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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

Immediate Loading Alternative After Failed Dental Implant:

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Abstract

Though failure rates of endosseous dental implants are relatively low, the increasing number of implant surgeries being performed worldwide is leading to a greater number of implant failures. This is creating a challenge for both the implantologist and the patient. Patients, who have been treated successfully with implants in the past, will likely select implants again in lieu of prostheses in the event of an implant failure. However, most patients do not understand, nor do they want to experience, the long waiting period necessary for returning to normal masticatory function after initiating the re-implantation process.

This waiting period can be eliminated with the application of basal implants (e.g. BOI®). The case presented here demonstrates the possibility of returning the patient to normal masticatory activity in a short period of time after failed screw implants.

Keywords:
immediate loading; dental implant failure; basal implants; blade implants

Survival rates for conventional dental implant systems are relatively high in normal healthy bone.[1] However, since osseointegration represents a dynamic process both during its establishment and its maintenance, even implants which initially integrate well, may occasionally show unexpected mobility when the bone/implant/restoration system has been in actual function and the forces imposed by the mastication increases or some of the abutments involved in carrying a bridge yield.

A large number of dental implants have been performed worldwide. In the USA alone, it has been estimated that more than 300,000 dental implants are performed annually.[3,4] According to a recent report, those actually implanted in the USA in 2000 numbered 910,000 (Annual Industry Report, 2000). Therefore, despite a relatively low failure rate in today's dental implant environment, the absolute number of failures is high and presents a clinical challenge to the dental implantologist. Because of the growing demand for dental implants, their failure is becoming one of the most challenging dental complications of our times.[5-8] The major problem in implant dentistry in the future will become late-stage failure and loosening.[6] In recent years the use of screw and cylinder implants has become very popular. Whenever the bone supply is reduced, bone augmentations are recommended today. The results of augmentation procedures are not as predictable as the implant procedure.[2] For some practitioners the use of blade implants are a good alternative to augmentations combined with screw implants, because

they help avoiding augmentations.

The likelihood for re-integration of a mobile crestal implant (i.e. screw, cylinder, blade) is small if the interface between the implant and the bone is bacterially contaminated (due to vertical or horizontal mobility) and the perfusion in the interface area is increased. In some patients, general and local contraindications may restrict the possibilities for re-implantation.[9] Methods to overcome this challenge therefore needs to be proposed and evaluated. We report on an alternative implant method that is ideal for the treatment of patients who present with a failed blade implant(s) and the desire to continue relatively normal uninterrupted mastication.

Case Report

This is a report of a 54 year-old female who was treated 25 years ago after the loss of the molars in the lower left mandible. The patient had received a crown block with four chewing units through a two-stage procedure. About 14 years later the upper jaw had been treated with 4 cylindrical implants, and two of them survived for 9 years in full function Fig. 1.

The patient presented to our dental clinic, with increased loosening of the bridge in the lower left mandible. The anterior tooth-support had yielded: the second premolar was fractured and the first premolar by itselve was not suitable to carry the masticatory load of this whole quadrant. The bridge incl. the implant was mobile in the vestibular-lateral direction. The patient did not report any pain but was bothered by restricted chewing ability on the right side. The following treatment alternatives were discussed with the patient:

a) removal of the bridge in quadrant III and removal of the blade implants with a subsequent two-stage approach with screw implants after bone augmentation. After a regeneration period of 3 months after the removal of the implant, the patient could undergo bone augmentation, followed by a new implant treatment; or

b) removal of the bridge in quadrant III and removal of the blade implant followed by immediate insertion of 3 basal implants (BOI®)[10-13] taking advantage of the intact cortical bone available. The patient chose the second option as it would allow him immediate return to normal masticatory activity. Inserting another blade implant into the existing implant cavity did not seem possible, taking into account the total bone height left.

After extraction of the implant and the two premolars under local anesthesia, three basal implants were inserted laterally using multi-cortical support by taking advantage of the existing cortical bone available. In region 34, a three-segment, one-piece, basal implant was inserted directly into the extraction alveole. Region 35 was equipped with a single base-plate basal implant. In region 37, directly to the extraction alveole, an asymmetrical basal implant was inserted.

The impression was taken directly after the implant installation. The sutures were removed at the next appointment, at which time metal casting was examined, and the final metal/ceramic bridge was incorporated on the 4th post-operative day. Figures 1 and 2 show enlarged sections of the treatment process from the panoramic

overview shots.

The vertical insertion slots as well as the extraction slot left after the removal of the blade impant was covered with autologous fibrin membranes.[15]

Clinically, the patient showed visible swelling of the left cheek for 3 days and she took pain medications for three days. The patient was asked to refrain from the consumption of hard food for 2 months; however, she began using the new bridge immediately for all other masticatory function and reported similar use and oral function compared to her bridge in the contralateral jaw. Although we recommended the refrain from smoking, she continuously smoked several cigarettes throughout the treatment phase. This affected the soft tissue healing, leading to delayed healing.

Discussion

Failed implants pose a significant challenge to both the implantologist and the patient, especially when using conventional dental implant systems (i.e., screw implants). From the patient's perspective, who has grown accustomed to normal mastication with the existing implant system before experiencing symptoms, the thought of "starting over" and having to wait a significant amount of time before returning to normal function is daunting. However, the implantologist must be prudent in his/her surgical treatment and rehabilitation so as to avoid another failed implant. It could be argued that one should be particularly careful during the initial operation so as to avoid this scenario. However, failed implants are inevitable despite the use of a quality implant and a skilled implantologist. Though failure rates have declined over the past several decades, more implant operations are being performed. The absolute number of failures, therefore, is on the rise.

In the patient case that has been presented, the patient decided to have basal implants inserted because she could avoid the 6 months of treatment and rehabilitation necessary for return to normal mastication if screw implants were re-inserted. With the option of basal implants that are inserted from the lateral aspect of the jaw bone, using the resorption-resistant cortical bone, we were able to provide the patient a viable alternative which allowed for a single surgical procedure followed by immediate masticatory function. Prosthetic constructions which combine teeth and basal implants also have proven to be favorable options for future success.[14]

The replacement of failed screw implants with basal implants, regardless of the etiology (e.g., infection, functional loosening, etc.), constitutes an important indication for BOI® implantology.[10-13] The remaining bone quality and quantity available is also not an issue – in fact, that is a strength of the BOI® procedure. When conventional dental implant systems fail, there is typically little bone for immediate re-implantation. For BOI® implants, almost any amount of bone remaining is sufficient for corrective procedures in most cases. This, coupled with the patient benefit of immediate functional use, makes BOI® an

excellent alternative for treating a patient with failed dental implants.

Conclusion

Basal osseointegrated implants are an excellent alternative for the implantologist faced with a patient who has experienced an implant failure(s). They provide a new implant(s) and allow the patient to return to normal masticatory function with little-to-no delay.

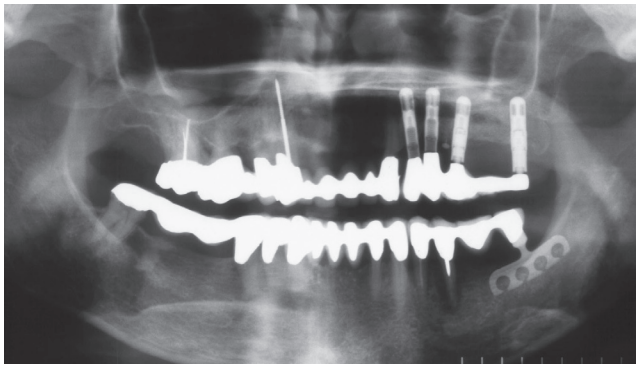

Figure 1. The radiolucent areas around the enossal implant 37 and the tooth 35 are shown in the preoperative overview photo.

