

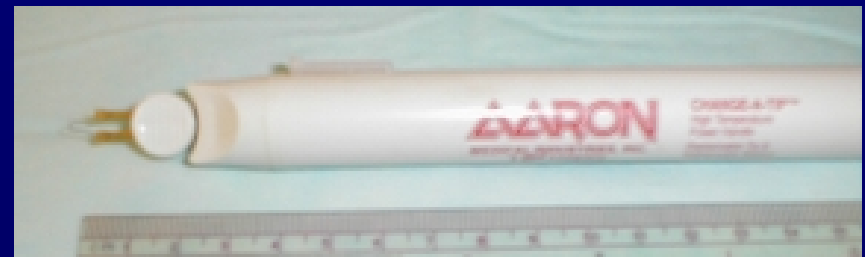
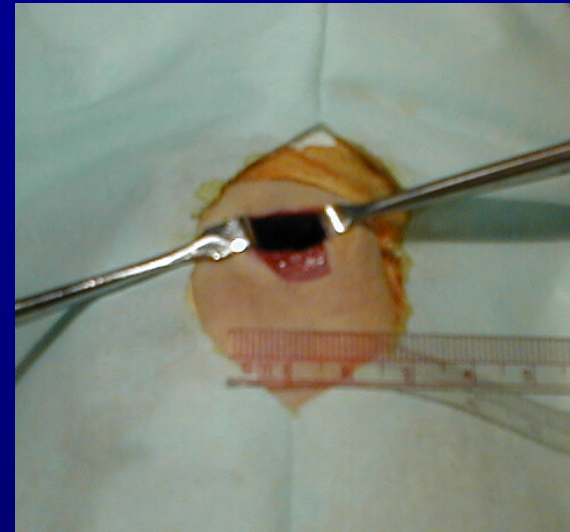
Particle toxicity and pollutant gas/particle
interactions in a rat model of acute
myocardial infarction

