Original Article / Özgün Araştırma

Use of Cone-beam Computed Tomography in Regenerative Treatment of Residual Bone Gaps around Implants: A Feasibility Study

İmmediyat İmplantlar Çevresindeki Defektlerin Rejeneratif Tedavisinde Konik Işın Hüzmeli Bilgisayarlı Tomografinin Kullanılması: Bir Fizibilite Çalışması

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Keywords
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Abstract

Objective: The cone-beam computed tomography (CBCT) has been recently used to monitor changes in alveolar bone. The aim of this study was to determine the feasibility of the use of CBCT in assessment of osseous regeneration with different regenerative materials around immediate implants.

Materials and Methods: Twenty implants were immediately placed after extraction in the anterior maxilla of eight systematically healthy patients. One group received bovine-derived xenograft (BDX) (n=10); and the other group was treated with demineralized freeze-dried allograft (DFDA) (n=10). Patients in both groups also received platelet-rich plasma. Clinical measurements and CBCT analyses were performed at the day of implant placement (baseline) and after 9 months just before placement healing abutments. The intragroup change was analyzed by ANOVA test. The clinical and CBCT measurements were compared with Pearson correlation analysis.

Results: Clinical measurements demonstrated that the defect depth and width improved with a similar gain compared to baseline in both BDX and DFDA-treated sites ($p<0.05$). There was no significant difference between two different bone substitutes clinically. CBCT measurements revealed a significant bone gain for both graft-treated gaps, compared to baseline ($p<0.05$) with no difference between groups. Clinical measures and CBCT values were highly and significantly correlated ($p<0.05$).

Conclusion: The results demonstrated that the CBCT may be a reliable method for evaluation of the change over time for the regenerative procedures around dental implants.

Öz

Amaç: Konik-ışın hüzmeli bilgisayarlı tomografi (KIBT) son yıllarda alveol kemiğindeki değişikliklerin tespit edilmesinde kullanılmaktadır. Bu çalışmanın amacı immediyat implantların çevresindeki defektlere farklı rejeneratif materyallerin uygulanmasının sonuçlarının değerlendirilmesinde KIBT fizibilitesinin incelenmesidir.

Gereç ve Yöntemler: Çalışma kapsamına sistemik olarak sağlıklı 8 bireyin üste çene anterior bölgesine immediyat olarak uygulanan 20 implant dahil edilmiştir. Bir gruba (n=10) sığır kaynaklı ksenogreft diğer gruba ise (n=10) demineralize dondurulmuş kurutulmuş kemik allogrefti uygulanmıştır. Her iki gruptaki tüm defektlere ilave olarak trombositten zengin plazma greft materyali ile karıştırılarak uygulanmıştır. Klinik ölçümler ve KIBT ile değerlendirme, implantların yerleştirildiği gün ve 9 ay sonra (iyileşme başlıkları yerleştirilmeden önce) yapılmıştır. Grup içi değişiklikler ANOVA testi ile analiz edilmiştir. Klinik ve KIBT ölçümlerini karşılaştırmak için Pearson korelasyon analizi kullanılmıştır.
Bulgular: Defekt derinliği ve genişliğindeki kazanç başlangıç değerlerine kıyasla her iki grupta da benzer ve anlamlıdır ($p<0,05$). İki farklı kemik grefti arasında anlamlı fark bulunamamıştır ($p>0,05$). KIBT ölçümleri ile her iki greft ile tedavi edilen defektler için de başlangıç değerlerine göre anlamlı bir kemik kazancı tespit edilmiştir ($p<0,05$). KIBT değerleri ve klinik ölçümler ileri derecede anlamlı korelasyon göstermiştir ($p<0,05$).
Sonuç: Çalışmanın bulguları ışığında KIBT'nin immediyat uygulanan diş implantlarının çevresindeki rejeneratif işlemlerin başarısının ölçülmesi için güvenilir bir yöntem olabileceği söylenebilir.

