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ORIGINAL ARTICLES

SYSTEMATIC REVIEW

REVIEWS

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Turkish Journal of Orthodontics (Turk J Orthod) is a scientific, open access periodical published by independent, unbiased, and double-blinded peer-review principles. The journal is the official publication of the Turkish Orthodontic Society, and it is published quarterly in March, June, September, and December.

Turkish Journal of Orthodontics publishes clinical and experimental studies on on all aspects of orthodontics including craniofacial development and growth, reviews on current topics, case reports, editorial comments and letters to the editor that are prepared in accordance with the ethical guidelines. The journal's publication language is English and the Editorial Board encourages submissions from international authors.

Journal's target audience includes academicians, specialists, residents, and general practitioners working in the fields of orthodontics, dentistry, medicine and other related fields.

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TURKISH JOURNAL of ORTHODONTICS

Original Article

The Condylar Effects of Mesenchymal Stem Cells, Low-Level Laser Therapy and Grape Seed Extract on Functional Mandibular Advancement of the Rat Mandible

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Cite this article as: Eğlenen MN, Tuğlu Mİ, Aydemir İ, Güleç A. The Condylar Effects of Mesenchymal Stem Cells, Low-Level Laser Therapy and Grape Seed Extract on Functional Mandibular Advancement of the Rat Mandible. *Turk J Orthod.* 2023; 36(2): 79-86 [Epub Ahead of Print].

Main Points

- In rats, condylar remodeling can be achieved using experimental functional appliances.
- The injected adipose tissue -derived mesenchymal stem cells successfully remained in the condylar area and were found to be effective.
- The use of low -level laser therapy and grape seed extract increases the effects of adipose tissue -derived mesenchymal stem cells.
- The combination of adipose tissue -derived stem cells, low -level laser therapy, and grape seed extract with mandibular advancement is the most effective.
- Adipose tissue -derived mesenchymal stem cells are a promising cell source in bone tissue production and regeneration.

ABSTRACT

Objective: Functional treatment of Class II malocclusion is expected to lead to adaptation in the condyle. This study aimed to evaluate the effects of adipose tissue-derived mesenchymal stem cells (ADMSCs), low-level laser therapy (LLLT), and grape-seed extract (GSE) on condylar growth after functional mandibular advancement.

Methods: Forty-five rats were randomly divided into 8 groups. Functional appliances were applied to all groups (n=6) except the control group (n=3). One group was treated with appliances only; the other six groups received various combinations of ADMSCs, LLLT, and GSE. Analyses for new osteoblasts and new bone formation, vascular endothelial growth factor, and Type II collagen were performed on condylar tissues, after an experimental period of four weeks. The quantitative data obtained from the results of the experiments were evaluated by H-score and analyzed using One-Way ANOVA by Tukey-Kramer multiple comparisons test ($p \leq 0.05$).

Results: Levels of all investigated parameters increased in all groups ($p \leq 0.05$). The highest increases were achieved by a combined application of functional appliance, ADMSCs, LLLT and GSE ($p \leq 0.05$). Single LLLT administrations or single GSE applications did not create a statistical difference from appliance alone ($p > 0.05$). A positive effect of ADMSCs or LLLT on osteoblast formation, neovascularization, and Type II collagen level was apparent ($p \leq 0.05$), however, neither affected new bone formation ($p > 0.05$).

Conclusion: This study shows that ADMSCs with LLLT and GSE applications provide differing levels of new osteoblast and bone formation, new vascular formation, and Type II collagen formation in rat condyles after functional mandibular advancement.

Keywords: Functional mandibular advancement, grape-seed extract, laser therapy, mandibular condyle, stem cell therapy

Previous Presentation: Oral presentation at 22nd Balkan Stomatological Society (BaSS) Congress, May, 4-7 2017, Thessaloniki, Greece.

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INTRODUCTION

Class II malocclusion with mandibular retrognathism is one of the most common clinical orthodontic problems that can be addressed using functional appliances. These appliances reposition the mandible in a forward-and-downward direction, which may accelerate and increase mandibular growth.[1] Previous studies have shown that forward positioning of the mandible leads to increased new bone formation in the condyle and the posterior region of the glenoid fossa.[2] This new bone formation can be reached its maximum level within four weeks in the rats.[3,4] The mandibular condylar cartilage can respond to environmental stimuli, such as ultrasound application, laser application,[4,5] systemic administration of hormones[6] and steroids,[7] as well as mechanical stimulation with functional appliances.[8]

The development of genetic research has facilitated investigations into the effects of adipose-derived mesenchymal stem cells (ADMSCs) on growth and development. ADMSCs have the ability to differentiate into various types of cells with mesenchymal origins, including osteoblasts, chondroblasts and myoblasts and are easily obtained from adult bone marrow, cartilage and adipose tissue. They are considered vital components for new bone formation.[9] Bone-marrow stem cells have been used to increase osteogenic differentiation in orthodontically expanded maxilla in rats. Local administration of ADMSC led to new bone formation, osteoblast formation and vascularization in the maxilla.[10]

LLLT has been used to increase the tissue regeneration.[11] Previous research on rabbit condyles indicated that LLLT had beneficial effects in accelerating condylar remodeling and enhancing new bone formation during mandibular advancement.[12] In rats, increased osteoblast and chondroblast activities resulting in condylar growth and mandibular length increase were observed after functional mandibular advancement and LLLT.[5]

Various physical and chemical stimuli can induce the differentiation of ADMSCs and LLLT is one such stimulus that allows ADMSCs to remain in the implanted area for longer periods, aiding regenerative events by increasing the release of various growth factors by ADMSCs.[13]

GSE is a flavonoid derivative with important antioxidant properties.[14] It has been shown to stimulate angiogenesis and possess anti-inflammatory, anti-oxidative, anti-cancer, anti-diabetic, anti-allergic, cardioprotective, vasodilator, cholesterol-lowering, and dermal wound healing mechanisms.[15] Proanthocyanidins, which are the active components of GSE, have not been found to have toxic and mutagenic effects at high-doses (1400-1500 mg/kg/day).[14] Alternatively, use of GSE combined with calcium has been shown to increase bone formation by enhancing osteoblast differentiation.[16]

The aim of the present study is to investigate the effects and synergy of LLLT, and GSE on the action of ADMSCs, in functionally induced condylar growth. The use of these stimulants in various combinations was evaluated in terms of their effects on condylar growth, with respect to the amount of new osteoblast and bone formation, condylar vascularization, and Type II collagen. The hypothesis of the study was that the applications of ADMSCs with LLLT and GSE would not significantly change the investigated parameters in rat condyles after functional mandibular advancement.

METHODS

Animals

All animal experiments were carried out in accordance with the National Institutes of Health Guide for Care and Use of Laboratory Animals, and ethical permission was obtained from the Manisa Celal Bayar University Ethics Committee of Experimental Animal Use and Research Scientific Committee (approval no: 71, date: 22.11.2016).

Forty-five Wistar-albino rats (6-week old, weighing 250±50 gr) were randomly divided into 8 groups. Functional appliances were administered to all study groups (n=6) except the control group (group C; n=3). Groups were treated with appliances only; the other six study groups received single administration or various combinations of ADMSCs, LLLT, and GSE, as shown in Table 1.

All the rats were housed in the same well-controlled environment, maintained under 12-hour light-dark cycles (with lights on 7:00 AM to 7:00 PM), at room temperature of 18-22 °C and a relative humidity of 40-60%. The study groups were housed in separate cages and provided with a soft diet to prevent weight loss due to the appliances. Water was available ad libitum to all rats throughout the experimental period.

Appliance Fabrication

Plaster models were prepared from impressions of the lower anterior teeth. 1 mm thickness vacuum-formed clear acrylic plates were the fabricated (Clear Advantage, OrthoTechnology, USA) on the models to create an inclined plane, which would move the mandible forward. The acrylic appliances were positioned in a way that caused mandibular forward-downward positioning during both resting rest and functional bite in the rats. When the appliance was bonded, the lower incisors of the subjects were positioned in front of the upper incisors, creating an anterior crossbite. In this state, the subjects were unable to retract their lower jaw.[3,8] The subjects were anesthetized intraperitoneally using a mixture of 20% lidocaine and 80% ketamine-hydrochloride. The lower incisors were washed, dried, and coated evenly with Transbond™ Plus self-Etching Primer (3M Unitek, Monrovia, California, USA) and the acrylic appliances were bonded to lower incisors using light-cured composite (3M™ESPE™Z100™, USA) (Figure 1).

Preparation and Administration of ADMSCs

ADMSCs were collected from adipose tissue of two rats not included in the study groups, following the procedures described by Aydemir et al.[17] The cells were cultured until passage P3, and ADMSC characterization was performed immunocytochemically using Stro-1, c-kit, CD45, and CD105 markers (Figure 2).

After the characterization of ADMSC, each condylar region received a dose of $1x10^6$ ADMSCs/mL through intra-articular injections under general anesthesia. To locate the temporomandibular joint (TMJ), the mandible was positioned forward to allow palpation of the TMJs, which are located approximately 5-10 mm posterior to the lateral canthus of each eye. A 30-gauge needle was then inserted posterior to the zygomatic process of the temporal bone and moved medio-anteriorly into the TMJ spaces[18] where ADMSCs were slowly injected (Figure 3A). In addition to local administration, ADMSCs were also given intraperitoneally[19] on the same day and at the same hour to prevent the decline of ADMSCs and to enhance the involvement of the condyle and the efficacy of ADMSCs. The intraperitoneal injection was intended to improve the treatment's effectiveness.

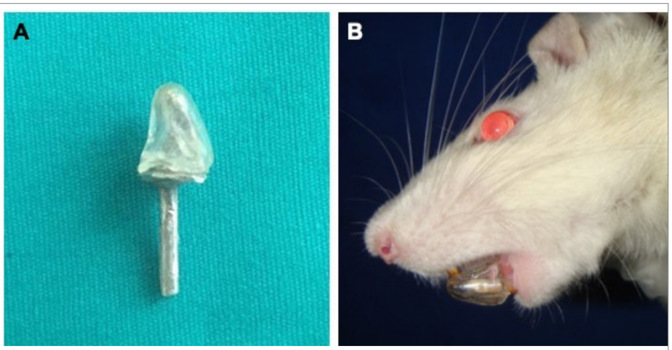

Figure 1. Acrylic appliance (A) was cemented on the lower incisors of experimental rats to move the mandible into a forward position during rest and function (B)

LLLT Irradiation

A low-level diode laser (SiroExtend Laser, 8 J/cm^2, 970 nm, 0.5 watt, 16 seconds) was used to irradiate each rat condyle once in every two days for four weeks (Figure 3B) (Table 1).[8]

Administration of GSE

GSE was obtained from grapes (Vitis-Vinifera L.) of the Denizli province in Turkey, known for their large and isomorphic seeds and prepared according to the method described by Erdemli et al.[20]. The extracts were stored at +4 °C and administered systemically by way of orogastric gavage, diluted with distilled water. The amount of extract given to each group and the number of applications are shown in Table 1 (Figure 3C).[20]

Histopathological Analyses

All rats were euthanized after four weeks through a high-dose of anesthesia. Mandibles were dissected and divided into right

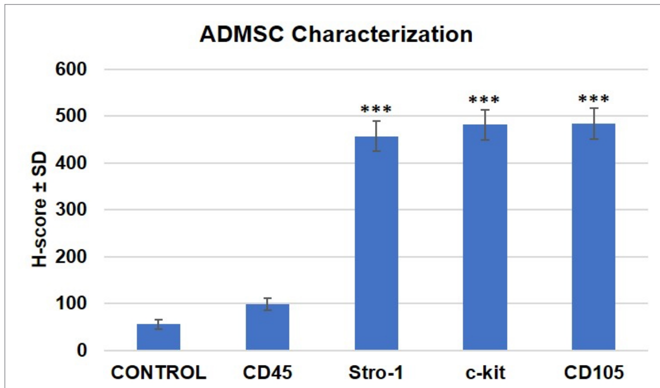

Figure 2. The characterization of ADMSCs immunocytochemically via CD45, Stro-1, CD44, and CD90 markers. Because of the H-score evaluation, Stro-1, c-kit, and CD105 positivity and CD45 negativity were detected ADMSCs, Adipose tissue-derived mesenchymal stem cells

Table 1. Applications and procedures for the experimental groups

Group (n)	Procedure	Application type	Dose	Frequency	Total application number
Control group (3)	-	-	-	-	-
Appliance group (6)	-	-	-	-	-
ADMSCs-LLLT group (6)	MSCs	Local	$1x10^6$ UI/mL	1/4 weeks (begining)	1
		Systemic	$1x10^6$ UI/mL	1/week	4
	LLLT	Local	8 J/cm^2	1/2 day	15
ADMSCs-GSE group (6)	MSCs	Local	$1x10^6$ UI/mL	1/4 weeks (begining)	1
		Systemic	$1x10^6$ UI/mL	1/week	4
	GSE	Systemic	300 mg/kg/day	1/day	30
ADMSCs-LLLT-GSE group (6)	MSCs	Local	$1x10^6$ UI/mL	1/4 weeks (begining)	1
		Systemic	$1x10^6$ UI/mL	1/week	4
	LLLT	Local	8 J/cm^2	1/2 day	15
	GSE	Systemic	300 mg/kg/day	1/day	30
LLLT group (6)	LLLT	Local	8 J/cm^2	1/2 day	15
LLLT-GSE group (6)	LLLT	Local	8 J/cm^2	1/2 day	15
	GSE	Systemic	300 mg/kg/day	1/day	30
GSE group (6)	GSE	Systemic	300 mg/kg/day	1/day	30

LLLT, Low-level laser therapy; ADMSCs, Adipose tissue-derived mesenchymal stem cells; GSE, Grape-seed extract

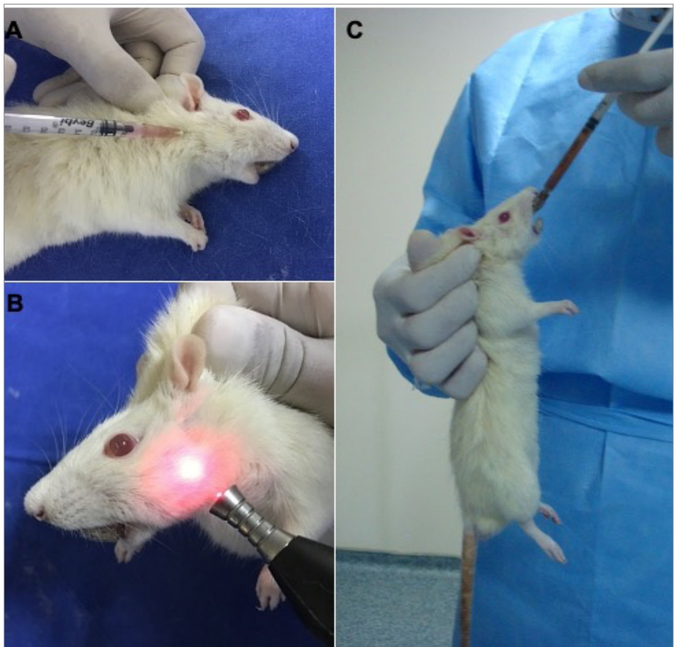

Figure 3. The applications of ADMSCs in the temporomandibular joint spaces (A), LLLT (B), and GSE via orogastric gavage (C)

LLLT, Low-level laser therapy; ADMSCs, Adipose tissue-derived mesenchymal stem cells; GSE, Grape-seed extract

and left parts at symphysis, and kept in a 10% formaline solution (Merck, Germany) until histochemical analyses were performed. The condyle was chosen as the side for cell counting because the most prominent cellular responses to mandibular repositioning occur in the condyle.

The left side condyle of each mandible was used for examination. Samples were embedded in parafine and cut into 5 µm thickness, and sections were taken from the posterior region of the condyles. Tissue sections were stained with hematoxylin-eosin and Masson's Trichrome dyes.[17] Sections were evaluated with a light microscope (BX43, Olympus, Japan) and photographed (SC50, Olympus, Germany) to investigate two histological parameters (Figure 4). The histomorphometrics evaluation was conducted by two histologists. The number of new osteoblasts was classified as mild (+, 0–15 cells), moderate (++, 15–30 cells), and strong (+++, >30 cells). The bone formation was scored between +1 to +5.[17]

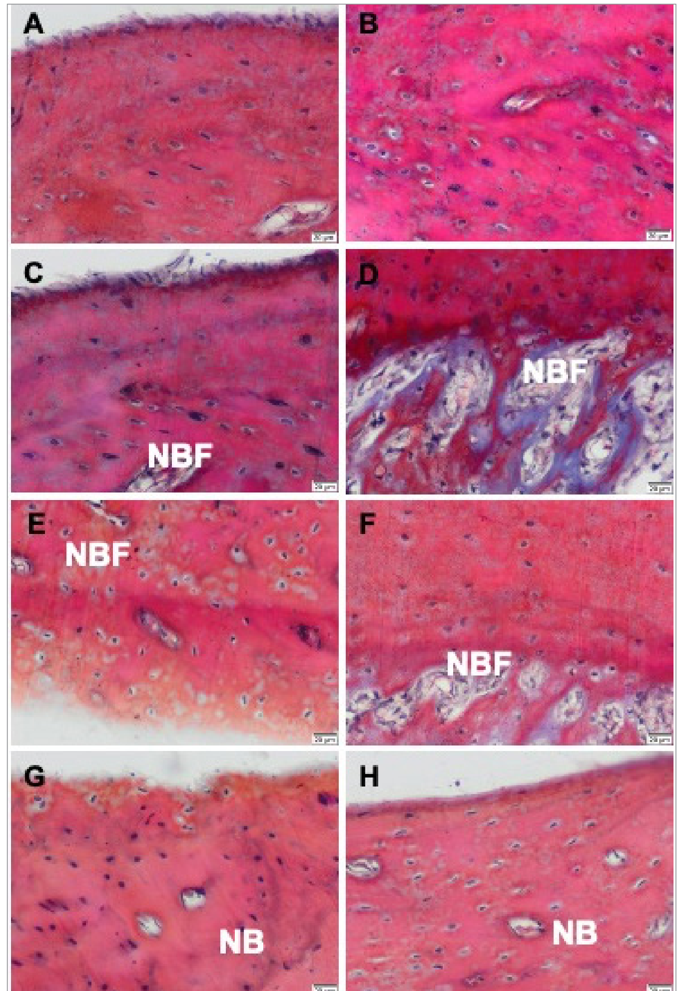

Figure 4. Histochemical staining of experimental groups with Masson's Trichrome; A) Control group, B) Appliance group, C) GSE group, D) LLLT group, E) LLLT-GSE group, F) ADMSCs-GSE group, G) ADMSCs-LLLT group, H) ADMSCs-LLLT-GSE group

LLLT, Low-level laser therapy; ADMSCs, Adipose tissue-derived mesenchymal stem cells; GSE, Grape-seed extract; NBF, New bone formation; NB, New bone; Scale bars, 20 µm

Immunohistochemistry

To detect vascularization and collagen formation, primary antibodies anti-VEGF (Sigma V1253, St Louis, Mo , USA) and anti-Type-II collagen (Sc7763, Santa-Cruz Biotechnology, Calif, USA) were used. After dewaxing in xylene, the sections were dehydrated with ethanol. They were then incubated with 0.5% trypsin at 37 °C for 15 minutes and endogenous peroxidase activity was inhibited using hydrogen peroxide (Merck). Blocking serum was applied for 1 hour, followed by incubation with primary antibodies anti-VEGF and anti-Type-II collagen at 4 °C overnight. The sections were then treated with the anti-mouse biotin-streptavidin hydrogen peroxidase secondary antibody (85–9043 Zymed Histostain kit). Immunoreactivity was made visible using diaminobenzidine (DAB, 00–2014, Invitrogen), and counterstaining was performed using Mayer's hematoxylin (800-729-8350, ScyTek). The sections were coated with entellan; and evaluated using a light microscopy (BX43, Olympus, Japan) by three independent researchers.[17] The procedure was performed three times. The immunoreactivity was evaluated as no (0), weak (+), moderate (++), and strong (+++), and stained cells were counted for each staining degree. The H-score value was calculated using the formula: Pi (intensity of staining + 1), where Pi is the percentage of stained cells for each intensity.[17]

Statistical Analysis

The data were presented as mean±standard deviation and analyzed using GraphPad software (San Diego, USA) after performing a normality test. Statistical significance was considered at p≤0.05, and the One-Way ANOVA followed by Tukey-Kramer multiple comparisons test was performed for data analysis.[17]

RESULTS

Clinical Observations

Daily observations were performed for appliance irritation on tissues and feeding behaviors. During the experiment, an appliance was broken and replaced. The rats were weighed on the first day of the experiment and immediately before they were euthanized. None of the animals showed any weight loss at the end of the experiment.

Histochemical and Immunohistochemical Results

Descriptive statistics of the groups for all four parameters (New osteoblast formation, new bone formation, VEGF and Type II collagen) and test results of paired group comparisons can be found in Tables 2 and 3.

Compared to the control group, all study groups showed an increase in all parameters, with the most significant increase observed in ADMSCs-LLLT-GSE group (p<0.001). Although all combinations of stimulants resulted in significant differences compared to the appliance only group (Appliance vs ADMSCs-LLLT; Appliance vs ADMSCS-GSE; Appliance vs ADMSCs-LLLT-GSE; Appliance vs LLLT-GSE groups), single LLLT administrations or single GSE applications did not create a statistical difference (Appliance group vs LLLT group; Appliance group vs GSE group) (p>0.05).

Table 2. Comparison of new osteoblast and bone formations between groups

		Mean±SD	Differences between appliance group	Differences between ADMSCs-LLLT group	Differences between ADMSCs-GSE group	Differences between ADMSCs-LLLT-GSE group	Differences between LLLT group	Differences between LLLT-GSE group	Differences between GSE group
Control group	New Osteoblast Formation	15.0±2.0	-4.8*	-13.0***	-12.0***	-14.5***	-8.3***	-11.0***	-5.7**
	New Bone Formation	1.4±0.6	-1.0*	-3.2 ***	-2.3***	-3.3***	-1.8**	-2.2***	-1.3*
Appliance group	New Osteoblast Formation	19.9±2.1		-8.2***	-7.1***	-9.7***	-3.5 NS	-6.2***	-0.8 NS
	New Bone Formation	2.4±0.4		-2.2***	-1.3**	-2.3***	-0.8 NS	-1.2*	-0.3 NS
ADMSCs-LLLT group	New Osteoblast Formation	28.2±1.7			-1.0 NS	-1.5 NS	-4.7**	-2.0 NS	-7.3***
	New Bone Formation	4.6±0.5			-0.8 NS	-0.2 NS	-1.3**	-1.0 NS	-1.8***
ADMSCs-GSE group	New Osteoblast Formation	27.4±1.9				-2.5 NS	-3.7*	-1.0 NS	-6.3***
	New Bone Formation	3.7±0.6				-1.0 NS	-0.50 NS	-0.2 NS	-1.0 NS
ADMSCs-LLLT-GSE group	New Osteoblast Formation	29.4±2.3					- 6.2**	-3.5 NS	-8.8***
	New Bone Formation	4.7±0.5					-1.5**	-1.2*	-2.0***
LLLT group	New Osteoblast Formation	23.3±1.9						-2.7 NS	-2.7 NS
	New Bone Formation	3.2±0.9						-0.3 NS	-0.5 NS
LLLT-GSE group	New Osteoblast Formation	26.0±1.4							-5.3***
	New Bone Formation	3.6±0.6							-0.8 NS
GSE group	New Osteoblast Formation	20.7±1.9							
	New Bone Formation	2.7±0.6							

Tukey-Kramer multiple comparisons test. *p<0.05; **p<0.01; ***p<0.001; NS: p>0.05 and SD: Standard deviation. The units for New Osteoblast Formation: Cell count; for New Bone Formation: Trabeculae count

Table 3. Comparison of VEGF and Type-II Collagen immunoreactivities between groups

		Mean±SD	Differences between appliance group	Differences between ADMSCs-LLLT group	Differences between ADMSCs-GSE group	Differences between ADMSCs-LLLT-GSE group	Differences between LLLT group	Differences between LLLT-GSE group	Differences between GSE group
Control group	**VEGF**	56.7±3.2	-6.8*	-24.2***	-21.7***	-28.5***	-10.5***	-12.5***	-8.5**
	Type-II Collagen	45.3±3.5	-13.1***	-39.7***	-33.8***	-44.3***	-19.7***	-22.5***	-17.3***
Appliance group	**VEGF**	63.5±1.8		-17.3***	-14.8***	-21.7***	-3.7 NS	-5.7*	-1.7 NS
	Type-II Collagen	58.5±4.3		-26.5***	-20.7***	-31.2***	-6.5 NS	-9.3**	-4.2 NS
ADMSCs-LLLT group	**VEGF**	80.5±2.9			-2.5 NS	-4.3 NS	-13.7***	-11.7***	-15.7***
	Type-II Collagen	85.0±2.9			-5.8 NS	-4.7 NS	-20.0***	-17.2***	-22.3***
ADMSCs-GSE group	**VEGF**	78.3±3.3				-6.8**	-11.2***	-9.2***	-13.2***
	Type-II Collagen	79.1±4.2				-10.5***	-14.2***	-11.3***	-16.5***
ADMSCs-LLLT-GSE group	**VEGF**	85.3±2.6					-18.0***	-16.0***	-20.0***
	Type-II Collagen	90.8±2.1					-24.7***	-21.9***	-27.0***
LLLT group	**VEGF**	67.1±2.6						-2.0 NS	-2.0 NS
	Type-II Collagen	65.0±3.2						-2.9 NS	-2.3 NS
LLLT-GSE group	**VEGF**	69.1±2.4							-4.0 NS
	Type-II Collagen	67.8±3.8							-5.2 NS
GSE group	**VEGF**	65.2±2.1							
	Type-II Collagen	62.7±3.9							

Tukey-Kramer multiple comparisons test. *p<0.05; **p<0.01; *** p<0.001; NS: p>0.05 and SD: Standard deviation. The units for VEGF and Type-II Collagen: H-scores

The positive effects of ADMSCs or LLLT (ADMSCs-GSE vs ADMSCs-LLLT-GSE; LLLT-GSE vs ADMSCs-LLLT; LLLT-GSE vs ADMSCs-GSE; GSE vs ADMSCs-GSE groups) were evident on neovascularization (VEGF), and Type II collagen levels compared to other groups (ADMSCs-GSE vs ADMSCs-LLLT-GSE; LLLT-GSE vs ADMSCs-LLLT; LLLT-GSE vs ADMSCs-GSE; GSE vs ADMSCs-GSE) ($p \leq 0.05$). However, neither ADMSCs nor LLLT affected new bone formation [LLLT group vs ADMSCs-GSE group, ($p>0.05$)]. Comparisons of the triple combination group (ADMSCs-LLLT-GSE group) with LLLT-GSE group indicated that the addition of ADMSCs increased new bone formation ($p \leq 0.05$), but had no visible effect on the number of osteoblasts ($p>0.05$). Osteoblast formation was high in all stimulant combinations, and the increase in the triple combination group was not statistically different.

GSE did not increase the effect of LLLT or ADMSCs for any of the four parameters being examined (ADMSCs-LLLT vs ADMSCs-LLLT-GSE; ADMSCs-GSE vs ADMSCs-LLLT; LLLT vs LLLT-GSE; GSE vs LLLT groups) ($p>0.05$). When applied together, ADMSCs and LLLT proved more effective than a single GSE administration (GSE vs ADMSCs-LLLT; GSE vs ADMSCs-LLLT-GSE groups) ($p<0.001$). ADMSCs and GSE together were very effective; they even increased the effectiveness of LLLT on all parameters, although new bone formation was slightly lower than the increase in the other three parameters. (Appliance vs ADMSCs-GSE; LLLT vs ADMSCs-LLLT-GSE groups). When applied together, LLLT and GSE were more effective compared to an appliance only (Appliance group vs LLLT-GSE group) ($p \leq 0.05$); but not compared to single LLLT or single GSE administration (LLLT vs LLLT-GSE; GSE vs LLLT-GSE groups) ($p>0.05$).

DISCUSSION

Many studies have contributed to our knowledge of condylar growth stimulation in rats, including an increase in the number of osteoblasts and new bone formation in the condyle, increased growth potential of the mandible,[8,9,21] an increase in neovascularization,[22] and Type-II collagen expression.[2] These findings are consistent with with the results of this study and support the deduction that osteoblast formation, new bone formation, VEGF, and Type-II collagen might be enhanced with the active advancement of the lower jaw in rats. Different combinations of ADMSCs, LLLT and GSE in addition to appliance use, increased these findings to varying degrees. While the increases due to the use of LLLT and GSE alone or together, did not reach statistically significant levels, the highest statistically significant increases were seen in the groups administered with ADMSCs. These results lead us to assume that appliance use, LLLT or GSE, can activate ADMSCs, which in turn, increases chondroblastic and osteoblastic activity.

Transformation of ADMSCs into osteoblasts and chondroblasts can increase bone and cartilage production.[10] Additionally, ADMSCs can increase vascularization.[9] Similarly, in this study, the number of osteoblasts increased significantly in all ADMSC groups. In order for to the ADMSCs to be activated and able to differentiate, they must be stimulated. They remain in a non-proliferative silent phase until they are activated by stimulatory signals initiated by remodeling forces or tissue damage, which prompts them to differentiate into the desired cell type for repair and remodeling.[23] The effects of intra-articular injection of ADMSCs combined with low-intensity pulsed ultrasound on developing rats increased the growth of the mandibular condyle according to CBCT and histological analyses. This change was not significant when ADMSCs were applied alone.[24] Therefore, in this study, ADMSCs were not administered alone, but rather in combination with a functional appliance, LLLT and GSE to achieve activation of ADMSCs.

Current studies indicate that LLLT increased osteoblast differentiation and cellular proliferation, as well as collagen deposition,[25] leading to new bone formation.[5,12] Based on these findings, LLLT is expected to increase bone and cartilage formation, promoting faster and more permanent remodeling of bone during orthodontic treatment.[26] Therefore, different protocols for LLLT application have been reported in the literature. The safe dose range for LLLT applications is known as 6-10 J/cm^2.[27] In this study, an 8 J/cm^2 protocol was selected as it fell within the middle of the safe dose range reported in the literature.[4,8] However, in this study, the increase in four parameters using LLLT and appliance, was not statistically significant. This may be attributed to differences in doses and methods used between studies, as well as the short duration, terminating the experiment at an early stage of bone formation. Nevertheless, the addition of LLLT to the ADMSCs-GSE combination managed to increase VEGF and Type-II collagen levels.

Some studies that investigated the effects of LLLT on ADMSCs, with some reporting a bio-stimulatory effect of LLLT on ADMSC proliferation under favorable conditions,[28] while others failed to confirm this synergic effect.[29] In the present study, the use of LLLT combined with ADMSCs resulted in increased levels of all parameters. These findings suggest that the application protocols for LLLT and ADMSCs may have an impact on the outcomes obtained.

The administration of GSE has been shown to induce bone formation, accelerate osteoblast differentiation, increase the amount of cortical bone and mineral content of trabecular bone,[30] particularly in the condyle,[15] when combined with dietary calcium.[15,30] It is believed that proanthocyanidin is responsible for inhibiting bone resorption by inhibiting proteolytic enzyme activity.[31] In this study, GSE was systemically administered, and while its use in combination with the appliance increased the effect on all parameters in the condyle, the increase was not statistically significant. It is possible that differences in methodology may have a greater impact on the results than anticipated.

Study Limitations

A limitation of this study was the absence of a single ADMSC group. This decision was based on previous studies that demonstrated that ADMSCs are not effective without an external stimulant and to avoid increasing the number of animals used in the study.

