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Original Article

Long-term side effects of sleep apnea treatment with oral appliances: nature, magnitude and predictors of long-term changes

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ABSTRACT

Objectives: Oral appliances for the treatment of obstructive sleep apnea (OSA) reduce upper airway collapse by advancing the mandible (OAm) and associated soft tissues. OAm are well tolerated but have side effects, mainly dental movement. It is not yet clear whether there are irreversible skeletal changes associated with treatment. As oral appliance treatment for OSA is a life-long therapy, careful and extended follow-up of patients is required. The objectives of this study were to evaluate the magnitude and progression of the dental and skeletal changes associated with long-term treatment, in addition to determining the predictors of the changes.

Methods: Lateral cephalograms of adults treated for primary snoring or mild to severe OSA with a custom-made titratable OAm for a minimum of eight years were retrospectively studied. The magnitude and rate of progression of any changes over time was determined and initial patient and dental characteristics were investigated as possible predictors of the observed side effects.

Results: Records of 62 patients with an average treatment time of 12.6 years (range:8–21 years) were included. Cephalometric analysis revealed significant ($p < 0.001$) maxillary incisor retroclination (mean of $\approx 6^\circ$) and mandibular incisor proclination (mean of $\approx 8^\circ$) over the observation period. Maxillary incisors demonstrated a constant rate of retroclination -0.5°/year, the rate of mandibular incisors proclination was variable. The number of treatment years was significantly associated with these variables ($p < 0.001$). A greater body mass index (BMI) and Subspinale, Nasion, Supramentale angle (ANB) were associated with more maxillary and mandibular incisor proclination respectively. Although statistically significant ($p < 0.001$) skeletal changes were noted over this extended observation period, the difference in the Sella, Nasion, Supramentale point B (SNB) and mandibular plane angles were approximately 1° and were deemed not clinically significant.

Conclusions: This study represents the longest observation period to date examining OAm side effects with up to 21 years of follow up for some patients. It confirms that there are significant and progressive dental changes with prolonged OAm use. Conversely, over the same time period skeletal or postural changes were negligible. Additionally, treatment duration was the predictor consistently associated with the magnitude of the observed side effects.

1. Introduction

Obstructive sleep apnea (OSA) is a chronic condition in adults which, at present, has no permanent cure and all currently available treatment options require life-long adherence. An increasingly common treatment option are oral appliances, which protrude the mandible (OAm), improves the upper airway patency and decrease its collapsibility [1]. The short-term side-effects of OAm treatment have been shown to be mild and transient [2,3].

Tooth movement leading to changes in occlusion is a common side effect of long-term OAm use. Dental cast analysis and cephalometric analysis have been used to assess the dentoalveolar changes and studies have shown decreased overbite and overjet [4–12], maxillary incisor retroclination and mandibular incisor proclination [4,7,13,14] mesialization of the mandibular molars and distalization of the maxillary molars [7,15,16] as well as changes in dental arch crowding [8,15]. These dental changes develop as a result of the forces exerted on the upper and lower dental arches by the oral

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appliance as it holds the protrusion, resisting the counteracting forces trying to return the mandible to its resting position [15].

Unlike the data on the dentoalveolar changes that seem to be mostly consistent between studies, cephalometric data on the skeletal side effects are conflicting with some studies showing skeletal changes [13,17] and others showing no such alterations [2,11]. Furthermore, previous studies have shown contradictory results in terms of the skeletal characteristics that demonstrate changes in addition to contradictory results in relation to the direction of the changes. For example, some have shown changes to be in the position of the maxilla as indicated by the Sella, Nasion, Supramentale point A (SNA) angle but not in the position of the mandible (SNB angle) [4] and vice versa [7]. Similarly, an increase in the vertical dimension of the mandibular plane angle and lower face height has been inconsistently reported [10,11]. Regarding the direction of change, some have shown a statistically significant decrease in the SNA angle [4], an increase in the SNA angle [13] or no statistically significant changes in SNA angle [7,15,18]. A recent systematic review and meta-analysis has concluded that there are no significant changes in the skeletal variables however, the duration of follow-up in the included studies that assessed skeletal changes was short [12].

A common limitation reported in the existing literature on OAm side effects are the relatively short observation periods, leaving the nature of the progression of skeletal and dental changes inadequately characterized considering the life-long need for treatment. It has also been previously speculated that the occlusal changes observed may be a combination of tooth movement and mandibular posturing. The aim of this study is to determine the nature of the occlusal changes associated with long-term oral appliance treatment (ie, dental and/or skeletal), to evaluate the magnitude and progression of these changes, and to determine if initial patient and dental characteristics are possible predictors of the observed long-term side effects of treatment.

