Ultrasonography for Chairside Evaluation of Periodontal Structures: A Pilot Study

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Contribution statement:

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Abstract

Background: The crestal bone level and soft tissue dimension are essential for periodontal diagnosis and phenotype determination; yet existing measurement methods have limitations. The aim of this clinical study was to evaluate the correlation and accuracy of ultrasound (US) in measuring periodontal dimensions, compared to direct clinical and cone-beam computed tomography (CBCT) methods.

Methods: A 24-MHz US probe prototype, specifically designed for intraoral use, was employed. Periodontal soft tissue dimensions and crestal bone levels were measured at 40 teeth and 20 single missing tooth gaps from 20 patients scheduled to receive a dental implant surgery. The US images were interpreted by 2 calibrated examiners. Inter-rater agreement was calculated by using inter-rater correlation coefficient (ICC). US readings were compared to direct clinical and CBCT readings by using ICC and Bland-Altman analysis.

Results: The following six parameters were measured: (1) interdental papilla height (tooth), (2) mid-facial soft tissue height (tooth), (3) mucosal thickness (tooth), (4) soft tissue height (edentulous ridge) (5) mucosal thickness (edentulous ridge), and (6) crestal bone level (tooth). Intra-examiner calibrations were exercised to achieve an agreement of at least 0.8. ICC between the two readers ranged from 0.482 to 0.881. ICC between US and direct readings ranged from 0.667 to 0.957. The mean difference in mucosal thickness (tooth) between the US and direct readings was -0.015 mm (95% CI: -0.655 to 0.624 mm) without statistical significance. ICC between US and CBCT ranged from 0.654 to 0.849 among the measured parameters. The mean differences between US and CBCT range from -0.213 to 0.455 mm, without statistical significance.

Conclusion: Ultrasonic imaging can be valuable for accurate and real-time periodontal diagnosis without concerns about ionizing radiation.

Introduction

Ultrasound (US) was proposed to image periodontal soft and hard tissues in as early as the 1970's, owing to its non-ionizing, real-time, and cost-effective properties.[1] It functions by transmitting sound waves from the US probe through a medium, and recording time-dependent reflections from tissue structures (object). On the basis of the travel time and the speed of sound, the distance between the probe and the object can then be determined. Primarily designed for soft tissue evaluation, US was validated for measuring soft tissue thickness in various anatomical locations of the oral cavity.[2-6] However, a single element US device was used in these studies, meaning that only values of soft tissue thickness were derived, as opposed to images. Efforts have also been made to design an ultrasonic device to identify periodontal attachment level.[7] This device has a probe that directs sound waves

into pockets with water for coupling. A computer algorithm could then identify the junction of the periodontal ligament and gingival connective tissue due to the impedance difference between the two structures. A recent study[8] applied US in the measurement of facial soft tissue thickness changes around implants following connective tissue graft procedures. Two studies demonstrated accurate periodontal images using a one-dimensional US array.[9, 10] As for periodontal hard tissue evaluation, an ophthalmetric US device was previously used to define alveolar bone topography intraorally in four participants.[11] Low image resolution unfortunately resulted in inaccurate alveolar bone measures. On the other hand, higher frequency, i.e. higher image resolution, US probes showed promising outcomes in cadaverous porcine models.[12-15] A human cadaver study[16] reconstructed 3-dimensional jawbone surface image for the diagnosis of periodontal bony defects and a recent study of our group presented proof-of-principle, that US can image oral structures, including periodontal hard and soft structures on a human cadaver.[17] Another study demonstrated accurate US readings of alveolar bone height and thickness with cadaverous human specimens.[18] In this study, a probe for general purposes (center frequency of 14 MHz) was used. The mean absolute differences of US measures from direct measures and cone-beam computed tomography (CBCT) radiographic measures are within 0.1 mm. A recent meta-analysis provides preliminary evidence to support US for measuring alveolar bone level.[19] By collaborating with an US scanner manufacturer, a prototype dental US probe was made. Satisfactory accuracy was demonstrated by using this prototype to measure peri-implant tissue dimensions on human cadavers.[20] The mean absolute differences between US and direct/CBCT measurements range from 0.033 to 0.24 mm. For the first time, we validated in human participants this dental US prototype for assessing periodontal structures. The primary aim is to compare US soft and hard periodontal and edentulous ridge tissue dimensions to direct and CBCT measurements.

