# The Impact of Utilizing Injectable Platelet-rich Fibrin and Collagen Plugs for Maintaining the Tooth Extraction Socket: A Review Study

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# تأثير استخدام الفيبرين الغني بالصفائح الدموية القابل للحقن وسدادات الكولاجين في الحفاظ على تجويف السن بعد الخلع: دراسة مراجعة

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## Abstract

Tooth extraction initiates a cascade of biological changes that result in alveolar bone resorption, compromising both the esthetic and functional outcomes of future dental rehabilitations, particularly implant placement. Socket preservation strategies have emerged as crucial interventions aimed at minimizing post-extraction ridge collapse. This review explores the synergistic effects of injectable platelet-rich fibrin (I-PRF) and collagen plugs in enhancing socket preservation outcomes. Collagen plugs serve as biocompatible scaffolds, promoting hemostasis, cellular migration, and angiogenesis, while supporting soft tissue healing and bone regeneration. Concurrently, I-PRF—an autologous, growth factor-rich biomaterial—provides a dynamic reservoir of platelets, leukocytes, and key cytokines such as Platelet-Derived Growth Factor (PDGF), Transforming Growth Factor-beta (TGF-β), and Vascular Endothelial Growth Factor (VEGF), which collectively accelerate tissue regeneration and vascularization. The injectable form allows for versatile application, either alone or in combination with grafting materials. This review highlights current evidence on the biological mechanisms and clinical benefits of combining I-PRF with collagen plugs for socket preservation, demonstrating promising potential for improved ridge maintenance and accelerated healing in post-extraction sites.

**Keywords: socket preservation, socket dimensions, alveolar bone loss, collagen plug, injectable platelet concentrate.**

## المستخلص

تُحدث عملية خلع الأسنان سلسلة من التغيرات البيولوجية التي تؤدي إلى ارتشاف العظم السنخي، مما ينعكس سلبًا على النتائج الجمالية والوظيفية لإعادة التأهيل السني المستقبلية، لا سيما في حالات زراعة الأسنان. وقد برزت استراتيجيات الحفاظ على تجويف الخلع كإجراءات مهمة تهدف إلى تقليل انهيار الحافة السنخية بعد الخلع. تستعرض هذه المراجعة التأثيرات التآزرية للفيبرين الغني بالصفائح الدموية القابل للحقن (I- PRF) وسدادات الكولاجين في تعزيز نتائج الحفاظ على تجويف السن. إذ تعمل سدادات الكولاجين كدعامات متوافقة حيويًا، تُسهّل عملية الإرقاء، وهجرة الخلايا، وتكوين الأوعية الدموية، كما تساهم في التئام الأنسجة الرخوة وتجديد العظم. وفي الوقت نفسه، يوفر الفيبرين الغني بالصفائح القابل للحقن —وهو مادة ذاتية المنشأ وغنية بعوامل النمو— مستودعًا ديناميكيًا يحتوي على الصفائح الدموية، والكريات البيضاء، وسيتوكينات رئيسية مثل عامل النمو المشتق من الصفائح الدموية (PDGF)، وعامل النمو المحوِّل بيتا (TGF-β)، وعامل نمو بطانة الأوعية الدموية (VEGF)، التي تُسهم مجتمعةً في تسريع تجديد الأنسجة وتكوين الأوعية.

وتُتيح الصيغة القابلة للحقن تطبيقًا مرنًا، سواء بشكل منفرد أو عند دمجها مع مواد التطعيم العظمي. تسلط هذه المراجعة الضوء على الأدلة الحالية المتعلقة بالآليات البيولوجية والفوائد السريرية لاستخدام I-PRF بالاقتران مع سدادات الكولاجين للحفاظ على تجويف الخلع، مما يُظهر إمكانيات واعدة في تحسين صيانة الحافة السنخية وتسريع الشفاء في مواقع الخلع.


