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# Effect of dental implantation on the hard and soft tissues around the adjacent natural teeth

## Wpływ implantacji na twarde i miękkie tkanki otaczające sąsiednie zęby

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## Abstract

**Background.** Dental implantation has become widespread for esthetic and functional rehabilitation following single tooth loss as a preferred alternative to conventional tooth-supported restorations. The main advantage of dental implant placement is that it does not require the preparation of the adjacent sound teeth.

**Objectives.** The aim of this cohort study was to assess the effect of dental implantation on the hard and soft tissues around the adjacent natural teeth.

**Material and methods.** In this historical cohort, 34 'connect-type' TBR® implants (bone level), 4 mm in diameter, were submerged in the intact bone of 22 patients (7 males and 15 females). The intraoral and extraoral clinical examination as well as periapical radiography were carried out preoperatively or right after surgery (baseline), at 3 months postoperatively (the time of prosthetic delivery), and at 3 and 6 months after prosthetic delivery. The data was analyzed using the Friedman test (due to the non-normal distribution of the data). In case of presence of a significant difference, pairwise comparisons were performed using the post-hoc Wilcoxon test with the Bonferroni correction. All statistical analyses were performed with a 95% confidence interval (CI) using the SPSS for Windows, v. 16.0 software. The  $p$ -value  $<0.05$  was considered statistically significant.

**Results.** The distance from the cemento-enamel junction (CEJ) of the adjacent teeth to the bone crest significantly increased at different postoperative time points compared to baseline ( $p < 0.001$ ). The changes in the papillae of the adjacent teeth were also significant at different postoperative time points ( $p = 0.04$ ). The pocket depth of the adjacent teeth increased, although the value at 3 months postoperatively was not significantly different from the baseline value ( $p = 0.842$ ). The distance from the implant shoulder to the bone crest of the adjacent teeth significantly increased at different postoperative time points compared to baseline ( $p < 0.001$ ).

**Conclusions.** Our results indicate that implant surgery significantly affects the soft and hard tissues around the adjacent natural teeth.

**Key words:** dental implants, alveolar bone loss, dental papilla

**Słowa kluczowe:** implanty dentystyczne, zanik kości wyrostka zębodołowego, brodawka zębowa

## Introduction

Dental treatment is applied with the aim of restoring oral and dental function, comfort, esthetics, speech, and tissue health.<sup>1</sup> The use of dental implants is increasing because of the growth of the elderly population and tooth loss due to aging, the failure of conventional fixed partial dentures, the poor performance of removable dentures, the psychological consequences of tooth loss, and the predictable long-term results of implant-supported restorations.<sup>1,2</sup> Thus, dental implantation has become a common alternative to tooth-supported restorations to regain esthetics and function after single tooth loss. The main advantage of dental implant placement is that it does not require the preparation of the adjacent sound teeth.<sup>3</sup>

Oral rehabilitation by dental implant placement in the esthetic zone is among the most complex treatment procedures, with the aim of creating optimal esthetics. With regard to the soft tissue contour, it is imperative to achieve a uniform gingival margin with no significant change in gingival height.<sup>4</sup> The presence of an adequate papilla and a convex contour over the alveolar crest are also important. The incision line, the flap design and the suturing technique are important surgical factors influencing the final results. The results should be predictable and stable. They depend on the interaction of several variables, including biological factors (the anatomy of the region and the host response), surgical factors (the three-dimensional (3D) implant position), implant-related factors (the implant surface and design), and prosthetic factors.<sup>5,6</sup> The interdental area is composed of the contact area, the interproximal embrasure and the interproximal dentogingival complex. This area is the primary site for the development of periodontitis and carious lesions, since it is prone to microbial plaque accumulation. The loss of the interproximal papilla can cause functional problems in the anterior maxilla, and lead to serious phonetic and esthetic problems.<sup>6,7</sup>

The level of papillae around the single-tooth implants in the anterior maxilla is mainly affected by the level of the interproximal bone crest around the adjacent teeth. On the other hand, the level of the facial gingival margin is affected by a number of factors, including the peri-implant gingival biotype, the facial bone level, implant fixture angulation, and the level of the interproximal bone crest.<sup>7</sup> Moreover, evidence shows that the level of the bone crest affects the soft tissue height.<sup>8</sup> Several classifications have been suggested to assess and quantify the loss or regeneration of the interdental or interimplant papilla. Jemt's classification is a commonly used index for the assessment of mesial and distal papillae.<sup>9</sup> According to this classification, a score of 0 indicates the absence of a papilla and the soft tissue contour around the implant restoration. A score of 1 indicates the presence of less than half of the papillary height and a concave soft tissue contour between the single-tooth implant crown and the adjacent teeth.

A score of 2 represents the presence of half or more of the papillary height; however, the papilla is not located above the interdental contact area at any point. A score of 3 indicates that the papilla fills the entire interproximal space and is in good harmony with the adjacent papillae; an ideal soft tissue contour is also present. A score of 4 indicates the presence of a hyperplastic papilla which covers a large portion of the single-tooth implant restoration or the adjacent teeth; the soft tissue contour is more or less irregular.<sup>9</sup>

It is believed that soft and hard tissue changes around implant-supported fixed partial dentures occur in the first 6 months after 1-stage implant placement, and the pattern of tissue alterations is different between the tooth and the implant on the one hand and between 2 adjacent implants on the other.<sup>10</sup> The magnitude of proximal bone loss between 2 adjacent implants is on average 0.6 mm at 6 months, whereas this value is less than 0.1 mm between the implant and the adjacent tooth. Evidence shows that further changes are not often observed in the period from 6 months to 3 years.

The aim of this study was to assess the effect of dental implantation on the hard and soft tissues around the adjacent natural teeth.

## Materials and methods

The study design was approved by the Research and Ethics Committee of Hamadan University of Medical Sciences, Iran (IR.UMSHA.REC.1395.324). In this historical cohort, 34 implants were placed in 22 patients (7 males and 15 females) who had an edentulous region adjacent to the natural teeth. Written informed consent was obtained from the patients who were willing to participate in the study. Data forms were filled out by the patients and the clinical examination was carried out. The diagnostic radiographic examination included periapical radiography and cone-beam computed tomography (CBCT). The patients were followed up for 9 months following implant placement.

The exclusion criteria comprised the presence of all teeth, a restoration covering the cemento-enamel junction (CEJ) of the teeth adjacent to the edentulous area, smoking, alcohol consumption, substance abuse, immunocompromised patients, patients with active periodontitis, those requiring guided bone regeneration, uncontrolled active systemic diseases, diabetes mellitus, hypertension, uncontrolled cardiac disease, radiotherapy, chemotherapy, the intake of immunosuppressive medications, and long-term steroid therapy.

In this study, 34 'connect-type' TBR<sup>®</sup> implants (bone level) (TBR Dental Group, Toulouse, France), 4 mm in diameter, were used. The implants were completely submerged in the intact bone. After ensuring the presence of the sufficient width of the keratinized gingiva, a crestal

incision was made with a surgical scalpel size 15 (KLS Martin GmbH + Co. KG, Freiburg im Breisgau, Germany). A full-thickness flap was elevated so that the papilla of the adjacent tooth could also be reflected. No crestal osteotomy was performed on the patients, and the preparation of the implant site for fixture installation was carried out according to the manufacturer's instructions. We used figure-8 sutures (silk 4-0; Supa Medical Devices Co., Tehran, Iran). One week after surgery, the sutures were removed. The patients received 500 mg amoxicillin (Farabi Pharmaceutical Company, Isfahan, Iran) thrice daily (TID), 600 mg ibuprofen (Zahravi Pharmaceutical Co., Tehran, Iran) TID and 0.2% chlorhexidine mouthwash (Behsa Pharma Co., Arak, Iran) twice daily (BID) for 1 week postoperatively.<sup>11</sup> The prosthetic restoration was delivered 3 months postoperatively. The digital periapical radiographs of the implant and of the adjacent teeth were obtained in all patients before surgery or right after surgery (baseline), and also at 3 months (at the time of prosthetic delivery), 6 months and 9 months postoperatively (Fig. 1). All radiographs were obtained by the same X-ray unit in order to standardize the exposure settings and projections. Variables in this study included the presence of papillae around the natural teeth adjacent to the implant according to Jemt's classification, and the pocket depth at the proximal, buccal and palatal/lingual surface of the adjacent teeth measured with a Williams probe (Hu-Friedy Mfg. Co., LLC, Chicago, USA). The maximum

value was recorded in millimeters, and eventually the distance from the implant shoulder to the bone crest as well as the distance from the bone crest to the CEJ of the adjacent teeth were measured using a digital caliper.

The data was analyzed using SPSS for Windows, v. 16 (SPSS Inc., Chicago, USA). Since the data was not normally distributed, the Friedman test was used to compare the changes in the respective variables. In case of a significant difference, pairwise comparisons were carried out using the post-hoc Wilcoxon test. The generalized estimating equation model was used to analyze Jemt's classification at different time points. The Bonferroni adjustment was also applied. All of the analyses were performed with a confidence interval (CI) of 95%. The *p*-values <0.05 were considered statistically significant.

## Results

Of the patients, 31.82% were males and 68.18% were females. The mean age of the patients was 39.23 years. The frequency distribution of implants in terms of position was as follows: 58.8% in the maxilla; 41.2% in the mandible; 32.35% in the anterior region; and 67.65% in the posterior region of the jaws.

As shown in Table 1, the distance from the CEJ of the adjacent teeth to the bone crest at different time points significantly increased compared to baseline ( $p < 0.001$ ). The pairwise comparisons of the distance from CEJ to the bone crest at different time points revealed that the increase in this distance was statistically significant at 6 months postoperatively compared to 3 months and at 9 months postoperatively compared to 3 months ( $p < 0.001$ ). However, the increase at 9 months postoperatively compared to 6 months was not statistically significant ( $p = 0.583$ ) (Table 2).

As shown in Tables 1 and 2, the changes in the pocket depth of the adjacent teeth showed an ascending trend starting at 3 months postoperatively ( $p < 0.001$ ). The pocket depth at 3 months postoperatively decreased compared to baseline, but the change was not significant ( $p = 0.842$ ). The distance from the implant shoulder to the bone crest around the implant significantly increased at different time points postoperatively compared to baseline ( $p < 0.001$ ). The pairwise comparisons of this parameter at different time points revealed a significantly ascending trend ( $p < 0.001$ ) (Tables 1,2).

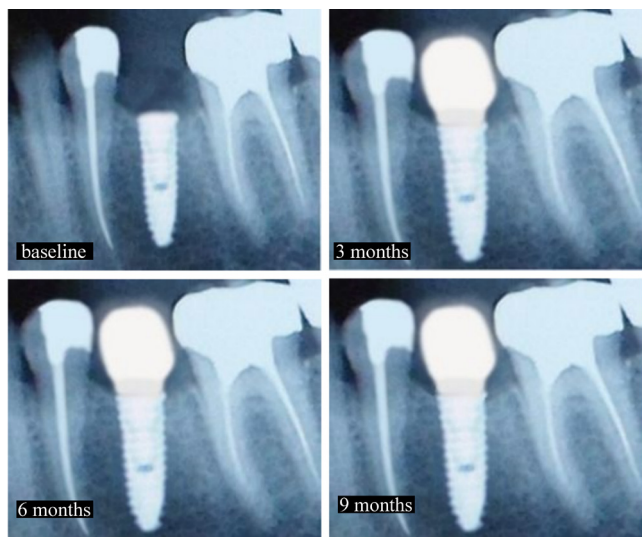


Fig. 1. Standard periapical radiographs at different time points (baseline, and 3, 6 and 9 months postoperatively)

Table 1. Mean changes in the level of the cementoenamel junction (CEJ), pocket depth and shoulder-to-crest distance at different postoperative time points compared to the baseline values (the Friedman test)

Variables	Baseline	3 months	6 months	9 months	<i>p</i> -value
CEJ [mm]	3.05 ±0.77	3.15 ±0.73	3.32 ±0.74	3.32 ±0.73	<0.001
Pocket depth [mm]	3.83 ±0.90	3.81 ±0.91	4.31 ±0.81	4.69 ±0.76	<0.001
Shoulder-to-crest distance [mm]	0.24 ±0.13	0.47 ±0.14	0.64 ±0.18	0.74 ±0.19	<0.001

Data presented as mean ± standard deviation (SD).

**Table 2.** Pairwise comparisons of the mean differences for the variables studied at different time points

Time	CEJ		Pocket depth		Shoulder-to-crest distance	
	mean difference $\pm$ SE	p-value	mean difference $\pm$ SE	p-value	mean difference $\pm$ SE	p-value
3 months–baseline	0.103 $\pm$ 0.33	<0.006	–0.021 $\pm$ 0.890	<0.842	0.228 $\pm$ 0.024	<0.001
6 months–baseline	0.273 $\pm$ 0.36	<0.001	0.479 $\pm$ 0.107	<0.001	0.397 $\pm$ 0.035	<0.001
9 months–baseline	0.276 $\pm$ 0.43	<0.001	0.853 $\pm$ 0.109	<0.001	0.499 $\pm$ 0.036	<0.001
6 months–3 months	0.171 $\pm$ 0.34	<0.001	0.500 $\pm$ 0.088	<0.001	0.169 $\pm$ 0.028	<0.001
9 months–3 months	0.174 $\pm$ 0.35	<0.001	0.874 $\pm$ 0.103	<0.001	0.270 $\pm$ 0.027	<0.001
9 months–6 months	0.003 $\pm$ 0.35	<0.583	0.374 $\pm$ 0.104	<0.002	0.101 $\pm$ 0.025	<0.001

CEJ – cementoenamel junction; SE – standard error; Bonferroni adjustment  $\alpha = 0.008$ .

As shown in Table 3, the frequency of Jemt's classification score 0 in the adjacent teeth decreased postoperatively compared to baseline. The frequency of score 1 at 3 months postoperatively was the same as at baseline, but it decreased at 6 months postoperatively and increased at 9 months postoperatively compared to baseline. The frequency of score 2 in the adjacent teeth increased at 3 months postoperatively (the time of prosthetic delivery) compared to baseline, and then remained constant (Table 3). The change in the presence of papillae around the adjacent teeth was statistically significant at different postoperative time points ( $p = 0.04$ ) (Table 4).

In general, according to Jemt's classification for the adjacent teeth, the presence of papillae increased at 3 months postoperatively (the time of prosthetic delivery; 85.3%), at 6 months postoperatively (79.4%) and at 9 months postoperatively (88.2%) compared to baseline (76.5%).

**Table 3.** Frequency of Jemt's classification scores at baseline, and at 3, 6 and 9 months postoperatively

Jemt's index	Baseline	3 months	6 months	9 months
0	8 (23.5)	5 (14.7)	7 (20.6)	4 (11.8)
1	24 (70.6)	24 (70.6)	22 (64.7)	25 (73.5)
2	2 (5.9)	5 (14.7)	5 (14.7)	5 (14.7)

Data presented as number (percentage).

**Table 4.** Comparison of the frequency of Jemt's classification scores at different time points

Time points	p-value
Baseline–3 months–6 months–9 months	0.040**
Baseline–3 months	0.085*
Baseline–6 months	0.338*
Baseline–9 months	0.036*
3 months–6 months	0.634*
3 months–9 months	0.798*
6 months–9 months	0.173*

\*  $\alpha = 0.008$ ; \*\*  $\alpha = 0.05$  (Bonferroni adjustment).

## Discussion

Commonly used implant success criteria mainly focus on the functional and technical aspects of dental implants, including successful osseointegration, achieving a stable

peri-implant bone margin and a high survival rate. However, in the case of implant-supported restorations in the anterior region, the success of the treatment depends on the esthetic results as well.<sup>12</sup> The expectations of optimal esthetic results create a challenge for implant treatment in the anterior maxilla, especially in patients with scalloped margins. On the other hand, coronal reconstruction should be performed with regard to the crowns of the adjacent natural teeth.<sup>4</sup> Evidence shows that the soft tissue margin around the natural teeth is determined by the attachment of the connective tissue to the root, the bone height, the alveolar bone support, and the soft tissue thickness. However, it seems that soft tissue appearance in the proximal regions around the single-tooth implants is influenced by the periodontal support of the adjacent natural teeth.<sup>3</sup> The esthetic outcome of implant treatment is not merely related to the crown shape; the topography and appearance of the surrounding soft tissues also affect the esthetic results.<sup>13</sup> Chang et al. observed that the soft tissue margin at the proximal and facial aspects of the implant was positioned much more apically than the gingival margin at similar sites in the adjacent teeth.<sup>3</sup> Such differences may manifest themselves immediately after crown delivery due to the loss of the bone height following tooth extraction. However, soft tissue marginal recession may also occur following crown placement.<sup>14–16</sup> Moreover, Jemt et al. showed that the gingival margins of the natural teeth around the single-tooth implants were at a higher risk of gingival recession in the long term compared to the untreated natural teeth.<sup>17</sup>

In the present study, we made efforts to standardize the status of the patients. As mentioned earlier, the patients had no systemic diseases and were generally healthy, did not have active periodontitis, and did not require guided bone regeneration. They were non-smokers and had no parafunctional habits. Also, they had good oral hygiene, did not use any immunosuppressive medications, were not alcoholics, and did not report substance abuse. Furthermore, they had at least 1 edentulous region with the adjacent natural teeth which did not have restorations covering CEJ. All implants were placed by the same expert surgeon.<sup>18</sup> A total of 22 patients participated in the study and received 34 'connect-type' TBR implants (bone level), 4 mm in diameter, which were totally submerged in the intact bone.

The distance from the CEJ of the tooth mesial to the implant to the bone crest increased by 0.103 mm at 3 months postoperatively, by 0.273 mm at 6 months postoperatively and by 0.276 mm at 9 months postoperatively compared to baseline. The distance from CEJ to the bone crest had an ascending trend up to 6 months postoperatively, which was probably due to the effects of flap elevation and the retraction of the periosteum.<sup>1</sup> Our findings in this respect are consistent with those of Meijndert et al., who observed that the bone loss of the teeth around the implants was small but statistically significant for up to 1 month after treatment.<sup>19</sup> Block et al., however, evaluated 76 patients and divided them into 2 groups.<sup>18</sup> The patients in group 1 had lost 1 maxillary tooth (premolar, canine, lateral incisor, or central incisor) and underwent immediate socket preservation by bone grafting followed by implant placement, and received a temporary restoration for 4 months. Group 2 underwent immediate implant placement and received a temporary restoration. The patients were examined at baseline, and at 6, 12, 18, and 24 months. The researchers concluded that the bone level around the teeth adjacent to the implant did not change over time and found no significant differences in the bone level between the 2 groups.<sup>18</sup> Immediate implant placement had no significant effect on the level of bone around the adjacent teeth and delayed implant placement had similar effects to immediate implant placement.<sup>20</sup> The difference between our study and that of Block et al. may be due to the different treatment protocols employed and the scheduled follow-ups. As shown in previous studies, the maximum changes occur in the first 6 months following treatment (1<sup>st</sup> phase).<sup>8</sup> In other words, osseointegration and the adaptation of the marginal soft tissue occur separately in 2-stage implant placement, whereas these steps occur simultaneously in the first 3–6 months following 1-stage implant placement.<sup>21</sup> The current results revealed that the frequency of score 0 decreased in the teeth adjacent to the implants over time compared to baseline. The frequency of score 1 remained constant until 3 months after surgery, but decreased at 6 months and increased at 9 months postoperatively compared to baseline. The frequency of score 2 in the teeth adjacent to the implants increased at 3 months compared to baseline and remained constant thereafter. Our results are in agreement with the findings of previous studies. Chang et al. evaluated 20 patients and observed a statistically significant increase in the papillary index in both the mesial and distal areas over time.<sup>3</sup> Scores 0–1 were obtained at the time of placing a crown in 12 out of 26 areas (46%), whereas in the follow-up examination, only 2 areas (8%) were scored 0–1. Moreover, only 1 interdental area was completely filled by the papilla at the time of crown placement (score 3), whereas this value increased to 11 regions (42%) during the follow-up sessions. Cosyn and De Rouck found a significant difference in the mesial papillary height between the implant and its adjacent natural teeth.<sup>22</sup> Shorter papillae

(0.4 mm on average) were observed at the implant site and the distal papillae were on average 1 mm shorter at the implant site compared to the adjacent teeth.<sup>22</sup> The results of those studies are in agreement with ours in terms of increases in the papillary index. However, the studies differ regarding the shorter height of the papillae distal to the implants compared to the mesial papillae. This controversy can be attributed to the difference in the sites studied, the teeth replaced with dental implants and the type of surgical procedure. As in our study, Palmer et al. and Lee et al. found no significant difference in the prevalence of complete papillae in the mesial and distal areas, which may be due to the anatomical differences in the embrasure space.<sup>21,23</sup> Moreover, the distal contact point is usually located more apically than the mesial contact point, by 1.5 mm on average; this anatomical difference can affect the shape of papillae.<sup>21</sup>

Our findings revealed that the pocket depth of the teeth mesial to the dental implants did not change for 3 months postoperatively, but later showed a significant increase, which may be due to the tissue reaction to the prosthetic restoration, the patient's oral hygiene status or similar issues.<sup>24</sup> Avivi-Arber and Zarb evaluated 41 patients who were followed up for 1–8 years.<sup>25</sup> Examinations performed 1 year after implant loading revealed that the mean annual bone loss was 0.03 mm in the mesial region and 0.11 mm in the distal region for all implants.<sup>25</sup> That study also showed an ascending trend in bone loss postoperatively; however, the magnitude of bone loss was smaller than the value reported in our study. This difference may be due to the type of surgical procedure (which was 2-step in the study by Avivi-Arber and Zarb), the time of assessment, the location of the implant, and the implant design.<sup>25</sup> Kourkouta et al. indicated that crestal bone loss increased following implant loading, but in our study, this value was smaller.<sup>24</sup> The comparison of their results with ours is difficult, since the treatment sites and the assessment time points were different in the 2 studies. Moreover, bone loss between the implant and the tooth (due to the presence of the natural tooth) was smaller than that between 2 adjacent implants.<sup>24</sup> On the other hand, our results were different from those of Grunder, who evaluated 10 patients that received single-tooth implants in the anterior maxilla and did not have periodontal disease.<sup>26</sup> Their results indicated that no areas around the natural teeth adjacent to the implants had a probing depth >4 mm before or within 1 year after treatment. Comparing their results with ours, there are differences in the methodology and the implant sites. In the present study, the distance from the implant shoulder to the first bone-implant contact at the mesial and distal surfaces was measured on radiographs using a digital caliper. The results showed that the distance from the implant shoulder to the bone crest around the implant significantly increased at different time points postoperatively compared to baseline. Similarly, some studies have demonstrated that when the implant shoulder is placed









subcrestally, greater bone loss occurs around the implant neck compared to the situation where the implant is placed at the level of the alveolar crest.<sup>27</sup>

We should mention that the small size of the study group is a limitation of our study. The results should be re-evaluated in a study with a larger sample size.

## Conclusions

The results of our study indicate that implant surgery significantly affects the soft and hard tissues around the adjacent natural teeth.

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# Comparison of two intravenous sedation techniques for use in pediatric dentistry: A randomized controlled trial

## Porównanie dwóch technik dożylniej sedacji w stomatologii dziecięcej – randomizowane badanie kliniczne

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## Abstract

**Background.** Psychological methods are the preferred behavior management techniques (BMTs) for children in the dental clinical set. However, sometimes they are not successful. On such occasions, pharmacological methods can be good alternatives. Intravenous sedation is one of these methods, which are very useful in behavior management. It is highly effective when applied appropriately.

**Objectives.** The aim of this study was to evaluate the efficacy of intravenous sedation using dexmedetomidine in comparison with ketamine and atropine in uncooperative children during dental treatment.

**Material and methods.** The study was performed on 40 healthy uncooperative children aged 2–6 years. They were equally and randomly divided into 2 groups: group D – intravenous dexmedetomidine with a loading dose of 1 µg/kg body weight (b.w.), which was followed by 0.2 µg/kg b.w./h via continuous infusion; and group K – intravenous ketamine 2 mg/kg b.w. with atropine 0.01 mg/kg b.w. Vital signs, recovery time and adverse effects were all recorded. Behavior was also evaluated using the Ohio State University Behavioral Rating Scale (OSUBRS).

**Results.** Statistically significant differences appeared in the degree of behavior between the 2 groups ( $p = 0.03$ ). Group D did better than group K. The mean recovery time was shorter in group D than in group K, but there were no statistically significant differences ( $p = 0.12$ ). No side effects, episodes of cardiovascular or respiratory instability were reported in either group.

**Conclusions.** The use of intravenous sedation in managing uncooperative children is more effective with dexmedetomidine than with ketamine. The addition of atropine as an adjunct to intravenous ketamine sedation helps in preventing complications.

**Key words:** behavior, ketamine, dexmedetomidine, intravenous sedation

**Słowa kluczowe:** zachowanie, ketamina, deksmedetomidyna, dożylna sedacja



## Introduction

Uncooperative behavior is the greatest challenge faced by pediatric dentists in daily practice. It can be a barrier to completing dental treatment or providing quality care.<sup>1,2</sup> Generally, most of the children showing a lack of cooperation or fears should be managed by behavioral management techniques (BMTs). However, the use of pharmacological methods, like conscious sedation or general anesthesia, is required in some children who are unable to tolerate dental procedures despite the use of all gentle psychological methods.<sup>3,4</sup>

Among the drugs used for conscious sedation, one can mention ketamine, which is a phencyclidine derivative and provides amnesia and dissociative sedation, associated with an analgesic effect by blocking N-methyl-D-aspartate receptors, without the loss of consciousness when given in appropriate doses.<sup>5</sup> When ketamine is administered alone intravenously, it produces an adequate sedative effect. However, it may have different side effects,<sup>5</sup> including hallucinations and nightmares during the recovery,<sup>6</sup> as well as nausea, vomiting and excessive salivation, which may lead to potential coughing and laryngospasm.<sup>7</sup>

Dexmedetomidine is a potent, highly selective alpha-2 agonist that has sedative and analgesic effects.<sup>8</sup> It acts on adrenoceptors in many tissues, including the nervous, cardiovascular and respiratory systems.<sup>9</sup> When dexmedetomidine is administered within the recommended doses provided by the clinical guidelines, it results in dose-dependent analgesia with no accompanying respiratory depression.<sup>10</sup> Some researchers even claim that the results of the action of dexmedetomidine resemble normal sleeping due to its alpha-2 agonist effect on the sympathetic system.<sup>11</sup>

Although there has been a lot of research on various drugs used individually and/or in sort of a combination (a cocktail) to achieve sedation in children, the 'golden' sedative drug – with better outcomes, a higher impact (but unquestionably safe) and with fewer side effects – is still being sought.<sup>12</sup> Consequently, the present randomized controlled study was conducted to evaluate the efficacy and safety of intravenous sedation with dexmedetomidine in comparison with ketamine administered with atropine in uncooperative children aged 2–6 years during dental treatment. It is worth mentioning that this age group is widely considered to be the most difficult to manage in pediatric dentistry.

## Material and methods

In this randomized controlled study, ethical and licensing approvals were obtained from the related specific review board (the number of the ethical approval is 2088, dated October 7<sup>th</sup>, 2017, and all parents gave informed written consent. This trial was carried out from November 2017 to January 2019.

The study consisted of 40 healthy (according to the American Society of Anesthesiology (ASA) scale, ASA I) children aged 2–6 years, requiring dental treatment (pulpotomy) under conscious sedation for exhibiting negative and definitely negative behavior on the Frankl scale.<sup>13</sup> Each child was assessed by a pediatric dentist prior to the sedation procedure. Moreover, preoperative medical questionnaires were completed by the children's parents or guardians with the help of the dentist.

The exclusion criteria embraced any children with known allergy to the drugs used, and children with respiratory infections or any systemic disease.

All the children were requested to fast preoperatively for 6 h (solid foods and nonhuman milk), 4 h (human milk) and 2 h (water and clear liquids).<sup>14</sup> Baseline heart rate (HR), oxygen saturation (SpO<sub>2</sub>) and blood pressure (BP) were recorded before any drug administration, at a 10-minute interval and at the end of the dental procedure.<sup>14</sup> An intravenous (IV) line was inserted before the start of conscious sedation using EMLA™ cream (Astra-Zeneca, Wilmington, USA).

The children were randomized into 2 equal groups – group D and group K – using a computer-generated table of random numbers.

The children in group D received intravenous dexmedetomidine with a loading dose of 1 µg/kg b.w. administered over 10 min, followed by 0.2 µg/kg b.w./h dexmedetomidine as continuous infusion using a syringe pump, until the desired level of sedation was achieved.<sup>15</sup> Dexmedetomidine was prepared and diluted with 0.9% sodium chloride saline to obtain the required concentration (4 µg/mL); then, it was gently shaken to mix it well prior to administration.<sup>15</sup>

In group K, the children received intravenous ketamine hydrochloride 2 mg/kg b.w. along with atropine 0.01 mg/kg b.w.

After the drug administration, the dental procedure was initiated and completed by an experienced pediatric dentist. All sedation procedures were handled by 1 anesthetist and all dental procedures were performed by 1 experienced pediatric dentist.

The sedation onset and recovery time were recorded, and also the behavior of each child during treatment was assessed by an external assessor using recorded videos according to the Ohio State University Behavioral Rating Scale (OSUBRS) (Table 1), which was also used by Hitt et al. in 2014.<sup>16</sup>

Table 1. Ohio State University Behavioral Rating Scale (OSUBRS)

Score	Behavior
1	quiet behavior, no movement
2	crying, no struggling
3	struggling movement without crying
4	struggling movement with crying

Adverse events were noted, if any existed, and then the children were discharged when full consciousness was regained and all vital signs were within normal ranges. The parents were contacted by telephone approx. 24 h post-operatively to check for any complications experienced by the children.

Data analysis was performed using the Mann–Whitney *U*-test and Student's *t*-test. The statistical package used for all data was IBM SPSS Statistics for Windows, v. 21 (IBM Corp., Armonk, USA). Statistical significance was defined as  $p < 0.05$ .

## Results

A total of 40 healthy children aged 2–6 years completed the study protocol and the dental procedures. They were comparable with respect to the demographic data (Table 2). With regard to age, weight, gender, and type of procedure, the differences were not statistically significant. Throughout the procedures and during the recovery, no episodes of oxygen desaturation, hypotension, airway obstruction, or bradycardia were noted in any of the children. Oxygen saturation was  $SpO_2 > 97\%$  in both groups.

In the dexmedetomidine group, the behavior score according to OSUBRS was 1 (quiet behavior, no movement) in 11 children (55%), 2 (crying, no struggling) in 4 children (20%), 3 (struggling movement without crying) in 2 children (10%), and 4 (struggling movement with crying) in 3 children (15%). On the other hand, in the ketamine group, 9 children (45%) had a score of 1, 2 children (10%) had a score of 2, the behavior score was 3 in 7 children (35%), and 4 in 2 children (10%).

The mean OSUBRS scores for both groups are presented in Table 3. There were statistically significant differences between the 2 intravenous sedation groups in the mean OSUBRS scores as recorded by the external assessor during treatment (Table 3). Group D showed better behavior than group K ( $p = 0.03$ ; the Mann–Whitney *U*-test).

Table 2. Characteristics of the patients

Characteristic	Group D (n = 20)	Group K (n = 20)
Ratio male:female	10:10	9:11
Age [years] mean $\pm$ SD	9.1 $\pm$ 0.9	8.9 $\pm$ 0.7
Weight [kg] mean $\pm$ SD	14.9 $\pm$ 9.1	15.2 $\pm$ 8.2
Sedation time [min] mean $\pm$ SD	24.41 $\pm$ 4.74	22.58 $\pm$ 4.44
Recovery time [min] mean $\pm$ SD	15.13 $\pm$ 2.4	17.93 $\pm$ 2.5

Group D – administered dexmedetomidine; group K – administered ketamine along with atropine; SD – standard deviation.

Table 3. Comparison of the behavior scores during the procedure

Group	OSUBRS score mean $\pm$ SD
Group D (n = 20)	1.2 $\pm$ 0.6
Group K (n = 20)	2.3 $\pm$ 1.1

In this study, the mean recovery time for dexmedetomidine was shorter than that for ketamine (15.13  $\pm$ 2.4 min and 17.93  $\pm$ 2.5 min, respectively) (Table 2). However, there were no statistically significant differences according to Student's *t*-test; the *p*-value for this comparison was 0.12 (non-significant).

No serious side effects were noted, either during the procedures or in the recovery room. Also, no late complications were reported by the children's parents in the 24 h following the operation in either group.

## Discussion

The ideal sedative for the outpatient dental clinic would be effective, easy to titrate, fast in onset and offset, predictable in response, able to preserve the airway tone, and inexpensive. Most importantly, it should exhibit minimal cardiovascular or respiratory effects, and minimal risk of the central nervous system (CNS) depression.

Dexmedetomidine has been shown to possess some of the desirable properties mentioned. Despite these excellent attributes, data regarding the use of dexmedetomidine in pediatric dentistry is still limited.<sup>17</sup>

Based on the present investigation, there is promising potential in the use of intravenous sedation techniques to overcome children's interfering behavior in the dental office. The outcomes of the present study indicate that both the intravenous sedation protocols used in this trial (with dexmedetomidine or with ketamine along with atropine) could provide effective and safe sedation for children undergoing outpatient dental procedures, still dexmedetomidine resulted in superior sedation in comparison with ketamine. Most children in the dexmedetomidine group (55%) showed quiet behavior and no movement, i.e., score 1 according to OSUBRS. This superiority can be attributed to the pharmacological sedative and analgesic effects of dexmedetomidine.<sup>18</sup> In a previous study by Hall et al., the authors reported that alpha-2 agonists behaved differently from other sedatives due to their unique characteristics that make their action in inducing sedation closer to normal sleep, yet obtaining the level of consciousness sufficient to respond to orders.<sup>8</sup> This is consistent with the results obtained in the present study.

There is no research in the dental field comparing the use of intravenous dexmedetomidine to ketamine with atropine. This is the first comparative study of its kind,

especially with the dosage mentioned. Therefore, the results of the present study could not be compared with any other. Studies that resemble the present one the most were conducted in the medical field, and compared dexmedetomidine to ketamine alone. In our study, the use of dexmedetomidine led to an earlier recovery than ketamine, but this difference was not clinically or statistically significant. However, intravenous dexmedetomidine has a longer time of onset, and ketamine has the advantage of having a quicker onset. Similar results were found in a study conducted by Gyanesh et al., who reported that children in the dexmedetomidine group had an earlier awakening and discharge than those in the ketamine group, but this difference was statistically non-significant.<sup>19</sup>

Dexmedetomidine is a potent centrally-acting alpha-2 agonist, and its action is characterized by easy titrating and a quick recovery from sedation, actually mimicking some aspects of natural sleep,<sup>8,20</sup> as the drug has a short half-life of 1.5–3 h after administering the intravenous doses, and because the main site of action of dexmedetomidine is the locus ceruleus rather than the cerebral cortex in the CNS.<sup>8,20,21</sup>

In the present study, the results of recovery time for ketamine were consistent with the clinical pharmacokinetics and pharmacodynamics of ketamine. It is an anesthetic that has a short acting time, so it is used mainly in children and elderly adults for short procedures. The later half-life of ketamine (beta phase) is 2.5 h, making the awakening from anesthesia fast.<sup>22,23</sup>

In our study, no patients experienced serious adverse events in either of the sedation groups, nor did any require the termination of the procedure or the administration of any emergency medications. This finding supports the aspect of safety relating to the use of intravenous dexmedetomidine,<sup>24,25</sup> and it is in accordance with the findings of several other studies that utilized intravenous dexmedetomidine.<sup>26</sup>

It also confirms the benefit of the prophylactic co-administration of atropine (an anticholinergic) as an adjunct to intravenous ketamine sedation in children. This is consistent with many studies, which have reported that atropine counters the effects of some sedatives, like ketamine, and reduces hypersalivation, excessive secretion from the respiratory tract, nausea, and vomiting,<sup>27–29</sup> which are the most common complications related to the use of ketamine.<sup>6,7,30</sup>

## Conclusions

In summary, both dexmedetomidine and ketamine presented satisfactory and good sedation, and were effective in behavior management in children undergoing outpatient dental procedures, but intravenous sedation with dexmedetomidine proved to be more effective than that with ketamine. Although intravenous dexmedetomidine

led to an earlier awakening than ketamine, this difference was not statistically or clinically significant. The addition of atropine as an adjunct to intravenous ketamine sedation in children prevents the occurrence of complications and adverse effects.

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# Effect of etching the coronal dentin with the rubbing technique on the microtensile bond strength of a universal adhesive system

## Wpływ wytrawiania zębiny koronowej techniką wcierania na mikrorozciągliwą siłę wiązania uniwersalnego systemu adhezyjnego

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## Abstract

**Background.** The adhesion of composite resins to the dentin substrate is influenced by the treatment of the smear layer. While etch-and-rinse systems require dentin to be conditioned with phosphoric acid, self-etching systems preserve the smear layer by incorporating it into the adhesive layer.

**Objectives.** The objective of this study was to evaluate the influence of etching with the rubbing technique on the microtensile bond strength ( $\mu$ TBS) of a universal adhesive to dentin.

**Material and methods.** Eighteen extracted teeth were selected. Two etch-and-rinse techniques (with and without rubbing) and a self-etching technique were used to bond the dentin surfaces with a universal adhesive system. After 24 h, the bonded samples were prepared for the  $\mu$ TBS testing. The specimens were loaded with a tensile force at a crosshead speed of 0.5 mm/min until failure. The scanning electron microscope (SEM) analyses were used to reveal the failure modes. The data were statistically analyzed with the one-way analysis of variance (ANOVA) and  $\chi^2$  tests.

**Results.** The etch-and-rinse system with rubbing produced significantly lower bond strength ( $42.11 \pm 9.26$  MPa) than the etch-and-rinse system without rubbing ( $47.30 \pm 8.12$  MPa) and significantly higher bond strength than the self-etching system ( $38.07 \pm 9.49$  MPa).

**Conclusions.** Under the conditions of this study, dentin etched with phosphoric acid for 3 s in the etch-and-rinse mode with the rubbing technique for a universal adhesive system decreases the  $\mu$ TBS of the composite to dentin.

**Key words:** etching, phosphoric acid, universal adhesive, rubbing technique

**Słowa kluczowe:** wytrawianie, kwas fosforowy, uniwersalny materiał adhezyjny, technika wcierania

## Introduction

Dentin is capped by a crown made of highly mineralized and protective enamel.<sup>1</sup> The composition and structure of the enamel and dentin matrices are different, so the adhesion mechanisms for these tissues are also dissimilar.<sup>2</sup> Bonding to dentin has been considered more difficult treatment because of the complex histology and composition of dentin.<sup>3</sup> A universal system has been described as ideally a single-bottle one, which can be used in the total-etching, self-etching and selective-etching modes.<sup>4</sup> Bonding to dentin with total-etch adhesives is accomplished in 2 steps. The 1<sup>st</sup> step is to etch the surface by applying a strong acid, and the 2<sup>nd</sup> step is the penetration and then polymerization of the resin in situ inside the etched surface.<sup>5</sup> On the other hand, self-etch adhesives do not require a separate etching step, as they contain acidic monomers.<sup>6</sup> Etching dentin with phosphoric acid for 15 s removes almost all mineral content, exposes collagen fibers and allows them to be infiltrated with the adhesive material.<sup>7</sup> In the self-etching mode, a universal adhesive partially dissolves the smear layer without demineralizing the tooth surface too profoundly, thereby removing hydroxyapatite at the interface. Preserving hydroxyapatite at the interface provides calcium for chemical bonding to the functional monomer.<sup>6</sup> Selective dentin etching is a relatively new approach used to improve resin–dentin bonding by preserving hydroxyapatite crystals inside the intrafibrillar collagen spaces.<sup>8,9</sup> Universal adhesives used in the self-etching mode produce superior, long-term dentin bonding compared to the etch-and-rinse method<sup>10,11</sup>; reducing the etching time may be useful for achieving complete penetration and for sealing the dentin surface.<sup>12</sup> Selective etching for 3 s using 37% phosphoric acid improves the effectiveness of dentin bonding.<sup>13</sup> Phosphoric acid is the most suitable acid conditioner in dental restoration.<sup>14</sup>

Hanabusa et al., who compared the self-etching mode with ‘dry-bonding’ and ‘wet-bonding’ etch-and-rinse techniques, noted that the self-etching approach was preferred on the dentin surface.<sup>15</sup> Zecin-Deren et al. recommended using triple adhesive layers with simplified adhesive systems in order to improve their performance.<sup>16</sup>

The present study highlights another application protocol, and discusses the rubbing action of phosphoric acid in the etch-and-rinse technique on the dentin surface before the rinsing and bonding procedures.

The bond strength measurement is one of the most effective methods for characterizing commercial dentin bonding products.<sup>17,18</sup>

The purpose of this in vitro study was to evaluate and compare the microtensile bond strength ( $\mu$ TBS) of 2 different etch-and-rinse protocols and a self-etching protocol for universal adhesive systems. The null hypothesis was that there are no differences in the  $\mu$ TBS of a dentin bond after the bonding procedure between the 3 different etching techniques.

## Material and methods

### Specimen preparation

This study was revised and approved by the Ethics Committee of the Faculty of Dental Medicine at the University of Strasbourg and Strasbourg University Hospital, France (protocol No. 201905).

In total, 18 recently extracted caries-free human mandibular molars were selected. The teeth were washed with physiological serum and stored in 70% ethanol for 2 weeks at 4°C. We divided the extracted teeth into 3 groups. The dentin bonding sites were prepared by sectioning the teeth and removing the root structure.

One section was made perpendicular to the longitudinal axis of the tooth crown to obtain a single coronal dentin wafer, 4 mm in thickness, then polished with P320-grit silicon carbide paper (Escil, Chassieu, France) for 60 s under water cooling conditions to get the same surface as in the case of using a dental diamond burr drill.<sup>13</sup>

The 1<sup>st</sup> group (G1) consisted of 6 teeth which were bonded in the self-etching mode using a universal adhesive (Prime & Bond<sup>®</sup> active – P&Ba; Dentsply DeTrey GmbH, Konstanz, Germany) (Table 1). The 2<sup>nd</sup> group (G2) consisted of 6 teeth which were bonded using the same universal adhesive in the etch-and-rinse mode – etching with 37% phosphoric acid (Itena Clinical, Villepinte, France) for 3 s, followed by rinsing with water for 30 s.<sup>13</sup> The 3<sup>rd</sup> group (G3) consisted of 6 teeth which were bonded in the etch-and-rinse mode with the rubbing technique – etching with 37% phosphoric acid for 3 s with the rubbing method using a micro-brush, and then rinsing with water for 30 s. The adhesive was applied according to the manufacturer’s

Table 1. Chemical composition of and instructions for the material used

Material and manufacturer	Composition	pH	Instructions for use
Prime & Bond Active (P&Ba); Dentsply DeTrey GmbH, Konstanz, Germany	– bisacrylamide 1 (25–50%) – 10-methacryloxydecyl dihydrogen phosphate (10-MDP) (10–25%) – bisacrylamide 2 (2.5–10%) – 4-(dimethylamino)benzotrile (0.1–1%) – dipentaerythritol pentaacrylate phosphate (PENTA), propan-2-ol (10–25%) – water (20%)	2.5	apply adhesive, slight agitation (20 s), mild air-blowing (5 s), light-curing (20 s)

protocol (brushing for 20 s, air-drying for 5 s and light-curing for 20 s). The adhesive was light-cured for 20 s with the aid of an Optilux® 501 apparatus (Kerr Dental France, Ivry-sur-Seine, France) at a light intensity of 600 mW/cm<sup>2</sup>.

## Microtensile bond strength

The samples from each group were prepared for the  $\mu$ TBS tests. Resin composite build-ups were performed using a resin composite (Ceram® X; Dentsply Sirona) in 3 increments of 2 mm each. Each increment was light-cured for 40 s, according to the manufacturer's instructions, until a height of 6 mm was reached. The teeth were stored in distilled water in an incubator for 24 h at 37°C. This experimental study was carried out in accordance with the International Standards Organization's ISO TR 11405. The samples were longitudinally sectioned using a diamond wire saw (WELL Diamond Wire Saws SA, Le Locle, Switzerland) in both X- and Y-axes with a cross-sectional area of approx. 1 mm<sup>2</sup>. The sticks (9–12 from each sample) were kept moist until testing. For the  $\mu$ TBS tests, the specimens were attached to a testing machine (Instron® 3345; Instron, Norwood, USA) with a cyanoacrylate adhesive. The specimens were loaded with a tensile force at a crosshead speed of 0.5 mm/min until failure. The microtensile bond strength [MPa] was calculated by dividing the load at failure [N] by the bonded surface area [mm<sup>2</sup>].

## Scanning electron microscope preparations and observations

After the  $\mu$ TBS testing process, the dentin sides of all samples were dehydrated in a graded ethanol series. The samples were sputter-coated with gold-palladium alloys (20/80) using a Hummer® JR sputtering device (Technics, San Francisco, USA). Later on, a Quanta® 250 FEG scanning electron microscope (SEM) (FEI Company, Eindhoven, the Netherlands) functioning with an accelerating voltage of 10 kV was used for the observation of all coated specimens (61 samples from G1, 60 samples from G2 and 60 samples from G3).

The dentin surfaces were examined under SEM at  $\times 100$  magnification in order to determine the mode of failure. The failure modes were categorized into the following 3 types<sup>19</sup>:

- type 1: adhesive failure;
- type 2: cohesive failure in the composite or dentin; and
- type 3: mixed failure, in the case when one area exhibited cohesive failure while other areas exhibited an adhesive fracture.

## Statistical analysis

Any samples that exhibited cohesive or mixed failures were excluded from the statistical analysis.<sup>20,21</sup> The data analysis was performed with SigmaPlot, v. 11.2 (Systat Software Inc., San Jose, USA). The one-way analysis of variance (ANOVA) test was applied in the comparisons of the  $\mu$ TBS data of the 3 groups. The  $\chi^2$  test was performed to compare the effects of the 3 different etching protocols used on the mode of failure. In all tests, a statistical significance level of  $\alpha = 0.05$  was adopted.

## Results

### Microtensile bond strength test

A total of 181 specimens (sticks) were available for the  $\mu$ TBS testing. The mean values of  $\mu$ TBS with standard deviations (*SDs*) are shown in Table 2. The ANOVA test revealed a statistically significant difference between the means corresponding to the different etching techniques. In a pairwise comparison for the pair (G1, G2), the test resulted in  $p < 0.001$ , and for the pairs (G2, G3) and (G1, G3),  $p = 0.034$  and  $p = 0.05$ , respectively. Therefore, the null hypothesis was rejected ( $p < \alpha$ ).

Table 2. Descriptive statistics of the microtensile bond strength ( $\mu$ TBS) of a dentin bond in adhesive failure samples

Experimental group	N (total)	n (cohesive and mixed failures)	n (adhesive failures)	$\mu$ TBS mean $\pm$ SD [MPa]
G1	61	19	42	38.07 $\pm$ 9.49
G2	60	26	34	47.30 $\pm$ 8.12
G3	60	23	37	42.11 $\pm$ 9.26

*SD* – standard deviation.

### Scanning electron microscope failure analysis

The dentin side of each stick was observed in order to identify the failure type. Higher  $\mu$ TBS values were mostly associated with a higher tendency toward cohesive failure in the composite (Fig. 1A) or mixed failure (Fig. 1B,C), in particular for G2 and G3. Most of the self-etching samples (G1) revealed adhesive interfacial failure (Fig. 1D). The interaction between the groups and the failure modes indicated a non-statistically significant correlation ( $p > 0.001$ ). The etch-and-rinse mode interfaces (G2, G3) often presented with intra-tubule tags as well (Fig. 2), particularly when the adhesive was applied in the etch-and-rinse mode without the rubbing technique (G2).



