Published online: 2019-04-23

Establishment of a large animal model for Eustachian tube functional study in miniature pigs

Zhao-hui Hou ， Feng-Wei AN, Shi-ming Yang

Department of Otolaryngology & Head Neck Surgery, Chinese PLA General Hospital, Beijing, China ； Key Lab of Hearing Impairment Science of Ministry of Education ， Key Lab of Hearing Impairment Prevention and Treatment of Beijing City ， Chinese PLA Medical School, Beijing, China.

INTRODUCTION

The precise mechanisms underlying Eustachian tube dysfunction (ETD) are complex and not fully understood, but are directly related to the structural features and concealed location of the ET, as well as to the lack of a valid ET animal model.

The present study was performed to improve Miniature pigs model of the auditory system and bridge the gap to the human auditory system, and to determine whether the miniature pig could be used as a valid animal model to test surgical treatments for ETD in humans.

METHODS

Sixteen Chinese experimental miniature pigs were used in this investigation. Ten animals were used for anatomical and morphometric analyses to obtain qualitative and quantitative information regarding the ET. Three animals were used for histological analysis to determine the fine structure of ET cross-sections. Three animals were used to investigate the feasibility of balloon dilation of the Eustachian tube (BDET).

RESULTS

Anatomical study

The tympanic orifice of the miniature pig was identified as a flat aperture that intrudes into the anterior wall of the middle ear cavity, whereas it protrudes from the middle ear cavity in humans.

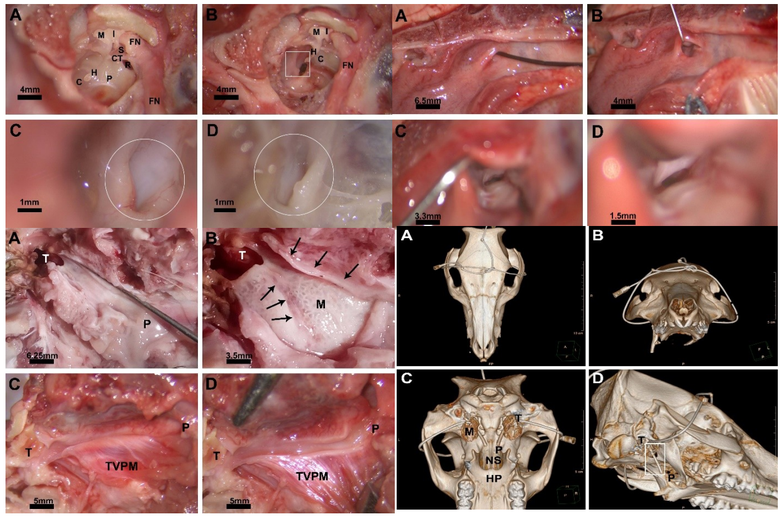
The pharyngeal orifice of the ET appears as an arc-shaped seam in a static state, which is located at the posterior end of the nasal lateral wall. On retraction, the cross-section of the pharyngeal orifice had a tadpole-like appearance. The ET lumen narrowed gradually from the pharyngeal orifice to the tympanic orifice, and was narrowest at the tympanic orifice, which presents as a flat aperture.

After removing the thin mucosal layer, the mastoid could be observed at the proximal tympanic orifice. A bony groove on the surface of the mastoid engaged with the cartilaginous tube. The superior wall was composed of mucosa and cartilage, which tended to curl up during removal. Its inner surface could be observed when pulling the tensor veli palatini muscle (TVPM). The attachment of the TVPM to the anterior edge of the ET cartilage was thought to result in whole-ET dilatation when contraction occurred. The cartilaginous tube extended throughout the whole length of the ET, although the upper third ran in a bony channel composed of the skull base and mastoid. The cartilage was thin at the tympanic end of the tube but became increasingly thicker toward the pharyngeal orifice.

Morphometric study

Whole-specimen reconstructions were done by applying a pixel value threshold and the isosurface function. Figure shows a representative reconstruction of the miniature pig skull, and indicates the position of the ET. The reconstructions could be manipulated in the software and rotated to allow viewing at any angle.

Measurements of the miniature pig skull and ET, including the intrinsic parameters, relative parameters. The cross-section was largest at the pharyngeal orifice, which had a tadpole-like appearance, and narrowest at the tympanic orifice, which had the appearance of a flat aperture.



