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Disclaimer

Typical contents in ID

- **Evidence Reports** summarize the latest «Hot Topics» from relevant journals putting similar studies «side-by-side». This unique presentation of studies allows you to compare and contrast the patient populations, the treatment interventions, and the quality of the scientific methods. The «evidence-based bottom line» is presented with an overall summary statement at the beginning. Clinical notes by implantologists with special expertise on the topic complete the Evidence Report by providing their expert clinical opinion. **ID** is an implantology publication that provides attention to detail in balancing science with clinical opinion in such a clear, concise, and visually-friendly presentation.

- **Literature Analyses** provide you with an in-depth look at the research on a given topic. A «Literature Analysis» is a critical review of the literature on the epidemiology, treatment methods, and prognosis for implant-related topics or conditions. Literature Analyses are broader than «Evidence Reports» and are written to serve as a reference tool for implantologists to help them make decisions regarding how to manage patients, to assist them in evaluating needs for future research, and to use the material for future presentations.

- **Critical Appraisals** summarize the findings from important papers used for clinical decision making or marketing by implant companies. In addition to the summary, the study's methods and clinical conclusions are critically reviewed in an effort to challenge the implantology community into not accepting everything that is published, while fostering alternative explanations and ideas.

- **Case reports** give implantologists the opportunity to publish on unique patients using innovative or alternative methods for treating challenging patient conditions.

- **Research in Context** is a helpful «what is» section to consult if you've ever read a study and asked «what is a p-value» or any other research method question. It assists clinicians with the critical evaluation of the literature by briefly describing relevant aspects of research methods and statistical analysis that may bias results and lead to erroneous conclusions.

Case Report

Replacement of a maxillary denture, extraction of residual teeth and implant borne reconstruction in an immediate load protocol

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ABSTRACT

For many patients removable upper dentures are acceptable, as long as it is possible to leave parts of the palatum free from an un-desireable denture plate and a long as the dentures are not overly mobile. When the last teeth are lost, the patients expect a fast solution, they try to avoid full dentures. They consider full dentures outdated. Dental implantology provides the desired solution. In the case shown here the residual teeth were extracted and replaced by basal implants. Both types of basal implants were used: lateral implants and screw-type implants. Due to the surface properties and the reduced diameter of the basal implants the extraction sockets could be equipped immediately after the extraction. The first fixed restauration was incorporated on day two after the operation.
The use of basal implants with thin, polished vertical implant portions allows immediate reconstruction even after extractions and in unfavourable bone situations. Cortial bone areas may be reached with basal implants in several areas of the jaw bone.

INTRODUCTION

In the last decades intricate connection elements between anchouring teeth and have been developed. The disadvantage of those dentures is that the teeth included into these constructions are overloaded and that they must provide strong retention for the crowns carrying connection elements. The fixed & removable reconstruction in the case shown here had been incorporated shortly before the patient requested our help, Fig. 1: the bridges in the upper jaw had become loose several times, because the retention was to small for the masticatory load. We did not see any possibility to re-cement the bridges with permanent success. After discussing several treatment alternatives, the patient decided for a reconstruction on implants.

MATERIAL & METHOD

In local anaesthesia the extraction of all remaining teeth in the upper jaw was attempted. Both canines resisted a complete extraction: only part by part was taken out until only very little access to the root was given. In this situation we decided to open a large vestibular flap. Using the FG-vertical cutter for basal implants a vertical cut through the vestibular cortical to the root was made and the root of both canines were cut into two halves. After this the two root-haölve were taken out easily. With a 9mmd contra-angle cutter (with inter –disk-distance of 5mm) two horizontal slots were prepared. The Crestal slot was enlagened to 10 mmd, the basal slot was enlargened to 15 mmd. After prepar-

ing the implant bed in this way a XBBS 14/10 H6 double-BOI-Implant was inserted from the lateral. The alveolus of the centrals were equipped with BCS 3.5 17 mm implants. Those implante engaged into the resistant bone of the anterior alveolar spine. The area of the 1st premolars was equipped with a BCS 3.5 23 mm and also the area of the 2nd Promolar received a basal screw implant. In order to extend the support of the bridge to the first molar we inserted two long basal implants BCS 3.5 23 in an oblique manner in front of the sinus. Those two implant bypassed the other implants on the palatal side of the alveolar crest. (Fig. 2)

We did not observe and contacts between the implants during insertion. The intention was, to ensure cortical anchorage of the basal screw implants in the cortical bone provided by the floor of the nose and the sinus respectively. Both distal implant were equipped with cemented angulation adapters immediately after the placement. Following to the setting of the cement, the distally projecting parts of the implant heads were cut of with a herd metal cutter on the turbine. Impression caps were placed onto the 10 anterior implants. An impression was taken immediately and a temporary bridge was inserted. During the next day the metal frame was tried in and at the end of the following day the metal-to plastic-bridge was incorporated using temporary cement.

RESULTS

The unfavorable situation of the masticatory system of this patient was changed into a stable, implant-borne bridge within 48 hours. The healing occurred uneventful, the situation remained stable and no changes in the temporary bridge were necessary. The patients expectations had been met completely.

RESULTS

Traditional concepts in implantology include wide diameter implants and an unloaded, mostly covered healing time after placements into sockets. Conventional screw tye implants seem unpractical for applications in extraction cases in combination with open healing protocols. The reason is, that their surface is sand-blasted and/or etched, and provides considerable retention for bacteria. Hence traditional protocols with these implants include a covered healing time, allowing the woven bone to close the socket in a sterile environment.

Our concept becomes possible through using appropriate implants with the following features: thin, polished vertical parts, without threads or other retentive elements near the location of the potential bacterial attack. This demand is fulfilled by both types of basal implants used here; laterally inserted BOI®-implants, and vertically inserted BCS implants.

For safe immediate loading protocols today two concepts are used widely:

- One concept (shown here) includes cortical & macro-mechanical anchorage of implants. The cortical bone is known to be quite resistant to resorption (because it is required for structural reasons) and due to its high degree of mineralization this bone is prepared for carrying large loads. This concepts applies the strategy of orthopaedic surgeons & the principles of fracture treatment. When chosing the best implants, the width of the bone is considered (for lateral implants) and the distance between the alveolar crest and the opposing cortical is considered (for basal screw implants). Integration along the vertical implant part is not essential for the success of the implant, but of course osseo- integration will occur over time also along the vertical implant parts.

- The second concept includes corticalisation of spongeous bone through with conical implants providing 1retentive threads. Corticalized (compressed) bone looses the capability of the initiation of osteonal remodeling. Hence the compressed bone areals may not be origin of new osteons but only the target. The implants used for this concepts must either provide a surface enlargening (sandblasting) or large retentive elements (e.g. thread) or a combination of both. The width of the implant is chosen according to the available bone (between 3 and 5 mm) and the length of the implant varies between 10 and 15 mm in most cases.

In extraction cases the lateralization of bone is not an option in the crestal part of the alveoli, because this would require the involvement of implants with overly large diameters. Also the usage of implants with rough surfaces adds risks to the procedure, if the sockets remains open because the implants are loaded immeditely.
For this reason we prefer to use implants anchoured in cortical areals: this offers safety both with respect to infections and with respect of loss of stability during early function. In our view, to avoid early infection of the extraction socket, implants exposed to the unsterile oral environment should be machined (polished) at least in the crestal portion of the implant. To prevend peri-implantitis, the mucosal penetration diameter must be as thin as possible.
This design contradicts the traditional concept of creating an "emerging profile" for the implant crown. In our view the introduction of the "emerging profile-concept" is a blessing only in selected cases, e.g. when enough vertical and horizontal bone is available and where teeth have remained adjacent to the implant. The teeth help to maintain the vertical bone level in those cases. Our concept however, is applicable and successful in all cases and it avoids risky augmentations.
Immediate implant placement in extraction cases leads occasionally to the requirement of re-basing the bridge after several weeks: the shrinkage of the gums can`t be anticipated completely in the design of the bridge, and remodeling will also reduce the vertical and horizontal bone height. Therefore the cemen-

tation should be done with temporary cement (e.g. Temp Bond®). In some cases the veneering needs to be replaced completely after the bone and the soft tissues have healed. If the same metal framework is used for the "second bridge" we can be sure, that the frame will sit tension-free (passive) on the implants.

CONCLUSION

The patients demand for immediate restoration after extractions can be met by using lateral and basal implants. Depending on the situation after the extraction, either basaly anchoured screw implants (BCS) or bi-cortically anchoured lateral implants (BOI) may be used alone or in combination. Our concept does not include any augmentation. If vertical bone is missing, we use the horizontal bone supply and keep the implant anchoured in the lateral cortical walls of the mandible or in the lateral walls of the maxilla, the palatal wall of the alveolar crest of the maxilla, the lateral and/or basal borders of the maxillary sinus or in the lateral cortical walls of the nasal cavity.

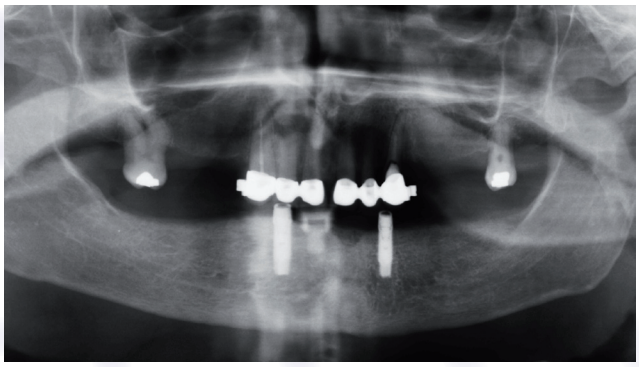


Figure 1. Preoperative panoramic view of the dentition in upper and lower jaw. The remaining teeth did not provide enough retention for the blocks of crowns holding the denture. Both molars were mobile. Severe intra-bony infections with suppuration and pronounced bone loss around the left canine were diagnosed immediately before the implant placement.

