



DEPARTMENT OF BIOMEDICAL ENGINEERING MARQUETTE UNIVERSITY MEDICAL COLLEGE OF WISCONSIN




**Acute Respiratory Distress Syndrome (ARDS):
Developing a Better Diagnostic Tool**

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OUTLINE

1. Present an ARDS case study.
2. Review ARDS prevalence, causes, disease progression, and current diagnosis criteria.
3. Describe the approach we are using to develop a better tool for diagnosing ARDS.




ARDS Case Study

- 80 year old male admitted to the ER with:
 - Shortness of breath, rapid breathing rate, and low blood oxygen saturation.
- Diagnosed with ARDS, and admitted to the ICU.
- Placed on mechanical ventilation to improve blood oxygenation.
- Blood oxygenation improved within the first 24 hours, but worsened by the second day.
- Day 4: kidneys failed.
- Patient died later that day.



Less than a week from ER admission to death!



What caused the ARDS in this patient?

- 7 weeks prior to admission to ICU, the patient was diagnosed with **cancer** (lymphoma).
 - **Lung CT scan was normal** at the time of cancer diagnosis.
- Received **2 doses of chemotherapeutic drugs** with low risk for lung injury in most patients.
- Drugs caused lung injury and ARDS, which in turn caused death from multi-organ failure.

Could a better diagnostic tool have changed the outcome for this patient?



Review ARDS prevalence, causes, disease progression, and current diagnosis criteria.



ARDS: Prevalence, Mortality, and Healthcare Costs

- A devastating lung disease.
- One of the most frequent causes of admission to Medical ICUs.

○ **Severe ARDS:**

- Accounts for 10-15% of ICU admissions.
- Occurs in **~200,000** patients in the US per year.
- Carries a mortality rate of **~40%**.
- Accounts for **75,000 deaths**, **3.6 million hospital days**, and **\$5 billions** in healthcare costs in the U.S. alone per year.



- **Lack of clinical means for early diagnosis.**
- **Lack of effective therapies.**

- The long-term goal of my research is to address these **critical clinical needs**.



Clinical Causes of ARDS

<p>Direct Injury to the Lung</p> <p>Common:</p> <ul style="list-style-type: none"> ▪ Pneumonia <p>Less common:</p> <ul style="list-style-type: none"> ▪ Inhalation injury ▪ Pulmonary contusion ▪ Fat emboli ▪ Near drowning 	<p>Indirect Injury to the Lung</p> <p>Common:</p> <ul style="list-style-type: none"> ▪ Sepsis ▪ Severe trauma <p>Less common:</p> <ul style="list-style-type: none"> ▪ Multiple blood transfusions ▪ Severe burns ▪ Head injury ▪ Drug overdose
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Gas Exchange in a Normal Lung: "Tight" Air-Blood Barrier

The diagram illustrates the normal state of the air-blood barrier. On the left, a cross-section shows a capillary (red) and an alveolus (green) separated by a "Thin and tight" air-blood barrier. Arrows indicate the exchange of O_2 and CO_2 . On the right, a small anatomical diagram shows the pulmonary circuit (red) and systemic circuit (blue). A key indicates:

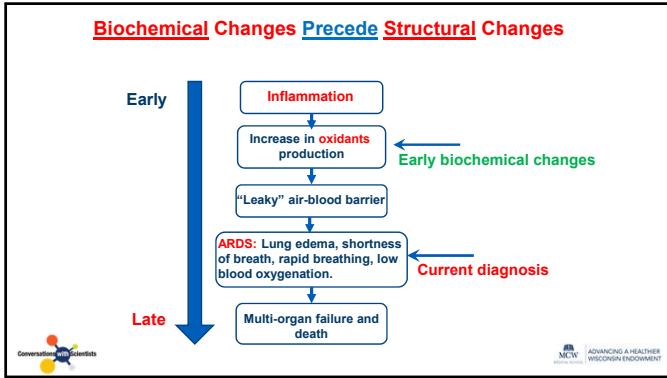
- Red box: Oxygen rich, CO_2 -poor blood
- Blue box: Oxygen poor, CO_2 -rich blood

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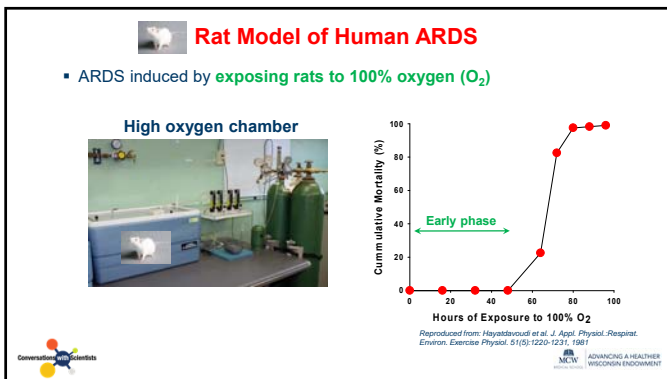
ARDS: "Leaky" Air-Blood Barrier

