Immediate implantation in the maxillary esthetic zone: results from two decades of clinical research

PhD Thesis

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LIST OF PUBLICATIONS PROVIDING THE BASIS OF THE THESIS

1. Klinger A, Mijiritsky E, Kohavi D. Biological and clinical rationale for early implant loading. Compend Contin Educ Dent. 2006; 27:29-34; quiz 5-6.

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2. Mijiritsky E. Plastic temporary abutments with provisional restorations in immediate loading procedures: a clinical report. Implant Dent. 2006; 15:236-40.

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3. Mijiritsky E, Mardinger O, Mazor Z, et al. Immediate provisionalization of single-tooth implants in fresh-extraction sites at the maxillary esthetic zone: up to 6 years of follow-up. Implant Dent. 2009; 18:326-33.

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4. Barone A, Marconcini S, Giammarinaro E, et al. Clinical Outcomes of Implants Placed in Extraction Sockets and Immediately Restored: A 7-Year Single-Cohort Prospective Study. Clin Implant Dent Relat Res. 2016; 18:1103-12.

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5. Kolerman R, Nissan J, Mijiritsky E, et al. Esthetic assessment of immediately restored implants combined with GBR and free connective tissue graft. Clin Oral Implants Res. 2016; 27:1414-22.

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6. Kolerman R, Mijiritsky E, Barnea E, et al. Esthetic Assessment of Implants Placed into Fresh Extraction Sockets for Single-Tooth Replacements Using a Flapless Approach. Clin Implant Dent Relat Res. 2017; 19:351-64.

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7. Kolerman R, Qahaz N, Barnea E, et al. Allograft and Collagen Membrane Augmentation Procedures Preserve the Bone Level around Implants after Immediate Placement and Restoration. Int J Environ Res Public Health. 2020; 17.

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ABBREVIATIONS

BOP - bleeding on probing
CBL - crestal bone level
DIM - distance from the mucosal margin to the implant shoulder
FDBA - freeze demineralized bone allograft
FSTL - facial soft tissue level
GBR - guided bone regeneration
HA - hydroxyapatite
IC - implant crown
IIP - immediate implant placement
IPR - immediate placement and restoration
ISQ - implant stability quotient (stability as measured by the Osstell device)
mBI - modified bleeding index
MBL - marginal bone loss
mPI - modified plaque index
NIH - National Institutes of Health
OHI - oral hygiene index (by O'Leary)
PD - probing depth
PES - pink esthetic score
PI - papilla index
RFA - resonance frequency analysis
SLA - sand-blasted and acid-etched
TPS - titanium plasma spray
WES - white esthetic score
WKG - width of the keratinized gingiva

I. INTRODUCTION[1]

I.1. Background and key terms

The history of dental implantation begins with an attempt to reimplant homologous teeth in 2000 BC.1 In 400 BC, the use of gold or wood tooth-shaped implants was reported. A 2-stage surgical procedure was explored by Adams in 1938, using a cylindrical screw and a healing cap. In 1943, Dahl reported using a subperiosteal implant,1 followed by the Linkow's blade implant in 1966 and the mandibular staple by Small in 1975 [1].

The dramatic change in the way we practice implant dentistry today was brought about by the introduction of titanium for this purpose by Brånemark in 1952 and the subsequent development of the osseointegration concept. The Brånemark group defined osseointegration "a direct structural and functional connection between ordered, living bone and the surface of a load-carrying implant" and described the ability of titanium threads to integrate into cortical bone [2].

Brånemark's protocol for the placement of titanium dental implants recommends machined titanium implants, a 2-stage procedure, stress-free healing period of 3 to 6 months, atraumatic surgery, a mucobuccal incision (rather than a crestal incision), sterile conditions, radiographs upon completion of healing, and acrylic occlusal surfaces [3, 4]. This strict protocol has led to high implant success rates ever since [5].

Brånemark described the stages of osseointegration as follows:

1. primary fixation

2. callus formation

3. remodeling into mature functional bone

When this desirable sequence of events is disturbed, pseudointegration takes place. Among the etiologic factors for this phenomenon are preparation trauma, infection, preintegration loading, and postintegration overload. Preintegration loading, or early loading, is defined as loading within physiologic limits, applied on implants before completion of the osseointegration process [6]. Postintegration overload is loading applied to implants after completion of the osseointegration process that exceeds physiologic limits [6-9]. For instance, Isidor [7] induced

[1] The introductory part is based on Klinger A, Mijiritsky E, Kohavi D. Biological and clinical rationale for early implant loading. Compend Contin Educ Dent. 2006; 27:29-34; quiz 5-6.

occlusal trauma by creating supraocclusal contacts with antagonist jaw and lateral displacement of the intercuspation during function after 6 months of healing in monkeys. Loss of osseointegration occurred within 41/2 months. At the cellular level, overload may affect gene expression of pluripotential mesenchymal cells, fibroblasts, and chondrocytes, inducing a reversed differentiation [8].

I. 2. Early or immediate loading: the uncertain beginnings

As discussed before, the Brånemark protocol suggests that dental implantation should always happen in a 2- stage procedure, with 3 to 6 months of unloaded healing between implantation and loading. This implicitly suggests that immediate or early implant loading should be avoided, which was supported by a few earlier studies of the Brånemark group and others. Specifically, Brunski discovered that excessive micromotion results in scarlike fibrous healing [10]; studies conducted in the late 1970s by the Brånemark group confirmed that premature loading may lead to fibrous tissue interposition. At the same time, the authors stated that insufficient healing time greatly increased the risk of immediate or late implant mobility. Necrotic bone formed by early loading may respond like fibrous tissue capsules at the implant border and is not capable of load-bearing as mature bone [3, 4]. That is, early loading seemed to lead to mere fibrous encapsulation. This was no good news, and based on these results, the idea of early or immediate loading should have been completely discarded. However, there was more to this question, and - unexpectedly - it was Brånemark himself who gave the first experimentally supported hint as to why early loading should, in fact, work. This was in 1985, when he wrote: “Bone-implant border zone remodels from callus of woven bone to mature functional bone in response to the masticatory load applied” [6]. To put it simply, this means that the transition from the callus formation stage to the remodeling stage into mature bone depends on the masticatory function of the implants. Indeed, the literature soon started to support this opinion, and several factors came to light that could have led to the unfavorable early opinions about early/immediate loading - factors that the early studies most probably did not consider at all. Notably, part of these new results came from the Brånemark group.

I.3. Animal studies support the concept

Only a year after Brånemark’s hint, a dog model study of early loading after 4 weeks of healing demonstrated no fibrous encapsulation around the implant [11]. Provision of a soft diet for 2 weeks after-implantation in monkeys and hard food afterward on splinting of the implant to

adjacent teeth showed no fibrous encapsulation at the 3-month histological examination [12]. Bone apposition averaged 52% for loaded implants and 48 % for unloaded implants in monkeys [13]. No difference was demonstrated between bone-to-implant contact of nonsubmerged (40.1%) and early loaded (35.5%) splinted implants in dogs given a soft diet [14]. Another study showed that, when comparing a test group receiving a soft diet without implant splinting to a control group receiving a hard diet with implant splinting, no difference between groups in bone-to-implant contact was found between groups [15]. In the posterior mandible, even higher bone density around immediately loaded implants was found in monkeys [16]. These studies demonstrated that, in carefully controlled conditions, it was possible to successfully load implants at early stages of healing.

I.4. The issue of micromovements

As mentioned earlier, Brunski and colleagues, in a dog model, found that excessive micromotion resulted in scarlike fibrous healing around implants [10]. Only a few years later, based on a study in the same dog model, Pilliar concluded that integration with bone will occur in the presence of implant micromovement but not micromovement [17]. Displacements of 150 μm to 500 μm are considered excessive micromotion, and disrupt the process of osteogenesis [18]. Even micromotion of above 100 μm was found to potentially cause the implant site to undergo fibrous repair rather than osseous integration [19]. However, micromotion of 30 μm to 50 μm was found to be tolerated for bony ingrowth into endodontic implants [19]. These studies indicated that the most important single factor for successful osseointegration was not the uncovering of the implant, nor the time elapsed between implant placement and the initiation of its function; rather, it was implant stability.

I.5. The importance of the implant surface properties

Surface roughness is a factor that was shown to influence bone density around the implant[20]. For example, the implant surface influences the stress transfer from the implant to the bone [21]. A few studies point to the fact that the effect of micromotion on the outcome of the implantation depends on the implant's surface. In less-than-optimal conditions, the porous cylinder shows bone apposition, while the smooth screw loses its primary fixation and is encapsulated by a membrane [22]. It appears that smooth surfaces will not always provide adequate biomechanical coupling with soft bone.

On the other hand, the texture of titanium plasma-sprayed (TPS) or sandblasted implants generates heterogeneous stress fields around implants in function, promoting bone formation [23]. Calcium phosphate (CaP)-coated implants tolerate more micromovement than implants that are not CaP-coated [24]. A study by Orenstein is an additional demonstration of the interconnecting nature between surface roughness, implant mobility at placement, and successful osseointegration. According to this study, survival of hydroxyapatite (HA)-coated implants mobile at placement was 91.8 %, compared with only 53.6% of implants not coated with HA [25].

I.6. Conclusions from some human studies

In one study, immediate loading was compared with the original 2-stage concept in the interforaminal area [26]. The authors concluded that it was possible to immediately load implants via a permanent fixed rigid cross-arch supraconstruction. This concept was then successfully expanded to the fully edentulous arches [27]. In the study of Tarnow, ten patients received stable cross-arch, screw-retained provisional restorations using rigid metal casting for the permanent restorations. No removable partial prosthesis or cantilevers were used, and no efforts were made to remove cemented provisional restorations by tapping off for 4 to 6 months. Bone-to-implant contact after 5 years was 46% to 82%, indicating that osseointegration was achieved [28].

In another study, no difference between maxilla and mandible was demonstrated after several weeks of healing using TPS implants. Bone apposition measured 67.2% in the maxilla and 80.7% in the mandible. Tight contact between the TPS implant surface and bone with no fibrous encapsulation was found [29].

Roccuzzo and colleagues studied 835 sand-blasted and acid-etched (SLA) implants inserted after 6 weeks of healing in 371 patients. No failures were found 2 years after restoration [30].

Ericsson and co-workers studied the immediate functional loading of Brånemark implants for single-tooth replacement. 13 mm implants with a diameter of 3.75 mm were used. Bilateral occlusal stability was verified and bruxer patients were excluded. 2 of the 14 studied implants were lost. The remaining implants were stable both clinically and radiographically [31].

Cooper studied early nonfunctional loading of single-tooth restorations. Provisional restorations were delivered 3 weeks after implantation, and the final restorations were delivered

12 weeks later. Inclusion criteria included nonmobile adjacent teeth, no bruxism, balanced posterior occlusion, and no type 4 bone. Results demonstrated a 96% success rate [32].

Immediate loading following immediate implantation of single teeth was addressed as well by Chaushu and colleagues, who demonstrated a 20% failure rate. The authors concluded that immediate loading is feasible in healed sites only [33].

The issue of early loading specifically in soft bone was investigated by Summers. In his study, 143 press-fit implants were inserted. HA-coated and TPS-coated implants were inserted in the maxilla and left to heal for 11 weeks. The bone in the implant site was condensed by osteotomes. The success rate was 96% [34].

Yet another study examined 36 SLA implants in the posterior maxilla. The implants were loaded after 6 weeks of healing. In all cases, primary stability was achieved. The torque for abutment connection was gradually increased from 15 Ncm at 43 days to 35 Ncm at 6 weeks. Only 1 implant was lost before the final restoration [35]. The authors suggested that when preparing soft bone for early loading, osteotomes should be used to condense bone and keep the amount of drilling within reasonable limits.

I.7. A fresh look at the protocol

Data from the literature disproved the claim that early/immediate loading should almost invariably lead to failed osseointegration and suggested that deviations from the classical protocol of Brånemark in this respect could be safe and reliable, as long as certain guidelines are adhered to. These include that a) the clinician should use a suitable technique for surgical preparation of the implant site concerning bone type; b) precise planning and execution of the implant direction during drilling sequences should be implemented; c) final burs should not be drilled to the total implant length; and d) primary implant stability should always be assessed for the decision making on implant loading [34, 35].

