Relationship of implant stability and bone density derived from computerized tomography images.

Authors: Joe Merheb, MAS, Doctor¹; Marjolein Vercruyssen, PhD, Doctor¹; Wim Coucke, PhD, Doctor³, Marc Quirynen, PhD, Professor^{1, 2}.

Author's affiliation:

¹Unit of Periodontology, Department of Oral Health Sciences, University of Leuven (Belgium)

² Research group Periodontology & Oral microbiology, Department of Oral Health Sciences, University of Leuven (Belgium)

³Scientific Institute of Public Health, Brussels (Belgium).

Correspondence:

Joe Merheb,

KU Leuven, Faculty of medicine, department of periodontology

Kapucijnenvoer 33, 3000 Leuven (Belgium)

Tel: +32 16 332483

Email: joe.merheb@med.kuleuven.be

Running title: implant stability and bone density

Key words: ISQ, RFA, resonance, implant, density, stability, Osstell

Funding: Dentsply Implants, (Mölnådal, Sweden) provided the implants and abutments free of charge. Materialise Dental (Heverlee, Belgium) provided the stereolithographical guides free of charge.

Conflicts of interest:

Joe Merheb reports no conflict of interest.

Marjolein Vercruyssen reports no conflict of interest.

Wim Coucke reports no conflict of interest.

Marc Quirynen reports no conflict of interest.

Authors' Contribution:

Joe Merheb: Concept/Design, Data analysis/interpretation, Drafting article.

Marjolein Vercruyssen: Concept/Design, Data collection.

Wim Coucke: Statistics.

Marc Quirynen: Concept/Design, Critical revision of article, Approval of article, Securing funding.

Abstract:*Background & purpose:*

Implant stability is one of the most important factors influencing osseointegration. Using stereolithographical guides for maximizing precision, this study aimed at investigating the relationship between implant stability and bone density derived from CT (Computerized Tomography) analysis.

Materials & methods:

195 implants were placed in 48 patients using digitally designed stereolithographical surgical guides. 95 implants were placed using a mucosa supported guide and 100 implants were placed using a bone supported guide. Implant stability was measured by means of Resonance Frequency Analysis (RFA) and damping capacity assessment (Periotest, PTV). Bone density (Hounsfield units) was measured at different ROI (regions of interest) and cortex thickness was measured around each implant.

Results:

Implant stability correlated significantly with the different ROI. The best correlation for RFA was obtained for the spongy bone ROI ($r = 0.64$) and PTV best correlated with the coronal cortex density ($r = -0.41$). Shorter implants (9 mm) had a significantly lower primary stability than longer implants (11, 13, 15 mm). Primary stability was also significantly higher in 4mm diameter implants than in 3.5mm diameter implants. A formula for the prediction of primary stability based on the different variables investigated was developed.

Conclusions:

Bone density and cortex thickness have a significant influence on implant primary stability. Longer and wider implants reached higher primary stability than shorter and narrower implants. These correlations lose their significance after osseointegration has taken place. Implant stability can be predicted based on an pre-operative analysis of bone characteristics.

Background & purpose:

Implant osseointegration is the process by which a functional, permanent and intimate bone-to-implant surface contact is formed and maintained without movement even when subjected to load ¹. An array of rules and precepts should be respected if successful osseointegration is to be achieved. The implant characteristics are of utmost importance. Surface treatment and roughness have also been proved to enhance the quality and velocity of the osseointegration process ²⁻⁴.

The surgeon has control over those factors related to the surgical phase of implant placement. The adoption of sterile operating conditions, the performance of a minimally traumatic surgery and the respect of biological imperatives are among such factors. Implant stability is one of those per-operative variables that are of major impact on the achievement of osseointegration, especially in the case of immediate and early placement or loading protocols ⁵ and Implant micromobility has been identified as a possible cause for the development of a fibrous capsule around the implants and the absence of an intimate bone-implant contact⁶.