2. Materials and methods

2.1. Design

This observational study evaluated the demographic and radiographic data obtained from adults treated for snoring or mild to severe OSA using an OAm. Patients were referred to the Sleep Apnea Dental Clinic at the University of British Columbia or to an affiliated private practice for their OAm treatment. The OAm used by patients were either Klearway (Space Maintainers Laboratories Canada Ltd., Calgary, Canada) or SomnoDent (SomnoMed, Ontario, Canada). These appliances are custom made and titratable, constructed of a semi-rigid thermoplastic material covering the occlusal surfaces of all teeth. The amount of initial advancement set at two-thirds of maximum protrusion, and then further advancements were prescribed by 0.25-mm increments until self-reported resolution of snoring and daytime sleepiness symptoms, or until uncomfortable for the patient. Optimal titration was then verified by a follow-up polysomnography for the OSA patients. The vertical opening was kept to a minimum to avoid downward rotation of the mandible during use. In the aforementioned clinics, it is standard protocol to obtain lateral cephalometric radiographs prior to the initiation of treatment and with each OAm replacement if the replacements are ≥1 year apart. Approval for the study was obtained from the UBC Clinical Research Ethics Board H11-01661.

Charts and lateral cephalometric radiographs were retrieved for patients who were treated for a minimum of eight years exclusively with OAm, between 1992 and 2016. Patients were excluded if the pre-treatment radiograph was of a poor quality due to image degradation as determined by a single investigator. The number of lateral cephalograms analyzed for each patient ranged between 2 and 9 and the duration of OAm treatment was calculated as the interval between the date of the initial and most recent cephalogram.

2.2. Cephalometric analysis

Pre-treatment and follow-up lateral cephalometric radiographs were obtained with the patients standing upright with their head oriented so that the Frankfurt Horizontal plane is parallel to the floor and the teeth in centric occlusion.

A custom-made analysis was developed in the cephalometric analysis software Dolphin (Dolphin® Imaging 11.7, Chatsworth, CA) to include the pre-selected variables of interest. All tracings were conducted by a single investigator (BTP). The main data collected pertained to the sagittal position of the maxilla and mandible, vertical dimension, intermaxillary relation, in addition to maxillary and mandibular dentoalveolar position. Fig. 1 shows the cephalometric landmarks and reference planes used.

2.3. Statistical analysis

The data are presented as the mean values and standard deviations. The magnitude of change in each of the variables was

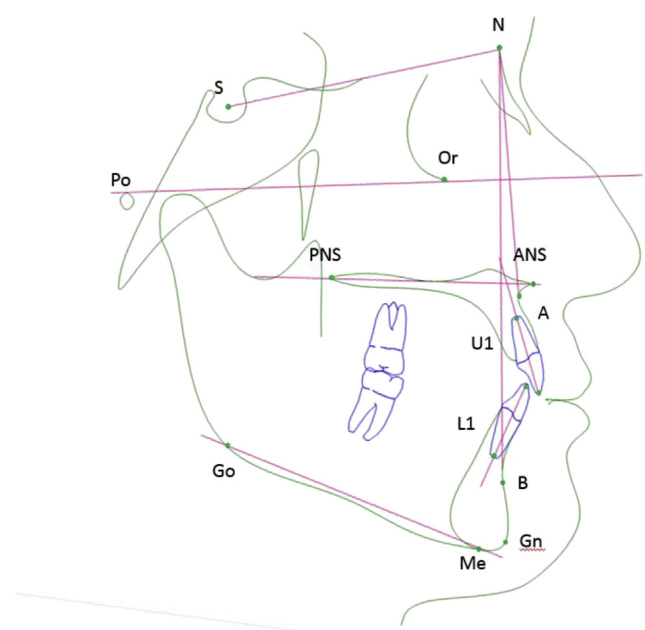


Fig. 1. The following landmarks and planes were identified on lateral cephalograms. *Landmarks*: S (sella) —center of the sella turcica, N (nasion) — deepest point in the concavity of the frontonasal suture, Po (Porion) — midpoint of the upper contour of the external auditory canal (Anatomic Porion), Or (Orbitale)—a point midway between the lowest point on the inferior margin of the two orbits ANS (anterior nasal spine) — tip of the median, sharp bony process of the maxilla, PNS (Posterior Nasal Spine)— tip of the posterior nasal spine of the palatine bone, at the junction of the soft and hard palate, A (Point A) — deepest point in the concavity of the anterior maxilla, B (Point B) —deepest point in the concavity of the anterior mandible, Me (menton) — intersection of the bony inferior symphysis with the inferior margin of the mandibular body, Go (gonion) — constructed point at the intersection of the ramus plane and the tangent to the lower border of the body of the mandible, Gn (Gnathion) — most anteroinferior point on the bony chin. *Planes*: SN (sella-nasion line) — line through the Sella and Nasion, FH (Frankfort Horizontal)— a line connecting Porion to Orbitale, PP (palatal plane) — a line through ANS and PNS, NA — a line through Nasion and A point, NB — a line through Nasion and B point, U1 (upper incisor line) — line through the upper incisor root apex and the upper incisor incisal edge of the most prominent upper incisor, L1 (lower incisor line) — line through the lower incisor root apex and the lower incisor incisal edge of the most prominent lower incisor, MP (mandibular plane) —a plane from constructed gonion to menton, GoGn —a line through Gonion and Gnathion.

determined to be the difference between the pre-treatment baseline (T_0) value and the last follow-up (T_F) value. Dental and skeletal characteristics at baseline (T_0) and at the last follow-up (T_F) were compared using the Student paired t-test in the SPSS statistical package version 21 (SPSS Inc., Chicago, Illinois, USA). A p value <0.05 was considered statistically significant.