Materials and Methods

Recruitment

This study was approved by the University of Michigan Institutional Review Board (Study ID: HUM00099062) and was conducted in accordance with the Helsinki Declaration of 1975, as revised in 2013. It was registered at ClinicalTrials.gov (Study ID: NCT03657589). All patients signed an informed written consent to participate in the study. A sample of 20 participants scheduled for a single implant surgery, at the University of Michigan School of Dentistry, Department of Periodontics and Oral Medicine, were recruited for this pilot study. The participants were deemed eligible if they had a maxillary or mandibular single edentulous area at the anterior or premolar site with two immediately adjacent teeth on both sides available. The sites of interest in each individual patient were the mesial and distal tooth, in addition to the edentulous site for an implant placement.

Quantitative Data Acquisition

The following 6 parameters were measured and compared (Figure 1):

(1) **Interdental papilla height (PH)**: the vertical distance from the tip of the facial papilla to the crestal bone on the mesial and distal papillae of a given tooth.

(2) **Mid-facial soft tissue height at teeth (STHt)**: the vertical distance from the free gingival margin to the crestal bone at the mid-facial site of a given tooth.

(3) **Mucosal thickness at teeth (MTt)**: the horizontal distance between the mucosal surface to the underlying bone or root surface measured at 2 and 5 mm from the gingival margin at mid-facial sites.

(4) **The crestal bone level (CBL) at teeth**: the vertical distance between the alveolar crest and the cemento-enamel junction (CEJ) or the restoration margin on the mid-facial site of the imaged tooth.

(5) **Soft tissue height at the edentulous ridge (STHe)**: the vertical distance from the external border of the cortical bone to the most superficial level of the crestal soft tissue in the center of the gap.

(6) **Mucosal thickness at the edentulous ridge (MTe)**: the horizontal distance between the mucosal surface to the underlying bone surface, measured at 3 and 6 mm from the mucosal margin at mid-facial and mid-palatal sites.

CBCT Scans

CBCT scans were acquired for participants who did not have a clinically ordered scan for the planned implant surgeries. The CBCT scans were used to acquire crestal bone levels and soft tissue-related parameters as an additional reference for comparison to US readings. All scans, regardless of being clinical or research-related, were obtained using a CBCT device[#], with scanning parameters of 120 kVp, 18.66 mAs, scan time of 20 seconds, and resolution of 250 µm. The captured CBCT scans were reconstructed in 3D using the built-in software, saved in DICOM format, and subsequently exported into commercially available implant-planning software[**] for measurements by 2 calibrated examiners (MT and KS).

US Scans

The US scan was a separate visit usually within 2 weeks before the implant surgery date when direct measurements were made. A single examiner (HC) performed the US scanning procedure using the 24 MHz imaging probe prototype, while a second examiner (OK) specialized in US imaging operated the US scanner[††].

The scanning set-up and procedure has been described in previous publications.[17, 18] Briefly, the probe prototype dimension is comparable to that of a toothbrush and its cable runs

perpendicular to the aperture, allowing for cross-sectional scans to the 2nd molars. The maximal transducer thickness, width and length is 15, 16.2 and 30 mm. Its axial and lateral image resolution is 64 and 192 μm, respectively, with an optimal penetration depth of 15 mm, and in real-time image acquisition. To enhance image resolution of bone and tooth edges, a built-in function for spatial compounding was selected. Acoustic coupling was achieved with mounting a gel-based stand-off-pad‡‡ to the probe aperture and applying US gel between the pad and the oral structures. The mesial and distal teeth adjacent to the edentulous gap in each participant were scanned at the mesial and distal papillae and mid-facial surface with the transducer placed approximately in line with the long axis of the particular tooth (Figure 2). The included edentulous gaps were scanned at the mid-facial and mid-lingual surfaces. The participants wore a customized acrylic reference guide during the US scans. The same guide was used during the CBCT scan and direct measurements to minimize measurement site variability among the three methods. Several US scans with minute differences in the facio-lingual scan plane in relation to the teeth were acquired to capture the anatomical structures needed for linear tissue quantification and saved in Digital Imaging and Communications in Medicine (DICOM). US readings were performed in millimeters via commercially available software§§ with a built-in caliper accurate to 0.01 mm by two independent, calibrated investigators (MT and KS).

At the implant placement visit, prior to elevating a full thickness flap, the papilla and mucosal height of teeth and mucosal thickness at the dentate and edentulous sites were measured by a calibrated examiner (HC). Soft tissues in situ before flap elevation facilitated easier and more accurate measurements. Interdental papilla height and facial mucosal height around teeth were measured with a calibrated periodontal probe‖‖ to the closest 0.5 mm. Both parameters were measured from the respective soft tissue margin to the crestal bone. After facial flap elevation, the remaining measurements (i.e. the mucosal height at the edentulous gap and crestal bone level) were made with the same periodontal probe.