Legends

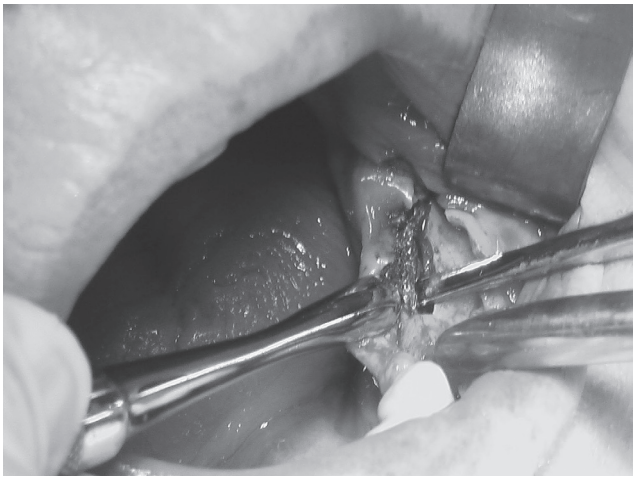

Fig. 2. The blade implant was mobilized through a small vertical slot

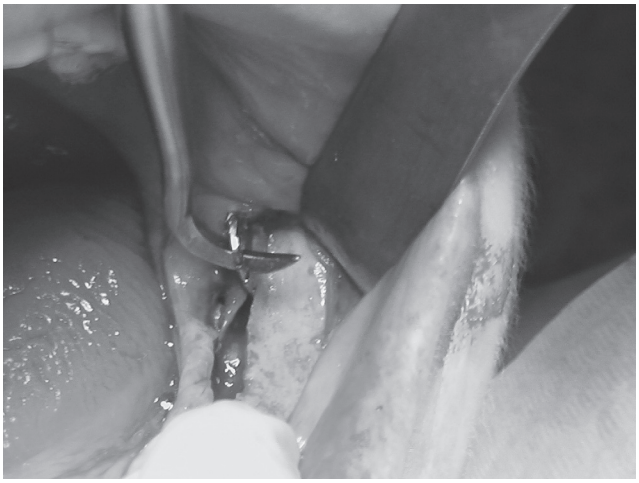

Fig. 3. The implant was quite resistant to extracting forces and had to be removed with the help of a crown click instrument

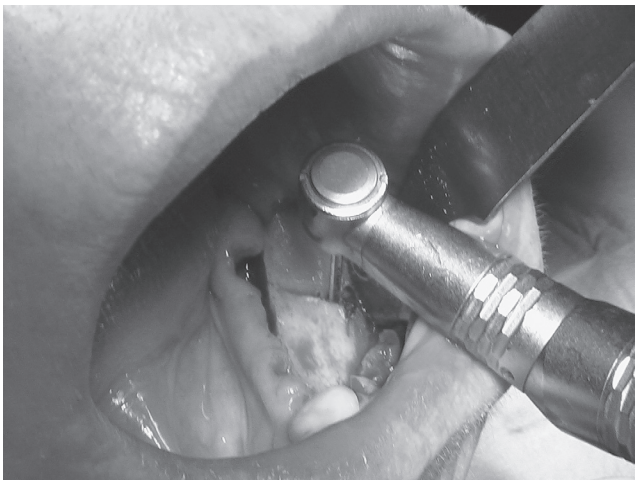

Fig. 4 .After a right-to-left vertical cut, the horizontal cut for the basal implant created the horizontal osteotomy

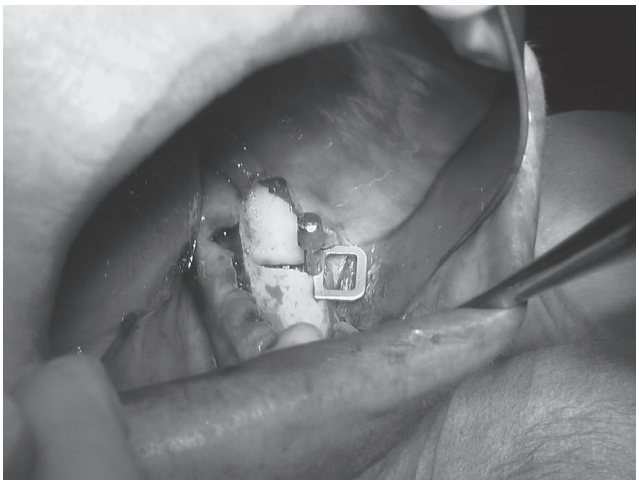

Fig. 5. The 9/12 single piece BOI®-implant during the insertion

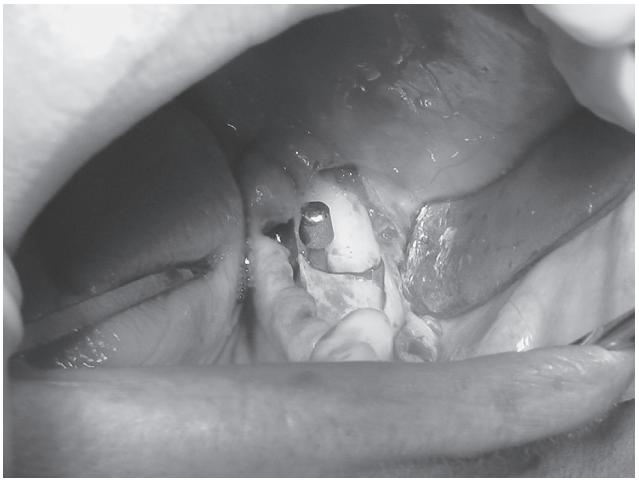

Fig. 6. The fully inserted BOI-implant fits the available bone exactly. Note that the extraction slot was not touched by the vertical implant part. The baseplate however projected through the basal slot areas into the medial cortical wall of the mandible.

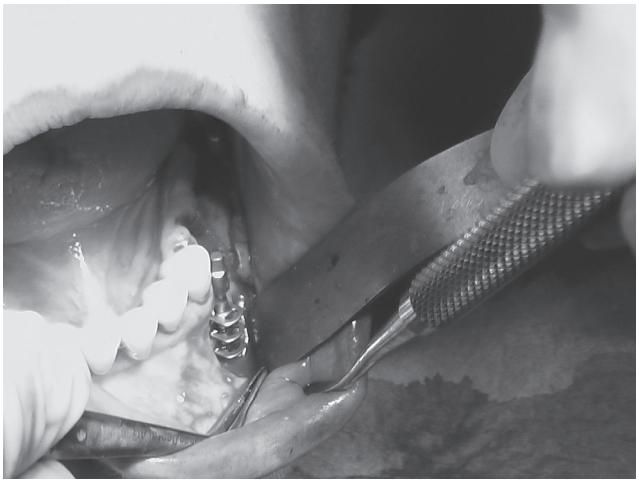

Fig. 7 A tripple-BOI®-Implant before insertion in the area if the first premolar.

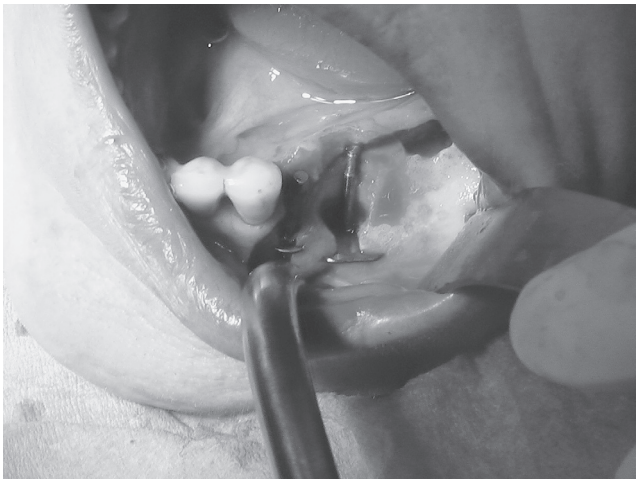

Fig. 8 . Lateral view of the implants in the areas of the premolars, immediately after insertion.

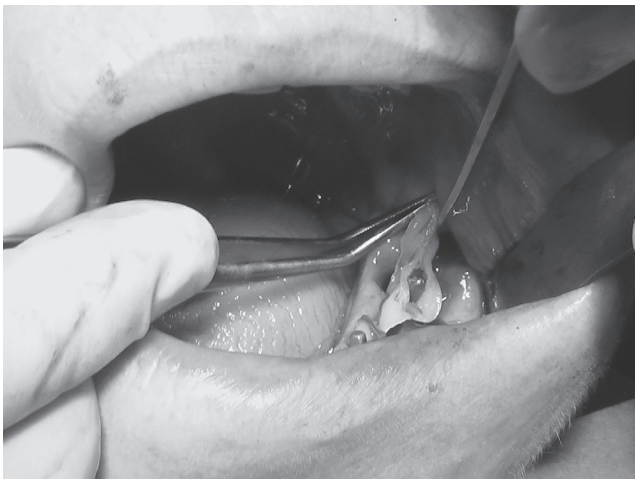

Fig. 9 Placement of a fibrin membrane over the vertical implant parts. The membrane covers the vertical slot and the extraction slot where the blade implant was extracted before.

