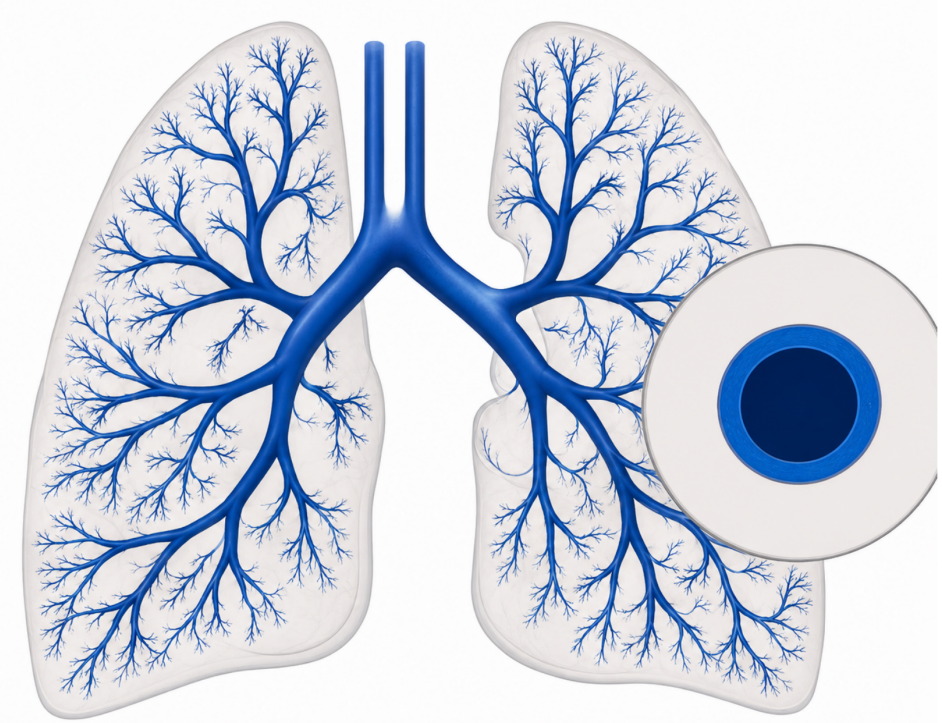


## 1. THE CLINICAL CHALLENGE

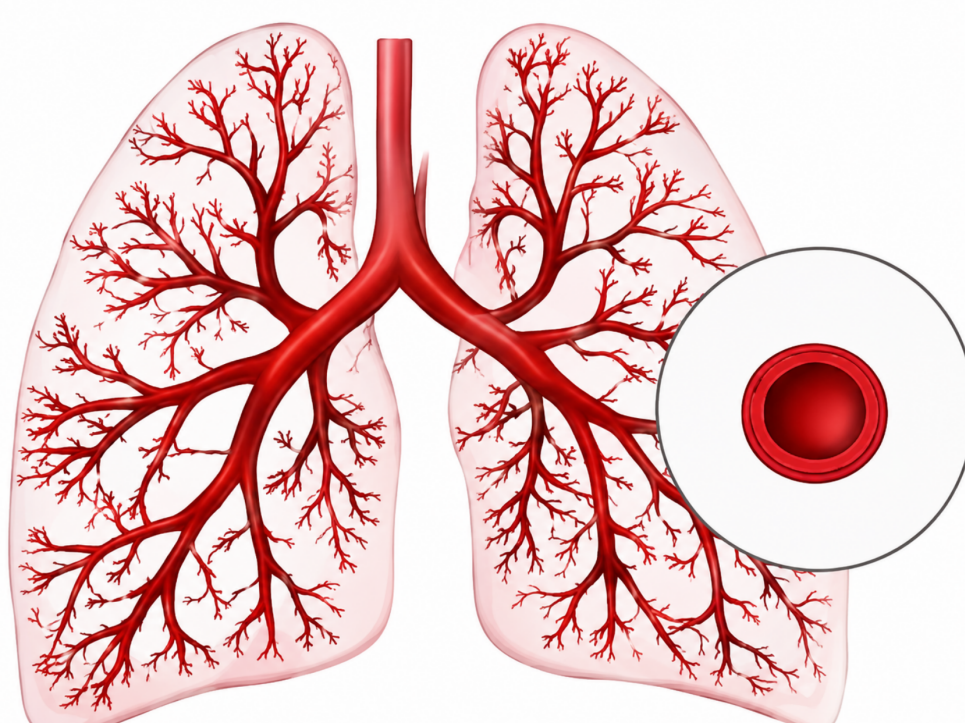
PAH is a progressive vasculopathy characterized by distal arteriolar narrowing, rarefaction, heterogeneous remodeling, sustained elevation of pulmonary vascular resistance, right-ventricular failure, and high mortality.

