Lars Schropp, Ann Wenzel

Timing of single implant placement and long-term observation of marginal bone levels

Lars Schropp, DDS, PhD
Associate Professor, Oral Radiology, Department of Dentistry, Aarhus University, Aarhus, Denmark

Ann Wenzel, DDS, PhD, Dr. Odont
Professor, Oral Radiology, Department of Dentistry, Aarhus University, Aarhus, Denmark

Correspondence to:
Lars Schropp
Associate Professor, Oral Radiology, Department of Dentistry, Aarhus University, Aarhus, Denmark.
Tel: +45 87168087
Email: lars.schropp@odont.au.dk

Key words *dental implant, long-term, marginal bone level, outcome, review, timing*

Aim: To assess the outcome of immediate or early placement of implants after tooth extraction supporting a single-tooth restoration with focus on the marginal bone level and its stability over time.
Material and methods: An electronic literature search without time restrictions was conducted of the Medline/PubMed database accompanied by a handsearch. Clinical human studies reporting on peri-implant marginal bone level (BL) and/or changes in bone level (BLC) and with a follow-up period of at least 12 months were selected for the present review.
Results: The search strategy resulted in 816 articles and 115 relevant publications were included for full-text analysis. Only few randomised controlled trials exist comparing immediate or early implant placement with placement in healed bone (the conventional protocol). Summarising the results from prospective studies, it was found that the mean marginal bone loss around immediately or early placed implants from baseline (at implant placement or placement of restoration) to the latest follow-up visit (between 1 and 10 years) was less than 1.5 mm.
Conclusion: The current literature indicates that immediate or early placement of single-tooth implants after tooth extraction may be a viable treatment with long-term survival rates and marginal bone level conditions matching those for implants placed conventionally in healed bone ridges.

■ Introduction

Peri-implantitis can affect the supporting soft and hard tissues around an oral endosseous implant and is characterised by bleeding and/or suppuration on probing and marginal bone loss. Poor oral hygiene, misfit between implant components and remnants of cement in the marginal sulcus are some of the contributors to peri-implantitis, which may compromise the survival of the implant and overall success of treatment[1]. Inappropriate loading conditions have been blamed for causing loss of peri-implant bone however the level of evidence is weak and does not indicate that overload per se can lead to peri-implant bone loss[2]. In contrast, in the presence of peri-implant inflammation, excessive mechanical occlusal load seems to aggravate the plaque-induced tissue breakdown[3], which in the worst case may lead to total loss of osseointegration.

A myriad of treatment concepts for implant-based prosthodontic rehabilitation has been suggested and it is imperative to clarify if the protocol, for example the timing of treatment, has an impact on marginal bone loss or gain after implant placement as well as the long-term marginal bone level.

The conventional protocol for treatment with intra-oral implants proposed by Brånemark[4] dictates a time interval of 3 to 6 months between extraction of a tooth and placement of the implant allowing soft tissue and bone healing at the extraction site. Furthermore, the protocol advocates a waiting period of at least 3 months before loading the inserted implant.

Two strategies have been followed to challenge the original protocol in order to reduce the treatment time. One alternative is to insert the implant immediately or soon after tooth extraction (termed immediate/early implant placement). Another alternative is to restore the implant (with or without occlusal loading) immediately or soon after placement (termed immediate/early restoration or loading). The strategies combined could minimise the overall treatment time dramatically. Ultimately, a patient may have one or more teeth extracted and will leave the dental office the same day with a single or multi-unit implant-supported restoration. This new protocol has been termed immediate or early replacement in the literature[5,6].

The reduction in treatment time is mainly due to fewer interventions and visits at the clinic and may be appealing for both the surgeon/clinician and patient in terms of increased effectiveness and satisfaction, and lower expenses. However, it is important to emphasise that this new approach should not be associated with a higher risk and more complications compared with the conventional protocol or require a disproportionate amount of extra training or special skills.

It has been speculated if placement of implants in fresh extraction sockets (immediate placement protocol) may also be beneficial from a biologic point of view. It is widely accepted that height and width (buccolingual) alterations in the alveolar ridge occur after tooth extraction and that most of these changes will occur within the first 3 months of socket healing[7]. These physiological dimensional changes may have a negative impact on the subsequent implant placement. By placing the implant immediately or early after tooth extraction and therefor before the narrowing and loss of bone ridge height has taken place, it might be easier to ensure proper positioning (apicocoronal and buccolingual) and angulation, which is indeed important for the functional and aesthetic outcome of implant-supported prosthodontics. Another potential advantage of preserving the bone walls would be that ridge augmentation is needed to a lesser extent.

Even though the immediate implant placement concept seems appealing, one could imagine some critical factors associated with it. Are we in fact sure that bone height around the implant can be preserved by immediate placement? Presence of periodontal or periapical/endodontic infections may interfere with healing and survival of the implant. The socket anatomy may influence the potential for obtaining primary implant stability, for example it appears reasonable to assume that a missing buccal bone plate or a molar extraction site would be more challenging. Furthermore, the surgical and prosthetic protocols may play a role. Flapless surgery has been suggested as an attempt to avoid bone resorption that may occur due to exposure of the underlying bone after raising a surgical flap[8]. It is also relevant to consider if immediate or early loading of an implant placed in a fresh extraction socket would be detrimental for the healing process or if this approach on the contrary may be beneficial.

Several studies have reported that successful outcomes are achievable when implants are inserted immediately after tooth extraction, with similar survival rates in comparison to implants inserted in healed sites, while other studies have found higher failure rates[9,10].

This systematic review was conducted to assess the outcome of immediate or early placement of implants after tooth extraction, supporting a single-tooth restoration, with focus on the long-term marginal bone level.

Material and Methods

Search strategies

An electronic literature search of the Medline/PubMed database, without time restrictions, was conducted and was completed on March 17, 2015. The following terms were used in the search strategy:
("Dental implant" OR "Oral implant" OR "Dental implantation" OR "Oral implantation" OR "Tooth implant" OR "Tooth implantation" OR "Dental

implants" OR "Oral implants" OR "Tooth implants") AND ("Single implant" OR "Single-tooth" OR "Single tooth" OR "Single-crown" OR "Single crown" OR "Single restoration" OR "Single implants" OR "Single-teeth" OR "Single teeth" OR "Single-crowns" OR "Single crowns" OR "Single restorations") AND ("Fresh extraction socket" OR "Fresh-socket" OR "Immediate placement" OR "Immediate insertion" OR "Immediate installation" OR "Immediate implant" OR "Immediate implants" OR "Immediately placed" OR "Immediately inserted" OR "Immediately installed" OR "Immediate-delayed placement" OR "Immediate-delayed insertion" OR "Immediate-delayed installation" OR "Immediate-delayed implant" OR "Immediate-delayed implants" OR "Immediate-delayed placed" OR "Immediate-delayed inserted" OR "Immediate-delayed installed" OR "Delayed-immediate placement" OR "Delayed-immediate insertion" OR "Delayed-immediate installation" OR "Delayed-immediate implant" OR "Delayed-immediate implants" OR "Delayed-immediately placed" OR "Delayed-immediately inserted" OR "Delayed-immediately installed" OR "Early placement" OR "Early insertion" OR "Early installation" OR "Early implant" OR "Early implants" OR "Early placed" OR "Early inserted" OR "Early installed" OR "Delayed placement" OR "Delayed insertion" OR "Delayed installation" OR "Delayed implant" OR "Delayed implants" OR "Delayed placed" OR "Delayed inserted" OR "Delayed installed" NOT ("animal" OR "animals" OR "dog" OR "dogs" OR "pig" OR "pigs" OR "in vitro" OR "cadaver" OR "case report").

Furthermore, the reference list of 16 recent and relevant reviews[9-24] was manually searched.

Study selection

Titles and abstracts of the identified publications were screened by the authors and full-text articles were obtained for all potentially relevant studies.

Clinical studies were included in this systematic review, while the following criteria for exclusion were applied: case reports, technical reports, animal studies, *in vitro* studies and review papers. In addition, to be eligible for inclusion, publications must be published in English, include at least 10 implants in the test group (immediate or early implants), have a follow-up period of at least 12 months and report on peri-implant marginal bone level (BL) and/or changes in bone level (BLC). In studies including both single and multiple implant restorations, data on BL and BLC had to be reported separately for the single-tooth restorations. Similarly, in studies evaluating different timing protocols for implant placement, publications were excluded if data reporting did not differentiate amongst the protocols.

