Immediate Postoperative Dimensional Changes Following Implant Placement

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IMMEDIATE POSTOPERATIVE DIMENSIONAL CHANGES FOLLOWING IMPLANT PLACEMENT

by

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ABSTRACT

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Objective: Hard tissue outcomes after implant placement have been well documented. However, there is scarce evidence on immediate soft tissue and patient-centered outcomes. The aim of this prospective study is to quantify post-implant placement edema and to correlate it with oral health-related quality of life.

Methods: Patients undergoing a standardized two-stage implant placement at a single tooth-bound site were recruited (n=26; 54.1±3.3 years, 14 males). Soft tissue edema was recorded by using intraoral scans immediately pre- (PS) and post-operatively (IP), at 2 (2D), 7 (7D) and 14 days (14D) and 2 months (2M). After scan registration, ridge width, maximum height, and volume changes from IP were recorded. OHIP-14 and VAS for pain and swelling were recorded at preop and follow-up visits.

Results: Ridge width (1.9±0.04mm), height (1.4 ±0.02 mm) and volume (37.8±0.8%) peaked on 2D. Ridge width reached PS levels by 14D (p=0.44). Height increases from IP to 2D and 7D were the highest compared to all other time point increases (p<0.0001). OHIP-14 and VAS for pain and for swelling exhibited a similar trajectory, peaking at 2D and reaching PS levels by 7D (pain: PS/7D p=0.07; OHIP-14: PS/7D p=0.28) and 14D (swelling: PS/14D p=0.18). There were no statistically significant correlations between edema, OHIP-14 and VAS measurements.

Conclusion: Following implant placement, soft tissue changes show a maximal response at 2 days and patients experience the most significant pain and swelling and the worst oral health-related quality of life at the same time point. However, clinically measured and patient-reported outcomes were not correlated.

ACKNOWLEDGMENTS

Juan Valencia Rincon, DMD.

Special gratitude to my parents that have devoted their lives supporting me during my years of education. To my wife and daughter for their unconditional love throughout my periodontal career and to my program director for making this research thesis possible.

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Chapter 1
Introduction:

Implant placement is a commonly used surgical procedure aiming to replace and restore the functions of a missing tooth. Since Branemark's discovery in 1965 that titanium was biocompatible and could be osseointegrated, a plethora of investigations have been conducted on clinical parameters for optimal biological and prosthetic implant-related outcomes**.** [1] [2] [3] [4] [5] [6]

Salvi et al [7] summarizes the process of osteointegration into 3 major events categorized as early healing, bone modeling and bone remodeling. Several hours after implant placement, the implant threads are in contact with pristine bone and the pitches of the threads providing mechanical anchorage. The voids between the pitch and the body of the implant are filled with blood clots rich in erythrocytes, neutrophils, and monocytes in a network of fibrin. Four days later, the blood clots are replaced with a primitive granulation tissue which has numerous mesenchymal cells, matrix components and new blood vessels. One week after implant placement, the peri-implant provisional connective tissue presents with multiple vascular structures and a relatively small number of inflammatory cells. Immature bone or woven bone is first observed surrounding blood vessels. At 14 days, woven bone formation is more pronounced in all compartments, apical and lateral to the implant. Osteoclasts accumulate on pristine bone surfaces in order to resorb pristine bone resulting adjacent to the implant surface, especially in areas of pressure of the implant to the bony bed. At 6-12 weeks, bone remodeling is observed, while most of the wound chambers are now filled with mineralized bone. Bone has the clearly defined structures of primary and secondary osteons, and the mature bone has

high contact with the implant surface. The bone trabeculae become reinforced by lamellar or parallel fiber bone deposition, which has an adequate structure to bear loading forces.

Even though osseointegration is necessary for successful early peri-implant healing, soft tissue parameters are also important for the long-term success of implants after restoration. Thoma et al [8] published a detailed review discussing critical soft tissue dimension parameters when placing dental implants. Peri-implant health and esthetic considerations include supracrestal tissue attachment, papilla height, soft tissue volume, keratinized tissue width and periodontal biotype. Despite consensus on the biologic implications of peri-implant supracrestal tissue attachment and its differences with its periodontal counterpart as well as the established knowledge on esthetic demands related to papilla height [9] [10] [11] [12] [13], there is no general consensus on the last three parameters. Specifically, the amount of soft tissue volume can influence the esthetic outcome and may even partly compensate for missing bone on the buccal side of the dental implant. Several authors have pointed out that a critical soft tissue dimension of 2mm on the buccal aspect of the implant is necessary for tissue stability and esthetic prosthetic demands. [14] [15]. Reduced peri-implant keratinized tissue (less than 1.5mm) may be more prone to plaque accumulation, bleeding on probing as well as soft tissue recessions [16] [17] [18]. A thin periodontal biotype may be associated with an increased risk for recession [19] and unfavorable treatment outcomes following surgical procedures [20] [21] [22]. In the past decades, titanium implants have become the standard of care for restoring an edentulous area due to advantages they possess over fixed partial dentures [23].

Patient-reported outcomes studies have shown that patients are highly satisfied with esthetic and functional demands of implants after a 10-year follow-up period [24]. Another advantage is the low frequency of complications (approximately 15%) [25]. Misch et al [26] in the study "Implant surgery complications: etiology and treatment" categorized the different implant-related complications. They were grouped into categories of procedure-related complications (lack of primary stability, mechanical complications, ingestion/aspiration of the implant components), anatomy-related complications (nerve injury, bleeding, cortical plate perforation, sinus perforation and/or deviation of adjacent teeth), treatment plan-related complications (wrong angulation, improper implant location, to close or too far apart, lack of communication between lab and clinician) and miscellaneous (iatrogenic or human error).

Camargo et al [27] focused on the post-operative biological complications after implant placement encompassing early-stage and late complications. Early-stage complications include pain, swelling [28] [29] [30] [31], infection (prevalence of 2.80% [28]), ecchymoses, hematomas, emphysema, bleeding, flap dehiscence and sensory disorders. Late complications include perforation of the mucoperiosteum, maxillary sinusitis, mandibular fractures, failed osseointegration, bony defects and periapical implant lesion [32].

Out of the aforenoted complications, pain is the most common one after any surgical procedure [33]. Postoperative pain constitutes not only an unpleasant sensory reaction most often associated to injury, but it also, appeals to the emotional experience and well-being of the individual [34] [35]. It may be recorded in a quantitative manner using Visual Analogue Scale and factors that have been associated with it include age

[29] [36] [37], gender [37] [38] [39], socioeconomic status [40] [41] [43], , untreated dental problems [42] [43], previous dental experiences, psychologic state of patient [37] [38], duration of surgery [29] [30] [31] [36], pain during surgery [36], operator experience [36], and type of dental intervention [37].

Implant placement is generally associated with less pain compared to other surgical procedures such as third molar extractions or other periodontal surgeries [29] [30] [44] [45]. Patients experience maximum pain severity the same day after implant placement surgery (VAS median of 1/10) which subsides by 3 days (VAS median of 0/10) [31]. In terms of pain prevalence, the majority of the patients feel zero pain during surgery (84%) and mild pain 24 hours (70%) and one week after the procedure (57%) [36]. During the first postoperative week, patients reporting discomfort decreased from postoperative day 1 (57%) to day 3 (36.1%) and at the 7 days pain was practically absent in all participants (17.5%) [33].

Even though pain experience affects oral health-related quality of life, it is not the only factor that can negatively impact it. The Oral Health Impact Profile-14 (OHIP-14) is a questionnaire that measures people's perception of the social impact of oral disorders on the well-being of the patient. Developed by Slade [46] in 1997, OHIP-14 showed high reliability, validity, and precision to quantify functional limitations, physical discomfort, psychological discomfort, physical disability, psychological disability, social disability, and handicap [47] [48]. OHIP-14 has been consistently used to assess overall patient reported outcomes in several fields of dentistry as well as after implant placement [49] [50] [51]. Kahn et al [45] assessed patients' perception of recovery after dental implant placement using this questionnaire. Individuals were evaluated for 7 consecutive days

post-surgery and the investigators' found out that the most serious difficulties were maximal pain (became minimal after 3 days), analgesics consumption (became minimal after 2.5 days), swelling (experienced in the first 5 days), and mouth opening and speech (became minimal after 2 days), difficulty eating everyday foods and ability to enjoy foods. All other parameters had minimal levels within 1 day post op. With this information, we should expect to see patient's worst health related outcomes in the first 5 days after implant placement with a subsequent improvement in the 5-7 days range. Along with pain, swelling is also a common postoperative outcome [29] [30] [31]. It has mainly been reported as a patient-centered outcome using the Visual Analogue Scale [30] [31] and Numeric Rating Scale [29] after implant placement, bone grafting and other periodontal and oral surgical procedures. It peaks on the second and third day and its severity is dependent on procedure type, duration of surgery, amount of anesthetic used and periosteal releasing incisions [29] [30] [31].