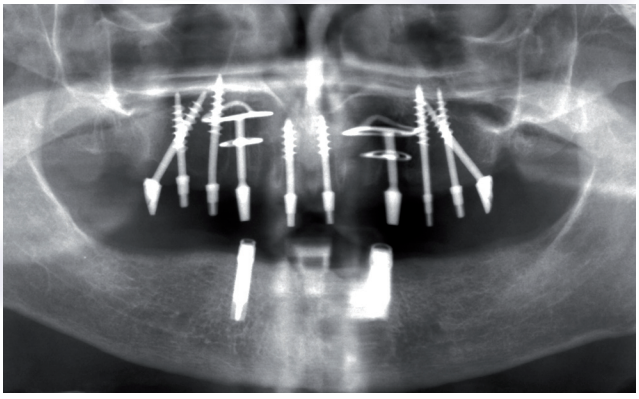


Fig. 2: Postoperative panoramic view of the same patient after placement of implants and cementing angulation-adapter on the distal implants. Note that the anterior segment of the maxilla need strong support by the implants, because the anterior mandibular dentition will be supported strongly by the two anterior implants.

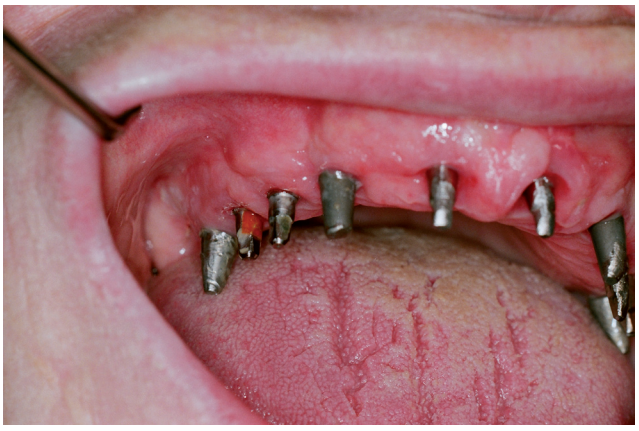


Fig. 3. 10 weeks postoperatively the gums appeared well healed and infection free. All extraction sockets had closed uneventfully.

Fig. 4. The metal-to-plastic bridge placed on the second day after implant placement.

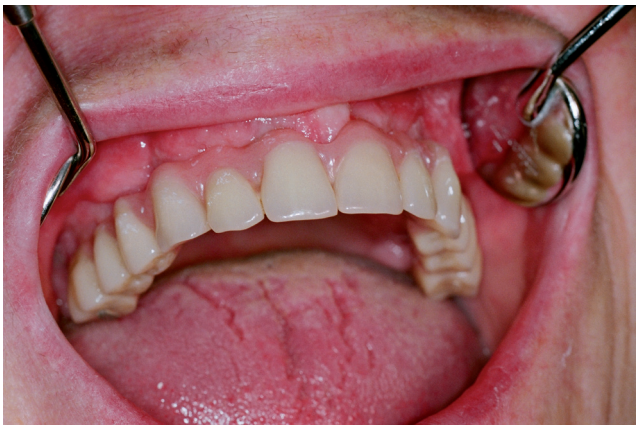


Fig. 5. Intra-oral view, 10 weeks after implant placement. No request from the patient to replace this bridge for a ceramic bridge without pink base.

Evidence Report

Title: The influence of inter-implant distance upon dental implant outcomes

EVIDENCE REPORT PURPOSE

In dental implantology, the establishment of a supracrestal soft tissue seal for protection of the osseointegration is considered to be important for the success of the treatment. Because the bone crest constitutes the base for the soft tissue seal, alterations in the peri-implant bone level will affect the position of the soft tissue margin, which in turn may have a significant impact on the aesthetic outcome of the implant therapy. It has been suggested that both vertical and lateral bone loss at implants could have an effect on the level of the bone crest and soft tissue between two implants.

OBJECTIVE

To critically summarize the recently published literature examining the influence of inter-implant distance upon outcomes of intraoral dental implants.

SUMMARY

One study reported a greater mean crestal bone loss for implants with ≤ 3mm distance between compared to implants that were > 3mm apart. Another study reported that crestal bone loss was related to a decreased inter-implant distance. One other study found that, when the tooth/implant or inter-implant distance was ≤ 2.5 mm, dental papilla was absent. Studies were of moderate to poor quality so conclusions based on reported differences should be considered with caution. However, this particular study question is a finite one that would unlikely be assessed in a higher quality study, at least as a primary objective. This Evidence Report, therefore, provides some insight into this interesting clinical question. Additional methodologically rigorous comparative studies with comparable characteristics between groups should be considered to better evaluate the effect of inter-implant distance upon dental implant treatment outcomes.

SAMPLING

A MEDLINE search was performed to identify recent human studies published between January 2000 and June 2008 examining the influence of inter-implant distance upon intraoral dental implant treatment outcomes. Four articles evaluated the treatment comparison of interest and are included in this report, Table 1.

Table 1. Medline Search Summary

Terms	Hits	Reviewed
Search dental implants OR dental implantation, endosseous [MeSH]	17,556	
Search (dental implants OR dental implantation, endosseous [MeSH]) AND (implant distance OR thin OR platform switch), Limits ENGLISH, Human, Literature containing Abstracts	121	4
Bibliographies from existing literature	0	0
Total Reviewed	4	

Common Outcome Measures

- Vertical bone loss
- Lateral bone loss
- Soft-tissue parameters

Interventions

Studies that evaluated outcomes of inter-implant distance for intraoral dental implants were described as follows. All details regarding implant type are reported if reported by the author. If implant type is not reported, author failed to report it in the text of the manuscript:

Lee (2005)

- Fifty-two patients who had implant-supported, fixed prostheses in posterior sites for more than 12 months underwent evaluation of interproximal papillae between two adjacent implants. Subjects had various implant types, designs and surfaces (turned, titanium dioxide-blasted, and acid-etched).

Gastaldo (2004)

- Interproximal sites between adjacent implants (group 1) and between a tooth and an implant (group 2) were evaluated in 48 patients who had implant-supported, fixed prostheses for a minimum of 18 months and a maximum of 6 years.

Cardaropoli (2003)

- In a retrospective study, 28 partially dentate patients had been fitted with partial fixed prostheses supported by 3 standard Branemark implants and underwent post-treatment follow-up at 1 and 3 years.

Tarnow (2000)

- In a radiographic study, radiographic measurements were taken between 1 and 3 years after implant exposure in 36 patients who had 2 adjacent machined titanium implants separated by different distances.
-

Table 2. Studies evaluating the influence of inter-implant distance upon outcomes for intraoral dental implants

Author (year)	Study Design	Population	Diagnostic Characteristics	Follow-up: %	LoE*
Lee (2005)	Case series	N=52; Ninter = 72 female: 42.3% age: 52.4 (40-62) yrs	Partially edentulous, rehabilitated with implant-supported, fixed prosthesis	N/A	Poor
Gastaldo (2004)	Case series	N=48 female: 58.3% age: 45 (19-72) yrs	Partially edentulous, rehabilitated with implant-supported, fixed prosthesis	N/A	Poor
Cardaropoli (2003)	Retrospective Cohort	N=28; Npros=35 female: 64.3% age: 65 (48-81) yrs	Partially edentulous in lateral jaw, rehabilitated with implant-supported, fixed prosthesis	3 years: NR	Moderate
Tarnow (2000)	Case series	N=36 female: NR age: NR	Two adjacent implants separated by different distances	N/A	Poor

N=number of subjects; Ninter=number of interproximal sites; Npros=number of prostheses

*Level of Evidence (LoE) is based on study design and methods (Very high, High, Moderate, and Poor)

†NR (not reported) = for follow-up rate either not reported or precise follow-up rate could not be determined since the initial number of eligible patients or number lost to follow-up were not provided.

Table 3. Evaluation of articles studying inter-implant distance upon outcomes for intraoral dental implants

Study design and methods	Lee (2005)	Gastaldo (2004)	Cardaropoli (2003)	Tarnow (2000)
1. What type of study design?	Case Series	Case Series	Retrospective Cohort	Case Series
2. Statement of concealed allocation?*	N/A	N/A	N/A	N/A
3. Intention to treat?*	N/A	N/A	N/A	N/A
4. Independent or blind assessment?	NO	NO	NO	NO
5. Complete follow-up of >85%?	NR	NR	NR	NR
6. Adequate sample size?	YES	YES	YES	YES
7. Controlling for possible confounding?	YES	NO	YES	NO
LEVEL OF EVIDENCE	Poor	Poor	Moderate	Poor

* Applies to randomized controlled trials only

RESULTS

Inter-implant Bone Loss

Vertical bone loss

- Mean crestal bone loss for implants with a 3mm or less distance between (n=25) them was 1.04mm, while mean crestal bone loss for implants that were more than 3.0mm apart (n=11) was 0.45mm (Figure 1; no significance statistics presented) [Tarnow].

- The mean distance from the base of the contact point to the inter-implant crestal bone was 4.7 ± 1.2mm [Lee].

