



DIAGNOSTIC TRIAL

Ultrasonography for noninvasive and real-time evaluation of peri-implant tissue dimensions

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Abstract

Aim: Existing methods for evaluating marginal bone loss and tissue biotype around dental implants present with many limitations. The aim of this study was to examine the accuracy of high-resolution, 3-dimensional ultrasound to measure peri-implant tissue dimensions.

Material and Methods: A 25-MHz ultrasound probe prototype was used to scan peri-implant tissues of 17 implants from seven fresh human cadavers. Four ultrasonic measurements were made as follows: the marginal bone level/thickness, and mucosal level/thickness. The readings were statistically compared to cone beam computed tomography (CBCT) and/or open bone measurements.

Results: The correlations (*r*) between the ultrasound and direct/CBCT readings of the four parameters ranged from 0.85 to 0.98 ($p < 0.0001$). The mean absolute difference in the four parameters between ultrasound-direct and ultrasound-CBCT ranged from 0.033 to 0.24 mm.

Conclusion: Encouraging evidence is shown that ultrasound can accurately measure peri-implant tissue dimensions. Following clinical trial validations, ultrasound offers potential as a valuable tool to evaluate long-term peri-implant tissue stability without concerns of ionizing radiation and image artefacts around implants.

KEYWORDS

alveolar bone, cone beam computed tomography, dental implants, peri-implantitis, soft tissue, ultrasonography

1 | INTRODUCTION

Dental implants are nowadays a mainstream approach for replacing missing teeth. High implant survival rate and patient satisfaction are the driving force for the popularity of this treatment option. While achieving osseointegration and providing function are predictable outcomes, recent emphases have focused on improving long-term implant functional and aesthetic results. These outcomes are highly dependent on the quality and quantity of peri-implant supporting tissues (Fu, Lee, & Wang, 2011; Kan, Rungcharassaeng, Umezu, & Kois, 2003; Lin, Chan, & Wang, 2013; Spray, Black, Morris, & Ochi, 2000). Peri-implant tissue volume determines tissue biotype (Fu

et al., 2010), which is currently evaluated by a visual examination, probing and bone sounding (Kan, Morimoto, Rungcharassaeng, Roe, & Smith, 2010; Kan et al., 2003). Each method has its own advantages and limitations. There is little doubt that an aesthetic outcome can be more easily achieved with thick rather than thin soft tissues (Fu et al., 2011). Thick tissues can camouflage metal restoration hues and imperfect implant locations better than thin tissues (Jung, Sailer, Hammerle, Attin, & Schmidlin, 2007; Steigmann, Monje, Chan, & Wang, 2014). It is now understood that the mucosal level could be maintained when a certain amount of peri-implant hard tissue is present (Miyamoto & Obama, 2011; Spray et al., 2000). In addition, tissue biotype may dictate extraction socket and implant healing

process. Thin tissue biotype is associated with greater horizontal and vertical bone loss in extraction sockets after immediate implant placement (Ferrus et al., 2010). There is some evidence that thick crestal soft tissue can reduce implant marginal bone remodelling (Linkevicius, Apse, Grybauskas, & Puisys, 2009; Suarez-Lopez Del Amo, Lin, Monje, Galindo-Moreno, & Wang, 2016). Therefore, it is very important to evaluate tissue volume at all implant treatment phases for achieving optimal outcomes.

It is a prerequisite to measure and monitor the amount of hard tissue loss in the presence of peri-implant diseases. Peri-implant bone loss is the hallmark of peri-implantitis, a prevalent disease that occurs in approximately 20% of dental implants (Derks & Tomasi, 2015). Costly and traumatic surgical revisions impact patients' quality of life tremendously. The amount of bone loss defines the disease diagnosis, indicates the severity and determines treatment options. Two-dimensional 2-D bone evaluation by intraoral radiographs is the current gold standard (2013; Sanz & Chapple, 2012, Tyndall et al., 2012). However, this imaging modality only shows superimposed interproximal bone level but not the radicular (facial and palatal/lingual) bone levels. Unlike teeth, facial bone around implants is more susceptible for resorption (Kehl, Swierkot, & Mengel, 2011; Parlar et al., 2009), resulting in nonuniform bone loss in 34%–45% of peri-implantitis-affected implants (Schwarz et al., 2007; Serino, Turri, & Lang, 2013). It becomes apparent the current 2-D radiographs are inadequate to evaluate peri-implant bone loss (Christiaens et al., 2017, 2018).

