T.C.

YEDITEPE UNIVERSTY

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EVALUATION OF ALVEOLAR BONE RESORPTION AFTER TOOTH EXTRACTION WITH DENTAL VOLUMETRIC TOMOGRAPHY

DOCTOR OF PHILOSOPHY THESIS

BERKAY ÖZATA, DDS

Istanbul-2023

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Doctor Of Philosophy Thesis

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APPROVAL

This thesis has been deemed by the jury in accordance with the relevant articles of Yeditepe University Graduate Education and Examinations Regulation and has beenapproved by Administrative Board of Institute with decision dated .....and numbered .....

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DECLARATION

I hereby declare that this thesis is my own work and that,to the best of my knowledge and belief, it contains no material previously published or written by another person not material which has been accepted for the award of any other degree except where due acknowledgment has been made in the best.

31.07.2023
Berkay ÖZATA

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TABLE OF CONTENT

LISTS OF TABLES

LISTS OF FIGURES

ABBREVIATIONS

®	Registered Trademark
CBCT	Cone Beam Computered Tomography
TGF-β	Transforming Growth Factor-β
RANK	Receptor Activator of Nuclear Factor Kappa
MSCs	Mesenchymal Stem Cells
ECM	Extracellular Matrix
MMP	Matrix Metalloproteinases
CHX	Chlorhexidine
FGF	Fibroblast Growth Factor
PDGF	Platelet-Derived Growth Factor
EGF	Epidermal Growth Factor
VEGF	Vascular Endothelial Growth Factor
FMPS	Full Mouth Plaque Score
FMBS	Full Mouth Bleeding Score
MPR	Multiplanar Reconstruction
ICDAS	International Caries Detection and Assessment System
PD	Probing Depth
VAS	Visual Analogue Scale

ABSTRACT

OZATA, B (2023) Evaluation Of Alveolar Bone Resorption After Tooth Extraction With Cone Beam Computer Tomography. Yeditepe University Health Sciences, Periodontology Department. Ph.D Thesis, Istanbul

Resorption occurring in the buccal bone after tooth extraction negatively affects the patient's health and aesthetic expectations. several atraumatic tooth extraction methods have been developed to minimize damage to the buccal bone. The aim of this randomized controlled clinical study is to compare the amount of alveolar bone resorption, soft tissue healing, and patient's pos-operative pain following tooth extraction using a periotome and an elevator. In the test group, tooth extraction was performed by using a periotome whereas in the control group with an elevator and dental forceps. Cone-beam computed tomography (CBCT) imaging was performed within 24 hours and at 3 months after tooth extraction for both groups. Visual analog scale (VAS) was provided to assess the post-extraction pain, and patients were asked to rate the pain experienced during the first 7 days. No statistically significant difference was observed between the two groups in terms of pain and soft tissue healing evaluated at the 7th day after tooth extraction ($p>0.05$). Radiological evaluation using CBCT at 3 months showed no statistically significant difference in buccal bone height and bucco-lingual/palatal bone width between the groups ($p>0.05$). However, the socket filling percentage was found to be statistically higher in the test group compared to the control group ($p<0.05$). Within the limits of this study, no superiority of the periotome over the traditional elevator could be established. Long-term follow-up studies with increased sample size and histological evaluations are needed.

Key Words: Atraumatic tooth extraction, periotome, buccal bone reserption

ABSTRACT (TURKISH)

OZATA, B (2023). Diş Çekimi Sonrasi Meydana Gelen Alveolar Kemik Rezorpsiyonunun Konik Işınlı Bilgisayarlı Tomografi ile Değerlendirilmesi. Yeditepe Üniversitesi Sağlık Bilimleri Enstitüsü, Periodontoloji Bölümü, Doktora Tezi. İstanbul

Diş çekimi sonrasında bukkal kemikte meydana gelen değişiklikler, hastanın sağlığını ve estetik beklentisini olumsuz etkilemektedir. Bu sebeple bukkal kemiğe minimum zarar veren birçok atravmatik diş çekim yöntemi geliştirilmiştir. Bu randomize kontrollü klinik çalışmanın amacı periotome ve elevatör kullanılarak yapılacak diş çekimi sonrası meydana gelen alveolar kemik rezorpsiyon miktarı, yumuşak doku iyileşmesi, ve hasta post-operatif ağrı miktarının karşılaştırılmasıdır. Diş çekimi endikasyonu verilen 26 dişte, test grubunda periotome yardımıyla periodontal fibriller kesilirken, kontrol grubunda elevatör yardımıyla dişler eleve edilmiştirve sonrasında davye ile diş çekimi yapılmıştır. Diş çekimi sonrası her iki gruptanda 24 saat içerisinde ve 3. ayda konik ışınlı bilgisayarlı tomografi(CBCT) ile görüntüleme yapılmıştır. Hastalara diş çekimi sonrası meydana gelen ağrıyı değerlendirebilmesi için görsel analog ölçek (VAS) verilmiş, ilk 7 gün boyunca oluşan ağrıyı puanlaması istenmiş ve 7. Günün sonunda veriler toplanmıştır. Hastaların yumuşak doku iyileşmesi 7. Gün sonunda kontrol edilmiş ve diş çekimi sonrası iyileşme indeksi yardımıyla değerlendirilmiştir. Diş çekimleri sonrası 7. Gün değerlendirilen ağrı ve yumuşak doku iyileşmesi açısından her iki grup arasında istatiksel açıdan anlamlı fark gözlenmemiştir ($p>0.05$). 3. Ay sonunda CBCT yardımıyla yapılan radyolojik değerlendirmede bukkal kemik yüksekliği ve çekim soketinin bukko-ligual/palatal mesafesinde istatiksel açıdan herhangi bir fark gözlenmemiştir ($p>0.05$). Alveol soketinin dolma yüzdesi ise test grubunda, kontrol grubuna göre istatiksel açıdan daha yüksek bulunmuştur ($p<0.05$). Bu çalışmanın limitleri dahilinde, periotome'un geleneksel elevatöre göre üstünlüğü bulunamamıştır. Uzun dönem takipli, örnek sayısı artmış ve histolojik değerlendirmelerin yapıldığı çalışmalara ihtiyaç bulunmaktadır.

Anahtar Kelimeler: Atravmatik diş çekimi, periotome, bukkal kemik rezorpsiyonu

1.INTRODUCTION and PURPOSE

The healing process of the alveolar socket following tooth extraction has gained importance due to the increased aesthetic expectations of patients and the popularity of implant-supported prostheses in modern dentistry (1). In the past, tooth extraction was merely considered as tooth loss. However, it is now understood that local changes occurring in the socket lead to permanent deformations in the hard and soft tissues. The success in preserving the alveolar socket after tooth extraction relies on preserving the integrity of the alveolar crest while minimizing trauma to the surrounding soft and hard tissues (2).

Tooth extraction is performed in cases of extensive decay, periodontal diseases, orthodontic treatment, symptomatic impacted teeth, and traumatic injuries (3). The process of local changes that occur to close the wound and achieve tissue homeostasis following extraction is referred to as "socket healing" (2). During this healing process, morphological and dimensional changes occur in the alveolar socket, leading to bone resorption (4–6). Studies have indicated that alveolar bone resorption peaks in the first month following tooth extraction, although it continues for an extended period. A study by Amler et al. (7) reported vertical bone resorption ranging from 3 to 5 mm and horizontal resorption ranging from 0.4 to 3.9 mm at 6 months after tooth extraction.

It has been reported in studies that the extraction technique and the instrument types used have an impact on alveolar bone loss. In modern dentistry, tooth extraction can be performed with classic manual instruments such as rubber band, physics forceps, benex extractor, easy X-trac system periotome, as well as power-driven instruments like piezosurgery, sonosurgery and powered periotome (8).

Following traumatic tooth extraction resulting in the loss of supporting bone walls, healing leads to the formation of narrow and short bone crests. This situation not only poses a risk to the long-term success of subsequent prosthetic treatments but also paves the way for aesthetic problems in the patient (9).

The use of periotome, which is believed to reduce both bone and soft tissue damage while preserving bone integrity during extraction, is considered an important advancement in modern dentistry (10). This instrument, developed by Directa (Sweden)® company, is inserted into the periodontal ligament space between the tooth and the gum using its sharp tip, cutting the periodontal ligament fibers in the space. During the cutting process, a gentle but firm rotational movement is applied to the tooth.

The continuous rotational movement facilitates cutting the fibers while expanding the alveolar socket. Although it resembles an elevator, tooth extraction is performed with significantly less force using a periotome (11). The use of a periotome reduces trauma to the alveolar socket during tooth extraction (12).

Based on this information, the aim of this study is to compare the amount of alveolar bone resorption, soft tissue healing and patient perception/comfort following tooth extraction using a periotome with forceps and an elevator with forceps.

2.LITERATURE REVIEW

2.1. Bone Tissue

Bone tissue is a specialized connective tissue, which is one of the hardest tissues in the body composed of cells, fibers, and intercellular substance. Unlike other connective tissues in the body, the mineralization of its extracellular components provides it with significant strength and stability, making it ideal for providing mechanical support. Bones are responsible for the storage and regulation of ions in the body, providing internal support against gravity, protecting internal organs, and converting muscle contractions created by striated muscle into movement. To perform these functions, bone must be rigid to resist deformation, yet flexible to absorb energy (13).

2.1.1. Bone Cells

Bone is primarily composed of four types of cells. Osteocytes, which are responsible for bone formation and originate from mesenchymal stem cells, periosteal cells, osteoblasts, and osteoclasts, which are responsible for bone resorption and originate from hematopoietic stem cells (13).

2.1.1.1. Osteoblasts

These are the cells responsible for new bone formation during skeletal development and bone remodeling processes. Osteoblasts originate from the differentiation of mesenchymal cells associated with osteoprogenitors in the periosteum, bone marrow, endosteum, and bone canals. Osteoblasts are arranged tightly on the bone surface and have an oval shape. They contain mitochondria, a Golgi apparatus, endoplasmic reticulum, and cytoplasmic extensions that enable communication with neighboring cells (14).

Osteoblasts produce growth factors and enzymes, such as type 1 collagen, collagenase, alkaline phosphatase, Transforming Growth Factor-β (TGF-β), and osteocalcin, to create new bone. Osteoblasts are responsible for the formation of the bone matrix, and the resulting unmineralized tissue is called osteoid. There are three different pathways that osteoblasts can follow: they can remain as active osteoblasts, become surrounded by the matrix and become osteocytes, or become relatively inactive and form periosteal cells, after completing bone formation (14).

2.1.1.2. Osteocytes

Osteocytes make up 90-95 % of bone cells and have an average lifespan of 25 years. They are formed when some of the osteoblasts that have completed their bone-building function become surrounded by matrix. Osteocytes originate from mesenchymal stem cells as a result of the differentiation of osteoblasts. This transformation occurs in four stages: osteoid-osteocyte, preosteocyte, young osteocyte, and mature osteocyte. During this process, many changes occur in osteoblasts, including a decrease in the number of organelles such as endoplasmic reticulum and Golgi apparatus, as well as an increase in the number of nuclei in the cytoplasm. These changes decrease protein synthesis and secretion. Branched osteocytes are located within lacunae surrounded by mineralized bone matrix. Osteocytes within bone differ depending on the structure of the bone in which they are found. Osteocytes within trabecular bone have a long morphology, while those within cortical bone are more spherical. Osteocytes regulate the protein and mineral content of the matrix and maintain the viability of bone tissue. Their long cytoplasmic extensions allow nutrients and critical hormones for bone cells to pass from cell to cell, providing nourishment to bones without blood vessels that have completed calcification (15).

2.1.1.3. Osteoclasts

Osteoclasts are multinucleated giant cells responsible for osteonecrosis, typically found on the surface of bone. They are derived from mononuclear cells of hematopoietic stem cells under the influence of factors such as macrophage colony-stimulating factor (MCS-F) and Receptor Activator of Nuclear factor Kappa (RANK), which are secreted by osteoblasts and osteocytes. MCS-F binds to receptors on osteoclast precursors and stimulates their proliferation. RANK plays a critical role in osteoclastogenesis by binding to receptors on osteoclast precursors and inducing the formation of osteoclasts (15).

Osteoclast cells on the bone surface begin to break down the matrix of the bone through the enzymes they secrete and create erosive cavities called Howship's lacunae through enzymatic pathways. The debris that results from this breakdown is also eliminated through MCS-F (15,16).

2.1.2. Bone Membranes

2.1.2.1. Periosteum

Periosteum, which covers the outer surface of the bone, consists of two layers, inner and outer. The outer layer is composed of a fibrous structure rich in collagen fibers and fibroblasts, and contains numerous capillaries surrounded by pericytes that serve as stem cells for bone. Pericytes play a crucial role in periosteal bone formation and have the ability to differentiate into many different cell types, including osteoblasts. Collagen fibers in this layer, which contains sympathetic nerve fibers, run parallel to the bone surface in a capsule-like structure. These collagen fiber bundles penetrate into the bone and attach it to the periosteum and are called Sharpey's fibers. The inner layer is densely composed of osteogenic progenitor cells and osteoblasts and plays an active role in bone formation and repair. Although it begins to thin with age, it always maintains a pool of progenitor cells (17).

2.1.2.2. Endosteum

Endosteum, which is known as the membrane that lines the cavities inside the bone marrow, covers the inner surface of the bone, including the Haversian canals throughout the bone. Compared to periosteum, endosteum has a much thinner structure and is composed of flattened osteoprogenitor cells and type 3 collagen fibers (18–20).

There are three types of endosteum: cortical endosteum, which covers the cavities in the bone marrow and is rich in nerves and blood vessels, osteon endosteum, which covers the Haversian canals, and trabecular endosteum, which covers the developing bone regions. Endosteum plays a role in the formation of an internal matrix through the absorption and accumulation of tissue, and continuously stimulates internal bone resorption. Endosteum also contributes to the accumulation of calcium in the bone matrix and facilitates the transfer of calcium between the bone matrix and the blood (21–26).

2.1.3 Structure of Bone

2.1.3.1. Primary Bone Tissue

Primary bone tissue, also known as immature or woven bone, is a type of bone that is seen during embryological formation, fracture, repair, and

healing stages. This type of bone, which is present temporarily, gives way to secondary bone after a certain period of time. This bone type is weak in terms of minerals, is not sufficiently calcified, and contains a large number of irregularly distributed osteocytes. The collagen fibers in it also have an irregular distribution (27).

2.1.3.2. Secondary Bone Tissue

Secondary bone tissue, also known as lamellar bone due to its mature, lamellar structure, contains hydroxyapatite crystals on the fibrils of its lamellae, which are parallel to each other but form cross or spiral connections to adjacent lamellae. Thanks to these special connections and hydroxyapatite crystals, bone gains a much stronger structure. Both collagen fibers and osteocytes are arranged in an organized manner compared to primary bone tissue. As a result, it is much more calcified and durable than primary bone tissue (27). There are two types of secondary bone tissue: spongy bone and cortical bone.