John Godleski, MD

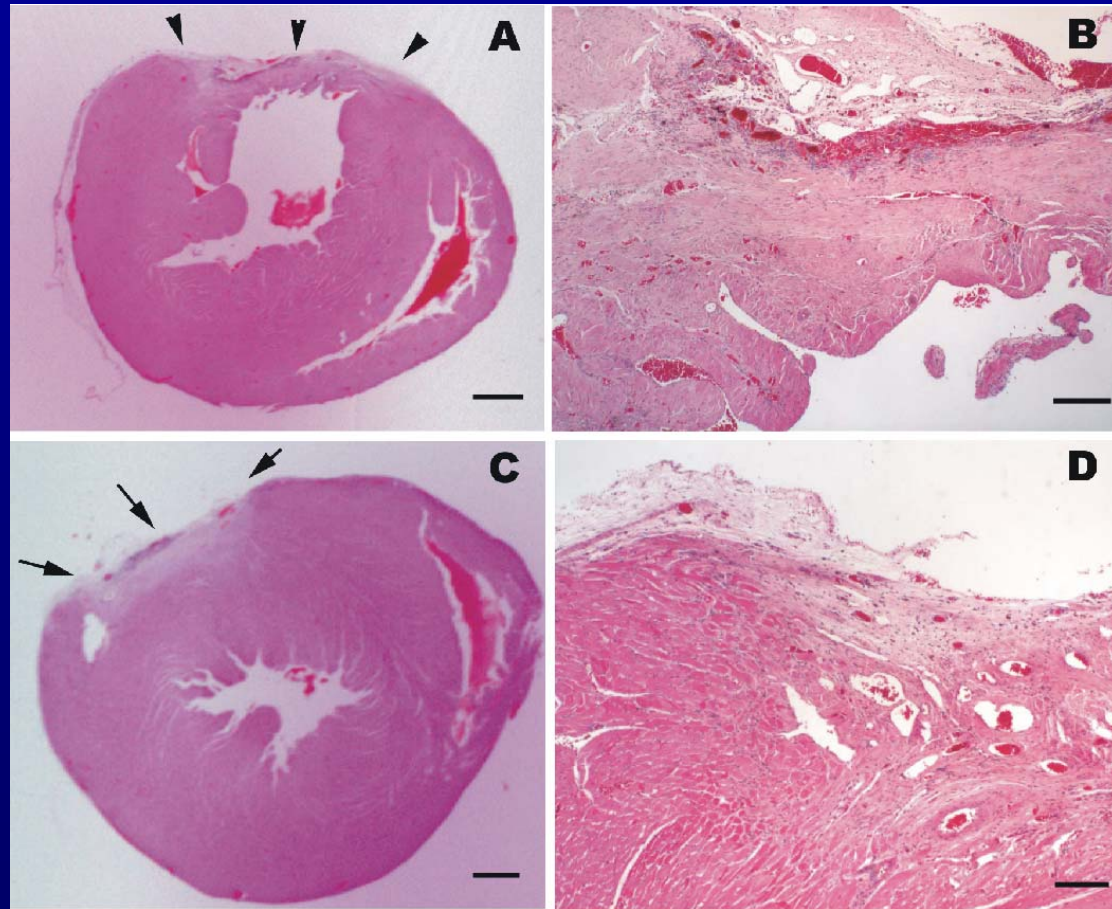
Harvard School of Public Health

Rat Model of Acute MI

- Perform left thoracotomy to expose heart.
- Cauterize left main coronary artery to induce MI.
- Close chest.