Cone beam computed tomography CBCT, capable of providing cross-sectional images, has been used to evaluate bone loss (Mengel, Kruse, & Flores-de-Jacoby, 2006). Although CBCT has generally shown clinically acceptable results, the presence of artefacts around metallic implants and the inability to identify thin bone limit its use (Fienitz et al., 2012; Kuhl et al., 2016; Ritter et al., 2014; Schliephake, Wichmann, Donnerstag, & Vogt, 2003). In addition, repeated radiation exposures and cost prohibit its routine use for monitoring bone loss clinically.

Ultrasonography was primarily designed for soft tissue evaluation; therefore, it has been validated for measuring soft tissue thickness in various anatomical locations of the oral cavity (Eghbali, De Bruyn, Cosyn, Kerckaert, & Van Hoof, 2016; Muller, Barrieshi-Nusair, & Kononen, 2007; Muller & Kononen, 2005; Tzoumpas, Mohr, Kurtulus-Waschulewski, & Wahl, 2015). A recent study (De Bruyckere, Eghbali, Younes, De Bruyn, & Cosyn, 2015) applied ultrasound to measure facial soft tissue thickness changes in two dimensions around implants after connective tissue grafting procedures. It has also been proposed to evaluate periodontal hard tissues. An early study reported unfavourable results, suffering from low image resolution (Palou, McQuade, & Rossmann, 1987). In a contrasting manner, others (Chifor et al., 2011; Nguyen, Le, Kaipatur, & Major, 2016; Nguyen et al., 2016; Tsiolis, Needleman, & Griffiths, 2003) showed promising outcomes using higher frequency ultrasound that yield better image resolution. A recent proof-of-principle study (Chan, Wang, Fowlkes, Giannobile, & Kripfgans, 2017) showed that ultrasound can image important oral

Clinical relevance

Scientific rationale for the study: Tissue biotype determines healing behaviour and aesthetic outcome of implant therapy. This study was to test the feasibility of a prototype probe with high-resolution and small-footprint for imaging peri-implant tissues.

Principal findings: Ultrasound can image peri-implant tissues accurately on human cadavers, compared with direct and CBCT measures. It is feasible to evaluate peri-implant tissues in a noninvasive and real-time fashion.

Practical implications: Ultrasound tissue volume evaluation will be beneficial for clinicians to select appropriate surgical and restorative modalities to achieve optimal aesthetic and functional outcome. It could be used to monitor peri-implant bone loss after implant placement.

anatomical structures. Later, another study from our group (Chan, Sinjab, et al., 2017) demonstrated accurate ultrasound readings of alveolar bone height and thickness on human cadaverous specimens. The mean absolute differences in ultrasound measures from direct measures and radiographic measures from CBCT images were within 0.1 mm. These promising results prompted us to evaluate the potential of ultrasonography for measuring peri-implant tissue dimensions in a preclinical model. In addition, the feasibility of ultrasonography for imaging peri-implant tissues was evaluated in humans.

2 | MATERIALS AND METHODS

2.1 | Preclinical study

The preclinical experiment was deemed exempt and nonregulated, as determined by the University of Michigan Institutional Review Board (Study ID: HUM00134643).

2.1.1 | Sample size calculation

To test a mean difference in 0.5 mm marginal bone level between ultrasound and direct readings, with 50% standard deviation and 80% power, 5% significant level, 16 implants were required.

Seven fresh cadaveric heads from four males and three females (mean age: 82.0 ± 11.7 years) donated to the University of Michigan for educational and research purposes were used. The specimens were kept frozen at -20°C and thawed at the initiation of the experiment. A total number of 17 implants were studied, of which 13 (3.7×13 mm TSV, Zimmer) were placed via a flapless approach during this experiment and 4 were already present in one cadaver head. Of the 13 implants, seven were placed using a computer-generated guide and the other six were placed free hand. For fabricating the surgical guides, presurgical CBCT

