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Timing of Therapeutic Extractions Can Affect En Masse Anterior Retraction: A Split Mouth Randomized Clinical Trial

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Main Points

- The rate of space closure at the recent extraction site was faster than the healed site.
- There was no significant difference in the mesial movement of anchorage molars or rotation of canines into the extraction site between the two sides.
- Orthodontic retraction should be initiated immediately following therapeutic extractions; this would be a practical and non-invasive way of hastening tooth movement.

ABSTRACT

Objective: To investigate the effect of deferred timing of therapeutic extraction on the rate of space closure during en masse anterior retraction.

Methods: Twenty-six patients (aged 16-24 years) with bimaxillary protrusion, crowding <3 mm, requiring bilateral extraction of four first premolars were recruited. Permuted block randomization was done. Allocations were concealed in opaque envelopes which were numbered and sealed. Each patient's right and left quadrant was randomly assigned for premolar extraction. The extraction of the contralateral side was deferred until the commencement of retraction. The primary outcome was the rate of space closure, and the secondary outcomes were anchorage loss and canine rotation. Blinding was applied only during the outcome assessment. The independent t-test and Intraclass correlation tests were used for statistical evaluation.

Results: Twenty-four patients completed the study. The mean rate of space closure over a period of 4 months was found to be significantly higher for the recently extracted site (0.818±0.208) when compared with healed site(0.426±0.184)($p<0.001$). The tipping of the canine was also significantly higher for the former (6.042°±1.398°) than the latter (5.125°±1.035°) ($p<0.05$). However, the amounts of anchorage loss and canine rotation were insignificant. No adverse effects were noted.

Conclusion: The rate of space closure at the recent extraction site was faster than that at the healed site. There was no significant difference in the mesial movement of anchorage molars or rotation of canines into the extraction site. The tipping of canines was significantly greater in the recent extracted quadrant. The results of this trial indicate a clinical recommendation to initiate orthodontic retraction immediately following therapeutic extractions and offer a practical, non-invasive, safe procedure for increasing the rate of tooth movement.

Keywords: Accelerated tooth movement, regional acceleratory phenomenon, rate of space closure, recently extracted site, healed site

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INTRODUCTION

The long-time span required for orthodontic treatment is a significant concern for both patients and orthodontists. The average duration of treatment is reported to range from 19.4 and 27.9 months and 18.1-24.5 months for extraction and non-extraction therapies, respectively.[1] Prolonged treatment times can lead to increased risks of dental caries, periodontal problems, and root resorption.[2,3] It can also adversely affect patient compliance and satisfaction.

Literature reveals an impetus to accelerate tooth movement by various means in the last decade.[4-10] These include surgical and non-surgical interventions (mechanical vibration, low-level laser therapy, low intensity pulsed ultrasound). Surgical approaches range from highly invasive procedures like corticotomy-facilitated orthodontics,[4] Periodontally Accelerated Osteogenic Orthodontics,[5] and dentoalveolar distraction[6,7] to minimally invasive procedures such as corticision,[8] piezocision,[9] and micro-osteo perforations (MOPs).[10] All invasive modalities were performed to take advantage of the "Regional Acceleratory Phenomenon" (RAP)[11] which is reported to induce transient functional osteopenia and decreased mineral density, thereby accelerating bone turnover and facilitating tooth movement through remodeling. RAP begins within a few days of injury, peaks at 1-2 months and lasts typically for approximately 4 months.[5,12]

The above procedures, whether invasive or minimally invasive, are all performed as additional interventions. It is possible that routine orthodontic extractions could also trigger the RAP phenomenon and thereby accelerate tooth movement. Hence, the timing of therapeutic extractions is important.

The literature regarding tooth movement into recent and healed extraction sites is controversial. While an animal study by Murphey[13] reported greater movement on the healed side, other animal studies have reported faster tooth movement at recent extraction sites.[14,15] Hasler[16] in his study involving 22 patients reported faster canine distalization on the recent extraction side. One trial comparing retraction of canine into healed versus recent extraction sites reported significantly faster movement in the latter.[17] However, data in this trial were analyzed after only one month of retraction, and no information was provided regarding anchorage loss, canine angulation, or rotation.