Introduction

Tooth extraction results in reduced width and height of the alveolar crest over time (1,2). Immediate placement of a dental implant after tooth extraction has been recommended for preventing the alveolar bone loss and shortening the time for prosthetic treatment (3-6). In order to fill the gaps between the implants and the bone walls during immediate implantation, various procedures and techniques, including the use of grafting materials and barrier membranes, have been suggested. Regenerative methods include biologically active agents to augment bone not only in the fresh extraction sockets but also around the dehiscence or fenestration defects. These techniques have been collectively referred to as "minor augmentation procedures" (7,8). Both demineralized freeze-dried allografts (DFDA) (9), and bovine-derived deproteinized xenografts (BDX) have been shown to become integrated and replaced by newly formed bone (10). Since the "quality" of new bone formed as a result of grafting is still being debated, the efficacy can be enhanced by the use of biologics such as growth factors. Platelet-rich plasma (PRP) include multiple growth factors such as PDGF and IGF-1 that have been shown to accelerate wound healing through parenchymal cell proliferation and tissue regeneration (11). El-Sharkawy et al. (12) also suggested that PRP facilitates healing by acting as an anti-inflammatory agent. Thus, PRP can enhance the success of grafting and quality of new bone alone (13) or in combination with other regenerative materials (14-17). The use of PRP with grafting may also be useful in enhancing the biological integration of the dental implants in the extraction sockets after immediate placement.

Accurate assessment of new bone formed and its quality after regenerative procedures is a critical determinant of success. Various clinical approaches are used as conventional methods. Dental radiographic techniques can enhance the quality and accuracy of outcome measures and to monitor changes in alveolar bone and dental structures and regenerative procedures around implants (18-20). Three-dimensional scanning techniques such as computed tomography (CT) and cone-beam computed tomography (CBCT) can be alternatives to conventional two-dimensional methods while eliminating the need for clinical re-entry procedures (19,20). CBCT enables the construction of a real-size dataset with multiplanar cross-sectional images with a low radiation dose (21). CBCT technique has been suggested to be reliable where the linear measurements between anatomical sites are required such as pre-operative assessment (21,22). Limited data indicate that CBCT may be used for the evaluation of regenerative periodontal treatment outcomes after bone replacement graft procedures (19). However, only a limited number of clinical studies are available for reaching definitive conclusions regarding the use of the CBCT after grafting around immediate implants. Thus, this study has been designed as to determine the feasibility of CBCT for assessment of bone regeneration around immediately placed implants in fresh extraction sockets.

Materials and Methods

Patient and Site Selection

Eight patients (8 females; age range: 42-50; average age: 45±5) were recruited at İstanbul University Faculty of Dentistry, Department of Periodontology.

The parallel-design study was approved by the Local Ethical Committee of İstanbul University (2006/1889), and it was carried out in accordance with Helsinki Declaration (1975; revised, 2002). Signed consent by patients was obtained. The study was conducted between 2007 and 2010. In total, 20 peri-implant sites were included. The inclusion criteria were: 1) a medical history that would not inhibit a physiological wound healing response, 2) hopeless maxillary anterior teeth due to periodontal infection, 3) radiographic assessment of at least 4 mm of bone beyond the root apex for primary implant stability during placement, and 4) age between 18 to 65 years. Exclusion criteria included 1) smoking; 2) immunosuppressive treatment or known use of any medication with a potential of affecting osseointegration and bone tissue during the previous 6 months; 3) pregnancy; 4) systemic diseases (e.g., diabetes); and 5) fractured teeth.

Surgical Procedures

All surgical procedures were performed by the same investigator under local anesthesia (Ultracaine D-S forte, Hoechst Marion Roussel, Frankfurt, Germany). Intrasulcular incisions were made around the maxillary teeth to be extracted, and the adjacent teeth; and mucoperiosteal flaps were elevated. Periotomes (Anterior Periotome, Hu-Friedy, Chicago, IL, USA) were used to extract teeth without trauma and by avoiding bucco-lingual movements and preventing damage to the labial wall of the alveolar socket. Granulation tissues were removed from the extraction sites using surgical curettes and irrigated with sterile saline. Remnants of the sulcular epithelium in the inner surface of flaps were removed by surgical scissors. After the extraction, Bränemark System MKIII TiU (Bränemark System, MkIII TiU RP; Nobel Biocare, Göteborg, Sweden) implants (Ø=3.75 mm, 11.5 or 13.0 mm in length) were inserted.

