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ORIGINAL RESEARCH

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Validity of fractal analysis of implants in individuals with healthy and diseased peri-implant mucosa

Melissa S. Lang[1,2] | Takanari Miyamoto[1,2] | Martha E. Nunn[1]

[1]Department of Periodontics, School of Dentistry, Creighton University, Omaha, NE, USA

[2]Private Practice, La Vista, NE, USA

Correspondence
Melissa S. Lang, Department of Periodontics, School of Dentistry, Creighton University, 2500 California Plaza, Omaha, NE 68122, USA.
Email: MelissaLang@creighton.edu

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Abstract

Objective: The purpose of this study was to determine whether fractal analysis could discriminate the peri-implant trabecular bone between individuals with healthy peri-implant mucosa and peri-implant disease using digital periapical radiographs.

Material and Methods: The electronic health records of patients with a dental implant were reviewed to determine their eligibility. One hundred four patients (aged 27–89 years) were included and divided into three groups. Group 1) Individuals with healthy peri-implant mucosa; Group 2) Individuals with peri-implant mucositis; or Group 3) Individuals with peri-implantitis. The following clinical measurements for each dental implant were extracted: probing depth (PD), clinical attachment level (CAL), and the presence or absence of bleeding on probing (BOP). Digital periapical images of the implant were used to calculate the fractal dimension (FD) for each implant at two regions of interest (ROI). Summary statistics were calculated for mean PD, mean CAL, mean percent BOP, and mean FD by group. Differences among groups were tested using one-way analysis of variance (ANOVA). Spearman nonparametric correlations were tabulated for mean PD, mean CAL, mean percent BOP, and mean FD.

Results: The only measure that did not demonstrate significant differences among groups was FD ($p = .559$) with all other measures demonstrating a significant difference ($p < .001$).

Conclusions: Based on this study, FD of the peri-implant bone calculated from a periapical radiograph does not appear to be a valid method to distinguish between healthy and diseased implants, while clinical measures of PD, CAL, and BOP are useful for the diagnosis of peri-implant health, peri-implant mucositis, and peri-implantitis.

KEYWORDS

analysis, dental implants, fractals, peri-implantitis, radiology

1 | INTRODUCTION

Peri-implant mucositis has been defined by the presence of inflammation in the soft tissues surrounding a dental implant with no loss of supporting bone beyond initial bone remodeling during healing, whereas peri-implantitis has been defined as a disease in which the inflammatory process involves both soft tissue and bone around a dental implant with progressive loss of supportive bone beyond physiological bone remodeling (Heitz-Mayfield & Salvi, 2018; Schwarz, Derks, Monje, & Wang, 2018). Peri-implant

mucositis falls between a continuum from healthy peri-implant mucosa to peri-implantitis, establishing peri-implant mucositis as a precursor to peri-implantitis (Jepsen et al., 2015). The transition from peri-implant mucositis to peri-implantitis, marked by radiographic bone loss >0.5 mm, was determined to occur early within 3 years of prosthesis insertion for 81% of patients (Derks et al., 2016b). Hence, early detection of peri-implant mucositis is critical to prevent the progression to peri-implantitis due to the reversible nature of peri-implant mucositis, and the unpredictable outcome of treatment of peri-implantitis (Lindhe & Meyle, 2008; Salvi et al., 2012).

The diagnosis, prognosis, and treatment of peri-implant diseases depend upon an accurate assessment of the clinical and radiographic data (Rosen et al., 2013). There is no single test to accurately diagnose peri-implantitis. Rather, the diagnosis of peri-implant disease is based on the collective analysis of radiographic changes in alveolar bone over time and the clinical presentation of the peri-implant mucosa (presence or absence of inflammation-bleeding on probing (BOP) coupled with an increased probing depth (PD)) (Rosen et al., 2013). However, two-dimensional radiographs are subject to distortion and magnification which makes comparison of sequential films difficult (Sener, Cinarcik, & Baksi, 2015). Furthermore, a baseline radiograph of the implant may not be available from which to make such comparisons.