Evidence on clinically-measured swelling is scarce due to methodological challenges, as wound healing is a delicate process and the tissue should be left undisturbed. Rotenberg and Tatakis [52] measured intraoral swelling after connective tissue grafting using a stent. Ege and Najavof [53] measured extraoral swelling following third molar extractions as the distance between the facial landmarks of the angle of the mandible, ear tragus, ala of nose, outer corned of eye, labial commissure and mentus. On the other hand, Weber and Griffin [54] measured extraoral swelling following orthognathic surgery using standardized photos.

Despite technological advances, swelling following implant placement is still mainly reported subjectively as a patient-centered outcome and clinical measurements are

lacking. Our group previously developed a novel digital protocol to evaluate swelling following guided bone regeneration. Therefore, the aim of this prospective study is to quantify post-implant placement edema and to correlate it with oral health-related quality of life.

Chapter 2
Materials and Methods:

Study population and design

Study population comprised of patients referred to the Graduate Periodontics Clinic of Marquette University School of Dentistry for single implant placement. Patients were recruited for this prospective observational study from October 2020 to November 2022 (IRB# HR-3502, approved on 11/21/2019). Patients were adults (18-75 years) with a stable periodontium and systemically healthy or with controlled conditions (American Academy of Anesthesiologists classification I or II). Specific health-related exclusion criteria were: (1) smoking, (2) uncontrolled periodontal or systemic disease, (3) pregnancy, (4) use of medication that impairs wound healing (bisphosphonates, steroids, etc.) and (5) inability to use ibuprofen. Patients, able and willing to provide informed consent, agreed not to wear a tooth replacement for 14 days following the procedure and site-specific inclusion criteria were: (1) single tooth-bound site, (2) simple implant placement without addition of autogenous or non-autogenous hard or soft tissue grafting or need for sinus lift (3) placement of cover screw and healing by primary closure.

Surgical procedures and intra-surgical measurements

All surgical procedures were performed by trained periodontal residents who followed standardized surgical protocol under the direct faculty supervision. All measurements were recorded by a trained clinician (JVR). After administration of local anesthesia (lidocaine 2% and epinephrine 1:100,000), a crestal incision (lingually/palatally biased) was made on the edentulous site extending to intrasulcular incisions on the distal aspect of the anterior tooth and mesial aspect of the posterior tooth

adjacent to the edentulous site. A full thickness flap was reflected for complete visualization of the bone anatomy by elevating past the mucogingival junction and approximately 5mm past the alveolar crest on the buccal aspect. The lingual flap was minimally elevated. Flap thickness was recorded at 1mm coronal and 1mm apical to the mucogingival junction using a wax caliper (Iwanson spring wax caliper, HuFriedy, Chicago, IL). Implant drilling sequence was followed according to manufacturer's instructions and a tapered rough surface implant was placed at crestal bone level. Implant placement was confirmed by faculty clinically and radiographically and flaps were secured using 4-0 vicryl (Coated Vicryl suture, Ethicon, Guaynabo, Puerto Rico, USA) simple interrupted sutures. If a dehiscence or fenestration was detected following implant placement dictating need for grafting, the patient was excluded from the study and biomaterials were added to the area according to patient needs. Duration of surgery was recorded in minutes starting from first local anesthetic administration until the completion of last suture.

Patients were prescribed antibiotics (amoxicillin 500mg three times a day for 7 days or clindamycin 300mg three times a day for 7 days if penicillin allergy was present). Ibuprofen 600mg was recommended for pain management (three times a day for the first 2 days and as needed afterwards). An antimicrobial rinse (Chlorhexidine rinse 0.12% two times a day for 2 weeks) was prescribed to all patients, whereas corticosteroids were not prescribed. Sutures were removed at the 14-day follow-up appointment.

Intra-oral scan measurements: ridge width, height, and volumetric measurements

Intra-oral scans (Trios3, 3Shape, Copenhagen, Denmark) were recorded immediately pre-surgery (PS), immediately post-operatively (IP), and at 2 (2D), 7 (7D), 14 days (14D) and 2 months (2M). The scans were converted to STL files and a professional engineering software (Geomagic Control X, Santa Clara, CA, USA) was used for calculation of ridge width, height, and volume by a trained clinician (JVR). The IP scan was used as the reference scan and mesiodistal, buccolingual and occlusal axes were defined based on the orientation of the teeth adjacent the edentulous space and the occlusal plane (Figure 1). An initial automatic registration of all scans was performed by the software and then, the remaining teeth were used as masks to increase accuracy of registration.

Ridge width and height measurement methodology

The reference IP scan was paired with all other scans for a pairwise recording of width and height measurements. The middle sagittal cross section of the edentulous ridge was used for analysis. As in Figure 2, a reference line parallel to the occlusal plane was drawn on top of the edentulous soft tissue crest on the IP scan. Then, a line parallel to the reference line and 3mm apical to it was drawn. At that level, the measurements of ridge width, and ridge width difference toward the buccal and lingual were recorded. A height difference measurement between IP and all other scans was recorded in the buccolingual middle of the edentulous site as well as at the site with maximum height distance between the scans.

Volumetric measurement methodology

After all scans were merged, the region of interest (ROI) was defined. ROI references were the mesial and distal aspects of the teeth adjacent to the edentulous area, the occlusal plane and a plane parallel to the occlusal which was located 5mm apical to the soft tissue crest (Figure 3). ROI volume was calculated in each scan and data are presented as percentage volume difference from IP scan.

Clinical measurements

Gingival width was measured before surgery and at 2 months with a UNC periodontal probe.

Patient-reported outcomes measures (PROMs)

Visual Analogue Scale (VAS) for pain, swelling and difficulty of mouth opening as well as Oral Health Impact Profile -14 (OHIP-14) were recorded immediately before the procedure and at 2 (2D), 7 (7D) and 14 days (14D) and 2 months (2M).

Statistical analysis

Using G*Power version 3.1.9.6 (Universitat Kiel, Germany), an estimated study sample of 26 patients with 5 measurements over time is expected to achieve more than 90% power with an effect size of 0.25 and an alpha of 0.05. Anticipating a drop-out rate of 20%, finally 31 subjects were recruited.

Statistical Software R 4.2.2 was used for all analysis. Statistical significance was determined when p value is less than 0.05. Summary statistics including mean and standard error were calculated. Pearson correlations were computed, and linear regression analysis was performed by R package-Im. Paired two sample t-test was implemented to

test the within group differences across different time points and non-paired two samples t-test was used to test the difference between different variables.

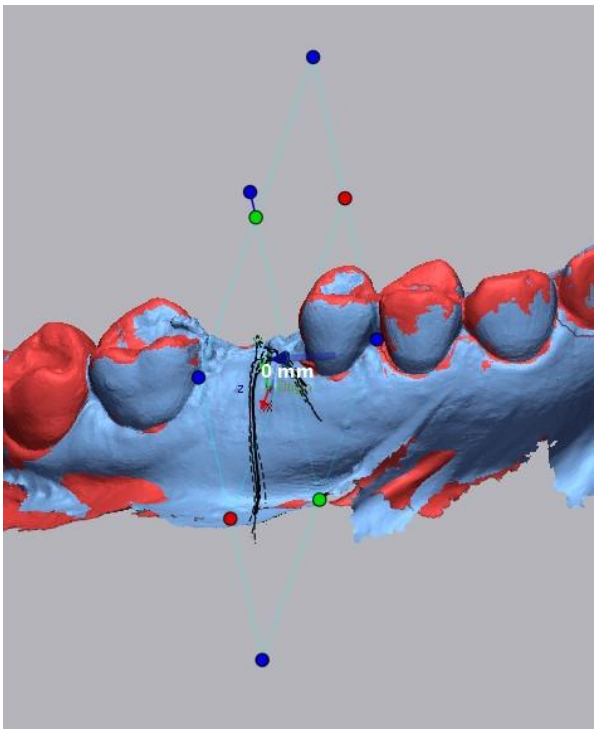

Figure 1: Intra-oral scan measurement methodology: Selection of measurement location. After registration of all scans, the cross section in the middle of the edentulous site was selected as the location for width and height measurements.