The following study information and treatment outcomes were extracted for randomised clinical trials (RCTs) and prospective controlled clinical trials (CCTs): author and publication year, follow-up period, implant placement protocol(s), number of patients and implants, implant survival rate, BL and/or BLC, implant site, loading protocol, implant system and tissue augmentation. Furthermore, for studies reporting on the buccal bone level assessed by cone beam computed tomography (CBCT), the same information was obtained for RCTs, CCTs and prospective clinical studies without a control group (PCTs).

Definitions

Various terms have been suggested in the literature with regard to defining the time of implant placement after tooth extraction. In the present review, the terms used in the included publications were presented in the text and tables, and in the tables, the actual interval between tooth extraction and implant placement was stated if mentioned by the author. The term immediate referred to implant placement in fresh extraction sockets (on the same day as tooth extraction).The terms early or delayed-immediate referred to implants placed up to 8 weeks after extraction. The terms delayed or late implants, or healed sites referred to placement after a healing period of at least 2 months.

Marginal bone level (BL) in radiographs (periapical and CBCT) was defined as the distance from implant shoulder/platform to the first visible bone-to-implant contact (BIC). A positive value indicates a BL located apical to the shoulder and vice versa. A positive value for marginal bone level change (BLC) indicated a bone gain. A negative value for BLC indicated a bone loss.

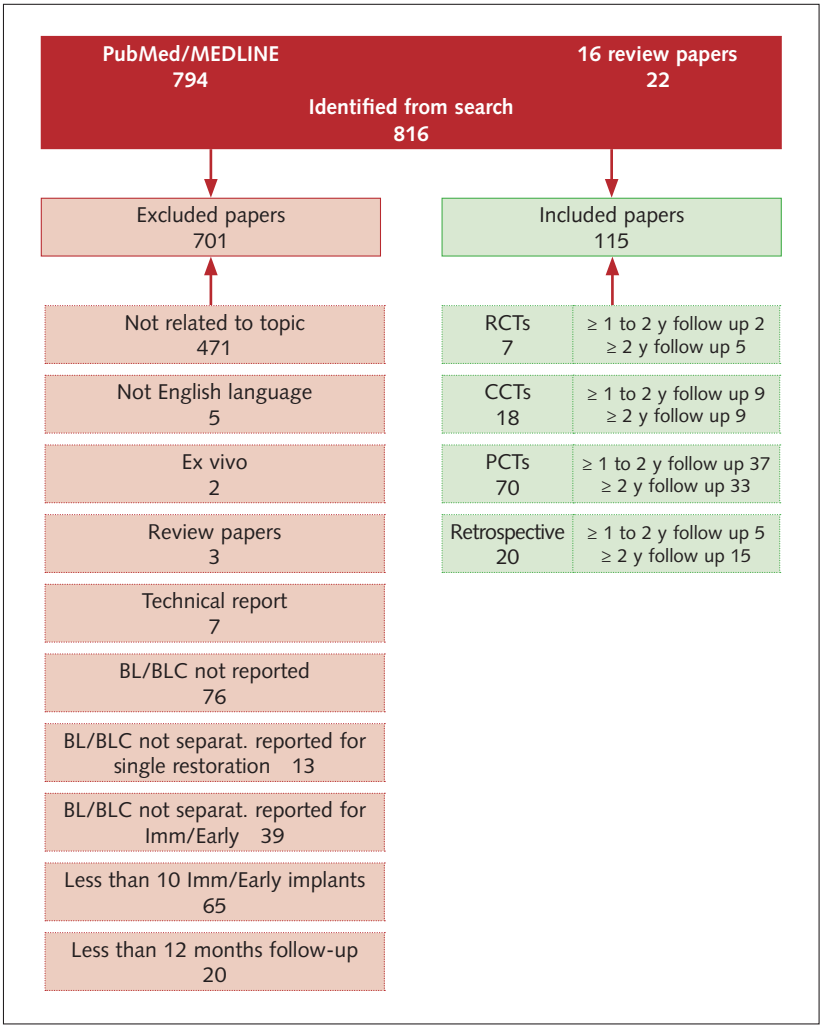

Fig 1 Study search strategy.

Results

Literature search

The PubMed/Medline search resulted in 794 potential articles and screening of the 16 review papers identified an additional 22 possible articles. Titles and abstracts (and full-texts in case the authors were in doubt if the inclusion criteria were fulfilled) were screened and 701 of the total 816 articles were excluded: 471 unrelated to the topic, five not in the English language, two *ex vivo*, three review papers, seven technical reports, 76 not reporting BL or BLC values, 13 not reporting BL/BLC separately for single-tooth restorations, 39 not reporting BL/BLC separately for immediate or early placed implants, 65 including less than 10 implants in the test group and 20 with a follow-up period of less than 12 months. Thus, 115 relevant publications were included for full-text analysis (Fig 1).

Description of studies

Forty-five studies had an observation period of 1 year, seven studies a follow-up between 1 and 2 years, and 63 studies a follow-up period of 2 years or more. Seven publications with an RCT design were identified; six of them with a follow-up period ≥ 2 years, however, four papers were from the same author group and dealt with the same study population. Eighteen publications reported on CCTs with one or more control groups, of which half had a follow-up period ≥ 2 years. Seventy studies were PCTs, i.e. without a control group (33 with a follow-up ≥ 2 years, 37 with a follow-up of 1 to < 2 years). Additionally, 20 retrospective studies (15 with an observation period ≥ 2 years, five with an observation period of 1 to < 2 years) were identified (Fig 1). The latter group of studies was not considered in detail in the following review of data. Ninety of the 95 prospective, clinical studies retrieved through the present search strategy reported on the interproximal bone level in intraoral, periapical radiographs, while five reported on the buccal bone level analysed by CBCT.

Publications from six RCTs are displayed in Table 1 while one RCT reporting on the buccal bone level analysed by CBCT is displayed in Table 2. Three articles by Schropp et al[25-27] compared the interproximal marginal bone level of implants placed early (also termed delayed-immediately) with that of delayed-placed implants at 2 and 5 years, respectively, after implant placement, and after 10 years these groups were compared with a late group comprising of implants placed approximately 1.5 years after tooth extraction in the premolar or molar regions. From crown delivery to 10-year follow-up, no changes in mean BL for the early group, a minor bone loss of 0.2 mm for the delayed group, and a minor bone gain of 0.2 mm for the late group were found. No statistically significant differences in mean BL values at 10 years were seen amongst the groups. Since the groups were not equally represented with implants in the incisor and molar regions, the authors carried out a separate analysis for implants replacing a premolar[28] and also found for this region alone

Table 1 RCTs reporting on interproximal bone level (BL) or bone level change (BLC) with a minimum mean follow-up period of 12 months.

Author/ year	Follow-up	Test group No. of patients / implants Protocol SR, BL and/or BLC	Control group(s) N of patients / implants Protocol SR, BL and/or BLC	Implant site	Loading protocol	Implant system	Augmentation
Schropp et al 2014[27]*	9.7 years	22/22 early (approximately 10 days after extraction) SR: 92% BLC: 0.00 mm; L: 1.15 mm NS difference in BL between groups	22/22 delayed (approximately 3 months after extraction) SR: 95% BLC: -0.23 mm; BL: 1.53 mm 19/19 late (approximately 1.5 years after extraction) SR: 100% BLC: 0.17 mm (gain) BL: 1.42 mm	Anterior and premolar for early/delayed Premolar and molar for late Maxilla/mandible	After 3 months	3i Parallel-walled Osseotite	Autogenous bone at dehiscences and fenestrations
Schropp and Isidor 2008[25]*	5 years	23/23 early (approximately 10 days after extraction) SR: 91%; BLC: -0.6 mm; BL: 1.2 mm NS difference in BL between groups	22/22 delayed (approximately 3 months after extraction) SR: 95% BLC: -0.8 mm BL: 1.5 mm	Anterior and premolar Maxilla/mandible	After 3 months	3i Parallel-walled Osseotite	Autogenous bone at dehiscences and fenestrations
Schropp et al 2005[26]*	2 years after implant placement	23/23 delayed-immediate (approximately 10 days after extraction) SR: 91% BLC: -0.8 mm; BL: 1.4 mm NS difference in BL between groups	23/23 delayed (approximately 3 months after extraction) SR: 96% BLC: -0.7 mm BL: 1.6 mm	Anterior and premolar Maxilla/mandible	After 3 months	3i Parallel-walled Osseotite	Autogenous bone at dehiscences and fenestrations
Palat-tella et al 2008[29]	2 years	8/9 immediate (in fresh extraction sockets) SR: 100%; BLC: -0.54 mm NS difference between groups	8/9 early (8 weeks after tooth extraction) SR: 100%; BLC: -0.46 mm	Anterior maxilla	Immediate restoration (non-occlusal loading)	Straumann TE implants	NM
Block et al 2009[30]	18 to 24 months	26/26 immediate (in fresh extraction sockets) SR: 85%; BL: 0.09 mm mesially, 0.18 mm distally NS difference in BL between groups	29/29 delayed (16 weeks after tooth extraction) SR: 97% BL: 0.32 mm mesially, 0.32 mm distally	Anterior and premolar maxilla	Immediate restoration	3i Straight wall, roughened surface	Human mineralised bone graft in gaps Grafting of extraction sites in delayed group
Linde-boom et al 2006[32]	1 year	25/25 immediate (in periapically infected extraction sites) SR: 92% BLC: -0.49 mm mesially, -0.53 mm distally NS difference between groups	25/25 delayed (12 weeks after tooth extraction) SR: 100% BLC: -0.52 mm mesially, -0.52 mm distally	Anterior and premolar maxilla	Loading after 6 months	Frialit-2 Synchro	Buccal bone augmentation in all cases (34 chin and 16 mandibular ramus bone grafts)

SR: survival rate; NM: not mentioned, NS; not statistically significant.