Fractal analysis is an alternative method of assessing changes in alveolar bone trabeculation patterns on radiographs, which avoids the problems associated with projection geometry (Sener et al., 2015). Fractal dimension (FD) measurements, calculated through fractal analysis, were shown to be relatively insensitive to variations in radiographic angulation, radiodensity, or radiographic machine settings, supporting its use as a diagnostic tool of non-standardized periapical radiographs (Jolley, Majumdar, & Kapila, 2006). Repeat exposures of periapical radiographs are taken over time in clinical practice to assess peri-implant bone. If changes in FD of peri-implant bone are noted in successively taken radiographs of dental implants, this could represent a true change in trabecular bone structure around the implant, which could aid in the diagnosis of peri-implant disease.

The use of fractal analysis for the assessment of alveolar bone, peri-implant bone, and periapical reactive bone using nonstandardized panoramic and periapical radiographs has been described (Jolley et al., 2006; Shrout, Potter, & Hildebolt, 1997; White & Rudoloph, 1999; Yaşar & Akgünlü, 2005; Yu et al., 2009; Zeytinoğlu, İlhan, Dündar, & Boyacioğlu, 2015). Fractal analysis of periapical radiographs was shown to discriminate between patients with healthy gingiva and moderate periodontitis (Sener et al., 2015). As similarities exist between healthy gingiva in the natural dentition and healthy peri-implant mucosa, and between periodontitis and peri-implantitis, this study evaluated the potential for fractal analysis to discriminate between patients with healthy peri-implant mucosa or peri-implant mucositis or peri-implantitis using digital periapical radiographs (Rosen et al., 2013). The null hypothesis was that diseased sites should display different patterns of interdental bone; thus, FD would differ significantly ($p < .05$) among implants with healthy peri-implant mucosa, peri-implant mucositis, and peri-implantitis.

2 | MATERIAL AND METHODS

This study was approved by the human subject ethics board of Creighton University and was conducted in accordance with the Helsinki Declaration of 1975, as revised in 2000. The study was conducted using the appropriate Standards for Reporting Diagnostic accuracy studies (STARD). The electronic dental health records of patients with dental implants who have had a prophylaxis or periodontal or implant maintenance in the Creighton University School of Dentistry undergraduate clinics were reviewed by the authors to determine their eligibility to be included in the study. Medical and dental histories, as well as previous periodontal charting and existing periapical (PA) radiographs, were reviewed. Inclusion criteria for this cross-sectional study included subjects ≥19 years with at least one dental implant with an internal conical abutment connection design and (a) diagnosis of healthy peri-implant mucosa or peri-implant mucositis or peri-implantitis, (b) no systemic diseases or medications which significantly impact periodontal inflammation or bone metabolism (e.g., steroids, bisphosphonates, >325 mg aspirin/day), and 3) have had the final restoration placed on the dental implant for a period of at least 6 months. Three hundred thirty-five patients' records were screened for inclusion in this study (Figure 1). Two hundred thirty-one patients were excluded for one or more of the following reasons:(a) Dates of PA radiograph and periodontal charting did not match, (b) periodontal charting at the implant site was not available, (c) PA radiograph of the implant was not available, and (d) health history was positive for rheumatoid arthritis, aspirin, or nonsteroidal anti-inflammatory drug therapy >325 mg/day, methotrexate use, bisphosphonate use, steroid use, or estrogen use. One hundred four patients (56 males and 48 females, aged 27–89 years; mean age: 65.72 ± 13.8 years) met the inclusion criteria and were divided into three groups as shown in Table 1. Group 1) Individuals with healthy peri-implant mucosa (no BOP and no radiographic signs of alveolar bone loss at the implant site beyond initial remodeling); Group 2) Individuals with peri-implant mucositis (BOP with no radiographic signs of alveolar bone loss at the implant site beyond initial remodeling); or Group 3) Individuals with peri-implantitis (BOP with radiographic signs of alveolar bone loss beyond initial remodeling) (Figure 1). The distribution of single implant sites included in the study is shown in Table 2.

