

# Interactive real time simulation of cardiac radio-frequency ablation

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## Abstract

*Virtual reality based therapy simulation meets a growing interest from the medical community due to its potential impact for the training of medical residents and the planning of therapies. In this paper, we describe a prototype for rehearsing radio-frequency ablation of the myocardium in the context of cardiac arrhythmia. Our main focus has been on the real-time modeling of electrophysiology which is suitable for representing simple cases of arrhythmia (ectopic focus, ventricular tachycardia). To this end, we use an anisotropic multi-front fast marching method to simulate transmembrane potential propagation in cardiac tissues. The electric propagation is coupled with a pre-recorded beating heart model. Thanks to a 3D user interface, the user can interactively measure the local extracellular potential, pace locally the myocardium or simulate the burning of cardiac tissue as done in radio-frequency ablation interventions.*

*To illustrate this work, we show the simulation of various arrhythmias cases built from patient specific medical images including the right and left ventricles, the fiber orientation and the location of ischemic regions.*

Categories and Subject Descriptors (according to ACM CCS): I.6.3 [Simulation and Modeling]: Applications—Medical interactive real time simulation

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## 1. Introduction

Virtual-reality based surgery simulation opens up new fields in medical training and planning of therapies. In this paper, we investigate the development of a simulator prototype for rehearsing radiofrequency (RF) ablation of the myocardium. This intervention which is performed through interventional radiology, consists in burning cardiac tissues responsible for arrhythmias.

Arrhythmias are pathologies characterized by an abnormal heart beat or rhythm. The contraction and relaxation of the heart is indeed controlled by the depolarization and repolarization of an electric wave that propagates through the myocardium, from the sinus node, the natural pacemaker of the heart, to the ventricles. This electrical activity of the heart can be measured at the level of the thorax through the electrocardiogram but can also be measured by electrodes positioned inside the heart during RF ablation. The abnormal propagation of the electric wave inside the heart leads to dysfunction of cardiac mechanics causing a loss of efficiency when pumping the blood to the general circulation.

While there exists a large variety of cardiac arrhythmias, some of them, like atrial flutter or atrial fibrillation are fairly common with up to 6 million people concerned in Europe. Ventricular tachycardia (VT) is not as common as atrial fibrillation but is considered as a potentially life threatening pathology which may evolve into ventricular fibrillation and death. In case of severe and chronic atrial fibrillation or ventricular tachycardia, RF ablation is widely used to burn the pathological cardiac cells responsible for abnormal electrophysiological propagations. One source of difficulty for cardiologists when performing this intervention is to locate those cells based on the reading of multiple electrical signals acquired in the heart. In many cases, the therapist adopts a trial and error approach where he continuously checks if the electric propagation is altered by performed ablation. Furthermore, partly due the challenge in performing the intervention, a large proportion (around 50 %) of patients being ablated for atrial fibrillation experiments have a recurrence of the pathology at least 6 months after the intervention.

### 1.1. Context and Objectives

To improve the success of RF ablation procedures, several research groups are developing computational models of the heart [BUM04] with the objective of predicting the optimal location of the ablation lines given some patient specific electrophysiological measurements and medical images of the heart function.

In this paper, we propose a complementary objective which is to develop a simulator to train cardiologists in performing RF ablation. To be complete such simulators should also reproduce the catheter navigation performed under X-ray guidance which contributes to the difficulty in performing the intervention. Several research groups [DMD\*08], [LV09] and commercial companies [Men], [Sim] are developing such endovascular navigation simulators, but in this paper, we have chosen to focus on the simulation of electrophysiology propagation which is suitable for real-time interaction. Fast and realistic simulation of cardiac electrophysiology is indeed fairly challenging since the physiological phenomenon occurring at the level of the cardiac cells involves different ion channels with various dynamics. Most electrophysiological models proposed in the literature [LR91] are way too complex to be implemented in real-time. Based on previous work, we have developed a multi-front Eikonal model which captures the main characteristics of electrophysiology propagation (anisotropy, refractory period, restitution curve) at a low computational cost. Furthermore, we show on several examples that such model can be combined with a 3D user interface in order to simulate the pacing of the myocardium and the ablation of pathological cells.