To clinically measure mucosal thickness, a #25 endodontic file was penetrated into the mucosa at the corresponding sites until bone/tooth root resistance was detected, during which the rubber stop was positioned in contact with the mucosal surface. The file was inserted perpendicular to the mucosal surface. The distance between the tip of the file to the rubber stop (i.e. the mucosal thickness) was measured using a metric digital caliper, precision to 0.01 mm.

Intra-examiner and inter-examiner calibration

The two readers (MT and KS) for US and CBCT images were first calibrated with the gold standard reader (HC) using two randomly selected cases in one day delay, to allow for memory washout, until an agreement of at least 0.8 was achieved.[21] Subsequently, intra-examiner calibration of the US and CBCT readings were performed in the same way. Intra-examiner calibration of direct measurements was performed in a previous study, with an agreement of 0.8.[20]

Data Analysis

A masked biostatistician (EL) performed statistical analysis. The inter-rater correlation coefficients (ICC), root mean square error (RMSE) and maximum differences were calculated to evaluate the strength of agreement between US measurements from both readers. The pairwise agreement between the direct, US and CBCT measurements were also assessed by ICC.[22] Because 6 hypotheses were tested to examine whether or not the agreement is strong enough for the 6 parameters listed above, Bonferroni corrections were used to adjust the significance level as 0.0083 (=0.05/6). F-tests were employed to examine if the p-values of the ICC were significantly greater than 0. The ICC ranges from -1 to 1, where an estimate of 1 indicates perfect agreement and 0 means random agreement. Negative ICCs indicate a systematic disagreement. Commonly-cited cutoffs are poor for ICC values less than .40, fair for values between .40 and .59, good for values between .60 and .74, and excellent for values between .75 and 1.0.[21] Bland-Altman plots were also created to

evaluate the differences between US, direct measurements, and CBCT readings[23] and clinical significance. All statistical analyses were conducted using statistical software[¶¶].

Results

Descriptive Analysis

A total of 20 participants (15 male and 5 female), with a mean age of 61.2 ± 13.4 years were included in this study. The study sample accounted for 40 teeth (anterior teeth (27) and posterior teeth (13) sites) and 20 edentulous ridges (anterior (16) and premolar (4)). Of these sites, 51 sites were in the maxilla (34 tooth sites and 17 edentulous sites), while 9 were in the mandible (6 tooth sites and 3 edentulous sites).

Inter-rater agreement

Table 1 summarizes the inter-rater agreements on US measurements. US measurements of PH, STHt, MTt, MTe and CBL had excellent agreement (ICC=0.78 to 0.88), except for STHe with fair agreement (ICC=0.48). Excellent agreement was demonstrated for CBCT derived CBL measurements, (ICC=0.97). Dual-investigator measurements were averaged for further analysis (US and CBCT).

Pairwise *correlation between US, direct and CBCT readings*

US soft tissue measurements demonstrated good agreement with direct measurements of STHe and MTt (ICC=0.667 and 0.707, respectively), and excellent agreement for the remaining parameters (ICC=0.829 to 0.918) (Figure 3). Excellent agreement was observed for both US and CBCT with direct CBL measurement (ICC= 0.957 and 0.798, respectively). When US soft tissue parameters were compared with CBCT, the resulting ICC values demonstrated good to excellent agreement (0.654 to 0.849) (Table 2). The RMSEs and maximum differences between US and direct measurements were reported in

supplementary Table S1 in online *Journal of Periodontology*. The RMSEs range from 0.324 to 0.656 mm for the measured parameters except for soft tissue height at the edentulous ridge (0.933 mm). The average maximum differences show a similar pattern with values from the edentulous ridge being the greatest.

Bias and variability of US relative to direct and CBCT readings

The mean differences and limits of agreement generated by the Bland-Altman plots were used to depict the clinical significance of the US measurements (Table 2). In each plot of Figure 4, the blue solid line represents the mean differences between the US and direct measurements, while the red dotted lines show the upper and lower 95% limits of agreement. Supplementary Figures S1 and S2 in online *Journal of Periodontology* illustrate the direct/CBCT and US/CBCT comparisons, respectively. Among the 5 soft tissue parameters, the smallest difference between US and direct readings is 0.015 mm, found in the MTt measurements; whereas the largest mean difference is 0.48 mm for STHe measures. Similarly, the differences between US and CBCT soft tissue measurements were 0.213 (MTt), 0.351 (PH) and 0.455 (STHt) mm. The mean difference in CBL for US/direct and US/CBCT is 0.078 and 0.412 mm, respectively. All the 6 US parameters are not significantly different from the direct and CBCT readings ($p>0.05$), suggesting there are no systematic deviations.