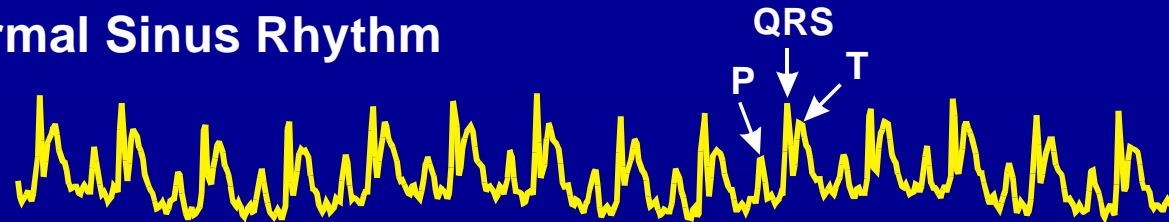


Surgical Outcomes

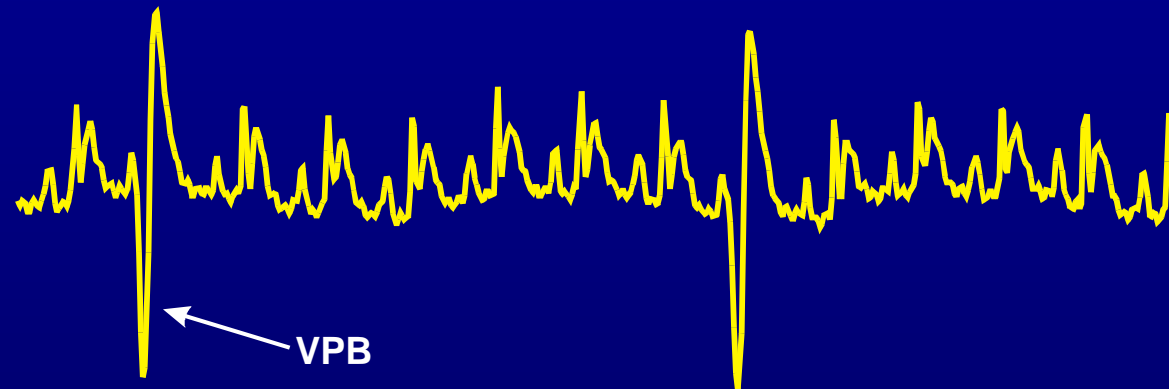


Sample ECG

Normal Sinus Rhythm



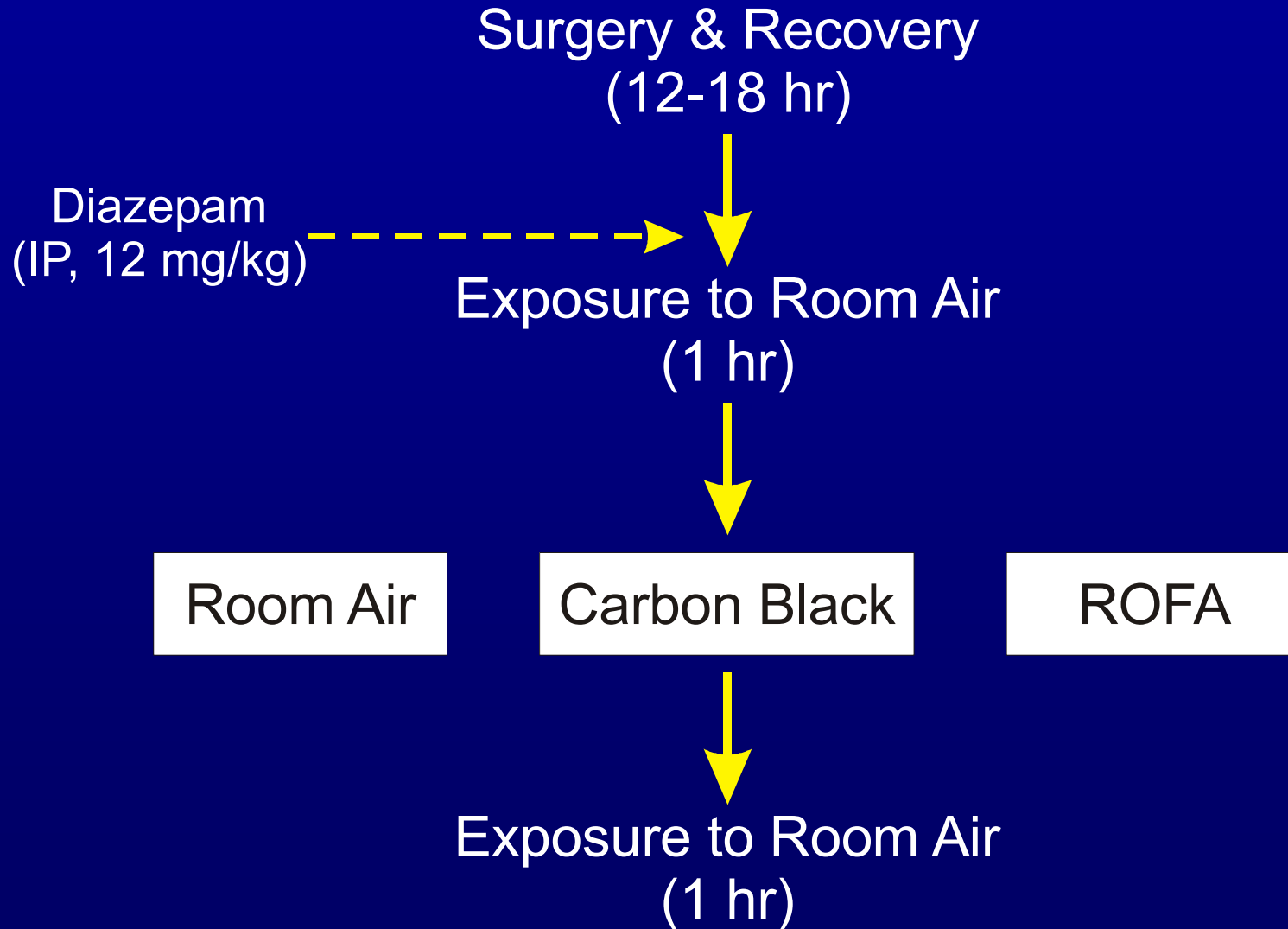