scans and digital scanning of cast models acquired from alginate impressions were obtained. With an open-source software package (Blue Sky Bio, Grayslake, IL), CBCT and model images were merged using existing teeth as references. The surgical guides were designed based on virtual implant locations on the merged images and 3-D printed. The implant locations were planned in three dimensions following the prosthetic-driven concept. In a specific manner, the vertical implant position was planned so that the smooth-rough surface junction was at the crestal bone level. Implants were placed following manufacturer instructions. Postsurgical CBCT scans were performed for peri-implant tissue dimension measurements. The remaining four implants in one cadaver specimen had been in function and splinted by a metal bar for supporting a mandibular removable overdenture. Therefore, only one CBCT scan was taken for that specimen. CBCT images were acquired by a scanner (3D Accuitomo 170, JMorita, Japan), with scanning parameters of 120 kVp, 18.66 mAs, scan time of 20 s, and resolution of 80 μm . A plastic cheek retractor and cotton rolls were used to separate facial mucosae from gingiva/alveolar mucosae. The captured CBCT scans were three-dimensionally reconstructed with the built-in software, saved in Digital Imaging and Communications in Medicine (DICOM) format.

2.1.2 | Ultrasound scanning and measures

The scanning set-up and procedures were performed by two examiners (HC and OK) based on methods previously described (Chan, Sinjab, et al., 2017; Chan, Wang, et al., 2017). A built-in function of spatial compounding was selected to obtain well-resolved bone and implant edges (ZS3 Zonare/Mindray, USA). Acoustic coupling was achieved with the application of ultrasound gel (Aquasonic, Parker Inc., PA, USA) and the use of a gel-based stand-off-pad (Parker Inc.). Each implant was scanned at 3 sites, the mesio- and disto-facial line angles and the mid-facial site, with the ultrasound probe (25-MHz) placed in line with the long axis of the implant. Once the implant surface was identified, the probe was slightly rotated in a range of few degrees along its long axis until the maximal implant surface and adjacent hard and soft tissue structures were clearly identified. The implants were displayed on ultrasound images as a bright white line, with hyperechoic veils behind the line because of the internal acoustic reverberation. The veils were used as a useful feature for identifying implants. Consecutive 2D cross-sectional images generated during the course of probe movements were saved as cineloops in DICOM format for each site to assist image interpretation.

Ultrasound images were read with a commercially available software package (Osirix, Bernex, Switzerland) on a 27" display desktop computer. On the representative ultrasound image, four parameters were measured by one calibrated examiner (HC) at each site of an implant with a built-in caliper accurate to 0.01 mm. Intraexaminer calibrations were performed through measuring all parameters on one randomly selected implant repeatedly, with 1 day apart, to achieve an agreement of at least 0.8. Hard tissue measures included: (a) marginal

bone level, that is, the vertical distance between the implant platform and the marginal bone crest, and (b) marginal bone thickness, that is, the horizontal distance between the outer surface of the bone crest and the implant surface 1 mm from the bone crest. Soft tissue measures included: (a) mucosal level, that is, the vertical distance from the mucosal margin to the marginal bone and (b) mucosal thickness, that is, the horizontal distance from the mucosal surface to the bone surface, measured at 5 mm from the mucosal margin. Corresponding hard tissue measurements were performed by one calibrated examiner (KS) from CBCT images with a commercially available implant planning software (Invivo5, Anatomage Dental, San Jose, CA, USA). Intraexaminer calibrations were conducted and an agreement of >0.8 was achieved before measuring the full set of data.

The calibrated examiner (HC) made direct measurements of marginal bone level/thickness and soft tissue height with a calibrated periodontal probe (University of North Carolina [UNC] Probe, Hu-Friedy, Chicago, IL, USA) accurate to the nearest 1 mm. This was conducted after intraexaminer calibration achieved an agreement of >0.8 . Soft tissue thickness was measured by penetrating a #30 endo file into the mucosa at the corresponding sites until bone resistance was felt. The distance from the tip of the file to the rubber stop represented the mucosal thickness and measured by a metric digital caliper accurate to 0.01 mm.

2.2 | Statistical analysis

The means and standard deviations of ultrasound, radiographic and direct measurements were calculated. The correlations and agreement between measurements of the three methods were evaluated with the Pearson's correlation coefficient test and the Bland-Altman analysis. The significant level was set at $p = 0.05$ for all statistical analysis.