**الكلمات المفتاحية: الحفاظ على تجويف الخلع، أبعاد التجويف، فقدان العظم السنخي، سدادة الكولاجين، مركز الصفائح الدموية القابل للحقن.**

# 1. INTRODUCTION

Tooth extraction initiates a physiological remodeling process within the alveolar bone, characterized by a gradual loss in both crystal height and buccolingual width of the ridge. This dimensional reduction can significantly hinder the optimal placement, stability, and esthetic integration of prosthetic restorations, particularly endosseous dental implants (1). Socket preservation is an essential technique aimed at minimizing bone loss following tooth extraction. A range of materials, such as bone grafts, platelet-rich fibrin derivatives, and barrier membranes, are employed to enhance healing and preserve the natural shape of the alveolar ridge (2). The collagen plug, made from a biocompatible extracellular matrix, promotes osteoblast migration, helps stabilize the blood clot, improves soft tissue repair, and contributes to bone regeneration and the preservation of the alveolar ridge(3). Its porous architecture offers a scaffold that enables the migration and proliferation of cells such as fibroblasts and endothelial cells, which is essential for the development of new connective tissue and vascular networks(4). I-PRF is a novel autologous blood-derived biomaterial that remains in a liquid state while incorporating a fibrin meshwork resembling that of solid PRF. Unlike traditional PRP, it offers a unique combination of flowable consistency and regenerative potential, making it ideal for enhancing tissue healing(5). Injectable PRF retains its liquid form temporarily before coagulating, allowing for straightforward mixing with grafting materials or direct injection into the surgical site(6). This substance contains high concentrations of platelets, leukocytes, and essential growth factors such as PDGF, TGF-β, and VEGF, which play crucial roles in promoting angiogenesis, soft tissue regeneration, and osteogenesis(7).

## 2. Socket healing

Tooth removal initiates a complex cascade of localized biological events involving both the alveolar bone and adjacent soft tissues. These processes are essential for promoting socket closure and reestablishing tissue homeostasis, collectively described as the phenomenon of socket healing(8). Alveolar healing progresses through distinct phases, beginning immediately after tooth extraction and extending over several months, typically up to six. Extensive research has shown that both modeling and remodeling of the alveolar bone can continue beyond the initial healing period, often lasting over a year post-extraction (9). Socket healing is influenced by a diverse array of determinants, encompassing local tissue conditions, systemic health status, clinician-related (iatrogenic) interventions, and external environmental factors(10). "Socket healing is typically associated with notable morphological changes in the alveolar bone, including a reduction in its dimensional volume and alterations in its structural configuration(11).

## 3. Morphological Alterations in Alveolar Bone Post-Socket Healing:

Following tooth extraction, remodeling affects all surfaces of the alveolar bone—including the buccal, palatal, mesial, and distal regions—resulting in dimensional alterations. The bundle bone, which is a tooth-associated component, has been identified as the initial site of resorption and plays a key role in the subsequent vertical reduction of the alveolar ridge(12). The most pronounced decrease in alveolar ridge dimensions occurs within the initial three months following tooth extraction, after which bone resorption persists at a more gradual rate over the individual's lifetime(13). The accelerated bone loss observed shortly after tooth

extraction is thought to be associated with heightened osteoclastic activity during the early phases of alveolar bone modeling and remodeling(14). Schropp *et al.* carried out a forward-looking investigation assessing alterations in both osseous and soft tissues following tooth extraction, employing clinical assessments and radiographic analysis. Their findings revealed that nearly half of the buccopalatal ridge width was lost within the first three months of the healing process(9, 15). A systematic review encompassing 12 studies evaluated dimensional changes during the post-extraction healing phase and reported a mean horizontal reduction of approximately 3.87 mm in ridge width. Additionally, vertical bone loss was observed, ranging from 1.67 to 2.03 mm clinically, and approximately 1.53 mm as measured radiographically(16). A detailed analysis conducted by Tan *et al.* (17) demonstrated that within six months following tooth extraction, vertical bone loss ranged from 11% to 22%, while horizontal dimensional reduction in ridge width varied between 29% and 63%. Resorptive activity was found to be more substantial on the buccal aspect of the alveolar bone compared to the palatal side, with the mandible exhibiting more significant changes than the maxilla. These alterations were most prominent in the molar region relative to the premolar area. As a result, the remodeling process of the alveolar ridge leads to a ridge that is both reduced in height and width, predominantly due to buccal bone resorption, ultimately causing a palatal displacement of the residual alveolar structure(18).

## 4. Factors that affect socket healing

The variability in alveolar socket healing outcomes can be attributed to a multitude of factors, including systemic conditions, clinician-induced

(iatrogenic) factors, localized anatomical or pathological influences, and environmental determinants.

