

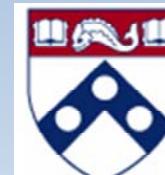
Lung Imaging and Personalized Care in ARDS

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UNIVERSITY OF PENNSYLVANIA

Disclosures

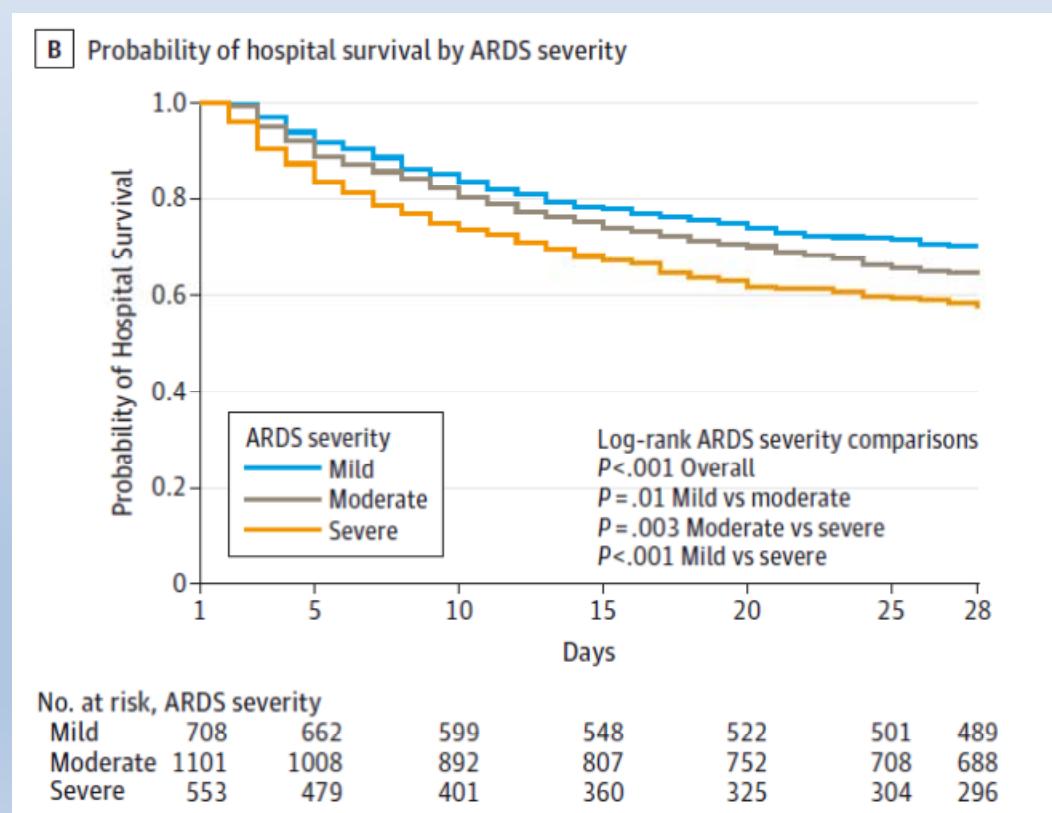
- Conflicts of interest: none
- Funding:
 - NIH
 - FAER
 - ITMATT
 - Hill-Rom

Overview

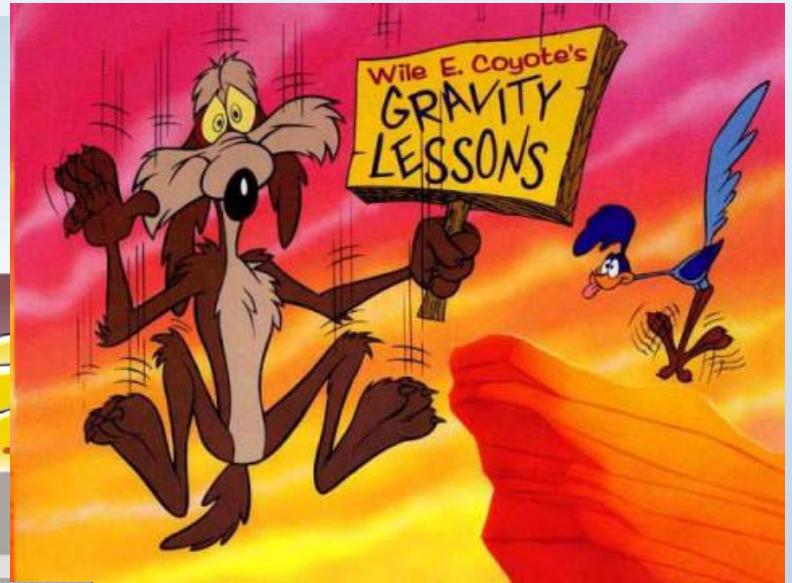
- Heterogeneity of the ARDS population and the need for better characterization of lung injury
- Can lung imaging help personalize ARDS care?
- Measuring small scale inflation and the progression of early lung injury

Epidemiology, Patterns of Care, and Mortality for Patients With Acute Respiratory Distress Syndrome in Intensive Care Units in 50 Countries

Giacomo Bellani, MD, PhD; John G. Laffey, MD, MA; Tài Pham, MD; Eddy Fan, MD, PhD; Laurent Brochard, MD, HDR; Andres Esteban, MD, PhD; Luciano Gattinoni, MD, FRCP; Frank van Haren, MD, PhD; Anders Larsson, MD, PhD; Daniel F. McAuley, MD, PhD; Marco Ranieri, MD; Gordon Rubenfeld, MD, MSc; B. Taylor Thompson, MD, PhD; Hermann Wrigge, MD, PhD; Arthur S. Slutsky, MD, MASc; Antonio Pesenti, MD; for the LUNG SAFE Investigators and the ESICM Trials Group

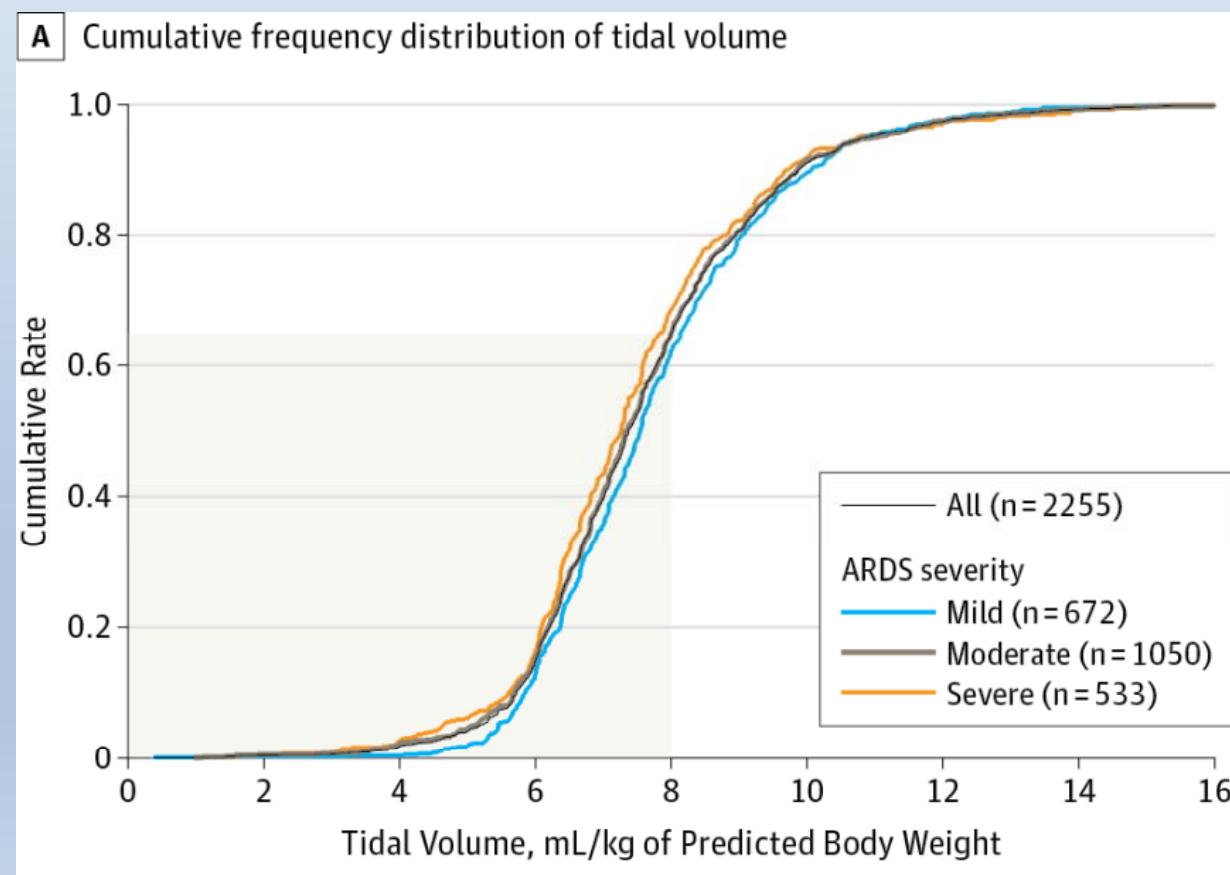


How to Improve ARDS Survival



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ARDS Sniffer



Sun, Jan 29, 11:07 PM

ARDS Finder<LF>The ARDS Finder identified your patient, JF, in 0983A as having ARDS. Use of the Low Stretch Protocol (SCM) is life-saving & strongly recommended, unless contraindicated.

Wednesday 7:32 AM

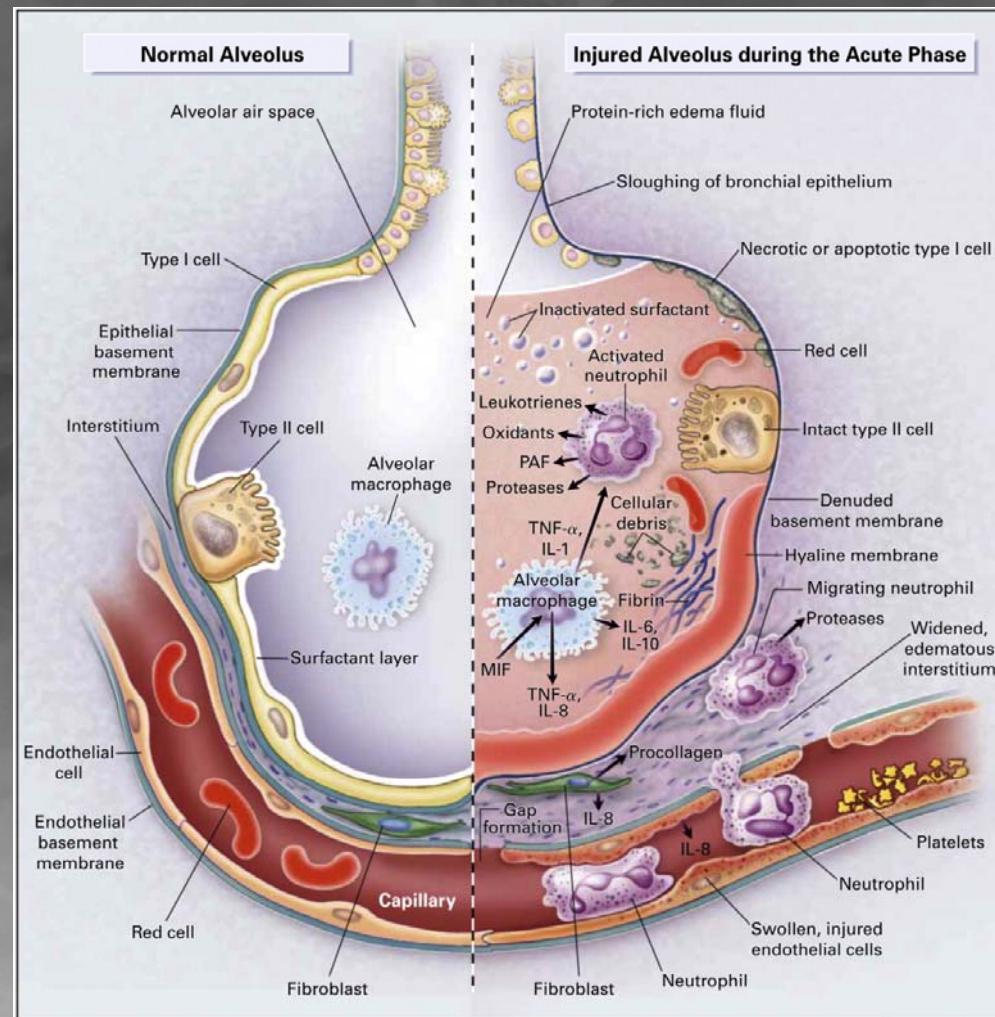


iMessage



L

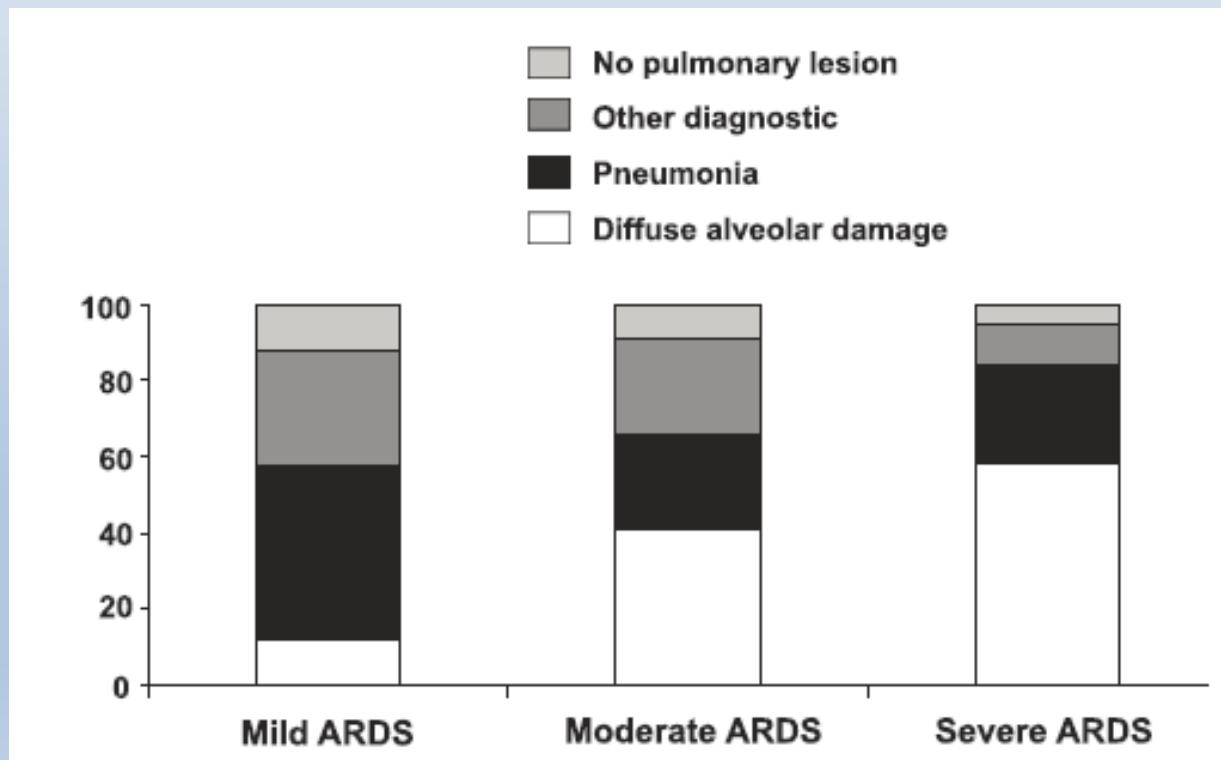
78



Comparison of the Berlin Definition for Acute Respiratory Distress Syndrome with Autopsy

