

Original article

Dentoskeletal effects of oral appliance wear in obstructive sleep apnoea and snoring patients

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Summary

Objectives: To evaluate the dentoskeletal changes associated with long-term and continuous mandibular advancement device (MAD) use in sleep-related breathing disorder patients.

Methods: Cephalometric measurements and three-dimensional model analysis were performed at baseline and after 3.5 ± 1.1 years in 20 snoring and obstructive sleep apnoea patients treated with the Silensor® appliance. Intra-group differences were compared using paired *t*-test or Wilcoxon signed-rank test. A regression analysis was performed for variables that showed a statistically significant difference between time points to evaluate the influence of treatment time and patient's initial characteristics on their variations. The statistical significance was set at P < 0.05.

Results: At cephalometric assessment, the maxilla revealed a significant decrease in horizontal position (SNA: -0.4 ± 0.72 degree, P = 0.021) and a significant retroclination of the upper incisor (-1.59 ± 1.07 degree, P < 0.001), while the mandible displayed a significant downward rotation (0.88 ± 1.28 degree, P = 0.006) and a proclination of the lower incisor (2.27 ± 1.38 degree, P < 0.001). Model analysis showed a decrease in upper total space discrepancy (-0.66 ± 0.72 mm, P < 0.002), overjet (OJ; -0.34 ± 0.47 mm, P < 0.011), and overbite (-0.4 ± 0.52 mm, P < 0.004). In the regression analysis, treatment time influenced the lower incisor inclination (Beta = -0.713, P = 0.018) and OJ (Beta = -0.218, P = 0.018); patients' initial characteristics had an effect on OJ (Beta = -0.195, P = 0.011).

Limitations: A larger sample size could increase the generalizability of the findings.

Conclusion: MAD wear after a mean of 3.5 years determines statistically significant but clinically irrelevant dentoskeletal changes. Their potential occurrence should be thoroughly discussed with patients; regular follow-up visits by a specialist experienced in dental sleep medicine are also mandatory during treatment in addition to polysomnographic examinations.

Introduction

Obstructive sleep apnoea syndrome (OSAS) is a common sleep disorder characterized by repetitive episodes of complete or partial collapse of the upper airway during sleep, causing a cessation (obstructive apnoea) or a significant reduction (obstructive hypopnea) of airflow (1). Mandibular advancement devices (MADs) are widely used for treatment for mild-to-moderate OSAS patients [$5 < apnoea-hypopnea index (AHI) \le 30$] and for those patients with severe OSAS (AHI > 30) who are neither able nor willing to tolerate the standard continuous positive airway pressure therapy and/ or refuse or are not good candidates for surgery (2–5). MADs are removable orthodontic devices that move the mandible forward and

therefore increase the upper airway patency during sleep by diminishing the upper airway collapsibility and elevating upper airway muscle tone (6). A certain degree of variability exists with respect to the amount of protrusion, but the success of therapy (i.e. AHI improvement) seems to be not proportional to the mandibular advancement increase (7). There is also a high inter-individual variability in response to the therapy with MAD, and current research is focusing on the identification of parameters capable of reliably discriminating between poor and good responders (8).

Patients often experience minor side-effects during the first months of MAD wear, including excessive salivation or dry mouth, myofascial stiffness, temporomandibular joint discomfort, tooth pain, and gum irritation (4). In the longer term, most of these side-effects disappear, but dentoskeletal changes can occur because the protrusion of the mandible with MADs generates reciprocal forces on the soft tissues and the muscles that attempt to move the mandible backward to its normal position (9–12). The appliance transmits these forces both to the teeth to which it is anchored and to the maxilla and the mandible (13).

Cephalometric analysis on lateral head radiographs is a widely available way to assess dentoskeletal side-effects, but it provides only a two-dimensional (2D) representation of a three-dimensional (3D) object. Dental cast analysis is complementary to cephalometry, because it allows an evaluation of the entire intra-arch and inter-arch changes. Moreover, 3D dental cast analysis enhances the ability to measure the individual tooth position in more detail compared with traditional 2D manual measurements and allows the execution of 3D measurements (e.g. Curve of Spee and precise tooth inclination) (14). The dentoskeletal side-effects of long-term MAD wear have already been described (13, 15-28), but only five authors used both cephalometric and dental cast analysis (13, 18, 21-23, 25, 26). So far, only one study has analysed in detail the dental side-effects with a 3D measurement tool in order to help clinicians to better understand the changes induced by the therapy (24). Since dentoskeletal changes may represent a potential reason for discontinuing the therapy (4), it is important to get more insight into these side-effects, especially due to the growing use of MADs in the treatment of OSAS. Therefore, the purpose of this retrospective study was to evaluate the dentoskeletal changes in sleep-related breathing disorder patients after longterm and continuous MAD wear using cephalometry and 3D dental cast analysis.