The decision to extract the first premolar is often included in the treatment plan for the correction of bimaxillary protrusion to achieve the desired outcomes. Both en masse and two-step retraction are effective methods of space closure through which incisors and canines can be retracted to correct proclination and crowding. Sliding mechanics using the MBT prescription are widely used for en masse retraction. After leveling and aligning using sequential heat-activated nickel-titanium (HANT) wires, en masse anterior retraction is performed using 0.019x0.025 stainless steel working wires. This leads to a time delay of around 4-5 months by which time the extraction sites can heal. There was no delay in treatment timing in this study, as retraction began as soon as the 19x25 stainless steel wires were inserted and sliding was effectivelyinitiated, as in a typical case. If extraction is performed after the completion of leveling and alignment, immediately before the start of en masse retraction, it is possible that tooth movement may be accelerated.

Although studies have compared canine retraction into healed and recently extracted sites, no studies have investigated en masse anterior retraction under similar conditions. En masse anterior retraction may not necessarily produce the same response as individual canine retraction. Hence, this study was conducted as a randomized clinical trial comparing en masse anterior retraction into healed and recently extracted sites, with monitoring over a period of at least 4 months. According to the literature, RAP begins within a few days following any surgical intervention, peaks at 1-2 months, and subsides by 4-6 months. Hence, we chose a 4-month observation period.[5,12] Furthermore, variables such as the amount of mesial movement of molars, rotation, and angulation changes in the canine etc. have not yet been evaluated, highlighting the need for further investigation.

Specific Objectives and Hypotheses

Assessment of rate of space closure into recently extracted and healed extraction sites was the primary objective. Evaluation of anchorage loss, canine rotation, and canine tipping were included as secondary objectives. The null hypothesis generated was that "there may be no difference in terms of the above outcomes between healed and recently extracted sites during en masse anterior retraction using MBT mechanics".

METHODS

Trial Design and Any Changes After Trial Commencement

This study was a single-center, split-mouth, randomized clinical trial with an allocation ratio of 1:1 between the right and left maxillary quadrants. The methodology remained unchanged after trial commencement.

Participants: Eligibility Criteria and Study Setting

This study is part of a postgraduate dissertation that was approved by the Institutional Research Board and Institutional Ethics Committee of Government Dental College, Kozhikode (approval no.: 162/2019/DCC, date: 14.11.2019) and registered under the Clinical Trials Registry (CTRI no.: CTRI/2020/05/025436). Participants were recruited from patients registered for orthodontic treatment at the postgraduate clinic of the Government Dental College, Calicut, Kerala, India. The inclusion criteria were as follows: Angle's Class I malocclusion with bimaxillary protrusion[18] necessitating bilateral extraction of premolars, presence of all permanent teeth (excluding third molars), age between 16-24 years, well-aligned arches with crowding of ≤3 mm, absence of transverse discrepancies, and maxillo-mandibular plane angle ranging between 23º and 31º.[19]

Exclusion criteria included poor oral hygiene, periodontal problems, alveolar bone loss, medications or medical conditions affecting bone biology, active systemic problems, smoking, presence of severe rotation of anterior and posterior teeth, any developmental anomalies of crown and root, deleterious oral habits, and those who were not willing to participate in the study were later excluded. Withdrawal criteria included missing routine appointments, appliance breakage, and failure to maintain proper oral hygiene. Both male and female participants were recruited. Informed consent was obtained from all participants or their legal guardians after providing all explanations and clarifications regarding the trial.

Sample Size

The nMaster software (Biostatistics Research & Training Centre, Christian Medical College, Vellore-2, India) was used for calculating the sample size. Based on the results from a previous study, for change in the anteroposterior movement of canine (T1-T3)[16] with a pooled standard deviation of 1.14, if the true difference between the means is 1.1, a sample size of 24 subjects per group was required to reject the null hypothesis. This calculation achieved a power of 0.9, with a Type I error probability of 0.05. It was decided to include more patients so as to increase the power of the study and compensate for possible dropouts during the study period. Thus, 26 patients were recruited.