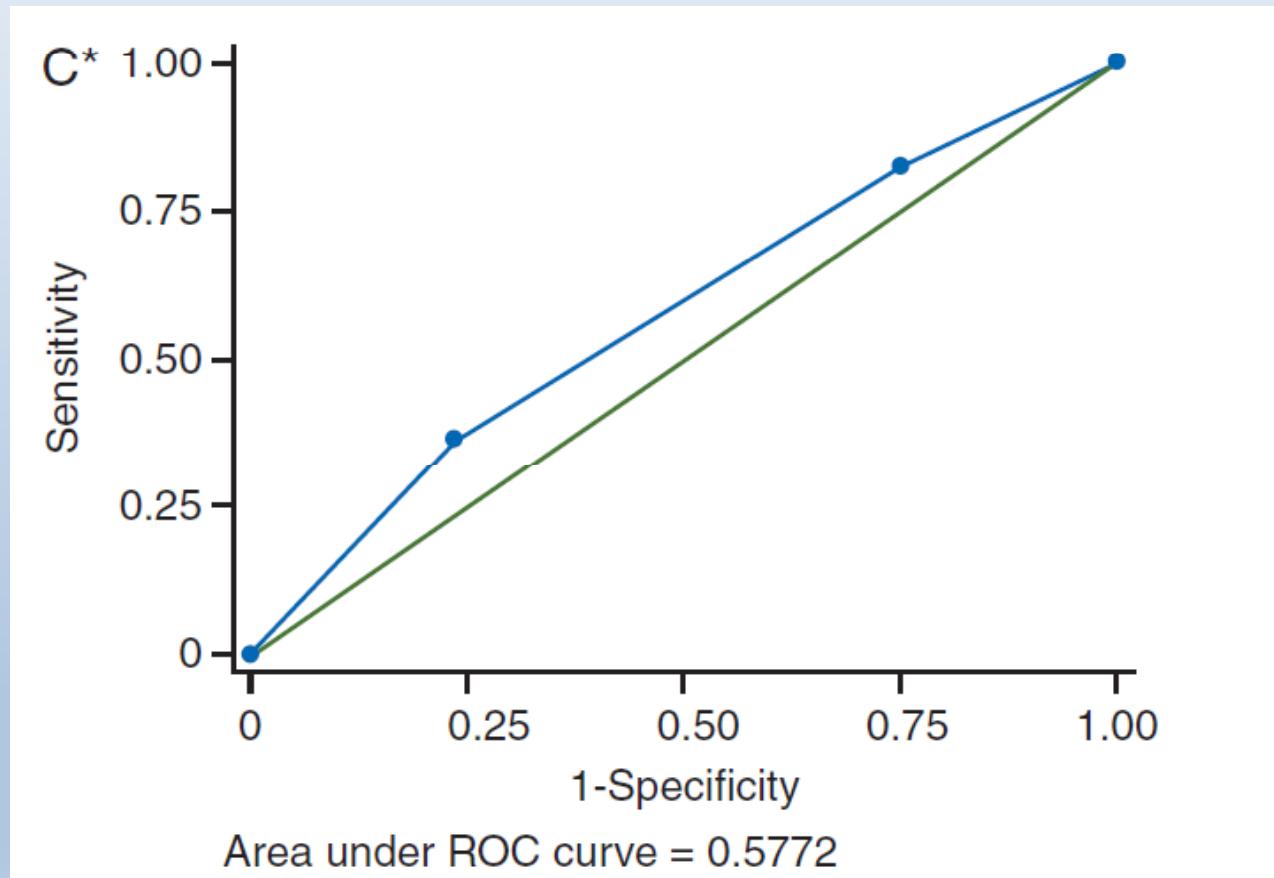
Arnaud W. Thille^{1,3}, Andrés Esteban¹, Pilar Fernández-Segoviano², José-Maria Rodriguez², José-Antonio Aramburu², Oscar Peñuelas¹, Irene Cortés-Puch¹, Pablo Cardinal-Fernández¹, José A. Lorente¹, and Fernando Frutos-Vivar¹

356 Autopsies of patients meeting Berlin criteria



ARDS: progress unlikely with non-biological definition

S. Fröhlich^{1,2*}, N. Murphy^{1,2} and J. F. Boylan¹

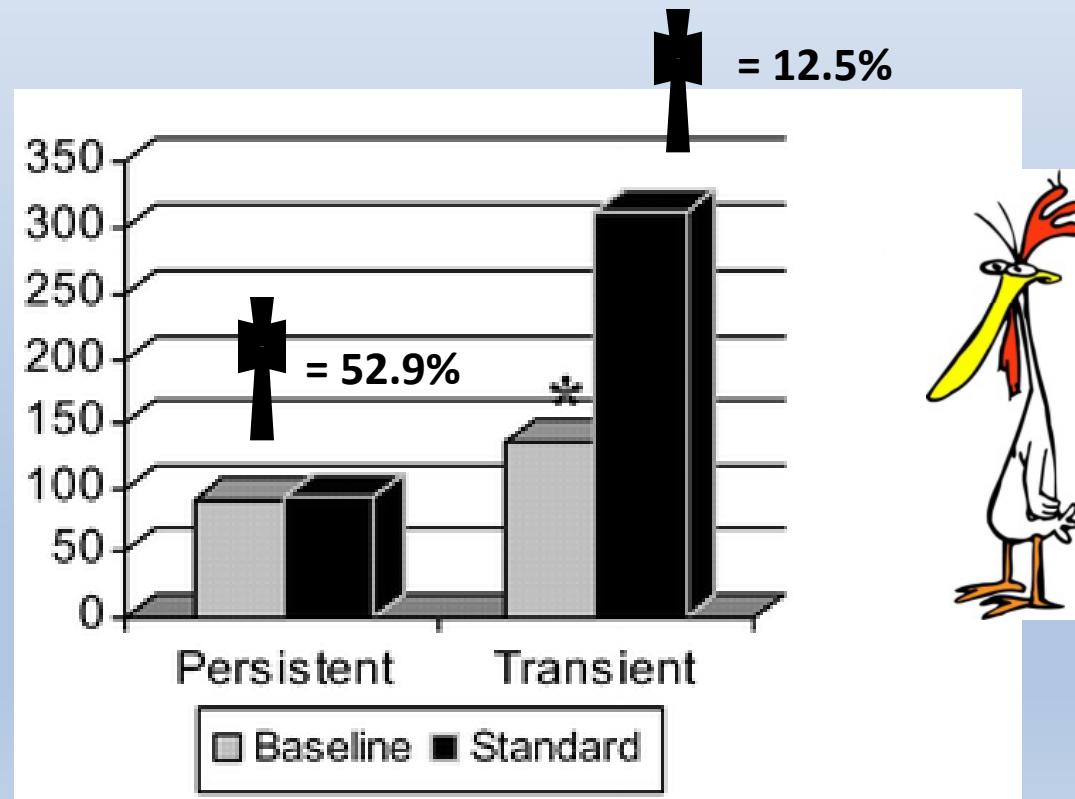


Outcome heterogeneity is unmasked by standardized ventilator settings

- 41 ARDS pts screened at baseline and with standardized ventilator settings (PEEP 10, FiO₂ 1.0)
- 24 did not meet ARDS criteria with the new settings



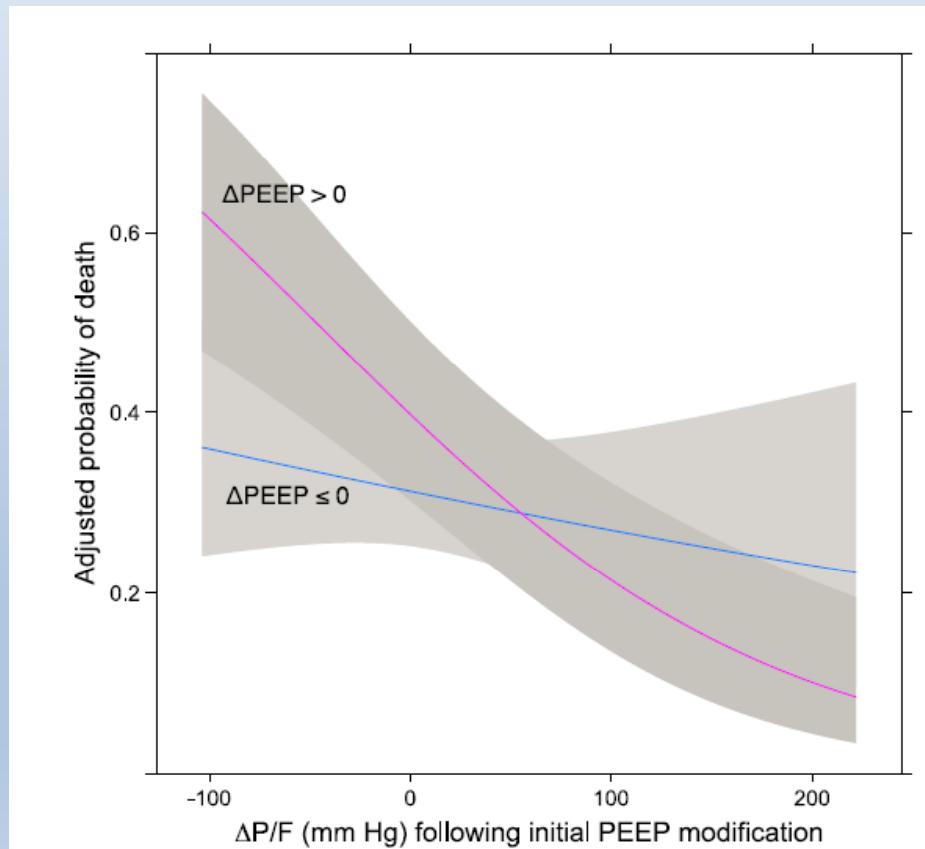
PaO₂/FiO₂



Oxygenation Response to Positive End-Expiratory Pressure Predicts Mortality in Acute Respiratory Distress Syndrome

A Secondary Analysis of the LOVS and ExPress Trials

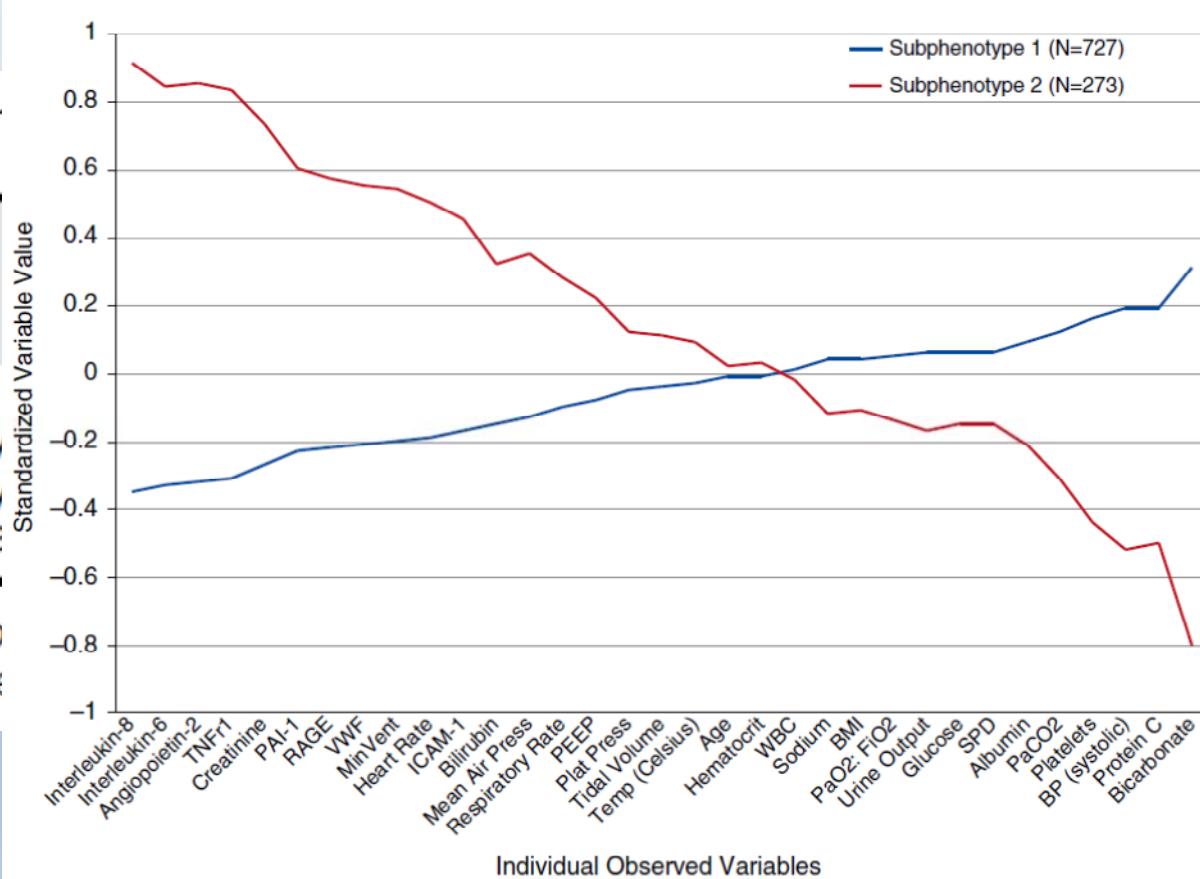
Ewan C. Goligher^{1,2,3,4}, Brian P. Kavanagh^{1,5,6}, Gordon D. Rubenfeld^{1,2,7}, Neill K. J. Adhikari^{1,2,7}, Ruxandra Pinto⁷, Eddy Fan^{1,2,4}, Laurent J. Brochard^{1,2,8}, John T. Granton^{1,2,4}, Alain Mercat⁹, Jean-Christophe Marie Richard¹⁰, Jean-Marie Chretien¹¹, Graham L. Jones¹², Deborah J. Cook^{12,13}, Thomas E. Stewart^{1,2,4}, Arthur S. Slutsky^{1,2,4}, Maureen O. Meade^{12,13}, and Niall D. Ferguson^{1,2,3,4}



Acute Respiratory Distress Syndrome Subphenotypes Respond Differently to Randomized Fluid Management Strategy

Katie R. Famous¹, Kevin Delucchi², Lorraine B. Ware^{3,4}, Kirsten N. Kangelaris⁵, Kathleen D. Liu^{6,7}, B. Taylor Thompson⁸, and Carolyn S. Calfee^{1,7}; for the ARDS Network

Table 3. Clir



60-d mortality
90-d mortality
Ventilator-free days

Definition of abbreviations
P value represents comparison of Subphenotype 1 vs Subphenotype 2

P Value

<0.0001
<0.0001
<0.0001

ventilator-free days.

ARDS Subtypes

Gas exchange

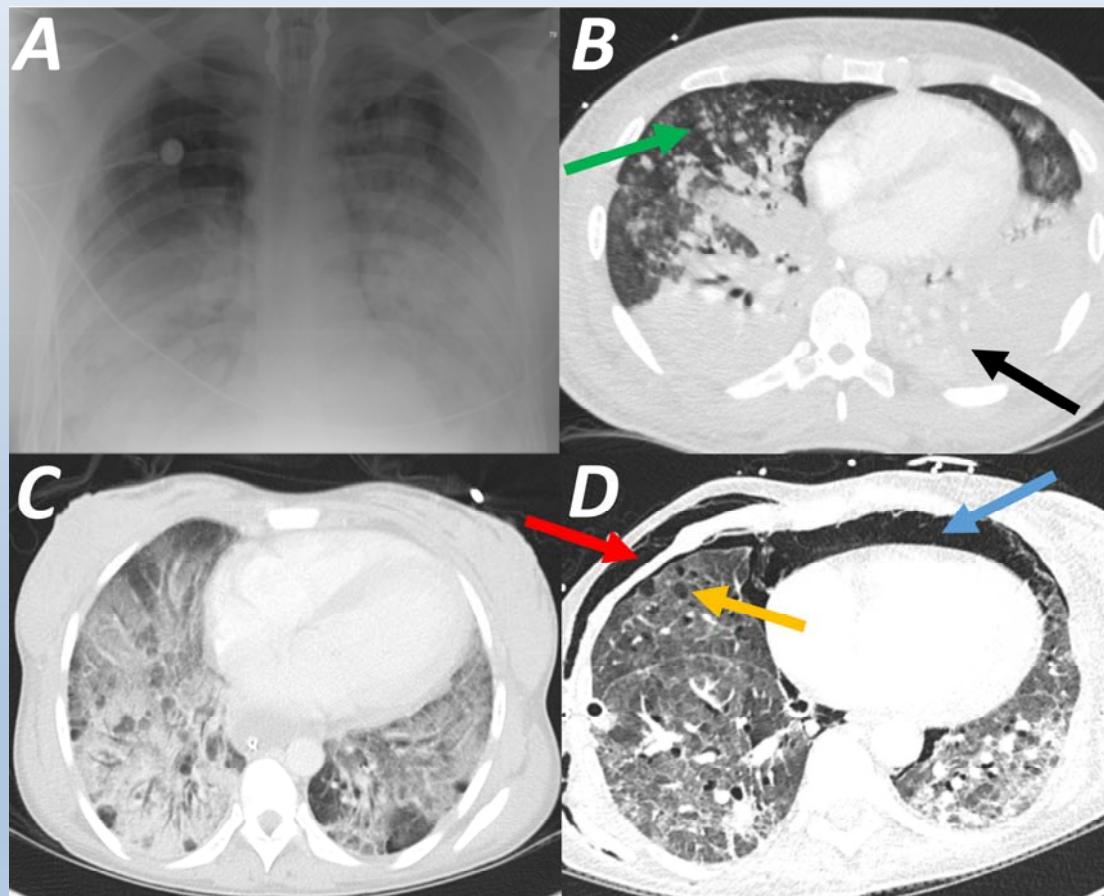
Imaging



Biomarkers

Lung mechanics

Imaging the Injured Lung



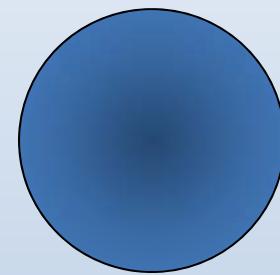
The ‘Baby Lung’

