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T.P. Chau Minh,
MSc., DDS, faculty Odonto-stomatology
N.L. Lam,
PhD, DDS, head of Department of Pediatrics Dentistry and Orthodontics, vice dean of faculty of Odonto-Stomatology
V.L. Khanh Phuong,
DDS, faculty Odonto-stomatology

Can Tho University of Medicine and Pharmacy, 900000, Can Tho, Vietnam

# The effect of platelet-rich fibrin (PRF) on orthodontic tooth movement: A split-mouth randomized controlled trial

**Abstract. Objective** — to evaluate the effectiveness of injectable platelet-rich fibrin (i-PRF) in accelerating orthodontic tooth movement (OTM) and reducing treatment duration. **Materials and methods.** This study used a split-mouth randomized clinical trial with 31 patients (14—31 years old, 9 males and 22 females) with Angle Class I malocclusion indicated bilateral maxillary first premolar extraction with a double-blind design. The i-PRF was obtained from each patient's blood and then injected into the buccal and palatal areas of the extraction sites right before the canines were retracted. The i-PRF was used on the left side, and physiological saline was used on the right side of the patients with even numbers. On the other hand, the i-PRF was used on the right side for patients with an odd number, whereas physiological saline was used on the left side. After the leveling and alignment phases, the canines were retracted with 150 g of force. Digital models were obtained at five time points: before tooth extraction, in the fourth, eighth, twelfth, and sixteenth week from the beginning of distalization. **Results.** In the current study, the rate of canine tooth movement was higher in the study group (PRF injection) than in the control group at all time points ($p<0.001$). PRF injection increased orthodontic tooth movement during the early stage (first 2 months). The average acceleration of canine movement in the PRF injection group was 1.21 times. There was no statistically significant difference between the male and female genders. **Conclusion.** i-PRF can be an effective method for accelerating orthodontic movement with minimal invasion, safety, and being autogenous.

**Key words:** injectable platelet-rich fibrin, i-PRF, orthodontic tooth movement, OTM, canine retraction

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Т.Ф. Чау Минь,
доктор стоматологических наук, факультет стоматологии
Н.Л. Лам,
доктор стоматологических наук, зав. кафедрой детской стоматологии и ортодонтии, проректор факультета стоматологии
В.Л. Кхань Фуонг,
доктор стоматологических наук, факультет стоматологии

Университет медицины и фармации Кантхо, 900000, Кантхо, Вьетнам

# Влияние фибрина, обогащенного тромбоцитами (PRF), на ортодонтическое перемещение зубов: рандомизированное контролируемое исследование с использованием модели «разделенной зубной дуги»

**Реферат. Цель** — оценить эффективность инъекционного фибрина, обогащенного тромбоцитами (i-PRF), в ускорении ортодонтического перемещения зубов (ОТМ) и сокращении продолжительности лечения. **Материалы и методы.** В данном исследовании использовался рандомизированный клинический эксперимент с использованием модели «разделенной зубной дуги», в котором участвовал 31 пациент (возраст от 14 лет до 31 года, 9 мужчин и 22 женщины) с аномалией прикуса I класса по Энглю. Им было показано двустороннее удаление первых премоляров верхней челюсти. PRF получали из крови каждого пациента, а затем вводили в щечную и нёбную области мест удаления непосредственно перед ретрагированием клыков. Пациентам с четными номерами i-PRF вводили на левой стороне, а физраствор — на правой стороне, а с нечетными номерами — наоборот. После этапов выравнивания и коррекции клыки были ретрагированы с усилием 150 г. Цифровые модели были получены в 5 моментов времени: до удаления зубов (Т0), на 4, 8, 12 и 16-й неделе с начала дистализации. **Результаты.** В настоящем исследовании скорость движения клыков была выше в исследуемой группе (инъекция PRF) по сравнению с контрольной группой во все временные точки ($p<0,001$). Инъекция PRF ускорила ортодонтическое движение зубов на ранней стадии (первые 2 месяца). Среднее ускорение движения клыков в группе с инъекцией PRF составило 1,21 раза. Статистически значимой разницы между мужчинами и женщинами не было. **Заключение.** i-PRF может быть эффективным методом ускорения ортодонтического движения с минимальной инвазивностью, безопасностью и аутогенностью.