For BLC, a positive value means gain and a negative value means a loss. For BL a positive value means the BL was positioned apically to the implant shoulder/platform.

* The three studies reported from the same study population.

Table 2 Clinical studies reporting on buccal bone level (BL) or BL change (BLC) with a minimum mean follow-up period of 12 months.

Author/year Study type	Follow-up	Test group N of patients / implants Protocol, SR, BL and/or BLC	Control group(s) N of patients / implants Protocol, SR, BL and/or BLC	Implant site	Loading protocol	Implant system	Augmentation
Schropp et al 2015[28] RCT	9.7 years	22/22 early (on average 10 days after tooth extraction) SR: 92% BL: 2.39 mm NS difference in BL amongst groups	22/22 delayed (3 months after tooth extraction) SR: 95% BL: 2.22 mm 19/19 late(1.5 years after tooth extraction) SR: 100% BL: 1.85 mm	Anterior and premolar for early/ delayed Premolar and molar for late Maxilla/mandible	After 3 months	3i Parallel-walled Osseotite	Autogenous bone at dehiscences and fenestrations
Miyamoto and Obama 2011[40] CCT	28.2 months Range 6 to 57 months	Overall 18 patients in the three groups 7 implants immediate SR: NM BLC: -3.25 mm SS difference in BLC between Imm and D1 ($P<0.05$) NS difference between D2 and Imm or D1	16 implants delayed (D1) SR: NM BLC -0.13 mm 8 implants delayed (D2) SR: NM BLC: -0.70 mm	Anterior maxilla	Immediately placed abutments with non-occlusal loading	3i Osseotite / NobelBiocare Nobel Replace	Imm: autogenous bone D1: non-resorbable membrane and xenograft D2: resorbable membrane and xenograft
Raes et al 2013b[41] CCT	1 year	12/12 immediate SR: NM BL 0.16 mm (range 0-0.6) NS difference in BL at 1-year between groups	14/14 healed sites SR: NM BL: 0.20 mm (range 0-0.8)	Anterior and premolar maxilla	Immediate loading	Astra Tech OsseoSpeed	No augmentation
Benic et al 2012[43] PCT	7 years	24/24 immediate SR: 100% BL 5.2 mm at 7-year Almost no buccal bone detected in approximately one third of implants In two-thirds, the buccal bone plate covered the entire surface		Anterior and premolar Maxilla and mandible	Delayed loading	Straumann	Xenogenic bone graft and resorbable membrane
Buser et al 2013[55] PCT	7 years Range 5 to 9 years	4¼1 early (4 to 8 weeks after tooth extraction) SR: 100% BL not reported! Mean thickness of the facial bone wall of 2.2 mm		Anterior and premolar maxilla	Delayed loading	Straumann	Xenograft, autogenous bone, resorbable membrane

SR: survival rate; NM: not mentioned; NS: not statistically significant; SS: statistically significant; RCT: Randomized controlled trial; CCT: Controlled clinical trial; PCT: Prospective clinical trial (without control).

For BLC a positive value means a gain and a negative value means a loss.

For BL a positive value means BL was positioned apically to the implant shoulder/platform.

no significant difference in interproximal BL among the groups (early: 2.29 mm, delayed: 1.61 mm, late: 2.16 mm; $P = 0.56$). The three other RCTs[29-31] evaluated the patients at 1 year, 1.5 to 2 years or 2 years, respectively, after implant placement. All implants in these studies had replaced anterior/premolar teeth in the maxilla. Palattella et al[29] compared immediate implants with implants placed 8 weeks after tooth extraction (early); Block et al[30] compared immediate implants with implants placed 16 weeks after extraction (delayed); and Lindeboom et al[32] compared implants placed in periapically infected extraction sockets (immediate) with implants placed 12 weeks after extraction. For those RCTs, a mean marginal bone loss of 0.5 mm interproximally was found, or the BL was situated less than 0.5 mm apically to the implant shoulder, during the most recent control visit, irrespective of timing protocol; no statistically significant differences existed between test and control groups.

The trend for the CCTs comparing immediate or early placement with delayed or late placement, or immediate with early placement (Table 3) was the same as that for RCTs. Statistically significant differences between test and control groups were noted in only three out of 16 papers[33-35]. Cooper et al[33] demonstrated marginal bone gain at immediate implants and bone loss at implants placed in healed bone (statistically significant difference in BLC), resulting in a non-significant difference in bone levels between the groups at 1 year. This was the only CCT where the mean bone level was situated more than 1 mm apical to the implant shoulder, which was at immediate implants. Vandeweghe et al[35] found a significant difference in bone loss (0.4 mm; $P = 0.016$) between immediate and delayed implants in favour of the former timing, while Carini et al[34] found a significant difference in bone loss (0.15 mm; $P = 0.016$) between immediate and early implants, also in favour of the former timing. The maximum mean bone loss was 1 mm during the observation period, except in two studies[35,36], that revealed a bone loss of 1.6 and 1.3 mm, respectively, for implants placed in healed bone. A bone gain interproximal to immediate implants was observed in several studies (Table 3).

Thirty-one PCTs with a follow-up ≥ 2 years reported on the interproximal bone level (Table 4). All studies were dealing with immediately placed implants except one study[37] where the implants were placed early (4 to 8 weeks after tooth extraction). Summarising the results, it was found that the mean marginal bone loss from baseline (typically at implant placement or placement of restoration) to the latest follow-up visit was less than 1.5 mm. Two-thirds of the studies had an observation period of 3 years or more. Seven studies reported the absolute marginal bone level (BL) measured as the distance between implant shoulder/neck and BIC. The maximum mean BL was 1.5 mm except in one study where mean BL was 1.5 and 1.7 mm for two groups[38]. In a study evaluating 116 implants, BL after 6 to 9 years was > 3.5 mm for 20% and 66%, respectively, of immediate implants with or without a connective tissue graft[39].

The five prospective clinical studies reporting on the buccal bone level analysed by CBCT are listed in Table 2. Schropp et al[28] presented data of the buccal bone level in patients from the same RCT included in Table 1. Ten years after implant placement, the bone level was situated more apically in the early group compared with the delayed and late groups, however, the statistical tests revealed no significant differences amongst the groups. When analysing the premolar implants (represented in all three groups) separately, there was similarly no significant difference in BL amongst groups (early: 2.11 mm, delayed: 1.95 mm, late: 2.01 mm; $P = 0.85$). In a CCT by Miyamoto and Obama[40], more buccal bone loss was found at immediate implants (BLC: -3.25 mm) than at delayed implants augmented with a xenograft and a non-resorbable membrane (BLC: -0.13 mm; statistically significant difference), or a resorbable membrane (BLC: -0.70 mm; No statistically significant difference), during the observation period (28 months on average). Raes et al[41] found no statistically significant difference in bone level buccal to immediate implants compared with implants placed in healed bone at 1-year follow-up.

Survival rates were high for implants irrespective of whether they were placed according to the immediate/early or conventional protocol. In one RCT[30], four out of 26 immediate implants placed in the maxillary anterior or premolar regions had failed after 2 years corresponding to a survival rate

Table 3 Prospective clinical studies with control group(s) (CCT) reporting on mean interproximal bone level (BL) or bone level change (BLC) with a a minimum mean follow-up period of 12 months.