Baby Lung

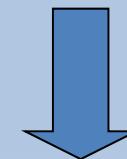


Consolidation/Atelectasis

Lung Strain



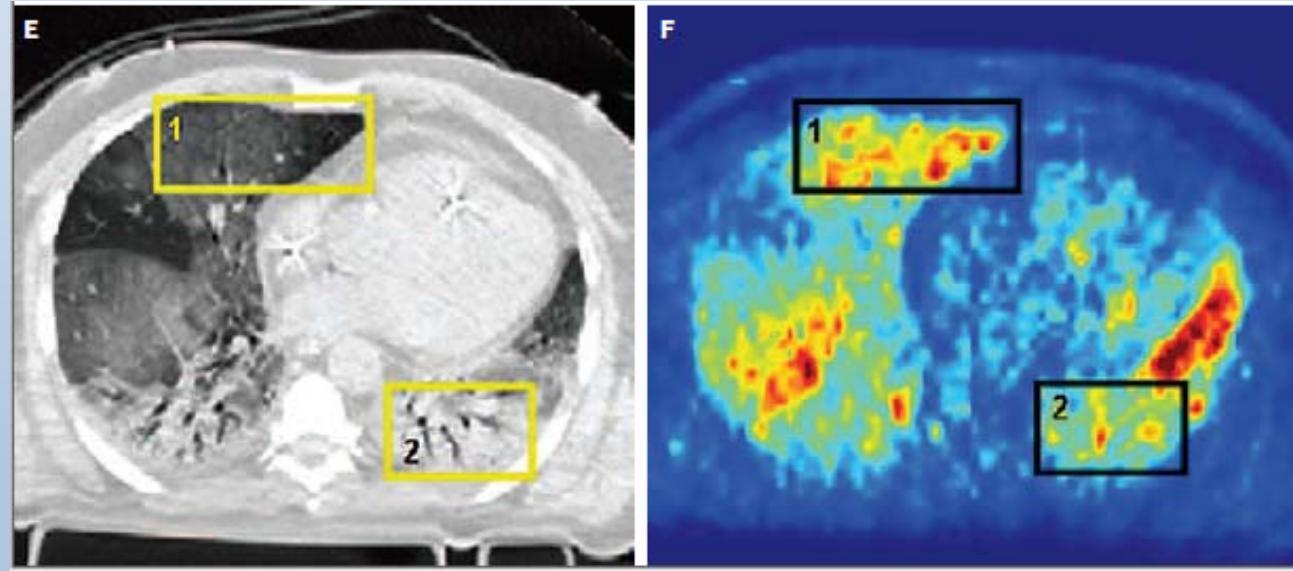
Mechano-signaling



Ventilator Induced Lung Injury
(VILI)

Lungs of patients with acute respiratory distress syndrome show diffuse inflammation in normally aerated regions: A [18F]-fluoro-2-deoxy-D-glucose PET/CT study

Giacomo Bellani, MD; Cristina Messa, MD; Luca Guerra, MD; Ester Spagnolli, MD; Giuseppe Foti, MD; Nicolò Patroniti, MD; Roberto Fumagalli, MD; Guido Musch, MD; Ferruccio Fazio, MD; Antonio Pesenti, MD

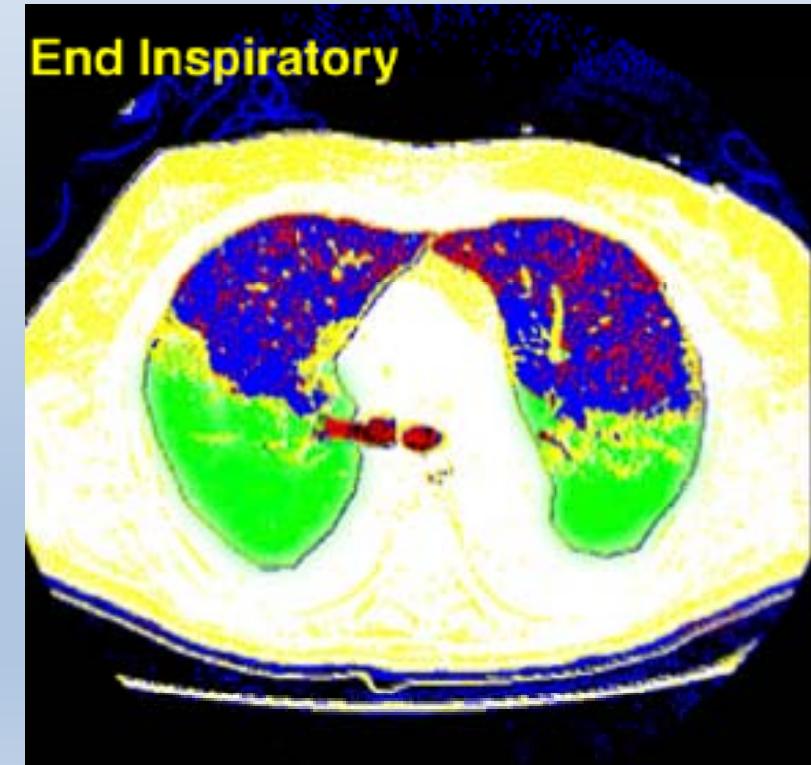
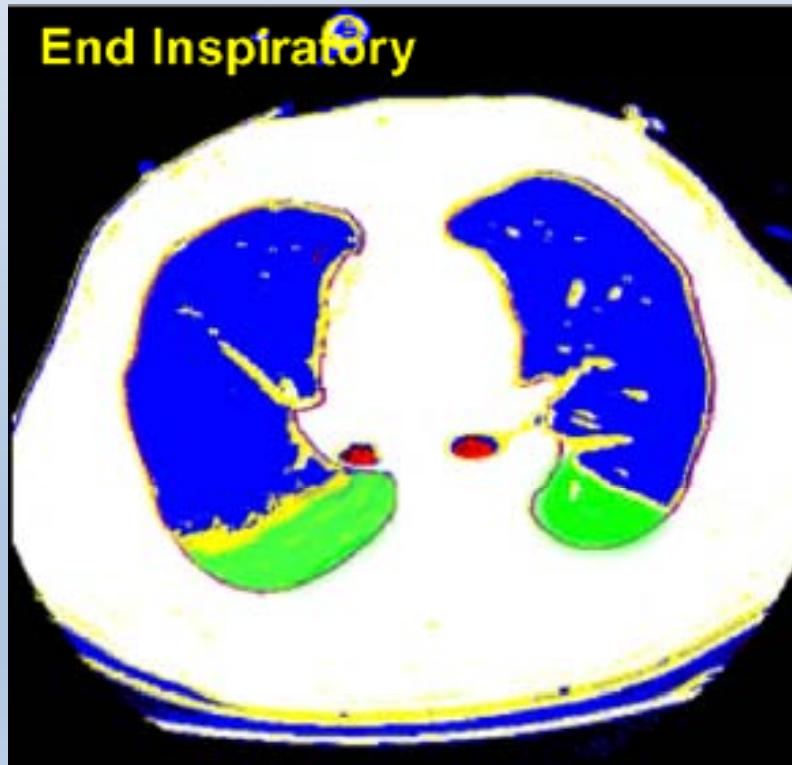


One size fits all?

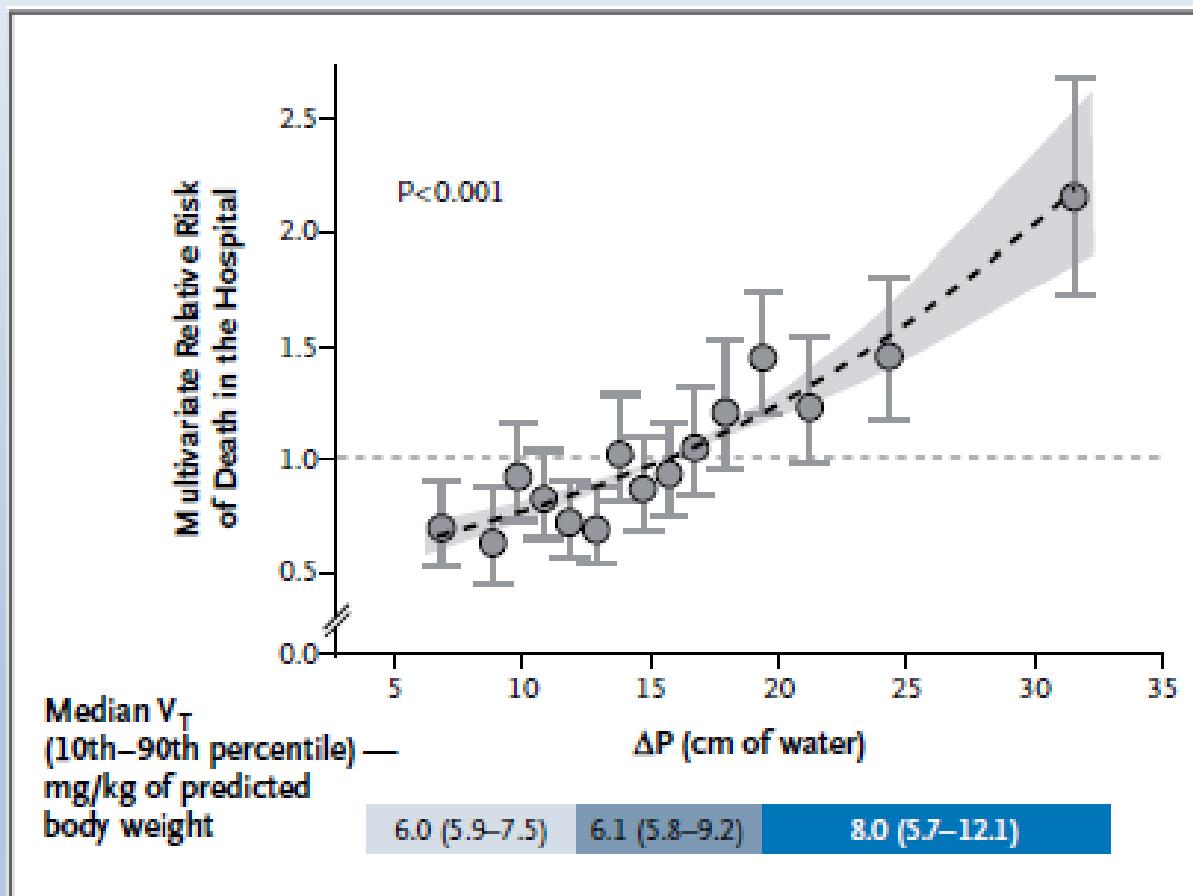


Tidal Hyperinflation during Low Tidal Volume Ventilation in Acute Respiratory Distress Syndrome

Pier Paolo Terragni, Giulio Rosboch, Andrea Tealdi, Eleonora Corno, Eleonora Menaldo, Ottavio Davini, Giovanni Gandini, Peter Herrmann, Luciana Mascia, Michel Quintel, Arthur S. Slutsky, Luciano Gattinoni, and V. Marco Ranieri



Driving Pressure and Survival in the Acute Respiratory Distress Syndrome



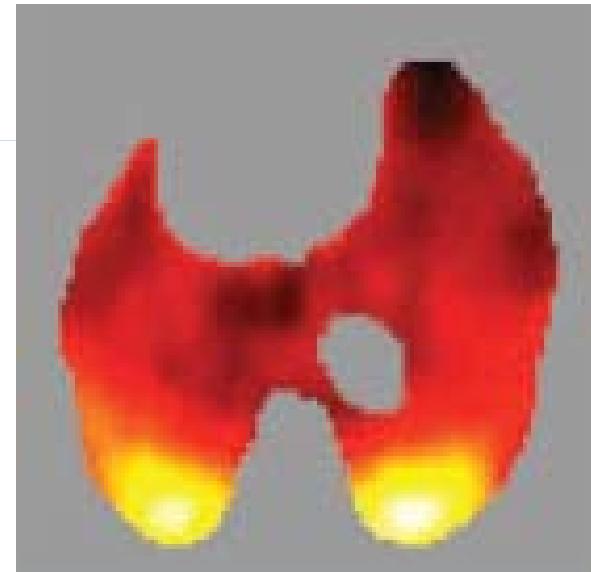
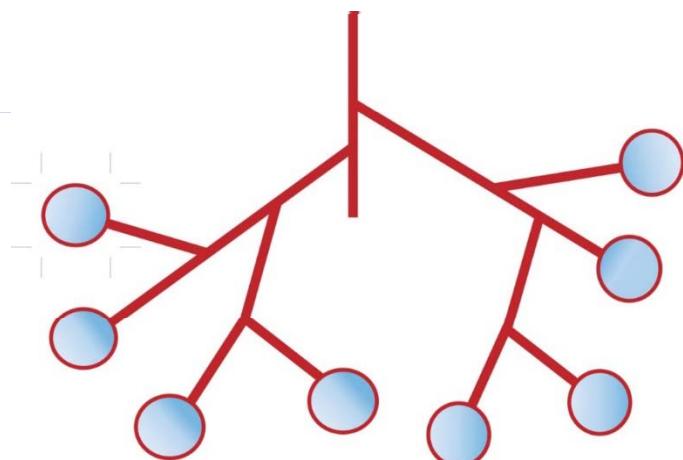
Marcelo Amato et al. N Engl J Med 2015;372:747-55.

Unstable Recruitment and Atelectrauma



Courtesy of J. Hermann, D. Kaczka

Mechanisms of atelectrauma



Wellman et al. et al. CCM 2014

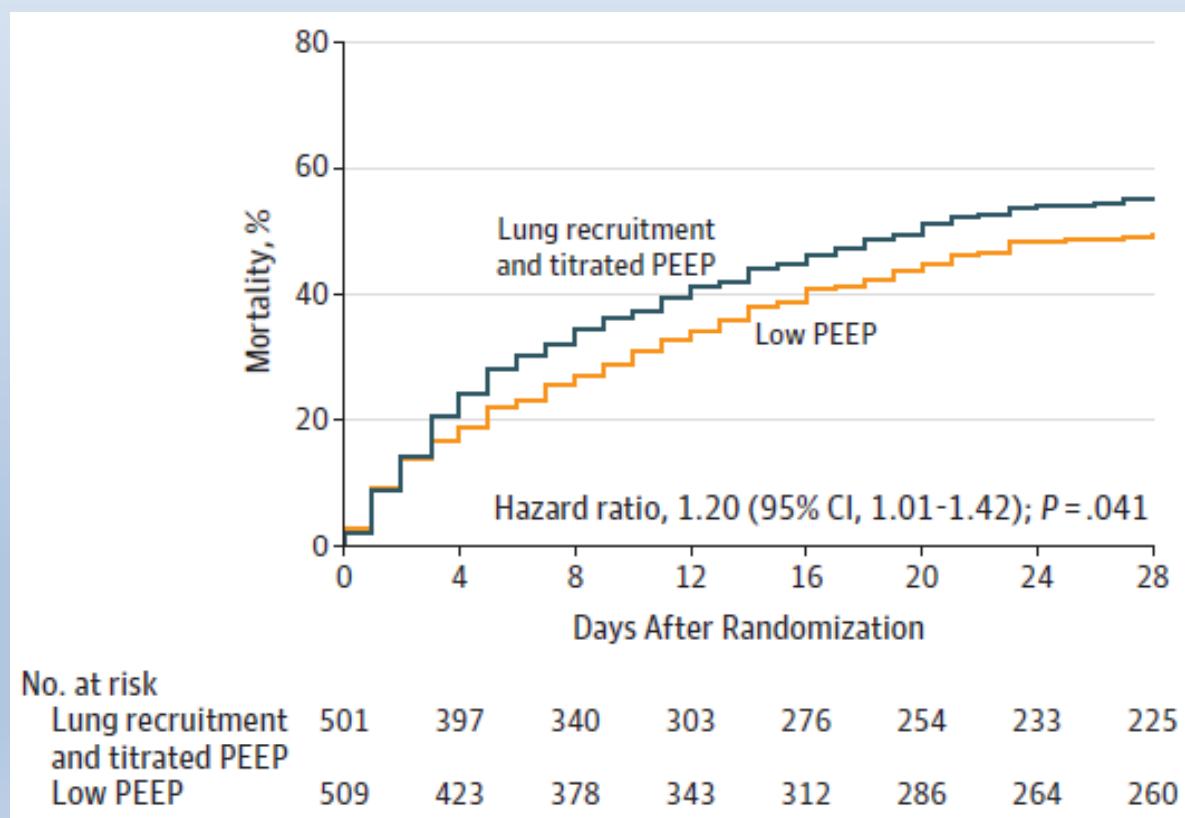
“Open up the lung and keep it open!”