Discussion

US accuracy relative to established methods

This study is among the first, to the authors' best knowledge, to image periodontal tissues on live humans with US.[9, 10] The measurement accuracy generated by US imaging is categorized into two broad categories: soft tissue and hard tissue dimensions. For soft tissue dimensions, direct clinical measurements were considered the gold standard. Good to excellent correlations (0.657 to 0.918) of US soft tissue measures to the direct measures were obtained. Additionally, the mean differences of direct versus US soft tissue

measurements range from -0.015 to -0.159 mm, with an exception of soft tissue height at the edentulous sites, which is 0.479 mm. The limits of agreement (95% CI) between US and direct interdental papilla height and mid-facial soft tissue height is -0.991 to 0.840 mm and -0.942 to 0.623 mm. The limits of agreement between US and direct mucosal thickness at teeth is -0.655 to 0.624 mm. The results are in general consistent with a recent human cadaver study.[24] Overall the results suggest that US assessing periodontal soft tissue dimensions agrees with direct measurements. Variability between US and direct soft tissue dimension measures at edentulous ridge is greater, with the limits of agreement between 1 to 2 mm. The primary reason for inconsistent soft tissue height measures at the edentulous sites is believed to be associated with the uneven ridge bone contour due to the use of bone allografts for ridge preservation in these cases. For hard tissue delineation, US measured crestal bone level was found to be highly correlated with direct measures. We also noticed that, US may differentiate thin alveolar bone better than CBCT. In approximately one third of the cases, CBCT is unable to locate the crestal bone level due to either a thin buccal plate or due to artifacts from metallic restoration materials (Table 1). These findings are in accordance with the results of our previous study.[18] Inter-examiner agreements were between fair (ICC=0.482 for soft tissue height at edentulous ridge) and excellent (ICC ranges between 0.77 and 0.88 for the rest parameters) for US readings, possibly indicating a learning curve for this new dental imaging modality.

Clinical significance

Alveolar bone loss is the hallmark of periodontal disease. Microbial dysbiosis in the periodontium elicits an inflammatory response, resulting in a reduction of collagen and mineral content within the alveolar bone, and eventually manifests as bone loss on radiographs. In a healthy periodontium, crestal bone level is on average 1-2 mm below the CEJ. When the reading is greater than this average, alveolar bone loss is suspected. Intra-

oral radiographs only provide superimposed interproximal bone levels. The consequence is that periodontal destruction in the facial and palatal/lingual sites may be undiagnosed, especially in the molar regions with furcation involvement. Similarly, when using the free gingival margin as a reference, crestal bone level is located at 3-4 mm below the margin in a healthy periodontium. This dimension is composed of clinical probing depth, junctional epithelium, and connective tissue attachment. When the reading is beyond this normal range, periodontal tissue loss or gingival overgrowth is suspected. Therefore, the combined US crestal bone level readings using both the free gingival margin and a fixed reference point (i.e., CEJ) could provide value in the diagnosis of periodontal disease. Current scan times are 1 minute/tooth; in the future, an automated probe positioning system could be developed to aim for full mouth scanning in 5 minutes. This way, it can provide a high-throughput screening of periodontal patients during the initial visit and follow-up visits as well. A series of standard full-mouth US scans then can be superimposed in a clinical setting, and the difference in bone levels compared for evaluating periodontal disease activity. The acceptance of this new technology by clinicians for use in a clinical setting will heavily depend on cost-benefit considerations, easiness of use, and if US scanning can be a reimbursable procedure, etc. Training acceptance is anticipated to be high. For this study, readers were calibrated within 2 weeks. This included machine (US scanner) use, scanning, and image interpretation. Image interpretation time is less than 1 minute/per image.