All residual defects after the placement of implants were treated with either BDX (Bio-Oss, Particle size: 0.25-1.00 mm, Geistlich Pharma AG, CH-Wolhusen, Swiss) or DFDA (Dembone, Particle size; 0.25-0.5 mm, Pacific Coast Tissue Bank, Los Angeles, USA) graft materials. The randomization of the choice of treatment groups was made using a randomization code. PRP was prepared with the PRP-20 mL prep kit and activated with autologous thrombin kit (Harvest Technologies Smart Prep2, Harvest Technologies Corp., Plymouth, MA, USA). Twenty mL of peripheral blood was drawn from each patient 1 hour before the surgery, for the preparation of autologous thrombin, 10 mL of venous blood were drawn syringe from each patient. Graft particles were mixed with PRP and then condensed to fill the peri-implant gap.

In all groups, flaps were sutured to allow a submerged healing with polyester sutures (Doğsan AS, Trabzon, Turkey). All patients received oral and written instructions for postoperative care; amoxicillin + clavulanic acid (1000 mg, b.i.d. for 5 days), naproxen sodium (550 mg, 2x1, for three days), and chlorhexidine gluconate (0.12%, 2x1, for two weeks). Sutures were removed after ten days. Patients were recalled every month and used temporary dentures. Implants were exposed and restored after 9 months.

Clinical Measurements

Occlusal stents were custom-fabricated on a cast model acquired from an alginate impression in order to uniform the guidance of periodontal probe for the pre- and postoperative measurements. Using these stents, the intrabony component was measured at the deepest point of the peri-implant space (Figure 1).

Depth of the defect (DD) was measured from the most apical region of the gap to the coronal aspect of the implant. Defect width (DW) was measured bucco-lingually from the most buccal area of the implant to the labial alveolar bone. In addition, distance between stent margin and bone crest and distance between stent margin and defect base (SDB) were measured. Measurements were performed with a PCP UNC-15 (PCP UNC-15, Hu-Friedy, Chicago, IL, USA) manual

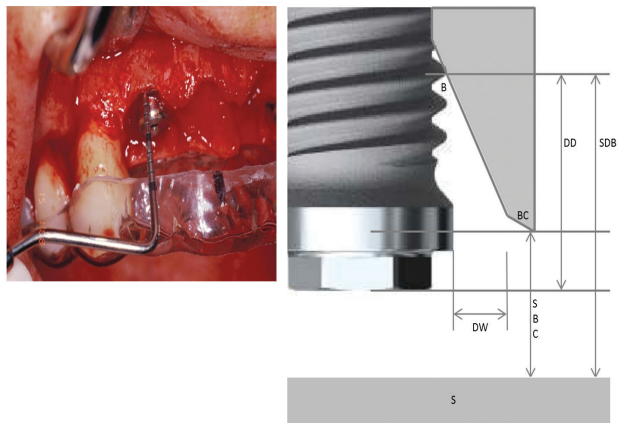

Figure 1. Clinical measurements with occlusal stent

B: Base of the defect, BC: Bone crest, S: Stent margin, DD: Defect depth, DW: Defect width, SBC: Distance between stent margin and bone crest, SDB: Distance between stent margin and defect base

periodontal probe and transferred to the scheme. When a single probe was not long enough to measure the distance a second probe was used. All measurements were performed by the same investigator, who was calibrated at intra-examiner level.

The data was collected by the same investigator and in order to prevent bias at analysis level and analyzed by a researcher who was unaware of the groups. Measurements were repeated at the end of the ninth month when implants were exposed.

Radiographic Measurements

CBCT images were obtained in patients immediately after the implantation and just before the placement healing abutments of the implants after nine months using Newtom 3G (Newtom 3G, Quantitative Radiology, Verona, Italy). The radiation dose and exposure were individually adjusted by CBCT automatically based on the patient size. The screening specifications were as follows: voxel size 0.19 mm^3; pixel size 0.11 mm×0.11 mm. The maximum output of scanner was 110 KV and 15 mAs. The average scan time was 36 seconds and ordinary exposure time was 5.4 seconds. CBCT examinations on 0.5 mm cross-section images were performed by one investigator. The following landmarks were defined in the cross-section images: Implant shoulder and the most coronal level of radiological bone in contact with the implant [i.e., radiographical bone level (RBL)]. For standardization, linear measurements were made by drawing a vertical line, following the long axis of the implant, from IS to RBL at the buccal aspect. The most coronal bone level on each side of the implant was identified at each axial cross section at the first radiographic visible the most coronal bone parallel to the implant was assessed on the buccal aspect of the jaw.