Ventricular Premature Beats



Atrioventricular Block



Experimental Design



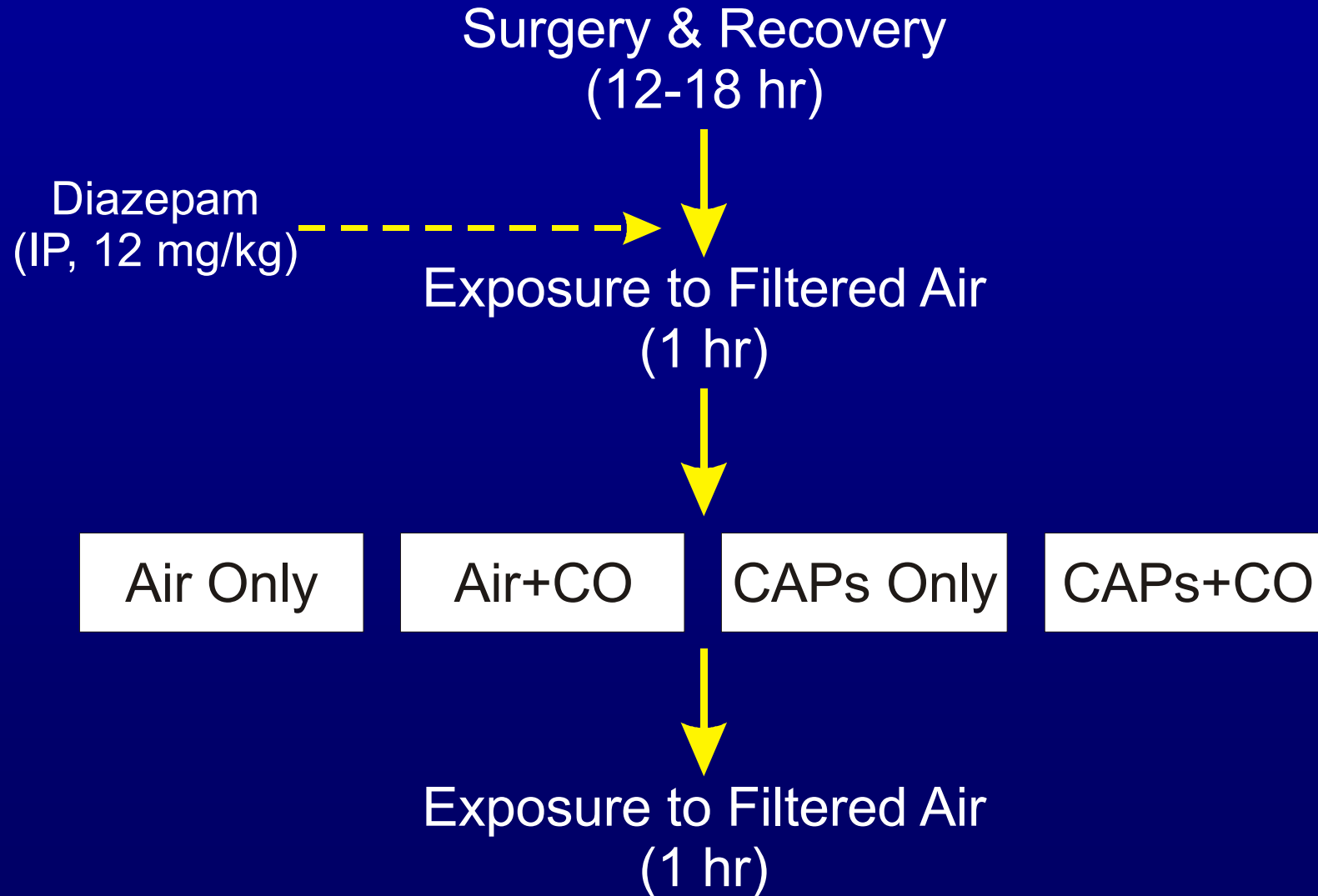
Change in VPB Frequency During Exposures as Compared to Room Air

