“Matching the Mechanical Breath with Dynamic Alveolar Pathophysiology to Reduce VILI”

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So what is the Magic Trick?

Science

Nieman Disclosures

• None of the funding organizations or sponsors had any role in the design and conduct of any of our studies including the collection, management, analysis, or interpretation of the data, preparation, review, or approval of any of our manuscripts.

• Consultant for Interxon Corporation
• Consultant for the DoD developing Mechanical Ventilators for Marine Mammals
• NIH R01 grant: Gene therapy to treat acute lung injury using
• Travel and honorarium funded by Draeger Medical
• Draeger Medical equipment used in our studies
• CDMRP DoD grant: A novel drug (TRB-N0224) to reduce ARDS incidence
• Established a APRV Network website
• Conduct an APRV Workshop Sponsored by Upstate Medical University
• Patent for: “Method of preventing acute lung injury”
• Patent for: “A device (MIRT) to remove toxic ascites and prevent MODS and ARDS
• Patent for: “Apparatus, system and method of assessing alveolar inflation”
How do we ‘Trick’ the ARDS Lung into Ventilating and Oxygenating without Exacerbating Tissue Injury?

• Understanding the science of ARDS pathophysiology

• Combine this understanding with the science of VILI in terms of applied stress and resultant strain on lung tissue

“Physiology is the basis of medical reasoning, not statistics. Statistics are a tool”

Luciano Gattinoni

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Hypothesis

Properly adjusted Mechanical Ventilation can reduce the severity of all components that comprise the Pathologic Tetrad of ARDS.

Why does the ARDS Tetrad Render the Lung so Vulnerable to VILI?
• It changes lung physiology from:
  – Homogeneous stable ventilation
  – Heterogeneous unstable ventilation

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Mechanism of VILI at the Alveolar Level

- Dynamic alveolar strain (R/D)
  - Tetrad: Edema/Surfactant deactivation
- Stress-Concentration (S-C)
  - Tetrad: Edema/Surfactant deactivation
- Over-distension
  - In the presence of R/D or S-C adjacent alveoli and ducts can over-distend
Normal Alveolar Micro-Anatomy

Lung Parenchymal Mechanics

Normal Homogeneous Alveolar Minimizes Dynamic Strain and OD

~2% in Alveolar Area with each breath.
What happens to this homogeneous ventilation when alveoli become unstable with Acute Lung Injury?
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Non-lobar atelectasis generates inflammation and structural alveolar injury in the surrounding healthy tissue during mechanical ventilation.

Stress-Concentration

Homogenous Ventilation

Heterogeneous Ventilation

Lines of Force

Stress is not evenly distributed

Stress is uniformly distributed
Mechanism of VILI at the Alveolar Level

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How must the Mechanical Breath be Adjusted to Minimize the Problems caused by ARDS Pathophysiology:

- Maintain homogeneous alveolar ventilation – *(Open the lung: prevent stress-concentration)*
- Prevent alveolar collapse at expiration – *(Keep the lung open: prevent dynamic strain)*

“Open the Lung and Keep the Lung Open”

B. Lachmann

*Intensive Care Med* 1992

**We Create the Problem and then Attempt to Devise Solutions for the Problem that We have Created!**

- Wouldn’t it make more sense to prevent the problem in the first place?
- The problem is *Heterogeneous Loss of Lung Volume* – Causing high inspiratory drive with the potential of SB-induced VILI – Causing stress-risers and alveolar instability – Causing over-distension of ‘Baby Lung’ – If the lung is open, VILI disappears, no problem to fix!
ARDS Pathogenesis

EALI  
Insidious-ARDS  
Established-ARDS

Prevent the Lung from Collapsing

Before Collapse  After Collapse

What is the Current Ventilation Strategy to Open the Lung and Keep it Open?

- Recruitment maneuvers
  - Open the lung
- PEEP
  - Keep the lung open
- Reduced Vt and Pplat
  - Minimize alveolar over-distension in the presence of dynamic strain and stress-concentrators
Current Protective Ventilation Strategies use the same 4-Parameters

Vt

Pplat

PEEP

RM

No Reduction in ARDS Mortality since 1998

Villar J. Curr Opin Crit Care 2014;20:3-9

Insanity: doing the same thing over and over again and expecting different results

Albert Einstein
Why haven’t these strategies worked?

Upstate

Understanding Dynamic Alveolar Physiology

- Alveoli are *not* elastic in nature
  - Do not inflate and deflate in a linear fashion like a balloon

- Rather, alveoli are a *viscoelastic* system
  - *Time lag* from when the force (i.e. Vt) is applied or removed and when the alveolus begins to change volume

- Dynamic alveolar inflation and deflation can be modeled as a *Spring and Dashpot* model

Upstate

Spring and Dashpot Model

*Spring* = Rapid Strain

*Dashpot* = Slow Strain

Time Lag between the time the stress is applied or released and the initiation of the strain

Force = Vt

Applies Stress to the Lung

Nieman GF, JAP. 2017.
How can we use this knowledge of dynamic alveolar physiology to design a better protective ventilation strategy?