### 1.2. SOFA Framework design

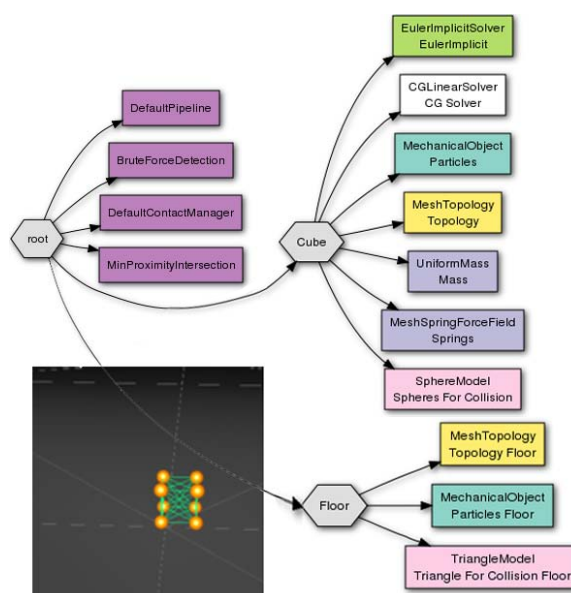
The proposed work has been implemented in an open source framework, SOFA. In this section, we overview the overall design of the framework but more details can be found in [ACF\*07]. This framework is targeting real-time modeling of deformable structures and mechanical behaviours, particularly for medical simulation.

SOFA is an open-source library mostly written in C++ and using XML script language. It can be used either as an external library, or used with its own user interface and 3D OpenGL views. The architecture main goals are to keep an high modularity implying, on one side, a lean core containing the overall architecture and prototype functions and on the other side, a large set of modules derived from the core. Thus, it allows to represent different aspects of the same object, e.g. mechanical behaviour, collision model, topology description or visual model, etc. Although all these models are connected together and synchronized, each one can be parametrized independently.

To create a data structure and link the different components (C++ module of the framework) together, scene graphs

(simulation tree in XML format) are used to describe a simulation. In terms of simulation tree, nodes are used to create hierarchical levels of modeling (e.g. behaviour model, collision model, visual model, etc.), whereas a large collection of components corresponds to leaves under the nodes and covers a large set of fields (e.g. mechanical behaviour, force fields, topology, mass, etc. ).

This description using a XML file allows an high flexibility in designing a simulation scene. Indeed, it is easy to replace one simple component by another. For example for the computation of forces acting on a mechanical system, one can replace a spring-mass force with a finite element force. This versatility also applies to the choice of the time integration schemes or collision detection pipelines. Changing a component does not affect other components in the scene due to the library architecture.



**Figure 1:** Scene graph and view of a simple system: a cube on a floor. They both have mechanical behaviours and collision models.

Figure 1 shows one simple example of a simulation tree describing two simple objects, a cube and a plane. Both objects are described in terms of geometry and topology (the relationship between vertices) and have a specific representation for the collision detection. It is important to note that the XML scene graph describes implicitly the simulation tasks and their scheduling similar to a script pipeline. Then, the simulation tree is constantly traversed by visitors which call appropriate functions of the different components, carrying information and propagating them. Finally, each component has its own list of parameters which can be changed in the XML scene and at runtime.