The introduction of 3D computerized tomography (CT) to implant therapy allowed a better pre-operative visualization of the surgical site which in turn allowed a better and more precise planning. Additionally, CT allowed the assessment of bone density through the measurement of Hounsfield Units (HU), named after the founder of the CT technology⁷. Cone Beam Computerized tomography (CBCT) is a technology that stemmed from the original Multi-Slice Computerized tomography (MSCT) and has the advantages of allowing a faster acquisition, lower subject irradiation and a reduction of the equipment costs. Despite technical limitations inherent to CBCT technology, several protocols are being introduced in order to allow the reliable measurement of density values⁸⁻¹⁰.

Several methods are available for the assessment of primary stability. Traditionally, implant primary stability was assessed either by the clinician tactile perception or by the evaluation of insertion torque with the help of a torque wrench or a dedicated implant motor. However, these methods either lack objectivity or measure the rotational component of primary stability which is of lesser clinical relevance than the translational component of primary stability. Resonance Frequency Analysis (RFA) and damping capacity assessment (Periotest) are two widely

investigated objective and reliable methods of measuring translational (lateral) primary stability^{11, 12}.

Several studies have investigated the relationship between bone density and primary implant stability¹³⁻¹⁵. However, the evaluation of bone density was done on 2D slices and in none of the studies was the volumetric density value assessed. Given the important variability of density between adjacent slices¹⁶, a volumetric assessment of density is of great added value.

The aim of this prospective study was to assess the relationship between implant stability and a number of bone and implant related features. Additionally, this study aimed at elaborating a mathematical formula that could help predict implant stability based on a pre-operative assessment of the radiographic images.

Materials & methods:

Patients Selection:

This study project was submitted to and approved by the ethical committee of the KU Leuven university (B32220095376). The enrolled subjects were patients seeking treatment with dental implant at the University Hospitals Leuven. At the moment of implant placement, the patients had been fully edentulous for at least 6 months. Patients were excluded if they showed signs of alcohol or tobacco abuse, insufficient motivation and willingness to follow the study protocol requirements or if bone metabolism diseases were detected. Further inclusion and exclusion criteria are to be found in Table 1. In total 48 patients were recruited and 195 implants were placed.

Computerized tomography analysis and radiographic superposition:

The prostheses of the patients were modified by the inclusion of eight gutta percha markers homogenously spread across the prosthesis and a bite index was made.

Each patient underwent a Computerized Tomography (CT) scan while wearing their traditional full prosthesis using a Siemens Volume Zoom helical CT (Siemens, Erlangen, Germany). The accuracy of the prosthesis position in the mouth was enhanced by having the patients occlude on the bite index which was previously made. The following settings: of intensity and tension were used: 120kV, 90mAs. The primary slice thickness was 0.75mm and a 0.3mm slice increment was adopted. Additionally, a separate scan (CBCT) of the patient's prosthesis alone was made. Both CT and CBCT data were saved in Dicom format (.dcm) and loaded in an implant planning software (Simplant®, Dentsply Implants, Mölndal, Sweden). After the matching of both scans, implant positions were picked in function of the teeth positions on the scanned prosthesis and in function of the available bone volume. Hounsfield values of the following regions of interest (ROI) were measured (Figure 1):

- The volume occupied by the virtual implant.
- The 1 mm thick bone shell surrounding the virtual implant.
- The spongy bone at the placement site
- The coronal cortical plate.
- The coronal 3 mm of the virtual implant volume.

Moreover, the cortical thickness vestibular and palatal at the level of the implant shoulder was measured.

Surgical procedure and implant stability measurement:

For every patient, according to the clinical situation, 4 to 6 implants (Astratech Implant System™, Dentsply Implants, Mölndal, Sweden) were placed according to the standard procedure with the help of stereolithographical surgical guides (Figure 2) obtained following the dual scan procedure and subsequent planning in Simplant software (Materialise Dental, Heverlee, Belgium). The choice of stereolithographical guides was randomized and the patients were assigned to one of two subgroups:

- Group M: (n = 24 patients, 95 implants). Mucosa supported stereolithographical guides. Flapless surgery.
- Group B: (n = 24 patients, 100 implants). Bone supported stereolithographical guides. Flapped surgery.

