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Effectiveness of laser-engineered copper-nickel titanium versus superelastic nickel-titanium aligning archwires: A randomized clinical trial

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Objective: To compare the effectiveness of laser-engineered copper-nickel titanium (SmartArch) and superelastic nickel-titanium (SENT) archwires in aligning teeth and inducing root resorption and pain experienced by patients. **Methods:** Two-arm parallel groups with a 1:1 allocation ratio were used. The participants were patients aged 11.5 years and older with 5–9 mm of mandibular anterior crowding who were indicated for non-extraction treatment. The primary outcome was alignment effectiveness, assessed using Little's irregularity index (LII) over 16 weeks with a single wire (0.016-inch) in the SmartArch group and 2 wires (0.014- and 0.018-inch) in the SENT group (8 weeks each). Secondary outcomes included root resorption evaluated by pre- and post-intervention periapical radiographs and pain levels recorded by the participants during the first week. **Results:** A total of 40 participants were randomly allocated into 2 groups; 33 completed the study and were analyzed (16 in the SmartArch group and 17 in the SENT group, aged 16.97 ± 4.05 years). The total LII decrease for the SmartArch and SENT groups was 5.63 mm and 5.29 mm, respectively, which was neither statistically nor clinically significant. Root resorption was not significantly different between the groups. The difference in pain levels was not statistically significant for the first 5 days following wire placement; however, there was a significant difference favoring the SENT group in the final 2 days. **Conclusions:** SmartArch and SENT archwires were similarly effective during the alignment phase of orthodontic treatment. Root resorption should be observed throughout the treatment with either wire. SmartArch wires demonstrated higher pain perception than SENT wires.

Key words: Alignment, Aligning archwires, Randomized clinical trial

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INTRODUCTION

Fixed orthodontic appliances have brackets attached to the teeth and archwires that connect them and induce stress in the teeth. The first set of archwires straightens teeth by reducing crowding and rotation. Light and continuous forces are assumed to move teeth in a regulated, predictable manner while causing minimal damage to the teeth and their supporting structures.[1-3]

Traditional nickel-titanium (NiTi) orthodontic archwires have a uniform composition; therefore, they exert the same force per deflection on all teeth.[4]

A patented pulsating laser technology was used to precisely program the transition zones in shape-memory alloys, creating SmartArch wires with different force zones. These force zones closely match Viecilli and Burstone's ideal resistance numbers, which represent the load proportion numbers between teeth to achieve similar stress in the compressive periodontal ligament zone.[5] In the incisor area, the force should be around 70 to 80 g, increasing to 300 g in the posterior segments.[6]

Manufacturers claim that SmartArch uses ideal forces to move teeth efficiently and reduces treatment time because it has seven preprogrammed zones to apply the right forces to each tooth;[7,8] however, it was reported that the pattern is inconsistent with the advertised force values.[9]

Many clinical trials have studied archwire effectiveness.[10-14] Results have shown inconsistent findings in alignment effectiveness and controversial outcomes in pain perception. Root resorption did not differ significantly among groups; however, one study suggested monitoring with superelastic nickel-titanium (SENT) wires. The results of the latest Cochrane systematic review found that there was insufficient evidence to determine the difference in the alignment rate between multistranded stainless steel wires and SENT archwires or heat-activated nickel-titanium (HANT) archwires. The same was found for conventional NiTi versus SENT or HANT, and SENT versus HANT.[1]

As no clinical trial (to our knowledge) has evaluated the efficiency of laser-engineered copper-nickel titanium archwires, this study was conducted to compare the alignment effectiveness, root resorption, and pain perception of SmartArch versus SENT.

Aim

This study compared the effectiveness of SmartArch and SENT in the early alignment phase of fixed appliance treatment.

Primary objective

To compare the degree of crowding relief among the anterior mandibular teeth at 4, 8, 12, and 16 weeks after treatment initiation.