3 | RESULTS

Peri-implant tissue dimensions of 17 implants were measured with the three methods on seven cadaverous specimens. The implants were located in the mandibular anterior region ($N = 6$), mandibular premolar region ($N = 5$), maxillary anterior region ($N = 5$) and maxillary premolar region ($N = 1$). The locations were based on the anatomical availability for placing implants. The landmarks, including the implant surface, marginal bone, mucosal margin, bone and mucosal surface were identified and demarcated (Figure 1). The mean hard and soft tissue measures from each method were summarized in Table 1. The mean ultrasound, CBCT and direct marginal bone level readings were 2.58 ± 1.74 , 2.82 ± 2.24 and 2.62 ± 1.78 mm. The corresponding mean marginal bone thickness was 0.93 ± 0.81 , 1.19 ± 0.75 and 0.96 ± 0.85 mm. The mean ultrasound and direct mucosal level were 2.04 ± 1.41 and 2.03 ± 1.42 mm. The mean mucosal thickness was 1.17 ± 0.53 and 1.29 ± 0.62 mm, respectively. The correlations of the four parameters among the three methods were summarized in Figure 2. High correlations were

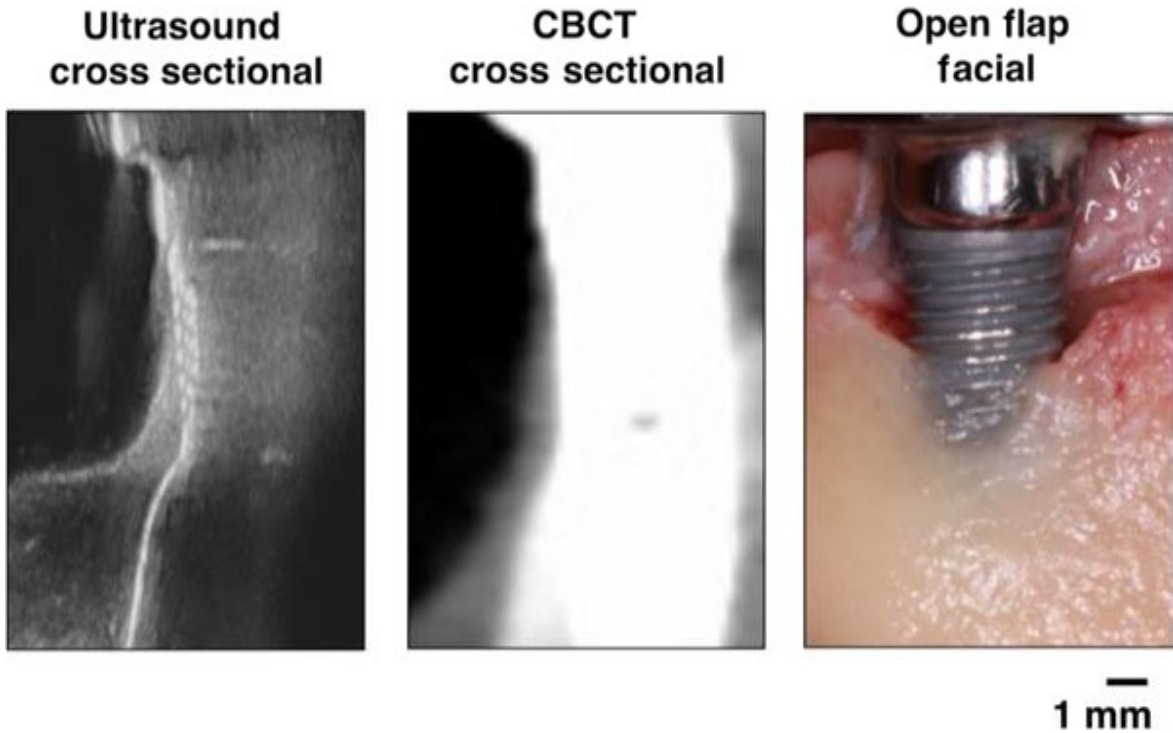


FIGURE 1 A representative cross-sectional ultrasound image of an implant on a human cadaver, in comparison with cone beam computed tomography (CBCT) and open-flap images. On the ultrasound image, the implant and bone surface, and the soft tissue can be clearly delineated. Note that ultrasound can show implant threads; CBCT image quality is affected by artefacts from implants

TABLE 1 Comparisons of the mean (SD) peri-implant hard and soft tissue dimensions among three methods, ultrasound, direct and cone beam computed tomography (CBCT)

