

# Comparison of quality of bone and insertion torque values of early implants placed at 6 and 8 weeks in sockets preserved with advanced platelet-rich fibrin: A randomized controlled trial

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## Abstract

**Aim:** Successful functional and esthetic rehabilitation of edentulous jaws with implants depends on the optimal timing of placement, surgical protocol, materials used, cost-effectiveness, and satisfying patient needs. Increasing demand for shorter treatment times necessitates the immediate placement protocol. However, researchers have demonstrated a higher failure rate. A-PRF (Advanced platelet-rich fibrin) has exhibited accelerated bone regeneration potential. Early implant placement with a limited healing period, along with A-PRF, can be beneficial over conventional and immediate implant placement.

**Settings and Design:** This prospective randomized clinical trial aims to assess the outcome of early implant placement in sockets preserved using A-PRF at six weeks and eight weeks of post-extraction. Two groups of 10 participants each were formed. All patients underwent atraumatic extraction and socket preservation using A-PRF.

**Materials and Methods:** A Partial-thickness pedicle graft was raised, and the extraction socket was closed. Implants were placed in at six and eight weeks of post-extraction in group A group B, respectively. The histomorphometric analysis assessed the bone quality present at the time of surgery. The insertion torque values were recorded during implant placement.


**Statistical Analysis Used:** The obtained data were statistically analyzed using parametric tests, namely independent T-test for intergroup comparison.

**Results:** T-test for torque values indicated a significantly higher torque value at eight weeks. The mean histomorphometric value showed a significantly higher percentage of bone formation at eight weeks than at six weeks ( $P = 0.03$ ).

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**Submitted:** 30-Jul-2021, **Revised:** 20-Aug-2021, **Accepted:** 20-Oct-2021, **Published:** 09-Nov-2021

Access this article online	
Quick Response Code:	Website: www.j-ips.org
	DOI: 10.4103/jips.jips_331_21

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**How to cite this article:** Chary NO, Raju MS, Sajjan MC, Gottumukkala S, Manyam R. Comparison of quality of bone and insertion torque values of early implants placed at 6 and 8 weeks in sockets preserved with advanced platelet-rich fibrin: A randomized controlled trial. J Indian Prosthodont Soc 2021;21:366-74.

**Conclusion:** Within the study's limitations, early implant placement in extraction sockets preserved with A-PRF had significantly higher insertion torque values and predictable bone at eight weeks compared to six weeks.

**Keywords:** Bone implant interactions, clinical research and trials, early implant placement, growth factors, platelet-rich fibrin

## INTRODUCTION

Various implant placement protocols have been described to date based on the duration of the healing period following tooth extraction before implant placement. The ideal timing of implant placement postdental extraction has been extensively discussed in the scientific literature. A waiting period of 6–8 months between tooth extraction and implant placement is traditionally considered, as suggested by Branemark.<sup>[1]</sup> This delayed implant placement protocol has its limitation like bone resorption, loss of gingival architecture, and migration of the adjacent teeth as the aging progresses. Other concerns include the increased time of edentulism, longer treatment duration, and increased patient demands.

Different alternative approaches<sup>[2,3]</sup> were proposed to overcome these potential drawbacks, which have shown promising results, such as immediate implant placement at the time of extraction or early implant placement following a few weeks post-extraction with optimum soft-tissue healing before implant insertion. Immediate implant placement reduces the treatment duration and surgical procedures. However, it has challenges like difficulty in soft tissue closure and chances of failures due to existing infection, thus increasing the risk of integrating dental implants.

Early implant placement could be an alternative treatment option to overcome these limitations. The early implant placement around 6–8 weeks could have better soft tissue, eliminating additional soft tissue augmentation techniques.<sup>[4]</sup> Debrided sockets have adequate time for the immune mechanism to resolve the existing infection. At the 6–8 weeks phase, the socket would have a provisional matrix with various healing stages. Placement of implant in this period may have an implant surrounded by a matrix with an osteogenic phase that could help integrate the implant.