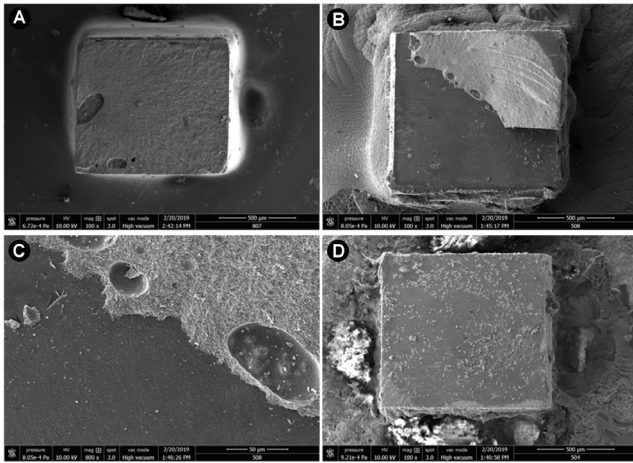


Fig. 1. A – scanning electron microscope (SEM) failure analysis of cohesive failure in the composite ( $\times 100$  magnification); B – SEM photomicrograph of mixed interfacial failure between the adhesive and composite layers ( $\times 100$  magnification); C – higher magnification of mixed failure showing the interface between the adhesive and composite layers ( $\times 800$  magnification); D – representative SEM photomicrograph of adhesive failure ( $\times 100$  magnification)

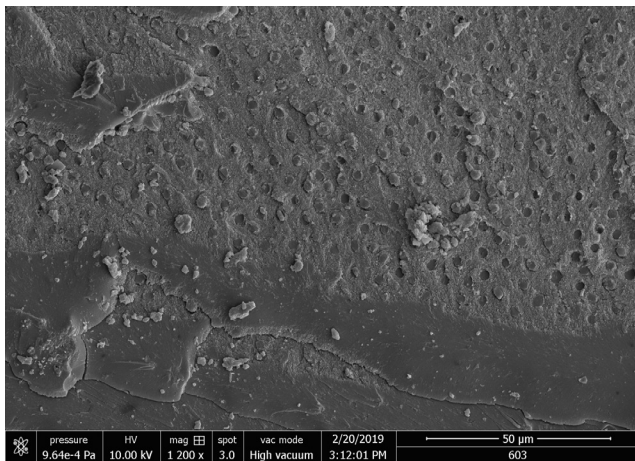


Fig. 2. Scanning electron microscope (SEM) image of the dentin–adhesive interface in bonded dentin using a universal adhesive in the etch-and-rinse mode without the rubbing technique (G2), showing the uniform and complete filling of dentinal tubules ( $\times 1,200$  magnification)

## Discussion

This study presents an investigation of the effects of etching with the rubbing technique on the resin–dentin interface. The tooth preparation processes bring important changes in the dentin thickness and density, leading to different resin bonding results.<sup>22</sup> In an attempt to improve the quality of the resin–dentin interface, some studies suggest specific clinical procedures, such as applying multiple adhesive coats, prolonging the exposure time during light-curing, using warm air to evaporate the solvent, and rubbing the adhesive onto the tooth surfaces.<sup>23</sup> Concerning the etch-and-rinse protocol (G2), it would appear that it is necessary to etch the dentin surface for 3 s before the bonding of a universal adhesive. Similar results were obtained by Stape et al., who noted that the use

of phosphoric acid for 3 s improves immediate and long-term resin–dentin bonding without overexposing demineralized collagen.<sup>13</sup>

In our study, the rubbing technique was proposed during etching in order to improve bonding quality. Under the experimental conditions defined in this *in vitro* study, the rubbing action (G3) does not enhance  $\mu$ TBS to dentin; on the contrary, this protocol statistically decreases  $\mu$ TBS.

The SEM images from the present study show that etching by means of phosphoric acid with or without the rubbing technique for 3 s before bonding removes the smear plugs, better opens up tubules which occur in the presence of resin tags (Fig. 2) and provides the micromechanical interlocking of the adhesive resin. It is generally accepted that the primary critical factor in determining an adequate bond is the micromechanical interlocking of the adhesive resin in the demineralized tooth surface.<sup>24</sup> Bahillo et al., in their use of an acidic monomer (glycerol phosphate dimethacrylate – GPDM), noted that selective dentin etching with phosphoric acid did not significantly improve marginal adaptation, indicating a self-etching effect most probably due to the presence of GPDM in the composition of the OptiBond™ FL primer.<sup>25</sup> There is still a point of discussion concerning the etching time. Etching dentin for 3 s in the case of a complex cavity is very difficult to translate into clinical application, because it is too easy to exceed this time, especially with rubbing.

The statistical analyses in our study revealed that etching associated with the rubbing technique decreased  $\mu$ TBS (Table 2). Phosphoric acid demineralized dentin and exposed the collagen matrix, containing hydroxyapatite.<sup>26</sup> Our hypothesis was that the rubbing action at the time of etching the dentin surface could crush and destroy collagen fibers and hydroxyapatite crystals. Hashimoto et al. noted that excessive acid-conditioning caused deeper demineralization of both intertubular and peritubular dentin, which in turn meant that the 2 kinds of dentin were not capable of being entirely infiltrated by resin monomers, leading to decreased bond strength.<sup>27</sup> Van Meerbeek et al. highlight the importance of keeping hydroxyapatite around collagen in order to better protect collagen against hydrolysis, and thus early degradation of the bond.<sup>28</sup> Therefore, functional monomers containing acidic groups cannot interact with hydroxyapatite. A functional monomer such as 10-methacryloxydecyl dihydrogen phosphate (10-MDP) can form stable calcium-phosphate complexes and self-assemble into the form of a regular layered structure at the apatite surface.<sup>29–31</sup> Preserving calcium at the bonded interface, in theory, could favor this peculiar chemical bonding process. Wang and Spencer noted that agitating acid gel facilitated etching and penetration into dentin, but it is not recommended, especially for longer etching times.<sup>32</sup>

The  $\mu$ TBS test is considered the most reliable technique for assessing the real strength of the interfacial bond between an adhesive material and a tooth.<sup>31</sup> One of the many

advantages of this test is that it can reveal the adhesive failure type and result in fewer cohesive and mixed failures.<sup>33</sup> Cohesive and mixed failures were observed more often when the  $\mu$ TBS values increased, which might be explained by the good mechanical properties of a bond, associated with the particular bonding technique used. In contrast, cohesive failures in the composite may have been caused by errors made during the build-up of the composite layers. The results in Table 2 present the incidence of each failure mode induced by particular etching techniques. The present study noted a higher tendency toward cohesive or mixed failure associated with higher  $\mu$ TBS values, but these results are not significantly different (the  $\chi^2$  test;  $p > 0.001$ ). In G1, bonding was weaker than in the specimens prepared with the etch-and-rinse mode, the most common failure type was adhesive fracture and minimal resin penetration occurred. Takamizawa et al. noted that using the etch-and-rinse mode for universal adhesives did not decrease dentin bond quality.<sup>34</sup>

The present in vitro study has some limitations. It did not address the effect of the rubbing action on dentin sensitivity, which should be followed with clinical studies. The relatively short period of water storage (24 h) was another limitation. Furthermore, dentin bonding by means of the etch-and-rinse method has been claimed to be technique-sensitive.<sup>32</sup>

## Conclusions

Etching with 37% phosphoric acid for 3 s without the rubbing technique is recommended before applying a universal adhesive on the dentin surface in order to improve bond strength.

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# Color and translucency stability of novel restorative CAD/CAM materials

## Stabilność barwy i przezierności nowych materiałów używanych w technologii CAD/CAM

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## Abstract

**Background.** The wide range of restorative materials available for use in the computer-aided design/computer-aided manufacturing (CAD/CAM) technology requires a better understanding of their esthetic properties.

**Objectives.** The aim of the study was to assess the stability of the color and translucency of different CAD/CAM restorative materials before and after being subjected to different staining solutions.

**Material and methods.** A total of 160 disc-shaped specimens were prepared from glass ceramic (IPS-e.max<sup>®</sup>-CAD and Celtra Duo<sup>®</sup>), high-translucency zirconia (Lava<sup>™</sup> Plus), resin nanoceramic (Lava<sup>™</sup> Ultimate), and hybrid ceramic (VITA ENAMIC<sup>®</sup>) CAD/CAM blocks (5 groups, n = 32). The specimen color and translucency parameter (*TP*) were assessed using a spectrophotometer at baseline and after subjecting the specimens to different staining solutions (coffee, cola, ginger, and water). Changes in color ( $\Delta E$ ) and *TP* ( $\Delta TP$ ) were calculated. The data was analyzed using the analysis of variance (ANOVA) and Tukey's post hoc test ( $p < 0.05$ ). The correlation between  $\Delta E$  and  $\Delta TP$  was investigated using Pearson's correlation coefficient.

**Results.** Staining significantly affected the baseline color of all specimens. Ginger had the most significant effect on Lava Plus ( $\Delta E = 4.01 \pm 1.2$ ), cola on Celtra Duo ( $\Delta E = 2.29 \pm 0.25$ ) and coffee on Lava Ultimate ( $\Delta E = 2.59 \pm 0.17$ ). Generally, IPS-e.max-CAD showed the smallest  $\Delta E$ . No significant differences in  $\Delta TP$  were found between different staining solutions. Increased  $\Delta E$  correlated with decreased translucency for all the tested materials and staining solutions.

**Conclusions.** Staining had a marked effect on the color and translucency of the tested CAD/CAM materials. The color change was staining solution- and material-dependent, with IPS-e.max-CAD showing the greatest color stability.

**Key words:** computer-aided design/computer-aided manufacturing, translucency parameter, color change

**Słowa kluczowe:** komputerowo wspomagane projektowanie/komputerowo wspomagane wytwarzanie, parametr przezierności, zmiana koloru

## Introduction

The use of computer-assisted design/computer-assisted manufacturing (CAD/CAM) has rapidly increased in recent years due to spectacular technological advances. The main advantage of this technology is the possibility of using homogenous and defect-free ceramic blocks<sup>1</sup> in the production of esthetic restorations during a single appointment.<sup>2</sup> The range of currently available materials includes glass ceramics, zirconia, resin nanoceramics, and – most recently – hybrid ceramics.

Conventional glass ceramics are generally highly esthetic but inherently brittle, which limits their use in the areas of high occlusal stresses.<sup>3</sup> Two variations of glass ceramics have been introduced to provide sufficient mechanical strength without affecting the esthetic outcome of the restoration – lithium disilicate and zirconia-reinforced lithium silicate ceramics.<sup>2</sup> Restorations made of lithium disilicate are initially milled in a partially crystallized form, and then subjected to crystallization firing to reach their ultimate strength and esthetic potential.<sup>4</sup> Zirconia-reinforced lithium silicate materials, on the other hand, are milled in their final form and may undergo an additional sintering cycle to enhance their mechanical properties. In addition to zirconia, which reinforces the ceramic structure and interrupts crack propagation, the material contains small silicate crystals in the lithium silicate glassy matrix, which has been shown to enhance the translucency of the material.<sup>5</sup>

In contrast, the zirconia-based ceramic restorative material has strong mechanical properties yet very low translucency, and thus is mainly used as a core structure to be veneered by a more translucent ceramic material.<sup>6</sup> To overcome this limitation, which often poses problems with maintaining the structural integrity of the restoration,<sup>7</sup> high-translucency monolithic zirconia has been introduced to the market. This material is claimed to have adequate esthetic properties for use without the need for an overlay material. The manufacturers of high-translucency zirconia attribute the improved optical properties to the use of high-quality zirconia processing techniques and to a reduction in the aluminum content (0.1% weight). These modifications are claimed to reduce light scattering, and thus to improve translucency.<sup>8</sup>

One alternative attempt to ensure the optimal properties of CAD/CAM restorative materials, such as adequate translucency, ease of polishing and high fracture resistance, involved combining the advantages of both ceramics and resins.<sup>9</sup> To this end, resin nanoceramics have been produced in machinable CAD/CAM blocks, and are claimed to have satisfactory mechanical and esthetic properties.<sup>10</sup> Another attempt involved the production of hybrid ceramics. These materials have a dual-network structure, in which the dominant porous sintered feldspathic ceramic network is strengthened by the methacrylate network, forming a ‘double network hybrid’ (DNH)

or a ‘polymer-infiltrated ceramic network’ (PICN). The reported high flexural strength, good internal and marginal fit,<sup>11</sup> and superior optical properties<sup>12</sup> make hybrid ceramics a valuable restorative option.

In terms of optical properties, all CAD/CAM restorative materials are currently available in different shades and degrees of translucency to better match the clinical situation. Reports on CAD/CAM material translucency vary. Several studies have demonstrated a higher translucency for zirconia-reinforced glass ceramics than for lithium disilicate ceramics.<sup>2,13</sup> The differences are attributed to the different grain size and crystalline structure of the materials. Resin nanoceramics have also been shown to have high translucency owing to their nano-sized zirconia and silica particles, decreasing light scattering.<sup>14,15</sup> Hybrid ceramics, on the other hand, have been reported to have a lower translucency than other ceramics, which is attributed to their higher alumina content.<sup>5</sup>

However, in addition to the initial color match and translucency of the material, its clinical esthetic stability is an important factor affecting its performance in oral conditions. It has been demonstrated that certain ceramic restorative materials may change color when subjected to staining solutions that simulate the consumption of regular beverages.<sup>16</sup> Nevertheless, how different beverage ingredients and acidities affect the color stability of different CAD/CAM restoratives based on their composition and structure requires further investigation. Furthermore, limited literature has been found to assess a potential change in the translucency of materials in the oral environment. In the case of esthetic restorative materials, their stain susceptibility as well as a change in their translucency after being subjected to common beverages are of utmost concern. The aim of this study was to assess changes in the color and translucency of currently available CAD/CAM restorative materials after being subjected to different staining solutions. The tested null hypothesis was that the color and translucency of the tested CAD/CAM restorative materials would not be significantly affected by immersion in different staining solutions.

## Material and methods

The properties and composition of the materials as well as their manufacturers are listed in Table 1.

A total of 160 ceramic specimens were prepared from the 5 tested CAD/CAM ceramic material groups ( $n = 32$ ). The specimens from each ceramic group were divided into 4 subgroups ( $n = 8$ ) according to the assigned staining solution. The color and translucency of the materials were assessed before and after staining. Thirty-two disc-shaped specimens (10 mm × 2 mm) were prepared from the 5 CAD/CAM restorative materials using a water-cooled low-speed diamond saw (IsoMet<sup>®</sup>; Buehler, Lake Bluff, USA). The EMC (IPS-e.max<sup>®</sup>-CAD; Ivoclar Vivadent,

**Table 1.** Computer-aided design/computer-aided manufacturing (CAD/CAM) materials used in the study (data provided by the manufacturers)

Classification	Brand	Composition	Average particle size	Code	Manufacturer
Lithium disilicate	IPS-e.max-CAD (LT, A2)	58–80% silicon dioxide, 11–19% lithium oxide, 0–13% potassium oxide, 0–8% zirconium dioxide, 0–5% aluminum oxide	3–4 μm	EMC	Ivoclar Vivadent, Schaan, Liechtenstein
Zirconia-reinforced lithium silicate	Celtra Duo (LT, A2)	58% silicon dioxide, 10.1% crystallized zirconium dioxide, 10% zirconium dioxide, 5% phosphorous pentoxide, 2.0% ceria, 1.9% alumina, 1% terbium oxide	400–800 nm	CD	Dentsply Sirona, York, USA
High-translucency zirconia	Lava Plus (Lava Plus Dyeing Liquid A2)	tetragonal polycrystalline zirconia partially stabilized with 3% yttria, 0.1% alumina (details withheld as a trade secret)	400 nm	LP	3M ESPE, Maplewood, USA
Resin nanoceramic	Lava Ultimate (LT, A2)	80% w/w ceramic (69% silicon dioxide and 31% zirconium dioxide) 20% polymer (Bis-GMA, Bis-EMA, UDMA, and TEGDMA)	silica nanomers: 20 nm zirconia nanomers: 4–11 nm	LU	3M ESPE, Maplewood, USA
Hybrid ceramic	VITA ENAMIC (2M2-T)	86% w/w fine-structure feldspathic ceramic (58–63% silicon dioxide, 20–23% aluminum oxide, 9–11% sodium dioxide, 4–6% potassium oxide, and 0–1% zirconium dioxide) 14% polymer (UDMA and TEGDMA)	–	VE	VITA Zahnfabrik, H. Rauter GmbH & Co. KG, Bad Säckingen, Germany

LT – low-translucency; T – translucent; Bis-GMA – bisphenol A-glycidyl methacrylate; Bis-EMA – ethoxylated bisphenol-A dimethacrylate; UDMA – urethane dimethacrylate; TEGDMA – triethylene glycol dimethacrylate.

Schaan, Liechtenstein) specimens were subjected to a crystallization cycle for 10 min at 850°C in an appropriate oven (Programat® EP 5000; Ivoclar Vivadent) according to the manufacturer's instructions. The LP (Lava™ Plus; 3M ESPE, Maplewood, USA) specimens were shaded with Lava Plus Dyeing Liquid shade A2, and then sintered according to the manufacturer's instructions.

The surfaces of all specimens were polished under water cooling conditions with P400, P600, P800, P1000, and P1200 silicon carbide paper at 300 rpm. The thickness of all specimens was confirmed using a digital micrometer (Mastercraft Electronic Caliper; Canadian Tire Corporation Ltd., Toronto, Canada) to be 2.0 ± 0.01 mm. All specimens were then ultrasonically cleaned in distilled water for 10 min. The specimen color was measured using a reflective spectrophotometer (model RM200QC; X-Rite GmbH, Neu-Isenburg, Germany). The aperture size was set to 4 mm and the specimens were positioned in the center of the measuring port. A white background (Commission internationale de l'éclairage (CIE)  $L^* = 88.81$ ,  $a^* = -4.98$ ,  $b^* = 6.09$ ) was selected and the measurements were made according to the CIE  $L^*a^*b^*$  color space relative to the CIE standard illuminant D65, where  $L^*$  refers to the degree of lightness (0–100),  $a^*$  to the color coordinate on the red/green axis and  $b^*$  to the color coordinate on the yellow/blue axis.<sup>17</sup> The spectrophotometer was calibrated before each measurement. Three measurements were taken for each specimen and the average was recorded.

For the translucency assessment, the color of the specimens was measured using the same spectrophotometer against white (CIE  $L^* = 88.81$ ,  $a^* = -4.98$ ,  $b^* = 6.09$ ) and black (CIE  $L^* = 7.61$ ,  $a^* = 0.45$ ,  $b^* = 2.42$ ) backgrounds relative to the CIE standard illuminant D65.

The translucency parameter ( $TP$ ) values were obtained by calculating the difference in the color of the specimens against black and white backgrounds using the following formula:

$$TP = [(L_b^* - L_w^*)^2 + (a_b^* - a_w^*)^2 + (b_b^* - b_w^*)^2]^{1/2} \quad (1)$$

where:

$TP$  – translucency parameter;

$L^*$  – degree of lightness;

$a^*$  – color coordinate on the red/green axis;

$b^*$  – color coordinate on the yellow/blue axis;

the subscripts  $b$  and  $w$  refer to the color coordinates against black and white backgrounds, respectively.<sup>18</sup>

The specimens from each tested group were randomly divided into 4 subgroups ( $n = 8$ ) according to the immersion medium (coffee, cola, ginger, and distilled water). To prepare the coffee solution, 20 g of coffee (Nescafé® Classic; Nestlé S.A., Vevey, Switzerland) was poured into 1,000 mL of boiled distilled water. The solution was stirred every 5 min for 10 s until it cooled to room temperature, and then it was filtered through a paper filter.

Cola (Coca-Cola®; Coca-Cola Company, Atlanta, USA) at room temperature was used as the 2<sup>nd</sup> staining solution. The ginger solution was prepared by pouring 20 g of ginger (Royal Herbs S.A.E, Ottoman Group, Shabramant, Giza, Egypt) into 1,000 mL of boiled distilled water. The solution was stirred every 5 min for 10 s until it cooled to room temperature, and then it was filtered through a paper filter. Distilled water (Health Aqua, Alexandria, Egypt) was used as the 4<sup>th</sup> immersion medium. After preparation, the pH of the solutions was measured using a pH meter (AD11; Adwa Instruments, Szeged, Hungary) and determined to be 2.5, 5.5, 8, and 6.9 for cola, the coffee solution, the ginger solution, and water, respectively.

The specimens were immersed individually in closed vials containing 5 mL of each immersion medium and stored in an incubator (model 431/V; C.B.M. S.r.l. Medical Equipment, Torre de' Picenardi, Italy) at 37°C for 28 days. The solutions were freshened daily to avoid yeast or bacterial contamination. To reduce the precipitation of particles in the staining solutions, the solutions were stirred twice a day. At the end of the immersion period, the specimens were rinsed with distilled water and wiped with gauze. Color and translucency were then reassessed.

The specimen color was assessed after employing different staining protocols as described for the baseline measurements. The color change ( $\Delta E$ ) of each specimen was calculated using the following formula:

$$\Delta E = [(\Delta L^*)^2 + (\Delta a^*)^2 + (\Delta b^*)^2]^{1/2} \quad (2)$$

where:

$\Delta E$  – change in color;

$$\Delta L^* = L^*_{\text{after staining}} - L^*_{\text{baseline}}$$

$$\Delta a^* = a^*_{\text{after staining}} - a^*_{\text{baseline}}$$

$$\Delta b^* = b^*_{\text{after staining}} - b^*_{\text{baseline}}$$

The  $\Delta E$  values greater than 1.2 were considered perceptible, whereas values greater than 2.7 were considered clinically unacceptable, according to the 50:50% threshold.<sup>19</sup>

Differences in the  $TP$  values were calculated using the following formula:

$$\Delta TP = TP_{\text{after staining}} - TP_{\text{baseline}} \quad (3)$$

where:

$\Delta TP$  – change in the translucency parameter.

The  $\Delta TP$  values greater than 2 were considered perceivable.<sup>20</sup> The mean and standard deviation ( $SD$ ) values of  $\Delta E$  and  $\Delta TP$  were calculated for each subgroup. The data was explored for normality using the Kolmogorov–Smirnov test and the Shapiro–Wilk test, and showed a parametric (normal) distribution. For  $\Delta E$ , the two-way analysis of variance (ANOVA) was performed to evaluate the effect of each variable (material group and staining solution). The one-way ANOVA followed by Tukey's post hoc test was used if ANOVA showed a significant  $p$ -value. For  $\Delta TP$ , the three-way ANOVA was performed to evaluate the effect of each variable (before vs after staining, material group and staining solution). The correlation between  $\Delta E$  and  $\Delta TP$  was investigated using Pearson's correlation coefficient. The significance level was set at  $p < 0.05$  throughout all statistical tests. The statistical analysis was performed with IBM SPSS Statistics for Windows, v. 20 (IBM Corp., Armonk, USA).

## Results

The means and  $SD$ s for  $\Delta E$  are presented in Table 2. Irrespective of the staining solution, LP generally showed the most significant  $\Delta E$ , whereas EMC showed the smallest  $\Delta E$ , as proven by the two-way ANOVA ( $F = 19.15$ ;  $p \leq 0.0001$ ).

The effect of different staining solutions on  $\Delta E$  in the tested materials also varied significantly. Ginger and coffee had the most significant effect, followed by cola, whereas water had the least effect on  $\Delta E$ , as demonstrated by the two-way ANOVA ( $F = 5.03$ ;  $p = 0.0035$ ).

Ginger had the most significant effect on LP ( $\Delta E = 4.01 \pm 1.2$ ), cola on CD (Celtra Duo®; Dentsply Sirona, York, USA) ( $\Delta E = 2.29 \pm 0.25$ ) and coffee on LU (Lava™ Ultimate; 3M ESPE) ( $\Delta E = 2.59 \pm 0.17$ ).

Table 2. Color change ( $\Delta E$ ) values

CAD/CAM restorative materials	Staining solutions				Total
	cola	coffee	ginger	water	
IPS-e.max-CAD	1.05 <sup>A</sup> <sub>a</sub> ± 0.25	1.23 <sup>A</sup> <sub>bc</sub> ± 0.29	1.27 <sup>A</sup> <sub>b</sub> ± 0.21	0.99 <sup>A</sup> <sub>b</sub> ± 0.21	1.14 <sub>b</sub> ± 0.27
Celtra Duo	2.29 <sup>A</sup> <sub>a</sub> ± 0.25	0.82 <sup>AB</sup> <sub>c</sub> ± 0.17	1.54 <sup>AB</sup> <sub>b</sub> ± 0.89	0.57 <sup>B</sup> <sub>b</sub> ± 0.09	1.32 <sub>b</sub> ± 0.78
Lava Plus	1.83 <sup>B</sup> <sub>a</sub> ± 0.04	3.88 <sup>A</sup> <sub>a</sub> ± 1.50	4.01 <sup>A</sup> <sub>a</sub> ± 1.20	2.66 <sup>AB</sup> <sub>a</sub> ± 1.50	3.20 <sub>a</sub> ± 1.50
Lava Ultimate	1.65 <sup>AB</sup> <sub>a</sub> ± 0.40	2.59 <sup>A</sup> <sub>ab</sub> ± 0.17	1.31 <sup>AB</sup> <sub>b</sub> ± 0.33	0.84 <sup>B</sup> <sub>b</sub> ± 0.07	1.59 <sub>b</sub> ± 0.66
VITA ENAMIC	0.88 <sup>AB</sup> <sub>a</sub> ± 0.04	1.60 <sup>AB</sup> <sub>bc</sub> ± 0.09	2.15 <sup>AB</sup> <sub>b</sub> ± 0.86	0.95 <sup>AB</sup> <sub>b</sub> ± 0.11	1.42 <sub>b</sub> ± 0.54
Total	1.53 <sup>AB</sup> ± 0.46	2.05 <sup>A</sup> ± 1.01	2.11 <sup>A</sup> ± 0.84	1.25 <sup>B</sup> ± 0.64	–

Data presented as mean ± standard deviation ( $SD$ ).

Different subscripts indicate significant differences within the same restorative material group after being subjected to different staining solutions. Different superscripts indicate significant differences between different restorative materials after being subjected to the same staining solution.

The means and *SDs* for  $\Delta TP$  are presented in Table 3. In general, *TP* was significantly higher before staining than after staining, as indicated by the three-way ANOVA ( $F = 35.56$ ;  $p \leq 0.0001$ ). There were no significant differences in  $\Delta TP$  between the different types of ceramic material groups ( $p > 0.05$ ). There were no significant differences in  $\Delta TP$  between the different types of staining solutions as well ( $p > 0.05$ ).

The correlation test showed that there was a moderate negative (inverse) correlation between  $\Delta TP$  and  $\Delta E$  ( $r = -0.693$ ), indicating that with increased  $\Delta E$ , a decreased translucency was observed for all the materials and all the immersion solutions tested (Fig. 1).

## Discussion

A thorough understanding of the optical properties of currently available CAD/CAM restorative materials is crucial for predicting the longevity of the esthetic outcome of monolithic restorations.

The consumption of a variety of foods and beverages exposes restorations to staining and pH fluctuations, which may influence their esthetic properties while in service.<sup>21</sup> In the current study, the effects of commonly consumed beverages (coffee, cola, ginger, and water) on the color and translucency of CAD/CAM restorative materials was investigated. The specimens were immersed in different solutions for 4 weeks, simulating an average of 2½ years of clinical aging.<sup>22</sup>

The results of the current study indicate that the most significant  $\Delta E$  after immersion in different staining solutions occurred in the LP group. Lava Plus is a high-translucency zirconia material, formulated to produce monolithic restorations without the need for a veneering ceramic. For this material, all changes were considered perceptible (above the 1.2 threshold), whereas changes resulting from immersion in coffee and ginger were above the 2.7 threshold of being clinically unacceptable. It has been shown that zirconia, when in contact with water, can undergo a progressive phase transformation, also known as low-temperature degradation (LTD), which can occur as soon as in 7 days of *in vitro* exposure.<sup>23</sup>

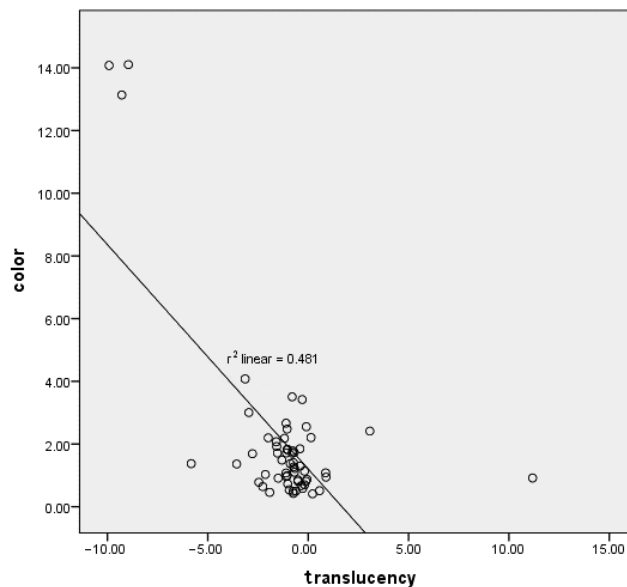


Fig. 1. Linear chart showing the correlation between color change ( $\Delta E$ ) and translucency parameter change ( $\Delta TP$ )

This transformation process, from the tetragonal to monolithic phase (T-M transformation), is accompanied by the roughness of the surface, particle displacement<sup>24</sup> and water penetration within the material.<sup>25</sup> This transformation can clearly explain a significant  $\Delta E$  observed in the high-translucency zirconia material after immersion in different staining solutions, even after immersion in distilled water. Notably, the ginger solution had the most significant effect on the color of LP. The ginger drink prepared in the current study had an alkaline pH. It has been shown that the exposure of zirconia to corrosive alkaline media may lead to an enhanced loss of the yttria stabilizer, more surface irregularities and an increase in the T-M transformation,<sup>26</sup> ultimately resulting in an increase in the staining potential. In fact, Novak and Kalin demonstrated the significance of the pH of an aqueous solution in terms of the wear of zirconia ceramics.<sup>27</sup> The authors noted that in alkaline media, zirconia exhibited exaggerated wear, probably due to a localized, hydrothermally induced phase transformation; this wear was accompanied by the severe fracture and degradation of the surface layer of the material.<sup>27</sup>

Table 3. Translucency parameter change ( $\Delta TP$ ) values

CAD/CAM restorative materials	Staining solutions				Total
	cola	coffee	ginger	water	
IPS-e.max-CAD	-2.39 ± 1.70	-0.87 ± 0.07	-1.59 ± 0.36	-1.06 ± 0.52	-1.47 ± 0.86
Celtra Duo	-1.09 ± 0.02	-0.34 ± 0.72	-0.81 ± 1.30	-0.56 ± 1.27	-0.53 ± 1.00
Lava Plus	-0.90 ± 0.35	-2.34 ± 1.00	-1.92 ± 1.60	-1.62 ± 1.68	-1.69 ± 1.27
Lava Ultimate	-0.61 ± 1.20	-0.97 ± 1.30	-1.97 ± 1.06	-0.48 ± 0.37	-0.70 ± 1.12
VITA ENAMIC	-0.57 ± 0.29	-1.44 ± 0.89	-1.41 ± 1.20	-1.06 ± 0.29	-1.12 ± 0.68
Total	-0.86 ± 0.63	-1.05 ± 0.22	-1.53 ± 0.49	-0.96 ± 0.31	-

Data presented as mean ± *SD*.



For the LU group, all  $\Delta E$  values were considered perceptible, except for a change resulting from water immersion. No changes were higher than 2.7, or clinically unacceptable. The greatest change was observed in the case of immersion in coffee. For EMC and VE (VITA ENAMIC<sup>®</sup>; VITA Zahnfabrik, H. Rauter GmbH & Co. KG, Bad Säckingen, Germany), only immersion in coffee and ginger resulted in changes that were above 1.2, or perceptible. Changes after immersion in cola and water were below the 1.2 threshold.

These results indicate that the tested ceramic materials having a resin component (LU and VE) generally showed a greater discoloration than the tested glass ceramics (EMC and CD). This greater discoloration tendency may be attributed to a greater water sorption potential of the resin<sup>28</sup> compared to the glass ceramic materials. According to the manufacturers, VE contains the urethane dimethacrylate (UDMA) and triethylene glycol dimethacrylate (TEGDMA) monomers, while LU contains a mixture of monomers comprising bisphenol A-glycidyl methacrylate (Bis-GMA), ethoxylated bisphenol-A dimethacrylate (Bis-EMA), UDMA, and TEGDMA.<sup>29</sup> Differences in the staining potential between the 2 materials, although statistically non-significant ( $1.42 \pm 0.54$  and  $1.59 \pm 0.66$  for VE and LU, respectively), may be explained by the different monomer composition of their resin components.<sup>30</sup> For both VE and LU, immersion in coffee resulted in perceptible color changes. A greater potential of coffee to stain resin-containing materials could primarily be due to the capacity of the yellow pigments in coffee to penetrate the microstructure of these materials. This change may also be enhanced by the low polarity of the coffee solution, which facilitates a deeper ingress of the pigments into resin matrices.<sup>22</sup> It has also been reported that solutions with pH ranging from 4 to 6 have a greater potential for ingress into resin materials, which in the case of the mildly acidic coffee solution (pH 5.5) would be an enhancing factor.<sup>31</sup> Our results are supported by those of Saba et al., who found that the VE material stained significantly compared to a feldspathic ceramic when subjected to coffee solutions.<sup>28</sup> If the same theory applied, i.e., that resins have a higher tendency to stain in mildly acidic media, then cola drinks, with their higher acidity, would have a reduced staining effect on resin-containing ceramic materials, as was observed in this study in the LU and VE groups. In fact, several studies have shown that despite their acidity, cola drinks result in minimal staining of resinous materials compared to other dark beverages.<sup>32,33</sup> Another factor that could reduce the staining effect of cola on resins is its phosphate ion content, which may decrease the dissolution of the resin surface, as these ions have been shown to have a similar effect on the tooth surfaces.<sup>34</sup>

In contrast, it was observed that cola had the greatest staining effect on the CD specimens. Interestingly, CD is composed of 5% w/w phosphorous pentoxide, which

is the same compound used to produce phosphorous acids for cola drinks. This may have enhanced the affinity of cola to the material. In addition, it has been reported that phosphorous pentoxide is highly hygroscopic, having extreme affinity for water,<sup>35</sup> which may have resulted in a greater sorption of the cola liquid into the CD material than into other tested CAD/CAM blocks containing no phosphorous pentoxide.

In addition to evaluating  $\Delta E$ , the current study aimed to assess a potential change in the translucency of CAD/CAM restorative materials after being subjected to different common beverages. The importance of translucency in determining the esthetics of the restoration has been well-recognized, as translucency refers to the passage of light through the material, which can give the restoration a life-like appearance.<sup>36</sup> The transparency parameter measures the difference in the color of the material of a uniform thickness when placed against white and black backgrounds, and has been shown to directly correspond to a visual assessment of translucency.<sup>32</sup> Variations in material translucency have been attributed to the different chemical composition, grain size, crystalline structure, pores, additives, defects, and surface texture of the materials.<sup>15,37</sup> Since preliminary options vary and can match the initial clinical situation, the current study focused on a potential change in the translucency of CAD/CAM restorative materials after being subjected to different common beverages rather than on their original translucency. The analysis of the change would allow a better understanding of the optical behavior of the material in different oral conditions and facilitate material selection to conform to different clinical situations.<sup>38</sup>

In the current study, the  $TP$  values recorded after staining were significantly lower than those at baseline in all the tested materials; nevertheless, according to Lee, these changes would not be regarded perceptible, as they did not exceed the limit of 2.<sup>20</sup> Changes in translucency can generally be attributed to changes in either the material body or surface texture.<sup>30</sup> There were also no significant differences between different materials or between different staining solutions. However, the greatest  $\Delta TP$  was recorded in the LP group, which may be attributed to possible LTD, which occurs on the surface of the material when in contact with moisture, as discussed for  $\Delta E$ . On the other hand, a decreased translucency of the tested resin-containing materials (VE and LU) may be attributed to changes in the material body resulting from possible water sorption by the resin component. The smallest  $\Delta TP$  was generally recorded for CD, which may be due to its structural composition, comprising nano-sized silicate crystals in the lithium silicate glassy matrix, enhancing its translucency and possibly stabilizing the material.

The correlation test indicated a moderate negative correlation between  $\Delta TP$  and  $\Delta E$  ( $r = -0.693$ ), suggesting that increased  $\Delta E$  corresponded to a decreased translucency for all the materials and all the immersion solutions

tested. This correlation could imply that  $\Delta E$  occurring due to the adsorption or absorption of pigments, water sorption, or a change in surface texture will be accompanied by a change in the light scattering properties of the materials.


The results of the current study have led to the rejection of the null hypothesis tested, as the color and translucency of the tested CAD/CAM restorative materials were significantly affected by immersion in different staining solutions. A factor that warrants further investigation is the surface texture of the material, since this feature has a determining effect on the optical properties of the material. In the present study, the finishing of the surfaces of all specimens was standardized at baseline using the same procedure; nevertheless, surface texture could have been affected by different immersion media, and in turn could have influenced  $\Delta E$  and  $\Delta TP$ . Studying changes in surface texture in response to immersion in different staining solutions was beyond the scope of this study and would require further investigation.

## Conclusions

Within the limitations of this in vitro study, the following could be concluded. Staining solutions had a marked effect on both the color and translucency of all the tested CAD/CAM materials. IPS-e.max-CAD showed the greatest color stability. Lava Plus stained with ginger and coffee showed a clinically unacceptable color change. The resin-containing materials were most affected by the coffee and ginger solutions, whereas the zirconia-reinforced lithium silicate material by cola drinks. Despite the differences in the initial translucency of the materials, staining had an equal effect on all materials.


The clinical judgment could include the consideration of the patients' beverage consumption habits, which might be a decisive factor when selecting the restorative material of choice.

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# Evaluation of the efficacy of the metal artifact reduction algorithm in the detection of a vertical root fracture in endodontically treated teeth in cone-beam computed tomography images: An in vitro study

## Ocena skuteczności algorytmu redukującego artefakty pochodzące od elementów metalowych w rozpoznawaniu pionowego złamania korzeni zębów leczonych endodontycznie w tomografii stożkowej – badanie in vitro

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D – writing the article; E – critical revision of the article; F – final approval of the article

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## Abstract

**Background.** Three-dimensional (3D) cone-beam computed tomography (CBCT) scans play an important role in dental diagnostics and treatment planning, especially in detecting vertical root fractures (VRFs). However, artifacts caused by high-density dental materials can negatively affect the quality of CBCT images by decreasing contrast and masking structures.

**Objectives.** The aim of this study was to assess the efficacy of artifact removal software in detecting VRFs in endodontically treated teeth on CBCT scans.

**Material and methods.** This study evaluated 70 endodontically treated single-rooted teeth. Half of the teeth were cracked by introducing a wedge into the canal and tapping gently with a hammer; the rest remained untouched as a control group. The teeth were then mounted in a bovine rib bone. Soft tissue was simulated using red dental wax. Cone-beam computed tomography scans were taken using the NewTom<sup>®</sup> 3G, ProMax<sup>®</sup> 3D and Cranex<sup>®</sup> 3D CBCT systems, and the MATLAB software was applied. The images were evaluated by 2 oral and maxillofacial radiologists, and the results were recorded in a checklist. The data was analyzed using the  $\kappa$  coefficient, McNemar's test and the receiver operating characteristic (ROC) curves.

**Results.** A significant inter-observer agreement was noted between the 2 observers in detecting VRFs using all CBCT systems. In all systems, the use of the MATLAB software improved the detection of VRFs, but the difference was not significant in the NewTom 3G ( $p = 0.119$ ) and ProMax 3D ( $p = 0.455$ ) systems. However, the difference was significant in the Cranex 3D system ( $p = 0.039$ ).

**Conclusions.** The MATLAB artifact removal software can enhance the detection of VRFs on CBCT scans to some extent.

**Key words:** cone-beam computed tomography, artifact, fracture, endodontically treated

**Słowa kluczowe:** tomografia stożkowa, artefakt, złamanie, leczony endodontycznie

## Introduction

Cone-beam computed tomography (CBCT) is an imaging modality with several applications and an increasing popularity in dentistry. It provides three-dimensional (3D) images and is commonly used in implantology, orthodontics, and oral and maxillofacial surgery. The majority of CBCT systems are capable of producing high-resolution images that visualize fine anatomical structures.<sup>1,2</sup> The advantages of CBCT compared to conventional radiography have increased its use in many dental fields.<sup>3,4</sup> The main advantage of CBCT in the detection of dental lesions is that it provides superior 3D images of the teeth and periodontal tissue compared to two-dimensional (2D) radiography. Moreover, the patient radiation dose in CBCT is lower than that in multi-detector computed tomography (MDCT).<sup>5,6</sup>

Exposure parameters, such as field of view (FOV) and voxel size, can affect the quality of CBCT images.<sup>7</sup> Cone-beam computed tomography systems with a small FOV provide images of higher quality and lower artifact incidence compared to CBCT systems with a large FOV.<sup>8,9</sup> Cone-beam computed tomography has been suggested as an efficient diagnostic modality for complex root canal treatment and for the assessment of the root canal system.<sup>10,11</sup> Recently, CBCT has been recommended as an efficient modality for the detection of vertical root fractures (VRFs) due to its numerous advantages.<sup>12</sup> Vertical root fractures are often detected by noticing a radiolucent fracture line. An X-ray beam needs to be parallel to the fracture line; otherwise a radiolucent trace is not visible on radiographs.<sup>13</sup>

Artifacts are the errors or distortions of the image reconstruction data.<sup>14</sup> Artifacts caused by high-density materials affect the quality of CBCT images by decreasing contrast and masking structures, which complicates diagnosis.<sup>13</sup> Gutta-percha, root-filling materials and metal posts can cause streak artifacts, which mimic the fracture lines and cause false positive results, hindering the detection of root fractures.<sup>3,7</sup>

Several methods have been suggested to reduce CBCT artifacts. The ProMax<sup>®</sup> CBCT systems (Planmeca Oy, Helsinki, Finland) have the artifact reduction algorithm.<sup>13</sup> In order to prevent unnecessary treatment due to false positive results, it is imperative to know the details of artifacts caused by root filling materials as well as methods to minimize them.<sup>12,13</sup>

To the best of our knowledge, studies on the efficacy of artifact removal software in enhancing the detection of VRFs of endodontically treated teeth on CBCT scans are limited. The aim of this study was therefore to assess the efficacy of an artifact removal program in detecting VRFs in endodontically treated teeth on CBCT scans.

## Material and methods

This study evaluated 70 single-canal teeth extracted for orthodontic treatment or severe periodontal disease (the number of approval from the ethics committee: IR.UMSHA.REC.1396.687). Multi-rooted and broken teeth, and those with root caries were excluded. The teeth were disinfected using 2% sodium hypochlorite solution. The root canals were instrumented by an endodontist using a stainless steel K-file size 40 (Dentsply, Ballaigues, Switzerland) and the passive step-back technique, and were filled with gutta-percha points size 40 (Pumadent Co., Ltd., Tianjin, China) using the lateral compaction technique. Next, the gutta-percha sealer was removed from the coronal third of the canal with a Gates–Glidden drill size 3 (Mani Inc., Utsunomiya, Japan). Teeth with a complete root fracture that occurred during root canal preparation were excluded. The teeth were then randomly divided into 2 groups ( $n = 35$ ). Cracks were induced in the experimental group by introducing a wedge into the canal and tapping gently with a hammer; the other group remained untouched as a control group. A fresh bovine rib bone was used in this study due to its resemblance to the alveolar bone. The ribs were cut into bone segments measuring 15 mm in length, 10 mm in width and 20 mm in height.

The teeth from each group were randomly mounted in rows (7 teeth in each row) in 10 bovine ribs in a curved fashion to simulate the dental arch, and then fixed with dental wax. The bovine ribs were coated with 3 layers of wax to simulate soft tissue (Fig. 1).

The teeth mounted in each bovine rib were subjected to CBCT using the following CBCT systems:

- NewTom<sup>®</sup> 3G (Quantitative Radiology, Verona, Italy) with 6-inch FOV, 10.65 mA and 90 kVp;
- ProMax 3D (Planmeca Oy) with 8 cm × 8 cm FOV, 14 mA, time of 12 s, and 84 kVp, with and without the metal artifact reduction (MAR) algorithm;
- Cranex<sup>®</sup> 3D (Soredex, Tuusula, Finland) with 6 cm × 8 cm FOV, 4 mA, time of 6.1 s, and 110 kVp, with and without the MAR algorithm.

The CBCT images obtained by means of the NewTom 3G system were evaluated in 2 modes: with and without the MATLAB ([www.mathworks.com](http://www.mathworks.com)) image processing software (Fig. 2,3).

The CBCT images obtained using ProMax 3D were evaluated in 3 modes: with and without the artifact removal



Fig. 1. Tooth placement

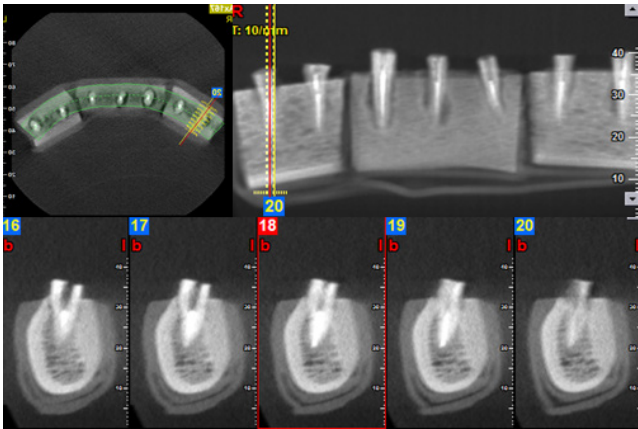


Fig. 2. NewTom 3G image

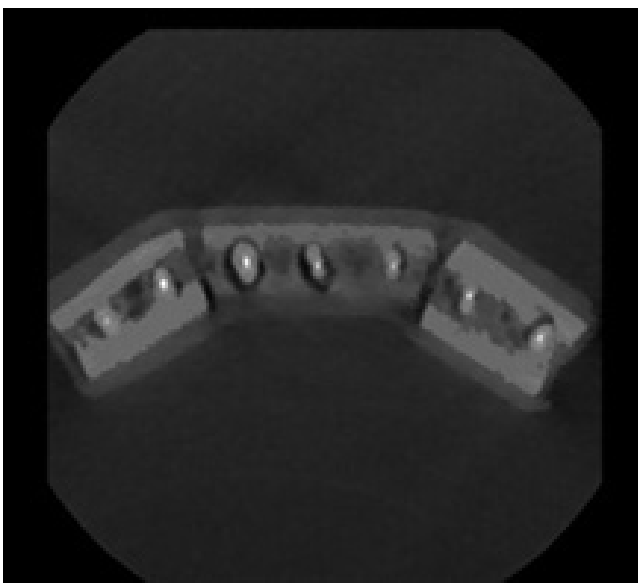


Fig. 3. NewTom 3G image with the MATLAB processing software

feature of the system, and also by applying the MATLAB artifact removal software (Fig. 4–6).

The CBCT images obtained with Cranex 3D were evaluated in 3 modes: with and without the artifact removal feature, and by applying the MATLAB artifact removal software (Fig. 7–9).

The CBCT scans of each group were assessed by 2 oral and maxillofacial radiologists with 10 years of clinical

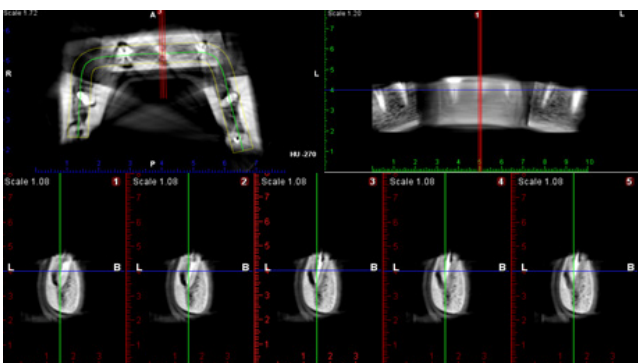


Fig. 4. ProMax 3D image

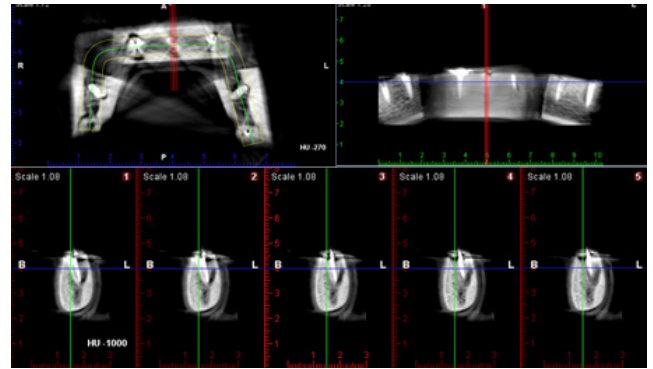


Fig. 5. ProMax 3D image with the metal artifact reduction (MAR) algorithm

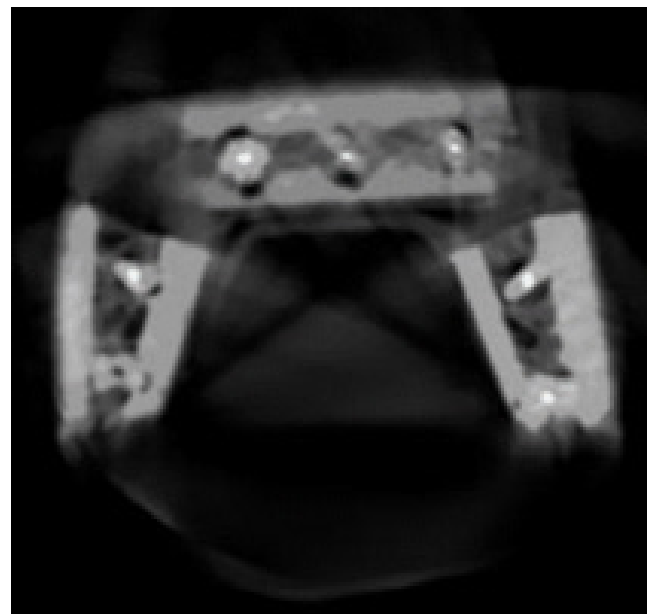


Fig. 6. ProMax 3D image with the MATLAB processing software

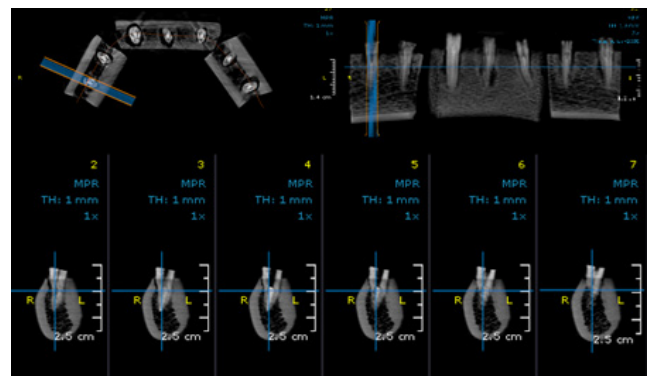


Fig. 7. Cranex 3D image

experience in a double-blind fashion on a 20-inch monitor (200P; LG Corporation, Seoul, South Korea) in a semi-dark room. The observers independently evaluated the images in the axial, coronal and sagittal planes by scrolling the mouse, and also assessed the cross-sectional images with a slice thickness of 1 mm and intervals of 0.5 mm. The observers were allowed to adjust the density and contrast of the images, and to use a magnification tool.

