1 **Original Article** 2 3 Use of computational fluid dynamics to compare upper airway pressures and airflow 4 resistance in brachycephalic, mesocephalic, and dolichocephalic dogs 5 6 R. Fernández-Parra a, b, c, *, P. Pey d, e, L. Ziberstein a, M. Malvè f, g, h 7 8 ^a Ecole Nationale Vétérinaire d'Alfort, Paris, France, 7 Avenue du General de Gaulle, 94704 9 Maisons-Alfort, France 10 ^b Department of Small Animal Clinical Science, Western College of Veterinary Medicine, 11 University of Saskatchewan, 52 Campus Drive Saskatoon, SK S7N 5B4, Canada 12 ^c Institut national de la santé et de la recherche médicale (INSERM), U955, Equipe 03, 51 13 avenue du Maréchal de Lattre de Tassigny, 94010 Créteil cedex, France 14 ^d Antech Imaging Services, Fountain Valley, CA 92708, USA 15 ^e Department of Veterinary Medical Science, University of Bologna, Ozzano dell'Emilia, Italy 16 ^f Department of Engineering, Public University of Navarre, Campus Arrosadía s/n, 31006 17 Pamplona, Spain 18 ^g Aragon Institute of Engineering Research, University of Zaragoza, C/María de Luna s/n, 19 50018 Zaragoza, Spain ^h Centro de Investigación Biomédica en Red - Bioingeniería, Biomateriales y Nanomedicina, 20 21 CIBER-BBN, C/Poeta Mariano Esquillor s/n, 50018 Zaragoza, Spain 22 23 24 25 26 *Corresponding author. Tel.: +33 (0) 1 43967349. 27 *E-mail address:* rocio.fernandez@vet-alfort.fr (R. Fernández-Parra). 28

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Abstract

Brachycephalic dog breeds are prone to breathing difficulties because of their upper airway anatomy. Several surgical techniques exist to correct anatomical pathologies and common surgical approaches aim to correct functional abnormalities in the nares and/or the soft palate. However, further research is needed to improve clinical outcomes. This study evaluated air pressure and airflow resistance in the upper airways and trachea in nine sedated, sternally recumbent dogs of different skull types (dolichocephalic, *n*=3; mesocephalic, *n*=3; brachycephalic, *n*=3). CT images were acquired from the nostrils to the caudal border of the lungs and geometrical reconstruction of the upper airway and trachea was performed. Analysis of computational fluid dynamics was performed using inspiratory flow adapted to bodyweight for each dog. Flow (L/min) and pressure (cmH₂O) were computed for the entire upper airway and trachea. Resistance (cmH₂O/L/min) was calculated using pressure differences between the nose, larynx, and trachea. In this pilot study, statistical comparisons were not performed.

Pressure maps, airflow, and resistance were similar in dolichocephalic and mesocephalic breeds. Median pressure difference (3.76 cmH₂O) and resistance (0.154 cmH₂O/L/min) between the nose and larynx were numerically higher in brachycephalic dogs than in other breeds (0.45 cmH₂O and 0.016 cmH₂O/L/min, respectively). Median pressure difference (0.205 cmH₂O) and resistance (0.009 cmH₂O/L/min) between the larynx and trachea was numerically similar in all dogs, except for the English bulldog. The methodology used in this preliminary study to quantify airflow characteristics such as pressure and resistance could improve the understanding of brachycephalic obstruction airway syndrome.

- 53 Keywords: Airway resistance; Brachycephalic dogs; Computational fluid dynamics;
- 54 Computerized tomography images; Pressure

Introduction

The anatomy of the upper airway is highly varied between dogs of different breeds and skull shapes. Dog breeds are classified according to their skull index (the ratio of skull width and length) into three basic types: dolichocephalic, mesocephalic, and brachycephalic (Evans and de Lahunta, 2012). A shorter muzzle carries a higher risk of brachycephalic obstruction airway syndrome (BOAS; Packer et al., 2015). This pathology is characterized by an elongated soft palate, stenotic nares, and/or everted laryngeal saccules. Some brachycephalic dogs can also have narrowed trachea, laryngeal collapse, and/or laryngeal paralysis, resulting in upper airway obstruction and clinical signs of BOAS (Dunié-Mérigot et al., 2010).

Pulmonary function tests are used in human medicine, but their application in veterinary medicine can be challenging (Hoffman, 2007; Balakrishnan and King, 2014). Spirometry or pneumotachography are used clinically in dogs and cats to obtain flow-volume and/or volume-pressure loops, which provides information about airflow rates, volumes over time, and inspiratory and expiratory peak pressures and times (Amis and Kurpershoek, 1986; Hoffman, 2007). This technique can also be used to identify tracheal collapse in dogs (Pardali et al., 2010), but is relatively insensitive to upper airway resistance to air flow. Whole-body barometric plethysmography can be used in unsedated dogs (Bedenice et al., 2006). One study reported that this technique could determine the severity of BOAS and diagnose the condition in French bulldogs with 95-97% sensitivity (Liu et al., 2015); however, it is purely a research technique. In brachycephalic dogs, there is high pressure in the pharyngo-laryngeal region during inspiration because of proximal obstruction to airflow (Amis et al., 1996), causing distortion and collapse of the laryngeal arytenoid cartilages (Koch et al., 2014).