The following clinical measurements for each dental implant were collected: diagnosis (Group 1, 2, or 3), PD, clinical attachment loss (CAL), and the presence or absence of BOP at six sites per implant (mesio-buccal, mid-buccal, disto-buccal, mesio-lingual, mid-lingual, and disto-lingual locations). Existing digital periapical images of each implant was saved as 8-bit TIF format files for the calculation of FD. All radiographs were digital using complementary metal–oxide–semiconductor (CMOS) detectors and photostimulable phosphor (PSP) plate detectors. Exposure parameters were set according to

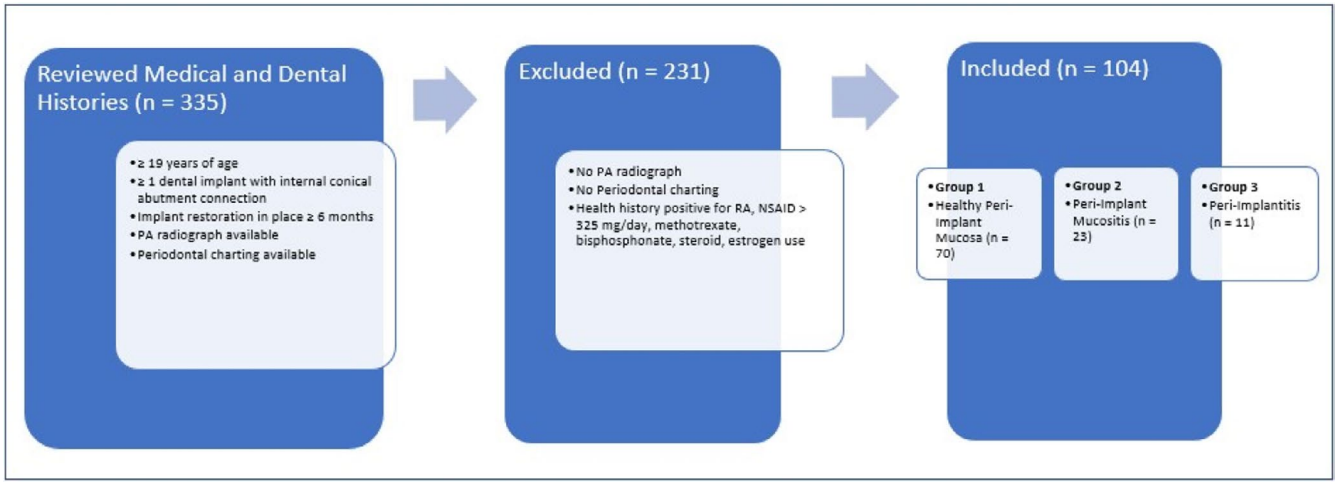

FIGURE 1 Flow diagram of patient inclusion/exclusion criteria

the 2012 American Dental Association recommendations for dental radiographic examinations on a per-patient basis. The FD was calculated for each implant at two regions of interest (ROIs): mesial and distal to the implant.

2.1 | Image analyses

FDs were calculated using the box-counting method described by White and Rudolph via an image software system (ImageJ v.1.46r software, National Institutes of Health, Bethesda, MD) (White & Rudolph, 1999). Two rectangular ROIs (100 x 50 or 100 x 40 pixels) were selected for each implant, one mesial to the implant and one distal to the implant within the interdental/implant bone, taking care to avoid periodontal ligament space, roots, and the implant surface (Figure 2). The size and position of each ROI was selected according to the available interproximal bone to be analyzed. FDs were calculated as described by Sener et al. Each ROI was duplicated (Figure 3a), and the Gaussian blur filter was applied using a diameter of 35 pixels (Figure 3b). The resultant blurred image was subtracted from the original ROI (Figure 3c). Subsequently, using the software features, the image was made binary, inverted, eroded once, dilated once (Figure 3d), and skeletonized (Figure 3e). The final image was used to calculate the FD with the fractal box count tool. Mean values of the two ROIs, one each mesial and distal to the implant, were used to calculate the FD for each implant.