- For tooth/implant units after 3 years, the mean marginal bone loss at the tooth was 0.4 ± 1.0mm, at the implant was 0.5 ± 1.2mm, and at the mid-proximal bone crest level was 0.3 ± 0.5mm [Cardaropoli].

- For tooth/implant units after 3 years, multiple regression analysis with respect to vertical bone loss at the mid-proximal bone crest level revealed a significant association with bone level change at the tooth site ($p<.01$) [Cardaropoli].

- For implant/implant units after 3 years, the mean marginal bone loss at the proximal implant surfaces facing the implant/implant unit was 0.7 ± 0.6mm and 0.6 ± 0.8mm. At the mid-proximal bone crest, there was a mean reduction of 0.5 ± 0.5mm [Cardaropoli].

- For implant/implant units after 3 years, multiple regression analysis revealed that a loss of mid-proximal bone crest level was related to decreased horizontal inter-implant distance ($p<.05$) [Cardaropoli].

Lateral bone loss

- The lateral distance from the implant to the crest of the ridge ranged from 1.34 to 1.40 ± 0.60mm [Tarnow].

- For implant/implant units after 3 years, the mean lateral bone loss was 0.3 ± 0.4mm and 0.4 ± 0.5mm for the anterior and posterior implant sites, respectively [Cardaropoli].

Interproximal soft-tissue parameters

- The mean length of the papilla from the crestal bone to the tip of the papilla was 3.3 ± 0.5mm. The width of keratinized mucosa from the mucogingival junction to the tip of the interproximal papilla between adjacent implants was 4.5 ± 1.7mm. The mean distance from the base of the contact point to the inter-implant crestal bone was 4.7 ± 1.2mm. The mean horizontal distance between adjacent implants was 3.1 ± 0.5mm [Lee].

- In a multiple regression analysis, the mean length of the papilla from the crestal bone to the tip of the papilla was directly related to the width of keratinized mucosa from the mucogingival junction to the tip of the interproximal papilla between adjacent implants (p=.001) [Lee].

- For the tooth/implant interproximal region, when the distance from the base of the contact point to the bone crest was from 3-5mm, the papilla was present 80-100% of the time (p<.05). The papilla filled the entire proximal space when this vertical distance was 3 and 4mm [Gastaldo].

- When the tooth/implant distance was 3 to 4mm, the papilla was present 75-88% of the time (p<.05, Figure 2). When this distance was ≤2.5mm, the papilla was present 0% of the time, independent of the distance from the base of the contact point to the bone crest (p<.05) [Gastaldo].

- For implant/implant interproximal regions, when the distance from the base of the contact point to the bone crest was 3mm only, the papilla was present 100% of the time (p<.05). The papilla filled the entire proximal space when this vertical distance was 3mm [Gastaldo].

- When the inter-implant distance was 3 to 4mm, the papilla was present 70-80% of the time (p<.05, Figure 2). When this distance was ≤2.5mm, the papilla was present 0% of the time, independent of the distance from the base of the contact point to the bone crest (p<.05) [Gastaldo].

Methodological considerations

- One study was a retrospective cohort study with a rating of moderate (low quality cohort), while the remaining studies were case series studies with a poor level of evidence rating. No high quality randomized controlled trials or high quality cohort studies were identified in the literature.

- However, this particular study question is a

finite one that would unlikely be assessed in a higher quality study, at least as a primary objective. This Evidence Report, therefore, provides some insight into this interesting clinical question.

- In general, these studies provided outcomes that were unique to each study and, therefore, were not comparable.

- Only one study [Cardaropoli] reported subject follow-up since the remaining studies were case series (cross-sectional) studies. This study did not provide a follow-up rate, though an 85% follow-up rate is necessary to ensure valid results.

REFERENCES

Studies

Study 1

Lee D-W, Park K-H, Moon I-S (2005)

Dimension of keratinized mucosa and the interproximal papilla between adjacent implants

J Periodontol 76:1856-60.

Study 2

Gastaldo JF, Cury PR, Sendyk WR (2004)

Effect of the vertical and horizontal distances between adjacent implants and between a tooth and an implant on the incidence of proximal papilla

J Periodontol 75:1242-6.

Study 3

Cardaropoli G, Wennstrom JL, Lekholm U (2003)

Peri-implant bone alterations in relation to inter-unit distances

Clin Oral Impl Res 14:430-36.

Study 4

Tarnow DP, Cho SC, Wallace SS (2000)

The effect of inter-implant distance on the height of inter-implant bone crest

J Periodontol 71:546-9.

Figure 1. Inter-implant Mean Crestal Bone Loss

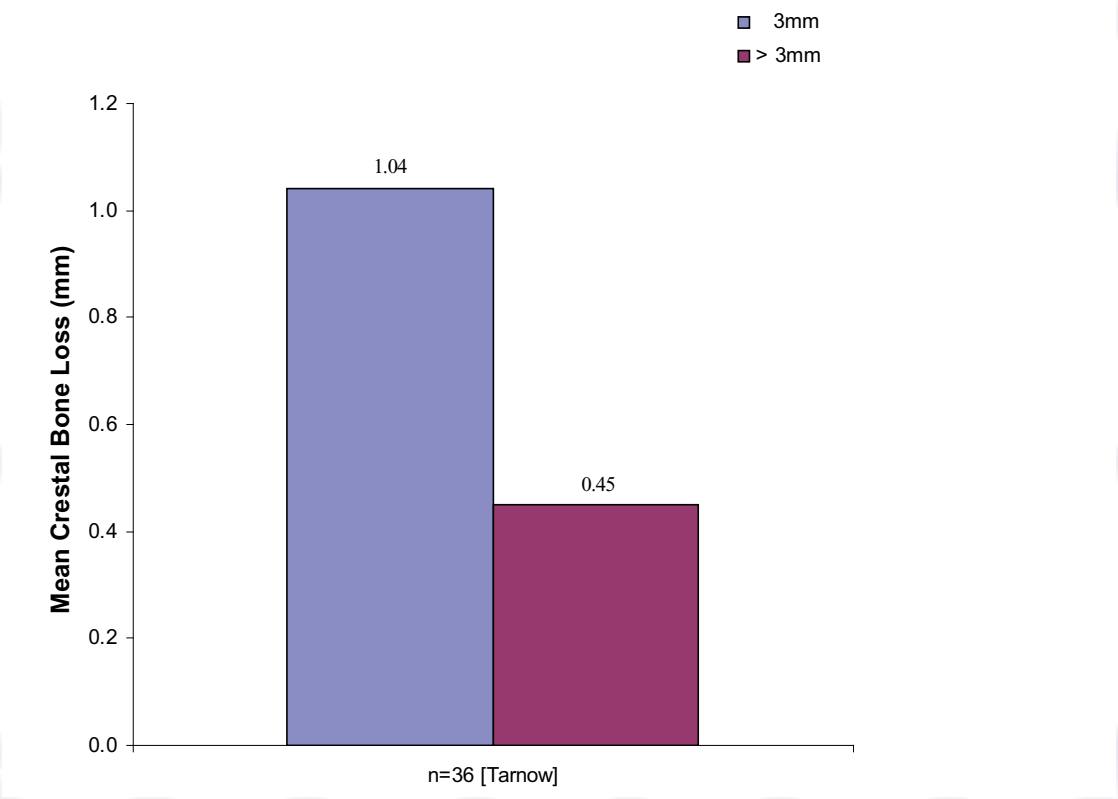
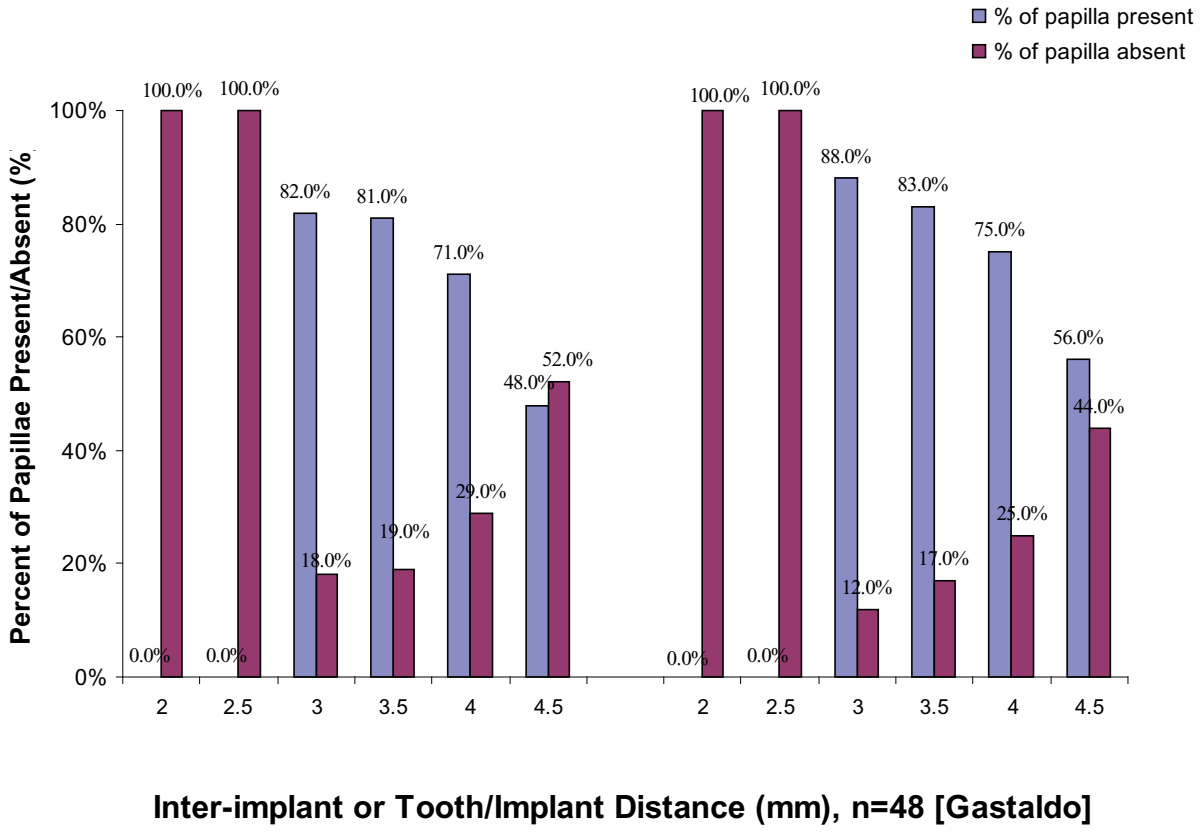