**Ключевые слова:** инъекционный фибрин, обогащенный тромбоцитами, i-PRF, ортодонтическое движение зубов, ОТМ, ретракция клыков

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## INTRODUCTION

One of the main goals of orthodontic treatment is reducing treatment time through faster tooth movement, acceleration of canine retraction and space closure would reduce overall treatment time. Tooth movement is essentially a biological response to a physical stimulus, speeding up this response should avoid common iatrogenic effects such as white spot lesions, caries, root resorption, and periodontal problems [1, 2]. Therefore, attempts to accelerate tooth movement and reduce treatment duration are of great significance to orthodontists and patients. Thus, various invasive and non-invasive modalities have been attempted to reduce the duration of orthodontic treatment by accelerating tooth movement such as surgical, vibration, pharmacological agents, low-level laser therapy, or other procedures [3—6]. However, none of these procedures have yet become a gold standard method. Platelet-based preparations from the patient's blood provide a safe alternative to commercially available bioactive materials. Platelet-rich fibrin (PRF) is the second generation and holds the advantages of easier preparations and longer effects [7—11].

The injectable platelet-rich fibrin (i-PRF) was developed as an advanced product of PRF by altering the centrifugation protocol by lowering the centrifugation speed and force to 700 rotations per minute within 3 minutes has many advantages over the conventional form such as higher rates of leukocytes, regenerative cells, and growth factors. The potential benefits of PRF have been widely investigated in regenerative dentistry and oral surgery such as tooth movement, implantology, oral pathology, and periodontal therapy [12, 13]. Wang et al. (2018) reported that i-PRF affected osteoblastic behavior remarkably by influencing its migration, proliferation, and differentiation. This promotes cellular activity and accelerates bone turnover and healing [11].

**The purpose of this study** was to investigate the efficiency of i-PRF in accelerating tooth movement.

## MATERIALS AND METHODS

### Study methods

This study was a randomized controlled clinical trial with a split-mouth study design with an allocation ratio of 1:1. It was a single-blind study where the statistician was blinded regarding the origin and grouping of data. It was also ensured that the coin investigator conducting the measurements was blinded. Both the principal investigator and patients were not blinded by the procedures. The research was accepted by the ethics committee in biological research at Can Tho University of Medicine and Pharmacy. All patients signed an informed consent form before participating in the study. Patients had the right to refuse to participate in the study without affecting the examination quality and/or treatment.

### Study participants

All 31 patients (9 males and 22 females) were classified into 2 groups according to a treatment method:

1) 31 patients with even numbers treated using the i-PRF was used on the left side, and physiological saline was used on the right side;
2) 31 patients with an odd number treated using the i-PRF was used on the right side, whereas physiological saline was used on the left side who needed bilateral maxillary canine retractions were involved in this study.

The same orthodontist provided the orthodontic treatment for all participants.

*Inclusion criteria*: Patients (14—31 years old) with Angle Class I malocclusion requiring extraction of maxillary first premolars, no missing teeth except third molars, no previous orthodontic treatment, absence of systemic diseases and dentofacial anomalies, had good periodontal health, had normal values of blood tests (e.g., bleeding time 1—4 minutes, coagulation time 5—10 minutes), and patients agreed to participate in the study. *Exclusion criteria*: Patients with periodontal diseases, craniofacial syndromes (e.g., cleft lip or palate), and systemic diseases related to bone metabolism, taking anticoagulants or medication that interferes with orthodontic tooth movement (e.g., heparin, warfarin, NSAIDs, cyclosporine, glucocorticoids, medroxyprogesterone acetate, thyroid hormones, etc.).

### Study procedure

**Step 1.**

General information, clinical examination, classification of facial symmetry while facing forward, profile, relationships between the first molar teeth, and canine relationship. Patients with bilateral Angle Class I malocclusion should be chosen, and orthodontic treatment was indicated for the upper first premolar extraction. Using customized software with copyright WebCeph, all cephalometric radiographs that complied with the study's requirements were calculated. Before beginning orthodontic treatment, check the patients who fulfill the inclusion criteria and test the bleeding time, clotting time, and platelet count. To participate in the study, patients must sign a permission form and get information about its goals and methods.