| Exposure | % Δ | 95% CI | p |
|-----------------|------------------------------|---------------|----------|
| ROFA | ↑ 566.7% | 185.4, 1457.2 | <0.0001 |
| Carbon Black | ↓ 52.3 | -90.6, 140.5 | 0.37 |

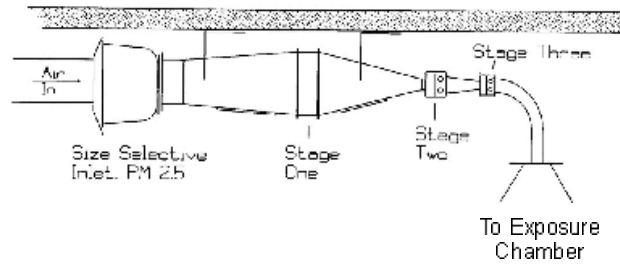
Study Hypotheses

1. Exposure to CAPs will increase arrhythmia incidence
2. Exposure to low levels of CO will increase arrhythmia incidence
3. Exposure to a combination of CAPs and CO will synergistically increase arrhythmia incidence

Experimental Design

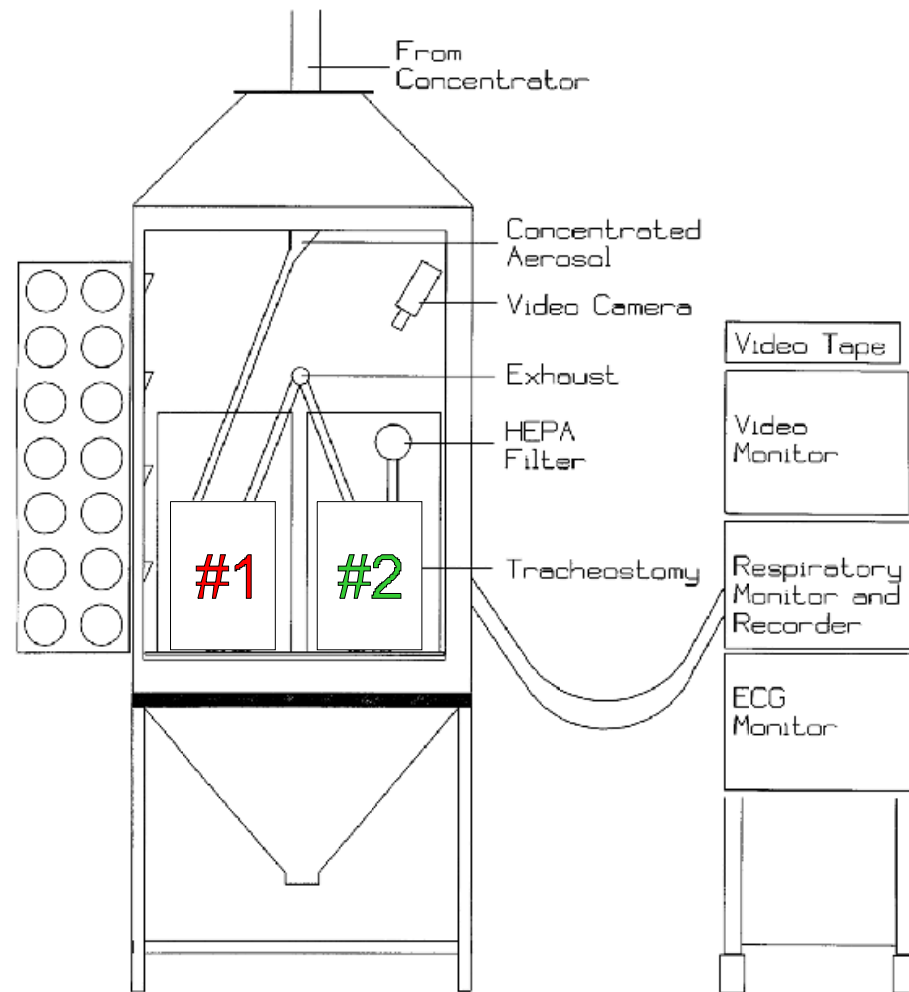


Harvard Ambient Particle Concentrator



CAPs:

- $PM_{2.5}$
- Concentration is ~30x ambient
- Composition is same as ambient



Exposure Characterization

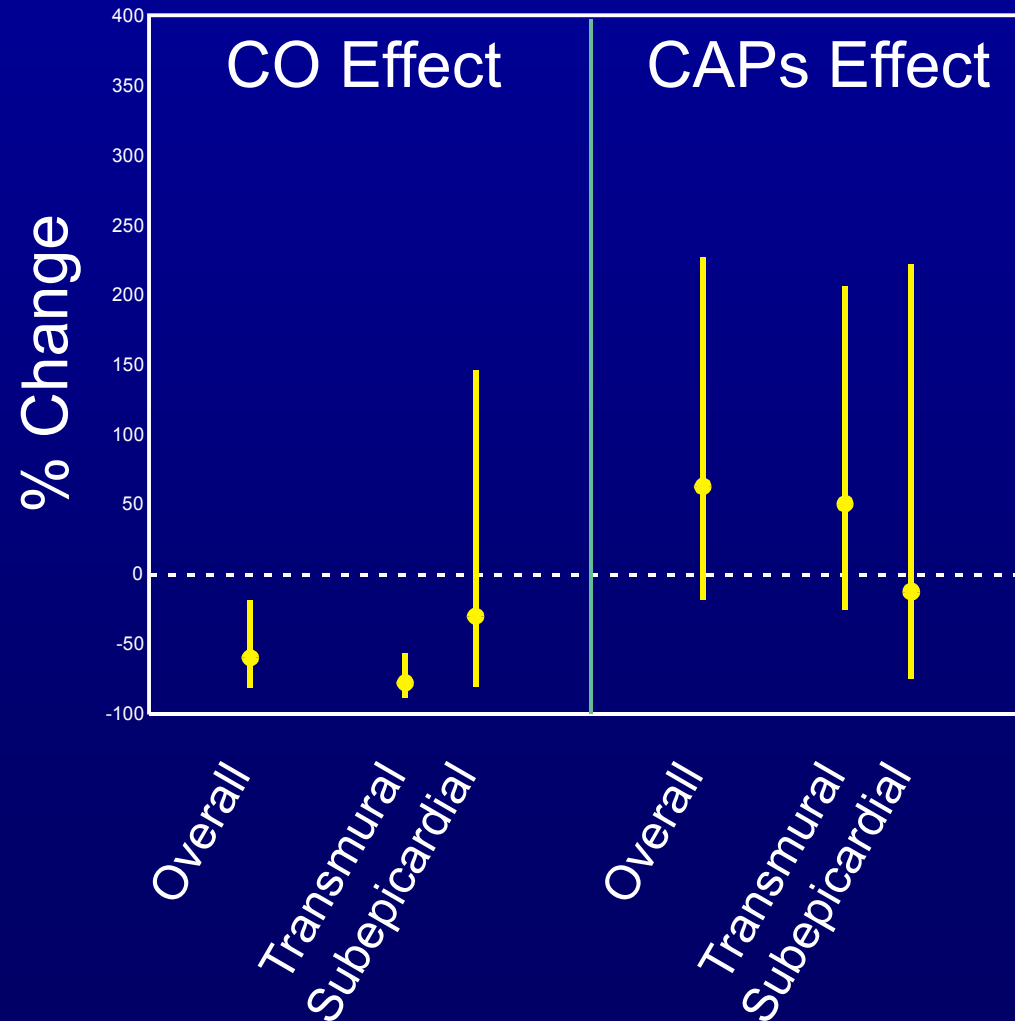
| Sampling Airstream | Sample Type | Parameter | Analytic Method |
|----------------------------|-------------|--------------------------------------|------------------------------------------|
| Ambient Air Particles | Integrated | Mass Concentration | Gravimetric Analysis |
| | | Sulfate | Ion Chromatography |
| | | Ammonium | Ion Chromatography |
| | | Particle Size Distribution | Gravimetric Analysis |
| | Continuous | Carbon Monoxide | Non-Dispersive Infrared |
| Concentrated Air Particles | Integrated | Mass Concentration | Gravimetric Analysis |
| | | Sulfate | Ion Chromatography |
| | | Elemental/Organic Carbon | Thermal/Optical Reflectance |
| | | Trace Metals | X-Ray Fluorescence |
| | | Endotoxins | KLARE Limulus Ameobocyte Assay |
| | Continuous | Non-Volatile Fine Mass Concentration | Tapered Element Oscillating Microbalance |
| | | Black Carbon | Aethalometer |
| | | Particle Number Concentration | Condensation Particle Counter |