Figure 2. Percent of Papillae Present/Absent by Inter-implant or Tooth/Implant Distance



Critical Appraisal

REFERENCE:

Tarnow DP, Cho SC, Wallace SS. The effect of inter-implant distance on the height of inter-implant bone crest. J Periodontol. 2000 Apr; 71(4):546-9.

PERFORMING CLINIC:

Department of Implant Dentistry, New York University College of Dentistry, New York, USA.

AUTHORS' SUMMARY:

There is a lateral component to the bone loss around implants in addition to the more commonly discussed vertical component. The clinical significance of this phenomenon is that the increased crestal bone loss would result in an increase in the distance between the base of the contact point of the adjacent crowns and the crest of bone. This could determine whether the papilla was present or absent between 2 implants as has previously been reported between 2 teeth. Selective utilization of implants with a smaller diameter at the implant-abutment interface may be beneficial when multiple implants are to be placed in the esthetic zone so that a minimum of 3 mm of bone can be retained between them at the implant-abutment level.

STUDY OBJECTIVES:

To evaluate the lateral dimension of the bone loss at the implant-abutment interface and to determine if this lateral dimension has an effect on the height of the crest of bone between adjacent implants separated by different distances.

STUDY DESIGN:

Case series consisting of 36 patients (age and gender not reported) who were part of a longitudinal study (no reference) at the New York University Department of Implant Dentistry.

INCLUSION/EXCLUSION CRITERIA:

- Patients who had previously received 2 adjacent machined titanium implants who had radiographs between 1 and 3 years after implant placement.

STUDY METHODS:

- Radiographic measurements were taken at a minimum of 1 and a maximum of 3 years after implant exposure to determine bone loss.
- Lateral bone loss was measured from the crest of bone to the implant surface.
- Crestal bone loss was also measured from a line drawn between the tops of the adjacent implants. The data were divided into 2 groups, based on the inter-implant distance at the implant shoulder (either greater than or less than 3mm).

RESULTS:

• Lateral bone loss was 1.34 mm (SD = 0.36mm) from the mesial implant shoulder to the bone crest and 1.40 mm (SD = 0.60) from the distal implant shoulder to the bone crest between the adjacent implants, Table.
• Crestal bone loss was 0.45 mm for implants > 3mm apart.
• Crestal bone loss was 1.04 mm for implants ≤ 3mm apart.

	Bone loss (mm)	
Lateral	**Distance A (n=36)**	**Distance B (n=36)**
Mean (± SD)	1.34 ± .36	1.40 ± .60
Crestal	**Mean vertical crestal bone loss**	
≤ 3mm (n=25)	1.04	
> 3mm (n=11)	0.45	

CONCLUSIONS PROVIDED BY AUTHORS:

The study demonstrates a trend of increased crestal bone loss as inter-implant distance decreases. Selective utilization of implants with a smaller diameter at the implant-abutment interface may be beneficial when multiple implants are to be placed in the esthetic zone so that a minimum of 3mm of bone can be retained between them at the implant-abutment level.

REVIEWER'S EVALUATION:

Methodological Principle	
Randomized design	NO
Independent or blind assessment	NO
Adequate sample size	NO
Appropriate analysis	NO
Appropriate measures	
Radiological analysis	YES

1. WHAT WERE THE STUDY'S METHODOLOGICAL STRENGTHS?

• Clearly defined objective.
• There were no other strengths identified.

1. WHAT WERE THE STUDY'S METHODOLO GICAL LIMTATIONS?

• The authors did not provide basic patient demographic data such as age and gender.

• The authors did not provide basic general health or comorbidity data that may influence crestal bone loss. Examples may include smokers, patients who are diabetic, or patients with bone conditions.

• The authors report that radiographs were performed between 1 and 3 years after implant placement; however, did report means or control for these differences when comparing crestal bone loss. Is it possible that 3 years could be significantly different than 1 year?

• The sample size was very small. The authors compared 25 subjects (≤ 3mm) to 11 subjects (>3mm) and concluded that distance between implants is associated with crestal bone loss. They did not report the variability of these findings (i.e., standard deviation, see table) and therefore we cannot calculate whether these differences were statistically significant.

• The authors did not report any analytical comparisons with p-values or confidence intervals. They only reported the mean crestal loss for the two categories. Again, this difference may be the result of chance with such a small sample size and no statistical analysis.

• Lastly, even if a statistical analysis was performed that demonstrated these changes in crestal bone loss as significant, the author did not report and therefore could not have controlled for other factors that might influence crestal bone loss such as age, bone conditions, smokers, or other comorbidities.

3. HOW MIGHT THE FINDINGS FROM THIS CRITICAL APPRAISAL BE APPLIED TO PATIENT CARE?

The authors used implants whose maximum collar diameter equals the maximum thread diameter. This is an untypical type of implant. Most of the implants available are of the Tulip-type (Straumann, SSO, STc, STO, etc.) or have at least some difference between collar-diameter and thread-width. We must doubt strongly, that the results are applicable to all types and designs of implants.

The authors should have registered the width of the bone at baseline. This way bone loss in sagitally reduced ridges could have been distinguished from wide ridges. We have to assume from the experience we have today, that the width of the ridge is a determining factor for bone loss around implants.

Furthermore the author should have made sure, that they work with a coherent study group: individuals "having two adjacent implants present", are not a coherent group, as a number of factors can influence the result:

- Next to the implants may be teeth which maintain the vertical level of bone well

- Next to the implant may be bone turning to atrophy, which by itselve leads to bone loss

-Bone loss in different regions varies

4. WERE ALL IMPORTANT ASSESSMENTS PERFORMED? IF NOT, WHAT ASSESSMENTS SHOULD BE CONSIDERED

Measuring distances "A", "B", and "C" are not clinically relevant outcomes, as implant loss occurs anyway in this type (design) of implants. The cases should have been grouped differently so that the result could be matched to the remaining dentition.

The diameter and type of the implants used should have been mentioned. The "results" are limited to these implants.

5. ARE THERE ALTERNATIVE EXPLANATIONS FOR THE FINDINGS OBSERVED IN THIS STUDY?

It seems that the authors have assumed, that bone loss occurs anyway in the implants used and that the bone loss will reach the first thread and stop there. This is the case for formerly sold Branemark implants etc.

The vertical crest height ("C" in the graphs of the authors) does not play any role under these circumstances. The authors should have prolonged the observation period to distinguish cases showing really progressing bone loss from typical bone loss.

6. HOW MIGHT THE FINDINGS BE APPLIED TO PATIENT CARE?

It is not possible to draw any conclusion to patient care. Especially the results may not be used to draw any conclusion on cases with thin diameter implants (e.g. less than 3.7 mm), to implant without crestal widening (e.g. not to KOS-implants) or to implants showing no threads along the crestal part of the bone (e.g. BCS-implants or thin necked basal implants).

Note also that the effect of reduced distance between endosseous parts of implants (screw threads or disk plates) was not investigated and conclusions may not be drawn to those implant types.

The results may also not be applied to implant without threads: bone loss in threaded implants is known to stop are slow down at the first tread. Patterns of bone loss in non-threaded implants have not been investigated yet.

Evidence Report

Effect of diabetes mellitus on dental implants survival and complications

EVIDENCE REPORT PURPOSE

Diabetes mellitus is a group of metabolic disorders characterized by an increase in plasma glucose levels. The resulting hyperglycemia is caused by a defect in insulin secretion, insulin action, or both. Chronically high levels of plasma glucose may be associated with a wide range of systemic complications such as retinopathy, nephropathy, neuropathy, micro- and macrovascular disease, and altered wound healing. In implantology, microvascular disease may contribute to delayed wound healing, reversed bone turnover, and increased susceptibility to infection

OBJECTIVE

To critically summarize the recently published literature examining implant survival and other outcomes in studies comparing patients with and without diabetes mellitus.

SUMMARY

There was a trend towards lower implant survival rates for subjects with diabetes mellitus compared to nondiabetic subjects. One study found increased implant survival rates in diabetic patients [1] when 0.12% chlorhexidine digluconate was used at the time of implant placement compared to not, [2] when pre-operative antibiotics were used compared to not, and[3] when hydroxyapatite (HA) coated implants were used compared to non-HA implants. Studies found significantly greater levels of peri-implant bone loss in (a) patients with diabetes compared to nondiabetics and (b) patients with poor diabetic control compared to those who were well-controlled. Further, there was a significantly greater prevalence of peri-implantitis in poorly-controlled diabetics compared to well-controlled individuals. Post-operative complications were also greater in poorly-controlled diabetics compared to those with good control, though the prevalences were not significantly different between these two groups. Additional methodologically rigorous comparative studies are needed to better evaluate the treatment outcomes of dental implants in relation to diabetes; however, these findings should be considered when treating patients with diabetes.

