitro testing of a 3D printing-based aortic polymeric heart valve", *II International Conference on Simulation for Additive Manufacturing - Sim-AM*, 11-13 September, Pavia, Italy, (2019).
- [11] L. Geronzi, E. Gasparotti, U. Cella, C. Groth, S. Porziani, M. E. Biancolini and S. Celi, "Advanced Radial Basis Functions mesh morphing for high fidelity Fluid-Structure Interaction with known movement of the walls: simulation of an aortic valve", submitted to *The International Conference on Computational Science*, Amsterdam (NL), 3-5 June (2020).

Acknowledgment

The MeDiTATe and SPINNER projects have received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement numbers 859836 and 766012 respectively.

Please visit also:

rbf-morph.com • meditate-project.eu • spinner-eid.eu

For more information

Marco Evangelos Biancolini, Ubaldo Cella

"Università di Roma Tor Vergata"

biancolini@ing.uniroma2.it - ubaldo.cella@uniroma2.it

Corrado Groth, Stefano Porziani - "RBF Morph"

corrado.groth@rbf-morph.com - stefano.porziani@rbf-morph.com