Optimal Inflating Technique to Maximize Small Airway Constriction in Precision-cut Lung Slices

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INTRODUCTION

3 Rs in animal research
- Replacement, Reduction and Refinement

Developing a useful technique to increasing the number of analysis that can be done in one animal and, thereby, reducing the number of animals.

The traditional inflating technique consists of inflating the whole lung through a direct infusion into the trachea.

The other technique is inspired by one technique commonly used with human's PCLS, whereby agarose is injected at multiple sites into the parenchyma to inflate one lobe.

Goal

Compare airway constriction in slices from lungs inflated by the traditionnal *versus* the needle technique.

METHODS

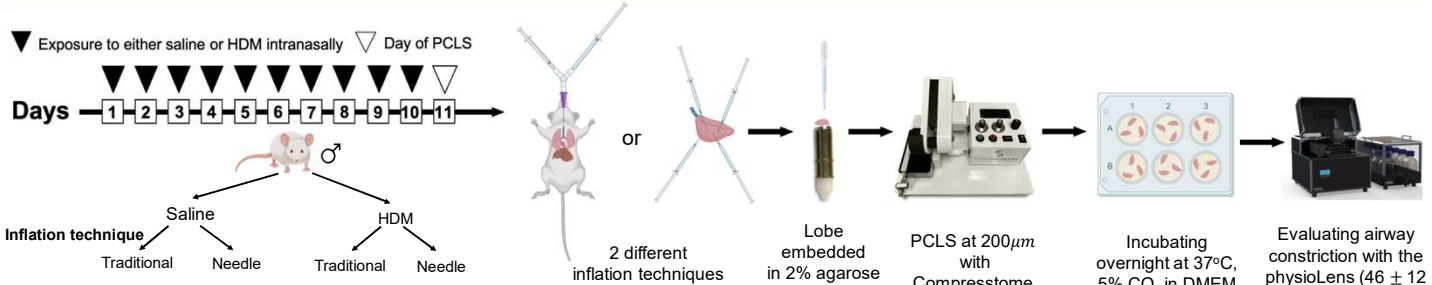


Figure 1: Schematic protocol

RESULTS

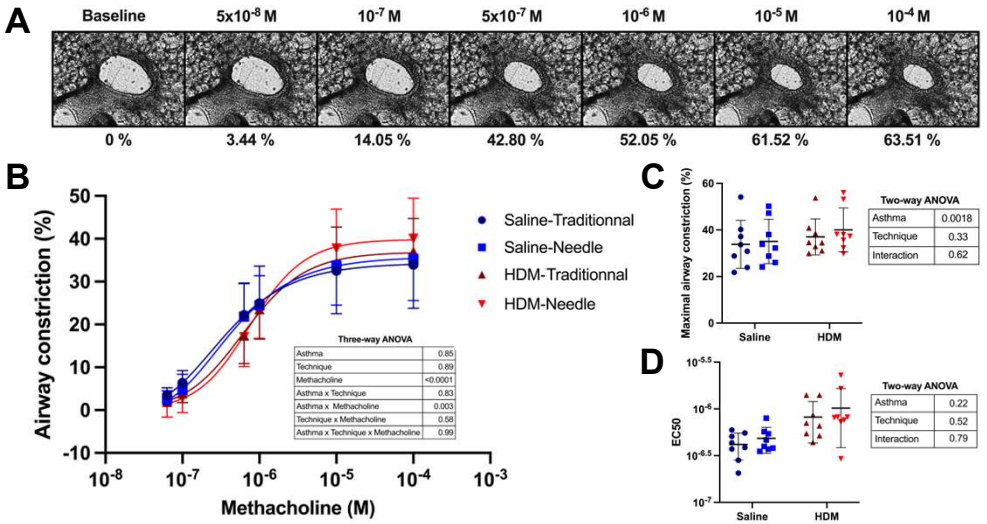
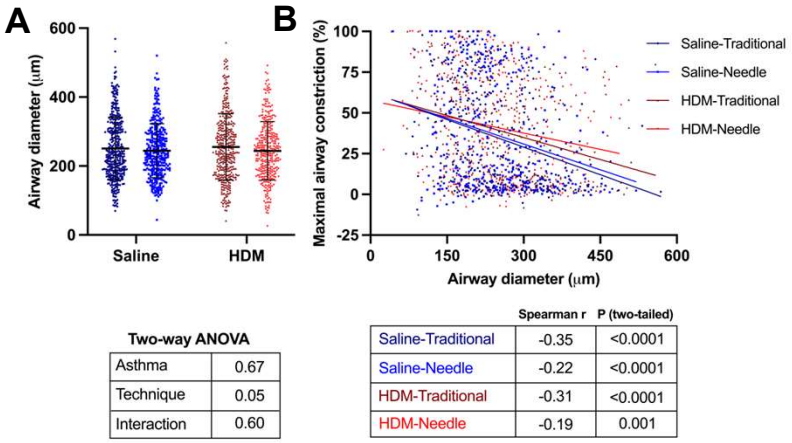


Figure 2: Airway constriction in PCLS. (A) An example of an airway constricting in response to incremental concentrations of methacholine. **(B)** Concentration-response curves displaying airway constriction over increasing concentration of methacholine, **(C)** maximal airway constriction at 10^{-4} M of methacholine, and the **(D)** EC50 showing the concentration of methacholine causing 50% of the maximal response in mice exposed to either saline (blue) or house-dust mite (red) with their lung inflated with either the traditional technique (darker colors) or with the needle technique (brighter colors).



Two-way ANOVA

Asthma	0.67
Technique	0.05
Interaction	0.60

	Spearman r	P (two-tailed)
Saline-Traditional	-0.35	<0.0001
Saline-Needle	-0.22	<0.0001
HDM-Traditional	-0.31	<0.0001
HDM-Needle	-0.19	0.001

Figure 3: Airway caliber at baseline on airway constriction. (A) Baseline airway diameters, and **(B)** correlations between baseline airway diameters and maximal constrictions are shown in slices from mice exposed to either saline (blue) or house-dust mite (red) with their lung inflated with either the traditional technique (darker colors) or with the needle technique (brighter colors).

CONCLUSION

- The needle inflating technique leads to similar airway constriction compared with the traditional technique.
- The HDM groups exhibit less sensitivity to methacholine.
- The airway constriction is greater in smaller airways for all groups.
- The needle technique slighly reduces airway diameter at baseline.

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