INTRODUCTION

Each year, over five million people die worldwide from putatively vaccine preventable infectious disease. In this study, we demonstrate the feasibility of aerosol vaccination with the recombinant poxvirus-based vaccine vectors NYVAC and MVA. In a first step, we selected an appropriate device for aerosol delivery of the NYVAC-HIV/MVA-HPV. Then, in order to trace the distribution of aerosol administered within the body, a deposition study was performed using radiolabeled recombinant vaccines. In vivo scintigraphic imaging of the head and thorax regions following inhalation revealed consistent deposition of the vaccines at various mucosal sites.

SCINTIGRAPHIC IMAGING AS A RESOURCE FOR OPTIMIZATION OF AEROSOL DEPOSITION

For immunization purposes via the respiratory tract, either Bronchial-associated lymphoid tissue (BALT) or Nasal-associated lymphoid tissue (NALT) has to be considered for rodents. In primates and humans BALT is the most efficient target.

For translational research, administration to the mouse can be achieved using nasal instillation or intratracheal nebulization, imaging being performed with a high-resolution dedicated gamma camera.

For primates and humans, administration using a facial mask of an aerosol previously optimized for granulometry is the rule.

RESULTS

✓ Labeling efficiency: >95%
✓ Nebulizer selection:

⇒ Of the two devices, the Fisoneb consistently produced higher amounts of aerosol with lower inter-test variability (Fig 1A)
⇒ After aerosolization there was a 40% net increase (p=0.026) in the viral titers in the Fisoneb (Fig 1B)
⇒ The Fisoneb dispensed a larger amount of biologically active vaccine, 15.76 ± 5.25%, than the Sidestream, 4.81 ± 2.90% (p=0.42) (Fig 1C)

Fisoneb was selected

✓ Monitoring aerosol NYVAC-HIV and MVA-HPV deposition by in vivo real-time scintigraphy:

⇒ Imaging of the head and thorax regions following inhalation revealed discreet deposition of the vaccines at various mucosal sites.
⇒ Efficient delivery was observed in all 8 animals as well as significant accumulations in the sinuses, mouth, oropharynx, stomach, and upper duodenum

✓ Histology:

Histology of various organs 72 hours post aerosolisation

MATERIAL AND METHODS

Animals: 10 C57BL6 mice were included in a feasibility study the aerosol administered with a Penn Century nebulizer;
8 rhesus macaques (Macaca mulatta) 4 to 9-year-old, 4 to 9 kg
Vaccines: Nyvac-C (Eurovacc initiative) and MVA-HPV (Transgene)
Radiolabelling: 2.51.10⁶ DCI50 NYVAC-C and 5.5.10⁶ pfu MVA-HPV were labeled with 500-800MBq Technetium 99m

Aerosol administration in macaques: 2 nebulizers were compared: the Fisoneb which generates aerosol by sonication and Sidestream which creates an aerosol mist via a pneumatic pump

Scintigraphic imaging: A 120 second static scintigraphic image (128x128 pixels matrix) was recorded in the posterior incidence of the thorax, as well as the head and neck region.

DISCUSSION / CONCLUSION

The results from this non-human primate pre-clinical investigation demonstrate the feasibility of aerosol vaccination using NYVAC and MVA in future human clinical trials. Aerosol delivery was immunogenic and no vaccine-associated pathology was observed.