Another potential limitation of this study is the relatively short duration of the experiment, which may have been insufficient to fully evaluate new bone formation. In future studies, longer durations could be considered to more thoroughly evaluate the effects of the interventions on bone formation. Additionally, more accurate methods such as micro-CT could be used to evaluate new bone formation in a more precise manner.

The results of the present study suggest that the combination of all three stimuli (appliance, LLLT and GSE) resulted in the most effective activation of ADMSCs. The triple group demonstrated the highest statistically significant increase in new bone formation, VEGF and Type-II collagen. ADMSCs appear to be a promising cell source for osteogenic, chondrogenic and vascular tissue generation. However, further animal studies are necessary before clinical application can be considered.

Based on the results of the present study, it is believed that vascularization could be enhanced with various combinations interventions, resulting in increased bone formation in a shorter time in the condyle. These clinical interventions may compensate for factors that prolong the treatment period, leading to more successful outcomes in a shorter time, reducing the need for patient cooperation and increasing the comfort of both the patient and physician.

CONCLUSION

The data obtained from this study suggest that the effects of LLLT, and GSE on the action of ADMSCs in functionally induced condylar growth were significant. The combined use of these stimulants showed the greatest synergy in terms of their effects on condylar growth, including the amount of new osteoblast and bone formation, condylar vascularization, and Type-II collagen.

Ethics

Ethics Committee Approval: Ethical permission was obtained from the Manisa Celal Bayar University Ethics Committee of Experimental Animal Use and Research Scientific Committee (approval no: 71, date: 22.11.2016).

Informed Consent: Animal experiment study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - M.N.E.; Design - M.N.E.; Data Collection and/or Processing - M.N.E., I.A., M.İ.T.; Analysis and/or Interpretation - A.G., I.A.; Literature Review - A.G.; Writing - M.N.E.; Critical Review - A.G.

Declaration of Interests: The authors have no conflicts of interest to declare.

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Original Article

Factors Affecting Patient Compliance during Orthodontic Treatment with Aligners: Motivational Protocol and Psychological Well-Being

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Main Points

- The psychological profile of individuals did not correlate with their compliance throughout the treatment, but the psychological well-being (PWB) questionnaire showed higher scores after 12 months of CA.
- The motivational protocol used in a group of adult patients already willing to improve their smile with clear and removable aligners did not show significant differences in treatment progress.
- The clinical progress evaluated both on gypsum casts and on digital clin-check demonstrated the efficacy of CA in patients with good adherence to treatment.

ABSTRACT

Objective: Compliance is critical for successful outcomes in orthodontics, and personality traits may play a role in determining patient adherence. This study aimed to monitor compliance during treatment with removable clear aligners (CA) [Align Technology Inc, San José, Calif], and evaluate the influence of motivational techniques and the patient's profiles assessed through the psychological well-being (PWB) questionnaire on clinical outcomes.

Methods: Thirty-nine consecutive patients in permanent dentition seeking treatment with CA were recruited from two universities. Casts were obtained before treatment and after 3, 6, and 12 months and the corresponding digital Clincheck©.STL files were used to calculate the discrepancy index to check for differences between virtual and real treatment stages. Patients were divided into two groups: the Case group, which received motivational techniques at each appointment, and the control group which received instructions only at the beginning. Psychological profiles were evaluated before treatment (T0) and after 3 (T1), 6 (T2), and 12 (T3) months.

Results: There were no differences between the Case and Control groups regarding the use of motivational reminders. The analysis of the PWB showed that almost all values increased, and there was a strong correlation between dental casts and correspondent. STL files at every time point. The PWB showed increased values from T0 to T3 in the sample.

Conclusion: Motivational techniques did not affect patient compliance, and treatment outcomes were achieved as planned. The PWB of all patients improved throughout the treatment with CA.

Keywords: Clear aligners, compliance, patient adherence, psychological well-being, motivational techniques, quality of life

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INTRODUCTION

Nowadays, malocclusion has a negative impact on people's quality of life, social interactions, and self-esteem[1,2] as well as on oral biological conditions and functions.[3,4] The increasing demand for orthodontic treatment in young adults, particularly women, is mainly due to their greater concern for aesthetics over dental health.[5-7] Orthodontic appliance designs also influence the judgments of adolescents, and comfort with the appliances seems to be one of the major factors in increasing treatment acceptance.[8,9] Patients treated with fixed orthodontic appliances report a more intense decrease in functional and psycho-social aspects of their daily lives, so they are more likely to accept removable clear aligners (CA) to avoid tooth soreness, mucosal irritation, esthetic and speech disturbances, as well as possible plaque accumulation and gingivitis that can be induced by fixed labial or lingual multibracket appliances.[10-12] The virtual diagnostic setup, provided before starting treatment, represents a useful consultation device to verify compliance and to show both improvements and the limits of the treatment to each patient. However, there may be some discrepancies between the digital setup and the effective clinical predictability.[10-13] Nevertheless, high compliance throughout the treatment remains the main critical benchmark for successful outcomes.[11-14]

In previous studies, it has been hypothesized that personality traits might partly determine the patient's adherence during orthodontic treatment.[15-18] Thus, understanding a subject's well-being before starting orthodontic treatment with CA may be clinically relevant.[19,20] Over the past few decades, researchers have developed a questionnaire to evaluate orthodontic treatment needs and outcomes in terms of oral health-related quality of life (OHRQoL). The Oral Impact on Daily Performance is one of the most widely used indicators to measure oral impacts. It assesses the impact of oral conditions on basic activities and behaviors that covers the physical, psychological, and social dimension of daily life.[21] However, only a few researchers have focused on the oral impacts of CA on daily performance in adults.[22,23] Nowadays, people of all ages search for information on CA treatment through web and social media, which have become the most commonly used marketing tools.[10,24,25] To improve patient compliance, the integration of new technologies can be considered as an effective solution due to their wider use among the whole population. The use of an app-based approach has shown positive effects in a sample of adolescents.[26]

Some researchers have reported that the use of motivation protocols during an orthodontic treatment can have a positive influence on patients' compliance and feelings.[27] For example, Noll et al.[28] analyzed users who liked to show great smile through selfies along with expressing high gratitude for the clinicians. A recent paper showed a consensus between clinicians and patient son the type of outcomes, that are important to be measured in orthodontic studies. Among the final core outcome sets identified, three were involved in this research strengthening the study rationale: the impact of self-perceived aesthetics, alignment, and patient-related adherence.[29] Currently, the treatment with aligners is the most affected by the patient's compliance and motivation.

Thus, the primary research questions were:

1) Does the use of motivational protocol influence patient adherence in CA treatment?

2) Does the patient's psychological profile, assessed through the psychological well-being (PWB) questionnaire, affect patient compliance?

A secondary objective was to evaluate whether the treatment outcomes measured on digital casts corresponded to the digital planning at different time points. The null hypotheses are represented by the improvement in patient compliance during CA treatment due to the use of motivational techniques and by a positive relationship between the patient's psychological profile and the related compliance during treatment evaluated by the outcomes on dental casts compared with the planned movements with the software.

METHODS

For this prospective study, consecutive patients seeking orthodontic treatment at the Orthodontic Program of the University of Campania Luigi Vanvitelli, and at the Orthodontic Division of the University of Turin, Italy, were selected from July 2017 to October 2019 using the following inclusion criteria:

- Full permanent dentition except for the third molars;

- Mild-to-moderate dental crowding with American Board of Orthodontics (ABO) Discrepancy index (DI) <30;

- Initial dental casts, panoramic and lateral skull radiographs of good quality;

- The ability to communicate in Italian based at least on primary education;

- Patient's approval for orthodontic treatment with CA without extractions.

Subjects with syndromes and/or craniofacial malformations, periodontal diseases, temporomandibular joint disorders,[30] history of previous orthodontic treatment, certified mental disorders, and chronic use of psycho-drugs, were excluded.

Approval for this study was granted from the Institutional Ethics Committee of the University of Campania Luigi Vanvitelli, Italy (approval number: 437, date: 24.07.2017). Informed consent was obtained from each adult patient or minor patient's parents before being involved in the study, after a detailed explanation of the research protocol.

Treatment and Study Protocols

Before beginning the treatment, the investigators measured the ABO DI using the initial printed dental casts, panoramic radiograph, and lateral skull radiograph of each patient.[31] The investigators were trained and calibrated beforehand to ensure the accuracy on the measurements. The ABO DI was used to grade only the pre-treatment digital casts with a numeric value correlated with the severity of both dental and skeletal craniofacial problems of each subject. Cephalometric analysis was performed using digital software (Viewbox 3.0. Dhal Software, Kifissia, Greece). Ten variables, 7 angular and 3 linear, were generated for each tracing. The enlargement factor was standardized to 0% (life size). All patients included in the study were treated with Invisalign (Align Technology, San José, CA, USA). Two trained orthodontists used the ClinCheck© software (Align Technology, San José, CA, USA) to design treatment plans. Every virtual setup was then revised by a third specialist to ensure a similar treatment approach was applied in the selected cases.

The patients were randomly assigned to two groups using online software to arrange the items of a list in a randomized order (www.randomizer.org). The first group, called Case, was composed of 20 subjects (10 females and 10 males, mean age 25±14 years) who received appropriate instructions on the use of aligners at each appointment (wear the aligners 22 hours per day, 7 days per week), and motivational and reminder text messages were sent twice a week by the doctor. The content of the text message included, for example, "Please, remember your aligners!", "Are you wearing your aligners right now?", "Let's enjoy your Invisalign!", "Keep smiling with your Invisalign!", "Cheer up and smile with clear aligners!".

The second group, called Control, was composed of 19 patients (10 females and 9 males, mean age 21±9 years) who were provided with verbal instructions about CA use only during the appointment in which the appliance was delivered.

After 3, 6, and 12 months, new dental casts were collected for each patient. The corresponding .STL files for each stage of treatment were extracted from the virtual setup and the list of patients and corresponding ClinCheck© stages were asked to Align Technology technicians who were randomly and anonymously assigned to this research project. The .STL files were emailed to the university responsible for the treatments. The patients, the investigators who calculated the ABO DI at different time points, and the data analysts were blinded to the group to which each subject was allocated. To evaluate treatment efficacy at the three-time points, only the dental DI was calculated on the conventional and printed models to avoid the need for further X-rays.[32] After 15 days, 30% of casts were remeasured to confirm measurement reproducibility.

PWB Questionnaire

The evaluations of the psychological profiles were collected before treatment (T0) and after 3 (T1), 6 (T2), and 12 (T3) months of CA treatment. The evaluations were based on a questionnaire that utilized the Italian version of Carol Ryff's PWB scales, which were used to analyze the psychometric characteristics.[33,34] The PWB is an 84-item self-rating inventory, consisting of six scales that represent the six dimensions of PWB: self-acceptance, autonomy, environmental mastery, personal growth, purpose in life, and positive relations. Participants were asked to rate their adherence to each item on a six-point Likert scale, with 1 indicating "strongly disagree" and 6 indicating "strongly agree".

The questionnaire was delivered in the university centers by the same two operators who explained the easy instructions to the patients and facilitated its completion on the same appointment. The total score for each dimension represented in the PWB questionnaire is calculated by adding together the degrees of agreement of each item, resulting in a score that potentially varies from 14 to 84. The overall values of the six scales could range from a minimum score of 84 to a maximum of 504. The effect of the PWB questionnaire on patients' compliance was evaluated indirectly through the evaluation of the treatment outcomes at different time points.

Statistical Analysis

Statistical analyses were conducted using the R statistical package (version 3.5.3, R Core Team, Foundation for Statistical Computing, Vienna, Austria). The normality assumption of the data was evaluated with the Shapiro-Wilk test. Multiple regression analysis was performed to estimate the differences at follow-up in the total sample, as well as in the Case and Control group. Three outcomes were considered for the statistical analyses: the cast models, the .STL files of dental models derived from Align Technology ClinCheck© software, and the PWB questionnaire responses at T0, T1, T2 and T3. The estimate of the regression model explains the mean difference (MD) i) between follow-up in all sample analyzes, and ii) between groups for the case-control comparisons. Tukey's multiple comparisons of means with a 95% family-wise confidence level and adjusted P value were considered, with a level of significance set at 0.05. Descriptive tables show the distribution of data. Spearman's correlation was used to evaluate the relationship between the three outcomes. Multiple regression analysis was also performed to estimate the differences at follow-up between the Case and Control groups to check for differences due to the motivational protocol.

The sample size was calculated a priori to obtain a statistical power of the study greater than 0.80 with an alpha of 0.05. The sample size calculation indicated that 16 participants were needed to reach an 80% power for considering differences between the group and during the follow-up, with T statistic and non-centrality parameters with the aim to detect an effect size ≥0.03 considering an average variation of the thickness related to the expected value and a standard deviation of 0.03.

RESULTS

The mean age in all samples was 22.6±2.7 years of age, and no statistical differences in age and gender were detected between the Case and Control groups. The results for intra-rater reliability, assessed with the Spearman rho correlation coefficient, showed an excellent agreement (r>0.8) for all performed measurements. Data before treatment showed no differences between the dental cast and the .STL digital models in all samples (Tables 1 and 2). Statistical significance was found on the DI measured at different time points compared to the baseline T0 and to T1 (after 3 months), with a decreased value as expected during CA treatment, in the whole sample (Tables 1 and 2).

Questionnaire scores increased from T0 to T3, and differences in the samples were similar at all time points analyzed (Table 3).

No significant statistical differences were found between the Case and Control groups in the evaluations of the collected records after 3, 6, and 12 months of CA treatment (Figures 1-3).

DISCUSSION

This study focused on adults due to the higher impact of their smile display on their social and professional life.[8,9] A recent scoping review evaluated the impact of poor dental appearance on employability and the potential enhancement in employment outcomes after dental treatment in adults.[35] This study assessed a "hot topic", and the responses to the different research questions provided high-impact outcomes for daily clinical orthodontic practices.

Table 1. Regression model: differences of DI measured on gypsum casts at different time points in all sample

	MD	95% CI	Adjusted p value
T1-T0	-5.03	-8.86 | -1.19	0.004*
T2-T0	-8.25	-12.08 | -4.41	0.008*
T3-T0	-10.31	-14.14 | -6.47	0.000*
T2-T1	-3.21	-7.05 | 0.61	0.132
T3-T1	-5.28	-9.11 | -1.44	0.002*
T3-T2	-2.06	-5.89 | 1.77	0.500

*p<0.05
MD, Mean differences; T0, Baseline; T1, After 3 months; T2, After 6 months; T3, After 12 months; CI, Confidence interval; DI, Discrepancy index

Our results indicated that the individual's psychological profile did not have a significant correlation with their compliance throughout the treatment. This is consistent with the findings of Bos et al.[15], who suggested that patients' personality characteristics could not be used to predict their compliance.

Thus, the previous studies that hypothesized that personality traits analyzed through different psychological scales could affect a patient's adherence to the prescribed orthodontic treatment were not confirmed in our study.[36,37] However, the PWB questionnaire showed higher scores after 12 months of CA in most cases, emphasizing the importance of facial and smile

Table 2. Regression model: differences of DI measured on printed casts at different time points in all sample

	MD	95% CI	Adjusted p value
T1-T0	-1.37	-5.41 | 2.66	0.812
T2-T0	-2.96	-7.01 | 1.07	0.228
T3-T0	-5.40	-9.45 | -1.36	0.003
T2-T1	-1.59	-5.63 | 2.45	0.734
T3-T1	-4.03	-8.07 | 0.01	0.051
T3-T2	-2.43	-6.48 | 1.60	0.399

*p<0.05
MD, Mean differences; T0, Baseline; T1, After 3 months; T2, After 6 months; T3, After 12 months; CI, Confidence interval; DI, Discrepancy index

Table 3. Regression model: Differences of PWB Questionnaire values at different time points in all sample

	MD	95% CI	Adjusted p value
T1-T0	4.62	-22.70 | 31.95	0.971
T2-T0	7.00	-20.32 | 34.32	0.909
T3-T0	13.15	-14.17 | 40.48	0.593
T2-T1	2.37	-24.95 | 29.70	0.995
T3-T1	8.53	-18.79 | 35.85	0.848
T3-T2	6.15	-21.17 | 33.48	0.935

*p<0.05
MD, Mean differences; T0, Baseline; T1, After 3 months; T2, After 6 months; T3, After 12 months; CI, Confidence interval; PWB, Psychological well-being

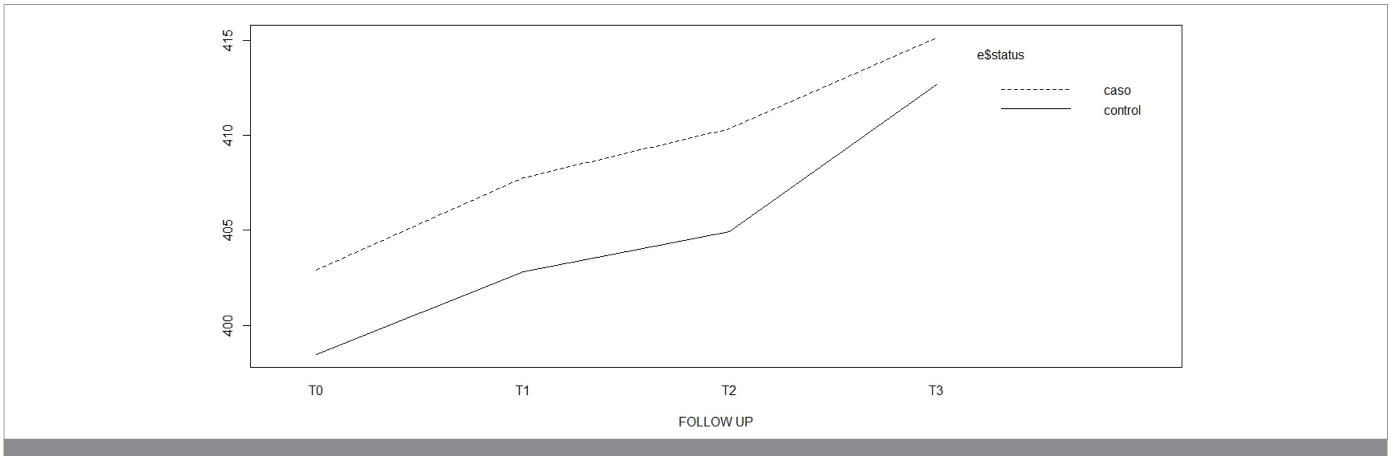

Figure 1. Psychological Well-being questionnaire scores between the Case (dashed line), and Control (continuous line) groups at T1, T2, and T3 (after 3, 6, and 12 months, respectively)

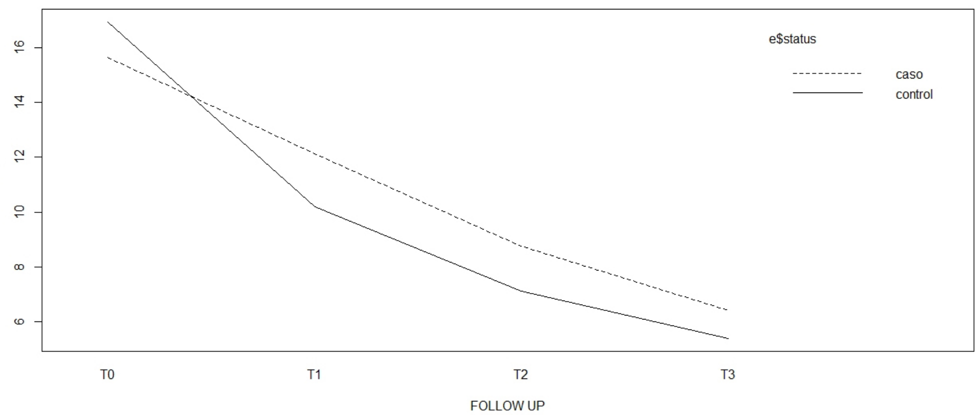

Figure 2. Gypsum cast Discrepancy Index between the Case (dashed line), and Control groups (continuous line) at T1, T2, and T3 (after 3, 6, and 12 months, respectively)

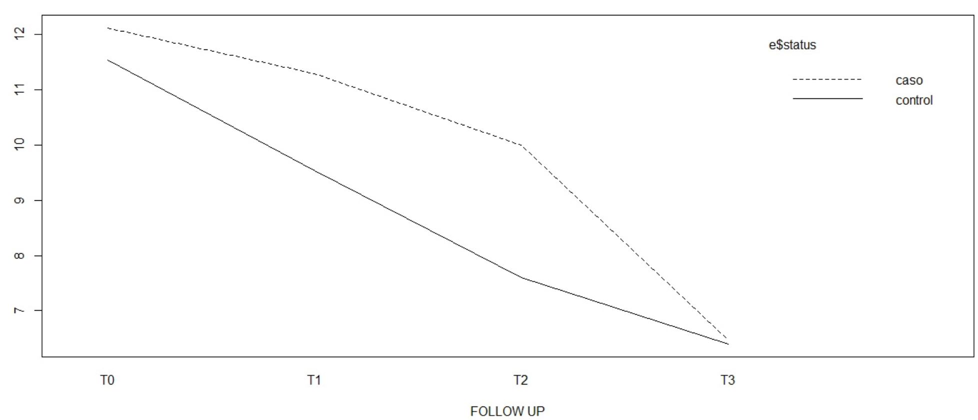

Figure 3. Printed cast Discrepancy Index between the Case (dashed line), and Control (continuous line) groups at T1, T2, and T3 (after 3, 6, and 12 months, respectively)

esthetic improvement related to a better quality of life for these patients. It was reported that for each of the six dimensions of the PWB representing the quality of life, an increasingly positive impact was reported at different times. In particular, the dimensions of self-acceptance and environmental controls were strongly associated with life-satisfaction measurements.

Agou et al.[19] demonstrated that better PWB in children was associated with better OHRQoL regardless of their orthodontic status. However, our data did not support this finding, possibly due to our sample including adolescents and adults, with a mean age of 22 years, who were seeking a specific esthetic treatment with CA.

The motivational protocol used in our Case group did not show significant differences in the treatment progress. The explanation may be the inclusion of adult subjects, who were already motivated to improve their smile with clear and removable appliances. Thus, the desire to straighten teeth and improve the esthetic smile seems to be a primary motivating factor for adults seeking orthodontic treatment, especially with the frequent use of digital social media. This may be a limitation of the study as it did not consider the importance of motivation and encouragement throughout the treatment, which is often highly crucial in younger patients. Communication between orthodontists and their patients should be considered a vital part of achieving patient adherence and satisfaction with treatment.[6] Finally, the satisfactory agreement between the clinical progress evaluated on gypsum casts, and the digitally prescribed models, demonstrated the efficacy of CA when there is good patient adherence to treatment.

Moreover, looking at a recent literature review,[38] deeper knowledge of the orofacial pain felt with CA versus fixed orthodontic treatment would be clinically interesting. Future research may include a larger sample and further evaluation at the end of treatment to obtain more information on the long-term impact of orthodontic treatment with CA.

CONCLUSION

The clinical progress evaluated on gypsum dental casts was comparable to those digitally prescribed before treatment, demonstrating the good adherence of all patients in wearing CA. The patients' compliance seeking orthodontic treatment with CA seems to be unaffected by motivational techniques delivered twice a week during treatment. The well-being questionnaire from all patients already showed high values at baseline that further improved throughout the treatment. However, no correlation between well-being values and compliance was found, as no differences were revealed in the treatment efficacy.

Ethics

Ethics Committee Approval: Approval for this study was granted from the Institutional Ethics Committee of the University of Campania Luigi Vanvitelli, Italy (approval number: 437, date: 24.07.2017).

Informed Consent: Informed consent was signed by each adult patient or minor patient's parents before being involved in the study after a detailed explanation of the research protocol.

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Original Article

Interobserver and Intraobserver Reliability of Cephalometric Measurements Performed on Smartphone-Based Application and Computer-Based Imaging Software: A Comparative Study

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Main Points

- The study compared interobserver and intraobserver reliability for cephalometric evaluation between smartphone-based applications (OneCeph®) and computer-based software (Dolphin imaging software®).
- Good to excellent reproducibility and repeatability of cephalometric evaluation seen with OneCeph, which is comparable to Dolphin software.
- OneCeph took double the time compared with Dolphin imaging software.

ABSTRACT

Objective: The aim was to compare the reliability of cephalometric analysis using a smartphone-based application with conventional computer-based imaging software.

Methods: Pre-treatment cephalometric radiographs of 50 subjects (26 males, 24 females; mean age, 19.2 years; ±4.2) were traced using the OneCeph® application and Dolphin imaging software®. Two independent observers identified seventeen landmarks and measured fourteen cephalometric measurements at an interval of. Interobserver and intraobserver reliability were evaluated using the intraclass correlation coefficient. Student's t-test was used to compare the means of two measurement methods for observer 1 and observer 2. Additionally, the time taken to complete the cephalometric measurements was also compared between the two methods.

Results: Good (ICC 0.75-0.90) to excellent (ICC 0.90-1.00) interobserver and intraobserver reliability was observed for all hard and soft tissue measurements with both methods. No significant differences were found between the two measurement methods for both observers ($p<0.05$). OneCeph application took significantly more time to complete the analysis than Dolphin imaging software ($p<0.001$).

Conclusion: Cephalometric measurements made through a smartphone-based application showed good to excellent interobserver and intraobserver reliability and are comparable with the computer-based software. Therefore, it can be recommended for clinical use. The time taken to complete the cephalometric measurements was more with a smartphone-based application (OneCeph application) compared to computer-based software (Dolphin imaging software).

Keywords: Cephalometrics, Reliabiity, OneCeph, Dolphin

INTRODUCTION

Evaluating and assessing dental malocclusion and underlying skeletal abnormalities require cephalometric radiography, which is widely used in orthodontics. However, the procedure is time-consuming and prone to various errors. Technical measures, radiography acquisition, and identification landmarks are some of the most

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common sources of inaccuracies in cephalometric radiography. In recent years, many computer-based cephalometric software programs have been introduced into the market. Clinicians and researchers have successfully adopted them, and they have been in use for the past two decades. Numerous studies have tested the consistency and reliability of Dolphin imaging software® (Dolphin Imaging and Management Solutions, Chatsworth, California, USA), which is considered almost a gold standard in the field.[1-4]

The advancement of technology has brought about the advent of the smartphones and their applications, leading many professionals to spend more time on them. Recently, mobile technology has evolved at par with computers with applications designed to mimic computer operations. Some smartphone-based applications have been developed for cephalometric analysis, allowing for easy access to various analyses at anytime. Promising results from recent research on smartphone-based applications have encouraged further investigation into their effectiveness.[5-9] Nevertheless, digital or smartphone applications should be designed to reduce the workload of orthodontists.

Livas et al.[7] assessed the diagnostic accuracy of two smartphone-based cephalometric analysis apps and found good to excellent reliability compared with the Viewbox software (Viewbox 4, dHAL Software, Kifissia, Greece). Another study compared the reliability of the OneCeph application® (version beta 1.1, NXS, Hyderabad, Telangana, India), a smartphone-based application, with the conventional hand tracing method and concluded that both methods can be used with good reliability.[8] Similarly, a study conducted on a smartphone-based app showed that most cephalometric parameters are comparable with the Dolphin Imaging software.[9] However, although smartphone-based apps have been used for quite some time, a robust study evaluating interobserver and intraobserver reliability is still lacking. None of the above studies have estimated the efficiency of cephalometric analysis in terms of time taken to complete the analysis.

This study aimed to compare the interobserver and intraobserver reliability of a smartphone-based application (OneCeph application) with the standard computer-based software (Dolphin imaging software). Our secondary objective was to compare the time required to complete the cephalometric analysis between the two methods. The null hypothesis was that there would be no significant difference in the interobserver and intraobserver reliability of the Dolphin imaging software and the OneCeph application.

METHODS

In this cross-sectional study, pre-treatment lateral head cephalograms were drawn from the archives of the Orthodontics Division, Department of Dentistry, All India Institute of Medical Sciences Jodhpur, between January 2016 and December 2018. The study received approval from Institutional Ethics Committee AIIMS Jodhpur (AIIMS/IEC/2018/689) Rajasthan, India..

A total of 50 pre-treatment standardized digital lateral head cephalograms were selected from healthy patients without any history of systemic diseases (26 males and 24 females), with a mean age of 19.2±4.12 years. The cephalograms were obtained using a standardized machine (NewTom GiANO CEFLA-SC, Cella Dental Group, Italy) in a natural head position. Only good-quality cephalograms without any artifacts were included for the study. Cephalograms on which landmarks could not be identified due to motion, resolution, or lack of contrast were excluded. Radiographs that did not show good superimposition of bilateral anatomical structures about the mid-sagittal plane were not included. Additionally, subjects with gross asymmetry, and craniofacial deformity were excluded.

Cephalometric Measurements

The lateral head cephalograms were imported into the semi-automated analysis software. For Method 1, Dolphin Imaging software® (Version 11.7, Chatsworth, California, USA) was installed on a Hewlett-Packard laptop (HP EliteBook Folio 9470m) with Windows 7 Professional (Service Pack 1) and an integrated Intel HD graphics 4000 chip. A14-inch HD Anti-glare SVA LED panel (Hewlett-Packard Company, Core i5, 8GB RAM, Graphics 2GB) was used as the output. Landmarks were identified manually within the software using a cursor (input). For Method 2, OneCeph application® (version beta 1.1, NXS, Hyderabad, Telangana, India) was downloaded from Google Play Store (Google Inc, Mountain View, Calif) on a OnePlus android smartphone with a 6.41-inch touch-screen (OnePlus 6T, Android 8, 6 GB RAM). Landmark identification was made manually using the index finger on the touch-screen and refined by repositioning it within the application. Each cephalogram was calibrated, and 17 digital landmarks were identified (Figure 1). A total of 14 parameters (nine angular and five linear) were chosen for measurements, including the commonly used skeletal, dental, and soft tissue parameters (Table 1). Figure 2 illustrates the linear and angular measurements used in the study.

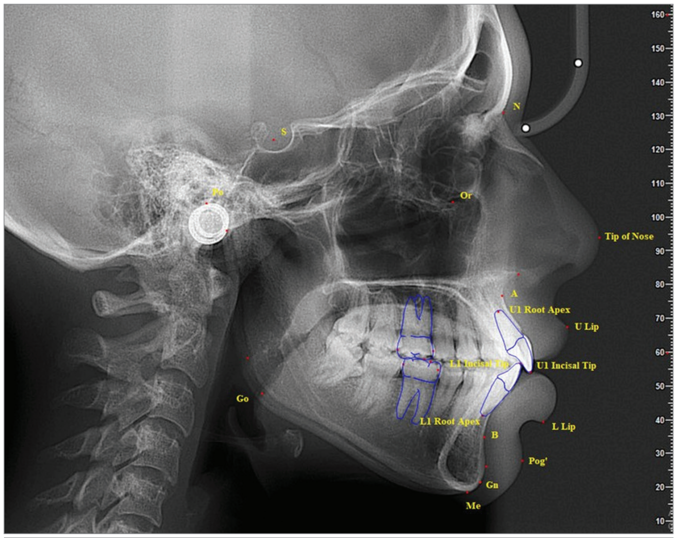

Figure 1. Cephalometric landmarks used in the study

Additionally, the time taken to complete all the measurements was recorded in minutes with the using a stopwatch. After importing the cephalogram in each software, time taken was recorded from the start of the analysis to the completion of all the measurements. An assistant not involved in the study operated the stopwatch, and he was blinded to the measurement being made.