Randomization

Random number generation, allocation concealment, and blinding

A splitmouth, paired design was used in which each participant had one "healed extraction side" and a recent contralateral extraction side. Extraction of first premolars were randomly allocated to the right or left sides at an allocation ratio of 1:1. Randomization was performed using random number tables occurring in permuted blocks of 2 patients, so that once all 26 patients were recruited, there would be equal numbers on either side. Random sequences were concealed in opaque, envelopes that were numbered and sealed. Ultimately, 50% of patients had the right premolar extracted, while the remaining 50%, had the left premolar extracted. Baseline information for each participant was stored by the investigator responsible for opening the next envelope in sequence and implementing the randomization process.

Blinding

This study did not allow the clinician or patients to be blinded. However, the co-investigator was blinded during the measurement and statistical analysis stages.

Intervention

A single investigator treated all the patients, using the pre-adjusted edgewise appliance (MBT prescription, 0.022×0.028" slot, 3M Unitek, Monrovia, CA, USA). As stated earlier, the upper and lower premolars on one side, be it left or right, was extracted at the beginning of treatment, based on randomization. This was considered the "healed extraction site". Only the upper arch was included in the investigation. The anterior segment was levelled and aligned using the following sequence of 0.014, 0.017x0.025, 0.019x0.025 HANT wires, with each archwire in place for 4 weeks. All six anteriors were consolidated (to prevent drifting of canine into extraction site) by tying them together using a single 0.010" ligature wire. This was followed by placement of the working wires, (0.019 x 0.025 posted stainless steel wires) in both the upper and lower arches for a period of 4 weeks, after which the contralateral first bicuspids were extracted, just before starting retraction. This was considered the "recent extraction site". Retraction was commenced simultaneously in both arches. Only the upper arch was included in the investigation. En masse retraction was initiated from the third day after the second extraction using closed coil Nitinol springs from the archwire hooks to the molar hooks, (3M Unitek; 9 mm), applied simultaneously on both sides of the arch. Activations were performed monthly. Upper molars were stabilized by placing a transpalatal arch at the first visit. Care was taken to maintain the retraction forces in the range of 150-200 g per side by delivering equal amounts of activation as measured by the force gauge every month ("Correx", Dentaurum, Germany). Patients were advised not to take anti-inflammatory NSAIDs as it may affect tooth movement. A positive overjet was maintained during the full treatment period. Impressions were taken using alginate, and casts prepared with die stone immediately before starting retraction, and also after the second and fourth months following retraction. The patients name, date and number were marked on all the casts before storage

Outcomes (Primary and Secondary) and Any Changes After Trial Commencement

The primary outcome was the rate of space closure at healed and recently extracted sites. The secondary outcomes were the rotational tendency of the canines, canine tipping, and changes in the first molar position. Outcomes were evaluated cephalometrically and using model analysis at two and four months. There were no changes after trial initiation.

Model Analysis

The midpalate raphe (MPR) served as the reference plane[20] and the medial aspects of the third rugae (RR-*rugae right*, RL-*rugae left*) as reference points for assessing anteroposterior changes in tooth position.[21] After identifying and marking the relevant landmarks on the pre- and post-retraction maxillary dental casts, they were scanned using an Epson perfection V700 scanner (maximum resolution-12,800 dpi). Perpendiculars were drawn on to the MPR reference plane from the mesiobuccal cusp tips of the maxillary permanent first molars (ML-molar left, MR-molar right) and the cusp tips of the maxillary permanent canines (CL- canine left, CR- canine right) (Figure 1). For determining rate of canine retraction, high accuracy digital calipers (Mitutoya, Kawasaki, Japan) with readings nearest to 0.1mm were used. After performing the measurements twice, the mean of the two measurements was recorded. The

difference in the linear distance between the CL (tip of left canine) and CR (tip of right canine) from pre-retraction to post-retraction was measured. After determining the extent of change in position, the duration of canine retraction was recorded as time intervals, with corresponding periods: first 2 months (T_{1-2}), second 2 months (T_{2-4}), and first 4 months (T_{1-4}). The rate of canine retraction was calculated by dividing the amount of retraction in millimeters by the time interval. This yielded the rate of canine retraction for each period (Table 1).