SAMPLING

A MEDLINE search was performed to identify recent studies published between January 2000 and September 2008 examining the effect of diabetes mellitus on dental implant treatment outcomes. From a list of 16 articles, 3 included implant treatment outcomes that met our criteria and are included in this report, Table 1.

Table 1. Medline Search Summary

Terms	Hits	Reviewed
Search dental implants OR dental implantation, endosseous [MeSH]	17,913	
Search (dental implants OR dental implantation, endosseous [MeSH]) AND [diabetes OR diabetes mellitus]), Limits ENGLISH, Human, Literature containing Abstracts	52	2
Search (dental implants OR dental implantation, endosseous [MeSH]) AND [diabetes OR diabetes mellitus] AND comparative studies), Limits ENGLISH, Human, Literature containing Abstracts	8	1
Total Reviewed		3

COMMON OUTCOME MEASURES:

- Implant survival
- Implant survival, categorized
- Peri-implant bone resorption
- Peri-implantitis
- Post-operative complications

INTERVENTIONS:

Dental implants were placed in subjects described as follows:

Tawil (2008)

• Forty-five Type 2 diabetic patients with a glycosylated hemoglobin (HbA1c) value ≤ 7.2% during the perioperative period were matched by age, gender and type of implant to 45 consecutively treated nondiabetic patients. Individuals were followed prospectively for 1 to 12 years.

Morris (2000)

• In a retrospective study, 255 implants were placed in individuals with Type 2 diabetes, and 2632 implants were placed in patients without diabetes. Implant outcomes were followed for 3 years after implantation.

Accursi (2000) (within Elsubeihi & Zarb 2002)

• In a retrospective study, 15 medically controlled diabetes mellitus patients were matched to 2 non-diabetic control subjects by age, sex, location of implants, type of prosthetic restoration, opposing dentition, and duration of edentulism. Individuals were followed for 1 to 17 years, and implant survival in diabetic patients (n=59 implants) was compared with that of non-diabetics (n=111 implants).

Note:

Glycosylated hemoglobin values reflect average blood sugar levels for the 2- to 3- month period before the blood test. Levels from 4% to 7% indicate well-controlled diabetes, and levels above approximately 7% indicate poor control.

Table 1. Medline Search Summary

Author (year)	Study Design	Population	Diagnostic Characteristics	Diabetes		Follow-up (%)	LoE†
				Diabetes Mellitus (Group A)	No Diabetes (Group B)		
Tawil -2008	Prospective cohort	N = 90 female: 37% age: diabetics = 64.7 (43-84) yrs; nondiabetics = 59.6 (29-85) yrs	Indication for dental implant placement	N=45; Ni=255	n=45; Ni=244	1-12 years (mean 42.4 months): NR*	Moderate
Morris (2000)	Retrospective cohort	N = 663 female: 5.9% age: NR	Indication for dental implant placement	N=NR; Ni=255	N=NR; Ni=2632	3 years: NR*	Moderate
Accursi (2000)	Retrospective cohort	N = 45 female: NR‡ age: NR‡	Indication for dental implant placement	N=15; Ni=59	N=30; Ni=111	1-17 years: NR*	Moderate

N = Number; Ni = Number of implants; NR = Not Reported
†Level of Evidence (LoE) is based on study design and methods (Very high, High, Moderate, and Poor)
*NR (not reported) = for follow-up rate either not reported or precise follow-up rate could not be determined since the initial number of eligible patients or number lost to follow-up were not provided.
‡ = Subjects with diabetes were age- and sex-matched to 2 control subjects without diabetes.

Table 1. Medline Search Summary

Study design and methods	Tawil (2008)	Morris (2000)	Accursi (2000)
1. What type of study design?	Prospective Cohort	Retrospective Cohort	Retrospective Cohort
2. Statement of concealed allocation?*	N/A	N/A	N/A
3. Intention to treat?*	N/A	N/A	N/A
4. Independent or blind assessment?	NO	NO	NO
5. Complete follow-up of ≥85%?	NR	NR	NR
6. Adequate sample size?	NO	YES	NO
7. Controlling for possible confounding?	YES	NO	YES
LEVEL OF EVIDENCE	Moderate	Moderate	Moderate

* Applies to randomized controlled trials only
NR = not reported

RESULTS

Overall implant survival (Figure 1)

There was a trend for lower survival rates in those subjects with diabetes.

- Overall implant survival for Type 2 diabetic subjects was 97.6%, while that of nondiabetics was 99.6% (p>.05) in a study in which subjects were followed for 1 to 12 years. [Tawil]
- At 3 years, subjects with Type 2 diabetes demonstrated a survival rate of 92.2% and those without diabetes had a survival rate of 93.2%; p>.05. However, in a multivariate regression, diabetes (p<.05) and health status (p<.02) were significant factors influencing implant survival. [Morris]
- In a retrospective study in which individuals were followed for 1 to 17 years, subjects with diabetes experienced a 93.2% survival rate, while those without diabetes had a survival of 94.6%; p>.05. [Accursi].

Implant survival, by treatment (Figure 2)

- When 0.12% chlorhexidine digluconate (CHX) was used at the time of implant placement in Type 2 diabetics, there was a significantly greater implant survival rate at 3 years compared to Type 2 diabetics on whom CHX was not used (95.6% vs. 86.5%; p<.05). In non-diabetic subjects, there was an increased, though non-significant, survival rate in those with CHX compared to those without CHX (94.3% vs. 91.8%, p>.05). [Morris]
- Pre-operative antibiotic usage in Type 2 diabetics provided a significant improvement in implant survival at 3 years (97.1% vs. 86.6%; p<.05). In

non-diabetics, there was an increased though non-significant implant survival rate in individuals in whom pre-operative antibiotics were used compared to those without pre-operative antibiotics at 3 years (95.1% vs. 90.6%, p>.05). [Morris]

• The use of hydroxyapatite (HA) coated implants compared to non-HA coated implants significantly improved implant survival in both Type 2 diabetics (97.9% vs. 84.7%; p<.05) and non-diabetics (96.7% vs. 87.2%; p<.05). [Morris]

Peri-implant bone loss

• One study reported a significantly greater mean loss of crestal bone height in the first year in subjects with medically controlled diabetes compared to those without diabetes (-0.25 ± 0.07mm vs. -0.06 ± 0.03 mm, respectively; p<.05) [Accursi].

• Another study found significantly greater peri-implant bone loss in Type 2 diabetic patients with poor diabetic control (HbA1c levels ≥ 7%) compared to those with good control (HbA1c levels < 7%) (-0.24 ± 0.28 mm vs. -0.5 ± 0.7 mm, respectively; p=.01). [Tawil]

Peri-implantitis (Figure 3)

• In Type 2 diabetics with different levels of diabetic control, there was a significantly greater prevalence of peri-implantitis in patients with HbA1c levels ≥ 7% compared to those with levels < 7% (30.4% vs. 0%, p=.05). [Tawil]

Post-operative complications (Figure 3)

• In Type 2 diabetics with different levels of diabetic control, there was a greater prevalence of post-operative complications in patients with HbA1c levels ≥ 7% compared to those with levels < 7%, though the difference was not statistically significant, likely due to small sample sizes (52.2% vs. 27.3%, p>.05). [Tawil]prevalence of peri-implantitis in patients with HbA1c levels ≥ 7% compare

Methodological considerations

• All studies reviewed were cohort studies with a rating of moderate (low quality cohort) level of evidence. No very high quality randomized controlled trials or high quality cohort studies were identified in the literature.

• All of the studies had small sample sizes, and two of the studies [Tawil, Accursi] had sample sizes that were likely inadequate to show a difference between the study groups, especially when samples were stratified into subgroups.

• Since multiple implants in the same subject are not statistically independent, either one implant should be chosen per patient or statistical analysis should account for multiple implants per patient. Only one of the studies reviewed [Tawil] accounted for multiple implants in the same subject, but only for complication rates.

• None of the studies reported a follow-up rate or provided data adequate enough to calculate the follow-up rate. A follow-up rate of ≥85% is necessary to ensure valid study results.

REFERENCES

Studies

Study 1

Tawil G, younan R, Azar P, Sleilati G (2008)

Conventional and advanced implant treatment in the type II diabetic patient: surgical protocol and long-term clinical results.

Int J Oral Maxillofac Implants 23:744-52.

Study 2

Morris HF, Ochi S, Winkler S (2000)

Implant survival in patients with type 2 diabetes: placement to 36 months.

Ann Periodontol 2000;5:157-65.