Interobserver Reliability

Two orthodontists (observer 1; SP & observer 2; NKB) with more than three-year experience performed all measurements on fifty lateral cephalograms. To calculate interobserver reproducibility, the first measurements of observer 1 were compared with the first measurements of observer 2.

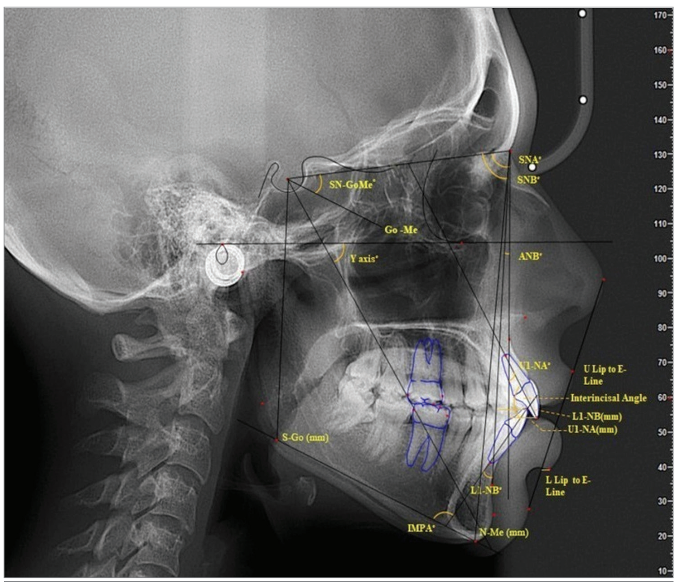

Figure 2. Linear and angular measurements used for two different measurement methods.

Before performing the cephalometric measurements, each orthodontist underwent a one-hour training session to become familiar with the use of the software and the method for make cephalometric measurements. Measurement periods for every session were set to one-hour to prevent operator fatigue. The study was initiated only after both observers demonstrated their ability to perform the cephalometric measurements independently using both software independently. All cephalometric radiographs were assigned a unique number in a list that did not follow any specific sequence. The images were randomized, and their order was blinded. Observer 1 was blinded to the measurements made by Observer 2 and vice-versa to ensure reproducibility.

Intraobserver Reliability

For the intraobserver reliability calculation, both observers' measurements were used. Thirty cephalograms were randomly selected and measured by two observers using both methods. An interval of at least four weeks between the repeated measurements (repeatability) was used.

For calculating time required to perform the cephalometric measurements, the first measurements by observer 1 and observer 2 were timed.

Statistical Analysis

The sample size was calculated using a web-based sample size calculator for reliability studies developed by Arifin.[10] The minimum acceptable reliability was set as 0.75 and the expected reliability was set as 0.90, which was observed for most variables according to the study by Livas et al.[7] With 90% power and a significance level of 95%, the minimum sample size needed per group was calculated to be 44. Fifty cephalograms per group were included to increase the power of the study.

Table 1. Linear and angular variables used in the study

Landmarks and variables	Definition
SNA (degree)	Anteroposterior position of the maxilla relative to the anterior cranial base
SNB (degree)	Anteroposterior position of the mandible relative to the anterior cranial base
ANB (degree)	Differences between the SNA and SNB angles
Mandibular plane angle (SN-Go Gn) (degree)	Angle between the sella turcica-nasion (SN) line and the mandibular plane (Go-Gn)
Jarabak ratio (S-Go/N Me)	The ratio between total posterior and anterior facial heights (Sella-gonion and nasion-menton)
Y-axis (degree)	The angle between S-Gn and FH planes
U1-NA (degree)	The angle between the nasion-A point (NA) line and the long axis of the upper incisor
U1-NA (mm)	The linear measurement from the tip of the upper central incisor to the NA line
L1-NB (degree)	The angle between the nasion-B point (NB) line and the long axis of the lower incisor
L1-NB (mm)	The linear measurement from the tip of the lower central incisor to the NB line
Interincisal angle (degree)	The angle between the long axis of the maxillary incisors and the long axis of the mandibular incisors
IMPA (degree)	The angle between the long axis of the lower central incisor and the mandibular plane (tangent to the lower border of the mandible)
UL to E-line (mm)	The linear measurement from the most prominent point of the upper lip to Rickett's E line
LL to E-line (mm)	The linear measurement from the most prominent point of the lower lip to Rickett's E line

The statistical analysis was conducted using the Dahlberg[11] formula to calculate the method error of each method for all cephalometric measurements.The data was analyzed using the SPSS for Windows (Version 23.0, Armonk, NY: IBM Corp). Interobserver and intraobserver reliability were assessed using the intraclass correlation coefficient (ICC; two-way mixed-effects model, single measures, absolute agreement) and the 95% confidence intervals (CI). ICC values less than 0.5 were considered to indicate poor reliability, values between 0.5 and 0.75 indicated moderate reliability, values between 0.75 and 0.9 indicated good reliability, and values greater than 0.90 indicated excellent reliability.[12] The Student's t-test was used to compare mean differences and the time it has taken to complete all the measurements between the two methods. A p-value of <0.05 was considered significant.

RESULTS

The measurement error measured with the Dahlberg[11] formula for Method 1 ranged between 0.35 to 0.88 degrees for angular measurements and 0.31 to 0.60 mm for linear measurements. The measurement error for Method 2 ranged between 0.42 to 1.08 degrees for angular and 0.42 to 0.66 mm for linear measurements.

Table 2 shows the result of ICC values for interobserver reliability (reproducibility) of the two measurement methods. For method 1, interobserver reliability was classified as "excellent" (ICC value >0.90) for all measurements. For method 2, interobserver reliability was classified as "excellent" (ICC value >0.90) for all measurements except upper and lower lip to E-line, which was classified as "good" (ICC value 0.75-0.90) reliability.

Tables 3 and 4 demonstrate the results of the intraobserver reliability (repeatability) for observers 1 and 2 using both measurement methods. For both the observers, the repeatability was classified as "excellent" (ICC value >0.90) for all measurements with methods made with 1 and 2 except for E-line to the upper lip and mandibular plane to SN, for which observer 1 showed "good" repeatability (ICC value 0.75-0.90).

The mean values of all cephalometric measurements using methods 1 and 2 are shown in Table 5. No significant difference was recorded with either observer 1 or observer 2 in performing the measurements using each method (p>0.05). A significant difference was observed in the time required to complete the cephalometric measurements between methods 1 and 2, with method 1 taking significantly lesser time (p<0.001) (Table 6).

DISCUSSION

This study showed excellent repeatability and reproducibility for hard and soft tissue measurements using Dolphin imaging software which is consistent with the findings of Kasinathan et al.[13], who reported higher reliability for hard tissue measurements using the same software. Compared to manual tracings, a high level of agreement (ICC >0.9) for cephalometric measurements has been reported with Dolphin imaging software.[14] It is known to have good intra-rater reliability for most cephalometric parameters and good inter-rater reliability for almost all parameters similar to this study.[15] The OneCeph application's measurements showed good to excellent reproducibility and repeatability for the cephalometric measurements. Previous studies have reported the OneCeph application to be reliable. However, most studies have used either the Pearson correlation

Table 2. The intraclass correlation coefficient for interobserver reliability of methods 1 and 2

Parameters (n=50)	Interobserver reliability			
	Method 1		Method 2	
	ICC (95% CI)	p value	ICC (95% CI)	p value
SNA	0.98 (0.96-0.99)	<0.001*	0.98 (0.96-0.99)	<0.001*
SNB	0.99 (0.99-0.99)		0.99 (0.97-0.99)	
ANB	0.99 (0.97-0.99)		0.99 (0.98-0.99)	
Sn-Go-Gn	0.99 (0.98-0.99)		0.99 (0.98-0.99)	
S-Go/N-Me	0.96 (0.89-0.98)		0.96 (0.90-0.99)	
Y Axis	0.98 (0.93-0.99)		0.96 (0.89-0.98)	
U1 to NA	0.99 (0.97-0.99)		0.84 (0.54-0.94)	
U1 to NA	0.99 (0.98-0.99)		0.99 (0.98-0.99)	
L1 to NB	0.99 (0.96-0.99)		0.98 (0.93-0.99)	
L1 to NB	0.98 (0.95-0.99)		0.98 (0.92-0.99)	
Interincisal angle	0.99 (0.86-0.99)		0.98 (0.87-0.99)	
IMPA	0.99 (0.97-0.99)		0.99 (0.98-0.99)	
E-Line UL	0.99 (0.98-0.99)		0.85 (0.49-0.95)	
E-Line LL	0.98 (0.95-0.99)		0.81 (0.44-0.94)	0.002*

*Statistical significance: p <0.05 ICC, Intraclass correlation was analyzed using a two-way mixed-effect model with absolute agreement
n, number of cephalograms; CI, confidence interval; Method 1, Dolphin software; Method 2, OneCeph application

coefficient or Student's t-test to the measure the reliability, which is an inaccurate method.[16,8] Livas et al.[7] reported the high validity of the OneCeph application with computer-based software using ICC. However, they did not investigate the Dolphin imaging software in their study.

Good reproducibility in upper and lower lip to E-line measurement was observed with the OneCeph application. Aksakallı et al.[5] found significantly lower values concerning lower lip to E-line in smartphone applications compared to the Dolphin imaging software however, the application was not investigated in their study. Shettigar et al.[9] did not find any difference in the measurement of the lower lip to E-line between the two software although, they did not report on the interobserver and intraobserver reliability of the OneCeph application and Dolphin imaging software. It should be noted that the OneCeph application works on a smaller smartphone screen and the absence of a contrast adjustment tool within the application may potentially affect the accurate identification of

Table 3. The intraclass correlation coefficient for intraobserver reliability of observer 1 using methods 1 and 2

Parameters (n=30)	Intraobserver reliability (Observer 1)			
	Method 1		Method 2	
	ICC (95% CI)	p value	ICC (95% CI)	p value
SNA	0.95 (0.87-0.98)	<0.001*	0.98 (0.95-0.99)	
SNB	0.95 (0.86-0.98)		0.99 (0.97-0.99)	<0.001*
ANB	0.99 (0.98-0.99)		0.99 (0.98-0.99)	
Sn-Go-Gn	0.99 (0.98-0.99)		0.79 (0.39-0.93)	0.003*
S-Go/N-Me	0.99 (0.99-0.99)		0.98 (0.91-0.99)	<0.001*
Y Axis	0.99 (0.98-0.99)		0.97 (0.91-0.99)	
U1 to NA	0.89 (0.55-0.96)		0.94 (0.84-0.98)	
U1 to NA	0.97 (0.85-0.99)		0.99 (0.98-0.99)	
L1 to NB	0.99 (0.99-1.00)		0.99 (0.98-0.99)	
L1 to NB	0.99 (0.99-0.99)		0.95 (0.85-0.98)	
Interincisal angle	0.97 (0.92-0.99)		0.99 (0.97-0.99)	
IMPA	0.99 (0.99-0.99)		0.99 (0.97-0.99)	
E-Line UL	0.98 (0.94-0.99)		0.80 (0.43-0.93)	0.002*
E-Line LL	0.99 (0.97-0.99)		0.91 (0.75-0.97)	<0.001*

*Statistical significance: p<0.05 ICC, Intraclass correlation was analyzed was analyzed using a two-way mixed-effect model with absolute agreement
n, number of cephalograms; CI, confidence interval; Method 1, Dolphin software; Method 2, OneCeph application

Table 4. The intraclass correlation coefficient for intraobserver reliability of observer 2 using methods 1 and 2

Parameters (n=30)	Intraobserver reliability (Observer 2)			
	Method 1		Method 2	
	ICC (95% CI)	p value	ICC (95% CI)	p value
SNA	0.99 (0.99-1.00)	<0.001*	0.97 (0.92-0.99)	<0.001*
SNB	0.99 (0.99-1.00)		0.98 (0.92-0.99)	
ANB	0.99 (0.99-0.99)		0.97 (0.92-0.99)	
Sn-Go-Gn	1.0 (0.99-1.00)		1.00 (1.00-1.00)	
S-Go/N-Me	0.96 (0.89-0.98)		0.99 (0.98-0.99)	
Y Axis	0.99 (0.98-0.99)		0.99 (0.90-0.99)	
U1 to NA	0.99 (0.99-0.99)		0.99 (0.99-1.00)	
U1 to NA	0.99 (0.98-0.99)		1.0 (0.99-1.00)	
L1 to NB	0.99 (0.99-1.00)		0.99 (0.99-1.00)	
L1 to NB	1.00 (1.00-1.00)		1.0 (0.99-1.00)	
Interincisal angle	0.99 (0.99-0.99)		1.0 (0.99-1.00)	
IMPA	0.99 (0.99-1.00)		1.0 (0.99-1.00)	
E-Line UL	0.99 (0.99-0.99)		0.99 (0.99-1.00)	
E-Line LL	0.99 (0.99-1.00)		0.99 (0.99-0.99)	

*Significant difference; p value <0.05 ICC, Intraclass correlation was analyzed was analyzed using a two-way mixed-effect model with absolute agreement
n, number of cephalograms; CI, confidence interval; Method 1, Dolphin software; Method 2, OneCeph application

soft tissue landmarks. While some landmarks can be refined in the application, there are limitations to adjusting the size and color of the landmark guide, which may reduce the precision of the identification of soft tissue landmarks.

Computer-based software allows not only the adjustment of the contrast of the cephalograms, but also provides users with a modifiable point cursor to locate the various landmarks with higher accuracy.

Dolphin imaging software offers various cephalometric analyses, as well as the ability to refine tracings of different structures. In contrast, the OneCeph application lacks advanced features of cephalometric superimposition, surgical treatment planning, and the ability to create STL files, or perform three-dimensional volume rendering. These limitations, along with the software's inability to conduct multiple analyses simultaneously, are significant drawbacks compared to the Dolphin software.

The overall reliability of the OneCeph application has been evaluated in multiple studies. However, most of them have only compared it with the manual tracing method.[7,8,17] This study is probably the first to report the method error, as well as the interobserver and intraobserver reliability of the OneCeph application. Only one study used Dolphin imaging software for comparison with the OneCeph application; however, they did not use a robust statistical method such as the ICC for reliability assessment.[9]

A significant difference in the time taken to complete the cephalometric measurements was found between the OneCeph application and Dolphin imaging software. It took nearly twice the time to complete the analysis compared to the Dolphin imaging software. This may be attributed to the small screen size of the smartphone, which makes landmark identification and marking more time-consuming with the OneCeph application as finger touch may not be as accurate as a cursor on a larger screen. Meriç and Naoumova[18] compared fully-automated, computerized, app-aided, and manual tracing in terms of time taken for tracing the landmarks and found that the shortest analysis time was obtained using CephX, followed by CephNinja and Dolphin, whereas manual tracing took the longest time. Since there is a significant difference in the speed of computers and smartphones, the performance of a computer is not only better but the landmark identification is also faster.

Both the software showed accuracy and reliability, although the Dolphin imaging software was faster. Dolphin imaging software provides more cephalometric evaluation features that may be added to smartphone-based applications in the future. However, it should be noted that measurements may vary depending on the screen size and specifications of the smartphone used. Nevertheless, smartphone-based applications are cost-effective, efficient, and readily accessible, making them an attractive option. The use of smartphone-based applications could play a vital role in cephalometric analysis in day-to-day practice, and

Table 5. Mean ± SD values of cephalometric measurement using Dolphin and OneCeph software for observer 1 and observer 2

Parameters (n=50)	Observer 1 (Mean ± SD)			Observer 2 (Mean ± SD)		
	Method 1	Method 2	p value	Method 1	Method 2	p value
SNA	82.5±4.56	82.7±4.59	0.836	82.3±4.42	82.2±4.25	0.940
SNB	79.1±4.45	79.3±4.58	0.806	79.3±4.97	78.9±4.55	0.823
ANB	3.5±4.66	3.5±5.12	0.974	2.8±5.26	3.2±4.72	0.882
Sn-Go-Gn	25.3±8.24	24.1±7.93	0.476	25.4±7.95	25.3±7.63	0.967
S-Go/N-Me	69.9±6.84	70.6±6.48	0.607	72.2±7.18	70.3±7.08	0.467
Y Axis	58.7±4.04	58.6±4.62	0.870	58.9±5.76	58.8±5.42	0.979
U1 to NA	7.4±3.93	6.9±3.88	0.547	6.6±3.18	6.4±3.36	0.795
U1 to NA	31.2±12.55	30.2±12.33	0.704	31.6±9.49	31.5±9.12	0.969
L1 to NB	6.8±3.65	7.9±8.59	0.424	6.7±3.58	6.8±3.76	0.941
L1 to NB	29.4±9.88	32.4±22.26	0.394	27.1±7.97	28.0±8.27	0.749
Interincisal angle	115.9±18.25	114.9±22.58	0.813	119.1±10.03	117.6±10.85	0.674
IMPA	101.0±10.22	99.5±16.18	0.575	100.0±9.09	98.9±9.38	0.750
E-Line UL	-2.67±3.17	-1.83±3.00	0.178	-3.61±3.24	-2.36±2.30	0.236
E-Line LL	0.05±3.28	-0.54±2.90	0.342	-0.20±3.12	-0.95±2.73	0.492

n, number of cephalograms; SD, standard deviation; method 1, Dolphin software; method 2, OneCeph application; analysis was done using Student's t-test; p value <0.05 was considered significant

Table 6. Comparison of the mean time taken to complete analysis by observer 1 and observer 2 using Dolphin and OneCeph softwares

Parameter (n=50)	Observer 1 (Mean ± SD)			Observer 2 (Mean ± SD)		
	Method 1	Method 2	p value	Method 1	Method 2	p value
Time taken (minutes)	1.4±0.76	2.4±0.45	<0.001*	1.5±0.61	2.6±0.33	<0.001*

n, number of cephalograms; SD, standard deviation; method 1, Dolphin software; method 2, OneCeph application; *Significant difference; analysis was performed using Student's t-test; p value <0.05 was is considered significant the findings of the current study indicate that their use may be advocated.

Study Limitations

Smartphones have different patterns of use, viewing positions, and distances from the eye compared to computers.[19] A recent study has shown that smartphones can aggravate subjective ocular symptoms, asthenopia and compromise tear film stability.[20] However, these aspects were not analyzed in this study. Another limitation of the study is that the time to complete the analysis was calculated after importing the cephalogram into the software from the start of analysis. The results may have been impacted if the time taken had been calculated from the import of cephalogram into the software to completion of the analysis.

CONCLUSION

The following conclusions can be drawn from the study:

- Both Dolphin imaging software and OneCeph application displayed good to excellent interobserver and intraobserver reliability for most cephalometric measurements.

- OneCeph application took nearly twice the time to complete the cephalometric measurements compared to Dolphin imaging software.

Ethics

Ethics Committee Approval: Ethical approval was obtained from the Institutional Ethics Committee, All India Institute of Medical Sciences Jodhpur, (AIIMS/IEC/2018/689) Rajasthan, India.

Informed Consent: Informed consent was obtained from all patients for orthodontic treatment.

Peer-review: Externally peer-reviewed.

Author Contributions

Concept - V.K.C., S.P.S.; Design - V.K.C., N.K.B.; Supervision - V.K.C., D.S.; Materials - S.P.S., R.S.; Data Collection and/or Processing - S.P.S.; Analysis and/or Interpretation - N.K.B., S.S.; Literature Review - N.K.B., D.S.; Writing - N.K.B., S.S.; Critical Review - V.K.C., D.S.

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Original Article

Evaluation of Orthodontic Treatment Method Preferences of Dentistry Students, Dentists and Orthodontic Residents

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Main Points

- Clear aligner was more preferred in terms of esthetics, advantage/disadvantage, health of the oral cavity, and short-term treatments, especially by orthodontic residents.
- Considering the success of treatment and long-term treatments, conventional metal brackets were preferred the most.
- Discrepancies in gender and income levels had little effect on treatment preferences.

ABSTRACT

Objective: The aim of this study was to evaluate orthodontic treatment method preferences among dentistry students, dentists and orthodontic residents taking into account factors such as esthetics, advantage/disadvantage, cost and treatment duration.

Methods: The study was carried out on three groups: dentistry students (n=318), dentists (n=110) and orthodontic residents (n=98), and a 17-question survey was applied. Questionnaire forms included informational photos of conventional metal brackets (CMB), esthetic ceramic brackets (ECB), self-ligating brackets (SLB), clear aligner (CA), and lingual brackets (LB). The participants' preferences for orthodontic treatment methods were evaluated using chi-square analysis, not only between groups but also considering gender and income level.

Results: Regarding esthetics, dentists (41%) and orthodontic residents (78%) mostly preferred CA, while dentistry students mostly preferred LB (44%). With regard to advantage/disadvantage, dentistry students (31%) and dentists (39%) mostly preferred SLB, while orthodontic residents mostly preferred CA (55%). Regarding the success of the treatment, all three groups mostly preferred CMB. (respectively 50%; 47%; 72%). While CA was mostly preferred for short-term treatments in all three groups (respectively 40%; 71%; 88%), CMB was mostly preferred for long-term treatments (respectively 35%, 51%, 55%). Gender and income-level differences had little effect on orthodontic treatment method preferences.

Conclusion: Except for long-term treatments and treatment success, there was generally great interest in CA, especially among orthodontic residents. Ceramic brackets and LB were generally the least preferred treatment methods among dentistry students, dentists, and orthodontic residents.

Keywords: Patient preferences, esthetics, orthodontic appliances, clear aligner

INTRODUCTION

Orthodontic treatments have traditionally utilized conventional metallic brackets (CMB). However, the appearance of metal brackets can lead to esthetic concerns, particularly in adults. As a result, there is a growing demand for orthodontic appliances that are less noticeable and more acceptable to patients.[1,2]

The change in the perspective of esthetics in dentistry, especially in orthodontics, has led to a sense of urgency in incorporating esthetics into orthodontic treatment requirements and has increased the demand for invisible

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orthodontic appliances.[3,4] Additionally, reducing chair-time and shortening the treatment time has become a desire for both clinicians and patients. For this reason, trends in orthodontic appliance usage are constantly evolving.[5] Currently, treatment modalities that prioritize esthetics and comfort during use are becoming the basic needs of patients seeking orthodontic treatment.[5]

Advancements in technology have resulted in the development of esthetic ceramic brackets, lingual brackets, clear aligner, and self-ligating brackets, which offer advantages over CMBs in terms of appearance and/or comfort and have impact on patient preference.[6] Although each of these new orthodontic systems has its advantages and disadvantages, some promise greater comfort, some offer a more esthetically pleasing appearance, and others provide shorter treatment times.[2]

Although there are different orthodontic treatment methods available, studies have shown that there are differences in the perception of orthodontic appliances among different age groups, as well as among those with different social and cultural values.[1,2,6] Understanding the factors involved in the perception of different orthodontic appliances in different populations can enable better planning of resources and treatment strategies in the clinical practice.[3] In the study by Marañón-Vásquez et al.[5], it was determined that before being informed in detail about orthodontic treatment methods, participants cared more about esthetics and attractiveness, and therefore preferred clear aligners and lingual brackets over traditional metal brackets, which were rejected at the highest rate. However, after being informed about the advantages and disadvantages of treatment methods, their preferences shifted towards clear aligner and traditional metal brackets, with lingual brackets being rejected more. This demonstrates that treatment preferences can change when patients are informed about orthodontic treatment methods. Since all these systems have some advantages as well as disadvantages, it is important to consider which orthodontic treatment method will be preferred by both orthodontists and patients who are informed about the various bracket systems in cases where orthodontic treatment is needed. Based on this idea, the current study aims to evaluate the preferred orthodontic treatment method in case of orthodontic treatment need considering factors such as esthetics, cost, advantage/disadvantage, health of the oral cavity, treatment success and treatment duration by dentistry students, dentists and orthodontic residents who are briefly introduced to different bracket systems.

METHODS

The study was conducted with three groups of participants: 3rd-4th year dentistry students, dentists, and orthodontic residents (post-graduate doctorate/specialty students studying in orthodontics). Ethical approval for the study was obtained from the Clinical Research Ethics Committee of Ankara University Faculty of Dentistry (date: 17.02.2021, decision number: 04/03).

Power analysis was used to determine the number of participants to be included in the study. The minimum sample size required for a significant relationship between the two categorical variables was determined to be 36 with an effect size of 0.80 (large effect), error level (a) of 0.05, test power (1-b) of 0.95 and degrees of freedom of 8. The questionnaire was applied to 559 volunteers and all participants provided written informed consent. Some questionnaire forms were excluded from the study after the preliminary examination based on the following criteria:

• Questionnaire forms in which all the questions were marked the same,

• Questionnaire forms in which the same answer was given to the control question put in the questionnaire to test whether the participants read the questions.

Accordingly, 526 questionnaires were evaluated. The numerical distribution of the number and gender of the participants in each group is given in Table 1. To avoid the problems that may be caused by numerical differences between the genders, it was attempted to have a similar percentage distribution of men and women among the groups. The participants were surveyed with 17 questions, evaluating demographic information (age, gender, study year for dentistry students, income level), and treatment preferences. Before the survey, the participants were briefly informed about the treatment methods with short introductions and intraoral photographs of conventional metal brackets (CMB), esthetic ceramic brackets (ECB), self-ligating brackets (SLB), clear aligner (CA) and lingual brackets (LB). Then, the participants were asked in case of need for orthodontic treatment, which orthodontic treatment method they would prefer in terms of esthetics, advantage/disadvantage, cost, health of the oral cavity, success of the treatment, long or short treatment time. Additionally, we evaluated whether there was a difference in treatment method preferences in terms of gender and income level.

Table 1. Distribution of the participants by gender

Participants	Women		Men		Total (N)
	(n)	(%)	(n)	(%)	
Dentistry students	222	70%	96	30%	318
Dentists	69	63%	41	37%	110
Orthodontic residents	76	71%	22	29%	98
Total (n)	367		159		526

Statistical Analysis

The differences in the participants' orthodontic method preferences were analyzed using chi-square analysis with SPSS Statistics 22.0 Software. Comparisons were made with a significance level of $p<0.05$. Also, gender and income-level differences were tested in each group.

RESULTS

The chi-square test results regarding the differences in orthodontic treatment method preferences among participant groups are presented in Table 2. Statistical significant differences were observed among the participant groups for all evaluated factors ($p<0.05$). In terms of esthetic concerns, lingual brackets were preferred by the students the most (44%), while clear aligners were preferred at the highest rate by the dentists (41%) and orthodontic residents (78%). Considering the advantages and disadvantages of the treatment methods, the students (31%) and dentists (39%) mostly preferred self-ligating brackets, whereas clear aligners were the top choice for orthodontic residents (55%). When considering esthetics, cost, and advantage/disadvantages together as well as oral cavity health, metallic brackets were mostly preferred by students (27%, 33% respectively), while the dentists (28%, 44% respectively) and orthodontic residents (55%, 85% respectively) mostly preferred clear aligners. In all groups, CMBs were mostly preferred in terms of treatment success (50%; 47%; 72% respectively) and long-term treatment (35%; 51%; 55% respectively), while clear aligners were preferred for short-term treatment (40%; 71%; 88% respectively).

Table 3 presents the relationship between the gender of the participants and their preferences for orthodontic treatment methods. The analysis revealed no significant gender difference in any group considering the advantage/disadvantage factor, health of the oral cavity, treatment success, and short-term treatments. However, in terms of esthetics, a gender difference

Table 2. Percentage distribution of the preferences of participants and the chi-square table showing the differences between groups

Group	CMB (%)	ECB (%)	SLB (%)	CA (%)	LB (%)	χ2	p value
Esthetics							
Students	5	22	3	26	44		
Dentists	9	14	4	41	32	96.224	
Orthod. Res.	1	0	3	78	18		
Advantage/Disadvantage							
Students	26	11	31	29	3		
Dentists	21	3	39	30	7	44.616	
Orthod. Res.	13	0	27	55	5		
Esthetics, Cost, Advantage-Disadvantage							
Students	27	21	23	23	6		
Dentists	18	18	19	28	17	57.744	
Orthod. Res.	10	19	8	55	8		
Health of the Oral Cavity							
Students	33	11	26	25	5		**0.000***
Dentists	31	7	13	44	5	117.074	
Orthod. Res.	4	5	6	85	0		
Success of the Treatment							
Students	50	9	28	8	5		
Dentists	47	6	25	11	11	34.962	
Orthod. Res.	72	0	18	10	0		
Short-Term Treatment							
Students	26	13	12	40	9		
Dentists	18	3	0	71	8	98.034	
Orthod. Res.	6	0	0	88	6		
Long-Term Treatment							
Students	35	18	23	13	11		
Dentists	51	11	20	14	4	38.839	
Orthod. Res.	55	0	27	14	4		

Orthod. Res., Orthodontic Residents; CMB, Conventional metallic brackets; ECB, Esthetic ceramic brackets; SLB, Self-ligating brackets; CA, Clear aligner; LB, Lingual brackets (χ2: Chi-square test; *: $p<0.05$ indicates statistically significance)

Table 3. Relationship between the gender of the participants and preferences of orthodontic treatment methods in each group

Group	Gender	CMB (%)	ECB (%)	SLB (%)	CA (%)	LB (%)	χ2	p value
Esthetics								
Students	Female	5	22	3	26	44	0.24	0.993
	Male	4	22	2	27	45		
Dentists	Female	10	16	6	41	28	2.65	0.617
	Male	7	10	2	42	39		
Orthod. Res.	Female	1	0	0	78	21	11.98	**0.007***
	Male	0	0	14	77	9		
Advantage/Disadvantage								
Students	Female	27	10	31	30	3	1.60	0.808
	Male	26	14	30	26	4		
Dentists	Female	17	4	45	30	3	9.37	0.052
	Male	27	0	29	29	15		
Orthod. Res.	Female	13	0	25	55	7	1.75	0.626
	Male	14	0	32	55	0		
Esthetics, Cost, Advantage/Disadvantage								
Students	Female	27	18	22	27	6	9.85	**0.043***
	Male	28	29	24	14	5		
Dentists	Female	19	17	23	28	13	3.61	0.46
	Male	17	17	12	29	24		
Orthod. Res.	Female	11	20	5	55	9	4.32	0.364
	Male	9	14	18	55	5		
Health of the Oral Cavity								
Students	Female	35	10	27	24	5	2.45	0.637
	Male	28	13	25	27	7		
Dentists	Female	26	10	16	45	3	7.28	0.122
	Male	39	2	7	42	10		
Orthod. Res.	Female	5	5	7	83	0	1.40	0.701
	Male	0	5	5	91	0		
Success of the Treatment								
Students	Female	53	6	28	7	5	6.84	0.144
	Male	44	15	27	9	5		
Dentists	Female	46	7	26	9	12	2.06	0.724
	Male	49	2	24	15	10		
Orthod. Res.	Female	71	0	18	11	0	0.04	0.979
	Male	73	0	18	9	0		
Short-Term Treatment								
Students	Female	23	14	13	43	8	7.04	0.131
	Male	34	9	12	33	12		
Dentists	Female	15	1	0	74	10	3.57	0.308
	Male	24	5	0	66	5		
Orthod. Res.	Female	7	0	0	87	7	0.26	0.877
	Male	5	0	0	91	5		
Long-Term Treatment								
Students	Female	35	18	24	14	10	1.94	0.746
	Male	33	19	23	10	15		
Dentists	Female	58	13	16	13	0	11.13	**0.025***
	Male	39	7	27	17	10		
Orthod. Res.	Female	57	0	28	13	3	2.33	0.506
	Male	50	0	23	18	9		

Orthod. Res., Orthodontic Residents; CMB, Conventional metallic brackets; ECB, Esthetic ceramic brackets; SLB, Self-ligating brackets; CA, Clear aligner; LB, Lingual brackets (χ2: Chi-square test; *: p<0.05 indicates statistically significance) was observed in orthodontic residents, where male residents preferred self-ligating brackets (14%) and female residents preferred lingual brackets (21%) as their second choice, while the most preferred treatment method was the same for both genders. When considering the esthetics - cost - advantage/disadvantage factors together, only female dentistry students showed a gender difference, as they preferred clear aligners more (27%). In terms of long-term treatments, only female dentists showed a gender difference, as they preferred CMBs (58%) more.