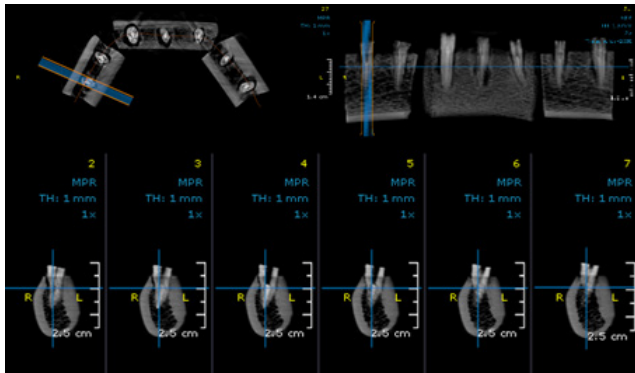


Fig. 8. Cranex 3D image with the metal artifact reduction (MAR) algorithm



Fig. 9. Cranex 3D image with the MATLAB processing software

The results were reported as the presence or absence of VRE, and recorded on a checklist.

The data was entered into IBM SPSS Statistics for Windows software, v. 24 (IBM Corp., Armonk, USA) and analyzed using the  $\chi^2$  test and McNemar's test. The weighted  $\kappa$  coefficient was also calculated to determine the level of inter-observer agreement. The level of significance was set at 0.01.

## Results

As shown in Table 1, the 2 observers had a significant agreement according to the  $\kappa$  statistic. The use of the MATLAB and MAR software programs improved the sensitivity and specificity of the detection of VREs. Cranex 3D with the MATLAB software yielded the highest sensitivity (85%) and specificity (80%), whereas ProMax 3D showed the lowest sensitivity (48%) and specificity (51%) (Table 2). According to the  $\chi^2$  test, the difference between NewTom 3G and NewTom 3G (MATLAB) was not significant ( $p = 0.119$ ). No significant differences were noted between ProMax 3D and ProMax 3D (MATLAB) ( $p = 0.455$ ), ProMax 3D and ProMax 3D (MAR) ( $p = 0.980$ ), or Cranex 3D and Cranex 3D (MAR) ( $p = 0.060$ ). However, the difference between Cranex 3D and Cranex 3D (MATLAB) was significant ( $p = 0.039$ ) (Table 3).

The independent  $t$ -test was used to assess the effect of the tooth position on the detection of VREs. It was also applied to compare the mean area under the curve (AUC) in the anterior and posterior teeth, which showed no significant difference ( $p = 0.137$ ) (Table 4).

Table 1. Inter-observer agreement for different cone-beam computer tomography (CBCT) systems determined by calculating the Cohen's  $\kappa$  coefficient

System/Mode	Coefficient of agreement
NewTom 3G	0.910
NewTom 3G (MATLAB)	1
ProMax 3D	1
ProMax 3D (MAR)	1
ProMax 3D (MATLAB)	0.910
Cranex 3D	0.910
Cranex 3D (MAR)	1
Cranex 3D (MATLAB)	1

MAR – metal artifact reduction.

Table 2. Sensitivity, specificity, false positive, and false negative values for the 3 cone-beam computer tomography (CBCT) systems assessed in the study

System/Mode	Sensitivity [%]	Specificity [%]	False negative [%]	False positive [%]	mean AUC	SE (AUC)	95% CI (AUC)
NewTom 3G	65	65	34	34	0.657	0.071	(0.770–0.543)
NewTom 3D (MATLAB)	77	71	22	28	0.743	0.068	(0.846–0.639)
ProMax 3D	48	51	51	48	0.557	0.059	(0.674–0.439)
ProMax 3D (MATLAB)	71	62	28	37	0.614	0.058	(0.727–0.500)
ProMax 3D (MAR)	57	60	42	40	0.586	0.060	(0.703–0.468)
Cranex 3D	68	68	31	31	0.686	0.056	(0.795–0.576)
Cranex 3D (MATLAB)	85	80	14	20	0.829	0.045	(0.917–0.740)
Cranex 3D (MAR)	82	70	17	21	0.743	0.052	(0.844–0.641)

AUC – area under curve; SE – standard error; CI – confidence interval.

**Table 3.** Differences between the 3 cone-beam computer tomography (CBCT) systems analyzed with the  $\chi^2$  test ( $p < 0.01$ )

System/Mode	mean AUROC	SE (AUROC)	p-value
NewTom 3G	0.715	0.055	–
NewTom 3D (MATLAB)	0.824	0.058	0.119
ProMax 3D	0.616	0.056	–
ProMax 3D (MATLAB)	0.549	0.052	0.455
ProMax 3D (MAR)	0.618	0.059	0.980
Cranex 3D	0.753	0.060	–
Cranex 3D (MATLAB)	0.906	0.081	0.039*
Cranex 3D (MAR)	0.847	0.052	0.060

AUROC – area under the receiver operating characteristic (ROC) curves;

\* statistically significant.

**Table 4.** Area under the receiver operating characteristic (ROC) curves for the anterior and posterior teeth ( $p < 0.01$ )

Position of the teeth	mean AUROC	SD (AUROC)	t-test	p-value
Anterior	0.602	0.149	–1/557	0.137
Posterior	0.702	0.100		

SD – standard deviation.

## Discussion

The detection of VRFs is challenging, because false negative diagnoses lead to periodontal disease over time, whereas false positive diagnoses lead to unnecessary dental treatment.<sup>15,16</sup>

The main limitations of periapical radiography include the superimposition of anatomical structures and the poor visualization of VRFs.<sup>17,18</sup> Researchers have long been searching for modalities alternative to periapical radiography and CBCT has been introduced for this purpose.<sup>19</sup> Considering the need for further investigation on this topic as well as the fact that CBCT systems may perform differently due to the differences in their FOV, voxel size and detectors, this study compared the efficacy of 3 CBCT systems, namely NewTom 3G, ProMax 3D and Cranex 3D, with or without the artifact removal software, in the detection of VRFs. The results showed that the sensitivity values for NewTom 3G, ProMax 3D and Cranex 3D were 65%, 48% and 68%, respectively; after applying the MATLAB software, they were 77%, 71% and 85%, respectively. Also, the sensitivity values for ProMax 3D and Cranex 3D after applying the MAR algorithm were 57% and 82%, respectively. The specificity values for NewTom 3G, ProMax 3D and Cranex 3D were 65%, 51% and 68%, respectively; after applying MATLAB, they were 71%, 62% and 80%, respectively. The specificity values for ProMax 3D and Cranex 3D after applying the MAR algorithm were 60% and 70%, respectively.

The anterior/posterior position of the teeth had no effect on the diagnostic efficacy of the systems in detecting the VRFs assessed in the study.

Hekmatian et al. evaluated the effect of the presence of gutta-percha on the detection of VRFs on CBCT images and reported that the presence of gutta-percha in the canal decreased the ability to detect VRFs.<sup>20</sup> Kamburoğlu et al. reported that dark areas around gutta-percha on the CBCT images of endodontically treated mandibular premolars caused false positive results and led to misdiagnoses of root fracture.<sup>21</sup> Hassan et al. evaluated the effect of root filling materials on the detection of VRFs on CBCT images, and reported that they significantly decreased the accuracy and sensitivity of the detection of VRFs.<sup>22</sup>

The manufacturers of CBCT systems are searching for methods to enhance image quality by developing image processing tools, such as the MAR algorithms.<sup>23,24</sup> The MAR algorithm is a post-processing program which is applied during image reconstruction and has no effect on image acquisition. The MAR algorithm decreases or eliminates artifacts. This kind of software increases the contrast-to-noise ratio; it also prolongs the image reconstruction time.<sup>3,25</sup> Tofangchiha et al. evaluated the effect of the artifact reduction algorithm on the detection of VRFs on CBCT scans.<sup>26</sup> They scanned the teeth with ProMax 3D. The results showed that the sensitivity and specificity values for VRF detection without the artifact reduction algorithm were 54% and 61%, which changed to 57% and 69%, respectively, after applying the artifact reduction algorithm. In fact, applying this algorithm did not increase the sensitivity or specificity of VRF detection.<sup>26</sup> In the present study, the sensitivity and specificity values for detecting VRFs were 48% and 51% for ProMax 3D without the artifact reduction algorithm, and 57% and 60%, respectively, after applying the algorithm. This was consistent with the results reported by Tofangchiha et al.<sup>26</sup>

Vasconcelos et al. evaluated the artifacts of endodontically treated teeth on CBCT scans taken by means of different systems – Cranex 3D, Accuitomo® 170 3D, WhiteFox® 3D, and Scanora® 3D – and showed that Cranex 3D had a significantly higher prevalence of artifacts (75%).<sup>11</sup> The application of the artifact reduction algorithm did not significantly improve the results.<sup>11</sup> In the present study, the prevalence of artifacts in Cranex 3D was smaller than in the case of other systems and the diagnostic value of this system for the detection of VRFs was higher than that of other systems. The difference between our findings and those reported by Vasconcelos et al. may be due to the different CBCT systems evaluated and the very high resolution of Accuitomo 170 3D (a voxel size of 0.08 mm<sup>3</sup>) compared to Cranex 3D (a voxel size of 0.2 mm<sup>3</sup>).<sup>11</sup>

Metska et al. evaluated the detection of VRFs on CBCT scans taken with Accuitomo 170 3D and NewTom 3G, and showed that the sensitivity and specificity values were 75% and 56%, respectively, for NewTom 3G, and



100% and 80%, respectively, for Accuitomo 170.<sup>27</sup> In the present study, the sensitivity and specificity values for NewTom 3G were 65% and 65%, respectively, which was consistent with the results of the study by Metska et al.<sup>27</sup> Bechara et al. scanned the teeth using the Master<sup>®</sup> 3D and ProMax 3D CBCT systems, and the results showed that ProMax 3D without software had the highest accuracy for detecting VRFs and Master 3D with software the lowest.<sup>13</sup> The accuracy of both systems significantly decreased after applying the artifact removal software; the accuracy of ProMax 3D with and without software was higher than that of Master 3D.<sup>13</sup>

Queiroz et al. assessed the effect of the CBCT MAR algorithm for different dental materials and indicated that the application of the algorithm caused a significant reduction in the prevalence of artifacts around dental alloys, but had no significant effect on artifact reduction around gutta-percha.<sup>23</sup> In the present study, the application of the MAR algorithm did not significantly decrease the prevalence of artifacts around gutta-percha, which was in agreement with the results of previous studies.<sup>13,23</sup> The atomic numbers of the main constituents of dental amalgam – silver (Ag) and mercury (Hg) – are 47 and 80, respectively, whereas gutta-percha is composed of zinc oxide, with the atomic number of zinc being 30, and isoprene rubber, with its components of much lower atomic numbers than in the case of amalgam. As a result, the number of artifacts caused by gutta-percha is smaller than of those caused by amalgam and other dental alloys, and therefore the MAR algorithm could not detect and minimize them.<sup>23</sup>

Johari et al. evaluated the detection of VRFs in sound premolars and endodontically treated teeth using a probabilistic neural network (PNN).<sup>28</sup> The teeth were scanned with the Kodak 2200 intraoral X-ray system and the NewTom VGi CBCT system. The results showed that the use of PNN is suitable for detecting VRFs in endodontically treated teeth.<sup>28</sup> De Martin e Silva et al. evaluated the effect of using filtering software for CBCT images (i-CAT<sup>®</sup> next generation) on the detection of VRFs in teeth with metal posts.<sup>16</sup> The results revealed that the presence of gutta-percha and metal posts decreased the accuracy of VRF detection, and that applying filtering software could not enhance the detection of VRFs.<sup>16</sup>

The MATLAB software used in the present study enhanced the detection of VRFs on images taken with the Cranex 3D, ProMax 3D and NewTom 3G CBCT systems to some extent. The difference caused by the application of MATLAB was significant for Cranex 3D, but it was not significant for the other 2 CBCT systems. The differences between our results and those of previous studies may be attributed to the fact that different software programs and CBCT systems were used.

When polychromatic X-ray beams pass through an object, low-energy photons are absorbed to a greater extent than high-energy photons. This phenomenon


increases the mean energy of X-ray beams and leads to beam hardening. The low-energy X-ray beams interact with materials with high atomic numbers and cause a further hardening of the beam. An increased voltage [kVp] increases the energy and penetration depth of the X-ray beam. Thus, increasing the voltage decreases beam hardening, and consequently the number of metal artifacts.<sup>29</sup> Panjnoush et al. evaluated the effects of various exposure settings on the level of metal artifacts when using different imaging modalities and concluded that increasing the voltage decreases the number of metal artifacts.<sup>30</sup> In the present study, Cranex 3D had the highest accuracy for detecting VRFs, followed by NewTom 3G and ProMax 3D in a descending order. Considering a lower voltage of ProMax 3D (84 kVp) compared to NewTom 3G (90 kVp) and Cranex 3D (110 kVp), the prevalence of metal artifacts would be higher in ProMax 3D.


Artifacts on CBCT images are not equally distributed over FOV. The position of an object in FOV affects the amount of scatter radiation, and consequently the level of noise and image quality; placing an object in the center of FOV is important to achieve a high-quality image.<sup>31,32</sup> In the present study, the simulated dental arch was in the center of FOV, and the anterior/posterior position of the teeth in the simulated dental arch had no significant effect on the detection of VRFs.


## Conclusions


The results of this study revealed that applying the MAR algorithm had no positive effect on the detection of VRFs on CBCT images obtained with the Cranex 3D and ProMax 3D CBCT systems. The use of the MATLAB software enhanced the detection of VRFs on CBCT images generated by the Cranex 3D, ProMax 3D and NewTom 3G CBCT systems to some extent. Cranex 3D with the MATLAB software had the highest diagnostic accuracy for detecting VRFs, with sensitivity of 85% and specificity of 80%.


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# Prevalence of traumatic dental injuries in Polish 15-year-olds

## Częstość występowania pourazowych uszkodzeń zębów u polskiej młodzieży w wieku 15 lat

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### Conflict of interest

None declared

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## Abstract

**Background.** Traumatic dental injuries (TDIs) can occur at any age. They may cause health, functional, esthetic, and psychological problems, negatively affecting quality of life.

**Objectives.** The objective of this study was to assess the prevalence, causes, treatment, and risk factors of TDIs among Polish adolescents.

**Material and methods.** As part of a cross-sectional national monitoring survey concerning the oral health condition and its determinants in the Polish population, 992 15-year-olds of both sexes were examined. The subjects were the residents of the urban and rural areas of 10 from a total of 16 provinces of the country. Caries-affected teeth were assessed according to the World Health Organization (WHO) criteria, and caries prevalence and the decayed, missing or filled teeth (DMFT) index values were calculated. Traumatic dental injuries were assessed with the use of the WHO criteria, modified for retrospective evaluation. The details of clinically diagnosed TDI were supplemented by a questionnaire and an interview.

**Results.** Overall, TDIs occurred in 22.0% of the subjects, similarly often in urban and rural areas (23.0% and 20.9%, respectively;  $p = 0.439$ ), and more frequently in males than in females (26.2% and 18.2%, respectively;  $p = 0.002$ ). The most common damage was crown fracture (46.2%), followed by luxation (43.9%) and avulsion (9.9%). Among the traumatized teeth, 73.8% received crown fracture restorations, 29.6% root canal treatment, and 17.5% were splinted due to luxation or avulsion. The most common cause of TDIs were accidental falls – 96.3%, including playing sports (27.1%), the other referred to violence/fight (3.7%). Nearly 14% of the accidents took place at school. The likelihood of TDI experience in males was 1.59-fold higher than in females. Males revealed a 2.76-fold higher probability of TDI incidence during participation in sports activities. Other predictors of TDIs were a low level of education of the mother, a poor socioeconomic status and a high DMFT score.

**Conclusions.** A relatively high prevalence of TDIs in Polish 15-year-olds calls for effective planning and intervention to prevent the occurrence of the injuries and their aftereffects.

**Key words:** traumatic dental injuries, 15-year-olds, prevalence, causes, treatment

**Słowa kluczowe:** pourazowe uszkodzenia zębów, młodzież w wieku 15 lat, występowanie, przyczyny, leczenie

## Introduction

Traumatic dental injuries (TDIs) can occur at any age. Their prevalence worldwide has not been assessed thoroughly, probably due to the usage of different classification criteria. Petti et al. evaluated the world TDI frequency on the basis of papers published in the years 1996–2016 and obtained the following results: 15.2% in permanent dentition; 22.7% in primary dentition; and 18.1% in 12-year-olds.<sup>1</sup> However, age is an essential risk factor of TDIs, since a higher occurrence rate has been found in the periods of childhood and maturation.<sup>2</sup> The injuries are most frequently observed between 2 and 5 years of age. During this developmental period, children learn to walk and run, but they often fall due to insufficiently developed coordination. Along with the development of coordination, the incidence of TDIs decreases, but then increases again in the age range of 8–12 years because of sports and physical recreational activities (riding a bicycle or a scooter, skateboarding, roller-skating, activities in the playground, etc.). Traumatic dental damage in children and adolescents may lead to health, functional, esthetic, and psychological problems, negatively affecting quality of life.<sup>3</sup> Demographic evaluations indicate a more frequent occurrence of dental traumas in boys than in girls, which is explained by greater physical activity.<sup>4–11</sup>

The main causes of TDIs are accidents, such as falls or being struck, as well as sports and fights; however, as the evaluation of their occurrence is carried out mostly retrospectively, the reasons can be inaccurately remembered.<sup>8,10,11</sup> Traumatic dental injuries have been reported to happen more frequently at home than at school, and then in the playground and on the street. Norton and O'Connell showed that in children aged 9–84 months, 46.7% of accidents resulting in TDIs took place at home and 35.7% in the area around home.<sup>12</sup> The occurrence of dental injuries at home is explained by the fact that children spend a lot of time at home, where safe conditions are not always provided, especially for little children.

The teeth most commonly injured are upper incisors, mainly central, especially when malocclusion factors predisposing to the risk of injury are present (predominantly incisal overjet, anterior open bite and protrusion). Another risk factor is an incomplete coverage of upper incisors by the upper lip when the jaw is at rest.<sup>3,7,9,10,12–14</sup> The TDI predisposing factors also include a lower socioeconomic status, and the behavior and psychological problems of adolescents.<sup>13,15,16</sup>

Odoi et al. examining 7–15-year-old children from the UK showed a 3.14-fold increase in the risk of dental injuries in the case of children who had problems with peer relations, whereas prosocial behavior proved to have a protective effect.<sup>16</sup> However, they did not reveal any relationship between hyperactivity behaviors and dental injuries.<sup>16</sup>

Surveys assessing the prevalence of traumatized teeth are important, because epidemiological data provides a basis for evaluating the problem, the treatment needs and the treatment effectiveness, as well as for planning preventive measures.

The aim of the study was to determine the occurrence and causes of TDIs, the treatment applied among Polish adolescents as well as the contributing factors for TDIs.

## Material and methods

This cross-sectional study was carried out in 2018 as part of a national monitoring survey concerning the oral health condition and its determinants in the Polish population.<sup>17</sup> The subjects were selected through a 3-stage cluster sampling procedure; 10 out of all 16 provinces of Poland, and then some administrative divisions of the 2<sup>nd</sup> (counties) and 3<sup>rd</sup> level (communes that are classified as urban and rural) were randomly selected. Then, 46 lower secondary schools were randomly chosen. Data on the total number of 15-year-olds in the country was derived from Statistics Poland (Demographic Yearbook of Poland 2017). The size of the sample under study was calculated based on the literature data concerning caries prevalence in this age group in Poland (about 90% of caries-affected subjects)<sup>18,19</sup> and the prevalence of TDIs (about 20% of subjects).<sup>20,21</sup> With such assumptions together with a 95% level of confidence and  $\pm 4\%$  error tolerance, approx. 600 participants represented a minimum sample size for caries assessment and 385 for TDI assessment.<sup>22</sup> Therefore, the number of 992 subjects included in the study covered these figures. Participation in the survey was voluntary. Parents were informed about the purpose of the study by means of a leaflet and asked for their children's participation. The inclusion criteria were as follows: adolescents attending lower secondary school; those who were 15 years old, not exceeding the age of 16; present at the time of conducting the survey; subjected to the oral examination; with the written consent of the parent; and with a fully answered questionnaire. The exclusion criteria were the following: lack of consent from lower secondary school authorities; adolescents younger than 15 or older than 16 years; uncooperative or absent adolescents on the day of the examination; no written consent from the parent; and an incomplete questionnaire.

The dental examination was performed with the use of artificial light, a plane mirror and a ball-ended dental probe – the World Health Organization (WHO) community periodontal index (CPI) probe. Caries-affected teeth were assessed according to the WHO criteria, and caries prevalence and the decayed, missing or filled teeth (DMFT) index values were calculated.<sup>23</sup> Traumatic dental injuries were assessed based on the WHO criteria, which were modified for retrospective evaluation. The following criteria were used: crown fracture, including enamel

or enamel and dentine fracture; luxation; avulsion; a missing tooth due to trauma, and treatment type (the restoration of crown fracture, root canal treatment or splinting). The clinical features of post-traumatic tooth injury were confronted with the questionnaire data and confirmed during an interview. The assessment of the dental condition was carried out by 12 teams; each consisted of 2 examiners who were pediatric dentists. The examiners were calibrated before the survey. Each examiner was asked to examine the same group of 14 patients and their findings were compared with those of an experienced supervisor. The questionnaire comprised the demographic and social background (gender, age, residence area, the mother's education, and the material status of the family) as well as data concerning TDI (experience of dental injury, cause, place, and type of treatment).

The study was approved by the Bioethics Committee of the Medical University of Warsaw, Poland (KB 185/2018).

## Statistical analysis

The obtained data was analyzed using descriptive statistics, the  $\chi^2$  test, the Mann–Whitney *U*-test, and the bivariate logistic regression analysis at a significance level of  $p < 0.05$ . The analyses were conducted with the use of the Statistica, v. 10 software (StatSoft Polska Sp. z o.o., Cracow, Poland).

## Results

Participation in the survey was voluntary. Approval from the chosen 46 lower secondary schools was obtained, 23 in urban and 23 in rural areas. Finally, 992 subjects were included in the study, out of which 51.8% were from urban and 48.2% from rural areas, and 47.4% of them were males (Fig. 1).

Most of the youth had mothers with a secondary level of education ( $n = 307$ ; 30.9%), and an average material status of the family ( $n = 543$ ; 54.7%) (Table 1). The subjects did not differ in caries prevalence and severity regarding the place of residence and gender, except for a higher DMFT score in rural area residents compared to urban areas (Table 2).

The intra-examiner reliability of the dental examination was 0.80 and the inter-examiner reliability was 0.97 (Cohen's  $\kappa$  coefficient).

Overall, TDIs affected 22.0% of the subjects, more males than females (26.2% and 18.2%, respectively;  $p = 0.002$ ), and similarly often the residents of urban and rural areas (23.0% and 20.9%, respectively;  $p = 0.439$ ). Five of the affected subjects (2.3%) had 2 teeth injured; the rest had only a single-tooth injury. The trauma-affected teeth were upper incisors. The overwhelming majority of TDI causes were accidental falls – 96.3%, including playing sports (27.1%); the other cause was violence/fight (3.7%).

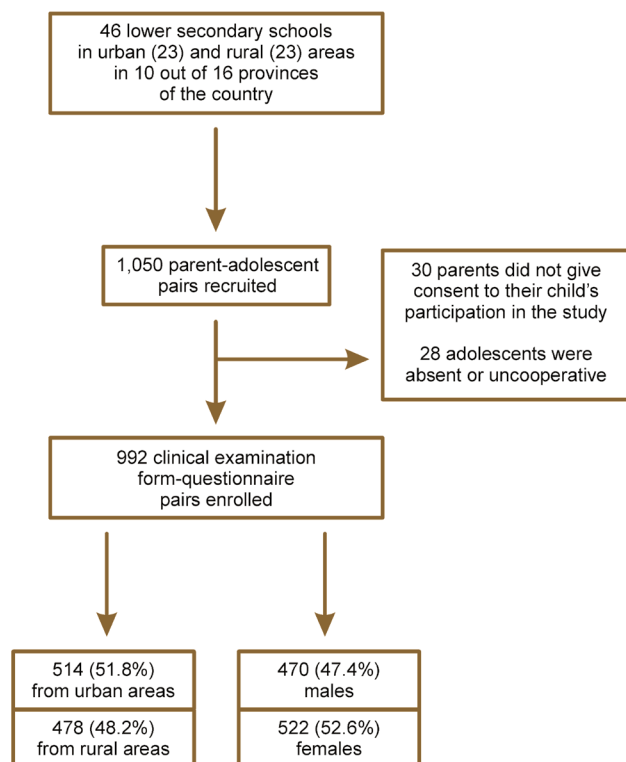


Fig. 1. Flow of participants

Table 1. Sociodemographic characteristics of the subjects

Sociodemographic parameters	n (%)
Residence area	
urban	514 (51.8)
rural	478 (48.2)
Gender	
male	470 (47.4)
female	522 (52.6)
Mother's education level	
primary	24 (2.4)
vocational	202 (20.4)
secondary	307 (30.9)
higher	290 (29.2)
no data	169 (17.1)
Material status of the family	
under average	16 (1.6)
average	543 (54.7)
above average	237 (23.9)
no data	196 (19.8)

Table 2. Caries experience of the subjects

Subjects	Caries prevalence n/N (%)	<i>p</i> -value	DMFT index score mean $\pm$ SD	<i>p</i> -value
All subjects	845/992 (85.2)	–	4.88 $\pm$ 3.84	–
Urban area residents	435/514 (84.6)	0.613	4.63 $\pm$ 3.58	0.034*
Rural area residents	410/478 (85.8)		5.15 $\pm$ 4.08	
Males	395/470 (84.0)	0.339	4.68 $\pm$ 3.95	0.123
Females	450/522 (86.2)		5.06 $\pm$ 3.92	

DMFT – decayed, missing or filled teeth;  
SD – standard deviation; \* statistically significant ( $p < 0.05$ ).

The percentage of teeth traumatized during practicing sports was 1.8-fold higher in males than in females (33.9% and 18.5%, respectively;  $p = 0.013$ ). Approximately 14% of TDI accidents took place at school. The most common type of dental damage was crown fracture (46.2%), followed by luxation (43.9%) and avulsion (9.9%). Regarding the treatment of the injured teeth, we found more fractured dental crowns that were restored in males than in females (82.1% and 63.8%, respectively;  $p = 0.035$ ). Similarly, males revealed more splinted teeth compared to females (23.5% and 9.6%, respectively;  $p = 0.007$ ). On the contrary, the number of traumatized teeth that required root canal treatment was similar in both sexes (Table 3).

The bivariate logistic regression analysis showed a 1.59-fold higher likelihood of TDI experience in males than in females (OR (odds ratio) = 1.59). Moreover, in males, an almost 3-fold higher probability of dental injury occurrence during sports activities was noticed (OR = 2.76); they also revealed a greater likelihood in terms of fractured crowns being restored (OR = 1.78) or tooth stabilization (OR = 3.64). However, regardless of gender, living in an urban area did not increase the risk of TDI experience. A lower educational status of the mother predicted a 2-fold higher likelihood of TDI experience in the school area. With regard to the material status of the family, the probability of TDIs due to violence among the adolescents

Table 3. Prevalence of traumatic dental injuries (TDIs)

Parameter	Males n/N (%)	Females n/N (%)	Urban area residents n/N (%)	Rural area residents n/N (%)	Total n/N (%)
Frequency of TDIs	123/470 (26.2)	95/522 (18.2)	118/514 (23.0)	100/478 (20.9)	218/992 (22.0)
<i>p</i> -value	0.002*		0.439		–
Number of injured teeth (n)	124	99	121	102	223
<b>Type of injury vs number of injured teeth</b>					
Crown fracture	56/124 (45.2)	47/99 (47.5)	58/121 (47.9)	45/102 (44.1)	103/223 (46.2)
<i>p</i> -value	0.134		0.335		–
Luxation	54/124 (43.5)	44/99 (44.4)	50/121 (41.3)	48/102 (47.1)	98/223 (43.9)
<i>p</i> -value	0.107		0.869		–
Avulsion	14/124 (11.3)	8/99 (8.1)	13/121 (10.8)	9/102 (8.8)	22/223 (9.9)
<i>p</i> -value	0.123		0.490		–
<b>Type of treatment</b>					
Dental crown restoration vs crown-fractured teeth	46/56 (82.1)	30/47 (63.8)	43/58 (74.1)	33/45 (73.3)	76/103 (73.8)
<i>p</i> -value	0.035*		0.927		–
Root canal treatment vs crown-fractured, luxated and avulsed teeth	36/124 (29.0)	30/99 (30.3)	36/121 (29.8)	30/102 (29.4)	66/223 (29.6)
<i>p</i> -value	0.713		0.935		–
Splinted teeth vs luxated and avulsed teeth	16/68 (23.5)	5/52 (9.6)	12/63 (19.0)	9/57 (15.8)	21/120 (17.5)
<i>p</i> -value	0.007*		0.622		–
<b>Cause and place of TDIs</b>					
Accidental dental injury	118/123 (95.9)	92/95 (96.8)	112/118 (94.9)	98/100 (98.0)	210/218 (96.3)
<i>p</i> -value	0.724		0.227		–
Violence	5/123 (4.1)	3/95 (3.2)	6/118 (5.1)	2/100 (2.0)	8/218 (3.7)
<i>p</i> -value	0.724		0.227		–
Playing sports vs accidental dental injury	40/118 (33.9)	17/92 (18.5)	34/112 (30.4)	23/98 (23.5)	57/210 (27.1)
<i>p</i> -value	0.013*		0.262		–
School area	19/123 (15.4)	11/95 (11.6)	18/118 (15.3)	12/100 (12.0)	30/218 (13.8)
<i>p</i> -value	0.411		0.487		–

\* statistically significant ( $p < 0.05$ ).

Table 4. Results of the bivariate logistic regression analysis

Variables	TDI experience	Cause			School	Treatment type		
		accident	violence	playing sports		crown restoration	root canal treatment	stabilization
Male gender	OR = 1.59 (1.18–2.16) <i>p</i> < 0.010**	OR = 1.20 (0.80–1.80) <i>p</i> = 0.380	OR = 1.86 (0.44–7.82) <i>p</i> = 0.389	OR = 2.76 (1.54–4.94) <i>p</i> < 0.010**	OR = 1.96 (0.92–4.16) <i>p</i> = 0.075	OR = 1.78 (1.10–2.87) <i>p</i> = 0.017*	OR = 1.36 (0.82–2.25) <i>p</i> = 0.228	OR = 3.64 (1.32–10.03) <i>p</i> = 0.006**
Urban area	OR = 1.13 (0.83–1.52) <i>p</i> = 0.439	OR = 0.98 (0.66–1.47) <i>p</i> = 0.933	OR = 1.81 (0.57–13.96) <i>p</i> = 0.177	OR = 1.40 (0.81–2.42) <i>p</i> = 0.221	OR = 1.41 (0.67–2.96) <i>p</i> = 0.360	OR = 1.23 (0.77–1.97) <i>p</i> = 0.382	OR = 1.12 (0.68–1.86) <i>p</i> = 0.646	OR = 1.25 (0.52–2.98) <i>p</i> = 0.621
Mother's lower education level	OR = 0.86 (0.71–1.05) <i>p</i> = 0.142	OR = 0.93 (0.71–1.20) <i>p</i> = 0.571	OR = 1.16 (0.46–2.93) <i>p</i> = 0.753	OR = 1.09 (0.77–1.55) <i>p</i> = 0.630	OR = 2.04 (1.18–3.51) <i>p</i> = 0.007**	OR = 0.97 (0.72–1.32) <i>p</i> = 0.869	OR = 0.84 (0.61–1.15) <i>p</i> = 0.273	OR = 0.86 (0.49–1.50) <i>p</i> = 0.599
Poorer material status of the family	OR = 1.07 (0.77–1.49) <i>p</i> = 0.681	OR = 0.98 (0.63–1.53) <i>p</i> = 0.929	OR = 5.34 (1.28–22.27) <i>p</i> = 0.019*	OR = 1.70 (0.98–2.94) <i>p</i> = 0.065	OR = 1.44 (0.68–3.08) <i>p</i> = 0.353	OR = 1.31 (0.80–2.16) <i>p</i> = 0.290	OR = 1.02 (0.59–1.77) <i>p</i> = 0.934	OR = 1.66 (0.69–4.03) <i>p</i> = 0.272
Higher DMFT score	OR = 1.08 (1.04–1.12) <i>p</i> < 0.001***	OR = 1.04 (0.99–1.09) <i>p</i> = 0.147	OR = 1.04 (0.88–1.24) <i>p</i> = 0.652	OR = 1.07 (1.00–1.14) <i>p</i> = 0.061	OR = 1.04 (0.95–1.14) <i>p</i> = 0.429	OR = 0.99 (0.94–1.06) <i>p</i> = 0.853	OR = 1.15 (1.08–1.22) <i>p</i> < 0.001***	OR = 1.09 (0.98–1.21) <i>p</i> = 0.112

Data in brackets presents 95% confidence interval (CI). OR – odds ratio; statistical significance: \* *p* < 0.05, \*\* *p* < 0.01, \*\*\* *p* < 0.001.

living in poor material conditions increased over 5-fold (OR = 5.34). Moreover, in the subjects with a higher caries severity, expressed as DMFT scores, TDI occurrence was greater (OR = 1.08) as well as the probability of necessary root canal treatment of the trauma-affected teeth (OR = 1.15) (Table 4).

## Discussion

This first cross-sectional national survey was carried out to determine the occurrence and causes of TDIs, their treatment, and contributing factors among Polish 15-year-olds. The findings showed that TDIs constituted a burden in this age group of the population, involving 22.0% of adolescents.

Epidemiological data concerning the incidence rate of TDIs in adolescents is diverse and difficult to compare due to the differences in social and cultural backgrounds between populations, the number of subjects examined, the age range, the assessment methods, and the data analysis. The retrospective evaluation presented in this study was based on the clinical examination, questionnaire data and an interview with the subject.

Reddy et al. studied patients aged 3–18 years who reported for treatment to a dental department within 6 years. They found the highest frequency of TDIs in 10–12-year-olds and the lowest in 3–6-year-old children.<sup>8</sup> Drosio-Bartosiak et al. analyzed patients aged 6–18 years undergoing dental treatment in a dental department in a period of 3 years and found that for 6.57% of them, the cause of the dental visit was traumatic tooth damage.<sup>24</sup> Bilder et al. reported a 10.4% prevalence of TDIs in 12–15-year-olds from Georgia.<sup>14</sup> Pattussi et al., studying 14–15-year-olds living in Brazil, found that the incidence rate of TDIs was 18.5% in boys and 13.5%

in girls.<sup>15</sup> Juneja et al., examining 8–15-year-old children from India, showed the greatest occurrence of traumatic tooth damage at the age of 15, which was 13.4%, with boys accounting for 17.0% (44/258) and girls for 8.6% (17/197) of the subjects.<sup>4</sup> The frequency of TDIs in the youth at the age of 16–18 years from urban areas in Albania was 8.9% and 10.5%, respectively.<sup>25</sup> In turn, a 10-year-period retrospective analysis of the dental records of patients from Brazil aged 6–63 years showed the highest incidence of TDIs at the age of 13–19.<sup>26</sup>

Therefore, our results in comparison with the above-mentioned data point to a more frequent occurrence of TDIs in Polish 15-year-olds (22.0%). They confirm a significantly higher prevalence of TDIs in males than in females (26.2% vs 18.2%), with the males-to-females OR over 1.5, which is in line with the previously published papers.<sup>4–7,15</sup>

Among the diagnosed traumatic injuries, crown fracture prevailed over luxation and avulsion, which is consistent with the results obtained in 12–15-year-olds and 3–18-year-olds from India,<sup>7,8</sup> and in 13–19-year-olds from Brazil.<sup>26</sup>

In contrast to the study carried out in Georgia, we did not find a higher prevalence of TDIs in rural areas compared to urban areas.<sup>14</sup> However, like Pattussi et al., we observed a lower occurrence of TDIs in adolescents from families with a higher than average material status.<sup>15</sup> Moreover, we found a 2-fold higher probability of TDI occurrence among subjects whose mothers represented a low education level, contrary to the results obtained in 12-year-old children from Brazil.<sup>9</sup>

Our data, similarly to other studies, showed that playing sports did not constitute the most frequent cause of traumatic tooth damage as opposed to other accidental falls.<sup>4,6–8</sup> However, we observed that in male students, sports activity increased approx. 3-fold the probability



of TDI occurrence. In the case of 13.8% of adolescents, TDI experience occurred on school grounds. However, an earlier study of Polish children and adolescents aged 6–18 years showed some more frequent occurrence of traumatic injuries at school than at home (14.96% vs 10.24%).<sup>24</sup> In turn, adolescents from India revealed more traumatized teeth at home than at school (58.4% vs 20.8%).<sup>7</sup>

An interesting observation resulting from our study was that the subjects with a higher DMFT score presented a significantly higher likelihood of TDI experience and a necessity of root canal treatment of the injured teeth. This could suggest that these subjects exhibit less concern about dental health in general, which is reflected in the postponed treatment of the trauma-affected teeth.

The strengths of the present survey are the recruitment of the subjects from the general population using a 3-stage cluster sampling procedure, in a sufficient number to be representative of the Polish population, and the examination of the subjects by calibrated dentists. Moreover, the obtained data is first to provide an overview of the burden of TDIs among 15-year-olds and it can be a benchmark for future comparison.


There are also some limitations: this was a retrospective study; the noticed associations could have been caused by other unexplored factors; and post-traumatic dental damage was detected visually, without taking radiographs.


## Conclusions

The data from the present epidemiological study indicated that 22% of Polish 15-year-olds experienced TDIs. A relatively high prevalence of TDIs calls for effective planning and intervention to prevent their occurrence in children and adolescents. The preventive measures should comprise the assessment of the risk of occurrence of TDIs during a routine dental examination, especially in individuals playing sports together with encouraging them to use protective appliances, and education, with the aim of increasing knowledge and awareness among children, adolescents, parents, and schoolteachers regarding the risk factors, and with the emphasis on the necessary immediate treatment of traumatized teeth.

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# Hypodontia – not only an orthodontic problem

## Hipodoncja – problem nie tylko ortodontyczny

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D – writing the article; E – critical revision of the article; F – final approval of the article

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### Abstract

**Background.** The meta-analysis of the data collected in the years 1939–1993 clearly shows an increasing incidence of hypodontia. The disorder is characterized by a congenital absence of deciduous or permanent teeth. It is a significant esthetical and functional problem, which may negatively affect the patient's psychosocial development.

**Objectives.** The aim of the study was to determine the scale of hypodontia using a sample of Polish orthodontic patients.

**Material and methods.** The orthopantomograms and medical records of 674 patients aged 6–15 years (376 girls and 298 boys) were analyzed in order to identify dental agenesis. Deciduous and wisdom teeth were excluded from the study. Data regarding gender, the location of the disorder as well as the number and type of missing buds was recorded.

**Results.** Hypodontia was found in 11.6% of the subjects (7.6% girls and 4% boys), more often in the mandible (44.9%) than in the maxilla (28.2%) or in both jaws (26.9%), and these differences were statistically significant ( $p = 0.096$ ). The occurrence rates of uni- and bilateral hypodontia were similar: 51.3% and 48.7%, respectively. The incidence of left-sided hypodontia (37.2%) significantly prevailed over right-sided hypodontia (14.1%) ( $p < 0.01$ ). Tooth 35 was the most frequently missing one (13.5%).

**Conclusions.** The large discrepancy in hypodontia prevalence indicates that geographical differences and varying sample sizes greatly affect the results of studies. The literature lacks comprehensive studies regarding hypodontia in Poland. More studies with similar sample sizes and selection criteria need to be carried out. Through an early detection of hypodontia, it is possible to plan comprehensive, interdisciplinary treatment. Regardless of the discrepancies in the literature as to the exact location of the problem, hypodontia affects over 10% of the population of patients treated orthodontically, which justifies the need to study this issue.

**Key words:** hypodontia, dental agenesis, oligodontia

**Słowa kluczowe:** hipodoncja, agenezja zębów, oligodoncja

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## Introduction

The meta-analysis of the data collected in the years 1939–1993 clearly points to an increase in the prevalence of missing teeth,<sup>1</sup> including hypodontia. This disorder, also referred to as dental agenesis, is the most common developmental irregularity affecting human teeth<sup>2</sup> and is characterized by a congenital absence of deciduous or permanent teeth. The term ‘hypodontia’ is usually used to describe the absence of 1–6 tooth buds, which distinguishes it from oligodontia – a systemic absence of tooth buds. In permanent dentition, the most commonly missing teeth (excluding third molars) are either lower second premolars or upper lateral incisors.<sup>2</sup> Hypodontia is often accompanied by microdontia, delays in tooth development, ectopic tooth positioning, taurodontism, shortened roots, or enamel hypoplasia. Having fewer teeth is a significant esthetic and functional problem, and it can severely impact one’s mental and social development.

The etiology of hypodontia involves multiple factors and is therefore complex. The patient’s genetic background is considered to be the dominant factor<sup>2–7</sup>; this is proven by the fact that hypodontia has frequently been reported in twins (more frequently in monozygotic than in dizygotic cases) and in successive generations, in the form of genetically conditioned defects (ectodermal dysplasia) or congenital defects (Down’s syndrome).

Environmental factors, such as diseases the mother suffered from during pregnancy (including viral and contagious diseases), poor nutrition, alcohol consumption, certain drugs (e.g., anticonvulsants), and past injuries, can also contribute to dental agenesis. In the postnatal period, tooth buds can be negatively affected by chemo- and radiotherapy being part of cancer treatment.<sup>2–4,6,7</sup> Regarding the absence of specific tooth buds, reports most commonly indicate the absence of second molars with simultaneous sella turcica calcification, and the absence of the second premolar and lateral incisor buds as a result of an innervation defect which occurred at the last stage of tooth bud development (neurogenic theory).<sup>2</sup>

Such a complex etiology of hypodontia requires any treatment applied to be highly specialized. Depending on the patient’s age, the location of missing teeth and any coexistent malocclusion, the patient must obtain an individualized treatment plan aimed at recreating the correct function and tooth esthetics, and at preventing complications of hypodontia, such as periodontal damage, the lack of alveolar growth or the development of malocclusion. The 2 main therapeutic options are the orthodontic closure of the space, and maintaining or recreating the space for future insertion.

In the frontal segment, the most proficient method – in terms of esthetics – is to mesialize a canine into the place of a missing lateral incisor. This method uses the patient’s own teeth to close the gap. It is also minimally invasive

and produces a relatively fast result, although it entails the need to change the shape and color of canines to make them resemble incisors. Furthermore, this method can distort canine guidance and the smile line.

The other treatment option – frontal dental implants – comes with even more issues. One must remember that the implantation procedure can be performed only after the jaw growth period is complete; until then, removable dentures or bridgeworks can be used. Furthermore, the bone surface under such dentures can disappear over time, which additionally limits the implantation possibilities.<sup>2,8</sup> The use of implants can be beneficial, but in the lateral section. Restrictions such as insufficient space and the proximity of important anatomical structures in this area should be taken into account, though.<sup>2,8</sup>

Due to its multi-factor etiology and treatment difficulties, hypodontia should not be ignored. Investigating the prevalence of hypodontia is essential in terms of early diagnosis and treatment planning; thus, it should be closely monitored, starting with the necessary basics, i.e., epidemiology.

The aim of the study was to determine the current prevalence and distribution of hypodontia in permanent dentition (excluding third molars) in Polish orthodontic patients, and to compare the results with other international studies.

## Material and methods

Initially, one clinician (Z.K.-G.) examined 2,000 patients and their orthopantomograms as they arrived at the Department of Maxillofacial Orthopedics and Orthodontics of Wroclaw Medical University, Poland, between 2014 and 2018, to identify congenitally missing teeth. All permanent teeth were investigated apart from third molars. A tooth was diagnosed as congenitally missing if the mineralization of its crown could not be recognized. If a clear diagnosis of hypodontia could not be made, the images were excluded from the study. Other exclusion criteria were developmental defects (craniofacial syndromes, or cleft lips and palates), a loss of permanent teeth caused by injury or decay, and extractions due to orthodontic indications.

The study group consisted of 674 panoramic radiographs of children and adolescents aged 6–15 years (376 girls and 298 boys). Data such as gender, the location of the disorder, and the number and type of missing teeth buds were also recorded.

The statistical analysis was carried out with the IBM SPSS Statistics for Windows software, v. 25 (IBM Corp., Armonk, USA). The package was also used to carry out the Shapiro–Wilk tests,  $\chi^2$  independence tests and Student’s *t*-tests for independent samples. The significance level was assumed to be  $p = 0.05$ , and  $0.05 < p < 0.1$  was considered statistically significant.

## Results

A total of 674 records were analyzed, including 376 girls and 298 boys. The results of the analysis of hypodontia occurrence, broken down by gender, are presented in Table 1. Hypodontia was found in 11.6% of the subjects ( $n = 78/674$ ); 7.6% were girls ( $n = 51/674$ ) and 4% were boys ( $n = 27/674$ ). The  $\chi^2$  independence analysis indicated that both variables were interrelated at the level of statistical tendency only ( $p = 0.07$ ).

At the next stage of the study, the 3 nominal variables were summarized using the frequency analysis. The absence of teeth was found more often in the lower jaw ( $n = 35/78$ ) than in the upper jaw ( $n = 22/78$ ) or simultaneously in both jaws ( $n = 21/78$ ) (Table 2). In terms of percentages compared, the difference was significant only at the level of statistical tendency ( $p = 0.096$ ).

The occurrence rates of unilateral hypodontia ( $n = 40/78$ ) and bilateral hypodontia ( $n = 38/78$ ) were similar (Table 3). The difference in the compared percentages was not statistically significant ( $p = 0.736$ ).

In the examined material, a greater number of patients were diagnosed with left-sided hypodontia ( $n = 29/78$ ) as compared to the right-sided hypodontia cases ( $n = 11/78$ ) (Table 4). The difference in the compared percentages was statistically significant ( $p = 0.010$ ).

The percentage share of particular tooth types in hypodontia is presented in Table 5. The most frequently missing tooth was 35 (13.5%). The second most frequently missing tooth was 12 (12.4%), followed by tooth 22 (11.2%), 45 (10.6%), 15 (10%), and 25 (9.4%).