Statistical Analysis

Data are presented as the average and standard deviations at baseline and endpoint values (SPSS Inc. Released 2008. SPSS Statistics for Windows, Version 17.0. Chicago: SPSS Inc.). Within groups, the change was analyzed by ANOVA for repeated measures followed by Friedman non-parametric test. Both tests gave similar results and were confirmatory. Inter-group differences were compared by normalizing the data for baseline levels and using the analysis of covariance. Pearson correlation analysis was used to compare the clinical and CBCT measurements. In all statistical evaluations, 0.05 was taken as the cutoff for the level of significance.

Results

All subjects successfully completed the study. Allergic reactions, swelling, abscess formation, or infections were not noted throughout the healing. All implants showed stability with no sign of mobility. A representative case is shown in Figure 2 including pre-operative, peri-operative, and post-operative images with clinical and radiological assessment.

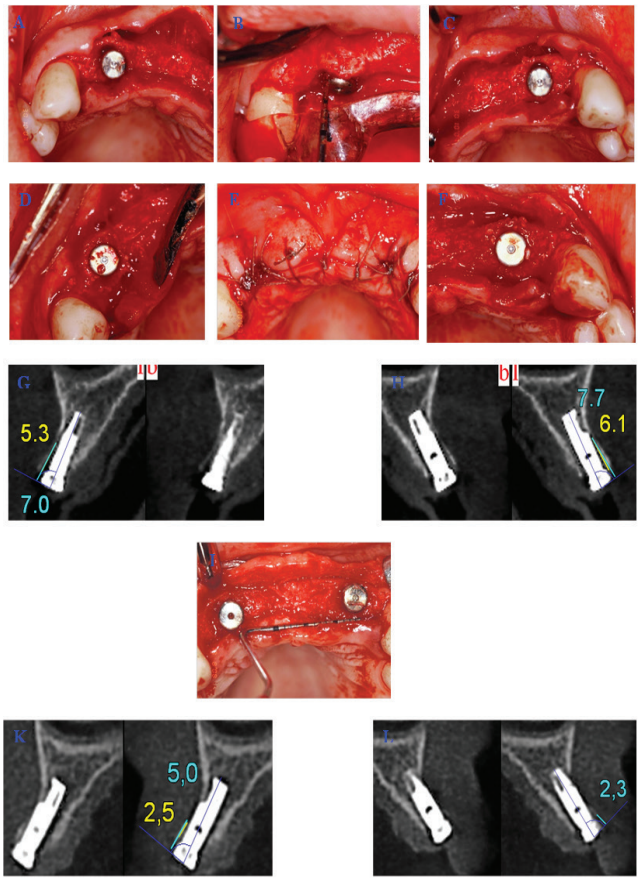

Figure 2. Representative series of pre-, peri-, and post-operative clinical and radiographical images

Panels A-C) Immediate placement of two dental implants in anterior maxilla, residual defects and clinical measurements using a custom-made occlusal stent in the same patient (A: Upper left second incisor site, B: Clinical measurement, C: Upper right second incisor site) Panels D-F) defects filled with bone grafts and PRP (D: BDX + PRP, E: Primary closure, F: DFDA + PRP) Panels G-H) CBCT measurements after the immediate implantation (G: Upper left second incisor site, H: Upper right second incisor site) Panel I) clinical re-entry Panels K, L) Second radiographic measurements with CBCT

BDX: Bovine-derived deproteinized xenografts, DFDA: Demineralized freeze-dried allografts, CBCT: cone-beam computed tomography, PRP: Platelet-rich plasma

The mean platelet count in whole blood from the donors was 283.000 cells/µL (198.000-398.000 cells/µL). On average, a 2.49-fold increase in platelet concentration was achieved by PRP preparation.

Clinically we have measured the amount of hard tissue fill in gaps during the time between two surgeries. There was no statistically significant difference in defect depth between BDX or DFDA-treated sites at baseline (Table 1). Both grafting approaches resulted in a statistically significant gain compared to baseline ($p<0.05$) with no statistical difference between grafting. Average DW for BDX or DFDA-treated sites at baseline. Both treatment methods resulted in a statistically significant and horizontal bone fill in both groups compared to baseline ($p<0.05$) regardless of the peri-surgical defect depth and width with no difference between groups.

CBCT measurements revealed that baseline and follow-up RBL measurements were similar between groups with significant differences compared to baseline ($p<0.05$; Table 1).

