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Original Article

Correlation study between fractal properties of pre-operative bone trabeculae and primary implant stability quotient

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Abstract

Background/objectives Resonance frequency analysis (RFA) is a non-invasive method for implant stability evaluation by implant stability quotient (ISQ) value. However, RFA cannot provide pre-implant placement prediction. Therefore, a new method for pre-surgical outcome projection is still needed. Fractal dimension (FD) is a radiographic quantitative analysis for bone complexity, which might be use as a stability predictor at the time of treatment planning. This investigation aimed to study the correlation between FD and ISQ.

Materials and methods Patients, receiving implant placement at Faculty of Dentistry, Chulalongkorn University between 2013-2017, were screened according to study criteria. Inclusion conditions included presence of ISQ and absence of systemic condition affecting bone quality. Demographic data of the patient and details of implant treatment were collected. CBCT data acquired within 6 months prior to ISQ measurement were reconstructed into cross-sectional slices for FD calculation, while imaging related variables were documented. Significant affecting factors to ISQ were inspected using multiple linear regression beforehand. Subsequently, a correlation between ISQ and FD with confounding factors was re-analyzed.

Results ISQ values at implantation time were significantly affected by implant diameter and placement jaw bones. ($R^2 = 0.307$, $p < 0.001$) No significant correlation was found between ISQ and FD when including age, sex, implant diameter, implanted jaw bone, image resolution and x-ray machine.

Conclusions No linear correlation between FD from pre-implant CBCT image under this study's condition and ISQ at the time of implant placement was found. Implant diameter and jaw type for implantation were found to influence ISQ value.

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Key words: *bone trabeculae; cone-beam computed tomography; dental implant; fractal dimension; implant stability quotient, resonance frequency analysis*

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Introduction

Dental implant is now widely used for tooth substitution with benefit of providing prosthesis support from bone integration without the needs for neighboring teeth destruction. However, comparing to other prosthodontic treatment, implant is more invasive. In addition, it demands both time and financial expense with risks from postoperative complication and failure. The suggested definition of successful implant osseointegration is clinical immobility of the implant or the ability to support axial, lateral and rotational loads. (Sennerby and Meredith, 2008; Suer, et al., 2016) Implant stability, in other words, plays major role in assessing treatment outcomes. (Atsumi, et al., 2007; Huang, et al., 2016; Swami, et al., 2016) Several techniques have been proposed in order to evaluate implant stability. (Mistry, et al., 2014; Saurabh and Rubina, 2016; Swami, et al., 2016)

Resonance frequency analysis (RFA), one of the commonly used clinical methods, provides an objective measurement for implant stability and bone osseointegration at implant placement and post-implant placement stages with a non-invasive resonance frequency analyzer and transducer. (Atsumi, et al., 2007; Suer, et al., 2016) The analysis is based on structural and vibration principle where a magnetic impulse is generated and transferred onto an implant or implant abutment via a transducer. Response signals are then picked up by a receptor vibration to induce an electric voltage in the resonance frequency analyzer. (Sennerby and Meredith, 2008; Mistry, et al., 2014; Huang, et al., 2016) The frequency with the highest amplitude, representing the implant-bone unit's stiffness, is translated to implant stability quotient (ISQ) value of 0 to 100. (Atsumi, et al., 2007; Pattijn, et al., 2007; Lee, et al., 2010; Veltri, et al., 2011; Suer, et al., 2016) The higher ISQ value indicates greater implant stability. (Atsumi, et al., 2007) At implantation stage, ISQ values of at least 55 could represent clinical stability and possibly predict future successful osseointegration. (Sennerby and Meredith, 2008; Huang, et al., 2016) However, RFA can only be done in the presence of the bone-implant interface, so it cannot provide pre-surgical information for treatment planning and outcome prediction.

