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# Cranial base and airway morphology in adult Malays with obstructive sleep apnoea

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*Background:* Obstructive sleep apnoea (OSA) has been described as a public health problem comparable to smoking in its impacts upon society.

*Objective:* To compare the differences in cranial base and airway morphology in Malay adults with and without OSA using finite element analysis (FEM).

*Method:* Lateral skull radiographs of 38 adult Malays aged 18–60 years were divided into two groups of 19 (13 male, 6 female). The first group consisted of 19 patients with OSA, defined as an apnoea-hypopnea index > 5/hr of sleep, diagnosed with overnight polysomnography. The second group consisted of 19 healthy, non-OSA control subjects. For each lateral skull radiograph 27 homologous landmarks, which encompassed the naso-oropharyngeal airway, were digitised using MorphoStudio software. The mean OSA and control 2D airway configurations were computed and subjected to *t*-tests and FEM.

*Results:* The mean 2D OSA airway was statistically different from the mean control airway ( $p < 0.01$ ). Inter-landmark analysis revealed that the cranial base saddle angle was more acute in the OSA group (153.9 degrees  $\pm$  3.4) compared to the control group (158.3 degrees  $\pm$  2.5;  $p < 0.01$ ). In addition, using pseudo-coloured FEM a relative 58 per cent decrease in nasopharyngeal airway area was found above and behind the soft palate. As well, a 32 per cent decrease in oropharyngeal airway area was located behind the base of the tongue, with a 23 per cent decrease in hypopharyngeal area near the level of the hyoid bone. In contrast, a 96 per cent increase in area associated with downward displacement of the hyoid bone was detected.

*Conclusion:* Functional airway impairments associated with OSA can be quantified and localised in Malay patients, and are predominantly associated with the morphology of the posterior regions of the cranial base.

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## Introduction

Obstructive sleep apnoea (OSA) has come to the forefront in the last 30 years, and has been described as a public health problem comparable to smoking in its effects upon society.<sup>1</sup> The Wisconsin Sleep Cohort study suggested that the prevalence of OSA among middle-aged women and men is 9 per cent and 24 per cent respectively (regardless of the presence of symptoms), while the prevalence of OSAS (OSA plus presence of excessive daytime sleepiness) is 2 per cent in women and 4 per cent in men.<sup>2</sup> It is thought that the pathophysiology of OSA involves factors that relate to the anatomical dimensions of the upper airway, upper airway resistance and upper airway muscle activity during sleep.<sup>3</sup> Therefore, upper airway

morphology is often measured in investigations of upper airway mechanics and OSA pathophysiology. The upper airway has been categorised into three anatomical regions: the nasopharynx (the area behind the nose and above the soft palate); the oropharynx (the area from soft palate to upper border of the epiglottis), which is subdivided into the retropalatal area (behind the palate) and the retroglottal area (behind the tongue); and the hypopharynx (laryngopharynx), which is the area from the upper border of epiglottis to the inferior border of the cricoid cartilage.<sup>4</sup>

Many techniques have been used to measure upper airway morphology, including nasopharyngoscopy,<sup>5</sup> acoustic reflectance,<sup>6</sup> computerised tomography<sup>7</sup> and

magnetic resonance imaging.<sup>8</sup> Although all these techniques can be used to accurately measure upper airway morphology, the invasive nature of some of them is disadvantageous. As well, while most previous studies compared OSA airway morphology using conventional techniques,<sup>9–10</sup> only a few studies have used robust geometric morphometric methods such as finite element morphometry (FEM). For example, FEM was used to model the upper airway and to create anatomically correct sagittal pharyngeal airways, as well as to assess the collapsibility of the upper airway.<sup>11</sup> Similarly, pharyngeal cross-sectional areas were assessed using FEM.<sup>5</sup> Recently, Singh et al.<sup>12</sup> used FEM to quantify changes in the upper airway in children undergoing functional orthodontic treatments.