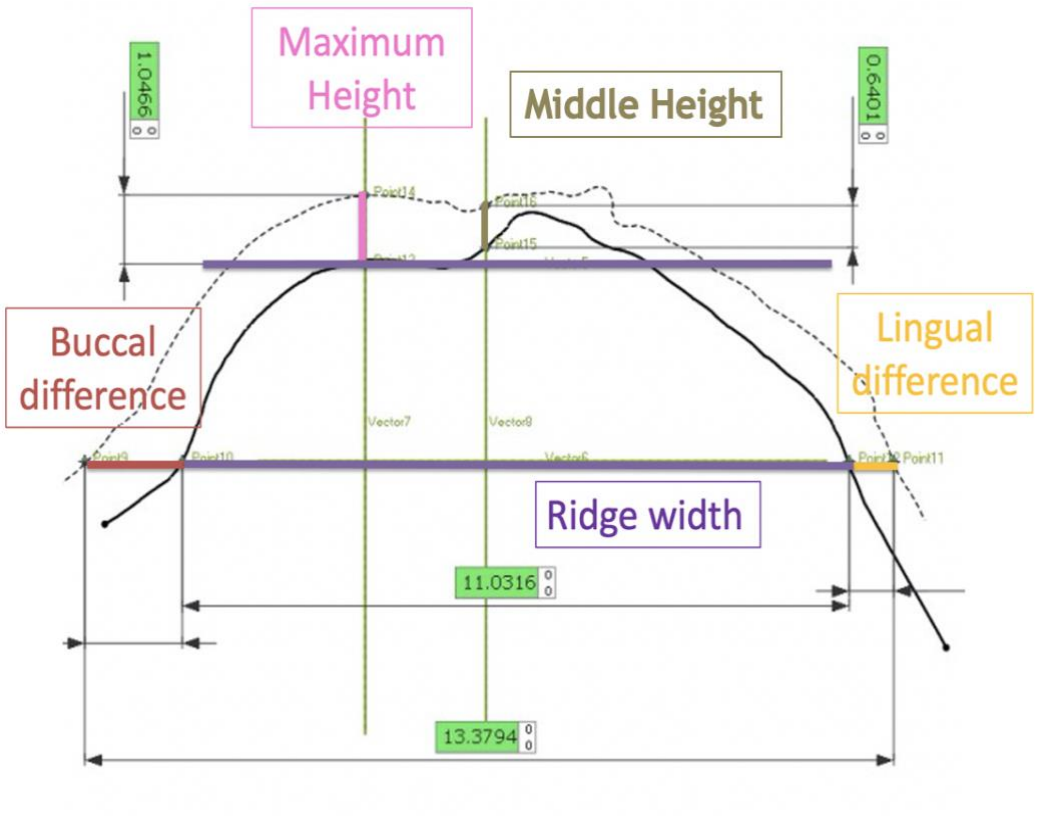

Figure 2: Intra-oral scan measurement methodology*:* Width and height measurement. A pair-wise analysis was done at selected location (figure 1) between the IP scan and all other scans. In the middle cross section (presented in this figure), a reference line (top purple line) was drawn parallel to the occlusal plane on the soft tissue crest. Ridge width as well as ridge width difference toward the buccal (red line) and lingual (yellow line) were measured 3mm apical to the soft tissue crest line (bottom purple line). Height difference in the middle of the ridge (brown line) and maximum height difference (pink line) were also measured.

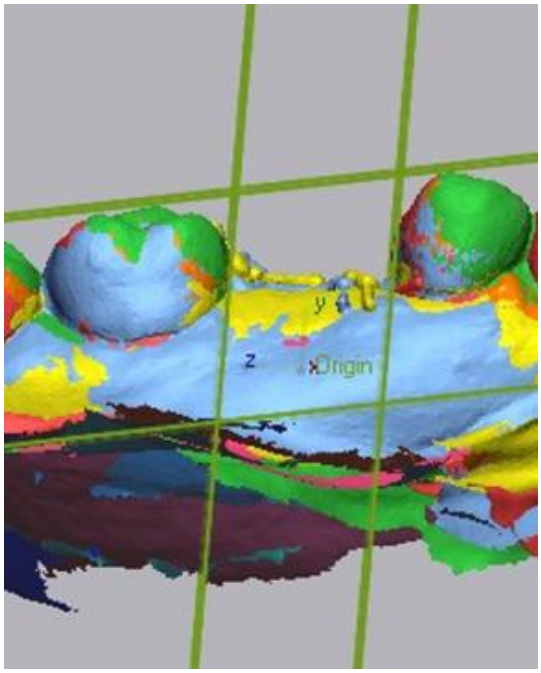

Figure 3: Intra-oral scan measurement methodology: Volumetric measurement.
After scan registration, ROI was selected based on landmark lines in the image. The landmark lines included were the most mesial and distal aspects of the teeth adjacent to the edentulous area, the occlusal plane and a plane parallel to the occlusal which was located 5mm apical to the soft tissue crest

Chapter 3
Results:

Thirty-one subjects were recruited for the study and 26 subjects completed all measurements (14 males; 54±3.3 years). Out of the five excluded subjects, two subjects had postoperative infections, two subjects received healing abutments instead of cover crews, and one subject received the healing abutment before recording the 2-month measurements. All included subjects (n=26) experienced uneventful wound healing, with no postoperative infection or cover screw exposure. None of the patients wore a provisional restoration during the entire follow-up period. Implants were placed at sites of 12 molars, 12 premolars and 2 anterior teeth. Pre-implant placement procedures included extraction and ridge preservation (10 sites), guided bone regeneration (6 sites), sinus lift (6 sites) and extraction alone (4 sites).

Intra-surgical measurements

Gingival width was 6.8±0.4mm and 6.9±0.5mm preoperatively and at 2M, respectively. Gingival and mucosal thickness was 0.7±0.08mm and 0.6±0.08mm, respectively, and were positively correlated ($r=0.62$, $p<0.0001$). Mean duration of surgery was 108.7±6.3 minutes.

Ridge width measurements

As in figure 4, ridge width increased from 11.3±0.3mm preoperatively to 12.9±0.4mm at IP, reached its peak value at 2D (14.6±0.3mm; difference with all-time points $p<0.01$), decreased at 7D to 13.3±0.3mm and reached IP levels at 14D

(12.7±0.3mm; 14D/IP p=0.44). At 2M, ridge width mean was 11.5±0.3mm (p=0.11 vs. PS).

Overall ridge width difference (figure 5) reflected a similar trend, increasing between PS/IP (1.5±0.04mm) and 2D/IP (PS/IP: 1.9±0.04mm vs. 2D/IP, p=0.28; 2D/IP vs. all postoperative time points p<0.001) and decreasing thereafter (Figure 5). As in figure 6 and 7, ridge width differences occurred toward both buccal (PS/IP: 0.9±0.04mm and 2D/IP: 1.2±0.03) and lingual (PS/IP: 0.67±0.02mm and 2D/IP: 0.5±0.01mm), with buccal experiencing more pronounced ridge increase at 2D/IP compared to lingual (p<0.0001). In a multiple regression analysis model, width difference toward the buccal affected overall ridge width difference at all early postoperative time points except 2D/IP (PS/IP p=0.0008, 2D/IP p=0.16, 7D/IP p=0.0008, 14D/IP p=0.0003). The opposite occurred between 2M/IP (lingual p=0.0056).

Ridge height measurements

As in figure 8 and 9, ridge height difference from IP was highest (p<0.001 compared to all other time points) at 2D (middle 1.1±0.03mm and maximum 1.4±0.02mm) and 7D (middle 0.7±0.03mm and maximum 1.2±0.03mm). The most significant decrease in height occurred between IP and 2M, (middle -0.22±0.03 and maximum -0.5±0.04mm; p<0.0001 for both).

Volumetric measurements

The percentage of volumetric difference (figure 10) presented a similar trend with the other parameters, peaking at 2D/IP (37.8±0.8mm^2; p<0.003 with all other time

points). Furthermore, volumetric changes from 2M/IP were statistically significantly different with all other time points (-11.4±0.5mm^2; p<0.0001).

Patient-reported outcome measures (PROMs)

VAS for pain, swelling and difficulty of mouth opening as well as OHIP-14 reached their peak values at 2D (1.7±0.1, 1.7±0.1, 0.7±0.05, 11.3±0.4). Severity and duration of pain, swelling and difficulty of mouth opening are summarized in table 1. VAS for pain (p=0.003), swelling (p=0.006) and difficulty of mouth opening (p=0.01) as well as OHIP-14 (p<0.001) improved between 2D and 7D. VAS for swelling (p=0.03) and OHIP-14 (p=0.008) further improved between 7D and 14D. All VAS variables reached preoperative levels by 7D (pain; p=0.07 and difficulty of mouth opening; p<0.0001) and 14D (swelling; p=0.18). OHIP-14 values at 14D (p=0.007) and 2M (p<0.0001) were significantly lower than preoperative values (Figure 11).

