Electrophysiological significance of the inter-atrial conduction during atrial fibrillation: *in silico* modeling study

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Background: Atrial Fibrillation

- Projected prevalence rate of Korean population

- AF population in US

AF prevalence in Korea and US:
* 1.5~2.9% in 2015
* 5.6~5.8% in 2060

Background: Role of AF maintenance of LA

- LA: important role of AF induction & maintenance

Developmental, anatomical, and electrophysiological differences between the LA and RA

What about the role of IAC in AF maintenance?

- Inter-atrial conduction (IAC), the septum ablation improves the rhythm outcome.

→ It is unclear how the IAC contribute to AF maintenance mechanism.
→ “Can we predict these AF treatment outcomes?”
Cardiac simulation modeling

- Human cardiac AF modeling


Why we cannot apply simulation modeling to the clinical medicine?

→ Computing time
Purpose of this study

- To improve the computing time and simulation accuracy using customize software CUVIA.

- To evaluate the effect of additional interataial conduction (IAC) ablation after PVI on AF wave dynamics represented by the DF integrated with the patient’s cardiac imaging and realistic modeling.

- We observed AF wave dynamics by blocking the IAC, which was composed of BB, PS, AS, and CTI.

* BB: Bachmann’s bundle
* PS: Posterior septal conduction
* AS: Anterior septal conduction
* CTI: cavo-tricuspid isthmus
Method: 3D modeling

3D Biatrial Modeling

- Patient’s CT images are merged (10 AF patients, 64.9±10.1 years)
- 3D mesh generation by the customized software (CUVIA).
- Triangular type mesh 650,000~850,000 nodes.
Coordinate APD and CV based on Yonsei AF ablation cohort (n=3,030), the clinical mapping data.
Voltage map from clinic to virtual model

Using clinically acquired 400~1500 voltage points, we interpolated these voltage values on the surface of 3D model.

Clinical Voltage Data

Simulation Voltage Data

Low polygon mesh <20,000 vertices

Massive polygon mesh >400,000 vertices
Virtual Fibrosis modeling

- Fibrosis formation

Clinical voltage map

Degree of Fibrosis

\[
\text{Probability (voltage)} = -40.03648v^3 + 155.3882v^2 - 206.327v + 99.76
\]

Clinical vs Virtual Data (Voltage map & LAT)

A. Voltage maps

Clinical voltage map

Virtual voltage map

B. Local activation time (LAT) maps

Clinical local activation map

Virtual local activation map

C. Comparison of clinical and virtual voltage

R=0.962

D. Correlation of clinical and virtual LAT

R=0.908
Computing Time

1. **GPU based simulation** - parallel computing system

   Time required for 1-sec simulation of our model
   - 123 min
   - 1.2 min

2. **30-fold faster PS calculation time**
AF Simulation time in Core Lab Team

Successfully analysis within 50 minutes

Clinical Data

Patient CT images

Clinical Data

Virtual voltage map

Fiber Orientation

Fibrosis Map

Ablation line

CPVI   BB
PS    CTI

Area around IAC (blue)

pre-Ablation

post-Ablation

Report the virtual wavedynamic maps
### Cutting edge virtual AF simulation

<table>
<thead>
<tr>
<th>Reference</th>
<th>Geometry</th>
<th>Heterogeneous atrial characteristics</th>
<th>Computing time to simulate 1 sec</th>
</tr>
</thead>
</table>
| Trayanova et al. [a] | MRI-derived (CARP software since 2003 *)
Electrical mesh generation from MRI                                   | Fiber orientation (image-based estimation) Fibrosis acquired from MRI       | 47.33 min (Intel X5660 CPU, 1,638,120 nodes)                |
| Roney et al. [b]   | MRI-derived (using MUSIC software †) SA node structure applied Bilayer model | Fiber orientation Fibrosis modeling                                         | NA                                                         |
| Loewe et al. [c]   | MRI-derived Homogeneous wall thickness (2.5-3mm) Bilayer model             | Fiber orientation (Patient-specific)                                        | NA                                                         |
| Jacquemet et al. [d]| Geometry from patient’s imaging Cubic mesh formation Uniform wall thickness | Fiber orientation (Patient-specific)                                        | NA                                                         |
| Our Lab.          | CT-based geometry Monolayer model                                         | Fiber orientation (image-based estimation) Fibrosis acquired from clinical voltage map | 1.2 min (Intel i5 6600 + GPU TitanV)                        |

→ We are able to conduct prospective ablation studies because of fast computing time.