It also became clear that the implant's surface texture plays a key role in the healing process [20, 21, 23-25] and that micromotion is indeed a factor. As for the latter, it was recommended that prosthetic considerations should aim to keep micromotion below the physiologic threshold by bilateral splinting, the use of the tripod principle (using at least 3 implants that do not align), and by eliminating lateral occlusal forces [26, 28, 31].

The contraindications of early/immediate loading include insufficient bone quantity and/or quality and no achievement of primary fixation. Such an estimation could be carried out by monitoring the screwing torque, periotesting, or resonance frequency analysis (RFA) [36, 37].

All in all, after the uncertain beginnings, by the beginning of the 2000s, it became clear that early/immediate loading could be safely and reliably carried out if a number of previously overlooked factors are taken into consideration. This realization provided the basis of the work of our research group in the following two decades.

I.8. The body of work covered in the present thesis

In the last two decades, our group has concentrated mostly on immediate implantation and loading, and we have covered numerous aspects. Our general aim was to contribute to a firm scientific basis for the clinical use of this approach and to establish its safety and reliability. However, for reasons of space, it would be impossible to cover all the work that has been done in this thesis. Instead, this thesis talks about a clinically important and challenging segment.

In the studies covered in this thesis, we concentrated on the maxillary esthetic zone as the most challenging and sensitive area of dental implantation. In all studies, immediate single-tooth replacement with nonfunctional immediate provisionalization. Our aim with these studies was to prove that this approach is a safe and reliable one in this sensitive area, both in the functional and esthetic sense. Please note that some results were only short-term ones at the time of their publishing. Since then, time has proven them to be lasting.

For reasons of space, in this thesis we concentrate on the key aspects of each covered study. The interested reader may find everything else in the copies of the original studies attached in the Appendix.

All studies reported in this thesis conformed to the Declaration of Helsinki in all respects, and whenever ethics permission was needed, it was granted by the Human Ethics Committee at Tel Aviv University, Israel.

II. OBJECTIVES AND HYPOTHESES

1. As a technical prerequisite, we sought to prove that the use of plastic temporary abutments with provisional nonfunctional restorations is an optimal approach for immediate loading procedures. This we first demonstrated in a proof-of-concept case study and in other studies later, including the ones covered in this thesis [38].

2. Based on the literature (with short follow-up times), we hypothesized that immediate provisionalization of single-tooth implants in fresh extraction sites in the maxillary esthetic zone could offer long-term implant survival free of complications or other adverse events. This we aimed to prove with prospective studies with long-term follow-up [39, 40].

3. As esthetic outcomes are of utmost importance in the frontal region, two studies were entirely devoted to testing the hypothesis that immediate provisionalization is favorable not only in the functional, but also in the esthetic sense [41, 42].

4. Finally, we directly addressed the question of immediate implant placement combined with augmentation procedures. While this question is addressed partially in our other studies, we found that it was of high practical importance, thus we designed a study to examine it. We hypothesized that immediate replacement of a single maxillary tooth by implants combined with guided bone regeneration would be a predictable treatment modality with favorable peri-implant bony response [43].

III. DEMONSTRATION OF THE ACCOMPLISHED WORK

III.1. Plastic Temporary Abutments with Provisional Restorations in Immediate Loading Procedures

III.1.1. Background

After the placement of implants in areas in which 1 or several teeth have been lost, both the clinician and patient face many difficulties, particularly during healing. If a removable prosthesis is provided, the patient's quality of life suffers, and, for optimum mastication and speech, adjustments of the denture may become necessary during healing. In addition, the possibility of osseointegration failure increases because of transmucosal loads. Several advantages have been attributed to implant-supported fixed provisional restorations after second-stage surgery: (1) improved tissue contours related to emergence profile, (2) development of an interdental or interimplant papillae,(3) potential avoidance of a third surgical operation, (4) fixation of the prosthesis, and (5)customization during the healing process to form an esthetically contoured prosthesis [44-46]. Techniques for incremental loading can be used either directly or indirectly after second-stage surgery [47, 48]. Others have described similar techniques involving tissue contour development and esthetic concerns [49-52]. The classic implant-prosthetic protocol was to replace round gingival formers after implants were uncovered. Once the soft tissues around the implant healed, this round, non-anatomic soft-tissue contour was transferred to the master model by standard impression components. It was only at this point, at the final prosthetic stage, that the clinician faced the challenge of not only creating esthetic restorations but also having to rebuild the natural gingival contour to create an emergence profile. This process would often require extensive, time-consuming steps, which could just as well have been accomplished at the beginning. Placement of a provisional restoration during implant surgery may create soft tissue contours that resemble normal gingival topography before placement of the definitive prosthesis [53]. Previous studies confirm that provisionalization of a fixed temporary plastic crown can be used routinely immediately after implant placement to allow for a guided healing that eliminates the need for an additional soft tissue surgery [54-57]. If the provisional restoration is placed after the implant becomes osseointegrated, an additional 3–6-month healing period is needed for complete soft tissue healing [44, 52, 58, 59].

III.1.2. Methods

Our protocol includes the placement of single implants simultaneously with the connection of fixed provisional restorations to prefabricated plastic provisional abutments. In this case, any occlusal contacts were avoided, permitting immediate but reduced functional loading of the implants. The use

of plastic provisional abutments allows a quick intraoral preparation, without any danger of heat transmission to the fixture and surrounding bone. Figure 1 shows the application of the plastic abutments.

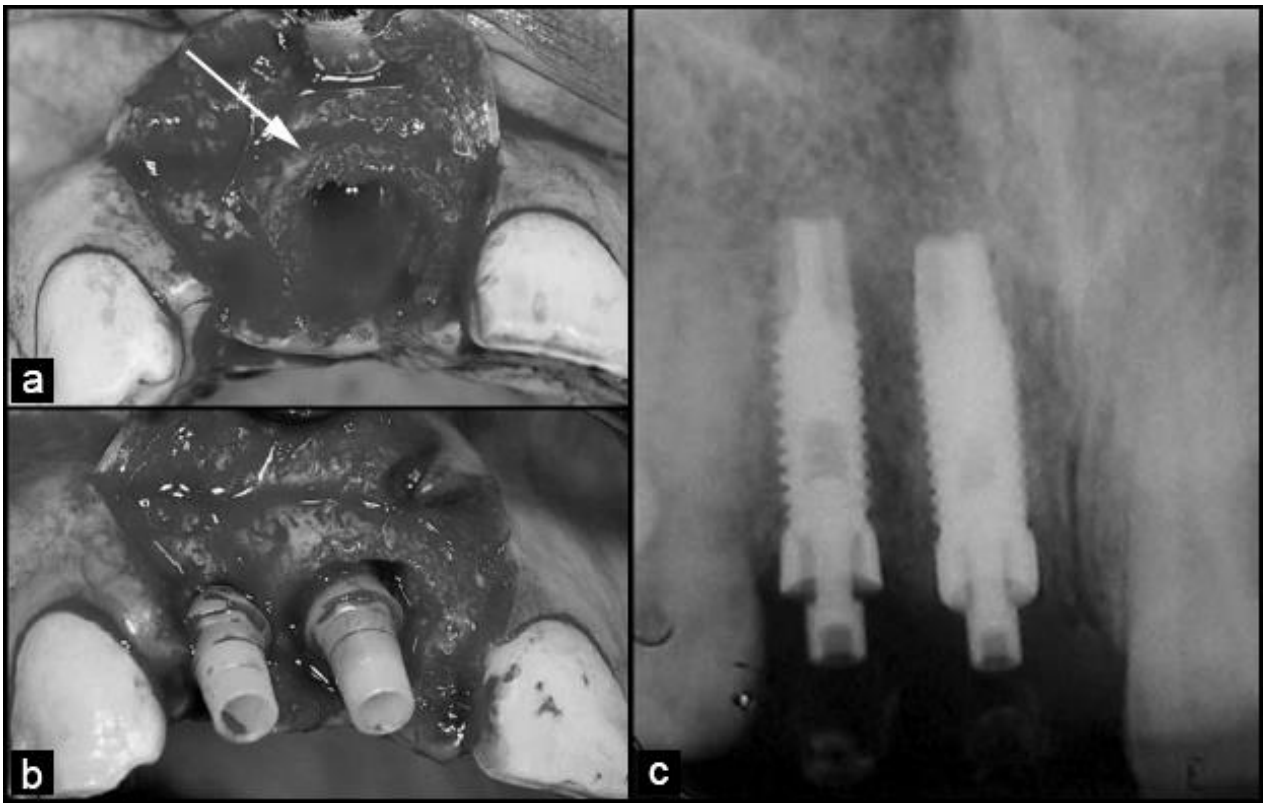

Figure 1. a) Atraumatic extraction of tooth No. 11. Note the preservation of the thin labial plate of the socket (arrow); b) Connection of 2 prefabricated temporary plastic abutments; c) Periapical radiograph taken immediately after implant placement and connection of 2 temporary abutments for immediate loading.

III.1.3. Results

The protocol that we proposed eliminated the period necessary for soft tissue healing and contouring because healing occurred concurrently with implant osseointegration. The resulting fixed provisional restorations are very effective in maintaining good esthetics and oral function for the patient.

III.1.4. Conclusions

The simultaneous placement of implants with the connection of fixed provisional restorations to prefabricated plastic provisional abutments is a viable and effective clinical approach. Occlusal contacts were avoided, permitting a reduced functional loading of the implants. The use of plastic provisional abutments allows for a quick and easy intraoral preparation of the abutments, without any danger of heat transmission to the fixture and surrounding bone. The resulting fixed provisional restoration is very effective in maintaining good esthetics and oral function for the patient. The

protocol followed in this case eliminated the period necessary for soft tissue healing and contouring because healing occurred concurrently with implant osseointegration. This treatment modality is especially useful in cases in which dental implants are to be immediately loaded in single, partial, or completely edentulous patients, with a good clinical outcome and no prosthetic complications.

III.2. Immediate provisionalization of Single-Tooth Implants in Fresh-Extraction Sites at the Maxillary Esthetic Zone: Up to 6 Years of Follow-Up

III.2.1. Background

The high levels of predictability in implant therapy have encouraged reevaluation of several aspects of the traditional Brånemark implant protocol [2, 60, 61]. Since its inception, this protocol has been progressively challenged to decrease treatment time, minimize the number of surgical procedures, and maximize esthetic outcomes. Several authors demonstrated successful immediate loading of dental implants in edentulous mandibles using fixed superstructures [26, 28, 55, 62], thereby preventing any movement or nonaxial loading by rigidly splinted implants. There is also data to show that immediate loading of the edentulous maxilla is also feasible if bone quality is suitable [63, 64]. The purpose of this study was to evaluate the long-term survival of single-tooth implants immediately placed in fresh extraction sites at the anterior maxilla and immediately loaded with infraocclusion-provisional restorations.

III.2.2. Methods

Sixteen patients (7 females and 9 males) ranging in age from 23 to 62 years (mean age 42 years) were treated for single-tooth replacement. Consecutive patients requiring extraction of a single tooth in the maxillary esthetic zone were proposed for the present study. After a thorough explanation of the treatment alternatives and risks, those accepting replacement by immediate loading and provisional crown placement were included. Informed consent was obtained from all patients. The oral examination focused on stable bilateral occlusion, soft tissue condition, buccolingual and mesiodistal width of soft and hard tissues, and intermaxillary relationship. Periapical radiographs, panoramic radiographs, and computerized tomograms were also obtained as necessary. Exclusion criteria from the study were uncontrolled diabetes; parafunctional habits (bruxism or clenching); infected adjacent teeth; and the need for tissue augmentation procedures during surgery. Indications for tooth extraction and immediate implant placement included root fracture, periodontal attachment loss, endodontic failures, nonrestorable crowns, and postdentoalveolar trauma.