Secondary objectives

First, to evaluate the extent of orthodontically induced inflammatory root resorption (OIIRR) in the apical region of the mandibular centrals after 16 weeks of treatment initiation. Second, to evaluate the level of perceived pain during the initial 7 days following placement of the first archwire.

The null hypothesis was that there would be no statistically significant difference in the effectiveness of SmartArch and SENT archwires during the leveling and alignment phase of orthodontic treatment.

PARTICIPANTS AND METHODS

Trial design

This was a multicenter randomized clinical trial with a matched allocation ratio (1:1) of 2 parallel groups and blinding of participants to the treatment groups.

On August 18, 2022, the trial was registered at ClinicalTrials.gov (NCT05510206).

Participants and settings

The participants were patients in need of orthodontic treatment who met the following criteria:

Inclusion criteria: (1) Patients with mandibular anterior teeth exhibiting 5–9 mm crowding according to Little's irregularity index (LII)[15] require fixed appliance orthodontic treatment. (2) All mandibular permanent teeth are present, excluding the third molars. (3) Overbite and overjet should not impede the placement of brackets on lower anterior teeth. (4) The lower incisors were not subjected to trauma or root resorption previously.

Exclusion criteria: (1) Past orthodontic treatment. (2) Severely crowded teeth such that proper engagement with the aligning archwire is not possible. (3) History of attachment loss and periodontal disease.

The study was conducted at 2 governments orthodontic centers in Baghdad by practicing orthodontists and clinicians during training. The Ethics Committee of the College of Dentistry, University of Baghdad, approved this study on April 10th, 2022 (reference number 611422).

Interventions

The universal bonding procedures were followed. The brackets (Pinnacle®, MBT prescription with 0.022-inch [-in] slot, Ortho Technology, Tampa, FL, USA) were bonded to the teeth using a light-cured composite (Light Bond; Reliance Orthodontic Products, Itasca, IL, USA).

One group received a 0.014-in SENT archwire, and the other received a 0.016-in SmartArch on the bonding

day. After 8 weeks, the first group replaced the 0.014-in archwire with the 0.018-in, while the second group kept the 0.016-in. The elastomeric modules fully tied the archwire to the brackets, which were replaced every 4 weeks in both groups.

Debonded brackets had to be replaced within 24 hours; otherwise, the patient was excluded from the study. Participants received appointment reminders 1 or 2 days in advance via phone. Lower arch impressions were obtained before the treatment (T0) and at 4 (T1), 8 (T2), 12 (T3), and 16 (T4) weeks. The study models were created using an extra-hard dental die stone (Elite Rock; Zhermack SpA, Badia Polesine, Italy). Periapical radiographs of the lower incisors were obtained at T0 and T4 using a paralleling technique. The participants recorded their pain levels using a visual analog scale (VAS) for 1 week following wire placement.

Outcomes

Primary outcome (alignment effectiveness)

Alignment effectiveness was measured according to the change in LII[15] by measuring the extent of mesio-distal displacement between the mesial contact points of the right and left mandibular canines using a digital Vernier caliper. Linear measurements were performed on good-quality study models free of impurities and defects acquired at T0, T1, T2, T3, and T4. Figure 1 shows the mandibular casts of patients in both groups at each stage of treatment, and Figure 2 shows the occlusal photographs taken at T0 and T4.

Secondary outcomes

Root resorption: Periapical radiographs captured with a digital sensor (NanoPix 2; Eighteenth, Changzhou, China) and a portable X-ray machine (HyperLight, Eighteenth) were used to evaluate the mandibular central incisors for root resorption at T0 and T4. The radiographs were produced with a 0.13-second exposure at 65 kV and 2.5 mA. The scoring index developed by Malmgren et al.[16] was used to evaluate root resorption. On a 5-point scale from grade 0 to grade 4, the score for the worst-affected central incisor, either left or right, was recorded.