Table 4 presents the relationship between the income levels of the participants and their preferences for orthodontic treatment methods. There was no significant difference in the preference of treatment method according to income levels of both dentistry students and orthodontic residents. However, significant differences were found for dentists, in terms of esthetics, advantage/disadvantage, and short-term treatment ($p<0.05$). In terms of esthetics, all low-income dentists (100%) preferred esthetic ceramic brackets, the middle-income dentists mostly preferred clear aligners (46%), and the high-income dentists mostly preferred lingual brackets (46%). Considering the advantage/disadvantage of the orthodontic treatments, all low-income dentists preferred conventional metallic or esthetic ceramic brackets (50%-50%), while the middle-income dentists mostly preferred self-ligating brackets (44%), and the high-income dentists mostly preferred CMBs (31%) and clear aligners (31%). Regarding short-term treatments, low-income dentists preferred esthetic ceramic brackets (50%) and clear aligners (50%) at similar rates, while middle and high-income dentists mostly preferred clear aligners (71%;73% respectively).

DISCUSSION

The perception of attractiveness, confidence, intelligence, social skills, popularity, employment, and success can be influenced by the appearance of orthodontic appliances.[7] Thus, the appearance of the orthodontic appliance plays a crucial role in patients' preference for orthodontic treatment. Also, the perceptions of individuals about orthodontic appliances differ and can vary according to various factors such as age, gender, social status, and income level.[1-3,6] In current orthodontic practice, the interaction between clinician and patient is crucial in determining the diagnosis and treatment planning. In this regard, determining patients' and clinicians' preferences is important in making recommendations that will guide the decision-making process effectively.[5]

This study was conducted with three groups of participants from the dentistry community: students (3rd and 4th year) currently studying dentistry, dentists, and orthodontic residents (post-graduate doctorate/specialty students studying in orthodontics at different levels). Therefore, participants' ages, education levels, and knowledge of orthodontic treatment varied. For this reason, it is expected that the issues that influenced them would differ.

The first question was which orthodontic treatment method they would prefer considering aesthetics in case of need for orthodontic treatment. It was observed that while the dental students mostly preferred lingual brackets (44%), dentists (41%) and orthodontic residents (78%) mostly preferred clear aligners in terms of esthetics (Table 2). In similar studies evaluating the attractiveness of orthodontic appliances in patients, lingual brackets and clear aligner have been found to be the most attractive treatment methods.[1-3] A study investigating young people's perceptions of different orthodontic appliances at different ages, reported that clear aligners are the most esthetically acceptable materials in all age groups, while lingual brackets are preferred in the second place, similar to our findings.[7] In some studies, age has been identified as an important factor in orthodontic appliance preferences considering esthetics, with metallic brackets being more attractive at younger ages, and interest in clear aligners increasing with age.[4,8] For example, in the study of Kuhlman et al.[4], it was found that while young individuals in the 8-12 age group preferred clear aligners the least, older individuals in the 13-17 age group found esthetic ceramic brackets and clear aligners without attachments more attractive. Alansari[7], who obtained similar results to us, stated that the increase in the interest in clear aligners was due to the increase in advertisement and presence on social media, as well as clinicians' efforts to keep up the times. Additionally, the attachments that are indispensable part of clear aligner treatments, were not completely clear in the photographs used for informational purposes, and this may have influenced the emergence of this preference.[7] Likewise in studies on adults and adolescents, clear aligners with attachments are less preferred than those without attachments.[3,4]

In terms of the advantages and disadvantages of orthodontic treatment methods, students (31%) and dentists (39%) mostly preferred self-ligating brackets, while orthodontic residents mostly preferred clear aligners (55%) (Table 2). The students and dentists based their decisions solely as patients receiving orthodontic treatment and not as providers. However, orthodontic residents answered the survey as both a patient and a specialist who performs orthodontic treatment. Generally self-ligating brackets which can deliver 3-dimensional tooth control are considered the most durable and possibly the most efficient because of their lower sliding friction.[9] Despite that, in this study, the orthodontic residents mostly preferred clear aligners in terms of advantages/disadvantages. It can be thought that factors such as social attractiveness of aligners', ease of use for eating, drinking and maintaining oral hygiene, the need to learn more about this new treatment method and an effort to set an example for their patients can be considered as the reasons for the emergence of this preference. Esthetic ceramic brackets and lingual bracket systems were the least preferred treatment methods in terms of advantage/disadvantage. It is thought that the handicaps of ceramic brackets such as fracturing during debonding and increased friction in sliding[10] and the handicaps of lingual brackets such as the difficulty of manipulating, increased oral discomfort, impaired speech performance,

Table 4. Relationship between participants income levels and preferences of the orthodontic treatment method in each group

Group	Income	CMB (%)	ECB (%)	SLB (%)	CA (%)	LB (%)	χ2	p value
Esthetics								
	Low	7	20	4	26	44		
Students	Middle	4	22	2	28	45	8.40	0.429
	High	3	36	0	19	42		
	Low	0	100	0	0	0		
Dentists	Middle	9	11	6	46	28	18.84	**0.016***
	High	12	15	0	27	46		
	Low	0	0	0	60	40		
Orthod. Res.	Middle	2	0	3	79	17	2.26	0.894
	High	0	0	4	78	19		
Advantage/Disadvantage								
	Low	29	9	35	25	3		
Students	Middle	26	11	30	30	4	8.32	0.357
	High	19	23	19	36	3		
	Low	50	50	0	0	0		
Dentists	Middle	17	2	44	31	6	23.53	**0.003***
	High	31	0	27	31	12		
	Low	0	0	0	100	0		
Orthod. Res.	Middle	15	0	30	49	6	5.94	0.43
	High	11	0	22	63	4		
Esthetics, Cost, Advantage/Disadvantage								
	Low	32	18	23	21	7		
Students	Middle	27	21	24	24	5	8.46	0.39
	High	16	36	13	29	7		
	Low	50	50	0	0	0		
Dentists	Middle	13	16	22	33	16	10.98	0.203
	High	31	19	12	15	23		
	Low	0	20	0	80	0		
Orthod. Res.	Middle	9	23	12	49	8	9.95	0.268
	High	15	7	0	67	11		
Health of the Oral Cavity								
	Low	30	13	27	25	5		
Students	Middle	32	10	28	25	5	7.85	0.448
	High	45	7	10	29	10		
	Low	50	50	0	0	0		
Dentists	Middle	31	5	13	46	5	8.44	0.392
	High	31	12	12	39	8		
	Low	0	0	0	100	0		
Orthod. Res.	Middle	3	6	8	83	0	2.53	0.864
	High	7	4	4	85	0		
Success of the Treatment								
	Low	50	10	26	9	5		
Students	Middle	51	8	31	5	5	6.22	0.622
	High	52	7	23	16	3		

Table 4. continued

Group	Income	CMB (%)	ECB (%)	SLB (%)	CA (%)	LB (%)	χ2	p value
	Low	50	50	0	0	0		
Dentists	Middle	45	4	28	13	10	12.11	0.146
	High	54	8	19	4	15		
	Low	80	0	0	20	0		
Orthod. Res.	Middle	68	0	21	11	0	2.38	0.666
	High	78	0	15	7	0		
Short-Term Treatment								
	Low	25	11	15	44	6		
Students	Middle	28	15	11	38	9	8.49	0.387
	High	26	7	13	36	19		
	Low	0	50	0	50	0		
Dentists	Middle	18	2	0	71	9	17.82	**0.007***
	High	19	0	0	73	8		
	Low	20	0	0	80	0		
Orthod. Res.	Middle	6	0	0	85	9	5.06	0.281
	High	4	0	0	96	0		
Long-Term Treatment								
	Low	32	17	29	14	9		
Students	Middle	35	20	22	11	12	8.43	0.392
	High	45	10	13	16	16		
	Low	50	50	0	0	0		
Dentists	Middle	49	12	21	16	2	6.97	0.539
	High	58	4	19	12	8		
	Low	100	0	0	0	0		
Orthod. Res.	Middle	49	0	32	15	5	6.33	0.387
	High	63	0	19	15	4		

Orthod. Res., Orthodontic Residents; CMB: Conventional metallic brackets; ECB, Esthetic ceramic brackets; SLB, Self-ligating brackets; CA, Clear aligner; LB, Lingual brawckets (χ2: Chi-square test; *: p<0.05 indicates statistically significance)

difficulty in eating, higher cost and the lack of adequate technical knowledge and training may have contributed to their rejection by orthodontists.[11-14] In the study of Marañón-Vásquez et al.[5], it was found that the use of the lingual bracket system is rejected with a rate of 80% due to a lack of experience with this method. Similarly, Riolo[15] states that orthodontists do not use lingual brackets because of inadequate training in lingual treatments despite their esthetic and biomechanical advantages. When considering esthetic concerns, cost, advantage/disadvantage together, dentists and orthodontic residents mostly preferred clear aligners (28% and 55% respectively), while students have similar preferences among treatment methods, except for lingual brackets (6%) (Table 2). However, there was a small difference in preference for CMBs (27%), which may be influenced by social, cultural, and economic conditions. In a previous study, while CMBs were mostly preferred by orthodontists, clear aligners were ranked second due to high clinical performance and low adverse effects.[5] In addition to their esthetic benefits, the direct access of clear aligner companies to patients via social media, and the inclusion of orthodontists and dentists in this aggressive marketing, may have contributed to their popularity in terms of many parameters, except for esthetics alone.[7]

In terms of oral cavity health and side effects, it was found that while lingual brackets and esthetic ceramic brackets were the least preferred treatment methods in all groups, clear aligners were more preferred, especially by the orthodontic residents (85%) (Table 2). This high rate of preference for clear aligners indicates the advantage of these appliances being "easy to remove and clean", which is one of the strongest aspects of this treatment system. Additionally, clear aligners cause less pain, and have a lower frequency of emergencies, incidence of periodontal damage and root resorption compared to conventional treatment methods.[16-18] In a study that examined the periodontal health of individuals treated with clear aligner and lingual brackets, it was stated that although clear aligner cover the keratinized gingiva of all teeth throughout the day, the periodontal risk is lower than lingual brackets because aligners are mobile and do not interfere with oral hygiene, which supports the results of this study.[19]

Considering treatment success, it was observed that all three groups of participants primarily preferred conventional or self-ligating metallic brackets, with orthodontic residents showing the highest preference rate (students: 50%, dentists: 47%, orthodontic residents: 72%) (Table 2). This is consistent with the consensus that the best-known classical methods are more effective in achieving successful orthodontic treatment. In the study by Marañón-Vásquez et al.[5], it was observed that participants who valued the finishing details and outcomes of treatment were more inclined to prefer CMBs and to reject clear aligners when they were informed about the advantages and disadvantages of different treatments. The fact that all three groups in the study predominantly preferred conventional or self-ligating metallic brackets in terms of treatment success shows that there is a consensus that successful orthodontic treatment can be achieved with the best-known classical methods.[20] Additionally, considering this result, it can be said that while the orthodontists trust clear aligner in terms of esthetics and advantage/disadvantages, they do not trust them enough regarding treatment success. Also, according to the results of our study, clear aligners were more preferred for short-term treatments in all groups, while CMBs were more preferred for long-term treatments, supporting our viewpoint on this matter (Table 2). Besides, the mild severity of malocclusion in short-term treatments may encourage the use of clear aligners, while the limitations of clear aligners may have led the participants to prefer metal brackets in long-term severe cases.[21,22] Similar to our findings, a study examining the priorities of individuals in the orthodontic treatment process, found that those who considered treatment time and smile esthetics more important, were more likely to prefer clear aligners and reject CMBs, while those who prioritized finishing details and cost were more likely to choose CMB and reject clear aligners.[5]

When the data were evaluated according to gender (Table 3), it was found that there were no significant differences between men and women in terms of advantage/disadvantage, oral cavity health, success of treatment, and short-term treatment. However, gender differences were observed among orthodontic residents regarding esthetics and among dentists in terms of long-term treatments. As in other studies[4,8] it is observed that gender has little effect on the preference of treatment methods in general. However, it can be said that women tend to be more sensitive to esthetics. Also, Feu et al.[3] reported that in adults men tend to assign lower scores than women for all evaluated appliances.

When orthodontic treatment preferences were compared based on income levels, no significant difference was observed among dentistry students and orthodontic residents in any income level (Table 4). However, in the group of dentists, considering the esthetics, all low-income dentists preferred esthetic ceramic brackets (100%), while the middle-income dentists (46%) preferred clear aligner and the high-income dentists (46%) preferred lingual brackets (Table 4). It is worth noting that clear aligner was preferred in all income groups (50%-73%) for short-term treatments, whereas lingual brackets (8%) were not preferred even in higher income groups. The preference of esthetic options such as lingual brackets or clear aligner appears to be related to the individual's economic status, with a higher income level being associated with a greater preference for lingual brackets. These findings are consistent with studies indicating that adults with higher socio-economic status are more willing to pay for esthetic options such as lingual brackets, clear aligner, or esthetic ceramic brackets.[2,3] A similar study found that adults with high income levels preferred clear aligners (73%), while low-income adults preferred CMBs (69%) and esthetic ceramic brackets (65%).[5] In contrast, another study conducted with children and adolescents, found no difference in treatment preferences based on income level for boys, but high-income adolescent girls were found to be more attracted to CA.[4]

When all parameters are evaluated in general, it is quite remarkable that the least preferred treatment methods among the orthodontic residents are esthetic ceramic and lingual brackets, respectively. Additionally, no orthodontic resident preferred esthetic ceramic brackets in terms of esthetics, advantage/disadvantage, treatment success, short-term or long-term treatment time. This situation calls into question the perspective and trust of orthodontists on esthetic ceramic and lingual brackets.

Although there are studies in the literature examining patients' preferences for bracket systems,[4,6,8] this is the first study to evaluate the treatment preferences of three different dentistry groups, with various levels of knowledge about orthodontic treatment systems, if they need orthodontic treatment. Additionally, studies comparing the perspectives of dentists and orthodontists in terms of clear aligner treatment exist in the literature; however, all treatment methods are not compared in these studies.[23,24] Furthermore, while other studies[1-8] have evaluated only the attractiveness and cost of the orthodontic appliances, our study examined different orthodontic treatment methods separately in terms of advantage/disadvantage, treatment duration, oral cavity health, and success of treatment. Also, both gender and income-level differences were evaluated. With this study, we aimed to clarify which factors are effective in orthodontic treatment method preferences in real terms and shed light on which factors clinicians should consider when deciding or directing the treatment method to be applied to their patients.

The number of adult orthodontic patients is increasing worldwide, and their concern about the appearance of the orthodontic appliance is growing.[4] For this reason, it is crucial for clinicians to assist patients in making informed decisions about their preferred orthodontic treatment method, guide them properly and respond correctly to their demands.[6] Understanding the general treatment method preferences of clinicians is crucial to empathize with patients and to guide and convince them effectively. Our findings are essential in representing the view points of both patients and clinicians regarding orthodontic treatment preferences.

It is thought that the preferences of dentistry students with limited knowledge about orthodontic treatment and can view the treatment from the patient's perspective, are closer to those of the general orthodontic patient population. The orthodontic treatment preferences of dentists may be related to their economic status and their esthetic concerns as dental professionals. When considering the parameters in general, it is seen that there is a great interest in clear aligners, especially in orthodontic residents, despite concerns over long-term treatment and treatment success. This interest among young orthodontists may be due to a desire to keep up with the latest developments in the field, as well as a curiosity and need for learning about the clear aligner system. In order to increase the use of clear aligners in clinical practice, efforts should be made to reduce costs, and eliminate inadequacies and uncertainties. The production of self-ligating brackets with a more aesthetically pleasing appearance, as well as better education on their advantages, may increase their popularity among patients and orthodontists alike. Lingual bracket systems have generally received little attention, and improving both orthodontist and patient comfort and optimizing costs may be beneficial for increasing use of lingual brackets in the clinical routine.

Study Limitations

One limitation of this study is that the informational photographs provided to the participants may not fully reflect the appearance of orthodontic appliances in real life, as they are demonstrative models photographs without including tissues such as lips and gingiva. Additionally, the fact that the attachments, which are indispensable for clear aligners, were not clearly visible in the photographs may have influenced participant preferences. Another limitation is that the number of women and men are not equal between the groups, since the female population is generally higher in the dentistry. However, efforts were made to ensure similar percentages of women and men in the groups to avoid gender related differences.

In future studies, it would be valuable to include patients from different age groups who require orthodontic treatment and orthodontists with varying levels of clinical experience to provide a more comprehensive understanding of the results.

CONCLUSION

- There are differences in orthodontic treatment method preferences among the dentistry students, dentists, and orthodontic residents in case of need for orthodontic treatment.
- Considering esthetic reasons, dentistry students tend to prefer lingual brackets, whereas dentists and orthodontic residents tend to prefer clear aligners.
- One notable finding is that orthodontic residents overwhelmingly prefer clear aligners in terms of advantage/disadvantage, short-term treatments and oral cavity health apart from esthetics.
- However, all three groups tended to prefer conventional metallic and self-ligating brackets regarding treatment success and long-term treatments.
- In general, ceramic and lingual brackets were the least preferred treatment systems among all three groups.
- Gender and income level had minimal impact on treatment method preference.

Ethics

Ethics Committee Approval: Ethical approval for the study was obtained from the Clinical Research Ethics Committee of Ankara University Faculty of Dentistry (date: 17.02.2021, decision number: 04/03).

Informed Consent: Written informed consent was obtained from the patients who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

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Original Article

Accuracy of Cone-Beam Computed Tomography Software in Predicting the Size of Impacted Canine: A Preliminary Study

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Main Points

- This study aims to compare and analyze the Precision & Accuracy of four CBCT software programs used in predicting the mesiodistal diameter of impacted canine and its reliability was compared with measurements made by digital vernier caliper.
- There were no clinical (in vivo) studies have been conducted to assess the accuracy and reliability of CBCT software.
- Every year many software programs have been introduced. Hence, it is highly essential to evaluate software programs for accuracy and reliability before they are implemented for medical practice.

ABSTRACT

Objective: To compare and analyze the precision, accuracy, and reliability of commonly used cone-beam computed tomography (CBCT) software in predicting the mesiodistal diameter of impacted canines.

Methods: This study was conducted on 11 patients (six males and five females, mean age: 17.5±5.5 years) with either unilateral or bilateral impacted canines in the maxilla or mandible. DICOM data sets of the patients obtained from CBCT scans were then loaded and visualized with four selected CBCT software to measure the widest mesiodistal diameter of the impacted teeth. Physical measurements using a digital vernier caliper, kept as a control, were also made on the extracted teeth and orthodontically erupted teeth. The collected data underwent statistical analysis, and the statistical significance level was set at $p<0.05$.

Results: The Bland-Altman analysis was performed to quantify the agreement between different software to the digital caliper, showing a narrow difference for all plots. Kruskal-Wallis ANOVA test followed by a post hoc test was performed to determine whether there was any difference in measuring the mesiodistal diameter of the impacted canine among the five methods, and tend no statistically significant difference was found among the five methods. Intraclass correlation (ICC) was performed, and measurements made with all CBCT software yielded an ICC greater than 0.95, indicating high reliability of the selected software.

Conclusion: All the evaluated CBCT imaging software exhibited a high degree of reliability, and accuracy in precise measurement of the mesiodistal diameter of an impacted tooth.

Keywords: Cone-beam computed tomography, software validation, data accuracy, tooth, impacted canine

INTRODUCTION

Predicting the size of unerupted or impacted teeth is one of the notable challenges in orthodontic practice for precise diagnosis and treatment planning. The variation between the space needed for the dentition and space available in the dental arch will lead to crowding or spacing,[1] consequently, an accurate estimation of the mesiodistal diameter (MDD) of the erupting permanent teeth is necessary to decide whether sufficient space is available for the permanent teeth to erupt correctly. Furthermore, it plays a vital role in determining eruption guidance, space maintenance, space regaining, or extraction during orthodontic treatment planning.

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Generally, the prediction of the MDD of unerupted permanent teeth is made either through direct measurements of unerupted tooth size on radiographs,[2] calculations from prediction equations, and tables,[3-5] or a combination of both methods.[6-8] For this purpose, numerous radiographic techniques have been suggested, such as periapical X-rays with central beam deviation (Clark's technique), occlusal, and panoramic radiographs.[2,6-8] However, several drawbacks of two-dimensional images in the visualization of unerupted teeth are challenging to differentiate the exact location of the teeth, impact on adjacent teeth/structures that cannot be accurately visualized, image distortions, image superimposition, artifacts, etc.[9] To overcome these glitches, conventional computed tomography (CT) scanning is sometimes used. However, this diagnostic aid is not highly recommended due to high radiation exposure during the procedure.[10]

Taking these considerations into account, cone-beam computed tomography (CBCT) is now commonly used in orthodontic practice for accurate diagnosis, especially in cases involving impacted teeth because it provides 3-Dimensional perspective at high resolution than conventional dental radiographs and provides better visualization of hard-tissue images than conventional CT images.[10-12]

Numerous software programs have been introduced every year to interpret and analyze Digital Imaging Communications in Medicine (DICOM) images. Hence, it is essential to evaluate software programs for accuracy and reliability before they are implemented for medical practice. However, thus far, no clinical (*in vivo*) studies have been conducted to assess the accuracy and reliability of CBCT software. Therefore, this study compares and analyzes the precision and accuracy of four CBCT software programs used in predicting the MDD of an impacted canine. Its reliability was compared with measurements made by a digital vernier caliper.

METHODS

Eleven patients (6 males and 5 females, mean age of 17.5±5.5 years) who were seeking orthodontic treatment with either unilateral or bilateral impacted canines in maxilla or mandible were selected for this study. Out of 11 patients, 4 patients had bilaterally impacted canines (for a total sample of 15 impacted canines). Informed consent was obtained from all selected patients, and the Institutional Review Board of Ragas Dental College and Hospital approved the study protocol (reference number: 201206IRB8 and the date: 12.06.2012).

CBCT imaging was used as part of the routine investigations to locate the impacted canine in three dimensions. The standardized scanning parameters were set to 5.0 mA, 120 Kv, 0.3 mm voxel size, and 9.6 second exposure time. After a comprehensive analysis based on the prognosis and severity of impaction,[13] the impacted teeth were either extracted or orthodontically brought into occlusion.

Nine impacted canines in 7 patients were extracted due to their unfavorable position and poor prognosis. Meticulous care was taken during the extraction to avoid any damage or alteration of crown morphology. One tooth was excluded from this study due to enamel fracture during extraction. A digital vernier caliper measured the extracted tooth widest MDD. Likewise, six impacted canines in 4 patients were surgically exposed and brought into occlusion byorthodontic treatment. After a complete eruption, the widest MDD of an erupted tooth was measured using the same digital vernier caliper.

To allow calculation of arithmetic means and avoid associated errors, all measurements made through a digital vernier caliper (Nominal resolution: $\pm$ 0.01 mm) were performed by a single investigator measured thrice with an interval of one week apart. Furthermore, intraclass correlation (ICC) to examine the intraexaminer reliability was calculated and found to be high with the ICC values ranging from 0.997 to 1. The physical measurement values were considered a control.

All DICOM images from CBCT scanning were uploaded separately into the four CBCT software. CBCT imaging software programs used in this study are:

1. Mimics software (Version 10.01; Materialise, Leuven, Belgium) (Figure 1):

Materialise Interactive Medical Image Control System (Mimics) was the first software to import DICOM files. Mimics have been used to set the sagittal (y-axis), vertical (z-axis), and transverse (x-axis) planes for three-dimensional image construction. After verification of three orthogonal views, landmarks were identified to quantify image variables of impacted canines.

2. Dolphin 3D software (Version 11.7; Dolphin Imaging & Management Solutions, Chatswort California) (Figure 2):

Dolphin Imaging is the most often used reconstruction program for CBCT imaging. Three planes, namely axial, coronal, and sagittal, have been used to reduce errors and relocate the images according to head position orientation while calculating volume sections of the impacted canine.

Figure 1. Mimics software (Version 10.01; Materialise, Leuven, Belgium)

3. OsiriX software (Version 3.8.3; Pixmeo, Geneva, Switzerland) (Figure 3):

OsiriX is an image processing application for the Mac operating system. DICOM files were loaded to assess the position of the canine and surrounding teeth in the multi-planar reconstruction planes. Images were magnified five times to delineate the tooth structure of an impacted tooth at a higher resolution to avoid calibration errors.

4. CS 3D Imaging software (Version 3.2.9; France) (Figure 4):

The CS 3D Imaging software is a user-friendly tool that includes advanced functions and applications to increase diagnostic and treatment planning capabilities. This software allows for the localization of impacted canines with a different interest viewpoint, such as axial, coronal, and sagittal using spatial relationships with excellent tissue contrast.

The 3D images of impacted teeth for each patient were visualized in three planes including axial, coronal, and sagittal. Then, the best-visualized plane to measure the maximum MDD of an impacted canine was identified according to the positional orientation of the impacted canine. Subsequently, to compute the widest MDD, the image of each tooth of interest was oriented perpendicular to the occlusal plane by extrapolating the 2-dimensional and 3D images simultaneously (Figure 5). After identifying and measuring the widest MDD in a particular slice, two more measurements were taken with one slice before

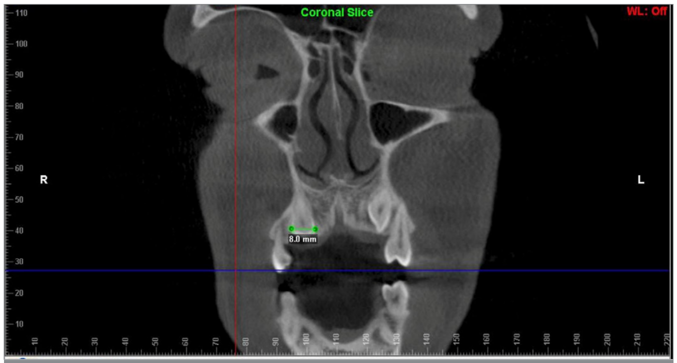


Figure 2. Dolphin 3D imaging software (Version 11.7; Dolphin Imaging & Management Solutions, Chatswort California)

Figure 3. OsiriX software (Version 3.8.3; Pixmeo, Geneva, Switzerland)

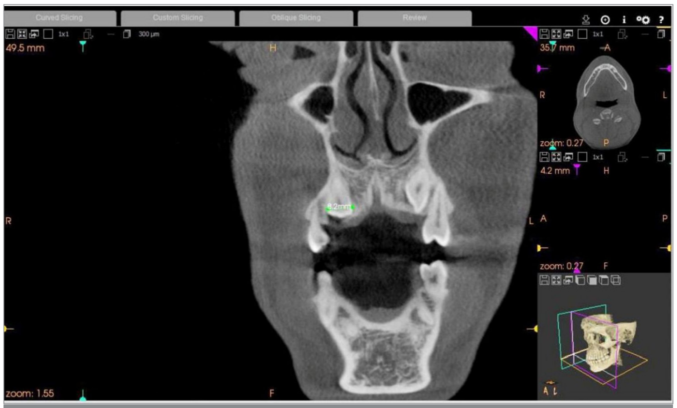


Figure 4. CS 3D Imaging software (Version 3.2.9; France)

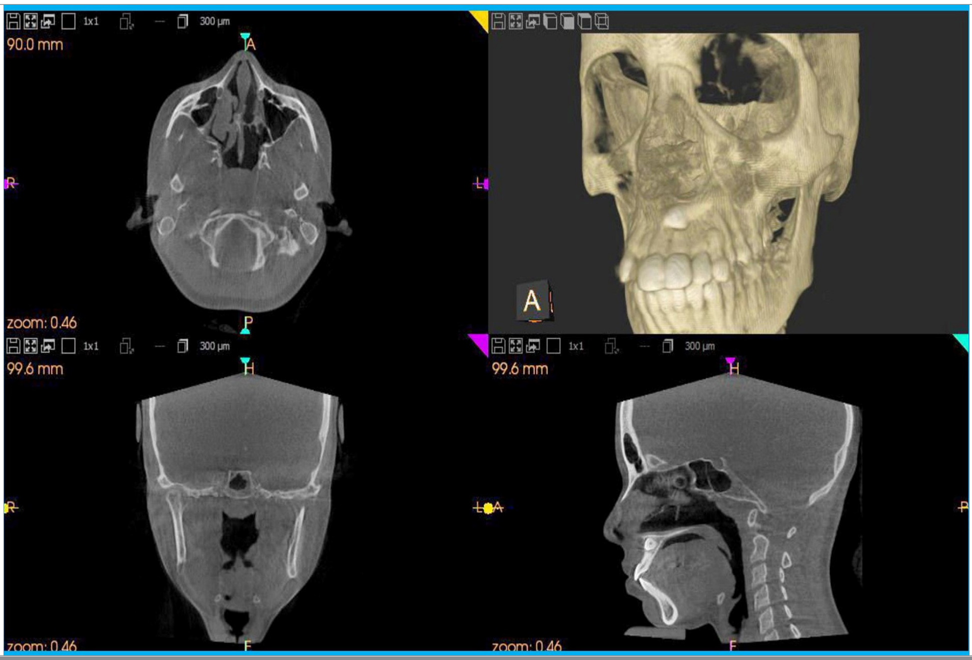


Figure 5. 3-Dimensional (3D) volume visualization displayed along with 2-Dimensional visualization

and one after the selected slice (slice thickness=0.3 mm). Consequently, the mean of these three values was considered as the maximum MDD of that particular tooth.

Statistical Analysis

The data obtained, were statistically analyzed using SPSS (version 19.0; IBM Corp., Armonk, NY, USA). Descriptive statistics for the mean difference and standard deviations were calculated for all variables. The Bland-Altman graph was quantify the agreement between two quantitative measurements by constructing limits of agreement between different software and the gold standard (digital caliper). Kruskal-Wallis ANOVA followed by a post-hoc test was used to compare the variables between the groups. ICC was performed to assess the reliability between the four CBCT software programs and a digital vernier caliper. The statistical significance level was set at $p<0.05$.

RESULTS

The widest MDDs of 14 impacted canines were measured. Mean differences and standard deviations were calculated for all variables. The Bland-Altman analysis was plotted to verify the extent of agreement or disagreement between different software and the gold standard (digital caliper) (Graph 1).

Bland-Altman plot compared two assay methods: software and digital caliper. It plotted the difference between the measurements of software and digital caliper on the y-axis, and the mean of the two measurements on the X-axis. Bland-Altman analysis generated two pages of results. The first page shows the difference and mean values of the two measurements, that were used to generate the plot. The second page shows the bias and standard deviation.

Bland-Altman plot-Digital caliper and Mimics: The graph shows that there is only a narrow difference, and it is within the limits of agreement for both methods. However, as the mean increases, the difference tends to increase as well, as depicted in Graph 1*.