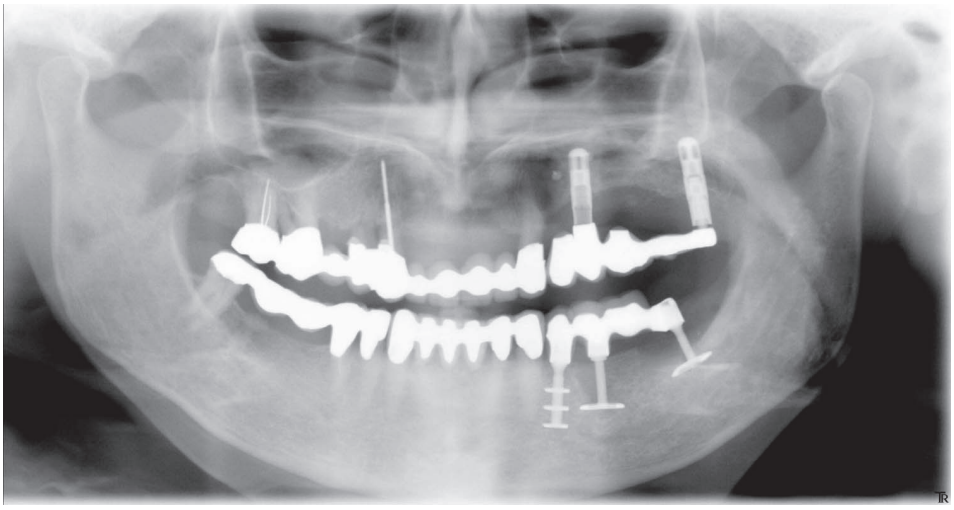

Figure 10. The newly placed and previously incorporated implants are shown four days post-operative. The extraction alveoles in the area of the teeth and the relation to the placed implants are clearly visible.

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Research in Context – Part IV

Blinding: What does this mean and who should be blinded?

Teaser

Blinding as a safeguard for preventing bias in study results is often confused with other methodological precautions, such as concealment of allocation during the randomization process – a concept discussed in the last edition of Implant Directions. Unlike pharmaceutical trials, surgical trials can typically not blind the implantologist to the type of implant. Does that mean you don't have to use blinding in your studies?

Text

Lack of blinding in medical studies has been associated with increased magnitudes of the observed effect. In a survey of orthopedic surgeons, 114 respondents (21%) had never heard of the term "blinding" as a method of reducing bias in surgical research. When those who heard of blinding were asked to define the term "double blind" from a series of options, 29 different definitions were given. In a meta-analysis entitled, "Reporting of Outcomes in Orthopaedic Randomized Trials: Does Blinding of Outcome Assessors Matter?", studies that blinded outcome assessors were associated with a significantly lower treatment effect than those studies with unblinded outcome assessors. This translated to relative risk reductions of 38% for blinded outcome assessments compared with 71% for unblended outcome assessments (a difference of 33%). There is clearly an exaggerated treatment effect reported in studies that do not blind the person evaluating the patients' outcomes! When evaluating a study, consider the following question and their definitions with respect to blinding.

Was there blinding of patients, investigators and study personnel assessing outcome?

Blinding, or masking, refers to keeping persons involved in a trial (RCT, cohort, or case-control study) unaware of which study subjects are in which treatment arm. The main reasons for doing this are:

- To avoid possible influences of this knowledge in assessing the outcome.
- To minimize a different rate of loss-to-follow-up between treatment groups.

When determining who should be blind, ask these three questions:

- Can I blind the patients? The best way to avoid the placebo effect is to prevent the patient from knowing if he or she received the treat ment of interest.
- Can I blind the implantologist or surgeon? Differences in patient care other than the intervention (such as rehabilitation care) can bias the results.

- Can I blind those that evaluate the outcomes? If study personnel are privy to treatment, out comes assessed by these personnel such as radiographs or clinical status may reflect the assessor's bias (conscious or subconscious)

- Can I blind the person who does the data analysis (e.g., biostatistician or epidemiologist)?

Generally,

- A trial is double-blind if both the patients and research staff members responsible for measuring outcomes are kept unaware.

- A trial is single-blind if only one of these parties (usually the subjects) are kept unaware.

- Blinding may also be extended to people with other roles, such as those performing the statistical analyses on the data.

In dental implant studies, it is often not feasible to blind the implantologists (they know what implant they put in the patient). If comparing two different screw type implants (e.g., SLA active versus SLA), it is possible to blind the patient, the person who assesses the outcome, and the statistician. We've never seen this done before but in order to claim one implant more effective than another, the blinding of the assessors is critical and if you can blind the patient even better!

Next issue of Implant Directions....

The importance of equivalent patient care and adequate follow-up in clinical studies

Critical Appraisal

Reference

Nkenke E, Hahn M, Weinzierl K, Radespiel-Tröger M, Neukam FW, Engelke K. "Implant stability and histomorphometry: a correlation study in human cadavers using stepped cylinder implants" Clin Oral Implants Res. 2003 Oct;14(5):601-9.

Performing Clinic

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ARTICLE SUMMARY

Authors summary

Resonance frequency analysis was superior to periotest in assessing implant stability based on histomorphometric data; however, it seems that the noninvasive determination of implant stability has to be improved in order to give a more comprehensive prediction of the bone characteristics of the implant site.

Study objectives

To determine the correlation between the primary stability of dental implants in edentulous mandibles and maxillae with bone mineral density and histomorphometric parameters.

Design

A human cadaveric study.

Subjects

Recently deceased, male edentulous patients who had bequeathed their bodies to the Anatomic Institute I of the University of Erlangen-Nuremberg for medical-scientific research and training purposes.

Implants

48 stepped cylinder screw implants (11mm length by 3.8mm diameter Frialit® 2, Friadent, Mannheim, Germany) were installed in two unfixed human maxillae and two unfixed human mandibles collected from three different recently deceased subjects (ages at death 75, 82 and 95 years).

Measurements

- Peak insertion torque (Ncm) was measured during implant placement.
- Bone mineral density was assessed using quantitative computed tomography (QCT).
- Implant stability was measured by the following (10 measurements/implant):
    - o Periotest values;
    - o Resonance frequency analysis.

•Histologic specimens were prepared (5mm slices in the bucco-oral direction parallel to the longitudinal axis of the implants and including them in the bone block) for the following assessments:

- o bone-to-implant contact;
- o trabecular bone pattern factor (TBPf);
- o density of trabecular bone (BV/TV);
- o height of the cortical passage of the implants.

•Linear regression was used to assess the correlation between each of these measurements .

Results

•The mean resonance frequency analysis values (maxilla 6130.4±363.2 Hz, mandible 6424.5±236.2 Hz) did not correlate with the Periotest measurements (maxilla 13.1±7.2, mandible -7.9±2.1) and peak insertion torque values (maxilla 23.8±2.2 N cm, mandible 45.0±7.9 N cm), Table.

•No correlations could be found between the resonance frequency analysis (see values above), the bone mineral density (maxilla 259.2±124.8 mg/cm3), mandible 349.8±113.3 mg/cm3), BV/TV (maxilla 19.7±8.8%, mandible 34.3±6.0%) and the TBPf (maxilla 2.39±1.46 mm-1, mandible -0.84±3.27 mm-1), Table. 1.

•Resonance frequency analysis values did correlate with bone-to-implant contact of the oral aspect of the specimens (maxilla 12.6±6.0%, mandible 35.1±5.1%) and with the height of the crestal cortical bone penetrated by the implants in the oral aspect of the implant sites (maxilla 2.1±0.7 mm, mandible 5.1±3.7 mm), Table.