**Protective Mechanical Ventilation: The Old and the New**

- **Old thinking:** RM+PEEP+LVt
  - **RM:** Reduce stress-concentrators (S-C)
  - **PEEP:** Reduce dynamic alveolar strain (R/D)
  - **LVt:** Minimize OD of ‘Baby Lung’

- **New Thinking:** Spring and Dashpot
  - **Long I-time:** Reduce stress-concentrators (S-C)
  - **Short E-time:** Reduce dynamic alveolar strain

**Extend the Duration at Inspiration**

Continually recruit alveoli with each breath: Reduce S-C
Extend Inspiratory Duration to Cause Full Alveolar Strain (i.e. Alveolar Recruitment)

Force = Vt
Applies Stress to the Lung

Spring = Rapid Strain

Dashpot = Slow Strain

Extended Inspiratory Duration will Continually Recruit Alveoli

Minimizing Stress-Concentrators

Nieman GF JAP 2017 INS

Reduce the Duration at Expiration

Minimize alveolar collapse and reopening: Reduce dynamic strain

Albert SP et al J Appl Physiol 2009
Short Expiratory Duration
Prevents reverse strain or compression (i.e. Prevents Alveolar Derecruitment)

Dashpot = Slow Strain

Force = Vt
Applies Stress to the Lung

Spring = Rapid Strain

Long Expiratory Duration

Short Expiratory Duration
What Mechanical Breath Strategies use Inspiratory and Expiratory Duration to Protect Alveoli?

- HFOV
- Inverse I:E
- APRV
Inspiratory Duration: ‘Nudge Alveoli Open with Each Breath’

Extend Inspiratory Duration to Cause Full Alveolar Strain (i.e. Alveolar Recruitment)

Dashpot = Slow Strain

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Extended Inspiratory Duration will Continually Recruit Alveoli

Minimizing Stress-Concentrators

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Albert SP et al J Appl Physiol, 2009
Extended *Inspiratory Duration* will Continually Recruit Alveoli

Inspiratory Pressure Held: 1 sec  Inspiratory Pressure Held: 5 secs

Minimizing Stress-Concentrators


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Short Expiratory Duration: Dual Alveolar Stabilization Mechanism

Positive end-expiratory Pressure (PEEP)

Jain S. Intensive Care Med Exp 2016

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Short Expiratory Duration: Dual Alveolar Stabilization Mechanism

Not enough time for alveoli collapse

Jain S. Intensive Care Med Exp 2016
Short Expiratory Duration
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Force = Vt
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Long Expiratory Duration

Short Expiratory Duration

Nieman GF JAP 2017 In Press

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Setting Expiratory Duration using the Expiratory Flow Curve
Setting Expiratory Duration using the Expiratory Flow Curve

-60L x 0.75 = -45L

Closed-Loop Feedback System

Input  Controller  Effector  Output

Sensor

Feedback Loop

Jain S. Intensive Care Med Exp 2016

EEF/PEF = 0.75, 45/60 = 0.75

Spring and Dashpot: Alveolar Recruitment and Stabilization

Nieman GF JAP 2017
APRV

Personalized, Adaptive, Flow Directed, Duration Dependent, Ventilator Strategy

Data Supporting our Hypothesis
PaO₂/FiO₂ Ratio

Gross Lung

Early application of airway pressure release ventilation may reduce mortality in high-risk trauma patients: A systematic review of observational trauma ARDS literature

Andrews et al. J Trauma Acute Care Surg 2013;75:635
Preemptive APRV in Humans

Andrews et al, J Trauma Acute Care Surg 2013;75:635

Hypothesis

Properly adjusted Mechanical Ventilation can reduce the severity of all components that comprise the Pathologic Tetrad of ARDS
Conclusion

APRV can block all 4-components of the Pathologic Tetrad of ARDS

Summary

• Mechanism of VILI in the Microenvironment
  – Alveolar stress-concentrators
  – Dynamic alveolar strain
  – Alveolar over-distension
    • Secondary to S-C and dynamic strain
• Dynamic Alveolar Physiology
  – Viscoelastic alveolar volume change
• Components of the Mechanical Breath that will Protect the Lung
  – Extended Inspiratory duration
  – Short Expiratory duration

Mechanism of VILI in the Microenvironment

- Alveolar stress-concentrators
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Dynamic Alveolar Physiology

- Viscoelastic alveolar volume change

Components of the Mechanical Breath that will Protect the Lung

- Extended Inspiratory duration
- Short Expiratory duration
Conclusion

• Properly set APRV acts like a splint to protect the lung with altered physiology keeping it open until the lung has a chance to ‘heal’.

• If we ‘Open the Lung and Keep it Open’ or better yet, ‘Never Give the Lung a Chance to Collapse’ all of the mechanisms associated with VILI will be significantly reduced or eliminated.
The Team