The anchorage loss in terms of mesial movement of first molars, as measured by the difference in the linear distance of their mesiobuccal cusp tips (ML, MR - molar left and molar right) before and after retraction was assessed (Figure 1). Rotation of the canine during retraction was assessed by drawing the rotation angle which is formed between a reference line parallel to the mid-palatine raphe and another line passing through the mesial-distal contact points of the concerned canine. Change in values between pre and post treatment rotation angles gives the rotation of that canine (Figure 2).

Cephalometric Analysis

Change in the long axis of the canine (tipping of canine) was assessed cephalometrically before and after retraction with the help of two differently shaped (by giving a bend toward mesial on right and distal on left) radiopaque markers made of 0.021 "stainless steel (SS) wire, ligated to canine brackets (Figure 3).[22] The change in marker angulation with respect to the palatal plane in pre- and post- treatment cephalograms depicted the amount of tipping undergone by the canine.[22] The direction of the bend helped to differentiate right and left canines. All measurements were performed to the nearest 0.5° with a protractor.

After two weeks, randomly selected models/radiographs of twelve patients were taken and all the above procedures repeated to assess the intraexaminer reliability.[22] There were no changes after trial initiation.

Statistical Analysis

All statistical analyses were performed using the SPSS statistical package (version 16.0, SPSS Inc., Chicago, Illinois, USA). The mean and standard deviation were calculated. The independent t-test was used to compare the amount of canine retraction between healed and recent extraction sites. A value of $p \leq 0.05$ was considered statistically significant. The intraclass correlation test was used to analyze intraexaminer variability.

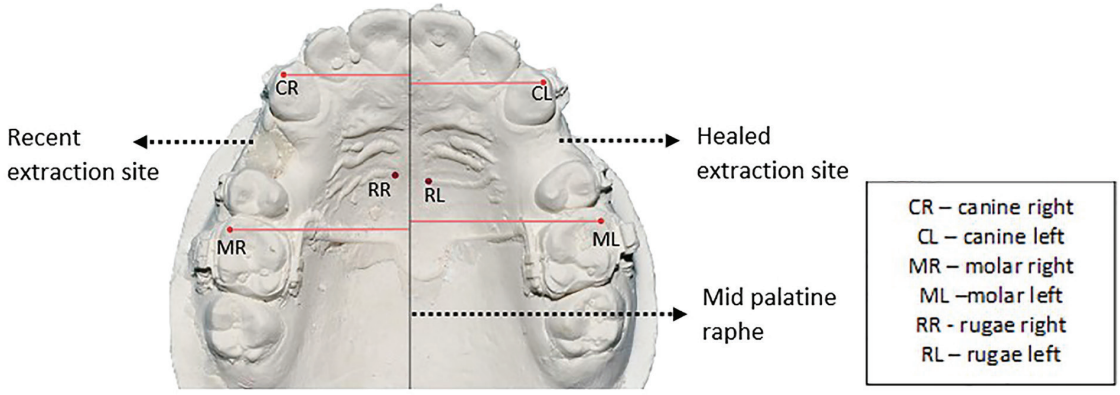

Figure 1. Landmarks on the maxillary cast showing recent and healed extraction sites