2.2 | Statistical methods

Summary statistics were calculated using analytics software (SAS®, Cary, North Carolina) for mean PD, mean CAL, mean percent BOP, and mean FD by group (healthy implants, implants with peri-implant mucositis, implants with peri-implantitis). Differences among groups were tested using analysis of variance (ANOVA). ANOVA assumptions of homogeneity of variance and normal distribution of residuals were validated. Pairwise differences between healthy implants and implants with peri-implant mucositis and between healthy implants and implants with peri-implantitis were tested using independent samples *t* tests with effect differences reported for all parameters. Spearman nonparametric correlations were tabulated for overall mean PD, mean CAL, mean percent BOP, and mean FD as well as for these measures by group.

3 | RESULTS

Summary statistics were calculated for mean PD, mean CAL, mean percent BOP, and mean FD by group with corresponding *p*-values for one-way ANOVA and pairwise *t* tests with effect sizes reported and are shown in Table 3. The only measure that did not demonstrate significant differences among groups was FD ($p = .559$ for ANOVA) with all other measures demonstrating a significant difference among groups ($p < .001$ for ANOVA for mean PD, mean CAL,

TABLE 1 Subject age by group and overall age

Group	*n*	Mean (years)	*SD*	Median (years)	Min (years)	Max (years)
1: Healthy peri-implant mucosa	70	64.76	14.9	67.5	27	89
2: Peri-implant mucositis	23	64.57	11.1	68.0	37	83
3: Peri-implantitis	11	74.27	8.9	73.0	59	87
Total	104					

and mean percent BOP) as well as significant pairwise differences for mean PD ($p < .001$ for healthy implants vs. implants with peri-implant mucositis and $p < .001$ for healthy implants versus implants with peri-implantitis), mean CAL ($p < .001$ for healthy implants versus implants with peri-implant mucositis and $p < .001$ for healthy implants vs. implants with peri-implantitis), and mean percent BOP ($p < .001$ for healthy implants vs. implants with peri-implant mucositis and $p = .027$ for healthy implants vs. implants with peri-implantitis). Analysis of FD based on implant site failed to yield a statistically significant difference in FD (data not reported). Spearman nonparametric correlations were also calculated for associations between mean FD and other measures and are shown in Table 4. No significant association was detected in overall correlation between FD and other measures. Spearman correlations were also calculated for these measures by group, but again, no statistically significant associations were detected between mean FD and other measures.

TABLE 2 Distribution of implant sites

Site	*n*	%
3	2	1.9
4	4	3.8
5	7	6.7
6	3	2.9
7	5	4.8
8	1	1.0
9	2	1.9
10	2	1.9
11	5	4.8
12	3	2.9
13	5	4.8
14	5	4.8
15	2	1.9
18	10	9.6
19	8	7.7
20	7	6.7
22	2	1.9
23	1	1.0
25	2	1.9
27	2	1.9
29	1	1.0
30	18	17.3
31	7	6.7
Total	104	100.0

4 | DISCUSSION

This study demonstrated a statistically significant difference in PD, CAL, and BOP at diseased implant sites compared to implants with healthy peri-implant mucosa ($p < .001$). The presence of BOP is commonly used in case definitions for peri-implant mucositis and peri-implantitis (Heitz-Mayfield & Salvi, 2018; Schwarz et al., 2018).

Furthermore, increased PD is a common finding among implant sites diagnosed with peri-implantitis (Schwarz et al., 2018). Accordingly, in an analysis of 2,277 implants in 588 patients, a higher percentage of implants with peri-implant mucositis (16.3%) and with peri-implantitis (58.7%) presented with PD ≥ 6 mm compared to healthy implants (3.3%) (Derks et al., 2016a). While the present study did not identify implants presenting with PD greater than 6 mm, a significant difference in PD was found between healthy implants and diseased implants.

Nevertheless, it is not possible to define a range of probing depths consistent with health or peri-implant disease, and a great degree of variability in the physiological PD in health has been documented (Berglundh et al., 2018; Fuchigami et al., 2017). Rather, of more importance in the diagnosis of peri-implantitis is the evidence of increased PD or CAL over time, which is supported by the findings of the present study (Berglundh et al., 2018).