In recent years platelet-rich fibrin (PRF) is widely used in implant dentistry to promote hard and soft tissue regeneration. PRF is a consistent fibrin biomaterial which releases a high amount of growth factors such as transforming growth factor  $\beta 1$  (TGF  $\beta$ -1), platelet-derived

growth factor AB (PDGF-AB), vascular endothelial growth factor (VEGF), and matrix glycoprotein (thrombospondin-1 [TSP-1]). Thus this biomaterial offers several advantages promoting wound healing, bone growth and maturation, socket sealing, and hemostasis.<sup>[5]</sup> Implants placed at 6–8 weeks in sockets preserved with advanced PRF (A-PRF) may produce better bone healing with higher torque values. However, deciding on the ideal timing for implant placement in early placement protocol ensures implants' success with good esthetic outcomes and minimal morbidity.

Therefore, given the paucity of the literature and dearth in the availability of existing data, the present study was conducted to evaluate treatment outcome for early implant placement in sockets preserved using A-PRF at 6 and 8 weeks following atraumatic extraction.

## MATERIALS AND METHODS

All the standards have been followed in conducting the study (i.e., Declaration of Helsinki; US Federal policy for the protection of Human Subjects). Clinical Trial Registration was done i.e CTRI /2018/08/015377. The study was conducted on volunteered patients indicated for the extraction of maxillary premolars due to decay. Patients of the age range of 20–50 years indicated for extraction of single-rooted maxillary premolar, desiring restoration with a dental implant, and teeth with straight root. Patients falling under the American Society of Anesthesiologists 1 category, with intact buccal cortical plate, minimum root length of 10 mm, and willingness to comply with study requirements were included in the study. Patients not fulfilling the inclusion criteria or not compliant with necessary procedural follow-up, inadequate pontic space, active systemic/local infection, medical conditions or medications known to alter soft tissue or bony healing, poor oral hygiene maintenance, smoking habit, pregnancy, roots extending into the maxillary sinus, dehiscence in buccal cortical plates after extraction were excluded from the study.

Sample size was obtained by using the formula:

$$n = \frac{2(Z\alpha + Z\beta)^2 \sigma^2}{d^2}$$

$$= \frac{2(1.96 + 0.84)^2(0.17)^2}{(0.15)^2}$$

$$= \frac{2(7.84)(0.29)}{0.0225}$$

$$= 20$$

Twenty patients fulfilling the criteria were selected and randomized into two groups. To avoid bias allocation concealment was done by using a computer-generated random table to randomly allocate the patients into groups. Prior consent was acquired from all the persons included in the study. Early implant placement was performed at 6 weeks in Group A patients and 8 weeks in Group B patients, after atraumatic extraction. All the patients were informed about the benefits and risks involving the treatment procedure, and consent was signed. Study approval was acquired from the institutional review board and ethical committee with Reference number IEC/VDC/MDS15 PROSTHO 06.

#### Atraumatic extraction

Two gram of amoxicillin as a preoperative antibiotic was prescribed 1 h before extraction. The surgical procedure was performed under strict aseptic conditions. Atraumatic extraction was done under local anesthesia (lignocaine 2% with adrenaline 1:80,000) using periostomes and luxators. 30 ml of blood was aspirated using a butterfly cannula into 3 A-PRF tubes for preparing the A-PRF plug and membrane by using centrifugation at 1500 rpm for 14 min.<sup>[6]</sup> Atraumatic extraction [Figure 1] was done using periostomes and luxators after making preoperative radiographs [Figure 2]. The extraction socket was [Figure 3] degranulated and irrigated with betadine and saline solution.

A partial-thickness palatal pedicle graft [Figure 4] was elevated and rotated onto the extraction socket's orifice. The underlying soft tissue in the course of the rotational flap was de-epithelialized to enable adequate adaptation and soft tissue healing. Two A-PRF plugs [Figure 5] were packed into the extraction socket and covered with the A-PRF membrane. The pedicle flap was rotated towards the extraction socket and approximated [Figure 6] by simple interrupted sutures using 4-0 resorbable (Vicryl) sutures. Postoperative antibiotics and analgesics were prescribed to the patient.