Among the local determinants influencing socket healing, the anatomical location of the extraction site plays a significant role. Mandibular molar regions have been associated with the most inconsistent and irregular healing patterns, whereas the maxillary incisor and canine areas tend to exhibit the most favorable and predictable healing responses(19). In a retrospective analysis, Pramstraller et al.(20) reported that extraction sites in the molar region experienced more substantial bone loss compared to premolar areas. They suggested that this discrepancy may be due to the increased complexity involved in extracting posterior teeth, which typically results in a broader post-extraction socket. Furthermore, the elevation of the entire muco-periosteal flap prior to tooth removal was identified as an additional local factor potentially affecting alveolar socket healing. This procedure has the potential to contribute to bone resorption, as it has been demonstrated to promote periodontal attachment loss and impair vascular supply to the regenerating socket, thereby negatively impacting the healing process(21). Moreover, studies have indicated that multiple adjacent tooth extractions tend to result in more extensive alveolar bone resorption compared to isolated single-tooth extraction sites(18).

The molecular and cellular mechanisms underlying post-extraction socket healing can be significantly influenced by systemic factors, with smoking being a notable contributor to impaired regenerative processes(22), uncontrolled systemic diseases such as post-menopausal osteoporosis(23), and diabetes mellitus(24). The specific mechanism by which smoking impacts socket healing remains unclear, but Kuśnierek *et al.* reported that the

prevalence rate of alveolar osteitis was 13.2% among smokers, compared to just 3.2% in non-smokers (25). Research on the harmful components of cigarette smoke, especially nicotine and carbon monoxide, indicates possible ways in which smoking could hinder wound healing (26). Nicotine causes vasoconstriction, which results in hypoxia, thereby obstructing tissue repair by limiting the availability of oxygen that is vital for cell movement, collagen formation, and immune function(25). Likewise, carbon monoxide worsens hypoxia by binding to hemoglobin more effectively than oxygen, which further diminishes oxygen supply to tissues(26). There is evidence indicating that osteoporosis in postmenopausal women may lead to a reduction in the residual ridge after tooth extraction, which can result in a mandibular ridge that appears knife-edge and a diminished maxillary alveolar ridge(23).

Likewise, Shahen *et al.* (27) observed that patients with poorly controlled insulin-dependent diabetes exhibited heightened alveolar bone resorption during socket healing, which was associated with diminished synthesis of the collagen matrix. Although patients with uncontrolled type 2 diabetes often experience poor socket healing, the application of hyaluronic acid to the socket after extraction may offer therapeutic benefits (28). Hyaluronic acid has been shown to play a beneficial role in the initial stages of post-extraction socket healing by enhancing fibroblast migration, proliferation, and survival, as well as promoting osteogenic differentiation. Additionally, it upregulates the expression of key wound healing-related genes, such as type III collagen and transforming growth factor-β3(29-31). Furthermore, research has indicated that post-extraction application of mouthwashes containing chlorhexidine may contribute to a reduction in alveolar bone loss, despite the precise biological mechanisms responsible

for this effect not yet being fully elucidated(32). Liao *et al.* (33). Demonstrated that hyperbaric oxygen therapy not only enhances the management of jaw osteoradionecrosis but also contributes to extraction socket healing and preservation of the alveolar ridge by reducing post-extraction alveolar bone resorption. This effect is achieved by promoting osteoblast formation and suppressing osteoclast activity. Therefore, they suggest that this approach could be applied clinically to accelerate alveolar socket healing and support ridge preservation in human patients.

The extent of tissue trauma caused by the surgeon during tooth extraction and the size of the resulting bone defect should also be considered, as these variables have the potential to significantly impact the regenerative outcome of alveolar socket healing. Under these circumstances, bone resorption tends to be more pronounced compared to less invasive cases (34).

## 5. Socket preservation

Extraction socket preservation (ESP) is a technique performed immediately after tooth extraction to minimize soft tissue and bone loss. Studies have shown that ESP helps maintain greater bone dimensions compared to sites where no preservation is done (35). Without restoration, extraction can lead to disuse ridge atrophy and significant vertical and horizontal bone loss, often requiring additional grafting procedures for successful implant placement (36). ESP allows for the placement of wider and longer implant fixtures and reduces the need for bone augmentation during implantation (37). However, ESP may not be necessary in all cases, and the decision should be based on the condition of the socket and surrounding tissues at the time of extraction(36).