Parameters	Site	Ultrasound (mm)		Direct (mm)		CBCT (mm)	
		Mean	SD	Mean	SD	Mean	SD
Marginal bone level	Mesial	2.62	1.75	2.66	1.77	2.82	2.32
	Mid	2.82	1.91	2.90	2.02	3.03	2.45
	Distal	2.32	1.62	2.30	1.59	2.62	2.04
	Overall	2.58	1.74	2.62	1.78	2.82	2.24
Marginal bone thickness	Mesial	0.84	0.72	0.96	0.91	1.28	0.89
	Mid	0.83	0.57	0.83	0.74	1.00	0.54
	Distal	1.11	1.11	1.09	0.95	1.30	0.83
	Overall	0.93	0.81	0.96	0.85	1.19	0.75
Mucosal level	Mesial	2.07	1.33	1.90	1.12	NA	
	Mid	2.23	1.80	2.45	1.84		
	Distal	1.82	1.14	1.74	1.23		
	Overall	2.04	1.41	2.03	1.42		
Mucosal thickness	Mesial	1.25	0.58	1.40	0.78		
	Mid	1.13	0.47	1.18	0.51		
	Distal	1.12	0.59	1.29	0.58		
	Overall	1.17	0.53	1.29	0.62		

Note. NA, not applicable.

found for bone margin level readings between ultrasound and direct methods ($r = 0.98, p < 0.0001$), between ultrasound and CBCT methods ($r = 0.85, p < 0.0001$), and between direct and CBCT methods ($r = 0.84, p < 0.0001$). A high correlation was also found

for bone thickness measurements obtained between ultrasound and direct ($r = 0.92, p < 0.0001$), between ultrasound and CBCT ($r = 0.91, p < 0.0001$), and between direct and CBCT methods ($r = 0.89, p < 0.0001$). Ultrasound and direct mucosal tissue height