Fractal analysis was shown to detect subtle changes in the interdental bone trabeculation pattern of patients with moderate periodontitis, and thus was recommended for the diagnosis and monitoring of changes in trabecular architecture associated with periodontitis (Sener et al., 2015). Given the similarities in clinical and radiologic features between periodontitis and peri-implantitis, the present study aimed to determine whether fractal analysis could

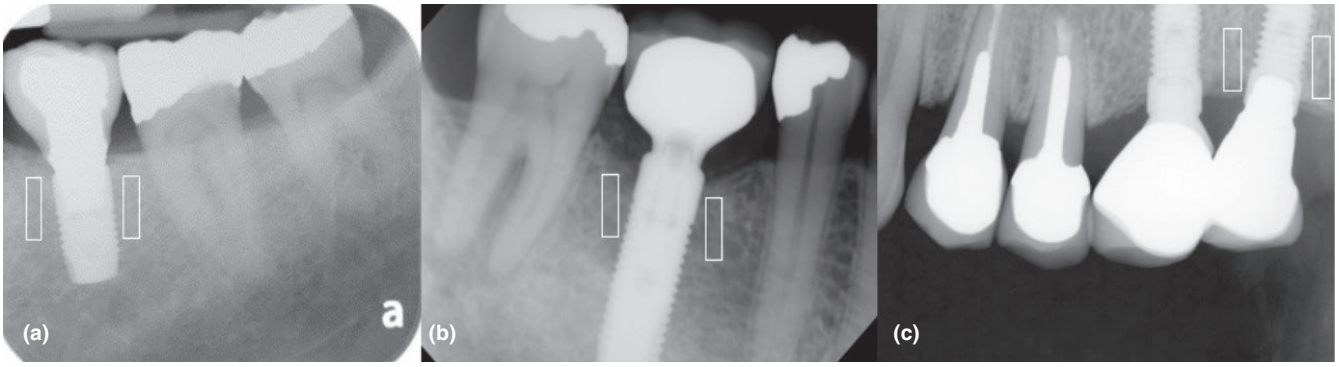

FIGURE 2 Digital periapical radiographic images with ROIs (white rectangular boxes) used in the calculation of FD for each implant. (a) Healthy implant. (b) Peri-implantitis implant. (c) Peri-implant mucositis implant

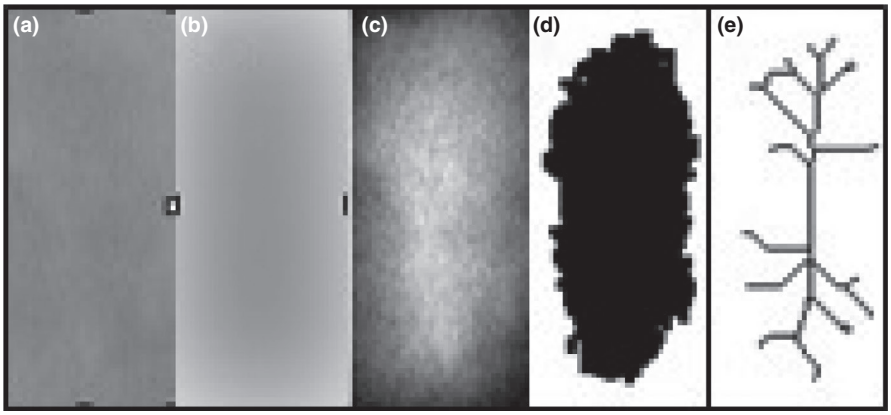

FIGURE 3 Process of FD calculation for each ROI. (a) Duplicated ROI. (b) Blurred ROI through Gaussian filter. (c) Resultant image from subtracting the blurred image from the original image. (d) Binary and inverted image. (e) Skeletonized image

discriminate the trabecular integrity alterations induced by peri-implant mucositis or peri-implantitis compared to peri-implant health.

The present study did not find a significant difference in FD among implants with healthy peri-implant mucosa and those with peri-implant mucositis or peri-implantitis, although a nonstatistically significant difference in FD was noted between implants with peri-implant mucositis (1.08 ± 0.03) compared to implants with peri-implantitis (1.07 ± 0.03; $p = .559$). The distribution of participants in the healthy peri-implant mucosa group ($n = 70$) exceeded the participants in the diseased groups ($n = 34$). The unequal participant distribution may have influenced the results. Supporting these findings, FD decreased in the transition from health to moderate periodontitis (Sener et al., 2015). Similarly, FD was lower in periodontitis patients compared to gingivitis patients (Shrout, Roberson, Potter, Mailhot, & Hildebolt, 1998; Updike & Nowzari, 2008). In contrast, FD of periapical reactive bone decreased after successful endodontic treatment (Yu et al., 2009).