Advances in radiography, CT (Grand and Bureau, 2011; Stadler et al., 2011), magnetic resonance imaging, and endoscopy (Bernaerts et al., 2010) have contributed to our understanding of the canine upper airway function and anatomy. CT and three-dimensional (3D) internal rendering can accurately indicate the presence and sometimes the cause of upper airway obstruction in dogs (Stadler et al., 2011). It is the imaging modality of choice for stent selection in dogs with tracheal collapse (Williams et al., 2016).

Computational fluid dynamics (CFD) uses numerical algorithms to analyse flow characteristics in a variety of situations, such as during respiration. CT and CFD in human patients has allowed computation of nasal airflow (Kyun Kim et al., 2013), upper airways (Gemci et al., 2008; Luo and Liu, 2008), stenosis (Brouns et al., 2007; Malvè et al., 2013), and sinonasal lesions (Lindemann et al., 2005). Numerical simulations have also been used to test medical devices and improve their design (Malvè et al., 2012). CFD studies have been performed in bats and rats to aid toxicology investigations (Zhao et al., 2006; Yang et al. 2007; Eiting et al., 2014), and airway fluid dynamics and stenting techniques have been reported in rabbits (Malvè et al., 2014; Chaure et al., 2016). CT and CFD techniques have been used in a mesocephalic dog (Labrador) to examine nasal airflow (Craven et al., 2007) and recently to quantify and compare airway resistance in 21 English bulldogs (Hostnik et al., 2017) to study BOAS.

The aim of this pilot study was to use CT-based CFD modelling to compare airway geometry, airflow, pressure, and resistance in dolichocephalic, mesocephalic, and brachycephalic dog breeds. Our hypothesis was that the computed airflow, pressures, and resistance would be more heterogeneous in brachycephalic breeds than in dolichocephalic or mesocephalic breeds.

Materials and methods

Dogs

Nine adult client-owned dogs presented to the Veterinary Medicine Hospital of Alfort, France were enrolled in this prospective study. All enrolled dogs required sedation for CT examination for reasons unrelated to this study. Respiratory signs were absent during physical examination in any of the dogs. From 135 dogs scheduled for CT over a period of 18 months, 12 dogs were recruited for this study after exclusion criteria were applied. Exclusion criteria were as follows: dogs requiring intubation for imaging, presence of respiratory or cardiovascular disease, closed glottis, pulmonary abnormalities, intraluminal tracheal mass, or invagination of the dorsal tracheal membrane, vomiting, hypersalivation, tremors or/and myoclonus. Three of the 12 initially enrolled dogs were excluded because abduction of the cordial cord of the larynx was observed during CT reconstruction. Three dolichocephalic dogs (Great Dane, Whippet, and Dachshund), three mesocephalic dogs (Belgian Shepherd, Labrador, and Brittany spaniel), and three brachycephalic dogs (French bulldog, Boxer, and English bulldog) were finally included, based on skull index. Median weight of the nine enrolled dogs was 27.4 kg (range, 10.3–78.6 kg). Food, but not water, was withdrawn 12 h prior to CT examination.

Ethical approval

All procedures were conducted as part of normal veterinary clinical practice with the owner's consent (Art. R242-48, Ordre National de Vétérinaire) and approval from the Head of the Veterinary Medicine Hospital of Alfort, France (7th September 2015).

Sedation and multidetector computed tomography (MDCT) protocol

All dogs were sedated IM with a combination of 5 µg/kg dexmedetomidine (Dexdomitor, Orion Pharma), 0.3 mg/kg midazolam (Hypnovel, Hoffmann-La Roche), and 0.3 mg/kg butorphanol (Torbugesic, Zoetis). Once sedated, an IV catheter (Delta Med) was aseptically placed in a cephalic vein. IV fluid therapy with crystalloids (Ringer's lactate, B. Braun) was administered at 5 mL/kg/h during the CT procedure. A multiparametric monitor (Vet Care Monitor, B. Braun Vet Care) was used; side-stream capnography in the nares measured respiratory rate and expired CO₂ (mmHg); pulse oximetry provided the pulse rate and arterial oxygen saturation; and body temperature (°C) was measured with a rectal thermometer. Physiological parameters were measured every 5 min. Dogs spontaneously breathed room air and were placed in sternal recumbency with the head elevated and the neck fully extended. Images were acquired from the nostrils to the most caudal border of the lungs (Hostnik et al., 2017). Non-contrast-enhanced MDCT examinations were carried out using a 64-detector-row CT system (Brilliance 64; Philips). Images were obtained using a collimation of 64×0.9 mm, a matrix of 512×512 , tube voltage of 120 kV, tube current of 400 mA, and tube rotation time of 50 s. One millimetre thick images were reconstructed using a highresolution algorithm. At the conclusion of the CT examination, atipamezole (Alzane, 5 mg/mL, Zoetis) was administered IM at the same volume as dexmedetomidine. Recovery was supervised until complete.