The operating surgeon was blinded towards the bone analysis and was unaware of the bone density measurements of the receiving sites. After placement, implant stability was measured by means of two different technologies:

- Resonance frequency analysis (RFA) using the Osstell device (Osstell ISQ™, Osstell AB, Göteborg, Sweden) and measured in ISQ units (Implant Stability Quotient).
- Damping capacity assessment test using the Periotest Classic device (PTV) (Medizintechnik Gulden, Modautal, Germany)

The measurements were performed in both the vestibulo-oral and mesio-distal directions and repeated twice for every direction and the mean of the four measurements was calculated. After a healing period of 3 to 6 months, the prosthetic rehabilitation phase could be started.

Statistical Analysis:

The relation between the various implant stability and bone density parameters was first assessed visually by means of a scatter plot on which a LOWESS (Local Weighted Estimated Scatterplot Smoothing)-fitted line and a linear regression line were drawn. In addition, the Pearson correlation with its P-value and the coefficients of the regression line were calculated. A P-value testing the hypothesis of a slope equal to zero was tested as well. The effect of the surgical technique on implant stability was assessed by means of an Analysis of Variance model in which a separate model was built for each explanatory variable separately. Finally, a stepwise regression was built to choose the combination of bone density measures that predicts implant stability the best. The correction for simultaneous

hypothesis testing was performed according to Tukey. Statistical significance was asserted for $p < 0.05$.

Results:

Influence of bone density and cortical thickness on implant stability:

The average RFA at surgery was 73.14 ± 9.50 and the average PTV at surgery was -4.34 ± 1.78 . Stability measures measured at abutment phase were on average lower than at surgery. RFA at abutment phase was 69.58 ± 8.54 and PTV at abutment phase was -3.16 ± 2.31 . No significant correlation between RFA at surgery and RFA at abutment phase was found ($p > 0.05$). Similarly, no significant correlation was found between PTV surgery and PTV abutment phase ($p > 0.05$). However, the correlation between mean RFA values and mean PTV values was found to be significant ($r = -0.42$, $p < 0.01$)

At implant placement, implant stability correlated strongly and significantly with bone density at all the regions of interest (Table 2). Broadly, the different ROI correlated better with Resonance frequency analysis and ranged from $r = 0.37$ to $r = 0.64$. than with the damping capacity assessment (r ranged from $r = -0.21$ to $r = -0.41$). The density of the spongy bone ROI showed the highest correlation with RFA ($r = 0.64$) while the Coronal cortex density ROI showed the highest correlation with PTV ($r = -0.41$).

The RFA measurements were repeated at the moment of the start of the prosthetic phase. The correlations between RFA and HU showed an important decrease and lost statistical significance ($p > 0.05$) except for the cortical bone density ($r = 0.40$, $p < 0.01$). The correlation between PTV measurements and bone density similarly decreased and lost significance ($p > 0.05$). Cortical thickness showed a high correlation with implant stability at implant placement. ($r = 0.58$) but this correlation decreased when measured at the start of the prosthetic phase ($r = 0.28$) and lost significance ($p > 0.05$)

Influence of implant length and diameter on implant stability:

At implant placement surgery, implant stability as measured by resonance frequency analysis averaged 68.7 ± 6.7 ISQ for 9mm long implants ($n = 16$), 73.1 ± 6.6 ISQ for 11mm long implants ($n = 60$); 75.4 ± 7.4 ISQ for 13mm long implants ($n = 80$) and 74.8 ± 7.2 ISQ for 15mm implants ($n = 39$). A significant difference in implant stability was detected between the “9mm” implants and the “11, 13 and 15mm implants” (Figure 3). The average PTV was -4.8 ± 1.5 PTV for 9mm long implants, -3.6 ± 1.7 PTV for 11mm long implants; -4.2 ± 1.7 PTV for 13mm long implants and -4.9 ± 1.9 PTV for 15mm implants. A significant difference in implant stability was only detected between the “11mm” and “15mm” (Figure 3).

At implant placement surgery, implant stability averaged 72.46 ± 7.42 ISQ for 3.5mm diameter implants ($n = 122$) and 76.65 ± 6.05 ISQ for 4mm diameter implants ($n = 73$). The difference in implant stability was significant between the two groups. Similarly, damping capacity demonstrated higher stability for 4mm implants (-4.75 ± 1.77 PTV) than 3.5mm implants (-3.86 ± 1.66 PTV) (Figure 4).

At the start of the prosthetic phase, significance was lost for all previously significant differences.