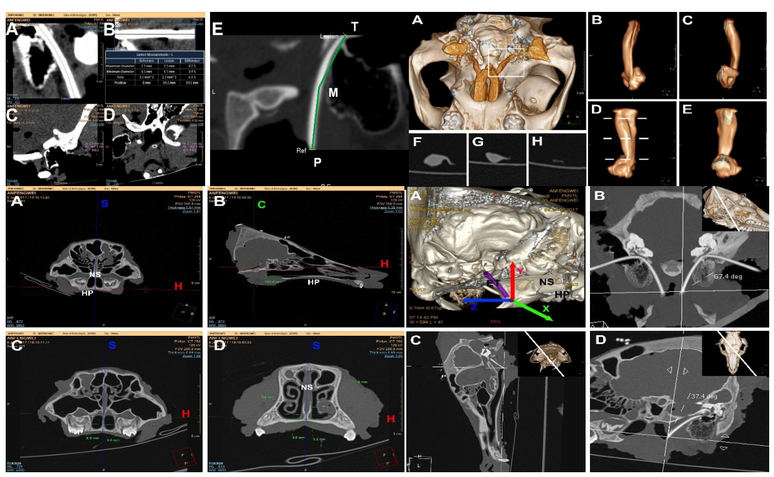
The cross-section of the midpoint was intermediate between the two outlined above, and had the appearance of a small fish. The tympanic orifice correspond to the isthmus of the ET.

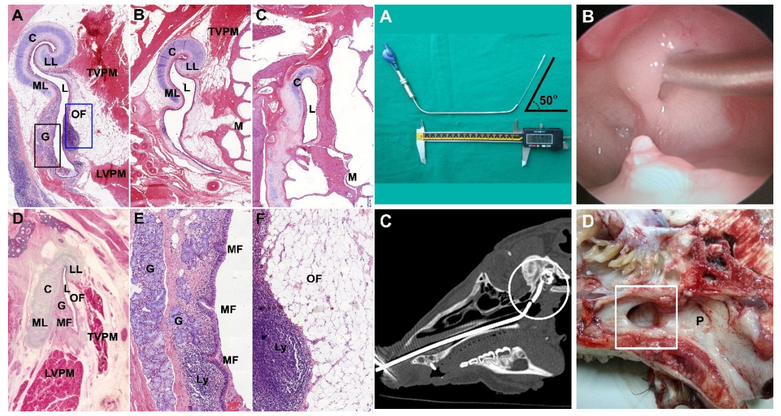
Histological study

The results of histological examination revealed the fine structure of miniature pig ET cross-sections in different planes. The curvature of the miniature pig cartilage decreased gradually from the pharyngeal orifice to the tympanic orifice. In the plane of the pharyngeal orifice, the ET cartilage was shaped like an “e”, while it was shaped like an inverted “J” in the plane of the tympanic orifice. The curvature of the miniature pig cartilage in the cross-section was greater than that in humans.

In terms of the relative proportions, the lumen of the miniature pig ET was greater than that in humans. In the pig, the lumen was shaped like an “ε” in the cross-sectional view. Its upper aspect was surrounded by the ET cartilage, while its lower aspect lacked cartilage.

In human, the S-shaped lumen, was completely surrounded by the ET cartilage. As in humans, the TVPM was firmly attached to the lateral lamina (LL) of the ET cartilage, consistent with the observations outlined above. The pig levator veli palatine muscle (LVPM) was located inferior to the ET lumen, but was more anterior than that in humans.





DISCUSSION

- With regard to the histology of the ET orifice, nasal cavity, and middle ear cavity, the miniature pig appears to be an appropriate large animal model for study of the ET. First, the pharyngeal orifice and tympanic orifice of the miniature pig ET are located at the posterior end of the nasal lateral wall and anterior wall of the middle ear cavity, respectively, which are identical to the positions in the human ET. Second, the nasal cavity is wide enough to allow endoscopic surgical procedures similar to transnasal endoscopic surgery in humans. Third, the arrangement and volume of the tympanic cavity are almost the same between the miniature pig and human.

- Our study indicated that the miniature pig possesses the osseocartilaginous junction of the ET in addition to the cartilaginous part. In humans, the osseocartilaginous junction of the ET is a clearly identifiable structure. There is a short extension of the cartilage into the protympanum or bony medial third of the ET, which is a continuation of the tympanic cavity (Berry et al. 1995). We found that the upper third of the ET lumen consists of cartilage and a bony groove on the surface of the mastoid, at which point the bony surface is lined by a very thin mucosa, identical to the arrangement of the osseocartilaginous junction in humans.

- By comparing human and miniature pig ET cross-sections, we found that the gross histology appeared to differ slightly, but the fine structures were essentially the same between the two species.
- A valid animal model of ET should allow for clinical operations in vivo, as well as preclinical trials. BDET was first applied in living animals in our study, which verified that the miniature pig is a valid animal model for ET studies.

CONCLUSION

In summary, the ET of the miniature pig corresponds very closely to that of humans. In addition, the miniature pig ET model allows in vivo clinical operations to be performed using procedures similar to those that would be applicable in humans. Therefore, the miniature pig is a valid animal model for use in ET studies.