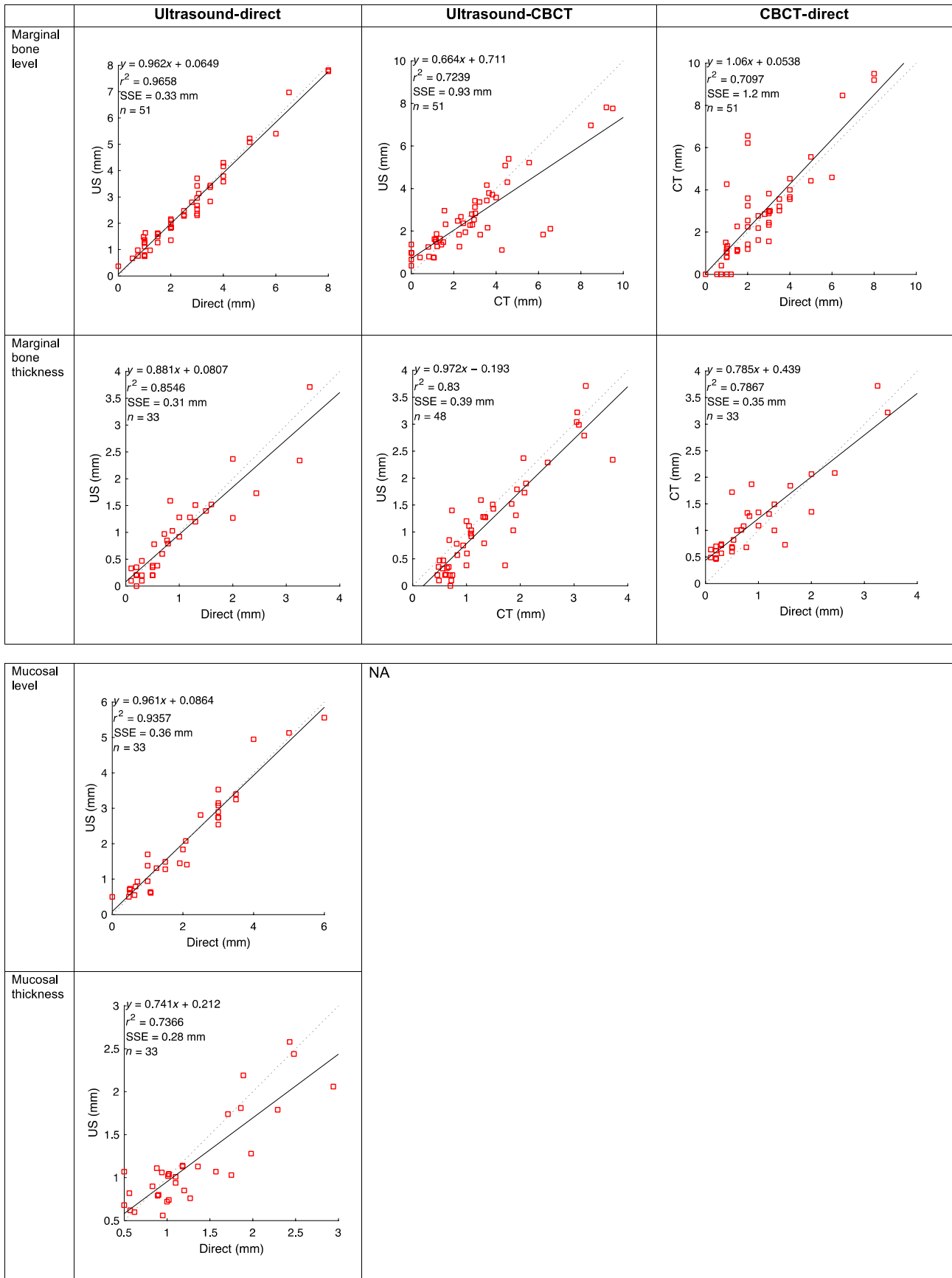


FIGURE 2 Correlations of the peri-implant hard and soft tissue dimensions among the three methods, ultrasound, direct and cone beam computed tomography

