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Title: LSC 2013 abstract - Early vascular remodelling in pulmonary fibrosis occurs concomitant with proliferation of vascular-associated cells

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Body: Introduction: Early manifestations of pulmonary fibrosis may include vascular symptoms e.g. vascular remodelling. Normally this phase goes unnoticed in patients, however to fully understand the pathogenesis, it is essential to understand this early phase. The aim was to investigate early vascular remodelling in pulmonary fibrosis, using a model with a specific initiation time. Methods: We injected mice subcutaneously with bleomycin (or saline) 3 times/week for 4 weeks. Animals were sacrificed after 1, 2, 3 and 4 weeks. α -SMA area/vessel perimeter (μ m²/ μ m) was used to determine vascular remodelling in small parenchymal vessels. Bleomycin induce proliferation and to determine the nature of these cells, the following double-stainings were done; PCNA/α-SMA, PCNA/CD31 and PCNA/NG2. Results: Vascular remodelling starts early; at 1, 2 and $3w \alpha$ -SMA was significantly increased compared to controls. At 4w, difference to controls was detected. A large proportion of the proliferating cells had perivascular localization and was often positive for NG2, whereas few cells were positive for α-SMA and CD31. Conclusions: Results suggest vascular remodelling to be an early feature in pulmonary fibrosis. The decreased remodelling at 4w may indicate a shift to a fibrotic phase, supported by our previous findings of increased fibrosis at 4w The remodelling was associated with increased proliferation of vascular-associated cells; smooth muscle and endothelial cells as well as a population likely to be pericytes (NG2-positive cells). Thus it appears that different cell-types contribute to vascular remodelling and the process is dynamic.