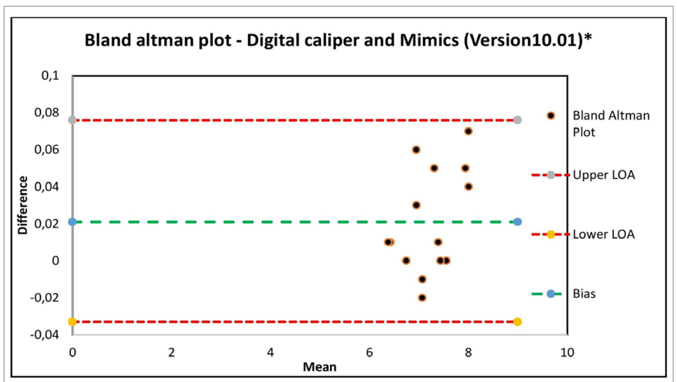
Bland-Altman plot-Digital caliper and Dolphin Imaging: The graph shows that there is only a narrow difference between the upper and lower lines of the agreement, which is depicted by being mostly above the bias line. However, the difference tends to be higher as most of the plots are above the bias line, as shown in Graph 2*.

Bland-Altman plot-Digital caliper and OsiriX: The graph shows that the difference is narrow and seems within the limit of agreement, which is similar to the other methods and further most since the plots are above the Bias line. This shows that the difference is greater than the mean of 7 (Graph 3)*.

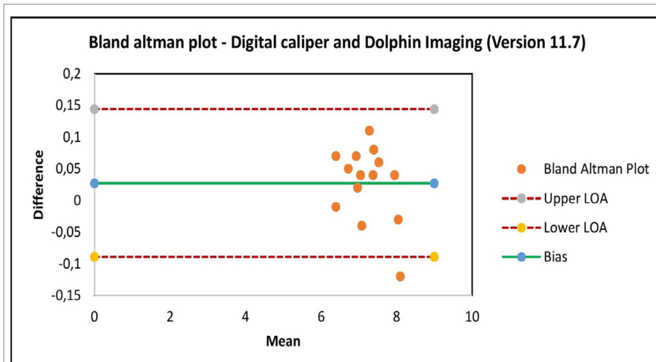
Bland-Altman plot-Digital caliper and CS 3D Imaging: The graph shows that there is a slightly wide difference between the lines of agreement. Most of the plots are near or precisely above the line, indicating a higher difference between both the methods (Graph 4)*.

From Graph 1, the limits of agreement for Mimics, Dolphin, OsiriX and CS 3D Imaging were 0.1, 0.2, 0.2, 0.3 respectively. The results obtained from Graph 1 show that for OsiriX and CS 3D Imaging software, most of the difference between the software and digital caliper were positive. The mean-positive differences in OsiriX and CS 3D Imaging were 0.0325 and 0.0688 respectively.

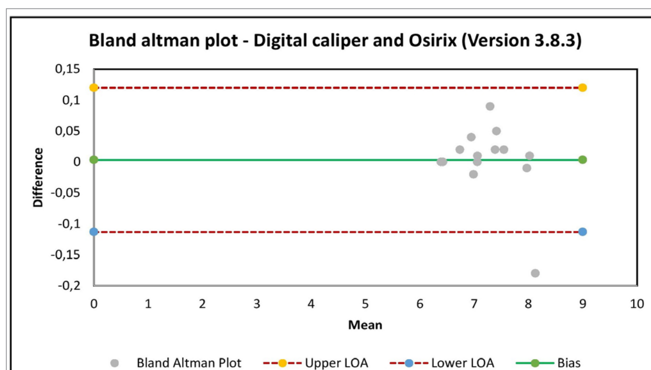
A Kruskal-Wallis ANOVA test was performed to compare and determine whether there were any differences in measuring the MDD of the impacted canine among the five methods (Table 1). The results revealed no statistically significant differences among all the five methods.



Graph 1. Bland altman plot - Digital caliper and Mimics (Version 10.01)



Graph 2. Bland altman plot - Digital caliper and Dolphin Imaging (Version 11.7)



Graph 3. Bland altman plot - Digital caliper and OsiriX (Version 3.8.3)

A post-hoc test was used to analyze inter-group comparison of the MDD of the impacted canine using each software and the gold standard method. This indicated that the comparison of all five groups agreed with these results and showed no statistically significant difference among all five methods (Table 2).

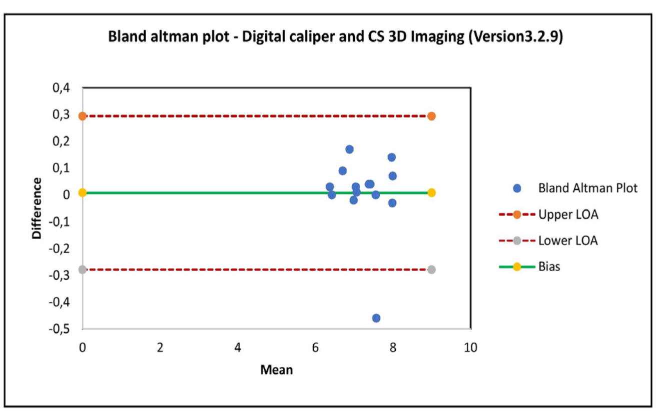
ICC was performed to assess the reliability between the four CBCT software programs and a digital vernier caliper (Table 3). The range of ICC values was from 0 to 1, with values close to 1 indicating strong evidence of reproducibility, and values close to 0 indicating less reproducibility. All CBCT software programs yielded an ICC greater than 0.95, indicating the high reliability of the selected software, with Mimics software (ICC: 0.999) having the highest correlation with the digital vernier caliper.

ICC was performed to assess the reliability between the four CBCT software programs and a digital vernier caliper (Table 3). The range of ICC values was from 0 to 1, with values close to 1 indicating strong evidence of reproducibility, and the values close to 0 indicating less reproducibility. All CBCT software programs yielded an ICC greater than 0.95, indicating the high reliability of the selected software, with Mimics software (ICC: 0.999) having the highest correlation with a digital vernier caliper.

DISCUSSION

Moyers[4] reported that overestimation of 1 mm above the actual widths of permanent canines and premolars would unfavorably influence the decision of extraction or non-extraction. Conversely, Proffit and Ackerman[9] suggested that an error of 1.5 mm is acceptable in expressing the error in tooth size prediction, and anything exceeding this is considered. However, significant variations in tooth size prediction can create problems and must be incorporated in the orthodontic problem list. Hence, the clinical significance in predicting unerupted tooth size becomes more critical.

To overcome the inadequacies and limitations of various prediction methods, CBCT was recommended toprecisely locate and accurately predict the MDD of an impacted tooth.[14] Walker et al.[15] established reference lines on anatomic landmarks in 2005 for three-dimensional localization of maxillary canines with CBCT. He also stated that 3D volumetric imaging systems precisely localization of impacted canines.[15]



Graph 4. Bland altman plot - Digital caliper and CS 3D Imaging (Version 3.2.9)

Table 1. Comparison of mesiodistal diameters measured by five methods using Kruskal-Wallis test

Group	Mean±SD	p value
Digital Vernier Caliper	7.24±0.54	
Mimics	7.22±0.52	
Dolphin 3D	7.21±0.56	0.99
OsiriX	7.24±0.56	
CS 3D Imaging	7.23±0.56	
Total	7.23±0.53	

Level of significance, p value<0.05.

Table 2. Inter-group comparison of mesiodistal diameters using post-hoc analysis

Group		Mean±SD	p value
Digital Vernier Caliper	Mimics	0.02±0.20	
	Dolphin 3D	0.02±0.20	
	OsiriX	0.00±0.20	
	CS 3D Imaging	0.00±0.20	
Mimics	Digital Vernier Caliper	-0.02±0.20	
	Dolphin 3D	0.00±0.20	
	OsiriX	-0.01±0.20	
	CS 3D Imaging	-0.01±0.20	
Dolphin 3D	Digital Vernier Caliper	-0.02±0.20	
	Mimics	-0.00±0.20	1.0
	OsiriX	-0.02±0.20	
	CS 3D Imaging	-0.01±0.20	
OsiriX	Digital Vernier Caliper	-0.00±0.20	
	Mimics	0.01±0.20	
	Dolphin 3D	0.02±0.20	
	CS 3D Imaging	0.00±0.20	
CS 3D Imaging	Digital Vernier Caliper	-0.00±0.20	
	Mimics	0.01±0.20	
	Dolphin 3D	0.01±0.20	
	OsiriX	-0.00±0.20	

Level of significance p value<0.05; SD, Standard deviation.

Table 3. Reliability between various softwares and digital caliper

Software vs. Physical Measurement	Intraclass Correlation	95% CI	
		Lower bound	Upper bound
MIMICS (version 10.01)	0.99	0.99	1.00
DOLPHIN 3D (version 11.7)	0.99	0.98	0.99
OSIRIX (version 3.8.3)	0.99	0.98	0.99
CS 3D (version 3.2.9)	0.96	0.89	0.98

CI, confidence interval.

The Bland-Altman plot shows that limits of agreement for Mimics were narrower than 0.1, indicating a greater precision. Dolphin and OsiriX limits of agreement were greater than 0.1, but narrower than 0.2, which could still be acceptable clinically. However, CS 3D Imaging was around 0.3, indicating poor precision associated with this software for this specific measure. From the result obtained from Graph 1, most of the differences were positive in OsiriX (0.0325) and CS 3D Imaging software (0.0688), which could be clinically acceptable. This result may be due to the underestimation of measurements by the software. Obviously, the sample size is small and the findings should be validated in future research.

The present study results reveal that all four CBCT software programs have high accuracy in predicting the impacted tooth's MDD. The mean MDD of impacted canine measured by digital vernier caliper (physical method) was equivalent to the mean MDD measured by all four CBCT software (digital method). Besides, the difference invalues between the four CBCT software ranges from 0.01 to 0.02. These values were statistically insignificant (p>0.05).

Moreover, the present study results revealed that CBCT methods tended to overestimate the MDD of the impacted tooth by 0.015 mm, but it is not clinically noteworthy. These results were analogous to a study by Sakabe et al.[16], who concluded that the measurements on the 3DX images overestimate a mesiodistal tooth diameter by 0.088 mm.[16] In contrast, Nguyen et al.[14] found that CBCT methods underestimate MDD by 0.4 mm.[13]

The ICC results of this study revealed high correlations (>0.95) between all four CBCT softwareprograms and the digital vernier caliper, which indicates that either of these CBCT software programs can accurately reproduce the dimensions of impacted teeth. Furthermore, among all these four CBCT software, the ICC test revealed that Mimics software was the most reliable (ICC: 0.999) compared to the physical method (Table 3).

Earlier, predictions of impacted tooth size were made by methods such as Moyers[4] prediction table, Tanaka and Johnston's[5] equation, etc. However, all these methods had limitations, as they were conducted with children from Northwestern European ancestry.[4,5] Therefore, the reliability of applying this methodology in other populations was questionable as tooth sizes differ within different population groups.[17,18] However, prediction methods using CBCT eradicate this population variations and are highly reliable because measurements are made individually with a precise 1:1 ratio and conflicting tables of average tooth sizes or regression models are avoided. In contrast to this study, Hofmann et al.[19] compared the imaging accuracy of CBCT data with multislice spiral computed tomography (MSCT) data sets for predicting the exact mesiodistal width of unerupted porcine tooth germs. They concluded that MSCT outperforms CBCT regarding determining tooth width.[19]

One constraint related to CBCT scanning is radiation exposure. Grünheid et al.[20] in 2012 compared the dosimetry of a CBCT with a digital X-ray in orthodontic imaging. They concluded that even though CBCT provides additional diagnostic and therapeutic benefits, patients are exposed to higher radiation levels than conventional digital radiography.[20] However, Hodges et al.[21] analyzed CBCT use in orthodontic diagnosis and treatment planning in 2013. They specified that obtaining a CBCT scan before orthodontic diagnosis and treatment planning is essential for patients with unerupted teeth due to uncertain location, as frequent modification is noted during orthodontic diagnosis and treatment planning.[21] In 2016, Detterbeck et al.[22] compared the accuracy of mesiodistal width measures with MRI to traditional 3D imaging techniques (MSCT, CBCT, and CT). The study concluded that magnetic resonance imaging (MRI) seems to be clinically equivalent to conventional ionizing 3D imaging techniques, and tooth germs are better appreciated than erupted teeth on MRI with less radiation exposure.[22] The smaller sample sizes can be considered a limitation of this study. Hence, further studies with a larger sample size are warranted to validate the reliability of CBCT software.

CONCLUSION

From the results obtained, it is prudent to conclude that there is no statistically significant difference between the measurements made using CBCT software and the digital vernier caliper. Furthermore, all four CBCT software programs revealed a high degree of reliability compared to the digital caliper.

Ethics

Ethics Committee Approval: The Institutional Review Board of Ragas Dental College and Hospital approved the study protocol (reference number: 201206IRB8 and the date: 12.06.2012).

Informed Consent: Informed consent was obtained from all selected patients.

Peer-review: Internally peer-reviewed.

Author Contributions: Concept - M.D., S.H.F., K.N.R.; Design - M.D., S.H.F., K.N.R.; Data Collection and/or Processing - M.D., S.H.F., K.N.R.; Analysis and/or Interpretation - M.D., S.H.F., K.N.R.; Literature Review - M.D., S.H.F., K.N.R.; Writing - M.D., S.H.F., K.N.R.

Declaration of Interests: The authors have no conflicts of interest to declare.

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Original Article

Evaluation of the Flash-Free Adhesive System for a 6-month Period: A Split-Mouth Trial

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Main Point
- The novel APC flash-free adhesive system is effective as well as efficient.

ABSTRACT

Objective: To compare the adhesive pre-coated (APC) flash-free (FF) appliance system (3M Unitek) with an operator-coated (OC) system (Transbond XT Light Cure Adhesive Paste; 3M Unitek) in terms of bond failure, bracket survival, and chair time.

Methods: This single-center study was planned with 30 non-extraction patients, 22 females and 8 males with an average age of 17 years and 5 months. A split-mouth design was used, and bonding time, failed brackets, reasons for failure, and adhesive remnant index (ARI) scores were noted. The data were analyzed with the chi-square, Kaplan-Meier, log-rank, and Mann-Whitney U tests.

Results: OC and FF adhesive-coated brackets demonstrated bond failure rates of 0.7% and 3.0%, respectively. Failure rates and survival rates presented a statistically significant difference (p=0.033). Although higher bond failure for the lower arch along with higher bond failure for the incisor teeth compared with the premolar teeth were found, these findings were not statistically significant (p=0.128; p=0.261, respectively). The effect of gender on the bond failure rate (p=0.463) and survival rate (p=0.473) was not statistically significant. A significant difference was obtained for the ARI scores (p=0.011). The bonding time for each bracket type (64.43 seconds for FF versus 98.97 seconds for OC) demonstrated a significant difference (p=0.174).

Conclusion: The bond failure rate was higher for the FF APC brackets, but the chair time reduction during bonding was recorded. Therefore, it seems that FF APC brackets are promising. Trial registration: ISRCTNand ISRCTN26731749. Registered October 7, 2020-Retrospectively registered, https://doi.org/10.1186/ISRCTN26731749

Keywords: Orthodontics, APC flash-free adhesive, bracket failure, bracket survival, and bonding time

INTRODUCTION

Bond failure hinders the efficiency of fixed orthodontic appliance therapy. Thus, a bond failure rate as low as possible is fundamental.[1] A survey reported a median bond failure rate as 5% for labial appliances.[2] Furthermore, an increase in the use of ceramic and adhesive pre-coated (APC) brackets was reported.[2] APC brackets were introduced approximately 30 years ago.[3] From then on, various APC bonding systems were developed.[4] In 2013, an APC flash-free (FF) adhesive coated appliance system was introduced. The FF adhesive is made up of a compressible fiber mat, soaked with an adhesive resin attached to the bracket base. This innovative design eliminates the flash removal step. Furthermore, the bond failure rate has been reported to be less than 2% with this unique technology.[4] To date, three studies evaluating the bond failure rate of the FF adhesive appliance system have been conducted,[5-7] which were performed with a split-mouth design. The efficiency of a split-mouth design to assess bonding agents has been stated.[8] The study by Grünheid and Larson[5] compared the bonding

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time and bracket failure rate of ceramic brackets over 1 year between the FF adhesive and a conventional adhesive. It was reported that the bonding time was significantly shorter with the FF adhesive, resulting in a time saving of approximately 30%. The bracket failure rate was 3.7% for the FF adhesive and 0.9% for the conventional adhesive. This outcome was found to be statistically equivalent. In the second study,[6] which was a continuation and completion of the aforementioned study,[5] the bracket failure rate was 4.3% for the FF adhesive and 1.9% for the conventional adhesive. The bracket failure and survival rates were not significantly different between the 2 adhesives. Also, no significant differences between the adhesive remnant index (ARI) scores were obtained. Finally, Tümoğlu and Akkurt[7] compared the bonding time and bond failure rate between the FF adhesive and a conventional adhesive using 0.018-inch-slot Clarity Advanced Ceramic brackets. The bond failure rates of the FF adhesive and the conventional adhesive were 1.21% and 1.81%, respectively. The bond failure rates were significantly different. The ARI scores did not demonstrate a significant difference. The FF bracket bonding time was significantly shorter. Bond failure rate is an acknowledged method for assessing bracket performance. Bond failure mainly occurs during the first 6 months of treatment.[9] In addition to the simple fact of bond failure, the survival rate presents the interval before bond failure.[10]

The objectives of this single center trial were as follows:

1. To compare the bond failure and survival rates of the APC FF Adhesive Coated Appliance System (3M Unitek) with an operator-coated (OC) system (Transbond XT Light Cure Adhesive Paste; 3M Unitek) for 6 months.

2. To compare the bond failure and survival rates of the upper and lower arches.

3. To compare the bond failure and survival rates of incisor, canine, and premolar teeth.

4. To compare the bracket failure and survival rates with respect to gender.

5. To compare the ARI scores.

6. To compare the chair time for each bonding procedure.

The null hypothesis was that there would be no difference in these parameters.

METHODS

Ethics approval was obtained from the Ondokuz Mayıs University Clinical Research Ethics Committee (OMÜ KAEK 2018/416). To determine the sample size for this trial, a power analysis using the G*Power software version 3.1.9.2 (University of Düsseldorf, Germany) was conducted, based on a previous trial.[11,12] It was found that a minimum of 27 patients were needed to observe a 4.2% difference in failure rates, with a power of 90% at a confidence rate of 95%. To account for potential dropouts, a total of 30 patients were enrolled. Patients included in the study had fully erupted maxillary and mandibular teeth with intact buccal enamel and were treated with a non-extraction protocol. They had Angle Class I or mild Class II malocclusion with normal overbite and teeth alignment without severe dental rotations. They had not undergone pretreatment of the enamel with any chemical agents and had good oral hygiene. Patients with skeletal problems, missing teeth, systematic disease and a previous history of orthodontic treatment were not included. Every patient and legal guardian (if the patient was under the age of 18) signed the informed consent. Table 1 presents the characteristics of the patient samples. Before the start of the trial, study models, X-rays, and photographs were obtained. 0.022 inch slot MBT prescription Clarity Advanced Ceramic Brackets (3M Unitek) were used. These brackets, designated as Interventions A and B (Figure 1), were bonded using OC and FF systems with the split-mouth method. The OC brackets were bonded with a conventional light cure adhesive (Transbond XT, 3M Unitek).

Light curing was carried out on the facial surface for 5 seconds using a new LED curing light (EliparTM DeepCure-L, 3M Unitek) with an output power of 1470 mW/cm^2 (milliwatts/square

Table 1. Sample characteristics

	Number	%
Number of total patients	30	-
Distribution of patients by gender		
Female	22	73.3
Male	8	26.7
Age range of patients		
13-22 years		
Distribution of patients by age		
<18	24	80
>18	6	20
Average age		
17 years 5 months		
Number of total brackets	600	
Distribution of brackets by gender		
Female	440	73.3
Male	160	26.7
Distribution of brackets by dental arch		
Upper	300	50
Lower	300	50
Distribution of brackets by tooth type		
Incisor	240	40
Canine	120	20
Premolar	240	40
Distribution of brackets by adhesive type		
Flash-free adhesive	300	50
Operator-coated adhesive	300	50

centimeter) and a wavelength range of 430-480 nanometers for both interventions. The distance between the light guide tip and the bracket base was approximated at 5 millimeters (mm) for optimum polymerization.[5,13]

The time required to bond each adhesive system was recorded. For FF, timing was started with the opening of each blister packaging and removal of the bracket until the completion of light curing for ten brackets (i.e., for both quadrants). For OC, timing was started from bracket removal until the completion of light curing. The maxillary and mandibular molar tubes, which were not evaluated in this study, were bonded with Transbond XT. Following the bonding procedure, patients received either a 0.014 or a 0.016 inch heat-activated nickel-titanium (HANT) arch wire, depending on their specific needs. Nevertheless, the following wire sequence was mainly used: round HANT, rectangular HANT, and rectangular stainless steel wires. Elastic and wire ligatures were used as needed.

Instructions for oral hygiene and care were provided to all patients and parents (if the patient was under the age of 18). All patients used the same orthodontic toothbrush (TePe, Sweden), floss (Oral-B Super floss), and toothpaste (Sensodyne Promine, Glaxo SmithKline, Brantford, Middlesex, UK). Patients were meticulously instructed to immediately report any issues concerning their appliances to the clinician for record keeping purposes (Table 2). The ARI is scored on a scale of 0 to 3, with higher scores indicating greater amounts of adhesive remaining on the tooth surface. To interpret the ARI values the following scale, based on the work of Artun and Bergland,[14] was used: ARI score 0: no adhesive remaining on the tooth surface; ARI score 1: less than half of the adhesive remaining on the tooth surface; ARI score 2: more than half of the adhesive remaining on the tooth surface; ARI score 3: all adhesive remaining on the tooth surface.[13] Only the first bond failure was registered. All clinical procedures were performed by one operator (DB) under the supervision of one faculty member (SET).

Statistical Analysis

Data were analyzed using a Statistical Package for the Social Sciences [(SPSS) Inc., Chicago; IL, USA]. The bond failure rates were determined for each bracket adhesive system, dental arch, type of tooth (incisor, canine, and premolar), and patients' gender. The chi-square test was used to compare the failure rates. The survival rates were estimated with the Kaplan-Meier

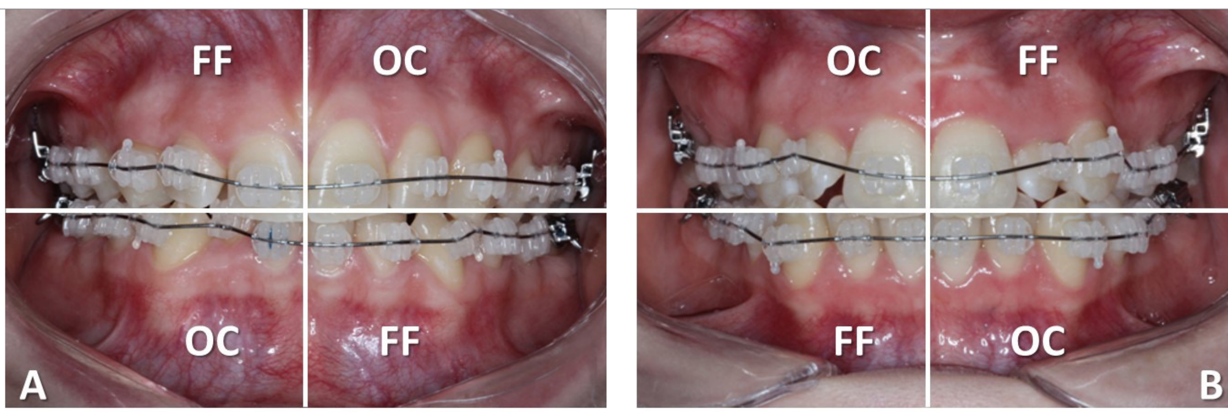

Figure 1. Intervention A and intervention B
FF, flash-free; OC, operator-coated

Table 2. Bond failure details*

Case	Gender	FF				OC			
		1st 3 months	2nd 3 months	ARI	Reason	1st 3 months	2nd 3 months	ARI	Reason
TA	♀	31 & 32**	---	0 & 0	Unknown	---	---	---	---
INU	♀	31	---	0	Unknown	---	---	---	---
USA	♀	31 & 33***	---	0 & 0	Popcorn and unknown	---	---	---	---
CA	♀	45	---	0	Olive pit	---	---	---	---
YD	♀	---	35	0	Olive pit	---	---	---	---
MD	♂	---	4**	0	Bread crust	---	15**	3	Bread crust
MBK	♂	---	22	3	Football trauma	12	---	3	Football trauma

♀, female; ♂, male
*FDI (Fédération Dentaire Internationale) dental numbering system was used
**Failure at the same time point
***Failures at different time points
ARI, adhesive remnant index; FF, flash-free; OC, operator-coated

test. Bracket survival distributions with respect to the bracket adhesive system, dental arch and type of tooth (incisor, canine and premolar) as well as patients' gender were compared with the log-rank test.

The differences in ARI scores between the failed brackets were determined with the chi-square analysis. Bonding time was measured in seconds for each adhesive bracket system in the two quadrants and divided into 10 (number of teeth). The difference between bonding times was compared with the Mann-Whitney U test. The significance was set at $p<0.05$ for all tests.

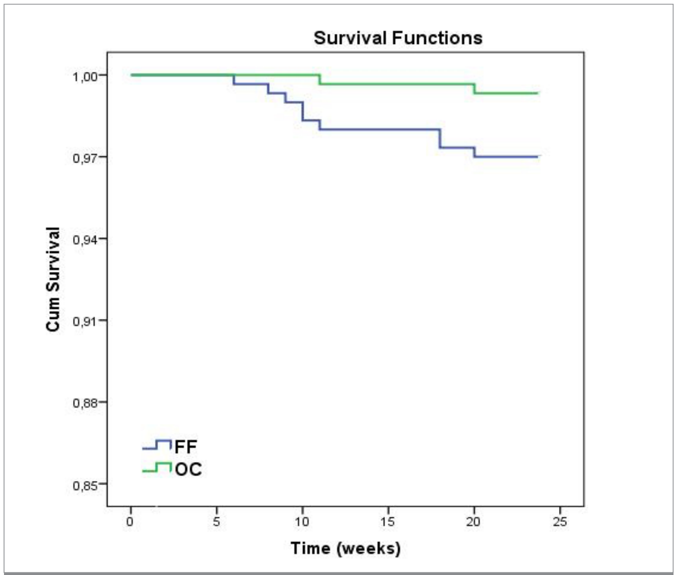

Figure 2. Bracket survival distributions
FF, flash-free; OC, operator-coated

RESULTS

During the observation period (6 months), 11 brackets failed: 2 (0.7%) for OC and 9 (3.0%) for FF (Table 3). A significant difference was found between the failure rates (χ^2=4,538; p=0.033). The survival curves were plotted with the Kaplan-Meier estimate (Figure 2). The bracket type showed a significant influence on the survival rates (Table 3; p=0.033). The probabilities of having brackets in place at the end of the observation period were 0.993 and 0.970 for the OC and FF brackets, respectively. Bond failure rates were 1.0% (3 brackets) and 2.7% (8 brackets) in the upper and lower arches, respectively. The difference was not statistically significant (Table 4; p=0.128).

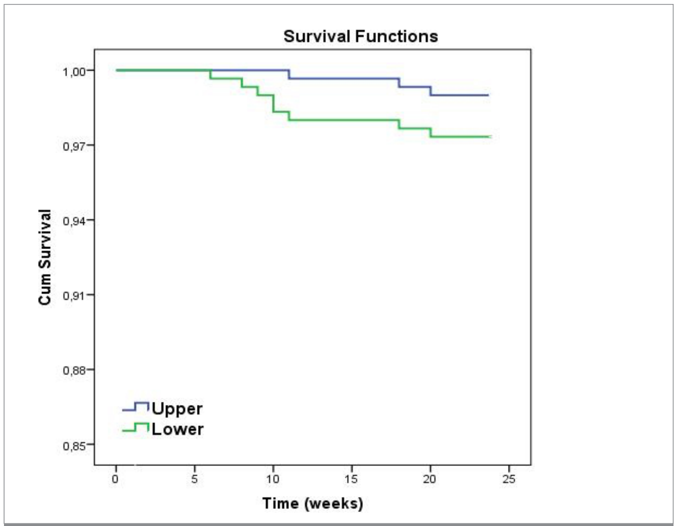

Figure 3. Bracket survival distribution for the dental arches

Table 3. Bond failure rate

OC			FF			p-value	Log-rank test
No failure	Failure	Failure rate	No failure	Failure	Failure rate		
298	2	0.7%	291	9	3.0%	0.033*	0.033

χ^2=4,538 on 1 df
FF, flash-free; OC, operator-coated, *: p<0.05

Table 4. Bond failure rates for the upper and lower dental arches*, for tooth type (incisor, canine and premolar)** and for female and male subjects***

	No failure	Failure	Failure rate	Log-rank test
Upper	297	3	1.0%	0.128
Lower	292	8	2.7%	
Incisor	233	7	2.9%	0.261
Canine	119	1	0.8%	
Premolar	237	3	1.3%	
Females	436	7	1.6%	0.463
Males	153	4	2.5%	

*χ^2=2,315 on 1 df; p=0.128
**χ^2=2,686 on 2 df; p=0.261
***χ^2=0.539 on 1 df; p=0.463

The influence of the dental arches on the bracket survival rate is depicted in Figure 3. The log-rank test showed no significant difference between the upper (S[t]=0.990) and lower (S[t]=0.973) dental arches (p=0.126). Bond failure rates were 2.9% (7 brackets) for incisor, 0.8% (1 bracket) for canine, and 1.3% (3 brackets) for premolar teeth (Table 4). Significant differences did not exist for the failure rates of incisor, canine, and premolar teeth (Table 4, p=0.261). Figure 4 depicts the influence of tooth type on the bracket survival rate. The log-rank test demonstrated no significant differences between the incisor, canine, and premolar teeth in terms of survival rate (p=0.260).

Female and male patients presented with a 1.6% (7 brackets) and 2.5% (4 brackets) failure rate, respectively (Table 4). This difference was not statistically significant (p=0.463). The influence of gender on the bracket survival rate is shown in Figure 5. No significant difference between females (S[t]=0.984) and males (S[t]=0.975) was obtained using the log-rank test (p=0.473). The frequency distribution and the result of the χ^2 analysis of the ARI scores are given in Table 5. A significant difference was obtained (p=0.011).

Bonding times demonstrated a significant difference (p=0.174).

DISCUSSION

During the first 6 months of treatment, the failure rates were 0.7% (2 failures) for the OC brackets and 3.0% (9 failures) for the FF brackets. These bond failure rates demonstrate a statistically significant difference, which is consistent with the findings of Tümoğlu and Akkurt.[7] Nevertheless, these researchers compared the FF brackets (1.21%) with the APC Plus brackets (1.81%). The findings of our study did not concur with the findings of Grünheid and Larson.[5,6] These researchers did not obtain a significant difference in the failure rates between FF brackets (3.7%; 4.3%) and APC II brackets (0.9%; 1.9%) during a longer observation period of 1 year and 19.9±5.4 months, respectively. In this study, the survival analysis for the OC (0.993) and FF brackets (0.970) showed a statistically significant difference. The survival analysis graph for the FF brackets and Table 2 demonstrate that most FF brackets (6 brackets out of 9 brackets) failed within the first 3 months of the 6 months observation period. Two patients reported specific reasons (olive pit, popcorn) for their bond failures (tooth 45, tooth 31). The remaining bond failures occurred in teeth 31 (2 failures), 32 and 33 with no specific reasons given by the patients. These failures may have resulted from inadequate enamel etching, poor moisture isolation, or inexpert handling of the brackets by the operator (DB), a second year resident. One OC bracket failed within the first 3 months (tooth 12) due to a soccer trauma.