Author/year	Follow-up	Test group N of patients / implants Protocol SR, BL and/or BLC	Control group(s) N of patients / implants Protocol SR, BL and/or BLC	Implant site	Loading protocol	Implant system	Augmentation
Gotfredsen 2012[56]*	10 years	10/10 early (4 weeks after extraction) SR: 100% BLC: -0.64 mm All: During the 10-year interval, 1 patient lost more than 1.5 mm of marginal bone, three patients lost 1.0 to 1.4 mm, and 16 lost less than 1.0 mm NS difference in BLC between groups	10/10 delayed (more than 12 weeks after extraction) SR: 100%; BLC: -0.86 mm	Anterior and premolar maxilla in early Maxillary incisors in delayed	After 6 months	Astra Tech ST	Non-resorbable membranes
Gotfredsen 2004[57]*	5 years	10/10 early (4 weeks after extraction) SR: 100% BLC: -0.34 mm NS difference in BLC between groups	10/10 delayed (more than 12 weeks after extraction) SR: 100% BLC: -0.26 mm	Anterior and premolar maxilla in early Maxillary incisors in delayed	After 6 months	Astra Tech ST	Non-resorbable membranes
Berberi et al 2014b[58]	5 years	Overall 42 implants in 36 patients, 22 immediate implants SR: 91% BLC: -0.21 mm	20 implants in healed sockets SR: 100% BLC: -0.19 mm	Anterior and premolar maxilla	Immediate loading	Astra Tech / Dentsply	Autogenous bone graft in gaps
Cooper et al 2014[59]**	5 years	55/55 immediate SR: 95% BLC: 2.06 mm (gain), bone gain in nearly all cases BL: 0.43 mm NS difference in BL between groups	58/58 healed sites SR: 98% BLC: 0.1 mm (gain), gain or no marginal bone change in 59%, marginal bone loss greater than 0.5 mm in only 21.6% BL: 0.38 mm	Anterior and premolar maxilla	Immediate restoration (non-occlusal loading)	Dentsply (Astra Tech) OsseoSpeed	No augmentation
De Bruyn et al 2013[60]**	3 years	55/55 immediate SR: 95% BLC: 1.56 mm (gain) BL: 0.7 mm	58/58 healed sites SR: 98% BLC: -0.40 mm BL: 0.77 mm	Anterior and premolar maxilla	Immediate restoration (non-occlusal loading)	Astra Tech OsseoSpeed	No augmentation
Merli et al 2012[61]	3 years	Overall 60 patients in the two groups 29 immediate implants SR: 100% BL: 0.2 mm more coronally (better) in immediate group than in healed group NS difference between groups	40 implants in healed sites SR: 100%	Anterior and posterior maxilla and mandible	Immediate or early non-occlusal loading (randomized)	Element (Thommen Medical)	Anorganic bovine bone in gaps
Vandeweghe et al 2013[35]	26 months Range 8 to 44 months	Overall 38 patients in the two groups 23 immediate implants SR: 100% BLC: -0.88 mm SS difference between groups (P = 0.016)	20 delayed implants SR: 100% BLC: -1.28 mm	Anterior and posterior maxilla, mandibular molars	Immediate loading	Southern Implants	No augmentation
Tsirlis 2005[62]	24 months	Overall 38 patients in the two groups 28 immediate implants SR: 100% BLC: -0.75 mm	15 delayed (N = 4) or late (N = 11) SR: 100% BLC: -0.875 mm	Anterior maxilla	Immediate loading	3i NT Osseotite or Friatec Frialit-2	GBR (grafting and membranes)

Aguirre-Zorzano et al 2011[63]	93.3 weeks (test) 91.4 weeks (control)	Overall 56 patients in the two groups 56 immediate implants SR: 98.7% BLC -0.4 mm NS difference in bone loss between groups Both groups: < 1 mm bone loss at 67 implants (no bone loss at 36 and a small bone gain in some cases)	22 implants in healed sites SR: 100% BLC: -0.1 mm	Between the second premolars Maxilla/mandible	Immediate restoration	Astra Tech	GBR
Atieh et al 2013[42]	1 year	12/12 immediate SR: 66.7% BLC: 0.41 mm (gain) NS difference in BLC between groups	12/12 delayed (minimum 4 months post-extraction) SR: 83.3% BLC: 0.04 mm (gain)	Mandibular molars	Immediate restoration	MAX Southern Implants	NM
Cooper et al 2010[33]***	12 months	55/55 immediate SR: 94.5% BLC: 1.30 mm (gain) BL: 1.18 mm SS difference in BLC between groups ($P < 0.05$) NS difference in BL between groups	58/58 healed sites SR: 98.3% BLC: -0.40 BL: 0.81 mm	Between the second premolars maxilla	Immediate restoration	Astra Tech OsseoSpeed	No augmentation
Raes et al 2013a[64]***	1 year	16/16 immediate SR: 94% BLC: 1.05 mm (gain) BL: 0.85 mm	23/23 healed sites SR: 100% BLC: -0.18 mm BL: 0.65 mm 9/9 grafted sites (implants placed 4 to 5 months after grafting) SR: 100% BLC: 0.27 mm (gain) BL: 0.56 mm	Anterior and premolar maxilla	Immediate loading	Astra Tech OsseoSpeed	No augmentation
Grandi et al 2013[65]	12 months	25/25 immediate SR: 92% BLC: -0.71 mm NS difference in BLC between groups	25/25 delayed SR: 96% BLC: -0.60 mm	Anterior and premolar maxilla	Immediate restoration	JDEvolution Tapered implants	Anorganic bovine bone in gaps
Luongo et al 2014[66]	1 year	Overall 46 patients in the two groups 10 immediate implants SR: 100% BLC: -0.22 mm	47 implants healed sites SR: 97.9% BLC: -0.35 mm	Anterior and posterior maxilla and mandible	Immediate loading	MegaGen Implant AnyRidge	Biphasic calcium phosphate granules in gaps
Carini et al 2014[34]	12 months	Overall 10 patients in the two groups 7/7 immediate SR: 90% BLC: -0.12 mm SS difference in BLC between groups ($P = 0.016$)	8/8 Early (4 to 8 weeks after tooth extraction) SR: 100% BLC: -0.275 mm	Anterior and premolar maxilla and mandible	Immediate restoration (non-occlusal loading)	Phibo TSA Advance	Autologous and alloplastic bone in gaps, resorbable membranes
Kan et al 2007[36]	12 months	19/23 immediate SR: 100% BLC: 1.0 mm (gain) BL: 0.2 mm	12/15 healed sites SR: 100% BLC: -1.6 mm BL: -0.1 mm (coronal to ref-line)	Anterior and first premolar maxilla	Immediate restoration	Nobel Biocare NobelPerfect	Autogenous bone and xenograft

SR: survival rate; NM: not mentioned; NS: not statistically significant; SS: statistically significant.
For BLC a positive value means a gain and a negative value means a loss.
For BL a positive value means BL is positioned apically to the implant shoulder/platform, and vice versa.
* The two studies were reported from the same study population; **The two studies were reported from the same study population; ***The patients from the Raes et al study were apparently part of those from the multi-center study by Cooper et al.

Table 4 Prospective clinical studies without control group(s) (PCT), reporting on interproximal bone level (BL) or BL change (BLC) with a minimum mean follow-up period of 2 years.

