CLINICAL ORAL IMPLANTS RESEARCH

Steven J. Kim Alexandre L. V. L. Ribeiro Alan M. Atlas Najeed Saleh Jamie Royal Mehrdad Radvar Jonathan Korostoff

Authors' affiliations:

Steven J. Kim, Department of Oral Biology University of North Carolina at Chapel Hill School of Dentistry, Chapel Hill, NC, USA Alexandre L. V. L. Ribeiro, Private Practice, Coconut Grove, FL, USA Alan M. Atlas, Najeed Saleh, Department of Preventive and Restorative Sciences, University of Pennsylvania School of Dental Medicine. Philadelphia, PA, USA Jamie Royal, Private Practice, North Massapequa, NY, USA Mehrdad Radvar, Department of Periodontics, School of Dentistry, Mashhad Dental Research Center, Mashhad, Iran Jonathan Korostoff, Department of Periodontics, University of Pennsylvania School of Dental Medicine, Philadelphia, PA, USA

Corresponding author:

Jonathan Korostoff Department of Periodontics University of Pennsylvania School of Dental Medicine Room NW3 Evans Building 240 South 40th Street Philadelphia, PA 19104, USA Tel.: 215 573 3965 Fax: 215 898 6094 e-mail: jkorosto@dental.upenn.edu

Date:

Accepted 4 November 2013

To cite this article:

Kim SJ, Ribeiro ALVL, Atlas AM, Saleh N, Royal J, Radvar M, Korostoff J. Resonance frequency analysis as a predictor of early implant failure in the partially edentulous posterior maxilla following immediate nonfunctional loading or delayed loading with single unit restorations. *Clin. Oral Impl. Res.* **00**, 2013, 1–8 doi: 10.1111/clr.12310 Resonance frequency analysis as a predictor of early implant failure in the partially edentulous posterior maxilla following immediate nonfunctional loading or delayed loading with single unit restorations

Key words: immediate loading, implant stability, maxilla, resonance frequency analysis

Abstract

Objectives: To assess the ability of baseline resonance frequency analysis (RFA) measurements to predict early implant failure in the posterior maxilla and to evaluate potential correlations between this measurement with Hounsfield units, bone quality variables, and implant dimension. **Materials and methods:** This prospective randomized study involved 46 SLActive Straumann implants placed in the posterior maxillae of 21 subjects. Each patient received at least one control (delayed loading) and one experimental (immediate nonfunctional loading) implant. Each site was evaluated with presurgical computer-assisted tomography (CT) scans, histomorphometric analysis of bone cores, and subjective determination of bone quality. Baseline implant stability quotients (ISQ) were determined by RFA measurements made at the time of fixture placement. Pearson's correlation analysis and Spearman's test were used to identify statistically significant correlations within the resultant data. Receiver operating characteristic (ROC) analysis was used to determine whether baseline ISQ values can accurately predict early implant failure.

Results: The mean baseline ISQ values for the two groups were 66.8 (experimental) and 66.2 (control). The 12-month survival rates were 86.4% (experimental) and 100% (control). There were no statistically significant correlations between baseline ISQ values and early implant failure, bone quality variables, or implant dimension. ROC analysis showed that baseline ISQ values cannot predict early implant failure.

Conclusion: Baseline RFA measurements were not able to predict early failure of immediately loaded implants placed in the posterior maxilla and therefore should not be used to determine whether an implant is a candidate for immediate nonfunctional loading in this region of the mouth.

As a result of improvements in implant surface characteristics and surgical instrumentation, immediate loading of dental implants is rapidly becoming a routine modality of tooth replacement therapy. Numerous clinical studies and meta-analyses of the existing literature indicate that this approach is extremely predictable in a variety of clinical scenarios (Ioannidou & Doufexi 2005; Esposito et al. 2007, 2009; Alsabecha et al. 2010; Atieh et al. 2010; Enriquez-Sacristan et al. 2011). However, there are circumstances under which the reliability of immediate loading is suspect. Foremost amongst these are situations in which (i) the quantity and/ or quality of available bone is compromised or (ii) cross-arch stabilization of the prosthesis is not feasible as is commonly encountered in patients presenting with a partially edentulous posterior maxilla or mandible. Under such conditions, the primary stability of the implant following surgical placement may be insufficient to resist the forces exerted on it during the subsequent early healing period. This results in micromotion of the implant and ultimately, failure to osseointegrate.

It is now well established that primary stability is a critical factor in determining the long-term success of immediately loaded implants (Javed & Romanos 2010). Primary stability of dental implants is most typically evaluated in a clinical setting by subjective methods including visual evaluation of implant mobility upon insertion and the percussion ("ping") test. When assessed visually, inadequate primary stability is defined as "lack of resistance during final tightening of the cover screw or mobility of the fixture mount when still on the implant" (Friberg et al. 1991). In reality, an implant that is visually stable upon insertion into an osteotomy does not always imply a successful clinical outcome. Neither visual evaluation of implant stability nor the percussion test is considered to exhibit an acceptable degree of reliability (Atsumi et al. 2007). Insertion torque, defined as "the rotational force applied to an object, usually a screw, during placement or tightening", has been proposed as a more objective measure of primary implant stability. Although it can be measured in a quantitative fashion it remains unclear as to whether insertion torque truly represents primary stability or contributes to it. Furthermore, the reproducibility of this measurement in a clinical scenario is virtually impossible to evaluate. Thus, it would be beneficial to a clinician if he or she was able to reproducibly measure primary stability and use the values to choose an appropriate loading protocol.