Correlations and regression analysis models

Clinically and statistically significant correlations are summarized in Table 2. Volume change was positively correlated with overall width difference at all time points except 2D/IP (PS/IP: r=0.67, p<0.0001; 2D/IP: r=0.15, p=0.45; 7D/IP: r=0.43, p=0.03; 14D/IP: r=0.46, p=0.02; 2M/IP: r=0.48, p=0.01) and both middle (7D/IP: r=0.7, p<0.001; 14D/IP: r=-0.68, p<0.0001; 2M/IP: r=0.56, p=0.003) and maximum height difference (7D/IP: r=0.57, p=0.002; 14D/IP: r=0.64, p<0.0001; 2M/IP: r=0.57, p=0.002). Mucosal thickness was correlated with ridge width at 7D days (r=0.42, p=0.03). Gingival (r=0.44, p=0.02) and mucosal thickness (r=0.58, p=0.002) were positively correlated with width difference between 2M/IP. Interestingly, patient-reported pain, swelling, difficulty

of mouth opening and OHIP-14 were not correlated with any of the clinically measured swelling parameters ($p>0.05$, data not shown).

In multiple regression analysis models with duration of surgery, gingival and mucosal thickness as independent variables, duration of surgery ($p=0.04$) negatively affected total ridge width difference between PS/IP and gingival ($p=0.04$) and mucosal thickness ($p=0.01$) affected maximum height difference at the same time point. At 2M, gingival thickness ($p=0.025$) and duration of surgery ($p=0.026$) had an effect on % volume difference from IP.

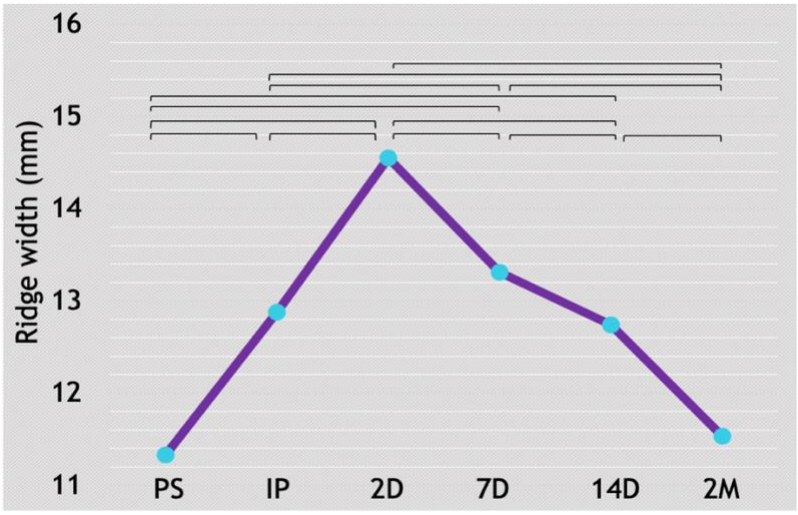

Figure 4. Ridge width.
The bars represent statistically significant differences between values of connected time points ($p<0.05$).

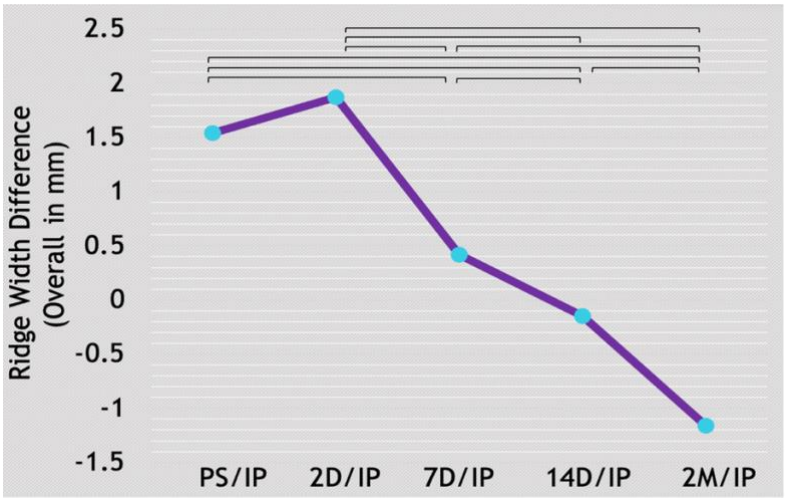

Figure 5. Overall ridge width difference from IP.
The bars represent statistically significant differences between values of connected time points ($p<0.05$).

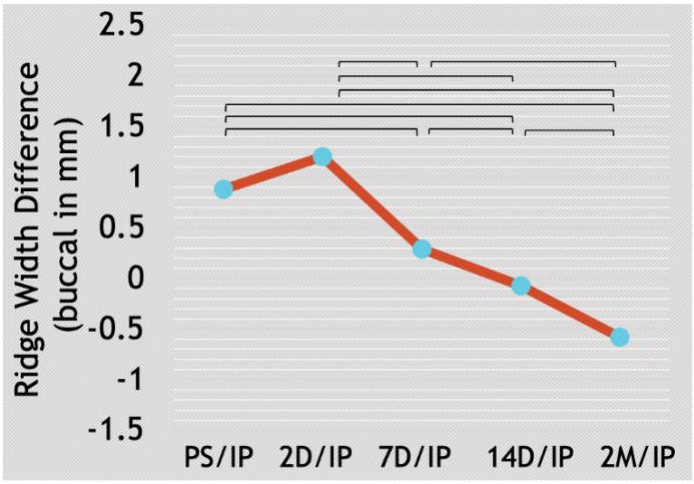

Figure 6. Ridge width difference toward the buccal aspect from IP.
The bars represent statistically significant differences between values of connected time points ($p<0.05$).

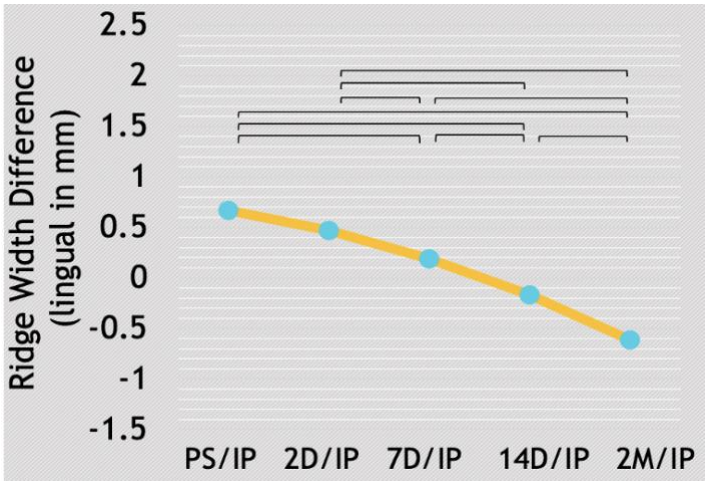

Figure 7. Ridge width difference toward the lingual aspect from IP.
The bars represent statistically significant differences between values of connected time points ($p<0.05$).

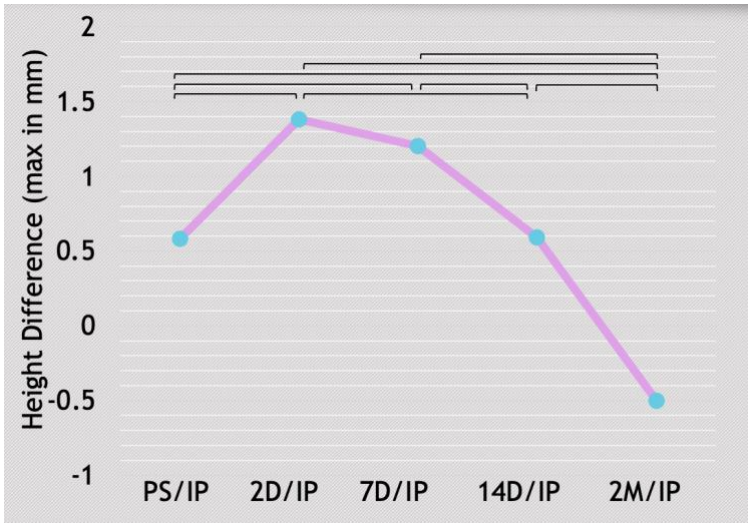

Figure 8. Maximum height difference from IP.
The bars represent statistically significant differences between values of connected time points ($p<0.05$).