FD rarely has been used to evaluate trabecular bone around dental implants, and to the authors' knowledge, this is the first report of the use of FD to evaluate changes in trabeculation around dental implants in health, peri-implant mucositis, and peri-implantitis using digital periapical radiographs. Intraoral digital radiographs to assess peri-implant bone in minipigs three months following implant placement failed to correlate FD with histological bone changes (Santos Corpas et al., 2011). In contrast, clinical and radiographic variables used to assess 94 implant-treated patients showed 26% of implants presented with peri-implantitis (bone level ≥ 3 mm apical to a fixed point and PD ≥ 5 mm) and a high FD correlated with less severe peri-implantitis (Papantonopoulos, Gogos, Housos, Bountis, & Loos, 2015). FD of peri-implant bone calculated from panoramic radiographs using the box-counting method decreased 6 months after prosthodontic loading with no additional changes after 12 months (Zeytinoğlu et al., 2015). However, FD of peri-implant bone on serial panoramic radiographs increased significantly during the period up to two years following implant placement ($p < .001$) (Wilding et al., 1995). The relationship between FD and initial implant stability as measured by resonance frequency analysis (RFA) showed a statistically significant correlation between peri-implant FD values acquired from panoramic radiographs and RFA (Lee et al., 2010). Some findings supported that FD increased in the diseased state, while others indicated that FD decreased in the diseased state due to reduced trabecular complexity, indicating that there appears to be no consensus on the relationship between FD and trabecular bone pattern.

Differences between reported results of FD in various studies may be influenced by discrepancies in the selection of jaw region or in the selection of ROIs (Zeytinoğlu et al., 2015). The use of small ROIs may not accurately reveal the differences in FD between selected areas (Updike & Nowzari, 2008). In the present study, all implant sites were included, both maxillary and mandibular, and anterior and posterior sites. Consequently, nonstandardized ROIs were necessitated by the varied amount of space available between the implant surface and the adjacent periodontal structures. Hence, smaller ROIs were necessitated in anterior regions which may have influenced the lack of statistically significantly different FD values among the groups in the present study. Additionally, the digital software used to calculate FD from ROIs on the periapical radiographs did not allow axial tilting of the ROIs to parallel implant surfaces, somewhat limiting the placement of the ROI very near the implant surface in some instances. Nevertheless, the effect of the location of the ROI on the FD calculation has not been determined (Sener et al., 2015).

Although clinical and radiologic features of periodontitis and peri-implantitis are similar, differences in patterns of disease evolution exist between the two diseases in terms of inflammatory reactions and histological characteristics (Berglundh, Zitzmann, & Donati, 2011; Carcuac & Berglundh, 2014). The cytokine profiles in connective tissue from peri-implantitis lesions differ distinctly compared to periodontitis lesions, indicating that anatomical differences in the connective tissue contribute to the difference in disease progression (Ghighi et al., 2018). A lack of collagen fiber insertion into the implant surface may contribute to progression of peri-implant disease, whereas a connective tissue attachment to cementum may limit the spread of the inflammatory process toward the bone in periodontitis (Albouy, Abrahamsson, Persson, & Berglundh, 2009). It is possible that the lack of confinement of the inflammatory infiltrate around implant sites in this study affected the peri-implant trabeculation pattern, and thus, influenced the FD calculation.