The rate of change in the variables that showed statistically significant changes between T_0 and T_F and the effect of baseline characteristics on dental and skeletal variables were assessed using a mixed-effect polynomial regression analysis. Baseline characteristics of interest included baseline Apnea-Hypopnea Index (AHI), body mass index (BMI), age at the start of treatment, initial Maxillo-Mandibular skeletal relation (ANB), initial mandibular plane angle and number of treatment years as possible predictors of change. The correlation between the dental changes and the number of teeth present at baseline was assessed using the Pearson correlation coefficient.

2.4. Method error

To evaluate systematic measurement errors, 22 randomly selected lateral cephalograms were retraced by the same investigator (BTP) six months following the initial tracing. The reassessment included all the previously assessed cephalometric measurements and used the same software. Test–retest reliability was calculated using the intraclass correlation coefficient (ICC) in SPSS (version 21). A two-way mixed effects model was used [19].

3. Results

A total of 62 patients (average age at start of treatment: 49 ± 8.6 years) were included in this study and average treatment length was 12.6 years (range: 8–21 years). The baseline characteristics of the study population are shown in Table 1. All the cephalometric variables assessed were angular measurements measured in degrees (Fig. 1). Continuous variables are presented as mean ± standard deviation. Intra-examiner reliability for the measurements showed a high agreement with ICC values ranging from 0.90 to 0.98. Values greater than 0.90 indicating excellent reliability [19]. Standard deviation of the repeated measures for SNB angle, Mandibular plane Frankfort Horizontal (MPFH) and Stella-Naison line, Gonion, Gnathion (SNGOGn) were 0.8, 1.3 and 1.3° respectively.

3.1. Direction and magnitude of change

3.1.1. Dental variables

Over the total treatment interval evaluated there was significant ($p < 0.001$) maxillary incisor retroclination (posterior tipping). Upper incisor inclination was assessed relative to multiple reference planes and a reduction of close to six degrees was consistently found (U1SN: −6.1° ± 5.9°, U1FH: −6.3° ± 6.2°, U1PP: −6.3° ± 6.0°, U1NA: −5.9° ± 5.6°) with a large amount of individual variation (Table 2 and Fig. 2). Significant ($p < 0.001$) mandibular incisor proclination (anterior tipping) was also noted; lower incisor inclination was assessed relative to the MP and the NB plane and the magnitude of change was 7.9° ± 6.2° and 8.2° ± 6.2° respectively (Table 2 and Fig. 2).

Table 1
Baseline patient characteristics.

N	62
Males/Females	52/10
Angle Classification (CI*, CII**, CIII***)	31/26/4
Age (y)	49.0 ± 8.6 (29–65)
BMI (kg/m^2)	29.1 ± 6.9 (18.7–63.6)
AHI (/hour) (N = 56)	30.0 ± 14.6 (7.4–66.2)
Treatment duration (y)	**12.6 ± 3.9 (8.0–21.4)**

Values presented as mean ± standard deviation (range).
*(ANB 0-5°), **(ANB >5°), ***(ANB <0°).

Table 2
Overall cephalometric changes during treatment (n = 62).

	Initial	Final	Final-Initial	P value
Dental Measurements				
U1 − SN (°)	95.3 ± 8.1	89.2 ± 9.0	−6.1 ± 5.9	<0.001
U1 − FH (°)	103.7 ± 8.0	97.4 ± 9.0	−6.3 ± 6.2	<0.001
U1 − PP (°)	105.1 ± 8.5	98.9 ± 9.5	−6.3 ± 6.0	<0.001
U1 − NA (°)	13.7 ± 8.2	7.8 ± 8.7	−5.9 ± 5.6	<0.001
L1 − NB (°)	23.1 ± 8.5	31.4 ± 10.9	8.2 ± 6.2	<0.001
L1 − MP (°)	91.1 ± 7.2	98.9 ± 10.5	7.9 ± 6.2	<0.001
Skeletal Measurements				
SNA (°)	81.6 ± 3.8	81.4 ± 3.8	−0.2 ± 1.6	NS
SNB (°)	77.1 ± 3.7	76.4 ± 3.7	−0.7 ± 1.3	<0.001
ANB (°)	4.6 ± 2.9	5.0 ± 2.8	0.4 ± 1.1	0.005
SNGoGn (°)	32.5 ± 6.5	33.4 ± 6.6	0.9 ± 2.1	0.001
MPFH (°)	26.7 ± 6.2	27.8 ± 6.3	1.1 ± 2.7	0.001

Values presented as mean ± standard deviation.
NS: not significant.
A negative value in Final-Initial indicates a decrease in value over time.