Subjects and methods

All procedures performed in this study, involving human participants, were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This study was approved by the Institutional Review Board (N. 268/15).

Subjects and eligibility criteria

A total of 35 OSAS patients (pts) who had been consecutively treated with MAD were recruited in the study.

Inclusion criteria were:

- MAD therapy for more than 2 years without treatment discontinuation during the whole study period;
- MAD use for a minimum of 5 nights per week and usually for the entire night (assessed through a questionnaire administered at the long-term follow-up day); and

Availability of good quality study models and lateral cephalograms at the baseline and follow-up visits.

From the original sample 15 pts were excluded:

- 8 pts used their devices for less than 5 nights per week;
- 4 pts had initial study models of poor quality; and
- 3 pts had initial lateral cephalograms of poor quality.

The study sample included 20 subjects (15 men, 5 women, mean age \pm SD = 57 \pm 11.4 years) referred for MAD therapy with a pretreatment AHI of 19.1 \pm 14.5 events/hour (ev/h) and a body mass index of 26.5 \pm 3.6 kg/m², who had a mean treatment duration of 3.5 \pm 1.1 years. Four pts (20 per cent) were primary snorers (AHI < 5 ev/h), 5 pts (25 per cent) had mild OSAS (5 \leq AHI < 15 ev/h), 5 pts (25 per cent) had moderate OSAS (15 \leq AHI < 30 ev/h), and 6 pts (30 per cent) had severe OSAS (AHI \geq 30 ev/h).

Dental casts and lateral cephalograms were taken at the day of first appliance placement as baseline (T0) and at the long-term follow-up day (T1). The period of MAD use was calculated as the interval between T0 and T1. The mean number of missing teeth at To was 1.8 ± 2.0 (excluding third molars); no teeth were lost at T1. Based on the ANB angle, the skeletal sagittal relationship at T0 was: Class I (ANB angle = 2 ± 2 degree, n = 7 pts), Class II (ANB angle > 4 degree, n = 13 pts), and Class III (ANB angle < 0 degree, n = 0 pts). All subjects used the same appliance (Silensor®, Erkodent Gmbh, Tuttlingen, Germany), an individually designed, titratable, and removable dental device that provides full coverage of the upper and lower dental arches. Two plastic connectors running from the upper canine to the lower molar regions maintain the mandible in protruded position, allowing forward movement of the mandible during opening, thus preventing or minimizing upper airway collapse during sleep. The MAD was gradually advanced until patients and their bedfellows reported that snoring ceased and daytime sleepiness symptoms improved. The final advancement was set on average at 60 per cent of each patient's maximum protrusion capacity $(6.7 \pm 1.6 \text{ mm})$ and the vertical height was fixed at 5 mm of the interincisal opening.

Cephalometric analysis

The lateral head radiographs were taken by means of a cephalostat (Scanning Planmeca 2002–10 Promax® 3D Classic Cephalostat, Helsinki, Finland) with the patient in an upright position, with natural head posture and centric occlusion. Tracings were constructed for each lateral head film; landmarks, and traditional contours of the anatomical structures were digitized (Delta-Dent, Outside Format, Paullo, Milan, Italy). The calibration of distances was performed by storing a millimeter scale with the images. The cephalometric measurements are shown in Supplementary Table 1 and Figure 1.

The examiner (CS), who had been extensively trained in digital cephalometric analysis, was blinded to patient names and radiograph dates. Each radiograph's order of submission (T0 and T1) was randomly assessed.