### Healthy Pulmonary Circulation



- Normal vessel hierarchy
- Wide distal arteries
- Balanced flow distribution
- Low pulmonary resistance
- Normal RV function

### PAH Vascular Remodeling

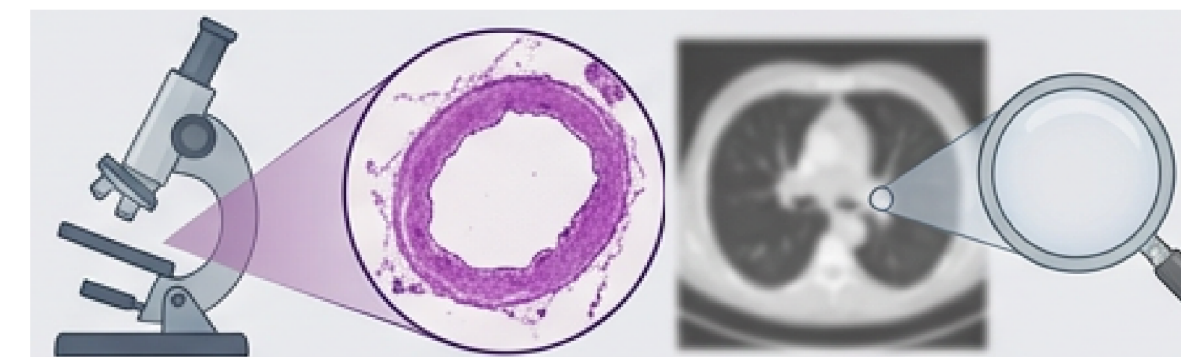


- Distal arteriolar narrowing
- Vascular rarefaction
- Heterogeneous remodeling
- Sustained ↑ resistance
- RV failure and high mortality

## 2. THE ENGINEERING GAP

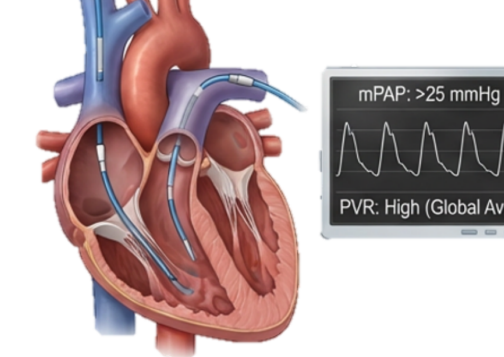
Current approaches quantify structure or provide a single global resistance value, but miss where and how resistance accumulates within the distal network.