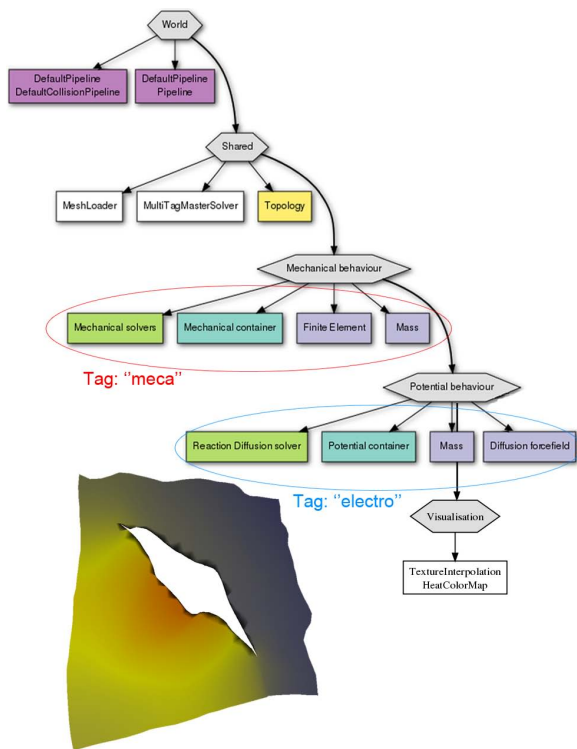
## 2. Interactive electro-mechanical simulation

### 2.1. Improved Software Framework

#### 2.1.1. Physical fields and their coupling

As explained before, the current framework has been mainly designed for the simulation of mechanical object interaction but not, for example, for the simulation of electrophysiology propagation and its coupling with mechanical objects. We have therefore extended the SOFA framework in order to simulate the evolution of a *physical field*, this field being any scalar, vectorial or tensorial quantity defined on a mesh. For instance, one may simulate the evolution of the electric potential (a scalar) on a mesh through a reaction-diffusion equation as shown in Figure 2.

A further extension of the framework has been to allow the coupling between mechanical and physical model evolution. To avoid confusion between models and to have an asynchronous behaviour, tag parameters defined as string identifiers were added to each component. Thus, all components having the tag "A" are processed by the visitor apart from components having the tag "B", whereas components without tags are shared with all visitors. As a result, we can

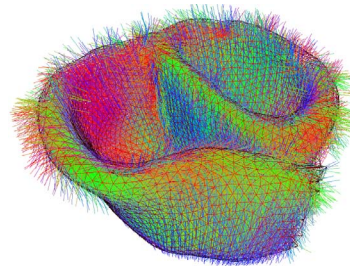


**Figure 2:** Simplified scene graph and view of a coupled model: a soft tissue model with electrical potential diffusion. Each behaviour is describe by one node and a shared node where components without tags are used by both behaviour.

design simulation scenes with a coupling between mechanical and electrophysiology variables. For example, Figure 2 shows a scene graph where the electric potential evolution is simulated on a deformable surface, the deformation of the surface having an influence on the diffusive process. Thus, on one hand, all components related to electrophysiology are tagged as "electro", and on the other hand, mechanical components are tagged as "meca". Note that the component *MultiTag-MasterSolver* is used to handle the sequential launch of visitors. Finally, some components such as the force fields components may require the knowledge of both mechanical and physical variables and a specific mechanism has been added to do so.

#### 2.1.2. Scene Description

For the simulation of cardiac electrophysiology, it is important to define volumetric meshes of the heart. In addition, it is required to define physiological structures attached to those meshes. For instance, 2D and 3D regions on the myocardium are useful to identify the endocardium, epicardium... Fiber orientations at each tetrahedron are also needed. These information are directly generated from a medical image processing toolbox which combines image segmentation, surface extraction and volumetric mesh generation [TMD\*08].



**Figure 3:** Example of data stored on topological elements: fiber directions are defined for each tetrahedron in a heart mesh which has been cut and deformed.

In the design of SOFA, all these informations stored in mesh files are loaded by a *MeshLoader* component. This last one will store all the data into specific C++ containers, called "Data", which are C++ components members reachable in the XML file. Thus, mechanisms are available to create dependency between those containers of same nature in the XML file (similar to "fields" in OpenInventor). Moreover, some containers have been specialized to store information associated with topological mesh elements like vertices, triangles, tetrahedra... For instance, *TriangleData* are specific Data containers storing information on triangles (such as colour, conductivity...). This approach allows to provide an automatic mechanism to handle topological changes [AD08]. When simulating the ablation of cardiac tissues, the

content of those containers is automatically updated by call-back functions. As example, in Figure 3, fiber orientations are updated during the resection of the myocardium.