**Step 2.**

Apply TransbondTM XT Light Cure Adhesive and the Victory Series Metal Bracket System (MBT 0.022 slot, 3M Unitek, USA). Before beginning the canine distalization phase, we perform the optimal sliding process for the closing stage after the leveling and alignment stage. Before beginning to retract the canines, the patient must be equipped with a 0.016×0.022 stainless steel wire (3M, USA). After the leveling and alignment phase, mini-screws (Chaorum, Korea) were placed bilaterally between the maxillary second premolar and the first molar. Tooth extractions were performed at the same time in the study and in the control group. Canine distalization was performed on both sides by 150 gram force with an elastic chain following the study design of Pham et al. (2025), the patient data in this study were collected from the same original research that evaluated the effectiveness of injectable platelet-rich fibrin (i-PRF) in addressing root resorption and alveolar bone density. This article examines the effectiveness of injectable platelet-rich fibrin (i-PRF) in accelerating orthodontic tooth movement (OTM) and reducing treatment duration, utilizing an entirely different analytical approach [14].

**Preparation and application of i-PRF**

Venous blood was taken for each patient using 10 ml tubes (plastic tubes) without any additives or anticoagulants. This was done as fast as possible, and each tube was placed into the PRF centrifuge. The centrifuge spun tubes at 700 rpm for 3 minutes at room temperature. This separates the blood into two parts: the top layer contains the liquid i-PRF, and the bottom layer contains red blood cells. The i-PRF from the top layer was put into dental injectors that could hold 2.5 cc. We utilized a dental injector needle with a 27-gauge needle. The amount of i-PRF was standardized as 2 ml and was injected submucosally into the distobuccal and distopalatal sides of the canine tooth (1 ml for each side) under local anesthesia for pain control. Digital model casts were obtained at five time points: before tooth extraction (T0) and in the fourth week (T1), the eighth week (T2), the twelfth week (T3), and the sixteenth week (T4) from the beginning of distalization.

**Step 3.**

Used the same brand of elastic chain for all patients. These are placed on day 1 and changed every 4 weeks (fig. 1). Distalized the canines with chain elastics instead of NiTi closed coil springs because the force of the chain elastics gradually decreased over time, usually about 3—4 weeks coinciding with the patient's follow-up appointment, while the force of NiTi closed coil spring remained more continuous, making it difficult to control if the patient was late for an appointment [15].

The study models were scanned using the Medit i600 scanner (Samsun Vina, Korea). The matching digital models are oriented and superimposed on normalization points using vertical, horizontal, and anterior vertical reference planes (fig. 2). The difference between the prior distalize at the beginning (T0) and the measurements obtained each month up to the end of four months (T4) is used to determine all measures. The distance parallel to the canine cusp concerning the frontal plane is used to indicate the entire