Using FEM, change in morphology is viewed as a deformation of an initial geometric configuration, whose boundaries are formed by edges that connect anatomical landmarks into a final form.<sup>13</sup> Indeed, this technique has been employed previously in a study of craniofacial growth,<sup>14</sup> facial soft tissue changes<sup>15–17</sup> and dental arch features.<sup>18</sup> It is thought that FEM allows a better understanding and visualisation of the magnitude and direction of morphologic change.<sup>19</sup> Hence, this study was undertaken to determine whether any morphologic differences can be identified in the upper airway of adult Malays with and without OSA, using FEM. The aim of this study is to test the null hypothesis that no morphologic differences in terms of upper airway size and shape are identifiable in the two groups. Rejection of the null hypothesis might indicate how OSA might be better managed in patients of diverse ethnicity.

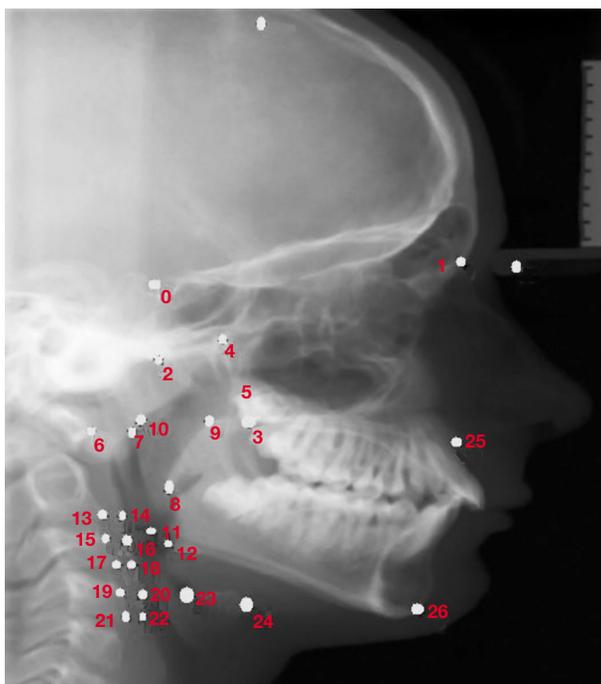
## Materials and methods

This multidisciplinary study took place in the Department of Otorhinolaryngology, Hospital Universiti Sains Malaysia (HUSM). After obtaining appropriate consent, lateral skull radiographs were taken for a total of 38 adult Malays aged 18–60 years. The first group consisted of 19 patients (13 males, 6 females) with OSA, defined as an Apnoea-Hypopnea Index (AHI) > 5/hr of sleep, diagnosed with limited overnight polysomnography (PSG). The second group consisted of 19 (13 males, 6 females) healthy, non-OSA control subjects who did not have any apnoeic symptoms as evaluated by the attending physician and limited channel PSG, but the Epworth

sleepiness scale was not used in this comparative, cross-sectional study. Exclusion criteria for sample selection were any subjects with psychiatric illness, sedative and/or alcohol intake, patient-specific disorders (such as neuromuscular disorders) and any craniofacial deformity, such as cleft lip and/or palate. An overnight hospital type III sleep study with PSG monitoring was performed on each subject between 2200 hours and 0600 hours. All variables were recorded simultaneously and continuously on a limited standard 8 channel PSG (Somnologica, Iceland) at HUSM Sleep Science Laboratory. Occurrence of OSA was scored when there was cessation of breathing for >10 seconds or associated with evidence of persistent respiratory effort. Hypopnea was scored when there was >50 per cent decrease in the airflow signal with >3 per cent decrease in arterial oxygen saturation.<sup>20</sup> Therefore, the severity of OSA was evaluated by the AHI, defined as the total number of apnoeas and hypopneas divided by the total sleep time in minutes.