## 2.2. Electrophysiology model: Fast-Marching method

Modeling the cell electrophysiology is an active research area since the seminal work of Hodgkin and Huxley [HH52]. We can divide these models into three categories, from the more complex to the simpler (numerically):

- Biophysical models: semi-linear evolution Partial Differential Equation (PDE) with ionic models. Up to fifty equations for ion concentrations and channels [LR91].
- Phenomenological models: semi-linear evolution PDE with mathematical simplification of biophysical models. Reducing to two equations representing the intra- and extra-cellular potentials (bi-domain, mono-domain [AP96]).
- Eikonal models: one static non-linear PDE for the depolarisation time derived from the previous models [KS98].

Solutions of the evolution PDE are very time-consuming, due to the space scale of the electrical propagation front being much smaller than the size of the ventricles. The motion of the front governed by the Eikonal equation is observed on a much larger scale, resulting in faster computations.

To simulate arrhythmias and radiofrequency ablation, we use a multi-front Eikonal model which was first proposed in the context of electrophysiology parameter estimation [SKD\*07]. This model makes the hypothesis that at each node of the mesh, the surrounding cardiac tissue may be in one of the three successive states : depolarized, refractory and repolarized. When a node is in refractory state, it cannot be depolarized (excited) anymore. When it is in repolarized state, it can be depolarized. The duration between the depolarized and refractory states is called the *Action Potential Duration* or APD whereas the duration between the refractory and repolarized states is called the *refractory period*. The APD and refractory periods change over time and space but there exists simplified relations called the *restitution curves* that can be measured experimentally and indicates how those durations vary as a function of frequency.

The transition between depolarized and repolarized states takes into account the anisotropic propagation of an electrical wave governed by the following eikonal equation :

$$F\sqrt{\nabla T^T \mathbf{D} \nabla T} = 1$$

where  $F$  is the conduction velocity,  $T$  is the time at which the wave reaches a given point and  $\mathbf{D}$  is a  $3 \times 3$  symmetric tensor defining the anisotropy of propagation. The conduction velocity  $F$  is not homogeneous in the myocardium. Ischemic or infarcted (necrotic) tissues in particular show low conduction velocities compared to normal tissue. The anisotropy matrix  $\mathbf{D}$  captures the fact that the electrical propagation is roughly three time as fast along the fiber orientation than in

its orthogonal direction. Therefore, this tensor is computed as :

$$\mathbf{D} = \frac{1}{9} \mathbf{I} + \frac{8}{9} f \otimes f$$

where  $\mathbf{I}$  is the identity matrix and  $f$  is the unit fiber orientation vector.

To establish in which state a node should be, we use an anisotropic fast marching method [KSC\*07] which computes the depolarization time at nodes located next to the front location. One issue with anisotropic fast marching is that the front propagation direction is no longer along the gradient of the isochrones which makes the classical fast marching method [Set99] fail. The anisotropic fast marching has been implemented on tetrahedral meshes and satisfactory results in terms of accuracy and computation times even in the case of large anisotropy ratios have been obtained.

To summarize, the proposed electrophysiology model is both discrete for the state of cardiac tissue and continuous for the propagation of the electrical wave. However due to the anisotropic *Fast Marching Method* (FMM), it is possible to simulate the cardiac electrophysiology in real-time for tetrahedral meshes of coarse medium resolution.

## 2.3. Mechanical model

The electrophysiological signal propagating through the heart is responsible for the contraction and relaxation of the heart muscle, the myocardium, during the cardiac cycle. The electro-mechanical coupling of the heart is rather complex phenomenon, but has been modeled in a fairly simplified way. Several research groups [GM91], [ROB04] have developed beating heart simulators that are coupled with electrophysiology models. However, simulating the cardiac mechanics in real-time (1 cardiac cycle per second) is still currently out of reach.