Resonance frequency analysis (RFA) was designed to evaluate the stiffness of the implant-to-bone interface by measuring the vibration (resonance frequency) of an implant in situ in response to application of a minute bending force. The resonance frequency of implants is most commonly reported as the implant stability quotient (ISQ) that can range from 0 to 100. It has been proposed that readings taken at the time of implant insertion can serve as a baseline measurement of primary stability; the higher the ISQ value the greater the stability of an implant. Additionally, it has been suggested that such readings can be used to determine whether an individual implant is a candidate for immediate loading. Hence, the aim of the present study was to conduct a randomized clinical prospective trial to determine whether the baseline RFA value serves as a reliable tool for predicting early implant failure following immediate nonfunctional or delayed loading with single unit restorations in the partially edentulous posterior maxilla. A secondary aim was to evaluate potential correlations between baseline ISQ values and other variables used to evaluate bone density as well as implant dimension.

Material and methods

Subjects

Twenty-one healthy individuals were recruited for the study from a pool of potential implant patients whom presented to the Post-Graduate Periodontics Clinic at the University of Pennsylvania School of Dental Medicine, regardless of sex, race, or other ethnic characterization. The protocol was approved by the Institutional Review Board of the University of Pennsylvania. The timeline for the study is shown in Fig. 1.

To participate in the study, patients were required to be:

- Between 18 and 80 years of age.
- Partially edentulous in the posterior maxilla for a minimum of 6 months requiring placement of two to four dental implants with sufficient bone volume as determined by CT to accommodate 4.1 or 4.8 mm diameter by 10 or 12 mm in length SLActive Straumann implants without the need for bone augmentation. Sites that were grafted at least 6 months before a subject's enrollment were included in the study if sufficient bone volume was present.
- Adequate intra-arch space allowing for satisfactory restoration of the edentulous area.
- At least 2 mm of attached (keratinized) gingiva on the buccal and palatal aspects of the edentulous ridge in the absence of active periodontal disease.
- Willingness and ability to comply with the pre- and postoperative diagnostic and

clinical evaluations required for the study.

- Willingness and ability (including financial) to comply with the final restorative treatment plan that would be accomplished upon completion of participation in the study.
- Willingness and ability to understand and comply with Institutional Review Board (IRB)/Ethics Committee requirements as outlined in consent form.

Exclusion criteria were:

- Pregnancy.
- Significant medical conditions known to interfere with bone healing.
- Bruxism and parafunctional habits.
- Medical conditions that preclude the subject from carrying out oral hygiene regimens (i.e. severe arthritis affecting the hands).
- Social history that indicates a risk of poor compliance (i.e. history of alcohol or drug abuse).

Evaluation of computer-assisted tomogram

SimPlant software (version 11.04; Materialize, Glenburnie, MD, USA) was used to evaluate the dimensions of residual bone in potential implant sites as well as the relative radiographic bone density as measured in Hounsfield units.

Surgical procedure

Patients were prescribed Amoxicillin and instructed to take 1 g 24 h prior to their surgical appointment and 500 mg every 8 h



Fig. 1. Study Design. Each patient received at least two implants in the posterior maxilla that were randomized to either an immediate nonfunctional occlusal loading protocol or a delayed loading protocol. Final impressions were made at 12 weeks postimplant placement and permanent cemented single unit PFM crowns were delivered in all cases at the 20–23 week follow-up visit. This study is focused on the ISQ values measured at the time of implant placement and its relationship to early failures.

thereafter for 7 days. Clindamycin (600 mg 24 h prior to surgery and 300 mg every 8 h thereafter) was prescribed for amoxicillin-sensitive patients. After administering local anesthesia, a crestal incision was made and a full-thickness mucoperiosteal flap was elevated. A surgical guide was used to identify the appropriate implant positions. The osteotomy was initiated with a 2-mm trephine to a depth of 5-10 mm, and a bone core was collected. The trephine with the intact bone core was placed in 10% neutral-buffered formalin and stored for future analysis. Implant sites were further prepared to receive 4.1 or 4.8×10 or 12 mm Straumann Standard Plus SLActive implants according to the manufacturer's instructions. Appropriately sized implants were placed to the correct depth with final seating torque values of 35 N cm or greater. All implants were placed using the nonsubmerged technique recommended by the manufacturer. Cover screws were placed on the implants randomized to the delayed loading group. Upon completion of implant placement, the flaps were coapted with 4-0 Vicryl sutures. Postsurgical instructions were reviewed with the patients. Prescriptions were given for suitable analgesics and 0.12% chlorohexidine gluconate oral rinse. Patients were reappointed for suture removal 1 week later and for follow-up visits 2, 6, 12, 20-23 and 52 weeks after their surgery.