All patients were given amoxicillin (1000 mg, 1 hour before the surgery). Gentle elevation of the tooth root was performed to preserve the alveolar housing around the extraction site. Flaps were avoided. Atraumatic extraction was done using a periotome to release the periodontal ligament. Once the tooth was removed the socket was carefully debrided and irrigated with sterile saline. Tapered titanium implants were placed (XIVE and Frialit-2, Dentsply/Friadent, Mannheim, Germany and Seven MIS, Shlomi, Israel). Implants with diameters of 3.3 to 5.5 and lengths of 13 to16 mm were selected based on the size of the tooth socket and mesiodistal diameter of the tooth to be replaced. The platform of the implant was set 1.5 to 2 mm below the level of the interseptal bone. Implant placement respected the minimal 1.5 to 2 mm space between the adjacent tooth and the implant. Implants were positioned palatally and autogenous bone graft obtained from the drill was used to fill space discrepancies in the cervical area when gaps were 2 mm or greater. Implant stability was monitored by using a manual torque wrench and recorded the insertion torque in Ncm. If insertion torque values were 32 Ncm or greater, the implants were included in the study. After placement, each implant was connected to a prefabricated plastic provisional abutment. The fixed provisional restorations were cemented to the abutments. Cementremoval was carefully performed using scalers and floss. Occlusal contacts were avoided using polyester film and articulating paper permitting immediate, nonfunctional loading of the implants. Patients were asked to limit their diet to soft food for one month and were routinely examined once a week for 3 weeks and then once a month for 6 months. Implant placement and immediate provisionalization were performed by a single clinician (the author). Assessment of the peri-implant tissue responses at the immediate provisionalized implants was done by a single examiner. The examiner measured the digital periapical radiographs acquired using a positioning device. The radiographs were used to evaluate the implant-bone interface and the level of marginal bone in relation to the top of the implant (marginal bone loss). Also, complications associated with abutments stability were recorded. An overview of the process is shown in Figure 2.

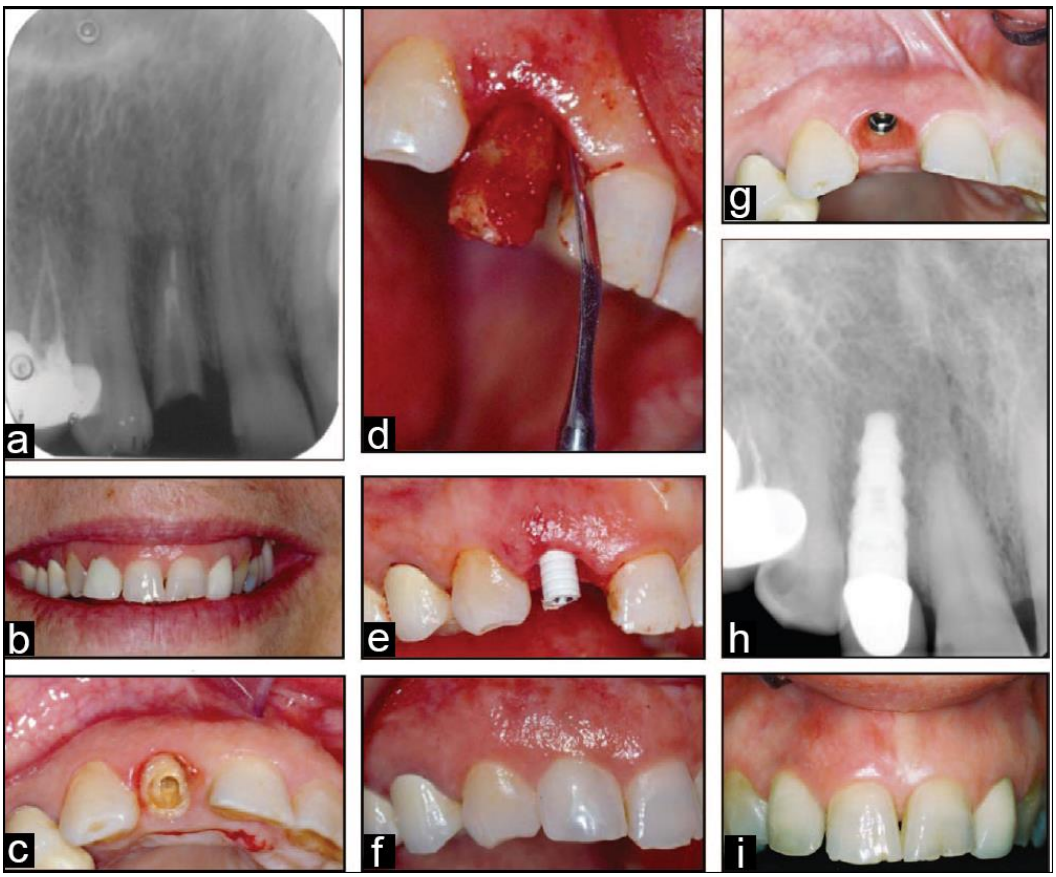

Figure 2. a-c: the preoperative status; d-f: extraction and provisionalization with plastic temporary abutment; g: condition of the soft tissues 6 months after implant placement; h-i: status at the 45-month recall.

III.2.3. Results

Table 1 presents an overview of the clinical data of patients and implants included in this study. A total of 24 implants were placed in 16 patients, 7 women, and 9 men, with an average age of 42 years (range: 23 to 62 years). The main reason for tooth extraction was non-restorable crowns followed by root fractures. All implants were placed in fresh extraction sites. Most of them were inserted in the maxillary lateral socket (12 implants). The mean implant length was 14.45 mm, the median length was 15 mm (range: 13 to 16 mm). The mean diameter was 4 mm (range: 3.3 to 5.5 mm). All implants were inserted with a final torque of 32 Ncm and were immediately reconstructed with provisional acrylic crowns. The follow-up started on the day of implantation and ranged from 24 to 72 months with a mean follow-up time of 40.7 months. One implant failed 1 month after placement due to unscrewing of the provisional abutment and overload. Successful reimplantation was made 2 months later. The overall implant survival rate was 95.8%. The preoperative and postoperative radiographs compared with the follow-up radiographs showed a maximum bone loss of 2 mm. The mean marginal

bone loss around the remaining implants increased by a mean of 0.9 ± 1.1 mm from placement to the final examination. No differences were found concerning abutment type or site.

Table 1. A descriptive summary of the results. Age is given in years, diameter and length are given in millimeters, follow-up time is given in months. Gender: 1- male, 2- female. Implant type: 1- Seven MIS Shlomi (MIS Implants, Israel); 2- Frialit 2 (Friadent, Germany); 3- XIVE (Friadent, Germany)

Patient	Gender	Age (yr)	Site	Implant	Diameter (mm)	Length (mm)	Failure	Follow-up (mts)
1	2	62	12	1	4.5	15		57
2	1	35	25	2	5.5	13	x	36
3	1	55	12	2	3.4	15		36
4	1	61	22	2	3.8	15		72
			11	2	5.5	15		64
5	2	47	12	2	3.8	15		65
6	2	50	12	1	3.75	16		35
			22	1	3.75	16		
7	2	23	11	2	4.2	16		50
			12	2	3.3	16		
8	1	57	21	1	4.7	13		46
			11	1	4.7	13		
9	2	52	24	3	3.8	13		30
10	1	25	12	1	3.75	13		30
			22	1	3.75	13		
11	2	25	25	3	3.8	13		27
			24	3	3.4	15		
12	1	32	12	3	3.8	15		35
			22	3	3.8	15		
13	2	50	13	2	3.3	13		49
14	1	26	22	2	3.75	16		48
15	1	26	13	3	3.8	15		24
			23	3	4.5	15		
16	1	28	21	3	4.5	15		26

III.2.4. Conclusions

Within the limits of this study, the data indicate that nonfunctional immediate loading of single-tooth implants in fresh extraction sites in the anterior maxilla can result in successful implant integration and stable peri-implant conditions up to 6 years.

III.3. Clinical Outcomes of Implants Placed in Extraction Sockets and Immediately Restored: A 7-Year Single-Cohort Prospective Study

III.3.1. Background

The placement of implants immediately after tooth extraction has proven to be a predictable treatment strategy with a very high success rate [65-67]. A recent systematic review on immediateimplants[68] reported that the timing of restoration was not associated with implant outcomes in terms of survival rate; moreover, this systematic review confirmed that the use of a flapless approach should be performed whenever possible to reduce the risk of soft tissue complications. The potential advantages of immediate restoration of single implants placed in fresh extraction sockets have been widely reported [69], even though there are still risks of implant failure/complications higher than those observed for implants placed in healed ridges [70, 71]. Several clinical studies have demonstrated that alveolar ridge volume loss after tooth extraction is an irreversible process that involves both arches with horizontal and vertical dimensional changes [72, 73]. In addition, implant placement into a fresh alveolar socket does not seem to alter the resorption changes that naturally occur after tooth extraction. While there is a consensus that careful tooth extraction is paramount, the use of bone graft, as well as the flapless approach for the ridge preservation procedures, have been reported to yield outcomes. In addition, the clinical agreement on the use of a flapless approach was based on the consideration that the buccal bone thickness of the anterior maxilla was 0.5 mm in the majority of the clinical cases. Therefore if a flap is raised the periosteal blood supply would be interrupted and thus compromised. With a thin buccal cortical bone, the remodeling process becomes critical and at high risk of aesthetic complications [74-78]. Several treatment approaches have been suggested to reduce the risk of aesthetic complications with the use of autogenous connective graft, low-resorption xenografts, and flapless approach. Del Fabbro and colleagues[78] supported the hypothesis that the graft materials were unable to completely prevent resorption of the buccal bone plate. Moreover, these authors highlighted that several factors seemed to be involved in the aesthetic success after tooth extraction and immediate implant placement, among which: appropriate implant positioning and maintenance of buccal bone architecture [78]. The present 7-year, prospective, single cohort study aimed to evaluate the success rate, marginal bone level (MBL), and soft tissue stability of implants placed in fresh extraction sockets and immediately restored. The study followed the STROBE guidelines for observational studies [79].

III.3.2. Methods

The study was a single-cohort prospective clinical study, and the patients were treated between 2005 and 2006. A total of 32 patients (19 women, 13 men, mean age: 40.1±13.3 years, range: 23 to 63 years) participated. The patients had at least one tooth in need of extraction to be replaced with immediate implant therapy. The inclusion criteria were: age >18 years; teeth adjacent to the experimental site were required to have complete occlusal surfaces and be free from infection; adequate bone volume for placement of implants of at least 13 mm in length and 3.75 in diameter; ability to follow the protocol and willingness to participate. The exclusion criteria were: general conditions with the potential to interfere with osseointegration; long-term steroidal and/ or amino-bisphosphonate therapy; severe intermaxillary discrepancy; severe parafunctional habits; poor oral hygiene; extraction sites with a partial or complete deficiency of buccal bone plate; smoking >10 cigarettes/day.

All patients received a detailed description of the procedures and signed informed consent before participation in the study. Potential participants underwent careful clinical evaluation before being enrolled in the study. Before the surgery, all patients received at least one session of professional oral hygienic treatment to reduce the risk of failure due to infection. Immediately before the surgery, the patients rinsed for 1 minute with 0.2% chlorhexidine (they were also instructed to do so twice a day for 3 weeks after the surgery). Treatment was done under local anesthesia (lidocaine with adrenaline 1:80.000). A flapless approach was chosen, and tooth extractions were carried without elevators to minimize the trauma; great care was taken to maintain the integrity of the buccal bone wall. An ultrasonic bone surgery approach was taken to allow easier tooth extraction. After extraction, the socket was carefully curetted and the implant osteotomy site was prepared according to the standard procedure (with standard drills following the palatal bony wall as a guide, making maximum use of the bone apical to the removed tooth). A periodontal probe was used to verify the integrity of the bone walls after implant osteotomy preparation. The extraction sockets were considered adequate for immediate placement if they fit the criteria of Juodzbalys and colleagues in 2008 [80]. The implants (Premium/Khono, Sweden&Martina, Padova, Italy) were placed with the implant platform at the marginal level of the buccal bone wall. All the implants were evaluated for primary stability with the Osstell device (Integration Diagnostic, Gothenburg, Sweden), as recommended by the manufacturer. Only implants with ISQ >62 were included in the study. For cases below that limit, delayed restoration was scheduled. The implants included in the study were temporarily restored within 24 hours from implant placement. The peri-implant bone defects between the implant surface and bone walls were grafted with corticocancellous porcine bone particles (MP3, Osteobiol- Tecnoss, Torino,

Italy). Subsequently, a resorbable membrane (Evolution, Osteobiol-Tecnoss, Torino, Italy) was used to stabilize the graft. The collagen membrane was exposed to the oral cavity, therefore, a secondary soft tissue healing was obtained. Patients were prescribed antibiotics (amoxicillin and clavulanic acid, 1000 mg twice a day, starting 1 day before surgery to be continued 4 days afterwards) and they were instructed to take ibuprofen (600 mg, 3 times a day, as long as required) to reduce inflammation. Sutures, when used, were removed after 10 days and oral hygiene instructions were given. The prosthetic protocol is described in detail in the article (see Appendix).

