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General discussion & Conclusions
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The PhD research described in this thesis was performed to provide evidence for the use of immediately placed dental implants and/or provisionalization in the aesthetic zone. At the start of this PhD project in 2009, studies with immediate implant placement were scarce. Based on the studies performed in this PhD study one could say in general that the 1-year results of immediately placed dental implants and/or provisionalization in the aesthetic zone are comparable and very promising.

Current knowledge

A Cochrane review on replacement of a single tooth with an immediate, early or delayed implant in a fresh extraction socket after tooth extraction evaluated success, complications, aesthetics and patient satisfaction among immediate, early and delayed implants and whether and when augmentation procedures are necessary and which is the most effective augmentation technique.1 The authors concluded that there was insufficient evidence to determine the possible advantages and disadvantages of immediate, early (immediate-delayed) and delayed implants. However, the authors mentioned that immediate and early (immediate-delayed) implants may be at a higher risk of implant failure and complications than delayed implants, while the aesthetic outcome might be better when placing implants just after tooth extraction. Moreover, there is yet insufficient evidence whether placement of implants in fresh extraction sockets have to be combined with augmentation procedure as well as which augmentation techniques is superior when indicated.

A systematic review was performed specifically assessing the clinical outcome of immediate placed implants in the aesthetic zone.2 This review (Chapter 2) learned that timing of provisionalization was not associated with outcome in terms of implant survival, which allows for immediate provisionalization after immediate implant placement. Regarding risk factors for change in marginal bone level (MBL), immediate provisionalization was associated with less bone loss, which is, to our opinion, a clinically relevant observation. Furthermore, the use of a flap and connective tissue graft was significantly associated with more bone loss. Unfortunately, the few included randomized clinical studies were based on short-term results (1 year), and studies with a longer follow-up period are needed to predict the aesthetic outcome on the long term. In future, we will report on the long-term results of our randomized clinical trials. In future trials, not only interproximal bone level dimensions should be taken into account, but also buccal bone level and buccal bone thickness. Loss of buccal bone after removal of a tooth is inevitable but there is insufficient evidence to set a threshold for minimum buccal bone thickness needed buccally of the implant to ensure the aesthetic outcome and the long-term stability.3,4 For example, most studies do not investigate the size of the bony defect after extraction. However, it has been hypothesized that an intact labial bony plate of the failing tooth might minimize facial gingival recession.5 Recently, due to altering techniques, the literature also reports a favourable treatment outcome of immediate implant placement in extraction sockets with buccal plate dehiscences.6,7 Thus, probably an intact buccal plate is not essential for immediate implant placement if the implant can be placed with sufficient primary stability. The current lack of clinical data regarding bone thickness at the buccal aspect of dental implants is probably related
to frequently encountered difficulties in how to reliably measure buccal bone thickness. A method was introduced to reliably measure buccal bone thickness after implant placement (Chapter 5), but still no reliable method is available to measure buccal bone thickness before implant placement.

Besides clinical and radiographic outcomes of the peri-implant tissues, aesthetic evaluation and patient-centered outcomes are gaining interest in the literature. The combination of unfavourable bony defects after extraction and thin overlying soft tissues are a considerable aesthetic risk for maintaining an acceptable long-term aesthetic outcome for immediately placed implants despite ideal placement and synchronous hard or soft tissue grafting procedures. The aesthetic result is mainly determined by the shape of these pink soft peri-implant tissues and the contour and colour of the definitive crown.

Immediate placement and provisionalization in the aesthetic zone has some important advantages for the patient: the patient immediately benefits from this treatment method which can substantially have a positive impact on the patient’s quality of life. Thus, patient satisfaction scales have to be applied, in addition to the already used treatment outcome parameters and aesthetic indexes in future studies assessing the treatment outcome of immediate placement of dental implants in the aesthetic zone (see Chapters 3 and 4). An aesthetic evaluation by professionals and a patient-centered outcome on quality of life should be a requirement for publications on single tooth replacement in the aesthetic zone.

Clinical outcome

Survival

In both clinical trials (Chapters 3 and 4) the survival rate of the immediate placed implants was 100%. Survival rate was defined as the percentage of functional implants one year after definitive crown placement. This is consistent with the one-year survival rates of around 98% in the literature. In a systematic review, factors were analyzed: reasons for extraction, antibiotic use, position of implant (anterior vs. posterior, maxilla vs. mandible) and type of loading. Only the regimen of antibiotic use reduced the survival rate significantly because provision of antibiotics may have helped to prevent post-operative infection.