#### Implant placement

A preoperative radiograph [Figure 7] was made for both the groups at 6 and 8 weeks, and a single operator performed the procedure. The patient was prescribed



**Figure 1:** preoperative image showing root stump of maxillary second premolar



**Figure 2:** Preoperative radiograph

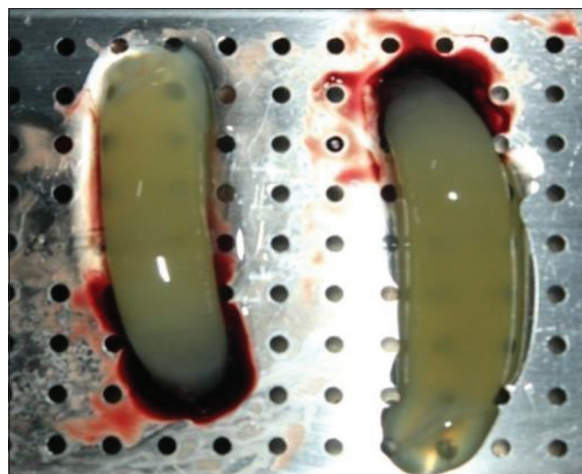


**Figure 3:** Extraction socket

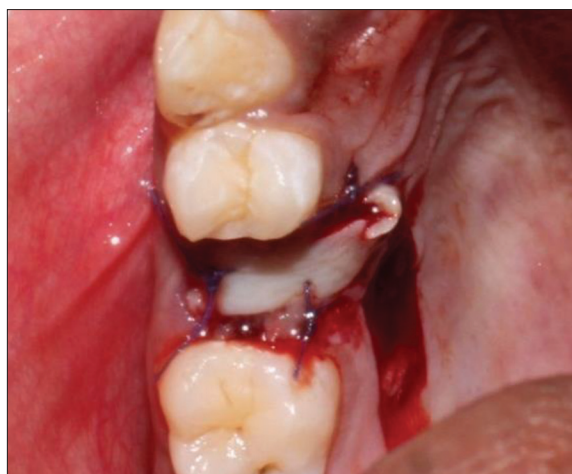
2 g of amoxicillin 1 h before surgery. 2% lignocaine with adrenaline was infiltrated at the surgical site. A mid-crestal incision was made, a full-thickness mucoperiosteal flap was elevated. A 2 mm internal diameter trephine bur was used at



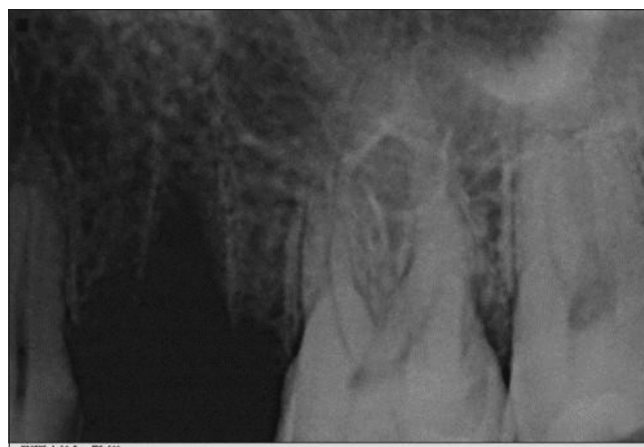
**Figure 4:** Partial thickness pedicle graft



**Figure 5:** Advanced platelet-rich fibrin plugs



**Figure 6:** Pedicle graft approximated



**Figure 7:** Radiograph before implant placement of 6 weeks subject

800 rpm to 8 mm depth, bone core [Figure 8] was collected and stored in 10% formalin neutral buffered solution. A 2 mm initial drill was used to extend the osteotomy up to 11.5 mm. The osteotomy site was prepared up to a diameter of 3.65 mm × 4.2 mm × 10 mm size implant was inserted in the final insertion torque value [Figure 9]. The radiograph was made after implant placement [Figure 10] and the cover screw placed. Simple interrupted sutures were placed using 4-0 Vicryl. Postoperative antibiotics and analgesics were prescribed for 3 days. The patient was recalled after 14 days, and suture removal was done. One bone core from each group was not ideal for analysis, and so the patients were excluded from the study. Overall, ten participants from each group were analyzed.