Dental casts analysis

The upper and lower dental casts were scanned by a 3D scanner (D800; 3Shape A/S, Copenhagen K, Denmark). Each cast was scanned from 10 or more views that were then combined and rendered into 3 dimensions using a specific software (3shape-ScanltOrthodontics™ 2010-2p3, 3Shape A/S, Copenhagen K, Denmark). During the scanning process of each dental cast, the scanner forms

G. Alessandri-Bonetti et al.

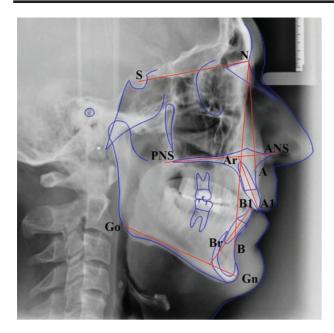


Figure 1. The baseline and the follow-up lateral cephalometric radiographs were measured and compared to evaluate the dentoskeletal changes after treatment with the Silensor® appliance. The following cephalometric analysis was used: Cephalometric landmarks. A point: deepest point on the contour of the premaxilla; anterior nasal spine (ANS): the most anterior point of the anterior nasal spine; B point: the deepest point on the contour of the mandibular symphysis; gonion (Go): midpoint of the curvature at the angle of the mandible; gnation (Gn): the most outward and everted point on the profile curvature of the chin; lower incisor (B1): incisal edge of the most prominent mandibular central incisor; lower incisor root apex (Br): root apex of the most prominent mandibular central incisor; nasion (N); most anterior point of the junction of the nasal and frontal bone (frontonasal suture); posterior nasal spine (PNS): the tip of the posterior nasal spine of the palatine bone; sella (S): centre of the hypophyseal fossa; upper incisor (A1): incisal edge of the most prominent maxillary central incisor; upper incisor root apex (Ar): root apex of the most prominent maxillary central incisor. Cephalometric reference lines. mandibular plane (MP): line joining the Go point and the Gn point; sella nasion line (SN); line through S and N; long axis of lower incisor (L1): line connecting the B1 point and the Br point; long axis of upper incisor (U1): line connecting the A1 point and the Ar point; maxillary plane (PNS-ANS): line joining the PNS point and the ANS point.

a point cloud and in a subsequent step converts it into a geometrical mesh of triangles. The output at the end of the scan process is a.STL file (stereolitography). The virtual 3D models were measured and analysed by a specific software (3shape-OrthoAnalyzer™ 2010, 3Shape A/S, Copenhagen K, Denmark). The models were digitized following this sequence: mandibular baseline model, maxillary baseline model, occlusion baseline models, maxillary follow-up model, mandibular follow-up model, and occlusion follow-up models. The dental casts measurements are shown in Supplementary Table 2 and Figure 2.

The examiner (CS), who had been extensively trained in the 3D model measurement process, was blinded to patient names and dental cast dates. The order of model analyses between T0 and T1 was randomly assessed.

Statistical analysis

Sample size

From the clinical point of view, a variation of 1.3 mm of the overjet (OJ) was found clinically relevant (22). The following assumptions

were used to calculate the required sample size: 1. the significance level of two-sided tests was set at 0.05; 2. the statistical power was set at 80 per cent; 3. the SD of OJ in a previous publication was found to be 1.57 mm (22), and 4. the intended inferential statistics approach was two-dependent sample (matched pairs) *t*-tests (if the assumptions of parametric tests were met, for example, normality). The calculation revealed that a sample size of 14 patients was required.

Method error

The technical errors of measurement were calculated from six randomly selected cephalograms and six randomly selected study models. A set of measurements was reassessed by the same examiner (CS) after a memory washout period of at least 8 weeks. The method error for all measurements was calculated using Dahlberg's formula (29).

Systematic differences between duplicated measurements were tested using a paired Student's t-test with the type I error set at P < 0.01.

The method error ranged between 0.14 and 0.28 degree for cephalometric angular measurements and between 0.09 and 0.24 mm for dental cast linear measurements.

There was no systematic error for any measurements (Student's t-test: P > .01).

Data analysis

Data were analysed by conventional descriptive statistics. A Shapiro—Wilk test to evaluate whether the samples are normally distributed was performed. Intra-group differences were compared by means of a parametric paired *t*-test or a non-parametric statistic Wilcoxon signed-rank test according to the data distribution.

Regression analysis was performed only for variables that showed a statistically significant difference between the two time points to evaluate the influence on the variations of the assessed variables of treatment time and patient's initial characteristics (values at T0).

Statistical significance was set at P < 0.05. All statistical analyses were conducted using the Statistical Package for Social Sciences Software (SPSS version 20.0, SPSS IBM, New York, NY).

Results

Skeletal and dental measurements at T0 and T1 and their relative changes over time are reported in Table 1 and Supplementary Table 3.

