Realistic simulation modeling for atrial fibrillation reflecting personal anatomy, histology, and electrophysiology
Background
Realistic modeling (Depended on extracellular field potential)의 시뮬레이션 모델이, 환자의 해부학/조직학/전기생리학 특성과 유사하다.
Progress (Realistic modeling)

Clinical Data → Voltage Mapping → Simulation Data → Fibrosis Map → LAT synchronization

CT Segmentation → Fiber Orientation Map

Probability (vol/k) = −40.0364v² + 1553.882v² − 206.327v + 99.76

Pashakhanloo F et al., 2016. Circ Arrhythm Electrophysiol

Clinical MAP Data → Realistic Modeling
Method: Voltage Map

Transporting to massive vertices mesh from clinical coordinates system and then extrapolation about the whole surface.

Clinical Voltage Data

Simulation Voltage Data

Low polygon mesh <20,000 vertices

Massive polygon mesh >400,000 vertices
Method: Fibrosis Map

Voltage P2P Map vs. Fibrosis Map

50% ↓ Inward rectifier potassium current [IK1]
50% ↓ L-type calcium current [ICaL]
40% ↓ Sodium current [INa]

Patient-derived models link re-entrant driver localization in atrial fibrillation to fibrosis spatial pattern, Sohail Zahid, 2016

Probability (volt) = 
\[-40.03648v^3 + 155.3882v^2 - 206.327v + 99.76\]

Fibrotic tissue
Resting Potential: -79.52mV

Non-Fibrotic tissue
Resting Potential: -84.32mV
Patient-derived models link re-entrant driver localization in atrial fibrillation to fibrosis spatial pattern, Sohail Zahid, 2016

Method: Fiber Orientation Map

Draw the yellow line for fiber orientation.

→ Interpolation each vector lines through the whole surface.

Monodomain conductivity (mS/mm)

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Longitudinal (σL, non-fibrotic)</td>
<td>0.1264</td>
</tr>
<tr>
<td>Longitudinal (σL, fibrotic)</td>
<td>0.0546</td>
</tr>
<tr>
<td>Transverse (σT, non-fibrotic)</td>
<td>0.0252</td>
</tr>
<tr>
<td>Transverse (σT, fibrotic)</td>
<td>0.0068</td>
</tr>
</tbody>
</table>
Method: Left Atrial Ion current mechanism & LAT Synchronization

Ionic mechanisms underlying human atrial action potential properties: insights from a mathematical model, Marc Courtemanche, 1998

<table>
<thead>
<tr>
<th>Ionic Currents</th>
<th>Model parameter</th>
<th>% change in PeAF from the control</th>
</tr>
</thead>
<tbody>
<tr>
<td>I(_{\text{Na}})</td>
<td>(g_{\text{Na}})</td>
<td>-10% [17]</td>
</tr>
<tr>
<td>I(_{\text{K}})</td>
<td>(g_{\text{K}})</td>
<td>-70%</td>
</tr>
<tr>
<td>I(_{\text{Ca,L}})</td>
<td>(g_{\text{Ca,L}})</td>
<td>-50% or -70%</td>
</tr>
<tr>
<td>I(_{\text{Kur}})</td>
<td>(g_{\text{Kur}})</td>
<td>-50%</td>
</tr>
<tr>
<td>SR leak</td>
<td>([\text{Ca}^{2+}]_{\text{L}}/\text{max})</td>
<td>-20%</td>
</tr>
<tr>
<td>I(_{\text{K1}})</td>
<td>(g_{\text{K1}})</td>
<td>+100%</td>
</tr>
<tr>
<td>I(_{\text{NOX}})</td>
<td>(g_{\text{NOX}})</td>
<td>+40%</td>
</tr>
</tbody>
</table>

Lee YS et al., 2016, PLoS ONE
Grandi E et al., 2011, Circulation Research
Sossalla S, et al., 2010, Journal of the American College of Cardiology

Initial stimulation
- Block area
- Normal cell

Calibration surface-to-volume ratio (Diffusion factor) referred to clinical LAT
\(S:\) Siemens \((1/\Omega)\)
Method: Reverse Engineering of MAP

Mono-phase Action Potential

Each sample has the data of randomized 20 ion channels.

500,000 samples

Match with database

Patient-specific ion parameter
More: Accelerated computing

1. Simplifying geometric information for the focusing on calculating ion mechanism. (e.g. FDM) <Boundary condition is Locked>

2. Using characterized lookup table of most high cost operation (e.g. Exponential, Logarithm..)

3. Heterogeneous CUDA parallel computing and own optimization

An Effective Finite Difference Method for Simulation of Bioheat Transfer in Irregular Tissues, Zhi Zhu He, 2013

Pipelined, Single Precision Floating-Point Logarithm Computation Unit in Hardware, Jing Chen, 2012

GPU-Accelerated Computing: What are the Perks for GNSS Simulation?, The Skydel Blog, Image
## Result (Computing Time)