The word "fractal" has been used to describe an entity with self-similarity, a property in which a magnified subset is indistinguishable from the whole object. (Geraets and van der Stelt, 2000; Lopes and Betrouni, 2009; Sánchez and Uzcátegui, 2011) Fractal analysis (FA) arises in order to quantify these complexities. (Lopes and Betrouni, 2009) Radiographic bone trabecular architecture could be analyzed, usually with modified tile counting method since cancellous bone has been shown to possess self-similarity and magnification-dependent metric properties. (Benhamou, et al., 1994; Lopes and Betrouni, 2009; Sánchez and Uzcátegui, 2011; Suer, et al., 2016)

According to position statement of American Academy of Oral and Maxillofacial Radiology, the need of cross-sectional images for pre-operative site-specific evaluation for implant planning was re-emphasized with cone beam computed tomography as a method of choice. (Tyndall, et al., 2012) As radiographic examination provides both quantitative details of bone dimension and qualitative information of bone density and microarchitecture, it is at best to explore the latter two major influences on implant stability for maximum benefit of implant planning and prognostic prediction pre-operatively. Previous studies demonstrated a correlation between ISQ and pre-surgical fractal dimension (FD) of bone trabeculae on panoramic radiograph. (Lee, et al., 2010; Suer, et al., 2016) However, Veltri and his colleagues (Veltri, et al., 2011) found no correlation between the two parameters in 16 rabbit femurs. Although no definite conclusion can be made, these findings suggest that FD could be considered as potential parameter to predict implant stability. Therefore, this study aimed to investigate a correlation between FD from pre-operative CBCT image and in vivo ISQ, taken multiple variables from clinical level into account.

Materials and methods

Treatment records of patients receiving implant treatment at Faculty of Dentistry, Chulalongkorn University, during 2013-2017, were screened. Study inclusion criteria included presence of ISQ at the time of implant placement and absence of systemic diseases affecting bone quality, like history of radiation and hypothyroidism. Demographic data of studied subjects, including age and sex, were extracted along with details of implantation sites, implant geometry (shape, thread and size) and ISQ values at implant placement time. (Categorization and distribution were shown in Table 1.) Multiple linear regression was used to test the correlation between all aforementioned factors and ISQ at 95% confidence level. (SPSS software version 17.0, SPSS Inc.)

In order to minimize effect from other physiologic bone changes through time, only CBCT images acquired within 6 months period before implant placement were reviewed, while implant sites with grafted bones or bone reconstruction before CBCT examination were also excluded. CBCT examinations were taken by two machines: 3D Accuitomo 170 (J.Morita, USA Inc.) and i-CAT next generation platinum Cone Beam 3D system (Imaging Sciences International, LLC, USA) with a resolution of 0.16 or 0.25 mm and exposure parameter of 80-90 kVp, 5-9 mA and 120 kVp, 5 mA, respectively. CBCT dataset were exported as DICOM files and reconstructed using CS3D Imaging Software (Carestream Dental, USA). Cross-sectional slices were reconstructed at 4.0-4.3 mm thickness in the center of implant site according to provided gutta percha markers and post-operative radiographs, by one operator. The images then underwent 4X magnification, and were captured as TIFF files. Imaging parameters were recorded.

Images were converted into 8-bits grey scale images using Image J software version 1.51 (National Institutes of Health, Bethesda, MD. http://rsb.info.nih.gov/nih-image). A rectangular region of interest (ROI) was selected to cover the highest height of alveolar ridge within the possible path of insertion excluding adjacent root surface and cortical bone. All ROIs were processed according to methods described previously as shown in Figure 1. (White and Rudolph, 1999) First, the ROIs were blurred with a Gaussian filter (Sigma = 10) to remove the fine and medium scale variations in image brightness. The blurred image was then subtracted from the original image and values of 128 was added to each pixel in the resultant image to set the intensity mean to 128. The image was then converted into binary image and underwent erosion and dilation process once to reduce the noise. The image inversion was done so that the trabecular part presented as black pixels. Lastly, the image was skeletonized and used for fractal dimension calculation by the modified tile counting method with a box size ranging from 5-12 and 3-7 pixels for 0.16 and 0.25 mm-resolution, respectively. The range of box sizes were adjusted according to the optimal range for the size of trabecular bone between 0.132-0.396 mm as described in previous study. (Huh, et al., 2011) A log-log plot of the number of boxes, used to cover all the black pixels was created against the varying box sizes. FD value was derived from slope of a straight fitted line.