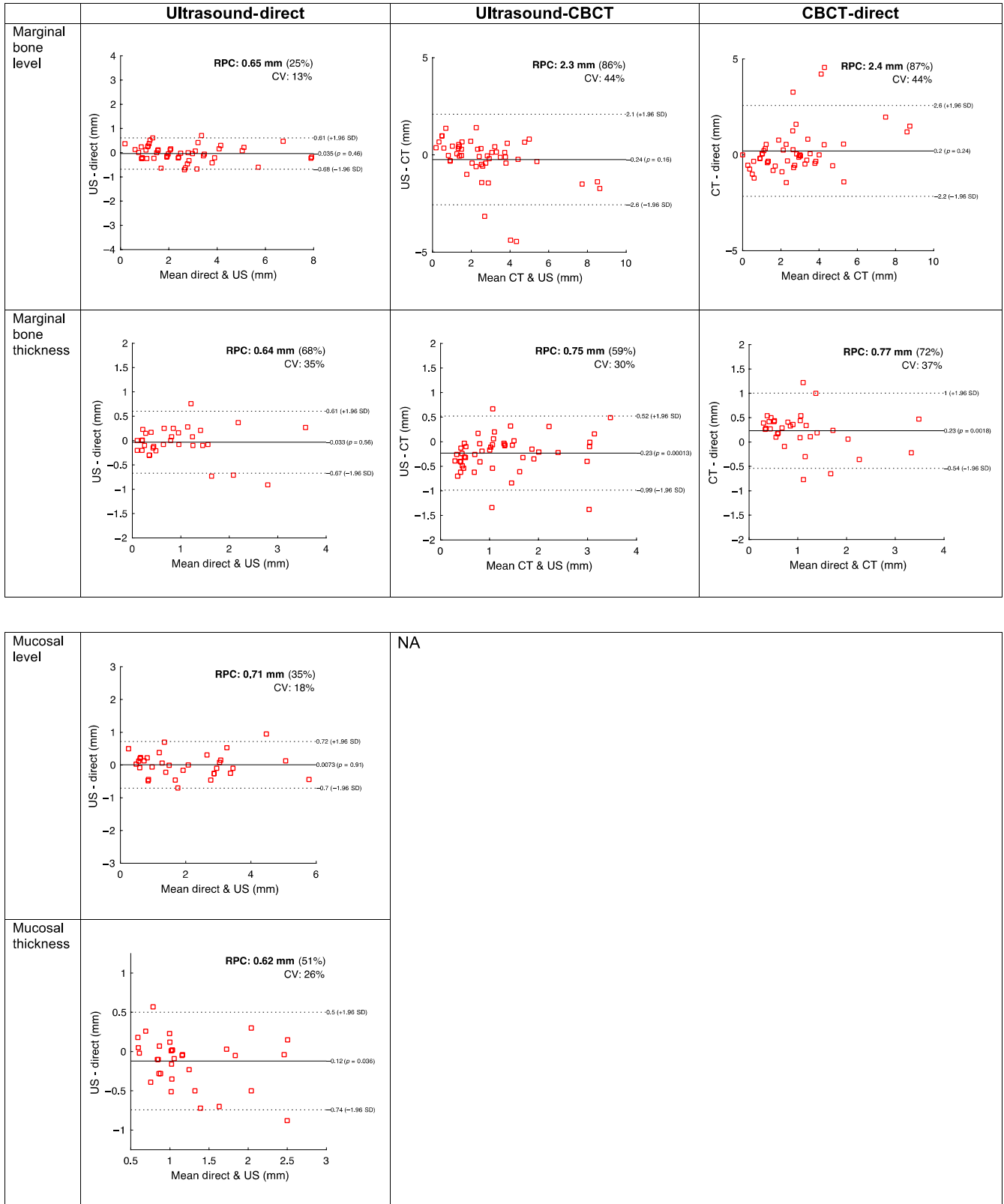


FIGURE 3 Results of Bland–Altman Plots for the peri-implant hard and soft tissue dimensions among the three methods, ultrasound, direct and cone beam computed tomography

and thickness were significantly correlated ($r = 0.97$ and 0.86 , respectively, $p < 0.0001$). Results of the Bland–Altman plots were summarized in Figure 3. The mean absolute difference (95% CI) in marginal bone level between ultrasound and direct, ultrasound and CBCT, CBCT and direct methods was 0.035 mm (-0.68 to 0.61 mm, $p = 0.46$), 0.24 mm (-2.60 to 2.10 mm, $p = 0.16$) and 0.20 mm (-2.20 to 2.60 mm, $p = 0.24$), respectively. The mean absolute difference (95% CI) in marginal bone thickness between ultrasound and direct, ultrasound and CBCT, CBCT and direct methods was 0.033 mm (-0.67 to 0.61 mm, $p = 0.56$), 0.23 mm (-0.99 to 0.52 mm, $p < 0.05$) and 0.23 mm (-0.54 to 1.00 mm, $p < 0.05$), respectively. The mean absolute difference (95% CI) in soft tissue height and soft tissue thickness between ultrasound and direct methods were 0.0073 mm (-0.70 to 0.72 mm, $p = 0.91$) and 0.12 mm (-0.74 to 0.5 mm, $p = 0.036$), respectively.

4 | DISCUSSION

Ultrasound was proposed to measure periodontal soft and hard tissue dimensions as early as in the seventies because of being nonionizing, real-time and cost-effective (Ghorayeb, Bertoncini, & Hinders, 2008). Earlier studies failed to show accuracy due to inferior image resolution. Technological advances have allowed us to construct an intraoral, high-resolution (25 MHz) device that provides high-resolution images with the size similar to a toothbrush. For the first time, this study demonstrates unprecedented ultrasound images of peri-implant hard and soft tissues that were compared with CBCT images and direct measures. One relevant study used 12.5-MHz ultrasound probe to image the amount of implant thread exposure (Bertram & Emshoff, 2008). Another study (Salmon & Le Denmat, 2012) showed images of peri-implant tissues in a case report using a prototype system. The results of the current investigation demonstrated that ultrasound readings are highly correlated and agreed with direct and radiographic readings. With clinical validation, it can be a useful tool to evaluate and monitor peri-implant tissue dimensions and changes.

Tissue biotype is considered an important determinant for outcomes of bone regenerative procedures (Chao, Chang, Fu, Wang, & Chan, 2015), and implant therapy (De Bruyckere et al., 2015; Fu et al., 2011; Lin, Chan, Bashutski, Oh, & Wang, 2014), etc. Several methods have been developed to evaluate soft tissue biotype, for example, visual, probing and direct methods (De Rouck, Eghbali, Collys, De Bruyn, & Cosyn, 2009; Kan et al., 2010). While visual examination is not a reliable method, the probing method is claimed clinically acceptable (predictive value = 70% and 83% for thick and thin tissues, respectively) (Kan et al., 2010). However, when the gingival thickness is between 0.6 and 1.2 mm, the probing method is unreliable for differentiating tissue biotype. Ultrasound is an excellent tool for soft tissue evaluation and has been validated to measure periodontal soft tissue thickness (Eghbali, De Bruyn, Cosyn, Kerckaert, & Van Hoof, 2014; Muller & Kononen, 2005; Muller et al., 2007). This outcome from our study suggests that ultrasound can be an objective and noninvasive method to evaluate peri-implant soft tissue biotype.