## 6. Socket preservation techniques:

To minimize alveolar bone loss to an acceptable extent, various surgical approaches have been suggested, including minimizing extraction-related trauma and restricting flap elevation(38). Socket preservation typically involves the following procedures:

### A. Immediate implants:

Dental implant placement is typically scheduled between 6 and 12 months following tooth extraction to ensure full maturation and healing of the alveolar socket. Nevertheless, during this period, alterations in the size and morphology of the alveolar bone can occur, potentially complicating implant placement and affecting treatment outcomes (39). To avoid these changes, Paolantonio *et al.* (40) proposed immediate implantation. Despite this, studies have reported inconsistent results. For instance, Velasco *et al.* (41) found an estimated reduction of about 2.6 mm in bone three months after immediate implant placement, and also observed initial bone-to-implant contact one month post-extraction, followed by buccal wall resorption and partial loss of contact by the third month (42). Mao *et al.* (43) confirmed that immediate loading does not alter the extent of buccal bone resorption. Nevertheless, using bone graft materials—either with or without immediate implantation—has been shown to reduce horizontal bone changes, especially within the coronal segment of the buccal alveolar plate, when contrasted with spontaneous or natural healing processes. Therefore, combining immediate implant placement with alveolar ridge preservation techniques, such as bone grafting, may be an effective strategy to limit modifications in osseous tissue structure and shorten the total duration of the therapeutic process(44).

## B. Bone graft and bone substitute:

Bone grafts are widely used to prevent alveolar bone loss after tooth extraction and can be combined with materials like barrier membranes (45). There are four main types:

- **Autogenous grafts** (from the patient) are the gold standard due to their ability to promote bone growth and biocompatibility, with common donor sites inside or outside the mouth (46).
- **Allografts** come from donors of the same species and have good bone-regenerating properties, but carry risks of immune response and disease transmission (47).
- **Xenografts** are animal-derived, mainly bovine or porcine, and are biocompatible but more immunogenic and riskier for disease transmission (48).
- **Synthetic substitutes** like hydroxyapatite and tricalcium phosphate mimic natural bone, provide consistent resorption rates, and avoid disease risks linked to biological grafts (49).

## C. Barrier membrane in socket preservation:

Barrier membranes play a key role in guided tissue and bone regeneration by protecting the bone site from surrounding soft tissues, promoting bone cell growth, and preventing infiltration by undesired cells. This helps manage bone defects and accelerates healing in a controlled way(50). These membranes are classified as absorbable or nonabsorbable based on their degradation properties. Nonabsorbable types include titanium mesh and various forms of polytetrafluoroethylene (ePTFE, high-density PTFE, titanium-reinforced PTFE), while absorbable membranes include polymeric, collagen, pericardium membranes, platelet-rich fibrin, and acellular dermal matrix(51).

## D. Collagen plug:

Collagen plugs are cylindrical collagen sponges designed to fit into extraction sockets, acting as scaffolds that support healing by attracting fibroblasts and aiding in hemostasis(52)(. As components of the extracellular matrix, they stabilize the blood clot, support osteoblast migration, promote soft tissue repair, and contribute to bone regeneration and ridge preservation(3).

These plugs are made from highly purified porcine or bovine collagen, offering excellent biocompatibility and seamless integration with host tissues. Their porous structure creates a favorable environment for the infiltration of key cells like fibroblasts and endothelial cells, essential for new connective tissue and blood vessel formation(53). One major advantage of collagen plugs is that they eliminate the need for flap elevation or graft harvesting, thus reducing postoperative morbidity(52). They also help minimize complications after extraction, such as bleeding and infection(54). Their flexibility and adaptability make them easy to shape and apply to sockets of various sizes(55). In addition, they can be used in different surgical procedures, enhancing soft tissue healing and reducing postoperative discomfort(56). However, while collagen plugs offer many benefits, a potential limitation is their lack of mechanical strength compared to other graft materials, which may affect their ability to support large defects. Nonabsorbable types include titanium mesh and various forms of polytetrafluoroethylene (ePTFE, high-density PTFE, titanium-reinforced PTFE), while absorbable membranes include polymeric, collagen, pericardium membranes, platelet-rich fibrin, and acellular dermal matrix(51).