Effect of Lung Recruitment and Titrated Positive End-Expiratory Pressure (PEEP) vs Low PEEP on Mortality in Patients With Acute Respiratory Distress Syndrome

A Randomized Clinical Trial

Writing Group for the Alveolar Recruitment for Acute Respiratory Distress Syndrome Trial (ART) Investigators



JAMA 2017

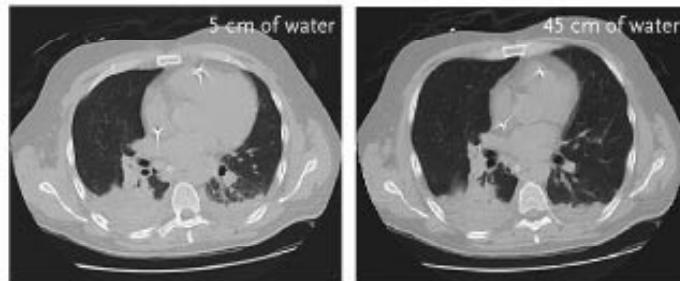
Recruit this!



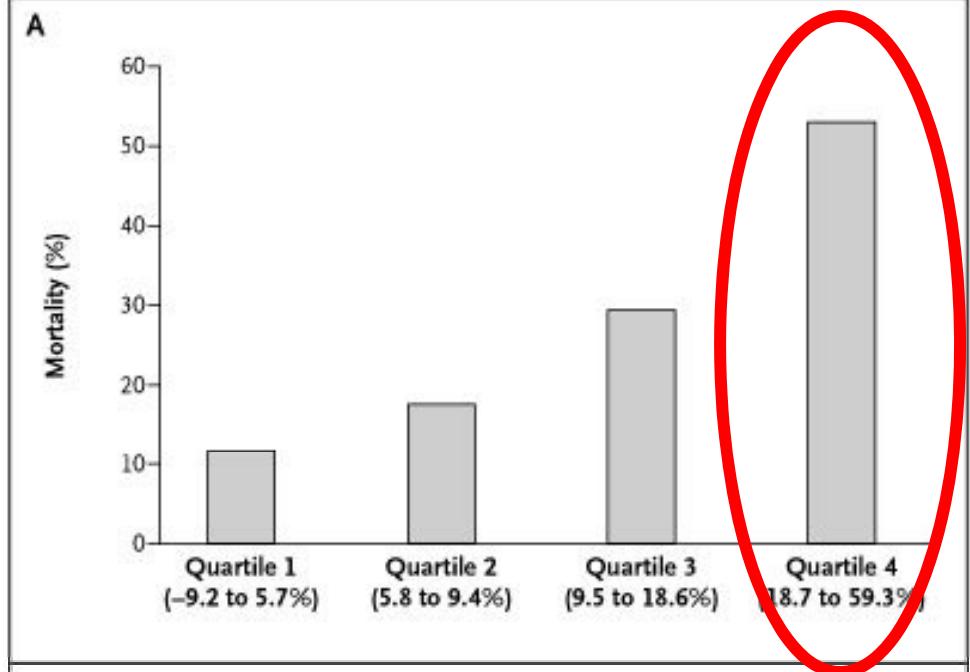
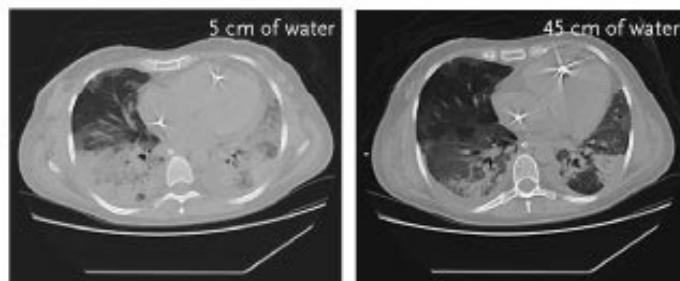
Lung Recruitment in Patients with the Acute Respiratory Distress Syndrome

Luciano Gattinoni, M.D., F.R.C.P., Pietro Caironi, M.D., Massimo Cressoni, M.D., Davide Chiumello, M.D., V. Marco Ranieri, M.D., Michael Quintel, M.D., Ph.D., Sebastiano Russo, M.D., Nicolò Patroniti, M.D., Rodrigo Cornejo, M.D., and Guillermo Bugedo, M.D.

B Lower Percentage of Potentially Recruitable Lung



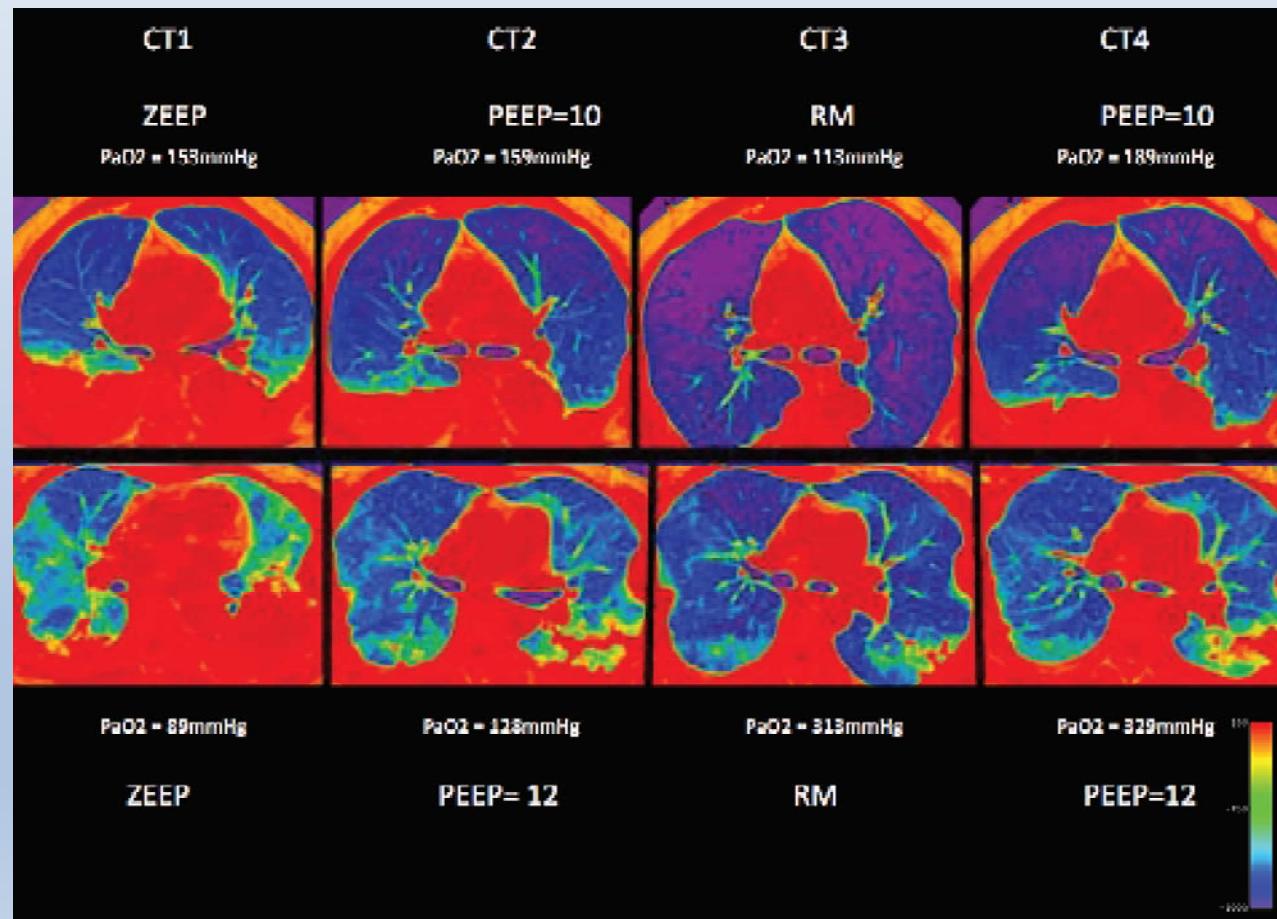
C Higher Percentage of Potentially Recruitable Lung



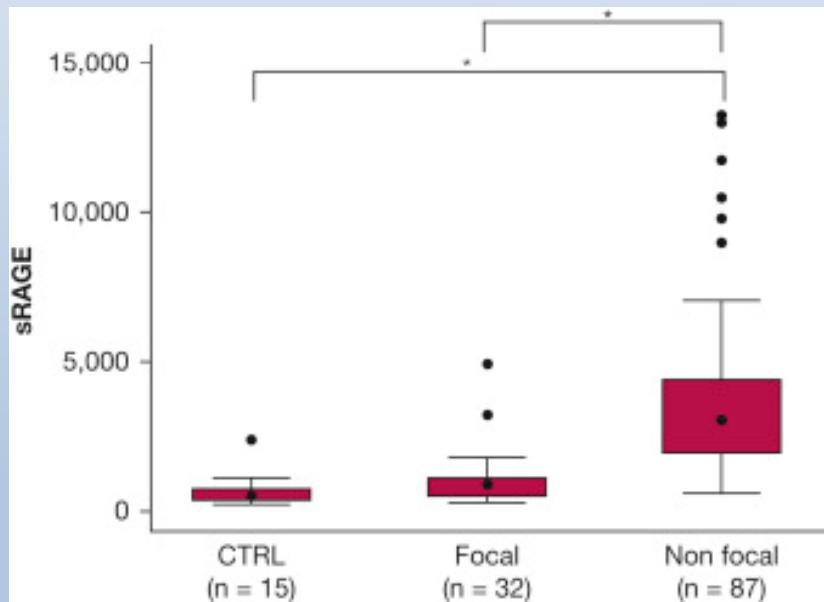
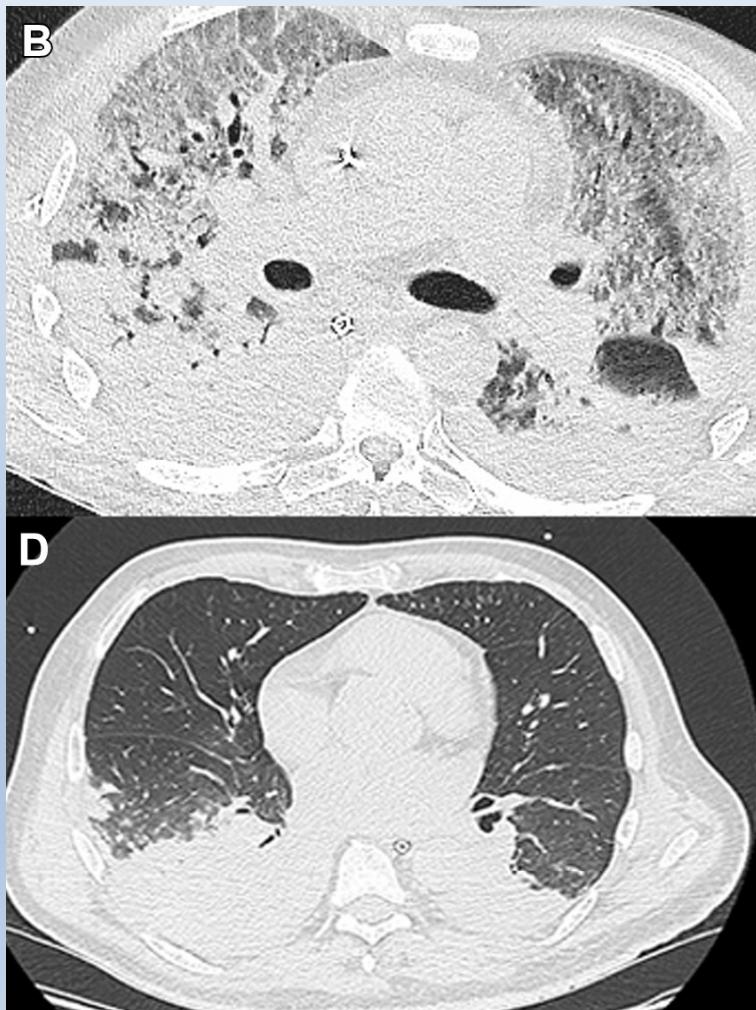
Gattinoni 2006

Lung morphology predicts response to recruitment maneuver in patients with acute respiratory distress syndrome

Jean-Michel Constantin, MD, PhD; Salvatore Grasso, MD, PhD; Gerald Chanques, MD; Sophie Aufort, MD; Emmanuel Futier, MD; Mustapha Sebbane, MD; Boris Jung, MD; Benoit Gallix; Jean Etienne Bazin, MD, PhD; Jean-Jacques Rouby, MD, PhD; Samir Jaber, MD, PhD

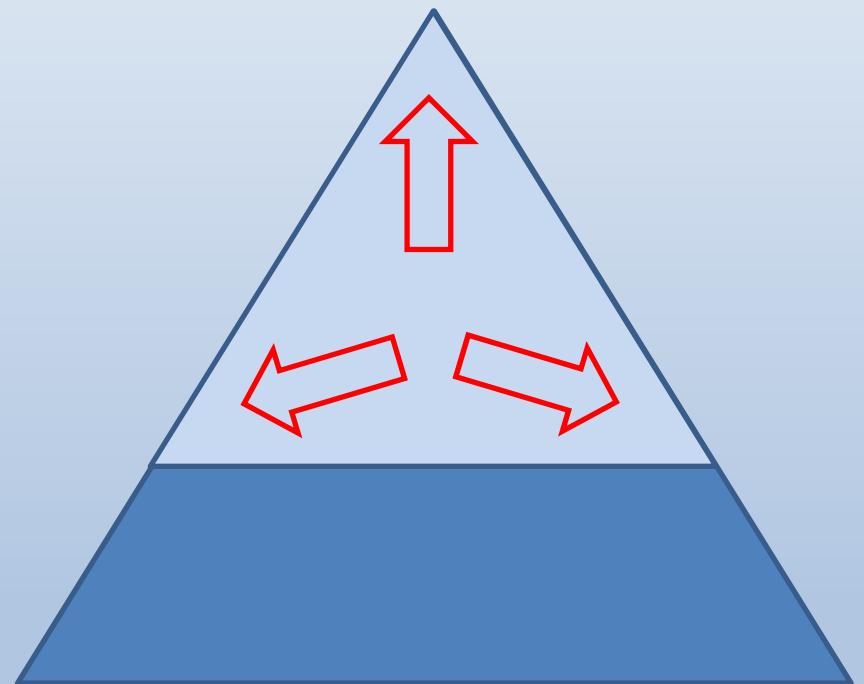
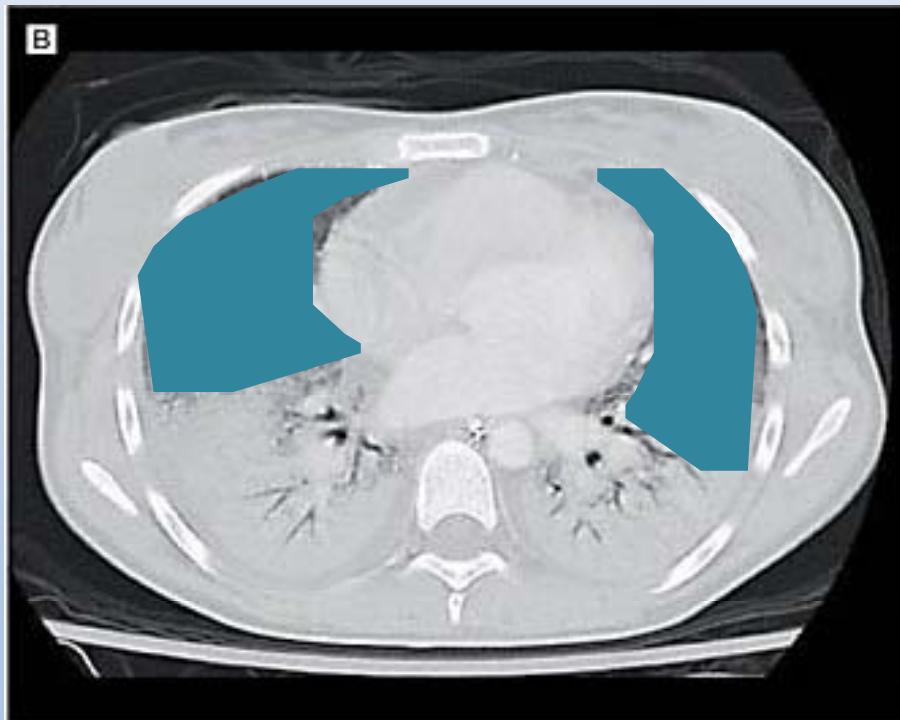