2.1.3.2.A. Spongy Bone

Spongy bone, also known as cancellous or trabecular bone, makes up 20% of the skeletal system morphologically. Despite being weaker and softer compared to cortical bone, it has a more flexible structure due to its lower density. It is made up of many interconnected trabeculae that are filled with bone marrow. The arrangement of trabeculae depends on the force of gravity and the mechanical force influenced by muscle contractions in the lower part of the bone. Spongy bone appears as a thin layer of bone called Diploë in long, short, and irregular bones, as well as in the flat bones of the skull. It has porosity between 50-90% and receives nourishment through the canaliculi via cytoplasmic extensions from blood vessels in the bone marrow (28).

Bone marrow is composed of hematopoietic tissue islands, stromal cells, and vascular sinuses interspersed within the trabecular bone network, surrounded by adipose cells. Bone marrow is the primary hematopoietic organ responsible for the production of erythrocytes, granulocytes, monocytes, lymphocytes, and platelets and an important source of stem cells. There are two types of bone marrow, red marrow consisting of hematopoietic tissues and yellow marrow consisting of adipocytes. Both types of marrow are rich in blood vessels and capillaries, but erythrocytes, leukocytes, and platelets are found in red marrow. In humans, primarily red marrow is found, but with age, yellow

marrow develops, and in an adult, there is a fifty-fifty ratio between red and yellow marrow. In case of severe blood loss, the body converts yellow marrow to red marrow to increase blood production. Although bone marrow does not directly participate in hematopoiesis, it creates a microenvironment suitable for hematopoiesis. For example, it produces colony-stimulating factors that have a significant effect on hematopoiesis. The bone marrow tissue is composed of fibroblasts, macrophages, adipocytes, osteoblasts, osteoclasts, and endothelial cells. The bone marrow stroma contains mesenchymal stem cells (MSCs), also known as marrow stromal cells, which are multipotent stem cells that can differentiate into various cell types. MSCs have been shown to differentiate into osteoblasts, chondrocytes, myocytes, adipocytes, and beta-pancreatic islet cells in vitro or in vivo. MSCs can also differentiate into neuronal cells (29).

2.1.3.2.B. Cortical Bone

Cortical bone surrounds the bone marrow cavity and the trabecular plates of spongy bone. It constitutes 80% of the mature skeletal system and forms the diaphysis of long bones. The outer surface of bones is composed of compact bone. In short bones, spongy bone in the center is surrounded by compact bone. Cortical bone in the secondary bone structure consists of osteons called Haversian canals, which are made up of loose connective tissue containing nerves and blood vessels. Adjacent canals communicate with each other through Volkmann canals, bone marrow, and periosteum. Blood vessels and nerves on the bone surface enter the Haversian canals through the Volkmann canals and penetrate the bone marrow. As a result, blood vessels reach all parts of cortical bone. The Haversian canals, arranged in a regular and tight pattern, make cortical bone much more resistant and rigid, providing high resistance to bending and flexion (30,31).

2.1.4. Mechanisms of Bone Formation

Bone formation, also known as osteogenesis or ossification, occurs through two pathways: intramembranous and endochondral ossification. In both types of bone formation, primary bone forms initially and is later replaced by secondary bone. During bone development, primary, secondary bone, and resorption areas are seen side by side (28,32).

2.1.4.1. Endochondral Ossification

In humans, except for the bones of the skull, most bones begin their formation with the formation of cartilage, followed by ossification. Ossification begins with the differentiation of mesenchymal cells of mesodermal origin into chondrocytes. Chondrocytes rapidly multiply and secrete an extracellular matrix to form a cartilage model for bone. The cartilage model contains hyaline cartilage, which resembles the future shape of the bone, and an enclosing membrane called perichondrium. Chondrocytes near the center of the bone model begin to hypertrophy and add collagen 10 and more fibronectin to the matrix they produce; this modified matrix allows calcification. Calcification of the extracellular matrix prevents nutrients from reaching chondrocytes and leads to apoptosis. The resulting cell death creates gaps in the cartilage template, allowing invasion by blood vessels. Blood vessels eventually merge, further expanding the gaps that become the medullary cavity; they also carry osteogenic cells and trigger the transformation of the perichondrium into the periosteum. Osteoblasts then form a thickened compact bone region called the periosteal ring in the diaphyseal region of the periosteum. This is where the primary ossification center forms. As cartilage is replaced by bone in the diaphysis, cartilage continues to grow at the ends of the bone, increasing bone length. These proliferative areas become epiphyseal plates (physeal plates/growth plates), which allow bones to grow longitudinally from birth to early adulthood. After birth, this entire process repeats in the epiphyseal region; this is where the secondary ossification center forms (33).

2.1.4.2. Intramembranous Ossification

This process is responsible for the formation of the skull bones and some other types of bones. In this process, mesenchymal cells transform directly into bone. It begins with the differentiation of mesenchymal cells, derived from the neural crest, into specialized bone-forming cells called osteoblasts. Osteoblasts cluster together to form an ossification center. They begin to secrete osteoid, a collagen-proteoglycan matrix that can bind calcium. The binding of calcium to osteoid causes the matrix to harden and traps the osteoblasts within it. This leads to the transformation of osteoblasts into osteocytes. Osteoid, secreted by osteoblasts, continues to surround the blood vessels and forms trabecular bone. These vessels will eventually form red bone marrow. The mesenchymal cells on the surface of the bone form a membrane called the periosteum. The cells on the

inner surface of the periosteum differentiate into osteoblasts and secrete osteoid in layers parallel to the existing matrix, forming cortical bone (34).

2.2. Alveolar Bone

The parts of the maxilla and mandible that support and form the alveolar socket of the teeth. It begins with the attachment between the periodontal ligament and the bone when the tooth erupts and disappears within a certain period of time after tooth extraction. They can also be referred to as bone structures attached to the tooth due to their shaping and eruption. Alveolar bone consists of cortical bone, alveolar bone proper, and cancellous bone. The interdental septum is composed of cancellous bone surrounded by a compact boundary. The part of the jawbone that does not come into contact with the teeth at the apical end is called basal bone.

Two-thirds of the alveolar bone is made up of inorganic material, and one-third is organic. The majority of inorganic material is made up of calcium and phosphate in the form of hydroxyapatite. 90% of the organic matrix is composed of type 1 collagen and a small amount of non-collagenous proteins such as osteocalcin, osteonectin, bone morphogenetic proteins, proteoglycans, etc. Osteopontin and bone sialoproteins play an important role in the adhesion of osteoclasts and osteoblasts. Cytokines, growth factors, and paracrine factors are also effective in bone development. Remodelling is the main factor that causes changes in bone shape and occurs with resistance to forces, wound healing, and calcium-phosphate balance. Factors are released to regulate the differentiation of osteoblasts and osteoclasts to balance bone formation and resorption in healthy individuals (29).

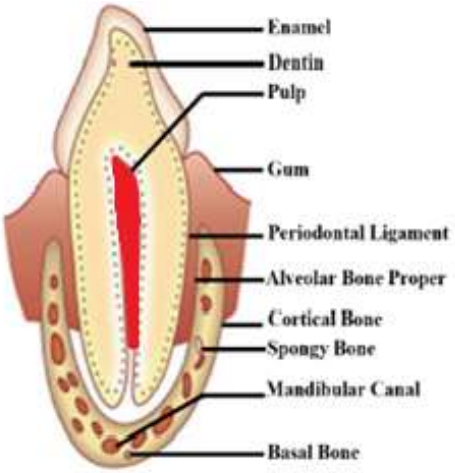


Figure 1. Schematic illustration of periodontium

2.3. Wound Healing

Wound healing is a complex and dynamic process that requires tight coordination of numerous cellular events to efficiently repair damaged tissue caused by trauma or surgical intervention (35). The wound healing process consists of four main phases: hemostasis, inflammation, proliferation, and tissue remodeling (36). These phases must occur in the appropriate sequence and continue at an optimal intensity for a specific period. Local factors such as foreign bodies, oxygenation, as well as systemic diseases such as age, stress, and diabetes can affect wound healing. These factors may interfere with one or more stages of wound healing, resulting in incorrect or impaired tissue repair (36–43).

2.3.1. Hemostasis

When the body sustains an injury, the process of hemostasis is immediately activated to minimize blood loss. The immune system responds within seconds to the damage caused to the endothelium of blood vessels (44). The immune system responds within seconds to the damage caused to the endothelium of blood vessels (44). The release of extracellular matrix triggers the hemostatic process by activating platelets in the local circulation (45,46). Platelets then release biologically active substances, including vasoactive mediators, proteases, cytokines, and growth factors, as well as chemotactic signals mediated by these factors (44,47,48). In order to prevent further bleeding, blood vessels constrict, and platelets adhere to each other to form a thrombus, which is strengthened by fibrin polymerization to close the wound.

Fibro-fibrinogen clots provide temporary extracellular matrix support and facilitate the migration of epithelial cells and fibroblasts to the wound site (44,48).

2.3.2. Inflammation

Following the hemostasis stage, the wound is exposed to sudden inflammatory infiltration in response to the chemokines that arrive at the wound site. The inflammatory response peaks 24 to 48 hours after injury and can last up to a week (45). In the early phase of inflammation, resident cytokines are scarce, blood vessels are reduced, and local fibroblast formation occurs swiftly in the wound bed (44)(49)(50). The initial inflammatory phase is crucial in preparing the wound matrix for tissue transformation by first clearing debris and pathogens through immune cell-mediated actions. Neutrophils are the first immune cells to migrate to the wound site, where they remove damaged extracellular matrix (ECM) components by secreting protease-like matrix metalloproteinases (MMP) (51). During the early inflammatory phase, neutrophils trigger a cascade of cytokines and growth factors to recruit other immune cells, including monocytes, which contribute to the initiation of reepithelialization (52). Once the wound area has been cleared of microbes, neutrophils undergo apoptosis and are subsequently phagocytosed and removed from the wound bed. In cases of impaired or prolonged wound healing, neutrophils may persist abnormally in the area during the prolonged inflammatory phase, leading to a chronic wound environment due to continuous protease production (53,54). Approximately 48 to 72 hours after the injury, monocytes migrate to the wound and differentiate into macrophages, becoming the predominant cell type during the inflammatory phase of wound healing through "proinflammatory" M1 macrophage polarization. Macrophages secrete various cytokines, such as interleukin-1, interleukin-6, fibroblast growth factor (FGF), platelet-derived growth factor (PDGF), epidermal growth factor (EGF), and TGF-β, which play crucial roles in regulating the migration of keratinocytes and fibroblasts to the wound site. During the late inflammatory phase, macrophages shift towards "anti-inflammatory" M2 macrophage polarization, supporting proliferative healing. They continue to secrete regenerative cytokines, like interleukin-10, and help up-regulate endogenous "anti-inflammatory" cytokines while down-regulating previously released

"proinflammatory" cytokines in the vicinity of the wound. As immune cells effectively remove pathogens, an increase in vascular permeability and transudate leakage from capillaries initiates the proliferation phase (55–58).

2.3.3. Proliferation

Following the hemostasis stage, the wound experiences a rapid influx of inflammatory cells in response to chemokines arriving at the wound site. The inflammatory response peaks 24 to 48 hours after the injury and can persist for up to a week (45). Successful wound healing is characterized by the reestablishment of existing vascular networks and the formation of new blood vessels. This process, known as angiogenesis, involves the formation of new blood vessels from existing vascular networks to restore tissue perfusion, establish microcirculation, and enhance oxygenation, which in turn supports collagen cross-linking and wound maturation (59,60). One of the key regulators of angiogenesis is vascular endothelial growth factor (VEGF), a protein that promotes blood vessel formation and plays a crucial role in endothelial cell proliferation, differentiation, and migration. However, impaired wound healing can occur when there is an imbalance in angiogenic mediators leading to abnormal angiogenesis, as observed in conditions such as diabetic venous stasis ulcers (59,61,62). As the wound proliferation phase progresses, capillary vessels increase near the healing edge, providing nutrients and cells essential for wound healing. The temporary fibrin-fibronectin extracellular matrix formed by temporary platelet plugs is eventually replaced by a highly vascularized stroma, which leads to the formation of granulation tissue. M2 macrophages are responsible for remodeling this granulation tissue by providing pro-regenerative growth factors such as EGF and VEGF.

Fibroblasts migrate to the temporary matrix and play a vital role in reshaping the extracellular matrix. These cells deposit matrix proteins, including collagen and fibronectin, to maintain the structural integrity of the healing tissue. Migratory fibroblasts undergo differentiation into myofibroblasts, initiating the wound contraction process, which supports wound edge healing and contributes to the maturation of the wound healing process (63–65).

2.3.4. Maturation and Remodeling

During the final stage of wound healing, the repaired tissue enters a reshaping and maturation phase, which typically begins around three weeks

after the injury and can extend up to two years (66). Protease activity, particularly that of Matrix Metalloproteinases (MMPs), plays a crucial role in promoting healing during the maturation phase by maintaining a balance between ECM accumulation and degradation. However, in cases of prolonged healing, the presence of pro-inflammatory cytokines may lead to elevated levels of MMP production, resulting in excessive ECM degradation. Consequently, local administration of protease inhibitors has been found to be beneficial in promoting healing by regulating protease expression in the wound area and facilitating ECM reshaping (67–69). During wound maturation, activated myofibroblasts gradually cease their production of matrix and play a key role in reshaping the granulation tissue as the wound bed moves towards a state of homeostasis. The cellular composition of the wound bed diminishes as certain cells, including fibroblasts and macrophages, undergo apoptosis. The initial temporary ECM transforms from a loose fibrin meshwork into larger, more densely packed collagen bundles. The extensive vascular networks begin to undergo pruning, and the fibrillar network of the ECM adopts a more cohesive structure. Meanwhile, resident cells like keratinocytes and macrophages continue to shape the remaining permanent ECM as the repaired tissue gradually returns to a state of homeostasis (70).

2.3.5. Types of Wound Healing

Wound healing is the body's response to repairing damage that occurs after injury. Wound healing occurs in three different ways: primary, secondary, and tertiary (delayed) healing.

2.3.5.1. Primary Wound Healing

This type of wound healing occurs when wound edges are brought together by sutures. The wound area is immediately filled with a clot containing fibrin and blood cells. The dehydrated clot on the surface forms a scab that covers the wound and isolates it from the external environment (71).

2.3.5.2. Secondary Wound Healing

This is a type of wound healing that occurs when the injured area is filled with excessive granulation tissue, followed by scar tissue. Compared to primary wound healing, this type of healing involves a certain amount of tissue loss and takes much longer to heal, and complications may arise (71).

2.3.5.3. Tertiary Wound Healing

This is the type of wound healing that occurs in large wounds with intense bacterial contamination. In order to minimize bacterial contamination, the wound is left open for a few days and then primary closure is applied to continue the wound healing process (71).

2.3.6. Factors Affecting Wound Healing

During the process of wound healing, various factors come into play that can influence the healing of the wound. These factors are generally categorized into two main headings: local factors and systemic factors and showed Table 1 (44).