As an alternative, we propose to simulate offline the heart mechanical deformation during a cardiac cycle and to store in a file the position of the mesh vertices at various instants during the cardiac cycle. During the electrophysiology simulation, the heart mesh is deformed by interpolating between the key frames stored in those files. The cardiac mechanics is simulated using the same tetrahedral mesh as for the electrophysiology modeling. This electromechanical model [SPC\*08] of the heart relies on linear tetrahedral finite elements and anisotropic linear elasticity and is able to capture the four phases of the cardiac cycle : contraction, isovolumetric contraction, relaxation and isovolumetric relaxation.

## 3. Simulation of radiofrequency ablation in case of arrhythmia

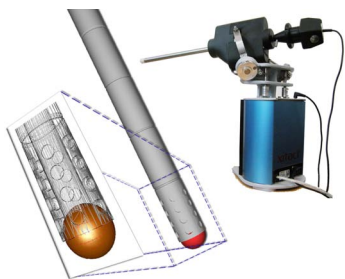
### 3.1. Basic User Interaction

As explained previously, FMM is an efficient computational method to approximate the propagation of transmembrane

potential in the heart and to visualize that potential as a coloured texture. Through the topological *Data* containers described in section 2.1, the user can easily read and change parameters that are stored for each vertex, edge or tetrahedron. For instance, the physiological states, action potential duration are stored for each vertex while the fiber orientation and anisotropy ratio are stored for each tetrahedron. Also, the mouse can be used to change locally the conductivity of a region of the myocardium or perform an electrical stimulation to generate additional electrophysiological waves.

### 3.2. 3D User Interface

To improve the realism of the simulation, we have interfaced our electrophysiology simulation with a 3D User Interface. Ideally, the user should interact with a force-feedback interventional radiology simulator which would allow the user to navigate a catheter through blood vessels and perform various actions (measuring potentials and ablating tissue). However, in a first prototype, we are using a Xitact ITP instrument [Men] as 3D positioning device which consists of one tracked instrument with a button and two pedals. In fact, the ITP instrument is designed for laparoscopic simulation with force-feedback. As the appropriate tools should have been the Xitact VIST, this choice of matériel lay on logistical choice and the fact that this tool allows user interactions. For this instrument the position and orientation of its tips can be read through a serial port at a high frequency. A complete description of the handling of haptic device, positioning and force feedback in the SOFA framework, can be found in [SDC08].



**Figure 4:** Picture of the ITP Xitact tool and its corresponding model. The tool tip corresponds to a sphere collision model.

### 3.3. Instrument Modeling

Due to nature of the 3D user interface, we assume that catheters are rigid instrument and avoid simulating the flexibility of a catheter that would be used for this kind of intervention. Figure 4 shows that the instrument is modeled as a thin rigid shaft with a sphere in its extremity. This tip is used to simulate the catheter interaction (potential stimulation and ablation). The sphere serves as a collision model for the collision detection with other objects.

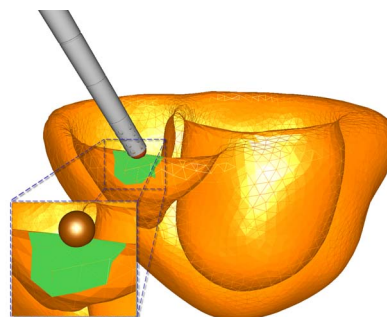
In terms of XML scene graph, the instrument is a stand-alone node with several branches corresponding to different types of models. It consists of two mechanical and visual models, for the shaft and the tip, linked together with an articulation. It also includes a sphere as a collision model and finally a device plugin which is in charge of communicating with the hardware system. Thus, at each time step, the plugin is in charge of refreshing the 3D position and orientation of the tool. This information is then propagated through the scene graph in order to update the different components.