### Histopathology/CT/MRI (Structure Only)



Anatomy & vessel structure

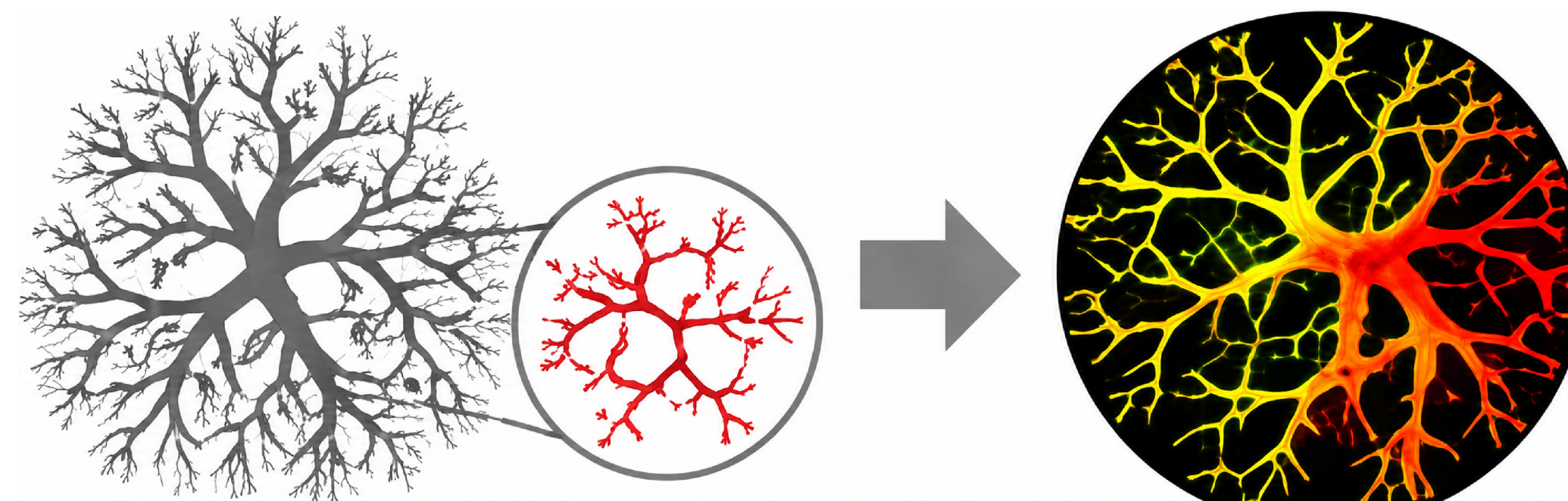
### RHC (Function Only)



One number for the whole lung

### THE MISSING INFORMATION

Where and how does resistance emerge within the distal vascular network?



Need a technology that links molecular recording, 3D architecture, and spatially resolved resistance.

## 3. OUR ENGINEERING VISION



### Molecularly record

Local hemodynamic burden encoded into stable AIE fluorescence during *in situ* gelation.



### Map spatial heterogeneity

Whole-lung 3D reconstruction reveals heterogeneous resistance burden across the arterial network.



