Noninvasive Detection of Coronary Artery Disease Using Resting Phase Signals and Advanced Machine Learning

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Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship
• None

Company
• None
Background

- *Artificial intelligence (AI)* techniques are increasingly being applied to cardiovascular (CV) medicine, yielding diagnostic tools that may significantly enhance the care of cardiac patients.

- *Cardiac Phase Space Tomography Analysis (cPSTA)* is a novel technology that employs machine learning to assess the presence of significant coronary artery disease (CAD).
Utilization of the *cardiac* Phase Space Tomography Analysis (cPSTA) System

1. **cPSTA System Scan**
   - The phase signals emitted by the heart are scanned while the patient is lying down.

2. **Data Transfer**
   - The patient’s data is automatically transferred to the cloud using Wi-Fi or cellular data connection.

3. **Cloud Computing**
   - Advanced mathematics and machine-learned algorithms transform and analyze the data.

4. **Physician Portal**
   - Imaging results from the scan are available in a secured web portal for interpretation.
Phase Space Tomography

Solid Appearing Uniform in Nature

Contains Arcs Angulation in Space

CAD-

CAD+
CADLAD is an ongoing prospective, multicenter, non-significant risk study sponsored by Analytics 4 Life designed to:

1. Develop machine-learned algorithms to assess the presence of CAD (defined as one or more ≥ 70% stenosis, or fractional flow reserve < 0.80)

2. Test the accuracy of these algorithms prospectively in a verification cohort
CADLAD Study Locations
Methods
Stage I of the CADLAD Trial

Gold Standard
Coronary Angiogram

Paired Data
(Clinical & Phase Signal)

Mathematical feature extraction

Machine Learning
(genetic algorithms, neural networks)

Algorithms
Embedded into cPSTA System

Naïve Phase Signal Data

cPSTA Result

Verify

Coronary Angiogram Result

VS.
The Stage I Cohort

606 phase signals were obtained from subjects at rest, just prior to angiography.

Angiographic results were paired with phase signal data.

A training set of 512 subjects were used for machine learning.

A verification set of 94 subjects was reserved for blind testing.
## Demographics of Population

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Development (n=512)</th>
<th>Test (n=94)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age - Years (Range)</td>
<td>61.5 ± 10.7</td>
<td>59.0 ± 9.8</td>
<td>0.04</td>
</tr>
<tr>
<td>Male (%)</td>
<td>60.2%</td>
<td>69.1%</td>
<td>NS</td>
</tr>
<tr>
<td>Female (%)</td>
<td>39.8%</td>
<td>30.9%</td>
<td>NS</td>
</tr>
<tr>
<td>Mean BMI (Range)</td>
<td>31.3 ± 7.0</td>
<td>32.5 ± 7.6</td>
<td>NS</td>
</tr>
<tr>
<td>Diabetes Mellitus (%)</td>
<td>31.4%</td>
<td>35.1%</td>
<td>NS</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>72.9%</td>
<td>75.5%</td>
<td>NS</td>
</tr>
<tr>
<td>Hypercholesterolemia/Hyperlipidemia (%)</td>
<td>71.3%</td>
<td>70.2%</td>
<td>NS</td>
</tr>
<tr>
<td>CAD Negative (%)</td>
<td>69.1%</td>
<td>73.4%</td>
<td>NS</td>
</tr>
<tr>
<td>CAD Positive (%)</td>
<td>30.9%</td>
<td>26.6%</td>
<td>NS</td>
</tr>
</tbody>
</table>

*All comparisons of p-values were greater than 0.05 except AGE which was p=0.04*
AUC-ROC Curve for cPSTA Assessment of CAD

CADLAD Stage I

<table>
<thead>
<tr>
<th>Metric</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of subjects (total signals)</td>
<td>606</td>
</tr>
<tr>
<td>Number of subjects for ML Training Cohort</td>
<td>512</td>
</tr>
<tr>
<td>Number of subjects in Validation Cohort</td>
<td>94</td>
</tr>
<tr>
<td>AUC-ROC Curve</td>
<td>0.80</td>
</tr>
</tbody>
</table>

(Sn 92%, Sp 62%)
## Results

### CADLAD Stage I

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity Range</th>
<th>Specificity Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>CADLAD (n=94)</td>
<td>92% (CI=74% to 100%)</td>
<td>62% (CI=51% to 74%)</td>
</tr>
<tr>
<td>Exercise SPECT(^1)</td>
<td>73 to 92%</td>
<td>63 to 87%</td>
</tr>
<tr>
<td>Exercise ECG(^1)</td>
<td>45 to 50%</td>
<td>85 to 90%</td>
</tr>
</tbody>
</table>

\(^1\) Eur Heart J, 2013. 34(38): p. 2949-3003

*Negative Predictive Value for CADLAD was 96% (CI=85% to 100%)*
Conclusions

The findings of Stage I of the CADLAD trial demonstrate:

• Features extracted from phase signals can be employed in machine learning to develop final mathematical predictors that assess the presence of significant CAD

• Performance of the cPSTA is comparable to the most commonly employed functional test of MPI

• Acquisition of phase signals:
  ▪ Requires no ionizing radiation or contrast
  ▪ Requires no physiologic or pharmacologic stress
  ▪ Requires minimal patient time
  ▪ No safety issues were observed (no AEs in 606 procedures)

• The cPSTA System holds promise for value-based healthcare
Thank You