Pain perception: For 7 days following bonding, the participants recorded their nightly pain or discomfort

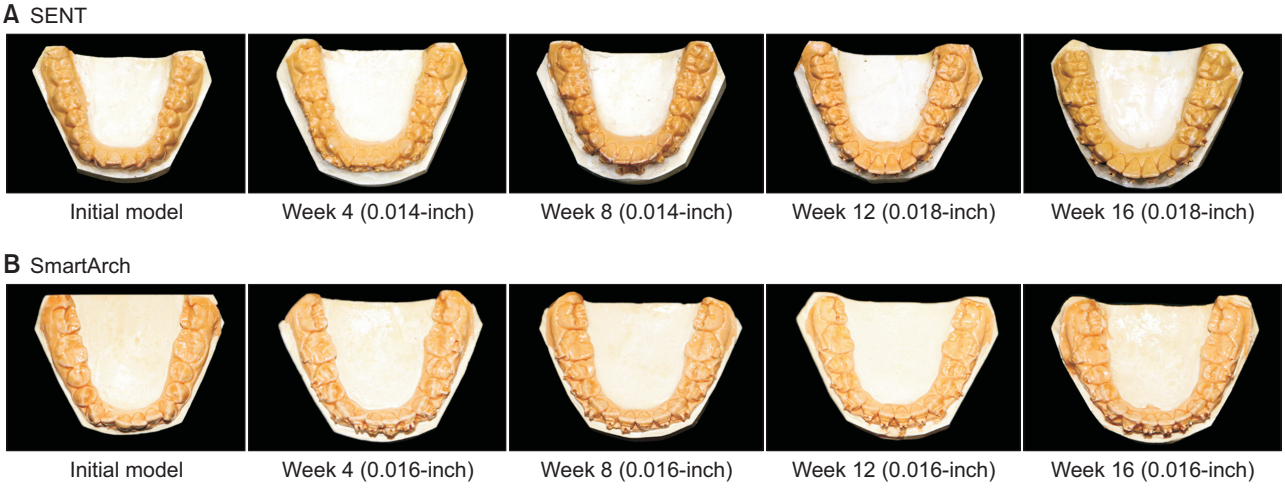

Figure 1. Mandibular casts of patients in both groups at each stage of treatment.
SENT, superelastic nickel-titanium.

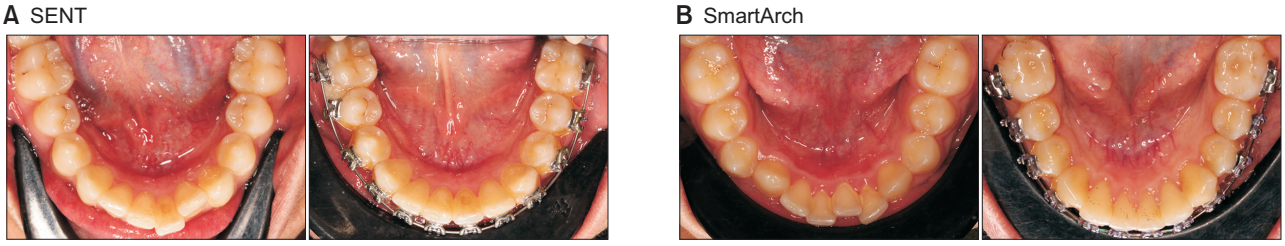

Figure 2. Occlusal photographs of patients in both groups before treatment and at the end of the trial.
SENT, superelastic nickel-titanium.

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on a 10-point VAS with a 10-cm length. Before taking the analgesics, they were instructed to mark the greatest daily pain level on the record sheet. To ensure compliance, participants were called or texted daily to complete the records, and the sheets were collected at T1.

Changes to the outcomes: No changes were made to the outcomes after the commencement of the trial.

Sample size calculation

The sample size for this study was determined based on an alpha level of 5% and 80% power to detect a 1.5 mm difference in crowding relief between the 2 treatment groups using data from a prior study by Nabbat and Yassir.[12] Thirteen patients in each arm were deemed sufficient to detect the clinical difference (26 total). To allow for a 15% dropout rate, the initial recruitment target was 30 participants, but 40 participants were ultimately enrolled due to seven early dropouts.