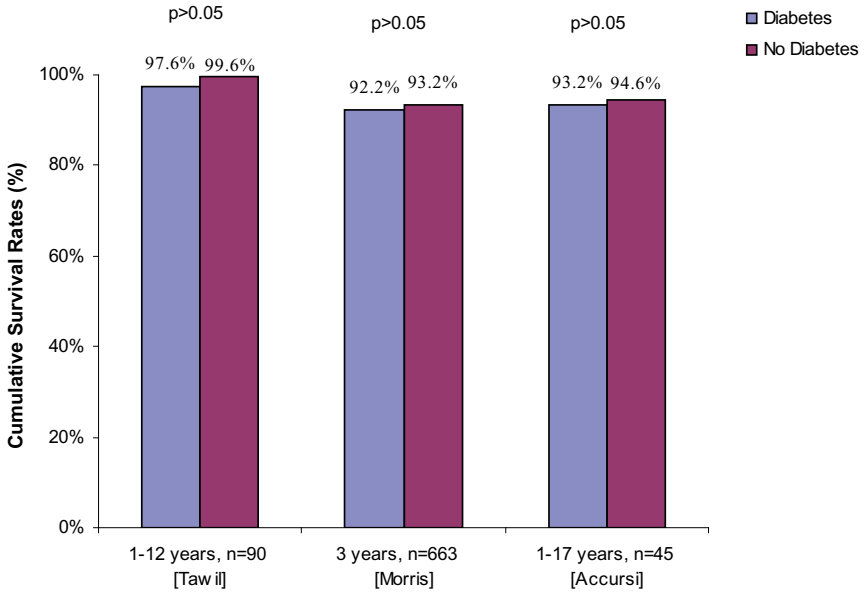
Study 3

Accursi GE (2000)

Treatment outcomes with osseointegrated Branemark implants in diabetic patients: a retrospective study [thesis]. Toronto (ON): University of Toronto.

In: Elsubeihi ES, Zarb GA. Implant prosthodontics in medically challenged patients: The University of Toronto experience. J Can Dent Assoc 2002;68(2):103-8.

Figure 1. Cumulative overall survival rates for dental implants by diabetic status.*



Statistical significance noted on graphs if provided by author
* n=number of subjects

Dowell S, Oates TW, Robinson M (2007)

Implant Success in people with Type 2 diabetes mellitus with varying glycaemic control – a pilot study; J Am Dent Assoc , 138: 355-361 (None of the implants places was lost during the observation period)

Behnke A., Behnke N., Hoedt B., Wagner W. (1998)

Diabetes mellitus – ein Risikofaktor für enossale Implantate im zahnlosen Unterkiefer?

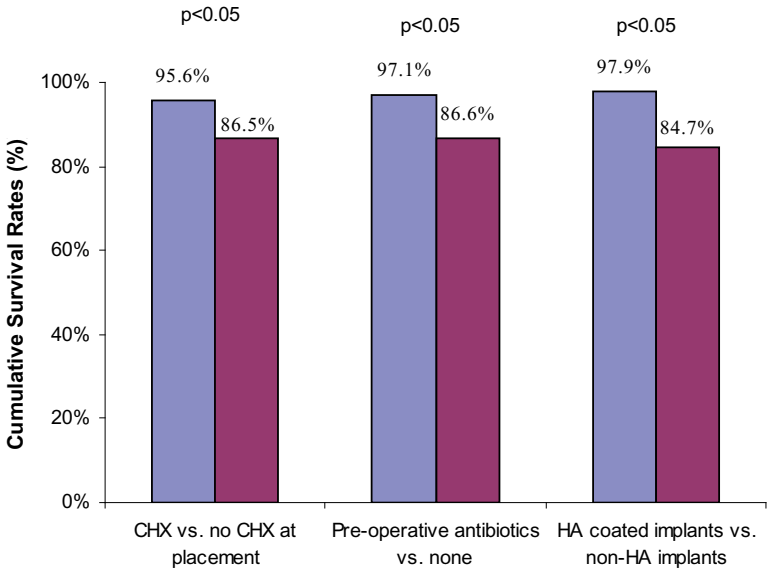
Dtsch Zahnärztl. Z. 5:332-329 (Controlled clinical study. Article in German: within a 5-year observation period implants placed in the anterior region of the mandible showed higher survival rate in diabetic patients (94,6%), compared to healthy subjects(91,6); the amount of bone resoption along the vertical axis of the implants was slightly higher (1.3mm) in diabetic patients, compared to healthy subjects (1mm), and the amount of resorption depended on duration of the diabetic condition.

Tawil G, Younan R et al; (2008)

A study on diabetic patients (Type II) showed that there is no statistic correlation between the group with well adapted hbA1c < 7%) compared to less well adapted HbA1c (7-9 %). However HbA1c values vorrelated to Plaque-Index and Bleeding Index BOP.

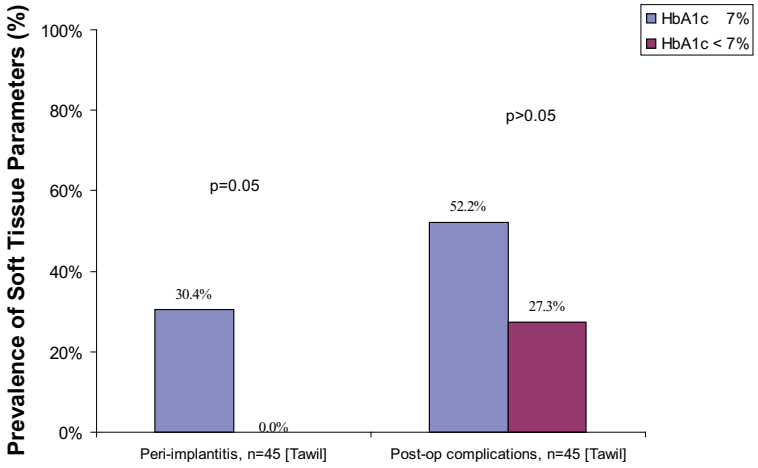
Int. J Oral Maxillofac Implants (2008) 23: 744-752

Figure 2. Cumulative survival rates for dental implants by diabetic patients by treatment.*



Statistical significance noted on graphs if provided by author
* blue indicates treatment, burgundy indicates no treatment or non-standard treatment

Figure 3. Post-operative soft tissue parameters of dental implants in diabetic patients by level of diabetic control.*



Statistical significance noted on graphs if provided by author
* n=number of diabetic subjects

Literature Analysis

A "Literature Analysis" is a critical review of the literature on the epidemiology, treatment methods, and prognosis for implant-related topics or conditions. Literature Analyses are broader than "Evidence Reports" (also published in each issue of Implant Directions) which focus on one specific treatment intervention by comparing and contrasting only 3 to 5 high quality articles in greater depth.

Literature Analyses are written to serve as a reference tool for implantologists:

- To help them make decisions regarding how to manage patients;
- To assist them in evaluating needs for future research;
- To use the material for future presentations.

This literature analysis on the effects of radiation therapy is the second of two parts. Part I evaluated and reported on ANIMAL studies. This analysis (Part II) will be published in the next edition of Implant Directions and will evaluate and report on HUMAN studies.

Purpose

The purpose of this Literature Analysis was to systematically search the literature to identify key articles in an effort to evaluate the effects of radiation therapy on craniomaxillofacial and dental implants. Part I of this literature analysis addressed the following objectives:

1. Provide an overview of implantology in irradiated craniomaxillofacial bone.
2. Summarize dental implant failure from ANIMAL studies with respect to the following:
   a. Irradiated versus non-irradiated bone
   b. Dosing of radiation
   c. Implant types
   d. Timing of radiation
   e. Hyperbaric Oxygen Therapy
3. Summarize the quality of the literature on ANIMAL studies and recommended future studies.

This edition (Part II) will address the following objectives:

1. .Summarize craniomaxillofacial (CMF) and dental implant failure from HUMAN with respect to the same parameters as reported in ANIMAL STUDIES.
2. Summarize complications from HUMAN studies associated with implants in irradiated bone in CMF and dental implants.
3. Summarize quality of literature on HUMAN studies and recommended future studies.
4. Discuss the role of BOI in the treatment of patients with irradiated bone.

The search methods and an overview of implants in irradiated bone are reported in the last edition of Implant Directions.

Summary of human studies on craniofacial implants in irradiated bone

An attempt was made to address the following categories by relying only on studies that made appropriate comparisons (i.e., cohort studies and case series with historical controls): irradiated versus non-irradiated bone, dosing of radia-

tion, timing of radiation, implant location, implant types, and HBO therapy. Studies were of poor (case series) to moderate (cohort studies) quality so conclusions should be made with caution, Table 1. Rates of failure are reported by implant location in the table so a single study may appear more than once in the table.

Irradiated versus non-irradiated bone

When comparing rates of implant failure in irradiated versus non-irradiated bone in CF applications, the risk of implant failure in irradiated bone was as high as 12 times greater than that for non-irradiated bone.[1-5] The increased risk was statistically significant in seven comparisons, however, only two were data from cohort studies (i.e., made the comparison in the same study population).[1, 2] Stronger associations were seen in case series compared to historical controls. Survival rates were based on as little as one year and as much as 5 years after implantation.

Dosing of radiation

Few studies were identified evaluating radiation dose in CF applications. One study reported no difference in failure based on dose (< 50 versus ≥ 50 Gy) in orbital implants, however the sample size was relatively small.[6] Cumulative radiation effect (CRE) as a measure of dose (≤30) was significantly related to implant failure in one prognostic study.[7] Radiation dose (above CRE30) was the only factor associated with implant failure (p=0.05) in this study.

Timing of radiation

Schoen evaluated failure rates based on whether the implants were placed prior to or after irradiation.[8] The sample sizes were too small to effectively determine the effects of timing or the risks associated with radiation prior to or after implant placement. No other studies were identified.