Author/year	Number of implants	BL or BLC	Follow-up	SR
Barone et al 2014[67]	30	BLC: -1.0 mm / -0.9 mm (two groups)	2 years	100%
Berberi et al 2014a[68]	20	BLC: -0.27 mm	3 years	100%
Berberi et al 2014c[69]	40	BLC: statistically significant bone loss (no values reported)	5 years	100%
Bianchi and Sanfilippo 2004[39]	116	BL > 3.5 mm: 20% of implants for test (connective tissue graft) and 66% of implants for control	6 to 9 years	100%
Buser et al 2011[37]	20	BLC: -0.18 mm	3 years	100%
Calvo-Guirado et al 2014a[70]	71	BLC: -0.86 mm	3 years	100%
Calvo-Guirado et al 2014b[71]	86	BLC: -1.01 mm	10 years	97.1%
Calvo-Guirado et al 2011[72]	64	BLC: -0.97 mm	5 years	97.1%
Canullo et al 2010[73]	25	BLC: -0.55 mm / -0.34 mm (two groups)	3 years	100%
Canullo et al 2009[74]	22	BLC: -0.30 mm / -1.19 mm (two groups)	25 months	100%
Chen et al 2007[75]	26	BLC: -1.00 to -1.30 mm (three groups)	4 years	100%
Cosyn et al 2011[76]	30	BLC: -1.13 mm (mesially) /-0.86 mm (distally)	3 years	96.0%
Covani et al 2014[77]	47	BLC: -1.08 mm	5 years	95.7%
Covani et al 2012[78]	159	Maximum BL was 1.50 mm in 98% of implants	10 years	91.8%
Covani et al 2004[79]	163	BL at or coronal to the first implant thread in 91% of implants	4 years	97.0%
Crespi et al 2009[80]	64	BLC: -0.78 mm / -0.73 mm (two groups)	24 months	100%
Crespi et al 2010[81]	30	BLC: -0.82 mm / -0.86 mm (two groups)	24 months	100%
Crespi et al 2008[82]	40	BLC: -1.02 mm / -1.16 mm (two groups)	24 months	100%
Groisman et al 2003[83]	92	Maximum BLC was 2.0 mm for all implants	2 years	93.5%
Guarnieri et al 2015[84]	21	BLC: -0.83 mm BL: 0.94 mm	5 years	95.2%
Kahnberg 2009[85]	40	BLC: -0.13 mm mesially / -0.19 mm (distally)	2 years	100%
Kan et al 2011[86]	35	BLC: -0.72 mm (mesially), -0.63 mm (distally)	4 years	100%
Kolinski et al 2014[87]*	60	BLC: 0.30 mm (gain)	3 years	98.3%
Malchiodi et al 2013[88]	64	BLC < 1.00 mm loss in 95% of implants BL: 0.80 mm	3 years	100%
McAllister et al 2012[89]*	60	BLC: -0.10 mm	2 years	98.3%
Migliorati et al 2013[90]	47	BLC: -0.06 mm / -0.17 mm (two groups)	2 years	100%
Mijiritsky et al 2009[91]	24	BLC: -0.90 mm	40 months	95.8%
Prosper et al 2010[92]	120	BL: 1.31 mm / 1.01 mm (two groups)	5 years	96.7%
Prosper et al 2003[93]	111	BL: 0.70 to 0.80 mm / 0.73 to 0.80 (two groups)	4 years	97.3%
Shibly et al 2010[94]	60	BLC: 1.19 mm (gain) / 1.00 mm (gain) (two groups)	24 months	95.0%
Truninger et al 2011[38]	29	BL: 1.54 mm / 1.57 mm (mesially), 1.69 mm / 1.59 mm (distally) (two groups)	3 years	100%

SR: survival rate
For the BLC a positive value means a gain and a negative value means a loss.
For the BL a positive value means the BL is positioned apically to the implant shoulder/platform.
* same study population

of 85% and a CCT[42] demonstrated a survival rate of 67% for 12 immediate implants and 83% for 12 delayed implants replacing molars in the mandible after 1 year. All other studies (Tables 1 to 4) demonstrated survival rates higher than 90% for immediate/early implants and approximately 80% of the studies showed a survival rate of 95% or higher. In comparison, all studies with a control group (except the CCT by Atieh et al) showed survival rates of 95% or higher for delayed/late implants.

Discussion

The marginal bone level around an implant is one important criterion for the success of treatment. Loss of marginal bone following implant placement will not only possess a risk of implant failure, but also reduce the chance of achieving an optimal aesthetic outcome[36], which in turn may affect patient satisfaction.

The present systematic review focused on long-term observation of the peri-implant bone level after placing single-tooth implants immediately in fresh extraction sockets or early after removal of the tooth. After scrutinising the literature for studies reporting on the peri-implant bone level at least 1 year after implant placement, it was revealed that only few RCTs exist, comparing immediate or early implant placement with placement in healed bone (the conventional protocol). An additional 18 prospective studies assessing a test group (immediate or early) together with a control group (delayed or late placement) were found.

Based on those studies that have monitored the marginal bone level around implants from 1 to 10 years in periapical radiographs, it could be concluded that the bone level or changes in bone level over time at the interproximal aspects differed only slightly between the alternative and conventional timing protocols, and no statistically significant differences were found for the majority of the studies. The buccal bone level was assessed by CBCT in a few trials. In an RCT, the bone level at early placed implants was positioned 2.4 mm apically to the implant shoulder at 10 years[28], which did not differ significantly from the buccal bone level for delayed/late implants. In a PCT[43], the buccal bone level at immediate implants was 5.2 mm from the implant shoulder at the 7-year follow-up, and almost no buccal bone was detected in approximately one-third of the implants, while a bone loss of 3.25 mm for seven immediate implants, 28 months after implant placement, was revealed in a CCT[40].

Even though no substantial differences in bone level or survival rate were found among the implant placement protocols, it should be noted that out of the 22 studies that compared the interproximal bone level between test and control groups, the survival rate was higher for the delayed/late implants than for the immediate/early implants in 14 studies while the latter outmatched the control group in only one study. In this context, it must be emphasised that data for the marginal bone level should only be reported for implants surviving through the whole observation period, and even when this is the case, selection bias cannot be ruled out when comparing groups.

Several studies have shown that determination of the marginal peri-implant bone level in periapical radiographs is reliable[44-47]. Two studies found a significant linear correlation between histomorphometric and radiographic parameters[44,45]. However, to be able to trust bone level measurements it is imperative that the periapical radiographs are recorded with optimal and standardised projections so that bone levels of the same implant can be compared at different time points. For example, a marginal bone gain observed over time when comparing two radiographs may be due to remodelling, but could merely be a radiological phenomenon (different projection angles applied in the two radiographs). In studies evaluating bone levels radiographically, it is therefore important that the radiographic technique is well-described. In most of the papers included in this review, it was reported whether the periapical radiographs were obtained with the paralleling technique and/or standardised. It is, however, relevant to discuss how parallelism and standardisation are best achieved. For the clinician, it can be difficult to figure out the angulation of the implant in the buccolingual plane after its insertion. Thus, even though a film holder with an aiming device is used, in some cases the central beam of the radiograph will not aim perpendicular to the long axis of the implant. Fortunately, it is easy to detect if parallelism has been obtained by assessing the sharpness of the implant threads. If the threads are blurred at one or both sides of the implant, the Right blur-raise beam/Left blur-lower beam (RB-RB/LB-LB) rule[48] can be applied to correct non-parallelism. Obtaining sharp implant threads in all images is also a simple way to standardise the projection angle so that reliable comparisons among them can be made. This has the advantage that fabrication of a bite-block attached to the film holder can be avoided.

One major drawback of intraoral, periapical radiography is that this radiographic technique only

displays the bone level mesially and distally to the implant. To radiographically detect the bone level at the buccal and oral aspects of the implant, it is necessary to apply a technique which can produce cross-sectional sections of the jaw. For that purpose, CBCT is a valuable tool. Corpas et al[44] found statistically significant correlations in the depth of bone defects adjacent to implants between CBCT and histological sections ($r = 0.61$, $P < 0.01$). However, CBCT images yielded a bone defect depth underestimation of 1.2 mm on average, compared with the histological data. In a comparison of CBCT and periapical images in measurements of the interproximal bone levels, no significant differences between the modalities were observed in one study[28], whereas Raes et al[41] found a low accuracy of CBCT ($r = 0.325$, $P = 0.019$) when assessing the bone level at implants placed in extraction sockets or in healed bone (BL was 0.70 mm in periapical images vs 0.23 mm in CBCT).

CBCT seems to be helpful in the evaluation of the peri-implant bone in the bucco-oral plane, however, it must be emphasized that besides higher radiation doses and higher expenses[49,50], this modality is also associated with challenges regarding image quality. The presence of metal objects or other materials with a high atomic number in the region of interest will inevitably cause beam-hardening artefacts in a CBCT image[51], and in turn may affect the image quality. Likewise, motion artefacts in CBCT are a well-known phenomenon because this image modality is associated with a longer exposure time compared with for example fan beam CT scanning[52]. Artefacts often appear as black and white stripes and have previously been shown to impair the visibility of the peri-implant bone and preclude accurate assessment of the bone level[44,53]. Due to the inherent disadvantages of current CBCT equipment, the authors suggest that this modality should not be used as a standard when monitoring the hard tissues around an oral implant.

When the marginal bone around implants is evaluated in longitudinal studies, data on bone level changes (loss or gain) during the observation period are usually reported. In contrast, relatively few papers report on the absolute bone levels at different follow-up visits. It seems relevant to know the marginal bone level expressed as the distance between a well-defined reference point (e.g. the implant shoulder/platform) and the first visible BIC, since this variable is more informative regarding implant prognosis than bone level changes. For example, bone gain at one implant placed in a fresh extraction socket (with BIC positioned apically to the implant shoulder at baseline), and bone loss at another implant placed in healed bone (with BIC positioned at or coronally to the implant shoulder at baseline) may result in a BIC positioned at the same level at the end of the follow-up period for both cases. It was also noted that publications most often only report mean (or median) values for the BL or BLC. It would be useful if, additionally, the implant cases were divided into subgroups, with respect to BL or BLC and frequencies calculated since specification merely of the average BL/BLC might conceal serious problems for some of the implants.