#### **Methodology for histomorphometric analysis**

Harvested bone specimens were fixed in 10% neutral buffered formalin for 24–48 h. Specimens were decalcified in 10% formic acid for 7–10 days. Once the decalcification was completed, as evidenced by the endpoint test, the tissue

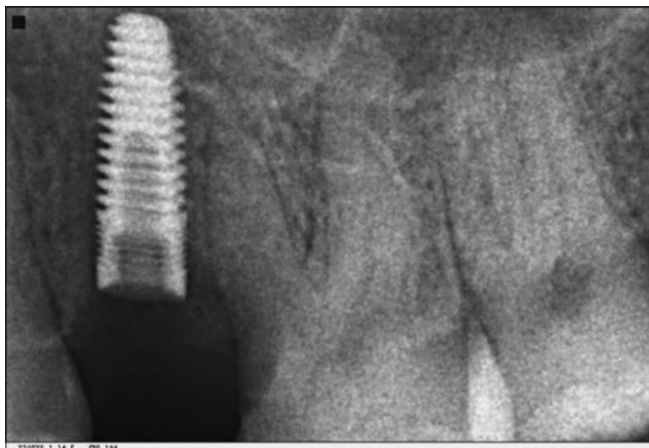
was subjected to processing for paraffin embedding. The blocks were sectioned in 4 μm thick serial longitudinal sections through the central part of core specimens; one section was stained using ehriles hematoxylin and eosin following the standard protocol. Another section was stained with Von Kossa stain. In the H and E stain, the osteoid appeared light pink, the mature bone pink, and the immature bone bluish. Von Kossa stain helps in differentiating osteoid from the mineralized bone. Von kossa staining is a combination of 1% aqueous silver nitrate, 2.5% sodium thiosulfate, and 1% safranin O. Deparaffinized sections were placed in silver nitrate solution, exposed to intense light for 10–60 min, and evaluated. The mineralized bone turned dark brown to black, indicating a completed reaction. Later washed in distilled water and treated with sodium thiosulfate for 5 min later washed in distilled water, followed by dehydration. Osteoid was seen in the red, mineralized bone as black. Using the BX51 research microscope, DP 71 camera, and Image Pro Plus software (Media Cybernetics, Inc., Rockville, USA), photomicrographs of at least three randomly selected fields



**Figure 8:** Trephined bone core 2 mm



**Figure 9:** Evaluation of final insertion torque value



**Figure 10:** Radiograph after implant placement

were taken to calculate the percentage of lamellar bone and woven bone, and provisional connective tissue matrix. The average value was taken for each specimen.

The histology image of size  $3072 \times 4080$  is an input to the algorithm. The input image was converted from the RGB color format into  $L^*a^*b^*$  color space to classify the colors in  $a^*b^*$  color space.

k – means clustering algorithm was applied to the “ab” component of the image to cluster into their different

groups, based on the tissue’s nature. Every pixel is labeled in the image as “osteoid” or woven bone or “connective tissue” based on the algorithm implemented on an i7 Intel core processor with 3–6 GHz frequency and 89GB RAM on Matlab R2014a version clusters obtained from k-means algorithm. The images have created and segmented the histology image by color. The volumetric analysis was performed for the images by using the given equation below.

$M \times N$  was the size of the image, and the resolutions of the image were 300 dpi for direction, then

$$\text{Volume in inch} = \frac{\text{number of pixels}}{M \times N \times 300^3}$$

### Statistical analysis

The obtained data were statistically analyzed using parametric tests, namely independent *t*-test for intergroup comparison. A probability value of  $P \leq 0.05$  was set for statistical significance and a value of  $P \leq 0.001$  for statistically highly significant relation.

### RESULTS

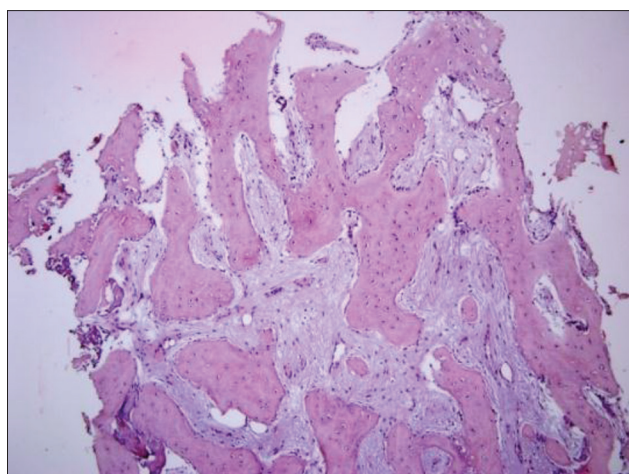
Intergroup comparison of mean torque values between Group A and B measured during implant placement was done. It was observed that the final insertion torque value is more at 8 weeks, i.e.,  $34.50 \pm 8.64$  when compared to 6 weeks [Figure 11], i.e.,  $25.50 \pm 5.99$ , and the difference was statistically significant [ $P = 0.02$ ; Table 1 and Graph 1].