Cephalometric analysis

In regard to the cephalometric comparison, the maxilla revealed a significant decrease in its antero-posterior position (SNA: -0.4 ± 0.72 degree, P = 0.021) and a significant retroclination of the upper incisor (U1–PP: -1.59 ± 1.07 degree, P < 0.001). The mandible showed a significant downward rotation (SN/GoGn: 0.88 ± 1.28 degree, P = 0.006) and lower incisors proclination (L1–MP: 2.27 ± 1.38 degree, P < 0.001).

There was no statistically significant difference in basal bone relation (ANB) and in the horizontal position of the mandible (SNB).

Dental casts analysis

Regarding the comparison of the dental casts between baseline and follow-up visits, the upper total space discrepancy decreased significantly (-0.66 ± 0.72 mm, P < 0.002).

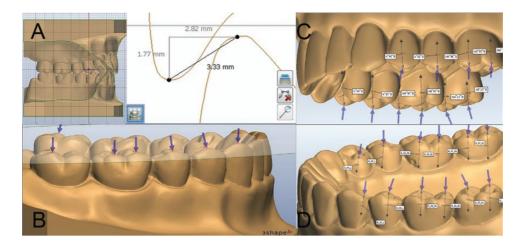


Figure 2. The baseline and the follow-up dental casts were measured using a 3D digital analysis and compared to evaluate the dental changes after treatment with the Silensor® appliance. Dental cast analysis showing (A) overjet (OJ, measured parallel to the occlusal plane at the level of the edge of the maxillary incisor) and overbite (OB, measured perpendicular to the occlusal plane); (B) right mandibular Curve of Spee (CS, measured as a perpendicular distance from the buccal cusp of each mandibular premolar and molar to a plane passing for the tip of the homolateral canine, the distobuccal cusp of the homolateral second molar and the distobuccal cusp of the contralateral second molar); (C) Maxillary teeth inclination (perpendicular distance from each buccal cusps of each maxillary molar, premolar and canine to a reference plane formed by three points); and (D) mandibular teeth inclination (perpendicular distance from each buccal cusps of each mandibular molar, premolar, and canine to a reference plane formed by three points).

Table 1. Cephalometric and dental cast measurements at baseline (T0) and at long-term follow-up (T1).

Measurement	T0 (mean \pm SD)	T1 (mean \pm SD)	T1-T0 (mean ± SD)	P
SNA (°)	81.36 ± 3.21	80.95 ± 3.50	-0.4 ± 0.72	0.021
SN/GoGn (°)	33.63 ± 6.07	34.51 ± 6.11	0.88 ± 1.28	0.006
U1-PP (°)	102.53 ± 7.30	100.94 ± 7.00	-1.59 ± 1.07	< 0.001
L1-MP (°)	91.25 ± 6.13	93.52 ± 6.33	2.27 ± 1.38	< 0.001
TOTAL UPPER DISCREPANCY (mm)	5.42 ± 6.46	4.76 ± 6.55	-0.66 ± 0.72	0.002
OVERJET_11 (mm)	3.79 ± 1.34	3.45 ± 1.22	-0.34 ± 0.47	0.011
OVERBITE_11 (mm)	3.03 ± 1.27	2.63 ± 1.32	-0.4 ± 0.52	0.004
INCLINATION_15 (mm)	4.46 ± 2.60	4.61 ± 2.69	0.15 ± 0.26	0.021
INCLINATION_14 (mm)	5.23 ± 2.50	5.51 ± 2.57	0.28 ± 0.52	0.025
INCLINATION_47DL (mm)	4.55 ± 1.93	5.08 ± 2.08	0.53 ± 0.92	0.014

Bold text indicates significant values.

Differences in OJ were found for the right central incisor (-0.34 ± 0.47 mm, P < 0.011). Likewise, the overbite (OB) showed a significant decrease (-0.4 ± 0.52 mm, P < 0.004).

The Curve of Spee in the bilateral premolar and molar area and the arch widths (AW) between molars and canines of the upper and lower arches did not show any significant difference.

Maxillary teeth inclination measurements in general increased, reflecting a tendency of the upper teeth towards palatal inclination; otherwise, mandibular teeth inclination measurements decreased, showing a tendency towards buccal inclination.

Teeth inclination variables had no significant differences except for the maxillary right first (INCLINATION_14 0.28 \pm 0.52, P < 0.025) and second premolars (INCLINATION_15 0.15 \pm 0.26, P < 0.021) and for the mandibular right second molar (INCLINATION_47 DL 0.53 \pm 0.92, P < 0.014).