When defect fill was compared between deep and shallow bone gaps (cut-off: 4 mm) at baseline, all groups showed statistically significant changes compared to baseline (Table 2; $p<0.05$) with no significant difference between BDX and DFDA ($p>0.05$). Likewise, when sites were categorized based on the baseline DW (cut-off: 2 mm), defect fill was significant in all test sites compared to baseline, with no significant difference between graft materials used (Table 3).

Correlation analysis demonstrated that the coefficient between RBL and DD was 0.959 ($p=0.000$). SDB and RBL was also significantly correlated ($p=0.000$; $R^2=0.761$). There was a significant correlation between DW and RBL ($p=0.000$; $R^2=0.787$). DD highly correlated with SDB ($p=0.000$; $R^2=0.729$) and DW ($p=0.000$; $R^2=0.850$).

Discussion

The aim of this study was to test the feasibility of CBCT in assessment of peri-implant residual bone fill after immediate implantation and grafting. The results demonstrated that the CBCT is a comparable and accurate method for evaluation of the change in response to regenerative procedures around dental implants over time. The data also showed that there was no difference between different materials/substitutes.

Table 1. Clinical and cone-beam computed tomography-based radiographical measurements of defect fill

	Baseline	9 Months	p
Defect depth			
BDX	5.9±2.5	0.3±0.5	0.000*
DFDA	5.1±1.6	0.2±0.4	0.000*
p	0.298	0.474	-
Defect width			
BDX	1.7±0.7	0.1±0.4	0.000*
DFDA	1.5±0.6	0.0±0.0	0.000*
p	0.491	0.302	-
Distance-stent margin and bone crest			
BDX	9.5±2.0	10.6±1.9	NS
DFDA	10.4±3.0	12.5±4.1	NS
p	0.345	0.480	-
Distance-stent margin and defect base			
BDX	15.4±2.8	10.9±2.0	0.000*
DFDA	15.4±3.0	12.7±3.9	0.001*
p	0.965	0.321	-
Radiographical bone level			
BDX	7.7±1.5	4.0±2.1	0.000*
DFDA	8.0±1.7	4.0±1.5	0.000*

NS: Not statistically significant, BDX: Bovine-derived deproteinized xenografts, DFDA: Demineralized freeze-dried allografts
*: Statistically significant

Table 2. Defect fill according to baseline defect depth

		Baseline	9 months	p
BDX	≤4 mm	3.50±1.00	0.00±0.00	0.002*
	>4 mm	6.82±2.36	0.50±0.58	0.000*
p	-	0.002*	0.134	-
DFDA	≤4 mm	3.20±0.84	0.00±0.00	0.003*
	>4 mm	6.00±1.00	0.20±0.45	0.000*
p	-	0.004*	0.512	-

BDX: Bovine-derived deproteinized xenografts, DFDA: Demineralized freeze-dried allografts
*: Statistically significant

Table 3. Defect fill according to baseline defect width. There was no statistically significant difference between groups for any parameter

		Baseline	9 month	p
BDX	<2 mm	1.07±0.19	0.00±0.00	0.000*
	≥2 mm	2.25±0.46	0.33±0.58	0.000*
p	-	0.000*	0.104	-
DFDA	<2 mm	1.06±0.30	0.00±0.00	0.000*
	≥2 mm	2.14±0.38	0.00±0.00	0.000*
p	-	0.000*	1.000	-

BDX: Bovine-derived deproteinized xenografts, DFDA: Demineralized freeze-dried allografts
*: Statistically significant

Previous studies on the use of CBCT offered a variety of applications during osseous healing in human and animal models (19, 23-26) with evidence that CBCT could be used to identify the alveolar defects with high accuracy (18,19, 25-27). While CBCT has become a part of the standard of care in implant dentistry in planning and guiding during the surgery (28-30), limited studies have investigated the use of CBCT for the assessment of changes in peri-implant defects (18,24,31,32). One limitation of the existing studies is that they were performed on artificially created on *ex vivo* defects in dissected jaws (31,32). Therefore, the current study represents an attempt for testing the feasibility of CBCT in a real clinical scenario where the accuracy of CBCT was compared to the clinical measurements in human peri-implant defects at baseline and after the regenerative treatment. The results suggested that the clinical and CBCT measurements were highly correlated and that the CBCT can be used to assess the peri-implant changes after grafting.

