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**Title:** Different pathology of pulmonary arterioles in centrilobular and panlobular emphysema

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**Body:** Two distinct pathological phenotypes have been described in patients with emphysema: Centrilobular Emphysema (CLE) and Panlobular Emphysema (PLE), with distinct clinical and functional characteristics. A different involvement of small airways and parenchyma has been described in CLE and PLE, but the involvement of pulmonary arterioles has never been analyzed. Therefore, we evaluated remodelling of pulmonary arterioles in surgical samples from 26 patients with CLE, 18 with PLE, 7 smokers without emphysema (SNE) and 8 non smokers (NS). By image analysis we measured total arterial wall, intima, media and adventitial thickness. Furthermore, since mast cells (MCs) are potentially involved in vascular remodeling, we quantified the infiltration of tryptase+ MCs in arterioles. Subjects with CLE have a higher total wall thickness compared to those with PLE (median[range] 61[21-198] vs 46[17-143]  $\mu$ m;  $p < 0,001$ ) and NS (51[20-123];  $p < 0,05$ ). In particular, thickness of the intima was greater in subjects with CLE than in those with PLE (9[2-66] vs 6[2-41];  $p < 0,05$ ), as was thickness of the media (19[7-94] vs 16[7-63];  $p < 0,005$ ). Finally subjects with CLE have a higher number of MCs in the adventitial layer than those with PLE (200[0-1200] cells/mm<sup>2</sup> vs 111[0-1000];  $p < 0,001$ ). In conclusion, our study demonstrates that pulmonary arterioles show a different pathology in CLE and PLE, suggesting that the mechanism responsible could be different in the two forms of emphysema.