On the lateral skull radiographs, 27 homologous landmarks, which encompassed the upper airway, were digitised using MorphoStudio software to obtain the x, y coordinates (Figure 1). All data were subjected to duplicate digitisation by the same investigator (SMB) on two different occasions. Next, Procrustes superimposition was implemented to obtain a generalised rotational fit, that is, all configurations were scaled to an equivalent size and registered with respect to one another. Thus, mean 2D nasopharyngeal airway morphologies were determined for both groups, and FEM was used to compare the mean OSA airway with the mean control airway. For statistical testing, the Procrustes means were subjected to Student's *t*-tests to identify elements showing significant changes. In addition, MorphoStudio software was used to perform an inter-landmark analysis to detect changes in length, and the statistical behaviour of the 2D linear distance between specific landmarks on the mandible (gonion) and the body of the hyoid bone in the Procrustes means. Finally, the cranial base 'saddle' angle (nasion-sella-basion, N-S-PPW1) was also measured and subjected to Student's *t*-tests. No other cephalometric parameters were utilised in this particular study, which was largely based on geometric morphometric techniques.

To demonstrate sources of cranial base heterogeneity, FEM was undertaken that incorporated a spline



**Figure 1.** Homologous landmarks employed for airway space evaluation.

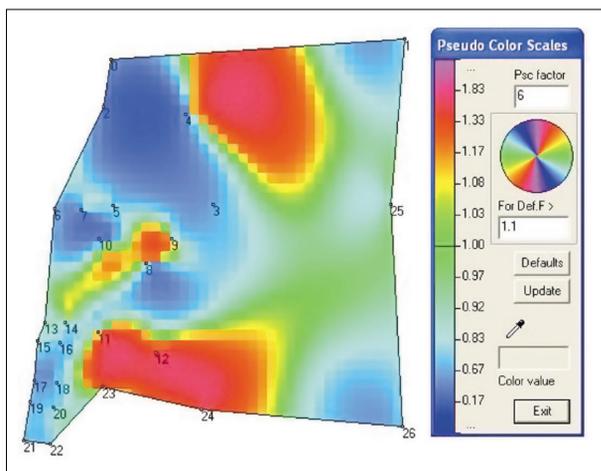
0. Sella: centre of sella turcica.
1. Nasion.
2. Posterior cranial base: point directly below sella in the vertical plane that intersects with the inferior surface of the posterior cranial base.
3. Posterior nasal spine.
4. Superior pterygomaxillare: superior point where pterygoid process of sphenoid bone and pterygoid process of the maxilla form the pterygomaxillary fissure.
5. Inferior pterygomaxillare: lowest point of the opening of the pterygomaxillary fissure as defined above.
6. Atlas: anterior-most point on anterior process of the atlas.
7. Atlas soft: anterior-most point on posterior pharyngeal wall in the horizontal plane directly opposing atlas.
8. Uvula: most inferior point on the tip of the uvula.
9. Uvula dorsum: point of maximum convexity on the dorsum of the uvula.
10. Posterior pharyngeal wall 1 (PPW1): point directly opposing PNS in the horizontal plane on the posterior pharyngeal wall.
11. Gonion: lowest and most posterior point on the angle of the mandible.
12. Base of tongue: most posterior point on the posterior surface of the dorsum of the tongue.
13. Second cervical vertebra lower: lowest point of the C2 intervertebral disc.
14. Soft second cervical vertebra: point on the surface of the posterior pharyngeal wall in the horizontal plane directly opposite point 13.
15. Third cervical vertebra: highest point of the intervertebral disc of C3.
16. Soft third cervical vertebra: point on the surface of the posterior pharyngeal wall in the horizontal plane directly opposite point 15.
17. Third cervical vertebra lower: lowest point of the C3 intervertebral disc.
18. Soft third cervical vertebra lower: point on the surface of the posterior pharyngeal wall in the horizontal plane directly opposite point 17.
19. Fourth cervical vertebra: highest point of the intervertebral disc of C4.
20. Soft fourth cervical vertebra: point on the surface of the posterior pharyngeal wall in the horizontal plane directly opposite point 19.
21. Fourth cervical vertebra lower: lowest point of the intervertebral disc of C4.
22. Soft fourth cervical vertebra lower: point on the surface of the posterior pharyngeal wall in the horizontal plane directly opposite point 21.
23. Epiglottis: superior tip of epiglottis.
24. Hyoid: anterior-most point on body of hyoid bone.
25. Anterior nasal spine.
26. Gnathion: most antero-inferior point on mandibular profile.

