

Pulmonary Hypertension - Challenges in Pathology

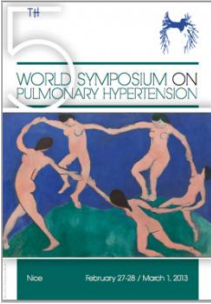


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INSERM Unit 999 "Pulmonary Hypertension: Pathophysiology and Novel Therapies"
Le Plessis Robinson, France

Disclosures

- None



Diagnostic classification of pulmonary hypertension

(Updated ESC/ERS guidelines 2015)

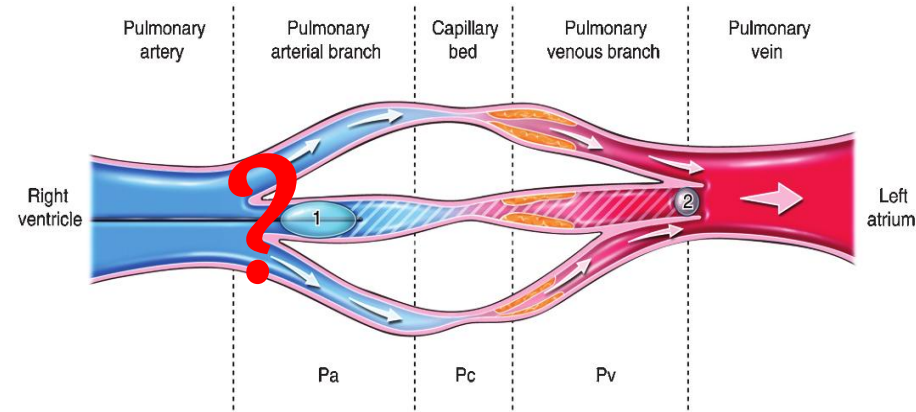
1 Pulmonary arterial hypertension

1' Pulmonary veno-occlusive disease / pulmonary capillary hemangiomatosis

1'' Persistent pulmonary hypertension of the newborn

2 Pulmonary hypertension due to left heart disease

3 Pulmonary hypertension due to lung diseases and/or hypoxia



4 Chronic thromboembolic pulmonary hypertension and other PA obstructions

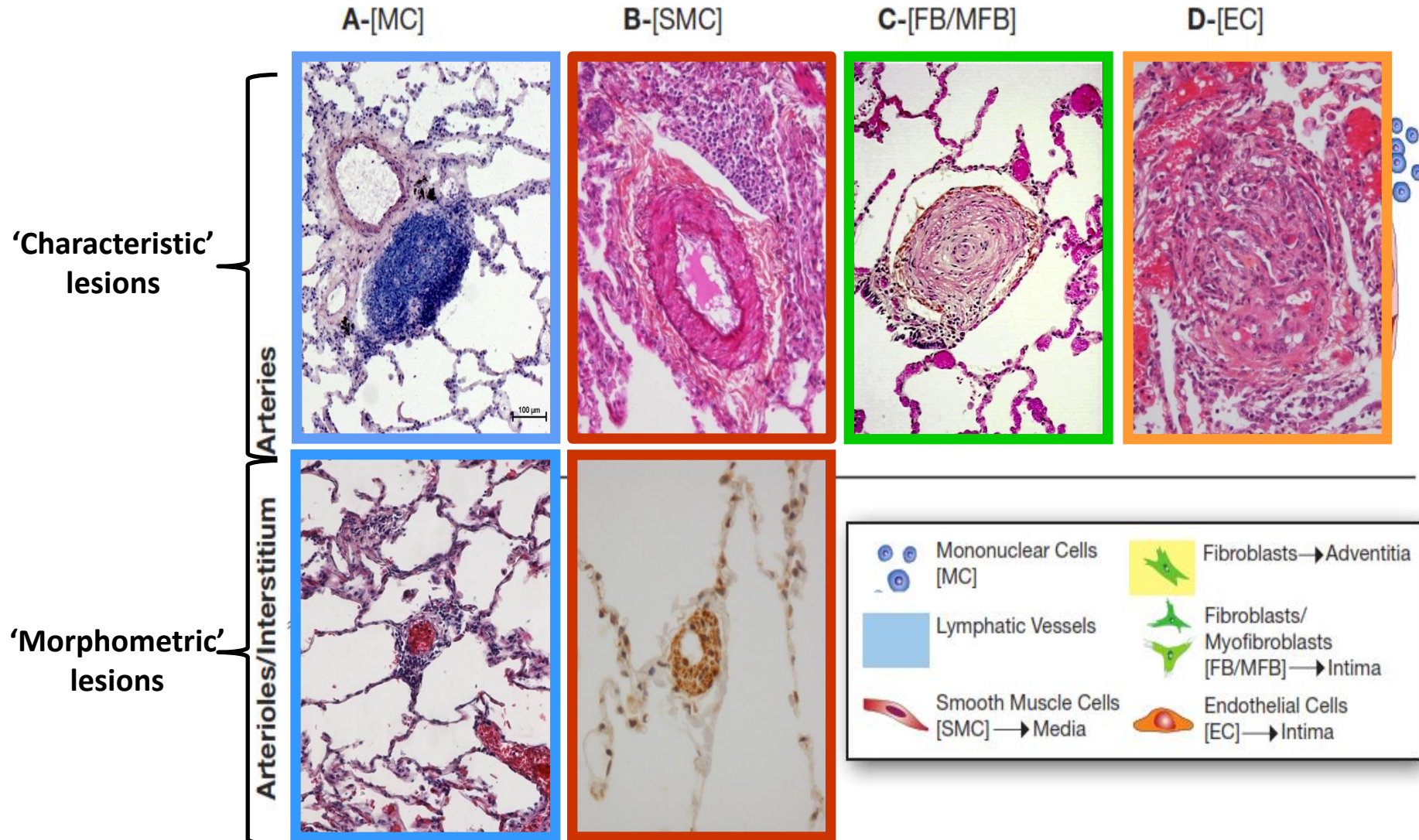
5 PH with unclear multifactorial mechanisms

Diversity of lesions in PAH: Variation of the prevailing cell type

AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE VOL 186 2012

Dorfmueller P, Humbert M.

Progress in Pulmonary Arterial Hypertension Pathology:
Relighting a Torch Inside the Tunnel

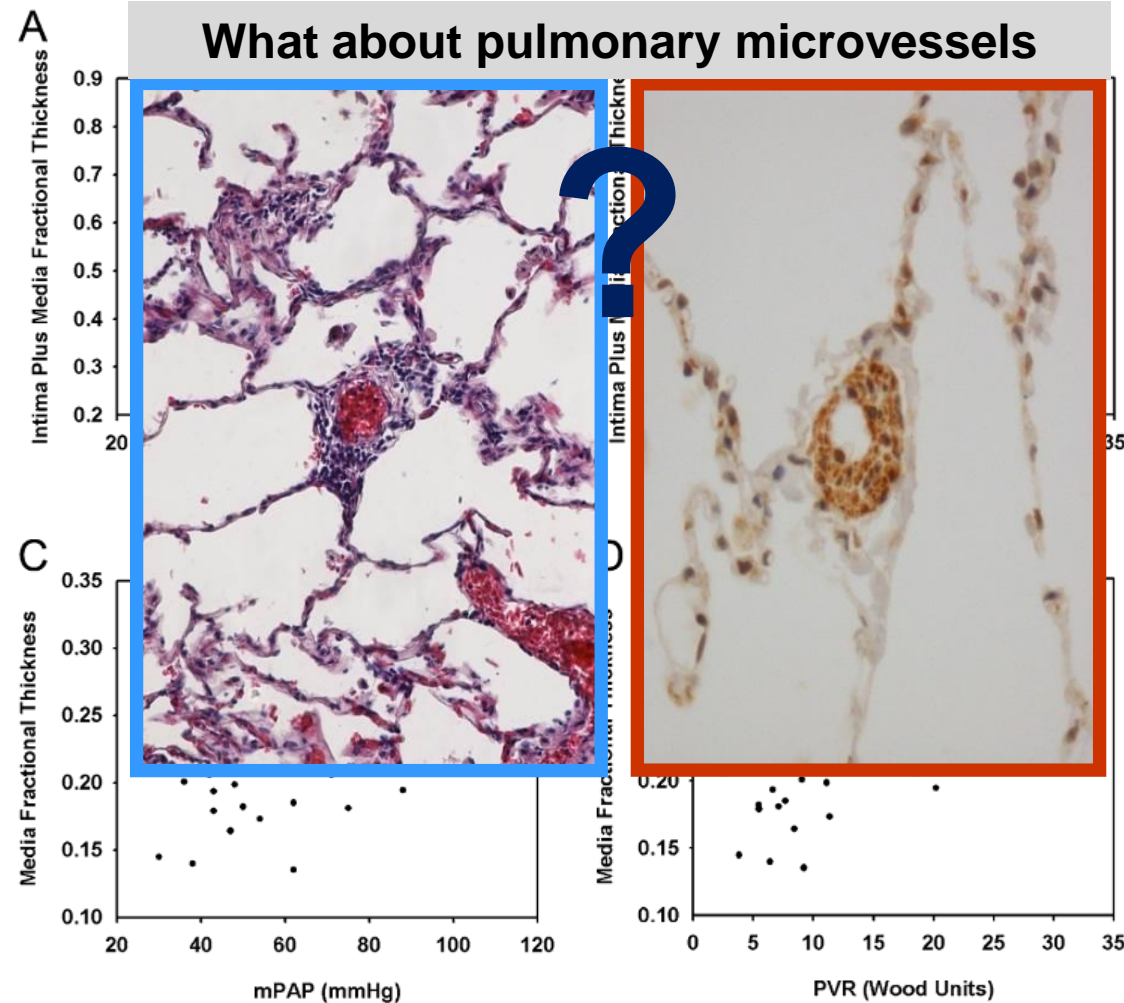


Sample images are presenter's own.