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* CARP: Cardiac arrhythmias research package
† MUSIC: Multi-modality Platform for Specific Imaging in Cardiology

**Result: Virtual ablation outcome**

### Ablation outcomes in 10 patients

<table>
<thead>
<tr>
<th>Ablation protocol</th>
<th>No. of episodes</th>
<th>No. of ablation lines</th>
<th>AF maintenance</th>
<th>AF termination or AT conversion</th>
<th>AF termination</th>
</tr>
</thead>
<tbody>
<tr>
<td>de novo AF induction</td>
<td>10</td>
<td>0</td>
<td>50% (5/10)</td>
<td>50% (5/10)</td>
<td>20% (2/10)</td>
</tr>
<tr>
<td>CPVI alone</td>
<td>10</td>
<td>2</td>
<td>50% (5/10)</td>
<td>50% (5/10)</td>
<td>30% (3/10)</td>
</tr>
<tr>
<td>Additional IAC ablation</td>
<td>70</td>
<td>3.7±0.7</td>
<td>26% (18/70)</td>
<td>74% (52/70)</td>
<td>59% (41/70)</td>
</tr>
<tr>
<td>CPVI+PS</td>
<td>10</td>
<td>3</td>
<td>30% (3/10)</td>
<td>70% (7/10)</td>
<td>40% (4/10)</td>
</tr>
<tr>
<td>CPVI+BB</td>
<td>10</td>
<td>3</td>
<td>50% (5/10)</td>
<td>50% (5/10)</td>
<td>20% (2/10)</td>
</tr>
<tr>
<td>CPVI+PS+BB</td>
<td>10</td>
<td>4</td>
<td>30% (3/10)</td>
<td>70% (7/10)</td>
<td>30% (3/10)</td>
</tr>
<tr>
<td>CPVI+CTI</td>
<td>10</td>
<td>3</td>
<td>30% (3/10)</td>
<td>70% (7/10)</td>
<td>70% (7/10)</td>
</tr>
<tr>
<td>CPVI+CTI+PS</td>
<td>10</td>
<td>4</td>
<td>10% (1/10)</td>
<td>90% (9/10)</td>
<td>90% (9/10)</td>
</tr>
<tr>
<td>CPVI+CTI+BB</td>
<td>10</td>
<td>4</td>
<td>20% (2/10)</td>
<td>80% (8/10)</td>
<td>80% (8/10)</td>
</tr>
<tr>
<td>CPVI+CTI+PS+BB</td>
<td>10</td>
<td>5</td>
<td>10% (1/10)</td>
<td>90% (9/10)</td>
<td>80% (8/10)</td>
</tr>
<tr>
<td>Ablation without a CTI</td>
<td>50</td>
<td>2.4±1.4</td>
<td>42% (21/50)</td>
<td>58% (29/50)</td>
<td>28% (14/50)</td>
</tr>
<tr>
<td>Ablation with a CTI</td>
<td>40</td>
<td>4.0±0.7</td>
<td>17% (7/40)*</td>
<td>83% (33/40)*</td>
<td>80% (32/40)†</td>
</tr>
</tbody>
</table>

* p=0.021 vs. ablation without a CTI; † p<0.001 vs. ablation without a CTI;

Result: DF depending on ablation conditions

A. DF values of baseline, CPVI, and IAC ablation

B. DF values with or without CTI ablation

* IAC: Interatrial conduction
Result: Example of 8 different virtual ablation strategies
We analyzed the role of the IAC in maintaining AF using 3D biatrial modeling reflected by the patients’ cardiac imaging.

We demonstrated in a 3D biatrial model that the IAC contributes to the maintenance mechanism of AF.

Patient-specific realistic AF modeling, reflecting the degree of fibrosis, activation pattern, and fiber orientation, was performed.

Virtual AF was induced based on a highly efficient computing algorithm (1.2-min calculation times for 1-s AF simulation).
Conclusion

The IAC contributes to the maintenance mechanisms of AF, and IAC including the CTI ablation significantly affects the wave dynamics of AF, especially the DF of the LA, facilitating the AF termination or AT conversion after a CPVI in 3D-biatrial modeling.

This high-performance model would enable a patient-specific virtual intervention or virtual drug therapy after further validation.
Thank you for your attention.
### Patients Characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years (Mean ± SD)</td>
<td>64.9 ± 10.1</td>
</tr>
<tr>
<td>&gt; 75 years old</td>
<td>1 (30%)</td>
</tr>
<tr>
<td>65-74 years old</td>
<td>4 (20%)</td>
</tr>
<tr>
<td>Male</td>
<td>9 (90%)</td>
</tr>
<tr>
<td>CHA2DS2-VASc score</td>
<td>1.30 ± 1.27</td>
</tr>
<tr>
<td>Paroxysmal AF</td>
<td>10 (100%)</td>
</tr>
<tr>
<td>Heart failure</td>
<td>1 (10%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>4 (40%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1 (10%)</td>
</tr>
<tr>
<td>Previous stroke</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Previous TIA *</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Vascular disease</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Left atrium dimension</td>
<td>39.6 ± 5.5 mm</td>
</tr>
<tr>
<td>Ejection fraction</td>
<td>62.0 ± 18.5 %</td>
</tr>
<tr>
<td>E/Em †</td>
<td>9.2 ± 4.6</td>
</tr>
</tbody>
</table>

* TIA, transient ischemic attack;

† E/Em, ratio of early diastolic mitral inflow velocity (E) to early diastolic mitral annular velocity (Em).