**Table 1.** Statistical analysis of the prevalence of hypodontia in boys and girls

Gender	n (%)	$\chi^2$	p-value	Yule's $\phi$
Boys	27 (9.1)	3.3	0.070	0.070
Girls	51 (13.6)			

**Table 2.** Statistical analysis of the prevalence of hypodontia in the maxilla and/or the mandible

Jaw	n (%)	Percentage of valid observations [%]	$\chi^2$	p-value
Mandible	35 (5.2)	44.9	4.69	0.096
Maxilla	22 (3.3)	28.2		
Both (simultaneous occurrence)	21 (3.1)	26.9		

**Table 3.** Statistical analysis of the prevalence of hypodontia in relation to the number of sides affected

Number of sides affected	n (%)	Percentage of valid observations [%]	$\chi^2$	p-value
1 (unilateral hypodontia)	40 (5.9)	51.3	0.11	0.738
2 (bilateral hypodontia)	38 (5.6)	48.7		

**Table 4.** Statistical analysis of the prevalence of hypodontia in relation to the side affected

Side affected	n (%)	Percentage of valid observations [%]	$\chi^2$	p-value
Right	11 (1.6)	14.1	14.54	0.010
Left	29 (4.3)	37.2		
Both (simultaneous occurrence)	38 (5.6)	48.7		

**Table 5.** Percentage share of missing teeth in hypodontia

Tooth number	Number of missing tooth buds	Percentage of all missing tooth buds [%]	Percentage of individuals with hypodontia [%]
12	21	12.4	26.9
13	1	0.6	1.3
14	3	1.8	3.8
15	17	10.0	21.8
17	2	1.2	2.6
22	19	11.2	24.4
23	1	0.6	1.3
24	2	1.2	2.6
25	16	9.4	20.5
27	3	1.8	3.8
31	11	6.5	14.1
32	3	1.8	3.8
33	4	2.4	5.1
34	1	0.6	1.3
35	23	13.5	29.5
37	7	4.1	9.0
41	4	2.4	5.1
42	4	2.4	5.1
43	3	1.8	3.8
44	1	0.6	1.3
45	18	10.6	23.1
47	6	3.5	7.7
Total	170	100.0	217.9

## Discussion

The analysis of the prevalence of dental agenesis among the Hutterite population of western Canada, isolated in religious and genetic terms, brought the result of approx. 47%.<sup>9</sup> However, the findings of the contemporary literature prove that the occurrence of hypodontia varies in different populations. According to the meta-analysis carried out by Khalaf et al., the prevalence of hypodontia is 13.4% for Africa, 7% for Europe, 6.3% for Asia, 6.3% for Australia, 5% for North America, and 4.4% for Latin America and the Caribbean.<sup>10</sup> This study confirms the results of an earlier systematic review, according to which dental agenesis is less frequent in North America than in Europe or Australia.<sup>11</sup>

Our finding (11.6%) is almost twice as high as that provided by Khalaf et al., and is also higher than that reported in Italian studies (Lo Muzio et al. – 5.17%, Polastri et al. – 5.14% and Gracco et al. – 9%),<sup>12–14</sup> Turkish studies (Celikoglu et al. – 4.6% and Sisman et al. – 7.54%)<sup>15,16</sup> or in an Iranian study (Amini et al. – 5.21%).<sup>17</sup> However, it is similar to the results of an analysis of hypodontia occurrence among the Korean population (Chung et al. – 11.2%)<sup>18</sup> and is even lower than the results obtained in a study carried out on German children (Behr et al. – 12.6%),<sup>19</sup> not to mention other results found in the Polish literature, where – depending on the group analyzed – the rate of hypodontia occurrence ranged from 9.5%<sup>6</sup> to as much as 14.8%.<sup>20</sup> Such data only stresses the extent of the problem of hypodontia in Asia and Europe.

Regarding the relationship between hypodontia and gender, the majority of studies indicate a higher occurrence rate among women, as in our study.<sup>5,14</sup> In women, the phenomenon was observed 1.22 times<sup>10</sup> to 1.37 times<sup>11</sup> more often than among the male population of the same race. The more frequent occurrence of missing teeth among girls is also confirmed by a Japanese study (10.8% in girls and 8.7% in boys)<sup>21</sup> and by a Polish study held in Cracow (10.8% in girls and 7.3% in boys).<sup>6</sup> However, this may be due to the fact that women seek dental care more often than men.

Our finding that dental agenesis is statistically more frequent in the lower jaw than in the upper jaw contradicts the results of other studies, according to which missing teeth is more often diagnosed in the upper arch.<sup>5,14,22,23</sup>

When it comes to the relationship between hypodontia and the quadrant of dentition, one Italian study confirms the results of our study, indicating similar occurrence rates of unilateral and bilateral hypodontia,<sup>14</sup> whereas a Turkish study contradicts these findings, instead indicating that unilateral hypodontia is more frequent (68.7%).<sup>16</sup>

As for the occurrence of hypodontia in the left or right side, no significant differences were indicated among the Iranian population<sup>17</sup> or among the Turkish population,<sup>16</sup> which differs from our results, where left-sided hypodontia was more frequently found than right-sided hypodontia.

The literature displays a certain inconsistency concerning the most frequently missing teeth. In the European population, agenesis more often affects teeth 35 and 45, 12 and 22, and 15 and 25,<sup>10</sup> as confirmed by the results of our study. According to Mattheeuws et al., Polder et al., Lo Muzio et al., and Gracco et al., the most frequently missing tooth is the second premolar of the lower jaw.<sup>1,11,12,14</sup> In turn, Iranian, Brazilian and American studies found that the lateral incisor of the upper jaw was the most frequently missing tooth.<sup>17,22,24</sup> All of these studies point to a certain interdependence – agenesis most often affects the distal tooth from a given group.

We are aware that the present results were obtained by examining only individuals visiting the orthodontist. On the other hand, orthopantomograms are a routine

diagnostic tool for the orthodontist, because who else can make diagnosis, for example, before cross bite treatment at an early age (absolute indication), and at the same time detect tooth agenesis in the maxilla, which may accompany class III malocclusion? Therefore, as orthodontists, we feel entitled and obliged to detect hypodontia, and thus to provide objective, evidence-based results of epidemiological research on this issue.

The unification of study groups is another limitation, but it does not apply only to our research, but to all of the abovementioned. It must be remembered that the more research is conducted, the easier it is to employ retrospective criticism, and to develop the criteria for optimal material and methods for further studies.

The age of patients in the study is the last limitation. The panoramic radiographs of patients younger than 9 years old should be retaken over time to prevent the classification of late mineralized teeth as congenitally missing and to confirm a diagnosis of hypodontia.

## Conclusions


The large discrepancy in hypodontia prevalence observed in all of the above studies indicates that geographical differences as well as different sample sizes greatly affect the research results. The literature lacks comprehensive studies regarding dental agenesis among the Polish population. More studies with the same sample size and selection criteria need to be carried out in order to gain an actual view on hypodontia.

Thanks to an early detection of hypodontia, it is now possible to plan comprehensive, interdisciplinary treatment to ensure correct functioning and esthetics. Regardless of the discrepancies in the literature as to the exact location of the problem, hypodontia affects over 10% of the population of patients receiving orthodontic treatment, which justifies the need to study the issue of congenital tooth absence.

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# Evaluation of the change in the tongue posture and in the hyoid bone position after Twin Block appliance therapy in skeletal class II subjects

## Ocena zmiany położenia języka oraz kości gnykowej po leczeniu aparatem Twin Block wady szkieletowej II klasy

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A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation; D – writing the article; E – critical revision of the article; F – final approval of the article

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### Abstract

**Background.** The tongue is posteriorly postured in a retrognathic mandible, and Twin Block appliance (TBA) therapy places the tongue and the hyoid bone in a favorable position to eliminate the risk of causing respiratory obstruction.

**Objectives.** The aim of this study was to evaluate the change in the tongue posture and in the hyoid bone position after TBA therapy.

**Material and methods.** This cross-sectional study was conducted using the pre-functional (PF1), post-functional (PF2) and post-treatment (PT) cephalograms of 30 growing subjects. The tongue posture at 6 distances and the hyoid bone position with 4 parameters were digitally measured using the Rogan-Delft View Pro-X<sup>®</sup> software. A digital vernier caliper was used to determine the inter-canine and inter-molar widths on the dental casts. The Wilcoxon signed-rank test was used to compare the PF1 and PF2 values, and the PF1 and PT values.

**Results.** The comparison of the PF1 and PF2 values showed significant differences in the tongue posture at distances 1–5. In the case of the hyoid bone, only the linear distance from the sella (S) to the most anterior point on the hyoid bone (H) – the SH distance – revealed a significant difference ( $p < 0.01$ ). The change in the tongue posture and in the hyoid bone position achieved at the PF2 stage remained stable at the PT stage. Significant differences occurred in the PF1 and PF2 maxillary and mandibular inter-canine and inter-molar widths ( $p = 0.01$  and  $p = 0.04$ , and  $p < 0.01$  and  $p = 0.02$ ), respectively.

**Conclusions.** Twin Block appliance therapy resulted in the advancement of the mandible with a lowered posturing of the tongue. The hyoid bone was displaced inferiorly after TBA therapy, whereas the angular position of the hyoid bone remained unchanged.

**Key words:** malocclusion, functional appliance, hyoid bone, class II

**Słowa kluczowe:** nieprawidłowy zgryz, aparat funkcyjny, kość gnykowa, klasa II

### Cite as

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## Introduction

Skeletal dysplasia between the jaws may affect the facial esthetics, oral function, speech, and social attitude of the patient.<sup>1,2</sup> Craniofacial morphogenesis is a complex interaction between the intrinsic and extrinsic stimuli.<sup>3</sup> In the study conducted by Gul-e-Erum and Fida,<sup>4</sup> 70.5% of orthodontic patients had class II malocclusion with a common diagnostic finding of mandibular retrognathism.<sup>5</sup> It is imperative to diagnose disharmony in the stomatognathic system, reestablish the oral function and improve the overall facial appearance.

The tongue is the most active muscular structure of the oropharyngeal system and is directly influenced by any modification in the dentoskeletal environment.<sup>6</sup> After skeletal discrepancy is corrected, the tongue adapts within the altered position of the dental arches and can enhance post-functional stability if the surrounding forces are in balance.<sup>7,8</sup> The hyoid bone has no bony articulation, and is connected through muscles and ligaments to the pharynx, tongue and mandible. The anteroposterior change in the position of the mandible tends to affect the hyoid bone position, altering its functions of airway maintenance and deglutition.<sup>9</sup> A retrognathic mandible with respect to the cranial base results in a decreased distance between the cervical vertebrae and the mandibular corpus.<sup>5,10</sup> This leads to a posteriorly postured tongue and soft palate, and a reduction in the distance between the hyoid bone and the mandibular plane, which may cause hypopharyngeal obstruction.<sup>11</sup> Mandibular and maxillary retrognathism and the retroposition of the tongue are implicated in causing obstructive sleep apnea (OSA).<sup>12</sup>

Functional appliances are the treatment of choice during the pubertal growth spurt for stimulating the sagittal growth of the mandible.<sup>13</sup> They work on the basis of the viscoelastic principle by stretching muscles to position the mandible forward. The purpose of functional appliance therapy is to achieve maximal skeletal correction and to transform malocclusion into optimally stable occlusion in the neutral zone.<sup>1</sup> A multitude of evidence-based studies have described the Twin Block appliance (TBA) to be efficient in the correction of mandibular deficiency.<sup>14–16</sup> The appliance therapy improves facial esthetics, and results in the functional relocation of the tongue and of the hyoid bone.<sup>17</sup>

Ozdemir et al. reported an increase in the tongue area and in the intermaxillary space after fixed functional appliance therapy, but found no statistically significant change in the hyoid bone position.<sup>18</sup> However, a significant forward movement of the hyoid bone was reported in the study conducted by Bavbek et al.<sup>2</sup>

The tongue is a muscular organ that may be retropositioned in a deficient mandible. With the use of a functional appliance such as TBA, the tongue and hyoid bone posture can be improved, resulting in increased dimensions of the retropalatal and retroglossal airways.<sup>10</sup>

To our knowledge, few studies have reported a change in the tongue posture after functional appliance therapy, and whether the achieved results remain stable after fixed orthodontic treatment. Therefore, the prime objective of the study was to evaluate the change in the tongue posture and in the hyoid bone position after TBA therapy in subjects with a retrognathic mandible.

## Materials and methods

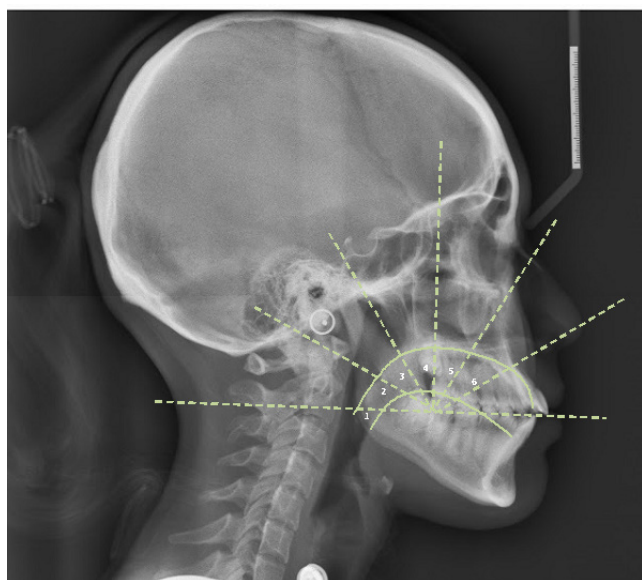
We conducted a cross-sectional study using the pre-functional (PF1), post-functional (PF2) and post-treatment (PT) cephalograms of orthodontic patients visiting our dental clinics. The data was gathered through screening the diagnostic records of patients reporting for orthodontic treatment since 2013 until 2017 after obtaining the approval from the ethical review committee (ERC No. 5430-18). The OpenEpi software ([www.openepi.com](http://www.openepi.com)) was used for the calculation of the sample size, taking into account the findings of Yassaei et al., who reported a statistically significant difference in the hyoid bone position after functional appliance therapy (31.98 ± 3.15 mm and 34.87 ± 4.25 mm in the pre- and post-treatment groups, respectively).<sup>19</sup> Keeping the power of study at the level of 80% and  $p \leq 0.05$ , we needed a total of 27 subjects. We inflated this sample by 10% to include a minimum of 30 subjects in our study. Male and female subjects were equally included to eliminate gender bias.

Subjects of Pakistani origin with skeletal class II malocclusion due to mandibular retrognathism, presented at cervical stage 3 and 4, and having standardized lateral cephalograms with clearly visible tongue and hyoid bone were included in the study. The subjects had the A point-nasion-B point angle (ANB) >4°, an overjet of 6–14 mm and were advised to undergo TBA therapy. Subjects who had the craniofacial syndrome or a systemic disease that might affect growth, or a history of trauma or surgery involving the facial structures as well as those wearing the appliance for less than 20 h were excluded. Patient cooperation and compliance were strictly monitored and documented during every visit.

The interocclusal wax bite registration for the fabrication of TBA was performed by the same clinician for all subjects and the appliances were made in the same laboratory by a trained technician. The therapy lasted for 8–9 months and was followed by fixed orthodontic treatment using a pre-adjusted appliance slot (0.022 × 0.028") in all subjects. The total duration of treatment was on average 30 months.

Lateral cephalograms were taken by trained technicians, with head fixation parallel to the horizontal plane at a film-to-tube distance of 165 cm for the standardization of radiographs. Following the protocol, the subjects were asked to bite in centric occlusion with their lips relaxed during the exposure. An Orthoralix® 9200 apparatus (Gendex-KaVo

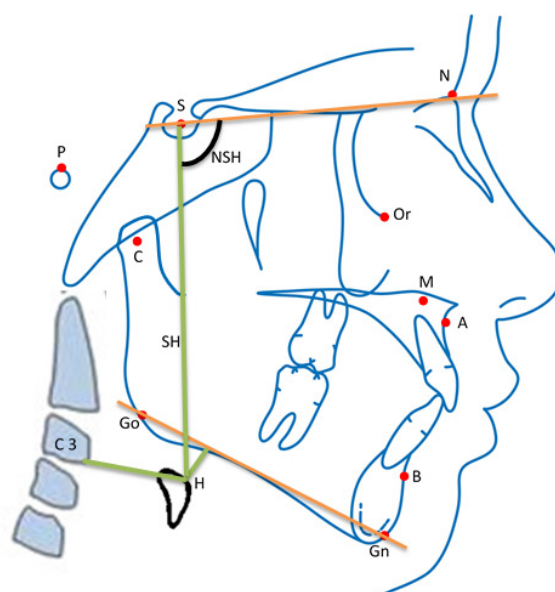
Italia, Milan, Italy) was used. Graber described a method which uses a template to evaluate the tongue posture in relation to the palate.<sup>11</sup> When the template is superimposed on a lateral cephalogram, the horizontal line should extend through the incisal edge of lower central incisor, the cervical third of the last erupted molar in the oral cavity, and its projection on the reference line between lower incisor and the distal point of molar. The contours of the dorsum of the tongue and of the bony palate were measured at 6 different angles. Six distances for each subject were recorded using the Rogan-Delft View Pro-X<sup>®</sup> software (Rogan-Delft BV, Veenendaal, the Netherlands) for precision and accuracy (Fig. 1). Distances 1 and 2 were considered as the posterior portion, distances 3 and 4 as the middle portion, and distances 5 and 6 as the anterior portion of the tongue.



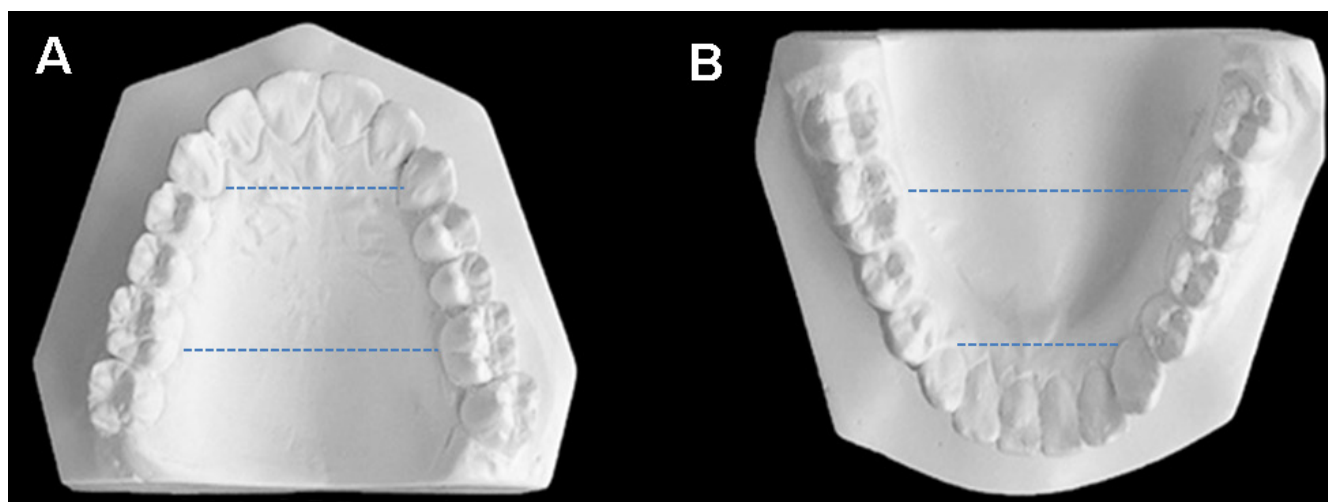
**Fig. 1.** Evaluation of the tongue posture on a lateral cephalogram  
The template was superimposed on a lateral cephalogram, and 6 distances between the dorsum of the tongue (lower green line) and the palatal contour (upper green line) were measured.

The mandibular length was measured from the gonion (Go) to the gnathion (Gn) and from the condylin (Co) to the gnathion (Gn) using the same software.<sup>20</sup> Linear and angular measurements for the hyoid bone position were also taken with the same software using the method described by Baybek et al. (Fig. 2).<sup>2</sup>

Dental casts were taken at the PF1, PF2 and PT stages. The inter-canine and inter-molar widths on the PF1 and PT dental casts were determined using a digital vernier caliper (0–150 mm ME00183; Dentaurem GmbH & Co. KG, Pforzheim, Germany) with an accuracy of 0.02 mm and a reliability of 0.01 mm, according to the manufacturer's specification (Fig. 3).



**Fig. 2.** Assessment of the hyoid bone position on a lateral cephalogram  
SH – vertical distance from the sella (S) to the most anterior point on the hyoid bone (H); C3-H – horizontal distance from H to the most anterior point of C3; NSH – angle between SH and the sella-nasion (SN) plane; H-GoGn – perpendicular distance from H to the mandibular plane (GoGn); Go – gonion; Gn – gnathion.



**Fig. 3.** Orthodontic cast analysis  
A – inter-canine and inter-molar widths of the maxillary cast; B – inter-canine and inter-molar widths of the mandibular cast.

The IBM SPSS Statistics for Windows, v. 21.0 software (IBM Corp., Armonk, USA) was used for the data analysis. Descriptive statistics were applied for the calculation of the mean age of the subjects. The Shapiro–Wilk test was applied to determine the normality of the data, which showed a non-normal distribution. The Wilcoxon signed-rank test was used to compare the PF1 and PF2 values, and the PF1 and PT values. The results were regarded statistically significant at  $p \leq 0.05$ .

The measurements on lateral cephalograms were taken by a single researcher; however, to test the intra-operator reliability, we randomly selected 30 lateral cephalograms and orthodontic casts, which were digitally re-measured using identical methodology after 3 weeks by the principal investigator. The intra-class correlation coefficient (ICC) showed a high degree of agreement, ranging from 0.85 to 0.9 between the 2 readings.

## Results

An equal number of male and female subjects was included. The mean age of the subjects was  $12.5 \pm 0.5$  years for males and  $12.3 \pm 0.7$  years for females. The comparison of the PF1 and PF2 values showed significant differences in the tongue posture at distances 1–5 and in the linear distance from the sella (S) to the most anterior point on the hyoid bone (H) – the SH distance ( $p < 0.01$ ) (Table 1). Similar results were found with regard to the PF1 and PT values, including the C3-H distance, which was also observed to be significantly different ( $p < 0.01$ ) (Table 2). A significant improvement in the overjet ( $p < 0.01$ ), ANB ( $p < 0.01$ ) and the mandibular length ( $p < 0.01$ ) was found when comparing the PT and PF1 values.

The medians and interquartile ranges (IRs) of the inter-molar and inter-canine widths of both arches at the PF1 and PT stages are presented in Table 2. Significant

differences in the maxillary inter-canine ( $p = 0.01$ ) and inter-molar ( $p < 0.01$ ) widths, and in the mandibular inter-canine ( $p = 0.04$ ) and inter-molar ( $p = 0.02$ ) widths were found in the PF1 and PT values.

## Discussion

Evidence from human and animal studies supports the claim that mandibular growth can be stimulated.<sup>21–23</sup> The goal of TBA therapy is to correct the craniofacial architecture by stimulating the growth of the jaws in a favorable direction.<sup>24</sup> The mandible is displaced anteriorly by TBA, influencing the position of the hyoid bone, and consequently the tongue posture.<sup>10</sup> Thus, the focus of this study was to evaluate the tongue posture and the hyoid bone position after TBA therapy.

The soft tissue profile improves after TBA therapy, reflecting substantial changes at the hard tissue level.<sup>25</sup> Johnston claimed that functional appliances hardly induce mandibular growth.<sup>26</sup> In contrast, the present study indicated a marked increase in the mandibular length after treatment with TBA. The skeletal change was also depicted by a decrease in the values of ANB from  $6^\circ$  to  $5^\circ$  and of the overjet from 9.5 mm to 3.0 mm, which is in close agreement to other studies.<sup>27,28</sup>

The hyoid bone acts as an anchor unit, and serves as an attachment area for several muscles of the tongue, mandible and throat.<sup>29</sup> The orthopedic outcome of TBA therapy is the displacement of the mandible and of the hyoid bone in a forward direction, leading to a beneficial effect on the posterior pharyngeal airway by the anterior traction of the tongue.<sup>28</sup> Our results showed significant changes in posture in the posterior and middle portion of the tongue after TBA therapy. However, distance 6 was maintained and it revealed a non-significant difference. In order to assess the stability of the appliance effects, the subjects were evaluated after

**Table 1.** Comparison of the pre-functional (PF1) and post-functional (PF2) values for the tongue posture and for the hyoid position

Cephalometric variables	PF1		PF2		p-value
	median	IR	median	IR	
Tongue posture					
Distance 1 [mm]	23.00	21.00–27.25	25.50	22.75–29.25	0.054*
Distance 2 [mm]	19.00	17.00–22.00	21.50	18.00–25.00	0.001**
Distance 3 [mm]	19.00	15.00–22.00	20.50	17.75–23.00	<0.001**
Distance 4 [mm]	20.00	17.00–23.25	23.00	20.75–26.00	<0.001**
Distance 5 [mm]	24.50	22.00–28.00	27.50	24.75–30.25	<0.001**
Distance 6 [mm]	35.50	33.00–38.25	36.00	33.75–37.25	0.289
Hyoid position					
SH [mm]	99.50	89.75–106.25	99.50	95.00–108.25	0.003**
C3-H [mm]	31.00	28.75–34.50	32.00	29.00–36.00	0.281
NSH [°]	92.00	89.00–97.50	91.00	88.00–98.00	0.385
H-GoGn [mm]	15.00	10.00–18.50	15.50	10.00–19.00	0.837

IR – interquartile range; \*  $p \leq 0.05$ ; \*\*  $p \leq 0.01$  (the Wilcoxon signed-rank test).

**Table 2.** Comparison of the pre-functional (PF1) and post-treatment (PT) cephalometric parameters

Cephalometric variables	PF1		PT		p-value
	median	IR	median	IR	
<b>Tongue posture</b>					
Distance 1 [mm]	23.00	21.00–27.25	30.00	26.75–32.00	<0.001**
Distance 2 [mm]	19.00	17.00–22.00	24.00	21.75–27.00	<0.001**
Distance 3 [mm]	19.00	15.00–22.00	22.00	20.00–25.00	<0.001**
Distance 4 [mm]	20.00	17.00–23.25	25.50	23.00–27.25	<0.001**
Distance 5 [mm]	24.50	22.00–28.00	29.00	26.00–30.00	<0.001**
Distance 6 [mm]	35.50	33.00–38.25	35.50	34.00–38.25	0.806
<b>Hyoid position</b>					
SH [mm]	99.50	89.75–106.25	108.00	98.00–117.25	<0.001**
C3-H [mm]	31.00	28.75–34.50	34.00	30.75–41.00	<0.001**
NSH [°]	92.00	89.00–97.50	92.50	89.75–94.25	<0.419
H-GoGn [mm]	15.00	10.00–18.50	15.00	11.00–22.00	<0.442
<b>Skeletal parameters</b>					
ANB [°]	6.00	5.00–8.00	5.00	3.00–6.00	<0.001**
Go-Gn [°]	70.00	68.00–74.50	77.00	72.00–82.50	<0.001**
Co-Gn [°]	102.00	98.00–110.75	110.00	104.75–119.50	<0.001**
<b>Dental parameters</b>					
Overjet [mm]	9.50	7.75–11.00	3.00	3.00–4.00	<0.001**
Maxillary inter-canine width [mm]	24.85	22.75–26.75	25.60	24.40–26.50	0.014**
Maxillary inter-molar width [mm]	34.55	33.37–35.92	36.95	35.77–39.00	<0.001**
Mandibular inter-canine width [mm]	21.60	20.67–23.07	21.35	19.85–21.82	0.046*
Mandibular inter-molar width [mm]	34.50	32.35–36.32	25.15	34.35–36.35	0.021*

Go-Gn – distance from Go to Gn; Co-Gn – distance from Co to Gn; \*  $p \leq 0.05$ ; \*\*  $p \leq 0.01$  (the Wilcoxon signed-rank test).

the 2<sup>nd</sup> phase of fixed orthodontic treatment. The improvement achieved by means of TBA therapy was sustained after fixed appliance treatment. The literature supports the claim that subjects with a retrognathic mandible have decreased airway dimensions.<sup>30,31</sup> A lowered posture of the tongue depicted in our study after TBA therapy minimizes the chance of collapsibility of the velopharynx; this occurs as a result of the tongue being attached to the lateral walls of the soft palate via the palatoglossal arch.<sup>32</sup> The gravitational influence of the tongue on the soft palate, though weak in nature, is also reduced by its lowered posture and, in effect, increases the airflow.<sup>32</sup> Our findings are in agreement with studies conducted by various authors who have reported an increase in the tongue area and in the intermaxillary space as a result of functional appliance therapy.<sup>18,19</sup> Liu et al. stated that the tongue dorsum is lowered after the use of mandibular anterior repositioning appliances in patients with OSA.<sup>33</sup>

There is a controversy in the literature regarding the change in the position of the hyoid bone.<sup>2,17,34</sup> Schendel and Epker and LaBanc and Epker reported that, due to compensatory action, the hyoid bone moves to its original position.<sup>35,36</sup> However, we found the vertical repositioning of the hyoid bone to be significant, whereas the change in angulation after TBA therapy was non-significant. Growth guidance may allow the mutual adaptability of form and function to the altered position of the hyoid bone.<sup>37</sup> Adaptations may

occur within the connective tissue attachments of the hyoid bone or in the belly of suprahyoid muscles.<sup>38</sup>

The transverse dimensions of the maxillary and mandibular arches were determined by measuring the inter-canine and inter-molar widths, which revealed significant differences. Active expansion during TBA therapy remains stable after fixed appliance treatment. Ozbek et al. state that the expansion of the dentoalveolar segments creates additional space for the tongue to accommodate within the oral cavity.<sup>39</sup> Improvement in the tongue posture and an increase in the nasal canal area result in better retropalatal and retroglottal airflows.<sup>40</sup>

An abnormal tongue posture is one of the causative factors for malocclusion and post-treatment relapse.<sup>6,40</sup> The normalization of the tongue posture might break the cycle of imbalanced muscular activity, thus leading to the harmonious growth patterns of the jaws and stable occlusion.<sup>29,40</sup> We speculate that this kind of intervention for treating a retrognathic mandible may help to eliminate the predisposing factors for OSA and prevent complex treatment modalities in adulthood.

It was a single-center study, which is why the results may not be extrapolated to different ethnic groups. The limitation of this cross-sectional study is that it was conducted on a group of treated patients using routine cephalograms, which provides two-dimensional (2D) information.


We recommend a prospective cohort study to compare the normal growth of the mandible, and changes in the hyoid bone position and in the tongue posture in non-treated individuals using a three-dimensional (3D) imaging modality for a comprehensive evaluation. Furthermore, there should be a long-term follow up to evaluate the changes achieved with TBA therapy and the stability of the results.

## Conclusions

This cross-sectional study demonstrated a lowered repositioning of the tongue and the inferior displacement of the hyoid bone after TBA therapy. There was improvement in the sagittal skeletal relationship due to an increased mandibular body length. The expansion achieved during TBA therapy was significant and stable after the completion of fixed appliance treatment.

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# Evaluation of the effectiveness of piezocision-assisted flapless corticotomy in the retraction of four upper incisors: A randomized controlled clinical trial

## Ocena skuteczności bezpłatowej piezokortykotomii w retrakcji czterech górnych siekaczy – randomizowane kontrolowane badanie kliniczne

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### Conflict of interest

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## Abstract

**Background.** Comprehensive orthodontic treatment may last for 20–24 months. Reducing the treatment time has become a common demand from both patients and orthodontists. Minimally invasive piezocision is one of the suggested approaches to accelerate the orthodontic tooth movement.

**Objectives.** The aim of this randomized controlled clinical trial was to assess the effectiveness of the flapless piezocision procedure in accelerating the retraction of upper incisors.

**Material and methods.** A single-blinded, parallel-group randomized controlled clinical trial was conducted at the Department of Orthodontics at the University of Damascus Dental School, Syria. The study involved 42 patients (11 males, 31 females) at the age of 16–31 years (mean age: 19.15 years). The patients had class II division I malocclusion and were treated with fixed appliances using the two-step retraction technique. With an allocation ratio of 1:1, the participants were randomly assigned to either the experimental group (n = 21) or the control group (n = 21) using a computer-generated list of random numbers. Allocation was concealed due to the use of sequentially numbered, opaque, sealed envelopes. The primary outcomes were the rate of incisor retraction (RIR) and the time required for retraction. The outcome assessor was blinded.

**Results.** The data analysis included 20 patients in each group. The rate of incisor retraction significantly increased in the experimental group by 53%, with a significant shortening of the retraction time in the experimental group by 27% ( $p < 0.001$ ). The rate of anchorage loss was significantly lesser in the experimental group ( $p < 0.001$ ). Regarding the cephalometric assessment, incisor tipping was significantly greater in the control group than in the experimental group. Skeletal measurements showed insignificant changes following retraction between the 2 groups.

**Conclusions.** The piezocision procedure was found to be effective in accelerating the retraction of 4 upper incisors, reducing the retraction time, preserving anchorage and enhancing root torque control during retraction.

**Key words:** acceleration, piezocision, incisor retraction, two-step retraction

**Słowa kluczowe:** przyspieszenie, dekortykacja przyzębia metodą Piezocision, retrakcja siekaczy, retrakcja dwuetapowa



## Introduction

The number of patients seeking improvement in dentofacial function and esthetics has increased over the past years.<sup>1</sup> The overall time of comprehensive orthodontic treatment with fixed appliances may amount to 24 months,<sup>2</sup> depending on the patient's characteristics and the complexity of malocclusion. Prolonged orthodontic treatment may lead to external root resorption, hypomineralization, dental caries, periodontal disease, pain, and discomfort.<sup>3</sup> Lengthy orthodontic treatment is considered a drawback; it is usually associated with poor patient compliance and may result in dissatisfaction.<sup>4</sup> Therefore, the acceleration of the orthodontic tooth movement has become one of the primary concerns among orthodontists worldwide. To date, several methods have been proposed to shorten the treatment time, such as the use of low-friction self-ligating brackets (SLBs), pharmacological approaches, physical stimuli, and surgical methods.<sup>5</sup> Surgical interventions have been found to be the most effective in enhancing the tooth movement and the most widely used, with predictable outcomes.<sup>6</sup>

These surgical interventions include conventional corticotomy, interseptal alveolar surgery, accelerated osteogenic orthodontics, dentoalveolar distraction, and periodontal distraction.<sup>7</sup> It has been demonstrated that surgical injury to the alveolar bone can temporarily accelerate the orthodontic tooth movement by evoking the so-called 'regional acceleratory phenomenon' (RAP), which is a physiological healing response that decreases the resistance of the alveolar bone to orthodontic forces and reduces the treatment time.<sup>8</sup>

Even though the conventional corticotomy procedures have been proven to be effective in reducing the orthodontic treatment time,<sup>9</sup> they have adverse sequelae, such as interdental bone loss, the loss of the attached gingiva, periodontal defects, and hematomas in the neck and face. These documented complications are due to the invasiveness of the traditional procedures with the need for elevating full-thickness periosteal flaps.<sup>10</sup> Consequently, several researchers have tended to investigate less invasive surgical acceleration modalities, such as laser-assisted flapless corticotomy, piezocision, corticision, and microosteoperforations.<sup>6</sup>

Piezocision has recently evolved as a novel approach of manipulating the cortical bone with minimal damage, less discomfort and greater patient acceptance,<sup>11</sup> and was first introduced by Vercellotti and Podesta.<sup>12</sup> In 2009, Dibart et al. used a piezoelectric knife to achieve flapless alveolar decortication, subsequently inducing RAP with the possibility of hard or soft tissue grafting, using selective tunneling procedures.<sup>13,14</sup> Piezocision-assisted corticotomy procedures have been investigated with several types of orthodontic tooth movement, such as resolving crowded lower anterior teeth with or without the extraction of premolars,<sup>15</sup> the retraction of maxillary canines,<sup>16</sup>

the en-masse retraction of maxillary anterior teeth,<sup>17</sup> and leveling and alignment in moderately crowded arches using SLBs.<sup>11</sup>

The camouflage treatment of class II malocclusion in non-growing patients includes the removal of upper first premolars with the subsequent retraction of upper front teeth.<sup>18</sup> There are 2 main strategies to retract the anterior teeth into the retraction space – en-masse retraction and two-step retraction. The most common technique is the sequential method, in which canines are independently retracted, followed by the retraction of 4 incisors in the 2<sup>nd</sup> stage.<sup>19</sup>

Several studies have reported speeding up canine retraction in the two-step retraction technique.<sup>16,20</sup> In the study of Alfawal et al., canines moved 1.5–2 times faster than those retracted in the conventional way, which meant a reduction of approx. 2 months or 10% with regard to the average total orthodontic treatment time.<sup>16</sup> Such a reduction is not clinically sufficient and it does not significantly decrease the overall treatment time. There is a need to accelerate incisor retraction in order to gain a considerable overall time reduction; however, this dimension has not yet been evaluated in the literature.<sup>6</sup> To the best of our knowledge, there is no randomized controlled trial (RCT) assessing the efficacy of flapless piezosurgery in the retraction of 4 upper incisors in the two-step retraction technique.

Therefore, the objectives of this trial were to investigate this treatment modality in terms of rate of incisor retraction (RIR), time required for retraction and molar anchorage loss, and to assess dental and skeletal changes following the treatment.

## Materials and methods

### Trial design and settings

This study was a two-arm, parallel-group RCT, and there were no changes regarding its published protocol following the trial commencement. This study was conducted at the Department of Orthodontics at the University of Damascus Dental School, Syria, between September 2016 and November 2017. Ethical approval was obtained from the related Local Ethics Committee of the University of Damascus Dental School (UDDS-2938-22112015/SRC-5927). This trial was registered in the Clinical Trials database with the identification number NCT03149016.

### Sample size calculation

The sample size was calculated using Minitab<sup>®</sup>, v. 17 (Minitab Inc., State College, USA) considering that the two-sample *t*-test was intended at a significance level of 0.05 and a power of 85%. It was assumed that the piezocision

intervention would decrease the overall treatment time by 40%, whereas the variability of this outcome measure in a previous study was  $9.27 \pm 2.55$  months<sup>17</sup>; therefore, the number of participants required in each group was 19. In order to compensate for sample attrition, 2 participants were added to each group with a total sample size of 42 patients.

## Participants and eligibility criteria

Recruitment was done by screening patients who had visited the Department of Orthodontics at the University of Damascus Dental School and were seeking orthodontic treatment. Out of the 109 patients who were initially examined, 42 participants were identified to be eligible for the study. The included patients were randomly assigned to 2 equal groups with a 1:1 allocation ratio: the piezocision group (PG;  $n = 21$ ), which received a surgical intervention, and the control group (CG;  $n = 21$ ), in which incisors were retracted in the conventional manner. All patients were chosen to meet the following inclusion criteria: class II division I malocclusion requiring the extraction of upper first premolars and the retraction of the upper anterior teeth; class II skeletal relationship ( $4^\circ < ANB < 10^\circ$ ); the clinical and radiological diagnosis of an average to vertical anterior facial height; an overjet not exceeding 10 mm and a normal overbite of 0–50%; well-aligned maxillary incisors with mild crowding ( $\leq 3.5$  mm); age of 15–26 years with a skeletal maturity stage of MP<sub>3U</sub> or R<sub>U</sub> depending on the hand-wrist radiograph; complete permanent dentition; no congenitally missing teeth (except for third molars); no orthodontic treatment received before; the absence of systemic disorders that could contraindicate oral surgery or affect the tooth movement; and good oral hygiene. Informed consent was obtained after a full explanation to patients and/or their parents about the purpose of the research, methods and procedures.

## Randomization, allocation concealment and blinding

Simple randomization was done by one member of the academic staff not involved in this trial, using a computer-generated list of random numbers (Minitab, v. 17). The participants were randomly assigned to either PG or CG. Allocation was concealed using sequentially numbered, opaque, sealed envelopes, which were opened only after the end of the canine retraction phase. The blinding of the principal investigator and the patients was impossible, and thus blinding was only employed in the data analysis.

## Orthodontic treatment in both groups

After setting up usual diagnostic records, orthodontic treatment in both groups was established using MBT pre-adjusted appliances with 0.022-inch slot size (American

Orthodontics, Sheboygan, USA). A soldered transpalatal arch was used to reinforce anchorage at the beginning of treatment. The teeth were leveled and aligned using the following archwire sequence: 0.014-inch NiTi (nickel-titanium); 0.016-inch NiTi; 0.016 × 0.022-inch NiTi; 0.017 × 0.025-inch NiTi; and finally 0.019 × 0.025-inch SS (stainless steel) (American Orthodontics).<sup>21</sup> After the leveling phase had been finished, upper first premolars were extracted and upper canines were retracted using elastic chains until class I canine relationship was achieved. The participants were then randomized into CG or PG. Incisor retraction was initiated by soldering 5-millimeter-long power arm hooks to the basal arch distal to the brackets of lateral incisors and NiTi closed coil springs were used to deliver a continuous force of the load of 150 g each side to retract upper incisors.<sup>22</sup> The force level was checked and measured every other week using a force gauge to keep it unchanged during the entire retraction stage. The incisors retraction stage was started by applying coil springs ( $T_0$  = start of observation) and considered complete ( $T_f$  = end of observation) when one of the 2 possible events occurred: spaces lateral to incisors were closed, or a contact between upper incisors and lower incisors or the brackets on lower incisors was observed.

## Surgical procedure in the experimental group

Piezosurgery was carried out at the Department of Oral and Maxillofacial Surgery at the University of Damascus Dental School, and was performed by an Oral and Maxillofacial Surgery (OMFS) Master's degree student (E.M.) under the supervision of an OMFS consultant (Y.M.). After rigorous rinsing with 0.12% chlorhexidine gluconate for 1 min, local infiltrative anesthesia was induced in the buccal and palatal aspects of the upper anterior segment. Using a blade size 15, vertical interproximal micro-incisions were made through the periosteum between the particular teeth, 4 mm above the interdental papillae, and extended along the middle third of the root (Fig. 1).



Fig. 1. Piezoelectric knife inserted to perform vertical incisions

A piezosurgical micro-saw was used to create buccal and palatal cortical alveolar incisions to a depth of approx. 3 mm, which was verified by a millimetric gradation on the piezosurgical knife (Fig. 2,3). The postoperative instructions given to the patients were as follows: analgesics to relieve pain (acetaminophen 500 mg tablets thrice daily (TID) for a week); antibiotics (Augmentin 1,000 mg twice daily (BID) for a week); nonsteroidal anti-inflammatory drugs (NSAIDs) were banned, as they were expected to interfere with RAP; the application of ice packs for the next 12 h; the avoidance of irritating food for 2–3 days after surgery; maintaining ideal oral hygiene; and rinsing with 0.12% chlorhexidine gluconate BID for a week.



Fig. 2. Minimally invasive incisions made on the buccal aspect to induce regional acceleratory phenomenon (RAP)

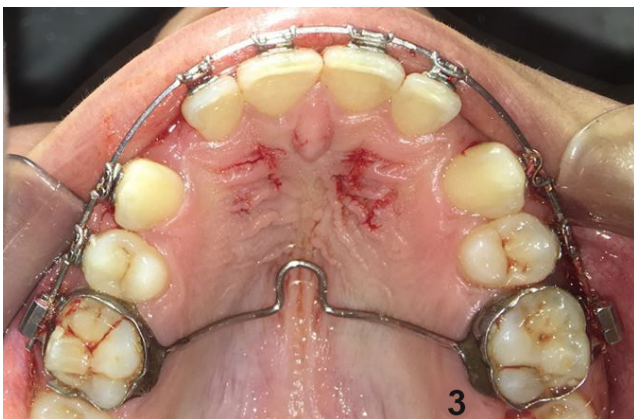


Fig. 3. Minimally invasive incisions made on the palatal aspect

### Primary outcome measures: Rate of incisor retraction and time required for retraction

The primary outcome was RIR in the 3<sup>rd</sup> week ( $T_1$ ), 6<sup>th</sup> week ( $T_2$ ), 9<sup>th</sup> week ( $T_3$ ), and 12<sup>th</sup> week ( $T_4$ ), which was calculated as the distance incisors moved each week. Maxillary alginate impressions were taken for each patient at 3-week intervals starting from the onset of retraction ( $T_0$ ) until the end of retraction ( $T_4$ ).

Using a 0.3-millimeter graphite pencil, the following landmarks were marked on the casts by the principal researcher and re-checked by the research supervisor:

the middle point of either the right or left central incisor; the medial end of the third palatal ruga as a stable landmark for assessing the anteroposterior movements of incisors and molars; and the central fossa of first molar (Fig. 4).<sup>23</sup> The standardized digital photographs of the poured study models were taken using Nikon D80 macro twin-flash 18–55-millimeter lens (Nikon, Shinagawa, Tokyo, Japan). The camera was attached to a holder specifically designed for this research project, with a model–lens distance of 30 cm, employing perpendicular projection. The models were placed against a dark background to aid visualization. A steel millimeter ruler was inserted into each image for size correction. After digitizing the marked landmarks, linear measurements were calculated on the digital photographs using the AudaxCeph<sup>®</sup>, v. 3.4.2.2710 orthodontic software (Audax d.o.o., Ljubljana, Slovenia). The displacement of the incisor segment was assessed by measuring the anteroposterior distance between the incisal edges of maxillary central incisors to the medial end of the third palatal ruga (Fig. 5). The time required for incisor retraction was recorded for both groups.

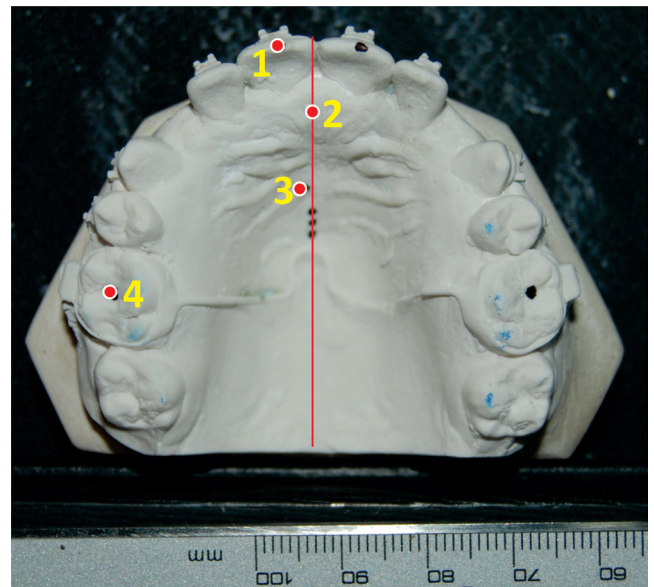


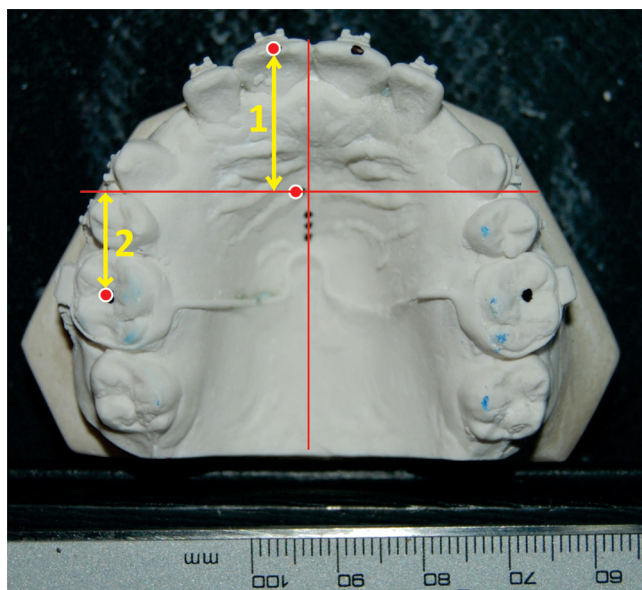
Fig. 4. Landmarks used for the plaster model analysis

1 – incisal edge of the right upper central incisor (representing all 4 incisors); 2 – mid-palatal suture line; 3 – medial end of the third palatal ruga; 4 – central fossa of the right upper first molar.

### Secondary outcomes: Molar anchorage loss and cephalometric variables

#### Molar anchorage loss

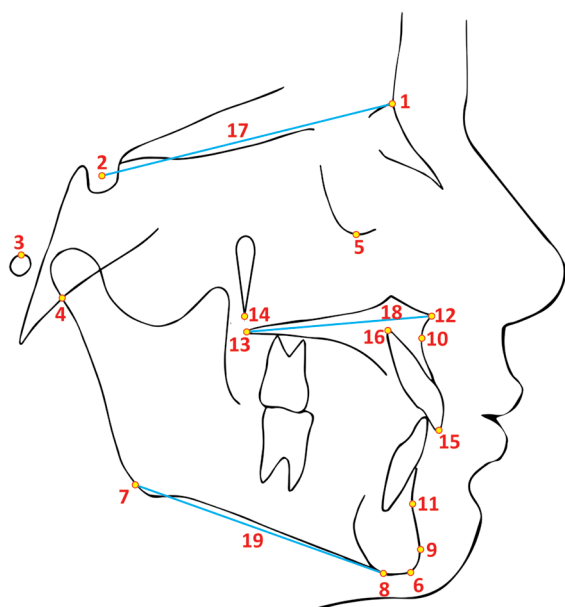
The amount and rate of the mesial displacement of upper first molar was assessed by measuring the distance from the medial end of the third palatal ruga to the central fossa of first molar on the digital photographs of the related dental casts (Fig. 5).