Regression analysis was performed for the statistically significant variables (Table 2).

Treatment time influenced only two variables: OJ for the right central incisor (Beta = -0.218, P = 0.018) and lower incisor inclination (Beta = -0.713, P = 0.018).

Moreover, the patients' initial characteristics had an effect on only one variable: OJ for the right central incisor (Beta = -0.195, P = 0.011).

Discussion

This study characterized the dentoskeletal changes in snoring and OSAS patients after a mean period of 3.5 years of treatment with the Silensor® appliance. The use of a 3D dental cast analysis attempted to improve the understanding of the dental changes induced by the therapy with MAD and allowed to evaluate for the first time the individual tooth inclination and the Curve of Spee, the latter without using the lower incisor as a landmark because the antero-posterior inclination of this tooth changes during treatment (13, 19–21, 23, 25, 28). These data may help clinicians in optimizing treatment protocols and intraoral device design, thus allowing maximum adherence to therapy and adequate information to the patients.

Cephalometric analysis showed a retroclination of the maxillary incisors and a proclination of the mandibular incisors. These results agree with those obtained in previous studies (13, 20, 21, 25, 28) and can be explained by the force required to maintain the mandible in forward position (30). During treatment with MADs, the muscles and the other soft tissues are stretched and try to pull the mandible back, thus transmitting a lingually directed force to the upper incisors and increasing their palatal inclination. Moreover, the mandible attempts to return to its baseline position, thus transmitting a labially directed force against the mandibular incisors and

G. Alessandri-Bonetti et al.

Table 2. Regression analysis assessing the influence of treatment time and patients starting forms (values at T0) on skeletal and dental changes.

	Treatment time		Patients starting forms	
	Beta	P	Beta	P
SNA (°)	0.115	0.453	0.071	0.182
SN/GoGn (°)	-0.091	0.809	-0.034	0.612
U1-PP (°)	0.113	0.62	-0.054	0.124
L1-PP (°)	-0.713	0.018	0.047	0.346
TOTAL UPPER DISCREPANCY (mm)	0.061	0.713	0.005	0.854
OVERJET_11 (mm)	-0.218	0.018	-0.195	0.011
OVERBITE_11 (mm)	-0.203	0.084	-0.105	0.289
INCLINATION_15 (mm)	-0.119	0.083	0.007	0.897
INCLINATION_14 (mm)	-0.155	0.2	-0.189	0.092
INCLINATION_47DL (mm)	-0.289	0.15	-0.346	0.072

Only variables that showed a statistically significant difference between the two time points were assessed in this analysis. Bold text indicates significant values.

increasing their vestibular inclination. A small but statistically significant decrease in SNA angle was also found, indicating a decrease in the antero-posterior position of the maxilla; it was accompanied by a non-significant decrease in SNB and ANB angles and a significant increase in SN/GoGn angle. These findings indicate a downward rotation of the mandible without antero-posterior repositioning. Previous studies did not find statistically significant changes in SNA angle (13, 16, 18, 19, 21, 23, 25, 28), with the exception of the work by Robertson et al. (20) who observed an increase in the anteroposterior position of the maxilla. These conflicting results can be attributed to the differences in study and appliance design (5 groups of 20 subjects each were reviewed either 6, 12, 18, 24, or 30 months after treatment beginning, but all the 100 subjects were combined into a single group to determine the extent of the dental and occlusal changes; a non-adjustable rigid splint was used and constructed to advance at 75 per cent of each patient's maximum protrusion). On the other hand, many studies have reported a downward rotation of the mandible (19, 21, 25, 28). In particular, a statistically significant increase in mandibular plane angle was found by Wang et al. (28) after 4 years on average of treatment with the Silensor® appliance; this skeletal change had been ascribed to the retroclination of the upper incisors and the proclination of the lower incisors (25, 28).

Dental cast analysis showed that the space discrepancy changes were within a small range. There was a slight but statistically significant decrease in total maxillary space discrepancy, reflecting a decrease in maxillary arch length, which can be a consequence of the retroclination of the upper incisors. Previous studies did not find statistically significant changes for this variable after an average of 29.6 months (13), 7.4 years (22), and 25.1 months (23) of treatment with MADs, while Chen et al. (24) observed an increased maxillary arch length after a mean treatment duration of 7 years and 4 months. The mandibular space discrepancy increased in our study, but none of the changes were statistically significant. An increased mandibular arch length has been previously reported (13, 22, 24), with the exception of the work by Hammond et al. (23) who found no statistically significant differences. These conflicting results can be ascribed to differences in study design (e.g. sample size and treatment duration).