Implant location

Location of CF implants may influence the survival rate. Numbers cited in the literature for implant survival in non-irradiated bone by location are as follows: mastoid region, >95%; orbital implants, 35-91%; nasal implants, 71-81%.[9] No significant differences were seen for implants in other CF locations. Several studies reported a tendency toward higher failure rate in the orbital area due to thin bone in this region,1, 10, 11 while others did not find any statistical difference between orbital implant success and other craniofacial implants, whether in irradiated or non-irradiated bone.[5-9] A review of patient data over a 25-year period comparing implant success in irradiated and non-irradiated populations indicated that implant location was not a factor in survival, with the possible exception of orbital implants which may show a trend toward lower survival rates (p=0.055), and gingival implants which may have a higher survival rate (p=0.05).[7]

Implant types

No studies attempting to compare different types of CF implants in irradiated bone were identified precluding any conclusions regarding superiority of one CF implant type over another.

HBO therapy

One study was identified evaluating the effect of HBO therapy in irradiated bone.[4] Failure was significantly less common (RR=0.15; 95% CI 0.7, 0.30) among radiotherapy patients treated with HBO compared with those who had radiotherapy but no HBO. There was no difference in failure rates comparing non-irradiated patients and those who had radiation and HBO.

Summary of human studies on dental implants in irradiated bone

An attempt was made to address the same categories of treatment effects reported in the CF section, Table 2.

Irradiated versus non-irradiated bone

The proportion of studies that reported statistically significant differences between irradiated bone and non-irradiated bone in the dental implant studies was far less than reported in the CF studies. Further the relative risks were not nearly as high. Of the eight studies that compared rates of implant failure in irradiated and non-irradiated bone, only three reported statistically significant differences. The risk of implant failure in irradiated bone was between 2-3 times greater than that for non-irradiated bone in these studies. In CF studies, the relative risk was as high as 12. Moy reported nearly a 3 times greater risk of implant failure in irradiated versus non-irradiated bone (RR= 2.73; 1.10, 6.81); however, after adjusting for diabetes and smoking status, the RR was still significant but less than two (RR= 1.87; no confidence interval was provided).[12] Raw data was not available so we did not present it in Table 3; however, the author produced the RRs and adjusted RRs that we report here.

Dosing of radiation

Visch et al [13] compared survival rates at 10-years in patients receiving a dose either less than or greater than or equal to 50Gy. Lower radiation dose (<50Gy) was significantly associated with improved implant survival compared with higher doses (≥50 Gy). This difference was greater than two-fold (RR = 0.49; 95% CI 0.29, 0.81). A review article noted that no failures were observed with radiation doses lower than 45Gy. [14]

Timing of radiation

Several studies compared failure rates for implants placed at varying intervals post-irradiation. No differences were seen when comparing placement less than or more than one year after radiation in one study. [13] Another study found no differences in timing but the number of subjects and implants was small.[15] One study observed that only the time interval between implant placement and the abutment operation showed significance, where patients receiving implant placement and abutment <4 months apart did significantly worse than those with the abutment procedure >4 months from time of implant (p=0.0001). [16] A second study agreed with this finding, noting that significantly more mandibular reconstruction plates were lost when radiation was administered during the perioperative period, defined as within 12 weeks of implant surgery.[15] A third study did not observe a statistically significant difference in survival rates between implants inserted less than or greater

than one year post-irradiation.[13] A review article comparing failure rates for implants placed either pre- or post- irradiation showed that failure rates were similar between the two groups and not statistically significant (5.4% and 3.2%, respectively).[14]

Implant location

Implant failure in irradiated maxillary bone was twice that of non-irradiated maxillary bone based on one study where the comparison could be made.[17] Complications based on radiation status were not well reported and generally not separated out in those studies reporting complications, making definitive statements about complications, including osteoradionecrosis difficult. Mandibular implants were significantly less likely to fail compared with maxillary implants. [13] An adjusted RR of 1.79 (p = 0.001, no CI provided) for implant failure in the maxilla compared with that in the mandible was reported (all bone). One study showed a survival rate of 59% in the maxilla, 85% in the mandible. (p=0.001).[13] In a comparison of total implant locations, high implant failures were seen after high dose radiotherapy and a long time after irradiation. All craniofacial regions were affected, but the highest implant failures were seen in frontal bone, zygoma, mandible, and nasal maxilla. Lowest implant failures were seen in oral maxilla.[7] A review article noted that implant location resulted in significant differences in failure rates, with mandibular implants failing less than maxillary implants (4.4% and 17.5%, respectively; OR=4.63; 95% CI: 2.25 to 9.49).[14]

HBO therapy

Two studies attempting to evaluate the effect of HBO therapy as an adjunct to irradiation for dental implants in irradiated bone were identified. [18, 19] Based on the criteria that the patient is expected to experience difficulty during osseointegration, Granstrom et al proposed the use of HBO therapy as potentially beneficial.[18] They reported from a multivariate analysis of 671 irradiated implants that HBO therapy improved implant survival with significance at the p<0.001 level (study in press). Conversely, Donoff et al contend that our understanding of wound healing is incomplete and constantly changing in the light of new research, and that our incomplete knowledge precludes any reliable conclusions regarding the necessity for HBO therapy.[19]

Summary of complications associated with implants in irradiated bone in human studies

Complication rates based on radiation status were not well described in any of the comparative studies. Failure to report complications should not be construed as meaning that none were present. Briefly, in the CF studies reviewed, several studies reported no complications,[8, 9] one study reported a low rate of osteoradionecrosis (4.7% (n=5/107)),[7] and grade 1-3 tissue reactions were observed in patients receiving radiotherapy (P<0.001 to 0.05).[7, 8]

For the dental implant studies, August et al reported the following early complications in an oral cancer population:[20] soft tissue overgrowth around pins (22.2% (n=4/18)), tongue ulcerations (11.1% (n=2/18)), and intraoral wound dehiscence(11.1% (n=2/18)). Late complications included orocutaneous fistula formation

(16.6% (n=3/18)), submental erythema (11.1% (n=2/18)), persistent tissue overgrowth around pins (5.6% (n=1/18)). Soft tissue ulcers have also been noted.[21, 22]

Radiation scattering

Implants placed before radiation therapy may cause scattering, resulting in a decreased dose delivered to the tumour and increased exposure to soft tissue and bone adjacent to the implant. [8] Implants of a higher atomic number material cause a greater back-scatter dose factor (BSDF), though the range is small (a few millimetres). Additionally, lower energy photons, i.e. ^{60}Co, caused greater backscatter than higher energy photons.[23, 24] A study of simulated head and neck radiotherapy showed that highest dose enhancement occurs at a distance of 0 mm from the bone-implant interface in all locations and implant materials studied. Transmandibular implants (high gold content, gold-copper-silver alloy) had scatter up to 1mm from the bone-implant interface. No significant difference was noted in buccal, lingual, mesial or distal directions. Hydroxyapatite-coated titanium implants demonstrated the best results.[25] An additional study of titanium implants in mandible confirmed that the risk of radionecrosis from backscatter is slightly but not significantly higher with post-implantation radiotherapay.[24]

A dosimetric evaluation of the effect of previously placed dental implants during radiotherapy concluded that the risk of osteoradionecrosis to the mandible is slightly but not significantly affected by the scattered dose in the radiation field exposed to 3 different radiation beams.[24]Granstrom et al recommend that if irradiation is to be performed post-implantation, all prostheses, frameworks and abutments should be removed prior to irradiation. Fixtures should be left intact but covered with skin or mucosa, as removal of osseointegrated implants is itself a potentially damaging procedure.[3]

Quality of literature and need for future research

In general, the quality of studies comparing implant failure/success and complication rates in irradiated versus non-irradiated bone is poor. For animal studies, no studies evaluated all important parameters such as timing, histomorphometric, biomechanical, and histological measurements in the same study using irradiated bone with a non-irradiated control leg. Furthermore, few animal studies were designed to compare implant types in irradiated bone.

For HUMAN studies, most were of poor to moderate quality. The majority of comparisons between irradiated bone and non-irradiated bone were with historical controls. However, a prospective study comparing patients who do and do not get irradiated in the same consecutive patient population may be difficult to perform. No studies were designed to compare implant types in irradiated bone. This may be the focus for future research.

We recommend the following two studies for future research and publication:

1. A well-designed animal study with adequate sample size that compares different implant types in irradiated and non-irradiated bone. This study should assess the following important parameters with respect to the implants evaluated:
   a. Timing of radiation
   b. Histomorphometric characteristics
   c. Biomechanical characteristics
   d. Histological characteristics

2. A well designed HUMAN observational cohort study that follows a group of similar patients during the same time period. This should be a population of patients who do and do not undergo radiation. Furthermore, this should be a large enough population with enough implantologists that more than one implant type is used in both irradiated and non-irradiated bone. This will allow for the comparison of implants in irradiated and non-irradiated bone with respect to the following outcomes:
   a. Time to loading
   b. Implant failure
   c. Complications
   d. Implant function
   e. Overall quality of life

Role of BOI in the treatment of patients with irradiated bone

The following key findings from this literature overview make BOI a potential solution for the management of patients with irradiated bone:

1. Patients are at greater risk of implant failure.
2. Patients typically undergo multiple procedures and very prolonged waiting times before loading their implants.
3. No implants have been identified from the literature superior for treating patients with irradiated bone.
4. If animal studies are successful, this may be an area of indication for BOI to market itself and find its way into the US market.
5. Furthermore, if BOI appears indicated for patients with irradiated bone then it may also be assumed it is indicated for all indications of "poor" bone quality or quantity.

Table 1: Summary of studies comparing implantation in irradiated versus non-irradiated bone: Craniofacial applications.