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Image analysis

Images were viewed using OsiriX software (v.5.8.2, 64-bit, Pixmeo SARL) with a lung window (window width [WW] 1600; window level [WL] –550). A board-certified radiologist evaluated the images for major abnormalities involving the airways and measurement of the skull index. Images were displayed using a bone window (WW: 1500; WL: 300).

Measurement of skull index

The skull index was obtained by dividing the skull width by skull length (skull width/skull length × 100). The width was taken at the widest interzygomatic distance. The length was taken as the distance between the inion (most prominent projection of the occipital bone, i.e., the external occipital protuberance) and the prosthion (most forward projecting point of the maxillary alveolar process at the midline). A previously reported skull index (Koch et al., 2012) was also calculated using the ratio of the length of the skull to the length of the cerebrum. The length of the cerebrum was defined as the length from the rostral border of the cranial cavity to the inion. The width and length were measured using multiplanar reconstruction CT images (high-resolution algorithm and displayed on the bone window). The results of the skull index measures are summarised in Table 1.

Geometrical reconstruction and numerical discretization

The DICOM (Digital Imaging and Communications in Medicine) files derived from the CT scans were imported into the image-based geometry reconstruction software (MIMICS, Materialise Software). A manual reconstruction of the upper airway and trachea geometry was conducted for each dog (Figs. 1 and 2). The air nasal passage was filled with a threshold throughout all contiguous images until the trachea (green colour in Fig. 1, sections 1, 2, 3, and 4), generating a 3D solid model. In Fig. 1, the model of the Great Dane is depicted in purple as an example.

The volume of each model was then subdivided in a CFD mesh consisting of tetrahedral elements in the software package (Ansys IcemCFD, v.16, Ansys). At this stage, the minimum size of all tetrahedral edge lengths was specified to control the number of

elements. Near-wall regions required a denser mesh with more elements (Fig. 3) to capture the gross geometry of the small airways. The minimum edge length varied depending on the skull index type, generating computational grids of approximately 20×10^6 elements. A mesh independence analysis was carried out to assess the effect of the computational mesh on the results. The number of elements of the computational mesh was progressively increased, and the pressures at the locations depicted in Fig. 3 were computed and plotted for different mesh densities. Nasal pressure (section 1) seemed independent of the global element number, while the laryngeal and tracheal pressures increased only slightly (in absolute value) with increasing mesh element number (section 2, 3, and 4; Appendix).

CFD analysis

The numerical grids from the nine dogs were imported into a simulation software package (ANSYS CFX, v.16, Ansys). The numerical approach used by this software is explained in the software manual (Ansys, 2016). Continuity and Navier-Stokes equations for turbulent flow were used to solve canine airflow for an incompressible and Newtonian steady fluid (Craven et al., 2009) using an air density of 1.185 kg/m³ and viscosity of 1.83 ×10⁻⁵ Pa·s, respectively (Malvè et al., 2013).

The imposed peak inspiratory flow was as previously published for dolichocephalic and mesocephalic breeds (1.125 L/kg/min; Rozanski et al., 1994) and brachycephalic dogs (0.83 L/kg/min; Bernaerts et al., 2010). These values were first adapted to individual bodyweight by computing different values for each dog and then applied at the nasal aperture representing the model inlet and at the distal tracheal section (model outlet; Fig. 3).

Resistance evaluation

The upper airway resistance was evaluated using pressure computed at different locations of each skull model (Fig. 3). Equivalent locations were used for each skull. The upper airway resistance was calculated as follows:

Resistance (cmH₂O/L/min) = Δp (cmH₂O)/flow (L/min) where Δp is the pressure difference between two anatomical locations and the flow is calculated as the mean airflow passing through these sections.

Additional details are as follows: section 1, between the nasal entrance and the proximal larynx, which was taken at 1 cm inside the nasal cavity; sections 2 and 3, between the proximal and distal larynx, which was taken 2 cm above and below the larynx, respectively; and section 4, between the larynx and trachea, which was taken 10 cm from the larynx, inside the trachea. The location of sections 2, 3, and 4 varied slightly and in proportion to the tracheal length for each dog. Pressure difference (Δp) and resistance between the nose and larynx were computed using sections 1 and 2 (Fig. 3), while Δp and resistance between the larynx and trachea were computed using sections 2 and 3. Section 4 was used only for the mesh sensitivity analysis described previously.