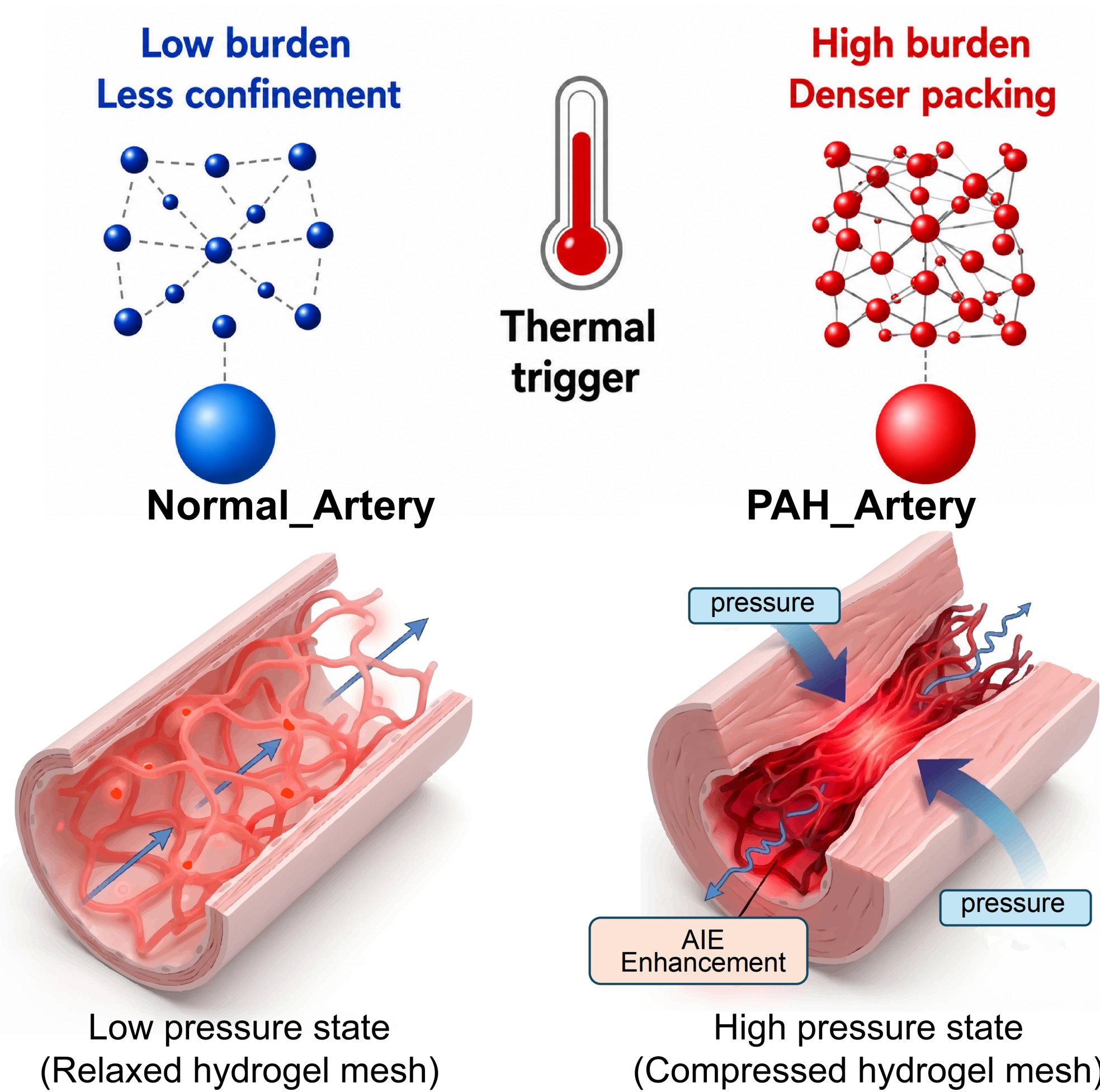
### Enable precision phenotyping

Identify high-burden microdomains linked to remodeling and disease severity.

From static anatomy to functionally informed vascular phenotyping.