A statistically significant decrease in OB and overjet was also observed at dental cast analysis, probably as a consequence of the retroclination of the maxillary incisors and the proclination of the mandibular incisors. The downward rotation of the mandible could have also contributed to OB reduction. Several previous studies

showed decreased OB and overjet after treatment with MADs using cephalometric and/or dental cast analysis (13, 16–18, 20–28). Only 1 study did not detect a statistically significant change in OB and OJ as well as in the inclination of the incisors after 4 years of continuous therapy with MADs (31). These differences may be attributed to the absence of incisal coverage in the MAD that, probably, did not impress a direct force on the maxillary and mandibular incisors. Furthermore, the study group included only patients with mild-to-moderate OSAS and the advancement was set at 50 per cent of each patient's maximum protrusion capacity. Since an association between the extent of side-effects and the mean mandibular protrusion has been postulated (25), these differences can probably explain the conflicting results.

Both maxillary and mandibular intermolar and intercanine AW tended to remain stable. These results are quite consistent with a decrease of 0.2 mm in maxillary intercanine width and an increase of 0.2 mm in mandibular intermolar width found after an average of 2.5 years of treatment (17), while more recent studies have reported an increased mandibular intermolar (0.57 mm and 1.1 mm, respectively) and intercanine width (0.40 mm and 0.7 mm, respectively) after a mean treatment duration of 7.4 and 11.1 years (22, 27).

The Curve of Spee, i.e. the anatomic curve established by the occlusal alignment of the teeth beginning with the cusp tip of the mandibular canine and following the buccal cusp tips of the premolar and molar teeth (32), was measured using a plane formed from the distal cups of the second molar, the cusp of the canine and the contralateral second molar distal cusp as a reference. No variations were found on both left and right sides. These results contradicted the findings by Chen et al. (24), that showed a significant decrease in the Curve of Spee in the bilateral premolar area. This discrepancy may be attributed to a difference in the reference plane; Chen et al. (24) calculated the distance from any cusp to the occlusal plane that is defined by the midpoint between the two central incisors and the distobuccal cusp tip of the most posterior molar on each side. On the contrary, we did not use the lower incisor as a landmark because the antero-posterior inclination of this tooth changes during treatment (13, 19–21, 23, 25, 28).

This is the first study that investigated teeth inclination from second molar to first premolar using a 3D measurement tool on digitized dental casts; this parameter can improve the understanding of the dental changes induced by the therapy with MAD, especially for the arch transverse changes. Three gingival points were used to define a reference plane in order to measure tooth inclination because they were

considered less affected by variations than dental points. As a general tendency, maxillary posterior teeth inclination increased (i.e. tendency towards palatal inclination) and mandibular teeth inclination increased (i.e. tendency towards buccal inclination). However, statistically significant differences were found only for the right maxillary first and second premolars and the right mandibular second molar.

Regression analysis revealed an effect of treatment time on overjet as well as on lower incisor inclination. The OJ decreased as long as treatment time increased; lower incisor inclination increased less during longer treatment period. This phenomenon could be explained by the long-term 'pushing' effect of the appliance on the lower incisors that could evoke a control pressure by the lower lip that stabilizes in part the lower incisors proclination (33). Nevertheless, an increased OJ at the beginning of the treatment provoked a greater reduction of the OI.

Since patient compliance is of critical importance for successful treatment outcomes when removable appliances are used, a limitation of our study is the impossibility to objectively assess the exact amount of time of MAD wear. In fact, compliance was evaluated based on patient self-reporting, and there was no available compliance monitor. Future studies incorporating newly developed compliance monitors embedded within the MAD should help to objectively evaluate wear times. Another shortcoming is the small sample size; probably a larger sample size could increase the generalizability of the findings. Future studies should consider to divide subjects into several groups according to malocclusion subtypes and to evaluate the side-effects separately.

Conclusions

A mean period of 3.5 years of MAD wear retroclined the upper incisors; proclined the lower incisors; increased the downward rotation of the mandible; and decreased upper space discrepancy, OJ, and OB. The observed mean changes were statistically significant but clinically irrelevant. However, since it cannot be excluded that even small changes can have an impact on individual's self-perception of dental occlusion, our findings reinforce the need for OSAS patients to receive a proper information about the potential occurence of these dentoskeletal changes; regular follow-up visits with a dentist specialized in dental sleep medicine should also be recommended in addition to follow-up polysomnographic examinations during treatment.