Table 1. Factors Affecting Wound Healing

Factors Affecting Wound Healing			
Local Factors Affecting Wound Healing		**General Factors Affecting Wound Healing**	
• Wound Size	• Presence of Necrotic Tissue	• Age	• Hypothyroidism
• Location of the Wound	• Edema	• Obesity	• Anemia
• Post-operative Bleeding	• Pathological Mobility	• Hereditary Diseases	• Antiresorptive Drugs
• Thermal Injury	• Traumatic Occlusion	• Nutritional Deficiencies	• Corticosteroids
• Maxillary Sinus Perforation	• Smoking	• HIV	
• Alveolar Bone Protrusions	• Venous Insufficiency	• Cancer	
• Local Anesthesia	• Mechanical Trauma	• Diabetes	
• Infection	• Local Toxins	• Alcoholism	
• Hypo-perfusion		• Chemotherapeutics	
• Ischemia		• Immunosuppressants	
• Foreign Body		• Vitamin A	

2.4. Changes Occurring in Alveolar Socket Space

2.4.1. Histological Changes

The studies conducted on tooth extraction have generally been performed on humans and dogs. Biopsy samples have been taken from the marginal area in human studies and from the alveolar socket in dog studies. Although bone formation observed in dogs is 3-5 times faster than in humans, the healing that occurs contains significant similarities. Accordingly, the healing that occurs has been histologically examined in four stages as mentioned above: hemostasis, inflammatory phase, proliferative phase, and maturation and remodeling (Table 2). In the hemostasis phase, bleeding begins in the socket after the tooth extraction, and the bleeding stops shortly after the formation of a blood clot. Then, the inflammatory phase begins, and inflammatory cells migrate to the wound area to clean the area before the formation of new tissue in the socket, which takes about 2-3 days. Inflammatory cells come together with immature fibroblasts and vascular buds to form granulation tissue. With the sterilization of the environment, granulation tissue is replaced by a temporary

connective tissue matrix rich in collagen cells and fibers, thus beginning the proliferative phase characterized by intense and rapid bone formation. This phase consists of two phases: fibroplasia and woven bone formation. In the fibroplasia stage, a rapid accumulation of temporary matrix occurs, and then bone-forming cells and blood vessels enter this matrix. Blood vessels begin to wrap around the finger-like projections of woven bone, and with complete wrapping, the first osteon is formed. The formation of woven bone occurs approximately 2 weeks after tooth extraction and remains in the extraction socket for weeks. However, it gives way to mature bone types such as lamellar bone and bone marrow since it does not have sufficient load-bearing capacity. The final stage is maturation and remodeling. While the shape of the bone changes in maturation, there is a change in remodeling without changing the shape of the bone. The transformation of woven bone into lamellar bone is remodeling, and bone maturation is the cause of volumetric changes in the alveolar crest. Bone remodeling continues for months after tooth extraction (7). According to a study conducted by Lindhe et al. (72), 65% of the bone formed after 16 weeks was lamellar bone, and it was observed that bone remodeling was still ongoing, and complete transformation took months or even years. Osteoclasts enter the area a few weeks after tooth extraction, and bone resorption begins. Bone modeling occurs equally in the lingual and buccal walls, but since the lingual wall bone is generally thicker than the buccal bone, the amount of resorption that occurs in the buccal bone is much higher. Maturation occurs much faster than remodeling, and two-thirds of bone remodeling is completed after the first three months (73). In a study conducted by Cardaropoli et al. (5) on animals, it was histologically observed that the socket was filled with woven bone one month after extraction, and a cortical ridge containing woven and lamellar bone was formed after three months. After six months, the woven bone was replaced by lamellar bone.

Table 2. The Healing of The Extraction Socket After Tooth Extraction (7)

Day 0 Tooth Extraction	After 2-3 days (48-72 hours) from tooth extraction	After 4 days (96 hours) from tooth extraction	After 7 days from tooth extraction	After 20 days from tooth extraction	After 40 days from tooth extraction
					
Haemostasis Blood clot	Blood clot Granulation tissue	Blood clot Granulation tissue Connective tissue Epithelium	Blood clot Granulation tissue Connective tissue Osteoid Epithelium	Connective tissue Osteoid (calcification has started) Epithelium	Connective tissue Bone Epithelium
Formation of clot	Replacement of clot with granulation tissue	Replacement of granulation tissue with connective tissue	Appearance of osteoid in the base of the extraction socket	Filling of 2/3 of the extraction socket with trabecular bone	Epithelialization

2.4.2. Volume Changes

After the loss of one or more teeth, alveolar bone undergoes atrophy (74) and the amount of atrophy has been evaluated by casting models, radiographs, and three-dimensional measurement methods. The socket healing process is completed clinically by the formation of tight epithelialized soft tissue at the socket entrance and radiographically by the filling of the socket with bone. Many studies have been conducted on the length of this process (73,75–77) and it is generally seen that the socket closure occurs between the 10th and 20th weeks (76,77) while radiographic bone formation occurs between 3 to 6 months (73). Although most of the volumetric changes occur in the first 3 months, complete socket healing is thought to be completed in the first year after the extraction (78). In the case of multiple tooth extraction with the use of total partial prostheses, the alveolar bone undergoes severe horizontal and vertical bone loss, and in some cases, the alveolar bone can be completely resorbed (79). In single tooth extractions, the bone thickness is more than 50% resorbed, and the bone loss in the buccal bone is greater than that in the lingual/palatal bone (2,80). Moreover, the amount of resorption in the mandible is greater than that in the maxilla (81).

2.5 Socket Classification

Although there are multiple variables in socket classification, the main factor determining the post-extraction socket condition is considered to be the presence of buccal hard and soft tissue. This classification is simplified by clinicians and divided into three main categories of extraction sockets: Type 1, Type 2, and Type 3 (Table 3, Figure 2) (82).

Type 1 sockets are the best healing sockets. There is no loss in both hard and soft tissues in the buccal region. The buccal bone and soft tissue level are similar to the enamel-cement border of the tooth before extraction and maintain this integrity (82).

In Type 2 sockets, the soft tissue in the buccal region is preserved, but there is partial loss in the hard tissue. This is the most confusing socket type for diagnosis by clinicians. In general, in this socket type, there is retraction in the soft tissue during the following periods as a result of the treatment methods preferred in Type 1 sockets. To eliminate this confusion, three subgroups have been identified in Type 2 sockets. In Type 2A socket, there should be no coronal third of the buccal wall of the socket, equivalent to 5-6 mm. In Type 2B socket, there is a loss in the middle third equivalent to 7-9 mm. In Type 2C socket, there is a bone loss up to the apical third, corresponding to 10 mm or more (83).

In Type 3 sockets, there is a loss in both hard and soft tissues. The treatment of these extraction sockets, which are difficult to manage, requires soft tissue grafting in addition to hard tissue grafting methods (82).

Table 3. Classification of The Extraction Socket Types(83)

		Residual Bone	Soft Tissue Level	Healing Process
Type 1		Intact	Intact	Good
Type 2	Type 2A	Coronal 1/3 buccal bone loss	Intact	Poor
	Type 2B	Middle 1/3 buccal bone loss	Intact	Poor
	Type 2C	Up to apical 1/3 buccal bone loss	Intact	Poor
Type 3		buccal bone loss	Buccal Gingival Recession	Very Poor

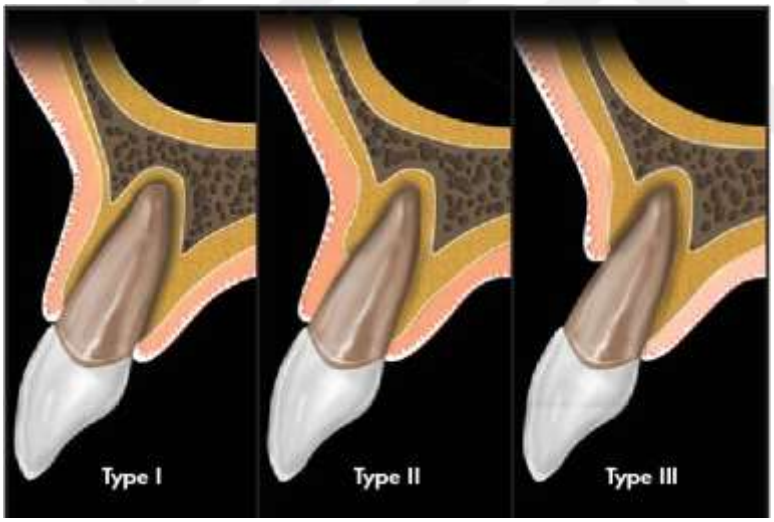


Figure 2. Schematic Illustration of The Extraction Socket Types (82)

2.6. Atraumatic Tooth Extraction Methods

Atraumatic tooth extraction is a method in which the dentist carefully removes the tooth and minimizes the trauma to the surrounding tissues. In particular, researchers have been focusing on safer and faster methods to reduce the trauma associated with tooth extraction over the past 20 years. Atraumatic tooth extraction offers several advantages, such as preserving the structural integrity of the tooth and surrounding tissues, enhancing bone regeneration ability and socket filling, reducing the risk of infection, preserving the gingival

contour, and improving post-extraction patient comfort (84). Atraumatic tooth extraction methods can be classified into two categories: mechanical methods (root preservation technique, rubber dam extraction, benex, periotome, X-trac systems, physics forceps) and motorized methods (piezosurgery, sonosurgery, and enhanced periotome techniques)(Table 4)(8).

Table 4. Atraumatic tooth extraction techniques

Atraumatic Tooth Extraction Techniques	
Mechanical	**Motorized**
• Root preservation Technique • X-Trac Systems • Tooth Extraction Using Rubber Band Assistance • Benex • Physics Forceps • Periotome	• Piezosurgery • Powered Periotome • Sonosurgery

2.6.1. Mechanical Atraumatic Tooth Extraction Techniques

2.6.1.1. Root Preservation Technique

In this technique is not a typical extraction method, however it is listed under atraumatic extraction method. Technique was developed by 2 Scandinavian researchers Dr. Nina Von Wowern and Dr. Svend Winther, a trapezoidal flap is reflected buccally or both buccally and lingually/palatally, and the coronal part of the tooth is cut and removed. The root canal is cleaned and filled with gutta-percha, and the flap is shaped according to the alveolar bone and closed (85). Although this method reduces bone resorption, it does not allow for implant placement and can only be applied to single-rooted teeth (8).

2.6.1.2. X-Trac Systems

In this system, the root pulp is drilled using a calibrated gauge adapted to the neighboring teeth, and a suitable screw is placed into the root pulp. After the placement of control plates, the tooth is extracted along with the screw in a more controlled manner using a key. This system includes three different colored drilling tips with increasing diameter, which minimizes wrist strain for the dentist and minimizes trauma to the surrounding tissues. To distribute pressure equally on both sides and facilitate the placement of the screw, protective plates and a key are used. There are two X-TRAC screws available, measuring 28 and 33 mm, respectively. This system can be easily used for ankylosed and horizontally impacted single-rooted and multi-rooted teeth, but it is contraindicated for teeth with vertical fractures and narrow roots (8).

2.6.1.3. Tooth Extraction Using Rubber Band Assistance

This system, developed by Dr. Regev et al. (86), aims to reduce the risk of osteonecrosis in patients, especially those using bisphosphonates. In this technique, an elastic band is placed in the cervical region of the tooth. Due to the flexibility of the elastic band, it tends to slide towards the narrower apical region of the root from the wider cervical area. As the band moves apically, it causes destruction of the periodontal ligaments, leading to extrusion of the tooth. To enhance the effectiveness of the technique, a new band is added around the root once a week, pushing the previous bands further apically. After an average treatment duration of 5-6 weeks, the tooth extraction is performed. This tooth extraction method is applied to single-rooted conical teeth, while in multi-rooted teeth, the roots are cut and endodontic treatment is performed before extraction. Regev's study, conducted on 21 roots, demonstrated successful healing in all roots with no signs of inflammation. However, the disadvantages of this system include a long follow-up period and associated patient complaints (86).

2.6.1.4. Benex Systems

Developed in Birmingham for the extraction of single-rooted teeth located below the marginal gum level, the primary goal of this method is to extract teeth without the need for flap elevation. Firstly, measurements are taken before the tooth extraction to ensure stabilization and comfortable vertical movement of the tooth. Depending on the root width, the pulp is cleaned with

1.6mm or 1.8mm diamond burs, and smart screws are placed. The measurements taken are placed on adjacent teeth, and the tooth is vertically extracted using the Benex system. It is not suitable for use in deeply decayed teeth (87). In a study conducted by Ren et al. (88) , a total of 25 patients underwent tooth extraction using the Benex system, followed by immediate implant placement. One year later, a periapical radiograph was taken during the follow-up visit, revealing an average bone loss of 0.21±0.23 mm. Post-operative pain was assessed using the Visual Analog Scale (VAS) after 7 days, with a recorded value of 3.32.

2.6.1.5. Physics Forceps

The forceps used in traditional tooth extraction methods allow the dentist to apply force but do not provide a mechanical advantage. These forceps, with their design, offer a mechanical advantage to the dentist, reducing the procedure time and minimizing post-operative pain (89). The forceps consist of two ends, one of which is cushioned. The cushioned part is placed on the buccal aspect of the tooth, while the straight part is placed on the palatal/lingual surface, similar to the principle of opening a bottle cap. Tooth extraction is performed using this method. The system allows for maximum results with minimum force applied. However, if unnecessary force is applied, fractures can occur in the tooth and bone (8). In the study conducted by Kapila et al. (90), a comparison was made between conventional forceps and physics forceps in 200 teeth with extraction indicated for orthodontic purposes. Similar results were obtained in terms of soft tissue healing and post-operative pain, but the duration of the extraction procedure was found to be shorter with the use of physics forceps.

2.6.1.6. Periotome

One of the tools designed to facilitate atraumatic tooth extraction is the periotome. These tools emerged approximately twenty-five years ago to enhance tooth luxation and assist conventional elevators. Periotomes are designed with thin and delicate working tips that can enter the narrow periodontal ligament space vertically along the long axis of the tooth. The design also allows for gentle vertical pressure to assist in luxation (91). Developed by the company Directa®, this tool is placed between the tooth and the gingiva using its sharp pointed tip, cutting the periodontal ligament fibers in

the gap. During the cutting process, a gentle but firm rotating movement is applied to the tooth. This continuous movement not only cuts the fibers but also expands the alveolar socket. Although it may resemble an elevator, tooth extraction is performed with much less force applied (92). In the study conducted by Kalyan et al. (93)periotome compare with conventional method on single-rooted teeth and the periotome technique offers several advantages. These include reduced soft tissue injury, elimination of buccal cortical plate and tooth fractures during extraction, decreased postoperative pain, and uncomplicated healing. Atraumatic extraction of single-rooted teeth can be effectively performed using a periotome, resulting in improved ridge contours that are beneficial for future prosthetic rehabilitations. Similarly, in a study conducted by Sharma et al. (92) involving 100 patients, the efficacy of periotome-assisted tooth extraction compared to traditional extraction methods was evaluated in terms of pain. It was observed that patients treated with the periotome technique experienced significantly less pain.