Other limitations of this study include that it was a cross-sectional study. Longitudinal data comparing the baseline FD data at

TABLE 3 Summary statistics for PD, CAL, BOP, and FD (mean ± *SD*)

Parameters	*n*	Mean ± *SD*	Median	Range	*p**
PD (mm)					<.001
Healthy	70	2.29 ± 0.64	2.33	1.00 to 3.67	
Perimucositis	23	3.01 ± 0.79	3.00	1.17 to 4.50	
Perimucositis versus Healthy		0.73 ± 0.16			<.001
Peri-implantitis	11	3.44 ± 0.78	3.50	1.83 to 4.33	
Peri-implantitis versus Healthy		1.15 ± 0.21			<.001
CAL (mm)					<.001
Healthy	70	2.28 ± 0.63	2.33	1.00 to 3.67	
Perimucositis	23	3.02 ± 0.77	3.00	1.33 to 4.50	
Perimucositis versus Healthy		0.74 ± 0.16			<.001
Peri-implantitis	11	3.59 ± 0.54	3.83	2.67 to 4.33	
Peri-implantitis versus Healthy		1.31 ± 0.20			<.001
BOP (% of sites per implant)					<.001
Healthy	70	0.0% ± 0.0	0.0%	0.0% to 0.0%	
Perimucositis	23	32.6% ± 19.8	33.3%	16.7% to 83.3%	
Perimucositis versus Healthy		32.6% ± 4.1			<.001
Peri-implantitis	11	24.2% ± 31.1	0.0%	0.0% to 66.7%	
Peri-implantitis versus Healthy		24.2% ± 9.4			.027
FD					.559
Healthy	70	1.08 ± 0.05	1.08	0.99 to 1.23	
Perimucositis	23	1.08 ± 0.03	1.07	1.02 to 1.13	
Perimucositis versus Healthy		0.009 ± 0.010			.344
Peri-implantitis	11	1.07 ± 0.03	1.07	1.02 to 1.13	
Peri-implantitis versus Healthy		0.014 ± 0.012			.243

*p-value on top line is for one-way ANOVA. Other p-values are for pairwise differences between healthy implants and implants with peri-implant mucositis and for differences between healthy implants and implants with peri-implantitis.

the time of implant placement to the FD at the time of the development of peri-implant disease could have revealed a statistically significant difference in FD between health and peri-implant disease. Such future longitudinal studies on FD could aid in the establishment of normal ranges of FD at various implant sites, age groups, genders and proximity to teeth or other implants. Additionally, this study included implants in the peri-implantitis group with an average CAL of 3.59 ± 0.54 mm, which may have represented relatively mild peri-implantitis. Perhaps a greater severity of peri-implantitis could have revealed a statistically significant difference among FD between health and peri-implant disease. However, the purpose of this investigation was to evaluate FD's use in early detection of peri-implant disease. Thus, inclusion of mild cases of peri-implantitis rather than implants with

TABLE 4 Spearman correlation between FD, PD, CAL, and BOP (mean ± *SD*)

		Mean PD	Mean CAL	% BOP
Mean FD	Correlation	.028	.018	−.005
	p	.775	.855	.962
	n	104	104	104
Mean PD	Correlation		.967	.426
	p		<.001	<.001
	n		104	104
Mean CAL	Correlation			.416
	p			<.001
	n			104

moderate to severe bone loss was more relevant to the study design and to the applicability of FD use in a clinical application. Furthermore, FD cannot be used to analyze the buccal and lingual bone of an implant due to the two-dimensional limitations of the periapical radiograph. Future studies in the arena of FD and peri-implant disease could focus on comparing FD as measured by higher resolution digital radiographic methods.

Based on the findings of this study, FD as calculated from a digital periapical radiograph is not a valid method to discriminate between peri-implant health and peri-implant mucositis or peri-implantitis. For now, an experienced clinician with the right diagnostic tools is the proven technique for the diagnosis of peri-implantitis.

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AUTHOR CONTRIBUTION

Melissa Sue Lang: Conceptualization (lead); Data curation (lead); Funding acquisition (equal); Investigation (lead); Methodology (equal); Project administration (lead); Software (equal); Writing-original draft (lead); Writing-review & editing (lead). **Takanari Miyamoto:** Conceptualization (supporting); Funding acquisition (equal); Project administration (supporting); Supervision (supporting); Writing-original draft (supporting); Writing-review & editing (supporting). **Martha E Nunn:** Formal analysis (lead); Methodology (supporting); Software (equal); Validation (lead); Writing-original draft (supporting); Writing-review & editing (supporting).

ORCID

Melissa S. Lang https://orcid.org/0000-0003-4616-0854

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