Bone quality assessment

Upon drilling with the trephine to harvest bone cores, the surgeon determined the bone quality utilizing the criteria of Leckholm and Zarb (Type I, II, III or IV; Lekholm & Zarb 1985).

Randomization of loading protocol

A minimum of two and a maximum of four implants in each subject were evaluated as part of the study with at least one fixture serving as the delayed loading control. When placed in the same quadrant, the most posterior implant was randomized to be loaded by either the immediate or the delayed protocol via a coin toss in which heads represented one loading protocol and tails the other. This was sequentially reversed for each subsequent patient. The remaining implant(s) was loaded via the alternative protocol. When placed bilaterally, the implant on the right side was randomized to one loading protocol and the fixture(s) on the contralateral side loaded via the alternative protocol. Three subjects in the delayed loading group each received three implants and one subject in the immediate load group required three implants.

Prosthetic procedures

Fixtures randomized to the immediate nonfunctional load group were provisionalized as single units immediately following placement. The temporary crowns were adjusted to avoid any vertical load or proximal contact on the implant during mastication. The temporary abutment and provisional restoration were screwed down as one unit and tightened to 10 N cm. Cover screws were placed in the fixtures in the delayed load group until all implants received single porcelain fused to metal (PFM) crowns 20-23 weeks after placement. Impressions for the final crowns were taken at the 12-week follow-up visit. Final abutments screws were torqued in place to 35 N cm, and the crowns were secured with a noneugenol containing provisional cement.

Histomorphometric assessment of bone quality

The bone specimens obtained upon initiation of osteotomies were removed from the trephines, decalcified in RDO rapid decalcifier (Apex Engineering Products Corporation, Aurora, IL, USA) for 2 h, then embedded in paraffin using a Leica tissue processing unit. Five micron sections were taken with a microtome and transferred to microscope slides. The tissue sections were stained with hematoxylin and analyzed with an Olympus SZH-ILLB dissecting microscope (Olympus America, Center Valley, PA, USA). Images were captured with an Olympus E-10 digital camera (Olympus America). The digital pictures were enlarged using Photoshop, version 9.0.2, and the trabeculi were outlined using a digital tablet (Wacom Intuos3 6×8 tablet; Wacom, Vancouver, WA, USA). ImageJ software (version 1.41; http://rsbweb.nih.gov/ij/, open source, public domain) was then used to determine the area of calcified tissue in each section and the total area of the section. The resulting ratio (×100%) was defined as the histologic bone density. This determination was made on five separate sections prepared from each bone core and averaged to obtain the mean histologic bone density of the specific implant recipient site.

RFA measurement

A wireless magnetic-based Osstell Mentor RF Analyzer (Ostell USA, Linthicum, MD, USA) was used to assess primary implant stability. The designated transducer (SmartPeg) was hand-tightened per the manufacturer's instructions to the fixture. ISQ values taken immediately after implant placement were measured in triplicate and averaged to yield the mean baseline ISQ value for each implant. Although additional RFA measurements were taken at the 6, 12, 20–23, and 52 week follow-up appointments, they are not relevant to this study and are therefore not reported in the results. These values will be presented and discussed in a subsequent manuscript.

Criteria used to evaluate implant survival and failure

Implant survival was evaluated according to a modification of the criteria proposed by Misch et al. (2008). These are as follows:

- The implant remains present in the patient's mouth.
- No pain on function.
- No mobility.
- Less than 1 mm of crestal radiographic bone loss.
- No history of periimplantitis.

Implants exhibiting clinically detectable mobility were removed and deemed failures.

Statistical analysis

A two-sample t-test was used to determine whether baseline ISQ values or the histologic bone densities were statistically significantly different between the two different loading groups. The Wilcoxon ranked sum test was employed to see whether there was a significant difference in Hounsfield units between the two groups. Pearson's correlation analysis was utilized to evaluate correlations between the baseline ISQ values with implant diameter and length, mean histologic bone density and Hounsfield units. The Spearman's test was used to evaluate the correlation between baseline RFA values and the subjective bone quality scores determined at the time of implant placement. Statistical significance was evaluated after adjusting for dependent data, because some patients received more than two total implants such that within these individuals, multiple implants were loaded via the same protocol. Consequently, 21 sites with one loading protocol were compared with 21 sites of the other loading protocol. For ISQ and histologic bone density, a two-sample t-test was employed. Wilcoxon ranked sum test was used for comparing radiographic bone densities (Hounsfield units) because they did not show a normal distribution.