•Periotest values showed a correlation with the height of the crestal cortical bone penetrated by the implants in the buccal aspect of the implant sites (maxilla 2.5±1.2 mm, mandible 5.4±1.2 mm), Table.

REVIEWER´S EVALUATION

1. Methodological strengths:

•The authors used humans for their assessment as opposed to animals which is more realistic to clinical practice.

•The sample size appeared adequate for the assessment.

•The authors evaluated several important clinical measurements in use today.

2. Methodological limitations:

•These subjects were very deceased elderly male patients and therefore not generalizeable to the average patient population receiving implants.

•It is unclear who performed the assessments and how the data was handled to ensure blinding to the findings of the other measurements that were being correlated.

•Despite a significant correlation with one histomorphometric measurement and height of cortical bone penetrated by the implant, resonance frequency analysis correlated the least (p=.900) with bone mineral density compared to insertion

torque and periotest which is conflicting with previous findings in the literature.

•The authors made multiple comparisons but did not adjust for this in their analysis through a Bonferroni correction or other comparable statistical technique. When multiple comparisons like this are made, statistical correlations can be observed simply by chance and therefore such an adjustment helps to ensure that findings are not by chance alone.

•The results can not be transfered to the real life situation, because biologic adhesion of the blood cloth to the impant and the bone surface could dramatically alter the results and ,- especially in soft bone-, could have a large influence on the clinical stability.

3. How might the findings from this Critical Appraisal be applied to patient care?

The reviewers do not any connection to the patients care. Although the study is technically well performed, the outcome is, that implants in more and more cortical bone are more stable. It was known before, that Periotest-measurements are unralyable and the device is hardly used any more for this reason..

4. Are the likely treatment benefits worth the potential harm and costs?

During this study neither humans nor animals were harmed. The costs of the study are assumend to be low and forthis reason it was justified to perform this study.

For future studies the results might have been grounds for comparison between RFA-measurements and CT-scans, however the authores did not perform this assessment (CT-scan) in their study.

Table: P-values* for the correlations between the different parameters

	Peak insertion torque	**Periotest**	**Resonance frequency analysis**
	p	p	p
Peak insertion torque	–	0.019	0.193
Periotest	0.019	–	0.28
Resonance frequency analysis	0.193	0.28	–
Bone mineral density	0.115	0.157	0.9
TBPf	0.114	0.602	0.292
BV/TV	0.122	0.14	0.86
Cortical bone density, oral aspect	0.764	0.954	0.178
Cortical bone density, buccal aspect	0.513	0.455	0.28
Bone-to-implant contact, oral aspect	0.156	0.277	**0.024**
Bone-to-implant contact, buccal aspect	0.278	0.808	0.454
Implant length within the implant site, oral aspect	0.196	0.151	0.906
Implant length within the implant site, buccal aspect	0.66	0.14	0.582
Height of the crestal cortical bone penetrated by the implant, oral aspect	0.343	0.244	**0.002**
Height of the crestal cortical bone penetrated by the implant, buccal aspect	0.323	**0.015**	0.067
TBPf: trabecular bone pattern factor; BV/TV: trabecular bone volume.			

*Items in bold indicate statistically significant correlations at $p < .05$.

Evidence Report

A comparison of survival and complications of dental implants placed in irradiated versus non-irradiated bone

Evidence Report Purpose

Irradiation of head and neck tumors cause permanent hypoxic, hypocellular and hypovascular changes in bone, skin, and mucosa, which may lead to tissue breakdown and chronic nonhealing wounds. Also, radiotherapy reduces the proliferation of bone marrow, collagen and periosteal and endothelial cells. The extent of changes is dependent upon dose, fields of radiation and type of radiation treatment (e.g. hyperfractionation vs. standard fractionation). The reduced viability of irradiated bone may not be capable of remodelling as the implant is subjected to stresses associated with supporting, retaining, and stabilizing prosthetic restorations. Furthermore, there is an increased risk of osteoradionecrosis in irradiated bone. Hyperbaric oxygen (HBO) treatment may help revitalize the bone by stimulating angiogenesis, leading to improved success rates, but long-term clinical follow-up data are still lacking.

Objective

To critically summarize the recently published literature examining implant survival and other outcomes in studies of intraoral dental implants placed in irradiated compared to non-irradiated bone.

Summary

There was a trend towards lower cumulative survival rates for dental implants placed in irradiated compared to non-irradiated bone. All studies reported lower rates of survival in irradiated implants by 5-13% compared to non-irradiated implants. One study found significantly greater peri-implant bone resorption and no differences in implant stability for dental implants placed in irradiated versus non-irradiated bone. Another reported greater than 3 times the risk of soft tissue healing complications in irradiated implants compared to non-irradiated implants. Studies were of moderate quality so conclusions based on reported differences should be considered with caution. Additional methodologically rigorous comparative studies with comparable characteristics between groups are needed to better evaluate the effect of irradiation upon dental implant outcomes.

Sampling

A MEDLINE search was performed to identify recent studies published between January 1999 and January 2008 examining treatment outcomes of intraoral dental implants placed in irradiated versus non-irradiated bone. Eleven articles evaluated the treatment comparison of interest. Five articles which included outcomes on implant survival 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]**	14,195	
Search **(dental implants OR dental implantation, endosseous [MeSH]) AND (radiotherapy OR radiation effects OR cranial irradiation OR ionizing radiation), Limits ENGLISH, Human, Literature containing Abstracts**	136	5
Bibliographies from existing literature	0	0
Total Reviewed	**5**	

Common Outcome Measures

- Implant survival
- Implant success
- Peri-implant bone resorption
- Implant stability
- Soft-tissue parameters

Interventions

Intraoral dental implants were placed in irradiated or non-irradiated bone and were described as follows:

Landes (2006)

• Thirty patients underwent surgical removal of oral cancer. Additionally, radiotherapy was performed on 19 of these patients within 100 days postoperatively. Radiated patients received 57 Grey (Gy) at single doses of 1.9 Gy. ITI full-screw dental implants were placed following cancer treatment (mean 21 months after radiotherapy for irradiated patients, mean 8 months after surgery for non-irradiated patients).

Nelson (2007)

• Ninety-three patients underwent surgical removal of intraoral cancers, 29 of whom also had postsurgical radiotherapy up to 72 Gy, delivered in fractions of 2 Gy given daily for 5 days each week. Implants were placed after a minimum of 6 months following radiation therapy.

Yerit (2006)

• Seventy-one patients underwent treatment (surgery, radiation therapy with total dosage of 50 Gy) for oral cancer, and mandibles were then reconstructed. Implants (n=316) were placed (range 0.34 to 6.35 years after reconstructive surgery) in irradiated or non-irradiated mandibular bone.

Shaw (2005)

• In a retrospective study, 81 consecutive patients underwent surgery for oropharyngeal cancer, 38 of whom also received radiotherapy, median 50 Gy, range 40-66 Gy. In 1995, HBO treatment was used routinely in irradiated pa-

tients at the time of implant insertion (n=24). Implant-based oral rehabilitation occurred approximately 1 year after surgery or completion of postoperative radiotherapy.

Werkmeister (1999)

• In a retrospective study, 29 patients underwent surgical resection of oral cancer, 12 of whom also received postsurgical radiotherapy with doses varying between 42 and 64 Gy (mean 54 Gy). Implants were placed at least 6 months after bony reconstruction and 24 months after irradiation.

Table 2. Comparative studies evaluating intraoral dental implants placed in irradiated compared to non-irradiated bone.