Influence of the surgical technique on implant stability:

At implant placement surgery, implant stability averaged 75.5 ± 6.7 ISQ for the implants placed with the help of a mucosa supported surgical guide ($n = 95$) and 72.6 ± 7.4 ISQ for implants placed with the help of a bone supported surgical guide ($n = 100$). The difference in implant stability ($p < 0.01$) was statistically significant. The difference in damping capacity was however statistically non-significant (-4.1 ± 1.8 PTV for the mucosa supported group versus -4.5 ± 1.7 PTV for the bone supported group) (Figure 5).

At the start of the prosthetic phase, no significant difference could be detected for either resonance frequency analysis or damping capacity assessment.

Prediction of primary implant stability:

A model for predicting implant primary stability (RFA) was constructed from the stepwise regression and isolated the following variables as most significantly influential on primary stability: HU_{OUTSIDE}, HU_{SPONGIOUS}, Cortical thickness. A formula was elaborated in an effort to predict primary stability based on radiological information:

$$\text{RFA (ISQ)} = 41.05 + 7.20 \cdot 10^{-3} \text{HU}_{\text{OUTSIDE}} + 3.56 \cdot 10^{-3} \text{HU}_{\text{SPONGIOUS}} + 7.85 \text{ Cortical thickness.}$$

The above-mentioned formula allowed to predict 96.92% of RFA measurements with an accuracy of 10 ISQ units and 78.46% of RFA measurements with an accuracy of 5 ISQ units.

Discussion:

The results of this study seem to confirm that a direct relationship exists between implant primary stability and bone density as derived from a reading of the Hounsfield values of the bone at the implant site. In previous investigations by this same group ^{17, 18} and other groups ^{14, 15, 19}, the relationship between implant stability and different bone and implants variables has been assessed and a correlation already established. However, to the difference of the previous investigations, this is the first time that this relationship is investigated in a well-established prospective setting combining the use of stereolithographical guides for maximal precision and measurement on three-dimensional regions of interest (ROI).

The use of three-dimensional ROI is justified by the observation that bone density can vary to a great extent following the cross-sectional cut on which the reading is being performed, even when those cross-sections are part of the same anatomical region and are only 1mm or less apart ¹⁸.

In the scope of those same concerns about the variability of bone density over minute distances, the use of stereolithographical guides offers a greater precision of

measurement by allowing a more reliable transcription of implant position but also, depth of insertion, direction and inclination. This method offers a significantly more accurate planning of the implants locations than the method used previously by our group and which relied on a photographic superposition of radiographs and/or intra oral photographs ¹⁷. The accuracy of the stereolithographical guides used in this study has been documented in previous publications²⁰. Vercruyssen and co-workers found a deviation of 0.9 mm at the entry point and of 1.2 mm at the apex, and an angular deviation of 2.7°. However, the precision of such guides depends significantly on the training and experience of the practicing surgeon.

Implant stability has repeatedly been acknowledged as a major factor for the survival of dental implants. Implant micromotion is believed to be responsible for the failure of osseointegration and previous reports have stated that implant micromotion should not exceed 50-100 micrometers if osseointegration was to take place²¹.

A general trend of loss of significance was observed for the correlation between the moments of implant placement surgery and prosthetic rehabilitation phase. Indeed, implant diameter, implant length, the surgical technique used, the various HU measurements (except for HU_{CORTEX}) and Cortex thickness, all lost their significant influence of implant stability as measured by the Osstell and Periotest devices. This trend is in accordance with previous conclusions on the progressive replacement of mechanical anchorage -which is the main component of primary stability- by a biological anchorage which is the result of bone healing and remodeling over the period of osseointegration and which is less influenced by the variables mentioned higher. However, Cortex density retained its significance even after osseointegration has taken place. This particularity may be related to its direct relation with the implant shoulder and the importance of the implant shoulder in achieving stability. Shoulder design is one of the focus points of an implant design in the light of its importance in stress distribution, implant stability and the formation of a stable biological connection between the implant surface on one side and the hard and soft peri-implant tissues on the other side.