The mean histomorphometric values of obtained bone core were compared between Groups A and B. It was observed that the percentage of bone formed was more at 8 weeks than at 6 weeks [Figure 12], and the difference was found to be statistically significant ( $P = 0.03$ ), with a mean value of  $78.52 \pm 9.38$  at 8 weeks and  $58.66 \pm 24.15$  at 6 weeks [Table 2 and Graph 2].

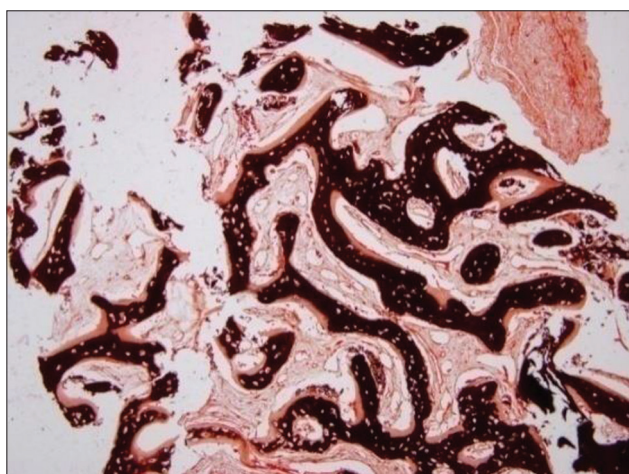
The mean values of osteoid formation were compared between the two groups, i.e., A and B [Figure 13], no statistically significant difference was found ( $P = 0.68$ ). In Group A the mean percentage of osteoid formation was  $19.22 \pm 15.59$  for 6 weeks, whereas in Group B, the osteoid formation was  $21.65 \pm 3.88$  for 8 weeks. Though there is a slightly greater amount of osteoid formation in Group B, the intergroup comparison showed no statistical significance [ $P = 0.65$ ; Table 3 and Graph 3].

### DISCUSSION

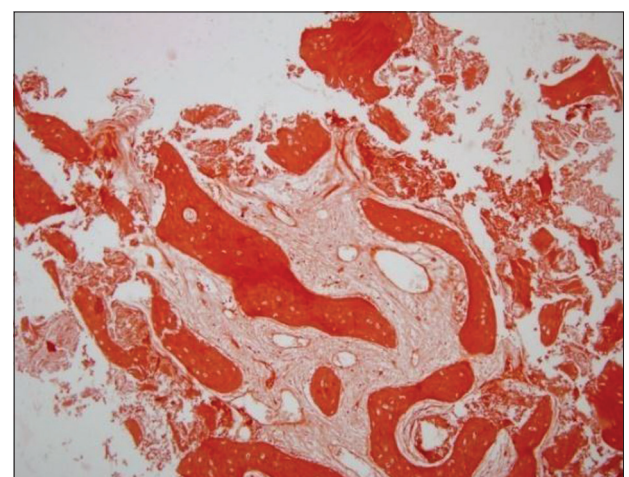
Delayed implant placement, following an extraction, with a healing period of 6–8 months before implant placement, has been conventionally considered the standard of care.<sup>[2]</sup>



**Figure 11:** H and E stained sections shows 57.66% woven bone (×10) in 6 weeks



**Figure 12:** Van Kossa stained sections shows 78.52% woven bone (×10) in 8 weeks



**Figure 13:** Van Kossa stained sections shows 78.52% woven bone (×10) in 8 weeks

Bone remodeling during the healing period would result in loss of bone volume in the buccolingual and occlusocervical

**Table 1: Intergroup comparison of mean final insertion torque values between the groups**

Parameters	Groups (weeks)	Samples	Mean±SD	t	P
Torque values	6	10	25.50±5.99	2.61	0.02 (S)
	8	10	34.50±8.64		

S: Significant, SD: Standard deviation

**Table 2: Intergroup comparison of histomorphometric values of obtained bone core between the groups**

Parameters	Groups (weeks)	Samples	Mean±SD	t	P
Bone formed	6	10	57.66±24.15	2.29	0.03 (S)
	8	10	78.52±9.38		