Author (year)	Study Design	Population	Diagnostic Characteristics	Implant Placement			Follow-up (%)	LoE*
				Irradiated Bone		Non-Irradiated Bone		
				No HBO	HBO			
Landes (2006)	Prospective Cohort	N=30; Ni = 114 female: 27% age: 63 (47-83) yrs	Surgical removal of oral cancer, indication for prosthetic rehabilitation	N=19; Ni=72	None	N=11; Ni=42	Median 36 (24-46) months: 83%	Moderate
Nelson (2007)	Retrospective cohort	N=93; Ni=435 female: 32% age: 59 (26-89) yrs	Surgical removal of oral cancer, indication for prosthetic rehabilitation	N=NR; Ni=124	NR	N=NR; Ni=311	Mean 10.3 (5-161 months) years: 94%	Moderate
Yerit (-2006)	Retrospective cohort	N=71; Ni=238 female: 21% age: 57.8±14.2 yrs	Surgical removal of oral cancer, indication for prosthetic rehabilitation	N=NR; Ni=154	None	N=NR; Ni=84	Mean 5.42 (0.3 to 13.6) years: 46%	Moderate
Shaw (-2005)	Retrospective cohort	N=81; Ni=364 female: 36% age: 58 (15-80) yrs	Surgical removal of oral cancer, indication for prosthetic rehabilitation	N=14; Ni=†	N=24; Ni=†	N=43; Ni=192	Median 3.5 (0.3-14) years: 95%	Moderate
	Retrospective cohort	N=29; Ni=109 female: 21% age: 55 (35-79) yrs	Surgical removal of oral cancer, indication for prosthetic rehabilitation	N=12; Ni=49	None	N=17; Ni=60	3 years: NR‡	Moderate

N=number of subjects; Ni=number of implants; HBO=hyperbaric oxygen treatment

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

†Total number of implants placed in irradiated bone=172 (HBO/no HBO distribution not reported)

‡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 comparing dental implants placed in irradiated versus non-irradiated bone

Study design and methods	Landes (2006)	Nelson (2007)	Yerit (2006)	Shaw (2005)	Werkmeister (1999)
1. What type of study design?	Prospective Cohort	Retrospective Cohort	Retrospective Cohort	Retrospective Cohort	Retrospective Cohort
2. Statement of concealed allocation?*	N/A	N/A	N/A	N/A	N/A
3. Intention to treat?*	N/A	N/A	N/A	N/A	N/A
4. Independent or blind assessment?	NO	NO	NO	NO	NO
5. Complete follow-up of ≥85%?	NO	YES	NO	YES	NO
6. Adequate sample size?	NO	YES	YES	YES	NO
7. Controlling for possible confounding?	YES	NO	NO	NO	NO
LEVEL OF EVIDENCE	**Moderate**	**Moderate**	**Moderate**	**Moderate**	**Moderate**

* Applies to randomized controlled trials only

Results

Implant survival (Figure 1)

All studies reported lower rates of survival in irradiated implants by 5-13% compared to non-irradiated implants; however, only two reported statistical signficance. One author [Landes] did not report dental implant survival rates.

- At 46 months, there were no statistically significant differences in cumulative survival rates between implants placed in irradiated versus non-irradiated bone (84% vs. 92%, respectively; p=.08) [Nelson].
- At 8 years, the survival rate of implants placed in irradiated bone was significantly lower than implants placed in non-irradiated bone (72% vs. 95%, respectively; p<.003) [Yerit].
- At a median follow-up of 3.5 years, there were no statistically significant differences in cumulative survival rates between dental implants placed in irradiated compared to non-irradiated bone (68% patients, 82% implants vs. 77% patients, 87% implants, respectively; p>.05). Further, no statistically significant differences were found between individuals who received HBO versus those without HBO therapy (62% patients, 85% implants vs. 72% patients, 83% implants, respectively; p>.05) [Shaw], Figure 2.
- At 36 months, there was a statistically significant lower cumulative survival rate in implants placed in irradiated compared to non-irradiated bone (73.3% vs. 85.3%, respectively; p<.05) [Werkmeister].

Implant success

Overall success was defined as pocket probing depth ≤ 5mm, negative bleeding on probing, and bone loss < 0.2mm annually.

- Implant success rates did not reveal any statistically significant differences between implants placed in irradiated compared to non-irradiated bone (98% vs 100%, p>.05) [Landes].

Peri-implant bone resorption

- One study reported a significantly greater mean marginal bone loss around implants placed in irradiated compared to non-irradiated bone at 2 years (-1.4 ± 0.9mm vs. 0.4 ± 0.5mm, p<.01) [Landes].

Implant stability

- No statistically significant differences were found for Periotest® values between dental implants placed in irradiated compared to non-irradiated bone at 2 years (p>0.05) [Landes].

Soft tissue parameters

There is a trend towards increased soft tissue complications associated with dental implants placed in irradiated compared to non-irradiated bone.

- Periodontal probing depths were significantly lower in irradiated versus non-irradiated cases at 2 years (3.4 ± 1.7mm vs. 2.6 ± 0.6mm, p<.002), and gingival recession was significantly greater in implants placed in irradiated compared to non-irradiated bone (0.8 ± 0.9mm vs. 0.4 ± 0.5mm, p<.015). No statistically significant differences

were found for peri-implant bleeding and plaque indices between dental implants placed in irradiated compared to non-irradiated bone at 2 years (p>0.05) [Landes].

• Soft tissue healing complications at 12 months (dehiscences of mucosa, local soft tissue infection, delayed wound healing) was significantly greater in implants placed in irradiated compared to non-irradiated bone (28.6% vs 8.3%, p<.05; Figure 3) [Werkmeister]. The relative risk of a soft tissue healing complication in implants placed in irradiated bone is more than 3 times greater compared to non-irradiated implants (RR=3.4, 95% CI: 1.3, 8.9).

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.

• Two of the studies [Landes, Werkmeister] had a sample size that was likely inadequate to show a difference between the study groups for some of the outcomes measured.

• 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 study reviewed accounted for multiple implants in the same subject [Shaw].

• Only two of the studies reported a follow-up rate of ≥85%, which is necessary to ensure valid study results.

References

Studies

Study 1
Landes CA and Kovacs AF (2006)
Comparison of early telescope loading of non-submerged ITI implants in irradiated and non-irradiated oral cancer patients
Clin Oral Impl Res 17:367-74.

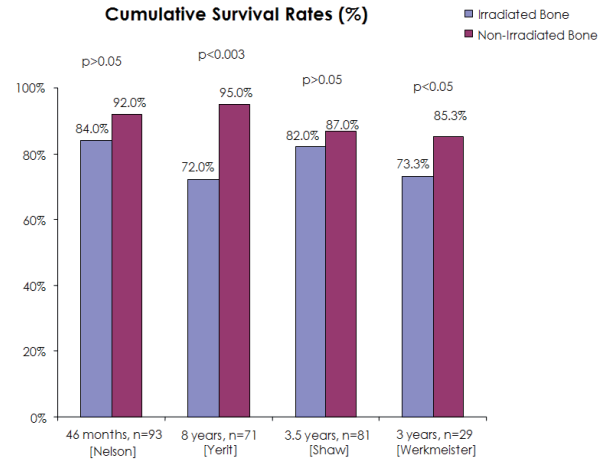
Study 2
Yerit KC, Posch M, Seemann M, et al.
Implant survival in mandibles of irradiated oral cancer patients
Clin Oral Impl Res 17:337-44.

Study 3
Shaw RJ, Sutton AF, Cawood JI, Howell, RA, et al (2005)
Oral rehabilitation after treatment for head and neck malignancy
Head and Neck 27:459-70.

Study 4
Nelson K, Heberer S, Glatzer C (2007)
Survival analysis and clinical evaluation of implant-retained prostheses in oral cancer resection patients over a mean follow-up period of 10 years
J Prosthet Dent 98:405-10.

Study 5
Werkmeister R, Szulczewski, D, Walteros-Benz, P, Joos, U (1999)
Rehabilitation with dental implants of oral cancer patients
J Cranio-Maxillofacial Surgery 27:38-41.