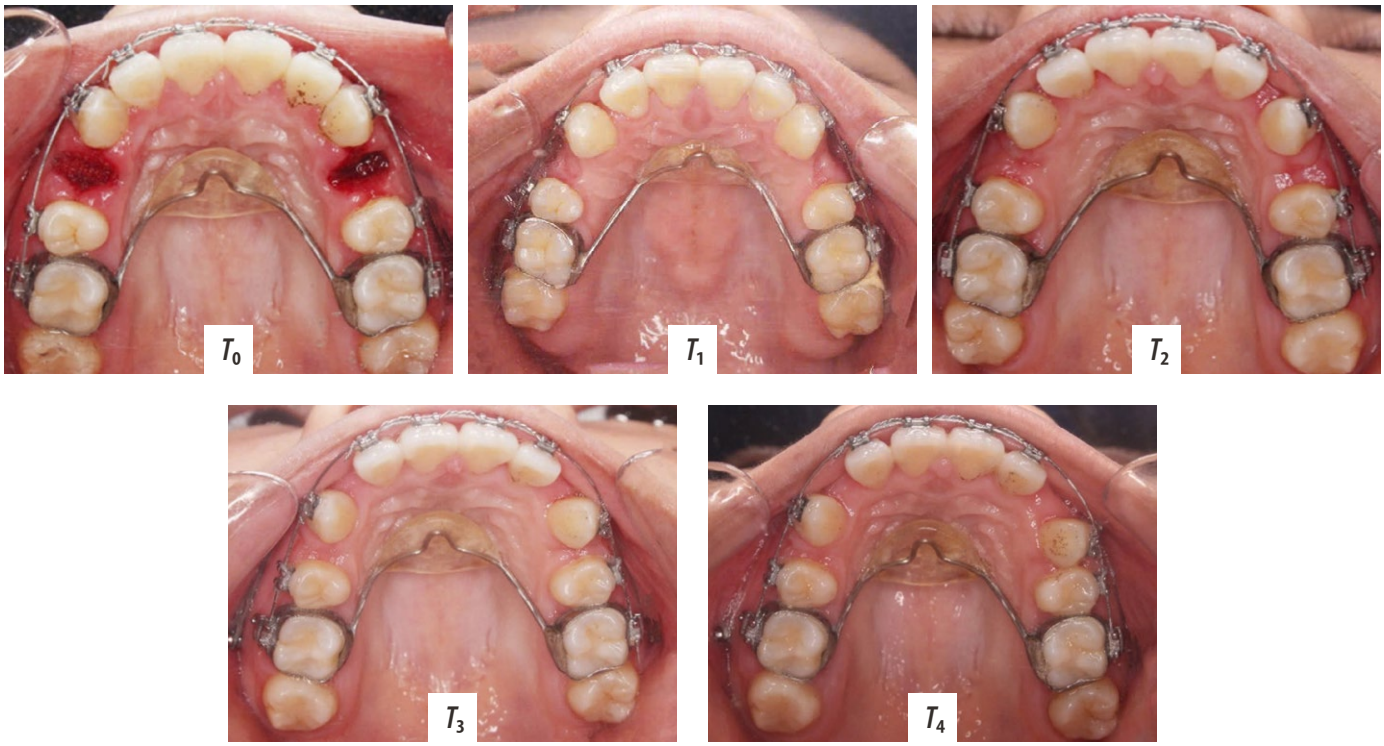


*Fig. 1. Intraoral maxillary occlusal views were taken at five-time points: before tooth extraction ($T_0$) and in the fourth week ($T_1$), eighth week ($T_2$), twelfth week ($T_3$), sixteenth week ($T_4$) from the beginning of distalization*

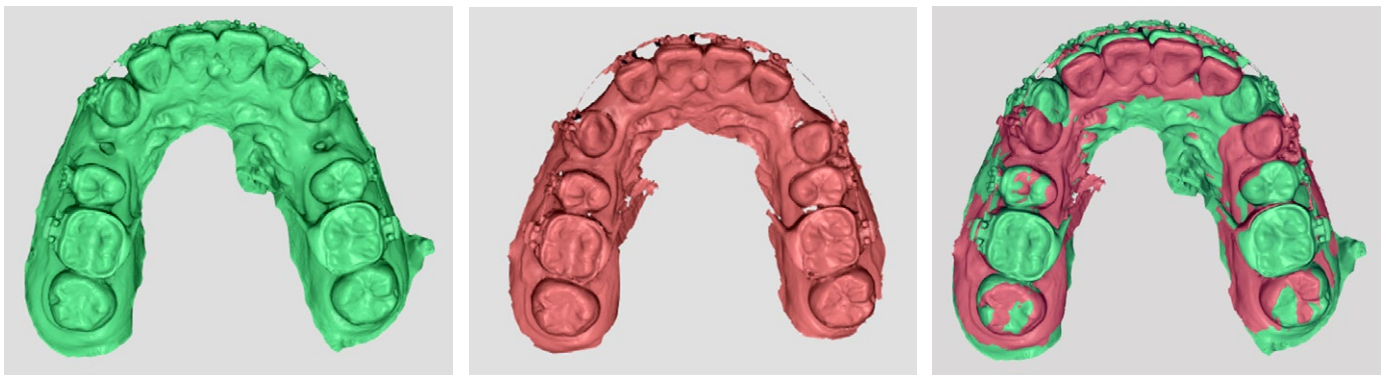

*Fig. 2. The intraoral scans before and after canine retraction and the digital 3D model superimposition*

canine retraction. In the following scans, the space lost by the first maxillary tooth about the anterior plane was calculated from the top of the canine crown. The angle between the projected line connecting the midpoint and point of contact for each canine and the frontal plane is used to estimate the canine rotation.