For further work, as indicated in previous part, the Xitact VIST model should be used for this simulation. In terms of integration in our simulator, the main part will be to simulate the catheter navigation taking into account blood fluid, vessel walls interaction and X-ray view which correspond to reality. However, some works on catheter navigation has already been done in the SOFA framework [DMD\*08]. Then, the interactions developed for the ITP model should be easily transferred to this one.

### 3.4. Collision Detection

A sphere collision model is used to represent the tip of the tool whereas tetrahedra are employed as the collision model for the myocardium, as shown in Figure 5. Thus, as soon as the sphere intersects a tetrahedron face, a collision is created and sent to the default collision pipeline of the SOFA framework [ACF\*07].

Upon the detection of a collision, no force-feedback is sent back to the device in such a case but instead we initiate some actions through a component called the *HeartSimulation-Manager*. When activated by a collision, this component allows the user to perform ablation or electrical stimulation by pushing on the tool button. Also, the pedal is used to change the type of interaction. To guide the user, the selected area after the collision is highlighted and its scale may be modified as seen in Figure 5.

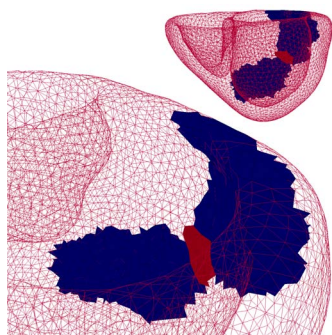


**Figure 5:** Collision model representations. A sphere model is used for the tool whereas the myocardium collision model consists of tetrahedra. The contact region is shown in green.

## 4. Results

### 4.1. Simulation Scene

In order to illustrate the radiofrequency ablation simulation, we build a simulation scene corresponding to ischemic ventricular tachycardia, an example of cardiac arrhythmia. In this pathology, the myocardium includes several necrotic regions or *scars* that appear after an infarct. Those scars can be imaged with a specific MR protocol, late enhancement MR, and are known to correspond to regions of very low conduction velocity. In the scene, we have decided to create synthetically an isthmus between two scars regions, which occurs frequently on patients suffering from VT. In this isthmus, represented in red in Figure 6, the propagation of electrical waves is also slowed down.



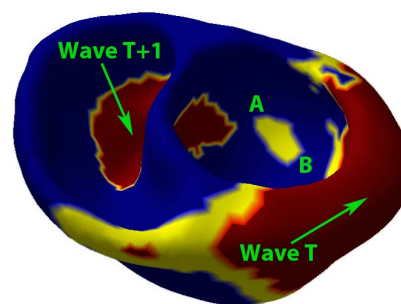
**Figure 6:** Conduction velocities of the myocardium. Zones in wireframe have normal conductivity while blue regions (scars) have very low values and red region (isthmus) has intermediate values.

To prevent fast heart beats and reentries, radio-frequency ablation has been shown to be an efficient therapy if performed properly [HUKS07]. During this procedure, catheters are used to permanently damage cardiac tissues with electromagnetic radiations having low voltage and frequencies in the radiofrequency range. When heated, the damaged tissue is no longer able to conduct electrical waves preventing the arrhythmia from occurring.

To simulate this pathology, a volumetric mesh of the right and left ventricles with scars has been generated from MRI images. This mesh is approximately composed of 10k vertices and 50k tetrahedra. Figure 6 shows the conductivity map on this mesh. Healthy tissues have a conduction velocity of  $50 \text{ cm}\cdot\text{s}^{-1}$  whereas the scar regions (in blue) have no conduction velocities and the isthmus (in red) has a conduction velocity of  $30 \text{ cm}\cdot\text{s}^{-1}$ .