Results

The airflow (Δp) and resistance between the nose and larynx and between the larynx and trachea for each dog breed are summarised in Tables 2 and 3, respectively. The flow inside the upper airway and trachea is depicted in Fig. 4, using streamlines that represented the spatial direction of the flow coloured with the velocity intensity (0-20 m/s).

The upper airway and trachea in dolichocephalic and mesocephalic dogs generated similar velocity and pressure maps. The flow velocity inside the sinus was low (<1 m/s;

depicted in dark blue in Fig. 4 and indicated by blue arrows). The flow velocity in nasal cavities and the ethmoidal- and maxillo-turbinate regions ranged from 0 to 11.11 m/s. In contrast, numerically higher flow velocity was observed for the Boxer and English bulldog in the hard palate at the maxillo-turbinate region and at the larynx, respectively (20 m/s, depicted in red and indicated by red arrows, Figs. 4g and 4i).

The pressure map inside the upper airway and trachea is shown in Fig. 5 (legend values range from –10 to 10 cmH₂O in terms of the atmospheric pressure). For each dolichocephalic and mesocephalic dog, the pressure contours showed an almost uniform pressure (2-4 cmH₂O) distribution in the upper airway (Fig. 5, upper and median panel). Only the Whippet (Fig. 5b) demonstrated some local pressure increase in the nares (depicted in yellow and indicated by a yellow arrow; Fig. 5b). In contrast, the brachycephalic dogs had highly nonhomogeneous pressure distributions (2-10 cmH₂O). In the French bulldog, a pressure difference of 2-4 cmH₂O was observed in the section just proximal to the soft palate (Fig. 5h, lower panel, depicted in yellow and indicated by a yellow arrow).

In the English bulldog, Δp of approximately 14 cmH₂O (from light green to dark blue) was observed (Figs. 5i and 6a, blue and green arrows; dark blue is due to sudden low pressure caused by the stenosis upstream). This was attributed to high velocity flow (20 m/s) immediately caudally to the stenosis (red colour in Fig. 4i and 6b, indicated by the red arrow).

In the Boxer (Fig. 5g), different colours (red, green, and yellow indicated by respectively coloured arrows) represent abrupt pressure changes. Red indicates peak pressure caused by a constriction downstream to the skull, proximal to the larynx. This dog had an

abnormal pressure decrease between the nasal cavities and the sinus (10-2 cmH₂O), which was not observed in the other eight dogs (Figs. 5 and 7). This indicates asymmetric left and right nasal cavities and uneven pressure distribution (Fig. 7a) and resistance due to local flow acceleration (Figs. 7a and 7b). There was a local increase in flow velocity in the left nasal cavity (depicted in red, Fig. 7b). The pressure in Fig. 7a has a different threshold to Fig. 5g. This emphasizes the dramatic increase in pressure in the Boxer compared with the other breeds and demonstrates that there were local variations in pressure regions in the skull of this dog.

Stenotic anatomical regions in brachycephalic breeds caused flow variations (Figs. 6 and 7) and, as a consequence, variations in pressure and the resistance (Figs. 8 and 9). In Figs. 8 and 9, respectively, Δp and resistance are plotted and compared between breeds, including data from a close-up view for each group. All dogs exhibited Δp proximal and distal to the larynx (Fig. 8), but this was especially enhanced in the English bulldog (Figs. 5i, 8b, and 8b.3). The largest pressure reduction was reflected in computed resistance (Figs. 8 and 9b). Resistance to airflow between the nose, larynx, and trachea (Fig. 9) was numerically higher in brachycephalic dogs (Tables 2 and 3). Brachycephalic dogs had numerically higher resistance between the nose and larynx than mesocephalic or dolicocephalic dogs (Figs. 9a and 9a.3).

Discussion

This study demonstrates that it is possible to examine pressure and resistance noninvasively in the canine upper airways and trachea for different skull conformations using a CT-based CFD technique that is widely used in humans. There are several reported approaches to determine skull index (Koch et al., 2012). The values obtained in the present

studies differ from those previously published (mesocephalic, *n*=39; brachycephalic, *n*=52; Evans and de Lahunta, 2012) and this may be related to the measurement technique, as previous studies used either conventional radiographic films (Regodon et al., 1993), or external measurements with a soft measuring tape (Packer et al. (2015), measuring the muzzle and cranial length. To our knowledge, there are no published studies investigating relationships between the degree of brachycephaly using skull measurements and the severity of clinical signs.