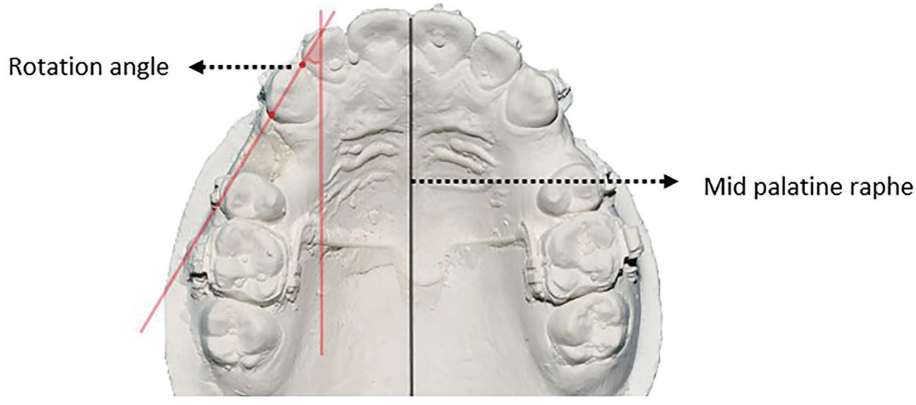

Figure 2. Determination of canine rotation

RESULTS

Participant Flow

Initially, 32 patients who presented to the Department of Orthodontics between July 2020 and December 2020 were assessed for eligibility by two clinicians not involved in the study. Six of the 32 patients not meeting the inclusion criteria were excluded from the study. Finally, 26 patients wereselected. The right and left quadrants were randomly allocated to either "healed"or "recent" extraction site in a 1:1 ratio. However, one patient was lost during follow-up. Another patient also had to be excluded due to breakage of the appliance. Information regarding each patient was stored in sealed envelopes to ensure confidentiality. Twenty-four patients finally completed the study and were analyzed (Figures 4 and 5).

Baseline Data

Of the 24 participants, 11 were male and 13 were female. The cephalometric variables included SNA (82.5°±3.7°), SNB (79.5°±4.6°), ANB (3.25°±2°), and maxillary incisor inclination to the palatal plane (120.5°±4.5°).

Numbers analyzed for outcome estimation and precision; subgroup analysis

Primary outcome: The mean rate of space closure (with standard deviation) for both healed and recent extraction