Results

A total of 46 implants were placed in 21 subjects. Twenty-two of the implants were immediately loaded and 24 were loaded via the delayed protocol (Table 1). Four patients Table 1. Dimensions, survival rates, baseline ISQ values, and measurements of bone quality (subjective, histomorphometric, and radiographic) for implants that were loaded utilizing a delayed vs. immediate nonfunctional loading protocol

Loading protocol	Delayed loaded		Immediately nonfunctionally loaded		P-value betwee groups, after adjustment*
Fixture length	10 mm	12 mm	10 mm	12 mm	
i mare length	14	10	15	7	
Fixture diameter	4.1 mm	4.8 mm	4.1 mm	4.8 mm	
	10	14	6	16	
Early failure	0		3		
Early survival rate (%)	100		86.4		
	(24/24)		(19/22)		
Baseline RFA (ISQ units)	Mean 66.2		Mean 66.8		0.61
	(SD: 6.5)		(SD: 7.4)		
	range of 53–76		range of 51–77		
Bone quality (ratio observed)	Type I: 3/2	Type I: 3/24		22	
	Type II: 11/24		Type II: 11/22		
	Type III: 9/24		Type III: 7/22		
	Type IV: 1/24				
Histologic bone density (%)	Mean 36.1		Mean 41.4		0.38
	(SD: 17.6)		(SD: 17.7)		
Radiographic bone density (HU)	Mean 584.9		Mean 524.2		0.92
	(SD: 415.9)		(SD: 353.1)		
SD, standard deviation. * $P < 0.05$ was considered to be sta	atistically sign	nificant.			

received more than three total implants. Forty-three implants were still present at the 12-month follow-up visit yielding an overall survival rate of 93.5%. Three of the 22 implants that were immediately loaded failed, yielding a 12-month survival rate of 86.4% for this group. In contrast, all of the implants that were loaded via the delayed protocol survived at the 1-year follow-up. The significance of these findings will be discussed in another manuscript to be submitted. The three implant failures all occurred within the first 6 weeks of immediate nonfunctional loading. The mean baseline ISQ values for these implants were 62.7, 66, and 72.

The baseline ISQ values measured upon insertion of each implant failed to show a significant correlation with early implant failure (Fig. 2; P value = 0.92). ROC analysis was performed on the data set to determine the utility of baseline ISQ as a tool to predict early implant failure for the fixtures in the immediate nonfunctional loading group (Fig. 3). The area under the curve (AUC) was



Fig. 2. Baseline ISQ values vs. loading protocol and outcome determined at the 1-year follow-up visit. Implants with redundant loading protocols (two loaded via the same protocol in one patient) were removed because they were dependent data. The resulting data set was made up of 21 implants for the delayed loading group and 21 implants for the immediate, nonfunctional loading group. The 1-year survival rate of the implants loaded with the delayed protocol was 100% (mean baseline ISQ = 65.6 [SD: 6.4], median = 67] and with the immediate nonfunctional loading protocol, it was 85.7% (mean baseline ISQ = 66.6 [SD: 8.1], median = 65.2). The mean baseline ISQ value for the three immediately loaded implants that failed was 66.9 (SD: 4.7) and the median 66. There was not a statistically significant difference in the mean baseline ISQ values between any of the three groups (P > 0.05). The red line is included for comparison and corresponds to an ISQ value of 60 that has been proposed to represent a threshold above which immediate loading can be considered (Sennerby & Meredith 2008; Atieh et al. 2012b).

calculated to be 0.50, indicating the test is indiscriminant.

None of the bone density variables evaluated in the study exhibited a statistically significant correlation with the baseline ISQ values (Fig. 4). Furthermore, the implant dimensions did not show a statistically significant correlation with the baseline ISQ values (data not shown).

Discussion

The clinical success of an implant-supported dental restoration is ultimately dependent upon the fixture becoming osseointegrated with the adjacent alveolar bone. As initially proposed by Brånemark, this process requires three to 6 months of load-free healing and is dependent upon initial mechanical (primary) stability of the implant. In recent years, a variety of immediate and delayed loading protocols have been described to decrease the overall treatment time a patient must endure. Some, but not all, of these procedures have been validated by well-designed controlled, randomized, prospective longitudinal clinical studies. What has become evident is that primary stability is of even greater importance in determining a successful outcome following loading via immediate or delayed approaches relative to the classic protocol. A quantitative noninvasive test to measure primary stability that predicts implant survival or failure would be of great use to clinicians and possibly allow them to choose an appropriate loading protocol for each patient's unique situation. The results of the current study indicate that RFA measurements taken at the time of implant placement do not meet these needs for implants placed in the posterior maxilla following immediate nonfunctional loading with single unit restorations.