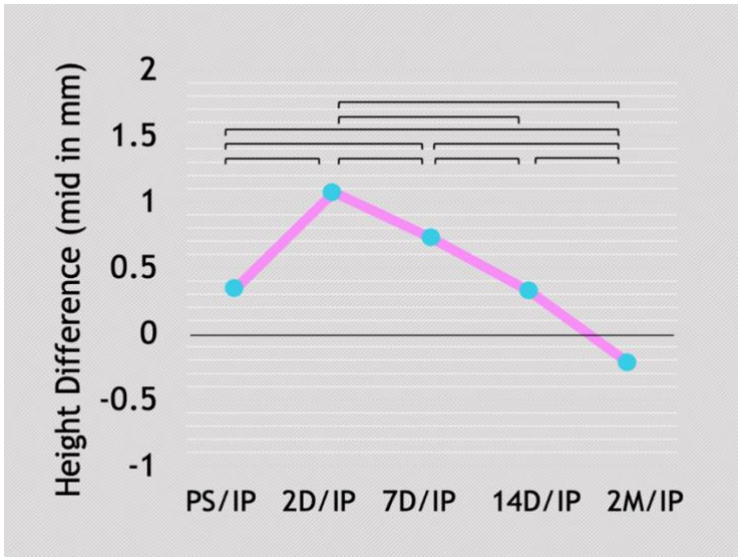

Figure 9. Middle (B) height difference from IP.
The bars represent statistically significant differences between values of connected time points ($p<0.05$).

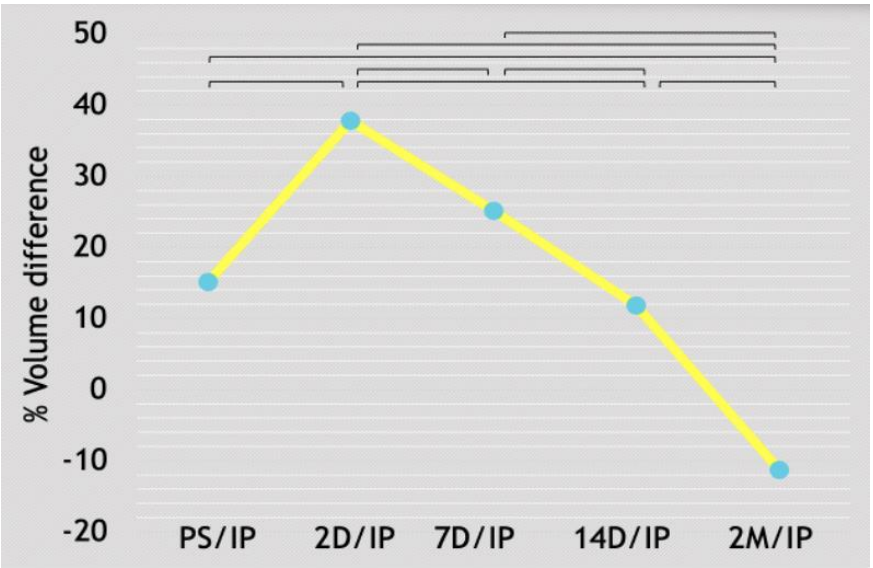

Figure 10. Percentage volume difference from IP.
The bars represent statistically significant differences between values of connected time points ($p<0.05$).

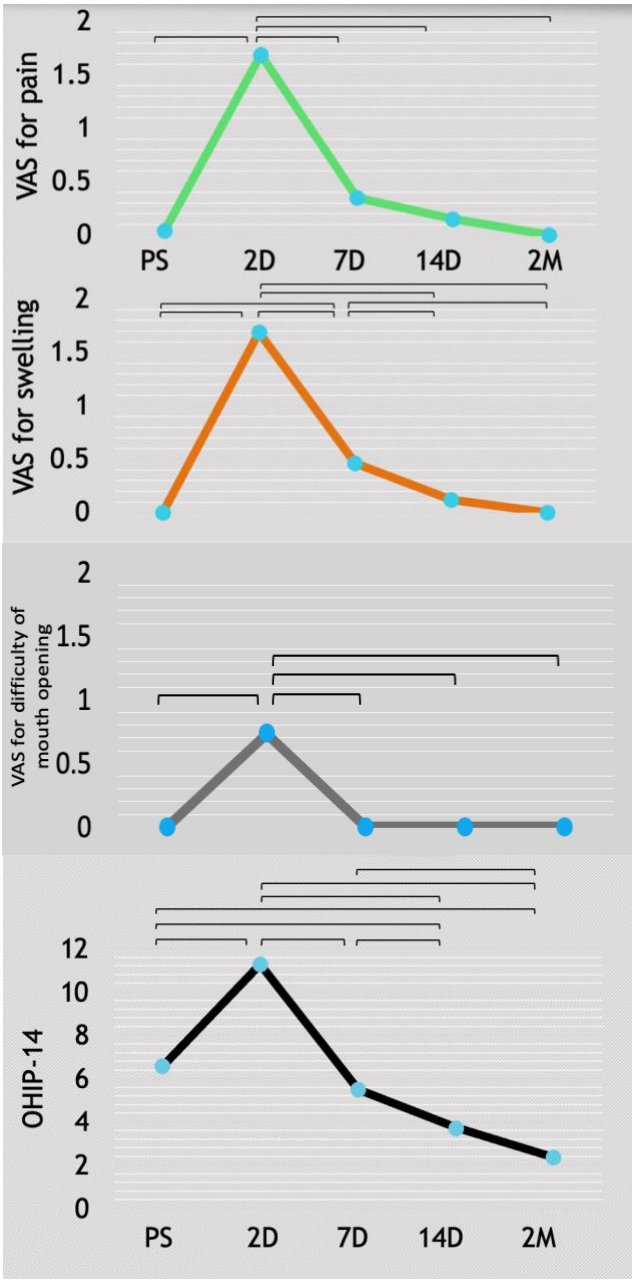

Figure 11. Patient centered outcome measures (PROMs); VAS for pain, VAS for Swelling, VAS for difficulty mouth opening and OHIP-14 questionnaire.
The bars on top of the graphs represent the statistically significant values.

Duration / Severity	Preop n/N (%)	2 days n/N (%)	7 days n/N (%)	14 days n/N (%)	2 months n/N (%)
No pain	25/26 (96.1)	9/26 (34.6)	21/26(80.7)	23/26 (88.4)	26/26 (100)
Mild (1-3)	1/26 (3.8)	14/26 (53.8)	4/26 (15.3)	3/26 (11.5)	0/26 (0)
Moderate (4-6)	0/26 (0))	2/26 (7.6)	1/26 (3.8)	0/26 (0)	0/26 (0)
Severe (7-10)	0/26 (0)	1/26 (3.8)	0/26 (0)	0/26 (0)	0/26 (0)

Duration / Severity	Preop n/N (%)	2 days n/N (%)	7 days n/N (%)	14 days n/N (%)	2 months n/N (%)
No swelling	26/26 (100)	11/26 (42.3)	20/26 (76.9)	24/26 (92.3)	26/26 (100)
Mild (1-3)	0/26 (0)	10/26 (38.4)	5/26 (19.2)	2/26 (7.6)	0/26 (0)
Moderate (4-6)	0/26 (0)	4/26 (15.3)	1/26 (3.8)	0/26 (0)	0/26 (0)
Severe (7-10)	0/26 (0)	1/26 (3.8)	0/26 (0)	0/26 (0)	0/26 (0)

Duration / Severity	Preop n/N (%)	2 days n/N (%)	7 days n/N (%)	14 days n/N (%)	2 months n/N (%)
No difficulty of mouth opening	26/26 (100)	17/26 (65.3)	26/26 (100)	26/26 (100)	26/26 (100)
Mild (1-3)	0/26 (0)	8/26 (30.7)	0/26 (0)	0/26 (0)	0/26 (0)
Moderate (4-6)	0/26 (0)	1/26 (3.8)	0/26 (0)	0/26 (0)	0/26 (0)
Severe (7-10)	0/26 (0)	0/26 (0)	0/26 (0)	0/26 (0)	0/26 (0)

Table 1. Severity and duration of pain, swelling and difficulty of mouth opening
n=number of patients experiencing specified symptom; N=total number of patients

Correlations (bolded p<0.05)										
Pearson's r	Width diff PS/IP	Width diff 2D/IP	Width diff 7D/IP	Width diff 14D/IP	Width diff 2M/IP	Height diff 2D/IP	Height diff 7D/IP	Height diff 14D/IP	Height diff 2M/IP	Width 7D
Vol % IP-PS/PS	**0.67**	-0.08	**-0.76**	**-0.56**	**-0.56**	0.06	-0.19	0.08	-0.24	-0.2
Vol % 2D-IP/IP	0.09	0.15	0.17	0.1	-0.01	0.38	0.37	0.11	0.28	-0.07
Vol % 7D-IP/IP	-0.13	0.07	**0.43**	**0.43**	0.1	0.21	**0.57**	0.35	0.35	-0.01
Vol % 14D-IP/IP	0.01	0.25	0.23	**0.46**	-0.14	0.05	0.3	**0.64**	0.31	-0.24
Vol % 2M-IP/IP	**-0.5**	0.17	**0.66**	**0.53**	**0.48**	0.19	0.28	0.25	**0.57**	0.02
Mucosal thickness	0.12	-0.36	0.17	0	**0.58**	0.37	0.25	0.09	0.05	**0.42**
Gingival thickness	0.16	-0.06	0.29	0.27	**0.44**	0.07	0.07	-0.01	0.16	0.33

Table 2. Pearson's correlations table.
Statistically significant correlations are bolded. ($p<0.05$).