S: Significant, SD: Standard deviation

**Table 3: Intergroup comparison of mean scores of osteoid formation between the groups**

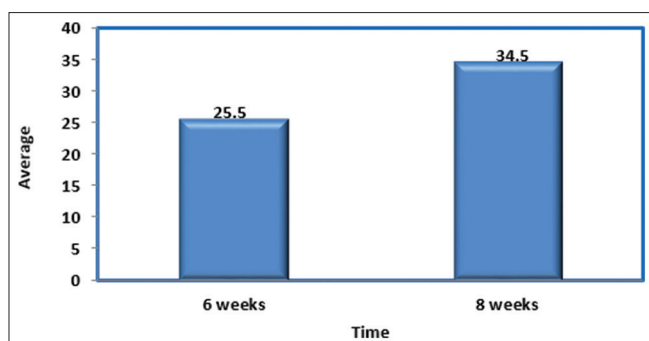
Parameters	Groups (weeks)	Samples	Mean±SD	t	P
Torque values	6	10	19.22±15.59	0.43	0.68 (NS)
	8	10	21.65±3.88		

NS: Not significant, SD: Standard deviation

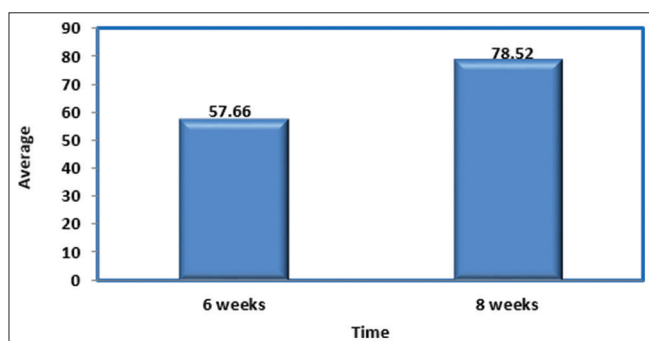
dimensions. Different alternative techniques have been proposed, namely, immediate and early implant placement.<sup>[2]</sup> Implant placement before the resorption of cortical plates of extraction socket could benefit from limiting resorption of bone during remodeling with the concept of atraumatic extraction, socket preservation using A-PRF, and early implant placement. These provide partial bone healing that is consistent with later phases of socket healing. Thus, implant placement could be performed before a large percentage of the alveolar ridge resorption occurs.<sup>[5]</sup> Early implant placement, i.e., 6–8 weeks following the extraction, provides satisfactory soft tissue healing before implant placement and may improve primary stability compared to immediate implant placement. However, there is an absence of scientific literature to identify the optimum timing for early implant placement. Therefore, the current clinical trial focuses on identifying the quality of bone at various time intervals, i.e., 6 and 8 weeks postextraction.

Six to eight weeks of healing period would allow the soft tissue approximation in early implant placement, thus reducing the risk of contamination and infection postoperatively. According to Sanz *et al.* 2012, early implant placement shows a reduction in bone resorption percentage. It also increases the esthetics and overall satisfaction of patients at the end of 2 years. However, these differences were negligible at the end of 5 years.<sup>[4]</sup>

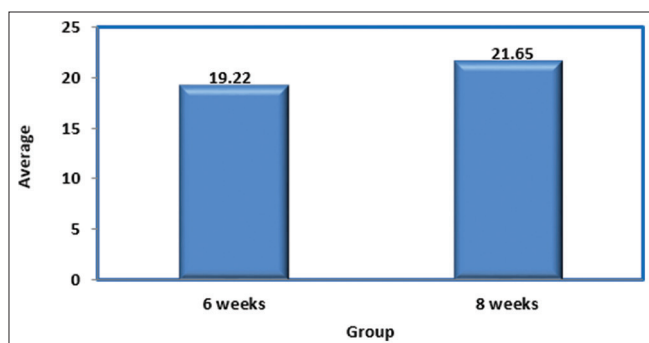
Traditional extraction methods have the disadvantage of producing postoperative pain and could damage the tooth's hard and soft tissues.<sup>[7]</sup> To overcome the various disadvantages of traditional extraction, atraumatic extraction was indicated. It requires an armamentarium like



**Graph 1:** Intergroup comparison of mean torque values between the groups



**Graph 2:** Intergroup comparison of mean histomorphometric values of obtained bone core between Group A and Group B



**Graph 3:** Intergroup comparison of mean values of osteoid formation between the groups

periotomes, luxators, and an advanced atraumatic extraction kit.<sup>[7]</sup> These instruments help extract teeth and retained roots without damaging the surrounding thin alveolar plates of bone and minimally lacerating the soft tissue. Preservation of the residual alveolar socket will limit ridge resorption and improve the foundation for implant placement.