interpolation function on a personal computer. FEM can be used to depict transformations in terms of allometry (size-related shape change) and anisotropy (directionality of shape change).<sup>21</sup> Based on this approach, differences can be described graphically as a size-change, shape-change or both. Change in form between the reference configuration and the final configuration is viewed as a continuous deformation, which can be quantified based on major and minor strains (principal strains). If the two strains are equal, the form change is characterised by a simple increase or decrease in size, but if one of the principal strains changes in a greater proportion, transformation occurs in both size and shape. The product of the strains indicates a change in size if the result is not equal to 1. A product greater than 1 represents an increase in size equal to the remainder, for example, 1.30 indicates a 30 per cent increase. On the other hand, a result of 0.80 indicates a 20 per cent decrease in size. Changes in shape are determined by the ratio of the principal extensions, where a value not equal to 1 represents an observable change in shape. The products and ratios can be resolved for individual landmarks within the configuration, and these can be linearised using a log-linear scale and pseudo-colour coded to provide a graphic display of size- and shape-change.

## Results

The control group included subjects whose AHI ranged from 0–4.<sup>20</sup> For the OSA group, patients with mild OSA presented with an AHI of 5–15. Patients with moderate OSA demonstrated an AHI of 15–30. Patients with severe OSA had an AHI >30. In this study, 6 patients had mild OSA, 4 had moderate OSA and 9 had severe OSA. The mean AHI for the OSA group was  $37.6 \pm 24.3$  per hour while the mean AHI for the control group was  $1.6 \pm 2.1$  per hour ( $p < 0.001$ ). The mean oxygen saturation of the OSA group was  $94.2$  per cent  $\pm 3.8$  while the mean oxygen saturation for the control group was  $98$  per cent  $\pm 0.9$  per hour ( $p < 0.001$ ). The mean BMI for the control group was  $20.5 \pm 2.6$  and the BMI for the OSA group was  $33.8 \pm 7.4$  ( $p < 0.001$ ).

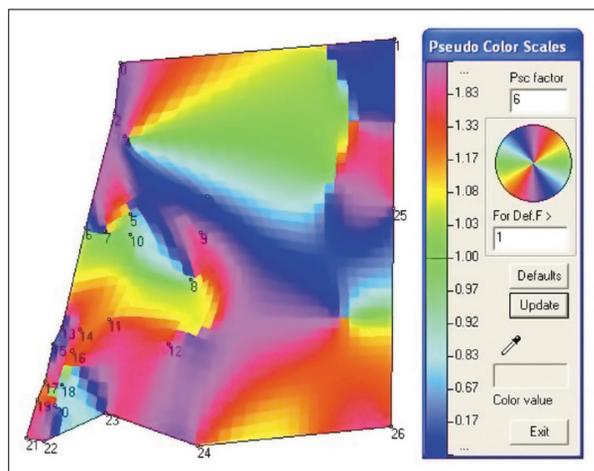
On duplicate digitisation of the landmarks, no significant differences were found ( $p > 0.05$ ) using a method equivalent to Dahlberg's formula, and therefore the study digitisation error was assumed to have no effect on the findings. The inter-landmark



**Figure 2.** Comparison of mean OSA and normal airway configurations for size change. Overall the airway space is narrower in the posterior region for the OSA group. Using the entire vertical pseudo-colour scale bar, which indicates the degree of size-change, a relative 58 per cent decrease in nasopharyngeal airway area is found above and behind the soft palate indicated by the light and dark blue pseudo-colouration.

analysis on the Procrustes means revealed that the linear distance from gonion (angle of the mandible) to the body of the hyoid bone increased in length by approximately 47 per cent ( $p < 0.01$ ) for the OSA group, and the cranial base saddle angle was more acute in the OSA group (153.9 degrees  $\pm$  3.4) compared to the control group (158.3 degrees  $\pm$  2.5;  $p < 0.01$ ). In addition, the results of the  $t$ -tests indicated that the normalised mean OSA airway was statistically different from the mean control airway ( $p < 0.01$ ).