Studies	Study Design	Implant Location	Outcome	Irradiated	Non-irradiated	Effect Size RR (CI)*
Roumanas[1]	Cohort	All	Implant Failure	40% (14/35)	12% (21/172)	3.3 (1.9, 5.8)*
Albrekteson[2]	Case series	All	Implant Failure	15% (4/34)	1.5% (6/389)	9.5 (3.1, 29.6)*
Granstrom[7]	Case series	All	Implant Failure	23%(147/631)	12% (76/614)	1.9 (1.5, 2.4)*
Granstrom[4]	Case series	All	Implant Failure	54% (79/147)	12%(12/101)	4.5 (2.6, 7.9)*
Wolfaardt[5]	Case series	All	No Osseointegration	30.5% (44/144)	2.5% (31/1221)	12.0 (7.9, 18.4)*
Roumanas[1]	Cohort	Various CF	Implant Failure	30% (3/10)	27% (9/33)	1.1 (0.37, 3,3)
Wolfaardt[5]	Case series	Nasal	No Osseointegration	20% (2/10)	17% (9/53)	1.18 (0.29, 4.66)
Roumanas[1]	Cohort	Auricular	Implant Failure	0%(0/6)	4.5 % (5/111)	Incalculable
Wolfaardt[5]	Case series	Mastoid	No Osseointegration	0%(0/10)	1.7% (9/516)	Incalculable
Schoen[8]	Cohort	Orbit	Implant Failure	11% (4/35)	0% (0/14)	Incalculable
Toljanic[6]	Case series	Orbit	Implant Failure	34% (31/92)	24% (21/89)	1.4 (0.89, 2.29)
Wolfaardt[5]	Case series	Orbit	No Osseointegration	49% (40/81)	6.1% (7/115)	8.1 (3.8, 17.2)*
Roumanas[1]	Cohort	Orbit	Implant Failure	59% (11/19)	25% (7/28)	2.3 (1.1, 4.9)*
				Rad + HBO	**Non-Irradiated**	
Granstrom[26]	Case series	All	Implant Failure	8.1% (8/99)	13.5% (12/89)	0.60 (0.26, 1.4)
				Rad + HBO	**RAD only**	
Granstrom[26]	Case series	All	Implant Failure	8.1% (8/99)	54% (79/147)	0.15 (0.7, 0.30)*
				Rad after Implant	**Non-irradiated**	
Schoen[8]	Cohort	Orbit	Implant Failure	14% (2/14)	0% (0/14)	Incalculable
				Rad prior to Implant	**Non-irradiated**	
Schoen[8]	Cohort	Orbit	Implant Failure	9.5% (2/21)	0% (0/14)	Incalculable
				Rad after Implant	**Rad prior to Implant**	
Schoen[8]	Cohort	Orbit	Implant Failure	14% (2/14)	9.5% (2/21)	1.5 (0.23, 9.4)
				< 50 Gy**	**≥ 50 Gy**	
Toljanic[6]	Case series	Orbit	Implant Failure	17% (2/12)	16% (10/61)	1.0 (0.25, 4.1)

*Indicates statistically significant findings. Cohort studies compare patients in the same treatment population. Case series compared results to historical controls.

**Gy= Grey

Table 2. Summary of studies comparing implantation in irradiated versus non-irradiated bone: Dental applications.

Studies	Study Design	Implant Location	Outcome	Irradiation	Non-irradiation	Effect Size RR (CI)*
Weischer[21]	Cohort	Mandible	Implant Failure	13.7% (10/73)	5.7% (5/87)	2.4 (0.85, 6.6)
			Wound disturbance	4.8% (4/83)	0 (0/92)	Incalculable
			Peri-implant inflammation	22.2% (4/18)	9.0% (2/22)	2.4 (0.50, 11.9)
Weischer[22]	Cohort	Mandible	Implant Failure	7.0% (4/57)	6.3% (3/48)	1.1 (0.26, 4.8)
Landes[27]	Cohort	Mandible	Implant Failure	1.4% (1/72)	0% (0/42)	incalculable
Schepers[28]	Cohort	Mandible	Implant Failure	3.3% (2/61)	0% (0/78)	incalculable
Esser[29]	Case series		Implant Failure	16.6% (29/221)	9.9% (7/71)	1.3 (0.81, 2.02)
			Osteoradionecrosis	3.4% (2/58)	NR	Incalculable
			Soft Tissue Necrosis	3.4% (2/58)	NR	Incalculable
Cao[17]	Cohort	Maxilla	Implant Failure	51% (27/53)	22% (17/78)	2.3 (1.4, 3.8)*
			Osteoradionecrosis	0 (0/53)	0 (0/78)	1.0
Ryu[15]	Case series	Mandible	Implant Failure	30.6% (11/36)	9.1% (1/11)	3.4 (1.49, 23.2)*
			Osteomyelitis or necrosis	11.1% (4/36)	0 (n=0/11)	Incalculable
			Chronic Pain	2.7% (1/36)	9.1% (n=1/11)	0.31 (0.02, 4.5)
			Complications	30.6% (11/36)	27% (n=3/11)	1.1 (0.38, 3.3)
Landes[27]	Cohort	Mandible	Peri-implant inflammation	3.2% (5/155)	2.2% (3/134)	1.4 (.35, 5.9)
				< 1yr post IR	**≥ 1 year post IR**	
Visch[13]	Cohort	HA-Titan screw	Implant Failure	16.5 %(n=29/175)	12.9% (n=35/271)	1.3 (0.81, 2.02)
				< 50 Gy* Dose	**≥50 Gy Dose**	
			Implant Failure	9.2% (19/207)	18.8% (45/239)	0.49 (0.29, 0.81)*
				10yr post IR		
				Mandible	**Maxilla**	
			Implant Failure	9.2% (31/338)	30.6% (33/108)	0.30 (0.19, 0.47)*
				IR > 10 mos post implant	**IR ≤ 12 wks post implant**	
			Implant Failure	0% (n=0/10)	42.3% (n=11/26)	Incalculable
			Osteomyelitis or necrosis	0 (n=0/10)	15.4% (n=4/26)	Incalculable
			Chronic Pain	0 (n=0/10)	3.8% (n=1/26)	Incalculable
			Complications	20% (n=2/10)	35% (n=9/26)	0.58 (0.15, 2.2)

Indicates statistically significant findings
* *Gy= Grey
NR=not reported

IR = irradiation

APPENDIX II
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Research in Context – Part VII

Title: Are the differences between two study groups real and applicable clinically or is it possible possibly they are simply due to chance?

Research in Context Question:

In the last edition of Implant Directions, we gave an overview of checking for appropriate analyses when critically reviewing a paper and considering the authors conclusions. For example, were there appropriate analyses that included descriptive statistics, analytic statistics using the primary outcome, ample sample size, and adjustment of potential confounding variables?

We listed the following 4 questions that need to be considered when evaluating the statistical analyses used for testing the hypothesis:

1. **Is the primary outcome used for the statistical analysis?**
2. **Is any difference between the groups likely due to chance?**
3. **Is the sample size large enough to test the hypothesis adequately?**
4. **Are potentially confounding variables considered in the analysis?**

The first point is self-explanatory – the authors should include the primary outcome outlined by the study question in the statistical analyses and present these data. It is amazing to see how often an author list the study's goal or objective but does not use an appropriate outcome measure to test this hypothesis. In a previous edition of Implant Directions, we discussed in detail the importance of outcomes measures in dental implant research and how to go about choosing the right one.

The second point relates to the role of chance as an explanation for any observed difference between the study groups. When you look at statistical significance (which is the measure of probability that the results you achieved occurred by chance) remember that statistical significance depends on three parameters:

- Sample size (the larger the sample size, the easier to demonstrate statistical significance; the smaller the sample size the possibility that the observed difference is simply due to chance)
- Variability in patient response, either by chance or by non-random factors (the smaller the variability, the easier to demonstrate statistical significance)
- Effect size, or the magnitude of the observed effect between groups (the greater the size of the effect, the easier to demonstrate statistical significance)

A real world example to address this issue is the published Critical Appraisal (CA) in this edition of Implant Directions evaluating an article by Tarnow, et al. The authors compared patients who had less than or equal to 3 millimeters (mm) of distance between implants to patients who had greater than 3 mm of distance between implants. They reported a mean of 1.04 mm vertical crestal bone loss in patients

(n=25) who had less than or equal to 3 mm distance between implants and a mean of 0.45 mm vertical crestal bone loss in patients (n=11) who had greater than 3 mm between implants. This sample size is very small and therefore this mean difference could be due to chance alone. One would want a much larger sample to make a conclusive statement regarding the cause of crestal bone loss.

One way to determine this would be to compare the groups analytically using a t-test which would reveal whether or not this difference is statistically significant ($p<.05$). This would require the mean values and the variability often reported in terms of the standard deviation. The authors failed to report the standard deviation of these findings. If the variability is small, then it is far more likely this difference is real than a result of chance. However, if the variability is high, with such a small sample size, these differences mean little and conclusions regarding the association of one factor (eg, lateral distance between implants) with another (eg, vertical crestal bone loss) are not warranted.

Lastly, if the differences are great, then fewer subjects are needed. For example, if the mean difference in crestal bone loss was 2 mm or more, then the difference is more likely to be real then a result of chance, assuming the variability is not too large.

It is important when reading a paper that one does not trust the author's conclusions without a critical review. Simple considerations such as those mentioned above, will go along way in helping you make informed clinical decisions.

The effect of confounding on the comparison of two groups will be discussed in the next edition of Implant Directions...

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