

Functional Imaging of Regional Airway and Ventilation Response to Intravenous Allergen and Methacholine Studied by Synchrotron Radiation CT in a Rabbit Model of Asthma

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Aim: Methacholine (Mch) and specific allergen challenges are commonly used to assess bronchial hyperresponsiveness in the diagnosis of asthma. However little is known of the regional differences in their effects on the airways. Since regional effects may be modified by non-uniform deposition of the particles, we aimed to compare the effects by using intravenous (i.v.) Mch and allergen challenge on large and peripheral bronchi in asthmatic rabbits. **Materials & methods:** We performed functional K-edge subtraction imaging using synchrotron radiation computed tomography (KES-CT) with inhaled xenon as a contrast agent in two protocols (A and B): at baseline, during i.v. infusions of Mch (A: 2.5 µg/kg/min and 5.0 µg/kg/min, B: 10.0 µg/kg/min), after recovery from the Mch effect, and following i.v. injection of the allergen, ovalbumine bolus (OVA, 2.0 mg). Protocol A was used on 6 healthy and 6 OVA-sensitized while protocol B on 6 healthy and 8 OVA-sensitized rabbits. Central airway cross-sectional area (CA), ventilated alveolar area (VA), and the heterogeneity of specific ventilation (sV) determined from coefficient of variation (CoV) were quantified from the KES-CT images. **Results:** The main results are shown in the table. Mch infusion induced a significant dose-dependent reduction in CA in healthy and sensitized animals with a smaller effect on VA and a small increase on CoV. Full recovery of all parameters occurred after discontinuation of Mch infusion. OVA bolus in the sensitized animals significantly reduced CA, VA, and increased CoV. However, the healthy animals did not show any airway reaction to OVA.

Variable	Cross-sectional Area [% Baseline] (p-value)		Ventilated Alveolar Area (VA) [% Baseline] (p-value)		Heterogeneity of Ventilation (CoV) [% Baseline] (p-value)	
	Healthy	Sensitized	Healthy	Sensitized	Healthy	Sensitized
Rabbits						
Baseline	100	100	100	100	100	100
Mch 2.5 µg/kg/min	84 (<0.05)	78 (<0.01)	98 (NS)	99 (NS)	103 (NS)	113 (NS)
Mch 5.0 µg/kg/min	58 (<0.001)	68 (<0.001)	97 (NS)	98 (<0.05)	109 (NS)	113 (NS)
Mch 10.0 µg/kg/min	46 (<0.001)	44 (<0.001)	97 (<0.05)	93 (<0.05)	127 (<0.01)	152 (<0.05)
Recovery	133 (<0.01)	129 (<0.05)	99 (NS)	99 (NS)	104 (NS)	107 (NS)
Ovalbumine	140 (<0.01)	109 (NS)	99 (NS)	77 (<0.001)	106 (NS)	244 (<0.001)

Conclusion: These results indicate that in asthmatic rabbits, sensitized with ovalbumine, non-specific airway challenge with methacholine has a predominant bronchoconstricting effect on central airways, whereas a specific allergen challenge with ovalbumine induces similar constriction both in central and peripheral airways.