Although numerous reports in the literature have indicated that successfully integrated implants exhibit an increase in ISQ from the day of placement up to 16 weeks postsurgery, there is no consensus regarding the use of baseline RFA measurements as true indicators of primary stability. Furthermore, it remains highly questionable as to whether baseline RFA measurements can be used to predict the risk of implant failure regardless of the loading protocol. Additional studies have been conducted to address these issues. A major problem in attempting to evaluate this body of work is the disparity between studies relative to the implant systems that were used, the loading protocol (s) that was followed, the clinical scenario



Fig. 3. Receiver operating characteristic (ROC) curve of the implants in the immediate nonfunctional loading group. ROC analysis was used to evaluate the capacity of baseline ISQ values to predict early implant failure. Dependent data were removed, resulting in the analysis including data from 21 implants placed in 21 subjects. The diagnostic specificity and sensitivity were determined for the predictability of early implant failure vs. survival at 1 year. Each baseline ISQ value was plotted as a false negative vs. a true positive outcome. Pretest probability was set to 95%, reflecting the widely accepted success rate of dental implants. This value is more forgiving than the 97.2% reported in a meta-analysis (Lindh et al. 1998), admitting for reporting bias. The confidence level was set a 95%. The ROC plot (blue line) of the data was along the nondiscriminatory line (red line) indicating that baseline ISQ values are not good predictors of 1-year clinical outcomes (survival vs. failure). The area under the curve (AUC) was calculated to be about 0.50. An AUC of 1.0 is considered an ideal discerning test, while one of 0.5 is representative of a worth-less test.

that was treated (e.g. maxillary vs. mandibular restorations and partial vs. full-arch restorations), and the iteration of the device used to make the RFA measurements. The ISQs that have been reported for stable, asymptomatic sand-blasted acid-etched Straumann implants similar to those used in the current study range from 46 to 65 (Nedir et al. 2004; West & Oates 2007; Kessler-Liechti et al. 2008; Rodrigo et al. 2010). Of these four studies, two attempted to determine whether the baseline RFA measurement predicted implant failure. Nedir et al. (2004) reported that all of the implants loaded via a delayed or immediate protocol with initial ISQ values of ≥49 and ≥54, respectively, "maintained osseointegration 1 year after loading". The investigators concluded that these values "might orient the practitioner to choose amongst various loading protocols". Although this study utilized two loading protocols, patients were not randomly assigned to the treatment groups. In contrast, Rodrigo et al. (2010) reported on a prospective case series and found that baseline RFA measurements could not predict implant outcomes. It should be pointed out that all four studies used different criteria in determining their thresholds indicative of a "stable" implant. Additionally, different types of transducers were utilized in this cohort of studies. While Rodrigo's group used magnetic transducers, West and Oates, Kessler-Liechti et al. and Nedir et al., used electronic-based transducers. The older generation electronic-based transducers tended to yield higher ISQ values



Implant with delayed loading and 1 year survival

Implant with immediate non-functional loading and 1 year survival

▲ Implant with immediate non-functional loading and failure after 1 year

Fig. 4. Evaluation of correlation between baseline ISQ values and the bone density of individual implant sites as determined by histologic (Panel a), subjective (Panel b), and radiographic (Panel c) criteria. The data from all 46 implants placed at baseline were pooled. The data failed to demonstrate a statistically significant correlation between the baseline ISQ values of the implants placed in the study and the mean histologic bone density (Pearson's correlation: r = 0.199, P = 0.185), subjective bone quality score (Spearman's rho: r = -0.258, P = 0.084) or Hounsfield units (Pearson correlation: r = 0.139, P = 0.356). The red line is included for comparison and corresponds to an ISQ value of 60 that has been proposed to represent a threshold above which immediate loading can be considered (Sennerby & Meredith 2008; Atieh et al. 2012b). Symbols representing data from the implants in each group were as follows: delayed loading (open circles); immediate load group that survived to 1 year (open squares); and the immediate load group that failed (closed triangles). compared with the newer magnetic Smart-Pegs (Valderrama et al. 2007).

The current study differed from those described above in that it was conducted in a randomized and controlled fashion with each patient having at least one control (delayed loading) and one experimental (immediate nonfunctional loading) implant. In addition, all of the implants were placed in the posterior maxilla and were restored with singleunit crowns. The other studies evaluated both maxillary and mandibular implants that were restored as single units, fixed partial dentures, fixed full-arch prostheses or implant-supported removable prostheses. By limiting the study to one anatomic site and a single type of prosthesis, we feel we were able to eliminate a number of confounding factors. A total of 46 implants were placed during our study; 24 were loaded via a delayed protocol and 22 by the immediate nonfunctional loading approach. Subjects were followed for 1 year and over this period three implants failed, all of which had been immediately loaded. The baseline ISQ values for the delayed and immediate groups ranged from 53 to 76 and 51 to 77, respectively. Our statistical analysis failed to demonstrate a correlation between the baseline ISQ measurements and implant failure. This finding is consistent with that of Rodrigo et al. (2010). It is also in agreement with a recently published systematic review that concluded RFA measurements made at the time of implant placement are not good predictors of failure following immediate loading (Atieh et al. 2012a). Interestingly, the baseline RFA measurements for the failed implants in our study were 62, 66, and 72, all being above the ISQ range of 60-65 that numerous studies have proposed to be the threshold below which immediate loading should not be carried out (Sennerby & Meredith 2008; Atieh et al. 2012a). In addition, three of the immediately loaded implants had baseline RFA measurements below the proposed threshold range (51, 54, and 58) yet survived to the 12month follow-up visit.