Stopping rule

The termination criteria for the experiment were set such that if any volunteer could not tolerate a certain level of pain, the trial was stopped.

Randomization

The participants were randomly assigned to either group using a non-stratified method with a 1:1 allocation ratio. A random number generator, available at http://www.randomization.com, was used to create a simple and straightforward allocation. An independent individual created a single allocation table that was used by the participants in both treatment centers. Each integer in the table represents the participant study number and allocation group.

The allocation and concealment processes were performed using sequentially numbered and sealed envelopes. The envelopes were numbered to correspond with the study numbers and contained the treatment allocation card and corresponding archwires for either Group 1 or 2.

The envelopes were sent to each center sequentially until the required number was reached. To enroll participants, practitioners were briefed on the criteria and notified by the investigator if the case met the criteria.

Blinding

A single blinding was executed for the patient.

Statistical analysis

Statistical analyses were performed using SPSS software (version 25.0; IBM Corp., Armonk, NY, USA). In addition to the descriptive statistics, several statistical tests were applied, including the following:

Reliability statistics: (1) To assess both the inter- and intra-examiner reliabilities of the LII, an intraclass correlation coefficient (ICC) was employed. Ten study models were measured twice, with a 4-week interval between each measurement. (2) The inter- and intra-examiner reliabilities of the root resorption scoring indices were assessed using the Kappa test. The test was performed by scoring 10 periapical radiographs twice at 4-week intervals.

Inferential statistics

The Shapiro–Wilk test was used to check the normality of variance between groups, and Levene's test was used to test for data homogeneity.

The statistical tests included: (1) An independent sample *t* test was used to compare the baseline readings for age and root resorption. (2) The chi-squared test was used to compare the sex distribution between the 2 groups. (3) A 2 × 2 mixed factorial analysis of variance (ANOVA) was used to analyze the difference in crowding relief between the groups with respect to time. (4) The Mann–Whitney *U* test was used to compare root resorption and pain perception scores between the groups at T0 and T4, while the Wilcoxon signed-rank test was used to assess the difference in root resorption scores within each group from T0 to T4. Significance was predetermined at $P < 0.05$.

RESULTS

Participant flow

The recruitment of the trial participants began in April 2022 and ended in August 2022 fulfilling the desired sample size.

Forty individuals initially participated in the clinical study, with 21 were allocated to the SENT group and 19 to the SmartArch group. However, seven participants withdrew from the study, leaving 33 patients (17 in the SENT group and 16 in the SmartArch group). The Consolidated Standards of Reporting Trials (CONSORT) flowchart of the study participants is shown in Figure 3.

Baseline data

The results of the Shapiro–Wilk test confirmed the normality of the data, even though this was not a concern given the assumption of a large sample size.

The results of Levene's test indicated the absence of inconsistencies. Table 1 shows baseline data. The independent sample *t* test showed that there was no significant age difference between the participants in the SmartArch and SENT groups. Similarly, there was no significant difference in sex distribution between the 2 groups, as indicated by the chi-square test. Additionally, the LII and root resorption scores showed no significant differences at T0, as indicated by the independent sam-

