Multiparametric QI Biomarker Measures: Plaque Morphology Example

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Plaque Morphology Example

1. Clinical Context of Use
2. Multi-dimensional descriptor
3. Readings as predictors in ML models:
   a) Classify phenotype
   b) Predict outcome
4. Beyond readings-based ML to image-based DL:
   a) Keeping it a biomarker by retaining a truth standard
   b) Avoiding a black-box by objective validation of intermediates
Clinical Context of Use

- CVD encompasses stroke, peripheral artery disease, and coronary artery disease.
- It is the most common cause of death and disability worldwide.
- The pathogenesis often manifests as circulating blood lipids evoking an inflammatory response and accumulating substances in and on walls.
- Lumenography is common across modalities, but the disease is in the wall. This results in overtreatment, missed cases, and lack of specificity as to optimal pharmacology.
- Clinical guidelines need robust biomarker measurements and models that combine them to classify phenotype, determine mechanism, and predict outcome.

Multi-dimensional Descriptor

Panel of individual, but related, biomarkers, each of importance:

<table>
<thead>
<tr>
<th>Measurement of</th>
<th>Units</th>
<th>Truth standard</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lumen Area</td>
<td>mm²</td>
<td>Phantom</td>
</tr>
<tr>
<td>Wall Area</td>
<td>mm²</td>
<td>Phantom</td>
</tr>
<tr>
<td>Maximum Wall Thickness</td>
<td>mm</td>
<td>Phantom</td>
</tr>
<tr>
<td>Plaque Burden</td>
<td>ratio</td>
<td>Phantom or histology</td>
</tr>
<tr>
<td>Calcified Area</td>
<td>mm²</td>
<td>Histology</td>
</tr>
<tr>
<td>LRNC Area</td>
<td>mm²</td>
<td>Histology</td>
</tr>
</tbody>
</table>
Readings as Predictors in ML

Classify Phenotype / Select Therapy

Predict Outcome / Stratify Risk

Beyond Readings-based ML to Image-based DL

**Keeping it a biomarker by retaining a truth standard**

1. Unsupervised clustering is a useful discovery tool, but supervised learning better suits biomarker validation. We use supervised.
2. Classification using a scheme defined apart from radiology keeps us grounded objectively. We use a reduced set of subtypes where subtypes fall within (rather than across) pathologist types.

**Avoiding a black-box by objective validation of intermediates**

1. Validating at intermediate points both enables use of reasonable size training sets while simultaneously increasing confidence that it will generalize to new patients.
2. Validating intermediate calculations from a truth basis ≥10x resolution of radiology, or otherwise being apart from imaging, with granularity higher than what radiology can do.