Multiple linear regression analyses were performed to test for significant affecting factor to ISQ and for correlation between FD and ISQ with confounding factors to ISQ from the first analysis and imaging parameter at 95% confidence level. (SPSS software version 17.0, SPSS Inc.) The study protocol was approved by the Human Research Ethics Committee of the Faculty of Dentistry, Chulalongkorn University,

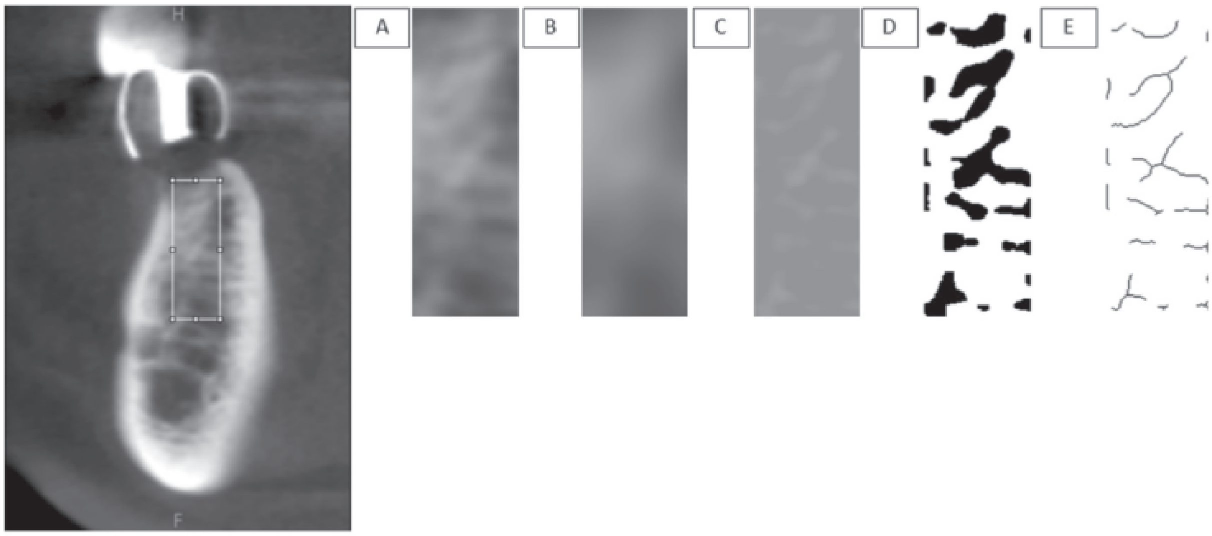

Figure 1: Morphological image processing prior to FD calculation. A. region of interest, B. blurred image, C. Subtracted image (add value of 128), D. Binary image, E. Skeletonized image.

Bangkok, Thailand. (HREC-DCU 2017-015)

Results

Part I: Identifying factors affecting ISQ

Seventy seven implant sites from 21 females and 12 males were included with mean age of 58.93 years and 56.18 years, respectively. After removing the 3 outliers, ISQ values range from 37 to 83, resulting in 69.62 ± 9.856 mean value. When taking all possible influencing factors on ISQ (age, sex, implant site, implant designs and geometry) into account, multiple linear regression analysis revealed statistically significant negative effect for maxillary location on ISQ, comparing to mandibular location. (p = 0.005) Implant diameter was also detected with significant positive outcome on ISQ. (p = 0.001) Table 2 demonstrated multiple linear regression analysis of all studied factors with possible influences on ISQ

Part II: Evaluating the correlation between FD and ISQ

Fifty four implant sites with available CBCT data were obtained from 18 females and 10 males with mean age of 57.74 years and 57.78 years, respectively. After removing the 2 outliers (ISQ value of 17, 30), ISQ values range from 37 to 83 and has 70.15 ± 9.251 mean value. All X-ray exposure parameters and implant data were included in the analysis. Since implant sites gave significant effect on ISQ in Part I, three multiple linear regression analyses were performed with a pooled data using both maxilla and mandible sites as confounding factor and 2 separated maxilla and mandible groups.

In pooled data, the result revealed no significant correlation between ISQ and FD values. There are Only the same 2 statistically significant factors related to ISQ, as shown in part I: implant diameter and implantation location. Table 3 revealed multiple linear regression results for all studied factors with possible influences on correlation between ISQ and FD. Scattered plot between ISQ and FD was illustrated in Figure 2.

Table 1: Distribution of subjects for each implant parameter regarding ISQ affecting factors.