### 4.2. Simulation Results

To display the electrophysiology simulations, we use a colour map from blue to red, to represent the electrophysiological state of each vertex. Depolarized vertices are set



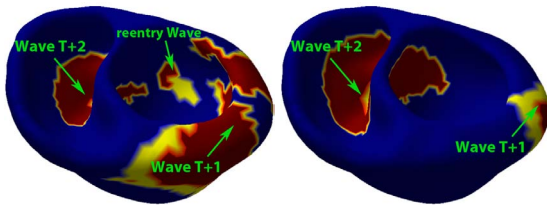
**Figure 7:** Electrophysiological wave propagation simulated with a multi-front Eikonal model. Successive waves are represented ( $T$  and  $T+1$ ) as well as isthmus boundaries (points  $A$  and  $B$ ).

to red, repolarized vertices to blue and refractory vertices to yellow. At the initialisation stage, all vertices are set to the repolarized state. Then, a stimulation is performed periodically at the apex of the right ventricle at a period of 300 ms to simulate a procedure called VT Stim. This procedure is performed to test the inducibility of ventricular tachycardia of a patient and decide whether a defibrillator should be implanted. The electrical wave resulting from the stimulation takes approximately 250 ms to traverse the two ventricles. These simulations are performed with a time step of 1 ms and we obtain a mean frame rate of 45 FPS.

Figure 7 shows the resulting wave propagation. As expected, the scars remain blue, since it is not conductive whereas the isthmus zone has a different behaviour than neighbouring healthy tissues. Indeed, the wave enters the isthmus through the upper side (point  $A$  in figure 7) and then exits by its lower bound (point  $B$ ). Then, due to different parameter values of the restitution curve, these vertices have a longer refractory period than healthy tissue. As a result, when the second wave (wave  $T+1$ ) reaches the upper bound of the isthmus, it can no longer go through this path. However, as the isthmus is no longer in refractory period when the second wave reaches the point  $B$ , it can then enter the isthmus through this point. This pattern is called a unidirectional block, and it can generate a reentry wave.

In ischemic VT, this reentry wave can turn around the scars through the isthmus and then create additional ventricular contractions leading to tachycardia. Non-sustained VT patterns (single reentries) could be simulated with specific patterns of stimulations. In those cases, when the wave  $T+1$  goes through the isthmus from the point  $B$ , on the other side (point  $A$ ), healthy tissues are already in repolarized state. Thus, when reaching the point  $A$ , the wave will be able to propagate into the heart, as it is the case in the right part of Figure 8, and potentially sustain itself by repeating this pattern.

A second set of tests has been performed to evaluate the



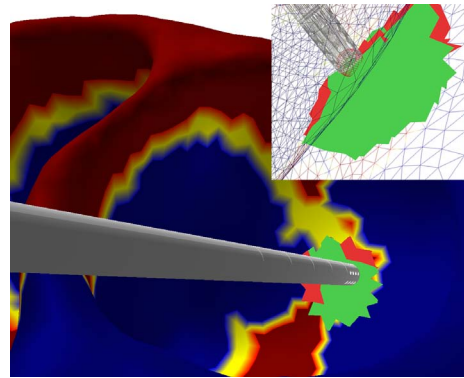
**Figure 8:** Potential wave propagations with different anisotropy ratios; (Right) isotropic propagation; (Left) 90% anisotropy propagation with a reentry wave at the top boundary of isthmus created by wave T+1.

importance of the anisotropy in those wave propagations. To this end, we modified the anisotropy ratio of conduction velocity in the anisotropy matrix  $\mathbf{D}$ . To quantify those changes, we used percentages, 0% meaning that we are in an isotropic case and 90% for realistic behaviour where the electrical propagation is roughly three times as fast along the fiber orientation than in its orthogonal direction. As expected, different anisotropy ratios lead to different conduction patterns. For instance, the left part of Figure 8 shows an isotropic potential propagation whereas the right figure shows a propagation with 90% anisotropy. In the anisotropic case, the propagation includes a reentry pattern while in the isotropic case no such pattern is observed. The anisotropic Fast Marching algorithm achieves a good accuracy even in strongly anisotropic cases.