Change in VPB Frequency During CAPs and CO Exposures as Compared to Filtered Air

| Exposures | % Δ | 95% CI | p |
|-----------|------------|--------------|-------|
| CAPs | ↑64.2% | -17.7, 227.6 | 0.16 |
| CO | ↓60.4% | -80.7, -18.8 | 0.012 |
| CAPs/CO* | ↓35.0% | -53.6, 246.6 | ns |

*: In a model assuming no interaction between CAPs and CO

Effects on Arrhythmia Frequency



Key Findings

- Animal model for studying arrhythmias is available
- Frequency ventricular arrhythmias
 - Significantly increased by ROFA
 - Tendency towards increase by CAPs
 - Significantly decreased by CO
 - No interaction was observed between the effects of CAPs and CO.

Magnitude of Effect by Exposure

| Exposure | % Δ | 95% CI | p |
|----------|------------|---------------|---------|
| ROFA | ↑ 566.7% | 185.4, 1457.2 | <0.0001 |
| CAPs | ↑ 64.2% | -17.7, 227.6 | 0.16 |
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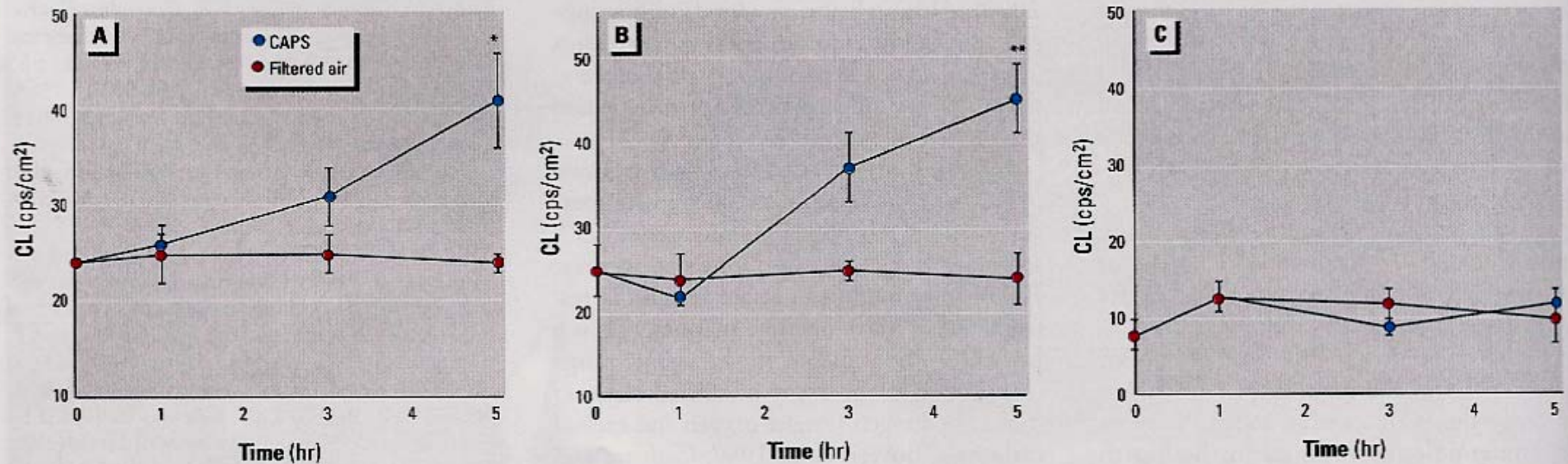
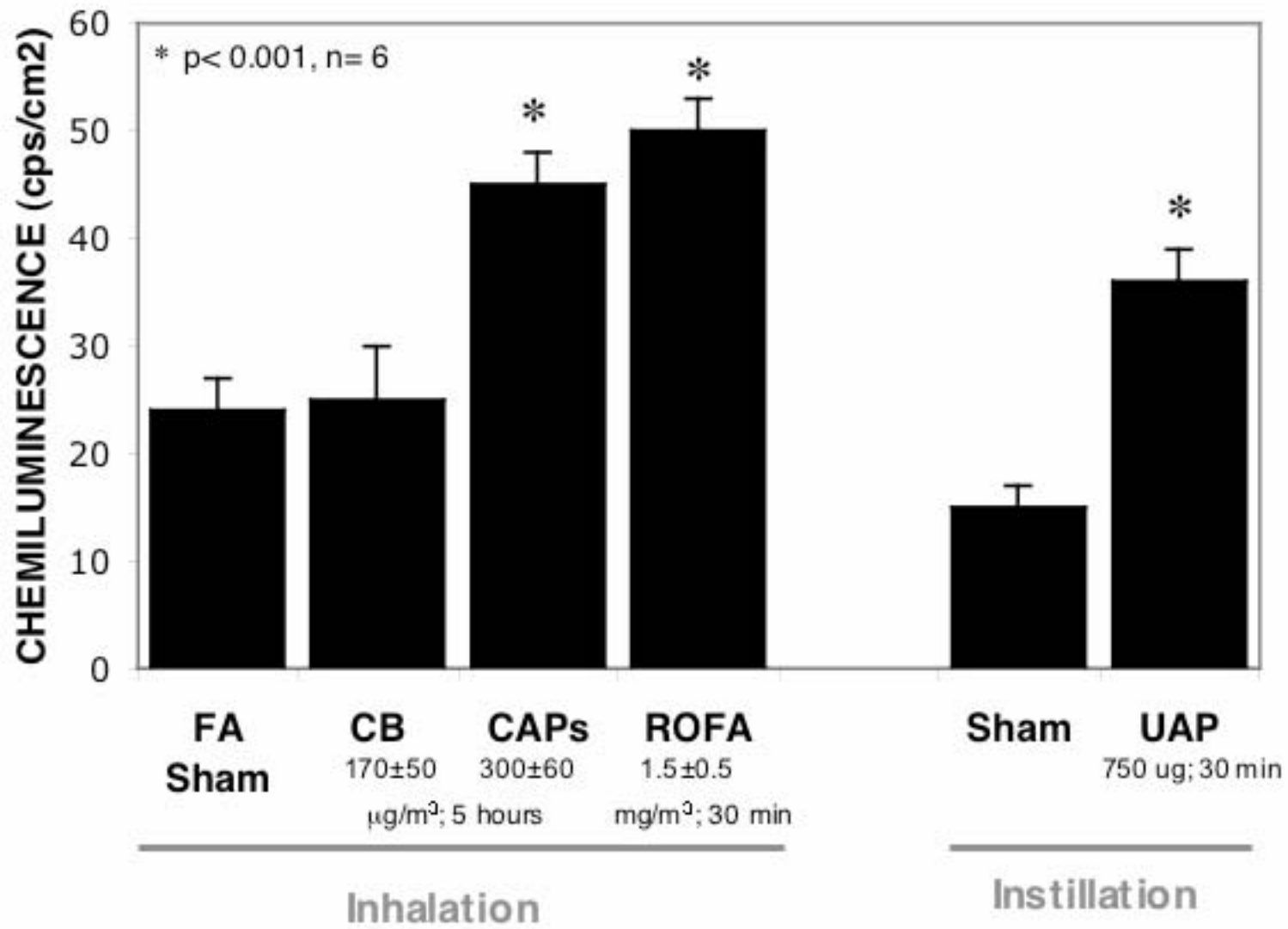