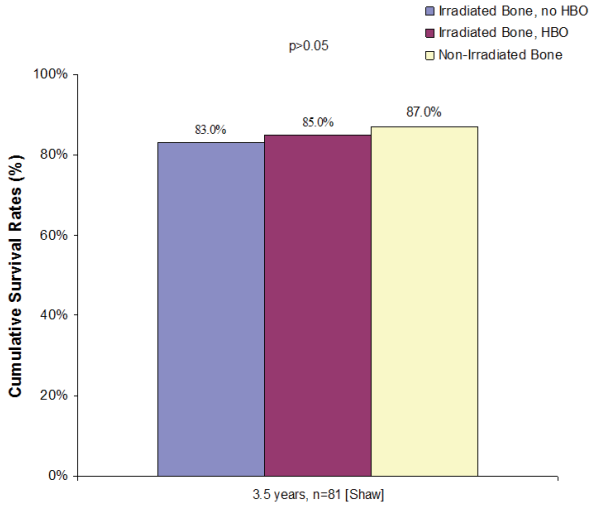
Figure 1. Cumulative survival rates for dental implants placed in irradiated versus non-irradiated bone†



Statistical significance noted on graphs if provided by author

† cumulative survival rates based upon number of implants

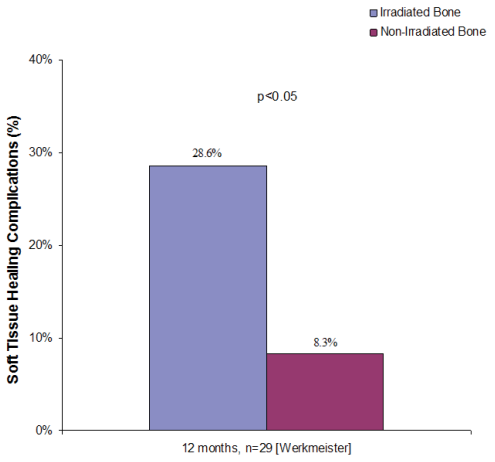
Figure 2. Cumulative survival rates for dental implants placed in irradiated versus non-irradiated bone, by hyperbaric oxygen treatment†



Statistical significance noted on graphs if provided by author

† cumulative survival rates based upon number of implants

Figure 3. Soft tissue healing complications for dental implants placed in irradiated versus non-irradiated bone*



Statistical significance noted on graphs if provided by author

* n=number of subjects

Literature Analysis

Bisphosphonate Therapy and Risk of Osteonecrosis of the Jaw SUMMARY of Findings and Implications

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.

Purpose

The purpose of this Literature Analysis was to systematically search the literature to identify key articles in an effort to better understand the risk of osteonecrosis in patients who are exposed to bisphosphonate medication. Moreover, we wanted to summarize any literature reporting osteonecrosis secondary to bisphosphonates in patients with dental implants. This literature analysis will address the following objectives:

- Provide background and details regarding mechanism/pharmacology of bisphosphonate medication
- Discuss risk factors for osteonecrosis secondary to bisphosphonate medication
- Report management recommendations for osteonecrosis secondary to bisphosphonate medication
- Summarize literature regarding implants in patients taking bisphosphonate medications

Data Sources and Search Strategy

The overall purpose of this report was to evaluate how bisphosphonates may cause osteonecrosis of the jaws with a particular interest in whether or not dental implants may contribute to oral complications of bisphosphonate medications. To accomplish this, we performed a MEDLINE search to identify studies reporting OSTEONECROSIS and BISPHOSPHONATE medication use (Table 1).

We also included some literature on animal studies in an effort to gain more knowledge regarding the mechanism of osteonecrosis of the jaws. An attempt was made to identify studies of high methodological quality (systematic reviews, RCT and cohort studies). Case series of 10 or more subjects were included due to minimal literature identified on this topic, and one case study was included since it discussed dental implants. Literature reviews were included for background information. Key articles that were identified from this strategy were explored further by using MEDLINE'S "Related Articles"

feature. In addition, bibliographies of retrieved articles were reviewed. There was no restriction on year published.

The following strategies were employed to identify literature to meet the objectives:

First strategy: Identify review articles describing osteonecrosis secondary to bisphosphonate medication.

Second strategy: Identify articles reporting osteonecrosis secondary to bisphosphonate medication. Topics such as definition, etiology, mechanism, risk factors and management were included.

Third strategy: Identify articles describing osteonecrosis secondary to bisphosphonate medication, with an emphasis on dental implants.

Table 1. Medline Search Summary

Terms	Hits	Reviewed
Search **"osteonecrosis" [MeSH] AND (bisphosphonates OR diphosphonates)**	207	
Search (**"osteonecrosis" [MeSH] OR jaw diseases OR maxillary diseases OR mandibular diseases) AND (bisphosphonates OR diphosphonates)**	441	
Search (**"osteonecrosis" [MeSH] OR jaw diseases OR maxillary diseases OR mandibular diseases) AND (bisphosphonates OR diphosphonates) NOT "technetium" [MeSH], Limits ENGLISH, Literature containing Abstracts**	91	12
Search (**"osteonecrosis" [MeSH] OR jaw diseases OR maxillary diseases OR mandibular diseases) AND (bisphosphonates OR diphosphonates)AND (device OR prosthesis OR implant)**	4	2
Bibliographies from existing literature	3	2
Total Reviewed		**16**

The following are results of the various search strategies:

First strategy: We identified one systematic review which provided background information, mechanism of action, oral complications risk factors in regards to jaw osteonecrosis secondary to bisphosphonate medication.

Second strategy: We identified 13 case series and one comparative study which summarized observational findings of osteonecrosis secondary to bisphosphonate medications.

Third strategy: We identified two case study articles describing oral implants placed in patients taking a bisphosphonate medication.

Background

Bisphosphonates

Definition:

Bisphosphonates are compounds used in the treatment of many metabolic and malignant bone diseases, such as bone metastases, osteoporosis, Paget's disease, hypercalcemia of malignancy and bone pain. Bisphosphonates are generally divided into two main classes based upon the presence or absence of a nitrogen side chain, and those which contain nitrogen are the most potent. The nitrogen side chain prevents these drugs from being metabolized, allowing them to accumulate with ongoing effects.

Mechanism/pharmacology:

The main pharmacological effect of bisphosphonates is the inhibition of bone resorption, mediated by a decreased function of osteoclasts. The exact mechanism of action is still unknown. Bisphosphonates are synthetic analogs of inorganic pyrophosphate that have a high affinity for calcium. They are rapidly cleared from the circulation and bind avidly to the mineralized bone tissue at the sites of osteoclast lacunae, and are then internalized by the osteoclasts [1]. They inhibit both osteoclastic activity and osteoclast recruitment and, moreover, diminish the lifespan of these cells.

- Non-nitrogen bisphosphonates can be incorporated metabolically into nonhydrolysable analogues of ATP. It is likely that the accumulation of these metabolites inhibits osteoclast function and causes osteoclast apoptosis.
- Nitrogen bisphosphonates are not metabolized, but act as transition state analogues of isoprenoid lipids inhibiting enzymes of the mevalonate pathway [2]. This leads to induction of osteoclast apoptosis, inhibition of bone resorption and reduction of bone remodeling, which compromises normal bone homeostasis.

Bisphosphonate-associated Osteonecrosis

Definition:

Osteonecrosis is necrotic, or dead, bone. Clinically, this condition begins with a superficial mucosal ulcer in either jaw, then progressing to detectable bone exposure, with extension of the ulcerated area in breadth and depth, with bone necrosis and sequestration. Some months later, it is common to find other and distant necrotic lesions in both jaws.

• In one study, the average size of the exposed areas of bone was 1.96 cm, with a mean of 2.3 lesions per patient in a population of 20 patients [3].

• The surrounding soft tissue is often inflamed due to secondary mucosal infection and is painful.

• The exposed bone surface in the early stage of the process is smooth. However, with progression of necrosis, some patients develop an irregular rough, bony surface that is likely due to fracture of the necrotic bone.

Mechanism/pharmacology for bisphosphonate-associated osteonecrosis of jaws (ONJ):

• Because the jaws have a greater blood supply than other bones and a faster bone turnover rate related both to their daily activity and the presence of teeth, bisphosphonates are highly concentrated in the jaws. Chronic invasive dental diseases and thin mucosa over bone are also contributors to this condition. The increased apoptotic rate of both osteoclasts and keratinocytes, which reduce and destruct the immune keratinocyte barrier of the oral mucosa, and the secondary infection by the oral flora, explain why osteonecrosis occurs only in the oral and maxillofacial region and not elsewhere in the body skeleton [4-7].

• Some reports have identified the anti-angiogenic effects of bisphosphonates [8,9]. Endothelial cell proliferation may be inhibited in the jaws, leading to loss of blood vessels and avascular necrosis.

Prevalence:

• Based on a web-based survey of 1203 patients with multiple myeloma or breast cancer, treated with zoledronic acid or pamidronate in the United States, 7% of patients with multiple myeloma and 4% of those with breast cancer reported osteonecrosis, and 6% and 8% of patients with multiple myeloma and breast cancer, respectively, reported lesions suspicious for osteonecrosis [10].