2.6.2. Motorized Atraumatic Tooth Extraction Techniques

2.6.2.1. Piezosurgery

The aim of newly developed tools is to reduce trauma during tooth extraction and accelerate the healing of the socket wall while preserving its integrity. Piezosurgery, also known as ultrasonic surgery, has recently become widely used in dentistry. With its various tips, piezosurgery is used in tooth extraction, sinus lift procedures, preparation of implant sites, crown lengthening, and gingivectomy. The use of vibrating tips for the extraction of teeth and roots is a newly developed method for atraumatic surgery. These vibrating tips are placed within the sulcus to separate the periodontal ligament fibers surrounding the socket, up to a depth of 10mm or more. The aim of this technique is to achieve atraumatic tooth extraction by gaining movement in the coronal portion without applying excessive force, primarily by cutting the apical fibers (11). Atraumatic tooth extraction preserves the integrity of the surrounding bone and gum structure in the extraction site, promoting faster wound healing and reducing the dimensions of alveolar bone resorption following extraction. A reduced level of post-extraction bone resorption provides a significant advantage for subsequent implant procedures (12).

2.6.2.2. Powered Periotome

Powered periotomes are precise electric tooth extraction tool developed to minimize bone loss. They work by using cutting and space creation mechanisms to assist in tooth extraction (94). These tools are made of very thin metal blades that are gently inserted into the periodontal ligament space and separate the Sharpey's fibers that secure the tooth within the alveolar socket. After most of the Sharpey's fibers are detached from the root surface, a slight rotational movement with minimal pressure facilitates the extraction of the tooth. The electric periotome is an electric unit activated by a foot control, providing precise control over the force applied by the periotome tip and the distance it travels within the periodontal ligament space. The tool has a microprocessor-run actuator that eliminates uncertainty while extracting a tooth. The electric periotome has a control box with 10 different power settings and often allows for flapless extraction of teeth, reducing postoperative pain and discomfort while maintaining periosteal blood supply to the alveoli (95). The electric periotome system also reduces the risk of bucco-lingual/palatal bone fractures. When using the electric periotome, it is believed to be most efficient to start from the interproximal area due to the thickness of the interproximal bone. It is important to keep the blade of the periotome parallel to the long axis of the extracted tooth. The blade should follow the tooth anatomy circumferentially in an apical direction with increments of 2 to 3 mm. Studies suggest that when extracting a multi-rooted tooth, cutting the tooth, and treating each divided root as a single-rooted tooth is the most effective method (12).

2.6.2.3. Sonosurgery

Sonosurgery is a hand tool originally designed by Dr. Ivo Agabiti for the preparation of gingival margins in the prosthetic preparation of abutment teeth. However, due to its specially designed cutting tips, it can also be used for atraumatic tooth extraction purposes. Sonosurgery vibrates at a high frequency of 6 kHz with a wavelength of 240 μm, allowing for precise and efficient cutting while working in close proximity to soft tissues, ensuring atraumatic procedures (96). The tool can break if it is inserted in the wrong direction during oscillation. Sonic tolls are contraindicated in patients with pacemakers, as they can interfere with their function. Additionally, the use of such tolls is not recommended in patients with infectious diseases due to aerosol production (8).

2.7. Radiological Evaluation Methods for Socket Space

In the past, various methods, such as preparing plaster models and taking measurements, have been attempted for the evaluation of extraction socket. However, these methods were not successful in obtaining the desired results as they only focused on the alveolar bone and did not consider the involvement of soft tissues. Radiological evaluation methods are among the most important evaluation techniques used in dentistry for diagnosis and treatment planning. The use of radiographic imaging in dental practice was first introduced by Dr. Otto Walkhoff and has become an essential part of dentistry with the acquisition of high-quality images using proper imaging techniques. Researchers have believed that radiological evaluation would provide much more successful results in the evaluation of alveolar bone (73,96).

2.7.1. Periapical Radiography

Periapical radiographs, derived from the combination of the prefix "peri," meaning around, and the term "apical," referring to the end of the tooth root, are an imaging method that reveals the health or disease conditions in the tooth and surrounding tissues. An ideal periapical radiograph should show the entire tooth and approximately 2 mm beyond the apical border. Periapical radiographs play a critical role in assessing periodontal health during intraoral examinations. Generally, they are frequently used by clinicians to detect bone resorption in interproximal areas and furcation regions, measure the distance between the bone loss and the cementoenamel junction to determine the prognosis of the tooth, monitor lamina dura, and evaluate the presence of periodontal pockets and open contacts within the periodontal space. They have various applications in dental practice (97).

In the 1930s, Zeidses des Plantes introduced the method of superimposing periapical radiographs to identify changes in teeth and surrounding tissues. With the development of digital periapical radiography, more accurate comparisons between images have been made. A study conducted by Lars Schropp and colleagues using digital superimposition of radiographs demonstrated a high correlation between two images. However, despite being standardized, some degree of magnification was necessary, and therefore, the measurements obtained were approximate values rather than true dimensions (73,96,97).

2.7.2. Dental Cone Beam Computed Tomography

In the late 1990s, the concept of Cone Beam Computed Tomography (CBCT) was introduced to dentistry by Mozzo and Aria. The advent of CBCT marked a new era in the field of dento-maxillofacial radiology. CBCT utilizes cone-shaped radiation that rotates 360 degrees around the patient's head to obtain the desired data (98–100). With its short scanning time and ability to generate high-volume data at a low dose, CBCT is ideal for imaging the dento-maxillofacial region (100–102). Two-dimensional imaging systems are insufficient in detecting three-dimensional changes in bone. The use of three-dimensional imaging systems allows for accurate measurement of bone changes by superimposing images using predetermined anatomical landmarks (102,103).

In older types of computed tomography, separate scans were required for the maxilla and mandible, exposing the patient to 400-600 times more radiation than a panoramic radiograph (105). However, CBCT scanners use a narrow cone beam that scans both the maxilla and mandible simultaneously. As a result, the radiation dose used in a panoramic radiograph is only 2-8 times higher than that of CBCT (105,106). When considering the risks and benefits, CBCT is a better choice for evaluating the socket space compared to panoramic radiography. Another advantage of CBCT is its increased accuracy. CBCT digital imaging is as accurate as the digital imaging produced by traditional medical computed tomography units, and unlike conventional computed tomography, it is not affected by head positioning during the scan (107,108).

3.MATERIALS and METHODS

3.1. Patient Selection

Systemically healthy patients, who were referred to Periodontology Department for premolar tooth extraction to the Yeditepe University Faculty of Dentistry Department of Periodontology participated the study. The study design of the present clinical trial was approved by the Yeditepe University Ethical Committee (1630-22.06.2022).

Patient selection criteria were as follows:

1) Patients who completed initial periodontal therapy and full mouth plaque score (FMPS) and full mouth bleeding score (FMBS) $\leq$ 20 after treatment
2) No smoking
3) No pregnancy
4) Teeth without alveolar bone loss or radiographically detectable horizontal bone loss <30%
5) Teeth aligned within the dental arc; no prominence
6) Probing depths $\leq$3 mm and mobility <2 at the study teeth
7) Premolars in maxilla or mandibule with an indication for extraction due to vertical fracture, pre-orthodontic treatment or deep dentin caries (ICDAS 6)(110) with irreversible advanced material loss.

A written informed consent was obtained from all participants after a through explanation of the purpose, the nature and the implications of participating in this study (Appendix 2). No changes in the trial design were made after approval by the local Ethics Committee.

3.2. Sample Size Calculation

Sample size calculation was performed using the study by Temmermen et al. (111). A sample size of 13 teeth was estimated to have an 80% power to detect a difference in socket fill with an effect size 1.064 between the treatment groups. The alpha error was set at 0.05.

3.3. Study Groups

I. Group (Periotome[a] forceps[b]) (test, n= 13):

Tooth was extracted with periotome and forceps. After application of infiltrative local anesthesia to the teeth to be extracted, atraumatic extraction was performed using the periotome and forceps to cut periodontal ligament fibrils from the root surface.

II. Group (Elevator[c] + forceps[b]) (control, n= 13):

Tooth was extracted with elevator and forceps. After application of infiltrative local anesthesia[d] to the teeth to be extracted, atraumatic extraction was performed using the elevator and forceps to separate periodontal ligament fibrils from the root surface.

3.4. Study Design and Flow-Chart

The study was designed as a randomized, parallel, double blind, prospective, controlled clinical trial. Selected patients who completed initial periodontal treatment and had an indication of premolar extraction were included. Following the initial periodontal therapy, patients were evaluated for FMPS and FMBS and were randomly assigned into two treatment groups according to a computer-based randomization table (www.grahpad.com). Patient's initial periodontal therapy was completed using ultrasonic device[e] and gracey curettes[f] and occlusal adjustment was performed if necessary. The study design was shown in Figure 1. In the test group, after cutting the periodontal ligament fibers with a periotome, extraction was performed with forceps; in the control group, after separating the periodontal ligament fibers with an elevator, extraction was performed with forceps. In both groups, sockets were carefully cleaned with surgical curettes following extraction, intactness of the buccal alveolar bone was checked with a periodontal probe. A Visual Analogue Scale (VAS) was explained to the patients for the evaluation of their pain level perceptions for 7 days. CBCT was taken within 24 hours following the extractions. On the 7th day, patients were recalled and the healing of the

[a]Friadent® Periotome blade P3 angle, Dentsply Sirona, Germany.
[b]Krowne® upper/lower premolar teeth forceps, Pakistan,
[c]Krowne® Elevator, Pakistan.
[d]Ultracain DS Fort 2 ml, Aventis Pharma Istanbul, Turkey.
[e]Newtron® P5 B.LED, Acteon, Merignac, France.
[f]Gracey SG 5/6, 7/8, Hu-Friedy®, Chicago, US

extraction sites was evaluated according to the soft tissue healing index(112). A control session was scheduled on day 21. At the end of the 3rd month, CBCT was repeated and the amount of bone resorption was compared with the baseline.

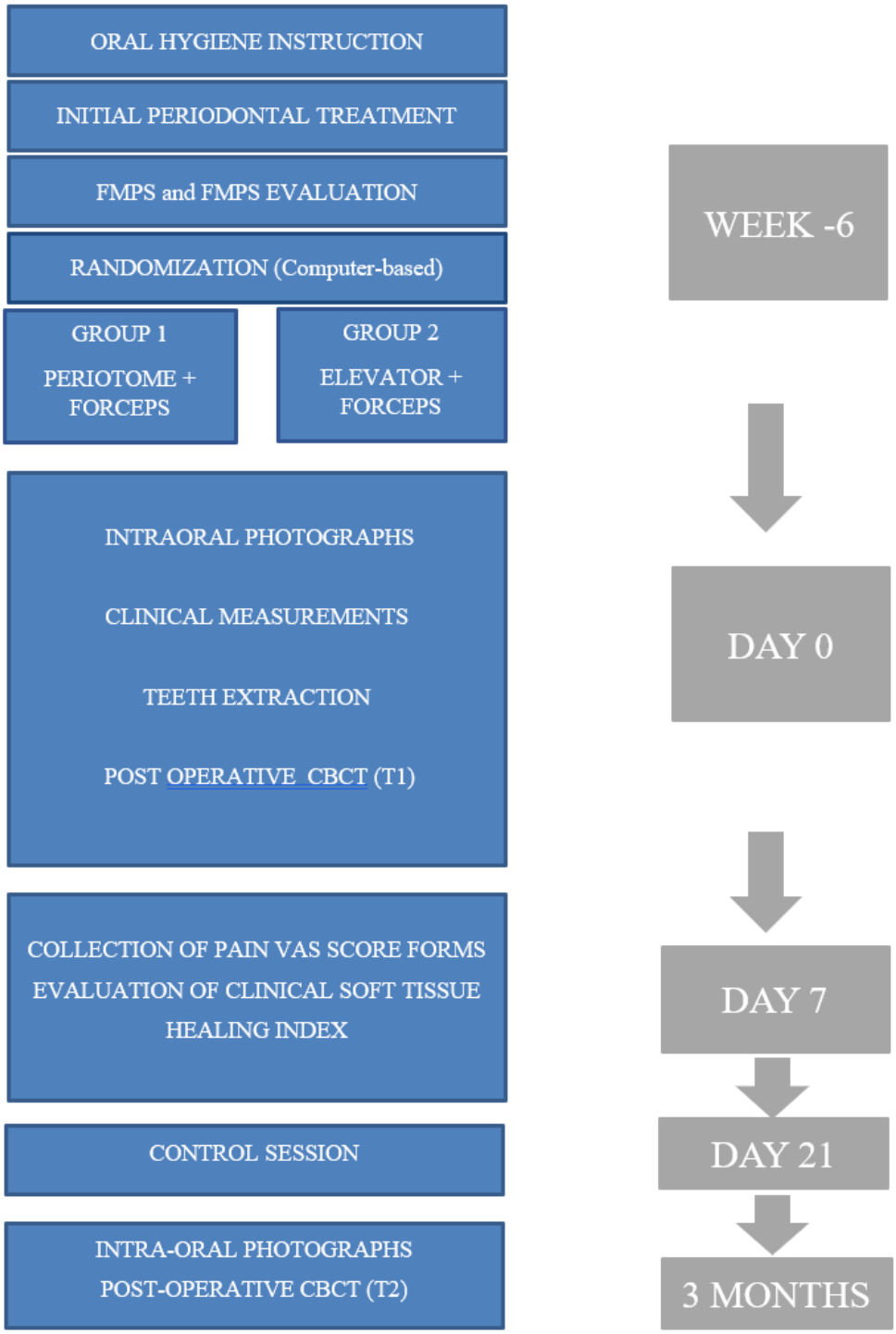


Figure 3. Flowchart of the study

3.5.Clinical Indices And Measurements

3.5.1. Periodontal Clinical Parameters

For the eligibility of the patients FMPS and FMBS were evaluated as described below:

3.5.1.1. Full Mouth Plaque Score (%)

At baseline, FMPS was assessed by the percentage of for tooth sites (mesiobuccal, buccal, distobuccal, and palatal) for the presence (+) versus absence (-) of plaque using a periodontal probe.

3.5.1.2. Full Mouth Bleeding Score (%)

At baseline, FMBS was determined by calculating the percentage of for tooth sites (mesiobuccal, buccal, distobuccal, and palatal) exhibiting bleeding upon probing (+) versus those without any bleeding (-).

3.5.1.3. Full Mouth Probing Depth (Pd) (mm)

Periodontal probe[b] is positioned parallel to the long axis of the tooth from the six points of each tooth (mesial, mid and distal points of the buccal and lingual surfaces) and pushed to the point where resistance is felt without losing contact with the root surface.

3.5.2 Soft Tissue Healing

Post-extraction alveolar clinical healing index was used (112) on day 7. The criteria and scoring used to evaluate the healing according to this index are given in Table 5.