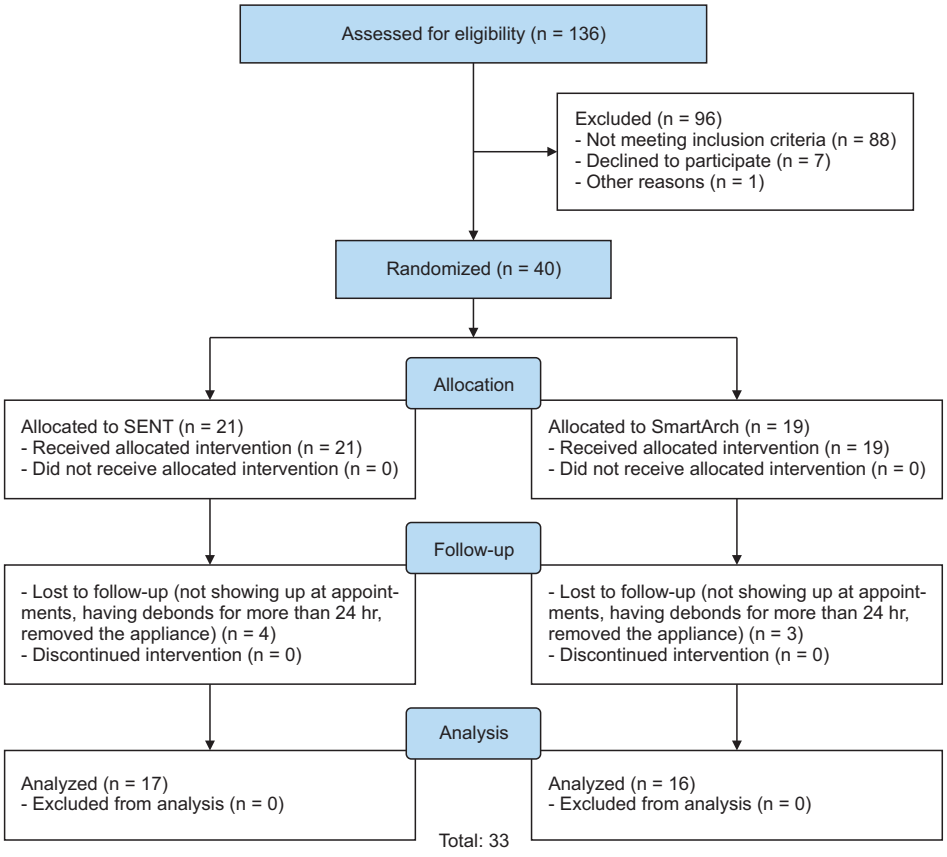

Figure 3. CONSORT flowchart of participants through each stage of the trial.
CONSORT, Consolidated Standards of Reporting Trials; SENT, superelastic nickel-titanium.

Table 1. Baseline characteristics of participants in each study group

Group	Age (yr)	Pre- treatment LII	Sex		Pre-treatment root resorption scores		
			Female	Male	0	1	2
SmartArch (n = 16)	18 ± 5.391	7.17 ± 1.31	9 (56.27)	7 (43.75)	10 (62.5)	6 (37.5)	0 (0.0)
SENT (n = 17)	16 ± 1.871	6.82 ± 1.39	12 (70.59)	5 (29.41)	6 (35.3)	10 (58.8)	1 (5.9)
P value	0.176[a]	0.470[a]	0.392[b]		0.101[c]		

Values are presented as mean ± standard deviation or number (%).
LII, Little's irregularity index; SENT, superelastic nickel-titanium.
[a]Independent sample *t* test; [b]Chi-square test; [c]Mann–Whitney *U* test.

ple *t* test and Mann–Whitney *U* test, respectively.

Reliability tests

The ICC values for inter- and intra-examiner reliability were 0.996 and 0.998, respectively, indicating an excellent level of agreement and reproducibility for the LII measurements. The kappa test showed very good reliability (0.8) for both inter- and intra-examiner root resorption measurements.

Outcome analysis

A total of 136 participants were assessed for eligibility; 40 met the study criteria, were randomized, and were almost equally allocated to the 2 groups (21 in the SENT group and 19 in the SmartArch group). Seven patients failed to continue the study for different reasons (not showing up at appointments, having debonded for more than 24 hours, removing the appliance, etc.). The remaining sample comprised 17 participants who received SENT and 16 participants who received SmartArch.