Chapter 4
Discussion

This is the first study to clinically quantify soft tissue edema and attempt to correlate it with PROMs after implant placement. Edema showed a maximal response measured in width, height, and volume on postoperative day 2. Clinically, this is significant because patient usually require a temporary restoration during the healing period. Due to the expected edema, an immediate temporary restoration should not have buccal and lingual ridge coverage and a safety distance between the restoration margin and the soft tissue crest should be carefully created. The maximum mean height difference from IP during healing was 1.38mm at 2 days, however the patient who experienced the most height increase from IP and marked the upper limit of all height difference ranges showed a 2.82mm increase on postoperative day 7. Therefore, and in order to account for all patients, it is suggested that temporary restoration placement should be delayed until day 7. If immediate temporary restoration is placed, a minimum distance of 3mm between the apical margin of the restoration and soft tissue should be present.

The difference in timing and magnitude of swelling toward the buccal and lingual provided insight on the relationship between flap manipulations and immediate postoperative soft tissue changes. The buccal flap showed maximal edema between 2D/IP, whereas the lingual flap exhibited more edema between PS/IP. This may be related to the different extent of flap elevation and intra-surgical flap manipulations between the buccal and lingual flap. On the buccal, the flap was elevated past the mucogingival junction and until approximately 5mm from the alveolar crest for

visualization of the bone architecture. Additionally, the elevated buccal flap is usually more manipulated by placing periosteal elevators on it for retraction and better visualization of the osteotomy and implant position. On the other hand, the lingual flap is minimally elevated past the lingual alveolar crest and is rarely manipulated to allow for visualization. These are novel findings regarding swelling after simple flap elevation and are consistent with findings from our group following guided bone regeneration where the buccal flap underwent full thickness elevation, vertical and periosteal releasing incisions compared to a minimally elevated and later minimally swollen lingual flap (Kofina et al unpublished data). However, the scarcity of data on clinically evaluated soft tissue swelling precludes further comparisons.

Gingival and mucosal thickness as well as duration of surgery were investigated as possible determinants of soft tissue swelling. All investigated determinants affect swelling in width and height recorded immediately after surgery. The deleterious effects of a longer surgery have been previously discussed in the literature [55] [Kofina et al unpublished data]. In a study by Levin et al [55], a longer duration of surgery negatively affects postoperative inflammation and flap collagen concentration. In thicker flaps (>1mm, 23% of sites in current sample), the increased proportion of connective tissue and therefore the increased number of intercellular spaces available for fluid retention may be responsible for the correlation between soft tissue thickness and immediate postoperative swelling due to longer surgical manipulations. Within the limits of this clinical study, this hypothesis is supported by the location of gingival and mucosal thickness measurements (1mm coronal and apical of the mucogingival junction) which is

an area where the flap allows for additional movement once mucosa is elevated. However, this hypothesis needs to be further investigated in animal studies.

VAS for pain, swelling and difficulty of mouth opening as well as OHIP-14 followed a similar trajectory as clinically measured swelling by peaking on postoperative day 2 and improving thereafter. Even though a small proportion of our patients experienced moderate or severe pain (3/26), swelling (5/26) and difficulty of mouth opening (1/26) on postoperative day 2, the majority of patients experienced no or mild symptoms (80.7-100%) throughout the first 2 weeks of healing (table 1). These findings are in accordance with previous studies reporting high frequency of patients with zero or mild pain on postoperative day 1 (89.4% by Al-Khabbaz et al [36] vs. 88.2% on postoperative day 2 in the current study) and significant recovery by postoperative day 7 (zero or mild pain prevalence: 96.2% by Al-Khabbaz et al [36] vs. 96% in the current study). Evidence on patient-reported swelling agree with the current study peaking on 1-3 days following implant placement with a median of 1/10 on postoperative day 1 [29] or 3 [31]. A significant decrease in swelling was observed by postoperative day 7 (96% of patients reporting zero or mild swelling) which is similar to the reported median recovery from swelling by 4-5 days [45]. Improvement in mouth opening occurred after postoperative day 2 in agreement with Kahn et al [45].

Oral-health related quality of life reached preoperative levels on postoperative day 7 as reflected by validated OHIP-14 questionnaire [46]. Interestingly, OHIP-14 values decreased further until postoperative month 2, while other PROMs reached preoperative levels by 7 or 14 days. Since patients were asymptomatic preoperatively, the continuous improvement of oral-health related quality of life after postoperative day 7 may be related

to the resumption of the overall dental treatment plan. Function and esthetics are areas that are also evaluated by OHIP-14 and their improvement may have been responsible for the decrease in OHIP-14 values during restorative therapy while waiting for implant osseointegration. OHIP-14 is rarely used for evaluation of postoperative oral health-related quality of life, therefore direct comparisons may not be possible. In a study by Lindeboom and van Wijk [56] following implant placement on edentulous maxillae with or without flap, OHIP-14 values were lower at one month after flap surgery compared to preoperatively. However, authors do not discuss why this happens.

Whereas clinically measured swelling and patient-reported outcomes follow the same trajectory, they were not correlated. This indicates that other factors are related to pain and swelling perception by patients. Psychological factors that have been correlated with acute post-surgical pain are pain catastrophizing, optimism, expectation of pain, neuroticism, state and trait anxiety, negative affect and depression [57]. Even though some of them such as optimism, neuroticism and anxiety trait are personality traits and remain stable over time, others such as state anxiety are transitory emotional states or conditions and vary over time. There is little evidence on effect of psychological factors on postoperative outcomes following oral surgical procedures. In a study by Eli et al [58], state of anxiety best predicted patient's pain perception. Similarly, Hashem et al [59] reported that state anxiety was highest the day of the surgery and according to Kim et al [60], it affected pain severity on postoperative day 1. Future studies should investigate the relationship between clinically evaluated wound healing and patient-reported outcomes by collecting clinical, patient-reported, and psychological data.

The strengths of this study rely on the standardization of the methodology including the surgical site extent (single tooth-bound), surgical technique as well as the use of a noninvasive instrument and novel methodology to record and measure the two- and three-dimensional soft tissue changes using an intraoral scanner. Additionally, only patients with uncomplicated healing were included in the study who did not wear a provisional restoration for the 2 postoperative months. They followed a standardized postoperative medication regimen which did not include corticosteroids. The limitations of the study include the low number of patients with implants placed in the esthetic area (n=12) as these patients usually require a temporary restoration. Due to the strict standardization of surgery, swelling at sites receiving implant placement and simultaneous healing abutment, biomaterial placement or crestal sinus lift were not followed-up. Future research should focus on sites receiving implant placement and simultaneous bone augmentation procedures such as guided bone regeneration or sinus lift in order to provide clinical guidelines for temporary restoration timing and reduction.

Chapter 5
Conclusion

The present study clinically quantified soft tissue swelling after implant placement with a novel two- and three-dimensional intraoral scanner methodology, provided guidelines to clinicians who deliver temporary restorations postoperatively and presented patient-reported pain, swelling and difficulty of mouth opening as well as oral health-related quality of life. Clinically measured and patient-reported outcomes showed maximal response on postoperative day 2 and improved thereafter. However, they were not correlated. Duration of surgery, gingival and mucosal thickness affected immediate postoperative swelling.

Bibliography

1. Holmgren EP, Seckinger RJ, Kilgren LM, Mante F. Evaluating parameters of osseointegrated dental implants using finite element analysis--a two-dimensional comparative study examining the effects of implant diameter, implant shape, and load direction. J Oral Implantol. 1998;24(2):80-8. doi: 10.1563/1548-1336(1998)024<0080:EPOODI>2.3.CO;2. PMID: 9835834.

2. Bahat O, Sullivan RM. Parameters for successful implant integration revisited part I: immediate loading considered in light of the original prerequisites for osseointegration. Clin Implant Dent Relat Res. 2010 May;12 Suppl 1:e2-12. doi: 10.1111/j.1708-8208.2010.00279.x. Epub 2010 Apr 23. PMID: 20455902.