To truly evaluate the baseline RFA measurement as a tool for predicting future implant failure, the data must be analyzed in terms of sensitivity and specificity. A ROC curve visualizes the whole spectrum of decision thresholds in one comprehensive graph of sensitivity vs. 1-specificity. The analysis, based on statistical decision theory, was originally developed for electronic signal detection and problems with radar (Metz 1986). It eventually was adopted in the medical field to determine cutoff values and to gauge the accuracy of clinical tests (Zweig & Campbell 1993). In dentistry, it has been used mainly to assess the validity of tests for predicting susceptibility to dental caries (White et al. 1990; Steiner et al. 1992; Hausen 1997; van Palenstein Helderman et al. 2001; Jamieson et al. 2009; Petersson et al. 2010; Fontana et al. 2011). In order for the ROC analysis to be utilized, there must be true positive (survival at the 12-month follow-up visit) and true negative (failure by the 12-month follow-up visit) results. We therefore applied the analysis to the data derived from the immediate load group since all of the failures that were encountered occurred in this group. The RFA plot of the data points was clustered around the nondiscrimination line, suggesting that many of the baseline ISQ values and their associated implant outcomes occurred by chance (Fig. 3). The area under the curve (AUC) is a common measure to quantify and compare accuracies between different diagnostic tests. An AUC of 1.0 is considered an ideal test while one of 0.5 is representative of a test with no diagnostic value. The AUC of our data was 0.50. Atieh et al. (2012b) evaluated the use of baseline RFA measurement as a predictor of failure for mandibular posterior implants loaded within 48 h following immediate placement into an extraction socket or a delayed loading protocol. Their ROC analysis resulted in a similar AUC to ours of 0.45. A suggested baseline ISQ threshold in our plot was 67, yielding sensitivity and specificity for diagnosing survival of 44% and 67%, respectively. Considering the overall random distribution pattern of our data, the use of this value as a predictor of implant failure is hardly better than the toss of a coin for which ROC analysis yields an AUC of 0.50. Thus, it appears that baseline ISQ values do not accurately foretell the early failure of immediately loaded implants in the posterior maxilla and should not be used to determine whether an implant can be loaded via an immediate, early or delayed approach. Noguerol et al. (2006) conducted a study somewhat similar to ours to evaluate the Periotest device as a prognostic test for implant survival. Acknowledging the differences in study design, we feel it is valid to compare their results to ours. The ROC analysis of the data from the Periotest device yielded an AUC value of 0.70 suggesting the device had only fair accuracy, at best, yet is apparently a better predictor of early failure relative to the baseline RFA measurement made at the time of implant insertion.

It is currently of considerable debate as to what variables affect RFA measurements.

Numerous studies yielding conflicting results have investigated a variety of patient-, siteand implant-associated factors that might impact RFA measurements. These include subjective evaluation of bone quality according to the criteria of Leckholm and Zarb (Barewal et al. 2003; Bischof et al. 2004; Lai et al. 2008), insertion torque (da Cunha et al. 2004; Schliephake et al. 2006; Kahraman et al. 2009), implant-to-bone contact (Degidi et al. 2010), Hounsfield units measured by computed tomography (Turkyilmaz et al. 2009), implant diameter and/or length (Karl et al. 2008; Lai et al. 2008), placement in the maxilla vs. the mandible (Balleri et al. 2002), gender (Balshi et al. 2005), and periimplant bone density (Su et al. 2009), amongst others. In the current study, we failed to detect a statistically significant correlation between baseline ISQ values measured at the time of implant placement and mean histologic bone density, Hounsfield units, subjective bone quality score, or implant dimension. Although our findings are in agreement with those reported by other investigators, they simply add to the uncertainty regarding the clinical significance of RFA measurements.

In summary, we did not detect a statistically significant correlation between the baseline RFA measurements made at the time of fixture placement and early implant failure. Thus, a coefficient of determination between the two could not be calculated. We also failed to find a statistically significant correlation between RFA measured at implant placement and clinical variables including mean histologic bone density, Hounsfield units, bone quality, or implant dimension. Within the limits of our study, these data suggest that RFA values measured at the time of implant placement are not a reliable predictor of early failure of immediately nonfunctionally loaded implants in the posterior maxilla. Furthermore, we would advise against using these measurements for determining whether an implant is a candidate for immediate nonocclusal vs. delayed loading.

Acknowledgements: The authors are grateful to Straumann USA and the ITI Foundation for supporting this study. The first author, SJK, is supported by the National Institute of Dental and Craniofacial Research through the T90 DE021986 institutional training grant. We would also like to thank Dr E. J. Macarack and Ms Sylvia Decker for their assistance with the histomorphometric analysis of the bone cores.