In addition to diagnosing periodontal disease, US could be used to evaluate periodontal tissue phenotype. Tissue phenotype is considered an important determinant of clinical outcomes following periodontal disease treatment[25-27,28], bone regenerative procedures[29] and implant therapy[8, 30-32]. Various methods have been developed to evaluate soft tissue type, including both visual and probing methods.[33, 34] US is an excellent tool for soft tissue evaluation and has been reportedly validated in the measurement of periodontal soft tissue

thickness.[2, 3, 24] Regarding hard tissue phenotype, the accuracy and reliability of CBCT has been studied using cadaveric specimens.[35] However, due to resolution limitations, CBCT cannot differentiate thin facial bone, where most facial bone exhibits a thickness of less than 1 mm in the maxillary anterior region.[36 37-39] The current prototype has an axial resolution of 64 μm, which is superior to 250-500 μm that commercially available CBCT machines can provide; therefore, US can complement radiographs in the measurement of facial bone thickness.[18] However, US can only measure bone thickness at the alveolar crest due to US attenuation at the bone surface.

All participants in this study are either periodontally healthy or stable. Therefore, neither deep pockets nor irregular bony destruction (e.g., infrabony defects) are present in this cohort. The current device can reliably imagine up to 15 mm of the depth. To further validate US for evaluating periodontal tissues, patients with varying degrees of periodontal disease severity need to be imaged. In those patients, the scanning angle may need to be adjusted to a straighter angle towards the periodontal pockets, in order for bony irregularities to be incorporated within the image. Additionally, anatomical imaging is only suitable for measuring tissue dimensions of interest; functional imaging is required to detect biological activity, e.g. estimation of the blood flow. US is capable of estimating the blood flow velocity and the amount of blood flow.[40] Therefore, US may be able to differentiate healthy from the inflamed tissue, in which microvasculature homeostasis is disrupted.[41] In addition, a new US-based imaging modality, photoacoustic imaging, may be useful in the fluctuation of minute changes in ratio of oxygenated/deoxygenated hemoglobin in periodontal tissues as a result of the presence of disease.[42, 43] Future research should focus on using photoacoustic imaging to evaluate disease activity, in order to allow for early intervention to be implemented for the purpose of minimizing tissue damage and maximizing treatment outcomes.

Conclusion

With encouraging 1st time human data displaying satisfactory measurements of periodontal soft and hard tissue dimensions, US imaging could become a valuable tool for real-time, cross-sectional evaluation of the periodontia without concerns of ionizing radiation and metallic artifacts. Future research should focus on the ability of US to differentiate periodontal disease from healthy status.

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Footnotes

3D Accuitomo 170, JMorita, Tokyo, Japan

** Invivo5, Anatomage Dental, San Jose, CA, USA

†† ZS3, Zonare/Mindray, Mountain View CA, USA

‡‡ Aquasonic, Parker Inc., PA, USA

§§ Osirix, Bernex, Switzerland

ǁǁ University of North Carolina (UNC) Probe, Hu-Friedy, Chicago, IL, USA

¶¶ R version 3.2.2, The R Foundation for Statistical Computing, Vienna, Austria

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Figures:

Figure 1. Illustrations depicting the parameters described in the methodology, including Interdental Papilla Height (PH), Crestal Bone Level (CBL), Mucosal Thickness at Teeth (MTt), Soft Tissue Height at the Edentulous Ridge (STHe) and Mucosal Thickness at the Edentulous Ridge (MTe).

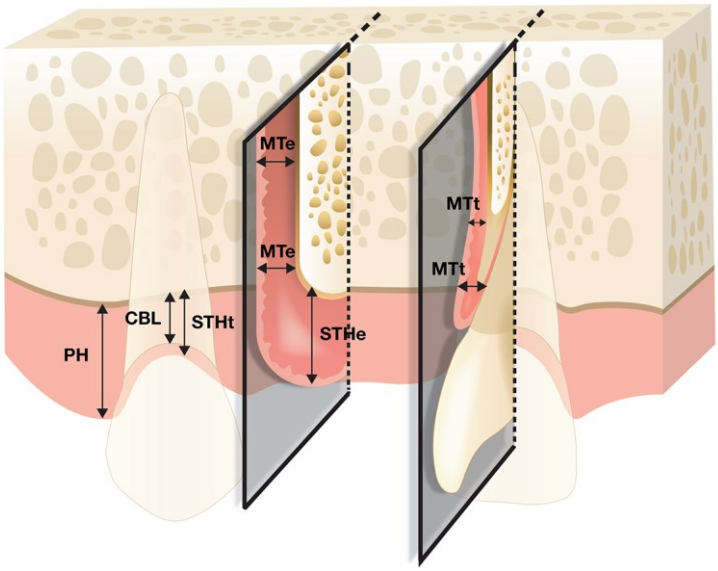


Figure 2. Implant treatment planning clinical photographs (A-C), with corresponding ultrasound images (D-F). ST: soft tissues, B: bone surface, C: crown surface, R: root surface, L: lip.