**Compare Other Simulation tools**

<table>
<thead>
<tr>
<th>Number of Vertices</th>
<th>Processor</th>
<th>Tools</th>
</tr>
</thead>
<tbody>
<tr>
<td>754893</td>
<td>AMD Opteron 6234</td>
<td>MATLAB</td>
</tr>
<tr>
<td>1638120</td>
<td>Intel Xeon X5660</td>
<td>CARP (Johns Hopkins &amp; Bordeaux Univ.)</td>
</tr>
<tr>
<td>486548</td>
<td>Intel i5-6600 + GPU (Titan V)</td>
<td>CUVIA (CUDA)</td>
</tr>
</tbody>
</table>

**Elapsed time to simulate 1 second**

- MATLAB: 185.분
- CARP: 47.33분
- Proposed SW (CUVIA): 1.8분

*Within 30 minutes*
Effectiveness of atrial fibrillation rotor ablation is dependent on conduction velocity: An in-silico 3-dimensional modeling study, Byoungyun Lim, 2017

1 September
2 Anterior wall
3 Left Atrial Appendage
4 Peri-mitral area
5 Posterior Inferior wall
6 Roof
7 LSPV
8 LIPV
9 RSPV
10 RIPV

Before CPVI

After CPVI

PAF(n=5)  PeAF(n=7)  PAF(n=2)  PeAF(n=3)

Clinical

Virtual
Effectiveness of atrial fibrillation rotor ablation is dependent on conduction velocity: An in-silico 3-dimensional modeling study, Byoungyun Lim, 2017

Region type and mean voltage

<table>
<thead>
<tr>
<th>Region Type</th>
<th>Clinical (mV)</th>
<th>Virtual (mV)</th>
<th>R</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Septum</td>
<td>1.22193 ±0.4</td>
<td>1.13281 ±0.36</td>
<td>0.9396</td>
<td>2.22E-08</td>
</tr>
<tr>
<td>Anterior Wall</td>
<td>1.63168 ±0.91</td>
<td>1.61598 ±0.77</td>
<td>0.9501</td>
<td>5.46E-09</td>
</tr>
<tr>
<td>LAA</td>
<td>3.37487 ±1.27</td>
<td>3.35841 ±1.34</td>
<td>0.9555</td>
<td>2.34E-09</td>
</tr>
<tr>
<td>Peri-mitral area</td>
<td>1.40044 ±0.85</td>
<td>1.38453 ±0.74</td>
<td>0.9276</td>
<td>1.02E-06</td>
</tr>
<tr>
<td>Posterior Inferior Wall</td>
<td>1.48904 ±0.65</td>
<td>1.64671 ±0.6</td>
<td>0.9429</td>
<td>1.47E-08</td>
</tr>
<tr>
<td>Roof</td>
<td>2.13586 ±1.23</td>
<td>2.35711 ±1.33</td>
<td>0.9850</td>
<td>7.45E-13</td>
</tr>
<tr>
<td>LSPV</td>
<td>1.05896 ±0.73</td>
<td>0.94845 ±0.5</td>
<td>0.9431</td>
<td>1.44E-08</td>
</tr>
<tr>
<td>LIPV</td>
<td>0.63907 ±0.47</td>
<td>0.49472 ±0.37</td>
<td>0.7270</td>
<td>9.44E-04</td>
</tr>
<tr>
<td>RSPV</td>
<td>0.77790 ±0.67</td>
<td>0.59504 ±0.56</td>
<td>0.9419</td>
<td>1.67E-08</td>
</tr>
<tr>
<td>RIPV</td>
<td>1.01687 ±0.8</td>
<td>0.80089 ±0.8</td>
<td>0.9528</td>
<td>3.64E-09</td>
</tr>
<tr>
<td>n=17</td>
<td></td>
<td>0.9466 ±0.07</td>
<td>&lt;.0009</td>
<td></td>
</tr>
</tbody>
</table>

n=17
Left atrial fibrosis quantification by late gadolinium-enhanced magnetic resonance: a new method to standardize the thresholds for reproducibility
Eva M. Benito, 2017
Result: Clinical Trial

Clinical Map

Mapping Fiber Orientation

Synchronize LAT map with adjust CV

Mesh volt mapping via clinical catheter volt

CPVI+V-Rotor ABL VS. Empirical ABL

Randomization

Clinicaltrials.gov. NCT2171364
Summary

Anatomy

Histology

Electrophysiology

Realistic AF Modeling (CUVIA AF II)

Virtual ABL

Virtual AAD

Basic Studies
Transformed paced clinical bipolar voltage and activation maps (300~500 points) to virtual bipolar voltage map (VVM) and virtual activation map (half million nodes). (r=0.95±0.07, p<0.0009).

Implemented of a fiber orientation in based prevailing knowledge and determined of overall fibrosis to spatiotemporal distribution using inverse non-linear relationship. (R=0.9876, p-value=0.017).

AF simulating of patient who pre-planned ablation procedure was successfully induced by ramp pacing and sustained for longer than 6 s in all cases.

Our operation was proceed 1 second simulation time within reality 120 second and analyzed PS(Phase Singularity) and DF(Dominant Frequency) data within 30 minutes about all progress sequence.
• We developed realistic simulation modeling for AF reflecting personal anatomy, histology, and electrophysiology by utilizing bipolar map and MAP recordings acquired during ablation procedure. This high performance modeling would enable patient-specific virtual intervention or virtual drug therapy in the future after further validation.