Elevated Plasma Levels of sRAGE Are Associated With Nonfocal CT-Based Lung Imaging in Patients With ARDS



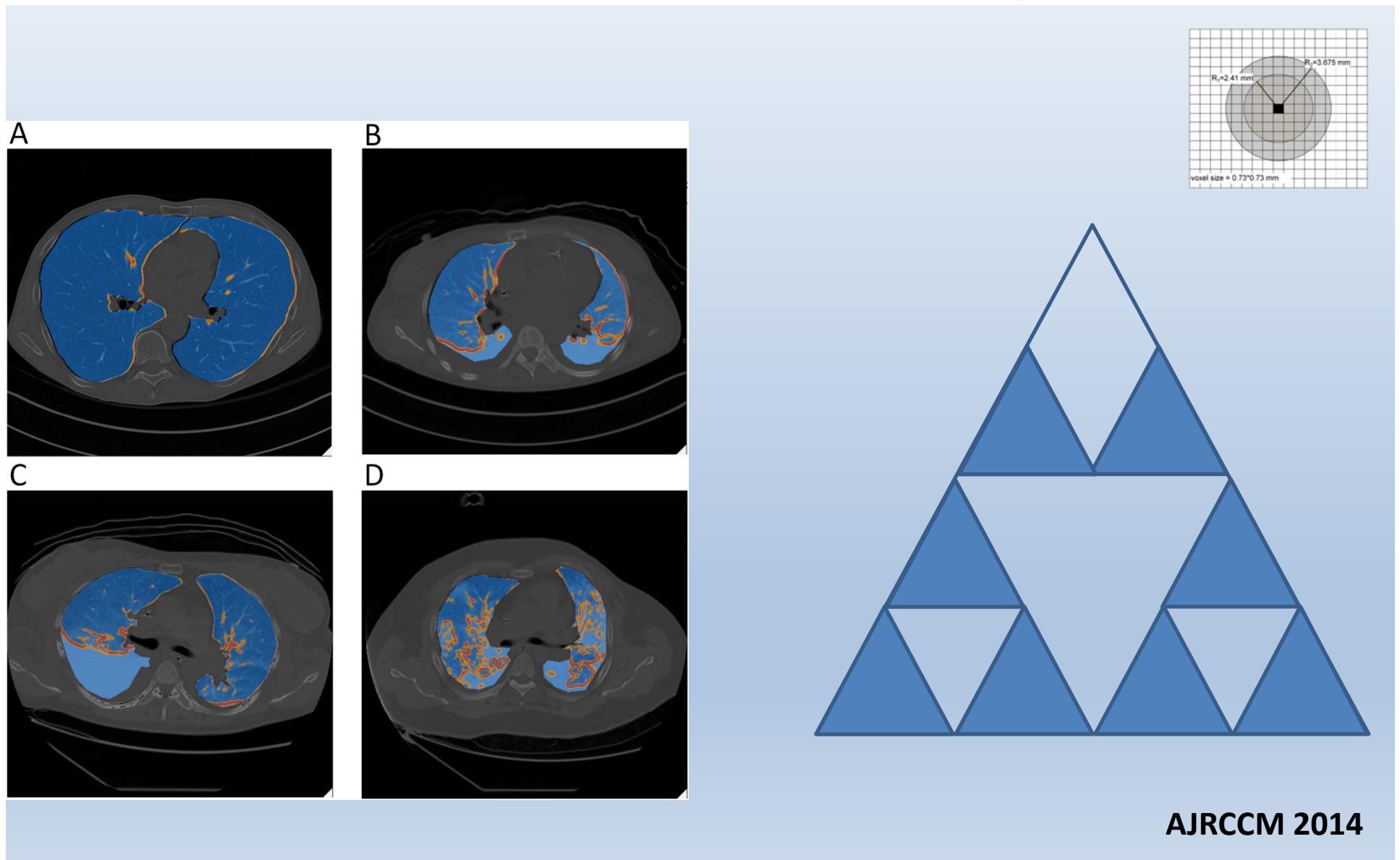
Mrozek et al. Chest 2016

'Baby Lung': a Binary Model



Lung Inhomogeneity in Patients with Acute Respiratory Distress Syndrome

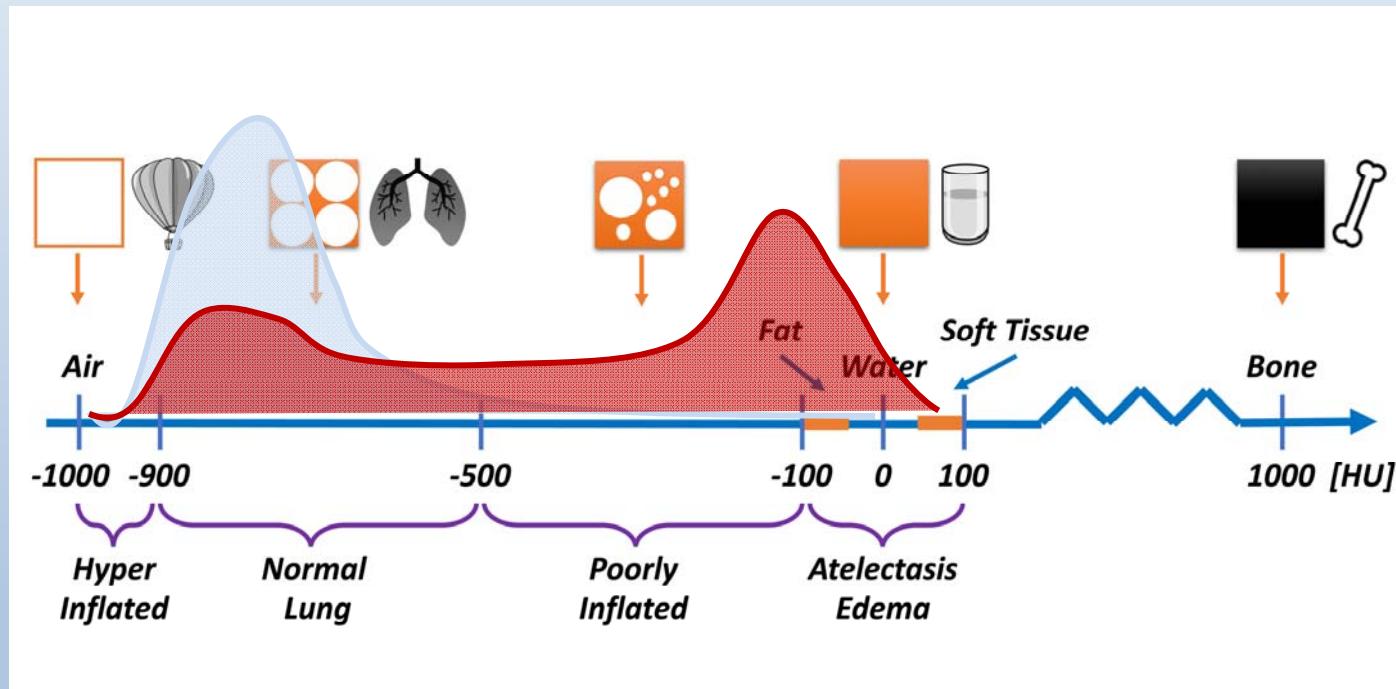
Massimo Cressoni¹, Paolo Cadringher¹, Chiara Chiurazzi¹, Martina Amini¹, Elisabetta Gallazzi¹, Antonella Marino¹, Matteo Brioni¹, Eleonora Carlesso¹, Davide Chiumello², Michael Quintel³, Guillermo Buggedo⁴, and Luciano Gattinoni^{1,2}



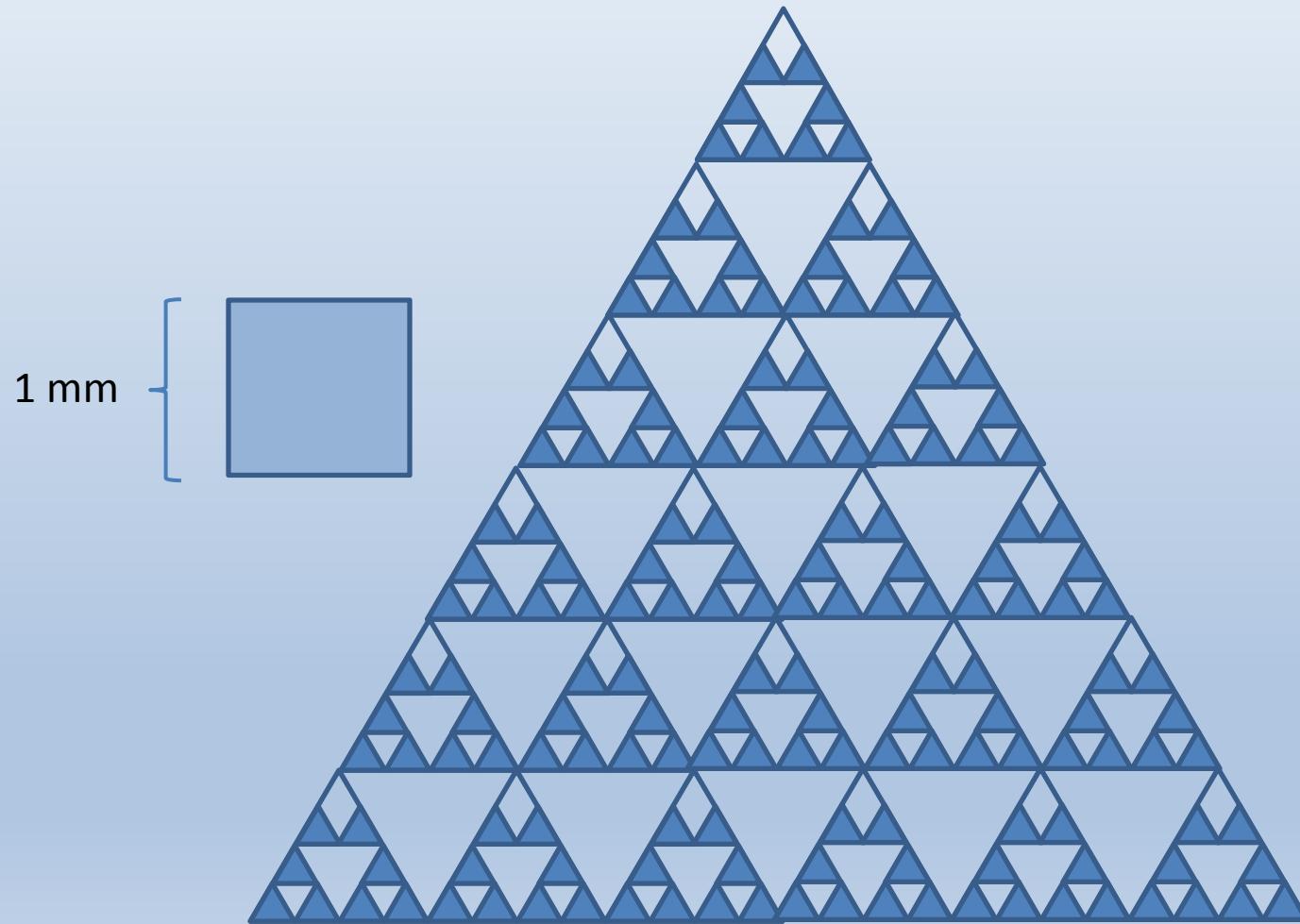
Find the ‘Normal’ Lung’