3. Bahat O, Sullivan RM. Parameters for successful implant integration revisited part II: algorithm for immediate loading diagnostic factors. Clin Implant Dent Relat Res. 2010 May;12 Suppl 1:e13-22. doi: 10.1111/j.1708-8208.2010.00280.x. Epub 2010 Apr 23. PMID: 20455906.

4. Alghamdi HS. Methods to Improve Osseointegration of Dental Implants in Low Quality (Type-IV) Bone: An Overview. J Funct Biomater. 2018 Jan 13;9(1):7. doi: 10.3390/jfb9010007. PMID: 29342830; PMCID: PMC5872093.

5. Feine JS, Dufresne E, Boudrias P, Lund JP. Outcome assessment of implant-supported prostheses. J Prosthet Dent. 1998 May;79(5):575-9. doi: 10.1016/s0022-3913(98)70179-9. PMID: 9597611.

6. Katsoulis J, Takeichi T, Sol Gaviria A, Peter L, Katsoulis K. Misfit of implant prostheses and its impact on clinical outcomes. Definition, assessment and a systematic review of the literature. Eur J Oral Implantol. 2017;10 Suppl 1:121-138. PMID: 28944373.

7. Salvi GE, Bosshardt DD, Lang NP, Abrahamsson I, Berglundh T, Lindhe J, Ivanovski S, Donos N. Temporal sequence of hard and soft tissue healing around titanium dental implants. Periodontol 2000. 2015 Jun;68(1):135-52. doi: 10.1111/prd.12054. PMID: 25867984.

8. Thoma, DS, Gil, A, Hämmerle, CHF, Jung, RE. Management and prevention of soft tissue complications in implant dentistry. *Periodontol 2000*. 2022; 88: 116– 129. doi:https://doi.org/10.1111/prd.12415

9. Kan JY, Rungcharassaeng K, Umezu K, Kois JC. Dimensions of peri-implant mucosa: an evaluation of maxillary anterior single implants in humans. J Periodontol. 2003 Apr;74(4):557-62. doi: 10.1902/jop.2003.74.4.557. PMID: 12747463.

10. Kan JYK, Rungcharassaeng K, Deflorian M, Weinstein T, Wang HL, Testori T. Immediate implant placement and provisionalization of maxillary anterior single implants. Periodontol 2000. 2018 Jun;77(1):197-212. doi: 10.1111/prd.12212. Epub 2018 Feb 25. PMID: 29478284.

11. Tarnow D, Elian N, Fletcher P, Froum S, Magner A, Cho SC, Salama M, Salama H, Garber DA. Vertical distance from the crest of bone to the height of the interproximal papilla between adjacent implants. J Periodontol. 2003 Dec;74(12):1785-8. doi: 10.1902/jop.2003.74.12.1785. PMID: 14974820.

12. Negruțiu BM, Moldovan AF, Staniș CE, Pusta CTJ, Moca AE, Vaida LL, Romanec C, Luchian I, Zetu IN, Todor BI. The Influence of Gingival Exposure on Smile Attractiveness as Perceived by Dentists and Laypersons. Medicina (Kaunas). 2022 Sep 13;58(9):1265. doi: 10.3390/medicina58091265. PMID: 36143942; PMCID: PMC9505136.

13. Brizuela M, Ines D. Excessive Gingival Display. [Updated 2023 Mar 19]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK470437/

14. van Brakel R, Noordmans HJ, Frenken J, de Roode R, de Wit GC, Cune MS. The effect of zirconia and titanium implant abutments on light reflection of the supporting soft tissues. Clin Oral Implants Res. 2011 Oct;22(10):1172-1178. doi: 10.1111/j.1600-0501.2010.02082.x. Epub 2011 Jan 20. PMID: 21251080.

15. Jung RE, Zembic A, Pjetursson BE, Zwahlen M, Thoma DS. Systematic review of the survival rate and the incidence of biological, technical, and aesthetic complications of single crowns on implants reported in longitudinal studies with a mean follow-up of 5 years. Clin Oral Implants Res. 2012 Oct;23 Suppl 6:2-21. doi: 10.1111/j.1600-0501.2012.02547.x. PMID: 23062124.

16. Adibrad M, Shahabuei M, Sahabi M. Significance of the width of keratinized mucosa on the health status of the supporting tissue around implants supporting overdentures. J Oral Implantol. 2009;35(5):232-7. doi: 10.1563/AAID-JOI-D-09-00035.1. PMID: 19882819.

17. Lin CY, Chen Z, Pan WL, Wang HL. Impact of timing on soft tissue augmentation during implant treatment: A systematic review and meta-analysis. Clin Oral Implants Res. 2018 May;29(5):508-521. doi: 10.1111/clr.13148. Epub 2018 Mar 30. PMID: 29603808.

18. Greenstein G, Cavallaro J. The clinical significance of keratinized gingiva around dental implants. Compend Contin Educ Dent. 2011 Oct;32(8):24-31; quiz 32, 34. PMID: 22073807.

19. Evans, C.D.J. and Chen, S.T. (2008), Esthetic outcomes of immediate implant placements. Clinical Oral Implants Research, 19: 73-80. https://doi.org/10.1111/j.1600-0501.2007.01413.x

20. Pontoriero R, Carnevale G. Surgical crown lengthening: a 12-month clinical wound healing study. J Periodontol. 2001 Jul;72(7):841-8. doi: 10.1902/jop.2001.72.7.841. PMID: 11495130.

21. Kalsi HJ, Bomfim DI, Hussain Z, Rodriguez JM, Darbar U. Crown Lengthening surgery: An overview. Prim Dent J. 2020 Jan 29;8(4):48-53. doi: 10.1308/205016820828463870. PMID: 32127094.

22. Mugri MH, Sayed ME, Nedumgottil BM, Bhandi S, Raj AT, Testarelli L, Khurshid Z, Jain S, Patil S. Treatment Prognosis of Restored Teeth with Crown Lengthening vs. Deep Margin Elevation: A Systematic Review. Materials (Basel). 2021 Nov 8;14(21):6733. doi: 10.3390/ma14216733. PMID: 34772259; PMCID: PMC8587366.

23. Goodacre CJ, Naylor WP. Single implant and crown versus fixed partial denture: A cost-benefit, patient-centred analysis. Eur J Oral Implantol. 2016;9 Suppl 1:S59-68. PMID: 27314112.

24. Wang, Y., Bäumer, D., Ozga, AK. *et al.* Patient satisfaction and oral health-related quality of life 10 years after implant placement. *BMC Oral Health* **21**, 30 (2021). https://doi.org/10.1186/s12903-020-01381-3

25. McDermott NE, Chuang SK, Woo VV, Dodson TB. Complications of dental implants: identification, frequency, and associated risk factors. Int J Oral Maxillofac Implants. 2003 Nov-Dec;18(6):848-55. PMID: 14696660.

26. Misch K, Wang HL. Implant surgery complications: etiology and treatment. Implant Dent. 2008 Jun;17(2):159-68. doi: 10.1097/ID.0b013e3181752f61. PMID: 18545047.

27. Camargo IB, Van Sickels JE. Surgical complications after implant placement. Dent Clin North Am. 2015 Jan;59(1):57-72. doi: 10.1016/j.cden.2014.08.003. Epub 2014 Sep 16. PMID: 25434559.

28. Camps-Font O, Figueiredo R, Valmaseda-Castellón E, Gay-Escoda C. Postoperative Infections After Dental Implant Placement: Prevalence, Clinical Features, and Treatment. Implant Dent. 2015 Dec;24(6):713-9. doi: 10.1097/ID.0000000000000325. PMID: 26384096.

29. Mei C-C, Lee F-Y, Yeh H-C. Assessment of pain perception following periodontal and implant surgeries. J Clin Periodontol. 2016;43:1151–1159.

30. Yao J, Lee KK, McGrath C, Wu YN, Li KY, Mattheos N. Comparison of patient-centered outcomes after routine implant placement, teeth extraction, and periodontal surgical procedures. Clin Oral Impl Res 2017;28:373–380.

31. Tan WC, Krishnaswamy G, Ong MM, Lang NP. Patient-reported outcome measures after routine periodontal and implant surgical procedures. J Clin Periodontol. 2014 Jun;41(6):618-24. doi: 10.1111/jcpe.12248. Epub 2014 Apr 21. PMID: 24593854.

32. Annibali S, Ripari M, LA Monaca G, Tonoli F, Cristalli MP. Local complications in dental implant surgery: prevention and treatment. Oral Implantol (Rome). 2008 Apr;1(1):21-33. Epub 2008 Jun 16. PMID: 23285333; PMCID: PMC3476500.