Peri-implant hard tissue dimensions

The presence of sufficient bone volume is the most important prerequisite to achieve primary stability in case of immediate implant placement in an extraction socket. The size of the bony defect after extraction is considered a considerable aesthetic risk for immediately placed implants despite ideal placement. Thus, peri-implant bone preservation is thought to be a key factor determining the outcome of peri-implant hard tissues as Marginal Bone level (MBL) and the amount of Buccal Bone Thickness (BBT).

In two clinical studies (Chapter 3 and 4) the outcome of single-tooth implants in the aesthetic zone were assessed. Patients were divided according to buccal bony defects of ≤5 mm and ≥5 mm. Unfortunately, in the literature, yet no publications are available indicating the effect of the size of the bony defects on treatment outcome. Although, not supported by evidence, recent studies report that buccal plate dehiscences possibly not influence the outcome of immediate implant placement. To achieve primary stability in case of immediate implant placement in an extraction socket is leading regarding a favourable
outcome, but it is not an easy procedure. Due to the complexity of the surgery (bone augmentation and soft tissue grafting in the same operation) the studies in this thesis focused only on the treatment outcome of immediate placement.

**Marginal Bone level**

Marginal Bone Level (MBL) change was the primary outcome measure for both clinical studies. MBL led to comparable outcomes in all patient groups subject to evaluation of immediate and delayed placement and independent of the size of buccal bone defect prior to implant insertion and timing of provisionalization. The change in MBL in this study is considerably less than the generally accepted magnitude of up to 1 mm for the first year after immediate implant placement described in the literature. MBL loss usually predominantly occurs during the first year after immediate implant placement and hardly progresses thereafter. Changes in MBL will probably not progress after this first year, but a longer follow-up period is needed.

**Change in Buccal Bone level**

A successful aesthetic outcome is suggested to be dependent on establishment of an optimal three-dimensional implant position within the available bone dimensions and the maintenance of adequate Buccal Bone Thickness (BBT) along the implant axis. If there is no buccal bone present due to a bony defect after extraction, the position and depth of the placed implant could be different compared to an intact extraction socket or healed site. In the present clinical studies, BBT at dental implants in the aesthetic zone, measured on CBCTs, appeared to be stable after 1 year, irrespective whether immediate or delayed implant placement used, and independent of size of defect, timing of implant insertion and provisionalisation. Still the interpretation of BBT adjacent to dental implants on the resolution of the CBCT is insufficient in comparison with light microscopy. In the case of very thin buccal bone, CBCT images seem not always reliable due to background scattering and problems with standardization of the measurements. The quality and accuracy of a three-dimensional (3D) model derived from a CBCT is dependent on scanner related factors such as type of scanner, field of view (FoV), artifacts and voxel size. In addition, patient related factors such as patient position and metal artifacts, and operator related factors as the segmentation process or interpretation of the CBCT are of influence. Although precise BBT measurements on CBCT scans rely on various factors, standardized measurements should be an integral part of the treatment evaluation as the amount of BBT influences the treatment outcome.

**Peri-implant soft tissues dimensions**

It has been described that immediate implant placement is associated with an increased risk for recession of peri-implant tissues. A midfacial recession of 1 mm is reported for the outcome of immediate implant placement. Larger bony defects are accompanied by a higher frequency and magnitude of facial gingival recession (1.5 mm) 1-year after immediate tooth replacement. Recession of the peri-implant tissues in our clinical studies were clinically acceptable after one year. Due to support of a provisional crown, peri-implant tissues have the possibility to establish their form around an anatomically shaped crown. In the aesthetic zone it is therefore a must to use a provisional crown before placement of the definitive crown.
All other parameters as the health of the keratinized gingiva remained stable throughout the study period, while the plaque and bleeding indexes remained low in all groups. Participating patients seem to be well aware of the necessity of an adequate oral hygiene to keep healthy peri-implant tissues on the long term. Good oral hygiene instructions by the treatment provider are therefore a must. The health, shape and form of the soft peri-implant tissues mainly determine the aesthetic result. It is therefore interesting that primary outcome measures in studies are particularly survival or the hard peri-implant tissues (MBL). The reason could be because the hard tissue dimensions support to a large extent the soft tissues. A shift towards outcome measures in soft peri-implant tissues is thought to be more logical in the aesthetic zone.

**Aesthetic assessments**

The clinical studies (Chapter 3 and 4) specifically asses the differences in the aesthetic zone. Interestingly, aesthetic scores did not differ between groups with regard to buccal bony defects of ≤5 mm or ≥5 mm. This is an important observation as differences in treatment outcome could have been expected. The aesthetic result is mainly determined by the shape of healthy pink soft peri-implant tissues and the contour and colour of the definitive crown. The total aesthetic outcome in these clinical studies was mainly influenced by the appearance of the implant crown (WES) and to a lesser extent by the peri-implant mucosa (PES). The PES/WES and ICAI scores were comparable to results published in the literature regarding immediately, early and delayed placed single tooth implants in the aesthetic zone.