Pathology of pulmonary hypertension

AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE VOL 186 2012

Stacher E et al. Modern age pathology of pulmonary arterial hypertension

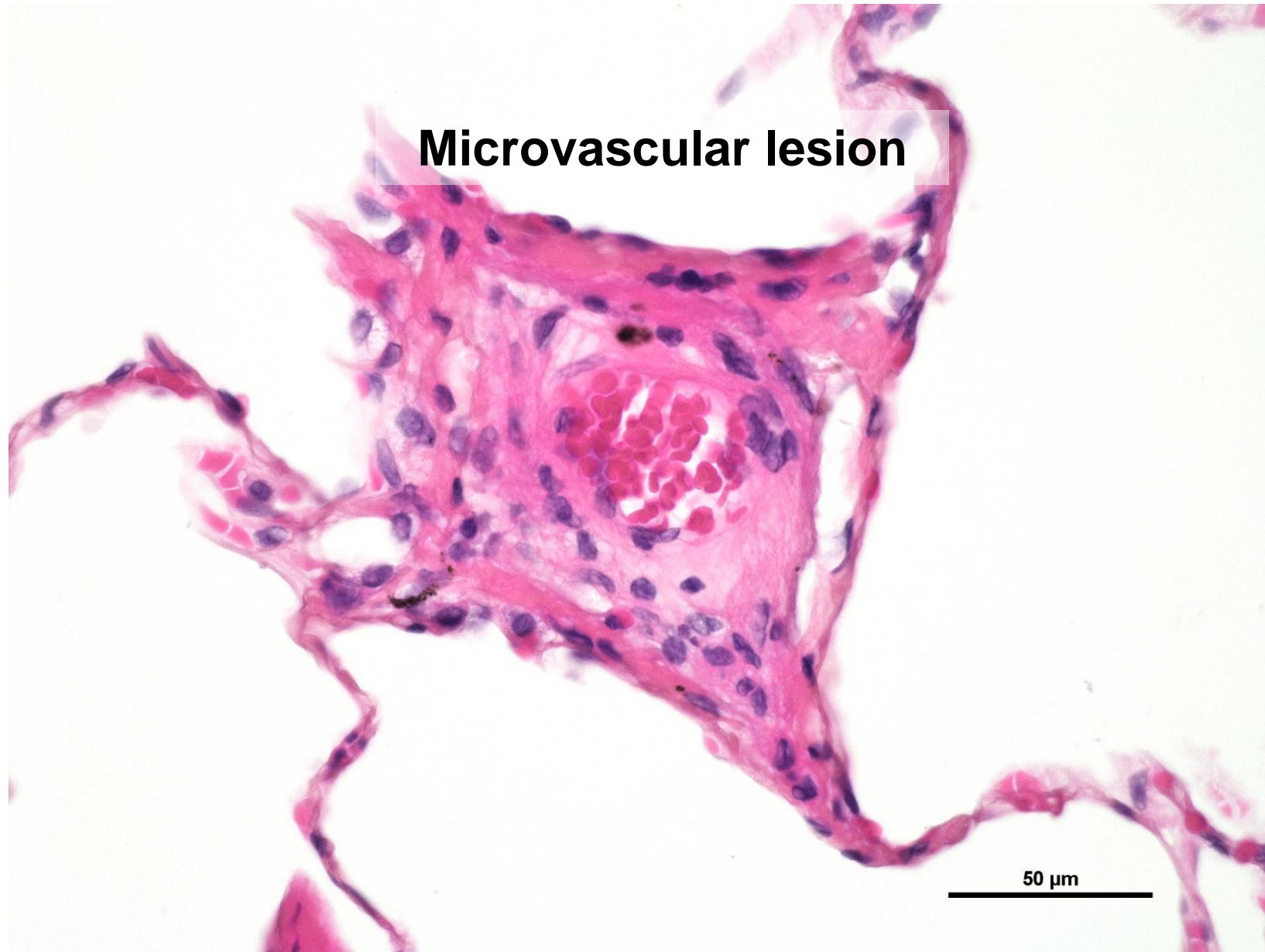


$R=0.235-0.267$

No true correlation can be seen between typical pulmonary artery remodeling and hemodynamics in PAH

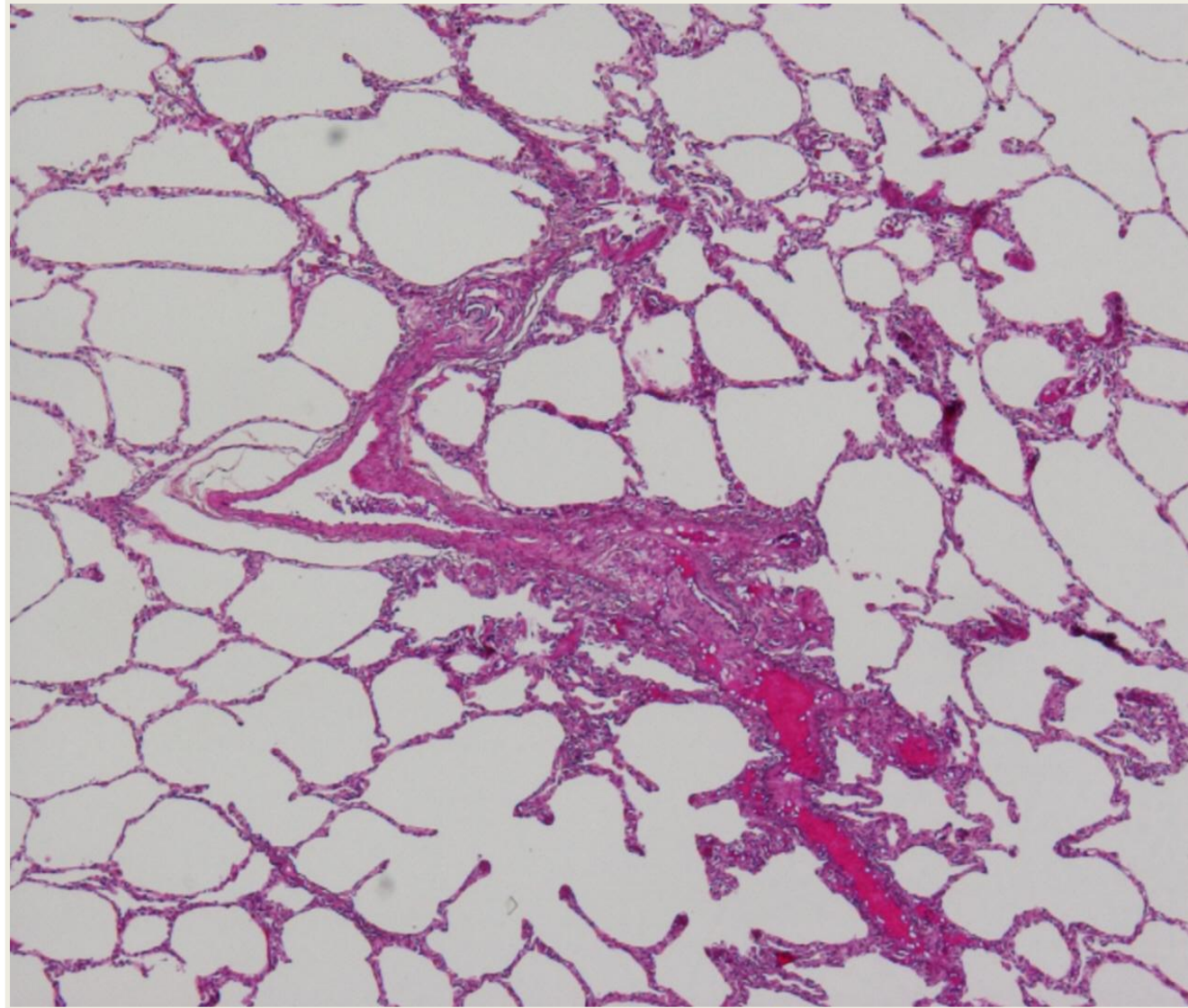
mPAP, mean pulmonary arterial pressure; PVR, pulmonary vascular resistance.

Lungs from a patient with HIV-associated PAH (Group 1)



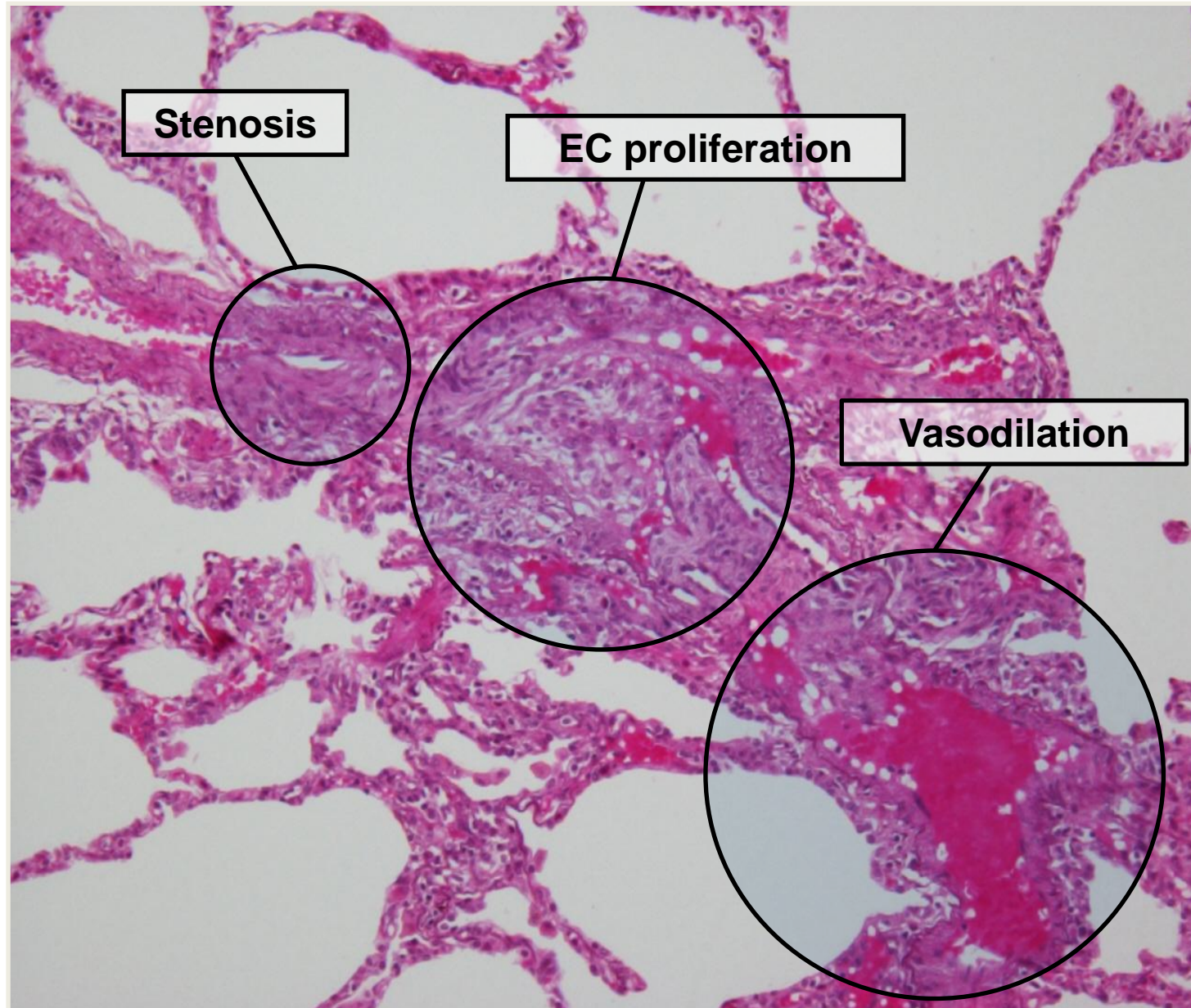
HIV, human immunodeficiency virus. Images are presenter's own.