• In a retrospective survey of 252 patients who had received intravenous bisphosphonates since January 1997, the 10% of multiple myeloma patients developed ONJ, while 3% of breast cancer patients developed osteonecrosis [11].

• In another retrospective survey of 202 patients with multiple myeloma, the prevalence of bisphosphonate-induced osteonecrosis was 7.4% [12].

Summary of Studies of Bisphosphonate-Associated Osteonecrosis

Thirteen case-series and one comparative (case control) study were identified evaluating bisphosphonate-associated osteonecrosis that met our objectives. Details of studies are reported in Tables 2 and 3.

Risk Factors for Complications

Definitions:

The cumulative hazard is the probability of the endpoint of interest (e.g. ONJ), taking into account the effect of several risk factors upon this probability. The odds ratio is an estimate of the strength of the association between the risk factor and the disease outcome. The adjusted odds ratio is an odds ratio that takes into account the effect of several risk factors upon the association. That is, controlling for other factors that may also be associated with the outcome (e.g., ONJ), the independent effect of the variable of interest (e.g., bisphosphonates).

Duration of therapy:

The cumulative hazard of developing ONJ increased above 1% after 12 months of IV bisphosphonate infusion treatments and up to 11-13% at 4 years [11,12].

Type of bisphosphonate

- The cumulative hazard of developing ONJ was significantly higher in those who received zoledronic acid alone (1% at 12 months, 15-21% at 48 months) compared to the group with pamidronate alone or with subsequent zoledronic acid (0% at 12 months, 5-7% at 48 months) [11,12].
- The reason for this difference is unknown. Regardless, a possible explanation is the more potent inhibitory effect of zoledronic acid on bone turnover and a stronger anti-resorptive activity compared with pamidronate [11,12].

Dental surgery:

The adjusted odds ratio of developing ONJ after an extraction is 9.0 (95% CI: 1.8, 50.0). Patients who had an extraction and those who received pamidronate followed by zoledronic acid had a higher odds of developing ONJ [13].

Other risk factors:

- cumulative bisphosphonate dose
- presence of medical and dental comorbidities
- presence of pre-existing dental disease

Current Management Strategies [4,5,14]

Prior to initiation of bisphosphonate therapy

- Patient should have a dental examination, and therapy should not be initiated until all dental treatment is completed. Dental treatment is aimed at eliminating infections and preventing the need for invasive dental procedures in the near and intermediate future. This may include tooth removal, periodontal surgery, root canal treatment, caries control, dental restorations, and dentures.
- Impacted teeth with an oral communication are recommended to be removed and given a one month healing period.

• Large, multilobed mandibular tori or midline palatal tori with thin overlyng mucosa are recommended to be removed one month before initiation of bisphosphonate therapy.
• Prosthodontic appliances should be evaluated for fit, stability and occlusion.

While receiving bisphosphonate therapy

• All patients receiving IV bisphosphonates should be referred to a dentist or oral surgeon for examination and surveillance.
• Routine restorative care may be provided, and scaling and prophylaxis should be done as atraumatically as possible.
• Tooth removal should be avoided if at all possible. If the tooth is nonrestorable because of caries, root canal treatment is a better option than removing the tooth. Similarly, teeth that demonstrate 1+ or 2+ mobility should be splinted rather than removed. If the mobility is 3+ or more or is associated with a periodontal abscess, remove the tooth and provide antibiotic treatment. Patients should be followed up weekly for 4 weeks and then monthly until the sockets are completely closed and healed.
• Elective surgery within the jaws is strongly discouraged at this time.
• Denture wearing is acceptable, but the prosthesis should be examined for areas of excessive pressure or friction and given a soft reline if needed.

Treatment of patients with osteonecrosis of the jaws

• Aside from rounding-off sharp bony projections that produce soft tissue inflammation and pain, debridement surgery is not recommended.
• 0.12% chlorhexidine and long-term antibiotics, if indicated, is recommended. Treatment should be directed at eliminating or controlling pain and preventing progression of the exposed bone.
• Patients should be followed every 2-3 weeks.
• There is no scientific evidence to support discontinuation of bisphosphonate therapy to promote healing of necrotic osseous tissues in the oral cavity[14,15]. Nevertheless, patients may benefit from bisphosphonate withdrawal, as there have been anecdotal reports of healing and complete resolution of existing sites of osteonecrosis after several months of therapy cessation[7].
• Hyperbaric oxygen is of no benefit to the patient with bisphosphonate-induced exposed bone.

Bisphosphonates and Implants

Recommendations:

Patients who will be initiating bisphosphonate therapy should not be considered as candidates for dental implants, which have no crevicular epithelial attachment and therefore would predispose the patients in the group to bone exposure 4.

Complications:

A careful review of the apparent event that resulted in the area of nonhealing exposed bone identified that 4 of 119 (3.4%) cases were related to a dental implant placement [4].

Existing Literature on Dental Implants and Bisphosphonates:

- A case report describes a patient who was undergoing bisphosphonate treatment for osteoporosis, and four implants were inserted into the anterior mandible. The implants were connected with a bar supporting an overdenture and were loaded the same day. At the 1-year follow-up, all four of the implants were clinically osseointegrated, and no mobility was present. Minimal bone resorption was present around all implants [16].
- A case is reported in which a patient lost five endosseous implants that had successfully osseointegrated and had been restored with a lower hybrid prosthesis. The implants were lost approximately 6 months after diphosphonate therapy for osteoporosis was started [17].

Summary of ANIMAL STUDIES using Bisphosphonates for Therapeutic Use

- Topical administration of a bisphosphonate clodronate solution was injected into the subperiosteum adjacent to an area of inflammatory periodontitis in a rat model. Administration of the solution significantly prevented alveolar bone loss compared to the control side, and the number of osteoclasts on the experimental side was decreased compared with the control side [18].
- An aminobisphosphonate (alendronate) or saline (control group) was injected subcutaneously to an area that underwent mucoperiosteal flap surgery in a rat mandible. The results showed that administration of alendronate caused a significant reduction in alveolar bone resorption activated by mucoperiosteal flap surgery compared to the saline group [19].
- There were no studies which compared the effectiveness of topical versus systemic bisphosphonates. Further studies, both animal and human, are warranted before determining the potential usefulness of topical bisphosphonates.

Summary and Recommendations

- There is minimal literature on this topic since bisphosphonate-associated osteonecrosis is a relatively recent finding.
- Literature on bisphosphonate-associated osteonecrosis in regards to implants is limited to two case reports.
- Prospective studies are needed to more precisely determine what additional risk factors, if any, may predispose the patient to the develop-

ment of osteonecrosis of the jaws. Such variables as age, sex, medications, preexisting medical conditions, and individual genetic variations need to be examined.

• In addition, clinical trials should be done to determine the most effective treatment protocols for patients with this condition.

• Implantologists should be careful when patients are taking bisphosphonate medications.

• In the event a case of bisphosphonate-associated osteonecrosis is identified, it should be published to include information on risk factors and management.