Table 5. Post-extraction alveolar clinical healing index

[g]15 UNC Color-Coded Probe, Hu-Friedy®, Chicago, USA.

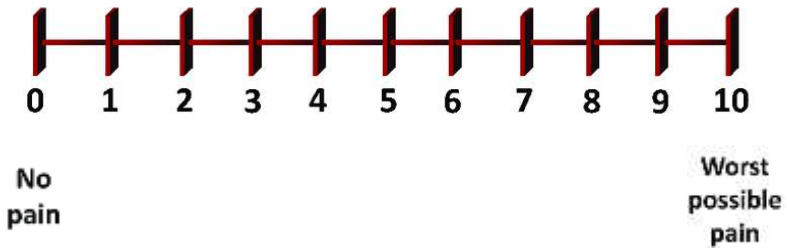
parameters	Score 0	Score 1	Score 0-1
Inspection			
Gingival color	Complete/ Partial red	Pink	
Granulation tissue	Present	Absence	
Epitelization degree	Partial	Complete	
Swelling	Present	Absence	
Palpation			
Bleeding	Present	Absence	
Pain	Present	Absence	
Suppuration	Present	Absence	
		Total Score (0-7)	

3.5.3 Evaluation of Patient Perception:

3.5.3.1. Post-Operative Pain:

During the first 7 days, patients recorded their VAS pain scores everyday, with 0 as absence and 10 as the highest pain level (Table 6).

Table 6. Visual Analogue Scale



The following form was given to the patients to score their pain status every day during the first 7 days (Table 7).

Table 7. VAS Score

Name-Surname:											
Extraction Date:											
	(VAS) SCORES GIVEN BY PATIENT										
DAYS	0	1	2	3	4	5	6	7	8	9	10
1. day											
2. day											

3. day											
4. day											
5. day											
6. day											
7. day											

3.5.4. Radiological Evaluation

3.5.4.1. Linear Measurements

RadiAnt DICOM Viewer v2023.1 (available at https://www.radiantviewer.com) was chosen as the software application for conducting a comparative analysis of buccal wall height, palatal wall height, and extraction socket width between the post-operation and 3-month after healing period in both the test and control groups. The CBCT scan images of the extraction socket were imported into program by selecting the appropriate CBCT DICOM files from the software's user interface. The Multiplanar Reconstruction (MPR) option was selected from the toolbar to generate MPR images from the CBCT scan data. MPR allowed for comprehensive visualization of the extraction socket in axial, sagittal, and coronal planes. The MPR images were carefully aligned within the software to ensure accurate measurements. Viewing angles and orientations were adjusted to achieve the desired visualization of the buccal and palatal walls. Using the "Measurements and tools" option from the toolbar, the "length" tool was selected for performing linear measurements. This measurement tool provided precise measurements of distances within the MPR images. The buccal wall and palatal wall of the extraction socket were identified on the MPR images by adjusting the gray-scale values for each scan, ensuring clear distinction. A linear measurement was conducted from the apical foramen of each root to the marginal edge of the buccal and palatal wall. Additionally, another measurement was performed between the marginal edges of the buccal wall and palatal wall to determine the extraction socket's width. The measurements were accurately recorded in an Excel file, specifying the unit of measurement (millimeters) used for documenting these distances. To ensure accuracy, the measurements were repeated twice. Intra-observer reliability tests have been conducted to assess the consistency of measurements performed by the same observer (Figure 4,5).

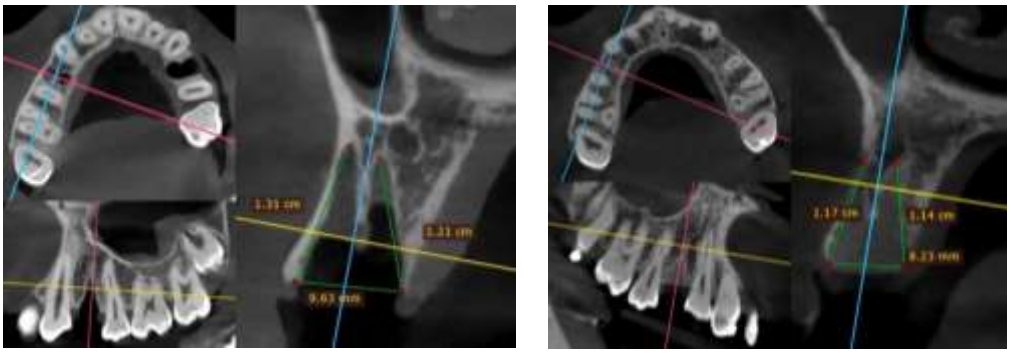


Figure 4,5. Post-op and 3 months linear measurements of buccal and palatal/lingual bone height and bucco-palatal/lingual width between the marginal edges

3.5.4.2. Volume Measurement

ITK-SNAP version 4.0.1 (www.itksnap.org) open-access image analysis software was launched, and the medical image file of the extraction socket was opened by selecting the "File" option from the menu bar and choosing the appropriate file. The "Active Contour" tool within ITK-Snap was selected to perform the segmentation of the extraction socket (Figure 5). The red square or rectangle on the image was adjusted to encompass the extraction socket's borders, defining the initial region of interest for the segmentation process (Figure 6). The presegmentation mode known as "speed image" within ITK-Snap was activated. This mode utilized gray-scale values to differentiate the extraction socket from surrounding structures. Different threshold values were experimented with in the speed image to determine the optimal value that accurately separated the extraction socket from surrounding structures. Bubbles were added to initialize the contour, acting as markers within various areas of the extraction socket. These bubbles provided initial information for the software to determine the shape and boundaries of the extraction socket. The contour evolution parameters were configured to fine-tune the contouring process, ensuring better alignment with the extraction socket's boundaries. The contour evolution process was executed, allowing for monitoring of the contour's movement and adjustments as it aligned with the boundaries of the extraction socket. The segmentation process was finalized by accepting the results, signifying the completion of the contouring process. The "Volumes and Statistics" option within the "Segmentation" tab of the ITK-Snap software was utilized to access the segmented area's volume measurement, typically presented in cubic millimeters (mm^3). This value represented the volume of the extraction socket (Figure 7).

By following these sequential steps, the volume of the extraction socket was accurately measured using ITK-Snap with snake contouring precisely. The segmentation process effectively separated the extraction socket from surrounding structures within the image.

For the visualization of the data and further analysis, 3D Slicer v.5.0.3., an open-source medical image computing platform widely used in biomedical research, was employed (3D Slicer, available at http://www.slicer.org). The segmented extraction socket was exported as a surface mesh file using ITK-Snap, enabling its representation as a 3D object. The "Export as Surface Mesh" option within ITK-Snap was selected, and the resulting file was saved in the designated location. The 3D Slicer software program, designed specifically for medical image visualization and analysis, was launched. The previously saved STL mesh file of the extraction socket, obtained from ITK-Snap, was loaded into 3D Slicer. This facilitated further analysis and exploration of the extracted data, providing additional visualization options and tools. Within the 3D Slicer software, the "Segmentations" module was accessed. By selecting the "Create new segmentation" button, a new segmentation node was generated, allowing for the subsequent segmentation of the volumes. The segmentation editor in 3D Slicer was utilized to segment the volumes individually. By selecting the "Add" button, a new segment was created. Various tools available in the segmentation editor, such as painting, thresholding, or contouring, were employed to delineate the volumes accurately. It was ensured that each segment was assigned to its respective volume. After segmenting both volumes, the "Calculate" button within the segmentation editor was selected. This action triggered the computation of volume measurements in cubic millimeters (mm^3) for each segment. The resulting volume values were recorded for subsequent comparison. To compare the volumes, the "Segment Statistics" module in 3D Slicer was accessed. The two segments representing the volumes of interest were selected within this module. The module provided various statistical measures, including the volume measurements in mm^3, facilitating a comprehensive comparison of the volumes. The volume measurements of each segment were carefully examined to perform a detailed comparison between the two volumes. The absolute difference in volume between the segments was assessed, and relative differences were calculated using appropriate mathematical operations. This rigorous analysis yielded valuable insights into the volumetric comparison of the two volumes (Figure 8).

By following these standardized procedures, the segmented extraction socket

was successfully exported as a surface mesh file from ITK-Snap and visualized in 3D Slicer. The volumes of interest were accurately segmented, and their respective measurements were obtained in cubic millimeters (mm^3).

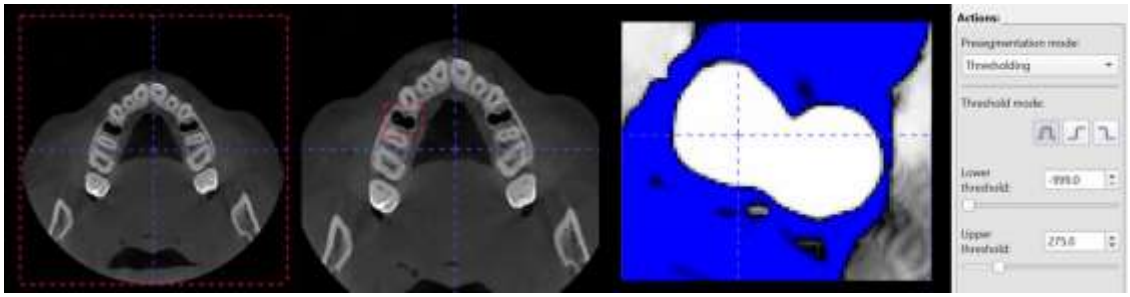


Figure 6. selection to perform the segmentation of the extraction socket

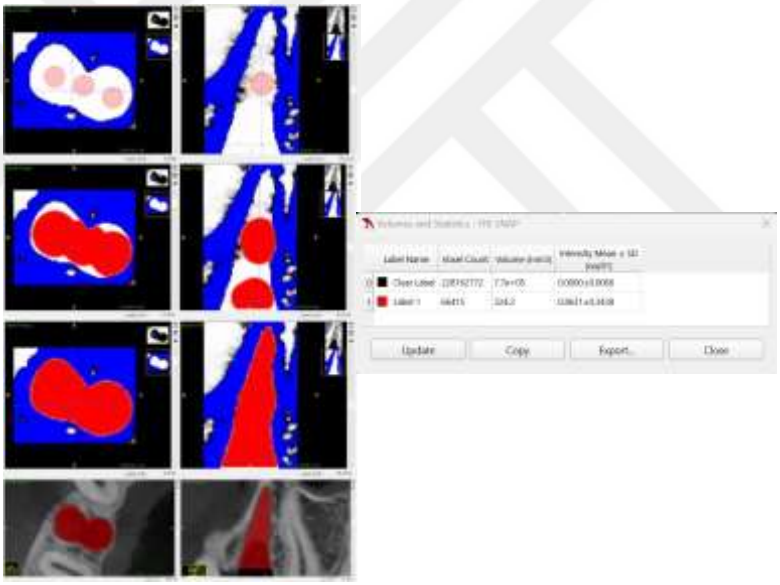


Figure 7. The red rectangle on the image was adjusted to encompass the extraction socket's borders

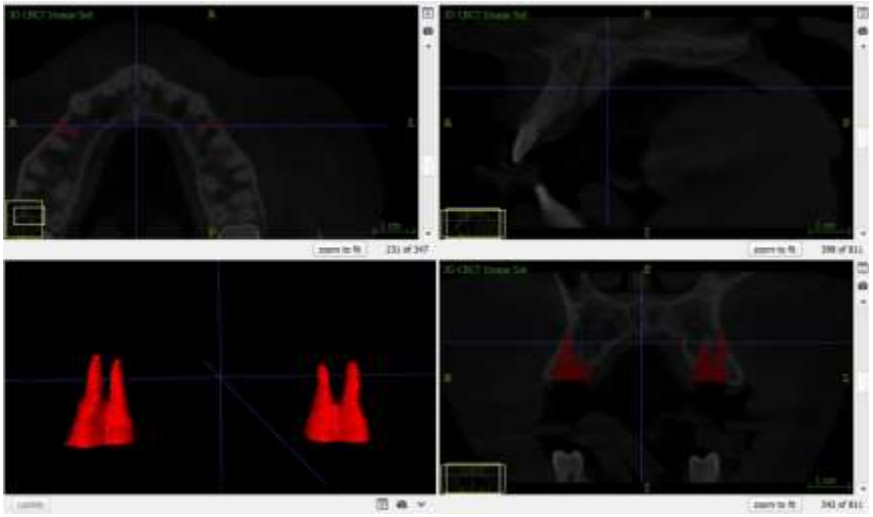


Figure 8. Different threshold values experimented with in the speed image

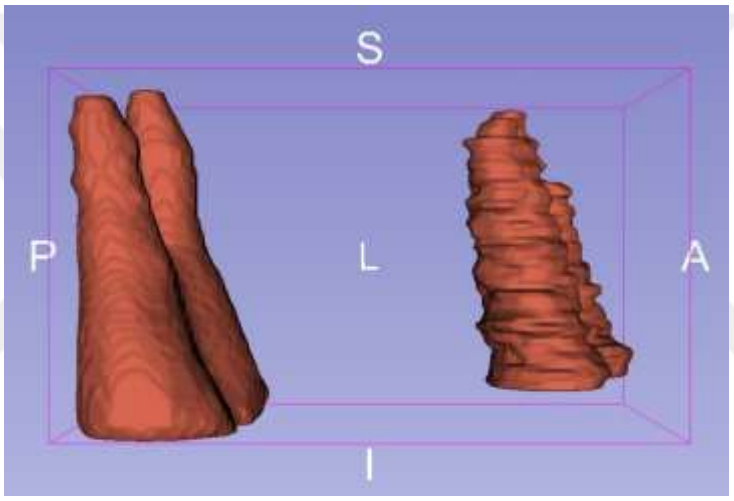


Figure 9. Pre-op and Post-op socket volume

3.6. Surgical Procedures

All patients were operated by applying infiltrative local anesthesia for the extraction. In the test group, periodontal ligament fibrils were cut with Periotome® and teeth was atraumatically extracted with a special forceps (Figure 9).

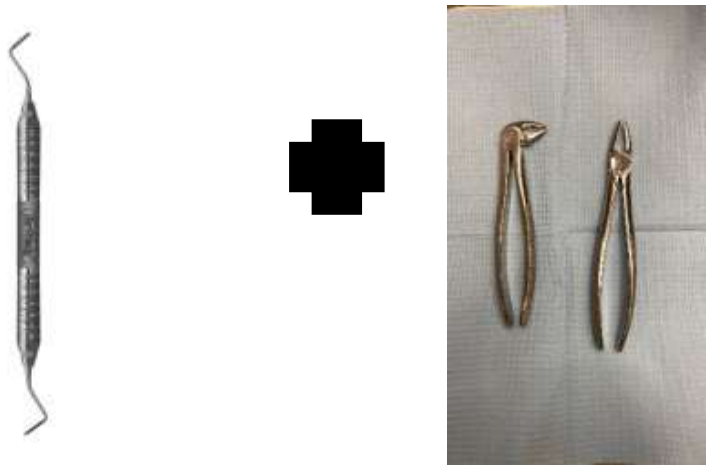


Figure 10. Periotome® + forceps

In the control group, periodontal ligament fibers were separated from the root surface by using a conventional elevator and atraumatically extracted with special forceps (Figure 10).