Plexiform lesion (1)



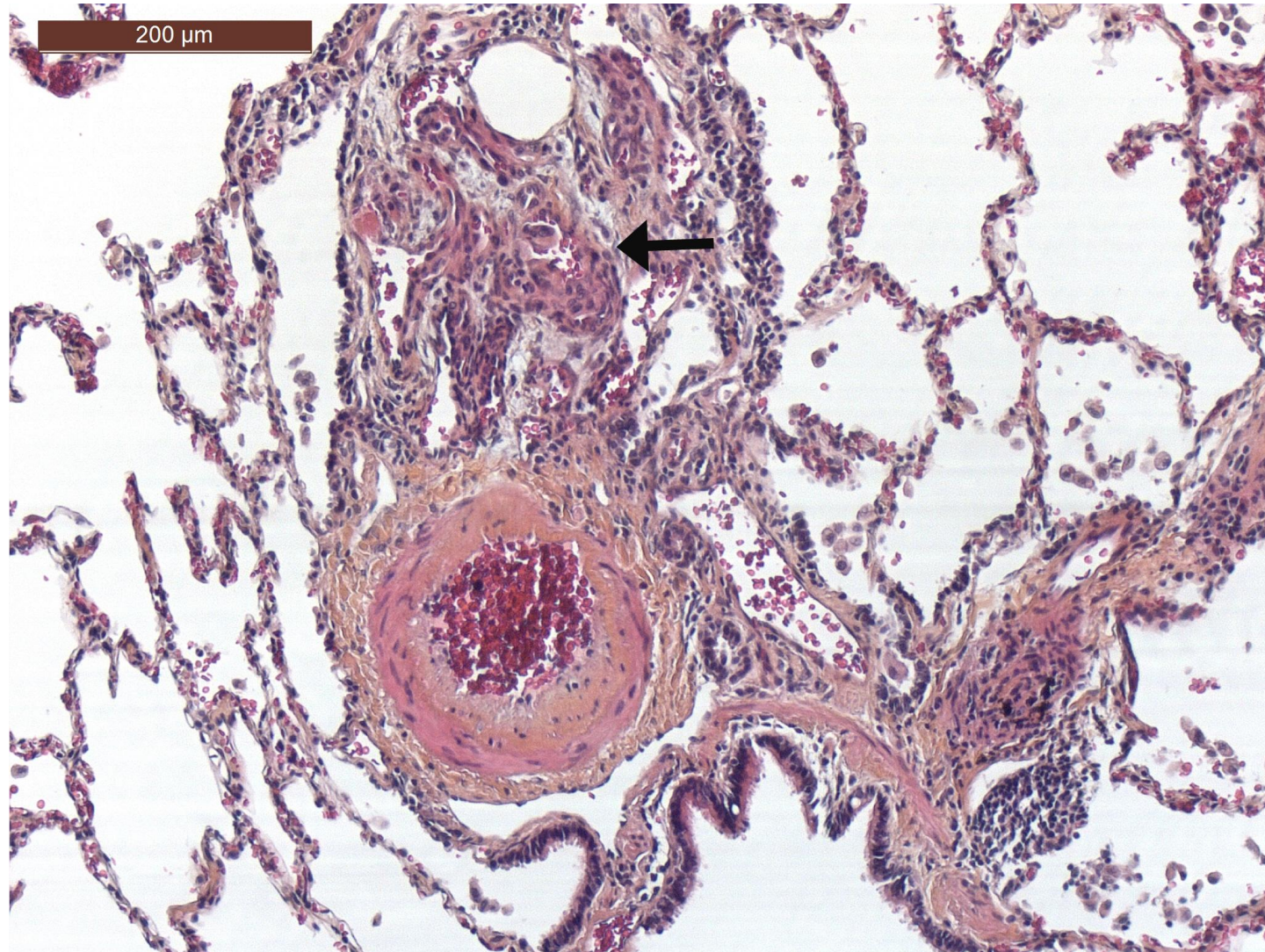
Arterial branch with two plexiform lesions

Plexiform lesion (2)



EC, endothelial cell. Image is presenter's own.

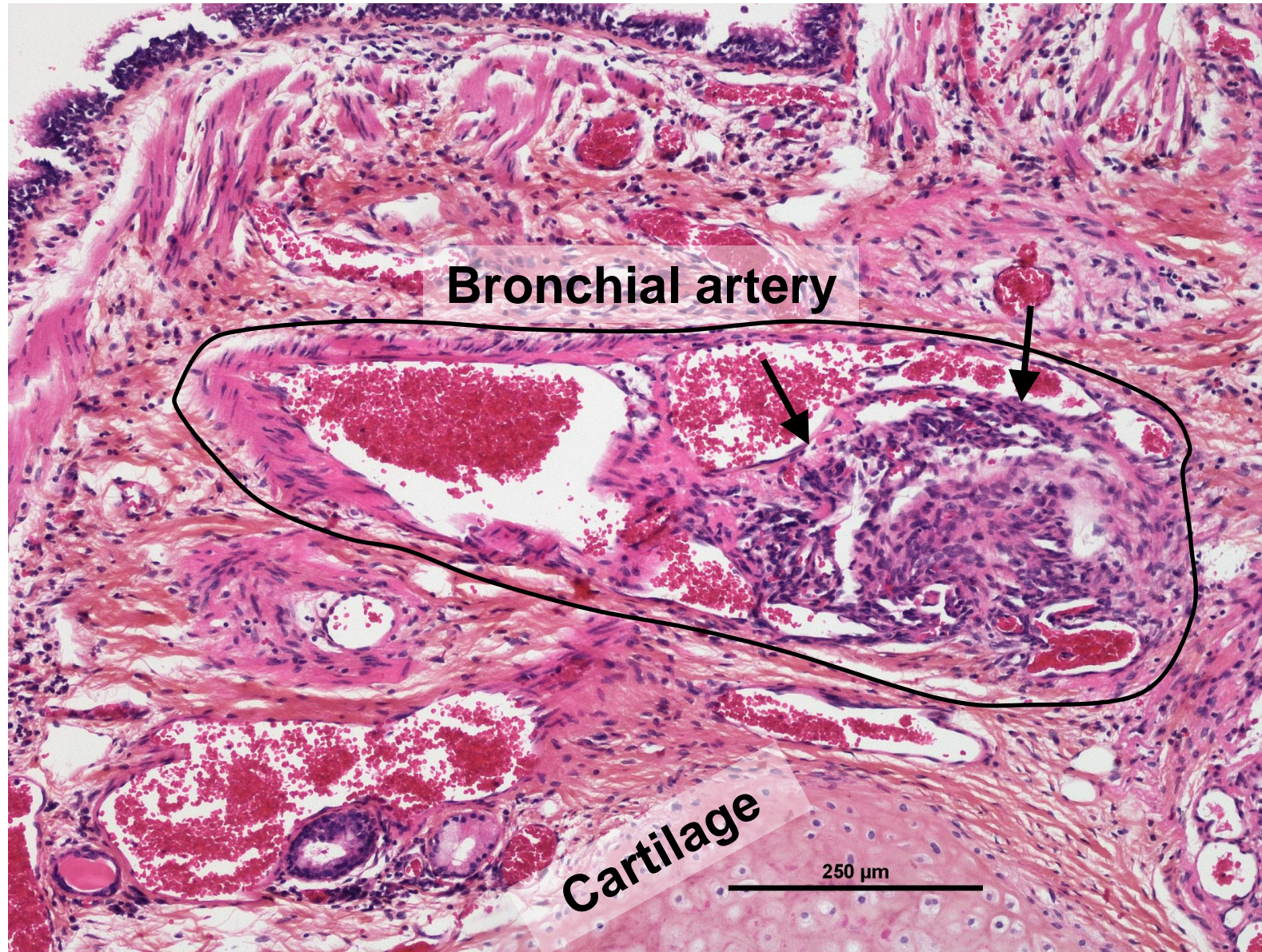
Plexiform lesion (3)



Note the para-arterial position of the lesion and its connection to the adventitia