In this pilot study, different brachycephalic breeds presented a wide degree of variation in computed airflow resistance, despite the lack of respiratory signs. Increased upper airway resistance results in increased respiratory effort, clinically visible as respiratory distress or decreased airflow due to prolonged inspiratory time (Pardali et al., 2010). Stenosis, high pressure and increased airflow resistance were detected in the hard palate at the maxilloturbinate region of the Boxer and in the larynx of the English bulldog. Furthermore, in the geometric reconstruction, we observed tracheal hypoplasia in the English bulldog, a breed known to be predisposed to tracheal hypoplasia (Coyne and Fingland, 1992). The computed resistance and Δp were extremely high. Brachycephalic breeds can have anatomical differences, potentially predisposing individual dogs to respiratory signs. Packer et al. (2015) concluded that breeding for flatter faces dramatically increases the risk of chronic airway obstruction in dogs and could result in an unintentional pathology which could be detrimental to animal welfare. Our results suggest that although the upper airway anatomy in the dogs we studied was genetically altered, they were able to compensate by breathing through their oral cavity during our examinations, resulting in high respiratory rates and lower tidal volumes, perhaps predisposing to a sedentary lifestyle.

We believe that simply resecting the nares and a portion of the soft palate does not correct the basic problem in dogs with BOAS. Upper airway resistance and Δp were numerically higher in all brachycephalic breeds in our study, especially in the ethmoidal region, reflecting the findings of Hostnik et al. (2017). The ethmoidal region, especially the edematous mucosa, has been proposed as important in airway disease of brachycephalic dogs; however currently, the only surgical correction available is nasal turbinectomy (Oechtering et al., 2016). Our findings document previously unreported (Lorenzi et al., 2009) anatomical regions that could be pathologically altered in brachycephalic dogs, which are not treated using current surgical techniques (Riecks et al., 2009; Fasanella et al., 2010). Hence, breed standards for at least some brachycephalic dogs could be problematic. Our numerical computations demonstrate that the entire skull shape of the brachycephalic dogs studied leads to severe airflow limitation and obstruction in the nasal passageways, larynx, and trachea.

A limitation of this study is that we used previously reported inspiratory flow rates (Rozanski et al., 1994; Bernaerts et al., 2010) and adapted them to each dog's bodyweight. Nevertheless, different breeds could have different inspiratory flow rates, especially brachycephalic dogs, and discrepancies might exist between computed and real values. Additionally, 3D geometries are considered rigid and therefore do not account for airway compliance. However, because of the relative inflexibility of the nasal cavity (Hostnik et al., 2017), this is not expected to affect our major conclusions. Another study limitation is that CT images were taken in sternal recumbency to maintain a physiological position. The natural standing position could somewhat modify anatomical geometry (Wei et al., 2017), as could sedation, which might relax the musculature around the larynx. Finally, statistical analyses to compare different skull index types was not performed. However, the goal of this work was not to determine statistically significant differences in airflow relationships

between skull index types, but rather to demonstrate the feasibility of CFD for the quantification of upper airway resistance in nine dogs of different breeds.

Conclusions

CT-based CFD is a non-invasive technique that can demonstrate changes in airway pressure and resistance in different dog breeds. In brachycephalic dogs, we were able to identify numerically different pressure distributions compared with dolichocephalic and mesocephalic dogs, demonstrating differences in the nasal apertures or soft palate. This method could support clinical decision making and surgical planning in cases of obstructive upper airway and tracheal disease. CT-based CFD simulations should be further evaluated as diagnostic tools to improve clinical outcomes and better understand anatomical predisposition the risk of BOAS.

Conflict of interest statement

None of the authors has any financial or personal relationships that could inappropriately influence or bias the content of the paper.

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355 **Appendix: Supplementary material** 356 Supplementary data associated with this article can be found, in the online version, at 357 doi: ...' 358 359 References 360 Amis, T. C., Kurpershoek, C., 1986. Tidal breathing flow-volume loop analysis for clinical 361 assessment of airway obstruction in conscious dogs. American Journal of Veterinary 362 Research 47, 1002-1006. 363 364 Amis, T. C., O'Neill, N., Van der Touw, T., Brancatisano, A., 1996. Control of epiglottic 365 position in dogs: role of negative upper airway pressure. Respiration Physiology and 366 Neurobiology 105, 187-194. 367 368 Ansys Inc., 2016. Ansys CFX Theory Manual v.16. Ansys Software Canonsburg, PA, USA. 369 370 Balakrishnan A., King LG., 2014. Updates on pulmonary function testing in small animals. 371 Veterinary Clinics of North America: Small Animal Practice 44, 1-18. 372 373 Bedenice, D., Rozanski, E., Bach, J., Lofgren, J., Hoffman, A. M., 2006. Canine awake head-374 out plethysmography (hop): characterization of external resistive loading and 375 spontaneous laryngeal paralysis. Respiration Physiology and Neurobiology 151, 61-376 73. 377 378 Bernaerts, F., Talavera, J., Leemans, J., Hamaide, A., Claeys, S., Kirschvink, N., Clercx, C., 379 2010. Description of original endoscopic findings and respiratory functional 380 assessment using barometric whole-body plethysmography in dogs suffering from 381 brachycephalic airway obstruction syndrome. The Veterinary Journal 183, 95-102. 382 383 Brouns, M., Jayaraju, S. T., Lacor, C., Mey, J. D., Noppen, M., Vincken, W., Verbanck, S., 384 2007. Tracheal stenosis: a fluid dynamics study. Journal of Applied Physiology 102, 385 1178-1184. 386 387 Chaure, J., Serrano, C., Férnandez-Parra, R., Peña, E., Lostalé, F., De Gregorio, M. A., 388 Martínez, M. A. and Malvè, M. On Studying the Interaction Between Different Stent 389 Models and Rabbit Tracheal Tissue: Numerical, Endoscopic and Histological 390 Comparison. Annals of Biomedical Engineering 44, 368-381. 391 392 Coyne, B. E., Fingland, R. B., 1992. Hypoplasia of the trachea in dogs: 103 cases (1974-393 1990). Journal of American Veterinary Medical Association 201, 768-772. 394 395 Craven, B. A., Neuberger, T., Paterson, E. G., Webb, A. G., Josephson, E. M., Morrison, E. 396 E., Settles, G. S., 2007. Reconstruction and morphometric analysis of the nasal airway 397 of the dog (canis familiaris) and implications regarding olfactory airflow. Anatomical