Figure 11. Elevator + forceps

3.7. Postsurgical Care

Post-extraction care and cautions were explained to the patients both verbally and handed in written form. Patients were instructed to rinse with chlorhexidine (CHX) solution (0.2%) twice daily for 1-minute commencing 24 hours after procedure and discontinue of using toothbrush in surgical area for 7 days. In the first week after the procedure, the patients were asked to consume warm and soft diet and to protect the extraction sockets against mechanical trauma. The patients were informed and asked to fill in the VAS form daily till day 7. All the patients were scheduled for a control visit at days 7, 21 and 3 months after surgical procedure. Post-extraction alveolar clinical healing index was recorded on day 7.

3.8. Data Analysis

The SPSS (Statistical Package for the Social Sciences) 24.0 software was used for statistical analyses. Descriptive statistical methods (Mean, Standard Deviation, Median, Minimum, Maximum) were employed to evaluate the study data on teeth basis. The normal distribution of the data was evaluated using Student's t-test. In cases where the quantitative parameters did not follow

a normal distribution, the Mann-Whitney U test was used for inter-group comparisons. The significance level was evaluated at $p<0.05$.

4.RESULTS

4.1. Demographic Results

26 premolar teeth in 18 patients aged between 18 to 50 years were evaluated in the study. There were 22 patients initially selected among the screened 45 patients. However, there were four dropouts, two in each group during the post-operative follow-up period. Teeth distribution according to gender and age of the patients are presented in Table 8,9.

Table 8. Age of the patients

	Test Group		Control Group		
	Mean±Sd	**Min-Max (Median)**	**Mean±Sd**	**Min-Max (Median)**	**p**
Age	35,01±11,93	18-49 (40)	40,77±10,72	18-50 (42)	0,207

Mann Whitney U test, p<0.05

Table 9. Teeth distribution according to gender of patients

		Test Group		Control Group		
		N of teeth	**%**	**N of teeth**	**%**	**p**
Gender	**Male**	8	61,5	6	46,2	0,431
	Female	5	38,5	7	53,8	

Mann Whitney U test, p<0.05

4.2. Baseline Clinical Parameters

Baseline clinical parameters regarding FMPS, FMBS and FMPD (mm) are presented in Table 10. No statistically significant differences were detected between the test and control groups at baseline (p>0.05).

Table 10. Inter-group comparison of the baseline clinical parameters in patient groups

	Test Group	Control Group	
	Mean±Sd (Median)	**Mean±Sd (Median)**	**p**
FMPD (mm)	1.96±0.53 (1.73)	1.85±0.61 (1.69)	0.418
FMPS (%)	14.68± 0.77 (10.3)	14.78± 1.08 (11.2)	0.803
FMBS (%)	12.76 ± 1.74 (10.7)	13.45± 1.94 (11.2)	0.316

Two-sample independent t test, p<0.05

4.3. Patient Perception Outcomes

The patient-based VAS score evaluation for post-operative pain is shown in Table 11. No statistically significant differences were observed between the two groups at any time point (p>0.05).

Table 11. Inter-group comparison of the post-operative pain (VAS) scores

	Test Group		Control Group		
	Mean±Sd	**Min-Max (Median)**	**Mean±Sd**	**Min-Max (Median)**	**p**
Day 0	4,31±1,44	1-6 (4)	3,54±1,39	1-6 (4)	0,149
Day 1	2,46±1,13	1-4 (2)	1,92±1,12	0-4 (2)	0,255
Day 2	0,92±0,86	0-2 (1)	1,08±0,95	0-3 (1)	0,725
Day 3	0,77±0,83	0-2 (1)	0,92±0,95	0-3 (1)	0,722
Day 4	0,62±0,87	0-2 (0)	0,69±0,85	0-2 (0)	0,773
Day 5	0,38±0,65	0-2 (0)	0,38±0,65	0-2 (0)	0,995
Day 6	0,23±0,44	0-1 (0)	0,31±0,48	0-1 (0)	0,665

Mann Whitney U Test, p<0.05

4.4. Soft Tissue Healing

Soft tissue healing in terms of alveolar clinical healing index scores is shown in Table 12. No statistically significant differences were observed between the two groups (p>0.05).

Table 12. Inter-group comparison of alveolar clinical healing index scores

	Test Group		Control Group		
	Mean±Sd	**Min-Max (Median)**	**Mean±Sd**	**Min-Max (Median)**	**p**
Alveolar Clinical Healing Index	5,08±1,04	3-7 (5)	4,92±1,44	2-7 (5)	0,830

Mann Whitney U Test, p<0.05

4.5. Vertical Buccal Bone Height

Buccal bone height after 24 hours post-extraction as baseline, post-operative buccal bone height after 3 months and the changes are shown in Table 13. Buccal bone height values were 10,37±2,84 and 9,67±3,12 at baseline; 9,08±3,07 and 8,49±3,58 at 3 months, in the test and control groups, respectively. Changes of vertical buccal bone height from baseline to 3rd month were not statistically significant (p>0,05).

Table 13. Inter-group comparison of vertical buccal bone height parameters

	Test Group		Control Group		
	Mean±Sd	**Min-Max (Median)**	**Mean±Sd**	**Min-Max (Median)**	**p**
Baseline Buccal Bone Height(mm)	10,37±2,84	6,06-16,8 (10)	9,67±3,12	4,74-13,4 (10,8)	0,739
Post-Buccal Bone Height (mm)	9,08±3,07	4,88-14,2 (9,1)	8,49±3,58	0-12,6 (9,53)	0,758
Changes (Post-Baseline)	1,29±1,8	1,45-(-5,09) (0,7)	1,18±2,42	2,64-(-6,57) (0,9)	0,995
Buccal Bone Height Changes (%)	0,12±0,19	0,19 -0,5 (0,06)	0,11±0,35	0,38-1 (0,11)	0,817

Mann Whitney U Test, p<0.05

4.6. Vertical Lingual/Palatal Bone Height

Lingual/palatal bone height after 24 hours post-extraction as baseline, post-operative lingual/palatal bone height after 3 months and the changes are shown in Table 14. Lingual/palatal bone height values were 11,19±2,05 and 8,99±3,48 at baseline; 10,34±2,03 and 8,62±2,9 at 3 months, in the test and control groups, respectively. Changes of vertical lingual/palatal bone height from baseline to 3rd month were not statistically significant (p>0,05).

Table 14. Inter-group comparison of vertical lingual/palatal bone height parameters

	Test Group		Control Group		
	Mean±Sd	**Min-Max (Median)**	**Mean±Sd**	**Min-Max (Median)**	**P**
Baseline Lingual/ Palatal Bone Height (mm)	11,19±2,05	8,92-16,3 (10,5)	8,99±3,48	2,71-14,2 (9,58)	0,137
Post-Lingual/Palatal Bone Height (mm)	10,34±2,03	7-15,2 (10)	8,62±2,9	4,53-13,4 (8,37)	0,174
Changes (Post-Baseline)	0,85±1,03	1,68-(-2,3) (0,8)	0,37±2,29	4,3-(-4,42) (0,8)	0,719
Lingual/Palatal Bone Height Changes (%)	0,07±0,10	0,19-0,25 (0,07)	-0,07±0,52	1,59-0,43 (0,07)	0,837

Mann Whitney U Test, $p<0.05$

4.7. Horizontal Extraction Socket's Width in Terms of The Distance Between Marginal Edges of Buccal and Lingual/Palatal Alveolar Bone

Baseline and post-operative horizontal bucco-lingual/palatal alveolar bone width, and the changes are shown in Table 15. Bucco-lingual/palatal bone width values were 7,40±1,36 and 8,05±2,15 at baseline; 6,23±1,35 and 5,57±2,21at 3 months, in test and control groups, respectively. The inter-group comparison of the changes revealed no statistical difference ($p>0.05$).

Table 15. Inter-group comparison of horizontal bucco-lingual/palatal bone width

	Test Group		Control Group		
	Mean±Sd	**Min-Max (Median)**	**Mean±Sd**	**Min-Max (Median)**	p
Baseline Bucco-Lingual/Palatal Bone Width (mm)	7,40±1,36	5,42-9,6 (7,3)	8,05±2,15	5,61-14,4 (7,85)	0,590
Post-Bucco-Lingual/Palatal Bone Width (mm)	6,23±1,35	4,3-8,8 (6,1)	5,57±2,21	0-8,23 (5,69)	0,720
Changes (Post-Baseline)	1,17±0,97	(-0,13)-(-3,64) (0,85)	2,47±3,25	(-0,26)-(-10,43) (0,97)	0,590
Bucco-Lingual/Palatal Bone Width Changes (%)	0,16±0,11	0,02-0,41 (0,13)	0,27±0,30	0,04-1 (0,12)	0,777

Mann Whitney U Test, p<0.05

4.8. Volumetric Socket Filling

Measurements of socket filling at baseline, post-operative and changes in percentages are shown in Table 16. Socket volumes (mm^3) values were 177,62±90,1 and 149,23±67,8 at baseline; 149,12±76,5 and 111,38±49,7 at 3 months, in test and control groups, respectively. The comparison of the percentage of socket filling changes between the groups revealed significant difference (p<0,05).

Table 16. Inter-group comparison of volumetric socket filling

	Test Group		Control Group		
	Mean±Sd	**Min-Max (Median)**	**Mean±Sd**	**Min-Max (Median)**	p
Baseline Socket Volume (mm^3)	177,62±90,1	90,79-386,3 (134,8)	149,23±67,8	63,76-286 (163,7)	0,412
Post-Socket Volume (mm^3)	149,12±76,5	68,14-329,3 (116,4)	111,38±49,7	53,41-199 (101,73)	0,205
Loss of Volume Change (%)	15,82±8,99	7,91-34,78 (11,68)	25,99±10,51	12,2-42,54 (26,64)	**0,016***

Mann Whitney U Test, p<0.05

4.9. Representative Case of the Test Group (Figures 12-27):

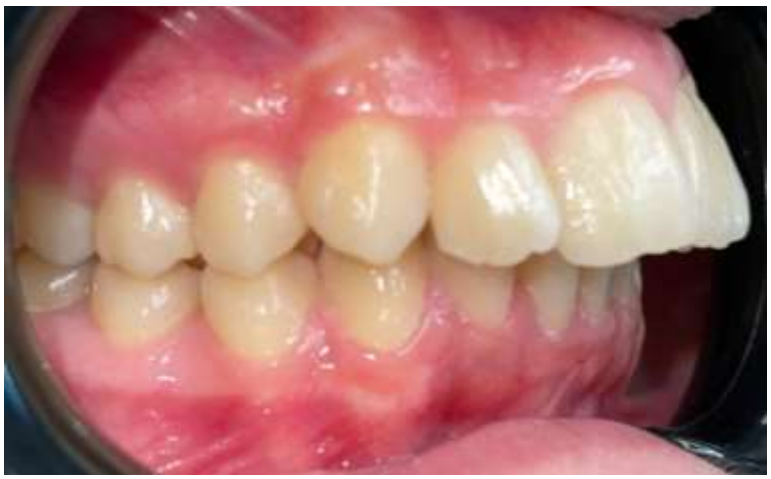


Figure 12. Pre-operative clinical view (test group)

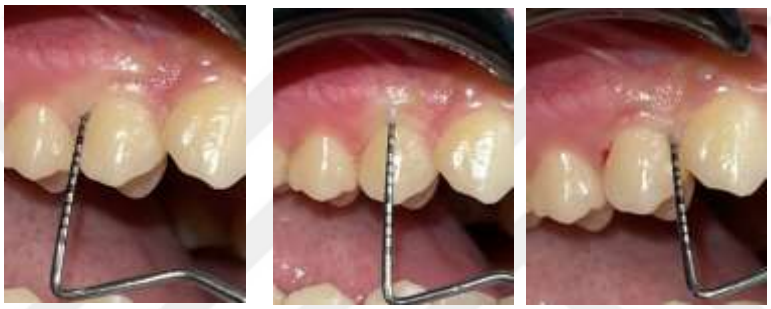


Figure 13-15. Pre-operative probing depths (test group)

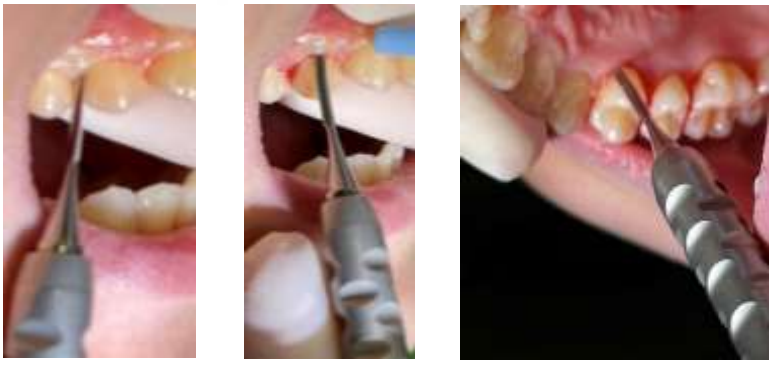


Figure 16-18. Application of Periotome® (test group)

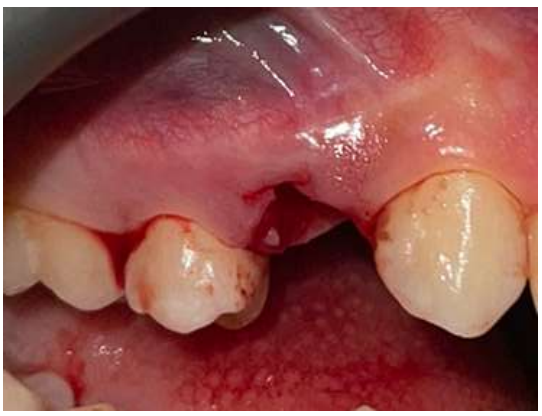


Figure 19. Post-operative clinical view (test group)

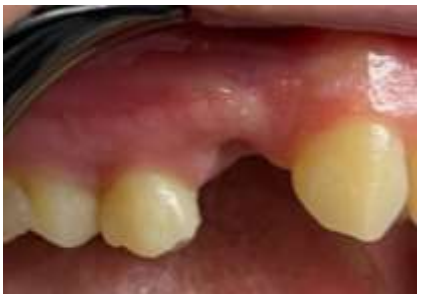
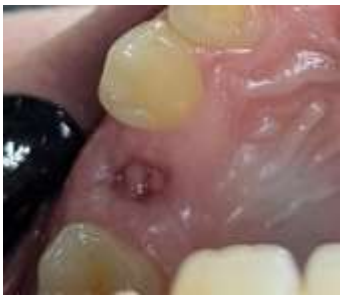



Figure 20,21. Post-operative clinical view on day 7 (test group)

