Regional Cardiac Blood Flow with Air Particle Exposure

John J. Godleski, M.D.
Harvard School of Public Health
Specific Aims

• To assess mechanisms by which exposure to ambient particles exacerbate myocardial ischemia during acute coronary occlusion through assessment of regional myocardial blood flow.

• To evaluate the role of the autonomic nervous system in regulation of regional myocardial blood flow with coronary occlusion and exposure to ambient particles.
Harvard Ambient Particle Concentrator, Inhalation Chamber and Monitoring Methods

- Size Selective Inlet, PM 2.5
- Stage One
- Stage Two
- Stage Three
- Exposure Chamber

**Ambient Monitors**
- Continuous CO
- MOI/ Size Distribution
- Ambient Mass
- Honeycomb Denuder
- Sulfate Cassette
- Endotoxin Cassette

**Stage & Chamber Monitors**

**Chamber Monitors**
- B/C Aethalometer
- TEOM
- EC/OC Quartz Filter
- Chamber Mass
- Elemental Cassette
- Sulfate Cassette
- Nitrate Cassette
- Endotoxin Cassette
Inhalation chamber setup and physiologic monitors
Canine Myocardial Ischemia Model

- Implantation of a balloon occluder for coronary artery occlusion
- Two - 5 min occlusions after each CAPs or sham exposure
## Exposure Protocol

<table>
<thead>
<tr>
<th>Day</th>
<th>Dog 1</th>
<th>Dog 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Filtered Air</td>
<td>Filtered Air</td>
</tr>
<tr>
<td>2</td>
<td>CAPs</td>
<td>Filtered Air</td>
</tr>
<tr>
<td>3</td>
<td>Filtered Air</td>
<td>CAPs</td>
</tr>
<tr>
<td>4</td>
<td>Filtered Air</td>
<td>Filtered Air</td>
</tr>
</tbody>
</table>

**CAPs = Concentrated Air Particles**
Myocardial Ischemia is Enhanced by CAPs
Peak ST-Segment Elevation

Wellenius et al. *EHP* 2003
Canine Myocardial Ischemia Model

Supply: myocardial blood flow

Demand: myocardial work

HR x BP
To assess mechanisms by which exposure to ambient particles exacerbate myocardial ischemia during acute coronary occlusion through assessment of regional myocardial blood flow.

**Hypothesis:** CAPs exposure results in coronary vasoconstriction and decreased collateral blood flow to the area of ischemia.

**Model:** Dogs with coronary occlusion

**Treatments:** CAPs
- Filtered Air -- Sham

**Outcomes:** Changes in cardiac blood flow using fluorescent microspheres assessing areas of ischemia, adjacent areas, and remote areas
- Preexposure normal flow
- Flow during occlusion
- Post exposure flow
- ECG and blood pressure by telemetry

**Statistics:** Comparisons of anatomic areas
- Size of ischemic area
- Flow to ischemic area
- Comparisons of Heart rate, BP, and Myocardial work
Fluorescent Microspheres for Regional Blood Flow Measurement

- 15 µm spheres
- 8 colors
- 400 microspheres per tissue piece
  
  - N min – 400(n) [Q organ/Q total]
    - N min – minimum number needed for injection
    - N – total number of organ pieces
    - [Q organ / Q total] = fraction of total cardiac output supplying the organ

- Recovery from tissue pieces and blood samples
  - Potassium hydroxide tissue digestion
- Filtration
- Extraction of dyes
- Read in spectrofluorometer
- Calculate flow to each piece in ml/gm/min
### Different Colors Permit Multiple Measures In the same Animal

<table>
<thead>
<tr>
<th>Color</th>
<th>Excitation (nm)</th>
<th>Emission (nm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blue</td>
<td>360</td>
<td>423</td>
</tr>
<tr>
<td>Blue-Green</td>
<td>420</td>
<td>467</td>
</tr>
<tr>
<td>Green</td>
<td>450</td>
<td>488</td>
</tr>
<tr>
<td>Yellow-Green</td>
<td>495</td>
<td>506</td>
</tr>
<tr>
<td>Orange</td>
<td>534</td>
<td>552</td>
</tr>
<tr>
<td>Red</td>
<td>566</td>
<td>598</td>
</tr>
<tr>
<td>Crimson</td>
<td>610</td>
<td>635</td>
</tr>
<tr>
<td>Scarlet</td>
<td>646</td>
<td>680</td>
</tr>
</tbody>
</table>

Optimal Excitation and Emission Wavelengths of FluoSpheres® in 2-ethoxyethyl acetate
Coronary Artery Flow Patterns with Microspheres

Pre Occlusion

During Occlusion of LAD

Base Apex

Microspheres/Gram

- 1000+
- 500 - 1000
- 100 - 500
- 0 - 100
Quantification of Cardiac Blood Flow Pre-occlusion, Occlusion and Occlusion with Vasodilator

Evenness Index: Microspheres/piece
Total Microspheres/Heart

Data Grouped by Distribution with Occlusion
To evaluate the role of the autonomic nervous system in regulation of regional myocardial blood flow with coronary occlusion and exposure to ambient particles.

**Hypothesis:** CAPs exposure results in coronary vasoconstriction via the sympathetic nervous system resulting in decreased collateral blood flow to the area of ischemia.

**Models:** Dogs with coronary occlusion, Stellectomy, parasympathetic antagonists

**Treatments:** CAPs vs Filtered Air -- Sham

**Outcomes:** Changes in cardiac blood flow using fluorescent microspheres assessing areas of ischemia, adjacent areas, and remote areas

- Preexposure normal flow, Flow during occlusion, and Post exposure flow
- ECG and blood pressure by telemetry

**Statistics:** Comparisons of anatomic areas

- size of ischemic area
- flow to ischemic area

Comparisons of Heart rate, BP, and Myocardial work