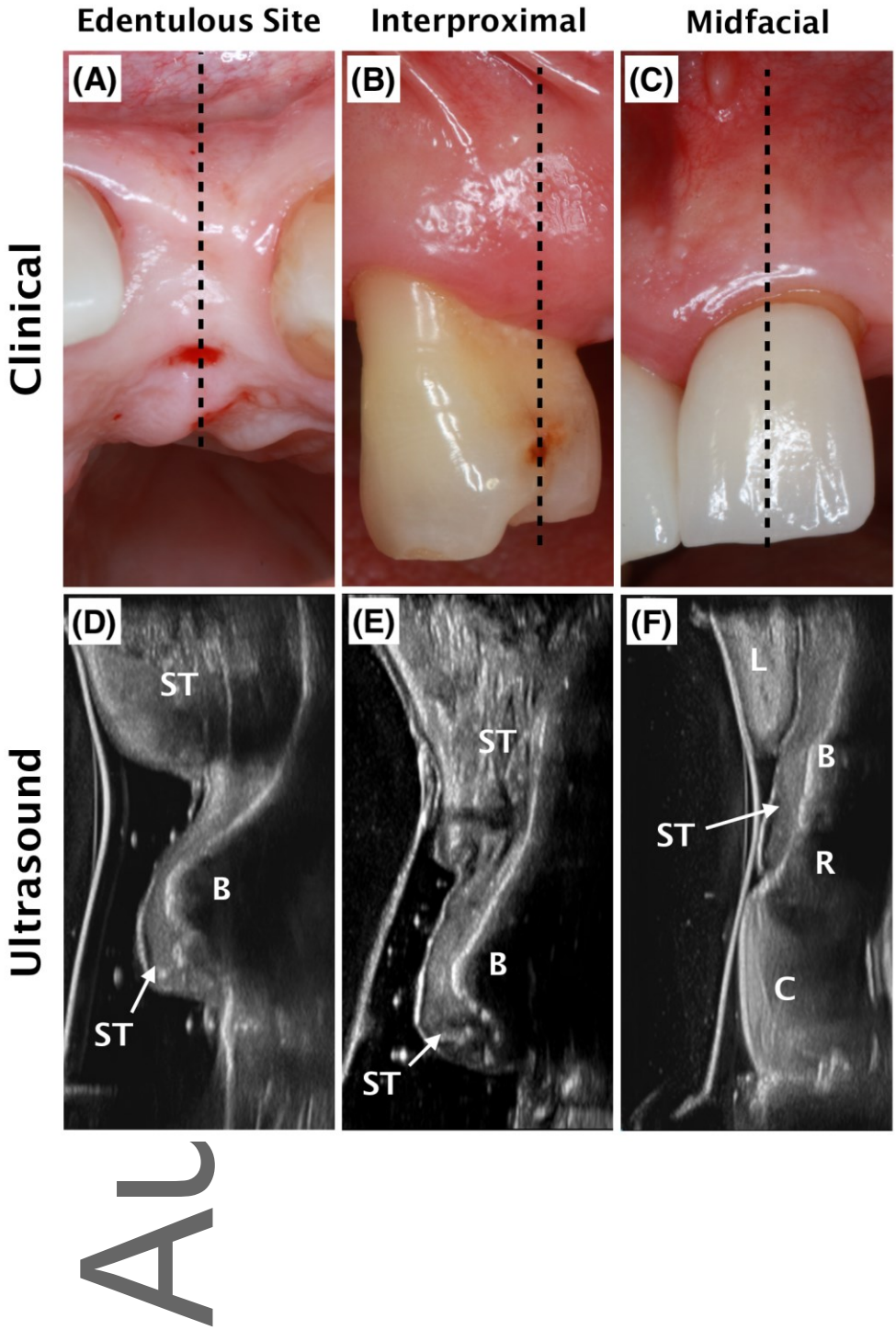


Figure 3. Scatter plots depicting the correlation between ultrasound (US) and direct measurements for each of the study parameters.

