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

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; Alsabeha 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.
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 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.
thereafter for 7 days. Clindamycin (600 mg
24 h prior to surgery and 300 mg every 8 h
thereafter) was prescribed for amoxicillin-sen-
sitive patients. After administering local
anesthesia, a crestal incision was made and a
full-thickness mucoperiosteal flap was ele-
vated. A surgical guide was used to identify
the appropriate implant positions. The osteot-
omy was initiated with a 2-mm trephine to a
depth of 5–10 mm, and a bone core was col-
clected. 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 manufac-
turer’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 poster-
or implant was randomized to be loaded by
either the immediate or the delayed protocol
via a coin toss in which heads represented
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 pic-
tures 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 soft-
ware (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 determina-
tion was made on five separate sections pre-
pared 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, Lintchrum, 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 measure-
ments 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 signifi-
cant difference in Hounsfield units between
the two groups. Pearson’s correlation analysis
was utilized to evaluate correlations between
the baseline ISQ values with implant diamete-

Results
A total of 46 implants were placed in 21 sub-
jects. Twenty-two of the implants were
immediately loaded and 24 were loaded via
the delayed protocol (Table 1). Four patients

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Kim et al. RFA as a predictor of implant failure
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 calculated to be 0.50, indicating the test is indiscernitant.

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 Branemark, 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

<table>
<thead>
<tr>
<th>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</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Loading protocol</strong></td>
</tr>
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<td>Fixture length</td>
</tr>
<tr>
<td></td>
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<td>Early survival rate (%)</td>
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<td>Baseline RFA (ISQ units)</td>
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<td>Bone quality (ratio observed)</td>
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<td>Histologic bone density (%)</td>
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<td>Radiographic bone density (HU)</td>
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SD, standard deviation.

***P < 0.05 was considered to be statistically significant.**

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].

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*Kim et al. RFA as a predictor of implant failure*
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.
compared with the newer magnetic SmartPegs (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 single-unit 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 12-month 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. Nogueiro 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-, site- and 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; Schlephake 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.

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