Only one patient had an anterior crossbite indicated by negative overjet pre-treatment, however the number of patients with a negative overjet at their last follow-up was 27 out of the 62 patients (≈44%) (see Fig. 3).

3.1.2. Skeletal variables

A significant change in the position of the maxilla, as indicated by the SNA angle was not observed. The average total change in the SNB angle, a measure of the anterior-posterior position of the mandible was a reduction of 0.7° ± 1.3° ($p < 0.001$), which coincided with a reduction in the ANB angle of 0.43° ± 1.1° ($p = 0.005$). The SNGoGn and the MPFH angles, measures of the vertical position of the mandible, demonstrated statistically significant changes of 0.9° ± 2.1° and 1.1° ± 2.7°, respectively, over the total observation period (Table 2).

3.2. Rate of change

The rate of change of the upper incisor inclination was constant over the years and was −0.47°, −0.49° and −0.49°/year for U1SN, U1FH and U1PP respectively (Table 3).

The rate of change of L1MP and L1NB was variable over the years. While the mandibular incisors on average continued to procline with time, the rate at which this anterior tipping occurred decreased from year to year, as indicated by the declining rate of change. At approximately 19 years of follow up, change in the lower incisor inclination appeared to stop (Fig. 4).

The rate of change of the SNB angle was constant and minimal, −0.05°/year. The rate of change of SNGoGn was inconsistent however, and the amount of change declined over time.

3.3. Predictors of change

Baseline OSA severity, age and number of teeth present at the start of treatment were not associated with the magnitude of changes observed. Contrary to this, the number of treatment years was most significantly associated ($p < 0.001$) with all of the measured cephalometric variables where changes did occur. Baseline patient BMI had a significant effect ($p = 0.02$) on U1SN and on U1PP ($p = 0.03$), where a coefficient of 0.39 indicates that patients with 1unit-higher BMI tend to have on average 0.39° less posterior tipping of the maxillary incisors over the years controlling

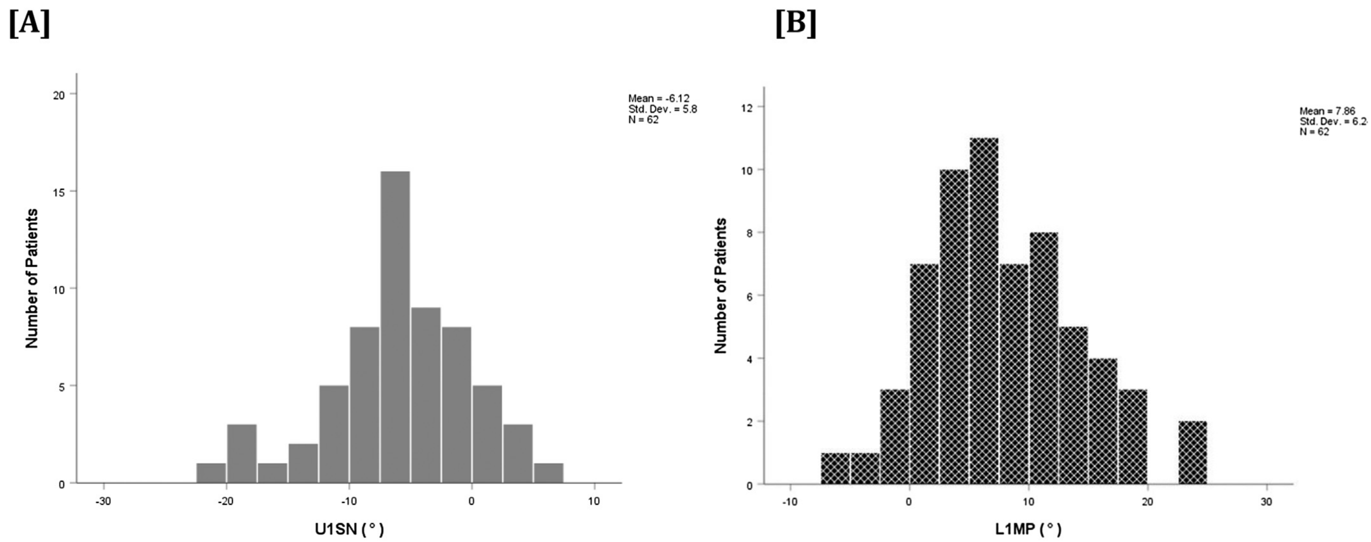


Fig. 2. Individual variations in the mean change of U1SN (A) and L1MP (B).