## 7. PLATELET CONCENTRATES

Platelet concentrates were introduced over 20 years ago to support tissue healing by using blood-derived growth factors that enhance revascularization and cell proliferation(57).

Platelet concentrates are classified into four main types based on their leukocyte content and fibrin structure (58):

- Pure platelet-rich plasma (P-PRP) or leukocyte-poor platelet-rich plasma (LP-PRP).
- Leukocyte- and platelet-rich plasma (L-PRP).
- Pure PRF (P-PRF)—or leukocyte-poor platelet-rich fibrin.
- Leukocyte- and platelet-rich fibrin (L-PRF).

### A. Platelet-rich plasma (PRP):

As a first-generation platelet concentrate, it is produced from the patient's blood and activated using calcium chloride and thrombin(59). Once activated, platelets rapidly begin releasing growth factors, with most being fully released within the first hour(60).

### B. Platelet-rich fibrin (PRF):

Leukocyte-PRF (Choukroun's PRF), introduced in 2000, is a second-generation platelet concentrate prepared without anticoagulants, aiming to promote wound healing and tissue regeneration(61). It is prepared by centrifuging venous blood at 3000 rpm for 10 minutes, forming a PRF clot that is then compressed into a strong membrane(62). The absence of additives reduces the risk of postoperative complications(63). A more recent version, Advanced PRF (A-PRF), is produced using a softer centrifugation

protocol—1300 rpm for 8 minutes—resulting in a dense fibrin network that enhances healing(64).

### C. Injectable platelet-rich fibrin (I-PRF):

An Injectable platelet-rich fibrin (I-PRF), developed by Choukroun and Ghanaati in 2018, is a liquid form prepared without anticoagulants using a gentle centrifugation of 700 rpm for 3 minutes(65). It separates into two layers, with the upper I-PRF layer used for regenerative procedures. This injectable form, “Fig. 1”, can be applied directly to defect sites or mixed with bone grafts to enhance graft stability and handling(66).

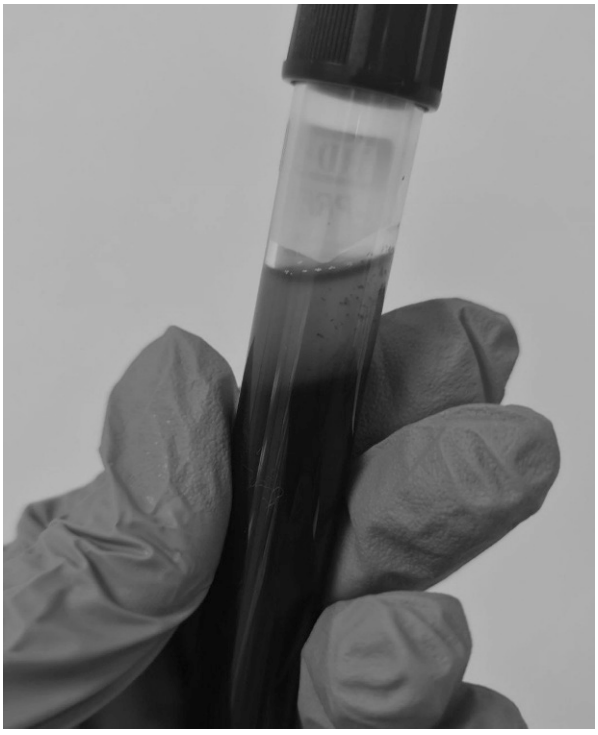

**Fig. 1: Upper I-PRF layer.**

Dohan Ehrenfest *et al.* (2010) reported that histological analysis of all PRF-based matrices shows three main components(67):

1. Blood cells: PRF matrices contain platelets, leukocytes, and red blood cells. Platelets release growth factors crucial for tissue repair, while leukocytes support wound healing and stimulate angiogenesis through immune regulation. Macrophages also aid angiogenesis by secreting growth-promoting factors. Injectable PRF (I-PRF) has the highest levels of platelets and leukocytes among solid PRF types(68-70).
2. The three-dimensional fibrin matrix: is crucial for tissue repair, even though most research has focused mainly on growth factors. It functions as a biological scaffold that supports the gathering of adherent cells at the healing site. Furthermore, the fibrin matrix serves as a carrier for growth factors, providing a controlled release that preserves their bioactivity throughout the healing process(71).
3. Growth factors of PRF:

   Key growth factors found in PRF include the following(72):

   1. Platelet-Derived Growth Factor (PDGF) regulates the growth and movement of mesenchymal cells.
   2. Transforming Growth Factor-beta (TGF-β) promotes the proliferation of mesenchymal cells and matrix production.
   3. Vascular Endothelial Growth Factor (VEGF) strongly stimulates tissue angiogenesis.
   4. Insulin-like growth factor (IGF) supports the differentiation, proliferation, and protection of mesenchymal cells.

I-PRF's slower centrifugation results in a higher concentration of regenerative cells and growth factors compared to other PRF types. Applying PRF to titanium implants improves early implant stability and promotes thicker fibrin networks on implant surfaces, enhancing cell migration and differentiation around the implant(73).

## 8. Effect of I-PRF on bone tissue engineering:

I-PRF is a recently introduced biomaterial in bone tissue engineering that has gained significant attention. It is recognized as a substantial reservoir of bioactive compounds with diverse functional properties.

### 1. Regenerative capability:

Research evaluating the osteoinductive properties of I-PRF has demonstrated favorable outcomes in promoting osteoblast attachment, maturation, mobility, and proliferation, as well as enhancing the mineralization capacity of stem cells.(74). Furthermore, Fernández-Medina *et al.* found that at low concentrations, I-PRF outperformed A-PRF, L-PRP, P-PRP, and blood clot in enhancing mineralization, making it a preferred option for tissue engineering that uses autologous factors to stimulate bone regeneration(64). Its injectable nature and ease of application have made I-PRF suitable for various clinical procedures in oral and maxillofacial bone restoration, including procedures like alveolar ridge reconstruction, maxillary sinus elevation, and surgical correction of cleft palate defects(75).

### 2. Anti-inflammatory capability:

Due to its slower centrifugation speed compared to traditional counterparts, I-PRF contains higher levels of growth factors and regenerative

cells. Additionally, I-PRF differs from L-PRF in cytokine composition, being richer in interleukin-10 (IL-10), which helps reduce inflammatory mediators and supports tissue regeneration(76). Its practical clinical use allows physicians to easily apply this liquid platelet concentrate alone or combined with other biomaterials to promote bone regeneration(77).

### 3. Anti-bacterial capability:

I-PRF has been shown to exhibit strong antibacterial properties against *Porphyromonas gingivalis* and *Aggregatibacter actinomycetemcomitans*. Consequently, it is proposed that, in addition to its osteoinductive potential, I-PRF may also exert antimicrobial effects(78).

## 9. Limitations of Injectable PRF in Socket Preservation:

The disadvantages of PRF include, but are not limited to:

### Resorption:

PRF, including injectable PRF (I-PRF), is susceptible to resorption over time. This means that the material breaks down and is absorbed by the body, potentially reducing its effectiveness in maintaining socket volume.

### Limited Duration of Action:

While PRF can stimulate initial healing and release growth factors, its effects on bone regeneration may not be sustained in the long term. Studies suggest that PRF is most effective in the early healing period after tooth extraction, but longer-term benefits may be limited(79).

**Variable Outcomes:**

The success of PRF in socket preservation can vary. Some studies show significant improvements in bone preservation and implant success with PRF, while others show less pronounced or no significant differences compared to control groups.

**Potential for Infection:**

Though generally considered safe, PRF, like any injectable material, carries a small risk of infection at the injection site.

**Cost and Availability:**

The cost of PRF preparation and the time required for its preparation can be a limiting factor for some patients and practices(80).

## 10. Conclusion

Combining injectable platelet-rich fibrin (I-PRF) with collagen plugs provides an effective and minimally invasive method for socket preservation after tooth extraction. This technique enhances soft and hard tissue healing by delivering growth factors and creating a bioactive scaffold that supports angiogenesis and regeneration. It reduces postoperative complications, preserves alveolar bone structure, and simplifies clinical procedures without the need for graft harvesting or flap elevation. Due to its biocompatibility, ease of use, and regenerative potential, this approach is a promising option in oral surgery and implantology.

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