A previous report by the same group ¹⁷ also investigated the relationship between implant stability and both implant diameter and length. Unlike the present investigation, the earlier study did not find a significant correlation between those

variables. This may be due to the fact that this study relies on a different implant system with different characteristics and a different surgical placement procedure was used. In a study by Coutant and co-workers, 2 different implants designs recorded very different patterns of correlation of primary stability with different variables even though the implants were from the same manufacturer, placed by the same operating team and in the same ex-vivo receiving bodies²². The differences in between our two studies may also owe to the fact that a newer and more precise of the Osstell measuring device was used in the present study (Osstell ISQ).

In vitro studies and previous in vivo investigations have advocated that RFA is a more precise measuring technique than the Periotest^{23, 24}. It presents the advantages of reproducibility by allowing the measurements to be independent of the position and direction of the probe while Periotest can vary significantly based on the position of the probe, its inclination relatively to the healing abutment and the contact point with the abutment surface. For those reasons, this study focused on the analyses of Resonance Frequency Analysis rather than Damping capacity.

The ability to predict primary stability during the pre-operative planning and before the moment of surgery would allow the operator(s) to better anticipate and optimize the per and post-operative phases. Surgical protocols could be modified in order to enhance primary stability. The choice of the loading protocol could be anticipated especially regarding immediate loading protocols and therefore the communication with the patient would be improved as the patients gets additional and sufficient information on the post-operative phase before the proceedings of the surgery. In this regard, a statistical formula based on the variables investigated in this study and which could predict primary stability is a tool that might be useful for the operating practitioners. The stepwise regression model allows to single out the most influential variables while discarding the confounding variables. The present formula should be validated with further investigations but it is important to mention that such a formula would only apply to the implant model which was used in this study.

In the present study, the radiographic images were derived from Multislice Computerized Tomography (MsCT) scans as MsCT is the golden standard in the measurement of HU derived bone density values⁷. In common practice however, Cone Beam Computerized Tomography (CBCT) has replaced MsCT as the preferred

method of radiographic 3D imaging in implant dentistry. This shift to CBCT is mainly to lay to the benefit of considerably lower operating costs, lower irradiation doses for the patient and much faster acquisition times. CBCT however lacks the ability to measure Hounsfield Units and can only measure grey values which are unreliable in the absence of proper calibration. Until recently, CBCT technology and algorithms did not allow reliable and reproducible calibrations but recent advancements in CBCT development now offer the promise of reliable measurements of HU derived bone density²⁵ and therefore future investigations in the field of HU measurements in the maxillary complex will most probably shift towards privileging the use of CBCT.

References:

1. Albrektsson T, Branemark PI, Hansson HA, Lindstrom J. Osseointegrated titanium implants. Requirements for ensuring a long-lasting, direct bone-to-implant anchorage in man. *Acta Orthop Scand* 1981;52:155-170.
2. Zechner W, Trinkl N, Watzak G, Busenlechner D, Tepper G, Haas R, Watzek G. Radiologic follow-up of peri-implant bone loss around machine-surfaced and rough-surfaced interforaminal implants in the mandible functionally loaded for 3 to 7 years. *Int J Oral Maxillofac Implants* 2004;19:216-221.
3. Ivanoff CJ, Hallgren C, Widmark G, Sennerby L, Wennerberg A. Histologic evaluation of the bone integration of TiO(2) blasted and turned titanium microimplants in humans. *Clin Oral Implants Res* 2001;12:128-134.
4. Wennerberg A, Albrektsson T. Effects of titanium surface topography on bone integration: a systematic review. *Clin Oral Implants Res* 2009;20 Suppl 4:172-184.
5. Ostman PO, Hellman M, Sennerby L. Direct implant loading in the edentulous maxilla using a bone density-adapted surgical protocol and primary implant stability criteria for inclusion. *Clin Implant Dent Relat Res* 2005;7 Suppl 1:S60-69.