Comparison of the nasopharyngeal region indicated that striking changes were detected using FEM, as the OSA configurations showed a relative 58–78 per cent decrease in area in the posterior cranial base and nasopharyngeal region above and behind the soft palate (Figure 2, vertical pseudo-colour scale). Specifically, the posterior pharyngeal wall (PPW1) was involved in the reduction in area. However, localised increases in area of 30–55 per cent were found further anteriorly (Figure 2). In addition, shape-changes were highly anisotropic (non-uniform). The directionality of these non-homogeneous shape changes is shown in Figure 3, which indicates a 45 degrees axis of narrowing with respect to the midsagittal plane (blue colour using the circular pseudo-colour scale). As well, antero-posterior narrowing is indicated by the green region visible in Figure 3 (using the circular colour scale).



**Figure 3.** Comparison of mean OSA and normal airway configurations for directionality of change. The circular pseudo-colour scale indicates direction. The two green areas indicate narrowing of the airway in the antero-posterior plane. The blue central zone indicates a 45 degrees axis of antero-posterior narrowing, while the purple regions indicate vertical.

Comparison of the oropharyngeal region indicated a 28–30 per cent increase in area posteriorly, allied with a 32–45 per cent decrease in oropharyngeal airway area located behind the base of the tongue (Figure 2, vertical pseudo-colour scale). In addition, shape-changes were highly anisotropic. The directionality of the shape changes identifies antero-posterior narrowing, as indicated by the green region using the circular pseudo-colour scale (Figure 3).

Comparison of hypopharyngeal region indicated a 23 per cent decrease in hypopharyngeal area near the level of the fourth cervical vertebra, C4 (blue colour, Figure 2, vertical pseudo-colour scale). Moreover, the hyoid bone moved more inferiorly with respect to the angle of the mandible (gonion), and C4 appeared to locate posteriorly. Accordingly, a 70–96 per cent increase in area was noted in the submandibular region associated with downward displacement of the hyoid bone. In addition, shape-changes were highly anisotropic. The directionality of the shape changes identifies supero-inferior elongation as indicated by the purple coloration but, antero-inferior (blue) and postero-inferior (red) deformations are also demonstrable in that region, using the circular pseudo-colour scale (Figure 3).

## Discussion

In this study, the characteristics of the cranial base and upper airway morphology in Malay patients with

obstructive sleep apnoea (OSA) were investigated using finite element analysis (FEM). While most previous studies compared OSA cranial base and airway morphology using conventional techniques,<sup>9–10</sup> only a few studies<sup>5,11–12</sup> have used FEM, a relatively new analytic tool. Although the FEM method appears to be somewhat theoretical, one advantage is that the results are presented graphically and one can view changes in size or shape. Nevertheless, the current study could not overcome some methodological limitations. For example, the radiographs employed for the study were obtained during wakefulness. However, there have been clearly documented abnormalities of upper airway anatomy and physiology in subjects with OSA during wakefulness. Therefore, we believe that careful anatomic/physiologic assessment during wakefulness may provide some valuable information even though cephalometric data cannot escape the limitations of 2D imaging.

In this study the mean cranial base configuration of the OSA group was compared to that of a non-apnoeic control group. For the groups studied, the inter-landmark analysis on the Procrustes means revealed that patients with OSA had a significantly more acute cranial base flexure angle ( $153.9$  degrees  $\pm 3.4$ ) when compared to the control group ( $158.3$  degrees  $\pm 2.5$ ). In addition, relative 58–78 per cent decreases in area of the posterior cranial base region were found using FEM (Figure 2). These findings support the view that an acute cranial base flexure angle may be responsible for a decrease in pharyngeal airway dimension in patients with OSA by reducing the distance between the anterior and the posterior pharyngeal walls, and bringing the cervical spine and posterior pharyngeal wall further forwards.<sup>22</sup> Both of these mechanisms would potentially reduce the space available for the airway.<sup>9</sup> Indeed, the presence of a narrower than normal pharyngeal diameter in OSA patients has been previously documented using conventional techniques. For example, in Japanese patients with OSA all upper airway cephalometric variables were smaller compared with a control group.<sup>23</sup> In addition, the majority of CT and MRI studies indicate that even during wakefulness the upper airway of patients with OSA is smaller than controls.<sup>24</sup>