PRF, the second-generation platelet concentrate, consists of fibrin membrane enriched with platelets and growth factors, induces bone formation, and accelerates wound healing. It also acts as a membrane scaffold to support the graft materials, release growth factors, and accelerates tissue regeneration.<sup>[5]</sup> With these advantages,

PRF has emerged as a new autologous material with numerous benefits in implant dentistry. Our study aims to verify PRF's efficacy by assessing bone quality using histomorphometric analysis.

PRF was introduced in 2000 by Choukroun.<sup>[8]</sup> Recent studies indicate that the PRF membrane has a sustained release of essential growth factors for 7 days and up to 28 days.<sup>[9]</sup> PRF can accelerate the socket healing due to its ability to release high quantities of growth factors, namely TGF  $\beta$ -1, PDGF-AB, VEGF, and a vital coagulation multi-domain matrix glycoprotein (TSP-1) during 7 days of placement in the study site. Apart from these, PRF also secretes endothelial growth factors, fibroblast growth factor (FGF), and three crucial pro-inflammatory cytokines-interleukins-1  $\beta$  (IL-1  $\beta$ ), IL-6, and tissue necrotic factor-alpha. These growth factors stimulate several functions, such as chemotaxis, angiogenesis, proliferation, differentiation, and modulation.<sup>[10]</sup> Recent studies showed that PRF could stimulate human osteoblast proliferation.<sup>[11]</sup> Simon *et al.* 2003 reported enhanced bone healing after placement of the PRF matrix in the extraction socket. This preserved site displayed rapid clinical healing, minimal flap reopening, and excellent bone density.

The PRF clot acts as a matrix scaffold for the conglomeration of tissue cells at the healing site. Specifically, fibrin is the end product of the coagulation cascade, a scaffold for the migration of various human cells to a wound. It is a natural ingrowth matrix for fibroblasts and endothelial cells. Fibrin, along with fibronectin, acts as a provisional matrix for the inflow of monocytes, fibroblasts, and endothelial cells. Apart from growth factors and chemotactic factors, an appropriate extracellular matrix is also necessary for angiogenesis.<sup>[12]</sup>

The temporal availability of growth factors sustains their chemotactic properties and accelerates cell growth and proliferation.<sup>[10]</sup> In animal studies, PRF with autogenous bone showed a new bone formation of 38.3% in contained defects in rabbits.<sup>[13]</sup> PRF is a prime source of growth factors that accelerate the initial healing steps, thus shortening an edentulous site's rehabilitation time. The concept of accelerated healing in extraction sockets has been previously validated in a controlled trial that compared healing in premolar sockets grafted with and without PRF.<sup>[14]</sup> At 8 weeks postextraction microcomputed tomographic analysis showed significantly improved microarchitecture and higher bone quality due to PRF.<sup>[15]</sup>

In an investigation on four mongrel dogs, Simon *et al.* 2003 evaluated the healing of sockets treated with platelet-rich

fibrin matrix (PRFM) and guided bone regeneration at 10 days and 2, 3, 6, and 12 weeks postoperatively. Extraction sites grafted with PRFM alone had more rapid healing and less bone resorption than areas treated with demineralized freeze dried bone allograft.<sup>[16]</sup> Considering the properties of PRF, its use as an effective scaffold matrix for osteogenesis, and the secretion of various growth factors and promoting soft tissue healing, in this study, A-PRF is used for socket preservation.

According to Kotsakis *et al.* 2016, the elevation and advancement of the buccal flap for primary closure may lead to the coronal repositioning of the mucogingival junction and reduction in the width of the keratinized mucosa.<sup>[5]</sup> Hauser *et al.* 2013 have reported that an invasive surgical procedure with a buccal mucosal flap appeared to neutralize the PRF's advantages.<sup>[15]</sup> Therefore, in the current investigation to overcome the above-said limitations, instead of coronally advancing labial mucosa, a palatal rotational pedicle flap was performed to attain primary closure after socket preservation.