Record (Hoboken N. J.) 290, 1325-1340.

398

400 Craven, B. A., Paterson, E. G., Settles, G. S., Lawson, M. J., 2009. Development and 401 verification of a high-fidelity computational fluid dynamics model of canine nasal 402 airflow. Journal of Biomechanical Engineering 131, 091002.

403

417

421

425

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432

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440

444

- Dunié-Mérigot, A., Bouvy, B., Poncet, C. M., 2010. Comparative use of CO₂ laser, diode laser and monopolar electrocautery for resection of the soft palate in dogs with brachycephalic airway obstructive syndrome. Veterinary Record 167, 700-704.
- Eiting, T. P., Smith, T. D., Perot, J. B., Dumont, E. R., 2014. The role of the olfactory recess in olfactory airflow. The Journal of Experimental Biology 217, 1799-1803.
- Evans, H.E., de Lahunta, A., 2012. The skeleton. In: Miller's anatomy of the dog, Fourth Edn. Saunders Elsevier, St. Louis, MO, USA, pp.87-88.
- Fasanella, F. J., Shivley, J. M., Wardlaw, J. L., Givaruangsawat, M. S., 2010. Brachycephalic airway obstructive syndrome in dogs: 90 cases (1991-2008). Journal of American Veterinary Medical Association 237, 1048-1051.
- Gemci, T., Ponyavin, V., Chen, Y., Chen, H., Collins, R., 2008. Computational model of airflow in upper 17 generations of human respiratory tract. Journal of Biomechanics 41, 2047-2054.
- Grand, J. G., Bureau, S., 2011. Structural characteristics of the soft palate and meatus nasopharyngeus in brachycephalic and non-brachycephalic dogs analyzed by CT. Journal of Small Animal Practice 52, 232-239.
- Hoffman, A. M., 2007. Airway physiology and clinical function testing. Veterinary Clinics of North America: Small Animal Practice 37, 829-843.
- Hostnik, E. T., Scansen, B. A., Zielinski, R., Ghadiali, S. M., 2017. Quantification of nasal airflow resistance in English bulldog using computing tomography and computational fluid dynamics. Veterinary Radiology and Ultrasound 58, 1-10.
- Koch, D., Wiestner, T., Balli, A., Montavon, P., Michel, E., Scharf, G., Arnold, S., 2012.
 Proposal for a new radiological index to determine skull conformation in the dog.
 Schweizer Archiv Für Tierheilkunde154, 217-220.
- Koch, D. A., Rosaspina, M., Wiestner, T., Wiestner, T., Mantovan, P. M., 2014. Comparative investigations on the upper respiratory tract in Norwich terriers, brachycephalic and mesaticephalic dogs. Schweizer Archiv Tierheilkunde 156, 119-124.
- Kyun Kim, S., Na, Y., Kim, J. I., Chung, S. K., 2013, Patient specific CFD models of nasal
 airflow: Overview of the methods and challenges. Journal of Biomechanics 46, 299 306.
- Lawson, M. J., Craven, B. A., Paterson, E. G., Settles, G. S., 2012. A computational study of odorant transport and deposition in the canine nasal cavity: implications for olfaction. Chemical Senses. 37, 553-566.

Lindemann, J., Brambs, H. J., Kech, T., Wiesmiller, K. M., Rettinger, G., Pless, D., 2005.
 Numerical simulation of intranasal airflow after radical sinus surgery. American
 Journal of Otolaryngology 26, 175-180.

452

Liu, N. C., Sargan, D. R., Adams, V. J., Ladlow, J. F., 2015. Characterization of brachycephalic obstructive airway syndrome in French bulldogs using whole-body barometric plethysmography. PLoS One 10, e0130741.