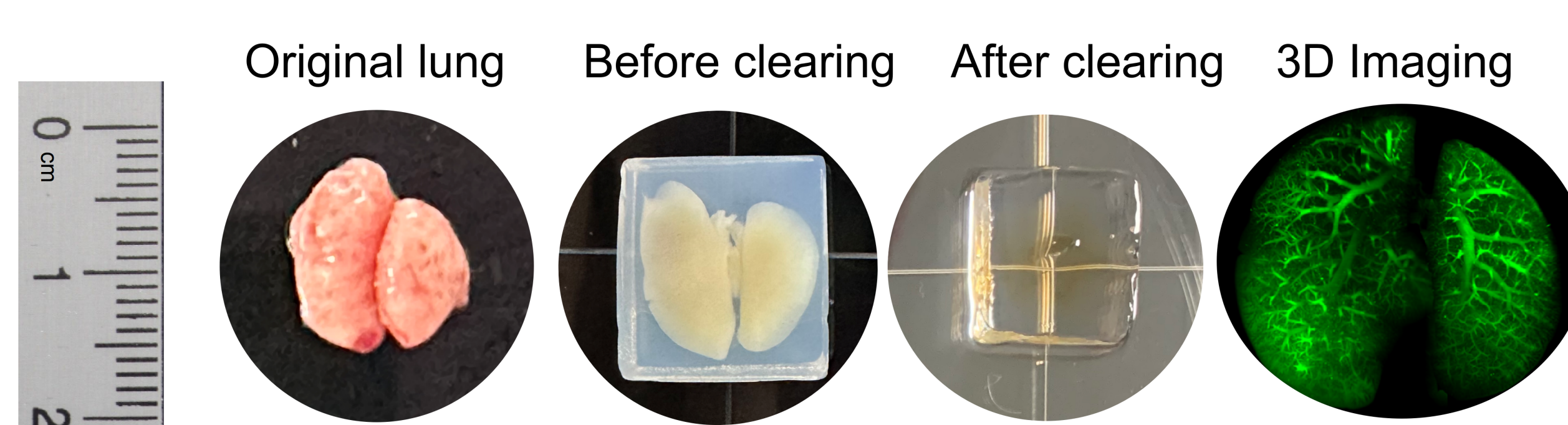
## 4. AIE-BASED MOLECULAR RECORDING

### Confinement-dependent emission mechanism