Grünheid and Larson[5,6] also carried out a survival analysis of their data and did not obtain a statistically significant difference. In fact, an equivalent number of bonds (two for each adhesive)

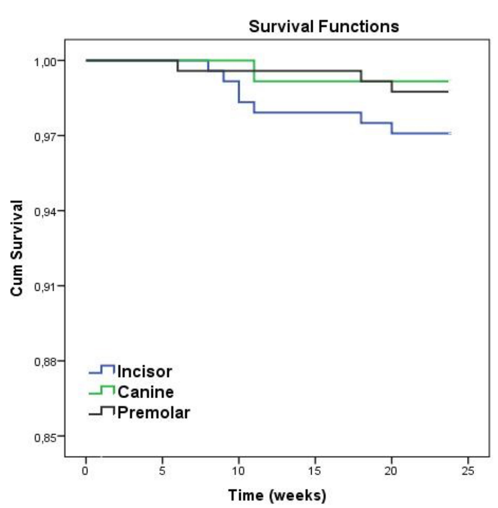

Figure 4. Bracket survival distribution for tooth type (incisor, canine and premolar)

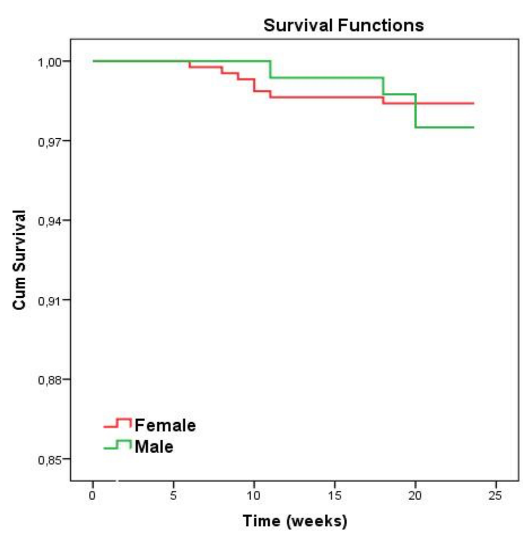

Figure 5. Bracket survival distributions for gender

Table 5. Frequency distribution and the result of the χ^2 analysis for the ARI*

	ARI scores				
	0	1	2	3	Total
OC	-	-	-	2	2
FF	8	-	-	1	9

*χ^2=6,519 on 1 df; p=0.011
ARI, adhesive remnant index; FF, flash-free; OC, operator-coated

failed during the first 3 months. However, these authors only evaluated the maxillary arch.

The comparison of clinical studies is difficult and must be carried out with caution due to differences in various aspects. For instance, the observation periods, number and experience of the operators, arch evaluation (maxillary arch only or both maxillary and mandibular arches), type of arch evaluation (an emphasis on quadrants), type of adhesives and bracket slot systems used. It has been reported that 0.018-inch slot brackets result in a greater number of bond failures than 0.022-inch slot brackets.[15] Furthermore, the inability to maintain the light-tip distance of 5 mm may have affected the degree of polymerization and bond durability.[16] In this study, the failure rate was 1% (3 brackets) for the maxillary arch and 2.7% (8 brackets) for the mandibular arch, with no statistical difference obtained for the failure and the survival rates. Nevertheless, the mandibular bonds failed more frequently and sooner when compared to the maxillary bonds. This outcome may be attributed to factors such as not abiding by the diet recommendations and potential traumatic occlusal contacts on the mandibular bonds. Poor control of moisture and saliva contamination control during bonding, when compared to the maxillary arch, may also have occurred. An effort to mitigate potential traumatic occlusal contacts, through a layer of cement placed on the molar occlusal surfaces for disclusion, might have lowered the failure of the mandibular bonds.[15]

It is noteworthy that all of the mandibular bonds (8 brackets) that failed belonged to the FF brackets. An *in vitro* study[17] compared 3 bonding systems (3M Unitek). The first group was bonded with the FF system, the second group with the APC Plus system, and the third group was manually bonded with the Transbond XT adhesive. One type of ceramic bracket (Clarity Advanced, 3M Unitek) was used. The three adhesive systems achieved comparable values; however, the mean shear bond strength (SBS) value for the FF group was lower when compared to the other groups. It is important to note that the FF adhesive is a low viscosity adhesive. Previous research has linked low viscosity, i.e., lower filler content, with reduced SBS.[18] Based on this information and the data from our study for the mandibular arch, it is possible that there is a threshold level for the FF adhesive, beyond which bond failure is likely to occur. The manufacturer determines the precise amount of low viscosity adhesive for each tooth type in the FF bracket mat. However, variations in tooth crown contour can weaken bond formation and compromise reliability. In contrast, Tümoğlu and Akkurt[7] reported only one FF bond failure for the mandibular arch. The significant difference between their study and the current study, which found eight FF bracket failures is likely due to the difference in methodology. Tümoğlu and Akkurt[7] worked on a quadrant basis; whereas in the current study acid etching was performed simultaneously on both upper and lower arches, making saliva and/or moisture contamination a possible factor.

During the current study, bond failures occurred with seven incisors, one canine, and three premolar brackets. Nevertheless, no significant differences were observed for the failure or survival rates. What is striking is that, despite the lack of a statistical significance, the anterior teeth (incisors and canine) experienced more bond failures than the posterior teeth. This finding contrasts with other studies, where more posterior than anterior bond failures were observed.[1,7,9,12,15] Similar to the current study, Manning et al.[19] also reported more anterior bond failures and suggested that habits, such as nail biting and pen chewing might contribute to this outcome. It has been reported that canines demonstrate the lowest bond failure rate.[1] Linklater and Gordon[15] stated that a potential contributing factor might include increased masticatory loading of the canines. Furthermore, these researchers[15] pointed out that moisture control of the mandibular canines is a greater challenge compared to the maxillary canines during bonding. In this study, one failure occurred with the mandibular left canine. No specific reason for this failure could be provided by the patient; thus, saliva and moisture contamination during the bonding process and inexpert handling by the right handed operator might have been the culprit for this bond failure. Right-handedness has been linked to superior bonding accuracy and moisture control on the right compared to the left side of the mouth.[7,20] A mild Class II canine relationship may have compounded this outcome.

Adolfsson et al.[21], speculated that females are more careful with their appliances than males. Thus, a higher bond failure rate for males was anticipated in this study. However, the bond failure and bracket survival rates did not demonstrate statistically significant differences. This might indicate that bond failure is strictly patient-related and gender-neutral. The bond failure sites were evaluated using the ARI. Both adhesives demonstrated a statistically significant difference. Most FF brackets (8 out of 9) had a score of 0 (no adhesive left on the tooth), indicating that bonds mainly failed at the mat-tooth interface. This outcome is consistent with Grünheid and Larson.[5] However, Grünheid et al.[13], suggested that the mat-tooth interface is not typically the site of failure, and that severance at the bracket base mat interface is predetermined due to a lower material density at that site. Hence, the outcome of this study, with an ARI score of 0 for 8 failures, is unexpected. ARI scores provide insight into the reason for failure, thus, this outcome may suggest inadequate etching and/or moisture or saliva contamination, which can prevent reliable bonding with the enamel. In this study, significant differences for the bonding times were obtained. This is not surprising given that two steps (adhesive application and flash clean-up) were eliminated with the FF bracket (mean: 64.43 seconds for one bracket) compared to the OC bracket (mean: 98.97 seconds for one bracket). Although, direct comparisons to the studies of Grünheid and Larson[5] and Tümoğlu and Akkurt[7] are not possible, these studies[5,7] also reported a significantly shorter bonding time. Cumulative time savings during the bonding of the upper and the lower arches with the FF system may enhance patient comfort by reducing chair time. The reduction in chair time might also imply a reduction in aerosols and droplets.

The current study used identical, polycrystalline, true twin brackets with a microcrystalline base design containing a stress concentrator. These ceramic brackets differed only regarding the adhesive on the bracket base. Notably no fractures of any ceramic bracket occurred. Eleven failed brackets did not have any fractures as well, i.e., they failed "intact" and remained ligated to the arch wire. This is a reassuring outcome, because tie-wing fractures may lead to numerous problems. Such fractures prevent efficient arch wire ligation and increase the risk of complete fragmentation of the bracket. Ceramic bracket fragments may become embedded in the oral soft tissues or they may be inhaled and/or swallowed. These fragments are radiolucent. Thus, not visible on radiographs.[22]

The short observation period and the Hawthorne effect are the two main limitations of this study. The Hawthorne effect has been described as an alteration in the patient's or therapist's behavior due to the awareness of being observed during a study.[23] This "good trial behavior" might lead to a superior performance of the participants. As a consequence, overoptimistic findings may be obtained. It has been pointed out that a short observation period, such as 6 months, might increase the risk of this effect.[24,25] Furthermore, an orthodontic adhesive system must be able to withstand the challenges posed by the oral environment.[26] The mean orthodontic treatment duration has been reported as 30.6 months.[1] Therefore, an extended observation period of preferably more than 12 months, would be necessary for the persistent and various degrading factors affecting this new technology in the oral environment[6,27] and mitigate the Hawthorne effect. Last but not least, future *in vitro* and *in vivo* research elucidating the effects of fluoride and non-fluoride remineralization agents with this new technology could be very interesting and beneficial, particularly since the APC FF adhesive does not release fluoride.[28,29]

CONCLUSION

The null hypothesis was rejected for parameters 1, 5, and 6, indicating a statistical difference in failure rates between the two adhesive systems. Despite this, the results for the FF brackets are promising. A significant difference in ARI scores was also found between the two systems. Six of the nine ARI scores for the FF adhesive system had a score of 0 during the first 3 months, indicating possible saliva or moisture contamination and inadequate handling during the bonding procedure. The bonding times were also significantly different between the two adhesive systems, suggesting that the FF adhesive system may improve patient comfort.

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Ethics

Ethics Committee Approval: Ethical committee approval was received from the Ondokuz Mayıs University Clinical Research Ethics Committee (approval no: OMÜ KAEK 2018/416).

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

Peer-review: Internally peer-reviewed.

Author Contributions: All of the following steps (conception of this work, data collection, data analysis and interpretation, drafting and the critical revision of this article as well as the final approval of the version to be published) were carried out by D.B. and S.E.T.

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Systematic Review

Accuracy of Invisalign® on Upper Incisors: A Systematic Review

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Main Points

- The accuracy of the tooth movements for the upper incisors ranged from 0% (when the teeth moved the opposite direction of the predicted movement) to 155.7% (when the achieved movement overcame the predicted one).
- For axial movements, the lateral incisors showed highly accurate (i.e., predictable) movements, especially in the labiolingual tip.
- For vertical movements, low accuracy was observed for intrusion, whereas the extrusion movement was proved to be highly accurate in both the central and lateral incisors.
- For horizontal movements, the central incisors presented highly accurate movements, especially in translation.
- Overall, the aligner showed good efficiency in reaching the desired movements in the upper incisors. Aligner features such as attachments and Power Ridge may be a good alternative to improve movement accuracy.

ABSTRACT

The current systematic review appraises the effectiveness of the types of tooth movements performed with Invisalign® clear aligner on the maxillary incisors. An electronic literature search of published trials was performed through PubMed, LILACS, Scopus, Cochrane Library, and Web of Science databases, and selected journals, from 2009 to 2020. Out of 291 references, five relevant publications were identified for analysis: four studies were performed retrospectively and one prospectively, all non-randomized. Despite the limited set of selected articles, the sample size is significant, with 148 subjects included in the reviewed studies involving the orthodontic treatment of upper incisors. We concluded that movements with the Invisalign® clear aligner on the upper incisors present distinct accuracy, possibly related with movement complexity; intrusion of the incisors has low accuracy (in some cases, 0% of accuracy was reported when the tooth extruded), while incisor extrusion exhibit some of the highest accuracy values reported in the included studies (45%-142%, when the achieved movement was greater than the predicted). Besides, axial (i.e., torque and tip) and horizontal (i.e., translation and rotation) movements are usually effective, with accuracy values between 39%-156% and 42%-79%, respectively. Overall, we determined that the efficiency of aligner to reach the desired movements in the upper incisors was low, as often refinements were required in the included studies. The use of aligner features must be more often considered to improve movement accuracy.

Keywords: Accuracy, efficiency, incisor, Invisalign®, tooth movement

INTRODUCTION

Invisalign® clear aligners (Align Technology Inc, CA, USA) are widely used in orthodontics nowadays, mostly in adult patients due to the improvement on aesthetics and comfort, as well as on hygiene and periodontal control.[1-4] Since its introduction in 1997 by Align Technology®, significant improvements were developed on the algorithms that can determine the necessary force systems to allow more accurate tooth movements.[5]

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Some studies have been conducted to evaluate the movement accuracy (i.e., the predictability of the movement; the difference between achieved and predicted tooth position) with Invisalign® clear aligners, although yet sparce evidence exists on the topic. The current knowledge is quite limited, and conflicting results are reported among the existing data. Thereby, despite the officially reported ranges for movement efficacy reported by Invisalign®, they remain far from being consensual among orthodontic professionals. To address this issue, three systematic reviews evaluating the accuracy of Invisalign® clear aligners were published in the last five years.[4,6,7] However, their conclusions were drawn regarding the type of movement instead of a specific tooth or tooth group. Accordingly, it is still difficult to assess specific clinical concerns such as those associated with upper incisors.

Having this in mind, the authors performed an electronic literature search to collect all the published evidence about the application of Invisalign® clear aligner to produce tooth movement in the upper incisors. Thus, this systematic review summarizes, compares and discusses the findings of different studies describing the tooth movement promoted by Invisalign® clear aligner in the upper incisors, aiming to identify the most affective parameters used so far by the clinicians. It also highlights and compare the accuracy and efficiency of the mechanisms triggered along the treatment.

METHODS

This systematic review followed the Preferred Reporting Items for Systematic reviews and Meta-Analyses checklist.[8] The protocol was registered in the PROSPERO database (CRD42020190272).

Identification of Relevant Studies

Articles that compare the predicted and achieved incisor movements and/or that evaluate the accuracy/efficiency of the movement during an orthodontic treatment to the upper incisors using Invisalign® clear aligner were included. Importantly, only papers published after 2010 were included, since 2009 marked the introduction of Invisalign® Smart Technology, that brought optimized features to the orthodontics community, namely, the SmartTrack material, SmartForce features (including the Invisalign Power Ridge®), and the SmartStage technology.[9-11] The review strategy was lined up according to the Population, Intervention, Comparison, Outcomes, and Study design tool, as presented in Table 1.

Thus, the aim of this systematic review is to answer the question: "What is the current knowledge on the accuracy of various tooth movements performed on maxillary incisors with Invisalign® clear aligners?"

Information Sources and Search Strategy

The database search plan was discussed among all authors, who decided to use the following databases: PubMed, LILACS, Scopus, Cochrane Library, and Web of Science. Given the introduction of optimized aligner features by Invisalign® designed to improve tooth movement accuracy in 2009, only studies published in or after 2010 were included in this review. Also, only papers written in English, French, Spanish, or Portuguese were considered. In addition, a manual search was also conducted in orthodontic journals of interest to refine the survey.

The following search terms were used: (humans* OR adult* OR malocclusion* OR male* OR female*) AND (Invisalign OR clear aligners OR aligners OR transparent aligners OR orthodontic appliances, removable*) AND (cephalometry* OR orthodontic treatment OR treatment outcome*) AND (incisor* OR incisors).

Study Selection and Data Collection

Three reviewers (AG, AC and FM) independently selected the articles for analysis. In the case of disagreement, other authors (DM and TP) intervened. The same methodology was used to process the articles through the previously set criteria for inclusion and exclusion, after the duplicates were removed. References of selected articles were searched in detail to find potentially relevant studies.

Data collected from each article included the authors, year of publication, study design and population, a type of intervention, and main results associated with the accuracy of tooth movement produced by Invisalign® clear aligner on upper incisors (Table 2). When possible, accuracy metrics were uniformized in percentage using the ratio between predicted and achieved movements/positions.

Methodological Quality Assessment

After data collection, two independent reviewers (AG and AC) evaluated the included studies according to the Risk of Bias in Non-randomized Studies - of Interventions (ROBINS-I) tool.[12]

Table 1. The PICOS strategy was applied to the current review

Categories	Applied Criteria
Population	Patients with permanent teeth undergoing treatment with Invisalign® clear aligner.
Intervention	Orthodontic treatment with Invisalign® clear aligner.
Comparison	Predicted vs achieved tooth position.
Outcomes	Clinical accuracy metrics of the tooth movements performed with Invisalign® clear aligner on upper incisors.
Study design	Controlled clinical trials (randomized or not), cohort studies, case control studies, and case series. Prospective, retrospective, and cross-sectional studies were also considered.

PICOS, Population, Intervention, Comparison, Outcomes, and Study design.

This approach is based on seven bias domains: confounding, participants selection, classification of interventions, deviations from intended interventions, missing data, measurement of outcomes, selection of the reported results, and overall bias. Bias assessments were tabulated with explanations when the studies were downgraded. Since assessments are inherently subjective and there are no strict and objective criteria to judge bias within the ROBINS-I tool, disagreements were resolved via a discussion between the two investigators. Bias was assessed per study rather than per outcome since there were no meaningful differences in bias across outcomes.

RESULTS

Study Selection

The electronic search initially identified 291 relevant articles. After 53 duplicate removal, 238 papers remained. Among these, 167 were excluded after title and abstract analysis. From these, 12 articles were selected for full-text reading, from which four studies were considered eligible for inclusion in the final analysis. One extra study was included from the reviewed literature, resulting in a total of five studies to be included in the current systematic review. The selection process is depicted in Figure 1.

Study Profile

Five relevant publications were identified: four retrospective non-randomized studies, and one prospective non-randomized study. There were variations in the total sample size (range 20-38 patients), totalizing 612 movements under study with upper incisors. Table 2 summarizes the main characteristics of the reviewed studies in a chronological order, enabling an intuitive comparison between the experiments and results.

The intervention among studies is similar, as all of them focus on the comparison of the final with the initial virtual models of the oral cavity, and the Invisalign® system only was used. We emphasize the classification of the intervention with the aligner features (i.e., auxiliary elements such as attachments and Power Ridge) used, compliance, and duration of treatment.

Accuracy results were written either as a mean accuracy percentage (i.e., ratio between achieved and predicted movements/positions)[13,14], or as the average difference (mean ± standard deviation) between predicted and achieved tooth positions.[15-17] Accuracy values greater than 100% mean that the achieved exceeded the predicted movement.[16,17] However, accuracy was deemed 0% when the achieved movement was in the opposite direction of the desired one.[16] Besides, different software was used to produce virtual models (e.g.,

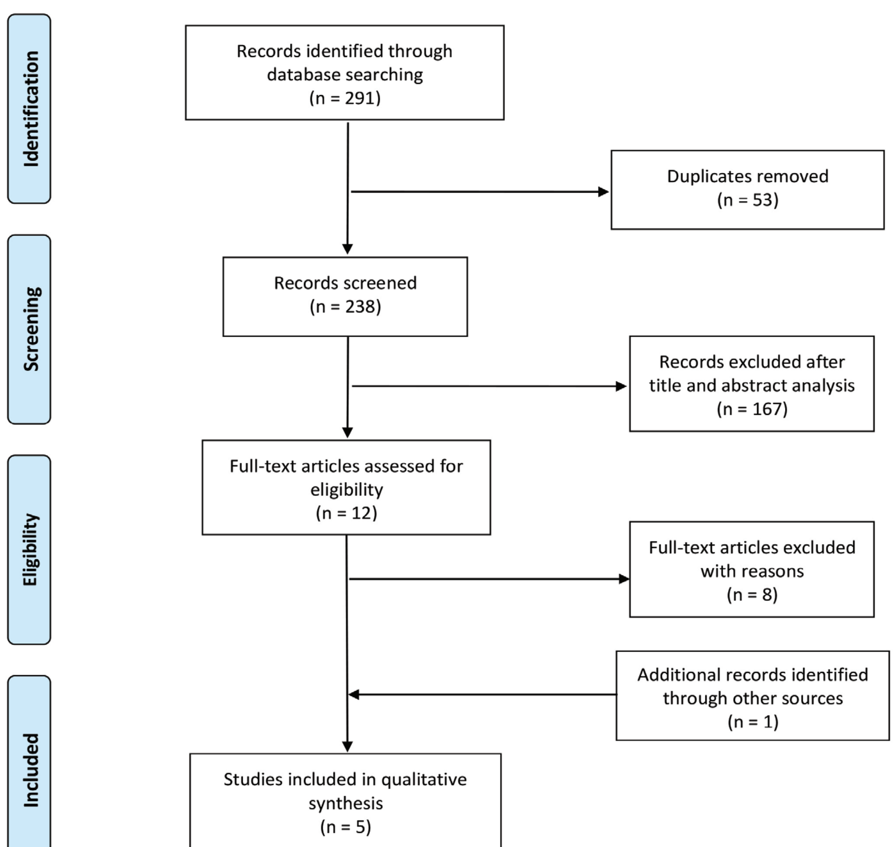

Figure 1. Flowchart from PRISMA method - articles selection process.[8]
PRISMA, Preferred Reporting Items for Systematic reviews and Meta-Analyses.

Table 2. Overview of the design and population, a type of intervention, and results of the included studies

Study	Study design	Invisalign® intervention	Results: Upper central incisors	Results: Upper lateral incisors	Results: General (other tooth movements)
Simon et al.[13] (2014)	Retrospective clinical study (30 patients)	- Time wearing the aligner: 22 h/day, except two patients who used 8 h/day - Time of aligner change: NR - Average treatment time: NR - Movement type: torque - Use of auxiliaries: torque with Power Ridge (n=7) and attachment (n=7)	- Lingual torque (with attachment): 49.1% - Lingual torque (with Power Ridge): 51.5%	NA	- Overall mean accuracy of tooth movement (upper incisor torque, premolar derotation and upper molar distalization): 59.3%
Grünheid et al.[15] (2017)	Retrospectivecohort study (30 patients)	- Time wearing the aligner: NR - Time of aligner change: 2 weeks - Average treatment time: 11 ± 4 months - Movement type: torque, horizontal and vertical movement - Use of auxiliaries: no	- Mesial rotation: 0.33° ± 2.80° - Lingual torque: 1.75° ± 2.86° - Distal tip: 0.42° ± 1.57° - Labial translation: 0.45 ± 0.64 mm - Mesial translation: 0.06 ± 0.40 mm - Extrusion: 0.30 ± 0.28 mm	- Distal rotation: 0.70° ± 3.23° - Lingual torque: 0.08° ± 2.93° - Distal tip: 0.35° ± 2.36° - Lingual translation: 0.01 ± 0.66 mm - Mesial translation: 0.14 ± 0.39 mm - Extrusion: 0.03 ± 0.26 mm	- Statistically significant differences between predicted and achieved tooth positions were found for all teeth except maxillary lateral incisors, canines, and first premolars.
Charalampakis et al.[16] (2018)	Retrospective clinical study (20 patients)	- Time wearing the aligner: NR - Time of aligner change: 2 weeks - Average treatment time: 12 ± 2.5 months - Movement type: horizontal, vertical displacements and mesiodistal rotations - Use of auxiliaries: no restrictions on attachment placement when needed	- Mesial-distal translation: 0.24 ± 0.90 mm; 78.9% - Extrusion: -0.36 ± 0.91 mm; 128.1% - Intrusion: 1.36 ± 0.63 mm; 0% - Rotation: 2.33 ± 3.65°; 57.2%	- Mesial-distal translation: 0.26 ± 0.83 mm; 77.2% - Extrusion: -0.27 ± 0.79 mm; 127.8% - Intrusion: 0.92 ± 0.70 mm; 0% - Rotation: 3.10 ± 7.34°; 66.2%	- Incisor intrusion and canine rotation were the most inaccurate movements, while other tooth rotations and vertical movements were the most accurate ones.
Dai et al.[17] (2019)	Retrospective clinical study (30 patients)	- Time wearing the aligner: NR - Time of aligner change: every 1-2 weeks - Average treatment time: 22.3 ± 4.6 months - Movement type: torque and vertical displacement - Use of auxiliaries: torque with Power Ridge and attachments, although rare	- Lingual tip: -5.16° ± 5.92°; 155.7% - Lingual translation: 2.12 ± 1.51 mm; 67.6% - Extrusion: -0.50 ± 1.17 mm; 142.4%	NA	- Low accuracy of the first molar anchorage control and central incisor retraction after the first premolar extraction treatment with Invisalign.
Haouilli et al.[14] (2020)	Prospective clinical study (38 patients)	- Time wearing the aligner: 22 h/day - Time of aligner change: 10 days - Movement type: torque and vertical displacement - Average treatment time: 8.5 months - Use of auxiliaries: average of six attachments	- Mesial rotation: 51.3 - 61.1 % - Distal rotation: 48.7 - 54.9% - Intrusion: 33.4 - 33.9% - Extrusion: 44.5 - 56.4% - Mesial tip: 47.7 - 57.5% - Distal tip: 45.5 - 49.8% - Lingual tip: 57.4 - 64.0% - Labial tip: 52.8 - 54.2%	- Mesial rotation: 52.6 - 56.4% - Distal rotation: 41.8 - 48.7% - Intrusion: 36.7 - 44.6% - Extrusion: 47.1 - 53.7% - Mesial tip: 38.5 - 47.3% - Distal tip: 47.3 - 51.5% - Lingual tip: 54.4 - 57.4% - Labial tip: 61.4 - 69.9%	- Overall mean accuracy for tooth movement (mesial-distal crown tip, buccal-lingual crown tip, intrusion, extrusion and rotation): 50%; - The most accurate movements were the labial crown tip of the maxillary lateral incisor, buccal-lingual crown tip, and rotation, whereas the least accurate movements were the mesial rotation of the mandibular first molarand intrusion of the maxillary and mandibular central incisors.

Negative values represent cases in which the achieved movement was greater than the predicted one - accuracy percentages over 100%.
Accuracy values of 0% are reported when the achieved movement occurred in the opposite direction of the predicted movement.
NA, not applicable.

ToothMeasure, Slicer CMF) to compare the predicted vs achieved tooth movement analysis.

Assessment of the Risk of Bias

Among the included studies, one was classified as having a low risk of bias (RoB)[17] three as moderate RoB,[13,15,16] and one study was scored with a serious risk of bias.[14] See the complete data on the quality assessment in Supplementary Table S1. RoB due to missing data was considered critical, as three studies excluded individuals and reported drop-outs with missing information.[13,14,16] Besides, three studies presented insufficient accuracy metrics, hampering result comparison.[13-15]

Effects of intervention on different types of movement

Torque: Four of five papers reported accuracy metrics of torque movement on upper confidence interval (CI).[13-15] Accuracy percentages of CI ranged from 49.1% to 51.5%,[13] while no information on accuracy percentages were provided for the LI. However, other authors reported a mean difference between predicted and achieved tooth positions of 1.75° ± 2.86° for the CI, and 0.08° ± 2.93° for the LI,[15] showing great accuracy for the lingual torque in the LI.

Labiolingual tip: Regarding the labiolingual tip, the accuracy of the lingual tip ranged from 57.4% to 155.7%[17] in the CI, and from 54.4% to 57.4% in the LI, while the accuracy for labial tip varied from 52.8% to 54.2% in the CI, and from 61.4% to 69.9% in the LI.[14]

Mesiodistal tip: The accuracy of the mesiodistal tip ranged from 45.5% to 57.5% on upper CI, and from 38.5% to 51.5% on upper LI.[14] Interestingly, Haouili et al.[14] found that the mesial tip was more accurate on the CI, while the tip in the distal direction showed more accuracy on the LI.

Intrusion and extrusion: Regarding the intrusion and extrusion movements, the accuracy reported by Haouili et al.[14] ranged from 33.4% to 33.9% for the CI, and 36.7% to 44.6% for the LI. However, Charalampakis et al.[16] observed that the vertical movement of intrusions initially predicted both for CI and LI were not accomplished, and the teeth moved toward the opposite direction (i.e., extruded). In these cases, the accuracy was deemed 0%. However, two studies reported highly accurate extrusion movements on upper CI, greater than predicted and therefore with accuracy values greater than 100%.[16,17] Moreover, mean differences between predicted and achieved extrusion movements ranged from -0.50 ± 1.17 mm (accuracy of 142.4%)[14] to 0.30 ± 0.28 mm[15] for the CI, which reflect high movement accuracy, and from 0.03 ± 0.26 mm[15] to 1.36 ± 0.63 mm for the LI.

Rotation: The accuracy of the rotation movement ranged from 48.7% to 61.1% on CI[14] and 41.8%[14] to 66.2%[16] on LI. Mean differences between predicted and achieved movements varied from 0.33° ± 2.80°[15] to 2.33° ± 1.21° (accuracy of 57.2%)[16] for the CI, whereas the same metrics for the LI ranged from 0.70° ± 3.23° to 3.10° ± 1.48° (accuracy of 66.1%),[16] which is almost negligible and suggest a high accuracy.

Labiolingual translation: The accuracy of labial translation was assessed in two of the included articles.[15,17] Dai et al.[17] obtained a mean differences between predicted and achieved movements of 2.12 ± 1.51 mm (accuracy of 67.6%) performing labial translation of upper CI. However, Grünheid et al.[15] observed a labial translation of 0.45 ± 0.64 mm and an even more accurate lingual translation of the LI of 0.01 ± 0.66 mm.

Mesiodistal translation: Only two studies evaluated the mesiodistal translation of incisors; regarding the CI, Grünheid et al.[15] reported a mean difference between predicted and achieved mesial translation of 0.06 ± 0.40 mm, while Dai et al.[17] observed a difference of 0.24 ± 0.90 mm between predicted and final positions. Concerning the LI, average differences of 0.14 ± 0.39 mm[15] and 0.26 ± 0.03 mm (accuracy of 78.9%)[17] were obtained.

DISCUSSION

Since the creation of Invisalign® clear aligner, issues associated with the movements of the upper incisors have been reported, as they fail to reach the programmed positioning.[4,7,18] This review identifies the major limitations of the revised studies, which constitute the current literature on orthodontic treatment using aligner in upper incisors. Nevertheless, multiple movements were assessed, for which a range of mean accuracy values is presented.

Although poorly discussed among the revised studies, the aligner-wearing time is critical for movement accuracy and effectiveness. The Invisalign® treatment protocol recommends a daily use of the aligner of 22 h. Here, three of five papers do not report the instruction given to the patients concerning the aligner wearing time.[15-17] However, the other two state that Invisalign® recommendations were followed.[13,14] Importantly, Kravitz et al.[19] described an individual case in which a patient with poor compliance to the aligner treatments (daily use of about 8 h/day) compromised the accuracy of premolar derotation. Thus, the wearing time seems to be a determinant for treatment succes; and therefore, future clinical studies using aligner must clearly describe the daily time recommended for the aligner usage.