**Fig. 5.** Measurements made on the digitized photographs  
 1 – distance between the incisal edge of incisor and a perpendicular line on the mid-palatal suture line at the medial end of the third palatal ruga;  
 2 – distance between the central fossa of first molar and a perpendicular line on the mid-palatal suture line at the medial end of the third palatal ruga.

**Lateral cephalometric analysis**

Standardized lateral cephalometric radiographs were obtained at 2 assessment times: T<sub>0</sub> (at the beginning of incisor retraction) and T<sub>4</sub> (after the end of retraction). The rate of incisor retraction was not assessed on the lateral cephalometric



**Fig. 6.** Cephalometric landmarks and planes used in the present study  
 Cephalometric landmarks: 1 – nasion (N); 2 – sella (S); 3 – porion (Po); 4 – articulare (Ar); 5 – orbitale (Or); 6 – gnathion (Gn); 7 – gonion (Go); 8 – menton (Me); 9 – pogonion (Pog); 10 – subspinale (point A); 11 – supramentale (point B); 12 – anterior nasal spine (ANS); 13 – posterior nasal spine (PNS); 14 – pterygoid point (Pt point); 15 – upper incisor edge (UIE); 16 – upper incisor root apex (UIA). Cephalometric planes: 17 – anterior cranial base (SN); 18 – palatal plane (PP); 19 – mandibular plane (GoMe).

radiographs for ethical reasons, i.e., to avoid exposing the patients to radiation every 3 weeks. Lateral cephalometric radiographs were taken using a Planmeca cephalometer (PM 2002 EC Proline®; Planmeca, Helsinki, Finland). All subjects were positioned in the cephalostat with the path of X-rays at a right angle to the sagittal plane, the Frankfort plane parallel to the horizontal plane, the teeth in centric occlusion, and the lips relaxed. All radiographs were digitized and traced by the principal researcher. Twelve angular and 5 linear measurements were made to evaluate skeletal, dental and soft-tissue changes following the retraction of 4 upper incisors. The definitions of these variables are given in Table 1, and the cephalometric landmarks, planes and measurements are presented in Fig. 6 and 7. There were no outcome changes after the trial commencement.

**Table 1.** Definitions of angular and linear measurements used in the present study

Variable	Definition (according to Al-Sibaie and Hajeer <sup>21</sup> )
SNA	the inward angle toward the cranium between the NA line and the SN plane
SNB	the inward angle toward the cranium between the NB line and the SN plane
ANB	the angle between the NA and NB lines obtained by subtracting SNB from SNA
SN-GoMe	the angle between the anterior cranial base plane and the mandibular plane
MM	the angle between the maxillary plane and the mandibular plane
Björk sum	the sum of the N-S-Ar, S-Ar-Go and Ar-Go-Me angles
Wits appraisal	the distance between the perpendiculars from the A and B points on the occlusal plane; it determines the skeletal anteroposterior jaw relationship
FHI	facial height index = posterior facial height (S-Go) / anterior facial height (N-Me) × 100
U1-SN	the angle between the long axis of upper central incisor and the anterior cranial base plane
U1-SPP	the angle between the long axis of upper central incisor and the maxillary base plane
U1-NA angle	the angle between the long axis of upper central incisor and the NA line; it defines the degree of inclination of upper central incisor in relation to the maxilla and the nasion
U1-NA distance	the distance between the anterior point of the crown of upper central incisor and the NA line; it relates the sagittal position of upper central incisor to the maxilla and the nasion
U1-L1	the angle between the upper incisor and lower incisor axes
Nasolabial angle	the angle formed by the lines from the columella to the subnasale and from the subnasale to the upper lip
Mentolabial angle	the angle formed by the lines from the columella to the point B and from the point B to the lower lip
U.L.Esth	the distance from the upper lip to the pronasale-pogonion line (E-line of Ricketts)
L.L.Esth	the distance from the lower lip to the pronasale-pogonion line (E-line of Ricketts)

Particular symbols are explained in the description for Fig. 6.

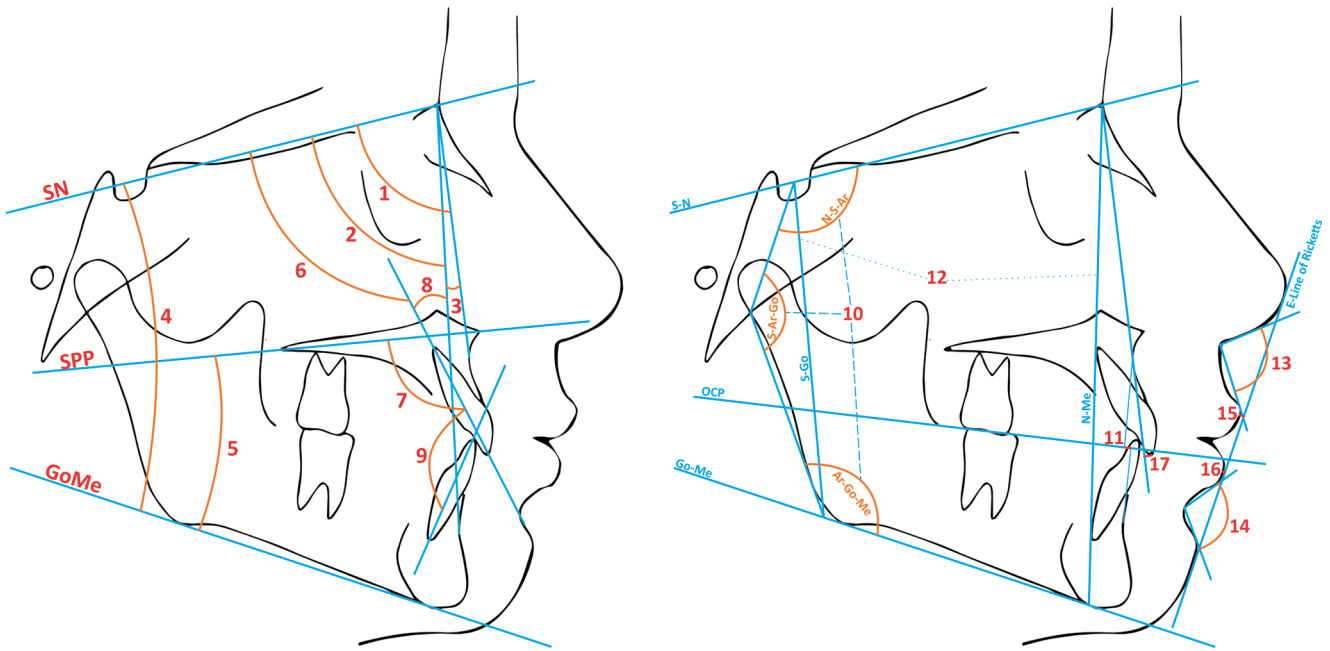


Fig. 7. Cephalometric angular and linear measurements

Cephalometric angular measurements: 1 – SNA; 2 – SNB; 3 – ANB; 4 – SN-GoMe; 5 – MM; 6 – U1-SN; 7 – U1-SPP; 8 – U1-NA angle; 9 – U1-L1; 10 – Björk sum; 11 – Wits appraisal; 12 – FHI; 13 – nasiolabial angle; 14 – mentolabial angle. Cephalometric linear measurements: 15 – upper lip-to-E-plane distance; 16 – lower lip-to-E-plane distance; 17 – U1-NA distance. OCP – occlusal plane.

### Statistical analysis

The IBM SPSS Statistics for Windows , v. 20 software (IBM Corp., Armonk, USA) was used to perform all statistical analyses. Parametric tests were used, as the data distribution was deemed normal according to the Shapiro–Wilk tests. In each group, changes that occurred between every 2 time points were calculated. The two-sample *t*-test was used to detect significant differences between the 2 groups regarding the observed changes in the primary and secondary outcomes. The level of significance was set at 0.05. The outcome data assessor was blinded to all patients’ data.

### Error of the method

To assess the reliability of measurements, 20 models and 20 cephalograms were randomly chosen and reanalyzed 1 month after initial assessment. The paired-sample *t*-tests were used to detect systematic errors, whereas intraclass correlation coefficients (ICCs) were used to evaluate the intra-examiner reliability (i.e., random error).

## Results

### Patient recruitment, follow-up, entry to data analysis, and baseline sample characteristics

Forty-two patients were enrolled in this trial and were randomly assigned to either PG or CG. One patient withdrew from CG for personal reasons and another patient

was excluded from the experimental group, because she did not follow the given oral hygiene instructions thoroughly, which caused acute post-surgical inflammation at the palatal side between upper central incisors. Therefore, the data analysis stage included 40 patients who were treated between September 2016 and November 2017. The Consolidated Standards of Reporting Trials (CONSORT) flow diagram is shown in Fig. 8.

The overall sample age ranged from 16 to 31 years (mean age: 19.15 ±3.4 years; 19.8 ±4.17 years for the intervention group and 18.5 ±2.32 years for CG). The difference in mean age between the 2 groups was insignificant (*p* = 0.231). Basic sample characteristics are given in Table 2.

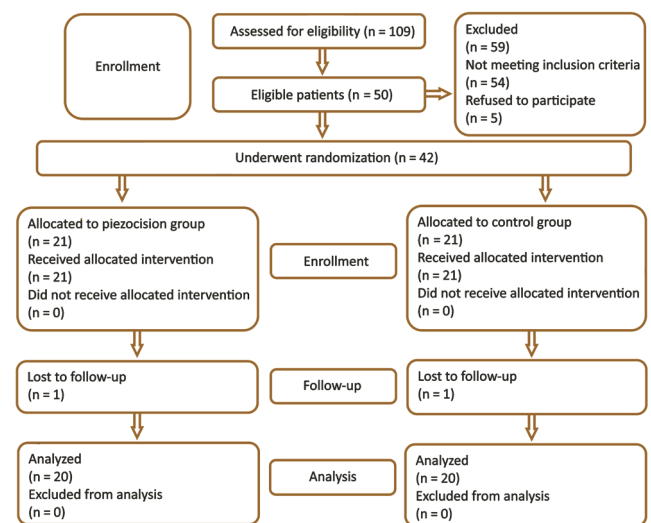


Fig. 8. Consolidated Standards of Reporting Trials (CONSORT) flow diagram of patient recruitment, inclusion and follow-up

**Table 2.** Frequency of Jemt's classification scores at baseline, and at 3, 6 and 9 months postoperatively

Group	Gender n (%)	p-value*	Age [years] mean ±SD	Max. age [years]	Min. age [years]	p-value**
CG	M: 4 (20) F: 16 (80)	1.000	18.50 ±2.32	31	16	0.231
PG	M: 5 (25) F: 15 (75)		19.80 ±4.17	23	16	
Whole sample	40 (100)		19.15 ±3.40	31	16	

CG – control group; PG – piezocision group; M – males; F – females; SD – standard deviation; \* the  $\chi^2$  test; \*\* the two-sample t-test.

## Changes in the retraction distance, the rate of incisor retraction and the time required for retraction

The mean incisor retraction distance was 6.48 ±0.51 mm and 4.21 ±0.38 mm in the experimental and control groups, respectively. In addition, the mean difference between the 2 groups regarding the palatal displacement of incisors was significant ( $p < 0.001$ ) (Table 3). Statistical significance was found between the 2 groups regarding RIR, which was greater in the experimental group (0.74 ±0.09 mm/week) compared to CG (0.35 ±0.04 mm/week) through the whole observation period ( $p < 0.001$ ) (Table 4). In the experimental group, RIR was increased by about 53% in comparison with the controls through the whole observation period. The mean difference in the retraction rate between the 2 groups through the entire 12-week assessment period was 0.39 ±0.02 mm/week.

**Table 3.** Changes in the upper incisor retraction distance (the linear distance between the medial end of the third palatal ruga and the mid-point at the incisal edge of either the right or left upper incisor) [mm] in the groups studied

Time	PG (n = 20) mean ±SD	CG (n = 20) mean ±SD	PG vs CG mean difference (95% CI)	p-value
T1–T0	-2.53 ±0.16	-1.16 ±0.23	-1.37 (-1.49, -1.23)	<0.001*
T2–T1	-2.13 ±0.12	-1.03 ±0.04	-1.11 (-1.16, -1.04)	<0.001*
T3–T2	-1.67 ±0.20	-0.99 ±0.21	-0.68 (-0.80, -0.54)	<0.001*
T4–T0	-6.48 ±0.51	-4.21 ±0.38	-2.27 (-2.56, -1.97)	<0.001*

T0 – start of observation; T1 – 3<sup>rd</sup> week; T2 – 6<sup>th</sup> week; T3 – 9<sup>th</sup> week; T4 – 12<sup>th</sup> week; CI – confidence interval; \* statistically significant (the two-sample t-test).

**Table 4.** Changes in the upper incisor retraction rate [mm/week] in the groups studied

Time	PG (n = 20) mean ±SD	CG (n = 20) mean ±SD	PG vs CG mean difference (95% CI)	p-value
T1–T0	-0.84 ±0.05	-0.39 ±0.07	-0.46 (-0.50, -0.41)	<0.001*
T2–T1	-0.71 ±0.04	-0.34 ±0.01	-0.37 (-0.39, -0.35)	<0.001*
T3–T2	-0.56 ±0.06	-0.33 ±0.07	-0.23 (-0.27, -0.18)	<0.001*
T4–T0	-0.74 ±0.09	-0.35 ±0.04	-0.39 (-0.43, -0.34)	<0.001*

\* statistically significant (the two-sample t-test).

The mean retraction time for the experimental group was 8.80 ±0.89 weeks and 11.95 ±0.68 weeks for CG. Statistical significance was observed between the 2 groups ( $p < 0.001$ ). Therefore, the upper incisor retraction time was decreased by 27%.

## Molar anchorage loss and cephalometric variables

The control group exhibited a significant increase in the mean of molar anchorage loss at all observation time points compared to the experimental group ( $p < 0.001$ ) (Table 5). Regarding the cephalometric measurements, changes that occurred in PG between T<sub>0</sub> and T<sub>4</sub> were compared to those observed in CG. The angles between upper central incisor and the anterior cranial base, the palatal plane, and the NA line showed a significant reduction in both groups ( $p < 0.001$ ), and the mean reduction was significantly greater in CG compared to PG (1.52°, 1.4° and 1.53°, respectively;  $p < 0.001$ ) (Table 6). Furthermore, a significant increase was observed in the mean inter-incisor angle in CG compared to PG (-1.11°;  $p < 0.001$ ) (Table 6). The upper and lower lips moved backward in relation to the esthetic line (E-line) of Ricketts after the end of retraction in both groups, but the movement was insignificantly greater in CG (0.41 mm and 0.33 mm, respectively;  $p > 0.05$ ) (Table 6). Regarding the skeletal assessment, the mean values of SNA, SNB and ANB insignificantly decreased in the 2 groups after the end of retraction ( $p > 0.05$ ); however, the mean difference between the 2 groups was also insignificant (-0.34°, -0.2° and -0.14°, respectively;  $p > 0.05$ ) (Table 6). All the other skeletal measurements changed insignificantly following retraction ( $p > 0.05$ ), with the differences between the 2 groups being also insignificant ( $p > 0.05$ ) (Table 6).

**Table 5.** Changes in the molar anchorage loss rate [mm/week] in the groups studied

Time	PG (n = 20) mean ±SD	CG (n = 20) mean ±SD	PG vs CG mean difference (95% CI)	p-value
T1–T0	-0.24 ±0.08	-0.39 ±0.17	0.15 (0.07, 0.24)	<0.001*
T2–T1	-0.21 ±0.07	-0.37 ±0.04	0.16 (0.11, 0.20)	<0.001*
T3–T2	-0.17 ±0.03	-0.39 ±0.05	0.22 (0.19, 0.25)	<0.001*
T4–T0	-0.22 ±0.04	-0.39 ±0.04	0.17 (0.40, 0.20)	<0.001*

\* statistically significant (the two-sample t-test).

**Table 6.** Comparison of the groups studied in terms of the cephalometric measurements

Variable	PG (n = 20) mean ±SD	CG (n = 20) mean ±SD	PG vs CG mean difference (95% CI)	p-value
SNA [°]	-0.56 ±0.58	-0.22 ±0.62	-0.34 (-0.73, 0.04)	>0.05
SNB [°]	-0.27 ±0.50	-0.06 ±0.60	-0.20 (-0.55, 0.15)	>0.05
ANB [°]	-0.29 ±0.29	-0.15 ±0.21	-0.14 (-0.31, 0.03)	>0.05
SN-GoMe [°]	-0.47 ±0.65	-0.67 ±0.41	0.20 (-0.16, 0.55)	>0.05
MM [°]	-0.39 ±1.00	-0.34 ±1.13	-0.05 (-0.73, 0.64)	>0.05
Björk sum [°]	-0.67 ±0.83	-0.63 ±0.97	-0.05 (-0.63, 0.53)	>0.05
Wits appraisal [mm]	-0.24 ±0.24	-0.45 ±0.39	0.21 (0.00, 0.42)	>0.05
FHI [mm]	-0.77 ±0.51	-0.82 ±0.63	0.05 (-0.32, 0.42)	>0.05
U1-SN [°]	-7.88 ±2.28	-9.40 ±1.39	1.52 (0.31, 2.73)	<0.001*
U1-SPP [°]	-8.08 ±2.01	-9.47 ±1.42	1.40 (0.28, 2.51)	<0.001*
U1-NA angle [°]	-6.80 ±2.38	-8.33 ±3.85	1.53 (0.13, 2.93)	<0.001*
U1-NA distance [mm]	-2.62 ±1.19	-3.23 ±1.55	0.62 (-0.27, 1.51)	>0.05
U1-L1 [°]	4.86 ±1.40	5.96 ±1.78	-1.11 (-2.14, -0.08)	<0.001*
Nasolabial angle [°]	5.91 ±2.81	5.98 ±3.41	-0.06 (-2.07, 1.94)	>0.05
Mentolabial angle [°]	8.06 ±6.60	6.69 ±4.51	1.37 (-2.25, 4.99)	>0.05
U.L.Esth [mm]	-1.52 ±0.40	-1.93 ±0.92	0.41 (-0.06, 0.87)	>0.05
L.L.Esth [mm]	-1.08 ±0.46	-1.41 ±0.59	0.33 (-0.01, 0.67)	>0.05

\* statistically significant (the two-sample t-test). The CG values were subtracted from the PG values.

## Discussion

This single-blinded, two-arm, parallel-group randomized controlled clinical trial was designed to investigate the efficacy of the piezocision technique in the retraction of 4 upper incisors using sliding mechanics. There was no significant difference between the 2 groups at  $T_0$  in the distance between the incisal edges to the third palatal ruga, which assured the similarity of the compared groups.

In order to retract incisors, NiTi closed coil springs were used, as they exert force at a constant level and maintain good oral hygiene. The 5-millimeter-long hooks enabled the adjustment of the force level so that the line of action of force could pass as much as possible through the center of resistance of upper central incisors, enabling the bodily movement of incisors during retraction. It has been demonstrated that the center of resistance during the retraction of 4 upper incisors is located within the mid-sagittal plane, approx. 6 mm apical and 4 mm posterior to the line perpendicular to the occlusal plane from the labial alveolar crest of central incisor, and 5 mm apical to the bracket position.<sup>24</sup>

The results of the current trial cannot be compared with those of other published papers, since this is the first RCT evaluating the piezocision-assisted retraction

of 4 upper incisors with sliding mechanics. In the present study, the piezocision procedure was found to be effective and shortened the overall time required for incisor retraction by 27% (approx. 4 weeks). Therefore, a 4-week time reduction in a procedure that usually takes 12–16 weeks can be considered clinically important. It has been emphasized that orthodontists would embrace a new adjunctive intervention to accelerate the orthodontic tooth movement if it shortened the treatment time by 20–40%.<sup>25</sup> Accordingly, piezocision-assisted upper incisor retraction may be an acceptable treatment modality to reduce the treatment time. Even though incisor retraction is part of overall extraction treatment, flapless piezocision can be redone to accelerate several stages of the treatment,<sup>26</sup> i.e., the canine retraction phase and the incisor retraction phase. In the current study, we looked at a specific period of the treatment sequence. We are totally aware that we evaluated a small portion of the whole scenario, but when we add the time reduction obtained in the current work with other time reductions revealed by other researchers in other portions of the treatment sequence, an overall reduction in the treatment time becomes apparent.

We found that upper incisors in the experimental group moved backward to a greater extent than those in CG (6.48 ±0.51 mm and 4.21 ±0.38 mm in PG and CG, respectively). This can be explained by the effect of piezocision surgery on reducing dense cortical bone resistance to the orthodontic tooth movement. The rate of upper incisor retraction in the experimental group during the first 3 weeks was approx. twice as big as that observed in CG (0.84 ±0.05 mm/week and 0.39 ±0.07 mm/week in PG and CG, respectively). These results indicate a 53% higher retraction rate. This mean rate slightly decreased to 52% and 41% between the 3<sup>rd</sup> and the 6<sup>th</sup> week and between the 6<sup>th</sup> and the 9<sup>th</sup> week, respectively. A recently published report on RCT conducted by Tunçer et al. addressed piezocision-assisted en-masse retraction.<sup>17</sup> The researchers reported an insignificantly higher rate of retraction in the experimental group at all time points except for day 90 (i.e., the 13<sup>th</sup> week), whereas the current trial showed a superior rate of retraction in the experimental group compared to the controls extending until the 9<sup>th</sup> week following surgery. Additionally, Tunçer et al. did not find any significant difference in the retraction speed between the 2 groups.<sup>17</sup> This can be attributed to the insufficient amount of bone injury that was performed in their study, since they restricted their incisions to the labial cortex of the alveolus with no intervention on the palatal side. In the current study, the palatal intervention was undertaken to initiate RAP at the sites where the teeth were moving forward.<sup>27</sup> Apparently, it is not logical to compare the en-masse retraction of the 6 anterior teeth with incisor retraction, as there are differences between the 2 treatment modalities, such as longer treatment time, higher anchorage requirements and a greater root surface area in the en-masse retraction technique. Besides, in the 2 techniques, different orthodontic biomechanics is employed.

Despite the conclusion of Tunçer et al. that piezocision was ineffective in accelerating the en-masse retraction of the maxillary anterior teeth,<sup>17</sup> 2 other publications reported opposite findings. Bhattacharya et al. used the so-called ‘accelerated osteogenic orthodontics’ (AOO) to enhance the en-masse retraction of the upper anterior teeth and found that the treatment time in the experimental group was approx. 45% shorter than that in the control group,<sup>28</sup> whereas Sakthi et al. assessed the corticotomy-assisted en-masse retraction of the anterior teeth in the treatment of bimaxillary protrusion and showed that the rate of space closure was significantly higher in the corticotomy group.<sup>29</sup> However, these 2 aforementioned studies are not comparable to our study due to the different number of teeth involved in the retraction technique and the invasiveness of the procedures undertaken in these 2 studies, i.e., the traditional elevation of full-thickness labial and lingual periosteal flaps.

The piezocision-assisted two-step retraction technique is expected to play an important role in our daily practice and might be superior to piezocision-assisted en-masse retraction, since it has been shown that a significant improvement in the speed of canine retraction can be achieved by minimally invasive methods,<sup>6,16</sup> and the results of the current trial show that also the time of incisor retraction can be significantly shortened when using these methods.

Regarding molar anchorage loss, CG exhibited a higher rate of molar mesial movement by about 44% compared to the experimental group in the whole observation period. It has been postulated that corticotomy procedures have the advantage of enhancing anchorage by providing the differential movement of the anchoring and non-anchoring teeth, i.e., the teeth located in the corticotomized regions tend to move more readily than those in the non-corticotomized regions.<sup>8</sup> Thus, piezocision seems to facilitate the tooth movement with lighter orthodontic forces and, therefore, reduces the load applied to the posterior anchoring teeth. These results are in agreement with previous investigations which addressed the acceleration of en-masse retraction.<sup>17,29</sup>

All skeletal measurements showed insignificant changes following the retraction of 4 upper incisors. It has been concluded that there are no significant differences in the changes in the skeletal measurements when comparing the accelerated to non-accelerated retraction of the maxillary anterior teeth.<sup>30</sup> However, in this trial, the significant post-retraction changes between CG and PG in the mean values of U1-SN, U1-SPP, U1-NA, and U1-L1 indicated that the type of movement of incisors after the end of retraction had a greater translational component in the experimental group, whereas in the controls, the type of movement was controlled tipping. This might be explained by the induced RAP effect, which may have facilitated the expression of the root torque during retraction.

There are some limitations of this study. A high percentage of female patients (77.5%) constituted this sample; therefore, inter-gender differences could not be investigated. Patient-centered outcomes, quality of life and the levels of acceptance were not evaluated in this trial. There was no post-surgical follow-up to investigate the effects of piezosurgical incisions on the labial gingivae (i.e., residual scars) as well as on the periodontal status. The blinding of the patients and the researcher was impossible; however, this could not be a source of bias, since no patient-centered self-assessed outcomes, such as the feeling of pain, discomfort or swelling, were evaluated.


One unexpected post-surgical complication in the experimental group was noticed in 1 patient who was excluded from the trial. One week after the piezocision procedure, an acute inflammatory response developed between central incisors in the midline at the palatal side. Appropriate care was provided for this patient, but a 2-millimeter recession of the interdental papilla in the midline was documented and retraction was resumed after 2 months. In the literature, there are no previous reports on periodontal complications following flapless corticotomy in the retraction of the anterior teeth.

## Conclusions


Piezocision proved to be effective in accelerating the retraction of 4 upper incisors, with the rate of retraction higher by 53% in PG compared to CG in the whole observation period. The incisor retraction period was shortened by 27% compared to the controls. The results of this study also showed a significant change in the type of incisor retraction movement, which was predominantly translational movement in PG and controlled tipping movement in CG. The rate of molar anchorage loss was significantly higher in CG compared to the corticotomy group.

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# Effects of the carbonic anhydrase VI gene polymorphisms on dental caries: A meta-analysis

## Wpływ polimorfizmów genu anhidrazy węglanowej VI na próchnicę zębów – metaanaliza

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## Abstract

**Background.** Carbonic anhydrase VI (CA VI) is considered to greatly participate in the buffering of saliva, ion transport, the regulation of pH, secretory processes, and saliva production. Various studies have been conducted to investigate the relationship between CA VI and dental caries.

**Objectives.** The goal of this study was to make a meta-analysis of studies that examined the effects of the CA VI gene polymorphisms on dental caries.

**Material and methods.** The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement guide was followed. Electronic databases (PubMed, Web of Science, Scopus, and Cochrane Library) were scanned by 2 independent researchers. The funnel plot, Egger's regression and Begg and Mazumdar's rank correlation test were used to determine publication bias. Cohen's *d* was used to measure the effect size.

**Results.** Four studies were included in the meta-analysis; a total of 3 polymorphisms (rs2274327, rs2274328, rs2274333) and a total of 13 polymorphism models were analyzed. According to Egger's regression and the Begg and Mazumdar's test, the meta-analysis had no significant publication bias ( $p > 0.05$ ). The highest susceptibility effect was noticed in the rs2274328 (AA vs CC) model ( $d = 0.18$ ; 95% CI (confidence interval):  $-1.77, 2.13$ ), but this effect was not significant ( $p = 0.237$ ), and the highest protective effect was observed in the rs2274328 (AA vs AC) model ( $d = -0.13$ , 95% CI:  $-1.36, 1.11$ ), but this effect was not significant, either ( $p = 0.195$ ). No association was found between any of the polymorphism models and dental caries ( $p > 0.05$ ).

**Conclusions.** Even though CA VI plays an important role in the buffering of saliva, it was shown that polymorphisms in the CA VI gene did not affect the process of dental caries.

**Key words:** single-nucleotide polymorphism, meta-analysis, caries susceptibility, dental caries resistance, human genome

**Słowa kluczowe:** polimorfizm pojedynczego nukleotydu, metaanaliza, podatność na próchnicę, odporność na próchnicę zębów, ludzki genom

## Introduction

Dental caries is one of the most common chronic diseases in the world and it can be affected by many factors, such as dietary habits, bacterial flora, fluoride intake, tooth position and morphological characteristics, oral hygiene, and amount and composition of saliva.<sup>1,2</sup> Although there are many environmental factors affecting dental caries, some individuals seem to be more prone to the formation of dental caries. This suggests that genetic factors, in addition to environmental factors, play an important role in the pathogenesis of dental caries.

Many genetic studies in the literature have analyzed the effects of genetic variances, such as single-nucleotide polymorphisms (SNPs), on dental caries. The studies have focused on genes encoding proteins that are related to mineralization, the immune system, taste sensation, and saliva.<sup>3–6</sup> Saliva is a complex body fluid containing essential protective components; it can regulate pH in the oral cavity due to its buffering capacity.<sup>7,8</sup> With regard to the functions of saliva, various studies have investigated the effects of gene polymorphisms related to salivary proteins, such as C-type lysozyme, beta-defensin-1, lactotransferrin, carbonic anhydrase VI (CA VI), mucin, and proline-rich proteins (PRPs).<sup>9</sup>

Carbonic anhydrase (CA) is a zinc-containing metallo-enzyme which catalyzes the reversible hydration of carbon dioxide. Especially, CA plays an important role in the regulation of pH, and in the transport of liquids and ions.<sup>10</sup> In mammals, 11 isozymes of CA have been identified. Four are cytosolic isozymes (I, II, III, and VII), 4 are membrane-bound (IV, IX, XII, and XIV), 2 are present in mitochondria (VA and VB), and 1 is a secretory isozyme (VI). Carbonic anhydrase VI is considered to greatly participate in the buffering of saliva, ion transport, the regulation of pH, secretory processes, and saliva production.

To date, according to our knowledge, there has been no meta-analysis to synthesize the effects of the *CA VI* gene polymorphisms on dental caries. This study aimed to perform a meta-analysis to synthesize the results of studies that investigated these effects.

## Material and methods

### Guidance and eligibility criteria

In this study, we abided by the guidance of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.<sup>11</sup> All studies that examined deciduous tooth caries (decayed, missing and filled teeth – DMFT) or permanent tooth caries (dmft) were included in the meta-analysis. In cases when there was no more than 1 study on a polymorphism, the relevant polymorphism was not included in the analysis. Additionally, studies that did not calculate the DMFT/dmft index as a caries index were excluded. Studies that did not present the frequencies

of genotype and phenotype polymorphisms clearly were also excluded. Studies published in English before 2019 were included. Letters to the editor, case reports, commentaries, and reviews were excluded from the meta-analysis.

### Information sources and search strategy

Electronic databases (PubMed, Web of Science, Scopus, and Cochrane Library) were scanned by 2 independent researchers. Related Medical Subject Headings (MeSH) terms and text words ('gene' OR 'genome' OR 'genetic' OR 'polymorphism' OR 'carbonic anhydrase' AND 'dental' OR 'tooth' OR 'decay' OR 'caries' OR 'saliva') were used in our search strategy. The reference list of each of the studies obtained was carefully reviewed to access subject-related studies. Additionally, recent articles citing the obtained studies were found.

### Study selection and data collection process

The titles and abstracts of the obtained studies were evaluated by 2 different researchers. The same studies retrieved from multiple databases were defined as single studies. Additionally, we contacted the authors to provide their articles in case the full-text access was not allowed. Polymorphisms investigated in no more than 1 study in the literature were excluded from the meta-analysis. Studies to be included in the meta-analysis were determined by a unanimous decision of the researchers.

### Publication bias and quality assessment

Egger's regression and Begg and Mazumdar's rank correlation test were used in assessing publication bias. The quality assessment was performed by 2 researchers based on the modified Newcastle–Ottawa Scale (NOS), employed in previous meta-analyses related to polymorphisms.<sup>12</sup> The scores on the scale range from 0 (the worst) to 10 (the best) points. In case the score of a study was  $\geq 5$ , it was accepted to have a low risk of bias, whereas if the score was  $< 5$ , it was accepted to have a high risk of bias (Table 1).

### Summary measures and the synthesis of the results

The David B. Wilson Meta-Essentials software, v. 1.2 (<http://mason.gmu.edu/~dwilsonnb/ma.html>) was used for the statistical analysis of the data. Weight calculation was performed separately for each group. Cohen's *d*-value was preferred in measuring the effect size. The DMFT/dmft caries index was used as a variable. The fixed effect model (FEM) with 95% confidence intervals (CIs) was used as the meta-analysis model. Heterogeneity was evaluated with Cochran's *Q* and *I*<sup>2</sup> test. The significance level of the effect size was determined based on the two-tailed test. In all tests, the level of significance was set at  $p < 0.05$ .

Table 1. Modified Newcastle–Ottawa Scale (NOS) for the quality assessment

Criteria	Score
<b>Representativeness of cases</b>	
Consecutive/randomly selected cases with a clearly defined sampling frame	2
Not consecutive/randomly selected cases or without a clearly defined sampling frame	1
Not described	0
<b>Source of controls</b>	
Population-based controls	2
Hospital-based controls and/or healthy controls	1
Not described	0
<b>Hardy–Weinberg equilibrium in controls</b>	
Hardy–Weinberg equilibrium	2
Hardy–Weinberg disequilibrium	1
Not available	0
<b>Genotyping examination</b>	
Genotyping done under blinded conditions and repeated again	2
Genotyping done under blinded conditions or repeated again	1
Genotyping done under unblinded conditions or not mentioned, and unrepeated	0
<b>Association assessment</b>	
Assessed the association between genotypes and caries with appropriate statistics and an adjustment for confounders	2
Assessed the association between genotypes and caries with appropriate statistics and without an adjustment for confounders	1
Inappropriate statistics used	0

## Results

### Study selection and characteristics

The literature review was performed between February 7, 2018 and May 10, 2019. The databases were scanned with the aforementioned queries and 5,112 papers were found (PubMed: 1,337; Web of Science: 1,903; Scopus: 1,826; and Cochrane Library: 46). This number was reduced to 2,372 after eliminating repetitive studies. The abstracts of the studies were examined and 2,244 studies that did not comply with the criteria were excluded. After thoroughly reviewing the full texts of the remaining 117 studies, 113 more studies that did not meet the meta-analysis criteria were excluded, and finally 4 studies were included in the meta-analysis (Fig. 1). The characteristics of the 4 studies published before 2019 are presented in Table 2.

### Publication bias and quality assessment

According to Egger's regression and Begg and Mazumdar's test, the studies had no significant bias ( $p > 0.05$ ) (Table 3). After the assessment of the modified NOS, all studies were found to have a low-risk of bias (Table 4).

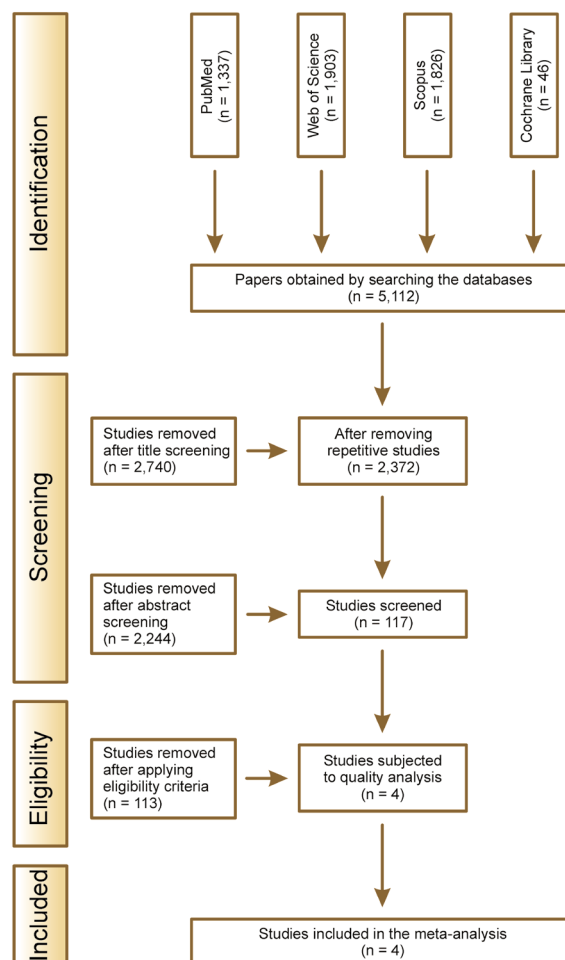


Fig. 1. Flow diagram of the studies involved in the meta-analysis

**Table 2.** Features of the studies included in the meta-analysis

No.	Study	Year	Population	Age [years]	Caries index (low; high)	Investigated genes (genetic variations)
1	Peres et al. <sup>21</sup>	2010	Brazilian 245 children	7–9	dmft/DMFT (0; ≥1)	CA6 (rs2274333, rs2274328, rs2274327)
2	Li et al. <sup>24</sup>	2015	Chinese 355 individuals	51.16 ± 9.48 (mean ± SD)	DMFT (≤2; ≥3)	CA6 (rs2274328, rs17032907, rs11576766, rs2274333, rs10864376, rs3765964, rs6680186)
3	Sengul et al. <sup>22</sup>	2016	Turkish 178 children (M = 81, F = 97)	6–16	dmft/DMFT (0; ≥1)	CA6 (rs2274327)
4	Yildiz et al. <sup>23</sup>	2016	Turkish 154 individuals	20–60	DMFT (≤5; ≥14)	CA6 (rs2274327)

M – males; F – females; SD – standard deviation; dmft/DMFT – the decayed, missing and filled teeth index, related to permanent/deciduous tooth caries.

**Table 3.** Meta-analysis model, the heterogeneity assessment and publication bias

Genetic marker (model)	Meta-analysis model	n	Q	pQ	I <sup>2</sup>	τ <sup>2</sup>	τ	EG	BG
rs2274327 (CC vs TT)	FEM	3	1.87	0.392	<0.01	<0.01	<0.01	0.341	0.059
rs2274327 (CC vs CT)	FEM	3	2.22	0.330	0.10	<0.01	0.07	0.752	0.301
rs2274327 (C vs T)	FEM	2	0.13	0.718	<0.01	<0.01	<0.01	NC	0.159
rs2274327 (CC vs CT+TT)	FEM	3	2.19	0.335	0.09	<0.01	0.06	0.567	0.301
rs2274327 (CC+CT vs TT)	FEM	3	2.37	0.306	0.16	0.01	0.10	0.543	0.301
rs2274328 (AA vs CC)	FEM	2	0.14	0.712	<0.01	<0.01	<0.01	NC	0.159
rs2274328 (AA vs AC)	FEM	2	<0.01	0.999	<0.01	<0.01	<0.01	NC	0.159
rs2274328 (AA vs AC+CC)	FEM	2	2.50	0.114	0.60	0.03	0.17	NC	0.159
rs2274328 (AA+AC vs CC)	FEM	2	0.10	0.754	<0.01	<0.01	<0.01	NC	0.159
rs2274333 (AA vs GG)	FEM	2	0.15	0.699	<0.01	<0.01	<0.01	NC	0.159
rs2274333 (AA vs AG)	FEM	2	0.45	0.500	<0.01	<0.01	<0.01	NC	0.159
rs2274333 (AA vs AG+GG)	FEM	2	0.19	0.662	<0.01	<0.01	<0.01	NC	0.159
rs2274333 (AA+AG vs GG)	FEM	2	0.42	0.519	<0.01	<0.01	<0.01	NC	0.159

FEM – fixed effect model; n – number of included studies; EG – Egger's regression (*p*-value); BG – Begg and Mazumdar's rank correlation test (*p*-value); NC – not calculated.

**Table 4.** Quality assessment of the studies with the modified Newcastle–Ottawa Scale (NOS)

No.	Study	Representativeness of cases	Source of controls	Hardy–Weinberg equilibrium in controls	Genotyping examination	Association assessment	Score
1	Peres et al. <sup>21</sup>	1	2	0	1	2	6
2	Li et al. <sup>24</sup>	1	1	2	1	2	7
3	Sengul et al. <sup>22</sup>	1	2	2	1	2	8
4	Yildiz et al. <sup>23</sup>	1	1	0	1	2	5

## Results of individual studies and the synthesis of the results

A total of 3 polymorphisms were included in the study and a total of 13 polymorphism models were analyzed. The number of studies in any analysis ranged from 2 to 3. No significant heterogeneity existed in any of the analyses ( $p_Q > 0.05$ ) (Table 3). Therefore, in all analyses, FEM was employed.

In rs2274327, the highest susceptibility effect was noted for the rs2274327 (C vs T) model ( $d = 0.08$ ; 95% CI: –1.03, 1.19) and the protective effect was observed only in the rs2274327 (CC+CT vs TT) model ( $d = -0.01$ ;

95% CI: –0.56, 0.54), but this effect was too low and non-significant ( $p = 0.944$ ). In rs2274328, the highest susceptibility effect was noticed in the rs2274328 (AA vs CC) model ( $d = 0.18$ ; 95% CI: –1.77, 2.13), but this effect was not significant ( $p = 0.237$ ), and the highest protective effect was observed in the rs2274328 (AA vs AC) model ( $d = -0.13$ ; 95% CI: –1.36, 1.11), but this effect was not significant, either ( $p = 0.195$ ). In rs2274333, all of the effects were protective and the highest protective effect was reported for the rs2274333 (AA vs AG) model ( $d = -0.10$ ; 95% CI: –1.34, 1.15), but this effect was also non-significant ( $p = 0.330$ ). No association was found between any of the polymorphism models and dental caries ( $p > 0.05$ ) (Fig. 2).

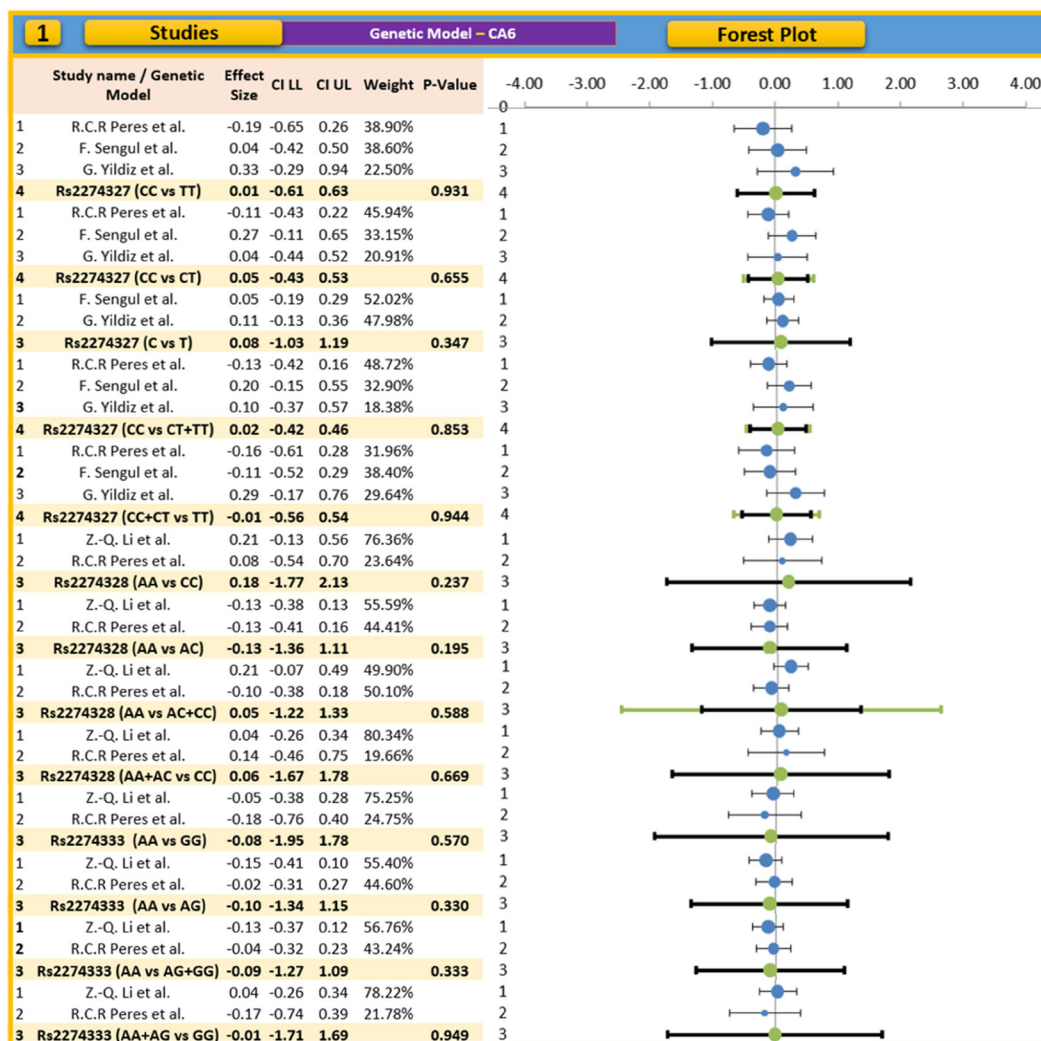


Fig. 2. Effect sizes of the polymorphisms of the carbonic anhydrase (CA VI) gene compared to the wild-type and forest plot presentation

## Discussion

Several measures of the effect size have been recommended for meta-analyses, such as Pearson’s correlation coefficient  $r$ , Cohen’s  $d$  or the odds ratio (OR). We preferred Cohen’s  $d$  in this meta-analysis. While the value of 0.00 indicates no association, (+) indicates that the related polymorphism is associated with susceptibility to dental caries and (–) indicates that the related polymorphism is associated with protection against dental caries. According to Cohen’s statistic,  $d = 0.2$  ( $OR \approx 2.3$ ),  $d = 0.5$  ( $OR \approx 8.07$ ) and  $d = 0.8$  ( $OR \approx 28.25$ ) indicate that the effect size is small, medium and large, respectively.<sup>13</sup> The value of  $p_Q < 0.05$  and high  $I^2$  values indicate that the meta-analysis has significant heterogeneity, and when heterogeneity is high in studies, the random effect model (REM) ought to be preferred. However, in this meta-analysis, none of the analyses showed heterogeneity, so we preferred FEM. Furthermore, deciduous and permanent tooth caries was not evaluated in subgroups due to the small numbers of studies examining the same polymorphisms.

Saliva plays an important role in oral homeostasis, and alterations in salivary secretion may cause oral infections and caries. Saliva contains inorganic compounds and various proteins that influence conditions in the oral cavity. The salivary buffering capacity has its share in protecting the tooth surface from caries.<sup>7</sup> Carbonic anhydrase VI is part of the defense system of saliva, increasing the buffering capacity by catalyzing the reaction of carbon dioxide.<sup>14</sup> In the literature, various studies have investigated the effect of CA VI on dental caries. Öztürk et al. performed a study on young adults, and they found no association between dental caries and CA VI concentration.<sup>15</sup> However, Kivelä et al., Frassetto et al. and Szabó reported that there was an association between low CA VI concentration and a higher caries index.<sup>16–18</sup> Esberg et al. performed a study on Swedish adolescents to determine the relationship between dental caries and variations in the CA VI gene.<sup>19</sup> In their study, it was found that the CA VI gene polymorphisms, such as rs10864376 (T), rs3737665 (T) and rs12138897 (G), and the TTG haploblock of CA VI are associated with *Streptococcus mutans* colonization, overall microbiota composition and dental caries.<sup>19</sup>

In the literature to date, only 5 studies have examined the relationship between the CA VI exon 2 polymorphisms and dental caries. In the study of Yarat et al., which was performed on 44 Turkish subjects, no significant negative correlation was obtained between DMFT and CA activity, and no correlation was found between SNPs and the salivary buffering capacity.<sup>20</sup> Similarly, Peres et al. investigated 3 different polymorphisms (rs2274333 A>G, rs2274328 A>C and rs2274327 C>T) in 245 Brazilian schoolchildren, and no association was found between the rs2274333 A>G, rs2274328 A>C and rs2274327 C>T polymorphisms and dental caries.<sup>21</sup> However, they found that the rs2274327 C>T polymorphism decreased the salivary buffering capacity.<sup>21</sup> In another study, performed on 178 Turkish children by Sengul et al., no correlation was found between rs2274327 and dental caries.<sup>22</sup> In the same year, Yildiz et al. performed their study on Turkish adults, and no association was found between rs2274327 and dental caries,<sup>23</sup> similarly to other studies. Li et al. investigated in their study 7 different SNPs (rs2274328, rs17032907, rs11576766, rs2274333, rs10864376, rs3765964, and rs6680186) related to CA VI and they found an association only in the rs17032907 genetic variant, which suggested that the rs17032907 polymorphism might be associated with dental caries susceptibility.<sup>24</sup>


In the present meta-analysis, 4 different studies were included. The study of Yarat et al. was not included due to insufficient knowledge about the frequencies of genotypes.<sup>20</sup> In the literature, there were 3 studies related to the rs2274327 polymorphism, and 2 studies related to the rs2274328 and rs2274333 polymorphisms. In any polymorphism model, no association could be obtained between the rs2274327, rs2274328 and rs2274333 polymorphisms and dental caries.

