

Introduction: Acute respiratory distress syndrome (ARDS) presents a significant clinical challenge, with ventilator-induced lung injury (VILI) being a critical complication arising from life-saving mechanical ventilation. Understanding the spatial and temporal dynamics of VILI can inform therapeutic strategies to mitigate lung damage and improve outcomes.

Methods: Histological sections from initially healthy mice and pulmonary lavage-injured mice subjected to a second hit of VILI were segmented with Ilastik to define regions of lung injury. A scale-free network approach was applied to assess the correlation between injury regions, with regions of injury represented as 'nodes' in the network and 'edges' quantifying the degree of correlation between nodes. A simulated time series analysis was conducted to emulate the temporal sequence of injury events.

Results: Automated segmentation identified different lung regions in good agreement with manual scoring, achieving a sensitivity of 78% and a specificity of 85% across 'injury' pixels. Overall accuracy across 'injury', 'air', and 'other' pixels was 81%. The size of injured regions followed a power-law distribution, suggesting a 'rich-get-richer' phenomenon in the distribution of lung injury. Network analysis revealed a scale-free distribution of injury correlations, highlighting hubs of injury that could serve as focal points for therapeutic intervention. Simulated time series analysis further supported the concept of secondary injury events following an initial insult, with patterns resembling those observed in seismological studies of aftershocks.

Conclusion: The size distribution of injured regions underscores the spatially heterogeneous nature of acute and ventilator-induced lung injury. The application of network theory demonstrates the emergence of injury 'hubs' that are consistent with a 'rich-get-richer' dynamic. Simulated time series analysis demonstrates that the progression of injury events in the lung could follow spatiotemporal patterns similar to the progression of aftershocks in seismology, providing new insights into the mechanisms of injury distribution and propagation. Both phenomena suggest a potential for interventions targeting these injury 'hubs' to reduce the impact of VILI in ARDS management.