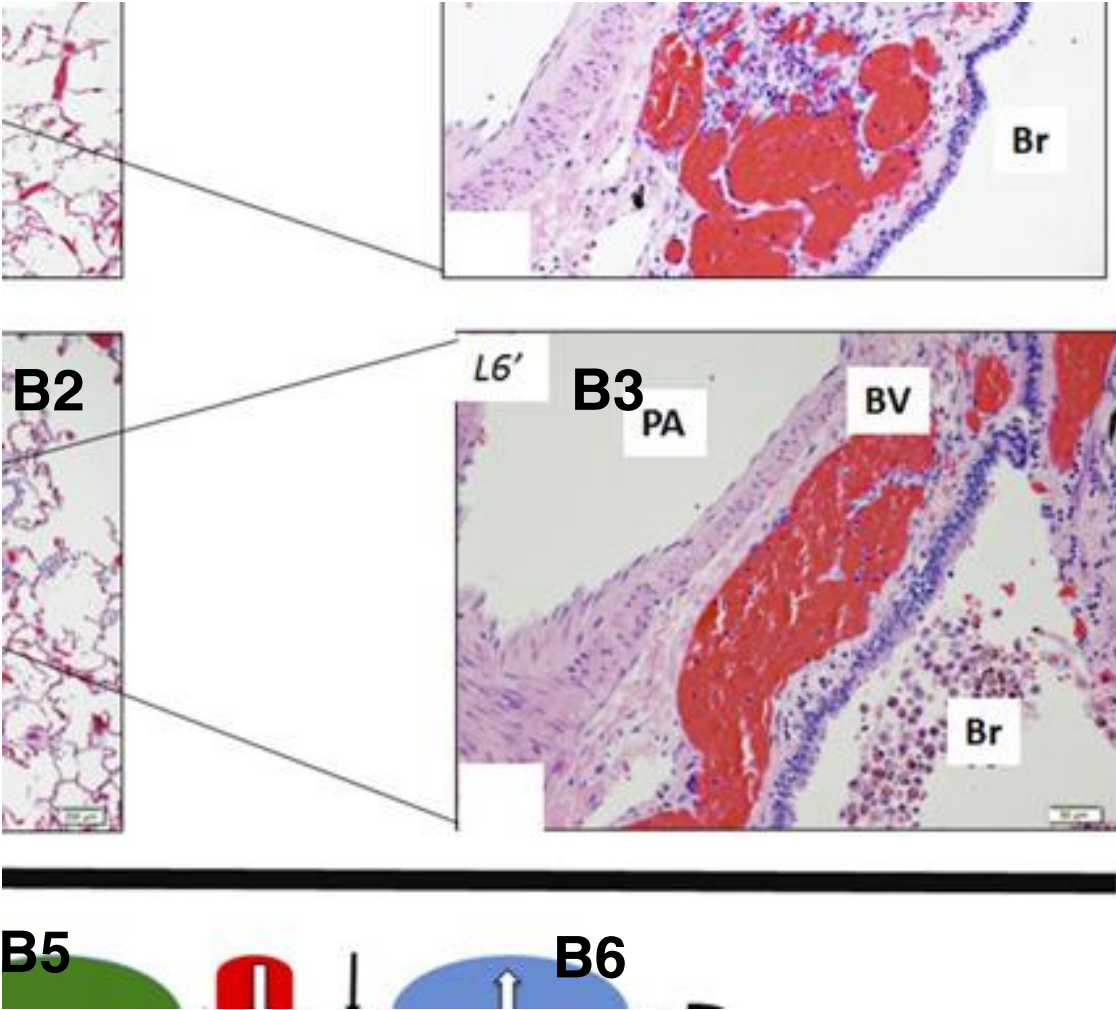
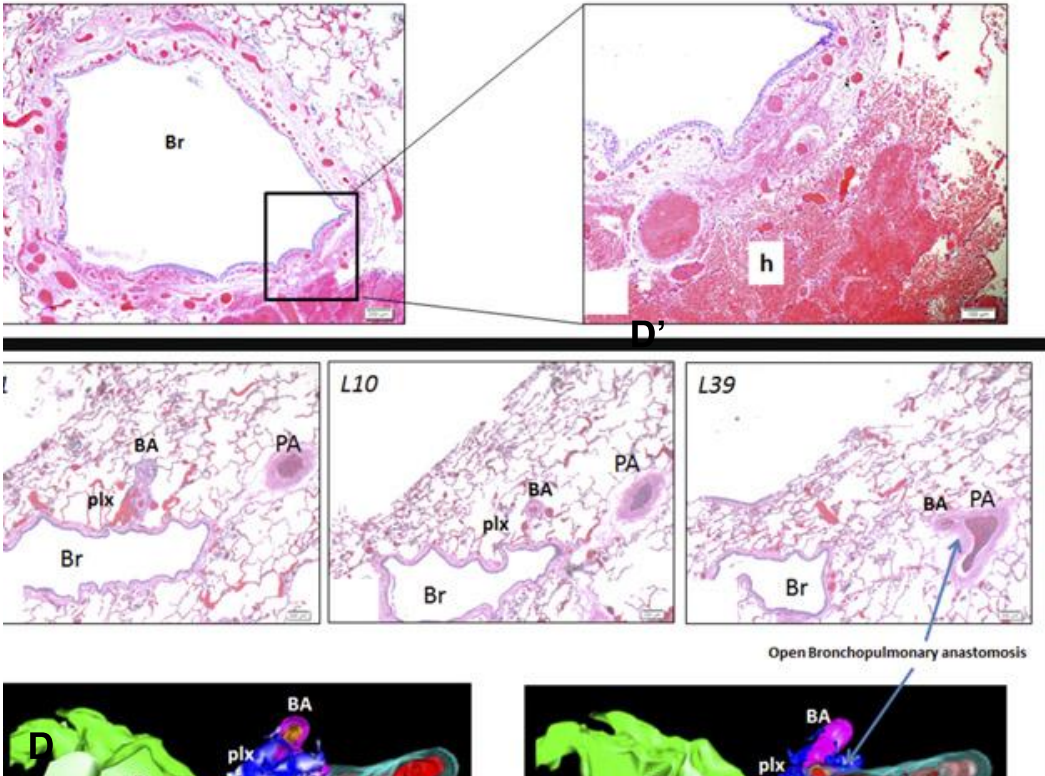
Ghigna *et al. Eur Respir J* 2016, in press.

IPAH displaying plexiform lesions in bronchial vessels

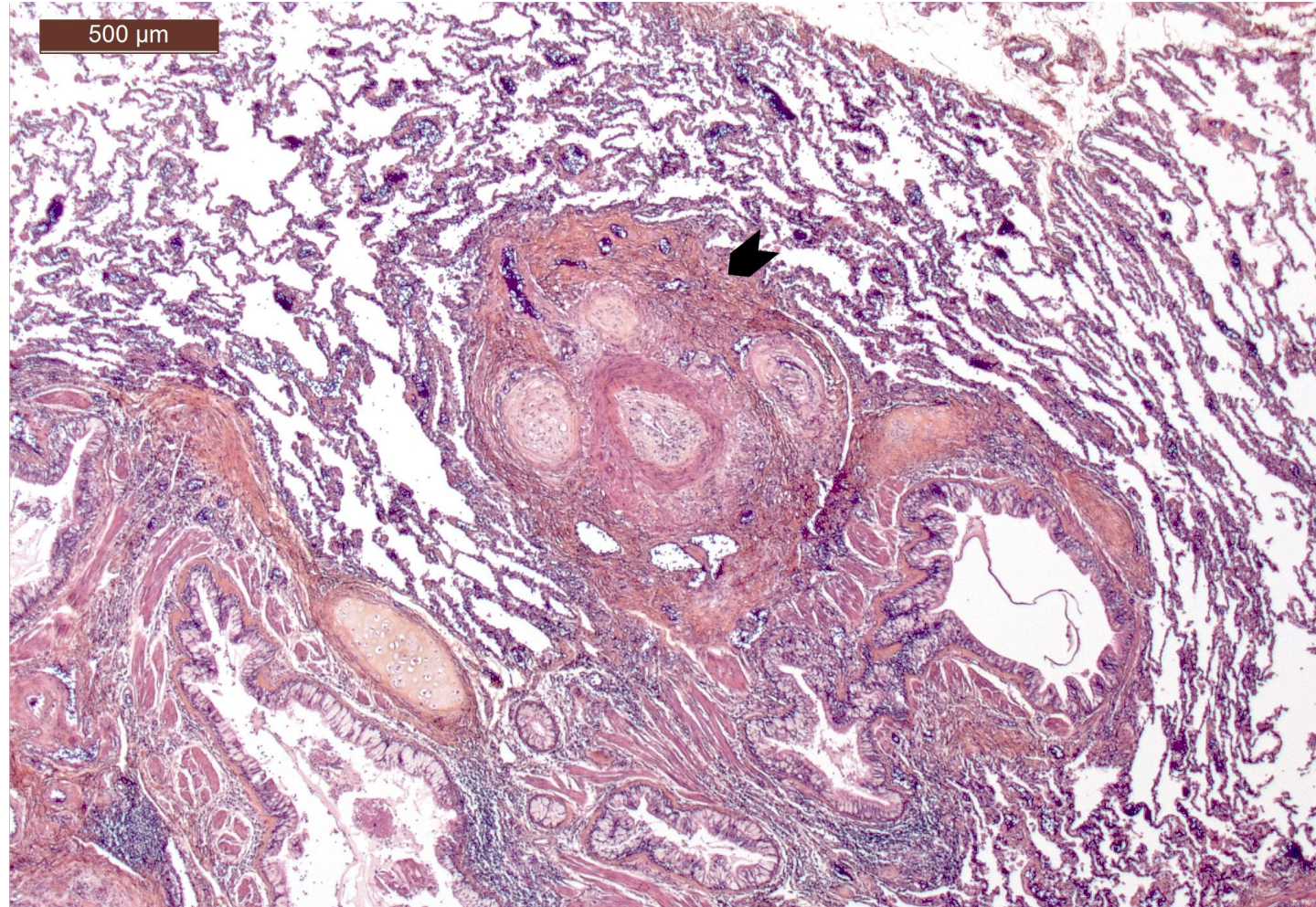


IPAH, idiopathic pulmonary arterial hypertension. Image is presenter's own.

Intrapulmonary Bronchopulmonary Anastomoses and Plexiform Lesions in Idiopathic Pulmonary Arterial Hypertension

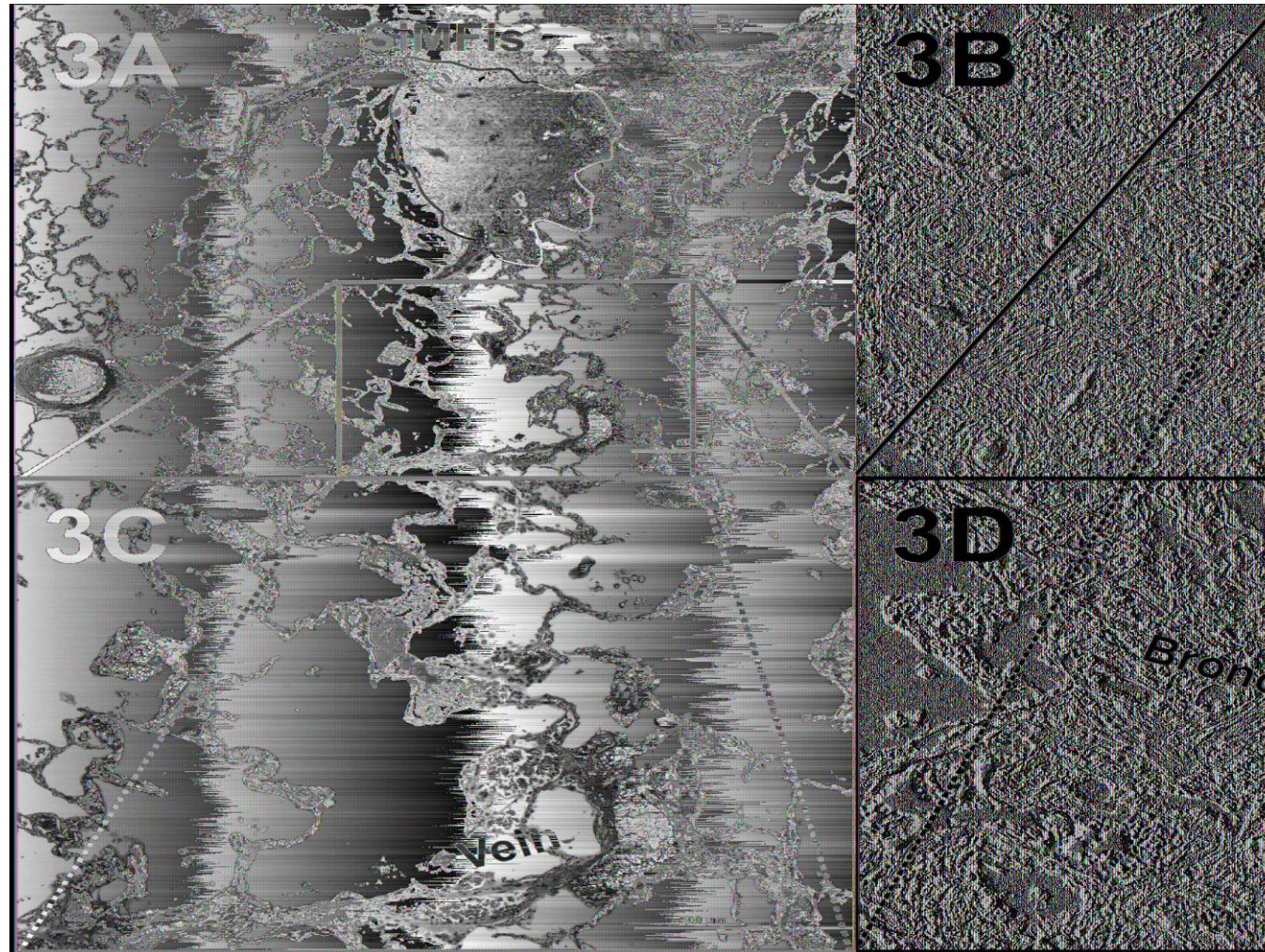


hPAH: Atypical, large (millimetric) fibrous lesions comprising several blood vessels (1)