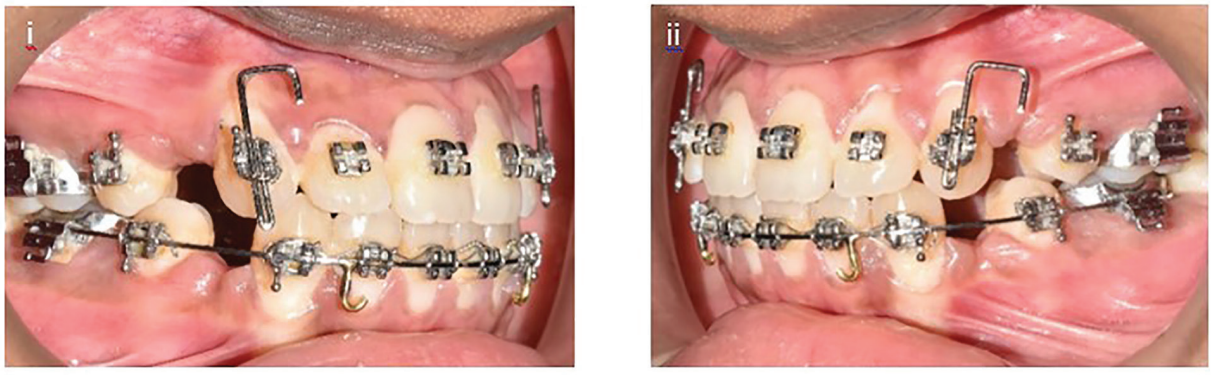

Figure 3. SS markers on right (i) and left (ii) canine
SS, stainless steel

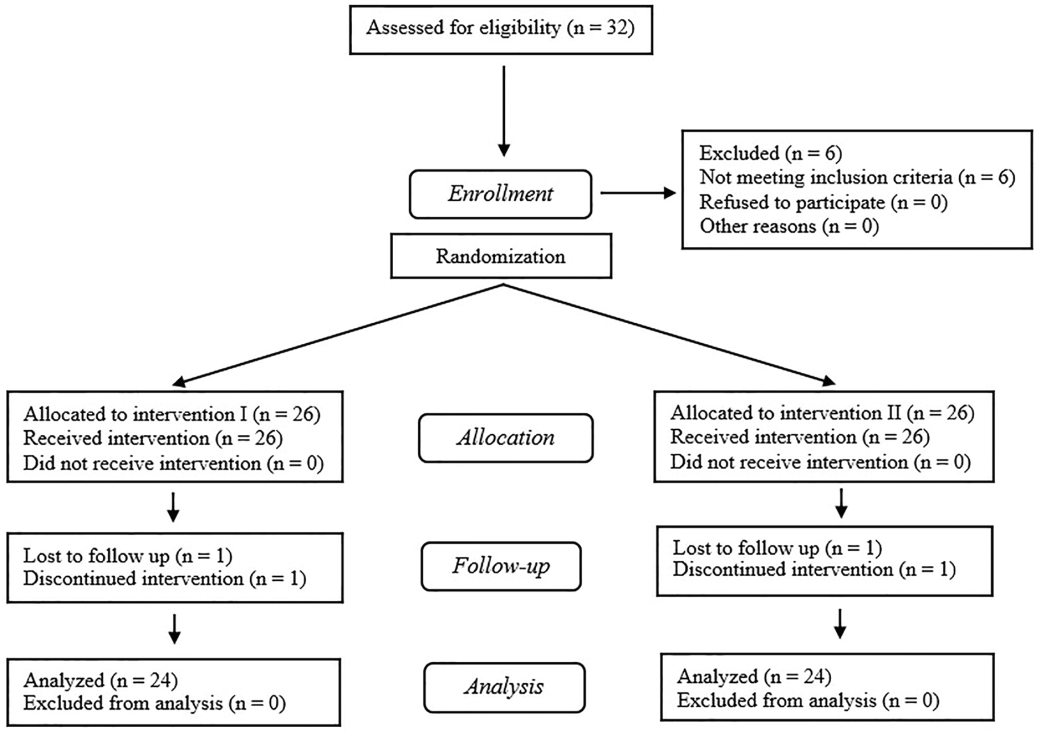

Figure 4. CONSORT diagram showing the flow of patients through the trial

sites is given in Table 1. The mean rate of space closure for a period of 4 months on the healed extraction site was found to be 0.426±0.184 mm/month, while for the recent extraction site it was 0.818±0.208 mm/month. This is highly significant ($p<0.000$). The rate of space closure during the first two months was higher than that during the second to fourth months for the recently extracted site.

Secondary outcomes (Table 1): Tipping of the canine into recent extraction side was 6.042° (±1.398°), which is significantly more than 5.125° (±1.035°) on the healed side ($p<0.05$). No statistically significant differences were observed in canine rotation and anchorage loss between the two sites. The intraclass correlation coefficient to test intra-examiner reliability is presented in Table 2, which demonstrates excellent agreement.

Harms

There were no harms or negative outcomes reported by any participant during the trial.

DISCUSSION

The rate of space closure on the side of recent extraction showed a 1.9-fold increase, as compared to the earlier healed side. This is relevant from a clinical standpoint as well. This can be explained by the "Regional accelerated phenomenon (RAP)", which is characterized by "transient functional osteopenia followed by accelerated bone turnover over time". In humans, RAP "begins within a few days following any form of surgical intervention, peaks at 1-2 months, and subsides by 4-6 months".[5,12] With respect to orthodontic tooth movement, RAP can be seen as a "tissue response to mechanical cyclical

Table 1. Comparison of mean rates of space closure, canine rotation, tipping, and anchorage loss between healed and recent extraction sites

	Healed extraction site		The recent extraction site		p-value
	Mean	SD	Mean	SD	
Rate of space closure (mm) R_{1-4} R_{1-2} R_{2-4}	 0.426 0.470 0.356	 0.184 0.243 0.115	 0.818 1.006 0.639	 0.208 0.266 0.239	 0.000***
Canine rotation (CR) (degree)	1.125	0.797	1.541	0.658	0.055
Canine tipping (CT) (degree)	5.125	1.035	6.042	1.398	0.013*
Anchorage loss (AL) (mm)	0.708	0.765	1.062	0.727	0.107