**Patient-centered outcome**

There is an increasing focus on patient-centered outcome measures within the field of implant dentistry. Immediate placement and provisionalization are known to be associated with high subjective satisfaction rates. The Visual Analogue Scales (VAS) and the Oral Health Impact Profile (OHIP) scores are in line with the patients’ satisfaction in our clinical studies. Regarding the OHIP-14, no differences were observed between both studies of all four groups during the entire follow-up, again in line with other studies regarding immediate implant placement. It seems that the advantage of immediate placement offering a shorter treatment time due to the lower number of surgical procedures by combining extraction, implant placement, and bone grafting in one operative procedure is experienced through the eyes of patients as a contribution to quality of life.
Future perspectives

In the clinical studies in this thesis patients were divided according to buccal bony defects of <5 mm or ≥5 mm. In the literature there is no division in the size or shape of bony defects.\textsuperscript{7,9,38} It is difficult to measure the exact dimensions of a bony defect when the failing tooth is still in situ. The diverse various osseous defects in the remaining alveolus after extraction can therefore pre-operatively not be predicted. It would be interesting to include the pre-operative peri-implant bone dimensions of the CBCT scan in relation to the actual position of the implant post-operatively. When information is available on the pre-operative BBT prior to removal of the failing tooth, it could be measured how much of this contour has been changed after dental implant treatment and what the influence is of the exact size and shape of the bony defect on the treatment outcome of immediate implant placement in the aesthetic zone.

In the literature there is insufficient evidence to set a threshold for minimum BBT to ensure the aesthetic outcome and the long-term stability.\textsuperscript{4,5} If standardized measurements are an integral part of the treatment evaluation, insight would be gained on alterations in BBT due to the surgical procedure and the remodeling process in the follow-up period. Not only BBT should be investigated with these standardized measurements, also interproximal and palatinal peri-implant bone dimensions as well as changes in BBT in the period between implant placement and provisionalization as this period was not assessed in the current study.

In the systematic review\textsuperscript{2} timing of provisionalization was not associated with outcome in terms of implant survival or changes in peri-implant hard and soft tissues. In the clinical study of buccal bony defects of <5 mm immediate provisionalization was non-inferior to delayed provisionalization. In buccal bony defects of ≥5 mm the results of immediate implant placement were very promising. In larger bony defects in the aesthetic zone it would be therefore interesting to investigate if immediate implant placement with immediate provisionalization is non-inferior to immediate implant placement with delayed provisionalization.

The phenomenon biotype is gaining interest.\textsuperscript{39} A thick or thin biotype could be of influence on the final aesthetic result. In the literature is described that biotype could be altered to gain more favourable results.\textsuperscript{40-41} Possibly the thickness of the mucosa can positively influence the stability of the peri-implant soft tissues. If pre- and post-operatively biotype is measured, possible alterations in the thickness of the mucosa can be investigated. In future studies, the effect of biotype on treatment outcome in the aesthetic zone should be an integral part of the treatment design.

Immediate single implant placement in the aesthetic zone shows good short-term results. The question remains how the performance is on the long term. Further research in prospective studies on immediate placed implants is warranted with a longer follow-up period than one year, preferably a follow-up of at least five years. If these studies, which are expected to be available in the next five years, show that immediate implant placement is stable on the long term, immediate implant placement should become the first treatment option if there is a failing single tooth in the aesthetic zone. If the tooth is already missing, the benefit of one operation combining implant placement and bone grafting in one operative procedure should be the first treatment option.
Conclusions

Immediate placement and/or provisionalization of dental implants in the aesthetic zone results in an excellent short-term treatment outcome in terms of survival, clinical outcome, aesthetic indexes and patient-centered outcome. Prerequisite is, however, primary stability of the implant.

Specific conclusions are:

- immediate implant placement with immediate provisionalization is non-inferior to immediate placement with delayed provisionalization in case of labial bony defects ≤5 mm;
- immediate implant placement with delayed provisionalization is non-inferior to delayed placement with delayed provisionalization in case of labial bony defects ≥5 mm;
- buccal bone at dental implants in the aesthetic zone, measured on CBCTs, is stable in thickness during the first year, irrespective of immediate or delayed placement as well as independent of the size of buccal bone defect prior to implant insertion and timing of implant insertion and provisionalization.
References