Implants are routinely placed with Torque  $\geq 30$  Ncm before the implants' immediate loading. In the present study, Group B's final insertion torque values were 35% higher than Group A. This significant increase could be attributed to better bone regeneration at 8 weeks compared to 6 weeks.

According to Bayarchimeg *et al.* 2013, implant stability at the time of surgery is crucial for the long-term success of dental implants. Primary stability is of paramount importance to achieve osseointegration. The author has investigated the correlation between the insertion torque and dental implants' primary stability using artificial bone blocks with different bone densities and compositions to mimic different circumstances encountered in routine daily clinical settings. Within the study's limitations, the author concluded that primary stability does not merely depend on the insertion torque but also bone quality.<sup>[17]</sup>

The mean comparison of histomorphometric values of the obtained bone core in Group-A and Group-B showed a more significant percentage of bone formed at 8 weeks (78.52%) [Figure 12] than at 6 weeks (57.66%). The reason could be the growth factors like TGF, PDGF, FGF found in PRF, which could have aided in new bone formation as seen histologically. The standard deviation values were 24.15 at 6 weeks and 9.38 in the 8<sup>th</sup> week. The higher standard deviations at 6 weeks suggest that bone formation's predictability is less reliable at 6 weeks than 8 weeks.

A case report by Kotsakis *et al.* 2015 similar to the current study on histologic evaluation of the bone specimen retrieved in a single patient at 6 weeks postextraction revealed the bone formation of approximately 30%. The bone gain obtained in the present study was comparatively higher (57.66%), which can be attributed to PRF, which has an earlier healing tendency than nonpreserved sites<sup>[18]</sup> [Figure 11].

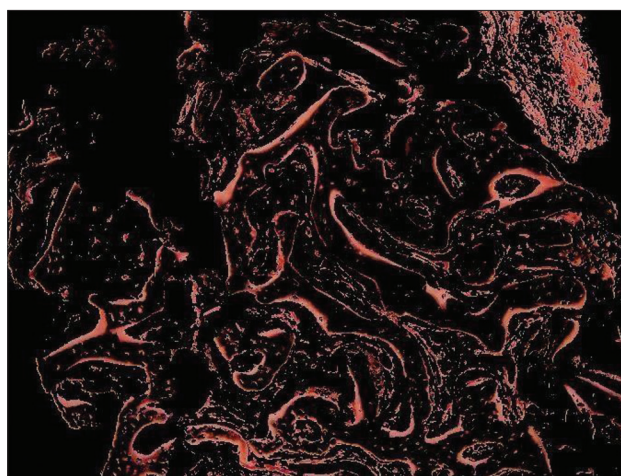
Evian *et al.* 1982 interpreted that maximum osteoblastic activity with osteoblasts laying down osteoid around immature islands of bone occurred between 4 and 6 weeks after extraction. The osteogenic process appears to slow down after 8 weeks.<sup>[19]</sup>

Osteoid is the unmineralized organic portion of the bone matrix that forms before the maturation of bone tissue.<sup>[6]</sup> The mean value of osteoid in the current study was 19.22% at 6 weeks and 21.65% [Figure 14] at 8 weeks. This finding suggests active bone formation was happening both at 6 and 8 weeks.

There is a scope for future research to assess early placed dental implants' long-term success by measuring implant stability using resonance frequency analysis. Also, evaluating bone density using computed tomography after socket preservation using A-PRF at 6 and 8 weeks can help in the correlation between primary stability and bone density.

## CONCLUSION

Within the limitations of the current study, early implant placement in extraction sockets preserved with A-PRF had significantly higher insertion torque values and predictable bone formation at 8 weeks when compared to 6 weeks.



**Figure 14:** Von Kossa stained sections shows 21.65% osteoid ( $\times 10$ ) in 8 weeks



### Acknowledgment

Dr. K. Padhmasavi for histomorphometric analysis, Professor, E.C.E. Department, Shri Vishnu Engineering College for Women.

### Financial support and sponsorship

Source of funding by corresponding author Nukalamarri Om Brahma Prasad Chary and Vishnu Dental College.

### Conflicts of interest

There are no conflicts of interest.

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