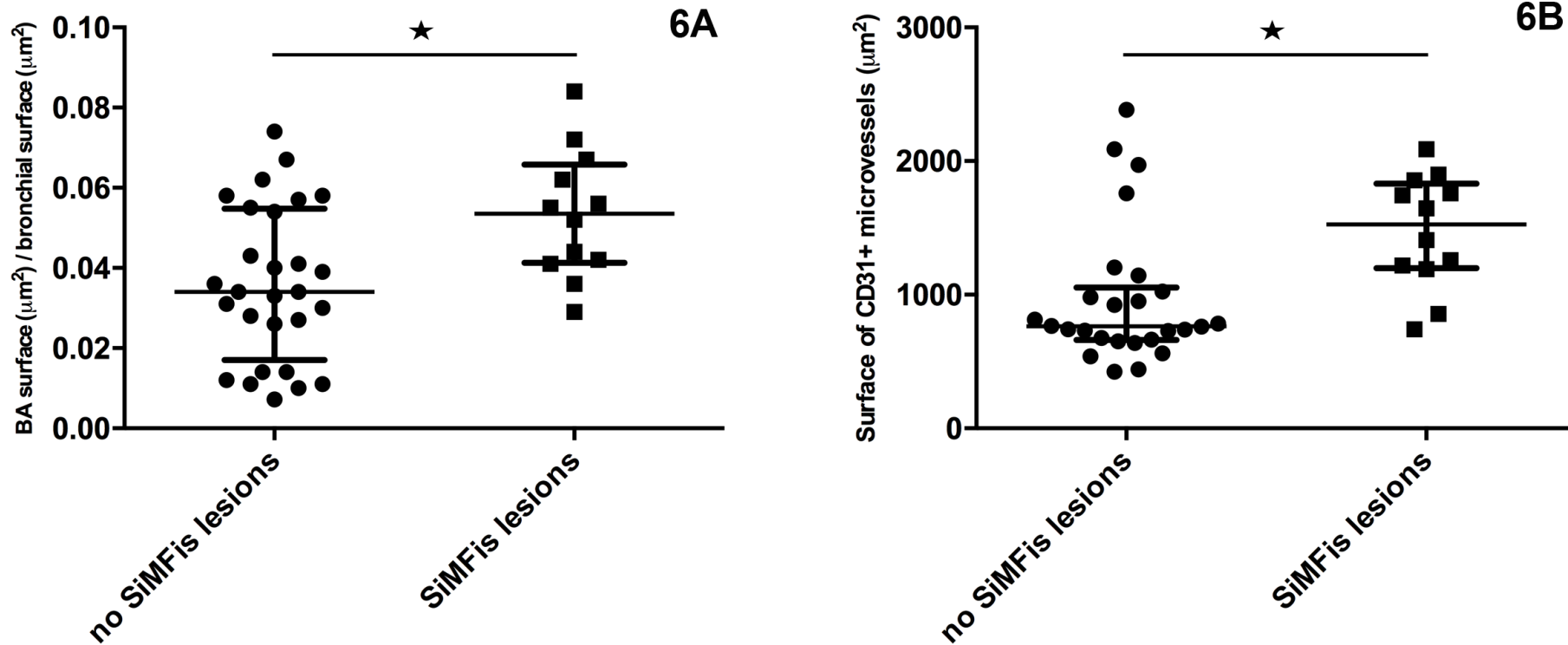
SiMFis: Singular millimetric fibrovascular lesions

hPAH: Atypical, large (millimetric) fibrous lesions comprising several blood vessels (2)



SiMFis: Singular millimetric fibrovascular lesions

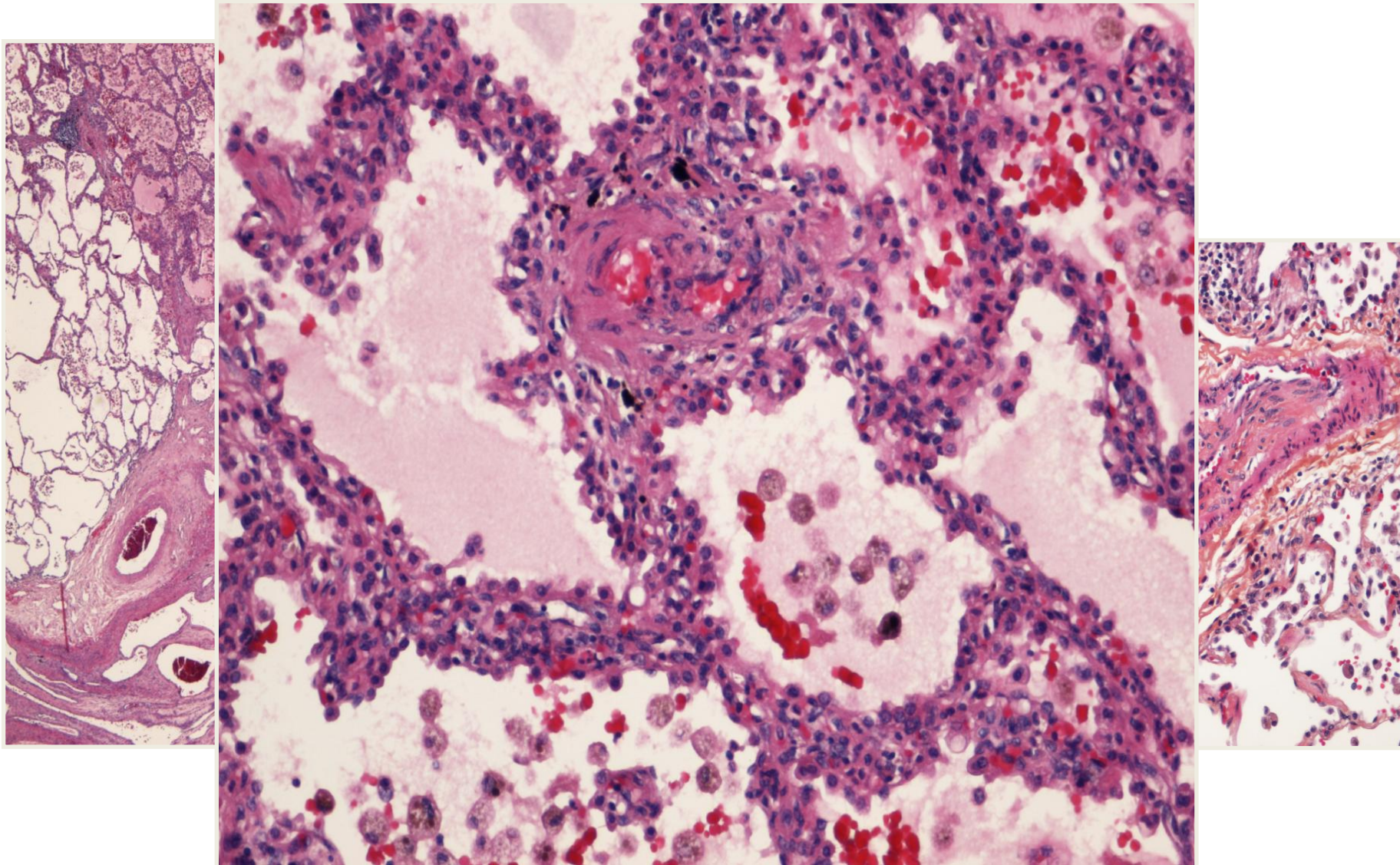
Association of SiMFis presence and hypertrophy of systemic (bronchial) vessels



43.5% of BMPR2+ (carriers) = SiMFis
9.5% of BMPR2- (non-carriers) = SiMFis

CTEPH (Group 4, peripheral disease)