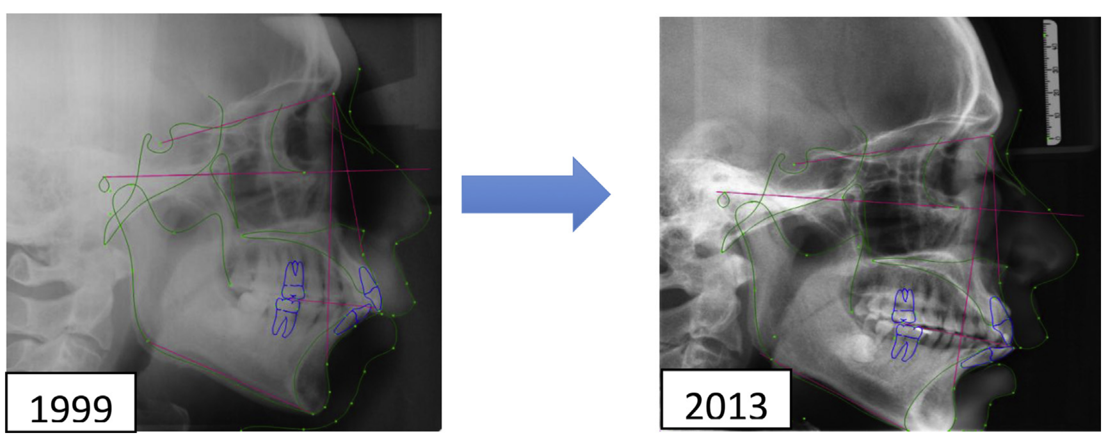


Fig. 3. Tracing of one of the study patient's initial (T_0) and final (T_F) lateral cephalograms showing the lower incisor proclination and upper incisor retroclination.

for other variables. Similarly, the initial ANB angle had a significant effect ($p < 0.001$ and $p < 0.01$) on L1MP and L1NB respectively. A higher ANB angle was associated with more anterior tipping relative to a lower ANB angle, controlling for other variables (Table 4).

4. Discussion

The present study confirms that there is significant dental movement associated with long-term OAm treatment but no clinically relevant skeletal changes. The principle effects noted were an approximate mean of 6° of maxillary incisor retroclination and a mean of 8° of mandibular incisor proclination. Combined, these changes in incisor inclination resulted in 44% of the study population having a negative overjet at the end of their latest follow-up visit, which on average corresponded to more than 12 years of treatment. Additionally, the observed changes were not reversible over the duration of the study and in fact were progressive in nature with a constant rate of retroclination for upper incisors of − 0.5°/year. The rate of change of the lower incisors proclination was not constant; the proclination overall increased with time, but at a declining rate of change year over year.

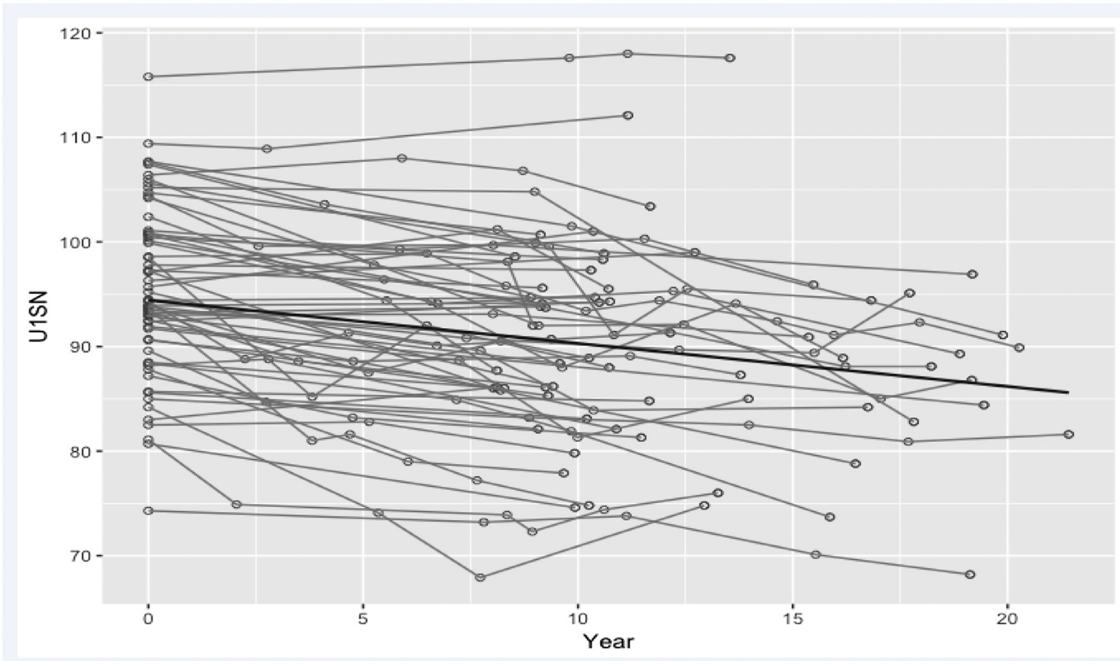
Maxillary incisor retroclination and mandibular incisor proclination have been previously documented in the literature [4,13,20] however, our findings indicate that these changes continue to progress over time. The rate of progression of maxillary incisor proclination was constant for nearly up to two decades of treatment. Proclination of the mandibular incisors was also progressive, however, the rate of proclination seemed to decline with prolonged follow up and appeared to stop after approximately 19 years of treatment. This decline followed by cessation of proclination may be attributed to the force exerted by the lower lip on the proclined lower incisors which might be counteracting the force created by the OAm. When the opposing forces from the OAm (exerted during