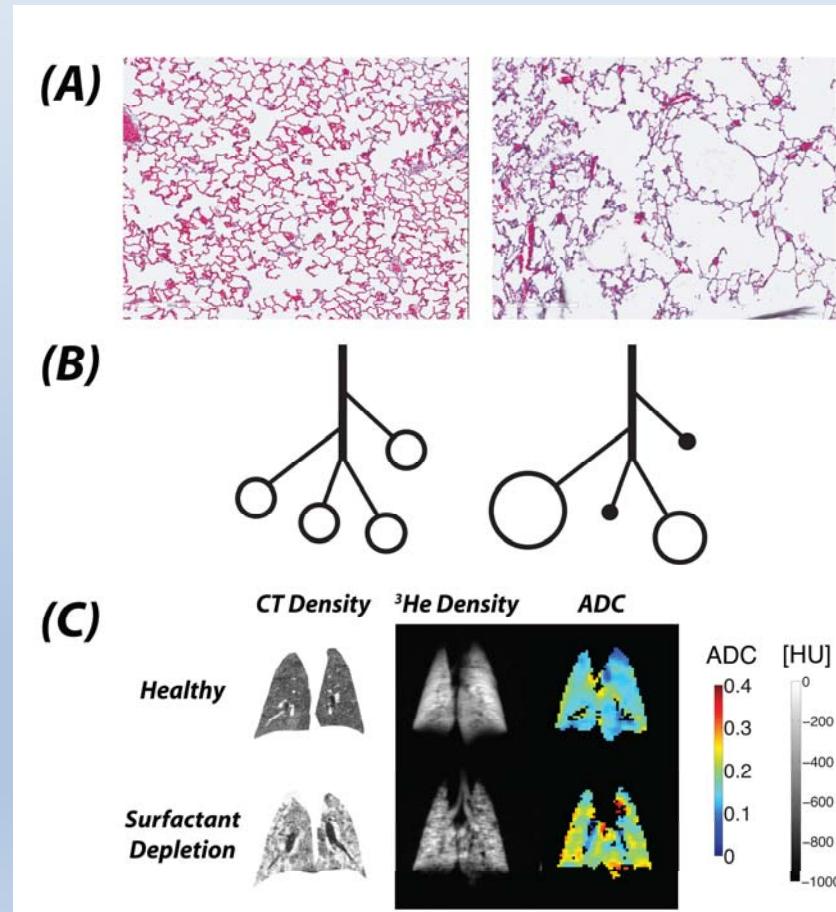
Interpretation of CT Densities



Sub-Voxel Heterogeneity of Inflation



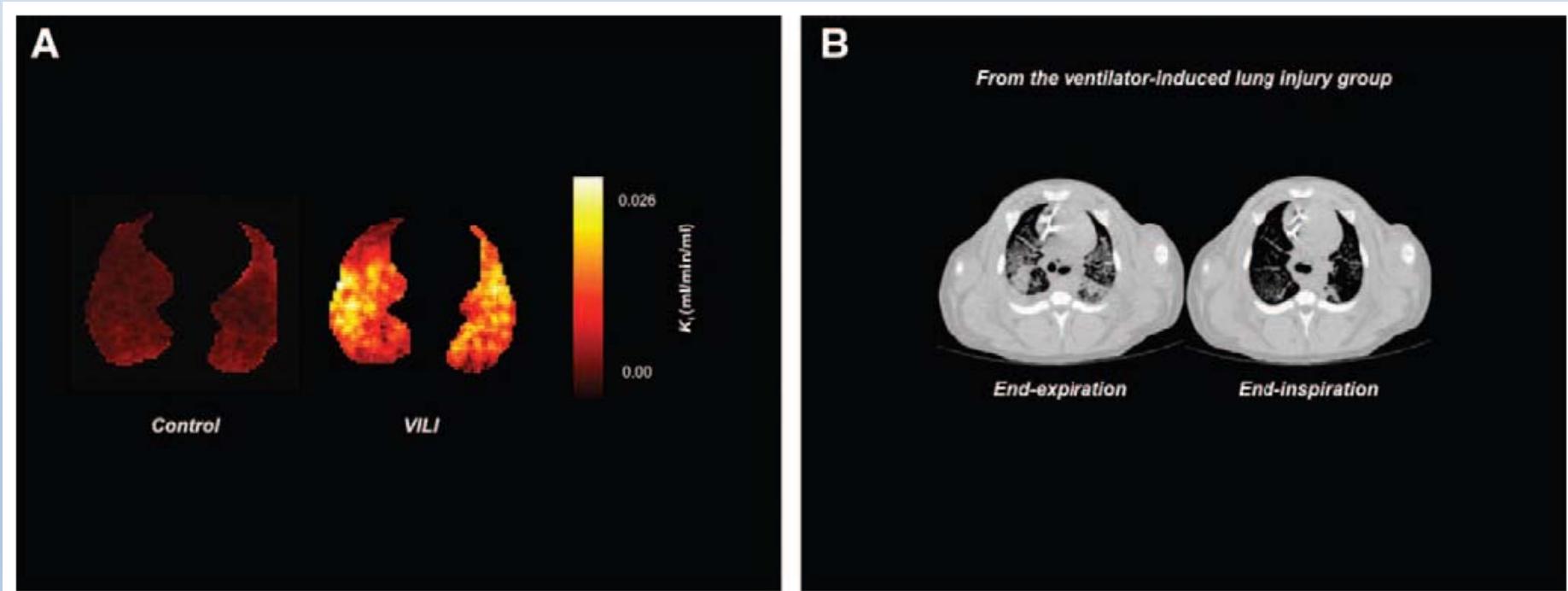
Imaging the Injured Lung



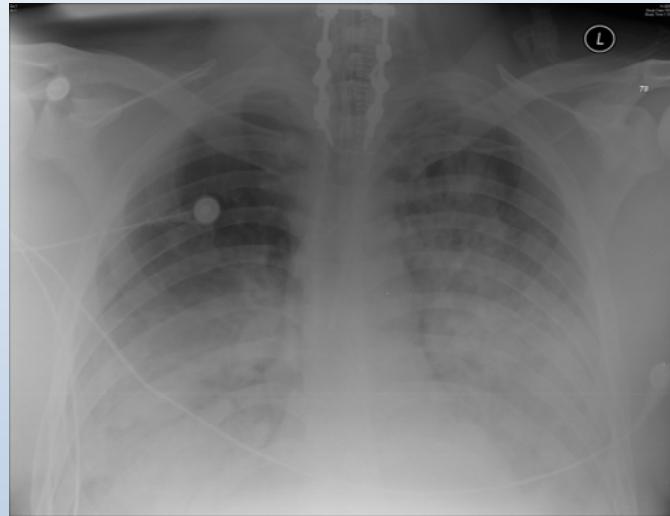
Early Inflammation Mainly Affects Normally and Poorly Aerated Lung in Experimental Ventilator-Induced Lung Injury*

João Batista Borges, MD, PhD^{1,2}; Eduardo L. V. Costa, MD, PhD^{2,3};

Fernando Suarez-Sipmann, MD, PhD^{1,4}; Charles Widström, MSc⁵; Anders Larsson, MD, PhD¹;
Marcelo Amato, MD, PhD²; Göran Hedenstierna, MD, PhD⁶



ARDS as a Spatially Evolving Process



Visualizing the Propagation of Acute Lung Injury

Maurizio Cereda, M.D., Yi Xin, M.S., Natalie Meeder, B.A., Johnathan Zeng, B.S.E., YunQing Jiang, M.S.E., Hooman Hamedani, M.S., Harrilla Profka, D.V.M., Stephen Kadlecak, Ph.D., Justin Clapp, Ph.D., Charuhas G. Deshpande, M.D., Jue Wu, Ph.D., James C. Gee, Ph.D., Brian P. Kavanagh, M.B., Rahim R. Rizi, Ph.D.

**HCl aspiration
(TV 12 ml/kg)**

1 h

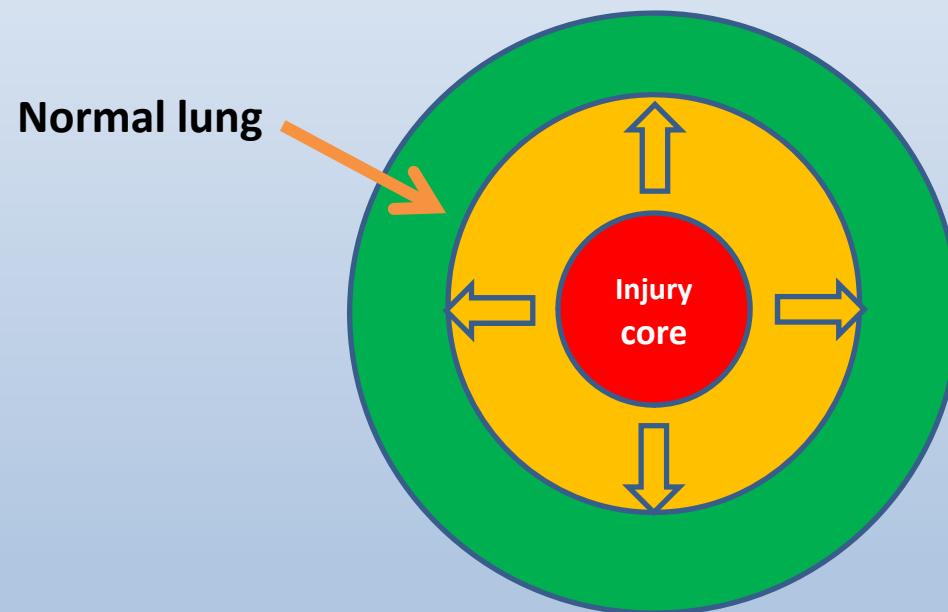
2 h

3 h

4 h



A Model of Lung Injury Propagation



Voxel-wise Tracking of Inflation and Injury Progression

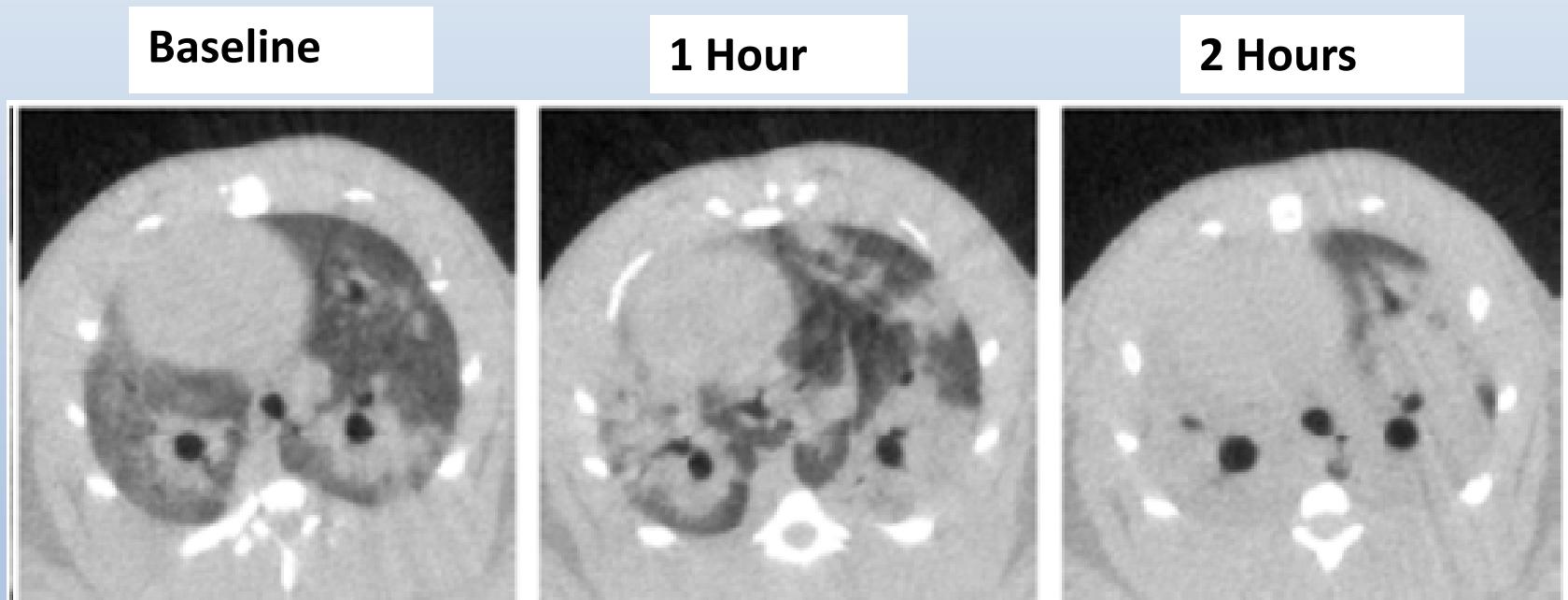
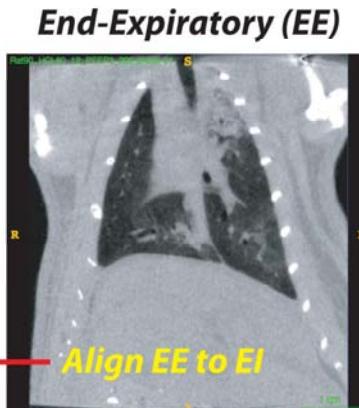
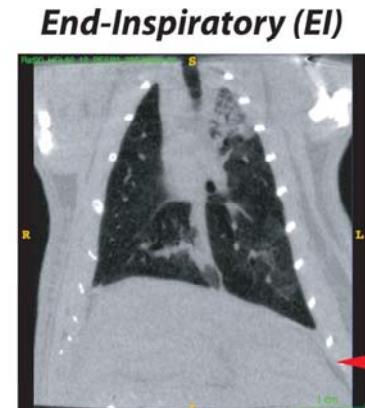
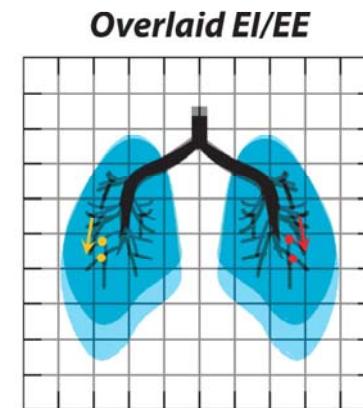
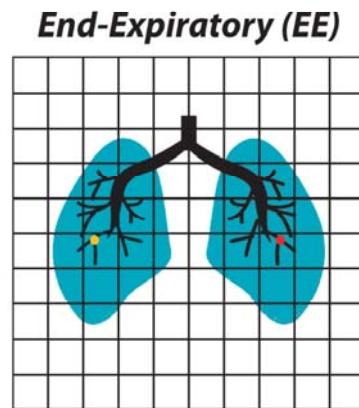
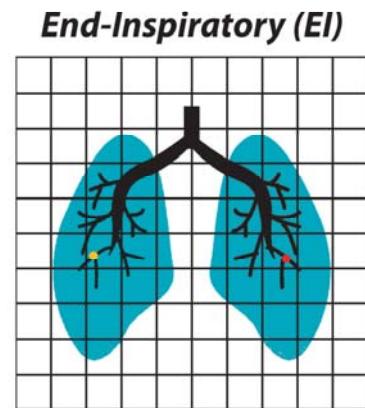
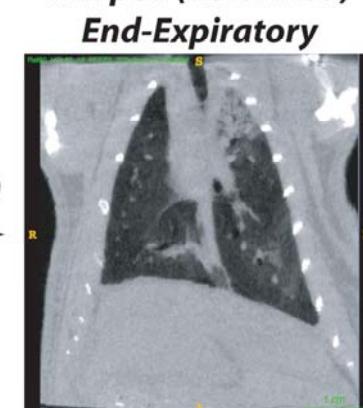