## Conclusions

Although CA VI plays an important role in the buffering of saliva, it was found that polymorphisms in the CA VI gene do not affect the process of dental caries. Due to an inadequate number of studies in the literature, we could only examine the rs2274327, rs2274328 and rs2274333 polymorphisms. Furthermore, due to an inadequate number of studies, the power of the meta-analysis was lower. In further studies, we recommend that researchers investigate also other polymorphisms related to the CA VI gene. Additionally, we recommend the separation of the dmft and DMFT variables as subgroups as the number of studies increases.

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# Effects of facemasks versus intraoral appliances in treating maxillary deficiency in growing patients: A systematic review and meta-analysis

## Porównanie zastosowania masek twarzowych i aparatów wewnątrzustnych w leczeniu niedorozwoju szczęki u rosnących pacjentów – systematyczny przegląd piśmiennictwa oraz metaanaliza

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D – writing the article; E – critical revision of the article; F – final approval of the article

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## Abstract

**Background.** Class III malocclusion is one of the most challenging types of orthodontic problems.

**Objectives.** The aim of this study was to compare the dentoskeletal effects of facemasks and intraoral appliances in treating class III maxillary deficiency in growing patients through a systematic review of the available literature.

**Material and methods.** Electronic and manual searches were performed in the Cochrane Central Register of Controlled Trials (CENTRAL), the Cochrane Database of Systematic Reviews (CDSR), MEDLINE (PubMed), Embase (OVID), and Scopus to find all the relevant studies published by January 2018. All randomized controlled trials (RCTs) recruiting 5–12-year-old patients who received maxillary protraction treatment with any type of facemask and comparing the facemasks with any type of intraoral appliance were included. The primary outcome measure was changes in the A point-nasion-B point angle (ANB), and the secondary outcomes included changes in the overjet, upper-1 (U1) inclination, the mandibular plane angle, and treatment time. The meta-analysis was carried out using the inverse variance-weighted random effects model.

**Results.** Out of 1,629 articles found in the initial search, 5 studies met the inclusion criteria. The meta-analysis showed no differences in the duration of treatment or in any of the cephalometric variables, with the exception of the overjet.

**Conclusions.** It seems that intraoral appliances and facemasks are similar in terms of dentoskeletal effects in the treatment of class III malocclusion as well as treatment duration. However, due to a lack of a sufficient number of high-quality studies, these results should be viewed with caution. Further high-quality, long-term studies are recommended.

**Key words:** systematic review, meta-analysis, class III malocclusion treatment, facemask, intraoral appliance

**Słowa kluczowe:** systematyczny przegląd piśmiennictwa, metaanaliza, leczenie wady zgryzu klasy III, maska twarzowa, aparat wewnątrzustny



## Introduction

The prevalence of class III malocclusion varies, with rates as high as 26.6% and a higher prevalence reported among East Asian populations,<sup>1,2</sup> which means that a remarkable proportion of orthodontic patients are affected.<sup>3</sup> The treatment of class III malocclusion is one of the most challenging kinds of orthodontic treatment.<sup>4–7</sup> This type of malocclusion can occur for a variety of reasons, including maxillary deficiency, mandibular prognathism, or a combination of the two.<sup>1,8,9</sup> Maxillary deficiency, with an incidence of approx. half of all cases, is the main cause.<sup>2,8,9</sup> Therefore, maxillary protraction is considered to be the primary treatment option in class III cases.<sup>8</sup> In growing patients, this goal can be achieved using either extraoral protraction facemasks<sup>9–13</sup> or intraoral appliances.

Generally, a facemask is the most widely used orthopedic device to treat growing patients with maxillary deficiency.<sup>14,15</sup> The therapeutic results are acceptable in terms of both skeletal and dentoalveolar aspects, and are achieved after a relatively short time.<sup>12,14,16–18</sup> This device has also some disadvantages, including soft tissue irritation and abrasion, and bulkiness. These factors can compromise the patient compliance, definitely affecting the therapeutic results.<sup>9,14,19</sup>

On the other hand, a large number of intraoral devices have been introduced to treat class III malocclusion, including Fränkel's functional regulator,<sup>20,21</sup> the reverse twin block,<sup>15</sup> the modified Jasper Jumper device,<sup>22</sup> the modified tandem traction bow appliance,<sup>13,14</sup> and fixed tongue appliances and plates.<sup>8,9</sup> They do not have bulky external appearance or the potential for soft tissue irritation, which are associated with a facemask. Fixed intraoral appliances also eliminate the patient compliance issues. Therefore, they seem to improve the results of maxillary protraction.<sup>2</sup> The efficacy of these devices has been investigated in various studies. However, there is some controversy in the literature over the issue, with some studies observing differences between these modalities and preferring one over the other,<sup>7,13,15,19,23</sup> and other studies showing no significant differences between these methods of treatment.<sup>2,8,9,14,24</sup> Two recently published systematic reviews on the early treatment of class III malocclusion focused on the comparison of groups treated with various kinds of appliances against untreated control groups.<sup>25,26</sup> Neither of these studies compared different therapies. Therefore, this systematic review and meta-analysis was designed and carried out to evaluate the efficacy of facemasks and selected intraoral devices in treating maxillary deficiency in growing class III malocclusion patients based on the studies previously published on the subject.

## Material and methods

### Protocol and registration

The study was carried out based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.<sup>27</sup> It was registered in the PROSPERO database under the code CRD42017063810 ([www.crd.york.ac.uk/PROSPERO](http://www.crd.york.ac.uk/PROSPERO)).

### Search strategy, the information sources and the type of included studies

All the relevant studies were searched for with no restrictions on the language or the date of publication until April 2017 (updated in January 2018) in the following databases: Cochrane Central Register of Controlled Trials (CENTRAL); Cochrane Database of Systematic Reviews (CDSR); MEDLINE (PubMed); Embase (OVID); and Scopus.

The search strategy was based on the one developed for PubMed (Table 1), but revised for each database according to their search strategy instructions.

Additionally, a manual search was carried out through the reference lists of the finally included articles, and the relevant systematic reviews and orthodontic journals not indexed in PubMed.

All searches were carried out by 2 independent investigators (S.S. and M.A.). Duplicate studies were removed in the 1<sup>st</sup> step of screening.

Only randomized clinical trials (RCTs) were considered for this systematic review and meta-analysis.

### Criteria of eligibility

The inclusion criteria for the studies were chosen according to the PICO guidelines for research and evidence-based practice.<sup>28</sup>

**Participants.** Studies on 5–12-year-old patients with skeletal class III malocclusion, with no craniofacial syndromes or any type of facial clefts, who underwent early orthopedic/orthodontic maxillary protraction treatment with any removable or fixed appliances were included; studies with any bone-anchored device or any surgical procedure to facilitate protraction were excluded.

**Intervention.** Maxillary protraction treatment using any intraoral appliances, including functional appliances and tongue appliances, or the modified versions of them were sought, with no restrictions on the treatment protocol or duration.

**Comparison.** Maxillary protraction treatment with any type of facemask, i.e., Delaire, Petit, Nanda, a rail-type facemask, or any other modifications, were included, with no restrictions on the treatment protocol or duration.

Table 1. MEDLINE search strategy

No.	Key words
#1	'malocclusion'; 'angle'; 'class III' (MeSH)
#2	'class III' AND 'angle' OR 'angle's' OR 'malocclusion' OR 'bite'
#3	'underbite' OR 'under-bite' OR 'under bite' OR 'reverse bite' OR 'reverse-bite' OR 'prognath' (MeSH)
#4	'prominent lower front teeth'
#5	OR/1–4
#6	'orthodontic appliances functional' (MeSH)
#7	'orthodontic appliances removable'
#8	'growth modif' AND 'maxilla' OR 'jaw'
#9	'growth modif' AND 'functional'
#10	'extraoral' OR 'extra oral' OR 'extra-oral' AND 'traction'
#11	'facemask' OR 'face mask' OR 'face-mask'
#12	'reverse headgear'
#13	'Delaire' OR 'Petit' OR 'Nanda' OR 'rail type'
#14	'orthopedic' OR 'orthopaedic' AND 'orthodontic' OR 'facial'
#15	'early' AND 'treatment' OR 'therapy' AND 'orthodontic'
#16	OR/5–15
#17	'intraoral' OR 'intra oral' OR 'intra-oral' AND 'appliance'
#18	'modified' OR 'reverse' AND 'twin block'
#19	'Jasper Jumper' OR 'modified Jasper Jumper'
#20	'tongue' AND 'plate' OR 'appliance'
#21	'Frankel III' OR 'FR III' OR 'FR-III'
#22	'Balter bionator'
#23	'double piece' AND 'corrector' OR 'appliance'
#24	'tandem' AND 'appliance' OR 'bow'
#25	'class III' OR 'cl III' AND 'activator'
#26	'sagittal' AND 'III' OR 'class III' OR 'cl III'
#27	'inclined plane'
#28	OR/17–27
#29	#5 AND #14 AND #28

MeSH – Medical Subject Headings.

### Outcomes:

- the primary outcome criteria were the A point-nasion-B point angle (ANB) changes obtained with a face-mask vs intraoral devices, measured on a lateral cephalogram;
- the secondary outcomes sought were other skeletal and dental differences between the treatment modalities, differences in the duration of treatment and any complications that occurred with regard to either treatment.

### Study selection and data extraction

After eliminating duplicates, all the studies selected by the search were examined in order to remove the irrelevant ones. Firstly, the names of authors and journals, and the result sections of the articles were deleted so as

to prevent any possible reviewer or publishing bias.<sup>29</sup> Then, the titles were screened. The articles with titles that made them potentially eligible were reviewed based on their abstracts. Then, the full texts of the selected articles were retrieved and screened for final inclusion based on the eligibility criteria. This selection of the studies was carried out by 2 investigators (S.S. and M.A.) independently and in duplicate. All doubts and disagreements were resolved after discussion.

A customized data extraction form was created by 2 researchers (S.S. and M.A.) and used by each of these investigators independently and in duplicate. The information collected in this form included the study and the author's name, the year of publication, the type of study, the appliances used for intervention and comparison, the number and age of participants in each group, and the mean differences and standard deviations (*SDs*) of the outcome measures.

For any missing information, an attempt was made to contact the corresponding author.

### Risk of bias and quality assessment

The risk of bias and methodological quality assessment was undertaken by 2 researchers (N.F. and S.S.) independently and in duplicate. It was carried out using the Cochrane Collaboration tool for assessing the risk of bias, comprising 6 categories: 1 – selection bias with a further division into 'randomization sequence generation' and 'allocation concealment'; 2 – performance bias, which evaluated the blindness of the person who performed the intervention; 3 – detection bias, which evaluated the blindness of the person who detected or interpreted the results; 4 – attrition bias, which refers to the withdrawal of the patients; 5 – reporting bias, which refers to selective outcome reporting; and 6 – other sources of biases.<sup>29</sup> The Review Manager (RevMan) software, v. 5.3 (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014) was used to summarize the risk of bias. Each category was judged as high, low or unclear.

### Data synthesis and analysis

The data analysis was carried out using comprehensive meta-analysis software (Comprehensive Meta-Analysis, v. 2; Borenstein M, Hedges L, Higgins J, Rothstein H. Biostat, Engelwood, NJ, 2005, 104). We calculated the summary measure with 95% uncertainty from different studies for each outcome. Due to the existence of heterogeneity, the meta-analysis was carried out with the inverse variance-weighted random effects approach. The  $\chi^2$  test was used to assess heterogeneity between the studies. Statistical significance was set at  $p < 0.05$ . Funnel plots were used to assess any publication bias of the articles.

## Results

### Search findings and study selection

The initial search after eliminating duplicates identified 1,629 records. Screening by title and abstract resulted in 167 and 60 studies, respectively. After reviewing the full texts by means of detailed inclusion and exclusion criteria, 55 articles were excluded, as they did not fulfill the inclusion criteria of the study (case reports, case series, retrospective studies or non-randomized studies, lacking a comparison group, including surgical intervention, or including any craniofacial syndromes or any kind of facial clefts). Finally, 5 studies were included in the systematic review.<sup>8,9,14,22,24</sup> Excluding Kurt et al.,<sup>22</sup> the 4 remaining studies were used for the meta-analysis after quality assessment (Fig. 1). The particulars of the selected studies are presented in Table 2.

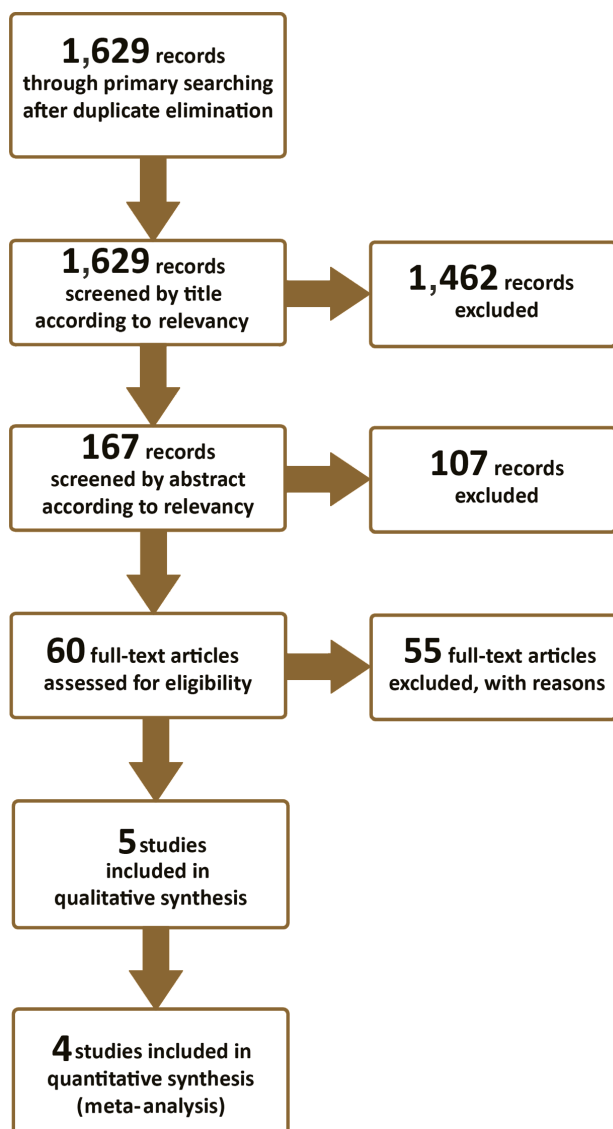


Fig. 1. Study flow diagram

### Risk of bias and quality assessment of the included studies

The quality assessment and the risk of bias assessment criteria for RCTs were adapted from *Cochrane Handbook for Systematic Reviews of Interventions* (Fig. 2,3).<sup>29</sup>

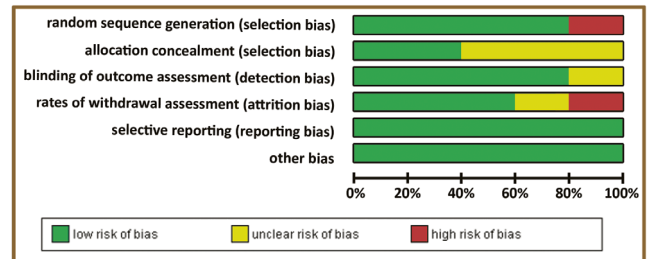


Fig. 2. Risk of bias assessment across all studies

	random sequence generation (selection bias)	allocation concealment (selection bias)	blinding of outcome assessment (detection bias)	rates of withdrawal assessment (attrition bias)	selective reporting (reporting bias)	other bias
Husson et al. 2016	+	?	+	+	+	+
Showkatbakhsh et al. 2015	+	+	?	-	+	+
Showkatbakhsh et al. 2013	+	+	+	+	+	+
Showkatbakhsh et al. 2012	+	?	+	+	+	+
Kurt et al. 2010	-	?	+	?	+	+

Fig. 3. Risk of bias assessment by study

### Selection bias (sequence generation and allocation concealment)

Sequence generation was adequate for all studies, with the exception of that by Kurt et al.<sup>22</sup> Husson et al.<sup>14</sup> and Showkatbakhsh et al. (2012)<sup>24</sup> used a random number generator. Showkatbakhsh et al. (2015)<sup>9</sup> and Showkatbakhsh et al. (2013)<sup>8</sup> used an unstratified subject allocation sequence. However, Kurt et al. assigned patients to treatment groups in accordance with their order of arrival at the clinic.<sup>22</sup>

Table 2. Characteristics of the included studies

Characteristic	Husson et al. (2016) <sup>14</sup>	Showkatbakhsh et al. (2015) <sup>9</sup>	Showkatbakhsh et al. (2013) <sup>8</sup>	Showkatbakhsh et al. (2012) <sup>24</sup>	Kurt et al. (2010) <sup>22</sup>
Study design	– RCT – single-center – single-blind – parallel-group	– RCT – single-center – single-blind – parallel-group	– RCT – single-center – single-blind – parallel-group	– RCT – single-center – single-blind – parallel-group	– RCT – single-center – single-blind
Participants	32 patients – 15 boys, 17 girls, randomly allocated to 2 groups: – MTA group (16 patients) – facemask group (16 patients)	56 patients – 26 boys, 30 girls, randomly assigned to 2 groups: – fixed tongue appliance group (26 patients) – facemask group (30 patients)	47 patients – 22 boys, 25 girls, randomly assigned to 2 groups: – tongue plate group (23 patients) – facemask group (24 patients)	45 patients – 22 boys, 23 girls, randomly assigned to 2 groups: – tongue appliance group (23 patients) – facemask group (22 patients)	46 patients – 23 boys, 23 girls, divided into 3 groups: – MJJ group (16 patients) – facemask group (17 patients) – untreated control group (13 patients)
Age [years]	7.98 ±0.68 (MTA group) 8.11 ±0.76 (facemask group)	8.9 ±1.7 (fixed tongue appliance group) 8.5 ±1.4 (facemask group)	9.1 ±0.9 (tongue plate group) 9.0 ±1.2 (facemask group)	10.1 ±0.7 (tongue appliance group) 9.3 ±1.2 (facemask group)	9.67 ±0.95 (MJJ group) 9.55 ±0.97 (facemask group) 9.14 ±0.40 (untreated control group)
Treatment/observation period [months]	8.11 ±0.76 (MTA group) 6.40 ±1.30 (facemask group)	14 ±2 (fixed tongue appliance group) 18 ±4 (facemask group)	16 ±2 (tongue plate group) 18 ±3 (facemask group)	17 ±3 (tongue appliance group) 18 ±3 (facemask group)	4.90 ±0.37 (MJJ group) 6.41 ±0.50 (facemask group) 6.00 ±0.00 (untreated control group)
Inclusion criteria	– early mixed dentition – class III molar relationship – anterior crossbite or edge-to-edge – ANB ≤ 0° – A-N perpendicular ≤ 1 mm – normal or horizontal growth pattern (Björk's sum: 396 ±5°)	– SNA ≤ 80° – SNB ≤ 80° – ANB ≤ 0° – Wits appraisal ≤ -1 mm – normal mandibular growth pattern (based on the assessment of Jarabak's ratio) – moderate class III molar relationship with a concave profile	– SNA ≤ 80° – SNB ≤ 80° – ANB ≤ 0° – class III molar relationship – classified as pre-pubertal according to CVM (CS1, CS2 and CS3)	– SNA ≤ 80° – SNB ≤ 80° – ANB ≤ 0° – class III molar relationship – a concave profile – the negative overjet	– skeletal class III malocclusion with maxillary retrognathism (SNA ≤ 79°) – ANB ≤ -1° – horizontal growth pattern (SN-GoMe = 30–32°) – class III molar relationship with the anterior cross-bite
Exclusion criteria	– extracted or congenitally missing teeth – deformity of the nasomaxillary complex – history of TMDs	– any syndromic or medically compromised patients – previous surgical intervention – use of other appliances before or during the treatment period – skeletal asymmetry – any possibility for a mandibular backward position in the centric relation	– any syndromic or medically compromised patients – previous surgical intervention – use of other appliances before or during the treatment period – skeletal asymmetry		– history of any craniofacial abnormalities – patients had undergone previous orthodontic treatment
Intervention	MTA: – protraction force of 230 g per side – 30° to the occlusal plane – at least 16 h per day	fixed tongue appliance: – combination of a maxillary hyrax (for loosening the maxillary sutures) and a palatal crib (wire width of 1.2 mm) – screw opening 0.25 of a turn per week for 3 months	tongue plate: – removable intraoral plate – acrylic plate mounted posterior to upper incisors – full-time wear of the appliance except for eating, tooth brushing and contact sports	tongue appliance: – removable intraoral plate – palatal crib attached to the acrylic plate – full-time wear of the appliance except for eating, tooth brushing and contact sports	MJJ group: – protraction force of 200 g per side – treatment discontinued once the class III molar relationship and the anterior cross-bite were corrected – use of a chin cap for retention 8 h per day
Comparison(s)	Petit-type facemask: – protraction force of 230 g per side – 30° to the occlusal plane – at least 16 h per day	multi-adjustable facemask: – removable intraoral plate with a midline screw – protraction force of 500 g per side – screw opening 0.25 of a turn per week for 3 months – full-time wear of the appliance except for eating	multi-adjustable facemask: – removable intraoral plate – protraction force of 500 g per side – full-time wear of the appliance except for eating, tooth brushing and contact sports	multi-adjustable facemask: – in combination with an edgewise fixed 0.018-inch appliance – protraction force of 500 g per side	Delaire-type facemask group: – protraction force of 400 g per side – 14 h per day – treatment discontinued once the class III molar relationship and the anterior cross-bite were corrected – use of a chin cap for retention 8 h per day untreated control group: – followed up for 6 months
Outcomes	skeletal changes: SNA – SNB – ANB – CoA – CoGn – Pog-N perpendicular – SN-PP – SN-GoMe – A-TW – Pog-TW – Pog-TV – dental changes: U6-TW – U1-TV – U1-TW – L6-TW – L1-TV – L1-TW – all measurements were taken before and after treatment	skeletal changes: SNA – SNB – ANB – Wits appraisal – ANS-PNS – GoGn-gonial angle – Jarabak's ratio – SN-GoGn – dental changes: inclination angle – U1-SN – IMPA – all measurements were taken before and after treatment	skeletal changes: SNA – SNB – ANB – ANS-PNS – GoGn – SN-GoGn – dental changes: inclination angle – U1-SN – IMPA – soft tissue changes: nasolabial angle – all measurements were taken before and after treatment	skeletal changes: SNA – SNB – ANB – ANS-PNS – GoGn – SN-GoGn – Jarabak's ratio – dental changes: inclination angle – U1-SN – IMPA – soft tissue changes: nasolabial angle – all measurements were taken before and after treatment	TMDs were evaluated with RDC/TMD in all groups before and after the treatment/observation period – presence of TMDs – myofascial pain – disc displacement – arthralgia – number of painful muscles – number of painful TMJs

Data presented as mean ± standard deviation (SD).

RCT – randomized control trial; MTA – modified tandem appliance; CVM – contingent valuation method; CS – CVM stage; MJJ – modified Jasper Jumper; TMD – temporomandibular disorder; RDC/TMD – Research Diagnostic Criteria for Temporomandibular Disorders; TMJ – temporomandibular joint.

Abbreviations related to the cephalometric variables: A – point A; B – point B; Co – condylion; Gn – gnathion; Go – gonion; IMPA – incisor mandibular plane angle; Me – menton; N – nasion; P – point P; Pog – pogonion; PP – palatal plane; S – sella (either angles or distances); and U – upper; L – lower; TV – tongue volume; TW – tongue width.

Allocation concealment was adequate for Showkatbakhsh et al. (2015)<sup>9</sup> and Showkatbakhsh et al. (2013),<sup>8</sup> whereas the studies by Husson et al.,<sup>14</sup> Showkatbakhsh et al. (2012)<sup>24</sup> and Kurt et al.<sup>22</sup> were judged as unclear on allocation concealment.

### Performance and detection bias

Due to the nature of the studies, comparing 2 different treatment modalities, the blinding of participants and clinicians could not be performed, and therefore it was not assessed. Conversely, the blinding of outcome detectors and statisticians was possible in all studies. Regarding detection bias, there was a low risk of bias in Husson et al.,<sup>14</sup> Kurt et al.<sup>22</sup> and in 2 studies by Showkatbakhsh et al. (2013, 2012),<sup>8,24</sup> whereas it was unclear in the study by Showkatbakhsh et al. (2015), where no blinding was mentioned.<sup>9</sup>

### Attrition bias

The rates of withdrawal were clearly reported in the 2013 study by Showkatbakhsh et al.<sup>8</sup> Interestingly, Husson et al.<sup>14</sup> and Showkatbakhsh et al.(2012)<sup>24</sup> reported no dropouts in their studies. These 3 studies were judged as having a low risk of bias. The attrition bias of the study by Kurt et al. was judged to be unclear.<sup>22</sup> On the other hand, Showkatbakhsh et al. (2015) reported that 4 patients had dropped out of the study due to personal reasons.<sup>9</sup> In response to our e-mail, the authors declared that these 4 patients rejected the facemask due to its bulky size. Therefore, the risk of attrition bias in this study was assessed as high.

### Reporting bias

The risk of reporting bias for all studies was judged to be low. All 5 RCTs reported the outcomes that they had set out to report and there was no obviously missing data.<sup>8,9,14,22,24</sup>

### Overall risk of bias of randomized controlled trials

The study by Showkatbakhsh et al. (2013)<sup>8</sup> showed an overall low risk of bias. Showkatbakhsh et al.'s (2015)<sup>9</sup> and Kurt et al.'s studies<sup>22</sup> were assessed as having a high risk of bias due to attrition bias and selection bias, respectively. The 2 remaining studies (by Husson et al.<sup>14</sup> and by Showkatbakhsh et al. (2012)<sup>24</sup>) were assessed to have an unclear risk of bias (Fig. 2,3).

### Summary of the studies and meta-analysis

The summary of findings of the final articles is reported in Table 3. Four cephalometric variables and treatment duration were selected, and the mean differences and SDs for each group were compared:

- overjet (Husson et al.<sup>14</sup>);
- ANB (all 4 studies);
- upper-1 (U1) inclination (all studies apart from Husson et al.<sup>14</sup>);
- mandibular plane angle (all 4 studies).

Furthermore, in order to investigate publication bias, funnel plots were constructed for each variable. These plots show symmetries in the publication of the studies (Fig. 4).

### Overjet

Since only 1 study (by Husson et al.<sup>14</sup>) had measured this variable, the meta-analysis could not be performed for the RCT subgroup. In the study by Husson et al., the overjet was  $3.53 \pm 1.24$  mm in the facemask group and  $2.52 \pm 1.45$  mm in the intraoral device group.<sup>14</sup> This difference was statistically significant ( $p = 0.04$ ).

### A point-nasion-B point angle

The mean difference in ANB was  $1.63^\circ$  in the facemask group and  $1.59^\circ$  in the intraoral device group. The meta-analysis was performed for all 4 RCTs. The pooled estimate

Table 3. Summary of findings of the final articles

Study	Design	Group	Age [years]	ANB changes [°]	Mandibular plane angle changes [°]	Overjet changes [mm]	U1 inclination changes [°]
Husson et al. (2016) <sup>14</sup>	RCT	MTA	7.98 ± 0.68	1.88 ± 0.72	1.00 ± 0.97	2.25 ± 1.45	–
		facemask	8.11 ± 0.76	2.13 ± 1.09	3.50 ± 1.41	3.53 ± 1.24	–
Showkatbakhsh et al. (2015) <sup>9</sup>	RCT	fixed tongue appliance	8.9 ± 1.7	1.1 ± 1.7	–0.9 ± 2.4	–	4.3 ± 7.4
		facemask	8.5 ± 1.4	1.4 ± 1.4	–0.2 ± 1.5	–	5.7 ± 5.0
Showkatbakhsh et al. (2013) <sup>8</sup>	RCT	tongue plate	9.1 ± 0.9	1.8 ± 1.2	0.4 ± 1.8	–	4.9 ± 4.5
		facemask	9.0 ± 1.2	1.2 ± 1.6	–0.4 ± 1.6	–	6.5 ± 6.0
Showkatbakhsh et al. (2012) <sup>24</sup>	RCT	tongue appliance	10.1 ± 0.7	1.6 ± 1.6	–1.0 ± 4.1	–	2.5 ± 6.1
		facemask	9.3 ± 1.2	1.8 ± 1.5	0.4 ± 1.9	–	11.1 ± 6.9

Data presented as mean ± standard deviation (SD).

U1 – upper-1.

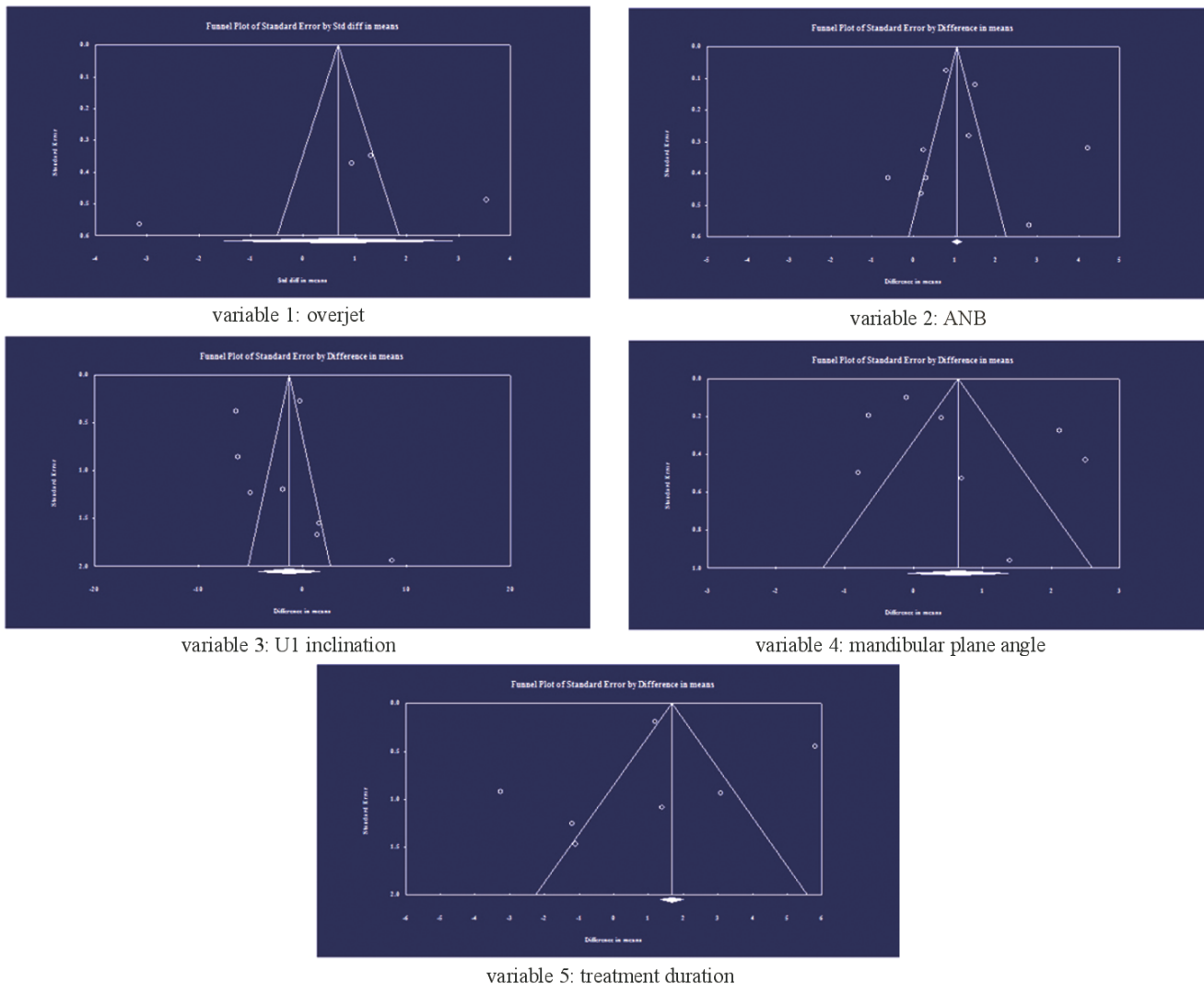


Fig. 4. Publication bias (funnel plots) for each variable

was 0.050 (95% CI:  $-0.351$ – $0.464$ ;  $p = 0.787$ ). The difference between the groups was not statistically significant and the  $\chi^2$  test showed heterogeneity ( $p < 0.001$ ) (Fig. 5).

### Upper-1 inclination

All studies, except for that by Husson et al.,<sup>14</sup> had measured the U1 inclination changes in terms of each modality. The mean difference in the U1 inclination was  $7.76^\circ$  in the facemask group and  $3.9^\circ$  in the intraoral device group. The meta-analysis showed that the pooled estimate was  $3.745$  (95% CI:  $-0.583$ – $8.074$ ;  $p = 0.09$ ). The difference between the groups was not statistically significant and the  $\chi^2$  test indicated heterogeneity ( $p < 0.001$ ) (Fig. 6).

### Mandibular plane angle

All studies had measured the mandibular plane angle changes in terms of each treatment modality.

The mean difference in the mandibular plane angle was  $0.82^\circ$  in the facemask group and  $-0.12^\circ$  in the intraoral device group. The meta-analysis showed that the pooled estimate was  $0.936$  (95% CI:  $-0.669$ – $2.542$ ;  $p = 0.253$ ). The difference between the groups was not statistically significant and the  $\chi^2$  test indicated heterogeneity ( $p < 0.001$ ) (Fig. 7).

### Duration of treatment

All studies mentioned the exact duration of treatment in both the facemask and intraoral device groups. The mean of treatment duration was 15.1 months in the facemask group and 13.77 months in the intraoral device group. The meta-analysis showed that the pooled estimate was  $1.266$  (95% CI:  $-1.470$ – $4.002$ ;  $p = 0.364$ ). The difference between the groups was not statistically significant and the  $\chi^2$  test showed heterogeneity ( $p < 0.001$ ) (Fig. 8).

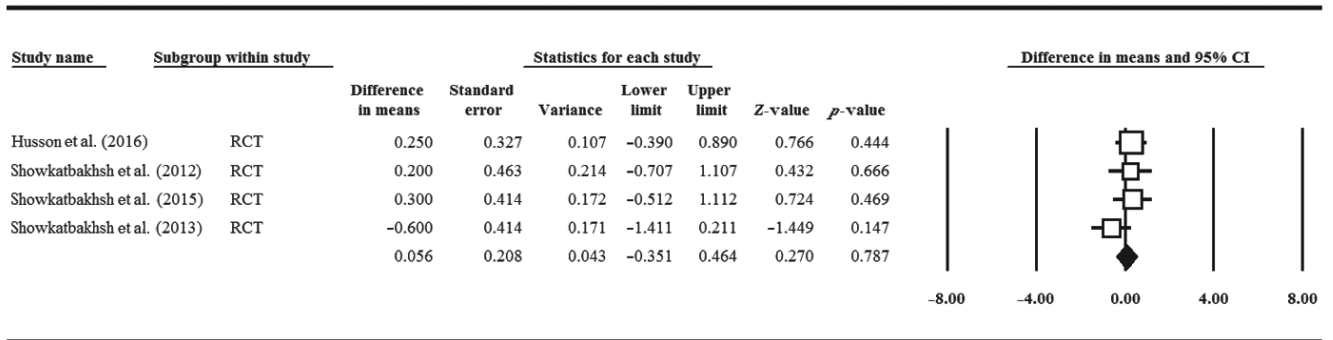


Fig. 5. Meta-analysis of the differences in the A point-nasion-B point angle (ANB)  
CI – confidence interval.

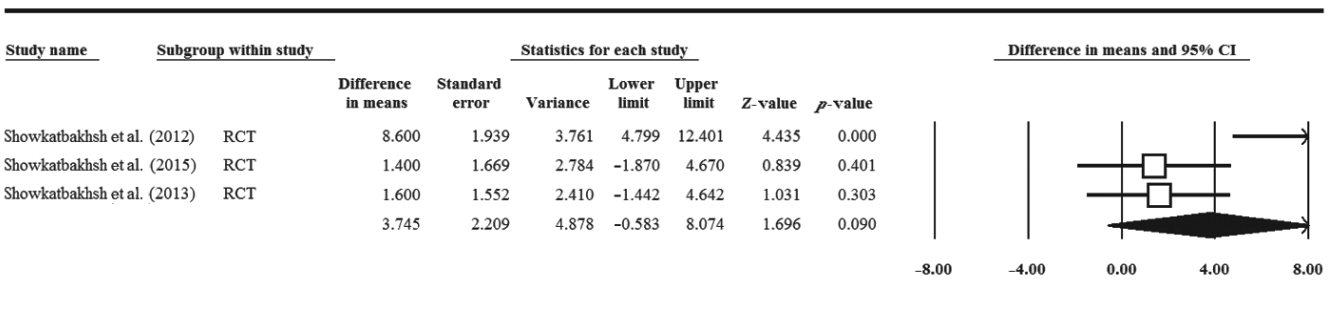


Fig. 6. Meta-analysis of the differences in the upper-1 (U1) inclination

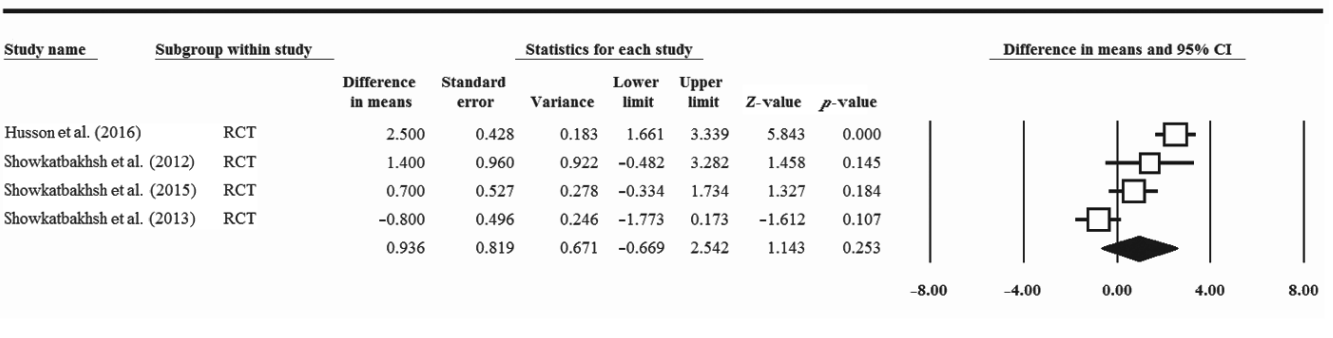


Fig. 7. Meta-analysis of the differences in the mandibular plane angle

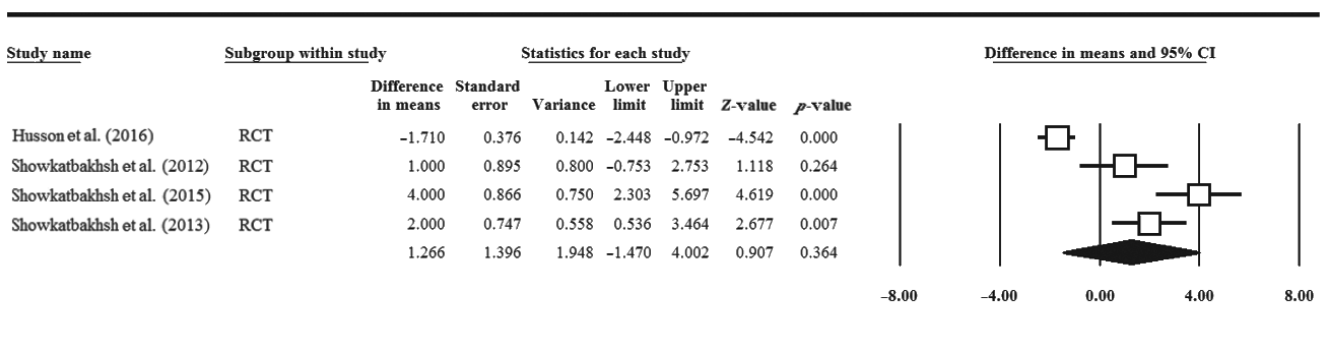


Fig. 8. Meta-analysis of the differences in treatment duration

## Discussion

### Summary of the main results

This systematic review was designed to appraise the available evidence comparing facemasks and intraoral devices in treating growing class III patients with maxillary deficiency. As shown in Table 2, 5 articles were included in this systematic review. Four articles had measured pre- and post-treatment cephalometric variables for the facemask and intraoral device groups, and had used them for meta-analysis.<sup>8,9,14,24</sup> These variables were measured with regard to different references in different studies (Table 2), but by measuring the mean differences between the pre- and post-treatment values, this limitation was overcome. However, Kurt et al. compared class III growing patients treated with a facemask or an intraoral appliance (the modified Jasper Jumper device) in the case of temporomandibular disorders (TMDs).<sup>22</sup> They concluded that both of these appliances were capable of reducing TMD-related symptoms, and thus could enhance the patient's quality of life, without affecting the incidence of TMDs.

As shown in Table 3, in the remaining studies, 4 cephalometric variables were compared and analyzed, in addition to the treatment duration differences between the facemask and intraoral device groups.<sup>8,9,14,24</sup> The comparison of the duration of treatment between these groups revealed no difference in the meta-analysis. On the other hand, no differences between the various cephalometric variables of the facemask and intraoral device groups were found, with the exception of the overjet.

Interestingly, although the analysis of the U1 inclination changes showed no differences, the results favored the intraoral device group. This might be attributed to the type of appliance used. All 3 of the relevant RCTs used a tongue plate/appliance.<sup>8,9,24</sup> These appliances transferred the low functional forces of the tongue to the palate and the whole maxillary arch. These kinds of forces may produce fewer changes in the U1 inclination.

Although a recent systematic review identified the reverse overjet as the main reason for a class III malocclusion patient to seek treatment, in our research, the overjet was assessed only in 1 study.<sup>14</sup> It seems that skeletal changes were more important to those authors, as they did not report the overjet changes throughout the treatment period.<sup>26</sup> It appears that most of the treatment modalities can lead to the positive overjet and that most authors are focused on finding the cause of an increase in the overjet. To make systematic reviews more informative for patients as well as for researchers, reporting changes in the overjet seems to be quite helpful.

Due to the nature of a facemask appliance, patient compliance in wearing elastics clearly influences the final outcome. Therefore, it seemed that the type of the intraoral part of the facemask, i.e., removable or fixed, did not affect the treatment outcomes. Conversely, in the intraoral appliance group, some fixed appliances did not require patient

compliance. Therefore, fixed or removable intraoral appliances might affect the final outcome. In 2 of the studies by Showkatbakhsh et al. (2013, 2012), removable intraoral appliances were used,<sup>8,24</sup> but Showkatbakhsh et al. (2015)<sup>9</sup> and Husson et al.<sup>14</sup> combined a hyrax expansion screw with the protraction protocol. Therefore, they had to choose a fixed design for their intraoral appliances. The efficacy of maxillary protraction with or without expansion was studied by Foersch et al. in 2015 in a systematic review, with no significant improvement being observed in maxillary protraction with expansion.<sup>1</sup> In the present review, due to a lack of new, high-level evidence regarding this issue since 2015, this variable was not assessed. Finally, it seems that there is no consensus regarding the best type of appliance in terms of fixed/removable and expansion/non-expansion.

### Quality of the evidence

Only the study by Showkatbakhsh et al. (2013) was judged to have a low risk of bias.<sup>8</sup> The studies by Husson et al. and Showkatbakhsh et al. (2012) were judged to have an unclear risk of bias.<sup>14,24</sup> Showkatbakhsh et al.'s study (2015) was assessed as having a high risk of bias.<sup>9</sup>

### Heterogeneity

Overall, facemask and intraoral appliances were effective in the treatment of class III malocclusion. Most of their effects seemed to be similar and they did not vary with respect to the duration of treatment. However, due to the high degree of heterogeneity in the pooled studies, the validity of this claim seems less conclusive.

### Potential for bias in the reviewing process

By using a comprehensive search strategy specified for multiple databases, updating the search results as the process of systematic review continued, and having no restrictions on the language or the date of publication, the potential for bias was kept low in this systematic review.

### Suggestion for future research

Due to a limited number of RCTs in the scope of this review, more well-designed RCTs seem to be necessary. The following suggestions should be considered:

- well-designed RCTs, which strictly follow the Consolidated Standards Of Reporting Trials (CONSORT) statement,<sup>30</sup> especially regarding the use of fixed/removable appliances and the expansion/non-expansion protocols;
- ruling out patients with pseudo-class III;
- long-term follow-up in order to determine the stability of the treatment results;
- a uniform set of variables, including the overjet and the maxillary skeletal position, in addition to all of the variables mentioned in this review.



## Conclusions

It seems that intraoral devices and facemasks have similar effects on class III malocclusion. However, due to a lack of a sufficient number of well-designed, high-quality RCTs, these conclusions must be viewed with caution.

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# Patient-reported outcomes and efficiency of complete dentures made with simplified methods: A meta-analysis

## Efektywność protez całkowitych wykonanych metodami uproszczonymi w opinii pacjentów – metaanaliza

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## Abstract

**Background.** An increasing lifetime expectancy of the elderly highlights the importance of prosthodontic techniques, such as preparing complete dentures, which can restore the complete loss of teeth.

**Objectives.** The present study compared patient-reported outcomes and efficiency in terms of preparation time and cost of a simplified complete denture (SCD) and a conventional complete denture (CCD) in edentulous patients using a meta-analysis of clinical trials (CTs).

**Material and methods.** A literature search was conducted for studies comparing SCD and CCD in MEDLINE (PubMed), Scopus and World of Science, and through analyzing the reference lists of the retrieved studies, without language or time limits. Studies fitting the pre-specified inclusion criteria were assessed for quality and the extracted data referred to the following issues: patient satisfaction measured using a 100-millimeter visual analog scale (VAS); impact on quality of life estimated using the Oral Health Impact Profile (OHIP)-19 on a scale from 0 to 38; the proportion of cost of SCD to CCD; and time in minutes to deliver dentures. The results were pooled in meta-analyses and displayed in forest plots.

**Results.** Eleven publications referring to 7 studies were included in the meta-analysis. There were no differences between SCD and CCD in patient satisfaction (mean difference: 0.896, 95% CI (confidence interval): –2.947, 4.739) or their impact on quality of life (mean difference: 0.379, 95% CI: –0.994, 1.751). It required significantly less time to deliver SCD (mean difference: –274.16, 95% CI: –348.37, –199.96) and it cost significantly less (proportion: 0.740, 95% CI: 0.597, 0.882). Both SCD and CCD similarly impacted the patient's quality of life and satisfaction. It took about 4.5 h less to deliver SCD to patients as compared to CCD and the cost of SCD was 75% of the cost of CCD.

**Conclusions.** Compared to CCD, SCD had a similar impact in terms of satisfaction and quality of life with reduced treatment time and cost. More studies are needed in low-resource settings, where SCD may have a greater advantage.

**Key words:** complete dentures, Health-Related Quality of Life, patient comfort, dental services

**Słowa kluczowe:** protezy całkowite, jakość życia uwarunkowana stanem zdrowia, komfort pacjenta, usługi dentystyczne

## Introduction

With life expectancy increasing worldwide,<sup>1</sup> more individuals reach the state of complete edentulousness, and therefore need prosthodontic rehabilitation. Despite the presence of a variety of prosthodontic modalities, complete dentures remain the most widely used solution.<sup>2</sup> In many parts of the world, the cost of complete dentures may be prohibitive, depriving those in need of rehabilitative services, which affects their quality of life and well-being.<sup>3</sup> Several studies have been conducted to assess the usefulness of a simplified complete denture (SCD) as a less costly alternative to a conventional complete denture (CCD).<sup>4-7</sup> A simplified complete denture is defined as a complete denture which is fabricated in less time compared to CCD through the omission of some steps during impression making, occlusal registration or try-in.<sup>3</sup> Two systematic reviews compared these 2 types of dentures regarding patient-reported outcomes, in addition to cost and time.<sup>3,8</sup> Neither of them provided an overall estimate of the differences between the 2 types of dentures with respect to these features. Several studies<sup>6,7,9,10</sup> have been conducted since the publication of the most recent of these 2 systematic reviews.<sup>3</sup>

The present study updates the information reported in the 2 previous systematic reviews and conducts a meta-analysis of the differences between both types of dentures. The aim of this systematic review and meta-analysis was to answer the PICO question whether there is a difference between SCD and CCD in terms of patient satisfaction, their impact on quality of life, their cost, and time needed to deliver the dentures.

## Material and methods

### Inclusion criteria

In this meta-analysis, the following inclusion criteria were adopted: studies conducted on completely edentulous adult patients; studies assessing the use of SCD; CCD as control; controlled clinical trials (CTs), whether parallel-group or crossover designs; studies assessing any or all of the following outcomes – patient satisfaction, impact on quality of life, cost, or time taken to provide the patient with a complete denture.