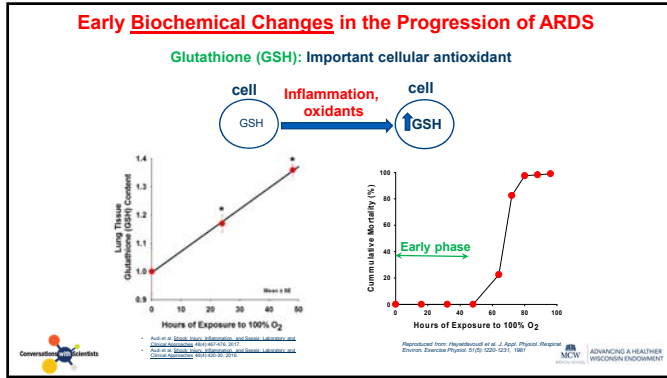
The diagram illustrates the pathophysiology of ARDS. It shows a "Leaky" air-blood barrier between a capillary and an alveolus. This leads to "Fluid (edema)" in the alveolus, which results in "Low blood oxygenation". This state can lead to "Multi-organ failure" and "Death", or "Recovery".

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Describe the approach we are using to develop a better tool for diagnosing ARDS.





Single-Photon Emission Computed Tomography (SPECT) Imaging

- Clinical **functional** imaging modality.
- Requires the delivery of a **biomarker** (compound labelled with a **gamma-emitting radioisotope**) into a patient.
- **Detection** of the accumulation of the biomarker in the lungs using a **gamma camera**.

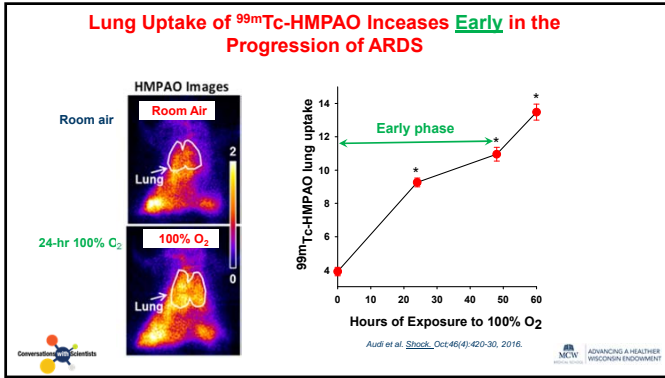
http://www.healthcare.waters.com/molecular-imaging/spect-and-spectroscopy.html
http://www.yourum.com/2013/10/16/primary-antibody-questions/

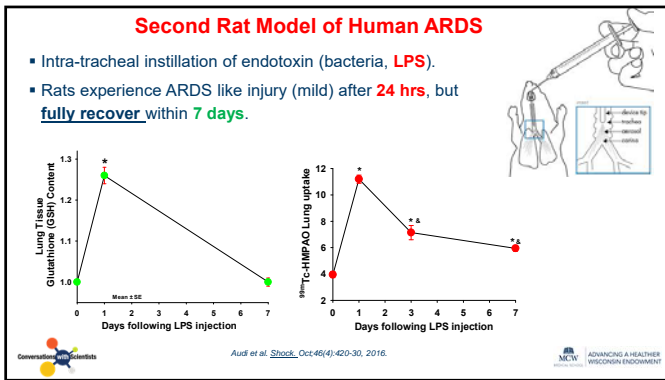
^{99m}Tc-hexamethylpropyleneamine (HMPAO)

- Clinical **SPECT** biomarker.
- **Biomarker** of tissue glutathione (**GSH**) content.
- When ^{99m}Tc-HMPAO enters the cells, it interacts with **GSH** and gets **stuck** within the cells.
- The more **GSH** present within the lung cells, the more lung uptake of ^{99m}Tc-HMPAO, and the **brighter** the image.

HMPAO Images
Room Air
Lung
100% O₂
Lung

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Could early detection of ARDS have changed the outcome for the patient in the case study?

- SPECT scan with ^{99m}Tc-HMPAO **after the first dose** of chemotherapy could have revealed early lung injury.
 - ✓ Assess the risk-to-benefit of the cancer treatment.
 - ✓ Use different drugs.
 - ✓ Take precautionary measures to reduce the risk of severe ARDS development.

http://usa.healthcare.basimg.com/molecular-imaging/spect-and-spect-ct/typical-a

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SUMMARY

- ❖ ARDS is a devastating lung disease with a high mortality rate, in part due to the lack of a clinical tool for **early diagnosis**.
- ❖ **Current** diagnosis is based on **late changes** in disease progression.
- ❖ Cellular biochemical changes that occur **early** in the progression of ARDS can be used for **early diagnosis** of ARDS using **clinical SPECT imaging**.
- ❖ The lung uptake of the SPECT biomarker **^{99m}Tc-HMPAO** increases early in the progression of ARDS, and tracks ARDS progression and regression.
- ❖ **Early diagnosis** of ARDS using SPECT imaging can enhance the efficacy of existing therapies, reduce the severity and healthcare costs of ARDS, and improve outcomes.



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