All measurements were acquired immediately after implant placement (baseline or time T0), and then at 1, 2, 3, 4, 5, 6, and 7 years. An examiner not involved in performing the surgical treatment performed all the measurements. The measured variables were as follows (all relevant procedures and calculations are described in detail in the Appendix): a) the diameter and length of the placed implants, b) marginal bone level (MBL), c) the width of keratinized gingiva (WKG), d) facial soft tissue levels (FSTL), e) prosthetic complications, f) implant failure (defined as mobility or infection requiring removal).

The aesthetic outcome was assessed only at the 5-and 7-year follow-up visits and was based on the modified papilla index and the pink aesthetic score. The papilla index (PI) was recorded at the dental implant site based on the papilla index proposed by Jemt[2]. The pink aesthetic score, devised by Belser in 2009 [81], was also utilized.[3]

III.3.3. Results

The most frequent reason for tooth extraction was root fracture (43%) followed by decay (28%), endo-failure (16%), and root reabsorption (13%). Thirty-seven implants were placed, of which 20 were inserted in incisor sites, 2 in canine sites, 15 in premolar sites. Region-wise, implants were placed most frequently in the maxillary incisor region (34.3%), followed by the maxillary premolar region (31.4%). The fewest implants were placed in the mandibular canine region (2.8%). The cumulative implant survival rate at the 7-year follow-up was 94.6%. No complications occurred during the healing period, no immediate post-operative infections were observed. Two patients showed acute infection and implant failure after final prosthetic delivery within the first year of treatment, which left us with 30 patients (35 implants) to follow-up during the entire study period.

[2] 0= no papilla; 1=less than one-half papilla is present; 2=greater than half ofthe papilla height is present but not to the full extent of the contact point; 3=papilla fills theentire proximal space and it is in good harmony; and 4=papilla is hyperplastic.

[3] It comprises five factors: the mesial papilla, the distal papilla, the curvature of the facial mucosa, the level of the facial mucosa, and root convexity/soft tissue color and texture on the facial aspect of the implant site.

The mean MBL recorded at baseline was -0.60±0.49mm. The changes of MBL were statistically significant ($p < 0.05$) for each year of the follow-up period. The highest difference was measured between the baseline and year 7 (1.60±0.50 mm). The mean WKG was 3.88±0.47 mm at baseline; the changes of WKG were statistically significant for each year of the follow-up period. WKG showed a reduction of 0.74±0.65 mm after 7 years. The mean FSTL was 0.40±0.69 mm at baseline; the changes of FSTL were statistically significant ($p < 0.005$) for each year of the follow-up period. By the last year of the follow-up, FSTL decreased by 0.37±1.00 mm, which is interpreted as an improvement in the discrepancy between the midfacial gingival level of the implant and that of the adjacent teeth. Figure 3 shows an example of the change of the soft tissue throughout the study.

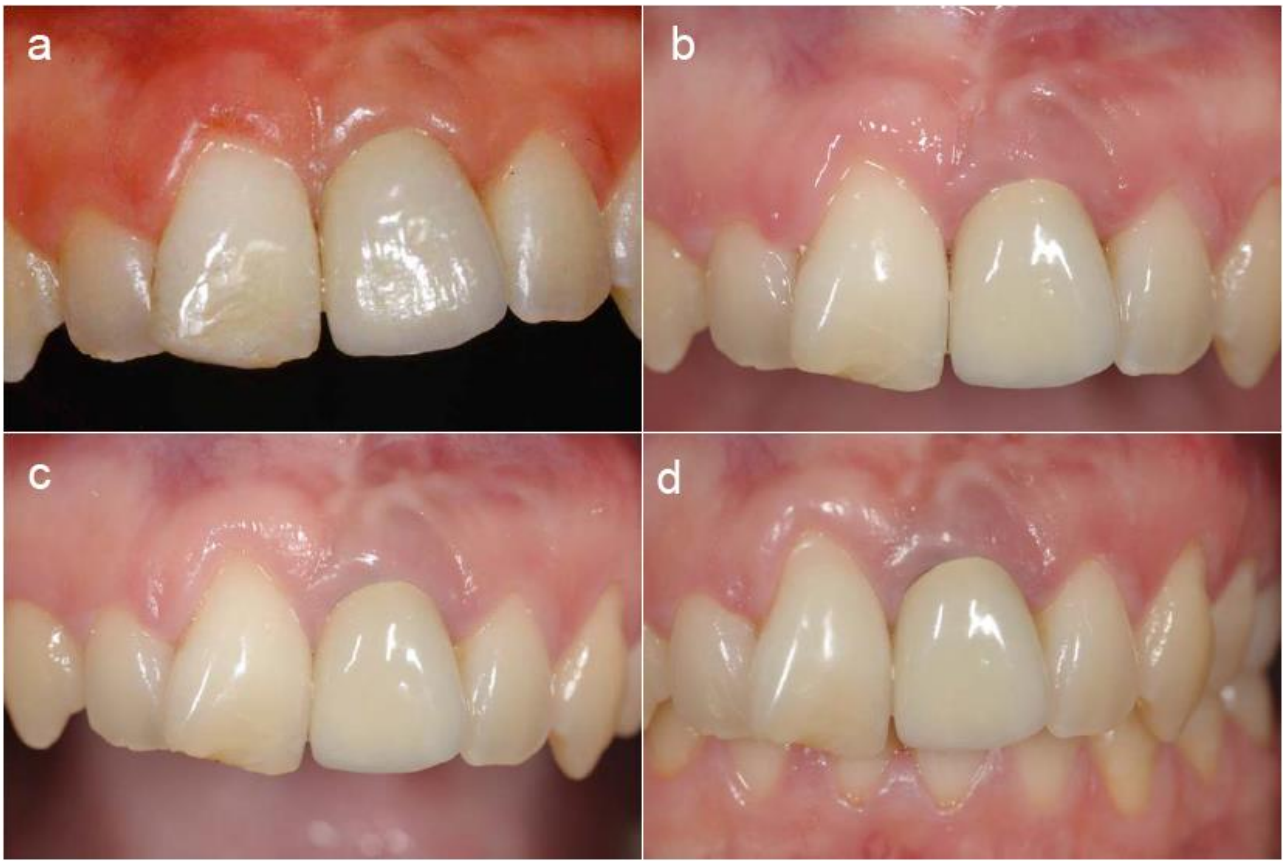

Figure 3. The final restoration and soft tissue conditions at a) baseline; b) 3 years; c) 5 years; d) 7 years.

The oral hygiene indices remained low throughout the study period (Table 4 in the original article, see Appendix). The results regarding the soft tissue parameters are summarized in Table 2.

Table 2. Soft tissue results. PES- pink esthetic score; PI- papilla index.

		Year 5	Year 7
PES	Mean	8.14±0.49	7.71±0.92
	95% CI	7.97–8.31	7.39–8.03
	Median	8	8
	Difference	-	-0.42±0.77
PI	Mean	2.71±0.45	2.71±0.45
	95%CI	2.55–2.81	2.55–2.81
	Median	3	3
	Difference	-	0.00±0.00

III.3.4. Conclusions

The data from the present study show that implants placed immediately after tooth extraction and immediately restored had predictable clinical and aesthetic outcomes. When interpreting these results, a few factors must be taken into consideration, though. First, the patients were treated according to strict, standardized treatment criteria. These included a flapless procedure, only with an intact buccal bone wall, the absence of soft tissue defects, the use of corticocancellous porcine bone to counteract postextraction tissue changes, and immediate restoration. Furthermore, all patients underwent a strict and tailored periodontal maintenance program. The data, thus, characterize a situation where the greatest possible care is taken from patient selection to maintenance.

III.4 Esthetic assessment of immediately restored implants combined with GBR and free connective tissue graft

III.4.1. Background

Advances in biomaterials technology and clinical methods over the past three decades have provided clinicians with efficient tools to improve treatment procedures. Accordingly, “osseointegration” has been redefined, influenced by contemporary patients’ increasing expectations for reduced treatment time and improved comfort and esthetic outcomes. The reduction of healing time by immediate implant placement into fresh extraction sockets has been previously described [82-87]. Provided that suitable implant primary stability is achieved, survival rates are like those recorded using the conservative delayed techniques (see citations above). Promising results in this field of research have led to further trials aiming to further shorten the healing period of maxillary multiunit implant reconstruction [88-91], and for single-tooth implants, ultimately resulting in immediate implant-retained provisional restoration [32, 33, 92, 93]. However, there was a concern that recession of the marginal peri-implant mucosa may occur,which, in turn, may compromise the final esthetic outcome

[94-96]. Several factors were claimed to influence the frequency and extent of marginal mucosal recession, including peri-implant soft tissue biotype [97], the connection of the provisional crown immediately after implant insertion [54, 98], the condition and thickness of the facial bone [99], the orofacial position of the implant shoulder [100, 101], and grafting of the facial peri-implant marginal defects with autogenous bone or bone substitutes [102, 103]. In addition, an experimental study [104] showed that following tooth extraction the facial socket wall, which is composed almost entirely of bundle bone, may be susceptible to resorption in the vertical and horizontal planes. This crestal bone resorption may lead to recession of the facial marginal mucosa. It was suggested that disruption of the vascular supply to the facial bone by the elevation of surgical flaps might be an important contributory factor. It has also been claimed that to maintain the stability of the buccal soft tissue, the buccal plate of bone should be at least 2 mm thick [105]. As in most cases suffering from bone loss and/or ridge deformations, there is a lack of soft tissue in addition to lack of bone, it is advisable to improve the soft tissue cover as early as possible, preferably at the time of hard tissue augmentation. Thin tissue biotype is considered a major risk factor for advanced midbuccal recession [106]. It has been proposed that increasing the thickness of the facial mucosa by the addition of a connective tissue (CT) graft beneath the facial flap at the time of implant placement may reduce this risk for recession [107, 108]. Postextraction healing and healing from implant insertion coincide, as there is only one surgical phase. The standard protocol with 2 to 3 consecutive surgeries in the same site may result in more tissue damage, scarring, and soft tissue loss. In addition, as the original gingiva may be preserved by the instant connection of a provisional restoration offering mechanical support to the papilla and midfacial gingival tissue, the need for additional soft tissue surgery may be eliminated [54, 98]. The aim of the present retrospective study was the esthetic assessment of immediately restored implants combined with GBR and free CT graft.

III.4.2. Methods

34 patients treated by the same periodontist during the years 2009 - 2013 with an immediate single implant in the esthetic zone of the anterior maxilla (central and lateral incisors, and canines) were included in the study. In all cases, immediate, non-functional loading was applied. The study was approved by the human ethics committee of Tel Aviv University, and patients signed an approved informed consent form.

The inclusion criteria were: age≥ 18 years; extraction of a single tooth in the anterior esthetic zone of the maxilla; both neighboring teeth mesial and distal to the extraction present; at least 5 mm of bone apically or palatally to the alveolus of the failing tooth (to ensure primary implant stability);

primary implant stability≥ 32 Ncm; compromised buccal plate width after extraction (thinner than 1 mm, dehiscenced or fenestrated, or combination of these) due to previous periodontal disease, periapical pathologies or traumatic extraction; the necessity of bone augmentation to address the latter. The exclusion criteria were the same as under III.3.2.

In all cases, a thorough presurgical evaluation was performed including clinical images, periodontal chart, smoking habits, periodontal diagnosis, and full-mouth periapical radiographs. The morphology of the alveolar process at the implant site, the location of the incisive foramen and the root to be extracted as well as the presence of periapical pathologies were evaluated preoperatively using CT. Special attention was given to the trabecular pattern between the buccal and palatal plates and the existence of bony contour undercuts, and indications for extraction. Light smokers (< 10 cigarettes/day) were committed to a smoking cessation protocol, which started 1 week before and lasted at least 1 month after implant placement. The initial periodontal therapy included oral hygiene instructions and training and was aimed at reaching a Hygiene Index (HI) of <10% [109]. Scaling and root planing were also carried out when indicated.