Our results localise the anatomical regions of the upper airway affected and quantify the decrease in airway area in the OSA group compared with a

matched, non-apnoeic, control group using a FEM technique. In a previous study, the antero-posterior width of the bony nasopharynx and oropharynx were also significantly reduced in obese and non-obese patients with OSA.<sup>25</sup> The smaller width of the bony pharynx may reflect a posterior position of the maxilla secondary to cranial base morphology, and together with an enlarged soft palate may contribute to upper airway narrowing. In addition, narrowing of the oropharynx as shown in this present study may displace the tongue into the hypopharyngeal space, and that displacement may play an important role in the development of OSA (Figures 2 and 3).

Another finding of our study is that the hyoid bone was displaced more inferiorly with respect to the angle of the mandible (gonion), and the fourth cervical vertebra (C4) appeared to relocate posteriorly. Accordingly, a 70–96 per cent increase in area was noted in the submandibular region. This displacement occurred in the vertical plane predominantly (Figure 3). Many previous studies have shown that patients with OSA have inferior displacement of the hyoid bone,<sup>2,10,25–27</sup> which is found lower at the level of cervical vertebrae C4–C6 compared to controls, in whom it is typically located at the level of C3–C4. Indeed, it has been suggested that a large neck circumference is caused not only by obesity or fat deposition, but also by inferior positioning of the hyoid bone allied with posterior positioning of C4.<sup>28</sup> It has also been suggested that an inferiorly placed hyoid bone relocates the tongue base into the hypopharynx, and thus the patency of the hypopharyngeal airway is adversely affected.<sup>29</sup> These ideas might also explain the case in Malay patients with OSA. The lower position of the hyoid bone in this group of patients might be a compensatory mechanism to ease the increased airway resistance caused by reduced airway space.<sup>30</sup>

Alternatively, in Asian patients with OSA other morphological abnormalities such as a ‘large’ cranial base might be a major contributor to the pathogenesis of OSA.<sup>31</sup> Indeed, habitual snorers show a significant decrease in sagittal cranial base dimensions<sup>32</sup> and for patients with OSA, craniofacial abnormalities include a greater flexion of the cranial base.<sup>33</sup> Similarly, compared with normal subjects, Chinese patients with OSA exhibit a shortened cranial base.<sup>34</sup> In Chinese-Singaporeans, a ‘narrower skull base’ has also been reported.<sup>35</sup> In Chinese males with severe

OSA craniocervical extension was significantly increased, while differences were also found for anterior cranial base length.<sup>36</sup> In terms of effect, Wong et al.<sup>28</sup> suggest that craniocervical angulation and head posture correlate with airway resistance associated with OSA in Malaysian patients. Robertson<sup>37</sup> also reported that while nearly all linear cranial base dimensions are smaller in patients with OSA, these failed to reach statistical significance, presumably due to the lack of normalisation in that study. Ono et al.<sup>38</sup> reported that when patients with OSA changed their posture from upright to supine, significant correlations were observed between the cranial base and upper cervical column angle. Tangugsorn et al.<sup>39</sup> also reported a shorter cranial base dimension with counterclockwise rotation and depression of the clivus in patients with OSA. Therefore, on the basis of the current results, we also conclude that an acute cranial base flexure angle is one important craniofacial factor, which may be responsible for OSA in Malays. Consequently, examination and evaluation of the cranial base and upper airway anatomy must be undertaken to confirm the diagnosis of OSA and support decision-making among various treatments. As the use of mandibular advancement devices would be contraindicated in patients presenting with Class III malocclusions secondary to cranial base morphology,<sup>40–41</sup> we suggest that changing the size of the apnoeic airway could be achieved by non-surgical alterations of structures that surround the upper airway. This notion is currently under investigation and remains as the premise for future studies.

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