### Statistical analysis

Paired sample and independent sample *t*-tests were used to compare the changes between groups, $p \leqslant 0.05$ was considered significant.

## RESULTS

*Distribution of study subjects according to age and sex.* Research results on 31 patients, in which men accounted for 29%, women accounted for 71%, and the mean age was 23.0±3.9 (minimum age was 14 years old, oldest age was 31 years old).

The maxillary canine distalization was longer in the PRF injection group (0.96 mm after 4 weeks, 2.19 mm after 8 weeks, 3.23 mm after 12 weeks, and 4.4 mm after 16 weeks) than in the control group (1.23 mm after 4 weeks, 2.82 mm after 8 weeks, 4.01 mm after 12 weeks, and 5.32 mm after 16 weeks; $p<0.001$; Table 1).

The total rate of canine movement was 5.32 mm on the experimental side and 4.4 mm on the control side, and the difference between the two groups was statistically significant ($p \leqslant 0.05$). The rate of canine traction after PRF injection showed that the OTM rate increased by 22% in the first month (1.23 mm vs 0.96, $p<0.001$), by 23% in the second month (1.59 mm vs 1.23 mm, $p<0.001$), by 14% in the third month (1.27 mm vs 1.1 mm, $p=0.011$), and by 9% in the fourth month (1.23 mm vs 1.12 mm, $p=0.048$). The PRF injection group had a noticeably higher rate of canine movement every 4 weeks (first month: 1.23 mm, second month: 1.59 mm, third month: 1.27 mm) than the control group. The rates of the canine movement were statistically significantly greater on the experimental compared to the control sides with $p<0.001$ except in the third month and fourth month ($p>0.05$; Table 2).

Moreover, the average speed of canine movement in a month of the PRF injection group was also significantly faster (1.33 mm) than the control group (1.10 mm) with a strong correlation ($r=0.793$, $p<0.001$). Furthermore, the average acceleration of canine movement in the PRF injection group was 1.21 times.

After 4 weeks, the distance between the maxillary canine and the gum was 1.02 mm, after 8 weeks it was 2.2 mm, after 12 weeks it was 3.27 mm, and after 16 weeks it was 4.46 mm. There was no statistically significant difference between the male and female genders (0.94 mm after 4 weeks, 2.18 mm after 8 weeks, 3.29 mm after 12 weeks, and 4.38 mm after 16 weeks; Tables 3 and 4). The male PRF group canine movement speed (1.34 mm/month) was nearly identical to the female PRF group canine movement speed (1.32 mm/month; Table 5).

**Table 1. Comparison of the accumulated amount of maxillary canine distalization between groups at 4-time points (in mm)**

| Time points | PRF injection group (*n*=31) | Control group (*n*=31) | *p* |
|---|---|---|---|
| **T1** | 1.23±0.16 | 0.96±0.12 | <0.001 |
| **T2** | 2.82±0.31 | 2.19±0.36 | <0.001 |
| **T3** | 4.01±0.34 | 3.23±0.34 | <0.001 |
| **T4** | 5.32±0.32 | 4.40±0.25 | <0.001 |

*Remarks. T1: 4th week, T2: 8th week, T3: 12th week, T4: 16th week. Paired samples t-test.*

**Table 2. Comparison of the monthly rate of canine retraction between groups (in mm)**

| Time points | PRF injection group (*n*=31) | Control group (*n*=31) | *p* |
|---|---|---|---|
| **ΔT1** | 1.23±0.16 | 0.96±0.12 | <0.001 |
| **ΔT2** | 1.59±0.23 | 1.23±0.30 | <0.001 |
| **ΔT3** | 1.27±0.24 | 1.10±0.22 | 0.011 |
| **ΔT4** | 1.23±0.26 | 1.12±0.20 | 0.048 |

*Remarks. ΔT1: 1st month, ΔT2: 2nd month, ΔT3: 3rd month, ΔT4: 4th month. Paired samples t-test.*