Table 2 presents data regarding the degree of crowding, pain perception, and root resorption at different stages of the study. After beginning with a slightly higher LII score for SmartArch (mean crowding of 7.17 mm for SmartArch vs. 6.82 mm for SENT), the final LII was in favor of SENT, with only 0.01 mm. To examine whether there was a significant difference between the groups as a consequence of the variable of time, as

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Table 2. Little's irregularity index scores, distribution of root resorption scores, and medians of pain perception in each group at different time intervals

Variable	SmartArch (n=16)		SENT (n=17)	
Little's irregularity index				
Start	7.17 ± 1.31		6.82 ± 1.39	
4 wk	3.98 ± 1.50		4.65 ± 1.51	
8 wk	2.84 ± 1.36		2.84 ± 1.02	
12 wk	2.11 ± 1.13		2.19 ± 0.77	
16 wk	1.54 ± 1.18		1.53 ± 0.72	
Root resorption (score)	**Count**		**Count**	
Pretreatment				
0	10 (62.5)		6 (35.3)	
1	6 (37.5)		10 (58.8)	
2	0 (0.0)		1 (5.9)	
16 wk of treatment				
0	3 (18.8)		0 (0.0)	
1	9 (56.3)		10 (58.8)	
2	4 (25.0)		7 (41.2)	
Pain perception (day)	**Median**	**Interquartile range**	**Median**	**Interquartile range**
First wk				
1st	6	5.50	5	5.5
2nd	5	4.50	5	5.5
3rd	2	3.75	3	4.5
4th	2	3.75	1	3.5
5th	2	2.75	0	3.5
6th	0	2.75	0	0
7th	0	2.00	0	0

Little's irregularity index: mean ± standard deviation; Root resorption: number (%); Pain perception: number.
SENT, superelastic nickel-titanium.

measured by the rate of change in LII, a 2 × 2 mixed factorial repeated measures ANOVA test was conducted.

Statistical analysis did not provide conclusive evidence for the effect of time interaction on the change in LII or for the effect of the 2 groups individually on this change. However, there was a statistically significant difference between the groups in terms of the rate of change in LII over time (Table 3).

The root resorption scores at T0 and T4 are shown in Table 2 for both the individual groups and for the entire sample. The SENT group scores were 0, 1, and 2, while the SmartArch group pretreatment scores were 0 and 1. After the therapy, the SENT group scored only 1 and 2, whereas the SmartArch group scored 0, 1, and 2. Compared with the SmartArch group, the SENT group had a somewhat higher level of root resorption at the T4 stage. The Mann–Whitney *U* test showed no statistically significant difference between the 2 groups regarding post-treatment root resorption scores (Table 4). The Wilcoxon signed-rank test showed that both groups had statistically significant differences between T0 and T4 (Table 5).

Table 3. A 2 × 2 mixed factorial ANOVA test for the difference between groups according to the change in LII with time factor (df = 1)

Source	*F*	*P* value
Time	76.956	< 0.001***
Time * type of wire	0.001	0.978
Type of wire	0.510	0.480

ANOVA, analysis of variance; LII, Little's irregularity index; df, degree of freedom.
***Statistically significant.

The Mann–Whitney *U* test revealed a non-significant

Table 4. Post-treatment root resorption Mann–Whitney *U* test between groups

Group	N	Mean rank	Sum of ranks	*P* value
SENT	17	19.18	326.00	0.129
SmartArch	16	14.69	235.00	
Total		33		

SENT, superelastic nickel-titanium.

Table 5. Difference in root resorption within each group using the Wilcoxon signed-rank test

Group	N	Mean rank	Sum of ranks	*P* value
SENT				
Post-PA - Pre-PA				
Negative Ranks	0[a]	0.00	0.00	0.001***
Positive Ranks	12[b]	6.50	78.00	
Ties	5[c]			
Total	17			
SmartArch				
Post-PA - Pre-PA				
Negative Ranks	0[a]	0.00	0.00	0.002***
Positive Ranks	10[b]	5.50	55.00	
Ties	6[c]			
Total	16			

[a]Post-PA < Pre-PA; [b]Post-PA > Pre-PA; [c]Post-PA = Pre-PA.
PA, periapical x-ray; SENT, superelastic nickel-titanium.
***Statistically significant.

difference between the groups regarding the perception of pain in the first 5 days after wire insertion. Nevertheless, for the last 2 days, there was a significant difference in favor of the SENT group, as shown in Table 6.