As for hard tissue determination, CBCT has long been used to evaluate facial alveolar bone dimensions. Its accuracy and reliability were studied using cadaveric specimens (Timock et al., 2011). However, because of resolution limits, CBCT could not differentiate thin facial bone. Most facial bone is <1 mm in thickness in the maxillary anterior region (Braut, Bornstein, Belser, & Buser, 2011) (Frost, Mealey, Jones, & Huynh-Ba, 2015; Vera et al., 2012; Wang et al., 2014). In addition, the presence of metal implants interferes with image interpretation (Ritter et al., 2014). At present, peri-implant bone level is primarily evaluated on 2-D intraoral radiographs (2013; Sanz & Chapple, 2012, Tyndall et al., 2012). However, 2D radiography only shows superimposed interproximal bone level. The radicular (facial and palatal/lingual) bone level and thickness cannot be seen on this imaging modality. Facial bone loss is inevitable and often it is more susceptible to resorption than interproximal bone. A recent study (Veltri, Ekestubbe, Abrahamsson, & Wennstrom, 2016) with 12 healthy implants concluded that the facial bone level was located 3.8 mm apical of the implant shoulder, and none of the implants displayed complete facial bone coverage. In another study (Kehl et al., 2011) that longitudinally followed 119 implants for 5–15 years, it was found that the mean facial bone loss (3.57 and 4.49 mm for two subgroups) is significantly more prominent than that in the remaining sites (2.49 and 3.00 mm). Another study (Serino et al., 2013) showed that 34% of implants experienced irregular bone loss, with more resorption at the facial site. From these studies, it becomes clear that facial bone loss follows a distinct pattern as compared to interproximal bone and should be monitored separately. Evaluating bone loss with 2D radiographs is inadequate. Ultrasound can complement radiographs for measuring facial bone dimensions at the crestal bone level. Therefore, the developed ultrasonography may add values to diagnose and characterize peri-implant bone loss and assist in treatment decision-makings.

The severity of marginal bone loss might influence ultrasound accuracy. Ultrasound achieved poorer accuracy (the intraclass correlation coefficient, ICC, with direct measures is 0.63) in cases with advanced bone loss (>6 mm) than those with normal (ICC = 0.72) or moderate (ICC = 0.76) bone loss. In the current study, the range of marginal bone level is from 0.8 to 7.7 mm. Limitations of using ultrasonography include (a) image quality is operator dependent, (b) the need of using a coupling medium, (c) only bone surface can be imaged with the currently used high frequency but not the intrabony structures, and (d) the bone thickness can only be measured close to the first bone-implant junction.

We demonstrate in this proof-of-concept study that high-resolution ultrasound can image human peri-implant tissues. For further validation, the next step is to image patients with varying severity of peri-implantitis in a larger sample size. Although anatomical imaging is adequate for measuring tissue dimensions of interest, it requires functional imaging to detect disease activity. Photoacoustic imaging, an emerging ultrasound-based modality, could be useful in differentiating changes in active blood vessels, ratio of oxygenated/deoxygenated haemoglobin and overall blood volume in peri-implant tissues. This new imaging modality could evaluate disease activity and deserves future research.

5 | CONCLUSIONS

Noninvasive, three-dimensional and high-resolution ultrasound was validated to evaluate peri-implant tissue dimensions in a human cadaver model. Ultrasound readings of peri-implant hard and soft tissue level and thickness were highly correlated with CBCT and especially with direct measurements. The ultrasound measurement differences, compared to the direct measures, range from 0.62 to 0.71 mm with 95% confidence for these four parameters. Once validated by large-scale clinical trials, it could become a valuable method to evaluate peri-implant tissue biotype and peri-implant diseases.

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CONFLICT OF INTEREST

The authors do not have any financial interests, either directly or indirectly, in the products or information listed in the paper.

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