456

Lorenzi, D., Bertoncello, D., Drigo, M., 2009. Bronchial abnormalities found in a consecutive series of 40 brachycephalic dogs. Journal of American Veterinary Medical Association 235, 835-840.

460

Luo, H. Y., Liu, Y., 2008. Modeling the bifurcating flow in a CT-scanned human lung airways. Journal of Biomechanics 41, 2681-2688.

463

Malvè, M., Barreras, I., López-Villalobos, J. L., Ginel, A., Doblaré, M., 2012. Computational
 fluid-dynamics optimization of a human tracheal endoprosthesis. International
 Communications in Heat and Mass Transfer 39, 575-581.

467 468

469

470

Malvè, M., Chandra, S., García, A., López-Villalobos, J. L., Finol, E., Ginel, A., Doblaré, M., 2013. CFD analysis of the human airways under impedance-based boundary conditions: application to healthy, diseased and stented trachea. Computer Methods in Biomechanics and Biomedical Engineering 16, 198-216.

471 472 473

474

Oechtering, G. U., Pohl, S., Schlueter, C., Schuenemann, R., 2016. A Novel Approach To Brachycephalic Syndrome. 2. Laser-Assisted Turbinectomy (LATE). Veterinary Surgery 45, 173-181.

475 476 477

Packer, RM., Hendricks, A., Tivers, MS., Burn, CC., 2015. Impact of Facial Conformation on Canine Health: Brachycephalic Obstructive Airway Syndrome. PLoS One, 28, 1-21.

478 479 480

Pardali, D., Adamama-Moraitou, K. K., Rallis, T. S., Raptopoulos, D., Gioulekas, D., 2010. Tidal breathing flow-volume loop analysis for the diagnosis and staging of tracheal collapse in dogs. Journal of Veterinary Internal Medicine 24, 832-842.

482 483 484

481

Regodon, S., Vivo, J. M., Franco, A., Guillén, M. T., Robina, A., 1993. Craniofacial angle in dolicho-, mesocephalic-, and brachycephalic dog: Radiological determination and application. Anatomischer Anzeiger 175, 361-363.

486 487

485

488 Riecks, T. W., Birchard, S. J., Stephens, J. A., 2009. Surgical correction of brachycephalic 489 syndrome in dogs: 62 cases (1991-2004). Journal of American Veterinary Medical 490 Association 230, 134-1328.

491

Rozanski, E. A., Greenfield, C. L., Alsup, J. C., McKiernan, B. C., Hungerford, L. L., 1994.
 Measurement of upper airway resistance in awake untrained dolichocephalic and
 mesocephalic dogs. American Journal of Veterinary Research 55, 1055-1059.

495

Stadler, K., Hartman, S., Matheson, J., O'Brien, R., 2011. Computed tomographic imaging of dogs with primary laryngeal or tracheal airway obstruction. Veterinary Radiology and Ultrasound 52, 377-384.

499 500 501 502 503 504	 Yang, G. C., Scherer, P. W. and Mozell, M. M., 2007. Modeling inspiratory and expiratory steady-state velocity fields in the Sprague-Dawley rat nasal cavity. Chemical Senses 32, 215-223. Wei, W., Huang, SW., Chen, LH., Qi, Y., Qiu, YM., Li ST1., 2017. Airflow behavior
505	changes in upper airway caused by different head and neck positions: Comparison by
506	computational fluid dynamics. Journal of Biomechanics 52, 89-94
507	
508	Williams, J. M., Krebs, I. A., Riedesel, E. A., Zhao, Q., 2016. Comparison of fluoroscopy
509	and computed tomography for tracheal lumen diameter measurement and
510	determination of intraluminal stent size in healthy dogs. Veterinary Radiology and
511	Ultrasound 57, 269-275.
512	
513	Zhao, K., Dalton, P., Yang, G. C., Scherer, P. W., 2006. Numerical modeling of turbulent and
514	laminar airflow and odorant transport during sniffing in the human and rat nose.
515	Chemical Senses. 31, 107-118.

Table 1
 Skull index (skull width/skull length x 100) and new skull index (Koch et al. 2012) obtained for each dog on multiplanar reconstructed computed
 tomographic images

Breed		Weight	Skull length	Skull width	Cerebrum length	Clayll in day	Novy almil inday
		(kg)	(cm)	(cm)	(cm)	Skull index	New skull index
Dolichocephalic	Great Dane	78.6	26.1	13.2	12.6	51	2.0
	Whippet	10.3	16.3	8.9	8.4	55	1.9
	Dachshund	12.2	16.8	9.0	8.5	54	2.0
Mesocephalic	Belgian shepherd	30.0	21.6	11.0	10.7	51	2.0
	Labrador	29.4	20.8	11.4	10.6	55	2.0
	Brittany spaniel	13.0	16.7	9.9	8.8	59	1.9
Brachycephalic	French bulldog	15.1	12.6	11.8	8.1	93	1.6
	Boxer	39.0	18.2	13.0	11.1	71	1.7
	English bulldog	19.0	14.3	11.1	8.6	77	1.6