Table 3
Rate of change per year for variables that showed a statistically significant change between final and initial measurements.

Variable (in degrees)	Rate of change per year
Dental	
U1-SN angle	−0.47°
U1-FH angle	−0.49°
U1-PP angle	−0.49°
U1-NA angle	Inconsistent rate of change
L1-MP angle	Inconsistent rate of change
L1-NB angle	Declining rate of change that is variable each year
Skeletal	
SNB angle	−0.05°
SN-GoGn angle	Declining rate of change that is variable each year

A negative value indicates a decrease in the angle over time.

[A]



[B]

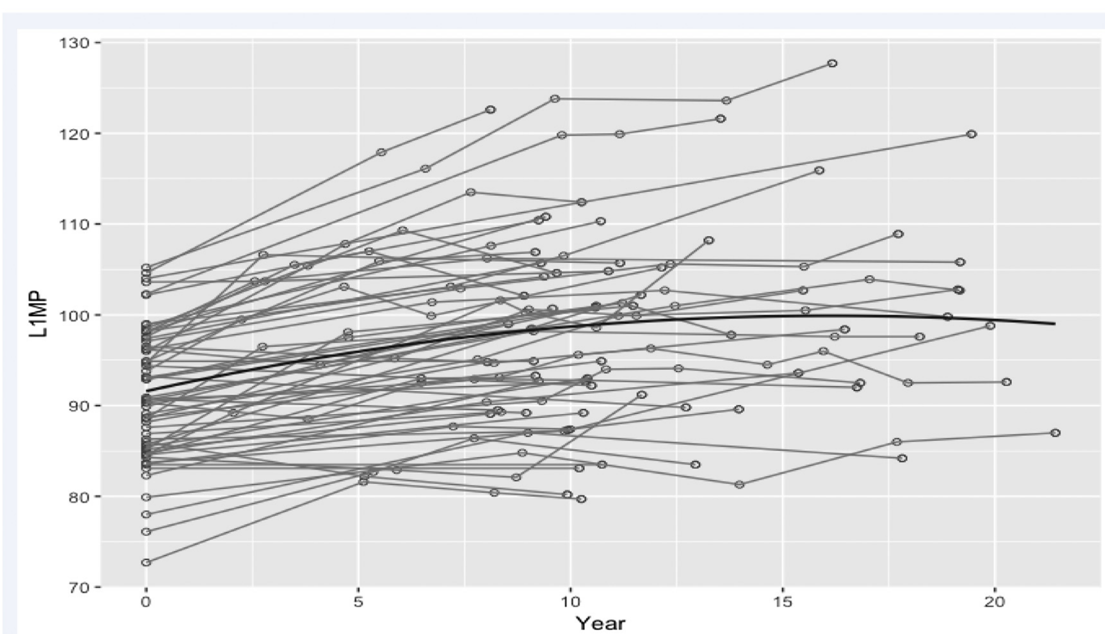


Fig. 4. All data points for the entire study population for U1SN (A) and L1MP (B) in degrees, as a function of number of years in treatment. Data for each patient are connected by a line.

OAm use) and from the lower lip (exerted during awake time) are balanced, a state of equilibrium may be reached leading to no net change in the position of the lower incisors. Alternatively, the decline in proclination may be attributed to the inclination of the tooth and the vector of the horizontal force from the OAm acting upon it. A tooth that is already severely proclined may not be as susceptible to further proclination compared to a tooth that is relatively upright.

In line with our findings regarding the rate of change in the maxillary and mandibular incisor inclination, it has been previously demonstrated that the maxillary incisors might retrocline an average of 1.9° and the mandibular incisors might procline an

Table 4
Adjusted models for the effect of BMI and ANB angle on upper and lower incisor inclination.