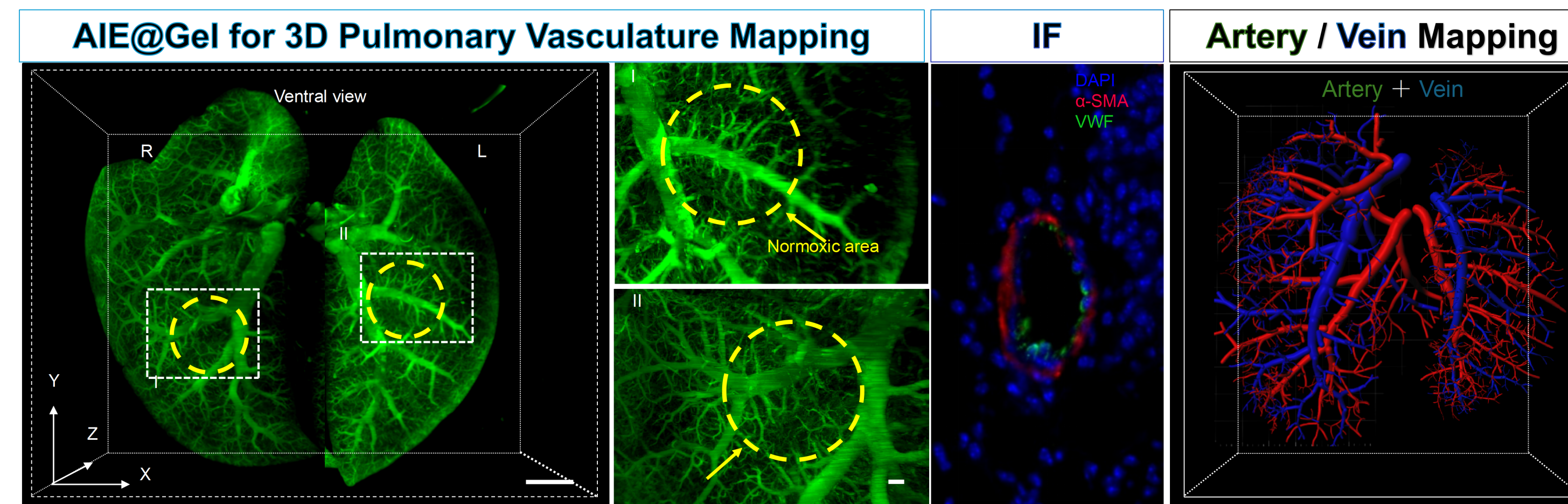


## 5. WHOLE-LUNG 3D VASCULAR RECONSTRUCTION

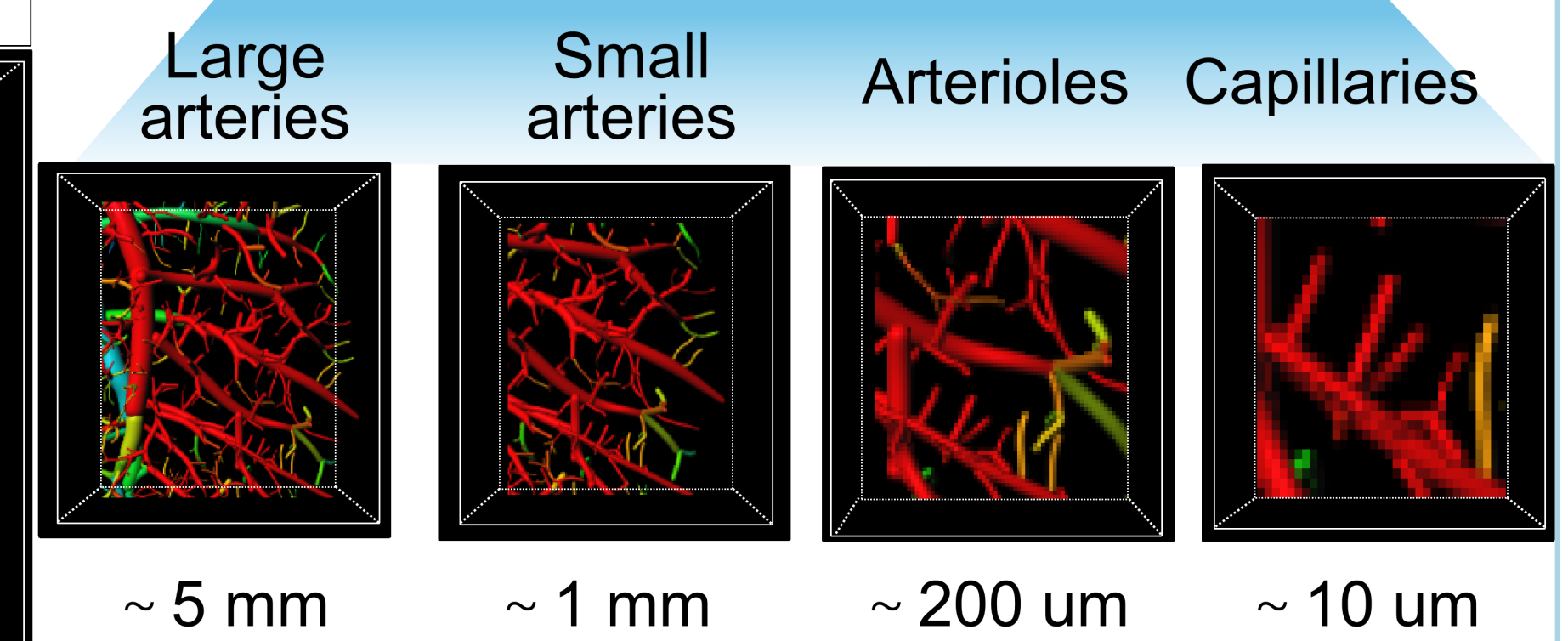