Independent t-test, *p<0.05, ***p<0.001
SD, standard deviation

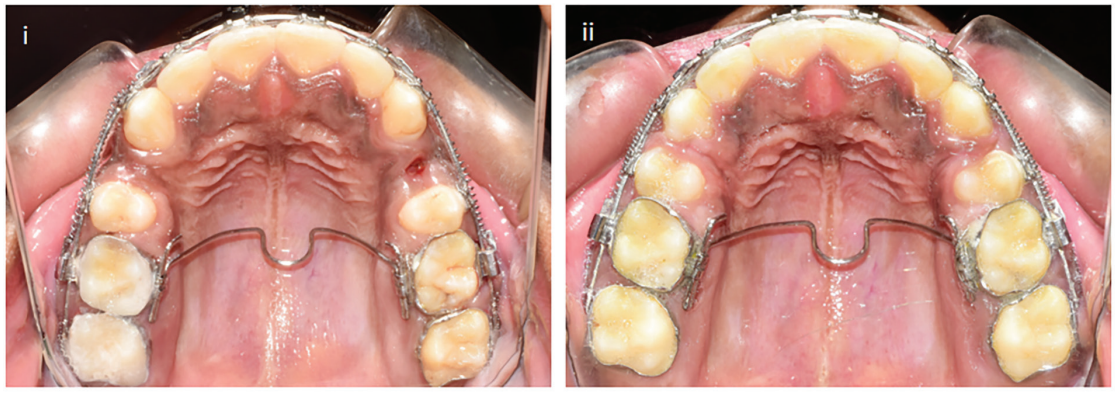

Figure 5. i) Pre-start of retraction, ii) 4 months post-retraction

Table 2. ICCs showing the level of agreement

Parameter	ICC
Retraction	0.991
Rotation	0.967
Anchorage loss	0.925
Tipping	0.936

ICC, intraclass correlation coefficient

perturbations" that induce microdamage which has to be removed to avoid their accumulation.[23] The adaptation to the "new orthodontically induced mechanical environment" is ensured by increased activation of the bone multicellular unit (BMU), which returns to normal levels after a few months. It is reported that the decreased mineral density allows easier orthodontic tooth movement during remodeling and healing.[23]

Previous research on the effects of timing of therapeutic extractions have all focused on individual canine retractions; hence, comparison of our findings with previous research was not possible. However, a recent study on the effects of micro-osteoperforations on en masse retraction reported a retraction rate ranging from 0.43±20 to 0.44±17 mm/month during the first 4 months for the control group, which is similar to the healed extraction side in this study.[24] They also reported a significant increase in the rate of retraction (0.71019 mm/month for the first month) in the group that underwent MOP. A recent publication by Zubair et al.,[17] has reported a rate of 1.17±0.27 mm/month for individual canine retraction into recent extraction site, (as compared to the healed site) during the first month. However, their study did not include evaluation beyond the first month. Alikhani et al.[10] hypothesized that "trauma amplifies the expression of inflammatory markers that are normally expressed during orthodontic treatment, and this response accelerates both bone resorption and tooth movement". High cytokine and chemokine levels help to convert osteoclast precursor cells into mature osteoclasts, thereby enhancing alveolar bone resorption at a faster rate.

Another important observation of this study is that the rate of tooth movement was considerably faster during the first two months (1.006 mm/month) for the recently extracted side, followed by a significant decline (0.639 mm/month). Observations by Raghav et al.[24] have also reported a similar decline in the rate of tooth movement after the first month in patients who underwent MOP. One possible explanation for the decline in the rate of tooth movement during 3rd and 4th month compared with the first 2 months could be the transient nature of RAP.