### Search strategy

The MEDLINE (PubMed) database was searched using the Medical Subject Headings (MeSH) term 'denture, complete' combined using the Boolean operator AND with 'simplified'; no time or language limits were applied. The Scopus and World of Science databases were searched using the term 'simplified complete denture'. The reference lists of the retrieved articles were also searched.

## Study selection

After the search, the titles and abstracts of the retrieved articles were scanned to assess if they fitted the inclusion criteria. If this could not be ascertained, full texts were scanned. The studies were excluded based on each criterion.

## Quality assessment

The quality of the studies was assessed using the method described by Egger et al.<sup>11</sup> The following issues were evaluated: randomization and allocation concealment, the sample size estimation method, reporting clear inclusion/exclusion criteria, the completeness of follow-up, the comparability of groups at baseline, and the blinding of outcome assessors. These items were scored on a scale from 0 to 2, with 0 indicating inadequate or absent information of a limited or no value as evidence, and 2 indicating clearly explained and adequate information of a high value as evidence. A total score was calculated for each study.

## Data extraction

From the studies included in the present meta-analysis, the following data was extracted to describe the study features: the year of publication; the place where the study was conducted; the study design; the SCD preparation steps that differed from those for CCD; the number of participants in each group; and the participants' age, in addition to patient satisfaction, impact on quality of life, cost, and delivery time. In the included studies, satisfaction was measured on a visual analog scale (VAS) ranging from 0 to 100, with higher scores indicating a greater satisfaction. In 1 study, satisfaction was measured on a scale ranging from 0 to 10, so the scores were multiplied by 10 to be similar to those from other studies included in the meta-analysis. Impact on quality of life was assessed using the Oral Health Impact Profile (OHIP), which is a 19-item questionnaire. In some studies, answers to these questions were scored from 0 to 4 (5-point Likert scale) and in others from 0 to 2 (3-point Likert scale), resulting in a potential total score ranging from 0 to 76 or from 0 to 38, respectively. Thus, this variable had different ranges. To produce similar scores to be used for the present meta-analysis, all values were transformed to scores ranging from 0 to 38. The absolute cost comprised the personnel cost, which is the cost of time needed for the dentist to deliver the denture to the patient, and the cost of materials and equipment. The proportion between the cost of SCD and CCD was calculated using a previously reported method.<sup>12</sup> The cost was also transformed to the USD value at the time of the study<sup>13</sup> and corrected for inflation.<sup>14</sup> In all studies, the time required to deliver the denture to the patient comprised the time for fabrication and the time for adjusting the denture to fit the patient's needs.

## Analysis

The analysis was conducted using the OpenMeta[Analyst] software.<sup>15</sup> The outcome variables were measured on continuous scales as mean differences (except for cost, which was measured as a proportion) and confidence limits were calculated. For the meta-analysis, the similarity between the results was assessed using  $I^2$ . The random effects model was used if the results were heterogeneous. Forest plots were developed for each outcome. We used the Meta-Essentials tool (<https://www.erim.eur.nl/research-facilities/meta-essentials/>) to draw a funnel plot and to calculate the  $p$ -value of Egger's test in order to assess publication bias.<sup>16</sup>

## Results

The MEDLINE search generated 110 articles, of which only 18 were CTs. In Web of Science, the corresponding

numbers were 213 articles, of which 20 were CTs, and Scopus generated 152 articles, of which 19 were CTs. All records were imported to the Mendeley reference management software (<https://www.mendeley.com/download-desktop/>) and after duplicates were removed, there were 27 articles left. Of these, 4 were excluded, because their study design did not fit the inclusion criteria; they were systematic reviews or clinical studies, not trials. Six were excluded, because they did not have either the intervention or the control specified in the inclusion criteria or both, or because the study took into consideration implant-supported prostheses. Two studies were excluded, because they were comments/summaries of another study. Four were excluded, because they did not assess the required outcomes. The remaining studies ( $n = 11$ ) were included in the analysis (Fig. 1).

The 11 papers included in the review described 7 studies (Table 1). There were 3 articles from Brazil, 1 from Chile, 3 from Canada, 1 from Germany, 1 from Italy, and 2 conducted in Japan.

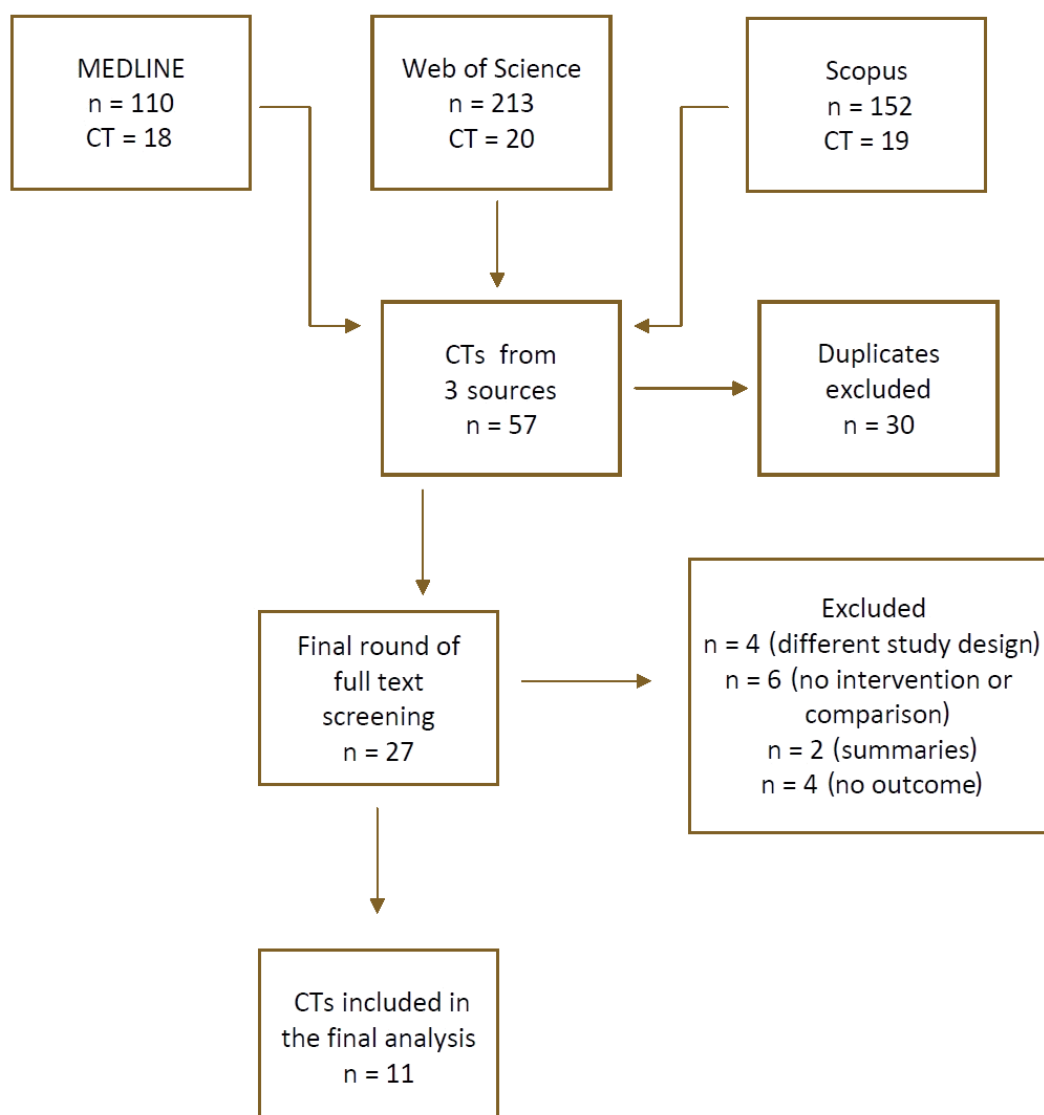


Fig. 1. Flow chart of clinical trials (CTs) included at different stages of the systematic review

Table 1. Features of the 11 studies included in the review

Study	Country	Follow-up [months]	n <sub>S</sub>	n <sub>C</sub>	Age [years]	Differences in the preparation steps S vs C	OHIP <sub>S</sub>	OHIP <sub>C</sub>	Time [min] <sub>S</sub>	Time [min] <sub>C</sub>	Cost <sub>S</sub>	Cost <sub>C</sub>	VAS <sub>S</sub>	VAS <sub>C</sub>
Regis et al., 2013 <sup>19</sup> (a)	Brazil	6	19	20	65.5	- no 2 <sup>nd</sup> impression; border molding and the final impression	6 (3.0–8.9)	5.5 (3.9–7.0)	-	-	-	-	-	-
Vecchia et al., 2014 <sup>18</sup> (a)	Brazil	6	19	20	65.5	- combining the anterior and posterior try-in in 1 step	-	-	1,669 ±487	2,174 ±414	138.62 ±36.34	216.50 ±57.64	-	-
Kawai et al., 2005 <sup>20</sup> (b)	Canada	6	54	51	45–75	- no final impression	-	-	-	-	-	-	79 ±23	79 ±20
Kawai et al., 2010 <sup>4</sup> (b)	Canada	6	54	51	45–75	- no face-bow transfer - monoplane articulator instead of a semi-adjustable articulator	-	-	-	-	726.0 ±50.3	892.1 ±41.1	-	-
Kawai et al., 2018 <sup>10</sup> (b)	Canada	6**	29	25	45–75	- no remount in the final step	81.7 ±23.9 ***	71.1 ±24.9	-	-	-	-	92	91.5
Núñez et al., 2015 <sup>21</sup> (c)	Brazil	6	25	25	64	- only 1 algininate impression - semi-adjustable articulator, no face-bow	4.7 ±6.6	5.0 ±6.1	-	-	-	-	8.7 ±2.2	8.1 ±1.8
Heydecke et al., 2008 <sup>22*</sup> (d)	Germany	3	20	20	69.1	- no face-bow transfer - anatomic teeth with canine guidance setup	-	-	-	-	-	-	69.9 ±35.5	54.8 ±36.1
Jo et al., 2015 <sup>**</sup> (e)	Japan	1	13	11	74	- a stock tray instead of a border-molded custom tray	19.0 ±14.3	19.5 ±15.5	-	-	-	-	84.5 ±39.0	91.0 ±16.3
Miyayasu et al., 2018 <sup>**</sup> (e)	Japan	1	13	11	74	- algininate instead of silicone	-	-	-	-	39,621 ±4,048	44,175 ±4,404	-	-
Ceruti et al., 2017 <sup>6</sup> (f)	Italy	6 m	32	32	70	- no preliminary impression - combining the definitive impression, the recording of the maxillo-mandibular relationship, and the selection and arrangement of the anterior teeth in 1 step	-	-	946.4 ±131.2	1,203.3 ±178.9	-	-	81.0 ±1.16	88.0 ±0.76
Lira-Oetiker et al., 2018 <sup>7</sup> (g)	Chile	6 m	21	17	72	- no functional impression (with a modelling compound and ZOE impression paste) - no assembly on the articulator	-	-	-	-	-	-	76.9 ±29.6	85.7 ±12.8

Data presented as mean ± standard deviation (SD), except for OHIP in the study by Regis et al., which is expressed as mean (confidence interval (CI)).

n – number of patients in particular groups; S – simplified (SCD – simplified complete denture); C – conventional (CCD – conventional complete denture); OHIP – Oral Health Impact Profile; VAS – visual analog scale; ZOE – zinc oxide eugenol; \* crossover designs (all other studies had parallel groups); \*\* satisfaction was also assessed at 10 years; \*\*\* used OHIP-20 and was not included in the meta-analysis (all other studies used OHIP-19); a–g – the 7 studies described in the 11 articles.

Three studies assessed impact on quality of life, 7 studies assessed patient satisfaction, 3 studies assessed cost, and 2 studies assessed time to deliver dentures to patients. Of these 7 studies that were included in the 11 papers, 2 were crossover studies and the remaining 5 included parallel groups. The total number of participants was 24–105. The follow-up period ranged from 1 month to 10 years. In most studies, the steps that were most frequently omitted in SCD preparation in relation to CCD were face-bow transfer and the final impression. The satisfaction estimates from 3 studies were not used in the meta-analysis, as 2 studies reported estimates after 1 month and 3 months,<sup>5,22</sup> respectively, whereas in the 3<sup>rd</sup> study (by Kawai et al.<sup>10</sup>), satisfaction was assessed after 6 months, but only for a subset of the sample of another study that was already included. In 1 study, impact on quality of life measured with OHIP-19 was assessed at 1 month and that study was not included in the meta-analysis.<sup>5</sup>

Table 2 shows that all 7 studies described in the 11 articles adequately explained the inclusion/exclusion criteria and reported that outcome assessors were blinded to the group the patients were allocated to. Patients were not informed of the differences between the 2 types of dentures so that their reporting on satisfaction and impact on quality of life could not be biased. All studies except 1 explained how the sample size was estimated and detailed the underlying assumptions. Two studies did not explicitly show the number of participants available at follow-up, and 3 studies

did not show differences between the groups at baseline or account for baseline differences in the analysis. Allocation concealment was the area where most studies showed weakness, with only 2 studies clearly describing the method of randomization and allocation concealment. The total quality score ranged from 6 to 12 (Table 2).

Figure 2 shows that the VAS score for satisfaction of the 4 included studies ranged from a mean difference of 6, favoring SCD, to a mean difference of –8.8, favoring CCD. None of the studies reported significant differences. These results were homogenous ( $I^2 = 0\%$ ) and the overall difference was not statistically significant, slightly favoring SCD (mean difference: = 0.896, 95% CI (confidence interval): –2.947, 4.739) (Fig. 2).

Figure 3 shows the differences in impact on quality of life between SCD and CCD reported in 2 studies. In both studies, the difference was not statistically significant. The overall difference slightly favored SCD (mean difference: 0.379), although the difference was not statistically significant (95% CI: –0.994, 1.751) (Fig. 3).

Figure 4 shows that each of the 3 studies assessing the cost difference between the 2 types of dentures reported a lower cost of SCD compared to CCD. When transformed to 2018 USD, the cost of SCD and CCD expressed as mean  $\pm$  standard deviation (SD) was 40.64  $\pm$  10.63 and 63.35  $\pm$  16.86, respectively, in the Brazilian study,<sup>18</sup> 844.68  $\pm$  47.71 and 1,037.93  $\pm$  39.23, respectively, in the Canadian study,<sup>4</sup> and 350  $\pm$  35.81 and 390.23  $\pm$  38.91, respectively,

Table 2. Quality assessment of the studies

Study	Randomization and allocation concealment	Sample size estimation method	Inclusion/exclusion criteria defined	Adequate number of participants available at follow-up	Comparability of groups at baseline	Outcome assessors blinded	Total
Regis et al., 2013 <sup>19</sup> Vecchia et al., 2014 <sup>18</sup>	2	2	2	2	2	2	12
Kawai et al., 2005, 2010, 2018 <sup>20,4,10</sup>	0	2	2	2	2	2	10
Núñez et al., 2015 <sup>21</sup>	0	2	2	2	2	1	9
Heydecke et al., 2008 <sup>22</sup>	0	0	2	2	0	2	6
Jo et al., 2015 <sup>5</sup> Miyayasu et al., 2018 <sup>9</sup>	0	2	2	0	2	2	8
Ceruti et al., 2017 <sup>6</sup>	0	2	2	0	0	2	6
Lira-Oetiker et al., 2018 <sup>7</sup>	2	2	2	2	1	2	11

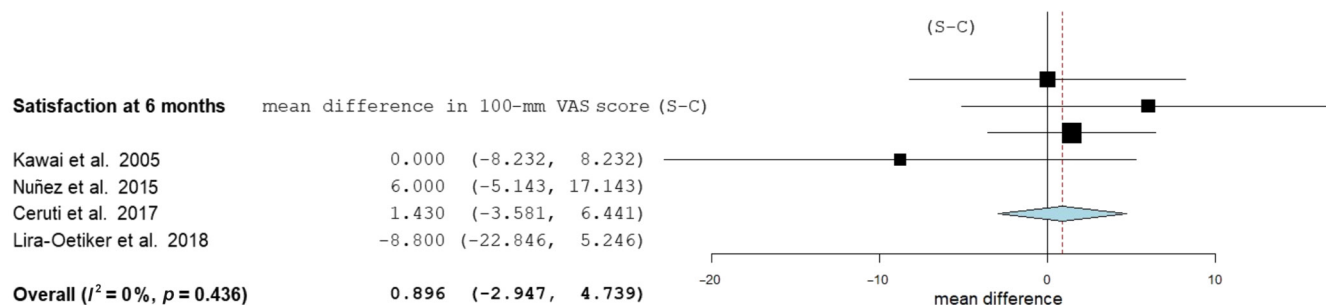


Fig. 2. Forest plot of the meta-analysis of the difference between simplified complete denture (SCD) and conventional complete denture (CCD) in satisfaction at 6 months

in the Japanese study.<sup>9</sup> The lowest proportion of cost of SCD to CCD that was reported by Veccia et al. was statistically significant and the absolute cost of the 2 types of dentures was the lowest.<sup>18</sup> The results of the 3 studies were homogenous ( $I^2 = 3.1\%$ ). The overall estimate indicated a significantly lower cost of SCD as compared to CCD (proportion: 0.740, 95% CI: 0.597, 0.882) (Fig. 4).

Figure 5 shows that significantly less time was needed for SCD delivery as compared to CCD in the Brazilian<sup>18</sup> and Italian<sup>6</sup> studies. The results were homogenous ( $I^2 = 0\%$ ;  $p = 0.1$ ) and the overall estimated difference between the 2 types of dentures was significant (mean difference: -274.16, 95% CI: -334.17, -199.96), indicating that less time was needed for SCD delivery (Fig. 5).

Figure 6 shows the funnel plot of the studies included in the present meta-analysis. The almost symmetrical distribution of the studies in the plot and the  $p$ -value of Egger's test of 0.79 indicate that there was no publication bias (Fig. 6).

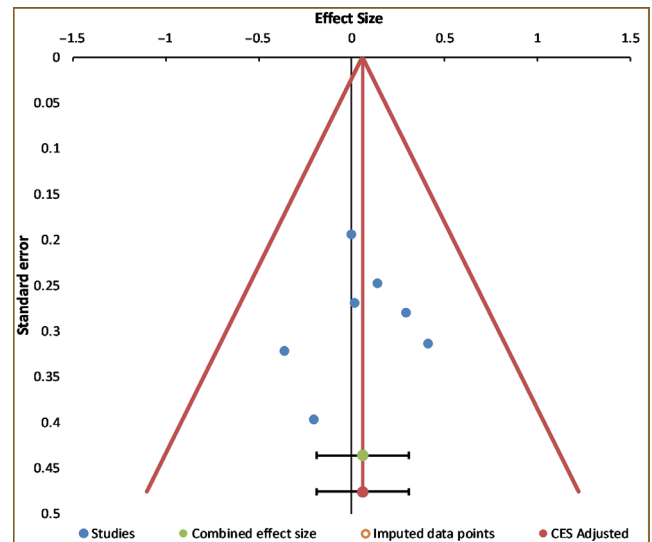


Fig. 6. Funnel plot to assess publication bias  
CES – combined effect size.

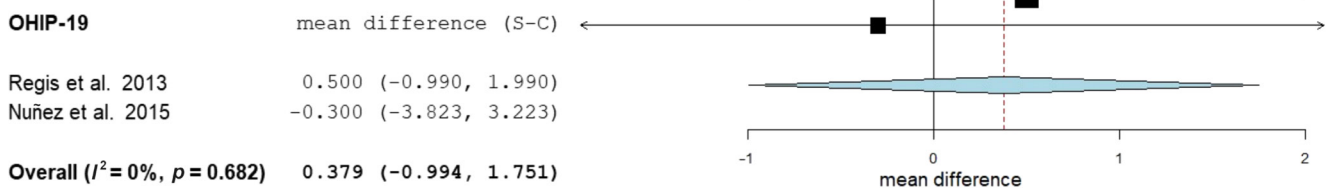


Fig. 3. Forest plot of the meta-analysis of the difference between simplified complete denture (SCD) and conventional complete denture (CCD) in impact on quality of life at 6 months

OHIP-19 – Oral Health Impact Profile-19.

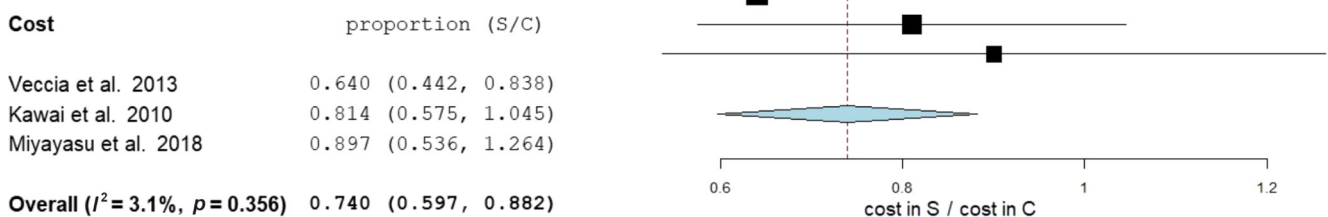


Fig. 4. Forest plot of the meta-analysis of the cost proportion (SCD / CCD)

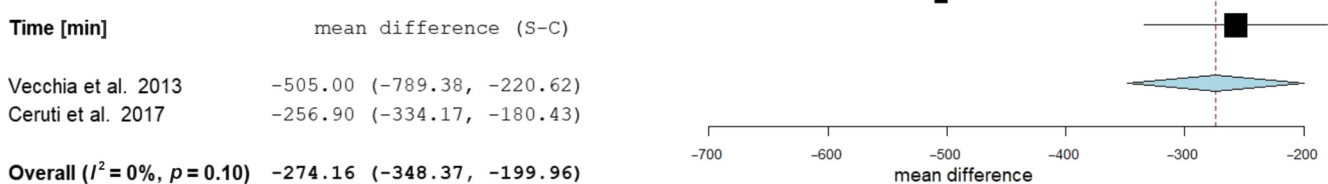


Fig. 5. Forest plot of the meta-analysis of the difference between simplified complete denture (SCD) and conventional complete denture (CCD) in the time needed to deliver the dentures

## Discussion

The present meta-analysis showed that the 2 types of dentures had a similar impact on quality of life and patient satisfaction. It took significantly less time (about 4.5 h (274 min)) to deliver SCD to the patient and the cost of SCD was significantly lower than in the case of CCD (75% of the cost of CCD). The results of the present meta-analysis are in agreement with the 2 previous systematic reviews, which reported a shorter treatment time, a lower cost, and similar satisfaction and impact on quality of life for SCD in relation to CCD.<sup>3,8</sup> The present meta-analysis has implications for patients who may be in need of less time-consuming or less costly complete dentures, and may thus benefit from the use of SCD. Our findings also have implications for dental education in the area of complete dentures. It is important to introduce dental students to SCD as an alternative to CCD in indicated cases, since the equality of the 2 types of dentures was demonstrated.

The Canadian study reported the highest absolute cost for both types of dentures.<sup>4</sup> This may be attributed to health care system characteristics, and is in agreement with a previous study assessing the direct and indirect cost of treating obesity.<sup>17</sup> In the same study<sup>4</sup> and also in the Japanese one,<sup>9</sup> the cost of SCD as compared to CCD was not significantly different. Only in the Brazilian study, where the absolute cost was the lowest for both dentures, was the proportion of cost of SCD to CCD significantly lower.<sup>18</sup> This indicates that the cost advantage of SCD was more evident in less expensive settings. The cost comparison between the 2 types of dentures forms the basis for recommending that more studies be conducted in low-resource settings to compare the expenditure for both types of dentures and the magnitude of cost reduction in the case of SCD in comparison with CCD.

Both studies evaluating the difference between the 2 dentures in the time needed to deliver the denture to the patient showed statistically significantly less time in the case of SCD. However, Vecchia et al.<sup>18</sup> reported almost twice as big time difference as Ceruti et al.<sup>6</sup> This may be explained by the number and type of steps used to fabricate SCD in the 2 studies. Vecchia et al. reported the absence of face bow transfer and the use of a single try-in for the anterior and posterior teeth together.<sup>18</sup> In the study by Ceruti et al., 3 steps (the definitive impression, the recording of the maxillo-mandibular relationship, and the selection and arrangement of the anterior teeth) were performed during 1 visit, which helped decrease rather the number of visits than the overall time.<sup>6</sup> This reduced time may be of greater usefulness to elderly patients, who have mobility and/or transportation problems; in their case, fewer visits and less time would be appreciated.

The maximum follow-up in the studies included in this meta-analysis was 6 months, with the exception of 1 study. This is a short time considering how long complete dentures are expected to be used. The similarity in

patient satisfaction and impact on quality of life would be expected to change with time. In the single study with a follow-up longer than 6 months, satisfaction and impact on quality of life was assessed also after 10 years.<sup>10</sup> On a scale ranging from 0 to 120, the mean OHIP-20 score for SCD was 81.7 and for CCD it was 71.1, with a difference of 10.6/120 or 8.8%, which is greater than the difference in the present study (0.38/38 or 1%). Similarly, the same study reported the VAS scores at 6 months of 92 and 91.5 for SCD and CCD, respectively, and the VAS scores after 10 years of 90 and 77.5, accordingly. This may point to a greater difference with time in satisfaction and impact on quality of life, favoring SCD. It is difficult, however, to generalize this conclusion based on a single study.


The present systematic review and meta-analysis has some limitations. It was based on studies having generally small sample sizes and – except for 1 study – short follow-up periods. The current evidence is derived from generally high-resource settings. Future studies are needed in low-resource settings to assess if the cost difference between the 2 types of dentures would still be significant. Such studies are needed before an evidence-based recommendation can be made for the use of SCD regardless of the economic background based on the equality of patient-reported outcomes and a reduced treatment time. The present meta-analysis was based on studies that seem to be free from publication bias, which further bolsters confidence in its findings.

## Conclusions

The present meta-analysis used data from 11 publications reporting on 7 studies conducted in 6 countries. A simplified complete denture was similar to CCD in terms of patient satisfaction and impact on quality of life. It required less time to be delivered in addition to having a lower cost.

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# Activity of enzymatic antioxidants in periodontitis: A systematic overview of the literature

## Aktywność antyoksydantów enzymatycznych w zapaleniach przyzębia – systematyczny przegląd piśmiennictwa

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A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation;  
D – writing the article; E – critical revision of the article; F – final approval of the article

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### Abstract

Periodontitis is initiated by a bacterial infection and an abnormal immune response of the host resulting in the formation of dysbiotic subgingival biofilm and the progressive destruction of the attachment apparatus of the teeth. It is believed that disturbances in the local and/or general indicators of oxidative stress are one of the mechanisms in the etiopathogenesis of periodontitis. Organisms using oxygen in their metabolic processes are equipped with mechanisms that protect against the activity of oxygen-free radicals. They are commonly referred to as 'the antioxidative barrier of the system'. The main enzymatic antioxidants which have been widely studied in the gingival fluid, saliva and blood serum of patients with periodontitis are superoxide dismutase (SOD), glutathione peroxidase (GPx) and catalase (CAT).

The aim of this systematic overview of the literature was to present the current research on the activity of these antioxidant enzymes in the gingival fluid, saliva and blood serum of patients with periodontitis.

Findings on the activity of these enzymes in the gingival tissue, gingival fluid, saliva, and blood serum in the course of the types of periodontitis that have been classified so far (chronic or aggressive) are quite disparate. Their activity in the gingival tissue was usually elevated, whereas in the saliva it was reduced. These differences may have resulted from the different methods of biochemically assessing their activity, and may have not reflected the stage and/or the risk of progression of periodontitis.

**Key words:** periodontitis, oxidative stress, antioxidants, superoxide dismutase

**Słowa kluczowe:** zapalenie przyzębia, stres oksydacyjny, antyoksydanty, dysmutaza ponadtlenkowa

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## Introduction

The existence of reactive oxygen species (ROS) is integrally connected to the metabolism of all aerobic organisms. In physiological conditions, ROS act as the mediators and regulators of many biochemical processes. However, a disturbance in the balance between the processes of production and degradation of ROS leads to damage to cellular components. Oxidative stress can be defined as a situation in which a disturbance in this oxidoreductive balance leads to a temporary or chronic increase in the production of ROS and, as a consequence, to a disturbance in the cellular metabolism and the degradation of cellular components.<sup>1</sup> Organisms using oxygen in metabolic processes are equipped with mechanisms that protect against the activity of oxygen-free radicals.<sup>2–4</sup> Enzymatic antioxidants include superoxide dismutase (SOD; EC (Enzyme Commission number) 1.15.1.1), glutathione peroxidase (GPx; EC 1.11.1.9) and catalase (CAT; EC 1.11.1.6), among others.

Periodontitis is a multifactorial disease which leads to progressive periodontal tissue destruction and is connected with dysbiotic biofilm. Pathogenic biofilm is a prerequisite for the development of periodontitis, but it cannot initiate the disease on its own. It has been proven that periodontitis may be related to the local and/or systemic indicators of oxidative stress.<sup>5</sup> After the immune reaction is initiated by the biofilm, neutrophils are the cells that most often occur in the gingival fluid of the periodontal pocket. In one study, polymorphonuclear leukocytes (PMNs) isolated from patients with early periodontitis produced much more superoxide anion radical ( $O_2^{\bullet-}$ ) than the cells from the control group.<sup>6</sup> During the ‘respiratory burst’, catalyzed by nicotinamide adenine dinucleotide phosphate (NADPH) oxidase, hyperactive neutrophils produce large amounts of  $O_2^{\bullet-}$ .<sup>7</sup> This radical can be transported to phagolysosomes and the extracellular environment and, subsequently, it can be transformed into hydrogen peroxide ( $H_2O_2$ ) by SOD or spontaneous dismutation. This compound can be further metabolized by GPx and CAT.<sup>8</sup>

Superoxide dismutase catalyzes the reaction of  $O_2^{\bullet-}$  dismutation into oxygen and  $H_2O_2$ . It has been proven that SOD also exhibits enzymatic activity toward other substrates, for example, singlet oxygen. Three isoforms of SOD (SOD-1, SOD-2 and SOD-3) have been distinguished; they differ by the type of cofactor, their sensitivity to inhibitors and their location in the cell.<sup>9–11</sup>

Glutathione peroxidase catalyzes the reduction of  $H_2O_2$  and organic peroxides with the use of reduced glutathione. Four isoforms of this enzyme have been distinguished (GPx-1, GPx-2, GPx-3, and GPx-4). In the active center of each type, selenocysteine can be found, an amino acid which enables the 2-electron oxidation of glutathione.<sup>9</sup> This enzyme plays an important role in the case of low concentrations of  $H_2O_2$  in the cell.<sup>12,13</sup> Salivary peroxidase (Px) can be further distinguished in the environment

of the oral cavity. The Px system consists of GPx and myeloperoxidase (MPO),  $H_2O_2$ , and a thiocyanate ion ( $SCN^-$ ).<sup>14,15</sup> In the presence of  $H_2O_2$ , Px oxidizes  $SCN^-$ , which leads to the formation of bactericidal products, and helps regulate the amount of  $H_2O_2$  produced by bacteria and leukocytes (antioxidative activity). Myeloperoxidase, synthesized by neutrophils and monocytes, catalyzes the oxidation of a chloride ion ( $Cl^-$ ) and the reduction of  $H_2O_2$  into hypochlorous acid (HOCl), which forms bactericidal chloramines with amines.<sup>14,16</sup> Peroxidase is one of the most important antioxidants synthesized by the salivary glands, even though it constitutes only 0.01% of the total protein content in the saliva.<sup>17</sup>

The activity of CAT is twofold, depending on the concentration of  $H_2O_2$  in the cell. At high concentrations of  $H_2O_2$ , the enzyme catalyzes the reaction of  $H_2O_2$  dismutation, which leads to the production of oxygen that is used by the body in metabolic processes. At low concentrations of  $H_2O_2$ , this enzyme acts as Px, whose activity is related mainly to the deactivation of  $H_2O_2$ .<sup>12,13</sup>

The aim of this systematic overview of the literature was to present the current research on the activity of antioxidant enzymes – SOD, GPx and CAT – in the gingival tissue, gingival fluid, saliva, and blood serum of patients with periodontitis. It can serve as the basis for establishing the role of enzymatic antioxidants in the course of periodontitis.

## Material and methods

This systematic overview of the literature was carried out in accordance with the guidelines of the Preferred Reporting Items for Systemic Reviews and Meta-Analyses (PRISMA).<sup>18</sup>

The questions regarding the overview were as follows:

- Is there a difference in the activity of SOD, GPx and CAT in the gingival tissue, gingival fluid or in the saliva in relation to the control group?
- In periodontitis, is there a difference in the activity of those enzymes in the blood serum in relation to the control group?

The overview referred to all publications in English, German, Polish, and Russian concerning research on the activity of SOD, GPx and CAT in the course of periodontitis. Only original in vivo human studies were considered; no abstracts, letters to editors, case reports, or review papers were included.

The inclusion criteria were as follows: chronic or aggressive periodontitis (CP or AgP) in generally healthy individuals; and the presence of at least 15 teeth. The following exclusion criteria were adopted: a systemic disease affecting the oxidoreductive balance; nicotine use; periodontal treatment within 6 months prior to the study; pregnancy; or a lack of a control group, defined as healthy periodontium or gingivitis.

The information was obtained from electronic databases. Electronic selection was carried out in the MEDLINE (PubMed), Scopus and Polish Medical Bibliography databases. Works published before the end of 2018 were included. The following key words were used while searching for the potential papers: periodontitis; periodontal diseases; oxidative stress; enzymatic antioxidants; superoxide dismutase (SOD); glutathione peroxidase (GPx); and catalase (CAT). The articles obtained in that manner were then independently verified by both authors (TK and JT) in terms of the inclusion and exclusion criteria.

In the preliminary selection, abstracts, case reports, review papers, animal studies, in vitro studies, and repeated publications were eliminated. Statistical differences between the activity of SOD, GPx and CAT in the gingival fluid, saliva, blood serum, or gingival tissue between patients with periodontitis (the study group) and individuals with healthy periodontium or gingivitis (the control group) had to be determined for the studies to qualify for the overview.

Both authors (TK and JT) independently obtained the following data from each study: the author, the year of publication, the country of the study, the sample size, the age of the participants, the definition of periodontitis, the method of the biochemical test, the average values of SOD, GPx and CAT in the biological fluids assessed, and the *p*-value along with the type of statistical test carried out.

## Results

The initial overview identified 1,108 items thematically related to the role of oxidative stress in periodontitis. After careful analysis, 19 papers meeting the inclusion criteria were selected. In the final qualification, 4 studies with endpoints different from the adopted ones were excluded.<sup>19–22</sup> Finally, 11 controlled clinical studies were classified for the overview,<sup>23–33</sup> along with 4 clinical intervention studies.<sup>34–37</sup> The process of selecting works for the systematic review is presented in Fig. 1.

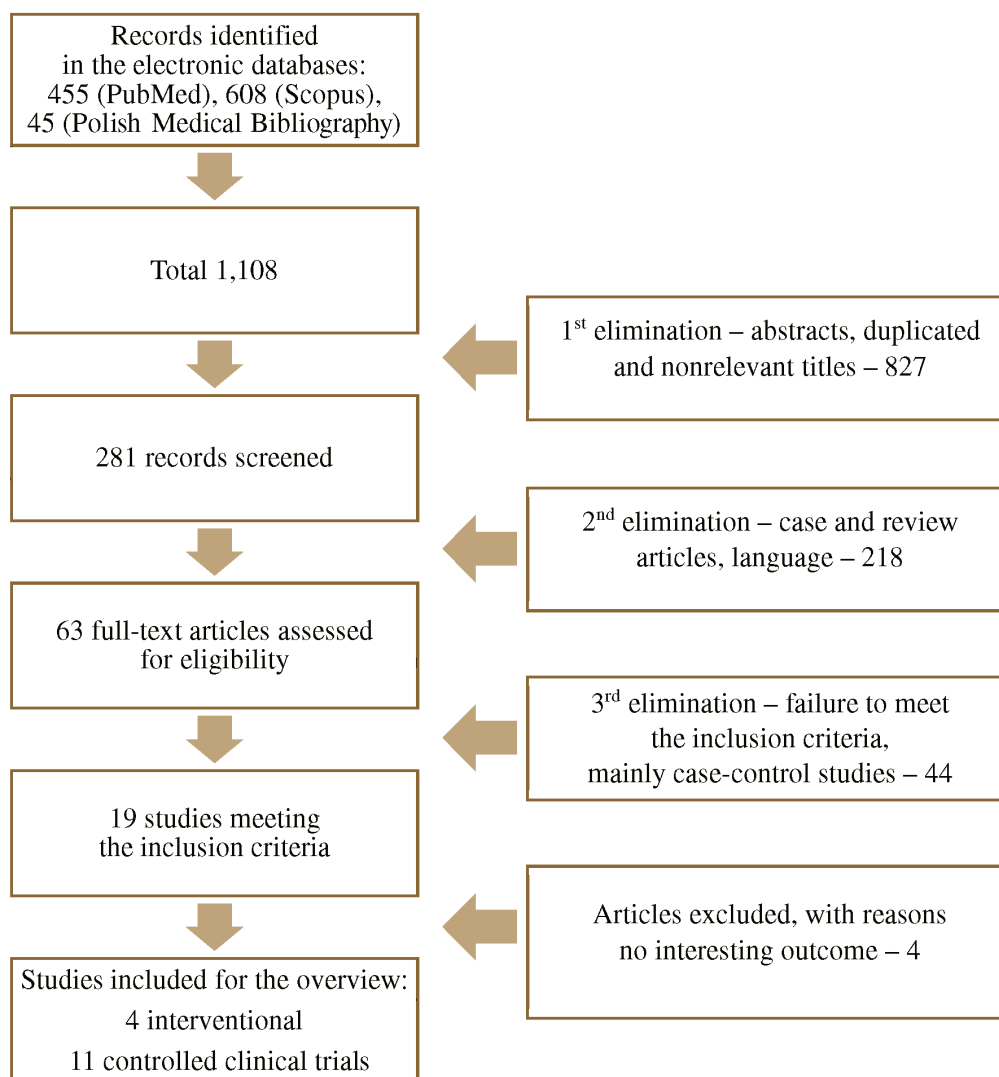


Fig. 1. Flow chart of the study selection process for the systematic review

## Superoxide dismutase

The qualified studies on the activity of SOD in patients with periodontitis in comparison with a control group are presented in Table 1. Three studies reported a higher activity of SOD in the gingival tissue of patients with periodontitis than in the control group.<sup>23,24,35</sup> A higher SOD activity in the blood serum of patients with periodontitis than in the control group was found in only 1 study,<sup>34</sup> and a lower activity was observed in as many as 5 studies.<sup>23,26,27,30,36</sup> The lowest SOD activity was found in the blood serum of patients with AgP.<sup>30</sup> In 1 study, a higher SOD activity occurred in the saliva of patients with periodontitis in relation to the control group,<sup>34</sup> and in 2 others it was lower.<sup>25,28</sup> In 1 paper, a higher activity of SOD was observed in the gingival fluid of patients with periodontitis than in the control group,<sup>34</sup> whereas in 2 other studies it was significantly lower.<sup>29,30</sup> The lowest activity of SOD was observed in the gingival fluid of patients with AgP.<sup>30</sup>

In 2005, Panjamurthy et al. carried out a study on a group of 25 males with CP.<sup>23</sup> The control group consisted of 25 males with clinically healthy periodontia. A higher activity of SOD was observed in both the gingival tissue and the blood serum of patients with periodontitis as compared to the control group ( $p = 0.001$ ).<sup>23</sup>

Also in 2005, Akalin et al. conducted a study on a group of 26 patients with CP, aged 31–52, and 18 people with clinically healthy periodontia, aged 22–29.<sup>24</sup> The activity of SOD in the gingival tissue in the CP group was significantly higher than in the case of the control group ( $p = 0.0001$ ). Although the experimental group showed a lower SOD activity in the gingival fluid than the control group did, the difference was not statistically significant ( $p = 0.356$ ).<sup>24</sup>

Canakci et al. assessed SOD activity in a group of 30 patients (15 males and 15 females), aged 31–63, with CP.<sup>25</sup> The control group consisted of 30 periodontically healthy patients (15 males and 15 females), aged 27–59. It was found that SOD activity in the saliva was significantly lower in patients with CP than in the control group ( $p < 0.05$ ). Additionally, in patients from the experimental group, a significant positive correlation between SOD and GPx was observed. A significant negative correlation between SOD activity in the saliva and the biomarkers of oxidative damage – the 8-OHdG protein and malondialdehyde (MDA) – was also observed. No significant correlations between SOD activity in the saliva and the indicators of the clinical condition of the periodontium were found.<sup>25</sup>

Wei et al. conducted a study on a group of 48 patients (27 males and 21 females), aged  $40.1 \pm 7.3$  years, with CP.<sup>34</sup> The control group consisted of 35 people (19 males and 16 females) with clinically healthy periodontia, aged  $42.1 \pm 7.7$  years. The concentrations of SOD were higher in the blood serum, saliva and gingival fluid of patients

with CP than in the control group ( $p < 0.05$ ). It was also observed that the highest concentrations occurred in the gingival fluid rather than in the blood or saliva of patients with periodontitis.<sup>34</sup>

Dhotre et al. assessed the activity of SOD in the blood serum of a group of 25 patients with periodontitis.<sup>26</sup> A lower activity of SOD was observed in this group than in the control group ( $p < 0.001$ ).<sup>26</sup>

Sukhtankar et al. studied the activity of SOD in the gingival tissue of 20 patients with CP, aged 24–55, and in 20 individuals with healthy periodontia the same age.<sup>35</sup> A significantly higher SOD activity was observed in the gingival tissue of patients with periodontitis than in the control group ( $p = 0.00003$ ).<sup>35</sup>

Thomas et al. carried out a test for the SOD concentration in the blood serum of patients with periodontitis, patients with gingivitis and individuals with no clinical changes in the periodontium.<sup>36</sup> It was found that the SOD concentration in the blood serum of individuals with periodontitis and gingivitis were significantly lower ( $p < 0.001$ ) than in the healthy group.<sup>36</sup>

Sreeram et al. assessed the concentration of SOD in the blood serum of a group of 150 patients with periodontitis, aged  $41.0 \pm 12.2$  years.<sup>27</sup> The control group consisted of 150 patients without clinically noticeable changes in the periodontium, aged  $34.2 \pm 12.0$  years. A significantly lower activity of SOD was reported in the blood serum of the study group ( $p = 0.000$ ).<sup>27</sup>

Trivedi et al. conducted a study on a group of 30 patients with CP, aged 25–45.<sup>28</sup> The control group consisted of 30 periodontally healthy people, also aged 25–45. A significantly lower activity of SOD was found in the saliva of patients with periodontitis than in the control group ( $p < 0.01$ ). Moreover, an inverse correlation was proven between salivary SOD activity and the concentration of MDA, a marker of lipid peroxidation.<sup>28</sup>

Ghallab et al. assessed SOD activity in the gingival fluid of 50 patients with periodontitis, broken down into 2 equal groups of CP and AgP.<sup>29</sup> The control group consisted of 15 people with no clinical lesions in the periodontium. The activity of SOD in the gingival fluid was significantly lower in both experimental groups ( $p < 0.01$ ) and it was the lowest in patients with AgP.<sup>29</sup>

Narendra et al. conducted a study on a group of 78 patients with periodontitis, including 32 patients, aged 18–28, with AgP and 46 patients, aged 30–62, with CP.<sup>30</sup> Fifty periodontally healthy individuals, aged 20–52, comprised the control group. A significantly lower SOD activity was found in the blood serum and gingival fluid of patients with AgP and CP in comparison with the control group ( $p < 0.001$ ). A lower SOD activity was also observed in the blood serum of patients with AgP than in patients with CP ( $p < 0.001$ ). Likewise, a significantly lower SOD activity was found in the gingival fluid of AgP patients as compared to those with CP ( $p < 0.001$ ).<sup>30</sup>

**Table 1.** Summary of the activity of superoxide dismutase (SOD) in patients with periodontitis

Study, year, country	Size of the control and experimental groups, age [years]	SOD in the experimental vs. control group	Periodontitis definition	p-value
Panjamurthy et al., 2005 <sup>23</sup> India	experimental group (CP): 25 age: 25–35 control group: 25 age: 25–35	gingival tissue ↑ blood ↓	PD > 3.5 mm, presence of furcation and tooth mobility	gingival tissue 0.001 blood 0.001
Akalin et al., 2005 <sup>24</sup> Turkey	experimental group (CP): 26 age: 31–52 control group: 18 age: 22–29	gingival tissue ↑ gingival fluid ↓ NS	PD ≥ 5 mm, 50% periodontal bone loss	gingival tissue 0.0001 gingival fluid 0.356
Canakci et al., 2009 <sup>25</sup> Turkey	experimental group (CP): 30 age 31–63 control group: 30 age: 27–59	saliva ↓	PD ≥ 4 mm, 30% periodontal bone loss	<0.05
Wei et al., 2010 <sup>34</sup> China	experimental group (CP): 48 age: 40.1 ± 7.3 control group: 35 age: 42.1 ± 7.7	blood ↑ saliva ↑ gingival fluid ↑	according to the AAP criteria from 1999	blood <0.05 saliva <0.05 gingival fluid <0.05
Dhotre et al., 2012 <sup>26</sup> India	experimental group (CP and AgP): 25 control group: 25	blood ↓	PD ≥ 4 mm, CAL ≥ 4 mm	<0.001
Sukhtankar et al., 2013 <sup>35</sup> India	experimental group (CP): 20 age: 24–55 control group: 20 age: 24–55	gingival tissue ↑	PD ≥ 5 mm or CAL ≥ 2 mm in at least 4 teeth, with radiographic evidence of bone loss	0.00003
Thomas et al., 2014 <sup>36</sup> India	experimental group (CP): 25 control group (gingivitis): 25 control group (healthy): 25	blood CP – lowest gingivitis – medium healthy – highest	CAL ≥ 5 mm in at least 30% of the sites	<0.001
Sreeram et al., 2015 <sup>27</sup> India	experimental group (CP): 150 age: 41.0 ± 12.2 control group: 150 age: 34.2 ± 12.0	blood ↓	BOP in >30% of the periodontal sites, with PD of 1–3 mm, BOP and CAL ≥ 3 mm in >30% of all sites in the mouth	0.000
Trivedi et al., 2015 <sup>28</sup> India	experimental group: 30 age: 25–45 control group: 30 age: 25–45	saliva ↓	PD > 5 mm in at least 30% of the sites	<0.01
Ghallab et al., 2016 <sup>29</sup> Egypt	experimental group (AgP): 25 age < 35 experimental group (CP): 25 age > 35 control group: 15 age: > 20	gingival fluid AgP – lowest CP – medium control – highest	according to the AAP criteria from 1999	<0.01
Narendra et al., 2018 <sup>30</sup> India	experimental group (AgP): 32 age: 18–28 experimental group (CP): 46 age: 30–62 control group: 50 age: 20–52	blood AgP – lowest CP – medium control – highest gingival fluid AgP – lowest CP – medium control – highest	according to the AAP criteria from 1999	blood <0.001 gingival fluid <0.001

Age presented as range or as mean ± standard deviation (SD).

CP – chronic periodontitis; AgP – aggressive periodontitis; NS – non-significant; PD – pocket depth; AAP – American Academy of Periodontology; CAL – clinical attachment level; BOP – bleeding on probing; ↑ – higher; ↓ – lower.