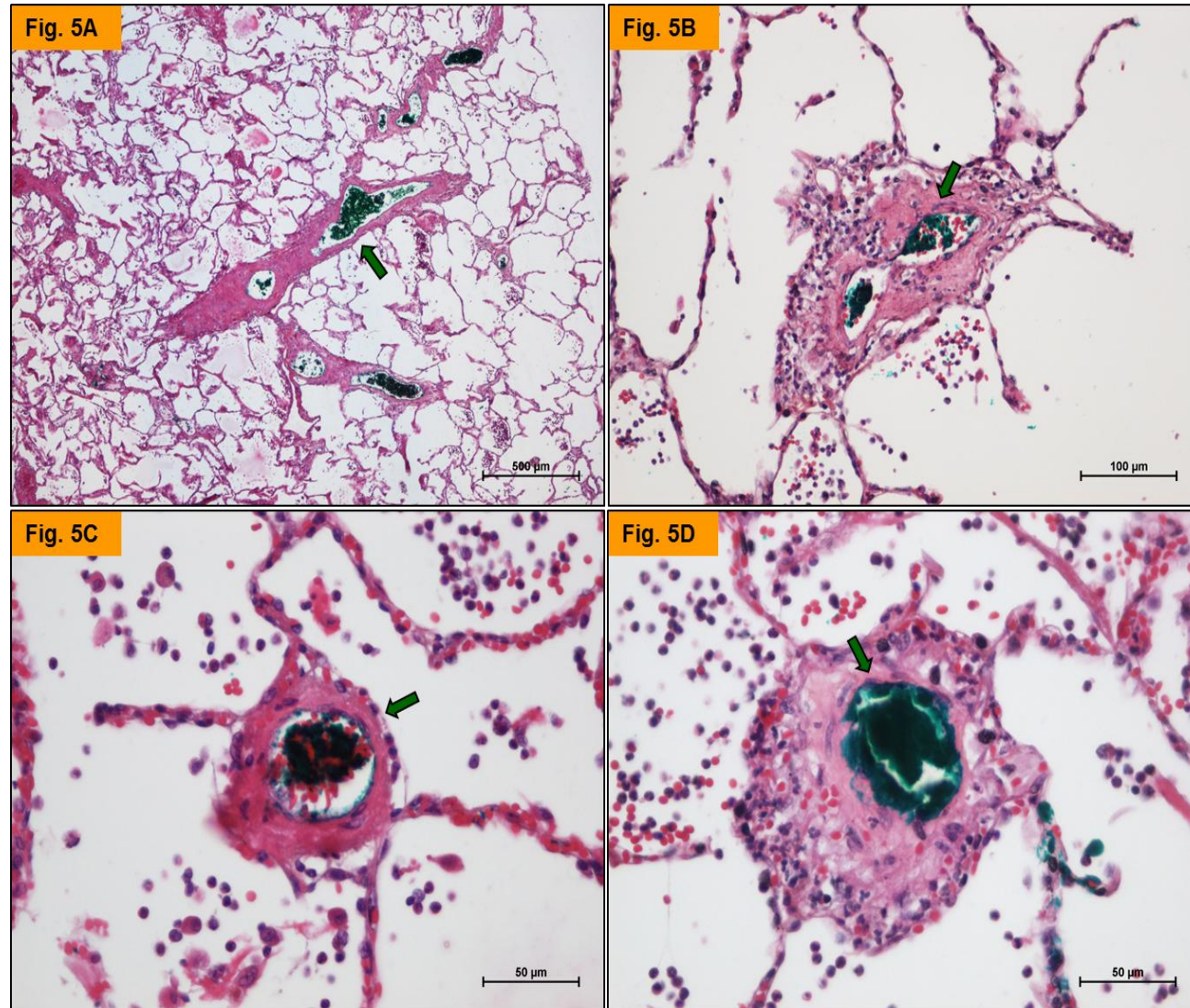
Dorfmüller P *et al.* Microvascular disease in chronic thromboembolic pulmonary hypertension: a role for pulmonary veins and systemic vasculature. *Eur Respir J* 2014;44:1275–88



CTEPH, chronic thromboembolic pulmonary hypertension.

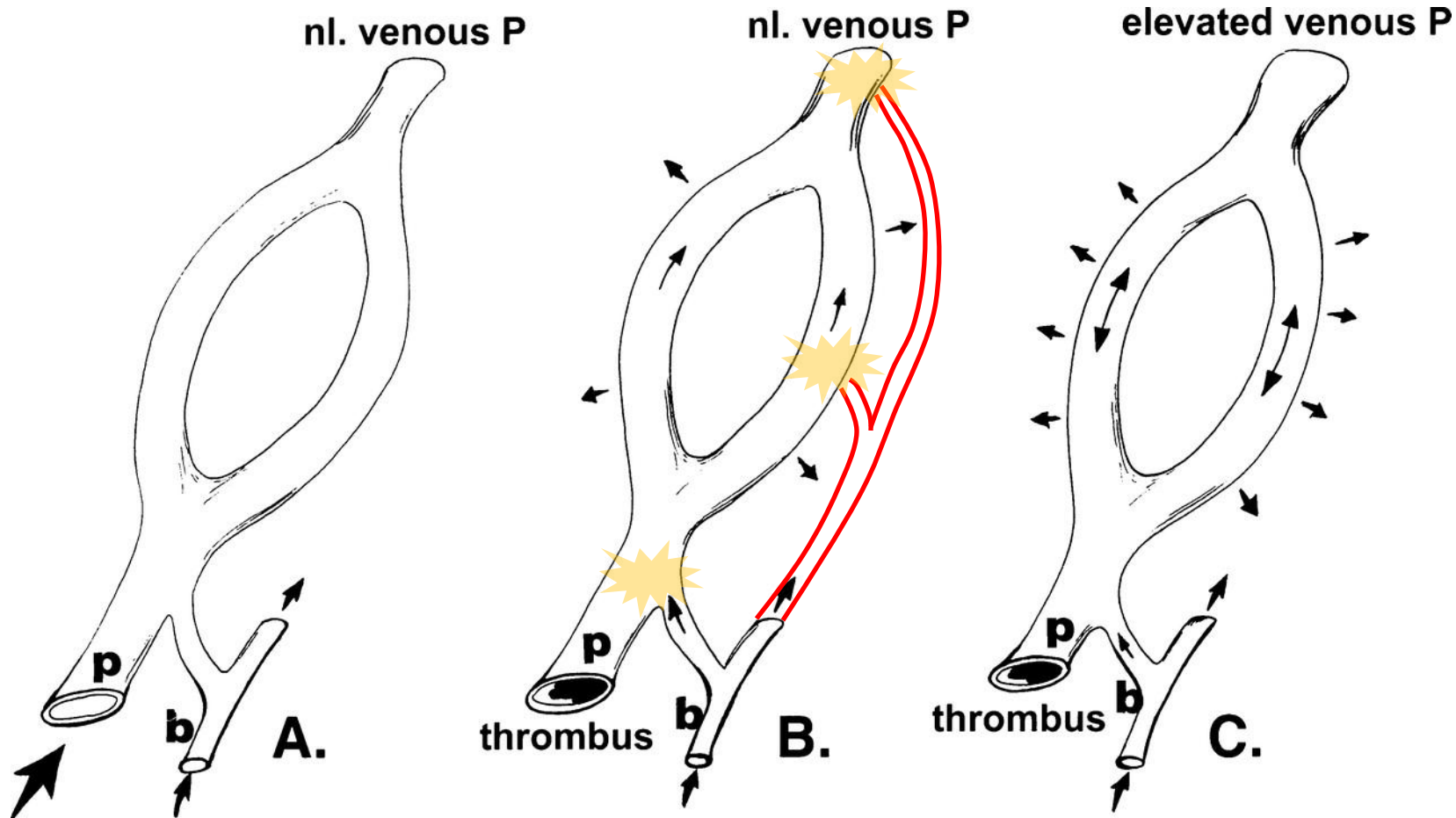
Microvascular disease in CTEPH

Dorfmüller P *et al.* Microvascular disease in chronic thromboembolic pulmonary hypertension: a role for pulmonary veins and systemic vasculature. *Eur Respir J* 2014;44:1275–88

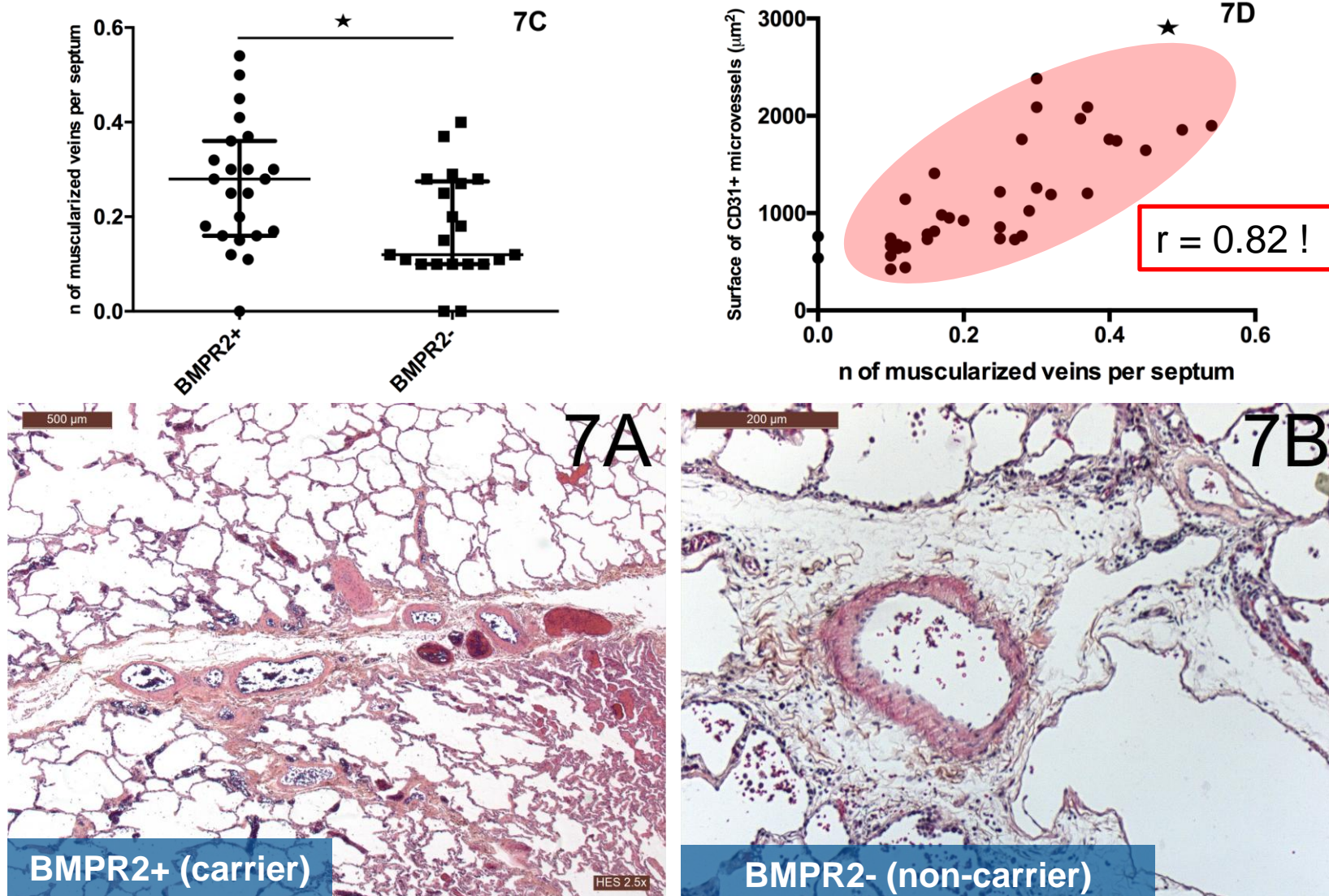


 = Pulmonary vein/venule

Anastomosis of a bronchial artery (b) and pulmonary arteriole (p) at an alveolar capillary loop