Supplementary material

Supplementary material is available at European Journal of Orthodontics online.

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Conflict of interest

None to declare.

References

- American Academy of Sleep Medicine. (2005) International Classification of Sleep Disorders: Diagnostic and Coding Manual. American Academy of Sleep Medicine, Chicago, Illinois, pp. 52–58.
- Hoffstein, V. (2007) Review of oral appliances for treatment for sleepdisordered breathing. Sleep Breath, 11, 1–22.
- Schmidt-Nowara W., Lowe A., Wiegand L., Cartwright R., Perez-Guerra F. and Menn S. (1995) Oral appliances for the treatment of snoring and obstructive sleep apnea: a review. Sleep, 18, 501–510.
- Ferguson K.A., Cartwright R., Rogers R. and Schmidt-Nowara W. (2006)
 Oral appliances for snoring and obstructive sleep apnea: a review. Sleep, 29, 244–262.
- Bonetti, G.A., Piccin, O., Lancellotti, L., Bianchi, A. and Marchetti, C. (2009) A case report on the efficacy of transverse expansion in severe obstructive sleep apnea syndrome. Sleep Breath, 13, 93–96.
- Ferguson, K.A. (2003) The role of oral appliance therapy in the treatment of obstructive sleep apnea. Clinics in Chest Medicine, 24, 355–364.
- Bartolucci, M.L., Bortolotti, F., Raffaelli, E., D'Antò, V., Michelotti, A. and Alessandri Bonetti, G. (2016) The effectiveness of different mandibular advancement amounts in OSA patients: a systematic review and metaregression analysis. Sleep Breath, 20, 911–919.
- Alessandri-Bonetti, G., Ippolito, D.R., Bartolucci, M.L., D'Antò, V. and Incerti-Parenti, S. (2015) Cephalometric predictors of treatment outcome with mandibular advancement devices in adult patients with obstructive sleep apnea: a systematic review. Korean Journal of Orthodontics, 45, 308–321.
- Clark, G.T., Sohn, J.W. and Hong, C.N. (2000) Treating obstructive sleep apnea and snoring: assessment of an anterior mandibular positioning device. *Journal of American Dental Association*, 131, 765–771.
- 10. Eckhart, J.E. (1998) Comparisons of oral devices for snoring. *Journal of the California Dental Association*, 26, 611–623.
- Lowe, A. (2000) Oral appliance for sleep breathong disorders. In Kryger, M., Roth, T. and Dement, W. (eds), *Principles and Practice of Sleep Medicine*. WB Saunders, Philadelphia, PA, 3rd edn, pp. 929–939.
- Marklund, M. (2006) Predictors of long-term orthodontic side effects from mandibular advancement devices in patients with snoring and obstructive sleep apnea. American Journal of Orthodontics and Dentofacial Orthopedics, 129, 214–221.
- Rose, E.C., Staats, R., Virchow, C., Jr and Jonas, I.E. 2002 Occlusal and skeletal effects of an oral appliance in the treatment of obstructive sleep apnea. *Chest*, 122, 871–877.
- 14. Chen, H., Lowe, A.A., de Almeida, F.R., Wong, M., Fleetham, J.A. and Wang, B. (2008) Three-dimensional computer-assisted study model analysis of long-term oral-appliance wear. Part 1: methodology. *American Journal of Orthodontics and Dentofacial Orthopedics*, 134, 393–407.
- Pantin, C.C., Hillman, D.R. and Tennant, M. (1999) Dental side effects of an oral device to treat snoring and obstructive sleep apnea. Sleep, 22, 237–240.
- 16. Bondemark, L. (1999) Does 2 years' nocturnal treatment with a mandibular advancement splint in adult patients with snoring and OSAS cause a change in the posture of the mandible? *American Journal of Orthodontics and Dentofacial Orthopedics*, 116, 621–628.
- Marklund, M., Franklin, K.A. and Persson, M. (2001) Orthodontic sideeffects of mandibular advancement devices during treatment of snoring and sleep apnoea. *European Journal of Orthodontics*, 23, 135–144.
- Fritsch, K.M., Iseli, A., Russi, E.W. and Bloch, K.E. (2001) Side effects of mandibular advancement devices for sleep apnea treatment. *American Journal of Respiratory and Critical Care Medicine*, 164, 813–818.
- Fransson, A.M., Tegelberg, A., Svenson, B.A., Lennartsson, B. and Isacsson, G. (2002) Influence of mandibular protruding device on airway passages and dentofacial characteristics in obstructive sleep apnea and snoring. American Journal of Orthodontics and Dentofacial Orthopedics, 122, 371–379.
- Robertson, C., Herbison, P. and Harkness, M. (2003) Dental and occlusal changes during mandibular advancement splint therapy in sleep disordered patients. *European Journal of Orthodontics*, 25, 371–376.