References

- Alsabeeha, N., Atieh, M. & Payne, A.G. (2010) Loading protocols for mandibular implant overdentures: a systematic review with meta-analysis. *Clinical Implant Dentistry and Related Research* 12(Suppl. 1): e28–e38.
- Atieh, M.A., Alsabeeha, N.H.M. & Payne, A.G.T. (2012a) Can resonance frequency analysis predict failure risk of immediately loaded implants? *The International Journal of Prosthodontics* 25: 326– 339.
- Atieh, M.A., Alsabeeha, N.H.M., Payne, A.G.T., de Silva, R.K., Schwass, D.S. & Duncan, W.J. (2012b) The prognostic accuracy of resonance frequency analysis in predicting failure of immediately restored implants. *Clinical Oral Implants Research* 1–7. [Epub ahead of print].
- Atieh, M.A., Payne, A.G., Duncan, W.J., de Silva, R.K. & Cullinan, M.P. (2010) Immediate placement or immediate restoration/loading of single implants for molar tooth replacement: a systematic review and meta-analysis. *The International Journal of Oral & Maxillofacial Implants* 25: 401–415.
- Atsumi, M., Park, S.H. & Wang, H.L. (2007) Methods used to assess implant stability: current status. The International Journal of Oral & Maxillofacial Implants 22: 743–754.
- Balleri, P., Cozzolino, A., Ghelli, L., Momicchioli, G. & Varriale, A. (2002) Stability measurements of osseointegrated implants using Osstell in partially edentulous jaws after 1 year of loading: a pilot study. *Clinical Implant Dentistry and Related Research* 4: 128–132.
- Balshi, S.F., Allen, F.D., Wolfinger, G.J. & Balshi, T.J. (2005) A resonance frequency analysis assessment of maxillary and mandibular immediately loaded implants. *The International Journal of Oral & Maxillofacial Implants* 20: 584–594.
- Barewal, R.M., Oates, T.W., Meredith, N. & Cochran, D.L. (2003) Resonance frequency measurement of implant stability *in vivo* on implants with a sandblasted and acid-etched surface. *The International Journal of Oral & Maxillofacial Implants* 18: 641–651.
- Bischof, M., Nedir, R., Szmukler-Moncler, S., Bernard, J.P. & Samson, J. (2004) Implant stability measurement of delayed and immediately loaded implants during healing. *Clinical Oral Implants Research* 15: 529–539.
- da Cunha, H.A., Francischone, C.E., Filho, H.N. & de Oliveira, R.C. (2004) A comparison between cutting torque and resonance frequency in the assessment of primary stability and final torque capacity of standard and Tiunite single-tooth implants under immediate loading. *The International Journal of Oral & Maxillofacial Implants* **19**: 578–585.
- Degidi, M., Perrotti, V., Piattelli, A. & Iezzi, G. (2010) Mineralized bone-implant contact and implant stability quotient in 16 human implants retrieved after early healing periods: a histologic and histomorphometric evaluation. *The International Journal of Oral & Maxillofacial Implants* 25: 45–48.
- Enriquez-Sacristan, C., Barona-Dorado, C., Calvo-Guirado, J.L., Leco-Berrocal, I. & Martinez-Gonz-

alez, J.M. (2011) Immediate post-extraction implants subject to immediate loading: a metaanalytic study. *Medicina Oral Patologia Oral Y Circugia Bucal* **16**: e919–e924.

- Esposito, M., Grusovin, M.G., Achille, H., Coulthard, P. & Worthington, H.V. (2009) Interventions for replacing missing teeth: different times for loading dental implants. *Cochrane Database of Systematic Reviews*: CD003878.
- Esposito, M., Grusovin, M.G., Willings, M., Coulthard, P. & Worthington, H.V. (2007) The effectiveness of immediate, early, and conventional loading of dental implants: a Cochrane systematic review of randomized controlled clinical trials. *The International Journal of Oral & Maxillofacial Implants* **22**: 893–904.
- Fontana, M., Santiago, E., Eckert, G.J. & Ferreira-Zandona, A.G. (2011) Risk factors of caries progression in a Hispanic school-aged population. *Journal of Dental Research* **90**: 1189–1196.
- Friberg, B., Jemt, T. & Lekholm, U. (1991) Early failures in 4,641 consecutively placed branemark dental implants: a study from stage 1 surgery to the connection of completed prostheses. *The International Journal of Oral & Maxillofacial Implants* 6: 142–146.
- Hausen, H. (1997) Caries prediction-state of the art. Community Dentistry and Oral Epidemiology 25: 87-96.
- Ioannidou, E. & Doufexi, A. (2005) Does loading time affect implant survival? A meta-analysis of 1,266 implants. *Journal of Periodontology* 76: 1252–1258.
- Jamieson, L.M., Mejia, G.C., Slade, G.D. & Roberts-Thomson, K.F. (2009) Predictors of untreated dental decay among 15-34-year-old Australians. *Community Dentistry and Oral Epidemiology* 37: 27– 34.
- Javed, F. & Romanos, G.E. (2010) The role of primary stability for successful immediate loading of dental implants. A literature review. *Journal of Dentistry* 38: 612–620.
- Kahraman, S., Bal, B.T., Asar, N.V., Turkyilmaz, I. & Tozum, T.F. (2009) Clinical study on the insertion torque and wireless resonance frequency analysis in the assessment of torque capacity and stability of self-tapping dental implants. *Journal* of Oral Rehabilitation 36: 755–761.
- Karl, M., Graef, F., Heckmann, S. & Krafft, T. (2008) Parameters of resonance frequency measurement values: a retrospective study of 385 ITI dental implants. *Clinical Oral Implants Research* 19: 214–218.
- Kessler-Liechti, G., Zix, J. & Mericske-Stern, R. (2008) Stability measurements of 1-stage implants in the edentulous mandible by means of resonance frequency analysis. *The International Journal of Oral & Maxillofacial Implants* 23: 353–358.
- Lai, H.C., Zhang, Z.Y., Wang, F., Zhuang, L.F. & Liu, X. (2008) Resonance frequency analysis of stability on ITI implants with osteotome sinus floor elevation technique without grafting: a 5month prospective study. *Clinical Oral Implants Research* 19: 469–475.
- Lekholm, U. & Zarb, G.A. (1985) Patient selection and preparation. In: Brånemark, P.I., Zarb, G.A. &