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Table 2. Case-Series Studies of Bisphosphonate-Associated Osteonecrosis of the Jaws (ONJ)

Author (year)	Study Design	Population	Primary Diagnosis	Sites w/ONJ	Length of Therapy before ONJ	Previous Surgical Procedure	Medications
Bagan (2006)	Case Series	N=20; Female 75%; Mean age 60.3 yrs (range 36-80 yrs); F/U: NR	Breast cancer, n=10; Multiple Myeloma, n=9; Prostate cancer, n=1	Maxilla n= 1, Mandible n=11; Maxilla + Mandible n= 8	Mean 30 months (range 10-59 months)	55% (n=11)	Zoledronic acid, n=17 Pamidronate, n=3 Zoledronate/ pamidronate, n=5
Dimitrakopoulos (2006)	Case Series	N=11; Female 55%; Mean age 61 yrs (range 47-76 yrs); F/U: 5 months (2-8 months)	Breast cancer n=1; Multiple Myeloma n=5; Prostate cancer n=2;	Maxilla n=3, Mandible n=7, Maxilla + Mandible n=1	6-60 months	64% (n=7)	Zoledronic acid, n=6 Pamidronate/ zoledronate, n=4 Pamidronate/ ibandronate/ Zoledronate, n=1
Purcell (2005)	Case Series	N=13; 46% Female; Age range 42-83 yrs; F/U: NR	Breast cancer n=5; Multiple myeloma n=3; Prostate cancer n=4, Osteoporosis n=1	Maxilla n=2, Mandible n=4, Unknown n=7	4 months to 4.5 years	38% (n=5)	Zoledronic acid, n=9 Pamidronate n=2, Pamidronate and zoledronic acid n=1, Alendronate n=1
Bagan (2005)	Case Series	N=10; 80% Female; Mean age 59.6 yrs (range 36-80 yrs); F/U: 6 months	Breast cancer n=6; Multiple myeloma n=4	Mandible n=5; Maxilla + Mandible n=5		70% (n=7)	Zoledronic acid IV n=2; Pamidronate n=4; Pamidronate/ Zoledronic acid n=4
Pires (2005)	Case Series	N=14; 71% Female; Mean age 63 yrs (range 43-84 yrs); F/U: NR	Breast cancer n=6; Multiple myeloma n=4; Prostate cancer n=1; Lung cancer n=1	Mandible n=10; Maxilla n=4	1 week to 24 months	64% (n=9)	Zoledronic acid n=3; Pamidronate n=4; Pamidronate/ Zoledronic acid n=5; Other n=2

Marx (2005)	Case Series	N=119; Female NR; Age NR; F/U: NR	Multiple myeloma n=62; Breast cancer n=50; Prostate cancer n=4; Osteoporosis n=3	Maxilla n=33; Mandible n=81; Maxilla + Mandible n=5	Pamidronate: 14.3 months; Pamidronate/ Zoledronic acid: 12.1 months; Zoledraonic acid: 9.4 months	46% (n=55)	Pamidronate n=32; Zoledronic acid n=48; Pamidronate/ Zoledronic acid n=36; Alendronate n=3
Zarychanski (2005)	Case Series	N=12; 42% Female; Age NR; F/U: NR	Multiple myeloma n=10; breast cancer n=1; renal cancer n=1	Maxilla n=1; Mandible n=10; Maxilla + Mandible n=1	12 to 77 months	58% (n=7)	Pamidronate IV n=12
Farrugia (2006)	Case Series	N=23; 70% Female; Mean age 69.6 yrs (range 50-92 yrs); F/U: NR	Multiple myeloma n=9; breast cancer n=6; prostate cancer n=2; renal cell cancer n=1; osteoporosis n=4; Paget's Disease n=1	Maxilla n=10; Mandible n=13;	NR	39% (n=9)	Zoledronic acid IV n=11; Pamidronate IV n=4; Paamidronate/ Zoledronic acid IV n=3; Fosamax PO n=5
Melo (2005)	Case Series	N=11; 36% Female; Mean age 69 yrs (range 59-83 yrs); F/U: NR	Breast cancer n=3; Multiple myeloma n=7; Lung cancer n=1	Maxilla n=2; Mandible n=8; Maxilla + Mandible n=1	Mean 34 months (range 18 to 70 months)	82% (n=9)	Pamidronate n=4; Zoledronic acid n=4; Pamidronate/ zoledronic acid n=3

Migliorati (2005)	Case Series	N=18; 78% Female; Mean age 62 yrs (range 37-74 yrs); F/U: NR	Breast cancer n=10;multiple myeloma n=3; ovarian cancer n=1; prostate cancer n=1; overian/breast cancer n=1; prostate cancer/ lymphoma n=1; osteopenia n=1		Mean 24 months (range 4-37 months)		Pamidronate n=3; Zoledronic acid n=8; Pamidronate/ zoledronic acid n=6; Alendronate n=1
Ruggerio (2004)	Case Series	N=63; 71% Female; Mean age 62 yrs (range 43-89 yrs); F/U: NR	Multiple myeloma n=28; breast cancer n=20; prostate cancer n=3, lung cancer n=1; uterine sarcoma n=1; plasmacytoma n=1; leukemia n=1; osteoporosis n=7	Maxilla n=23; Mandible n=39; Mandible + Maxilla=1	Range 6-48 months	86% (n=54)	Pamidronate n=34; Zoledronic acid n=8; Pamidronate/ zoledronic acid n=14; Alendronate n=5; Risedronate n=1; Alendronate/ Zolenronic acid n=1
Bamias (2005)	Case Series	N=17; 41% Female; Mean age 61 yrs (range 43-72 yrs); F/U: NR	Mulitple myeloma n=11; breast cancer n=2; prostate cancer n=3; other n=1	Maxilla n=3; Mandible n=14	Median 20 months (range 4-86 months)	76% (n=13)	Zoledronic acid n=7; Pamidronate/ Zoledronic acid n=9; Zoledronic acid/Ibandronate n=1
Dimopoulos (2006)	Case Series	N=15; 40% Female; Median age 64 yrs (range 26-73 yrs); F/U: NR	Multiple myeloma n=15	Maxilla n=2; Mandible n=13	Median 39 months (range 11-76 months)	67% (n=10)	Zoledronic acid n=7; Pamidronate n=1; Pamidronate/ Zoledronic acid n=6; Zoledronic acid/Ibandronate n=1

Table 3. Comparative Study of Bisphosphonate-Associated Osteonecrosis of the Jaws (ONJ)

Author (year)	Study Design	Population	Primary Diagnosis	Sites w/ONJ	Length of Therapy before ONJ	Previous Surgical Procedure	Treatment Group(s)	Results (Medications)	Complications
Badros (2006)	Case Control	N=90; 30% Female; Median age 58 yrs (range 27-78 yrs); F/U: median 9mo (range 2-14 mo)	Mulitple myeloma n=90	Maxilla n=2; Mandible n=15; Maxilla + Mandible n=5	Median 6.4 months, range 2.3-15.4 months;	ONJ Group: 55% (n=12/22); Non-ONJ Group: 22% (n=15/68)	Osteonecrosis of the jaw (ONJ) n=22; No ONJ n=68	ONJ Group: Zoledronic acid n=2; Pamidronate n=3; Pamidronate/ Zoledronic acid n=17; None n=0 Non-ONJ Group: Zoledronic acid n=32; Pamidronate n=14; Pamidronate/ Zoledronic acid n=16; None n=6	ONJ Group: Infections n=4 Recurrent ONJ n=4

New Standards

Basal implants are the new benchmark for oral rehabilitation

Journal of Maxillofacial & Oral Surgery 2008 Vol. 7: No. 1: Comparison of immediate vs. delayed basal implants (Kopp S, Kopp W)

Basal implants by Dr. Ihde Dental such as Diskos®, BOI® and BCS® have been scientifically proven to be useful for a wide range of indications, from single-tooth replacement to full-mouth reconstruction, including single-step surgical protocols. Recently, these implants have been evaluated for additional indications. A 4.5-year consecutive study was able to show that immediate placement of these implants in extraction sockets had no negative implications on success rates, even in the presence of severe infection at the sites of removed teeth or implants, under immediate-loading conditions. The survival rates were actually slightly higher (97.7 %; p = 0.493) in the fresh-extraction group than the overall average of 96.8%. Interestingly, these results were obtained under real immediate-loading conditions; only full-arch implant-supported fixed restorations had been included in this study. 75.5% of the implants were part of "all-on-four" designs and had a survival rate of 96.6% (p = 0.291). More than 80% of the fixed restorations examined were supported strictly by four basal implants, with no "redundant" implants available to compensate for "suboptimally" placed implants.

The study has shown that basal implants can be securely placed using immediate-loading protocols, both in extraction sites and in healed bone. The shortened treatment times made possible by basal implants need not be prolonged; no waiting periods are required after removing infected teeth or failed implants. Using this scientifically validated protocol avoids the – even temporary – use of removable dentures.

A new benchmark has thus been established: The results of all implantological research today must be compared to these innovative products and protocols. Full-mouth rehabilitation of periodontal patients, even in the presence of severe infection, in just one surgical step must be considered the "gold standard" in restorative dentistry today. Any additional treatment measure or surgical intervention required by competing protocols or products must be based strictly on facts and significantly improve on the high survival rates of basal implants, as shown in this study.

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