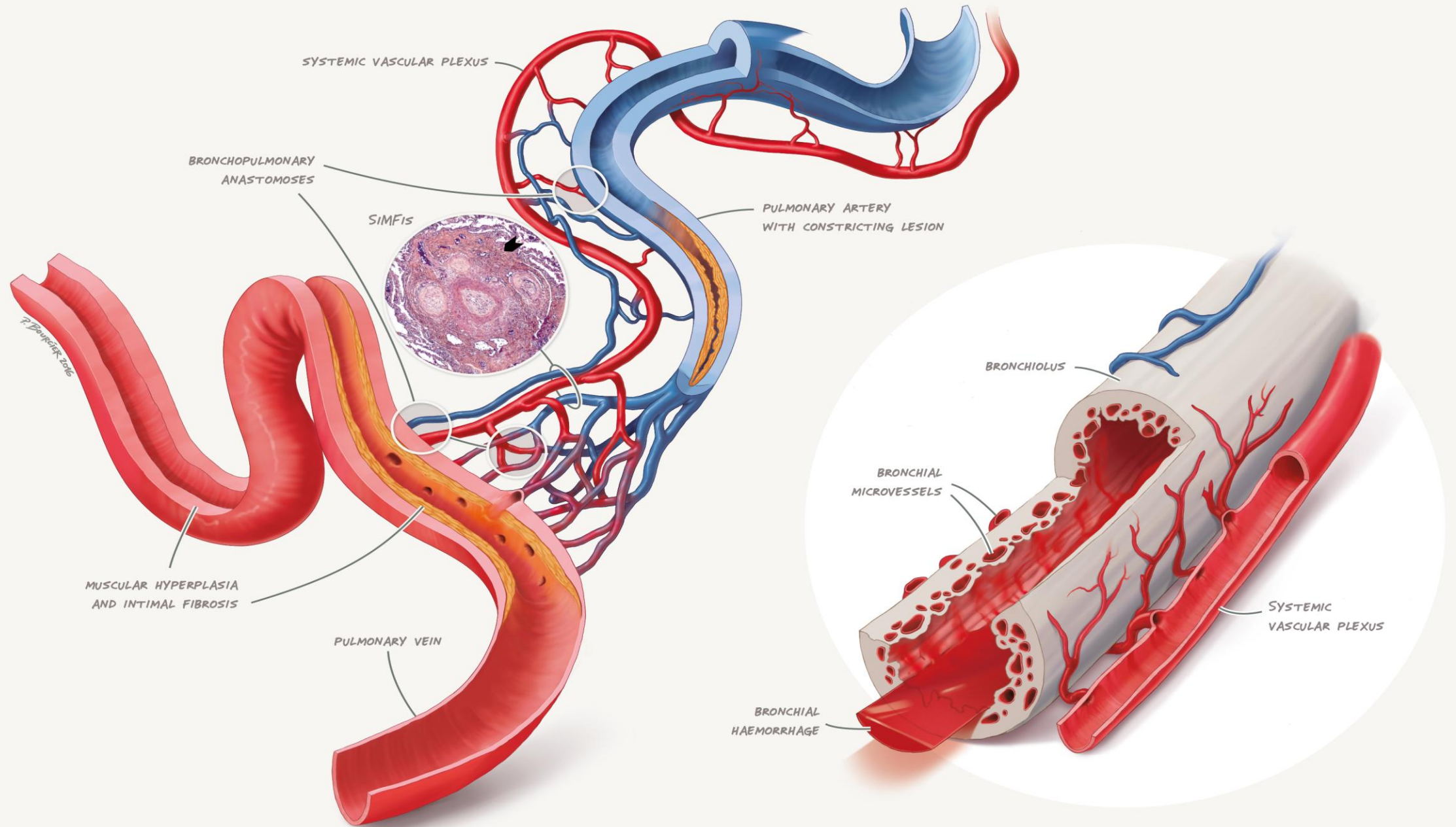
In PAH systemic (bronchial) vessel hypertrophy correlates positively with pulmonary venous remodeling



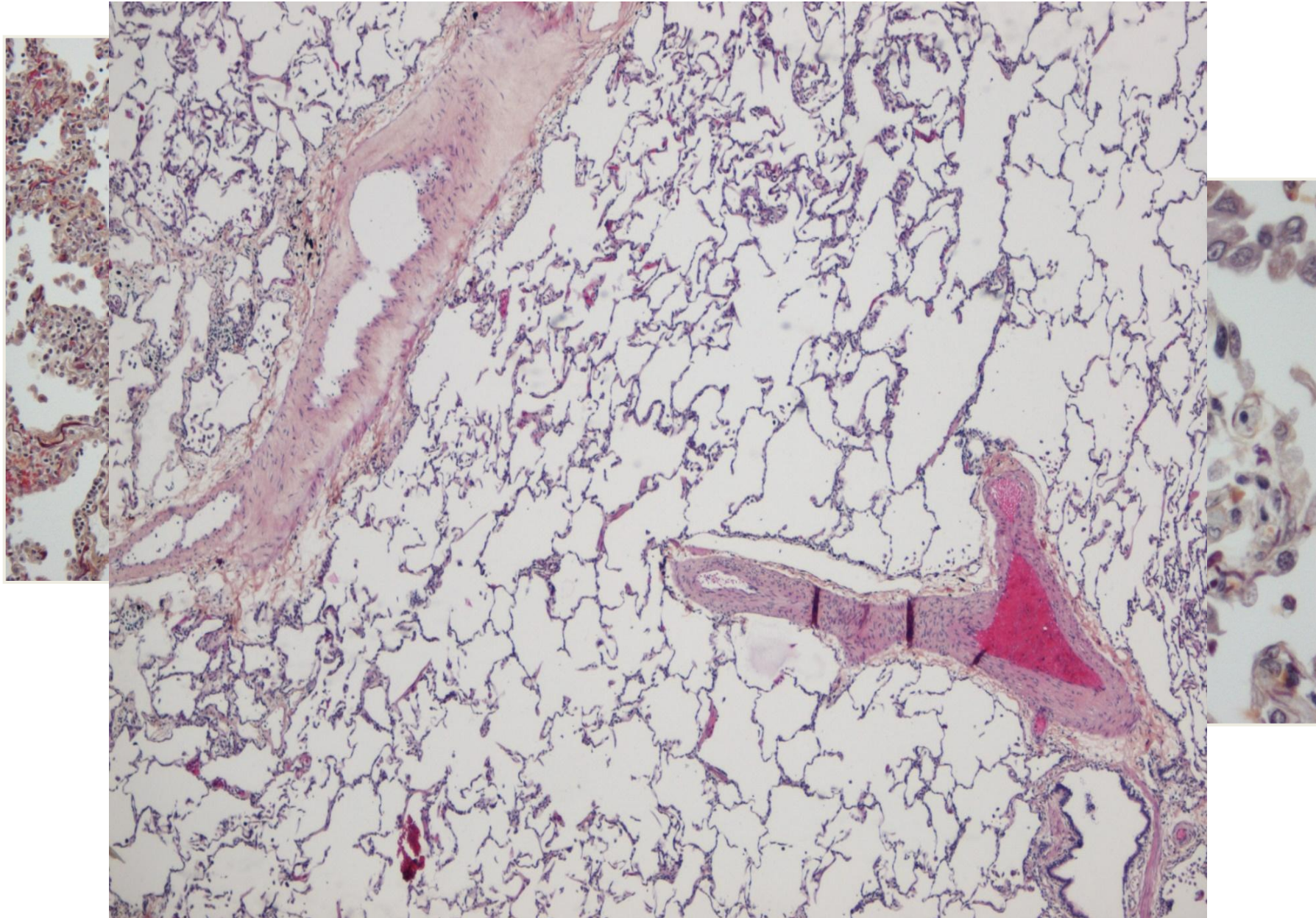
BMPR2, bone morphogenetic receptor type II

Ghigna *et al. Eur Respir J* 2016, in press.