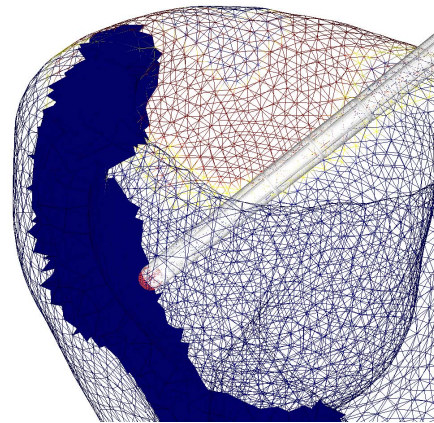
#### 4.3. Simulating radio-frequency ablation

Additionally to the simulation described above, we simulate interactively the radio-frequency ablation therapy. In this case, the aim is to close the isthmus in order to prevent reentry loops. Figure 9 is a screenshot of the interactive simulation while positioning the haptic device on the isthmus zone. The highlighted zone corresponds to the region impacted by the instrument, with green tetrahedra corresponding to healthy or isthmus tissues and red tetrahedra to scar tissues (with null conductivity). Adding collision detection and the prerecorded heart motion requires some additional computational time. Thus, we obtain for this simulation with a time step of 1 ms a mean frame rate of 15 FPS which is a bit lower than previous results but is still acceptable for interactive simulation.

With this setting, several radio-frequency ablations are performed around the isthmus in order to burn its tissue and get a large region with zero conduction velocity, as shown in blue in Figure 10, which blocks electric waves. To ensure that the path is completely blocked, stimulation can be performed during the intervention by actioning a pedal. By applying stimulations near the scars, one creates a new potential wave like in Figure 11 to check that the isthmus has been successfully ablated.



**Figure 9:** Simulation of radio-frequency ablation on the isthmus performed with a 3D user interface. The green zone corresponds to the tissues to be burned whereas the red zone represents tissues with no conductivity (scars).



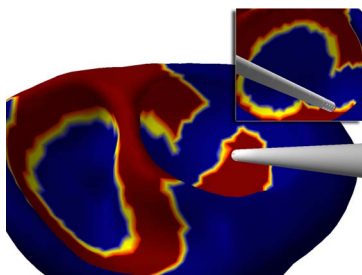
**Figure 10:** Wireframe representation of conduction velocity which reveals a large scar region (blue volume) resulting from the radio-frequency ablation.

A video clip describing the different stages of the simulation is provided as an electronic appendix.

#### 4.4. Discussion

To assess the accuracy of the simulation, it is possible to compare the simulated isochrone map with the one measured by catheters during the intervention using contact (i.e. the NavX or Carto systems) or non contact (such as the Ensite balloon) endocardial mappings. Further evaluation can be performed by comparing stimuli conditions for which one can induce VT.

In term of haptic simulation, no validation from clinicians can be performed at the moment since our prototype does not reproduce virtual catheter guidance to the heart, as it uses laparoscopic instruments for force feedback.



**Figure 11:** Potential waves propagation simulated after an ablation of the isthmus. Using the 3D user interface a stimulation is applied to generate a second wave near the isthmus.

## 5. Conclusion and perspectives

In this paper, an electrophysiology heart model based on an anisotropic multi-front Fast Marching Method has been presented. It provides a suitable means to represent in real-time the electrophysiological cardiac rhythm and its pathologies. This model has been coupled with pre-recorded realistic heart mechanical deformations and has been integrated in the open source framework SOFA, for which specific software components have been developed to handle the coupling between mechanical and electrophysiological behaviour.

Using a 3D user interface, we have presented a complete pipeline for the interactive simulation of cardiac radio-frequency ablation. A first prototype has been demonstrated for ischemic ventricular tachycardia where reentries may occur through an isthmus surrounded by scar regions. A 3D rigid instrument allows the user to interactively simulate radiofrequency ablation by zeroing the conduction velocity around intersected tetrahedra. The user can also apply focal stimulations to check the effect of ablations.

There are several ways to improve the realism of the current prototype. For instance, the electrophysiology model could be extended to better represent the pathological behaviour and to include patient specific restitution curves. Real-time coupling between mechanical deformations and electrophysiology propagations should be developed in order to provide additional realism. Finally, catheter navigation should be made more realistic by using interventional radiology force-feedback simulators.

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