Moreover, it is important to evaluate the accuracy of the orthodontic treatments considering the use or not of aligner features. Here, only one study did not use any type of auxiliary,[15] while three used attachments,[13,14,16] and one used Power Ridge. Dai et al.[17] referred that attachments and Power Ridge were rarely used to increase torque control. However, this study presented some of the greatest accuracy values for incisor lingual tip (155.7%), labiolingual translation (67.6%), and vertical movements (142.4%). Interestingly, the sample is presenting the lowest accuracy of incisor torque (49.1% and 51.5%) used either attachments or Power Ridge.[13] Nevertheless, the overall data suggests an increased accuracy of most of the incisor movements considered in the reviewed studies when aligner features, such as Power Ridge and attachments, are used.[14,16,17]

Axial movements: torque and tip

Three studies evaluated the clinical torque, either lingual[13-15] and labial. However, in the studies led by Simon et al.[13] and Grünheid et al.[15], the exact definition of the term "torque" is not totally clear. Statistically significant differences between the predicted and achieved tooth positions were found in both. Accuracies are only reported by Simon et al.[13], who studied the lingual torque movement: 49.1% (with horizontal ellipsoid attachment) and 51.5% (with Power Ridge). Note that, as reported by Simon et al.[13] and Grünheid et al.[15], the reference point was determined using the virtual crown positions. Therefore, these findings may need to be interpreted with caution, as one of them considers biomechanical torque evaluation.[14]

To notice, Haouili et al.[14] excluded the torque measurement due to the absence of radiographs evaluating the labiolingual tip, while others have been assuming the clinical torque as labiolingual tip action Items.[19] These findings illustrate the frequently misuse of the term "torque." Even though, Haouili et al.[14] found the highest value for labiolingual tip accuracy on LI (69.9%), although its small clinical crown has been reported as the main factor for loss of retention and movement failure throughout the treatment.[20-24]

Considering the labiolingual tip, the highest accuracy values were found for the lingual tip, with that of Dai et al.[17] reporting a mean difference between predicted and achieved movement of -5.16° ± 5.92°, corresponding to an accuracy of 155.7%, since the achieved movement overcame the initially predicted. It should be emphasized that the later study evaluated the accuracy of incisors' movement on a bicuspid extraction protocol.[17] This rises clinical issues that might compromise the evaluation of the torque movement since, although Power Ridge has been used, torque control is more difficult to achieve due to the premolar extraction.

Haouili et al.[14] also found that the labiolingual tip presented high accuracy metrics, both for CI and LI. Interestingly, the lingual tip was found to be more accurate in the CI, while the labial tip presented higher accuracy values for the LI.

Moreover, Haouili et al.[14] also measured the accuracy of mesiodistal tip in the CI and LI. The authors found that the mesial tip was more accurate in the CI, whereas the distal tip presented higher accuracy in the LI. Similarly, Grünheid et al.[15] reported the mean differences between predicted and achieved distal tip movements, and the results show that this movement was more accurate in the LI compared with the CI.

Vertical movements: extrusion and intrusion

Vertical movements are usually difficult to achieve, and therefore are often associated with low accuracy values, mainly with clear aligner.[4,16,25] However, among the reviewed studies, tooth extrusion was the most accurate movement, with two different papers reporting accuracy values greater than 100% (i.e., where the achieved movement was greater than the predicted.[16,17] Similarly, another study reported a mean difference between the predicted and achieved movement of 0.30 ± 0.28 mm, also revealing a great accuracy of the extrusion movement. Besides, Haouili et al.[14] reported accuracy values from 44.5 to 56.4% for CI, and 47.1 to 53.7% for LI, which reflects a good accuracy of the desired movement. Even though, in the referred study, a statistically significant difference between predicted and achieved tooth positioning was found for CI, but not for LI.[14]

In contrast, the accuracy of the intrusion movements among the included studies was typically low and, in some cases, null; specifically, Charalampakis et al.[16] found that the CI and LI for which an intrusion movement was predicted actually moved toward the opposite side (i.e., extruded), and thus the accuracy of the movement was considered to be 0%. However, Haouili et al.[14] observed that incisors intrusion ranged from 33.4 to 33.9% in the CI, and 36.7 to 44.6% in the LI. Among the movements studied in the work led by Haouili et al.[14], intrusion presented the lowest accuracy values.[16]

Despite the development of optimized attachments to improve aligner grip for a more reliable intrusion, the attachment hierarchy might interfere with its placement and with the movement. Moreover, data from Charalampakis et al.[16] reveal that an extrusion movement was achieved when the intrusion was programmed. The authors reported that, although tooth superimposition was based on unmovable teeth, the bite-block effect promoted some molar intrusion and it was responsible for the opposite movement observed.[16] For the same reason, the extrusion movement achieved was over the expected,[16] in line with what was reported by Dai et al.[17].

Horizontal movements: rotation, mesiodistal, and labiolingual translation

Regarding horizontal movements, translations presented higher accuracy than rotations. The greatest accuracy was found for mesiodistal translation - 78.9% for the CI and 77.2% for the LI.[16] Then, lingual translation also presented good accuracy values, with the only study reporting an accuracy percentage of such movement stating an accuracy of 67.6%.[17]

Additionally, mesial and distal rotation movements ranged from 48.7% to 61.1% for CI and 41.8% to 66.2% for LI.[14,16] Overall, the accuracy of mesiodistal rotation is similar comparing LI and CI. However, a lower accuracy of LI rotation could be expected due to the small clinical crown, which consequently allows a small distance between the point of application of the forces that generates smaller moments.

Overall, horizontal movements presented high accuracy metrics, with the efficiency of body movements (i.e., translation) being greater than the rotation. Specifically, the higher accuracy of rotation movement on the upper CI compared to the LI can be explained by their flat morphology. Despite the aligner material innovations, these findings are not surprising since labial and lingual tooths provide larger surfaces for the appliance to apply forces.

Study Limitations

Very few articles have met the objective of this systematic review. As a result, a rigorous methodology for researching the biases of each selected study has been implemented. Importantly, this literature review only covers articles describing studies using clear aligner on the upper incisors and published from 2010 till the present, since 2009 marked a great innovation regarding optimized features in Invisalign aligner - the introduction of Invisalign Smart Technology.[9-11] Within this period, no randomized clinical trials exist on the topic. This means that no randomized experiments were ever performed on the accuracy and efficiency of tooth movements performed on maxillary incisors since the introduction of optimized aligner features. Future efforts in the field must have this into account.

Among the included studies, few samples for each incisor movement were available. Additionally, inconsistent accuracy metrics were presented among the studies; only one study reported the complete data about the predicted and achieved tooth positions,[16] another study reports mean accuracy percentages without the predicted and achieved raw data,[13] others provide the average difference between predicted and achieved tooth positions,[15,17] while some present the maximum and minimum accuracy values.[14] This really hampers the comparison of the reported results, disabling a supported and constructive search for the best orthodontic parameters. To improve comparability, when possible, the achieved and predicted movement metrics were converted into an accuracy percentage.[16,17]

Overall, accuracy values of orthodontic movements of the upper incisors found in the literature are difficult to interpret and cross compare. Here, we uniformized the accuracy metrics reported and compiled the accuracy data (achieved vs predicted ration) into an easy-to-read and systematic table. We expect that future reports could present a complete descriptive analysis of the data, providing different accuracy metrics.

CONCLUSION

Within the limitations of this systematic review, the most important conclusions to be highlighted in the current systematic review are:

The accuracy of the tooth movements for the upper incisors ranged from 0% (when the teeth moved the opposite direction of the predicted movement) to 155.7% (when the achieved movement overcame the predicted one).

For axial movements, the lateral incisors showed highly accurate (i.e., predictable) movements, especially in the labiolingual tip;

For vertical movements, low accuracy was observed for intrusion, whereas the extrusion movement was proved to be highly accurate in both the central and lateral incisors;

For horizontal movements, the central incisors presented highly accurate movements, especially in translation;

Overall, the aligner showed good efficiency in reaching the desired movements in the upper incisors. Aligner features such as attachments and Power Ridges may be a good alternative to improve the accuracy of movement.

Ethics

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - A.G.; Design - A.G.; Supervision - A.G.; Materials - A.C.; Data Collection and/or Processing - A.G., A.C.; Analysis and/or Interpretation - A.C., F.M., R.A.; Writing - A.G., A.C.; Critical Review - F.M., D.M., Ó.C., R.A., F.S.S., T.P.

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Supplementary Table S1. Risk of bias of observational studies by ROBINS-I quality assessment scale

	Domains							
	Preintervention		Intervention	Postintervention				
Authors	Bias due to confounding	Bias in selecting participants for the study	Bias in classifying interventions	Bias due to deviations from intended intervention	Bias due to missing data	Bias in measuring outcomes	Bias in selecting reported result	Overall RoB judgment
Simon et al.[13]	green	green	green	green	yellow	green	yellow	yellow
Grünheid et al.[15]	green	green	green	green	green	green	yellow	yellow
Charalampakis et al.[16]	green	green	green	green	yellow	green	green	yellow
Dai et al.[17]	green	green	green	green	green	green	green	green
Haouili et al.[14]	green	green	green	green	red	green	yellow	red

Low RoB in green; Moderate RoB in yellow; and Serious RoB in red.

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Review

The Use of 3D Printers in Orthodontics - A Narrative Review

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Main Points

- The use of 3D printers and intraoral scanners eliminate the need for dental impressions and processes such as gypsum casting for some orthodontic workflows, providing a fully-digitalized workflow.
- A large percentage of the articles focused on the accuracy and precision of 3D-printed orthodontic models.
- There is limited information about the production of devices such as removable appliances with metal hooks consisting of multiple materials.
- The ability to produce completely patient-specific designs from 3D printers has allowed doctors to develop new solutions (customized chain for impacted tooth, replica tooth etc.).

ABSTRACT

Developments in computer-aided design and three-dimensional (3D) printing have revolutionized the workflow for orthodontic applications. The purpose of this review article is to provide information about 3D printer history and types, appliances manufactured using 3D printers, and new designs that can be used in different cases. Articles published between January 2010 and November 2020 were reviewed on PubMed, MEDLINE, ScienceDirect, Elsevier, and Google academic resources, and 69 were identified as appropriate for the study. It was seen that bracket and archwires, nasoalveolar molding devices, orthognathic surgical splints, removable appliances, expansion appliances, clear aligner, retainers, auxiliary attachments, and working models can all be made with 3D printers. The 3D printer is now a technology that is easily accessible to orthodontists, increasing the production of different customizable appliances and promising a transition to a digital clinical workflow in the future.

Keywords: Printing, three-dimensional, stereolithography, 3D printer

INTRODUCTION

Technological advances have affected dentistry in various ways, one of which is the utilization of three-dimensional (3D) printers and the additive manufacturing principle for producing appliances. This new system, unlike subtractive manufacturing, is based on building the desired product layer by layer, making it possible to produce more precise and complex objects. Particularly over the last decade, studies indicate that the demand for 3D printers has significantly increased in orthodontics.[1] The American Society for Testing and Materials defines 3D printing as: "the creation of an object from 3D model data by adding layer upon layer, unlike subtractive manufacturing techniques".[2] Each of these layers can be viewed as a thinly sliced horizontal cross-section of the object made.

The foundation for 3D systems were laid by Charles Hull in 1986, when he launched a Stereolithographic 3D printer.[3] A few years after the first 3D printer's release, Scott Crump developed the fused deposition modeling (FDM) (3), and in 1995, Prof. Ely Sachs invented the inkjet printer system, which could be used in metal materials and coined the term "3D printing" for the first time.[4]

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A file format STL, was developed by Charles Hull, to define the surface geometry of three-dimensional models through triangles and ensure their transfer to the printer.[5] It is available on almost all computer-aided design (CAD) and 3D printers due to its simplicity, open-source code, and universal format.[5] STL, which does not have any color scale and prints items in one color, is one of the most widely used file extensions even 30 years after its creation.[5]

The most commonly used types of 3D printers in orthodontics include stereolithography (SLA), FDM, digital light procession (DLP), Polyjet photopolymer (PPP), and selective laser sintering (SLS).[3] SLA is the first developed type of 3D printer.[4] The production process begins by sending an ultraviolet laser beam to the liquid photo-curable resin pool. The laser contact resin is cured and solid, and after the first layer is cured, the moving structure platform goes down until a layer thickness, creating space for the new layer to cure.[3,6] After the production of the object is finished, some post-curing processes are required to clean the non-polymerized resin and increase the degree of polymerization of the product. Although this process increases the cost and duration of the method, the high resolution and quality of the produced objects ensure the continued demand for SLA today.[6] In orthodontics, stereolithographic 3D printers have been reported to be used in surgical guides, clear aligners, occlusal splints, retraction hooks, removable appliances such as activator, nasoalveolar molding (NAM) devices, aligner attachments, and craniofacial - dental tissue engineering.[1,7-9] DLP is the same as SLA except for the light source. Unlike the spot laser on the SLA, light is projected as a plane to cure an entire layer immediately.[3] This difference allows DLP to produce in less time than the SLA. DLP and SLA are vat polymerization type (liquid chamber) printers.

FDM is separated from SLS and DLP by using a thermoplastic polymer. The head part called the Nozzle is preheated and melts the thermoplastic material during its passage and sends it to the platform in semi-liquid form, and the polymer begins to solidify as soon as it spreads to the surface. The product consists of layers and overlapping of the melting filament. The shrinkage of the material during hardening and the limited materials that can be used in production creates disadvantages, while the advantage is that they do not require post-processing after printing and produce quickly.[6] FDM, which is one of the most widely used 3D printer types in the world, has been used for production in orthodontic models, retainer, aligner, surgical guide, and bioprinting studies.[10,11]

PPP creates a model by spraying the photopolymer resin layer by layer on the table and curing it with ultraviolet radiation at the same time. High-end PPP printers can print multiple materials on a single model.[3] PPP printers typically waste more material than other technologies, which increases the cost of use.

SLS-selective laser melting (SLS-SLM), developed by the University of Texas in 1989, is a system where layers of powder material are melted with a CO_2 laser to create 3D objects.[6] Layers of powder material are applied to the surface via a cylinder, and a new layer of dust is added after each melting process. The selective structure of the laser allows complex geometries to be obtained. It also enables the use of various materials including polymers (such as polyamide, polycaprolactone), hydroxyapatite, glass, ceramics and metal powders such as Co-Cr, titanium, and stainless steel.[3] Due to the mechanically strong structure of printed objects, it has been used to fabricate rigid metal structures such as implants,[12] retainers,[13] or maxillary expansion appliance[14] used in orthodontic and oral surgery.

The current article examines the areas in which 3D printers can be used in orthodontics by conducting a review of the current literature. A review of the literature published between January 2010 and November 2020 was conducted on MEDLINE, ScienceDirect, Wiley Online Library, Google Scholar, and PubMed. The keywords "3D printing, orthodontics", "SLA, and orthodontics" were used. The articles were scanned by one researcher (T.E). The search results are presented in Table 1. Mendeley desktop software (Mendeley Desktop, version 1.19.8, Mendeley Ltd., Elsevier Inc., NY, USA) was used as a reference manager to manage the search results. Using this tool, 169 duplicate studies were removed. Books, book parts, editorial letters, generics, dissertations, non-English articles, and articles that cannot be viewed even their abstract were excluded. Additionally, articles non-associated with orthodontics, and those that do not focus on the use of 3D printers were excluded. The most recent 69 articles that meet our criteria were included in the review.

Orthodontic Models

Many studies have evaluated the precision, accuracy, and reproducibility of orthodontic models produced from 3D printers. Most studies have shown that models made from 3D printers are suitable for clinical use[15-21] except for the study of Nurazreena et al.[22] (Table 2). Various methods have been used to create digital models for 3D printers, such as intraoral scanning, re-scanning existing plaster models, or referencing a typodont model. In 2017, Dietrich et al.[15] examined models produced from SLA and Polyjet printing for accuracy and precision, and found that both were clinically suitable for use. Measurements taken on Polyjet models were more accurate than those on SLA models, while the SLA models had higher precision than the Polyjet models.[15] Kim et al.[23] evaluated accuracy and precision digitally by scanning models made with DLP, fused filament fabrication (FFF), SLA, and Polyjet rinting. Models produced with Polyjet and DLP were found to offer more accurate results than

Table 1. Distribution of the articles by database and keywords

	3D printing and orthodontics	Stereolithography and orthodontics
PubMed	226	67
ScienceDirect	275	193
MEDLINE	62	2
Elsevier	12	-
Google Scholar	374	593

3D, three-dimensional

Table 2. Details of 3D-printed model studies included in the review

Authors	Year	Model data source	3D printing system	3D printing material	Layer thickness (μm)	Postprocessing treatment	Modelbase shape	Assesment method	Advised printer type
Dietrich et al.[15]	2017	Patient ios 2 case	SLA Polyjet	Epoxy-based resin (Accura) Photopolymer resins	100 at base/50 tooth level	Unclear	Unclear	By software	Both types suitable
Rebong et al.[20]	2018	Plaster dental cast 12 case	SLA Polyjet FDM	Unclear	100 50 16	Unclear	Unclear	Digital caliper	FDM
Ledingham et al.[19]	2016	Typodont model 30 case	SLA	Calcium sulfate-based substrate	Unclear	High heat Low heat Epsom salt	Unclear	By Software	Epsom salt
Brown et al.[17]	2018	Paitent ios 30 case	DLP Polyjet	Unclear	Unclear	Unclear	Unclear	Digital caliper	Both types suitable
Camardella et al.[24]	2017	Paitent ios 10 case	SLA Polyjet	Light-curing methacrylic resin (E-Denstone; Envisiontec) Photopolymer resin (Full Cure 720; Stratasys)	100 16	Unclear	Regular base horseshoe-shaped horseshoe-shaped with bar	By software	Polyjet
Kim et al.[23]	2017	Typodont model, 14 case	SLA DLP FFF Polyjet	Unclear	50 75 100 16	Unclear	Unclear	By software	Polyjet DLP
Koretsi et al.[16]	2018	Plaster dental cast	Polyjet	MED620	Unclear	Unclear	Horseshoe-shaped	Digital caliper	Suitable
Hazeveld et al.[18]	2014	Plaster dental cast 6 case	DLP Polyjet Inkjet	Unclear	Unclear	Unclear	Unclear	Digital caliper	All replicas are accurate enough
Wan Hassan et al.[22]	2017	Patient impression 10 cast	FDM	High performance composite (Zp151; 3D Systems)	Unclear	Infiltrant modeling	Unclear	Digital caliper	Not suitable
Manuelli et al.[21]	2018	Patient impression 80 cast	Unclear	Unclear	Unclear	Unclear	Unclear	Digital caliper	Suitable
Favero et al.[25]	2017	Typodont model	SLA SLA DLP DLP Polyjet	Grey photopolymer resin (FLGPGR02; Formlabs), unclear	25, 50, 100 100 100 100 28	Immersion baths, unclear	Unclear	By software	All types suitable

Table 2. continued

Authors	Year	Model data source	3D printing system	3D printing material	Layer thickness (µm)	Postprocessing treatment	Modelbase shape	Assesment method	Advised printer type
Zhang et al.[26]	2019	Patient ios	SLA DLP DLP DLP	Dental model resin (Formlabs) Model Orthoresin (Union Tec) Enca-Model Resin (Encashape) E-Denstone Resin	25, 50, 100 50, 100 20, 30, 50, 100 50, 100	Unclear	Unclear	By software	Except of two groups all types suitable
Loflin et al.[27]	2019	Plaster dental cast 12 case	SLA	Gray photopolymer resin (FLGPGR03; Formlabs)	25, 50, 100	Unclear	Unclear	Aboriginal tool	100 um SLA
Scott et al.[38]	2019	Plaster dental cast 15 case	SLA	Gray photopolymer resin (GPGR03; Formlabs)	50	Immersion baths	Unclear	Hand-grading Suresmile	Need future research

IOS, intraoral scanner; SLA, stereolithography; FDM, fused deposition modeling; DLP, digital light procession; FFF, fused filament fabrication; Aboriginal, American Board of Orthodontics

models produced with SLA and FFF, but the highest accuracy was observed in the Polyjet models.[23] Although Polyjet models gave highly accurate results in some studies conducted,[15-17,23,24] there are studies that claim this is not the case.[20]

Print layer height is an important factor that affects the printing time and the precision and accuracy of models. Naturally, researchers have conducted studies on this issue.[25,26] Favero et al.[25] conducted a comparison by using SLA printing to produce models with print layer heights of 25, 50, and 100 µm. The 100 mm layer height group was found to be more accurate than the 50-µm and 25 mm layer height groups.[25] These results suggest that increasing the number of layers increases accumulated of errors and failures during printing, reducing the accuracy of the printed model.[26] Zhang et al.[26] compared models with different print layer heights (20, 30, 50, 100 µm) from 3 different DLP printers to models with different print layer heights (20, 50, 100 µm) from an SLA printer. The highest accuracy was observed in DLP models with a thickness of 50 µm, while SLA models with a thickness of 100 µm showed the lowest accuracy.[26] In contrast to Favero et al.[25], the researchers observed that when the SLA models were examined, the resolution increased with the reduction in the print layer height, the stair-stepping effect decreased, and the accuracy of the model increased.[26] Two studies used the American Board of Orthodontics Cast-Radiograph evaluation (ABO-CRE) rating system, which has proven to be an objective way to evaluate models produced from 3D printers.[27,28] Loflin et al.[27] evaluated the effect of print layer height on the accuracy of 3D printed models using the ABO-CRE system. The researchers compared models with print layer heights of 25, 50, and 100 µm produced from SLA printer, and ultimately concluded that all models are clinically acceptable.[27] Scott et al.[28] used the ABO-CRE system to compare SLA-printed 3D models with values measured manually and automatically by the software (Suresmile), and the software was found to have higher scores on some measurements. It is explained that the software can be used instead of manual measurements if properly scaled.[28]

Today, different base designs can be used for model production. Camardella et al.[24] examined the effect that different model base designs have on the accuracy of models made with SLA and Polyjet printing. They used three different model base designs: regular base, horseshoe-shaped base, and horseshoe-shaped base with bar.[24] The 3D-printed models from the Polyjet printer were accurate regardless of their model base design, but the same cannot be said for the models from the SLA printer.[24] Transverse shrinkage was observed in models using the horseshoe-shaped base design; however, but there was no significant difference in measurements with the horseshoe-shaped base with bar and regular base models.[24]

Orthodontic models are sometimes required for constructing appliances. To prevent the deformation of polymer materials at high temperatures, Ledingham et al.[19] produced 3D-printed models based on calcium sulfate hemihydrate and subjected them to different post-processing treatments to increase their strength. They applied high heat (30 min.-250 °C), low heat

(30 min.-150 °C) and Epsom salt treatment. Epsom salt-treated models might be a viable alternative to the production of soldered orthodontic devices, as they produced statistically significant improvements in their mechanical properties.[19] A review study of 3D-printed orthodontic models was conducted in 2020 and it was noted that several different techniques, production parameters, materials, and evaluation protocols are used, making a meta-analysis impossible.[29] It is recommended that studies be conducted in accordance with a standardized reporting protocol that details all printing parameters, materials used, the post-processing protocol and evaluation time.

Clear Aligners

Aligners can be made with plaster and 3D-printed models using traditional techniques or by printing directly from 3D printers. Geometric inaccuracies are common and frequent due to the heat-forming process and decay of models during the traditional technique in which a thermoforming material is vacuum-formed.[30] Jindal et al.[30] compared 3D-printed aligners with thermoform aligners vacuum-formed from 3D-printed models through finite element analysis (FEA). Eliminating the thermoforming printing process with 3D-printed aligner increased accuracy, while the mechanical resistance and geometric accuracy of the 3D-printed aligner were also high. The next year, Jindal et al.[30] chose thermoplastic materials such as Duran and Durasoft for the vacuum-forming technique and dental LT Resin for direct 3D printing, then compared them using FEA under forces equivalent to a human biting force.[31] Researchers have shown that Dental LT Resin provides an alternative to the conventional materials for manufacturing clear dental aligner due to its compatibility with 3D printers.[31] Jaber et al.[10] used FDM and DLP printing to evaluate the reliability of aligner produced from different 3D-printed models. 3D-printed models produced with FDM and DLP did not show any significant differences compared with the original models. Both 3D-printed models produced were suitable for clinical use, but neither guaranteed the production of clear aligner.[10] In another study, the cytotoxicity of thermoform (SmartTrackInvisalign) aligner produced from 3D-printed models and aligners made directly from different types 3D printers was compared.[32] Dental LT resin was selected for stereolithographic 3D printer, while E-Guard clear material was used in DLP type 3D printer.[32] Post-curing processes that eliminate uncured resin after printing had reduced cytotoxicity. Meanwhile, SmartTrack (a polyurethane material) was considered the most biocompatible material.[32] There was no significant difference in cell viability between Dental LT and E-Guard material. Dental LT and E-Guard Clear, used in the production of aligners from a 3D printer, had slight cytotoxicity (expressing cell viability of 60%-90% after incubation) within the acceptable range compared to thermoforming retainers.[32] However, Edelmann et al.[33] compared the thickness of the aligner they designed digitally and produced with an SLA 3D printer using 2 different types of resin (Dental LT and Grey V4) to the thickness values originally planned. According to the results of this study, Dental LT aligner showed noticeable overbuilding across all intaglio regions. They found that producing aligners directly from a 3D printer can increase aligner thickness by 0.2 mm, thus damaging the functionality of the aligner.[33] Although the resin they use meets most of the requirements that should be in an aligner material, they reported that there is no resin on the market just for aligner production.[34,35] In another study, they found that the print orientation of 3D-printed aligners (with Dental LT resin) and heat exposure and UV curing duration after printing had little effect on overall dimensional accuracy, but considered that the effects of positional differences on 3D-printed aligner should be considered.[34]

Retainers

The retention stage after orthodontic treatment has long been of great importance in maintaining occlusion. With models made from 3D printers, problems such as patient losing their retainer or the retainer degrading have been eliminated with the possibility of easily producing a replacement. In 2014, Nasef et al.[13] designed a virtual Essix retainer, obtaining a digital model from cone beam computed tomography (CBCT) images and producing it with SLS 3D printing. The compatibility of the retainer that was produced was good in the controls, but the opaque white was a disadvantage.[13] In 2017, Nasef et al.[35] compared Essix retainers made from 3D printers via CBCT scans with vacuum-produced thermoforming retainers, examined their accuracy, and found no significant difference between them. 3D-printed retainers have been found to be accurate and reliable compared to traditional vacuum-produced ones.[35] Cole et al.[36] compared 3D-printed Essix retainers, traditional vacuum-formed Essix retainers (TVF), and a group of commercial vacuum-formed retainers (CVF). Models for the CVF group were digitally scanned using an intraoral scanner and sent to Invisalign (AlignTechnology) for retainer production. In the printed group, the models were digitally scanned using a 3Shape TRIOS scanner and the retainers were produced with a 3D printer. Compliance was measured with software that superimposed digital images of Essex retainers and reference models. The TVF retainer group showed minimal deviation from the original reference models.[36] The printed group showed deviation at some points, but its results were similar to those of the TVF group.[36]

A more interesting study was conducted by Jiang et al.[11] to prevent problems that may arise because of patients forgetting their drug intake. They made Essix retainers from a 3D printer, designing them to release constant, low doses of drugs into the mouth. To do this, they chose clonidine hydrochloride, which is used to keep the blood circulation stable as an antihypertensive and pain-relieving agent and extruded it in a hot melt state into the orthodontic retainer made using FDM printing. Although drug release remained high for the first three days in their simulation experiments *in vitro*, the fact that it became stable over time showed that 3D-customised retainers could be promising in the future of regular drug release applications.[11]

Removable Appliances

The first semi-automatic acrylic orthodontic devices were made with 3D printers by Sassani and Roberts[37] in 1996, who stated that it was possible to use digital systems to create orthodontic devices, but that wires and screws had to be pre-attached to the model. Salmi et al.[38] produced two soft removable appliances using SLA printing. One of the appliances applied minimum force and the other applied moderate force, for use in patients who had not previously undergone orthodontic treatment. Although the moderate force-applying device reduced patient comfort, both appliances were tolerated and comfortable to use.[38]

Al Mortadi et al.[7] used SLA printing's stop feature during production for their own designs, Andreasen designs, and sleep apnea devices. They added grooves to the areas where the wires would pass and seated manually bent wires of their choice into these grooves.[7] In 2015, they then conducted a new study to produce metal elements, including Adams clasps and labial arcs, with computer-aided design (CAD) software (version 12, Geomagic FreeformModeling Plus; 3D Systems, Rock Hill, SC) and additive manufacturing technology.[39] A Hawley appliance was printed and then clasps and wires were printed on another 3D printer and added to the base part.[39] This Hawley appliance was produced through intraoral scanning alone without any impressions, also gives hope for future designs.[39]

Orthodontic Auxiliaries

Various orthodontic auxiliaries have also been produced with 3D printers. Nagib et al.[40] produced a customized chain from a 3D printer for impacted canine teeth by taking CBCT images. The attachment was easily inserted during operations and offered increased compliance and good bonding.[40] Ahamed et al.[1] reported that the retraction hook, bite turbo, lingual retainer, and attachments of an aligner can all be produced with 3D printing technology.[2] After creating digital models by scanning dental arches or models, auxiliaries were designed with software, such as Netfabb, and manufactured using FDM or SLA printing.[1] The authors noted that the biggest advantage of 3D printers is the ability to produce customized devices, emphasizing that it will quickly replace older technologies.[1] Park et al.[41] produced a replica tooth with rapid prototyping technology from CBCT images to guide the autotransplantation process. To increase the success of the process by reducing the extraoral time of the tooth they were transplanting, they placed the replica tooth in the recipient socket area.[41] They then extracted the impacted tooth, applied root canal treatment, and placed it in the recipient socket area prepared for it. Additionally, case reports using custom-made 3D-printed miniscrews are also available in the literature.[42]

Customised Brackets

Obviously, trends in the use of patient-specific devices have affected orthodontist's choice of bracket type. Wiechmann et al.[43] determined the bracket positions on digital models obtained from silicone impressions and designed the bracket bases in a tooth-compatible way. They applied the customized brackets created through rapid prototyping to the patient with indirect bonding.[43] Furthermore, in another study, they mentioned a Herbst appliance designed for use with customized lingual brackets.[44] To provide the strong anchoring required by the Herbst appliance, the upper first molar and canine brackets were designed in a band shape and produced as a single unit with pivots from a 3D printer.[44] Krey et al.[45] attempted to use an all-digital workflow to produce customized suspenders. Depending on the location of the customized brackets in the malocclusion model, the researchers created a transfer template and sent the dataset to the construction platform. The customized brackets were printed with DLP printing and then underwent post-processing, which improved biocompatibility.[45] Archwires were also produced according to a template.[45] Furthermore, Yang et al.[46] used DLP printing to convert virtual bracket models into wax patterns. In this study, 3D printing technology, lost-wax technology and selected glass-ceramic ingots were employed to fabricate a customized aesthetic ceramic bracket (CCB) system.[46] Duarte et al.[47] produced the transfer trays used in indirect bonding from a 3D printer for thirty-three orthodontists and investigated the effect they had on the reproducibility of bracket positions. They reported that the digitally-planned bracket and the bracket positions provided by the transfer tray were generally compatible. They also said that the orthodontist's previous experience and number of years of clinical practice had no significant effect on bracket positions with this technique. Plattner et al.[48] evaluated the production stages and durations of the digital and conventional indirect bonding tray and found that the digital laboratory process was longer, whereas the chair time per patient was shortened.