IMPACT OF HYPERTROPHIC SYSTEMIC VASCULATURE IN PAH

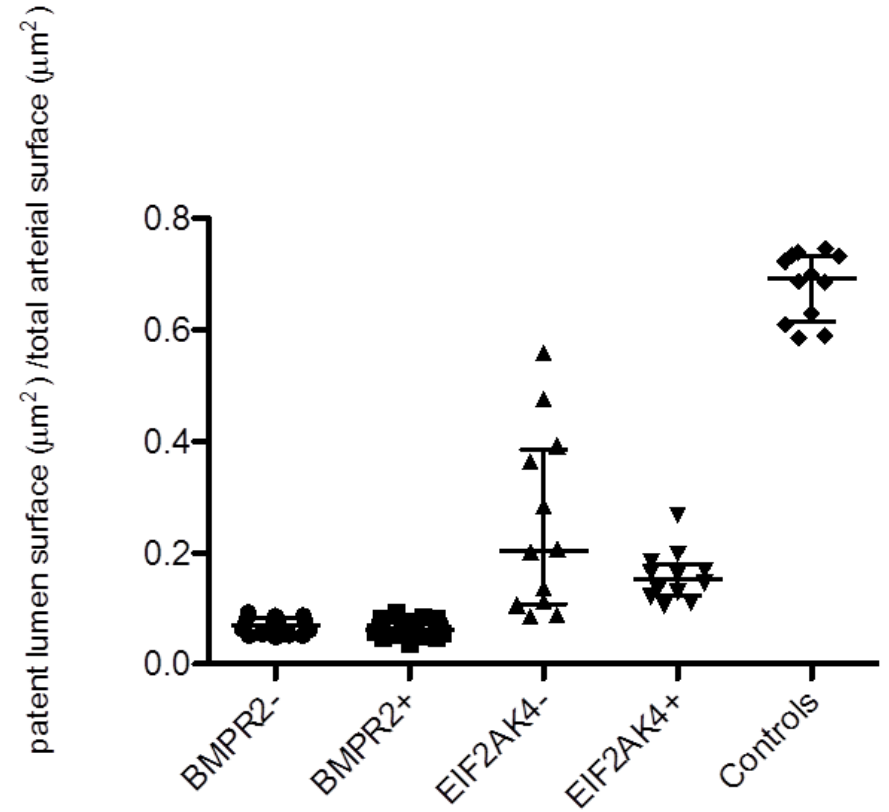
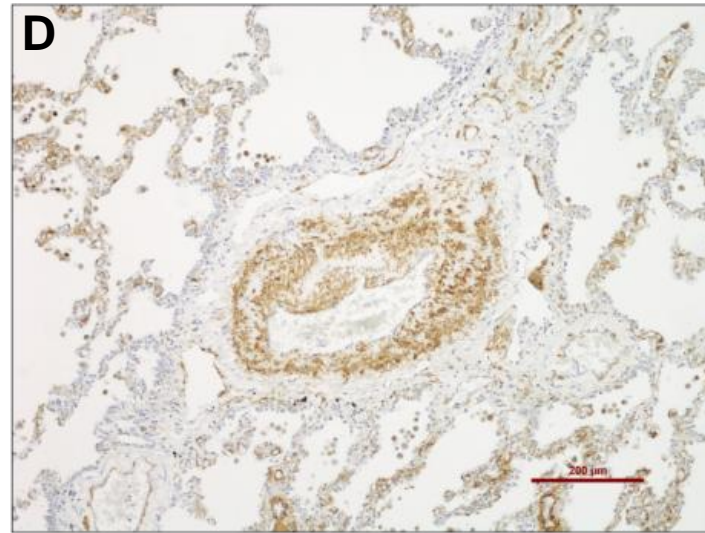
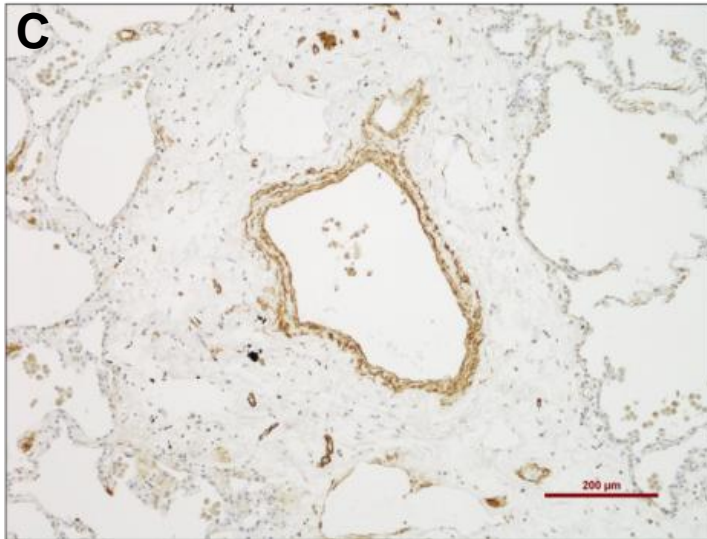
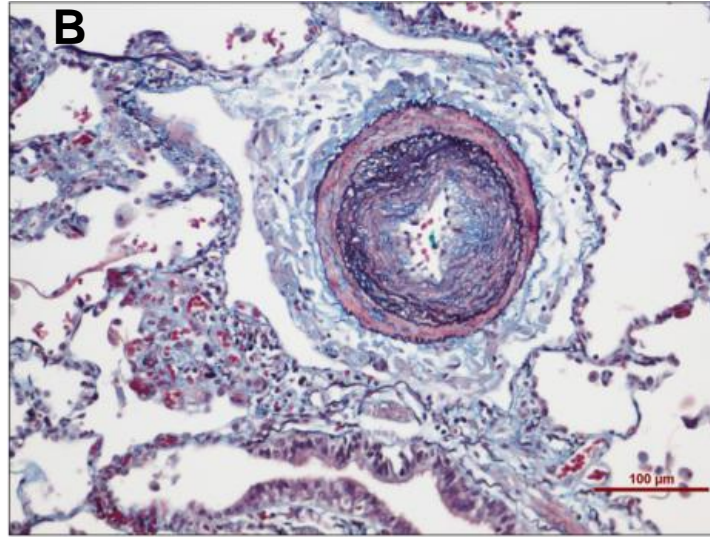
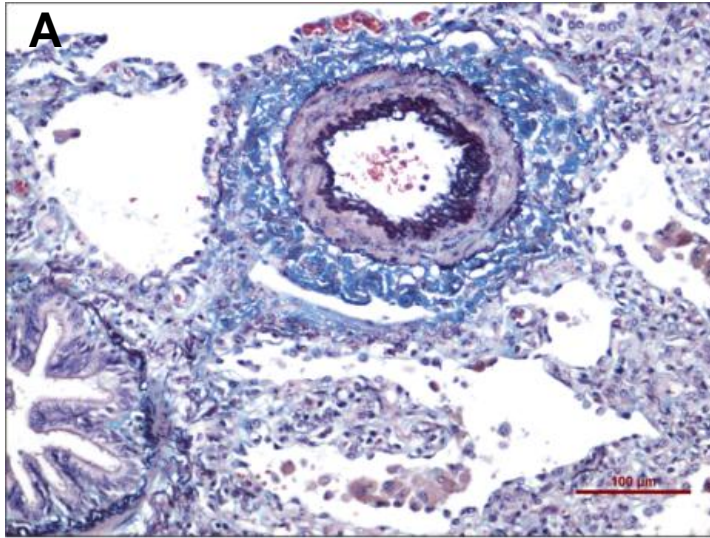


Typical vascular lesions in PVOD (Group 1') (1)

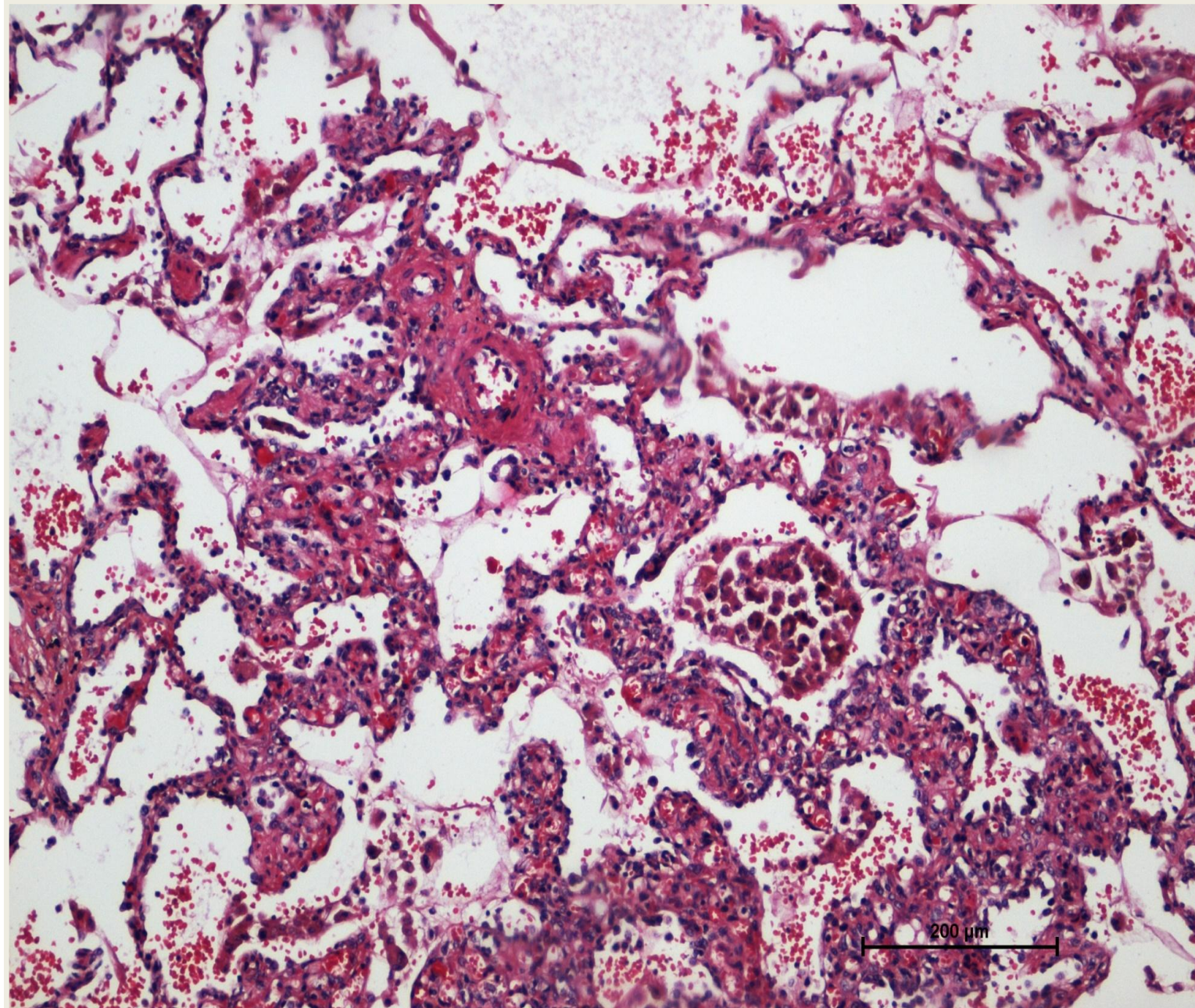


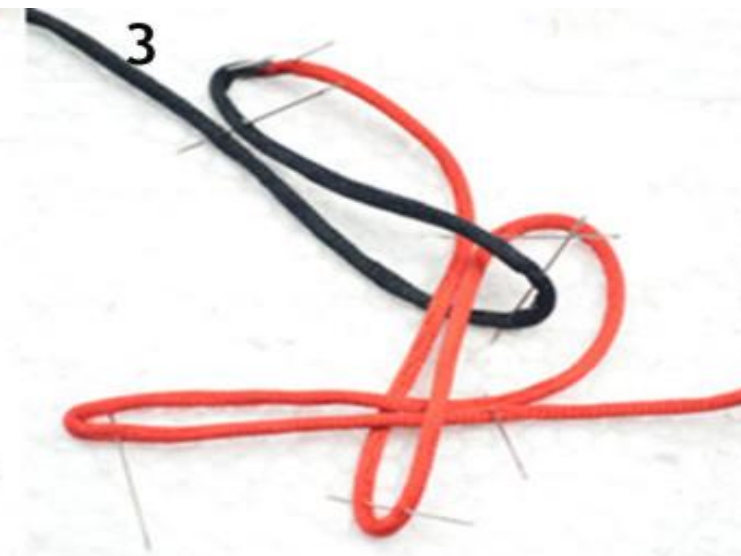
PVOD, pulmonary veno-occlusive disease. Images are presenter's own.

Typical vascular lesions in PVOD (Group 1') (2)



Typical vascular lesions in PVOD (Group 1') (3)





Conclusions

Pathology is an observational and descriptive discipline...

But it is also an important non-abstract (real) visual of the disease, the morphological correlate of what causes disease

We might have arrived at a turning point of PH pathology – same old lesions, but rebooting interpretation:

- It might be that, in the past, we were too focused on ‘the classic arterial lesions’ and have neglected the role of the microvasculature (arterioles and venules)
- The systemic lung vasculature appears to play an important role in different forms of PH, even if its part in disease evolution has yet to be elucidated
- All levels of the pulmonary vasculature (arteries, capillaries, veins) are involved in most forms of PH
- From pathology’s standpoint of view a clear-cut categorization into pre- and post-capillary PH / vascular remodeling appears more and more difficult: perhaps rather different conditions in one large spectrum of disease?