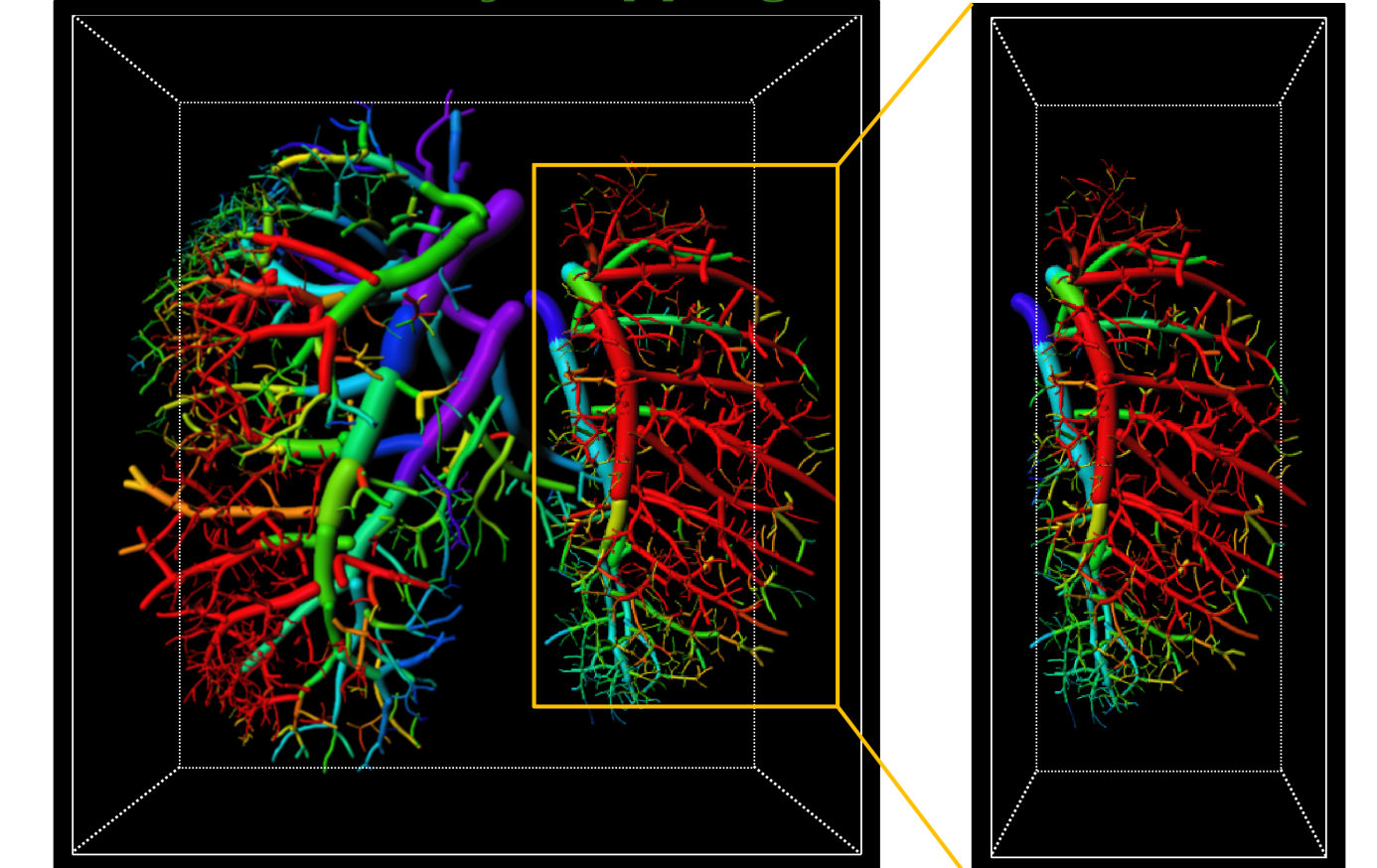
### TOC-LSFM imaging → Vessel segmentation → 3D reconstruction