**Table 3. Comparison of the accumulated amount of maxillary canine distalization between groups by gender at 4-time points (in mm)**

| Time points | PRF injection group | | | Control group | | |
|---|---|---|---|---|---|---|
| | Male (*n*=9) | Female (*n*=22) | *p* | Male (*n*=9) | Female (*n*=22) | *p* |
| **T1** | 1.18±0.09 | 1.25±0.18 | 0.298 | 1.02±0.14 | 0.94±0.11 | 0.109 |
| **T2** | 2.80±0.22 | 2.82±0.34 | 0,854 | 2.20±0.43 | 2.18±0.34 | 0.905 |
| **T3** | 4.12±0.19 | 4.07±0.39 | 0.697 | 3.27±0.46 | 3.29±0.29 | 0.902 |
| **T4** | 5.31±0.35 | 5.31±0.31 | 0.975 | 4.46±0.28 | 4.38±0.24 | 0.419 |

*Remarks. T1: 4th week, T2: 8th week, T3: 12th week, T4: 16th week. Independent samples t-test.*

**Table 4. Comparison of monthly rate of canine retraction between two groups by gender (in mm)**

| Time intervals | PRF injection group | | | Control group | | |
|---|---|---|---|---|---|---|
| | Male (*n*=9) | Female (*n*=22) | *p* | Male (*n*=9) | Female (*n*=22) | *p* |
| **ΔT1** | 1.18±0.09 | 1.25±0.18 | 0.298 | 1.02±0.14 | 0.94±0.11 | 0.109 |
| **ΔT2** | 1.62±0.18 | 1.58±0.25 | 0.631 | 1.19±0.32 | 1.25±0.29 | 0.619 |
| **ΔT3** | 1.32±0.21 | 1.25±0.26 | 0.433 | 1.07±0.75 | 1.11±0.26 | 0.700 |
| **ΔT4** | 1.19±0.27 | 1.25±0.26 | 0.583 | 1.19±0.24 | 1.09±0.18 | 0.230 |

*Remarks. ΔT1: 1st month, ΔT2: 2nd month, ΔT3: 3rd month, ΔT4: 4th month. Independent samples t-test.*

**Table 5. Correlation rate of i-PRF canine distal movement (mm/month) by gender after 16 weeks**

| | Male (*n*=9) | Female (*n*=22) | *p* |
|---|---|---|---|
| **PRF injection group (*n*=31)** | 1.34±0.09 | 1.33±0.08 | 0.975 |
| **Control group (*n*=31)** | 1.12±0.07 | 1.09±0.06 | 0.419 |

## DISCUSSION

There was a high demand for accelerated orthodontic tooth movement (OTM) among individuals requiring orthodontic treatment. The present study used a randomized, double-blind clinical trial design, where individuals were randomly allocated to distinct groups. Both the researchers and the participants were kept uninformed of the patient's assigned group, guaranteeing impartial outcomes and reducing any sources of prejudice in the study. This approach enabled a more thorough assessment of the efficacy of faster orthodontic tooth movement in comparison to conventional procedures. The design of the current research closely resembled that of Pacheco, El-Timamy, and Erdur [16—18].

Most studies used a canine distalization force of 150 g and were controlled with a tension gauge, which was reactivated every month [19]. Orthodontic force essentially changed blood flow pressure, and the local electrochemical environment, initiated cellular and biochemical responses, and reshaped the bone. The best orthodontic force was the force that effectively moves the teeth to the desired position without causing discomfort or tissue damage to the patient. According to canine distalization research on orthodontic patients, it was suggested that the best canine distalization force was 150—200 g on the tooth-bone interface, with this force the tooth movement speed was maximized. Light forces below this level do not produce tooth movement. While the force increased above this level, the rate of tooth movement would decrease and eventually reach zero in one week [19].