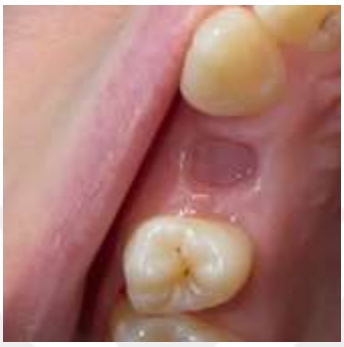
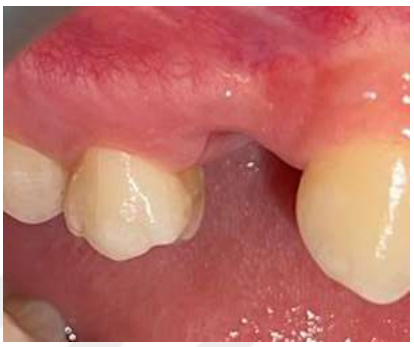



Figure 22,23. Post-operative clinical view on day 21 (test group)

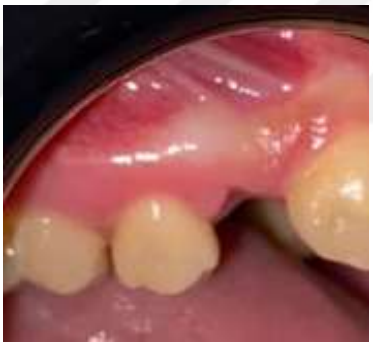
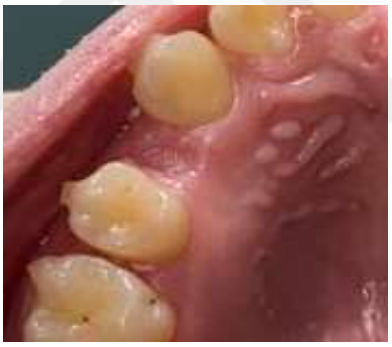



Figure 24,25. Post-operative clinical view at 3 months (test group)

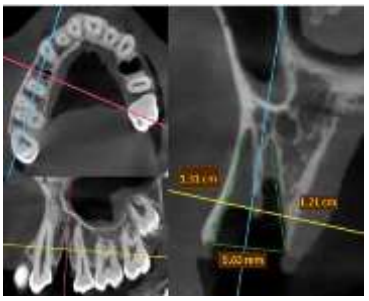
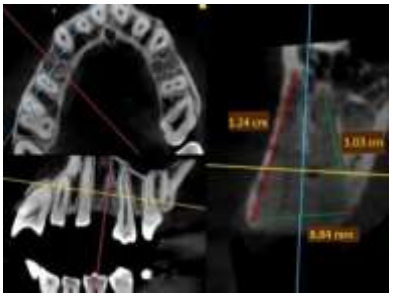



Figure 26,27. Baseline and post-operative 3 months radiographic view (test group)

4.10. Representative Case of the Control Group (Figures 28-40):

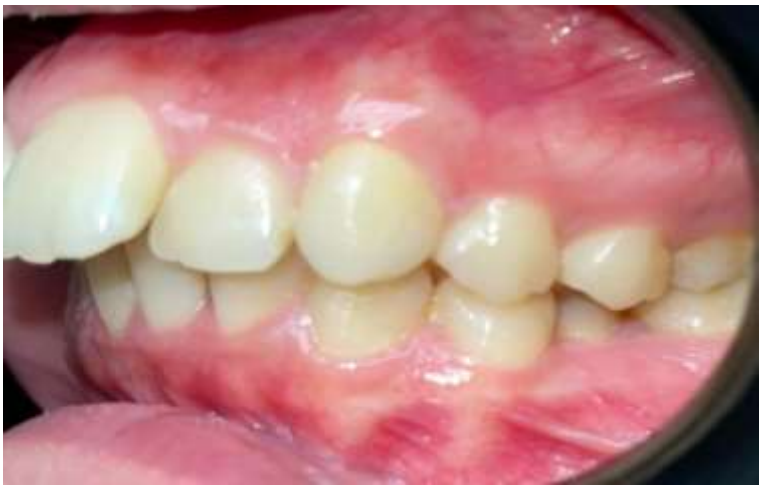


Figure 28. Pre-operative clinical view (control group)

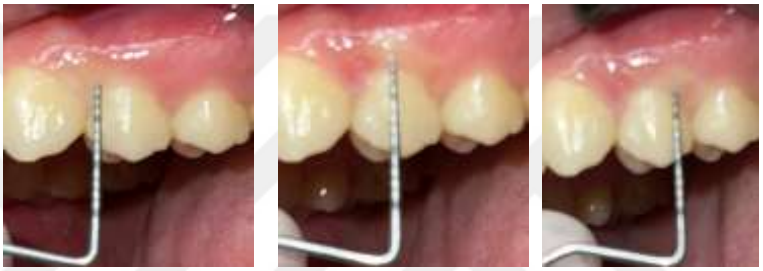


Figure 29-31. Pre-operative probing depth (control group)

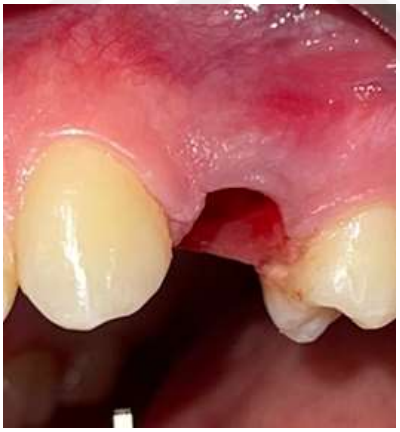


Figure 32. Post-operative clinical view (control group)

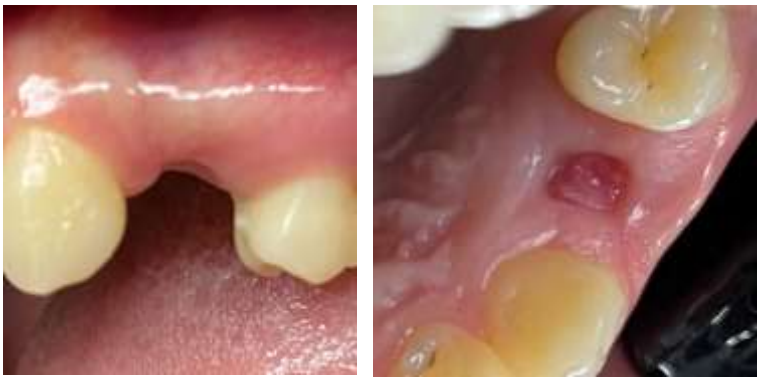


Figure 33,34. Post-operative clinical view on 7 day (control group)

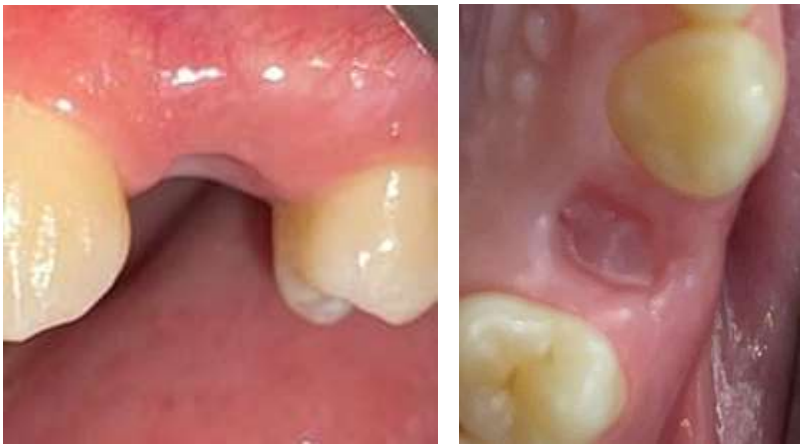


Figure 35,36. Post-operative clinical view on day 21 (control group)

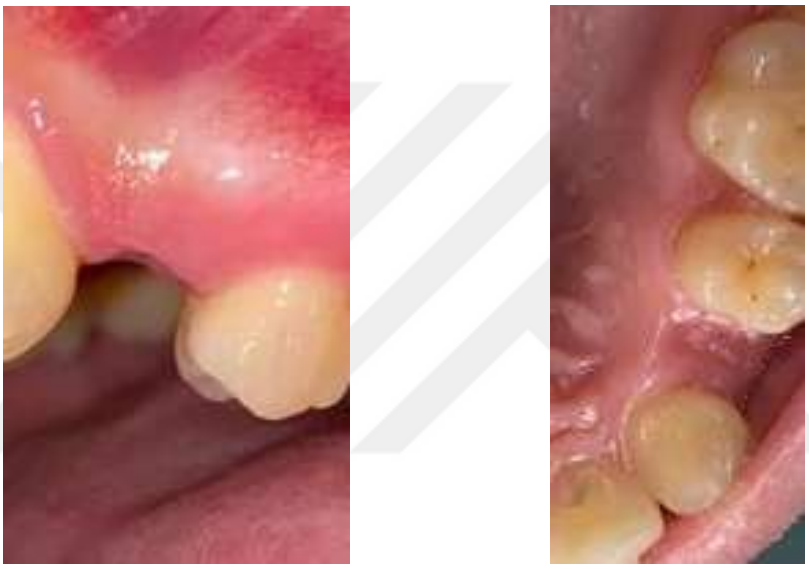


Figure 37, 38. Post-operative clinical view at 3 months (control group)

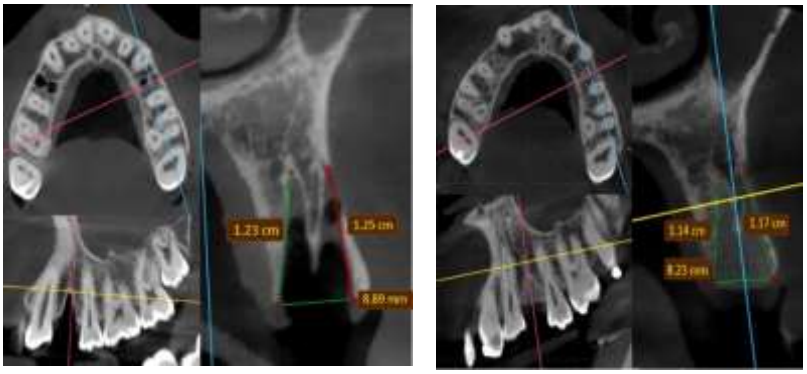


Figure 39, 40. Baseline and post-operative 3 months radiographic view (control group)

5.DISCUSSION

Tooth extraction is one of the primary oral minor surgeries preferred either when the condition of the patient is considered untreatable or to provide support for orthodontic treatments. The healing process of the extraction site, starting with the formation of a blood clot, concludes with the completion of new bone formation. The healing process of the surgical site after tooth extraction is crucial for prosthetic rehabilitation of the missing area. Besides the expected natural vertical and horizontal dimensional changes in alveolar bone after extractions, damage occurring in the extraction socket and defect areas give rise to therapeutic problems. Particularly, in modern dentistry, alveolar bone thickness and height play an important role in further implant supported treatments (113). Quayle et al. (10) proposed that the replacement of teeth with immediate implants subsequent to elective extraction necessitates the preservation of the alveolus with minimal surgical trauma through atraumatic extraction. The conventional elevator/forceps technique is the most employed extraction method, which can lead to bundle bone resorption due to the destruction of the periodontium, and further exacerbated by the involvement of the mucoperiosteum. The preservation of periosteal blood supply to the alveolus can be compromised due to the possibility of elevation of the mucoperiosteum during tooth extractions, resulting in marginal alveolar bone loss even in cases where the extraction is performed with minimal trauma (10,114).

Atraumatic tooth extraction techniques are comprehensive surgical methods preferred to preserve all surrounding hard and soft tissue structures during the removal of a tooth or its root/s (8). During tooth extraction performed with conventional methods, the periodontium is detached from the tooth and root surface, followed by luxation with an elevator and removal using forceps. However, this method may cause trauma to the surrounding hard and soft tissues and, due to reasons such as tooth fracture, it is sometimes not possible to extract the tooth only with forceps. If tooth extraction with forceps fails, the tooth is surgically removed by creating a flap in the extraction site. Removing the tooth by flap elevation leads to increased hard and soft tissue loss (12).

The conventional extraction technique is sometimes associated with various complications such as pain, fracture of the buccal cortical plate, root

fracture, dry socket, swelling, trismus, prolonged healing, alveolar bone loss necessitating the adoption of different surgical extraction approaches. Any damage inflicted on the bone tissue during tooth extraction leads to the sacrifice of alveolar bone, thereby causing bone loss and difficulties in preserving the socket integrity (115,116) . Traumatic extractions not only result in soft and hard tissue damage but also disrupt the healing process posing challenges (117). In a study conducted by Buser et al., it was observed that the buccal bone thickness should be at least 1 mm for an ideal implant placement (118). Similarly, in a study by Spray et al. performed on 2685 implants, significantly higher buccal bone resorption was observed in implants with buccal bone width less than 1.8 mm compared to implants with greater width (119). To preserve the alveolar bone, enhance the success rate of implants and achieve more favorable aesthetic outcomes, atraumatic extraction techniques that minimize damage to soft and hard tissues have been developed throughout the years. Atraumatic methods for the prevention of bone resorption can be categorized into two main groups: Manual approaches including root preservation technique, rubber dam traction, benex system, periotome, X-trac systems, physics elevators, and electrically assisted approaches such as piezosurgery, sonosurgery, and reinforced periotome (87).

In an animal study by Cardaropoli et al. (5), it was observed that a blood clot formed within the first three days, the clot was replaced by a temporary matrix on day 7, initial mineralized bone formation occurred between days 14-30, and approximately 88% of the extraction socket was filled at 3 months, forming a cortical ridge containing woven and lamellar bone. In a study by Amler, osteoid appearance was observed at the base of the socket on day 7 after extraction, and after 40 days, he reported trabecular filling in at least two-thirds of the extraction socket. In a study by Schropp et al. (73) with a 12-month follow-up period, it was found that most of the loss of vertical bone height took place within the first 3 months. With the presence of osteoclasts in the extraction site after tooth extraction, bone resorption begins, and along with the remodeling and maturation phases, almost two-thirds of bone remodeling is completed in the first 3 months. Based on these studies, in our study, bone formation was radiologically evaluated approximately three months after tooth extraction.