Although there are few clinical studies in this area, a histological explanation has been proposed by Diedrich and Wehrbein.[15] Their experiments on foxhounds reported that recent extraction sites were characterized by higher bone density with less maturity and broader alveolar processes, whereas older (12 weeks old) extraction sites had more mature lamellar bone, pronounced horizontal atrophy, and periosteal bone apposition in the direction of tooth movement. This makes orthodontic tooth movement challenging at older healed extraction sites. They opined that, according to histological finding, orthodontic retraction into extraction sites should be initiated at an early stage.

The contribution of the RAP phenomenon might explain the accelerated tooth movement rather than the existing histological differences in bone density. There is a reported difference in bone densities between healed and recently extracted sites (more denser in former than latter). In recently extracted sites, inflammatory markers are also reported to be amplified (than what is expressed during normal orthodontic treatment) due to the RAP phenomenon, which is induced without any additional surgical procedures. This response may be responsible for the difference in bone densities and for accelerating both bone resorption and tooth movement. The advantage of immediate retraction into the extraction site can definitely bring about rapid tooth movement, thereby decreasing the overall treatment time as well as the possible untoward effects on the periodontal tissues. Clinically, this information is applicable to cases with bimaxillary protrusion and minimal crowding. The clinical relevance of this approach is that it would be beneficial to delay extractions in such patients.

The results of our investigation revealed insignificant anchor loss and rotation of the canine on both sides. Although anchor loss was observed to be greater on the recent extraction side, it was not significant, probably due to reinforcement of anchorage with the transpalatal arch. A previous investigation of canine movement into healed and recently extracted sites reported similar findings.[16] However, their study involved sectional mechanics using Gjessing springs on either side for individual canine retraction. The tipping of the canine in our investigation was more toward the recent extraction site, with a difference of only 0.917º. Hasler[16] also reported significant tipping of canines in the quadrant that underwent a recent extraction. The angulation reported by them was 15.75º in recent and 14.25º in old extraction side, which is much higher than that obtained by us (mean 6.04º on recent extraction side and 5.13º on healed side). This is probably due to the fact that friction mechanics on continuous archwire (as advocated by MBT philosophy) were used in our investigation, which involved both tipping and uprighting during the course of retraction. The method of evaluation of canine angulation was also different in the two investigations.

Study Limitations

A limitation of our study is that evaluation was performed for only four months, and the complete closure of the extraction spaces was not considered. This is because RAP begins within a few days following any form of surgical intervention, peaks at 1-2 months, and subsides by 4-6 months. Treatment was continued thereafter, and all cases were debonded following the completion of space closure in all four quadrants. Moreover, no histological examination was performed to distinguish the bone qualities of both the experimental and control sides.

This clinical trial included patients with mild crowding and protrusion requiring extraction. Therefore, the findings are expected to be generalizable only to patients requiring extraction for orthodontic treatment.

CONCLUSION

The null hypothesis was rejected, as the results of the study showed that the rate of space closure was higher for the recently extracted site than for the healed site. The results of this randomized clinical trial show that:

• The rate of space closure at the recent extraction site was faster than at the healed site.

• There was no significant difference in the mesial movement of anchorage molars or rotation of canines into the extraction site between the two sides.

• Tipping of canines into the extraction site was significantly greater in the quadrant with recently extracted premolars.

The results of this trial support a clinical recommendation to initiate orthodontic retraction immediately following therapeutic extractions and offer a practical, non-invasive, safe procedure to enhance the rate of tooth movement.

Ethics

Ethics Committee Approval: Ethical permission was obtained from the Institutional Research Board and Institutional Ethics Committee of Government Dental College, Kozhikode (approval no.: 162/2019/DCC, date: 14.11.2019).

Informed Consent: Informed consent was obtained from all participants or their legal guardians after providing all explanations and clarifications regarding the trial.

Footnotes

Author Contributions: Concept - S.S.; Design- S.S.; Data Collection and/or Processing - D.P., N.M., Sr.S.; Analysis and/orInterpretation -Sr.S., D.P., B.J.; Literature Search - M.S., N.M., B.J.; Writing- M.S., D.P., S.S.

Conflict of Interest: The authors have no conflicts of interest to declare.

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