The current study assessed an innovative method to expedite the duration of orthodontic treatment. In this randomized controlled trial, i-PRF was administered to the control group to reduce the treatment time for patients undergoing tooth extractions. The use of platelet concentration, which releases a diverse range of proteins and growth factors, has grown to expedite the process of tissue repair and regeneration in several medical and dental disciplines. i-PRF was an enhanced version of PRF that was created by modifying the centrifugation process [20, 21]. This modification involved reducing the centrifugation speed and force to 700 spins per minute. As a result, i-PRF has a greater number of regeneration cells and higher quantities of growth factors compared to PRF [22]. The change in time and speed of centrifugation leads to the formation of a new formula of platelet concentrate with a high concentration of leukocytes and growth factors. Analysis of the results demonstrated that i-PRF stimulated the expression of inflammatory cytokines, which indicated osteoclastic activity and an increased rate of tooth movement. PRF, a completely autologous fibrin matrix, was developed as a second-generation platelet concentrate without the addition of anticoagulants and additives at lower centrifugation speeds [23, 24]. In a recently published systematic review, studies have suggested the potential function of platelet-rich concentrates in the OTM acceleration of animal models [25, 26]. In a clinical study, Tehranchi et al. (2018) demonstrated that PRF (membrane form) accelerated orthodontic tooth movement [26].

The positive effect of i-PRF on the rate of tooth movement started in the first week and was seen throughout the follow-up period. The current showed a maximal difference in OTM rate between the experimental side and control side in the 2nd month after PRF application, implying that PRF exerted the greatest effect on OTM acceleration after the first month [18]. Movement of the teeth with orthodontic forces depends on bone remodeling, which is associated with the activity of inflammatory markers, the quality and quantity of bone turnover, and the balance between osteoclastic and osteoblastic activity [27, 28]. Extraction of the teeth can increase the activity of inflammatory markers, which could obscure the effect of i-PRF. To minimize this possibility, tooth extractions were performed at the same time in the study and control groups. Karakasli et al. (2021) noted that the study group with PRF injection had faster incisor movement than the control group and the values were higher within the first week after PRF application [29].

The reason why this present study chose 4 weeks to inject PRF instead of 2 weeks like Kobayashi et al. (2016) studies is that i-PRF can release growth factors last to 28 days [22]. The prolonged release time enabled a greater span of beneficial effects, which may result in enhanced results as compared to shorter periods. In addition, the injection schedule lasting for 4 weeks may provide longer-lasting advantages for the process of tissue regeneration and the healing of wounds [30]. In summary, the prolonged release duration of growth factors from i-PRF over a period of 4 weeks may provide a more advantageous setting for the healing and renewal of tissues. The extended duration of therapeutic effects has the potential to improve the overall efficacy of the therapy. The initial results of this study also showed positive results similar to the majority of studies by previous authors. The cumulative distance of the canines in the PRF injection group was significantly higher than in the control group and the total movement was significantly higher in the study group (5.32 mm) than the control group (4.40 mm, $p<0.001$) in all time points (see table 1 and 2) similar to the research results of Erdur's study [18]. However, Zeitounlouian et al. (2021) reported no benefit of PRF to tooth movement [1]. Pacheco et al. (2020) even claimed that PRF decreased the rate of canine distalization [16]. These controversial results may be attributed to the different intervention procedures they adopted in dosage, delivery methods (plug, membrane, or injection), and observation periods.

It was highly recommended to do more trials that were well-designed, had more expansive sample numbers, and lasted for a longer duration of therapy. These studies have the potential to provide more definitive data about the efficacy of the therapy under investigation. Furthermore, the inclusion of diverse patient populations and control groups may enhance the validity of the findings. Additional research is required to investigate the impact of platelet number and quality, as well as the effects of illnesses and medications on PRF products. This would aid in gaining a more comprehensive understanding of the possible constraints and fluctuations in results. To advance our knowledge and enhance patient care, it is essential to adopt a holistic strategy for study in this field. Subsequently, consider the provided indications and contraindications for the product. No histology study has been conducted yet.

## CONCLUSION

In orthodontics, the i-PRF infiltration group showed a significantly faster retraction of teeth compared to the control group. i-PRF can accelerate the movement of the canine and be used in extreme situations. The speed of the PRF-injected canine was faster than the control group by 1.21 times. PRF injection increases orthodontic tooth movement during the early stage (first 2 months).

The use of i-PRF as a procedure that is safe, reproducible, and minimally intrusive to speed up the OTM, and shorten the amount of time it takes to complete. In addition, it is advantageous since it is autologous and biomimetic in nature, which eliminates the risk of an immunological response as well as other negative consequences that are associated with biocompatibility.

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