Application of the CBCT for testing the osseous changes around implants has several potential advantages but also presents an increased risk by repeated exposure to x-rays during radiographic imaging. Based on ALARA, which is the fundamental principle for diagnostic radiology, minimization of the dose should be achieved by clinician determination for patients' needs with obtaining a radiographic image of sufficient diagnostic quality (33). The International Commission on Radiological Protection Committee recommendations in 2007; included extrathoracic region, salivary glands, and oral mucosa in the calculation of adequate dose and suggested a re-appraisal of cancer risk from maxillofacial radiographic examinations (34). These issues limit the use of most radiographic techniques for the re-appraisal of changes in osseous tissues. On the other hand, CBCT has been considered as a dose-sparing technique in comparison with conventional medical CT scans for extensive oral and maxillofacial radiographic imaging assignments (35). Recent studies have confirmed that the doses from CBCT are far below compared to the conventional CT (35,36). In this study, the images were taken at baseline and after 9 months; therefore, the risk for the patients given the current guidelines is minimal. Yet, more research is required for the assessment of safety of repeated CBCT imaging.

Factors that can influence the outcomes (e.g. the variation in defect biotype, the width of the facial and palatal alveolar walls) need to be evaluated in larger clinical trials and for their potential impact on CBCT measurements. For example, Tyndall et al. (37) suggested that implant fixtures inherently produce beam-hardening artifacts concealing subtle alterations in marginal and peri-implant bone where intraoral radiographs may provide better results for the detection of these findings. Indeed, the accuracy of the imaging compared to the conventional intraoral periapical radiographs, which have been widely used to provide high-resolution images for accurate measures around the implanted sites (38,39) needs to be assessed. While periapical radiographs present as low-cost techniques with good patient tolerance and user-friendliness, they have critical limitations such as two-dimensional anatomical superposition and geometric distortion, limiting the visibility of intra-bony defects and their alterations over time (27,40). Newly-introduced digital panoramic radiography device may overcome some of these limitations

reaching a sufficient image quality. However, it has been noted that panoramic radiographs cannot be used to assess peri-implant defects adequately, due to the limited resolution, enlargement, and distortion (41). CBCT presents a solution for these limitations (19,40) allowing the examination of the implant and its surrounding tissues in different orthogonal planes (42) and offering an evaluation of osseous regeneration even on lingual and buccal aspects of implants (43,44).

Our results suggested that CBCT correlated well with the clinical measurements. We acknowledge, however, that there are limitations to the CBCT use around implants. Because of the radiopacity of various bone grafts, a non-osseous graft material might be wrongfully diagnosed as bone (24). In order to test this, we compared two different graft materials and demonstrated that there was no difference suggesting that the CBCT measurements were accurate regardless of the graft material. Another major image-distortion may be due to the metallic structure of implants on exposure quality and amount of artifacts and detection findings (39). A strong beam hardening artifacts can occur in CBCT images of titanium implants (45,46), which could becloud the detection of bone adjacent to the implant surface.

This study was not designed to test the efficacy of the use of PRP in addition to the graft materials in regenerative procedures. This is an area of research where there is extensive and current studies are underway, For example, some studies reported that DFDA combined with PRP did not significantly change bone mineral density or graft maturity levels (15) while Kim et al. (14) have suggested that the combination enhanced bone formation around the implant defects. Further conflicting results were noted in an animal study by You et al. (16), who have examined the effect of combination PRP and BDX, in the repair of bone gaps adjacent to dental implants. the addition of PRP into BDX graft actually decreased the peri-implant bone healing was demonstrated. In our current study, we have found no difference between two different grafting methods. Both approaches had the PRP added, and since we did not have the PRP-alone or graft alone groups, the impact of additional growth factor use during the grafting procedures around dental implants need to be tested in future studies.

Conclusion

The data suggested that the CBCT is an efficient method to assess vertical osseous changes around immediately placed implants in the anterior maxilla.

Ethics

Ethics Committee Approval: The parallel designed study was approved by the local ethical committee (2006/1889).

Informed Consent: All patients were informed about the aims of the study, risks, benefits and alternative treatment options. Signed consent by patients was obtained.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: C.Z.K., Ö.T., A.K., Design: C.Z.K., A.K., Data Collection and Processing: C.Z.K., Z.Y.S., I.S., S.M., Analysis or Interpretation: A.K., S.H., Literature Search: C.Z.K., I.S., S.M., Writing: C.Z.K., A.K.S.H., Ö.T.

Conflict of Interest: No conflict of interest.

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