Variable	Predictor	Unit change in variable with 1-unit change in predictor (in degrees)	P-value
U1SN	BMI	0.39	0.02
U1PP	BMI	0.40	0.02
L1NB	ANB CII	10.91	<0.01
L1MP	ANB CI	12.89	0.02
	ANB CII	20.19	<0.001

average of 2.8° [15,18,21] after approximately two years of treatment. However, this study is the first to characterize the yearly rate of progression of the dental changes. More recently a systematic review [22] reported on data assembled from 18 studies investigating dental and skeletal changes with OAm therapy ranging from a period of 2–11 years. The corresponding meta-regression analysis found that dental side effects are progressive in nature and strongly correlated to the duration of therapy; the longer the treatment time, the greater the magnitude of changes recorded. Also similar to the present study, this systematic review deemed the skeletal changes caused by long-term treatment to be clinically insignificant.

Differences between the findings of the various studies in terms of the magnitude of dental changes has been previously observed and could be attributed to several factors including appliance design or material [23,24], the amount of mandibular advancement and the adherence to treatment [23]. Discrepancies in the results of the various studies can also be attributed to the varying observation periods and different sample sizes [8]. In this study, there was a wide range of individual response to treatment side effects, as indicated by the standard deviations. While 85% of the patients showed maxillary incisor retroclination and 92% of the patients showed mandibular incisor proclination a few patients showed an opposite response. Notably, two individuals (both Class II at baseline and treated with the Klearway OAm) showed both maxillary incisor proclination and mandibular incisor retroclination. Additionally, the patients who showed change in the opposite direction were mostly the patients with a low AHI. The low AHI may have resulted in reduced appliance advancement or less frequent use of the OAm compared to patients with a higher AHI, hence their teeth were less prone to movement.

The number of teeth present at the start of treatment may be a reasonable additional factor determining the distribution of forces exerted on the dentition and consequently, impacting the amount of tooth movement. Our findings do not indicate a correlation between the number of teeth retained at the beginning of treatment and the magnitude of the observed dental changes. Minagi et al., have noted a weak negative correlation between the total number of teeth and overjet reduction [20]. The difference between the findings of the two studies could be attributed to the difference in the variables assessed. While Minagi et al., assessed the changes in overjet, the present study assessed tooth inclination relative to cephalometric planes. The variability in the findings could also be attributed to the difference in follow up duration between the two studies. While there may be a weak correlation observed during a short duration of follow-up, this correlation is not evident with a prolonged follow-up period.

The potential influence of appliance material (rigid versus flexible) and design on the magnitude and nature of the occlusal changes is not clear and warrants further investigation. Norrhem et al., [24] have shown that a flexible type of OAm without incisor coverage increased the irregularity of the lower anterior teeth compared to a more rigid OAm with incisor coverage. However, the overbite and overjet changes were similar between the flexible and rigid type of appliances. Ringqvist et al., [17] used an OAm with no incisor coverage and reported no significant changes to overjet and overbite over a period of four years. This could be attributed to the lack of incisor coverage or to limiting the mandibular protrusion to 50% of maximum protrusion which also has been suggested to influence the magnitude of the occlusal changes [11]. Changes in cephalometric variables were found to be similar between the traction and compression types of appliances [25].

The findings of the present study confirm the findings of Marklund [23] and Minagi et al., [20] who also reported that side effects increase with treatment duration. Our results also show that a higher BMI may have a protective effect against upper incisor retroclination, which may be attributed to the fact that individuals with increased BMI tend to have larger tongues [26]. During awake time, a large tongue will apply a force onto the lingual surface of the upper incisors and minimize their retroclination, relative to an individual with a smaller tongue. Previous findings by Pliska et al., [8] indicated no effect of BMI on occlusal changes in their study of dental models, while baseline AHI was positively associated with a reduction in overjet.

Our findings also show that a higher ANB angle is associated with greater lower incisor proclination relative to a lower ANB angle. This may be attributed to the amount of OAm advancement, as skeletal Class II patients are often retrognathic and therefore might need greater amounts of advancement and hence greater forces are applied on the teeth leading to more labial tipping. However the specific relationship between initial ANB angle (degree of retrognathia) and amount of therapeutic protrusion warrants further investigation. Alternatively, the lower incisors in retrognathic patients typically can be tipped labially to a greater extent before they meet an equilibrium with opposing pressure from the lips. In contrast to the present study, baseline AHI has been previously reported to correlate with the amount of overjet reduction. This discrepancy may be due to differences in the nature of the specific measurements (overjet vs. inclination of teeth), and in the length of the observation periods between studies.

Similar to previous findings, this study demonstrated a reduction in the SNB angle [7,18,27] and an increase in the SNGoGn [4,10] and the mandibular plane angle [10,17]. However, the skeletal changes observed in this study were approximately 1° in magnitude and although statistically significant, they are deemed clinically irrelevant, especially considering the standard deviation of the repeated measures of these variables. With prolonged follow up periods extending for over a decade, natural physiologic changes need to be considered. We attribute the skeletal changes recorded in this study, although clinically insignificant, to the physiologic changes that occur during mid to late adulthood. It has been shown that there are significant changes in total face height with aging, mainly due to an increase in the lower anterior facial height [28–30]. Sarnäs and Solow [31] reported a significant increase in total face height of 1.5 mm in five years, which was mostly attributed to the increase in lower anterior face height. Bondevik [32] reported a significant decrease in the SNB angle in women, while men showed no significant changes.