Implant site								Number (N)
Maxilla								25
Mandible								49
Implant design*	*Shape*		*Thread*		*Microthread*			Number (N)
1	Cylindrical		V-shaped		No			26
2	Cylindrical		Buttress		No			3
3	Cylindrical		V-shaped		Yes			17
4	Tapered		V-shaped		Yes			26
5	Tapered		Buttress		No			2
Implant size	*Diameter (mm)*							
Length (mm)	3.3	3.6	4.1	4.2	4.5	4.8	5.0	Total (N)
8	1		3			3		7
9		2		24	4		3	3.3
10	6		9			11		26
11				4	2	1		7
12	1							1
Total (N)	8	2	12	28	6	15	3	74

*1: Straumann, bone level implant

2: Straumann, standard plus implant

3: Osseospeed EV implant(S), Astratech

4: Osseospeed EV implant(C), Osseospeed TX implant, Astratech

5: Straumann, bone level tapered implant

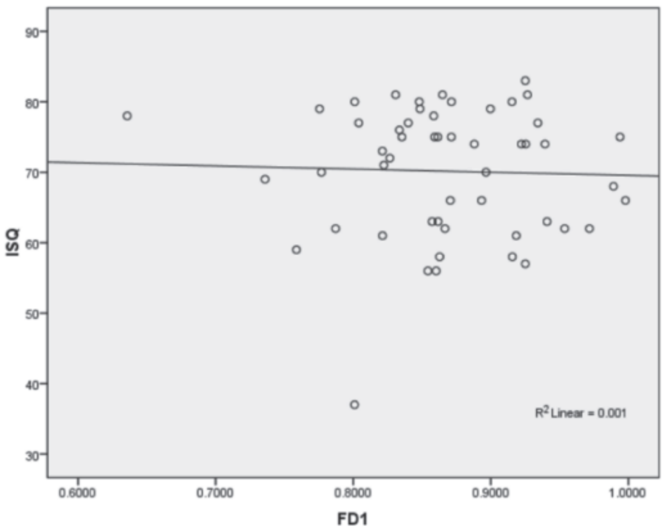

Figure 2: Scatter plot between ISQ and FD values.

Table 2: Multiple linear regression analysis of all factors effecting ISQ.

	Unstandardized Coefficients		Standardized Coefficients	t	Sig.
	B	Std. Error	Beta		
Constant	33.397	19.1593		1.705	0.093
Age	0.038	0.123	0.035	0.312	0.756
Sex	2.512	2.215	0.128	1.134	0.261
Maxillary location[a]	-6.865	2.380	-0.332	-2.884	0.005*
Implant diameter	7.948	2.306	0.366	3.447	0.001*
Implant length	-0.141	1.341	-0.012	-0.105	0.917
Implant design 2[b] Cylindrical Buttress	4.182	5.276	0.084	0.793	0.431
Implant design 3[b] Cylindrical V-shaped microthread	4.001	3.290	0.172	1.216	0.228
Implant design 4[b] Tapered V-shaped microthread	4.028	2.976	0.196	1.354	0.181
Implant design 5[b] Tapered Buttress	8.883	6.781	0.147	1.310	0.195

*Significant effect on dependent variable, ISQ

a: Mandibular location was used as reference.

b: Implant design 1 (Cylindrical V-shaped) was used as reference.

In maxillary group, 16 datasets were included from 4 females and 6 males with mean age of 62.27 years and 53.86 years, respectively. The ISQ values range from 30 to 81 (mean 63.69±14.131). The FD values range from 0.7769 to 0.9979 (mean 0.8786±0.0588). No significant correlation was found between ISQ and FD values. Table 4 showed multiple linear regression analysis of all possible influencing factors on a correlation between ISQ and FD in maxillary group.

In mandibular group, 37 datasets were included from 15 females and 7 males with mean age of 56.23 years and 60.02 years, respectively. The ISQ values range from 57 to 83 (mean 71.86±7.825). One outlier was removed from the regression analysis (ISQ value of 17). The FD values range from 0.6357 to 0.9939 (mean 0.8625±0.0718). No significant correlation was found between ISQ and FD values. However, significant effect of age on ISQ was present ($p = 0.007$). Table 5 demonstrates multiple linear regression analysis of all possible influencing factors on a correlation between ISQ and FD in mandibular group.