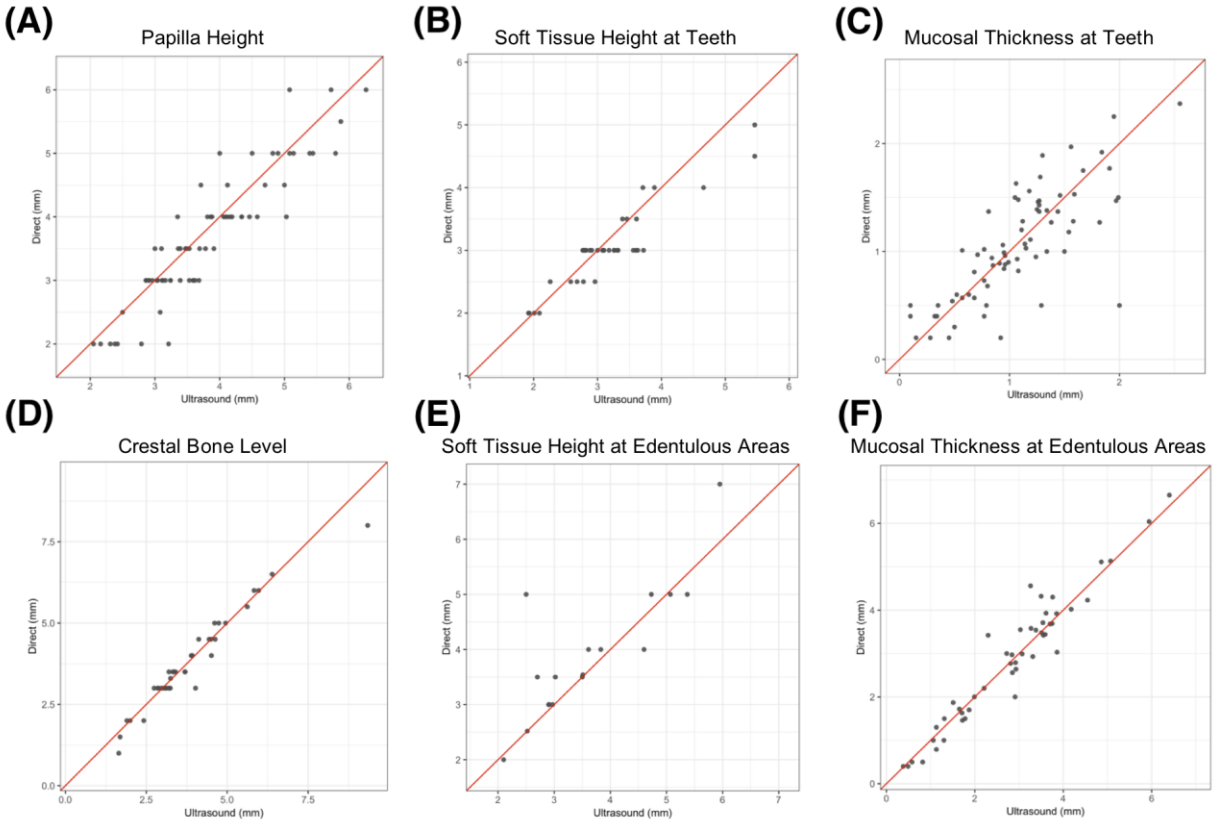
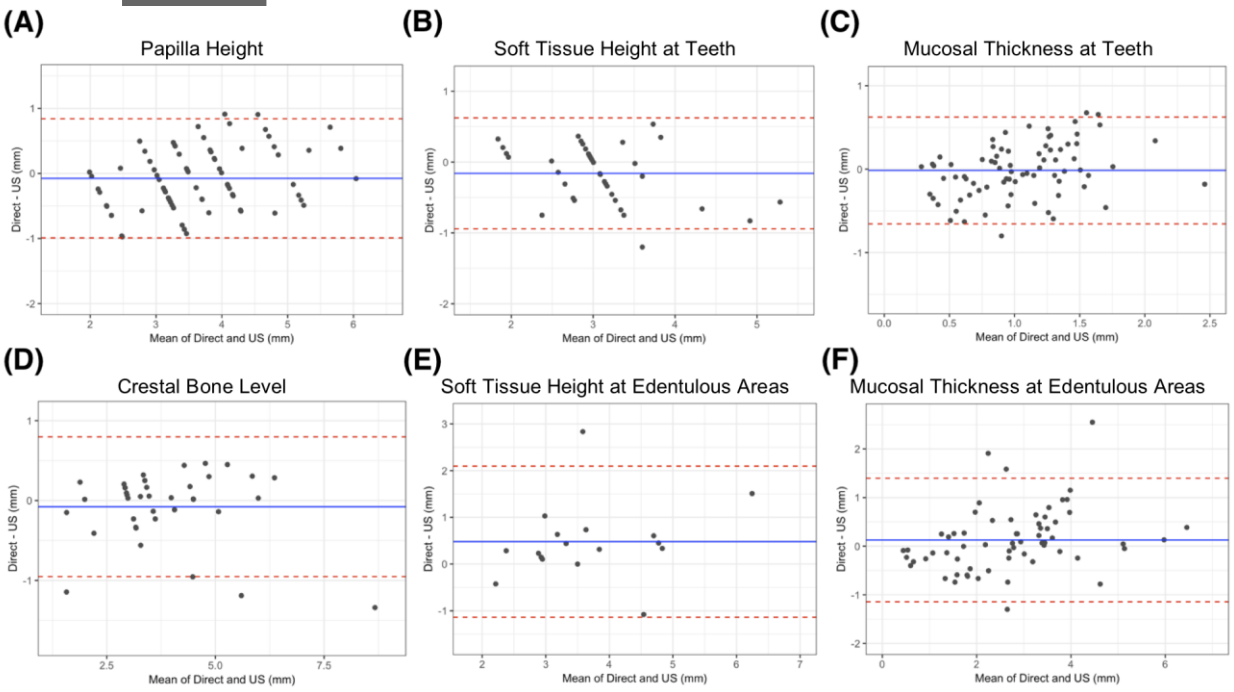


