Title: Improving surfactant therapy: Development of a neonatal upper airway model for in vitro aerosol deposition testing

Body: Background: Aerosolized surfactant is a promising technique to treat neonatal Respiratory Distress Syndrome (RDS). However, aerosol delivery to neonates is complex and few studies have addressed its feasibility in vitro. Methods: A computer-design of an infant airway model was drawn in CAD, and 3D pieces were printed by means of rapid prototyping. Natural surfactant aerosols were produced by a pneumatically-driven intratracheal inhalation catheter (driving pressure range 4-6bar). Characterization of surfactant aerosols (particle size and distribution) was performed using Time of Flight technology. Further, deposition of surfactant aerosols within the thermoplastic model of the upper airways was measured. Results: The printed neonatal tracheobronchial airway model successfully passed the quality control. Maximum surfactant aerosol production rate was achieved at 6bar (0.39±0.01ml/min; 31.54±0.52mg/min). Although a high percentage of deposition of the aerosolized mass (between 23.75±6.45% 4bar and 26.48±11.43% 6bar) was deposited within the printed model, the highest percentage of mass (between 64.95±7.40% 4bar and 66.43±11.46% 6bar) was measured beyond the distal exit of the model. The Mass Median Aerodynamic Diameter (MMAD) ranged between 8.52±0.16µm (6bar) and 9.36±0.35µm (4bar); higher MMAD values (13.26±3.41µm) were measured at the exit of the printed model. Conclusion: Surfactant aerosolization seems to be feasible and holds potential as a treatment for RDS; however, further research is needed to adapt current technology to the requirements of the neonatal population.