The lack of skeletal contribution to the occlusal changes observed aligns with what is found in the orthodontic literature, where the use of functional appliances for the correction of Class II malocclusion in adults occurs predominantly due to dental movement and not due to skeletal or postural changes. Bock and Ruf [33] used a herbst appliance in adults average age 25.6 years, where the objective was to move the lower jaw and dentition forward. Patients wore the herbst appliance which was bonded in place and therefore held the mandible forward 24 h a day for an average treatment time of nine months. It was found that at long term follow up the malocclusion was corrected as a result of dentoalveolar tooth movement, rather than the mandible being moved or postured forward.

There are some limitations to this study. First, selection bias might be a factor as severe long term side effects might have caused some patients to discontinue OAm therapy early on and this study attempted to assess patients who could continue OAm treatment long-term. Nevertheless, often occlusal changes go unnoticed by the patients and two previous studies have shown that only 4–14% [5,34] of patients notice the occlusal changes. Our observations concur with the study of Fritsch et al., who demonstrated that the benefits experienced from OAm therapy typically outweigh the inconveniences experienced by the patients with therapy and do not lead to discontinuation of treatment in the majority of the cases. Additionally, this study did not objectively assess patient adherence to treatment which may be an important factor when considering the rate of development of side-effects. Even though adherence to OAm treatment was self-reported in routine follow up questions for this study population. In the province where the study was conducted, patients pay out of pocket for oral appliance therapy. Therefore, it is highly unlikely that they would continue to purchase oral appliances if they are not being used continuously.

The amount of mandibular advancement has also been suggested as a factor affecting the progression of side-effects [20] and although the amount of mandibular advancement was not documented in this study, all patients were optimally titrated, as confirmed by a follow-up polysomnography. This study along with previous investigations, has not assessed the effect of the periodontal condition of the teeth on the magnitude of the tooth movement observed, though these factors may be related and warrant future study.

Despite the absence of a control group, as there is no justification to obtain routine lateral cephalograms for an untreated population, there is an abundancy of literature describing the progression of dental and skeletal changes in untreated populations. Most studies have shown no physiologic changes to occur in overjet during adult life, indicating that there are no changes in the inclination of the incisors [35–37] and confirming that the changes observed in maxillary and mandibular incisor inclination in this study are due to OAm treatment.

The strengths of this study include the prolonged follow-up period which averaged 12.6 years and up to 21 years of follow-up for some patients. Unlike most previous studies, a wide range of baseline OSA severities were included in this study with a mean AHI of 30 events/hour, which increases the generalizability of the results. Additionally, this study utilized multiple lateral cephalograms for each patient. Besides the high accuracy and reproducibility of lateral cephalographic measurements, the availability of multiple lateral cephalograms obtained at different time points for each patient allowed for a clear characterization of the progression of the changes and an analysis of the rate at which these changes occurred.

Oral appliances are well-tolerated and both objective and subjective assessments of adherence have shown a high adherence rate to treatment [38]. Long-term side effects are an important aspect of treatment that require further research to mitigate their deleterious effects. However, even major occlusal changes should not deter patients from continuing on OAm therapy if they are not willing to adhere to any other OSA treatment. We continue to believe that effective treatment of a serious and potentially life-threatening condition such as OSA supersedes the maintenance of a stable baseline occlusion [8,27]. Nevertheless, it is of utmost importance to inform the patient about the long-term side-effects prior to the initiation of treatment and careful and extended follow up of oral appliance patients by a specialized dentist is imperative. Interestingly, dental changes have also been reported with prolonged Continuous Positive Airway Pressure (CPAP) use [16,39,40] although the severity of the changes may be different.

Due to the inevitable dental movements associated with OAm therapy, we recommend that if a patient is using an OAm for snoring only, the patient should be advised to not use the appliance every night, which will likely decrease the amount of changes in the long term. For OSA patients, a balance between therapeutic effectiveness and side-effects must be reached.

5. Conclusion

This study represents the longest observation period to date examining OAm side effects, with up to 21 years of follow up for some patients. It confirms that dental changes are inevitable with long-term OAm treatment. Both clinically and statistically significant and progressive dental changes were observed with prolonged OAm use, and over the same time period skeletal or postural changes of the mandible appear to be negligible. Treatment duration is the factor most strongly associated with the magnitude of the reported dental side effects.

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Conflict of interest

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: https://doi.org/10.1016/j.sleep.2018.12.012.

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