Figure 4. Bland-Altman plots depicting the mean absolute differences of ultrasound (US) measurements for each of the study parameters.



Supplementary Figure S1. Bland-Altman and scatter plots depicting the (A) mean absolute difference and (B) correlation, between direct measurements and CBCT of crestal bone level.

Supplementary Figure S2. Bland-Altman plots depicting the mean absolute difference between US and CBCT measurements of (A) Interdental Papilla Height, (B) Soft Tissue Height at Teeth, and (C) Mucosal Thickness at Teeth.

Table 1. Inter-rater agreement of the two examiners for each of the study parameters measured via ultrasound (US) and CBCT depicted as inter-rater correlation coefficients (ICC) (*=statistical significance, p<0.05).

Parameter	*n*	Method	ICC	95% Confidence Interval		*P*
				Lower	Upper	
Interdental Papilla Height	71	US	0.818	0.724	0.882	<0.0001*
Facial Soft Tissue Height at Teeth	38	US	0.793	0.637	0.886	<0.0001*
Mucosal Thickness at Teeth	73	US	0.776	0.493	0.912	0.0001*
Soft Tissue Height at the Edentulous Ridge	17	US	0.482	0.286	0.640	<0.0001*
Mucosal Thickness at the Edentulous Ridge	45	US	0.881	0.794	0.933	<0.0001*
Crestal Bone Level	38	US	0.838	0.711	0.912	<0.0001*
	28	CBCT	0.965	0.926	0.984	<0.0001*

Table 2. Agreement between the methods of measurement (Direct, Ultrasound (US) and CBCT) depicted as inter-rater correlation coefficients (ICC) and mean differences. (*=statistical significance, p<0.05).

Parameter	*n*	Subgroup	Mean Difference (Limits of Agreement)	ICC	95% Confidence Interval		*P*
					Lower	Upper	
Interdental Papilla Height	68	US-Direct	-0.076 (-0.991 to 0.840)	0.873	0.803	0.912	<0.0001*
	45	US-CBCT	0.351 (-1.279 to 1.981)	0.654	0.371	0.810	0.0003*
Soft Tissue Height at Teeth	36	US-Direct	-0.159 (-0.942 to 0.623)	0.829	0.691	0.909	<0.0001*
	22	US-CBCT	0.455 (-0.456 to 1.365)	0.849	0.637	0.937	<0.0001*
Mucosal Thickness at Teeth	69	US-Direct	-0.015 (-0.655 to 0.624)	0.707	0.567	0.808	<0.0001*
	45	US-CBCT	-0.213 (-1.052 to 0.626)	0.657	0.377	0.812	0.0002*
Soft Tissue Height at the Edentulous Ridge	16	US-Direct	0.479 (-1.138 to 2.097)	0.667	0.284	0.868	0.0013*
Mucosal Thickness at the Edentulous Ridge	44	US-Direct	0.127 (-1.145 to 1.398)	0.918	0.855	0.954	<0.0001*
Crestal Bone Level	35	US-Direct	-0.078 (-0.952 to 0.797)	0.957	0.918	0.978	<0.0001*
	25	Direct-CBCT	0.412 (-1.160 to 1.985)	0.798	0.598	0.905	<0.0001*