Albrektsson, T., eds. Tissue Integrated Prostheses: Osseointegration in Clinical Dentistry, 199– 208. Chicago: Quintessence Publishing Co.

- Lindh, T., Gunne, J., Tillberg, A. & Molin, M. (1998) A meta-analysis of implants in partial edentulism. *Clinical Oral Implants Research* 9: 80–90.
- Metz, C.E. (1986) ROC methodology in radiologic imaging. *Investigative Radiology* 21: 720–733.
- Misch, C., Perel, M.L., Wang, H., Sammartino, G., Galindo-Moreno, P., Trisi, P., Steigmann, M., Rebaudi, A., Palti, A., Pikos, M.A., Schwartz-Arad, D., Choukroun, J., Gutierrez-Perez, J., Marenzi, G. & Valavanis, D.K. (2008) Implant success, survival, and failure: the international congress of oral implantologists (ICOI) Pisa consensus conference. *Implant Dentistry* 17: 5–15.
- Nedir, R., Bischof, M., Szmukler-Moncler, S., Bernard, J.P. & Samson, J. (2004) Predicting osseointegration by means of implant primary stability. *Clinical Oral Implants Research* 15: 520–528.
- Noguerol, B., Munoz, R., Mesa, F., de Dios Luna, J. & O'Valle, F. (2006) Early implant failure. Prognostic capacity of periotest: retrospective study of a large sample. *Clinical Oral Implants Research* 17: 459–464.
- van Palenstein Helderman, W.H., Mulder, J., van't Hoff, M.A. & Truin, G.J. (2001) Validation of a Swiss method of caries prediction in Dutch children. Community Dentistry and Oral Epidemiology 29: 341–345.
- Petersson, G.H., Isberg, P.E. & Twetman, S. (2010) Caries risk assessment in school children using a reduced cariogram model without saliva tests. *BMC Oral Health* **10**: 5.
- Rodrigo, D., Aracil, L., Martin, C. & Sanz, M. (2010) Diagnosis of implant stability and its impact on implant survival: a prospective case series study. *Clinical Oral Implants Research* 21: 255–261.
- Schliephake, H., Sewing, A. & Aref, A. (2006) Resonance frequency measurements of implant stability in the dog mandible: experimental comparison with histomorphometric data. *International Journal of Oral and Maxillofacial Surgery* 35: 941–946.
- Sennerby, L. & Meredith, N. (2008) Implant stability measurements using resonance frequency analysis: biological and biomechanical aspects and clinical implications. *Periodontology 2000* 47: 51–66.
- Steiner, M., Helfenstein, U. & Marthaler, T.M. (1992) Dental predictors of high caries increment in children. *Journal of Dental Research* 71: 1926– 1933.
- Su, Y.Y., Wilmes, B., Honscheid, R. & Drescher, D. (2009) Application of a wireless resonance frequency transducer to assess primary stability of orthodontic mini-implants: an *in vitro* study in pig ilia. *The International Journal of Oral & Maxillofacial Implants* 24: 647–654.
- Turkyilmaz, I., Sennerby, L., McGlumphy, E.A. & Tozum, T.F. (2009) Biomechanical aspects of primary implant stability: a human cadaver study.

Clinical Implant Dentistry and Related Research 11: 113–119.

- Valderrama, P., Oates, T.W., Jones, A.A., Simpson, J., Schoolfield, J.D. & Cochran, D.L. (2007) Evaluation of two different resonance frequency devices to detect implant stability: a clinical trial. *Journal of Periodontology* 78: 262–272.
- West, J.D. & Oates, T.W. (2007) Identification of stability changes for immediately placed dental implants. *The International Journal of Oral & Maxillofacial Implants* **22**: 623–630.
- White, S.C., Kaffe, I. & Gornbein, J.A. (1990) Prediction of efficacy of bitewing radiographs for caries

detection. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology 69: 506-513.

Zweig, M.H. & Campbell, G. (1993) Receiver-operating characteristic (ROC) plots: a fundamental evaluation tool in clinical medicine. *Clinical Chemistry* 39: 561–577.