Discussion

RFA is widely accepted as a non-invasive method to determine implant stability at various time points after implant insertion. (Atsumi, et al., 2007; Meredith, 2008; Huang, et al., 2016; Suer, et al., 2016) Primary implant stability depends mostly on immediate mechanical engagement between implant and surrounding

Table 3: Multiple linear regression analysis of factors effecting correlation of ISQ and FD. (pooled data).

	Unstandardized Coefficients		Standardized Coefficients	t	Sig.
	B	**Std. Error**	**Beta**		
Constant	48.938	25.978		1.884	0.066
Age	0.038	0.159	0.035	0.242	0.810
Sex	1.365	2.663	0.073	0.512	0.611
Implant diameter	7.520	3.075	0.339	2.445	0.019*
Maxillary location[a]	-6.426	2.835	-0.318	-2.267	0.028*
Image resolution	-6.962	44.490	-0.023	-0.156	0.876
X-ray machine[b]	-1.355	3.219	-0.064	-0.421	0.676
Fractal dimension	-11.687	20.115	-0.087	-0.581	0.564

*Significant effect on dependent variable, ISQ

a: Mandibular location was used as reference.

b: 3D Accuitomo 170, J. Morita was used as reference.

Table 4: Multiple linear regression analysis of factors effecting correlation between ISQ and FD in maxillary group.

	Unstandardized Coefficients		Standardized Coefficients	t	Sig.
	B	**Std. Error**	**Beta**		
Constant	54.398	74.345		0.732	0.483
Age	-0.603	0.447	-0.453	-1.348	0.211
Sex	-2.690	8.351	-0.098	-0.322	0.755
Implant diameter	9.090	8.394	0.343	1.083	0.307
Image resolution	-69.093	135.680	-0.150	-0.509	0.623
X-ray machine[a]	-9.027	16.802	-0.160	-0.537	0.604
Fractal dimension	26.674	70.887	0.111	0.376	0.715

a: 3D Accuitomo 170, J. Morita was used as reference.

bone during implantation. (Atsumi, et al., 2007) Therefore, degree of implant stability can be affected by various factors associating to bone-implant interface: quantity and quality of bone, implant geometry and surgical technique. (Sennerby and Meredith, 2008) Thus, 3 variables affecting the bone property (age, sex and implantation location) and other 3 variables affecting the bone-contact surface of implant (implant diameter, length and design-shape; thread and microthread) were included in multiple lincar regression analysis of ISQ in our study. However, due to a limitation of retrospective study, surgical technique and data regarding any complication cannot be retrieved for all subjects. Hence, these factors could not be included in our study.

Table 5: Multiple linear regression analysis of factors effecting correlation of ISQ and FD in mandibular group.

	Unstandardized Coefficients		Standardized Coefficients	t	Sig.
	B	Std. Error	Beta		
Constant	50.893	28.082		1.812	0.080
Age	0.548	0.189	0.509	2.906	0.007*
Sex	-1.549	2.972	-0.097	-0.521	0.606
Implant diameter	5.994	3.432	0.276	1.747	0.091
Image resolution	-25.834	49.127	-0.103	-0.526	0.603
X-ray machine[a]	1.107	3.014	0.067	0.367	0.716
Fractal dimension	-34.699	19.999	-0.318	-1.735	0.093

*Significant effect on dependent variable, ISQ

a: 3D Accuitomo 170, J. Morita was used as reference.

Our result was in accordance with previous studies that wider implant diameter increases primary stability due to the increased bone-implant contact surface area. (Östman, et al., 2006; Meredith, 2008; Gehrke, et al., 2016) Furthermore, recent retrospective analysis for effect of multiple factors on ISQ also revealed a positive effect of larger implant diameter on ISQ both at the time of implantation and before restoration when taking into account various factors that possibly effect ISQ, consisting of sex, age, maxillary mandibular location, immediate/delayed implantation, presence or absence of bone grafting, implant diameter, implant length, healing pattern, insertion torque and bone type. (Huang, et al., 2016) This finding gave a stronger model since the coefficient of correlation was weighted among other variables. Another recent multivariate study also yielded similar results, which demonstrated significantly higher ISQ with greater implant diameter. (Gehrke, et al., 2016) Moreover, RFA measures the stability when apply lateral force relevant to clinically bending force (Östman, et al., 2006; Meredith, 2008). Therefore, amount of circumferential bone surrounding implant, rather than longitudinal bone volume, should play an important role on RFA.