## Glutathione peroxidase

A summary of the studies on the activity of GPx in patients with periodontitis in comparison with a control group which were selected for this review is presented in Table 2. A higher activity of GPx in the gingival tissue of patients with periodontitis was found in 2 studies.<sup>23,32</sup> A higher activity of GPx was observed in the blood serum of patients with periodontitis as compared to the control group in 1 study,<sup>23</sup> and in 2 studies, the observed activity was lower.<sup>26,27</sup> A statistically insignificantly higher activity of GPx was observed in the saliva of patients with periodontitis in relation to the control group in 1 study,<sup>31</sup> and in 2 reports, the activity was lower.<sup>25,33</sup>

Panjamurthy et al. observed a higher activity of GPx in both the blood and the gingival tissue of patients with CP as compared to individuals from the control group ( $p = 0.001$ ).<sup>23</sup>

Tsai et al. carried out a study on the activity of GPx in the saliva on a group of 21 patients (13 males and 8 females) with CP and 22 patients with clinically healthy periodontia.<sup>31</sup> No significant differences were observed in the salivary activity of this antioxidant enzyme between the compared groups.<sup>31</sup>

Borges et al. assessed GPx activity in the gingival tissue of 9 individuals with CP, aged  $52.9 \pm 5.0$  years, and in 9 individuals with no inflammatory changes in the

periodontium, aged  $51.1 \pm 9.6$  years.<sup>32</sup> A significantly higher GPx activity was observed in patients with CP than in the control group ( $p = 0.006$ ).<sup>32</sup>

Canakci et al. found that the GPx concentration in the saliva was significantly lower in patients with periodontitis than in individuals from the control group.<sup>25</sup> Moreover, a significant positive correlation was observed between GPx and SOD in patients from the experimental group. A significant negative correlation was also observed between GPx activity in the saliva and the biomarkers of oxidative damage (8-OHdG and MDA) ( $p < 0.05$ ). No significant correlations between GPx activity in the saliva and the indicators of the clinical condition of the periodontium were found.<sup>25</sup>

Dhotre et al. observed a significantly lower SOD activity in the blood serum of patients with periodontitis than in the control group ( $p < 0.001$ ).<sup>26</sup>

Miricescu et al. carried out a study on the salivary activity of GPx in a group of 20 patients with CP (5 males and 15 females), aged  $51.26 \pm 7.40$  years.<sup>33</sup> Twenty individuals with no clinical lesions in the periodontium were selected for the control group. The activity of GPx in the saliva of patients with periodontitis was significantly lower than in the control group ( $p < 0.05$ ).<sup>33</sup>

Sreeram et al. observed that GPx activity in the blood serum of patients with periodontitis was significantly lower than in the case of the control group ( $p = 0.000$ ).<sup>27</sup>

**Table 2.** Summary of the activity of glutathione peroxidase (GPx) in patients with periodontitis

Study, year, country	Size of the control and experimental groups, age [years]	GPx in the experimental vs. control group	Periodontitis definition	p-value
Panjamurthy et al., 2005 <sup>23</sup> India	experimental group (CP): 25 age: 25–35	gingival tissue ↑	PD > 3.5 mm, presence of furcation and tooth mobility	gingival tissue 0.001
	control group: 25 age: 25–35	blood ↑		blood 0.001
Tsai et al., 2005 <sup>31</sup> Taiwan	experimental group (CP): 21	saliva ↑ NS	not specified	>0.05
	control group: 22			
Borges et al., 2007 <sup>32</sup> Brazil	experimental group (CP): 9 age $52.9 \pm 5.0$	gingival tissue ↑	PD ≥ 5 mm, CAL ≥ 3 mm	0.006
	control group: 9 age: $51.1 \pm 9.6$			
Canakci et al., 2009 <sup>25</sup> Turkey	experimental group (CP): 30 age 31–63	saliva ↓	PD ≥ 4 mm, 30% periodontal bone loss	<0.05
	control group: 30 age: 27–59			
Dhotre et al., 2012 <sup>26</sup> India	experimental group (CP and AgP): 25	blood ↓	PD ≥ 4 mm, CAL ≥ 4 mm	<0.001
	control group: 25			
Miricescu et al., 2014 <sup>33</sup> Romania	experimental group (CP): 20 age: $51.26 \pm 7.40$	saliva ↓	PD ≥ 4 mm, >30% periodontal bone loss	<0.05
	control group: 20			
Sreeram et al., 2015 <sup>27</sup> India	experimental group (CP): 150 age: $41.0 \pm 12.2$	blood ↓	BOP in >30% of the periodontal sites, with PD of 1–3 mm, BOP and CAL ≥ 3 mm in >30% of all sites in the mouth	0.000
	control group: 150 age: $34.2 \pm 12.0$			

Age presented as range or as mean ± standard deviation (SD).

## Catalase

Table 3 presents a summary of CAT activity in patients with periodontitis in comparison with a control group based on the studies which qualified for this review. A higher CAT activity was observed in the gingival tissue of patients with periodontitis in 1 study and the result was statistically significant.<sup>23</sup> A higher CAT activity was found in the blood serum of patients with periodontitis as compared to the control group in 1 study,<sup>23</sup> whereas in another study it was lower.<sup>37</sup> A statistically significant lower CAT activity was observed in the saliva of patients with periodontitis than in those from the control group in 1 study.<sup>28</sup>

Panjamurthy et al. observed a significantly higher CAT activity in both the blood and the gingival tissue of patients with periodontitis as compared to individuals from the control group ( $p = 0.0001$ ).<sup>23</sup>

Borges et al. did not observe any significant difference in CAT activity in the gingival tissue of the experimental group in comparison with the control group ( $p = 0.523$ ).<sup>32</sup>

Thomas et al. carried out a study on CAT activity in 25 patients with periodontitis, 25 patients with gingivitis and 25 periodontally healthy individuals.<sup>37</sup> They showed a significantly lower CAT activity in the blood serum of patients with periodontitis than in patients with gingivitis and individuals with no inflammatory lesions in the periodontium ( $p < 0.001$ ).<sup>37</sup>

Trivedi et al. reported a lower CAT activity in the saliva of patients with periodontitis than in the control group ( $p < 0.001$ ).<sup>28</sup> A negative correlation between CAT activity and the MDA concentration was also observed.<sup>28</sup>

## Conclusions

Antioxidant enzymes, such as SOD, GPx or CAT, protect the structural and tissue integrity by preventing the harmful activity of oxygen-free radicals. An imbalance between the production of oxygen-free radicals and antioxidative mechanisms plays an important role in the etiopathogenesis of periodontitis. The activity of enzymatic antioxidants varies greatly in the course of periodontitis, especially in the gingival fluid and saliva. In the gingival tissue and blood serum, their activity is usually higher. These differences may result from the initial mobilization of the antioxidative reserves, which leads to an increase in the activity of antioxidant enzymes. Another probable explanation is a pathological increase in neutrophil activity and the oxidative burst of PMNs. Even with the nominal activity of antioxidant enzymes, the oxidoreductive balance is disturbed. Thus, the varied advancement of periodontitis is reflected by the activity of the enzymatic antioxidants. It is possible that the current classification of the advancement and progression risk of periodontitis created by Page and Eke insufficiently translates into the tissue, salivary and serum activity of those antioxidative factors. Due to a small number of studies and the small sample sizes of the study groups, it was not possible to carry out a meta-analysis. Significant limitations of the studies that have been carried out so far include very diverse methodologies of the biochemical analyses (antioxidant activity expressed in different units, which makes it difficult to combine studies in a meta-analysis), very diverse definitions of periodontitis, failure to assess the influence of the duration of periodontitis, and incomplete eradication of local and general factors, which may affect the antioxidant activity under study.

**Table 3.** Summary of the activity of catalase (CAT) in patients with periodontitis


Study, year, country	Size of the control and experimental groups, age [years]	CAT in the experimental vs. control group	Periodontitis definition	<i>p</i> -value
Panjamurthy et al., 2005 <sup>23</sup> India	experimental group (CP): 25 age: 25–35	gingival tissue ↑	PD > 3.5 mm, presence of furcation and tooth mobility	gingival tissue 0.001
	control group: 25 age: 25–35	blood ↑		blood 0.001
Borges et al., 2007 <sup>32</sup> Brazil	experimental group (CP): 9 age 52.9 ± 5.0	gingival tissue NS	PD ≥ 5 mm, CAL ≥ 3 mm	0.523
	control group: 9 age: 51.1 ± 9.6			
Thomas et al., 2014 <sup>37</sup> India	experimental group (CP): 25	blood	CAL ≥ 5 mm in at least 30% of the sites	<0.001
	control group (gingivitis): 25	CP –lowest gingivitis – medium		
	control group (healthy): 25	healthy–highest		
Trivedi et al., 2015 <sup>28</sup> India	experimental group: 30 age: 25–45	saliva ↓	PD > 5 mm in at least 30% of the sites	<0.001
	control group: 30 age: 25–45			

Age presented as range or as mean ± standard deviation (SD).



Further studies aimed at explaining the role of oxidative stress in the occurrence and course of periodontitis are undoubtedly necessary. The inclusion and exclusion criteria should be unified, as they may affect differences in the results between authors. Perhaps the new classification of periodontitis created during the World Workshop on the Classification of Periodontal and Peri-implant Diseases and Conditions will be linked to the local and/or general activity of the enzymatic antioxidants in a better and more homogeneous way. These studies may have important therapeutic implications in the local use of antioxidants in periodontitis treatment.

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## Oculo-auriculo-vertebral spectrum with radial defects, a bifid condyle and taurodontism: A case report

### Spektrum objawów oczno-uszno-kręgowych z wadami promieniowymi, dwudzielnym kłykiem i taurodontyzmem – opis przypadku

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#### Abstract

Goldenhar syndrome (GS) is a rare congenital anomaly involving the first and second branchial arches. It is an autosomal dominant genetic disorder in which there is abnormal prenatal development of the head and face leading to the subsequent asymmetry of craniofacial structures. It is generally sporadic, with its incidence ranging from 1:3,500 to 1:5,600 live births and a gender ratio of 3:2 (male:female). Goldenhar syndrome is considered to be a variant of hemifacial microsomia, characterized additionally by vertebral anomalies and epibulbar dermoids. Facio-auricular dysplasias represent a single disorder with great variability of expression, and an isolated ear malformation may represent the mildest expression of the disorder.

This report presents a case of the oculo-auriculo-vertebral spectrum (OAVS) with radial defects, a unilateral bifid condyle and taurodontism. The presence of a bifid condyle and taurodontism has not been previously reported in the literature. Whether this is a coincidental or new finding has to be hypothesized and confirmed. The documentation of all such new findings is of utmost importance for updating the existing literature.

**Key words:** hypoplasia, bifid condyle, hemifacial microsomia, Goldenhar syndrome, taurodontism

**Słowa kluczowe:** hipoplazja, dwudzielnny kłykieć, mikrosomia połowy twarzy, zespół Goldenhara, taurodontyzm

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## Introduction

In 1861, Goldenhar syndrome (GS) was first observed by Canton, and later in 1881 by an Austrian physician Ferdinand von Arlt; however, it went unnoticed.<sup>1</sup> In 1952, Maurice Goldenhar, a Belgian-American ophthalmologist, described the syndrome in detail as Goldenhar syndrome.<sup>2</sup> In 1963, Robert James Gorlin described this syndrome with vertebral anomalies.<sup>3</sup> It is also known as oculo-auriculo-vertebral (OAV) syndrome, hemifacial microsomia, first arch syndrome, first and second branchial arch syndrome, Goldenhar–Gorlin syndrome, lateral facial dysplasia, unilateral craniofacial microsomia, otomandibular dysostosis, unilateral intrauterine facial necrosis, and auriculo-branchiogenic dysplasia.<sup>4–6</sup> Very few cases with a radial defect are documented in the literature along with various other findings.<sup>7,8</sup> In this report, the author illustrated another case of the oculo-auriculo-vertebral spectrum (OAVS) with radial defects, along with an interesting finding of a bifid condyle and taurodontism.

## Case report

An 18-year-old female patient visited the Department of Oral Medicine and Radiology at Jaipur Dental College, India, with a complaint of sensitivity in the lower anterior teeth in the preceding 6 months. Her medical history revealed that she had consulted various physicians in her childhood for unilateral hearing loss and the upper left limb defect below the elbow. No investigations were conducted and the patient did not carry any records. Due to the poor financial status, the family had not sought any treatment. She was born of a full-term normal delivery at home. There was no history of maternal illness during pregnancy. All other family members were normal. She was born of a non-consanguineous marriage and all milestones were reported as normal. She was afebrile, with normal pulse rate, blood pressure and respiratory rate. The physical examination revealed a well-nourished 18-year-old, ambulating well, without limp or support. The lower extremity and neurovascular examination showed no abnormalities. An altered posture was evident, as the head was not centered in the mid-sagittal plane with a prominent sternocleidomastoid muscle on the left (Fig. 1). Her upper left limb showed a radial defect. There was radius hypoplasia and thumb agenesis (Fig. 2). A deformed left ear and ear tags were evident (Fig. 3), which could be classified as third-degree microtia according to Weerda. The patient reported partial hearing on the same side. Ocular changes were manifested with a whitish covering of the sclera in the left eye (epibulbar dermoids) and diminished vision (Fig. 1). Speech was not clear, as she also presented with partial ankyloglossia.



Fig. 1. 18-year-old female patient with an asymmetrical face and epibulbar dermoids on the left side

An additional oral examination showed facial asymmetry with hemifacial hypoplasia, limited mouth opening and a deviation of the mandible to the right on opening the mouth (Fig. 4). The intraoral examination revealed the crowding of the anterior teeth, a deep bite and generalized recession suggestive of chronic periodontitis (Fig. 5). Orthopantomography (OPG) revealed a hypoplastic left body of the mandible (evident as a reduced height and width of the body), ramus (a reduced height and width of the ramus compared to the right side) and condyle (Fig. 6). A prominent antegonial angle and a bifid condyle on the left (heart-shaped condylar head), missing upper third molars,



Fig. 2. Radial defect with only 4 fingers



Fig. 3. Deformed left ear with ear tags

and impacted lower third molar taurodontism with teeth 37 and 47 were visualized. An underdeveloped orbit, maxilla and hard palate on the left side were noticed. Generalized alveolar bone loss was also evident. An intraoral periapical radiograph of the 3<sup>rd</sup> quadrant clearly depicts hypotaurodontism with tooth 37 (Fig. 7). A diagnosis of OAVS with radial defects, a bifid condyle and taurodontism was suggested. The patient was referred for thorough evaluation to rule out other systemic involvement, as she required a multidisciplinary approach and would be treated accordingly.

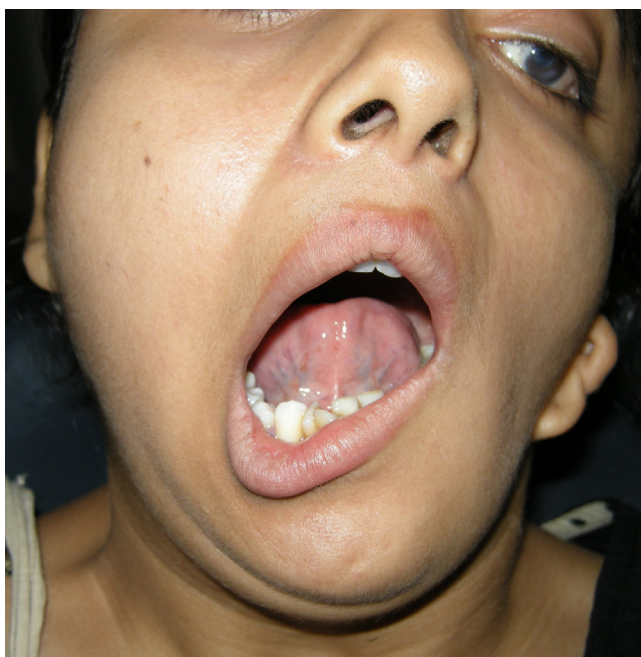


Fig. 4. Deviation of the mandible on mouth opening



Fig. 5. Intraoral view showing the crowding of the lower anterior teeth and gingival recession

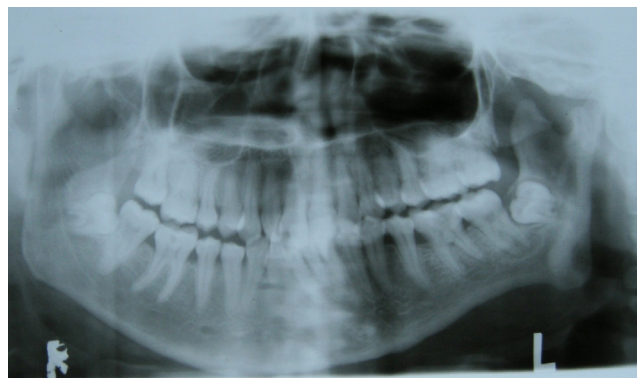


Fig. 6. Orthopantomography (OPG) revealing a hypoplastic mandible on the left side with a bifid condyle



Fig. 7. Intraoral periapical radiograph showing taurodontism with tooth 37

## Discussion

The oculo-auriculo-vertebral spectrum or GS is a well-recognized condition characterized by variable degrees of unilateral or bilateral involvement of craniofacial structures, including the first and second branchial arches, ocular anomalies and vertebral defects. In the present case,

a bifid condyle and taurodontism along with radial defects are presented, which has so far not been recorded in the literature in English.

Some authors suggested that GS might result from the interaction of many genes, possibly in combination with the environmental factors; others pointed to a possible link between genetic causes and vascular disruption, e.g., due to a fetal hemorrhage in the first and second branchial arches at the time when blood supply switches from the stapedial artery to the external carotid artery. Furthermore, disturbances in the development of the neural crest were indicated as possible reasons of this syndrome. The ingestion of drugs such as thalidomide, retinoic acid, tamoxifen, and cocaine by pregnant woman may be a risk factor as well. The pathogenetic mechanisms have been discussed theoretically and are a matter of controversy, but so far, no definitive causal agent has been confirmed. It has been postulated that GS represents a defect of blastogenesis that could be attributed to the interferences in cephalic neural crest cell migration; however, in some cases of OAVS with multisystemic malformations, the involvement of several developmental fields does not sustain localized damage.<sup>8–12</sup>

Clinically, it ranges from isolated microtia, with or without mandibular hypoplasia, to a more complex phenotype with skeletal, cardiac, renal, pulmonary, and central nervous system (CNS) manifestations. The oculo-auriculo-vertebral spectrum with radial defects is a subset within OAVS, mainly involving unilaterally or bilaterally the first branchial arches and limb primordium. The main signs include external, middle and internal ear malformations, facial asymmetry, orofacial clefts, mandibular hypoplasia, and a radial defect, which is a 'sine qua non' anomaly for the clinical diagnosis.<sup>8</sup> In the case presented, all of the signs were noticed, except for orofacial clefts. There was a bifid condyle and taurodontism with the lower left second molar, which has so far not been reported.

Due to the delay in growth and development, the effects of the syndrome appear more evident as the child grows, mainly as craniofacial microsomia. It is diagnosed clinically, but requires complementary evaluation that includes a hematological and hormonal study depending on the presentation as well as chromosome studies. An audiological investigation comprises pure tone audiometry, speech audiometry, tympanometry, stapedius reflex measurement, and brainstem auditory evoked response. Two-dimensional (2D) echocardiography for cardiac abnormalities, skull, facial, upper limb, and spine X-rays, temporal bone computed tomography (CT), spine CT, and magnetic resonance imaging (MRI) are also performed, if required.

The treatment depends on the patient's age and systemic manifestations, but generally requires a multidisciplinary approach.<sup>13–20</sup> In order to correct a craniofacial malformation, a team consisting of a maxillofacial and plastic surgeon, orthodontist, speech therapist, etc. is required,

along with a pediatrician, ophthalmologist, cardiologist, otolaryngologist, and genetic counselor.

At birth, the functional concerns in OAVS are the patency and adequacy of the airway, swallowing and feeding, hearing, vision, and the presence of other malformations that may have systemic implications.

Airway and oxygenation monitoring are essential. Airway problems can be treated by infant positioning, nasopharyngeal airway placement, tongue–lip adhesion, distraction osteogenesis to advance the mandible, or tracheotomy. Feeding difficulties are managed with nasogastric tube feeding or the placement of a gastrostomy tube to maintain a positive nitrogen balance while allowing sufficient oxygenation.

The aim of the treatment is to achieve better functioning and an esthetically pleasing outcome, allowing the patient to lead a normal life as much as possible. With the continued growth of the child, the effects of GS may become more pronounced, since the affected areas will show a significant delay in development. This can result in cosmetic concerns, breathing difficulties and malocclusion. The timing of primary and secondary reconstructions plays an important role in the complex treatment. Primary reconstruction consists of cleft repair, the corrections of colobomas and ear deformities, and the extirpation of dermoids and preauricular tags. Between years 2 and 4, no treatment is indicated for patients who are mildly affected. Reconstruction by a rib bone graft and the lengthening of the underdeveloped mandible with a bone distraction device is recommended in the case of a severely underdeveloped mandible, and modifications in the growth of teeth are made with the assistance of orthodontics. Orthodontic therapy may be started with removable appliances. With the appearance of permanent dentition, fixed orthodontic therapy can be initiated to create a proper occlusal plane, and to correct malocclusion and tooth discrepancies. The reconstruction of the external ear is performed in several stages over a period of 6–12 months between years 6 and 8, and the structural anomalies of the eye and ear can be corrected by means of plastic surgery. At the age of 8–10 years, the asymmetry of the cheeks is to be corrected. This may be the most important stage in the entire treatment program, in terms of physical appearance. Jaw surgery is carried out at or close to skeletal maturity, whereby in the case of mild involvement, no surgery is required. The extent of the temporomandibular joint (TMJ) dysmorphology is a principal factor when considering the timing of and techniques for mandibular reconstruction. Surgical correction includes costochondral rib grafts with osteotomy and distraction procedures.

Children with GS usually have reduced oral opening and/or malocclusion, and hence oral hygiene is more difficult, which exposes them to an increased risk of both dental caries and gingivitis. Toothbrushes with smaller heads and waterjet systems can be recommended to patients

with limited mouth opening to improve the mechanical removal of plaque. Regular dental visits that include topical fluoride application, with an emphasis on the prevention of future disease, should be an important consideration in these individuals, especially in the cases like the present one because of the disability of the limbs.<sup>21</sup>

The literature reveals that OAVS and radial defects have been reported in mothers with a history of diabetes and shows that pregnant women with pre-existing or gestational diabetes are at a higher risk of giving birth to a child with malformations. Therefore, special attention should be paid to maternal glycemia as a precautionary measure.<sup>8</sup>

## Conclusions

As OAVS subjects with radial defects are more frequently affected with cardiovascular defects, thorough systemic evaluation is mandatory for better quality of life and better prognosis. This case was a classical one with newer findings, and as such, it should be regarded as a contribution to the description of numerous GS features, updating the literature and knowledge.

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# Odontogenic keratocyst of the mandible: A case report and literature review

## Zębopochodna torbiel rogowaciejąca żuchwy – opis przypadku i przegląd piśmiennictwa

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## Abstract

Based on a literature review, we analyzed the World Health Organization (WHO) classification and the treatment algorithm for the odontogenic keratocyst (OKC), formerly referred to as keratocystic odontogenic tumor (KCOT).

The KCOT reclassification from benign odontogenic tumors to odontogenic developmental cysts resulted from the emergence of new evidence regarding their morphogenesis and biological behavior. The authors of the most recent 2017 classification do not provide specific guidelines for OKC. Nevertheless, it has been observed that conservative surgical management is not necessarily associated with recurrences characteristic of neoplastic disease.

The aim of this paper was to present the effective management strategy for a local recurrence that developed following conservative OKC enucleation in a 53-year-old patient. The treatment for recurrence consisted of enucleation, marginal osteotomy and augmentation with a cancellous bone graft harvested from a tibial tuberosity. A 6-year observation period (clinical and radiological monitoring) revealed normal bone regeneration and no evidence of recurrence.

The algorithm applied in our center for the treatment of OKC/KCOT was compared with the management strategies proposed by other authors.

**Key words:** odontogenic keratocyst, WHO classification, autogenic bone graft, recurrence

**Słowa kluczowe:** zębopochodna torbiel rogowaciejąca, klasyfikacja WHO, autogeny przeszczep kości, WZNOWA



## Introduction

The term 'odontogenic keratocyst' was first used in 1956 to describe an odontogenic cyst lined with keratinized stratified squamous epithelium. In 1992, the World Health Organization (WHO) introduced the term 'odontogenic keratocyst', synonymous with 'primordial cyst', to denote benign cysts of odontogenic origin and specific histological appearance. However, in 2005, considering a high risk of recurrence, aggressive clinical course, mutations in the tumor suppressor gene (*PTCH1*), the occurrence of satellite cysts, and the association with the Gorlin–Goltz syndrome, WHO reclassified this pathology as a benign keratocystic odontogenic tumor (KCOT).<sup>1,2</sup>

In 2017, though, WHO released a new classification of head and neck tumors. As there was insufficient evidence to categorize the abovementioned pathology as a neoplastic lesion, KCOT was moved back into the cyst category under the name of odontogenic keratocyst (OKC). However, the term 'keratocystic odontogenic tumor' is still in use. The authors of the 2017 classification do not specifically recommend any strict guidelines for OKC treatment. Nevertheless, it has been observed that conservative surgical management is not necessarily associated with recurrences characteristic of neoplastic disease.<sup>1–3</sup>

The aim of this paper was to analyze a 2-stage surgical intervention for OKC in a 53-year-old patient. We also analyzed a single-stage treatment for recurrence (which developed 2.5 years after the initial therapy), consisting of enucleation with marginal osteotomy and augmentation with a cancellous bone graft harvested from a tibial tuberosity.

## Case report

A 53-year-old hypothyroid – but clinically euthyroid – patient reported to the Outpatient Department of Dental Surgery at the University Dental Centre of the Medical University of Silesia in Bytom, Poland, for the diagnosis and treatment of a 2-chamber osteolytic lesion within the mandibular body (teeth 42–36), accidentally detected on a dental X-ray.

Extraoral examination revealed left facial asymmetry, but no submandibular lymphadenopathy. The following anomalies were also found: inactive fistula within the mucous membrane of the alveolar socket (tooth 45); mandibular body bulging (teeth 31–35); and bundle bone thinning characteristic of periapical cysts. Diagnostic imaging demonstrated a 2-chamber osteolytic lesion in the area of teeth 42–36. Teeth 42, 41, 31, 32, 33, 34, and 35 remained within the cystic lumen (Fig. 1).

The preparation for surgery consisted of the endodontic treatment of teeth 42, 41, 31, 32, and 33, and the extraction of teeth unsuitable for routine treatment (34 and 35). Then, intraoral cyst enucleation was performed (the area of teeth 33–36) and the root apex of tooth 33 was resected.

Subsequently, cyst decompression was carried out in the area of teeth 42–32. A cyst wall specimen was collected for histological examination. Based on the pathology reports, an initial diagnosis of mandibular body OKC was provided, and the decision was made to completely evacuate the lesion. A month later, cystectomy was performed in the area of teeth 42–32 with the apicectomy of teeth 42, 41, 31, and 32. Histological examination confirmed the initial diagnosis of OKC, a cyst with a connective tissue wall lined with parakeratinized stratified squamous epithelium (Fig. 2).<sup>4–6</sup>

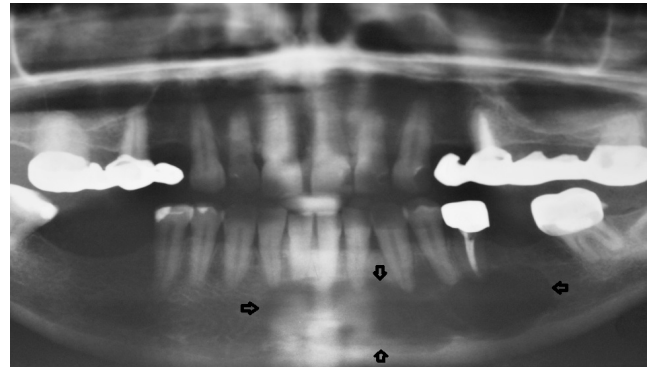


Fig. 1. Pre-treatment orthopantomogram showing a polycyclic osteolytic lesion in the area of teeth 42–36 (pointers)

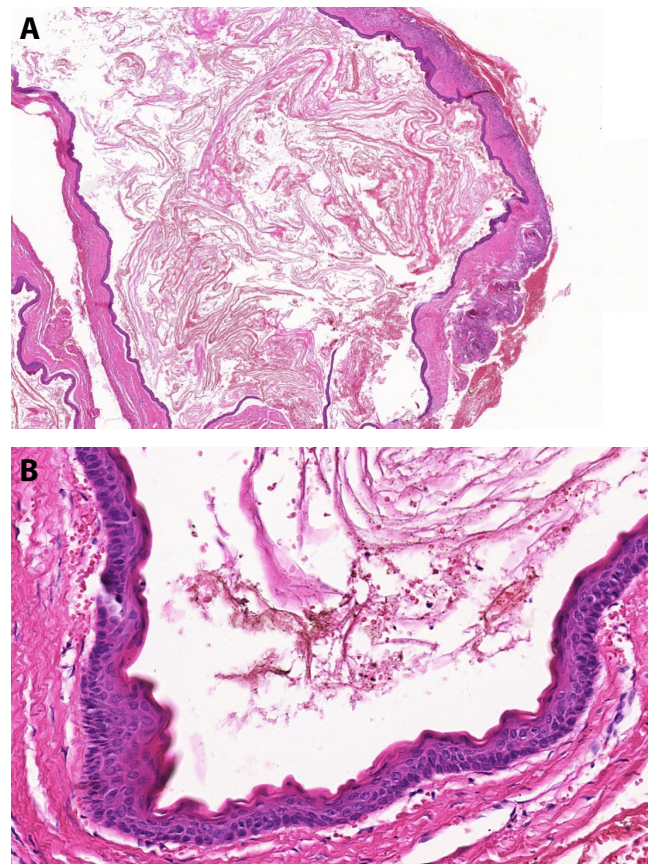
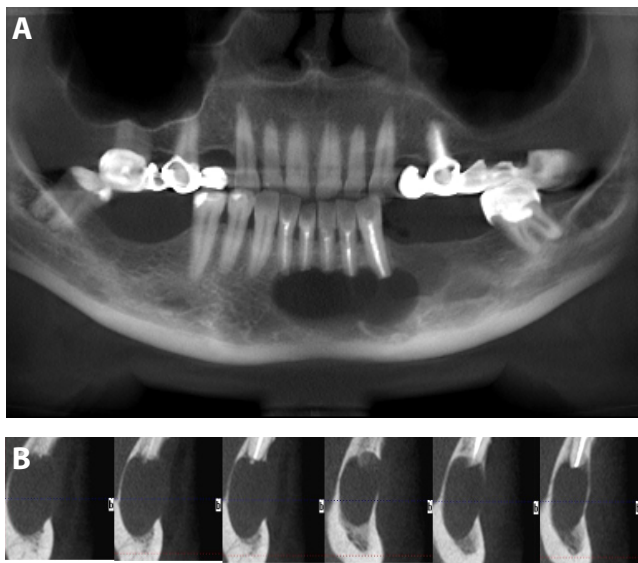
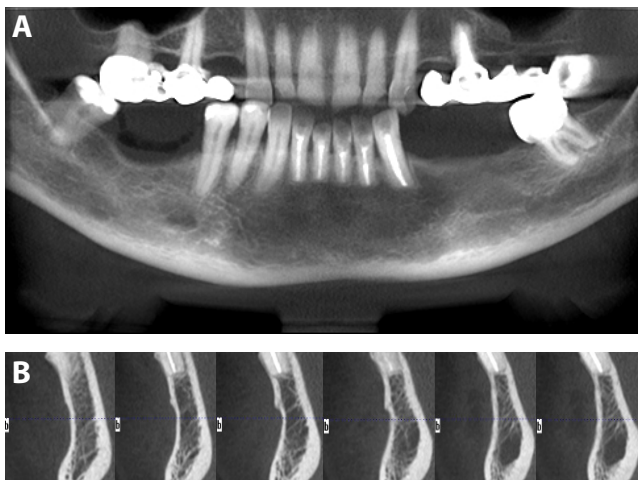


Fig. 2. A – cyst with a connective tissue wall lined with keratinized stratified squamous epithelium; the lumen contains a keratinaceous mass (hematoxylin and eosin (H & E);  $\times 5$  magnification); B – cyst with a connective tissue wall lined with parakeratinized stratified squamous epithelium; the lumen contains a keratinaceous mass (H & E;  $\times 65$  magnification)

The patient continued periodic monitoring at the Outpatient Department of Dental Surgery. A follow-up appointment 2.5 years after treatment revealed a local recurrence, an osteolytic lesion within the mandibular body between teeth 42 and 35 (Fig. 3). The patient was admitted to the Department of Maxillofacial Surgery at St. Barbara Provincial Specialist Hospital No. 5 in Sosnowiec, Poland, for radical surgery. Following the preparation for surgery, the lesion was resected along with a disease-free bone margin; re-apicectomy of teeth 42, 41, 31, 32, and 33 was also performed. The residual post-cystic cavity was augmented with a cancellous bone graft harvested from a left tibial tuberosity. Histological examination confirmed the recurrence of OKC; the bone margins were negative.



**Fig. 3.** A – orthopantomogram taken 2.5 years after the conservative surgical intervention, showing a mandibular keratocyst recurrence in the area of teeth 42–35; B – selected coronal sections of cone-beam computed tomography (CBCT) 2.5 years after the conservative surgical intervention, showing well-defined oval osteolysis beneath the previously resected root apices of teeth 42, 41, 31, 32, and 33 (keratocyst recurrence)

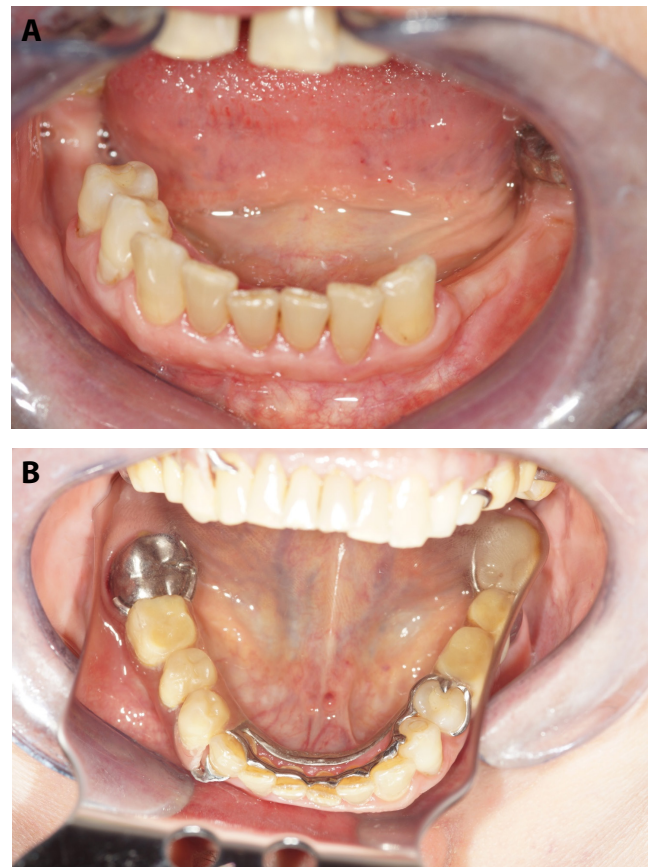


**Fig. 4.** A – follow-up orthopantomogram taken 4 years after marginal resection with the complete enucleation of the keratocyst in the area of teeth 42–35, showing normal bone regeneration; B – selected coronal sections of cone-beam computer tomography (CBCT) 4 years after marginal resection

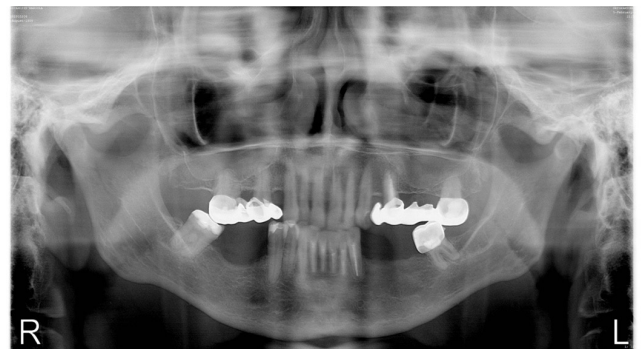
A follow-up X-ray and cone-beam computed tomography (CBCT) taken 4 years after marginal resection showed normal bone regeneration and no recurrence (Fig. 4).

The resected teeth (42, 41, 31, 32, and 33) demonstrated satisfactory stability within the dental alveoli, and hence served as sufficient support for frame dentures, which the patient continues to use (Fig 5).

The patient continues with annual follow-up appointments consisting of clinical and radiological monitoring of the post-cystic bone defect. A follow-up orthopantomogram taken 6 years after radical keratocyst resection demonstrated a complete remodeling of the autologous bone transplant (Fig. 6).



**Fig. 5.** Intraoral view 6 years after keratocyst resection and augmentation with a cancellous bone graft harvested from a left tibial tuberosity  
A – no clinical features of recurrence; B – no evidence of mandibular body deformities; wing defects restored with frame dentures.



**Fig. 6.** Follow-up orthopantomogram taken 6 years after keratocyst resection and augmentation with a cancellous bone graft harvested from a left tibial tuberosity: Complete bone remodeling within the post-cystic area

## Discussion

The reclassification of OKC from benign odontogenic tumors to odontogenic developmental cysts resulted from the emergence of new evidence regarding their morphogenesis and biological behavior. For example, it has been confirmed that a mutation of the *PTCH1* gene is not OKC-specific, as it also occurs in follicular cysts. Depending on whether the lesion is sporadic or associated with the Gorlin–Goltz syndrome, the *PTCH1* alterations are observed in 30–85% of OKCs. It has also been found that OKCs tend to regress following decompression or marsupialization, and that their lining spontaneously undergoes transition into normal oral epithelium. All of these features disqualify this clinical entity from being included in the category of neoplastic lesions and justify changing the name of the lesion to OKC.<sup>1</sup>

The abovementioned changes in nomenclature have had an impact on the strategy for OKC treatment, which mainly depends on the patient's age and compliance as well as the size and location of the lesion.<sup>1</sup> Bone resection offers the lowest recurrence rates. Segmental resection (removal of a bone segment without maintaining bone continuity) and marginal resection (removal of the lesion and a margin of uninvolved bone) are associated with recurrence rates ranging from 0% to 8.4%.<sup>1,7–10</sup> Despite their high efficacy, these interventions should be limited to multi-chamber lesions. Our patient presented with a recurrence 2.5 years after the initial conservative surgical intervention, hence the decision was made to perform marginal resection including a small bone fragment for histological examination.

Low recurrence rates are also characteristic of tumor enucleation with chemical curettage or cryodestruction. Chemical curettage consists in the application of Carnoy's solution (60% ethanol, 30% chloroform, 10% glacial acetic acid, and 1 g of ferric chloride) into the cyst cavity; the solution induces superficial tissue necrosis and helps eliminate the tumor remnants. In cryodestruction, the bony cavity is filled with liquid nitrogen. The recurrence rates are 14.5% and 11.5%, respectively.<sup>1,7–10</sup>


Conservative treatment, i.e., OKC decompression followed by enucleation or marsupialization (transformation of the cyst into an open pouch, allowing continuous drainage) is not recommended due to very high recurrence rates (17–56%).<sup>1,7–10</sup> Decompression should be followed by enucleation with chemical curettage, cryodestruction or marginal osteotomy, as it was in the case of our patient. The reported recurrence rate for 2-stage treatment is 14.6%.<sup>1,7–10</sup>


We decided on 1-stage radical surgery consisting of marginal resection and augmentation of the post-cystic defect with a cancellous bone graft harvested from a left tibial tuberosity. The treatment resulted in excellent mandibular bone regeneration. We have not come across any literature reports on similar augmentation methods

following OKC enucleation. It should be noted that this treatment allowed jawbone continuity to be maintained, and the teeth and the inferior alveolar nerve to be preserved. Naturally, there is some risk of disease recurrence in allogenic and autologous bone grafts, as reported by Tolstunov and Treasure and DeGould and Goldberg.<sup>11,12</sup> We would not define our method as superior to other treatment options, but it is undoubtedly worth recommending. An analysis of OKC recurrence with a larger sample size is needed, which we plan to be the subject of further research.


The patient's attitude and compliance with follow-up appointments (especially during the first 6 years after surgery, when the risk of recurrence is the highest) are prerequisites for successful treatment.<sup>7</sup> Based on our findings, we conclude that patients diagnosed with OKCs should be regularly monitored at outpatient clinics, including follow-up orthopantomography and CBCT – at least once a year and for 6 years following the surgical intervention.

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# Impact Factor Listing for Journals on Dentistry (2018)

## First part: Journals on General Dentistry (38 titles with IF: 0.72–5.13)

Journal title	Abbreviation	Country of publication	Frequency in a year	IF (change vs 2017)
Journal of Dental Research	J Dent Res	USA	12	5.13 (–0.26)
Dental Materials	Dent Mater	UK	12	4.44 (+0.41)
Journal of Dentistry	J Dent	UK	12 open access	3.28 (–0.49)
Molecular Oral Microbiology	Mol Oral Microbiol	Denmark	6	2.93 (+0.08)
International Journal of Oral Science	Int J Oral Sci	India	4	2.75 (–1.38)
Journal of the American Dental Association	J Am Dent Assoc	UK	12	2.57 (+0.09)
Clinical Oral Investigations	Clin Oral Investig	Germany	4 open access	2.45 (+0.07)
Community Dentistry and Oral Epidemiology	Community Dent Oral Epidemiol	Denmark	6	2.28 (+0.28)
BMC Oral Health	BMC Oral Health	UK	open access	2.05 (+0.44)
Odontology	Odontology	Japan	1–2 open access	1.813 (+0.36)
European Journal of Oral Sciences	Eur J Oral Sci	UK	6	1.81 (+0.16)
Brazilian Oral Research	Braz Oral Res	Brazil	4	1.77 (+0.55)
Journal of Esthetic and Restorative Dentistry	J Esthet Restor Dent	UK	6	1.72 (+0.18)
Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology	Oral Surg Oral Med Oral Pathol Oral Radiol	USA	12	1.69 (–0.02)
Archives of Oral Biology	Arch Oral Biol	UK	12	1.66 (–0.39)
International Dental Journal	Int Dent J	UK	6	1.63 (+0.24)
Acta Odontologica Scandinavica	Acta Odontol Scand	UK	6	1.57 (+0.04)
Journal of Applied Oral Science	J Appl Oral Sci	Brazil	4	1.51 (–0.20)
Dental Traumatology	Dent Traumatol	Denmark	6	1.49 (+0.08)
Gerodontology	Gerodontology	UK	2	1.46 (+0.03)
Journal of Oral & Facial Pain and Headache	J Oral Facial Pain Headache	USA	4	1.443 (–0.09)
British Dental Journal	Br Dent J	UK	24	1.44 (+0.16)
Dental Materials Journal	Dent Mater J	Japan	6	1.42 (+0.22)
Quintessence International	Quintessence Int	Germany	10	1.40 (+0.31)
Journal of Public Health Dentistry	J Public Health Dent	USA	4 open access	1.35 (–0.08)
Australian Dental Journal	Aust Dent J	Australia	4	1.28 (–0.21)
Journal of Evidence-Based Dental Practice	J Evid Based Dent Pract	USA	4	1.25 (–1.15)
International Journal of Dental Hygiene	Int J Dent Hyg	UK	4	1.233 (–0.15)
International Journal of Periodontics & Restorative Dentistry	Int J Periodontics Restorative Dent	USA	6	1.23 (–0.02)
Head & Face Medicine	Head Face Med	UK	open access	1.22 (–0.39)
International Journal of Computerized Dentistry	Int J Comput Dent	UK	4	1.21 (–0.48)
Journal of Craniomandibular Practice & Sleep Practice	Cranio	UK	6	1.14 (+0.05)
Journal of Oral Science	J Oral Sci	Japan	4	1.10 (+0.25)
Community Dental Health	Community Dent Health	UK	4	1.08 (+0.12)
Oral Health & Preventive Dentistry	Oral Health Prev Dent	UK	6	0.90 (–0.06)
Journal of Dental Sciences	J Dent Sci	China	4	0.78 (+0.17)
Journal of the Canadian Dental Association	J Can Dent Assoc	Canada	6	0.76 (–0.22)
American Journal of Dentistry	Am J Dent	USA	6	0.72 (–0.04)

**Second part: Journals on Specialist Dentistry (51 titles with IF: 0.07–7.86)**

Journal title	Abbreviation	Country of publication	Frequency in a year	IF (change vs 2017)
<b>Oral Surgery and Maxillofacial Surgery (8 titles)</b>				
Oral Oncology	Oral Oncol	UK	12	3.73 (−0.90)
International Journal of Oral and Maxillofacial Surgery	Int J Oral Maxillofac Surg	Denmark	12	1.96 (−0.20)
Journal of Cranio-Maxillo-Facial Surgery	J Craniomaxillofac Surg	UK	8	1.94 (−0.02)
Journal of Oral and Maxillofacial Surgery	J Oral Maxillofac Surg	USA	12	1.78 (−0.01)
Cleft Palate–Craniofacial Journal	Cleft Palate Craniofac J	USA	10	1.47 (+0.21)
British Journal of Oral & Maxillofacial Surgery	Brit J Oral Maxillofac Surg	UK	6	1.16 (−0.10)
Journal of Stomatology, Oral and Maxillofacial Surgery	J Stomatol Oral Maxillofac Surg	France	6	0.96 (+0.52)
Oral and Maxillofacial Surgery Clinics of North America	Oral Maxillofac Surg Clin North Am	USA	4	0.94 (−0.43)
<b>Dental Radiology (2 titles)</b>				
Dento Maxillo Facial Radiology	Dentomaxillofac Radiol	UK	8	1.53 (−0.32)
Oral Radiology	Oral Radiol	Japan	2 open access	0.68 (+0.22)
<b>Periodontology and Oral Pathology (8 titles)</b>				
Periodontology 2000	Periodontol 2000	Denmark	3	7.86 (+1.64)
Journal of Clinical Periodontology	J Clin Periodontol	USA	12	4.16 (+0.12)
Journal of Periodontology	J Periodontol	USA	12	2.77 (−0.63)
Oral Diseases	Oral Dis	Denmark	8	2.63 (+0.31)
Journal of Periodontal Research	J Periodontal Res	USA	6	2.61 (−0.26)
Journal of Oral Pathology & Medicine	J Oral Pathol Med	Denmark	10 open access	2.03 (−0.20)
Journal of Periodontal & Implant Science	J Periodontal Implant Sci	South Korea	6	1.47 (+0.4)
Medicina Oral Patologia Oral y Cirugia Bucal	Med Oral Patol Oral Cir Bucal	Spain	6 open access	1.28 (−0.39)
<b>Implant Dentistry (7 titles)</b>				
Clinical Oral Implants Research	Clin Oral Implants Res	Denmark	12	3.83 (−0.48)
Clinical Implant Dentistry and Related Research	Clin Implant Dent Relat Res	USA	4 open access	3.21 (+0.12)
European Journal of Oral Implantology	Eur J Oral Implantol	UK	4	2.51 (−0.29)
International Journal of Oral & Maxillofacial Implants	Int J Oral Maxillofac Implants	USA	6	1.73 (+0.04)
Implant Dentistry	Implant Dent	USA	6	1.21 (−0.09)
Journal of Oral Implantology	J Oral Implantol	USA	6	1.06 (−0.15)
Implantologie	Implantologie	Germany	4	0.07 (−0.06)
<b>Cariology and Endodontics (6 titles)</b>				
International Endodontic Journal	Int Endod J	UK	12	3.33 (+0.32)
Journal of Endodontics	J Endod	USA	12	2.83 (−0.05)
Caries Research	Caries Res	Switzerland	6	2.33 (+0.14)
Operative Dentistry	Oper Dent	USA	6	2.03 (−0.11)
Journal of Adhesive Dentistry	J Adhes Dent	Germany	4	1.88 (+0.18)
Australian Endodontic Journal	Aust Endod J	Australia	4	1.71 (+0.34)

Orthodontics (9 titles)				
American Journal of Orthodontics and Dentofacial Orthopedics	Am J Orthod Dentofacial Orthop	USA	12 open access	1.91 (+0.07)
Angle Orthodontist	Angle Orthod	USA	6	1.88 (+0.29)
European Journal of Orthodontics	Eur J Orthod	UK	6	1.84 (–0.19)
Korean Journal of Orthodontics	Korean J Orthod	South Korea	open access	1.48 (–0.14)
Orthodontics & Craniofacial Research	Orthod Craniofac Res	UK	4	0.95 (–1.13)
Journal of Orofacial Orthopedics	J Orofac Orthod	Germany	6 open access	0.927 (+0.20)
Progress in Orthodontics	Prog Orthod	Germany	2 open access	0.927 (–0.33)
Seminars in Orthodontics	Semin Orthod	USA	4 open access	0.47 (–0.04)
Australian Orthodontic Journal	Aust Orthod J	Australia	3	0.27 (–0.13)
Pediatric Dentistry (3 titles)				
Pediatric Dentistry	Pediatr Dent	USA	7	3.31 (+1.54)
International Journal of Paediatric Dentistry	Int J Paediatr Dent	UK	6	2.06 (+0.67)
European Journal of Paediatric Dentistry	Eur J Paediatr Dent	Italy	4	0.87 (–0.02)
Prosthetic Dentistry (6 titles)				
Journal of Prosthetic Dentistry	J Prosthet Dent	USA	12	2.79 (+0.44)
Journal of Prosthodontic Research	J Prosthodont Res	Japan	4	2.64 (–0.67)
Journal of Oral Rehabilitation	J Oral Rehabil	UK	12	2.34 (+0.29)
Journal of Prosthodontics	J Prosthodont	USA	6 open access	2.17 (+0.43)
International Journal of Prosthodontics	Int J Prosthodont	USA	6	1.53 (+0.20)
Journal of Advanced Prosthodontics	J Adv Prosthodont	South Korea	6	1.36 (+0.22)
Dental Education (2 titles)				
European Journal of Dental Education	Eur J Dent Educ	UK	4	1.53 (+0.19)
Journal of Dental Education	J Dent Educ	USA	12	1.51 (+0.42)

IF – impact factor.



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