6. Szmukler-Moncler S, Salama H, Reingewirtz Y, Dubruille JH. Timing of loading and effect of micromotion on bone-dental implant interface: review of experimental literature. *J Biomed Mater Res* 1998;43:192-203.
7. Hounsfield GN. Computerized transverse axial scanning (tomography). 1. Description of system. *Br J Radiol* 1973;46:1016-1022.
8. Razi T, Niknami M, Alavi Ghazani F. Relationship between Hounsfield Unit in CT Scan and Gray Scale in CBCT. *J Dent Res Dent Clin Dent Prospects* 2014;8:107-110.
9. Campos MJ, de Souza TS, Mota Junior SL, Fraga MR, Vitral RW. Bone mineral density in cone beam computed tomography: Only a few shades of gray. *World J Radiol* 2014;6:607-612.
10. Rafic M, Ravindran P. Evaluation of on-board imager cone beam CT hounsfield units for treatment planning using rigid image registration. *J Cancer Res Ther* 2015;11:690-696.
11. Olive J, Aparicio C. Periotest method as a measure of osseointegrated oral implant stability. *Int J Oral Maxillofac Implants* 1990;5:390-400.
12. Meredith N, Alleyne D, Cawley P. Quantitative determination of the stability of the implant-tissue interface using resonance frequency analysis. *Clin Oral Implants Res* 1996;7:261-267.
13. Beer A, Gahleitner A, Holm A, Tschabitscher M, Homolka P. Correlation of insertion torques with bone mineral density from dental quantitative CT in the mandible. *Clin Oral Implants Res* 2003;14:616-620.
14. Ikumi N, Tsutsumi S. Assessment of correlation between computerized tomography values of the bone and cutting torque values at implant placement: a clinical study. *Int J Oral Maxillofac Implants* 2005;20:253-260.
15. Turkyilmaz I, Tumer C, Ozbek EN, Tozum TF. Relations between the bone density values from computerized tomography, and implant stability parameters: a clinical study of 230 regular platform implants. *J Clin Periodontol* 2007;34:716-722.

16. Merheb J, Temmerman A, Coucke W, Rasmusson L, Kubler A, Thor A, Quirynen M. Relation between Spongy Bone Density in the Maxilla and Skeletal Bone Density. *Clin Implant Dent Relat Res* 2015;17:1180-1187.
17. Merheb J, Van Assche N, Coucke W, Jacobs R, Naert I, Quirynen M. Relationship between cortical bone thickness or computerized tomography-derived bone density values and implant stability. *Clin Oral Implants Res* 2010;21:612-617.
18. Merheb J, Temmerman A, Rasmusson L, Kubler A, Thor A, Quirynen M. Influence of Skeletal and Local Bone Density on Dental Implant Stability in Patients with Osteoporosis. *Clin Implant Dent Relat Res* 2016.
19. Turkyilmaz I, Tozum TF, Tumer C, Ozbek EN. Assessment of correlation between computerized tomography values of the bone, and maximum torque and resonance frequency values at dental implant placement. *J Oral Rehabil* 2006;33:881-888.
20. Vercruyssen M, Cox C, Naert I, Jacobs R, Teughels W, Quirynen M. Accuracy and patient-centered outcome variables in guided implant surgery: a RCT comparing immediate with delayed loading. *Clin Oral Implants Res* 2015.
21. Trisi P, Perfetti G, Baldoni E, Berardi D, Colagiovanni M, Scogna G. Implant micromotion is related to peak insertion torque and bone density. *Clin Oral Implants Res* 2009;20:467-471.
22. Coutant JC, Seguela V, Hauret L, Caix P, Ella B. Assessment of the correlation between implant stability and bone density by computed tomography and resonance frequency analysis in fresh cadavers. *Int J Oral Maxillofac Implants* 2014;29:1264-1270.
23. Zix J, Hug S, Kessler-Liechti G, Mericske-Stern R. Measurement of dental implant stability by resonance frequency analysis and damping capacity assessment: comparison of both techniques in a clinical trial. *Int J Oral Maxillofac Implants* 2008;23:525-530.
24. Oh JS, Kim SG, Lim SC, Ong JL. A comparative study of two noninvasive techniques to evaluate implant stability: Periotest and Osstell Mentor. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2009;107:513-518.

25. Sennerby L, Andersson P, Pagliani L, Giani C, Moretti G, Molinari M, Motroni A. Evaluation of a Novel Cone Beam Computed Tomography Scanner for Bone Density Examinations in Preoperative 3D Reconstructions and Correlation with Primary Implant Stability. *Clin Implant Dent Relat Res* 2015;17:844-853.