Table 2520 Flow, pressure difference (Δp) and resistance between the nose and larynx in the upper 321 airways

		Flow	Δp	Resistance
		(L/min)	(cmH_2O)	(cmH ₂ O/L/min)
Dolichocephalic	Great Dane	88.4250	0.6771	0.0077
	Whippet	11.5875	0.1843	0.0155
	Dachshund	13.7250	0.1892	0.0138
Mesocephalic	Belgian shepherd	33.7500	0.5585	0.0166
	Labrador	33.0750	0.8733	0.0264
	Brittany spaniel	14.6250	0.2240	0.0153
Brachycephalic	French bulldog	12.5571	1.5428	0.1228
	Boxer	32.4324	8.4442	0.2603
	English bulldog	15.8004	1.3012	0.0823

Table 3
 Flow, pressure difference (Δp) and resistance between the larynx and trachea in the upper
 airways.

-		Flow	Δp	Resistance
		(L/min)	(cmH_2O)	(cmH ₂ O/L/min)
Dolichocephalic	Great Dane	80.4174	0.6668	0.0083
	Whippet	22.6249	0.0676	0.0029
	Dachshund	11.1854	0.1892	0.0169
Mesocephalic	Belgian shepherd	28.1240	0.2732	0.0097
	Labrador	29.2017	0.1325	0.0045
	Brittany spaniel	10.2754	0.1071	0.0104
Brachycephalic	French bulldog	10.0294	0.1911	0.0191
	Boxer	12.1020	0.0148	0.0012
	English bulldog	16.2401	21.3551	1.3149

527 Figure legends 528 529 Fig. 1. CT-based three-dimensional model generation. One dog breed (Great Dane) is shown 530 as an example: the four green markers correspond to transverse sections on CT from the 531 rostral nasal cavity to the laryngeal entrance to the trachea, extracted from images and used 532 with the other sections (not shown) for building the entire model (represented in purple). 533 534 Fig. 2. Reconstructed CT-based geometry in the Great Dane (a), Whippet (b), Dachshund (c), 535 Labrador (d), Belgian shepherd (e) Brittany spaniel (f), Boxer (g), French bulldog (h) and 536 English bulldog (i). 537 538 Fig. 3. Boundary conditions and locations used for the computation (a): Sections 1-4 with 539 their respective computational grids along the canine upper airways and trachea were used for 540 computing flow, pressure decrease and resistance for a Labrador. The results of the mesh 541 independence study are shown in the lower panel (b). The average pressure (cmH₂O) 542 computed on the four sections is plotted as a function of the grid size. The plotted values refer 543 to the atmospheric pressure. 544 545 Fig. 4. Computed flow represented by velocity streamlines for Great Dane (a), Whippet (b), 546 Dachshund (c), Labrador (d), Belgian shepherd (e) Brittany spaniel (f), Boxer (g), French 547 bulldog (h) and English bulldog (i), respectively. Higher velocities are in red (red arrow) and 548 low velocities in blue (blue arrow). Velocity is expressed in m/s. 549 550 Fig. 5. Computed pressure represented by means of coloured surface for Great Dane (a), 551 Whippet (b), Dachshund (c), Labrador (d), Belgian shepherd (e) Brittany spaniel (f), Boxer

552 (g), French bulldog (h) and English bulldog (i). Different colours indicate different pressures 553 (cmH₂O) indicated by arrows. Higher pressures are in red and lower pressures in blue. 554 555 Fig. 6. Ventral view of the distribution of pressure (up, cmH₂O) and velocity streamlines 556 (down, m/s) in the English bulldog with the corresponding CT section, highlighting tracheal 557 stenosis (red arrow). 558 559 Fig. 7. Ventral view of the spatial distribution of pressure (up, cmH₂O) and velocity (down, 560 m/s) in the Boxer, with the corresponding CT sections highlighting the asymmetric nasal 561 cavity (red circle). Regions coloured in yellow, red, green and blue are characterized by 562 different pressure and velocity values. 563 564 Fig. 8. Computed pressure reductions (cmH₂O) between the nose and larynx (a) and between 565 larynx and trachea (b) with a close-up view on each single breed; dolichocephalic (a.1 and 566 b.1), mesocephalic (a.2 and b.2), and brachycephalic (a.3 and b.3). 567 568 Fig. 9. Computed resistance (cmH₂O/L/min) between the nose and larynx (a) and between the 569 larynx and trachea (b) with a close-up view on each dog; dolichocephalic (a.1 and b.1), 570 mesocephalic (a.2 and b.2), and brachycephalic (a.3 and b.3) skull types.