Occlusal Splints

Occlusal splints used for treating temporomandibular joint diseases have also been influenced by the development of 3D printers and digital workflows. Researchers have been able to use 3D printers to produce occlusal splints with adequate accuracy, and this development has shortened lab procedures, labor and patient waiting times compared to traditional manufacturing.Salmi et al.[38] designed an occlusal splint on a digital model obtained with a scanned plaster model and printed the splint using SLA printing.[8] They evaluated the wear and deformations on the splint by superimposing it with the digital model. Splints produced with a 3D printer were found to be as successful as splints produced with traditional methods and their use was recommended.[8] To assess the accuracy of 3D-printed splints, Ye et al.[49] conducted a study by placing digital splints that they designed with a Boolean operation on various offset models adjusted through CAD software (3D Systems, Rock Hill, SC). They produced an occlusal splint with DLP printing and measured the amount of impression material remaining in the airspace between the teeth and splint.[49] The results showed that 3D-printed splints generated from offset dental models can fit on teeth better.[49] 3D printers are used in surgery not only to produce surgical guides but also for the production of intermediate and final splints in serious operations, such as orthognathic surgery.[50-52] In 2014, researchers investigated the accuracy of splints by comparing traditional surgical splints and splints produced through rapid prototyping.[52] The error range of rapid surgical splints was shown to be wide, but they were acceptably accurate.[51] Shaheen et al.[51] supported the clinical use of 3D final

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occlusal splints after reporting a reduced error rate compared to previous studies. After a few years, Shaheen et al.[50] conducted a new study on 3D intermediate orthognathic splints. This gave acceptable clinical results and reproducibility, and they reported that this protocol can be used for 3D planning and fabrication of intermediate splints for bimaxillary orthognathic surgery.[50]

Nasoalveolar Moulding Devices

The development of digital technologies has also affected the treatment protocol in patients with cleft lip and palate. These developments, aimed at reducing the risk of aspiration using a scanner, seem to allow the clinician to produce appliances with less labor in a shorter time. Shen et al.[54] designed orthopedic devices in accordance with Grayson and Cutting's treatment protocol[53] using CAD software (Rapid Form software, 2006; INUS Technology, Seoul, Korea) from scanning models obtained from patients with alginate impressions. These special plates were designed to close the gap between the alveolar bones by 1 mm per week and were manufactured using maxillary models printed from 3D printers.[54] The results of the study were comparable to the results provided with traditional NAM treatment, while the number of visits to the clinic and device adaptation time decreased.[54] Grill et al.[55] investigated NAM devices using CAD/computer-aided manufacturing (CAD/CAM) technology (Geomagic® Studio 12, Morrisville, NC, USA) and devices that combine 3D printers with semi-automatic intraoral molding design (Rapid-NAM). This new system, called Rapid-NAM, automatically identifies the alveolar ridges with a graphical user interface and designs plates according to the growth data of healthy newborns, allowing plates to be produced in minutes.[55] At the end of treatment, both approaches narrowed the cleft line with leveling of the alveolar segments and produced successful results.[55] In Zheng et al.'s[9] 2019 study, devices designed with CAD software (Rhinoceros 5; Robert McNeel & Associates, Seattle, Wash) and printed from a 3D printer were manufactured independently of the nasal hook and were given the name "split type-NAM devices". In this technique, in which the two are separated to eliminate the negative effects of the nasal hook and NAM devices on each other, the nasal hook supports the nasal cartilage with a band that is supported from the forehead.[9] The resulting models were scanned (3Shape, Copenhagen, Denmark), designed with CAD software, and sent to a 3D printer in STL format.[9] The plates were replaced every week, and the patient was checked-up once a month.[9] With splint-type3D-PNAM treatment, the cleft distance was reduced, the form of the arch was improved, lip segments were brought closer together, and nasal morphology was significantly improved.[9] In 2019, Batra et al.[56] and the next year, Bous et al.[57] published a case series that combined the philosophy of clear aligners and presurgical infant orthopedics. Bous et al.[57] produced models using FFF printing for a patient with a unilateral cleft lip-palate with OrthoInsight 3D software (MotionView Software, Chattanooga, Tenn). This software could segment the alveolar crests and move them to a desirable position.[57] Researchers divided the total movement amount in the cleft line so that it could be digitally modeled with a sequence of 1-1.5 mm, then manufactured 3D-printed models from digital models and printed a clear aligner of 0.4 mm for each model.[57] They did not produce NAM plates directly from 3D printers as the FDA does not allow the use of 3D-printed plates on infants in the United States.[57] In their results, they reported that the clear aligner NAM plate succeeded at closing the segments but that a minor segment was in a more mesial position contrary to what was expected.[57]

There are studies in the literature related to the use of NAM devices manufactured directly from a 3D printer.[58-59] According to Abd El-Ghafour et al.[59], it is easier to treat patients with a full digital workflow, and the treatment results are successful compared to conventional methods. These findings also match the results found by other researchers.[58] Additionally, Gong et al.[58] reported, reduced patient visits and chairside thanks to its full digital workflow.

Surgical Guides

Customized surgical guides have been produced from 3D printers to ensure that miniscrews are positioned accurately, avoiding anatomical structures such as dental roots, the vascular-nerve pack, and thin bones during placement. To assess the accuracy of these guides, Liu et al.[60] determined suitable locations for the placement of miniscrews via CBCT and checked the locations of miniscrews after the use of guides via CBCT. They found that the guides produced with rapid prototyping have sufficient reliability.[60] Hard tissue (bone-teeth) images were provided to choose the appropriate area for the miniscrews, while tooth-bracket-mucous contours ensured that the surgical guide sat well in the mouth.[61] The surgical guide designed was sent in STL format and printed with FDM printing for use in clinical practice, helping ensure the accurate and safe placement of the miniscrews.[61] Some researchers preferred to place the miniplates on the models obtained from 3D printers in the appropriate position and to create a jig from the light-cured resin material.[61] Maino et al.[62] showed the effectiveness of the method they used for the placement of palatal miniscrews with a 3D-printed surgical guide called the MAPA system. In another study concentrating on a miniscrew-supported Hyrax appliance produced with CAD-CAM technology (3-Matic Medical v12.0 tools), a 3D-printed surgical guide was used for the placement of miniscrews.[63] In the literature, there are also studies in which surgical templates or computer-assisted piezocision guides have been produced from a 3D printer to guide a corticotomy carried out to accelerate orthodontic tooth movement.[64]

CONCLUSION

Having resolved storage and plaster model problems with scanners, and with the development of 3D printers, new-generation appliances are being produced cost-effectively and the workload caused by the traditional method is decreasing. This is transforming the traditional workflow into a digital one. While researchers focused more on 3D produced models in the first step, they now use 3D printers for the production of orthodontic appliances or attachments. Although one-stage production has not yet been achieved in the production of devices with acrylic parts and clasps, technological developments are promising.

Ethics

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - T.E., A.G., M.G.; Design - T.E., A.G., M.G.; Data Collection and/or Processing - T.E., A.G., M.G.; Analysis and/or Interpretation - T.E., A.G., M.G.; Literature Review - T.E., A.G., M.G.; Writing - T.E., A.G., M.G.

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Review

In-office Customized Brackets: Aligning with the Future

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Main Points

- 3D technology has been lately introduced in Orthodontics.
- Customized brackets have been used mainly for lingual orthodontics.
- A new Orthodontic CAD software allows the designing and printing of labial and lingual customized brackets in the orthodontic office.
- Hybrid ceramic crown resin and Zirconia slurry have been used to print customized orthodontic brackets. Scientific studies have been published regarding ceramic crown resin and zirconia slurry properties printing outcome.

ABSTRACT

Digital technology introduced many innovations in the field of dentistry and orthodontics in the last years. The most important advancement was the ability to digitize the oral cavity using intraoral scanners. CAD software have been around for decades, but only in the last twenty years started showing up in the field of dentistry and orthodontics. 3D printers are not new in the field of manufacturing. Nevertheless, their inclusion in the orthodontist armamentarium was made possible only the last few years, while new printing materials have been also invented, allowing the manufacturing of many appliances previously made using traditional laboratory procedures. Orthodontic treatment is mainly based on the use of fixed appliances. The vast majority of orthodontists use commercial straight-wire brackets while customized brackets are preferred mostly for lingual orthodontic treatment. New CAD software called Ubrackets allows the in-office designing and printing of customized brackets using hybrid ceramic crown resin or zirconia slurry. Some scientific studies have been conducted to investigate the bracket printing outcome in terms of mechanical properties. More studies must be performed to allow the inclusion of in-office designing and printing of customized brackets in the orthodontic armamentarium.

Keywords: 3D technology, in-office customized brackets, hybrid ceramic resin, zirconia slurry, printed brackets

INTRODUCTION

Orthodontics is a specialty that combines mechanics and biology. It has the unique feature of being the only dental and medical speciality that uses forces to move parts of the human body to correct, malposition of teeth and bones relative to each other. On one hand, there is the medical part that is biology, and on the other hand the mechanical part, engineering. As it is well-known, teeth move continuously in the oral cavity all our life. This characteristic has been used by pioneers in orthodontics such as Angle[1-4] to move teeth using fixed or removable appliances. All these appliances, at least at the beginning of the 20th century were hand-made. When orthodontics was recognized as a speciality, companies started manufacturing brackets, bands, archwires, etc. Fixed appliances were manufactured in one-size fits all manner, while treatment had to be adjusted to each patient by the orthodontist. In the early 70's, Andrews brilliantly thought to create an appliance that could fit most of the patients, taking into account that the labial surfaces of our teeth resembled in a high percentage.[5] Thus, he created the "straight wire" appliance where he incorporated into the brackets all the information needed for correcting malocclusion according to his 6 keys. In reality, Andrews attempted to create customized brackets,

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nevertheless, with the absence of digital technology at that time, that was not possible.

Irrefutably, digital technology has changed many aspects of our life the last 60 years. Dentistry and especially orthodontics have also been a field of great changes in the last years, with the main cause being digital technology. The ability to digitize the oral cavity, import it in orthodontic CAD software, design or edit appliances, and then manufacture them (undigitize) using 3D printers gave a different perspective on the practice of orthodontics. Unavoidably, this digitization-undigitization configuration mode transformed the traditional orthodontic laboratory into a digital one. Moreover, the ability to have a clean, dustless, with fewer machines laboratory, using scanners, computers, and printers allowed its inclusion in the space of an orthodontic office. Thus, a new modality called in-office manufacturing was introduced into the orthodontic society. The core of this digital laboratory is the computer, that handles all the designing, editing, and printing commands.

Due to this technology, dentists and orthodontists can design various appliances such as crowns, occlusal splints, indirect bonding (IDB) trays, dental models, orthodontic bands, rapid palatal expanders, and thermoformed and printed aligners, etc. Printing most of the appliances can be done using VAT technology printers or can be outsourced to powder bed fusion printers for metal appliances.

Due to this immense digital technological advancement, other technologies evolved simultaneously. Resin material for 3D printing was initially only for dental models, while over the course of time, more resins were introduced for occlusal splints, IDB trays, etc. In the last two years, hybrid ceramic permanent crown resin was introduced to the market for the printing of single crowns, inlays, and onlays. On the other hand, compact 3D printers using zirconia slurry that could be installed in the dental office appeared in the market in the last two years.

Another advancement was the introduction of the first orthodontic CAD software for the in-office designing and printing of customized brackets called Ubrackets (Coruo, Limoges, France).[6] Hybrid ceramic permanent crown resin and zirconia slurry were used to test the feasibility of such bracket printing.

Regardless of the current state of in-office printing customized brackets, it seems that the river can go back and that the orthodontist will be able to design and manufacture customized brackets in the office in a self-sufficient environment offering more accurate, easy, faster, and trouble less orthodontic treatments.

Clinical and Research Consequences

Customized bracket manufacturing is not something recently developed. More than 20 years ago, Wiechmann et al.[7] introduced the first fully customized lingual appliance called Incognito. Brackets and archwires were customized for each patient designed on a dental arch setup. In the following years, more companies appeared in the market offering customized lingual brackets to orthodontists. Ormco (Orange, Cal, USA) created Insignia customized brackets where customized brackets and archwires are delivered to the orthodontist following a digital setup of the patient's dental scans. Similarly, Light Force customized ceramic brackets (Light Force, Massachusetts, USA) were introduced in the last two years, offering the ability of online setup and design of customized brackets. 3D printing is performed at Light Force premises and the brackets with the IDB tray are then sent to the orthodontist. Despite the obvious advantage of customized brackets, manufacturing is done in a laboratory out of the orthodontic office, which has the disadvantage of considerably higher cost.

Customized brackets have not been extensively investigated due to the lack of customized fixed appliances and their limited use. Nevertheless, most of the studies show controversial results, which range from the finding that customized brackets do not offer something more compared to the straight wire appliance to findings like treatment with customized brackets is faster and has fewer archwire changes.[8-11]

Miethke and Melsen[12] stated that, it is unreasonable to expect that any straight-wire appliance without individual adjustments can be anticipated to lead to an optimal tooth position and that if the straight-wire approach should be followed, the bracket would have to be custom made.

In-office designing and printing, as previously mentioned were made possible due to the manufacturing of various software, machines, and materials such as orthodontic CAD software, 3D printers and printing resins. Various appliances can be designed and printed in an orthodontic office in a clean environment with the center of the digital lab being the computer. Until now, none of the existing orthodontic CAD software included a module for in-office designing customized brackets. The ability to design and print almost everything in the orthodontic office urged the invention of the first orthodontic CAD software for the design of customized orthodontic brackets. The software called Ubrackets (Coruo, Limoges, France) is a software, that allows the import of dental arch scans, which after a certain procedure pass to the setup stage (Figure 1).[6] All the CAD software for the design and manufacturing of thermoformed aligner resemble Ubrackets up to the setup stage. After setup, the orthodontist enters the customized bracket module where there is an option of labial or lingual brackets and an option of full customization or customization by using commercial brackets found in the software library and by adding composite onto their bases. The software library contains several series of brackets for printing. Some bracket series are special for hybrid ceramic resin printing and some for zirconia printing. The different series of brackets have the scope of counteracting the different shrinkage percentages that is observed when hybrid ceramic resin or zirconia slurry is used. By choosing labial brackets and full customization, the software automatically aligns the brackets on 0.018 x 0.025 inches flat archwire exactly opposite to the labial surfaces of the teeth but without getting in contact with them (Figure 2). Each bracket has a manipulator that appears after selecting the bracket to be moved. The manipulator allows the distal or mesial movement of the bracket, the lingual or labial movement, or the rotation of the bracket on the horizontal level (Figure 3). Each time a bracket is moved, the archwire adapts to the new position of the bracket. The whole archwire-brackets system can also be moved (translate or rotate) in any direction to facilitate proper positioning of the system relative to the gingiva and the incisal edges of the teeth (Figure 4). At this point, the base of the brackets is not touching the surface of the teeth. When the brackets are finalized at their proper position, a command tool enables the operator to extrude the surface of the bracket's base toward the tooth surface to create the customized base of the bracket (Figure 5). Thus, the brackets are designed on a flat archwire on the ideal setup, which will be later bonded at the initial malocclusion, hoping that by this procedure, the customized brackets with the customized prototype archwire will bring the teeth to the position that was defined at the setup stage. The whole procedure can be described as "treatment with the end in mind". At the next stage, the software designs a dental model with the brackets attached and the prototype archwire that will serve at all stages

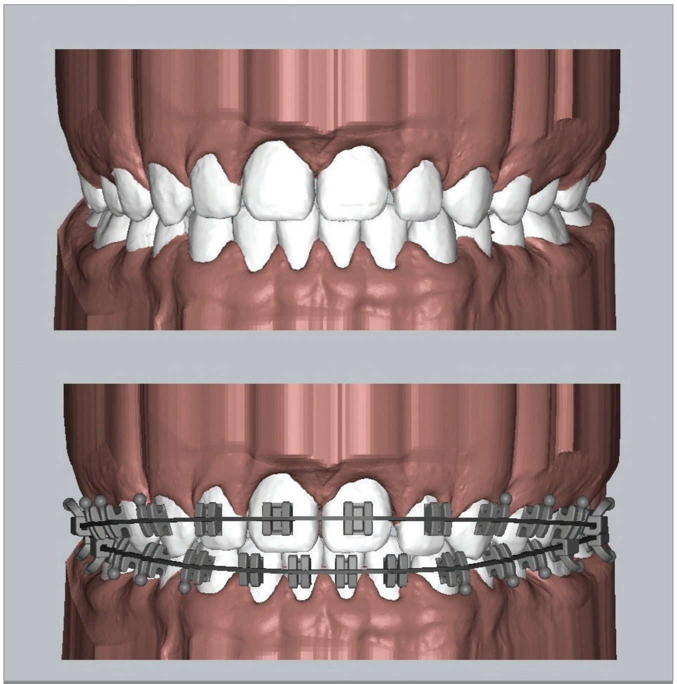

Figure 1. Dental setup in Brackets software and automatic positioning of the brackets

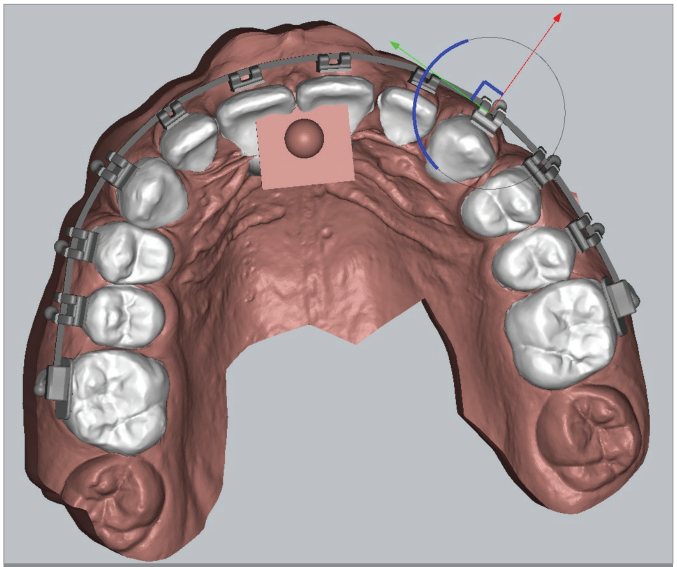

Figure 3. A manipulator can be used to move the bracket in all directions, mesiodistally, labiolingually, and rotationally on the horizontal level. The archwire in each movement adapts accordingly

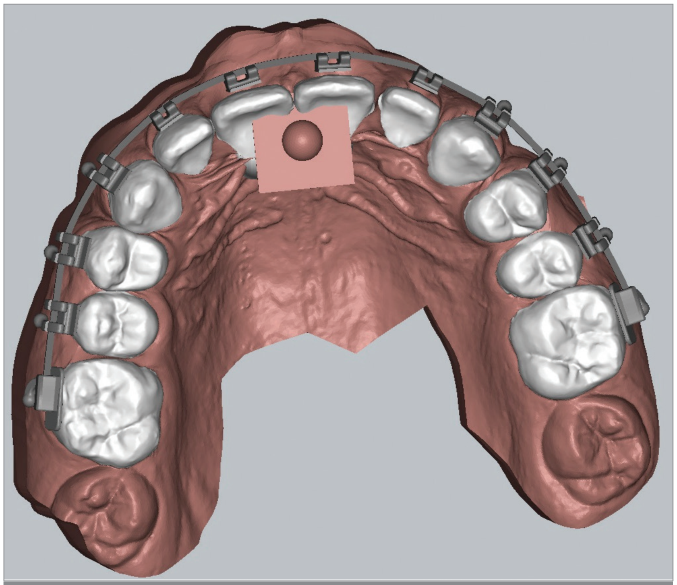

Figure 2. Automatic positioning of the brackets and flat rectangular archwire opposite the teeth' labial surfaces. Note the space between the bracket bases and teeth, which will be later filled by the software to create the customized bracket bases

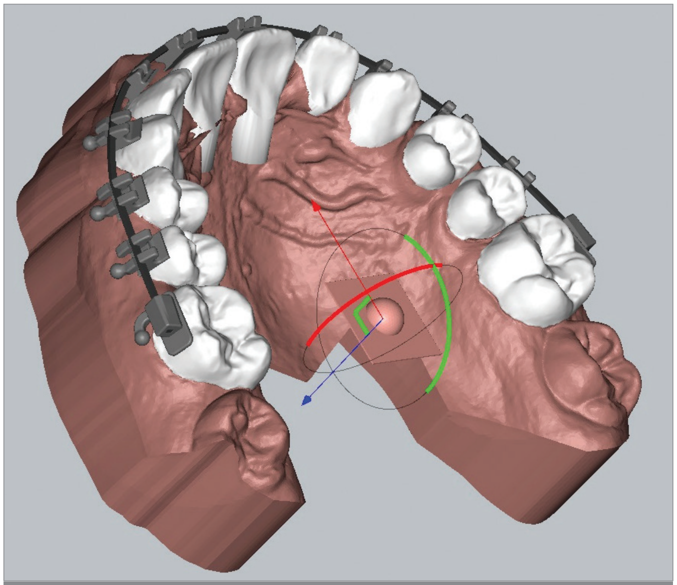

Figure 4. A central manipulator can be used to move the whole archwire-brackets complex in any direction to position them in a proper position away from the gingiva and the incisal edges of the teeth

of the orthodontic treatment. The archwire is exported from the software as a 1:1 ratio PDF drawing to help the orthodontist manually bend the archwires with pliers and as an STL file for the bending of the archwires using an archwire bending robot. The operator is enabled to design IDB trays at this stage that will be later printed in a 3D printer. A unique feature of the software is that it allows the designing of positioning keys for each bracket to facilitate accurate bonding (Figure 6). The positioning key is printed together with the bracket as one unit and removed using a bur after bonding. The positioning key can have a thickness of 0.3 to 1mm or more depending on the material to be used for printing. Usually, when printing zirconia brackets, the key should be thin enough to be easily removed after bonding.

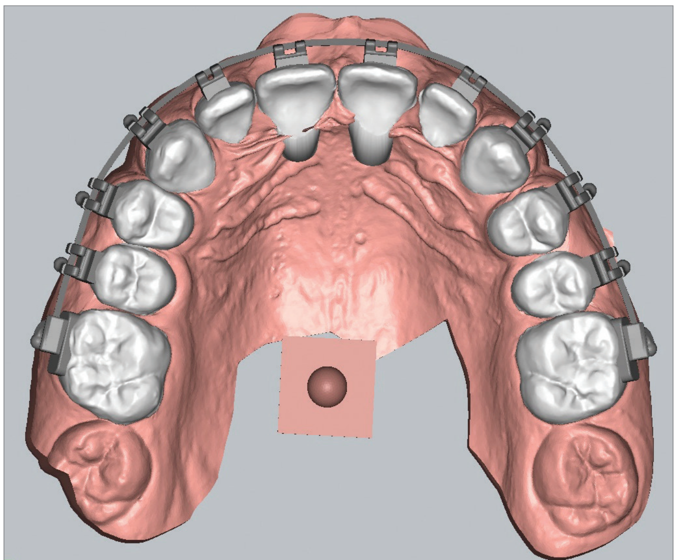

Figure 5. A command tool is used to extrude the bases of the brackets toward the teeth' labial surfaces, thus creating the brackets' customized bases

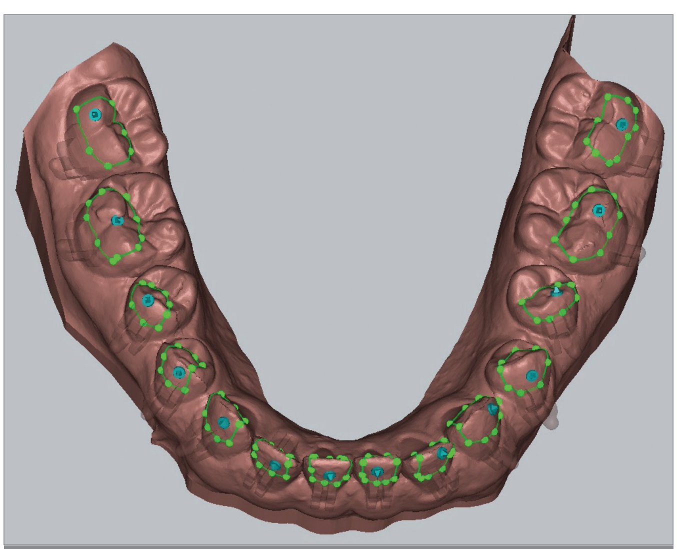

Figure 6. Individual positioning keys can be designed to allow the accurate placement of the brackets upon bonding. The keys were easily removed after bonding

Despite the huge technological advancement of creating software and printers, the real challenge in custom-made bracket manufacturing is the printing material.

The first attempt to design and print customized brackets in the office was done using Formlab's hybrid ceramic permanent crown resin.[13] The brackets were designed in Ubrackets software together with positioning keys for accurate bonding and printed in Formlabs 3B, while isopropyl alcohol 91% was used to clean the uncured resin excess followed by UV curing using a Cure M curing machine (Graphy, Seoul, Korea) (Figure 7). To investigate the mechanical properties of this resin, a study was conducted where the permanent crown resin was compared to temporary crown resin made by Formlab's.[14] The results showed a low value of hardness and elastic modulus (low stiffness) while fracture toughness was adequate. Nevertheless, hardness was almost double compared to commercial plastic brackets that were studied in a similar research article.[15] Hardness is an important property for brackets. Low hardness causes wear off of the brackets upon steel ligation or archwire insertion. Fracture toughness is also important as a property that is defined as the ability of a material to absorb energy when a force is applied to it without breaking. These findings encourage the invention of a hybrid ceramic resin with better properties to serve as a material for bracket printing.

Another material that the author used to print customized brackets was zirconia. Currently, there is a desktop zirconia 3D printer (AON, ZiproD, Seoul, Korea) that can be used for in-office printing of crowns, bridges, etc. Zirconia slurry comes in an A1 color and it is used as a material to print crowns.[16] As a proof of concept, brackets for a patient were designed and printed using Zirconia slurry (Figure 8). The procedure for zirconia bracket printing is longer and more complex as it requires the use of a debinding-sintering oven after the printing process. Printing is accurately performed using a 50 μm Z-axis resolution and

Figure 7. Customized brackets with their positioning keys were printed using hybrid ceramic permanent crown resin. After bonding, the keys were removed

it takes approximately two to three hours depending on the height of the brackets and supports that will be printed (Figure 9). Zirconia slurry contains, except zirconia, a polymer that helps bind zirconia particles at the printing time. Zirconia brackets pass a procedure of debinding after printing to remove the polymer, which is not needed anymore. The Zirconia slurry that is currently used is supplied by AON Company and it is called Inni-Cera. Brackets after printing are soft due to the presence of the polymer and the zirconia particles which are not firmly connected. After debinding, spaces remain between zirconia particles where the binding polymer used to be.[17] The next procedure is sintering, which brings the zirconia particle in touch with each other, creating a hard, strong zirconia bracket that will be later polished and colored to be bonded in the patient's mouth. Debinding and sintering take up to 13 hours depending on the kind of furnace and debinding-sintering furnace program. Coloring can be performed using special zirconia colorings in all shades of white according to the patient's teeth color. After debinding, the brackets are immersed in the zirconia painting for some seconds and then left to dry for some time.

Figure 8. Customized brackets were printed using zirconia slurry and bonded to a patient. The color is the standard slurry A1 color, which can be painted using zirconia painting. Here, no zirconia paint was used

Figure 9. Zirconia bracket after printing. The uncured excess slurry will be moved back into the printing tray to be used for other printings. Brackets can be easily removed and cleaned from the excess resin using isopropyl alcohol 91%

Later, the brackets are reinserted in the furnace for the last stage of sintering. Polishing is the last stage of the workflow using special brushes and zirconia polishing paste. To counteract the shrinkage of the bracket upon sintering, the virtual files of the brackets are enlarged by the printer's software before printing (Figure 10). This compensation enlargement is different for the x, y, and Z axis. Hybrid ceramic resin printing does not need any major virtual bracket compensation.

In an attempt to investigate the mechanical properties of zirconia-printed brackets, a study was undertaken where, zirconia, Clarity (3M, Monrovia, Cal, USA), and Light Force (Light Force, Massachusetts, USA) customized brackets were compared.[18] The main finding was that fracture toughness was significantly higher compared to the Clarity bracket and much higher compared to the Light force bracket. As it is well-known, ceramic brackets suffer from low fracture toughness, which causes them to be fragile. This finding proves that zirconia could be a better material concerning fracture resistance compared to alumina. Hardness was higher for the Clarity brackets followed by the Light Force and Zirconia brackets. Nevertheless, the difference in hardness between the three kinds of brackets is not found clinically significant as the amount of hardness for the brackets was very high and adequate for their clinical use. Ideally, a bracket should have high hardness, elastic modulus, and fracture toughness.

A disadvantage of this technology compared to the traditional manufacturing of commercial brackets (i.e. molding) is that it entails many steps that are prone to errors and could affect the final result. Designing the brackets is an important part while the STL file resolution is important to creating high-resolution brackets that will be printed accurately and that will be smooth. Different printers use different technology in printing, which could lead to different printing results. Under the same conditions, a printer could print the same brackets at successively printing sessions with different properties. The homogeneity of the resin or slurry is of great importance and they should be adequately stirred before printing. Positioning

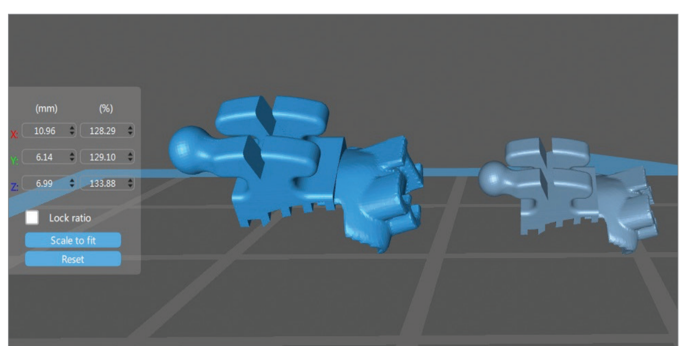

Figure 10. Zirconia brackets pass a different procedure to be printed. Debinding and sintering, which follow printing, decrease the size of the brackets due to material shrinkage. For this reason at the process of virtual bracket placement in the printing software, there must be compensation in dimensions. The right bracket is exactly as was exported from the software. The left bracket is enlarged in all three dimensions (x, y, z) according to the guidelines of the AON company providing ZiproD zirconia printers. The software that was used is Chitubox (CBD-Tech, Shenzhen City, China)

the brackets on the virtual printer platform is also an important aspect. The most important part of the bracket is known to be the slot, and it is the one that must be accurately printed. For this reason, brackets should be oriented properly to ensure accurate printing results. In the case of permanent hybrid ceramic crown resin, the use of a UV curing unit is essential. It is well known that oxygen prevents the full polymerization of oligomers and monomers.[19] An ideal condition would be to use UV curing units with a nitrogen generator that removes oxygen from the curing process in its chamber. All these stages should be investigated through *in vitro* research, while *in vivo* research should be carried out to check for example, material aging, leaching, etc.

It is obvious that the inclusion of a small digital lab in our orthodontic offices is not anymore a figment of our imagination. Moreover, the ability to design customized brackets and easy access to affordable 3D printers enables the orthodontist to create a self-sufficient orthodontic office offering personalized orthodontic treatment to the patients.

CONCLUSION

The time has come that the orthodontist should take the manufacturing of the appliances into his/her hands. 3D technology offers this ability to the orthodontist in a relatively low-cost, easy way. A self-sufficient office would be independent of most of the external companies creating tailor-made appliances that would target the patient's specific orthodontic problems. The software can design customized brackets in an easy and fast way based on the setup that the orthodontist will perform, which will be the imaginary orthodontic treatment result. Orthodontic associations should try linking all the orthodontic offices through a central server where all data will be gathered, and with the use of artificial intelligence software, there will be given feedback to the orthodontic offices for better and more efficient orthodontic treatments. Nevertheless, before this technology is fully used in the office, extensive research should be undertaken regarding new material for bracket printing and the material behavior in the oral aging. Additionally, there should be research proving the advantages of bracket customization over straight-wire appliances. Last but not least, protocols should be created to ensure the safety of the patients and personnel in the orthodontic office regarding the proper installation of the machines for bracket manufacturing.[20] It is obvious that the centralization of orthodontic appliances manufacturing in an orthodontic office is not a fantasy. The orthodontist could guide the production of the appliances according to the needs of every orthodontic case performing personalized treatments for each patient.

Ethics

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Competing interests: Dr. Nearchos Panayi declares that he is the inventor of Ubrackets orthodontic CAD software.

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