- Almeida, F.R., Lowe, A.A., Sung, J.O., Tsuiki, S. and Otsuka, R. (2006) Long-term sequellae of oral appliance therapy in obstructive sleep apnea patients: part 1. Cephalometric analysis. *American Journal of Orthodon*tics and Dentofacial Orthopedics, 129, 195–204.
- Almeida, F.R., Lowe, A.A., Otsuka, R., Fastlicht, S., Farbood, M. and Tsuiki, S. (2006) Long-term sequelae of oral appliance therapy in obstructive sleep apnea patients: part 2. Study-model analysis.
 American Journal of Orthodontics and Dentofacial Orthopedics, 129, 205–213.
- Hammond, R.J., Gotsopoulos, H., Shen, G., Petocz, P., Cistulli, P.A. and Darendeliler, M.A. (2007) A follow-up study of dental and skeletal changes associated with mandibular advancement splint use in obstructive sleep apnea. *American Journal of Orthodontics and Dentofacial Orthope*dics, 132, 806–814.
- 24. Chen, H., Lowe, A.A., de Almeida, F.R., Fleetham, J.A. and Wang, B. (2008) Three-dimensional computer-assisted study model analysis of long-term oral-appliance wear. Part 2. Side effects of oral appliances in obstructive sleep apnea patients. American Journal of Orthodontics and Dentofacial Orthopedics, 134, 408–417.
- Doff, M.H.J., Hoekema, A., Pruim, G.J., Huddleston Slater, J.J.R. and Stegenga, B. (2010) Long-term oral-appliance therapy in obstructive sleep apnea: A cephalometric study of craniofacial changes. *Journal of Dentistry*, 38, 1010–1018.
- Doff M.H., Finnema K.J., Hoekema A., Wijkstra P.J., de Bont L. G. and Stegenga B. (2013) Long-term oral appliance therapy in obstructive sleep

- apnea syndrome: a controlled study on dental side effects. *Clinical Oral Investigations*, 17, 475–482.
- 27. Pliska, B.T., Nam, H., Chen, H., Lowe, A.A. and Almeida, F.R. (2014) Obstructive sleep apnea and mandibular advancement splints: occlusal effects and progression of changes associated with a decade of treatment. *Journal of Clinical Sleep Medicine*, 10, 1285–1291.
- 28. Wang, X., Gong, X., Yu, Z., Gao, X. and Zhao, Y. (2015) Follow-up study of dental and skeletal changes in patients with obstructive sleep apnea and hypopnea syndrome with long-term treatment with Silensor appliance. *American Journal of Orthodontics and Dentofacial Orthopedics*, 147, 559–565.
- Dahlberg, G. (1940) Statistical Methods for Medical and Biological Students. Interscience Publications, New York, NY.
- Cohen-Levy, J., Pételle, B., Pinguet, J., Limerat, E. and Fleury, B. (2013)
 Forces created by mandibular advancement devices in OSAS patients: a pilot study during sleep. Sleep Breath, 17, 781–789.
- Ringqvist, M., Walker-Engstrom, M.L., Tegerlberg, A. and Ringqvist, I. (2003) Dental and skeletal changes after 4 years of obstructive sleep apnea treatment with a mandibular advancement device: A prospective, randomized study. American Journal of Orthodontics and Dentofacial Orthopedics, 124, 53–60.
- 32. The Academy of Prosthodontics. (1994) The glossary of prosthodontic terms. *Journal of Prosthetic Dentistry*, 71, 50–112.
- Jack, H.C., Kieser, J., Antoun, J.S. and Farella, M. (2014) The effect of incremental lower lip advancement on oral pressure and EMG activity of the lower lip. *European Journal of Orthodontics*, 36, 672–677.