Harms

The only documented side effects were minor discomfort and root resorption, both of which are common sequelae of orthodontic treatment.

DISCUSSION

Study design

In the latest Cochrane review of initial arch wires, the authors drew attention to the weak quality of the evidence and the necessity for more trials to assess the efficacy of aligning arch wires. They highlighted the importance of randomized clinical trials (RCTs) that adhere to the CONSORT declaration in properly evaluating various alignment archwires on the market.[1]

Table 6. Mann–Whitney *U* test for pain perception

Day	N	Mean rank	Sum of ranks	*P* value
1st day				
SENT	17	14.97	254.50	0.211
SmartArch	16	19.16	306.50	
Total	33			
2nd day				
SENT	17	17.15	291.50	0.928
SmartArch	16	16.84	269.50	
Total	33			
3rd day				
SENT	17	18.56	315.50	0.334
SmartArch	16	15.34	245.50	
Total	33			
4th day				
SENT	17	15.71	267.00	0.412
SmartArch	16	18.38	294.00	
Total	33			
5th day				
SENT	17	15.88	270.00	0.465
SmartArch	16	18.19	291.00	
Total	33			
6th day				
SENT	17	14.35	244.00	0.038***
SmartArch	16	19.81	317.00	
Total	33			
7th day				
SENT	17	13.50	229.50	0.003***
SmartArch	16	20.72	331.50	
Total	33			

SENT, superelastic nickel-titanium.
***Statistically significant.

Since no previous RCT has evaluated the performance of SmartArch, this study used an RCT design to compare SmartArch to SENT archwires to determine any differences in alignment effectiveness, root resorption, and patient discomfort during the first stage of orthodontic therapy.

Except for a slightly higher pain rate in the SmartArch group in the last 2 days, no statistically significant differences were found between the groups. The null hypothesis was accepted for alignment and root resorption but partially rejected for pain perception. Because the power analysis used to determine the sample size was for the primary outcome, the secondary outcomes were

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carefully interpreted.

Sample characteristics

Simple randomization was adopted, although stratified randomization is preferable because of the complexity of identifying stratifying factors and the unknown number of covariates, which may result in an unrecognized bias due to the omission of any relevant covariate.

The minimum age of recruitment was 11.5 years old to ensure that all permanent teeth had erupted and to avoid bias from incomplete root growth in the mandibular anterior teeth when assessing OIIRR severity. Age was not included as a selection criterion, although it may have affected bone maturity. This factor can be seen as a confounding variable, whose effect is thought to be mitigated by randomization, which balances the differences in all factors that might affect the outcome of the study among groups;[17] indeed, no significant difference was found between the 2 groups in terms of participant age. Both groups had more females than males, which is in line with previous research showing that more females than males seek orthodontic care,[12,18,19] which could be attributed to the fact that females are more concerned about their smiles and aesthetics than males.

Intervention

In this study, the appointment duration was set at 4 weeks. The SENT group followed an archwire sequence that started with a 0.014-in wire and then transitioned to a 0.018-in wire after 8 weeks. For the SmartArch group, only a 0.016-in wire was used according to the manufacturer's recommendation that this size should be maintained until alignment is achieved, after which it should be replaced with a 0.018 × 0.025-in wire.

If the patients required analgesics, they were instructed to take their medication after recording their pain level and to have either ibuprofen or acetaminophen, because when these are prescribed in the lowest recommended doses, they have no inhibitory effect on the rate of orthodontic tooth movement.[20]

Alignment effectiveness

The findings of this study add further scope to studies comparing different aligning archwires. In previous studies, SENT and Copper-NiTi were found to be equally effective for the alignment of lower anterior teeth,[11] HANT and SENT had similar performance in the alignment phase,[12] and 0.014-in SENT and 0.016-in HANT wires had no clinical difference in the amount of tooth alignment or perception of pain.[18] In contrast, a different study indicated that HANT wires were more effective than SENT wires in alleviating crowding.[21]

The current study found that expensive archwires manufactured using advanced technology have comparable effectiveness in aligning the mandibular anterior teeth to readily available SENT.