The choice of surgical and prosthetic protocols in relation to implant treatment and the immediate/early implant placement approach, specifically, may affect implant survival and the peri-implant marginal bone level. Information about implant system, supplementary tissue augmentation procedures as well as loading protocol was stated in Tables 1 to 3 for the RCTs, CCTs and studies reporting on the buccal bone level, which illustrated a high heterogeneity among the studies in this respect.

Unfortunately, no consensus has been reached in the classification or terminology in relation to timing protocols in implant treatment. For example, immediate implant placement has been called 'immediate' or 'post-extraction implants' or 'placement in fresh extraction sockets'. Early placement has also been called 'early implants' or 'immediate-delayed' or 'delayed-immediate placement', and further deferred placement after tooth extraction has been termed 'delayed' or 'late' (with varying definitions) or 'placement in healed bone'. To facilitate reading and comparison of outcomes from different studies, it would be practical if researchers use the same terms when defining the time between tooth extraction and implant placement. Thus, development of a simple classification system based on clear and exhaustive (all time points for implant placement are covered) definitions would be appreciated. Hämmerle et al[54] proposed a classification based on soft and hard tissue healing parameters: Type 1- implant placement immediately following tooth extraction and as part

of the same surgical procedure, Type 2- complete soft tissue coverage (typically 4 to 8 weeks), Type 3 - substantial clinical and /or radiographic bone fill of the socket (typically 12 to 16 weeks), Type 4 - healed site (typically > 16 weeks). This classification is in our opinion sensible and useful since it considers variations in the subjects' healing capacity.

Due to the limited number of existing RCTs on the topic of this review, it was decided to include prospective studies with (CCTs) or without a control group (PCTs), in order to base our conclusions on more study populations. However, one must recognise that most prospective studies have set several exclusion criteria (e.g. lack of or thin facial bone wall, post-extraction infection, need of GBR procedures, large peri-implant infrabony defects) when enrolling patients for post-extraction or early implants. Therefore, data from non-randomised studies should be interpreted critically with attention to the clinical setup. This fact also indicates that not all clinical cases are suitable for the immediate placement approach, and it is advocated a careful patient selection in the treatment planning phase should be followed. Since a significant number of prospective studies (RCTs, CCTs and PCTs) were available from the search, it was decided to exclude data extraction from retrospective studies that are considered to have a lower level of evidence.

Conclusion

This systematic review of the current literature indicates that immediate or early placement of single-tooth implants after tooth extraction may be a viable treatment with long-term survival rates and marginal bone level conditions, matching those for implants placed conventionally in healed bone ridges. However, interpretation of the results must be made with caution as only few RCTs and prospective, controlled clinical studies with a follow-up of 5 years or more are available. The authors advocate that careful patient selection for post-extraction implant placement is made and that a strict treatment protocol for the surgical and prosthetic procedures is followed. Furthermore, publications on this topic should report mean values, as well as frequencies and ranges for the absolute marginal bone levels, in addition to only bone level changes over time. Data on marginal bone level should only be provided for surviving implants, and survival rates should always be reported. Even then, if more implants are lost in one of the groups, there will be a risk of selection bias in follow-up studies.

References

1. Smeets R, Henningsen A, Jung O, Heiland M, Hammacher C, Stein JM. Definition, etiology, prevention and treatment of peri-implantitis--a review. Head Face Med 2014;10:34.
2. Duyck J, Vandamme K. The effect of loading on peri-implant bone: a critical review of the literature. J Oral Rehabil 2014;41:783–794.
3. Naert I, Duyck J, Vandamme K. Occlusal overload and bone/implant loss. Clin Oral Implants Res 2012;23(Suppl 6):95–107.
4. Brånemark PI. Introduction to osseointegration. In: Brånemark PI, Zarb G, Albrektsson T (eds). Tissue-integrated Prostheses: Osseointegration in Clinical Dentistry. Chicago: Quintessence Publishing Co, 1985:11–76.
5. Jofre J, Valenzuela D, Quintana P, Asenjo-Lobos C. Protocol for immediate implant replacement of infected teeth. Implant Dent 2012;21:287–294.
6. Garber DA, Salama MA, Salama H. Immediate total tooth replacement. Compend Contin Educ Dent 2001;22: 210–216, 218.
7. Schropp L, Wenzel A, Kostopoulos L, Karring T. Bone healing and soft tissue contour changes following single-tooth extraction: a clinical and radiographic 12-month prospective study. Int J Periodontics Restorative Dent 2003;23:313–323.
8. Romero-Ruiz MM, Mosquera-Perez R, Gutierrez-Perez JL, Torres-Lagares D. Flapless implant surgery: A review of the literature and 3 case reports. J Clin Exp Dent 2015;7: e146–e152.
9. Chrcanovic BR, Albrektsson T, Wennerberg A. Dental implants inserted in fresh extraction sockets versus healed sites: a systematic review and meta-analysis. J Dent 2015; 43:16–41.
10. Ortega-Martinez J, Perez-Pascual T, Mareque-Bueno S, Hernandez-Alfaro F, Ferres-Padro E. Immediate implants following tooth extraction. A systematic review. Med Oral Patol Oral Cir Bucal 2012;17:e251–e261.
11. Alvarez-Camino JC, Valmaseda-Castellon E, Gay-Escoda C. Immediate implants placed in fresh sockets associated to periapical infectious processes. A systematic review. Med Oral Patol Oral Cir Bucal 2013;18:e780–e785.
12. Atieh MA, Payne AG, Duncan WJ, de Silva RK, Cullinan MP. Immediate placement or immediate restoration/loading of single implants for molar tooth replacement: a systematic review and meta-analysis. Int J Oral Maxillofac Implants 2010;25:401–415.
13. Chen ST, Buser D. Clinical and esthetic outcomes of implants placed in postextraction sites. Int J Oral Maxillofac Implants 2009;24(Suppl):186–217.
14. Chrcanovic BR, Martins MD, Wennerberg A. Immediate placement of implants into infected sites: a systematic review. Clin Implant Dent Relat Res 2015;17(Suppl 1):e1–e16.
15. Corbella S, Taschieri S, Tsesis I, Del Fabbro M. Postextraction implant in sites with endodontic infection as an alternative to endodontic retreatment: a review of literature. J Oral Implantol 2013;39:399–405.