### Complete multiscale 3D vascular trees

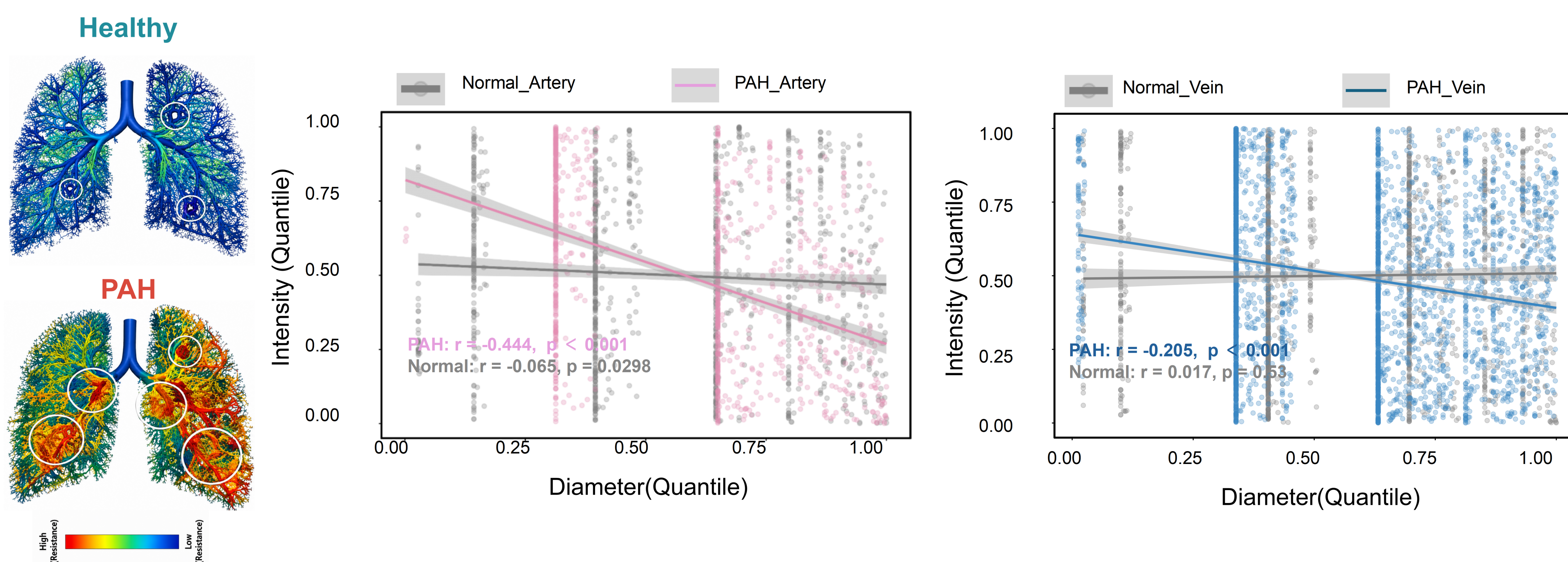


### FL Intensity Mapping



Reconstructed from whole-lung scale to the arteriolar-capillary level.

## 6. RESISTANCE-ASSOCIATED HOTSPOT MAPPING



## 7. IMPACT & FUTURE VISION

- Reveals hidden resistance distribution beyond global metrics, linking vascular architecture to function.
- Enables mechanism-guided understanding of where resistance emerges and how it propagates.
- Supports early detection of high-burden microdomains before hemodynamic collapse.
- Provides a foundation for personalized, spatially targeted therapies.
- Toward a digital twin of the pulmonary circulation for prediction, monitoring, and therapy optimization.

## CONCLUSIONS

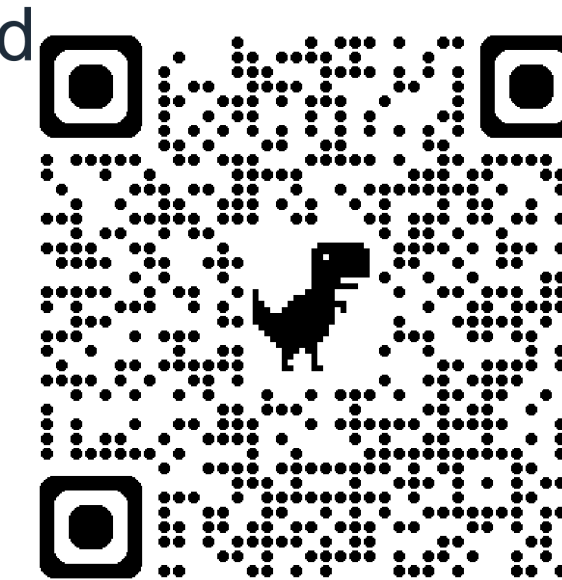
- We present an integrated platform that molecularly records hemodynamic burden with thermally triggerable AIE nanoparticles, reconstructs whole-lung 3D vasculature, and maps resistance-associated hotspots.
- Our approach reveals the hidden heterogeneity of resistance across the pulmonary arterial tree.
- This bridges the gap between vascular architecture and functional vascular phenotyping in PAH.

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Website: <https://media.au.tsinghua.edu.cn/cn/index.htm>



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- [2] Gong XT, Zhuang J, Chong KC, et al. Far-Red Aggregation-Induced Emission Hydrogel-Reinforced Tissue Clearing for 3D Vasculature Imaging of Whole Lung and Whole Tumor. *Adv Mater.* 2024;36(35):e2402853.

## Organizers

