**In vivo / in vitro comparison of aerosol deposition in nasal cavities**

**Introduction**

*In vitro* metrology methods based on particle size measurements do not allow an accurate prediction of the deposition of nasally inhaled drugs. Intranasal deposition can be measured *in vivo* by gamma camera imaging, but the risk of exposure to radiation and ethical considerations is present. As an alternative, anatomical models have been developed to study the nasal deposition but these models have not been validated as relevant to predict *in vivo* deposition.

The aim of this study is to validate anatomical models in order to predict aerosol deposition by comparing *in vivo* nasal aerosol deposition to *in vitro* using two nasal nebulizer systems. Two nasal cast models, a plastiñated head model and its replica in plastic, were tested.

**Materials and methods**

**In vivo study:**

*Human volunteers* were seven non-smoking healthy males (21 to 36 years).

**In vitro study:**

Two anatomical models of nasal cavities were tested (Figure 1):

- NC1 : *plastiñated head* model in which liquids and liquids replaced by silicone polymers.
- NC2 : Acrylonitrile Butadiène Styène (ABS) replica using 3D imaging analysis and 3D printing technique.

**Nebulizers:**

Two nasal nebulizer systems were used (Figure 2):

- **Sonic jet nebulizer** (NL11SN® Atomisor, DTF medical, Saint Etienne, France) used with a compressor generating a sound at 100Hz. (A)
- **Mesh nebulizer** (EasyNose®, DTF medical, Saint Etienne, France) connected to a specific compressor. (B)

The devices were used for both *in vivo* and *in vitro* studies, with nebulizers loaded with 74MBq / 3mL of **TE-DTPA** (Diethyl-Triamine-Penta-Acetic acid) during 10 min.

**Images acquisition and processing:**

Scintigraphic images were recorded with a planar gamma camera. The Regions Of Interest (ROIs) were defined from the images obtained with Krypton gas administration.

The gamma camera images were analyzed using ImageJ software. The distribution of the aerosol deposited in nasal cavities was analyzed along three axes : x, y, z (Figure 3)

- **X-axis**: from the nostrils to the cavum
- **Z-axis**: from the floor to the upper nasal cavities

In *in vitro* and *in vivo* distributions were normalized.

**Results**

**Images of aerosol deposition:**

Nasal deposition (Figure 4) was quantitatively similar in *volunteers* and in *in vitro* models.

Deposition of aerosol administered by mesh nebulizer was deposited from nostrils to the cavum, while jet nebulizer administration resulted in a predominant deposition in the nasal valve.

**Aerosol deposition in nasal cavities:**

- **In vitro nasal, ethmoid and maxillary sinuses** deposition in NC1 were similar to *in vivo* data, for both nebulizers (NS).
- **In vitro nasal deposition** in NC2 was significantly lower than *in vivo* (p<0.05). But deposition in the ethmoid and maxillary sinuses was similar to *in vivo* (NS) (Table 1)

**Aerosol distribution in nasal cavities:**

- **Distributions** of NC1 are similar to the distributions in *volunteers* for both nebulizers, except a wider peak along x-axis with the mesh nebulizer.
- **Slight differences** were observed between the *in vivo* and NC2 profiles: a peak value of jet nebulizer distribution along x-axis was higher than *in vivo* and a peak along y-axis was flatter than *in vivo* (Figure 5)

**Conclusion**

The study demonstrates that the deposition of nebulized aerosols in human nasal cavities could be predicted using a nasal cast model. In particular, it demonstrates that the prediction of deposition differs according to the nasal model used, and shows that the accuracy of the prediction depends on the quality of the model.