16. Esposito M, Grusovin MG, Polyzos IP, Felice P, Worthington HV. Timing of implant placement after tooth extraction: immediate, immediate-delayed or delayed implants? A Cochrane systematic review. Eur J Oral Implantol 2010;3:189–205.
17. Esposito M, Grusovin MG, Polyzos IP, Felice P, Worthington HV. Interventions for replacing missing teeth: dental implants in fresh extraction sockets (immediate, immediate-delayed and delayed implants). Cochrane Database Syst Rev 2010;(8):CD005968.
18. Kinaia BM, Shah M, Neely AL, Goodis HE. Crestal bone level changes around immediately placed implants: a systematic review and meta-analyses with at least 12 months' follow-up after functional loading. J Periodontol 2014;85: 1537–1548.
19. Koh RU, Rudek I, Wang HL. Immediate implant placement: positives and negatives. Implant Dent 2010;19:98–108.
20. Lee CT, Chiu TS, Chuang SK, Tarnow D, Stoupel J. Alterations of the bone dimension following immediate implant placement into extraction socket: systematic review and meta-analysis. J Clin Periodontol 2014;41:914–926.
21. Sanz I, Garcia-Gargallo M, Herrera D, Martin C, Figuero E, Sanz M. Surgical protocols for early implant placement in post-extraction sockets: a systematic review. Clin Oral Implants Res 2012;23(Suppl 5):67–79.
22. Schropp L, Isidor F. Timing of implant placement relative to tooth extraction. J Oral Rehabil 2008;35(Suppl 1):33–43.
23. Slagter KW, den Hartog L, Bakker NA, Vissink A, Meijer HJ, Raghoebar GM. Immediate placement of dental implants in the esthetic zone: a systematic review and pooled analysis. J Periodontol 2014;85:e241–e250.
24. Waasdorp JA, Evian CI, Mandracchia M. Immediate placement of implants into infected sites: a systematic review of the literature. J Periodontol 2010;81:801–808.
25. Schropp L, Isidor F. Clinical outcome and patient satisfaction following full-flap elevation for early and delayed placement of single-tooth implants: a 5-year randomized study. Int J Oral Maxillofac Implants 2008;23:733–743.
26. Schropp L, Kostopoulos L, Wenzel A, Isidor F. Clinical and radiographic performance of delayed-immediate single-tooth implant placement associated with peri-implant bone defects. A 2-year prospective, controlled, randomized follow-up report. J Clin Periodontol 2005;32:480–487.
27. Schropp L, Wenzel A, Stavropoulos A. Early, delayed, or late single implant placement: 10-year results from a randomized controlled clinical trial. Clin Oral Implants Res 2014;25: 1359–1365.
28. Schropp L, Wenzel A, Spin-Neto R, Stavropoulos A. Fate of the buccal bone at implants placed early, delayed, or late after tooth extraction analyzed by cone beam CT: 10-year results from a randomized, controlled, clinical study. Clin Oral Implants Res 2015;26:492–500.
29. Palattella P, Torsello F, Cordaro L. Two-year prospective clinical comparison of immediate replacement vs. immediate restoration of single tooth in the esthetic zone. Clin Oral Implants Res 2008;19:1148–1153.
30. Block MS, Mercante DE, Lirette D, Mohamed W, Ryser M, Castellon P. Prospective evaluation of immediate and delayed provisional single tooth restorations. J Oral Maxillofac Surg 2009;67:89–107.
31. Lindeboom JA, Frenken JW, Dubois L, Frank M, Abbink I, Kroon FH. Immediate loading versus immediate provisionalization of maxillary single-tooth replacements: a prospective randomized study with BioComp implants. J Oral Maxillofac Surg 2006;64:936–942.
32. Lindeboom JA, Tjiook Y, Kroon FH. Immediate placement of implants in periapical infected sites: a prospective randomized study in 50 patients. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2006;101:705–710.
33. Cooper LF, Raes F, Reside GJ, Garriga JS, Tarrida LG, Wiltfang J, Kern M, de Bruyn H. Comparison of radiographic and clinical outcomes following immediate provisionalization of single-tooth dental implants placed in healed alveolar ridges and extraction sockets. Int J Oral Maxillofac Implants 2010;25:1222–1232.
34. Carini F, Longoni S, Pisapia V, Francesconi M, Saggese V, Porcaro G. Immediate loading of implants in the aesthetic zone: comparison between two placement timings. Ann Stomatol (Roma) 2014;5:15–26.
35. Vandeweghe S, Nicolopoulos C, Thevissen E, Jimbo R, Wennerberg A, De Bruyn H. Immediate loading of screw-retained all-ceramic crowns in immediate versus delayed single implant placement. Int J Prosthodont 2013;26:458–464.
36. Kan JY, Rungcharassaeng K, Liddelow G, Henry P, Goodacre CJ. Periimplant tissue response following immediate provisional restoration of scalloped implants in the esthetic zone: a one-year pilot prospective multicenter study. J Prosthet Dent 2007;97 (Suppl 6):S109–S118.
37. Buser D, Wittneben J, Bornstein MM, Grutter L, Chappui V, Belser UC. Stability of contour augmentation and esthetic outcomes of implant-supported single crowns in the esthetic zone: 3-year results of a prospective study with early implant placement postextraction. J Periodontol 2011;82:342–349.
38. Truninger TC, Philipp AO, Siegenthaler DW, Roos M, Hammerle CH, Jung RE. A prospective, controlled clinical trial evaluating the clinical and radiological outcome after 3 years of immediately placed implants in sockets exhibiting periapical pathology. Clin Oral Implants Res 2011;22:20–27.
39. Bianchi AE, Sanfilippo F. Single-tooth replacement by immediate implant and connective tissue graft: a 1-9-year clinical evaluation. Clin Oral Implants Res 2004;15:269–277.
40. Miyamoto Y, Obama T. Dental cone beam computed tomography analyses of postoperative labial bone thickness in maxillary anterior implants: comparing immediate and delayed implant placement. Int J Periodontics Restorative Dent 2011;31:215–225.
41. Raes F, Renckens L, Aps J, Cosyn J, De Bruyn H. Reliability of circumferential bone level assessment around single implants in healed ridges and extraction sockets using cone beam CT. Clin Implant Dent Relat Res 2013;15:661–672.
42. Atieh MA, Alsabeeha NH, Duncan WJ, de Silva RK, Cullinan MP, Schwass D, Payne AG. Immediate single implant restorations in mandibular molar extraction sockets: a controlled clinical trial. Clin Oral Implants Res 2013;24:484–496.
43. Benic GI, Mokti M, Chen CJ, Weber HP, Hammerle CH, Gallucci GO. Dimensions of buccal bone and mucosa at immediately placed implants after 7 years: a clinical and cone beam computed tomography study. Clin Oral Implants Res 2012;23:560–566.
44. Corpas dos Santos L, Jacobs R, Quirynen M, Huang Y, Naert I, Duyck J. Peri-implant bone tissue assessment by comparing the outcome of intra-oral radiograph and cone beam computed tomography analyses to the histological standard. Clin Oral Implants Res 2011;22:492–499.
45. Hermann JS, Schoolfield JD, Nummikoski PV, Buser D, Schenk RK, Cochran DL. Crestal bone changes around titanium implants: a methodologic study comparing linear radiographic with histometric measurements. Int J Oral Maxillofac Implants 2001;16:475–485.
46. Choi KS, Lozada JL, Kan JY, Lee SH, Kim CS, Kwon TG. Study of an experimental microthreaded scalloped implant design: proximal bone healing at different interimplant distances in a canine model. Int J Oral Maxillofac Implants 2010;25:681–689.
47. Gotfredsen K, Berglundh T, Lindhe J. Bone reactions at implants subjected to experimental peri-implantitis and static load. A study in the dog. J Clin Periodontol 2002;29: 144–151.