Image Registration

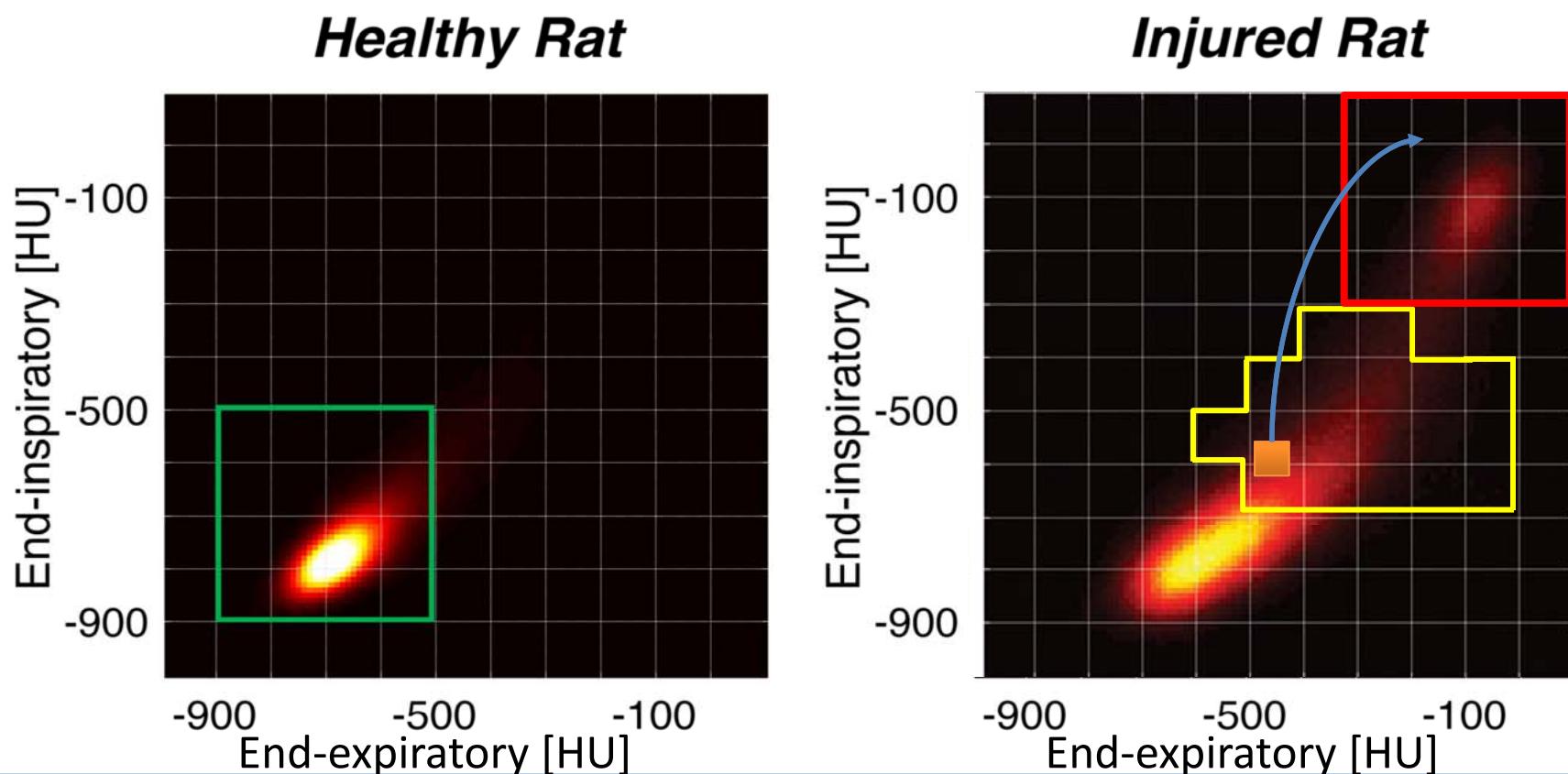


*3D Image
Registration*



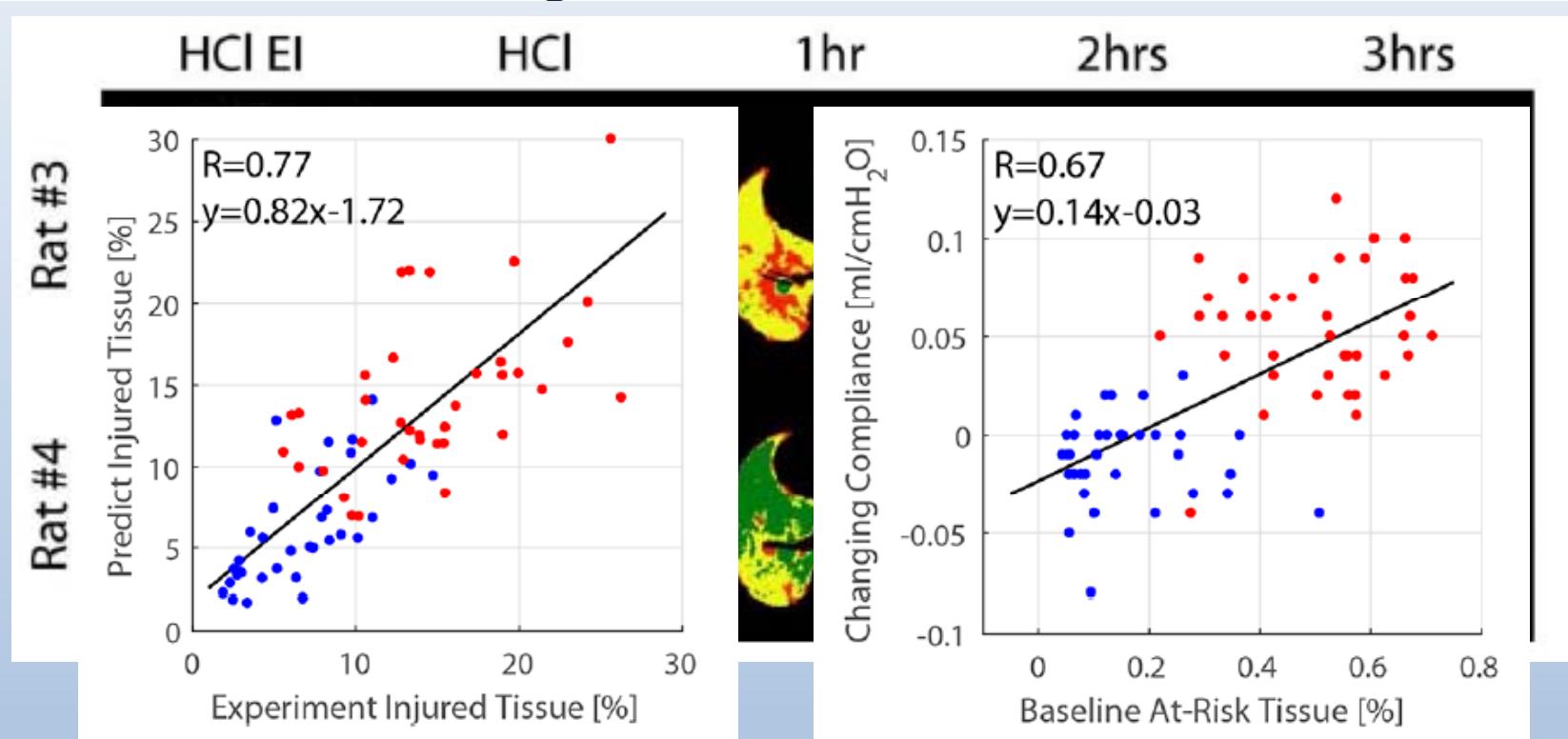
Tidal changes on CT and progression of ARDS

Maurizio Cereda,¹ Yi Xin,² Hooman Hamedani,² Giacomo Bellani,³ Stephen Kadlecak,² Justin Clapp,¹ Luca Guerra,⁴ Natalie Meeder,¹ Jennia Rajaei,² Nicholas J Tustison,⁵ James C Gee,² Brian P Kavanagh,^{6,7} Rahim R Rizi²



Tidal changes on CT and progression of ARDS

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Severe Injury



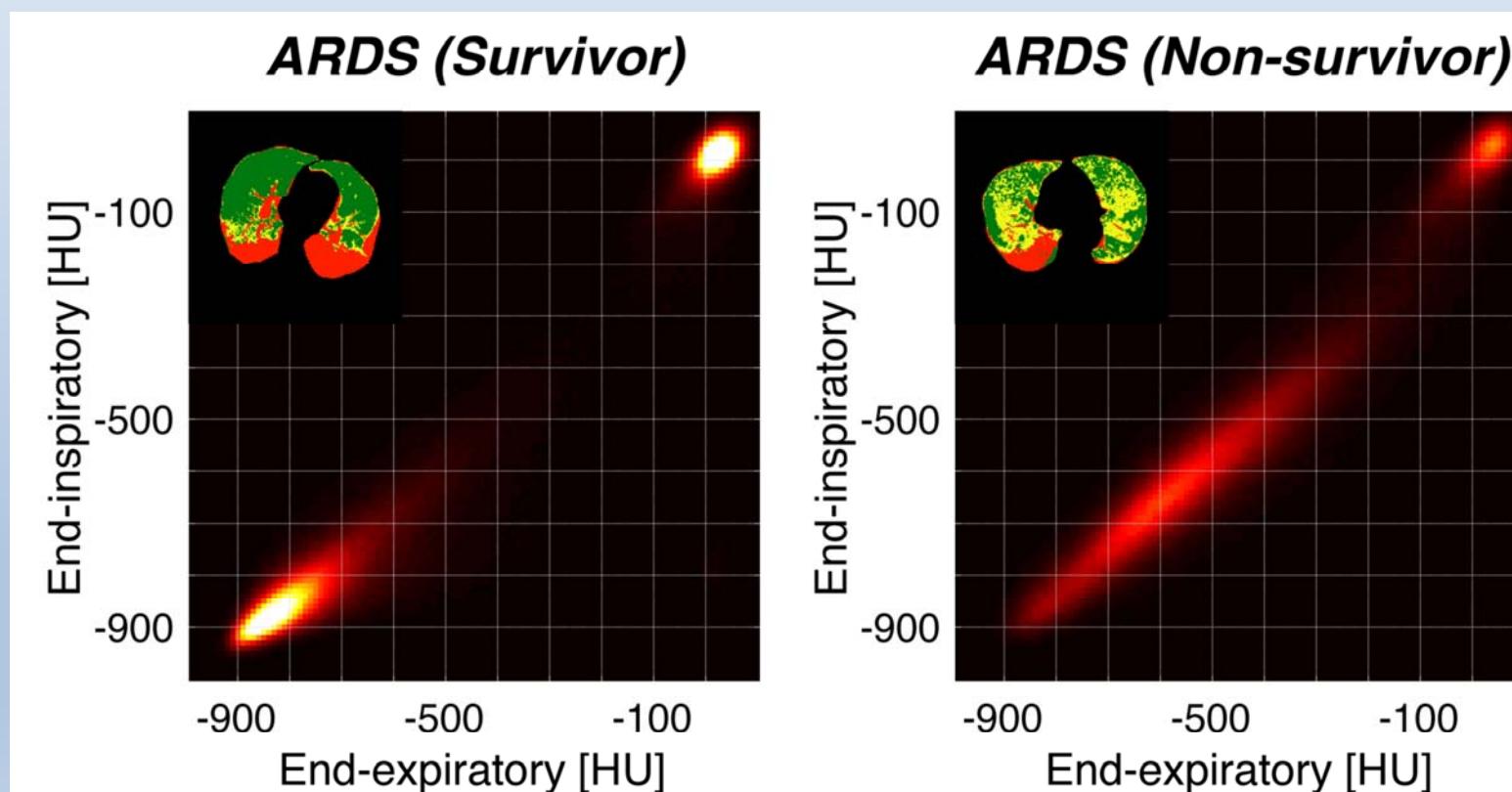
Normal Lung



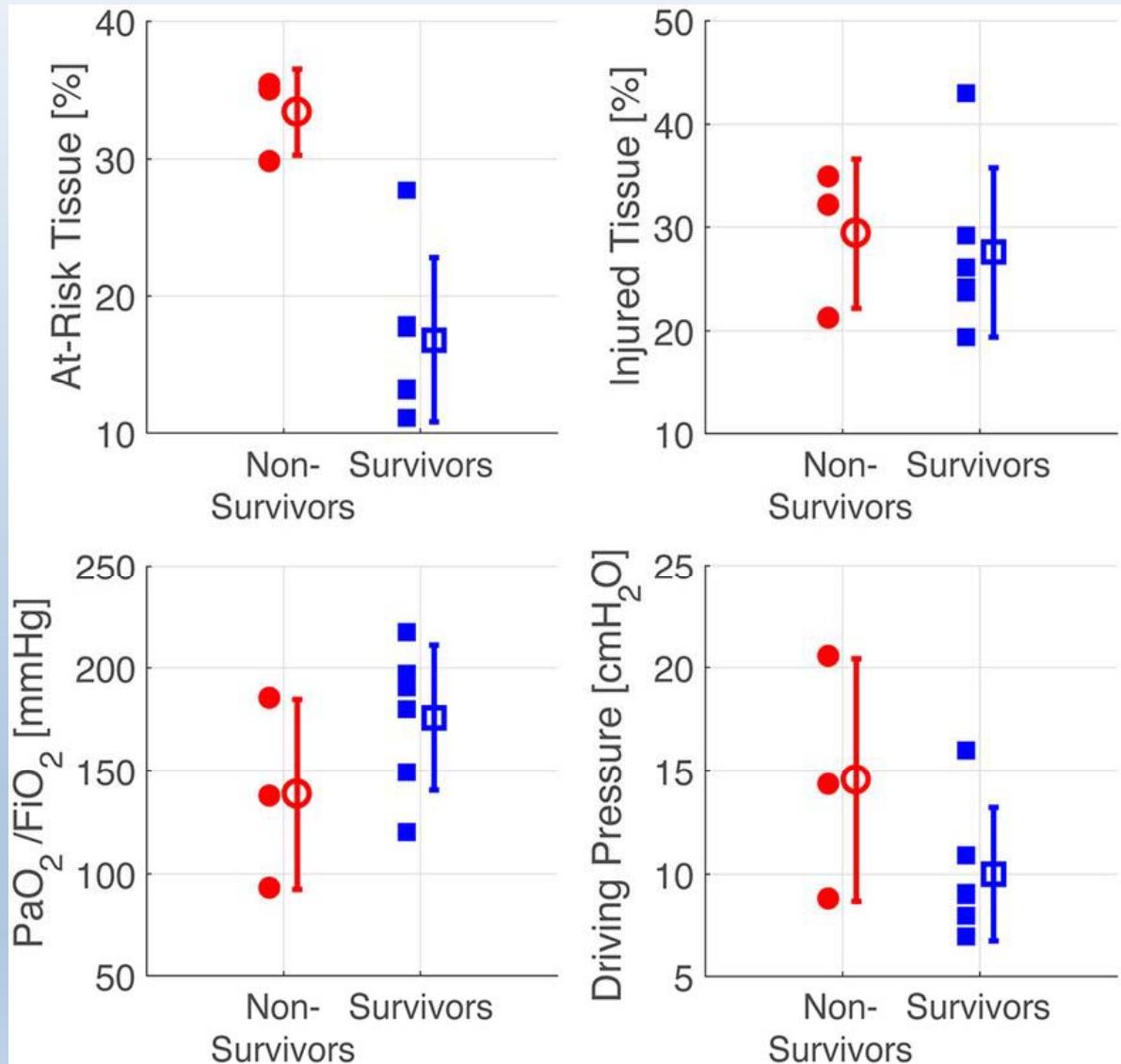
'High Risk' Unstable Inflation

Tidal changes on CT and progression of ARDS

Maurizio Cereda,¹ Yi Xin,² Hooman Hamedani,² Giacomo Bellani,³ Stephen Kadlecak,² Justin Clapp,¹ Luca Guerra,⁴ Natalie Meeder,¹ Jennia Rajaei,² Nicholas J Tustison,⁵ James C Gee,² Brian P Kavanagh,^{6,7} Rahim R Rizi²