The pre-and postoperative prophylaxis followed the generally accepted recommendations (see Appendix for details). After the surgical site was anesthetized, mucoperiosteal flaps were elevated including intracrevicular incisions extending to the mid-facial aspect of at least both neighboring teeth, thereby fully reflecting papillae. This was followed by atraumatic tooth extraction using periotomes (Hu-Friedy, Chicago, IL, USA) to maintain the integrity of the socket bony walls. Granulation tissue was removed using a spoon curette and a 3-mm diamond bur (Strauss Company, Raanana, Israel). The drilling was conducted to the palatal wall, and care was taken to avoid any contact between the implant and the compromised buccal plate. The final drilling was performed using a drill at least 1 mm less in diameter than the implant diameter. The implants were driven in with a torque of ≥ 32Ncm with a torque-controlled ratchet (MIS Implants Technologies, Bar Lev, Israel). Screw-type bone level titanium implants with a platform switch design (Seven MIS Implants Technologies, Bar Lev, Israel) were used. Proper implant positioning was considered of pivotal importance with the neighboring teeth serving as a reference for optimal implant positioning. A minimum distance of 1 mm (measured with a periodontal probe) in the M-D dimension between the implant shoulder and the neighboring tooth was achieved in all the cases. In the apico-coronal direction, the neck of the implant was 2 to 3 mm apically to the cemento-enamel junction or the crown-cervical margin of the neighboring teeth. In the orofacial dimension, an effort was made to place the buccal neck of the implant at least 2 mm palatal to the buccal contour of neighboring teeth.

After the adaptation of an appropriate abutment (0 to 25°, with 1 to 3 mm gingival neck height, at 15 Ncm), allograft material of 0.25 to 1 mm particle size (Raptos FDBA, Citagenics, Toronto, Canada) was applied in the residual gap and in excess above the buccal wall. A resorbable collagen membrane (Bio-Gide; Geistlisch Pharma AG, Wolhusen, Switzerland) was applied in an apron-like manner above the bone graft. At this stage, a free CT graft was harvested from the palate [107, 108] and placed over the collagen membrane (Fig. 4).

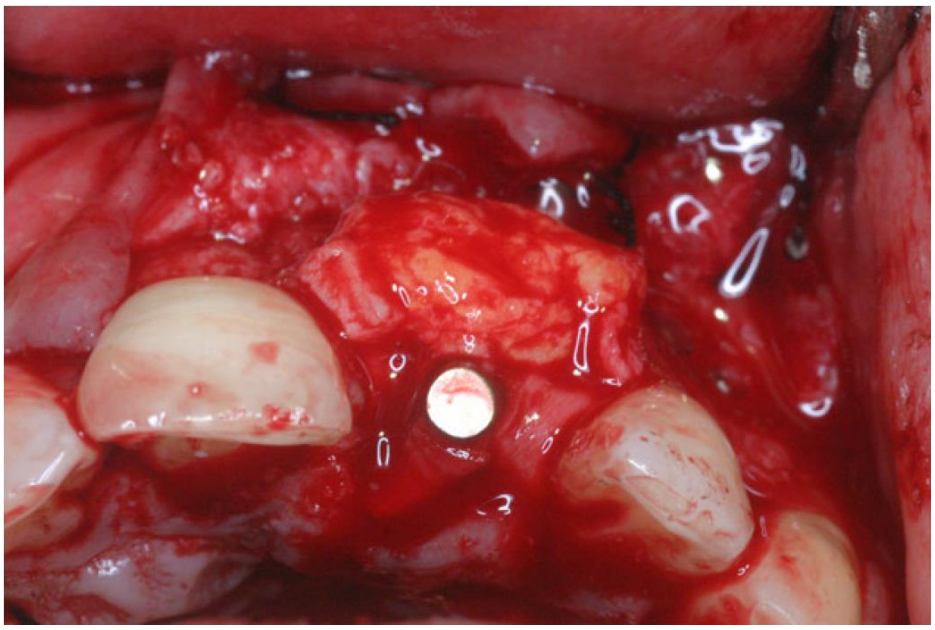

Figure 4. Free connective tissue graft placed over Type 1 collagen membrane and allograft.

The buccal flap was coronally positioned after periosteal releasing incision and sutured to the palatal flap using Vicryl 4/0 sutures (Vicryl Rapid-Ethicon Johnson, Diegem, Belgium). The connection of the abutment was followed by the adaptation of a prefabricated nonfunctional acrylic temporary crown (no occlusal contacts). Six months after implant placement, after removal of the temporary crown and abutments, color-coded transfers (MIS Implants Technologies, Bar Lev, Israel) were adapted and radiographic verification of transfer adaptation was done. Impressions were taken using putty-wash one-step technique (Express, 3M. ESPE dental products, St. Paul, MN, USA) using the closed tray technique with metal stock trays. A master model with a silicon image of the marginal gingiva was prepared, and interarch relations were recorded. At the following appointment, the zirconia base was tried. The permanent zirconia crown was cemented after occlusal adjustment and glazing with temporary cement (Temp-Bond Kerr corporation, 1717 West Collins Avenue, Orange, CA, USA). The abutments were tightened to 35 Ncm using a prosthetic ratchet (Anthogyr, torque-

controlled ratchet-Botzer ergonomics). The implants were considered successful if they fulfilled the criteria of Alberktsson and colleagues [110].

The entire follow- up lasted for a mean of 29 months (12-48 months). A wide variety of parameters were recorded during the follow-up (see Appendix), but the main goal of the study was to assess esthetics, so we focus only on the clinical esthetic outcomes here, assessed at 12 months after the adaptation of the final crown.

At 12 months after the adaptation of the final crown, a clinical examination was performed and frontal photographs were taken (Canon EOS 650 D, Tokyo, Japan with a 100-mm Canon macro lens and a ring flash). The photograph was centered slightly superior to the occlusal plane, centered at the contact region of the centrals at the midline to facilitate the subsequent analysis, which is primarily based on symmetry. Care was taken that the contralateral tooth was also completely and symmetrically represented. To comprehensively assess the esthetic outcome and performance, the approach described by Belser and colleagues [81] was adopted. To objectively examine the esthetic outcome of the ICs at the 12-month examination, the respective casts and intraoral pictures were critically analyzed by three examiners not involved in the surgical procedure, according to two specific indices, the pink esthetic score (PES) and the white esthetic score (WES). PES comprises the following parameters: mesial papilla, distal papilla, the curvature of the facial mucosa, the level of the facial mucosa, and root convexity/soft tissue color and texture at the facial aspect of the implant site. WES comprises five parameters: tooth form, tooth volume, tooth color, tooth texture, and translucency. A score of 0, 1, or 2 is assigned to each parameter, that is the maximum score on both measures is 10. The parameters were assessed by direct comparison with the natural, contralateral reference tooth, estimating the degree of match or eventual mismatch. In the case of an optimum duplication of the esthetically relevant features inherent to the control tooth, a maximum score of 10 is applied for each index. Hence, the highest possible combined PES/WES score was 20, which represents an optimal match of the peri-implant soft tissue conditions and the clinical single-tooth IC compared to the respective features present at the contralateral natural tooth site. Such a situation is shown in Figure 5. To facilitate the objective appreciation of some of the parameters, the examiners used the study casts. The threshold of clinical acceptability was at a value of 6/10 for each index. The details of the statistical analysis are given in the original publication in the Appendix.

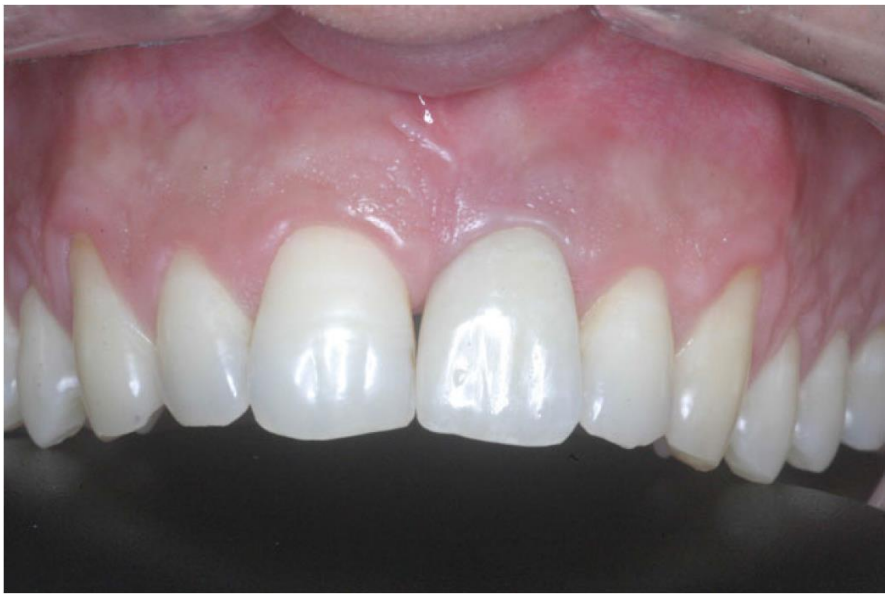

Figure 5. Final zirconia crown at the 1- year recall (PES–WES score 20)

III.4.3. Results

The data of thirty-four patients (14 males and 20 females, mean age: 52.68±14.35 years, range: 24 to 82 years) were included in the study. The majority (N=26, 76.5%) were nonsmokers, the rest smoked <10 cigarettes a day. Regarding prior pathologies, twenty-seven (79.4%) of the patients had suffered from chronic advanced adult periodontitis or aggressive periodontitis, and 7 (20.6%) had been diagnosed with gingivitis and/or mild adult chronic periodontitis. Eighteen teeth (53%) were extracted due to periodontal disease, 9 (26.5%) due to root fracture, 4 (11.7%) due to severe carious lesions, and 3 (8.8%) due to external root resorption.

Intraoperative examination of the buccal bony plate after extraction and debridement revealed dehiscence in 21 cases (62%, of which in 6 cases the residual buccal plate was both thin and dehiscenced), fenestration in two cases (6%), and in 11 cases (32%), the buccal plate was thinner than 1 mm. The diameter of the inserted implants varied between 3.3 and 5 mm, and their length varied between 13 and 16 mm (see Appendix for more details).

The clinical esthetic parameters are summarized in Table 3. The cumulative total PES/WES of the 34 cases shows that in 91.2% of the cases, good or acceptable esthetics (≥12) was achieved. Overall, the esthetic outcomes were favorable. As for mean PES, mesial papilla height scored the lowest (1.09), and the root convexity/soft tissue color and texture scored the highest (1.71).

Table 3. A summary of the clinical esthetic parameters.[4] 0,1 and 2 are the achievable scores and the values (given as N(%)) indicate what proportion of the examined teeth got that particular score in any given parameter.

Parameter	0	1	2	Average
Mesial papilla	5 (14.7)	21 (61.7)	8 (23.5)	1.09
Distal papilla	1 (2.9)	13 (38.2)	19 (55.8)	1.56
Curvature of facial mucosa	1 (2.9)	15 (65.2)	19 (55.8)	1.50
Level of facial mucosa	8 (23.5)	9 (26.5)	17 (50)	1.26
Root convexity/soft tissue color/texture	0 (0.0)	10 (29.4)	25 (73.5)	1.71
PES (mean ±SD)		**7.12 ± 1.89**		
Tooth form	0 (0.0)	13 (38.2)	21 (61.7)	1.62
Tooth volume/outline	1 (2.9)	17 (50)	16 (47)	1.44
Tooth color (hue value)	1 (2.9)	17 (50)	16 (47)	1.44
Surface texture	1 (2.9)	13 (38.2)	20 (58.8)	1.56
Translucency	1 (2.9)	23 (67.6)	10 (29.4)	1.26
WES (mean ±SD)		**7.32 ± 1.25**		
Total PES-WES		**14.44 ± 2.34**		

Altogether seventeen implants (50%) presented an optimal level of facial mucosa recession. A recession of < 1 mm was observed in nine implants (26.5%), and eight implants (23.5%) presented a recession of 1 mm or more. Of the WES parameters, tooth form (1.62) and surface texture (1.56) scored the highest, and translucency scored the lowest (1.26). Using the Mann-Whitney U-test, a marginally significant association (P=0.048) was found between the severity of the periodontal disease (advanced chronic and aggressive periodontitis group) and low scores of the PES total. Using the same test, no correlation was found between periodontal status and either total WES (P = 0.559) or total PES/WES (P = 0.066), neither between the cause for extraction or smoking status and esthetic outcomes. Using the Spearman test, no correlation was found between age and esthetic outcome (P < 0.2).