33. Wu X, Ye M, Sun J, *et al.* Patient-reported outcome measures following surgeries in implant dentistry and associated factors: a cross-sectional study. *BMJ Open* 2022;**12:**e059730. doi: 10.1136/bmjopen-2021-059730

34. Pippi R. Post-Surgical Clinical Monitoring of Soft Tissue Wound Healing in Periodontal and Implant Surgery. Int J Med Sci. 2017 Jul 18;14(8):721-728. doi: 10.7150/ijms.19727. PMID: 28824306; PMCID: PMC5562125.

35. Muller E, Ríos Calvo MP. Pain and dental implantology: sensory quantification and affective aspects. Part I: At the private dental office. Implant Dent. 2001;10(1):14-22. doi: 10.1097/00008505-200101000-00007. PMID: 11307642.

36. Al-Khabbaz AK, Griffin TJ, Al-Shammari KF. Assessment of pain associated with the surgical placement of dental implants. J Periodontol. 2007 Feb;78(2):239-46. doi: 10.1902/jop.2007.060032. PMID: 17274712.

37. Aldosari M, Mendes SDR, Aldosari A, Aldosari A, de Abreu MHNG. Factors associated with oral pain and oral health-related productivity loss in the USA, National Health and Nutrition Examination Surveys (NHANES), 2015-2018. PLoS One. 2021 Oct 11;16(10):e0258268. doi: 10.1371/journal.pone.0258268. PMID: 34634083; PMCID: PMC8504739.

38. Maggirias J, Locker D. Psychological factors and perceptions of pain associated with dental treatment. Community Dent Oral Epidemiol. 2002 Apr;30(2):151-9. doi: 10.1034/j.1600-0528.2002.300209.x. PMID: 12000356.

39. Tonetti MS, Fourmousis I, Suvan J, Cortellini P, Brägger U, Lang NP; European Research Group on Periodontology (ERGOPERIO). Healing, post-operative morbidity and patient perception of outcomes following regenerative therapy of deep intrabony defects. J Clin Periodontol. 2004 Dec;31(12):1092-8. doi: 10.1111/j.1600-051X.2004.00615.x. PMID: 15560811.

40. Villalobos-Rodelo JJ, Medina-Solís CE, Maupomé G, Lamadrid-Figueroa H, Casanova-Rosado AJ, Casanova-Rosado JF, Márquez-Corona Mde L. Dental needs and socioeconomic status associated with utilization of dental services in the presence of dental pain: a case-control study in children. J Orofac Pain. 2010 Summer;24(3):279-86. PMID: 20664829.

41. Prego-Domínguez J, Khazaeipour Z, Mallah N, Takkouche B. Socioeconomic status and occurrence of chronic pain: a meta-analysis. Rheumatology (Oxford). 2021 Mar 2;60(3):1091-1105. doi: 10.1093/rheumatology/keaa758. PMID: 33276382.

42. Nomura LH, Bastos JL, Peres MA. Dental pain prevalence and association with dental caries and socioeconomic status in schoolchildren, Southern Brazil, 2002. Braz Oral Res. 2004 Apr-Jun;18(2):134-40. doi: 10.1590/s1806-83242004000200008. Epub 2004 Aug 5. PMID: 15311316.

43. Bastos JL, Nomura LH, Peres MA. Dental pain, socioeconomic status, and dental caries in young male adults from southern Brazil. Cad Saude Publica. 2005 Sep-Oct;21(5):1416-23. doi: 10.1590/s0102-311x2005000500014. Epub 2005 Sep 12. PMID: 16158147.

44. Kamankatgan S, Pimkhaokham A, Krisdapong S. Patient-based outcomes following surgical implant placements. Clin Oral Implants Res. 2017 Jan;28(1):17-23. doi: 10.1111/clr.12608. Epub 2015 May 7. PMID: 25952925.

45. Kahn A, Masri D, Shalev T, Meir H, Sebaoun A, Chaushu L. Patients' Perception of Recovery after Dental Implant Placement. Medicina (Kaunas). 2021 Oct 15;57(10):1111. doi: 10.3390/medicina57101111. PMID: 34684148; PMCID: PMC8538387.

46. Slade GD. Derivation and validation of a short-form oral health impact profile. Community Dent Oral Epidemiol. 1997 Aug;25(4):284-90. doi: 10.1111/j.1600-0528.1997.tb00941.x. PMID: 9332805.

47. Husain FA, Tatengkeng F. Oral Health-Related Quality of Life Appraised by OHIP-14 Between Urban and Rural Areas in Kutai Kartanegara Regency, Indonesia: Pilot Pathfinder Survey. Open Dent J. 2017 Oct 31;11:557-564. doi: 10.2174/1874210601711010557. PMID: 29238416; PMCID: PMC5712656.

48. Papaioannou W, Oulis CJ, Yfantopoulos J. The oral health related quality of life in different groups of senior citizen as measured by the OHIP-14 questionnaire.

49. Campos, L.A.; Peltomäki, T.; Marôco, J.; Campos, J.A.D.B. Use of Oral Health Impact Profile-14 (OHIP-14) in Different Contexts. What Is Being Measured? *Int. J. Environ. Res. Public Health* **2021**, *18*, 13412. https://doi.org/10.3390/ijerph182413412

50. Klink A, Groten M, Huettig F. Complete rehabilitation of compromised full dentitions with adhesively bonded all-ceramic single-tooth restorations: Long-term outcome in patients with and without amelogenesis imperfecta. J Dent. 2018 Mar;70:51-58. doi: 10.1016/j.jdent.2017.12.011. Epub 2017 Dec 21. PMID: 29275170.

51. Alzarea BK. Assessment and Evaluation of Quality of Life (OHRQoL) of Patients with Dental Implants Using the Oral Health Impact Profile (OHIP-14) - A Clinical Study. J Clin Diagn Res. 2016 Apr;10(4):ZC57-60. doi: 10.7860/JCDR/2016/18575.7622. Epub 2016 Apr 1. PMID: 27190953; PMCID: PMC4866251.

52. Rotenberg SA, Tatakis DN. Dimensional changes during early healing after a subepithelial connective tissue graft procedure. J Periodontol. 2014 Jul;85(7):884-9. doi: 10.1902/jop.2013.130478. Epub 2013 Nov 11. PMID: 24215201.

53. Ege B, Najafov E. Comparison of two different suture knot techniques on postoperative morbidity after impacted mandibular third molar surgery. J Stomatol Oral Maxillofac Surg. 2020 Jun;121(3):206-212. doi: 10.1016/j.jormas.2020.02.002. Epub 2020 Feb 19. PMID: 32061709.

54. Weber CR, Griffin JM. Evaluation of dexamethasone for reducing postoperative edema and inflammatory response after orthognathic surgery. J Oral Maxillofac Surg. 1994 Jan;52(1):35-9. doi: 10.1016/0278-2391(94)90010-8. PMID: 8263640.

55. Levin MP, Grower MF, Cutright DE, Getter L. The effects of length of surgery on healing of full and partial thickness flaps. J Oral Pathol. 1977 May;6(3):152-60. doi: 10.1111/j.1600-0714.1977.tb01876.x. PMID: 405466.

56. Lindeboom JA, van Wijk AJ. A comparison of two implant techniques on patient-based outcome measures: a report of flapless vs. conventional flapped implant placement. Clin Oral Implants Res. 2010 Apr 1;21(4):366-70. doi: 10.1111/j.1600-0501.2009.01866.x. Epub 2010 Feb 1. PMID: 20128828.

57. Sobol-Kwapinska M, Bąbel P, Plotek W, Stelcer B. Psychological correlates of acute postsurgical pain: A systematic review and meta-analysis. Eur J Pain. 2016 Nov;20(10):1573-1586. doi: 10.1002/ejp.886. Epub 2016 May 2. PMID: 27136510.

58. Eli I, Schwartz-Arad D, Baht R, Ben-Tuvim H. Effect of anxiety on the experience of pain in implant insertion. Clin Oral Implants Res. 2003 Feb;14(1):115-8. doi: 10.1034/j.1600-0501.2003.140115.x. PMID: 12562373.

59. Hashem AA, Claffey NM, O'Connell B. Pain and anxiety following the placement of dental implants. Int J Oral Maxillofac Implants. 2006 Nov-Dec;21(6):943-50. PMID: 17190305.

60. Kim S, Lee YJ, Lee S, Moon HS, Chung MK. Assessment of pain and anxiety following surgical placement of dental implants. Int J Oral Maxillofac Implants. 2013 Mar-Apr;28(2):531-5. doi: 10.11607/jomi.2713. PMID: 23527356.