In our study, we opted for the periotome as the manual test group approach due to its handy, simple, and non-aerosol usage with dual tips and affordability enabling implementation in various clinical settings. The periotome is held using a modified pen grip technique to incise the gingival fibers circumferentially around the cervical area of the tooth. Initially, it is tilted in a mesiodistal direction starting on the buccal aspect of the tooth, parallel to the root surface and a few millimeters into the periodontal ligament space as a working action, Once access is achieved all around the tooth, subsequently the periotome is gradually advanced towards 2/3 of the root surface using the same technique. At this point, the tooth remains only attached to the alveolar bone through the most apical portion of the periodontal ligaments. Finally, with the aid of manual force, the tooth is extracted using a forceps. In a study conducted by Sharma et al. (92), the postoperative pain experienced by patients within the first 7 days following periotome-assisted extractions was evaluated, and it was found that the pain was significantly less compared to other extraction methods. However, in our study the postoperative pain experienced by patients was assessed within the first 7 days, and no significant difference was observed between the two groups. It is believed that the difference observed in this study compared to the aforementioned study may be attributed to the individual perception differences and disparity in sample size. In a study by Kalyan et al. (93), involving clinical and radiographic evaluations following periotome-assisted tooth extraction, no significant difference was found between the test and control groups regarding gingival injury. Similar to this study, our patients were assessed with the alveolar socket healing index at the 7th day after tooth extraction, and no significant difference was observed between the two groups. Quayle suggested in his study (10) that the periotome is an ideal manual method for extraction without causing damage to surrounding tissues. Lanning et al. (120) and Gargiulo et al. (121) recommended the use of periotome in cases of deep subgingival carious lesions terminating beneath the gingiva, root fractures extending beneath the gingiva, and situations where extensive osseous resection is contraindicated.

To the best of our knowledge, there are no similar studies evaluating buccal and lingual/palatal bone level changes and volumetric differences by using an accurate and sensitive method of CBCT. In a study evaluating the

vertical bone loss following periotome-assisted tooth extraction conducted by Kalyan et al. (93), only mesial and distal bone loss were assessed using periapical radiographs, and a statistically significant difference was observed in the bone levels between day 0 and month 3. In our study, putting a stronger emphasis on the buccal and lingual/palatal vertical bone height and alveolar socket width in terms of bone resorption according to the literature, we found no statistically significant differences between the groups at day 0 and month 3 ($p>0.05$). In another study by Hansson et al. (122) using a different evaluation method, it was reported that 3.06 mm of vertical and 1 mm of horizontal bone loss occurred at 6 months following tooth extraction assessed by using a fundamental principle of bone physiology based on the adaptation of bone mass and bone structure to the levels and frequencies of strain. In our study, the test group exhibited a buccal bone height reduction of 1.29±1.8 mm whereas it was 0,85±1,03mm lingually/palatally and a horizontal alveolar socket width change of 1.17±0.97 mm. The control group showed a buccal bone vertical height reduction of 1.18±2.42 mm, 0,37±2,29 mm of a lingual/palatal reduction and a horizontal alveolar socket width change of 2.47±3.25 mm. The differences in indications for extraction, study population and measurement methods, follow-up periods, as well as different population numbers between the studies are considered to have influenced the results.

After tooth extraction, four main stages can be observed in the healing process of the extraction socket: hemostasis, inflammatory phase, proliferative phase, and maturation and remodeling. Immediately after tooth extraction, the hemostasis phase begins, and the area is filled with a blood clot. Inflammatory cells migrate to the area within 48-72 hours to sterilize the wound site, and these cells, along with immature fibroblasts and vessel buds, form granulation tissue, constituting the inflammatory phase. The formed granulation tissue is replaced by temporary connective tissue matrix, initiating the proliferative phase characterized by intense and rapid bone formation. The formation of the first osteon occurs as blood vessels start to encase the woven bone. The formed woven bone occurs approximately two weeks after the tooth extraction and remains in the extraction socket for weeks before being replaced by mature bone types such as lamellar bone and bone marrow. The stage where resorption and volumetric changes occur in the alveolar bone is the remodeling and

maturation phase. The significant difference found between the groups in favor of the test group regarding the volumetric socket filling percentage can be explained by the fact that during the measurement of alveolar socket volume, the assessment is not confined to a single point but rather encompasses measurements from all areas of the socket and by denser bone tissue maturation reflected to the accuracy of volumetric evaluation, although there were no significant differences in the other millimetric parameters of our study.

With the increasing prevalence of dental volumetric tomography in dental practice, significantly higher levels of accuracy have been observed in clinical practice and research studies. Radiographic evaluation methods, including periapical radiographs and dental volumetric tomography, have been used in studies investigating socket healing. In a study by Raichur et al. (123), it was observed that patients evaluated with dental volumetric tomography had much closer values to reality compared to those evaluated with periapical radiographs. Similarly, in a study by Grimard et al. (124) comparing the measurement of surgical parameters after regenerative treatment, values obtained with dental volumetric tomography were significantly more accurate and precise. In a study by Schropp et al. (73) where socket healing was evaluated by superimposing periapical radiographs, despite standardization efforts, the study was completed based on approximate values due to factors such as the need for magnification.

Within the limits of this study conducted to obtain precise, detailed and accurate alveolar bone measurements by using dental volumetric tomography in buccal and lingual/palatal vertical bone changes, horizontal socket width changes in terms of the distance between marginal edges of buccal and lingual/palatal alveolar bone as well as socket filling, it is concluded that no superiority of the periotome extraction over the conventional elevator could be established except better socket fill percentage. Long-term follow-up studies with increased sample size and histological evaluations are warranted based on the current findings.

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7. APPENDICES

7.1. Ethical Approval

YEDİTEPE ÜNİVERSİTESİ KLİNİK ARAŞTIRMALAR ETİK KURULU KARAR FORMU

Araştırmanın Açık Adı	**"Diş Çekimi Sonrasında Meydana Gelen Alveolar Kemik Rezorpsiyonunun Dental Volumetrik Tomografi İle Değerlendirilmesi"**
VARSA ARAŞTIRMANIN PROTOKOL KODU	

ETİK KURUL BİLGİLERİ	ETİK KURULUN ADI	**Yeditepe Üniversitesi KAEK (2012-KAEK-70)**
	AÇIK ADRESİ:	Yeditepe Üniversitesi Hastanesi İçerenköy Mahallesi, Hastane Yolu Sokak no:102-104 34755 Ataşehir İstanbul
	TELEFON	+90 (216) 578 40 00 / 4797
	FAKS	+90 (216) 469 37 96
	E-POSTA	keak1@yeditepe.edu.tr

BAŞVURU BİLGİLERİ	KOORDİNATÖR/SORUMLU ARAŞTIRMACI UNVANI/ADI/SOYADI	Prof. Dr. Bahar Eren Kuru/Prof. Dr. Hare Gürsoy/ Dr. Öğr. Üyesi Gizem İnce Kuka/ Dt. Berkay Özata			
	KOORDİNATÖR/SORUMLU ARAŞTIRMACININ UZMANLIK ALANI	Periodontoloji AD.			
	KOORDİNATÖR/SORUMLU ARAŞTIRMACININ BULUNDUĞU MERKEZ	Yeditepe Üniversitesi Diş Hekimliği Fakültesi			
	VARSA İDARİ SORUMLU UNVANI/ADI/SOYADI				
	DESTEKLEYİCİ				
	PROJE YÜRÜTÜCÜSÜ UNVANI/ADI/SOYADI (TÜBİTAK vb. gibi kaynaklardan destek alanlar için)				
	DESTEKLEYİCİNİN YASAL TEMSİLCİSİ				
	ARAŞTIRMANIN FAZI VE TÜRÜ	FAZ 1			
		FAZ 2			
		FAZ 3			
		FAZ 4			
		Gözlemsel ilaç			
		Tıbbi cihaz klinik araştırması	☒		
		İn vitro tıbbi tanı cihazları ile yapılan performans değerlendirme çalışmaları	☐		
		İlaç dışı klinik araştırma	☐		
		Diğer ise belirtiniz	☐		
	ARAŞTIRMAYA KATILAN MERKEZLER	TEK MERKEZ ☒	ÇOK MERKEZLİ ☐	ULUSAL ☒	ULUSLARARASI ☐

YEDİTEPE ÜNİVERSİTESİ KLİNİK ARAŞTIRMALAR ETİK KURULU KARAR FORMU

Araştırmanın Açık Adı	**"Diş Çekimi Sonrasında Meydana Gelen Alveolar Kemik Rezorpsiyonunun Dental Volumetrik Tomografi İle Değerlendirilmesi"**
VARSA ARAŞTIRMANIN PROTOKOL KODU	

KLİNİK ARAŞTIRMALAR ETİK KURULU	
ETİK KURULUN ÇALIŞMA ESASI	İlaç ve Biyolojik Ürünlerin Klinik Araştırmaları Hakkında Yönetmelik, İyi Klinik Uygulamaları Kılavuzu
BAŞKANIN UNVANI / ADI / SOYADI:	Prof. Dr. Turgay Çelik

Unvanı/Adı/Soyadı	Uzmanlık Alanı	Kurumu	Cinsiyet		Araştırma ile İlişki		Katılım *		İmza
Prof. Dr. Turgay Çelik (Etik Kurul Başkanı)	Tıbbi Farmakoloji	Y.Ü. Eczacılık Fakültesi	E ☒	K ☐	E ☐	H ☒	E ☒	H ☐	
Prof. Dr. Ferda Özkan	Patoloji	Y.Ü. Tıp Fakültesi	E ☐	K ☒	E ☐	H ☒	E ☒	H ☐	
Prof. Dr. Pelin Yazgan	Fiziksel Tıp ve Rehabilitasyon	SBÜ Fatih Sultan Mehmet Eğitim ve Araştırma Hastanesi	E ☐	K ☒	E ☐	H ☒	E ☒	H ☐	
Prof. Dr. Esra Can	Diş Hekimi	Y.Ü. Diş Hekimliği Fakültesi	E ☐	K ☒	E ☐	H ☒	E ☒	H ☐	
Prof. Dr. Hasan Aydın (Etik Kurul Başkan Yrd.)	Endokrinoloji	Y.Ü. Tıp Fakültesi	E ☒	K ☐	E ☐	H ☒	E ☒	H ☐	
Doç. Dr. Gökhan Ertaş	Biyo Medikal	Y.Ü. Mühendislik Fakültesi	E ☒	K ☐	E ☐	H ☐	E ☐	H ☐	
Hasan Erdem	Hukuk (Av.)	Serbest Meslek	E ☒	K ☐	E ☐	H ☐	E ☐	H ☐	
Prof. Dr. Recep Erol Sezer	Halk Sağlığı	Y.Ü. Tıp Fakültesi	E ☒	K ☐	E ☐	H ☒	E ☒	H ☐	
Prof. Dr. Hatice Türe	Anesteziyoloji ve Reanimasyon	Y.Ü. Tıp Fakültesi	E ☐	K ☒	E ☐	H ☒	E ☒	H ☐	
Doç. Dr. Muhammed Hamitoğlu (Bildirimden Sorumlu Üye)	Eczacı	Y.Ü. Eczacılık Fakültesi	E ☒	K ☐	E ☐	H ☒	E ☒	H ☐	
Doç. Dr. Aylin Yaba Uçar	Histoloji ve Embriyoloji	Y.Ü. Tıp Fakültesi	E ☐	K ☒	E ☐	H ☒	E ☒	H ☐	
Dr. Öğr. Üyesi F. Ferda Kartufan	Anesteziyoloji ve Reanimasyon			K ☒	E ☐	H ☒	E ☒	H ☐	
Dr. Öğr. Üyesi Hale Arık Taşyıkan	Halk Sağlığı			K ☒	E ☐	H ☐	E ☐	H ☐	
Merve Çınar	Sivil Üye			K ☒	E ☐	H ☒	E ☒	H ☐	

*:Toplantıda Bulunma

YEDİTEPE ÜNİVERSİTESİ KLİNİK ARAŞTIRMALAR ETİK KURULU KARAR FORMU

Araştırmanın Açık Adı	"Diş Çekimi Sonrasında Meydana Gelen Alveolar Kemik Rezorpsiyonunun Dental Volumetrik Tomografi İle Değerlendirilmesi"
VARSA ARAŞTIRMANIN PROTOKOL KODU	

	Belge Adı	Tarihi	Versiyon Numarası	Dili
DEĞERLENDİRİLEN BELGELER	ARAŞTIRMA PROTOKOLÜ	21.06.2022	2	Türkçe ☒ İngilizce ☐ Diğer ☐
	BİLGİLENDİRİLMİŞ GÖNÜLLÜ OLUR FORMU	18.06.2020	1	Türkçe ☒ İngilizce ☐ Diğer ☐
	OLGU RAPOR FORMU	25.05.2022	1	Türkçe ☒ İngilizce ☐ Diğer ☐
	ARAŞTIRMA BÜTÇESİ	25.05.2022	1	Türkçe ☒ İngilizce ☐ Diğer ☐

	Belge Adı		Açıklama
DEĞERLENDİRİLEN DİĞER BELGELER	KLİNİK ARAŞTIRMA BAŞVURU FORMU GÖZLEMSEL RETROSPEKTİF	☐ ☐ ☐	
	TIBBİ CİHAZ TC KLİNİK ARAŞTIRMA (AKADEMİK) TC GÖZLEMSEL KLİNİK ARAŞTIRMA TC İN VİTRO KLİNİK ARAŞTIRMA	☒ ☐ ☐ ☒	
	SİGORTA	☐	
	ARAŞTIRMA BÜTÇESİ	☒	
	BİYOLOJİK MATERYEL TRANSFER FORMU	☐	
	ÖZGEÇMİŞLER	☒	
	HELSİNKİ BİLDİRGESİ	☒	
	ÇIKAR İLİŞKİSİ BELGESİ	☐	
	KURUM İZNİ	☒	
	CİDDİ ADVERS OLAY (CAO) BİLDİRİMİ	☐	
	SONLANIM BİLDİRİMİ BAŞVURU FORMU	☐	

KARAR BİLGİLERİ	**Karar No: 1630**	**Tarih: 22.06.2022**
	Yukarıda bilgileri verilen **"Diş Çekimi Sonrasında Meydana Gelen** **lumetrik Tomografi İle Değerlendirilmesi"** klinik araştırmanın başvuru dosyası ile ilgili belg daşım ve yöntemleri dikkate alınarak incelenmiş ve uygun bulunmuş olup araştırmanın/çalışmanın kleştirilmesinde etik ve bilimsel yönden yeterli bulunduğuna toplantıya katılan etik kurul üye İlaç ve Biyolojik Ürünlerin Klinik Araştırmaları Hakkında Yönetmeli in Türkiye İlaç ve Tıbbi Cihaz Kurumu'ndan izin alınması gerekmektedir.	

7.2Curriculum Vitae

Personal Information

Name-Surname	Berkay	**Surname**	Özata
Place of birth			
Nationality	T.C.		
E-mail			

Education

Derece	**Alan**	**name of the Institution Gradutated from**	**Graduation Year**
PhD	Periodontoloji	Yeditepe Üniversitesi	2023
University	Diş Hekimliği	Yeditepe Üniversitesi	2016
High School	-	Şehit Osman Altınkuyu Anadolu Lisesi	2010

.

Languages	**Grades**
English	62,5 (YÖK-DİL)

Scientific Works

SCI, SSCI, AHCI indekslerine giren dergilerde yayınlanan makaleler

Implant mucosal tunnel may be critical modifier for peri-implant health (Digest), Journal of clinical periodontology, 2019