III.4.4. Conclusions

In the present study, a hard and soft tissue augmentation concomitantly with immediate implant placement was employed to obtain stable hard and soft tissue. The results imply that the combined GBR and CT graft procedure may only partially compensate for buccal bone deficiencies and that a staged approach might be more favorable in cases with compromised buccal bone.

[4] Please note that Table 2 of the original publication (to be found in the Appendix) provides a case-by-case overview of all variables of the study; the table has been omitted from the present thesis for reasons of space.

III. 5. Esthetic Assessment of Implants Placed into Fresh Extraction Sockets for Single-Tooth Replacements Using a Flapless Approach

III.5.1. Background

This study aimed to objectively analyze the esthetic outcomes of single-tooth immediate implants placed and restored without flap elevation in the anterior maxilla. The working hypothesis was that flapless extraction, which preserves the integrity of the residual bone walls after extraction and allows immediate implant placement, is a predictable treatment modality in terms of both osseointegration and esthetic outcome.

III.5.2. Methods

Thirty-nine patients who had undergone maxillary anterior single-tooth immediate implants according to the concept of immediate nonfunctional loading between 2004 and 2013 were included in this retrospective case-control study. The study was approved by the ethics committee of Tel-Aviv University, and all patients gave written permission for the use of their medical files and records.
The inclusion criteria were the need for extraction of a single tooth in the anterior esthetic zone of the upper jaw (central/lateral incisors or canines), the presence of both adjacent teeth, perfect symmetry of the pre-extraction soft tissue contours, (or excess of soft tissue) at least 18 years of age, good oral hygiene (after initial preparation) with a plaque score $\leq 10\%$, the integrity of the residual bone walls after extraction (three wall defects were acceptable if the buccal dehiscence was < 3 mm), and at least 5 mm of bone apical or palatal to the alveolus of the failing tooth to ensure primary insertion torque of at least 32 Ncm. The exclusion criteria were the same as under III.3.2. The preoperative assessment and pre-and postoperative prophylactic procedures were the same as under III.4.2. with the exception that here open flap debridement was also utilized if necessary.

After the surgical site was anesthetized, intracrevicular incisions limited to the circumference of the hopeless tooth or retained root were performed using a 15c blade. This was followed by an atraumatic tooth extraction taking care to maintain the integrity of the socket bone walls, especially the buccal bone, using periotomes (Hu- Friedy, Chicago, IL, USA). Granulation tissue was removed using a spoon curette and a 3 mm diamond bur (Strauss Company, Raanana, Israel). The socket walls were then inspected for the presence of fenestration or dehiscence defects. At this stage, a decision was made as to whether or not to proceed with implant placement without flap elevation. To be included in the current study, the facial socket walls had to be intact or to contain only small defects (reducing

crestal bone height by < 3 mm). Patients with greater defects were treated with a flap procedure and underwent bone augmentation and their data are not included herein. Site preparation was performed along the palatal socket wall. The osteotomy was designed to achieve as much implant engagement as possible with the apical and palatal borders of the extraction socket. Depending on the residual bone density, final drilling was performed using a drill measuring at least 1 mm less than the implant diameter Screw-type sandblasted, and acid-etched surface bone level titanium implants that were used (Lans, MIS-Bar Lev Industrial Zone, Israel) or a conical type (Seven, MIS-Bar Lev). The implants were inserted at an insertion torque of at least 32 Ncm with a torque-controlled ratchet (MIS-Bar Lev). Proper implant positioning was considered of pivotal importance, with the adjacent teeth serving as a reference for optimal implant positioning (Figure 6). A minimum distance of 1 mm (measured with a periodontal probe) between the implant shoulder and neighboring tooth was achieved in all cases.

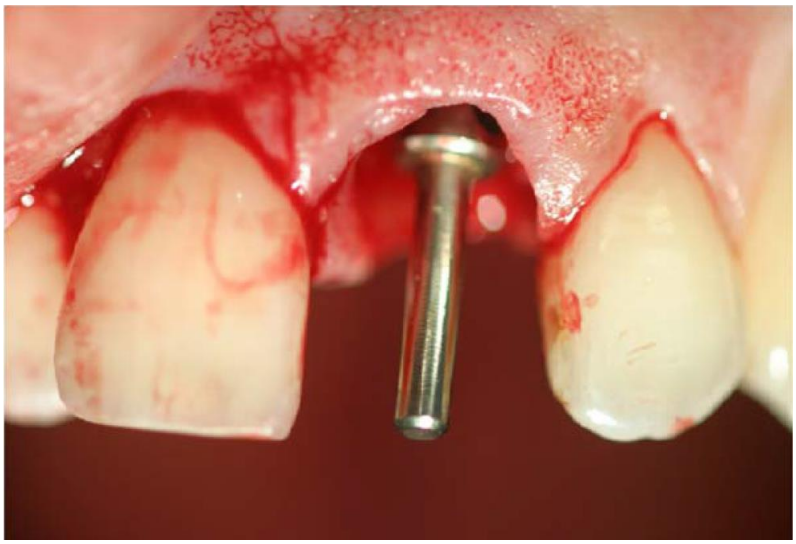

Figure 6. Flapless extraction and parallel pin

After adaptation of an appropriate abutment (0–258), with a gingival neck 1–3 mm in height and torqued with 15 Ncm (Anthogyr, torque-controlled ratchet, Botzer Ergonomics, Israel), 0.25 to 1 mm particle allograft material (FDBA-Raptos–Citagenix Toronto, Canada) was applied in the residual gap in all cases.

Abutment connection was followed by the adaptation of a prefabricated nonfunctional acrylic temporary crown (no occlusal contacts with the implant crown [IC] or during protrusive and lateral movements) (Figure 7).

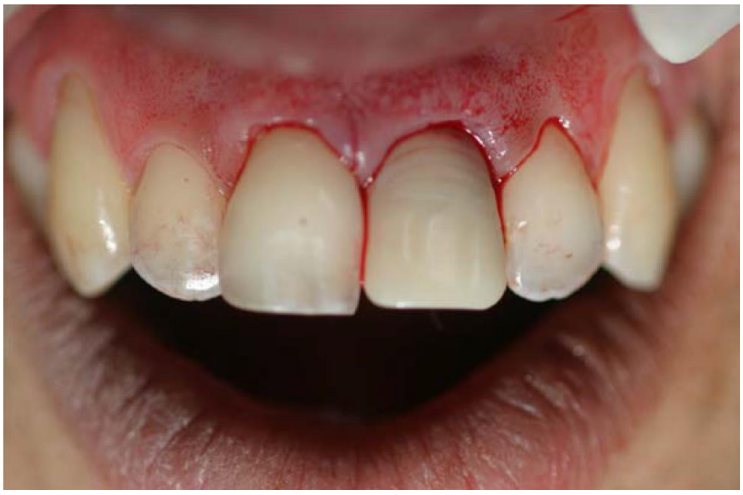

Figure 7. Temporary nonfunctional acrylic crown in the 21 position

Six months after implant placement, the temporary crown and abutments were removed, and color-coded transfers (MIS-Bar Lev, Israel) were adapted. Transfer adaptation was radiographically verified, and impressions were taken utilizing the putty-wash one-step technique (Express, 3M. ESPE Dental Products, St. Paul, MN, USA) using the closed tray technique with metal stock trays. A master model with a silicon image of the marginal gingiva was prepared, and interarch relations were recorded. Abutments were connected, and the Zirconia base was adjusted at the following visit. The permanent Zirconia crown was cemented after occlusal adjustment and glazing with temporary cement (Temp- Bond Kerr Corporation, Orange, CA, USA). The abutments were tightened to 35 Ncm using a prosthetic ratchet. The implants were considered successful if they fulfilled the criteria of Alberktsson et al.[111]

The entire follow-up lasted for a mean of 45 months (12 to 108 months). Like before, other parameters were also examined (see article in Appendix), but the main goal of the study was to assess esthetics, so we focus only on the clinical esthetic outcomes here, assessed at 12 months after the adaptation of the final crown. For clinical esthetics analysis, the PES and WES scores were used, as discussed under III.4.2. The details of the statistical analysis are given in the original publication in the Appendix.

III.5.3. Results

The data of 39 patients were included in the study (16 males and 23 females, mean age: 47.51 ± 18.09 years, range: 24 to 82 years). Most of them (N=32, 82.1%) were non-smokers, the rest smoked <10 cigarettes a day. Twenty (51%) of the patients were diagnosed as having gingivitis and/or mild adult chronic periodontitis, and 19 (49%) as having chronic moderate/advanced adult periodontitis or aggressive periodontitis. Eleven teeth (28%) were extracted due to periodontal disease, 17 (44%) due

to root fracture, 8 (21%) due to severe carious lesions, and 3 (7%) due to external root resorption. Three patients had a narrow and shallow (≤ 3 mm) buccal dehiscence. The implant diameter varied between 3.3 and 5 mm, and the implant length varied between 13 and 16 mm. The clinical esthetic parameters are summarized in Table 4.

Table 4. A summary of the clinical esthetic parameters.[5] 0,1 and 2 are the achievable scores and the values (given as N (%)) indicate what proportion of the examined teeth got that particular score in any given parameter.

Parameter	0	1	2	Average
Mesial papilla	3(7.9)	16(42.1)	19(50)	1.42
Distal papilla	0(0)	13(34.2)	25(65.8)	1.66
Curvature of facial mucosa	0(0)	12(31.6)	26(68.4)	1.68
Level of facial mucosa	5(13.2)	8(21)	25(65.8)	1.53
Root convexity/soft tissue color/texture	1(2.6)	12(31.6)	25(65.8)	1.63
PES (mean ±SD)		**7.92 ± 1.6**		
Tooth form	0(0)	13(34.2)	25(65.8)	1.66
Tooth volume/outline	0(0)	13(34.2)	25(65.8)	1.66
Tooth color (hue value)	0(0)	9(23.7)	29(76.3)	1.76
Surface texture	0(0)	28(73.7)	10(26.3)	1.26
Translucency	0(0)	26(68.4)	12(31.6)	1.32
WES (mean ±SD)		**7.66 ± 1.48**		
Total PES-WES		**15.50 ± 2.67**		

The esthetic parameters at 1 year after crown adaptation of the final restoration revealed a mean PES of 7.92±1.60 (range: 5-10) and a mean WES of 7.66±1.48 (range: 5-10), resulting in a total PES/ WES score of 15.50±2.67. The cumulative PES/WES demonstrated that good or acceptable esthetics (≥12) had been achieved in 35/38 patients (89.7%). Overall, the esthetic outcomes were favorable. Of the five parameters of the PES index, the mesial papilla height scored the lowest (mean: 1.42) whereas the curvature of facial mucosa scored the highest (mean: 1.68). Twenty-five implants (66%) had an optimal level of the facial mucosa, eight implants (21%) had recessions < 1 mm and five implants (13%) had recessions > 1 mm. Of the five parameters of the WES index, color scored the highest (mean: 1.76) while surface texture scored the lowest (mean: 1.26). Figure 8 shows a near-perfect outcome from this study (PES-WES = 19/20).

[5] Please note that Table 3 of the original publication (to be found in the Appendix) provides a case-by-case overview of all variables of the study; the table has been omitted from the present thesis for reasons of space.

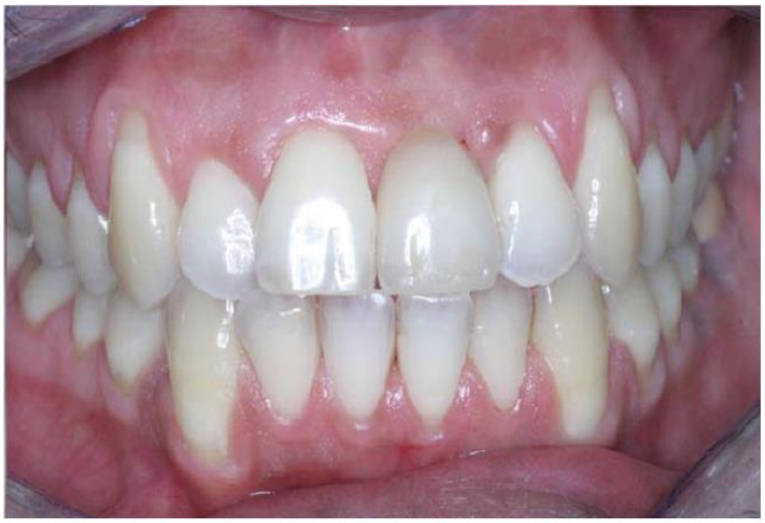

Figure 8. Near-perfect esthetic outcome 12 months after the adaptation of the final restoration.