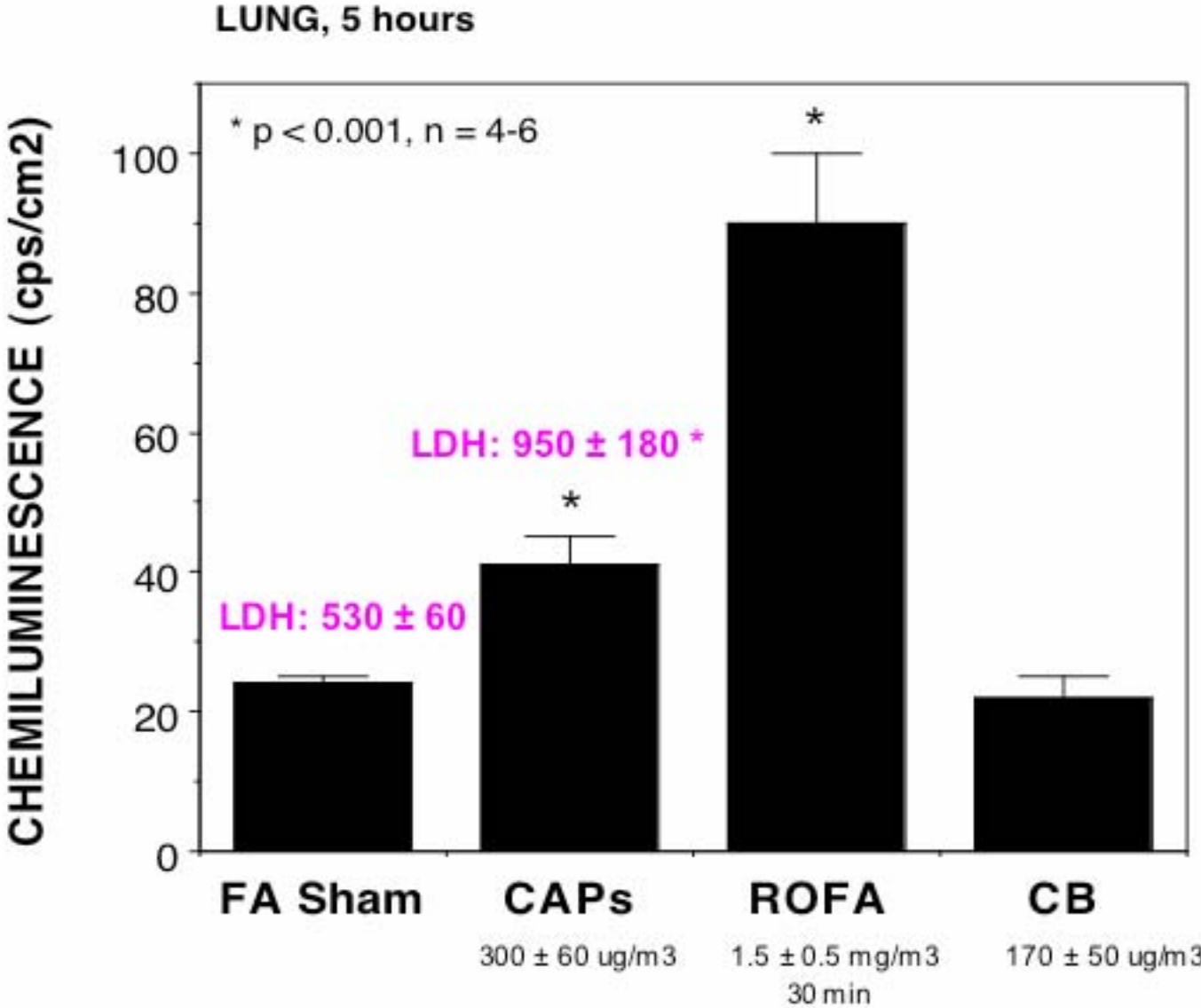
Figure 1. Time course of increase of *in situ* CL from the lung (A), heart (B), and liver (C) of rats exposed to CAPs (average mass concentration, 300 ± 60 µg/m³) or filtered air for 1, 3, and 5 hr. See "Materials and Methods" for details. Each point represents the mean ± SEM (n = 10 determinations). Compared with their sham controls or with time 0, *p < 0.001 and **p < 0.005.

Gurgueira SA, et al. Rapid Increases in the Steady-State Concentration of Reactive Oxygen Species in the Lungs and Heart after Particulate Air Pollution Inhalation. *Environ. Health Perspect.* 110:749-755 (2002)

PM exposure increases the steady-state concentration of oxidants in the heart



CAPs inhalation increases the steady-state concentration of oxidants in the lung.



Summary

- Particle / Gaseous pollutant effects can be disentangled in laboratory studies.
- Particles and environmentally relevant levels of CO have opposite effects on arrhythmias in a model of acute MI.
- Similar exposure protocols yield similar results in measurements of *in vivo* chemiluminescence in the heart and arrhythmias in the MI studies.
- ROFA has greater toxicity than CAPs.