Our result showed no significant effect on ISQ from implant length. Although longer implant also creates higher bone-implant contact, this positive effect could be minimized by longer drilling time leading to over preparation of the implant site and loosening the implant-bone interface. (Östman, et al., 2006) Moreover, the more number of threads moving through the bone in longer implant, the more bone deformity due to repeated contact, leading to reduced stability. (Kheur, et al., 2016) In addition, Friberg and co-worker reported a significant correlation between cutting torque, a parameter representing bone density, and ISQ only at the crestal bony region. (Friberg, et al., 1999) Therefore, increasing in implant length does not significantly alter the ISQ value.

Several implant designs have been released to improve implant stability with modifications in number, orientation and spacing of thread (thread pitch). Greater number of thread and smaller pitch result in larger functional surface area which increase resistance to applied force. (Misch, et al., 2004) However, due to limited information of thread pitch on our implants, this factor was excluded from our study. Thread geometry is another factor, reported as influencing factor

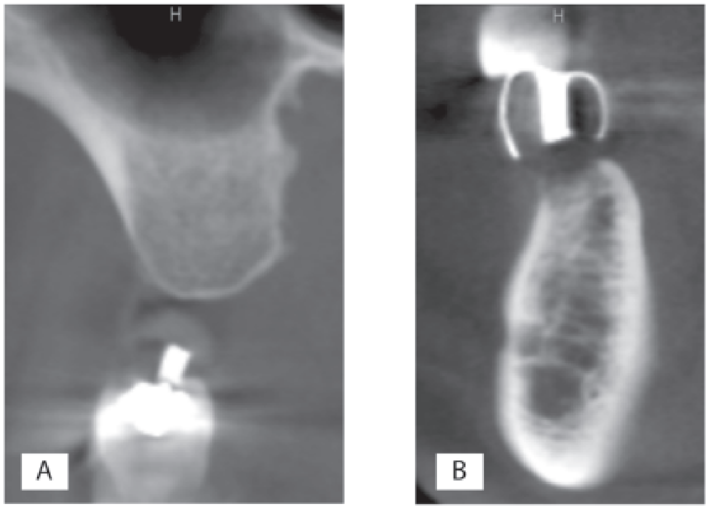

Figure 3: Difference in trabecular pattern between maxillary (A) and mandibular (B) sample with the same ISQ (value = 81) but different FD (A = 0.9267 and B = 0.8308).

for implant stability. Study of reverse torque and bone-implant contact (BIC) of 3 different implant threads, placed in rabbit tibia, reported significant more BIC and greater reverse-torque from square threaded-implants than the comparable values from both the V-shaped and reverse buttress thread designs. (Steigenga, et al., 2004) This is consistent with our finding. Since no significantly different effect on ISQ was found between buttress and V-shaped threads. Another adaptation is in the implant shape where tapered implants are developed to create a lateral compression to the bone during insertion thus increasing the bone-implant interface stability. (Glauser, et al., 2004; Meredith, 2008; Gehrke, et al., 2016) Additionally, implant with cervical microthread was also reviewed with greater stability, compared with cylindrical implant. (Gehrke, et al., 2016) In spite of a non-statistically significant difference, our findings followed the same trend. Comparing implant design 1 and 3 (without and with cervical microthread), the latter gave a higher positive effect on ISQ. Moreover, comparing implant design 2 and 5, tapered implant also showed a greater positive effect on ISQ as well. (Table 3) Nevertheless, these additional designs seem to be outshadowed by the effect of bone quality. Recent multivariate study also found lesser effect of tapered implant when taking other confounding variables of implant location, platform, gender and bone quality into account. (Östman, et al., 2006) Furthermore, these modified geometries may result in over-compression in good bone quality thus these implants may fail to seat or eventually fail. (Meredith, 2008)

Implantation location has been shown in several studies to affect ISQ. Maxillary implants often have lower ISQ than mandibular implants. (Gehrke, et al., 2016; Huang, et al., 2016) Previous study also reported that most implants in maxilla had ISQ < 60 while mandibular implants often had ISQ ≥ 60. (Nedir, et al., 2004) As bone quality plays an important role in primary stability, it also gives possible explanations to this finding as well. It was suggested that maxillary bone is often softer due to less cortex. (Östman, et al., 2006) Another study also reported a mean bone mineral density of the mandible at 1.11 g/cm^2, which is much larger than that in the anterior maxilla (mean = 0.55 g/cm^2) or the posterior maxilla (mean = 0.31 g/cm^2). (Devlin, et al., 1998)