Pain perception

Pain/discomfort was evaluated nightly for 7 days after bonding. Although some studies extended the VAS records for 1 month following the insertion of each aligning archwire,[22] pain is usually perceived in the first week after bonding. The pain-time pattern corresponds to the biological response to orthodontic forces. Interleukin-1β concentration in gingival crevicular fluid, which triggers the release of pain-inducing chemicals, increases after 1 hour, peaks at 24 hours, and returns to normal within 1 week to 1 month.[23] Detecting differences within this timeframe is clinically relevant.

The pain was evaluated in multiple RCTs, with two of them reporting similar pain levels with HANT and SENT wires,[11,12] while one study indicated higher pain levels associated with SENT wires compared to HANT.[10] In the current study, there was a statistically non-significant difference between groups in the first 5 days after wire insertion, but the last 2 days had a statistically significant and clinically relevant difference favoring the SENT group, which may be related to the fact that the SmartArch wire has 7 distinct zones that produce different forces. The higher forces in the molar region, which have been applied since the start of treatment, could have resulted in higher pain perception by the patient, which partially disagrees with the findings of the aforementioned RCTs.[11,12]

Root resorption

Root resorption studies are scarce, and comparing this to other studies is difficult because of the use of different appliances, archwires, assessment methods, assessment times, image types, and/or examined teeth than in the current study. Two RCTs concluded that there was no significant difference between HANT and SENT wires in terms of OIIRR, although one of the studies raised concerns about the use of SENT wires.[10,12] In contrast, 1 RCT reported increased root resorption with the use of SENT wires when compared to HANT wires.[21] In this study, neither type of archwire was found to significantly affect root resorption. The findings of this study corroborated those of a comprehensive overview of systematic reviews,[24] which concluded that there was no difference in the OIIRR with different archwire sequences.

The degree of root resorption was evaluated at baseline and after 16 weeks of treatment to determine any differences. Statistical analysis revealed a significant difference in the scores at T4 compared with those at T0 in both groups. This is a common finding and could be related to the consistent pressure these wires apply.[25] In-

termittent forces, on the other hand, might lead to less root resorption because the resorbed cementum has time to repair itself during periods of inactive tooth movement.[25,26] This finding supports the recommendation of radiographic monitoring of all patients, beginning with the preliminary stages of orthodontic therapy, to assess root resorption.

Strengths and limitations of the study

This is the first RCT to compare the effectiveness of a high-technology graded-force archwire with that of a conventional archwire.

Including both growing patients and adults in the current study, along with multicenter recruitment and the RCT design following the CONSORT guidelines, could make the outcome of this study more generalizable.

As with any randomized controlled trial involving orthodontic care, blinding of professionals to the allocation groups was not possible.

Root resorption was examined for only a limited time, which is another limitation of the present study.

Pain perception was compared only for the first wire because the SmartArch group had only 1 wire. In addition, variables such as age and sex and mental factors such as anxiety, sadness, and female hormone fluctuations during menstruation that may have occurred during the evaluation of pain were not taken into account.

Despite these limitations, the trial's primary and secondary objectives were met, suggesting that the research restrictions had little to no impact on the overall success of the research.

CONCLUSIONS

SmartArch and SENT archwires were similarly effective during the alignment phase of orthodontic treatment. A certain level of root resorption was observed, which requires monitoring during treatment with either wire. The SmartArch wires elicited higher pain perception than the SENT wires during the first week of treatment.

AUTHOR CONTRIBUTIONS

Conceptualization: ASK. Data curation: OKA. Formal analysis: ASK. Investigation: OKA. Methodology: ASK. Project administration: ASK. Resources: OKA. Visualization: OKA. Writing–original draft: OKA. Writing–review & editing: ASK.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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None to declare.

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