III.5.4. Conclusions

Objective PES/WES assessment validated immediate anterior maxillary single-tooth replacement and restoration as being a successful and esthetically predictable treatment modality in the short term (1 year), although the occurrence of buccal recessions is inevitable, even in patients with optimal soft- and hard-tissue configuration. The technique may be implemented in a selected group of implants: specifically, implants placed in sites where the buccal bone had been preserved during the extraction. More data are needed regarding the maintenance of the esthetic results in the medium and long terms.

III.6. Allograft and Collagen Membrane Augmentation Procedures Preserve the Bone Level around Implants after Immediate Placement and Restoration.

III.6.1. Background

Single-tooth immediate implant insertion and provisionalization, especially in the aesthetic zone, is a highly reliable treatment modality for replacing failing teeth [112]. Increasing patient expectations for reduced treatment time and improved esthetics and comfort have shifted research interest from implant survival toward optimal preservation of soft and hard tissue. Whenever possible, immediate placement and restoration (IPR) of implants is strongly recommended. There are a few factors that, in turn, may have an adverse effect on the final esthetic outcome. The recession of the marginal peri-implant mucosa [94, 97] is one of the most significant of these factors. Being related to the bone

levels surrounding the implant [113], maintenance of the soft tissue and underlying bone is of the utmost importance [113]. Several factors have been claimed to influence the frequency and extent of marginal mucosal recession, including the peri-implant soft tissue biotype [97], the connection of a provisional crown immediately following implant insertion [98], condition and thickness of the facial bone [99], the orofacial position of the implant shoulder [100, 101] and filling the gap and facial peri-implant marginal defects with autogenous bone or bone substitute grafts [102, 103]. During implant placement into fresh extraction sockets, gaps usually remain between the implant surface and the inner wall of the facial plate of the bone. Moreover, following tooth extraction, the alveolar bone-supporting tooth undergoes constant significant atrophy during the first 3 months [114, 115]. A marked reduction in the height of the alveolar ridge has been shown to consistently occur following tooth extraction; additionally, implant installation into the fresh extraction socket does not interfere with the process of bone modeling [116, 117]. Different approaches have been advocated to preserve or improve the dimension and contourof the ridge following tooth extraction, including the use of various graft or filler materials, such as autografts, allografts, xenografts and synthetic grafts, and/or barrier membranes [118]. The rationale for the use of graft materials and membranes is to prevent the migration of cells from the gingival epithelium and connective tissues into this gap, thus permitting osteoprogenitor cells to occupy the established gap [119] and eventually regenerate the bone tissue, thus supporting osseointegration [120]. Moreover, these grafts are used to partially prevent horizontal and vertical resorption following the extraction and to augment the buccal bone to achieve at least a 2-mm-thick bony plate buccal to the implant surface [121]. However, there is not enough evidence supporting or refuting the need for augmentation procedures concomitant with immediate implant placement [117] or whether any of the augmentation techniques are superior to the others [41, 122, 123]. Consequently, the purpose of this study was to validate the efficiency of an allogenic bone graft material and non-cross-linked collagen membrane in preventing marginal bone loss after the extraction of a single anterior maxillary tooth and treatment with IPR.

III.6.2. Methods

This historical prospective single-arm study was designed to evaluate the medium-term hard tissue changes around implants after immediate placement and restoration (IPR) in the anterior maxilla with simultaneous bone augmentation. A total of 90 patients were treated in the said way between 2010 and 2017. The data of 73 of them were included in the analysis. In all cases, the concept of immediate nonfunctional loading was utilized. The inclusion and exclusion criteria were the same as reported before. The preoperative assessment and pre-and postoperative prophylactic procedures were the same as under III.4.2.

After the surgical site was anesthetized, the mucoperiosteal flaps were elevated, including intracrevicular incisions extending to the midfacial aspect of at least both adjacent teeth. This was followed by an atraumatic tooth extraction aiming to preserve the integrity of the extraction socket walls. Granulation tissue was removed using a spoon curette and a 3-mm diamond bur (StraussCompany, Raanana Israel). The drilling was conducted to the palatal wall. Osteotomy was intended to achieve as much implant engagement with the apical and palatal bone aspects of the extraction socket as possible. Depending on the residual bone density, final drilling was performed using a drill measuring at least1 mm in diameter less than the implant diameter. Final placement of the implant was achieved with an insertion torque of at least 32 Ncm using a torque-controlled ratchet (MIS Implants Technologies, BarLev industrial center, Israel). Screw-type bone-level titanium implants (Seven, Lance MIS ImplantsTechnologies, Bar Lev industrial center, Israel) were used. Proper implant positioning was considered of pivotal importance. The neighboring teeth were used as references. A minimum distance of 1 mm (measured with a periodontal probe) in the mesiodistal direction between the implant shoulder and adjacent teeth was achieved in all cases. In the apicocoronal direction, the neck of the implant was flush with the palatal bone. In the orofacial dimension, an attempt was made to place the buccal neck of the implant at least 2 mm palatal to the buccal contour of neighboring teeth. An appropriate 0-25° abutment with a gingival neck of 1–3 mm height was adapted, (not related to the socket configuration or defect morphology) followed by the application of 0.25–1 mm freeze-dried bone allograft (FDBA) particles (FDBA-Life-Net, Virginia, FL, USA) in the residual gap and in excess above the buccal wall. A resorbable collagen membrane (Bio-Gide, Geistlich Pharma AG,Wolhusen, Switzerland) was applied in a draping manner over the abutment and above the bone graft. The buccal flap was coronally positioned after a periosteal releasing incision and sutured to the palatal flap using 4/0 sutures (Vicryl Rapid, Ethicon, Johnson Belgium).

Abutment connection was verified radiographically, followed by the adaptation of a prefabricated nonfunctional acrylic temporary crown. The sutures were removed after 7–10 days and were repeated when indicated. Six months after implant placement, the temporary crown and abutments were removed, color-coded transfers (MIS Implants Technologies, Bar Lev, Israel) were adapted and radiographically verified. Impressions were taken using putty and wash silicone (Express, 3M ESPE Dental Products, St. Paul, MN, USA) employing the closed-tray technique and metal stock trays. A master model with a silicone image of the marginal gingiva was prepared and inter arch relations were recorded. At the following appointment, new abutments were connected (Figure 1e) and porcelain fused to metal or zirconia was tried (Figure 1f). The abutments were tightened to 25 - 35

Ncm (depending on implant diameter) using a prosthetic ratchet. The permanent crown (Figure 1g) was cemented after occlusal adjustment and glazing with temporary cement (Temp-Bond, Kerr Corporation, 1717 West CollinsAvenue, CA, USA).

The patients were followed up at 6 and 12 months postoperatively and then annually (12 to 96 months; mean: 34 months). They participated in a personal maintenance program every 3 to 6 months performed by dental hygienists. At these sessions, plaque index, probing depth, and bleeding on probing were recorded. De-plaquing, scaling and root planing were performed as necessary.

Postoperative periapical radiographs were obtained immediately after implant placement at the time of impression taking, at the final crown installation, at the annual follow-up examinations and once again at the time of final data collection during 2018. Standardized radiographs were obtained with the film kept parallel (Schick Technologies, Long Island, NY, USA) using plastic film holders while the X-ray beam was kept perpendicular. Distance from the Implant Shoulder to the Coronal Bone-to-Implant Contact (DIB). The distance from the mesial and distal alveolar bone crest to the implant shoulder, which served as a reference level (RL), was digitally measured by computerized dental radiography based on parallel periapical X-rays (Schick Technologies, Long Island, NY) (Figure 2). The radiographic distortion was calculated by dividing the radiographic implant length by the actual implant length.

Peri-implant mucositis was defined as PD $\geq$ 5 mm with BOP and no bone loss. Peri-implantitis was defined as mucositis with implants showing more than 1.5 mm of bone loss during the first year and higher than an additional 0.2 mm for each successive year.

III.6.3. Results

The study population consisted of 73 patients (33 men and 40 women) aged 22 to 84 years (mean: 56.49 ± 14.56 years) who were treated according to a strict protocol consisting of single-tooth extraction, immediate implant placement, guided bone regeneration (GBR), and immediate restoration. Eleven central incisors, 17 lateral incisors, 6 canines, 23 first premolars and 16 second premolars were replaced. Forty-nine patients (67.1%) presented with chronic advanced adult periodontitis or aggressive periodontitis, whereas 24 (32.9%) were diagnosed with gingivitis or mild adult chronic periodontitis. Twenty-nine teeth (39.7%) were extracted due to periodontal disease, 19 (26 %) due to root fracture, 22 (30.1%) due to severe carious lesions, and 3 (4.1%) due to external root resorption. The diameter of the implants varied between 3.3 and 5 mm (mean: 3.83 ± 0.43 mm) and the implant length varied between 10 and 16 mm (mean: 14.84 ± 1.66 mm).

As for the radiographic findings, at the time of final data collection (at 12 to 96 months, depending on the particular case) all 73 (100%) implants were deemed successful according to the Albrektsson criteria, showing no more than 1.5 mm of bone loss during the first year and up to an additional 0.2 mm for each successive year [110]. Moreover, seventy patients presented with marginal bone coronal (positive) or at the level of the implant shoulder (RL). Only in three patients was the bone level apical to the implant shoulder (Figure 9).

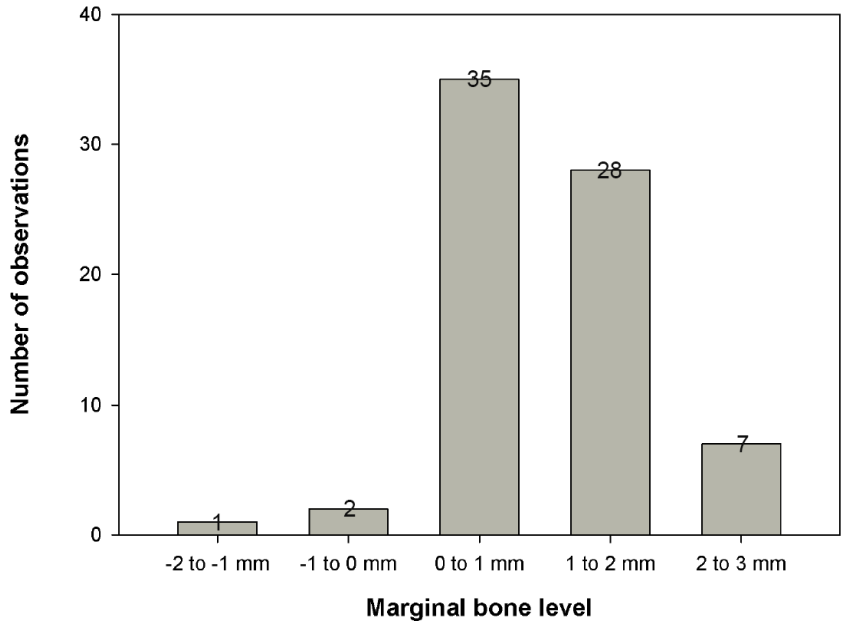

Figure 9. Marginal bone levels at the final follow-up.

Crestal bone level measurements revealed a mean mesial and distal bone level of 0.86 ± 0.86 mm (range: 0–3 mm) and 0.8 ± 0.84 mm (range: 0–3.3 mm), above the implant shoulder (RL) respectively. Splitting the study group at 3 years of follow-up (0-3 and 3-8), the measurements showed an average positive bone level of 0.90 ± 0.83 and 0.99 ± 0.87 mesial and distal to the implants, and 0.68 ± 0.88 and 0.74 ± 0.83, respectively. Neither the paired t-test nor the nonparametric signed t-test for paired samples showed a significant difference between the CBL on the mesial or distal aspect of the implants. No significant CBL difference was found between light smokers and nonsmokers, whereas the bone level was slightly significantly higher in males than in females ($p = 0.04$). CBL in advanced/aggressive periodontitis patients was higher than in gingivitis/ mild to moderate periodontitis: 1 ± 0.7 vs. 0.5 ± 0.9, respectively. No significant correlation was found with

periodontal status, age, or cause of extraction. The physical parameters of the implants (length and diameter) did not have a significant influence either.