Regarding CBCT, previous study (Pauwels, et al., 2015) concluded that kVp has no significant influence on FD at constant radiation dose. Therefore, this parameter was excluded from our analysis. Higher resolution is more capable in detecting fine bone structure. With lesser resolution, the images are blurred, and trabeculae become merging to adjacent bone, leading to significantly lower FD. (Bollen, et al., 2001; Baksi and Fidler, 2012; Pauwels, et al., 2015) However, higher resolution could result in higher radiation dose and might not be available in all CBCT machines. In this study, we included standard resolutions for our implant image protocol (0.16-0.25 mm) as one of study's factor.

Different CBCT machines using different exposure parameters and different image reconstruction algorithms give different image quality as a result from spatial resolution, contrast resolution, noise, and geometric accuracy. (Pauwels, et al., 2012) This inconsistency in image quality might affect in FD calculation. Thus, X-ray machine was also included in the model analysis as influencing factor to FD.

Since CBCT was raised as method of choice for implant planning with a benefit of less-superimposed bone image, it was seen as an appropriate modality with expectation to give a more distinct result, regarding ISQ-FD association. However, our study found no significant correlation between ISQ and FD. The first explanation might due to the fact that ISQ values represent coronal bone implant contact rather than at the deeper parts. (Akkocaoglu, et al., 2005) However, FD values were measured along the alveolar height in present study hence a correlation might be hard to obtain. Our result was also in contrast with previous studies using pre-operative panoramic radiographs, which had detected a significant correlation between ISQ and FD. (Lee, et al., 2010; Suer, et al., 2016) The second rationale could be contributed to the differences between imaging technologies. In general the sharpness of bone trabeculation seems to be higher in directly captured panoramic radiographs, but blurring in reconstructed CBCT images. The third reason could also be contributed to aforementioned lesser image resolution (0.25 mm) used in most of our samples. Since large FOV were needed in order to cover all implantation sites in one scan, the voxel size increased. As resolution decreased, fine bone structures became blurred and merged to each other. (Bollen, et al., 2001) Hence, lesser difference in bone complexity among different bone quality could be revealed. Therefore, with image resolution used in our study, the differences in FD among samples might not be large enough to differentiate various bone quality and ISQ. Furthermore, these two previous studies were controlled and investigated only for correlation between ISQ and FD without any confounding variables. When taking multiple variables from the clinical level into account, a decrease in the ability of the model to predict ISQ was foreseeable. Final explanation is due to CBCT grey values, which are affected by the partial volume effect (PVE). (Ibrahim, et al., 2013) The voxels that contain both bone and marrow information will have an ambiguous grey value, resulting in difficulty in classifying them as foreground or background. With large voxel sizes, the influence of PVE can result in thicker trabeculae or loss of thin trabeculae which might also lead to the FD alteration. (Kothari, et al., 1998) As a result, further prospective multivariate study with higher image resolution is needed to further investigate correlation between ISQ and FD. Additionally, direct comparison between FD from panoramic radiograph and CBCT image might be useful.

Although significant correlation between ISQ and FD was not found in both maxillary and mandibular group, one intriguing finding was that FD was reported with positive effect (correlation coefficient) in maxillary group while the effect was negative in mandibular group. We speculated that the difference lies in trabecular structure between maxilla and mandible in our subjects. Maxillary trabeculae tend to be finer and grainy thus with more trabecular number, the complexity increases, so does the FD value. In mandible, bone trabeculae tend to be coarser and thicker, similar to a linear structure. Hence, the denser the trabeculae, the more linear with less grain they become, leading to less complexity detected, so does the FD values. (Figure 3) With this finding, we proposed that should ISQ prediction using FD is possible, separation between maxillary and mandibular group might be warranted. However, our smaller maxillary sample might need further investigation to confirm this speculation.

Conclusions

Under this study condition, no significant linear correlation was found between ISQ and FD. ISQ values at implantation time were significantly affected by implant diameter and implantation sites.

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