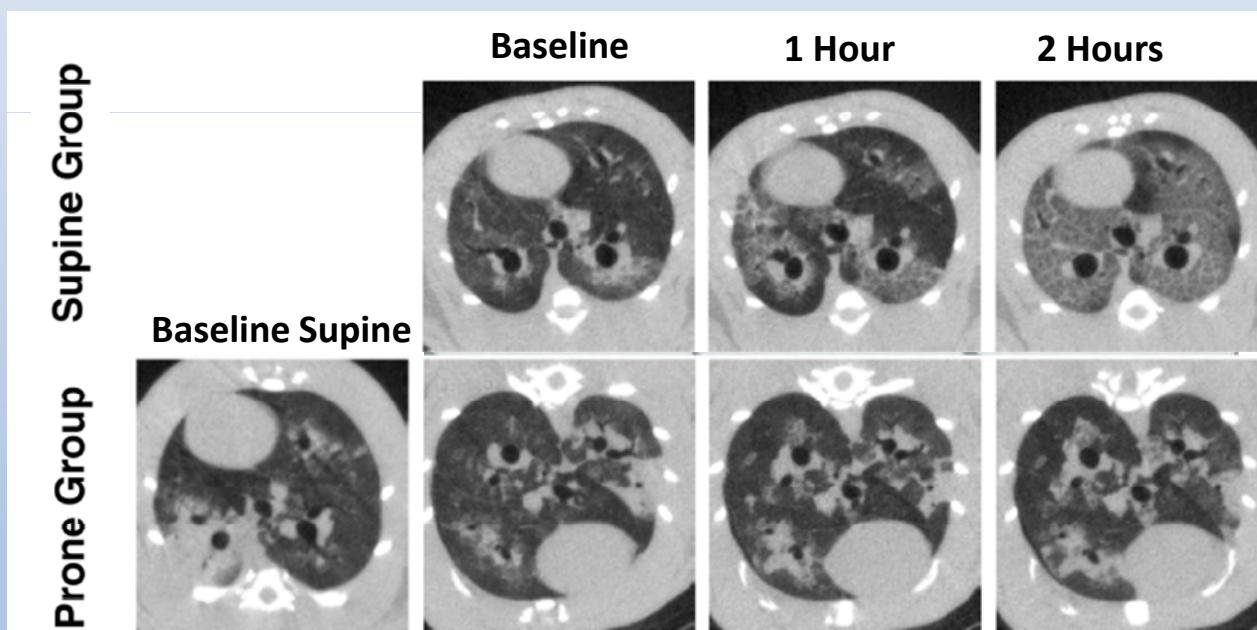
Unstable Inflation and ARDS Mortality



Unstable Inflation Causing Injury

Insight from Prone Position and Paired Computed Tomography Scans

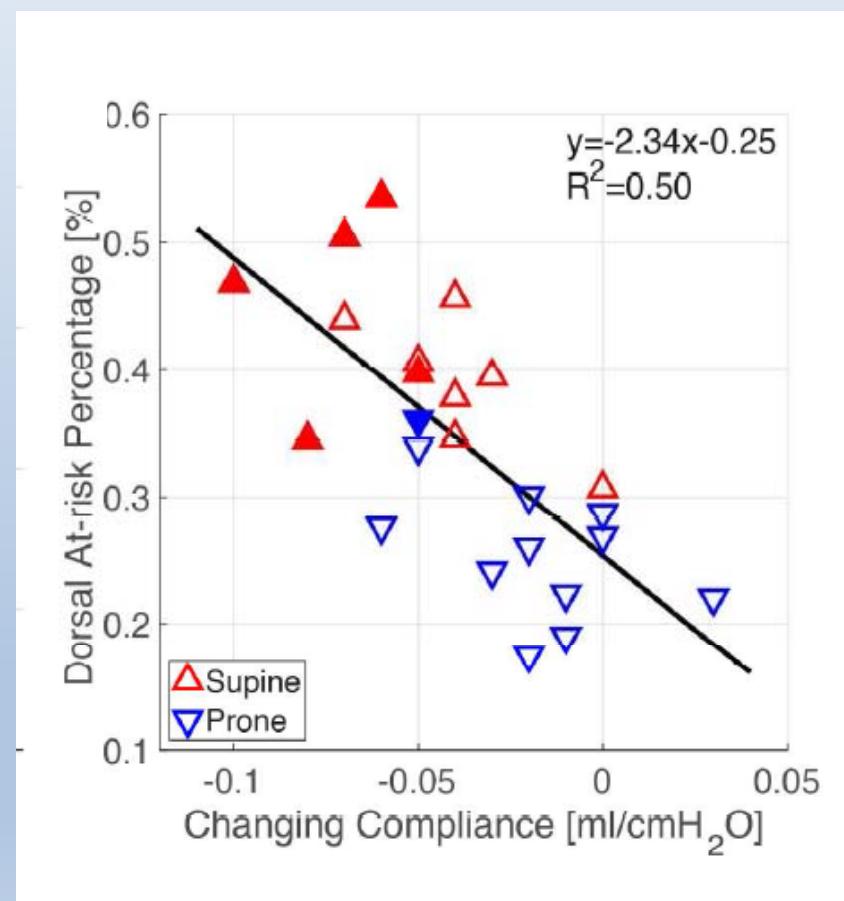
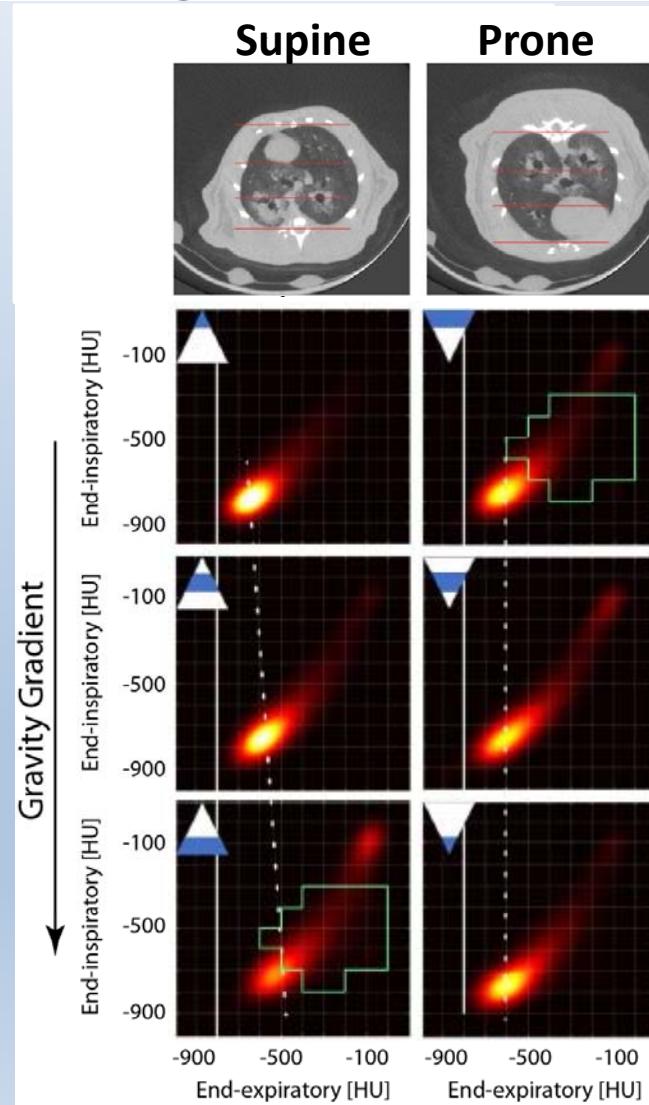
Yi Xin^{1*}, Maurizio Cereda^{2*}, Hooman Hamedani¹, Mehrdad Pourfathi¹, Sarmad Siddiqui¹, Natalie Meeder², Stephen Kadlecik¹, Ian Duncan¹, Harrilla Profka¹, Jennia Rajaei³, Nicholas J. Tustison⁴, James C. Gee¹, Brian P. Kavanagh^{5,6}, and Rahim R. Rizi¹



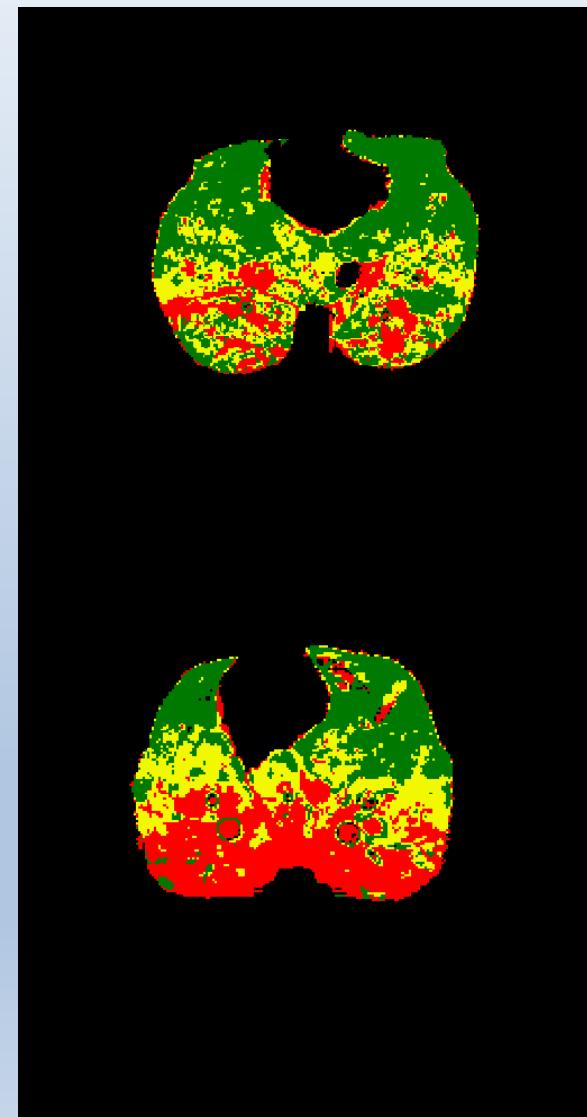
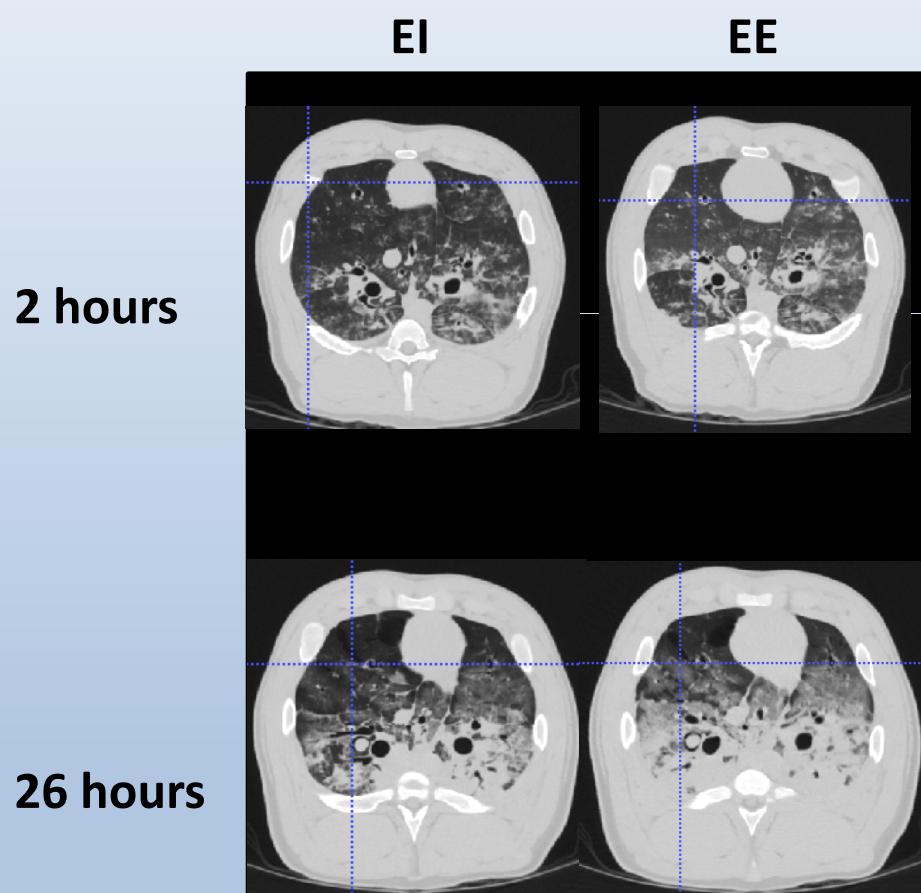
Unstable Inflation Causing Injury

Insight from Prone Position and Paired Computed Tomography Scans

Yi Xin^{1*}, Maurizio Cereda^{2*}, Hooman Hamedani¹, Mehrdad Pourfathi¹, Sarmad Siddiqui¹, Natalie Meeder², Stephen Kadlecik¹, Ian Duncan¹, Harrilla Profka¹, Jennia Rajaei³, Nicholas J. Tustison⁴, James C. Gee¹, Brian P. Kavanagh^{5,6}, and Rahim R. Rizi¹



Progression of Lung Injury in Ventilated Pigs



Conclusions

- Heterogeneity of the ARDS population is a major obstacle to progress in treatment
- The way we understand ARDS and ventilate patients is heavily influenced by lung imaging
- Small-scale heterogeneity and instability of lung inflation may promote ARDS progression
- Imaging research may provide the tools to predict outcomes and guide therapy

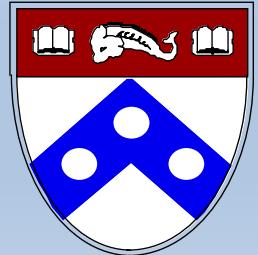
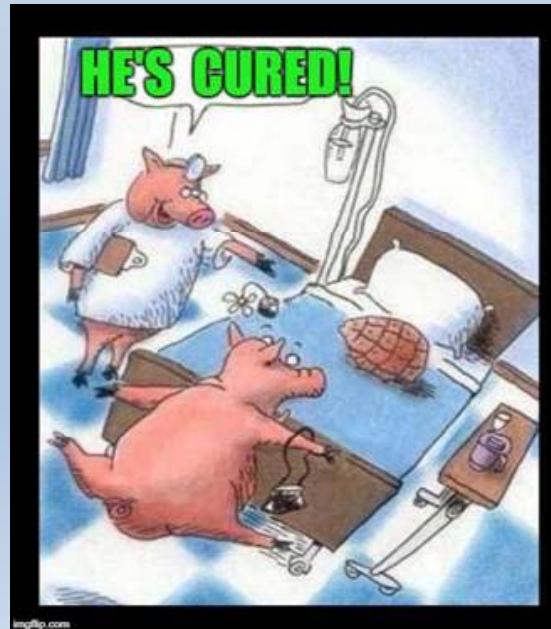
- In an autopsy study in patients meeting Berlin ARDS criteria, the fraction of patients who also had disseminated alveolar damage (DAD) was:
 - 90%
 - 45%
 - 25%

- A diffuse vs. focal pattern of CT infiltrates in ARDS is associated with the following:
 - Alveolar recruitment by positive pressure
 - Serum markers of epithelial injury
 - Worse mortality
 - All of the above

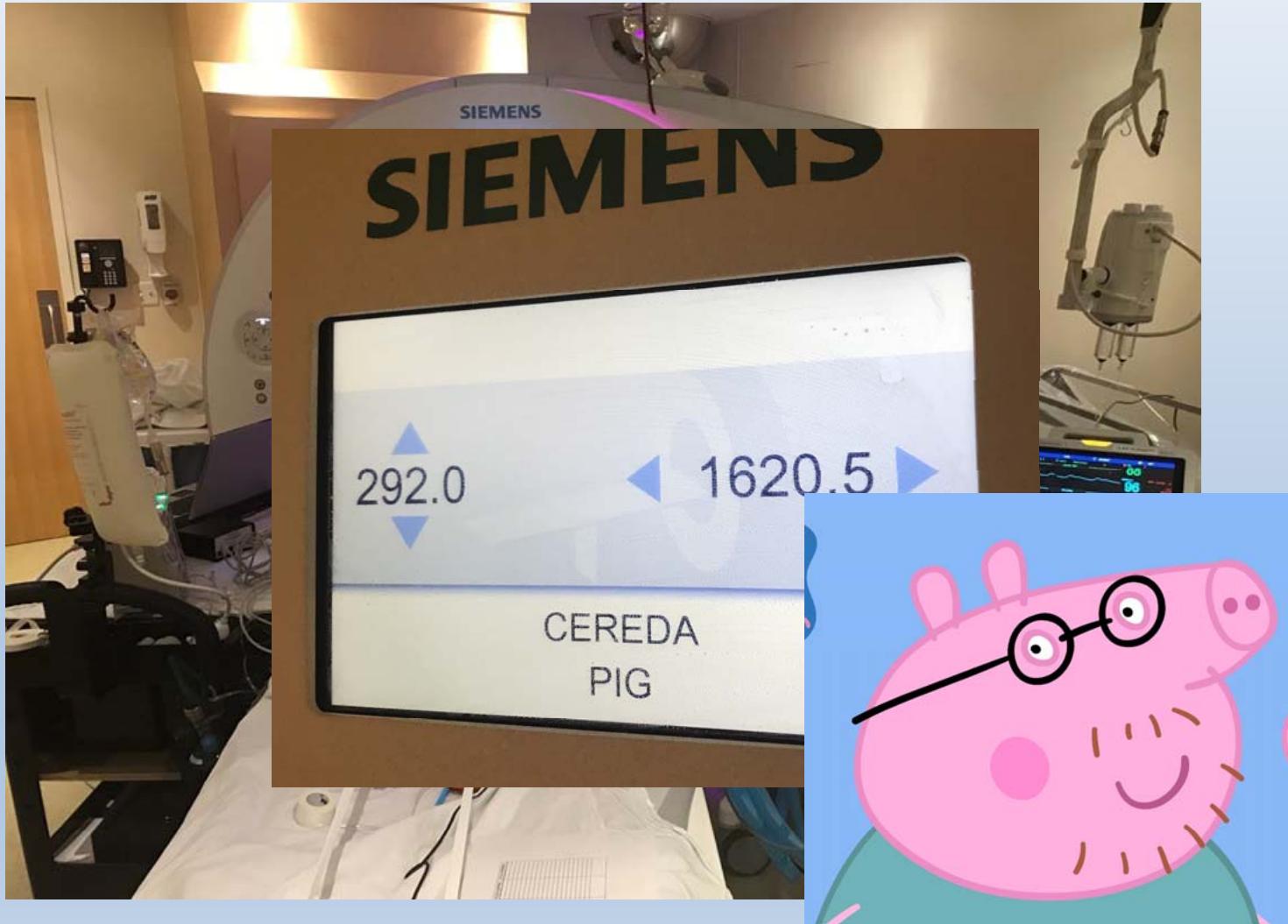
- PET imaging studies in human ARDS showed high metabolic activity in ventilated lung tissue.
 - True
 - False

Acknowledgements

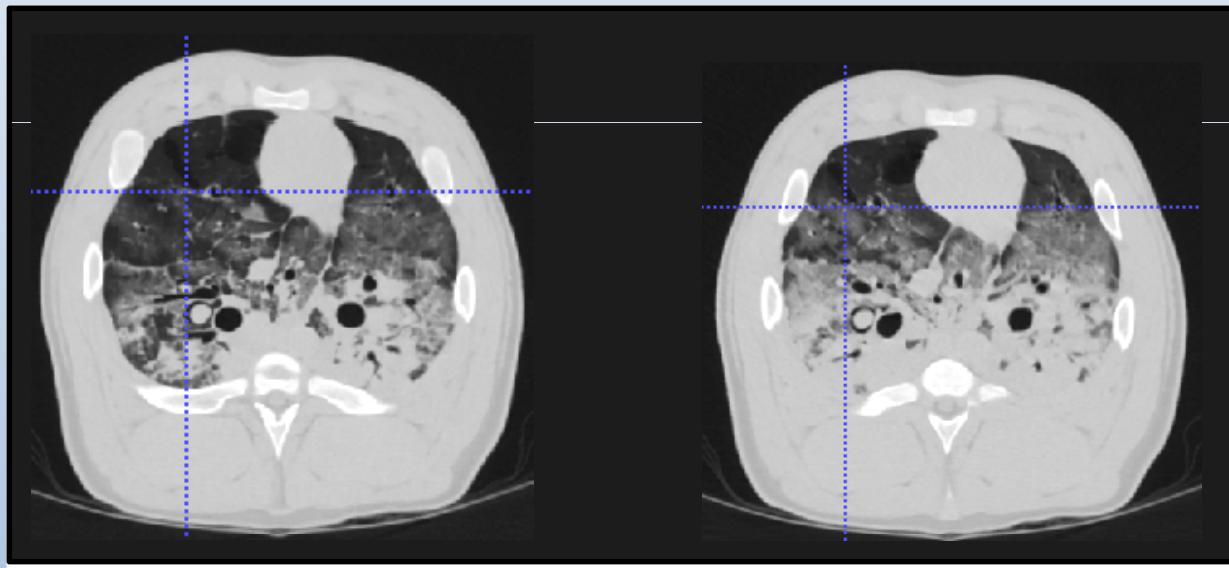
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Lung Injury Propagation in a Large Animal Model



Unstable Recruitment and Atelectrauma



INSPIRATION

EXPIRATION