III.6.4. Conclusions

Within the limitations of this study, we demonstrate that the regenerative technique presented, using mineralized FDBA particles combined with a non-cross-linked collagen membrane concomitant with immediate implant placement, preserved the crestal bone level surrounding the implant.

IV. DISCUSSION

In the studies covered in this thesis, we concentrated on immediate single-tooth replacement with nonfunctional immediate provisionalization in the maxillary esthetic zone as a challenging and sensitive area of dental implantation. The foremost aim of the studies was to provide evidence for the safety and reliability of this approach.

First, as sort of a preliminary technical question, we sought to prove that the use of plastic temporary abutments with provisional restorations is an optimal approach in immediate loading procedures. We managed to prove this point and we used these abutments throughout our studies. The prefabricated plastic provisional abutments are designed to allow for cementation of a provisional restoration because of horizontal retention sleeves, as well as the fabrication of screw-retained provisional restorations. The use of prefabricated plastic temporary abutments simplifies the connection and adaptation of provisional restorations, especially in immediate loading procedures. These abutments cost less than temporary titanium abutments and are easy and quick to prepare. Furthermore, preparation can be performed intraorally because this manipulation does not produce any heat transmission to the peri-implant bone as do titanium abutments.

The second aim was to prove that our approach could offer long-term implant survival free of complications and adverse events. This we studied through 6 to 7 years of follow-up and got a positive result. We must note that some studies reported low success rates in similar circumstances [26, 124-126]. However, in these studies, the prostheses were in full functional loading or primary occlusal contact. This is a crucial difference from our studies, where we always used nonfunctional provisionalization, and this underlines the benefits of our approach. The soft tissue reaction was also quite favorable due to the presence of a provisional crown during the healing phase. This preserved the gingival and interdental papilla, resulting in highly esthetic outcomes. In this respect, our results are in agreement with the literature [33, 127-129]. The same is true for marginal bone loss around single implants [128-131]. The technique of immediate (if nonfunctional) loading in extraction sites appeared to be beneficial in many ways. There was no need for second-stage surgery and the need for transitional removable dentures was eliminated, along with its harmful effects on soft and hard tissues. Furthermore, the technique maintains the existing hard and soft tissues, which allows highly aesthetic results without the need for hard and soft tissue augmentation (but it does not exclude the possibility either, as demonstrated elsewhere in this thesis). It cannot be overemphasized that we reached these outstanding results by strict patient selection and careful maintenance, which we consider as the key factors to success in general. Certainly, the outcomes are appealing, but it must

be kept in mind that any treatment will work only if it is applied with the right patients and if care is taken that all controllable factors that have the potential to interfere with long-term success are eliminated.

Esthetic outcome is a question we found so important that we studied it separately. We considered this a question of key importance because we experienced and still experience that patients expect higher and higher esthetic standards in dentistry, but also because it has been proven in several studies that dental esthetics is a major determinant of quality of life [132, 133]. The primary means of assessment was the PES/WES assessment, as proposed by Belser and co-workers [81]. PES/WES assessment validated immediate anterior maxillary single-tooth replacement and restoration as being a successful and esthetically predictable treatment modality, but with certain caveats.

In the first study of this kind, we assessed immediately placed implants combined with GBR and free connective tissue graft. The overall PES/WES score turned out to be 14.44 ± 2.34, a quite favorable outcome, comparable to 14.70 reported by Belser et al. [81], in connection with early placement, and 14.30 reported by Mangano et al.[134], in connection with immediate placement. Both studies focused on tooth replacement in the anterior maxilla. On the other hand, our results were somewhat inferior to the PES/WES value of 16.76 reported by Buser and colleagues [135, 136]. Our lower score may be explained by the fact that all the bony socket walls around the tooth to be extracted and replaced, were compromised in the vertical and/or horizontal dimensions, mainly due to previous periodontal disease. The high score obtained for the combined root convexity/soft tissue color and texture (1.71) may be attributed to the combined procedure of GBR and CT grafts. This combination seems to have enhanced soft tissue morphology, yielding an optimal emergence profile and texture of the buccal soft tissue. Of the 34 cases, 24 scored 2 (70.6%) while the remaining 10 cases scored 1 (29.4%). Our data confirm those reported by Kan et al. [137] that after CT grafting used for single immediate tooth replacement, the gingival level could be maintained regardless of the initial gingival biotype. Moreover, if the immediate placement is performed in patients with a thin biotype, there is a higher risk of soft tissue recession and underlying resorptive osseous remodeling, exposing the metal margin of the implant [97]. The GBR and CT grafts were used in this study to achieve favorable esthetics and to avoid recessions that would necessitate a second soft tissue intervention during the first year [138]. The cumulative total PES/WES of the 34 cases shows that in 91.2% of the cases, good or acceptable esthetics was achieved (≥12). The low scores of the mesial papilla (1.09 ± 0.62) and the level of facial mucosa (1.26 ± 0.83) were probably affected by the marginal bone loss of the neighboring teeth [139]. Our data of 23.5% regarding significant buccal soft tissue recessions (>1 mm) are lower than the 30–40% reported in studies utilizing immediate implant placement [96, 101,

140-142], but much higher than the 5% reported by Buser and co-workers, utilizing a staged approach [81, 136]. Thus, in almost 1 of 4 case, a notable recession of >1 mm was observed - a fact that raises the possibility that cases with a compromised buccal bony wall may benefit more from a staged approach.

The other study on esthetics dealt with a group of patients in whose cases a flapless approach was used, and extraction was carried out in a way that the integrity of the residual bone walls was spared. Not surprisingly, the PES/WES score in this patient group (15.50 ± 2.67) was superior to that of the patients of the first study, whose bony socket walls were compromised. Acceptable or good esthetics (PES/WES >12) was achieved in 34/38 cases (89.4%). PES scored 7.92 in this study, which is well withing the 7 to 8.1 reported for delayed or immediate implant placement and restoration [143]. Notably, the ratio of significant buccal soft tissue recessions (>1mm) was only 13.2%, which is much lower than the 30 to 40% ratio reported by authors who claim that a high incidence of mucosal recession is a frequent observation after immediate implant placement [96, 101, 140, 141]. Our observation points out that it is not necessarily so. The potential causes of this esthetic complication include a thin gingival biotype [137] and a U-shaped defect morphology, but such patients can be excluded by careful case selection. It must be noted that in the present study, patients with a thin biotype were not excluded from the analysis. Had those data been excluded, the ratio of significant recessions would probably have been even lower. As for the exact magnitude of recession, the reported mean value is usually less than a millimeter [143], so our finding of a mean of 0.41 mm is completely in line with the literature. Intriguingly, some studies reported no change or even a gain in mucosal height [144-146]. Those studies all used the flapless approach with immediate provisional restoration, as well as the concomitant incorporation of a connective tissue graft.

In the present study, the pre-extraction soft-tissue contours were in perfect symmetry with the surrounding teeth. Consequently, there was no need for soft-tissue augmentation or flap elevation, unlike in situations where the extracted teeth had a pre-existing gingival recession whose correction required connective tissue grafts in conjunction with coronally advanced flaps. Furthermore, the post-extraction bony socket walls were preserved as much as possible. These factors together added up to a favorable esthetic outcome.

To summarize our esthetic observations, immediate nonfunctional provisionalization in the anterior maxilla does not risk long-term soft- or hard tissue esthetics provided that the bony socket walls are well preserved, and no specific soft tissue risk factor (such as a thin biotype) is present. For patients with damaged socket walls, a staged approach is recommended. Significant mucosal recession is not

a necessary or even highly likely sequela of immediate provisionalization in the anterior maxilla. When used in the right patient population, the approach yields outstanding esthetic results.
Finally, we addressed the question of immediate implant placement combined with augmentation procedures directly. While this was implicitly a part of one of the esthetics-related studies [41], it was only in the last study of the thesis that we dealt with this per se.

After a mean follow-up of 34 months, the cumulative implant success rate was 100%. This is in agreement with several studies demonstrating the high predictability of immediate implant placement and provisionalization with simultaneous bone augmentation [42, 147, 148]. Most studies regarding IPR reported a bone loss of 0.2 to 1.0 mm after the first year of function [129, 149], but some reported even a minimal bone gain above the implant shoulder observed at the 1-year follow-up [150, 151]. In the current study, all but three implants (70/73) were characterized by bone gain, indicating that the peri-implant marginal bone level can be well maintained or enhanced using the proposed treatment protocol. The results of the present study regarding positive crestal bone level are in line with a recently published meta-analysis comparing immediately placed implant combined with GBR vs. the use of bone grafts alone [152]. Despite the presence of intact or dehisced sockets, the CBL was better preserved in IIP with bone graft and membrane compared with bone graft alone. The latter finding is logical since membranes assist in complete graft containment without soft tissue downgrowth [152]. The low mean PD around the implants (3.63 ± 1.06 mm) at the last follow-up examination indicated healthy peri-implant soft tissue. The remarkable maintenance of CBL in this study may be attributed to the surgical technique, which is characterized by the placement of mineralized FDBA granules into the gap in excess over the buccal bone, followed by covering with a non–cross-linked collagen membrane. Although this surgical technique has been used extensively in regenerative procedures [153, 154], there is insufficient scientific evidence to support its efficacy in immediate implant placement [152, 155]. A range of biomaterials, primarily bone xenografts, and allografts, have been found to improve bone volume [156]. Other preclinical [157] and clinical studies [158] have demonstrated that vertical bone loss is limited with the use of allografts covered with a resorbable collagen membrane. Moreover, aiming to compensate the volume reduction during the healing stage of the GBR procedure, over-augmentation was endorsed [41]. The low resorbability of the graft can be advantageous, as it limits buccal bone resorption [159]. Collagen membranes were used to reduce the risk of infection if soft tissue dehiscence occurs postoperatively [160, 161]. The osteoconductive properties of mineralized allografts have been previously described [42]. In comparison to autogenous bone and despite the lack of osteogenic properties of allografts [162], comparable volumetric results were achieved with or without autogenous bone when used to restore

alveolar ridge deficiency [163]. The use of bone replacement grafts and temporary acrylic restorations has been shown to improve the soft tissue height and thickness compared to those in the control groups [164, 165]. A possible explanation for these phenomena may be that the incorporation and encapsulation of graft particles in peri-implant soft tissue creates a sort of "benign foreign body reaction", consequently improving the soft tissue dimensions [166]. Another possible explanation for our results is that the pressure of the lips and tongue on the provisional crown had generated stress at the implant shoulder, stimulating cells directly within the peri-implant bone and initiating bone remodeling at the implant surface. Such a course of events should result in bone gain [167]. In any way, the findings confirm the positive contributions of the proposed regenerative techniques in terms of osseous volume preservation during implant placement.

V. CONCLUSIONS

Through the studies covered in this thesis, we have demonstrated the following and we consider these to be the novel scientific findings related to the work that has been accomplished:

1. The use of plastic temporary abutments with provisional nonfunctional restorations is an optimal approach for immediate loading procedures. This approach has become routine since its introduction.

2. Nonfunctional immediate loading of single-tooth implants in fresh extraction sites in the anterior maxilla results in successful implant integration and stable long-term peri-implant conditions.

3. Immediate nonfunctional provisionalization in the anterior maxilla offers predictably good esthetic outcomes provided that the bony socket walls are well preserved, and no specific soft tissue risk factor is present. As esthetics is a key factor in the anterior region, careful patient selection is essential for these procedures.

4. Mineralized FDBA particles in excess, combined with a non-cross-linked collagen membrane concomitant with immediate implant placement in the anterior maxilla preserves the crestal bone level around the implants.

Besides their particular importance, the results laid out in this thesis show that immediate nonfunctional provisionalization in the anterior maxilla is a safe and reliable approach, both in the functional and the esthetic sense.

VI. ACKNOWLEDGEMENTS

To be filled in.

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Appendix