48. Schropp L, Stavropoulos A, Spin-Neto R, Wenzel A. Evaluation of the RB-RB/LB-LB mnemonic rule for recording optimally projected intraoral images of dental implants: an in vitro study. Dentomaxillofac Radiol 2012;41:298–304.
49. Petersen LB, Olsen KR, Christensen J, Wenzel A. Image and surgery-related costs comparing cone beam CT and panoramic imaging before removal of impacted mandibular third molars. Dentomaxillofac Radiol 2014;43:20140001.
50. Petersen LB, Olsen KR, Matzen LH, Vaeth M, Wenzel A. Economic and health implications of routine CBCT examination before surgical removal of the mandibular third molar in the Danish population. Dentomaxillofac Radiol 2015;44:20140406.
51. Schulze R, Heil U, Gross D, Bruellmann DD, Dranischnikow E, Schwanecke U, Schoemer E. Artefacts in CBCT: a review. Dentomaxillofac Radiol 2011;40:265–273.
52. Spin-Neto R, Matzen LH, Schropp L, Gotfredsen E, Wenzel A. Factors affecting patient movement and re-exposure in cone beam computed tomography examination. Oral Surg Oral Med Oral Pathol Oral Radiol 2015;119:572–578.
53. Razavi T, Palmer RM, Davies J, Wilson R, Palmer PJ. Accuracy of measuring the cortical bone thickness adjacent to dental implants using cone beam computed tomography. Clin Oral Implants Res 2010;21:718–725.
54. Hämmerle CH, Chen ST, Wilson TG Jr. Consensus statements and recommended clinical procedures regarding the placement of implants in extraction sockets. Int J Oral Maxillofac Implants 2004;19(Suppl):26–28.
55. Buser D, Chappuis V, Bornstein MM, Wittneben JG, Frei M, Belser UC. Long-term stability of contour augmentation with early implant placement following single tooth extraction in the esthetic zone: a prospective, cross-sectional study in 41 patients with a 5- to 9-year follow-up. J Periodontol 2013;84:1517–1527.
56. Gotfredsen K. A 10-year prospective study of single tooth implants placed in the anterior maxilla. Clin Implant Dent Relat Res 2012;14:80–87.
57. Gotfredsen K. A 5-year prospective study of single-tooth replacements supported by the Astra Tech implant: a pilot study. Clin Implant Dent Relat Res 2004;6:1–8.
58. Berberi AN, Sabbagh JM, Aboushelib MN, Noujeim ZF, Salameh ZA. A 5-year comparison of marginal bone level following immediate loading of single-tooth implants placed in healed alveolar ridges and extraction sockets in the maxilla. Front Physiol 2014;5:29.
59. Cooper LF, Reside GJ, Raes F, Garriga JS, Tarrida LG, Wiltfang J, Kern M, De Bruyn H. Immediate provisionalization of dental implants placed in healed alveolar ridges and extraction sockets: a 5-year prospective evaluation. Int J Oral Maxillofac Implants 2014;29:709–717.
60. De Bruyn H, Raes F, Cooper LF, Reside G, Garriga JS, Tarrida LG, Wiltfang J, Kern M. Three-years clinical outcome of immediate provisionalization of single Osseospeed(TM) implants in extraction sockets and healed ridges. Clin Oral Implants Res 2013;24:217–223.
61. Merli M, Moscatelli M, Mariotti G, Piemontese M, Nieri M. Immediate versus early non-occlusal loading of dental implants placed flapless in partially edentulous patients: a 3-year randomized clinical trial. J Clin Periodontol 2012;39:196–202.
62. Tsirlis AT. Clinical evaluation of immediate loaded upper anterior single implants. Implant Dent 2005;14:94–103.
63. Aguirre-Zorzano LA, Rodriguez-Andres C, Estefania-Fresco R, Fernandez-Jimenez A. Immediate temporary restoration of single-tooth implants: Prospective clinical study. Med Oral Patol Oral Cir Bucal 2011;16:e794–e799.
64. Raes F, Cosyn J, De Bruyn H. Clinical, aesthetic, and patient-related outcome of immediately loaded single implants in the anterior maxilla: a prospective study in extraction sockets, healed ridges, and grafted sites. Clin Implant Dent Relat Res 2013;15:819–835.
65. Grandi T, Guazzi P, Samarani R, Grandi G. Immediate provisionalisation of single post-extractive implants versus implants placed in healed sites in the anterior maxilla: 1-year results from a multicentre controlled cohort study. Eur J Oral Implantol 2013;6:285–295.
66. Luongo G, Lenzi C, Raes F, Eccellente T, Ortolani M, Mangano C. Immediate functional loading of single implants: a 1-year interim report of a 5-year prospective multicentre study. Eur J Oral Implantol 2014;7:187–199.
67. Barone A, Toti P, Quaranta A, Derchi G, Covani U. The Clinical Outcomes of Immediate Versus Delayed Restoration Procedures on Immediate Implants: A Comparative Cohort Study for Single-Tooth Replacement. Clin Implant Dent Relat Res 2015;17:1114–1126.
68. Berberi AN, Noujeim ZN, Kanj WH, Mearawi RJ, Salameh ZA. Immediate placement and loading of maxillary single-tooth implants: a 3-year prospective study of marginal bone level. J Contemp Dent Pract 2014;15:202–208.
69. Berberi AN, Tehini GE, Noujeim ZF, Khairallah AA, Abousehlib MN, Salameh ZA. Influence of surgical and prosthetic techniques on marginal bone loss around titanium implants. Part I: immediate loading in fresh extraction sockets. J Prosthodont 2014;23:521–527.
70. Calvo-Guirado JL, Gomez-Moreno G, Aguilar-Salvatierra A, Guardia J, Delgado-Ruiz RA, Romanos GE. Marginal bone loss evaluation around immediate non-occlusal microthreaded implants placed in fresh extraction sockets in the maxilla: a 3-year study. Clin Oral Implants Res 2015;26:761–767.
71. Calvo-Guirado JL, Gomez-Moreno G, Delgado-Ruiz RA, Mate Sanchez de Val JE, Negri B, Ramirez Fernandez MP. Clinical and radiographic evaluation of osseotite-expanded platform implants related to crestal bone loss: a 10-year study. Clin Oral Implants Res 2014;25:352–358.
72. Calvo-Guirado JL, Gomez-Moreno G, Lopez-Mari L, Guardia J, Negri B, Martinez-Gonzalez JM. Crestal bone loss evaluation in osseotite expanded platform implants: a 5-year study. Clin Oral Implants Res 2011;22:1409–1414.
73. Canullo L, Bignozzi I, Cocchetto R, Cristalli MP, Iannello G. Immediate positioning of a definitive abutment versus repeated abutment replacements in post-extractive implants: 3-year follow-up of a randomised multicentre clinical trial. Eur J Oral Implantol 2010;3:285–296.
74. Canullo L, Goglia G, Iurlaro G, Iannello G. Short-term bone level observations associated with platform switching in immediately placed and restored single maxillary implants: a preliminary report. Int J Prosthodont 2009;22:277–282.
75. Chen ST, Darby IB, Reynolds EC. A prospective clinical study of non-submerged immediate implants: clinical outcomes and esthetic results. Clin Oral Implants Res 2007;18:552–562.
76. Cosyn J, Eghbali A, De Bruyn H, Collys K, Cleymaet R, De Rouck T. Immediate single-tooth implants in the anterior maxilla: 3-year results of a case series on hard and soft tissue response and aesthetics. J Clin Periodontol 2011;38:746–753.
77. Covani U, Canullo L, Toti P, Alfonsi F, Barone A. Tissue stability of implants placed in fresh extraction sockets: a 5-year prospective single-cohort study. J Periodontol 2014;85:e323–e332.
78. Covani U, Chiappe G, Bosco M, Orlando B, Quaranta A, Barone A. A 10-year evaluation of implants placed in fresh extraction sockets: a prospective cohort study. J Periodontol 2012;83:1226–1234.
79. Covani U, Crespi R, Cornelini R, Barone A. Immediate implants supporting single crown restoration: a 4-year prospective study. J Periodontol 2004;75:982–988.

80. Crespi R, Cappare P, Gherlone E. Radiographic evaluation of marginal bone levels around platform-switched and non-platform-switched implants used in an immediate loading protocol. Int J Oral Maxillofac Implants 2009;24:920–926.
81. Crespi R, Cappare P, Gherlone E. Fresh-socket implants in periapical infected sites in humans. J Periodontol 2010;81:378–383.
82. Crespi R, Cappare P, Gherlone E, Romanos GE. Immediate versus delayed loading of dental implants placed in fresh extraction sockets in the maxillary esthetic zone: a clinical comparative study. Int J Oral Maxillofac Implants 2008;23:753–758.
83. Groisman M, Frossard WM, Ferreira HM, de Menezes Filho LM, Touati B. Single-tooth implants in the maxillary incisor region with immediate provisionalization: 2-year prospective study. Pract Proced Aesthet Dent 2003;15:115–122, 124; quiz 126.
84. Guarnieri R, Ceccherini A, Grande M. Single-tooth replacement in the anterior maxilla by means of immediate implantation and early loading: clinical and aesthetic results at 5 years. Clin Implant Dent Relat Res 2015;17:314–326.
85. Kahnberg KE. Immediate implant placement in fresh extraction sockets: a clinical report. Int J Oral Maxillofac Implants 2009;24:282–288.
86. Kan JY, Rungcharassaeng K, Lozada JL, Zimmerman G. Facial gingival tissue stability following immediate placement and provisionalization of maxillary anterior single implants: a 2- to 8-year follow-up. Int J Oral Maxillofac Implants 2011;26:179–187.
87. Kolinski ML, Cherry JE, McAllister BS, Parrish KD, Pumphrey DW, Schroering RL. Evaluation of a variable-thread tapered implant in extraction sites with immediate temporization: a 3-year multicenter clinical study. J Periodontol 2014;85:386–394.
88. Malchiodi L, Cucchi A, Ghensi P, Nocini PF. Evaluation of the esthetic results of 64 nonfunctional immediately loaded postextraction implants in the maxilla: correlation between interproximal alveolar crest and soft tissues at 3 years of follow-up. Clin Implant Dent Relat Res 2013;15:130–142.
89. McAllister BS, Cherry JE, Kolinski ML, Parrish KD, Pumphrey DW, Schroering RL. Two-year evaluation of a variable-thread tapered implant in extraction sites with immediate temporization: a multicenter clinical trial. Int J Oral Maxillofac Implants 2012;27:611–618.
90. Migliorati M, Amorfini L, Signori A, Biavati AS, Benedicenti S. Clinical and Aesthetic Outcome with Post-Extractive Implants with or without Soft Tissue Augmentation: A 2-Year Randomized Clinical Trial. Clin Implant Dent 2015;17:983–995.
91. Mijiritsky E, Mardinger O, Mazor Z, Chaushu G. 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;18:326–333.
92. Prosper L, Crespi R, Valenti E, Cappare P, Gherlone E. Five-year follow-up of wide-diameter implants placed in fresh molar extraction sockets in the mandible: immediate versus delayed loading. Int J Oral Maxillofac Implants 2010;25:607–612.
93. Prosper L, Gherlone EF, Redaelli S, Quaranta M. Four-year follow-up of larger-diameter implants placed in fresh extraction sockets using a resorbable membrane or a resorbable alloplastic material. Int J Oral Maxillofac Implants 2003;18:856–864.
94. Shibly O, Patel N, Albandar JM, Kutkut A. Bone regeneration around implants in periodontally compromised patients: a randomized clinical trial of the effect of immediate implant with immediate loading. J Periodontol 2010;81:1743–1751.