Received:
15 May 2018

Revised:
20 August 2018

Accepted:
23 August 2018

<https://doi.org/10.1259/bjr.20180437>

Cite this article as:

Nicolielo LFP, Van Dessel J, van Lenthe GH, Lambrichts I, Jacobs R. Computer-based automatic classification of trabecular bone pattern can assist radiographic bone quality assessment at dental implant site. *Br J Radiol* 2018; **91**: 20180437.

FULL PAPER

Computer-based automatic classification of trabecular bone pattern can assist radiographic bone quality assessment at dental implant site

¹LAURA FERREIRA PINHEIRO NICOLIELO, DDS, MSc, ¹JEROEN VAN DESSEL, MSc, ²G. HARRY VAN LENTHE, MSc, PhD, ³IVO LAMBRICHTS, DDS, MSc, PhD and ^{1,4}REINHILDE JACOBS, DDS, MSc, PhD, Dr Hc

¹Department Imaging & Pathology, OMFS-IMPATh research group, KU Leuven and Oral and Maxillofacial Surgery, University Hospitals Leuven, Leuven, Belgium

²Department of Mechanical Engineering, Biomechanics Section, Leuven, Belgium

³Morphology Group, Biomedical Research Institute, Hasselt University, Diepenbeek, Belgium

⁴Department of Dental Medicine, Karolinska Institutet, Huddinge, Sweden

Address correspondence to: Ms Laura Ferreira Pinheiro Nicolielo
E-mail: laura.nicolielo@kuleuven.be

Objective: To develop and validate an automated classification method that determines the trabecular bone pattern at implant site based on three-dimensional bone morphometric parameters derived from CBCT images.

Methods: 25 human cadaver mandibles were scanned using CBCT clinical scanning protocol. Volumes-of-interest comprising only the trabecular bone of the posterior regions were selected and segmented for three-dimensional morphometric parameters calculation. Three experts rated all bone regions into one of the three trabecular pattern classes (sparse, intermediate and dense) to generate a reference classification. Morphometric parameters were used to automatically classify the trabecular pattern with linear discriminant analysis statistical model. The discriminatory power of each morphometric parameter for automatic classification was indicated and the accuracy compared to the reference classification. Repeated-measures analysis of variances were used to statistically compare morphometric indices between the three classes. Finally, the outcome of the automatic classification was evaluated against a subjective classification performed independently by four different observers

Results: The overall correct classification was 83% for quantity-, 86% for structure-related parameters and 84% for the parameters combined. Cross-validation showed a 79% model prediction accuracy. Bone volume fraction (BV/TV) had the most discriminatory power in the automatic classification. Trabecular bone patterns could be distinguished based on most morphometric parameters, except for trabecular thickness (Tb.Th) and degree of anisotropy (DA). The interobserver agreement between the subjective observers was fair (0.25), while the test-retest agreement was moderate (0.46). In comparison with the reference standard, the overall agreement was moderate (0.44).

Conclusion: Automatic classification performed better than subjective classification with a prediction model comprising structure- and quantity-related morphometric parameters.

Advances in knowledge: Computer-aided trabecular bone pattern assessment based on morphometric parameters could assist objectivity in clinical bone quality classification.

INTRODUCTION

Bone quality assessment prior implant placement is an important step to predict treatment prognosis. For many years, the ideal implant site was solely associated with primary implant stability linked to bone density and quantity. Thanks to the continuous improvement of implants' surface and a better understanding of implant osseointegration mechanism, vascularization of alveolar bone has become an important factor related to long-term implant

survival. While a well-vascularized bone can promote faster peri-implant healing,^{1,2} compact bone with small trabecular spaces and sclerotic areas could indicate poor vascularization and a higher risk of implant failure.²⁻⁶ Because bone vascularization cannot be directly assessed, one should look to the medullar area of the bone.⁶

Between the methods to assess bone quality, radiographic evaluation is certainly an important preoperative tool to

assist tactile perception during preparation of implant bed. This evaluation, is frequently based on the subjective assessment of cortical thickness and medullar bone space using two-dimensional (2D) conventional radiographs. Nevertheless, it often leads to discrepancies between clinicians, what in turn makes comparisons across studies difficult.^{7,8}

As a three-dimensional (3D) structure, bone architecture cannot be fully visualized on conventional 2D radiographs.⁹ With the rapid advancement of radiographic technology, cone-beam CT (CBCT) scans became an attractive method for implant planning, especially in cases of complex anatomy or risk factor. The full potential of the obtained 3D information, however, is in most cases not entirely exploited and bone quality radiographic evaluation often remains based on subjective 2D measurements and visual judgement. Recently, morphometric bone parameters derived from CBCT scans have been validated for standardized trabecular structure assessment by comparison with the gold-standard histomorphometry,¹⁰ micro-CT^{11–13} and clinical multislice CT alternative.^{12,13} High-resolution CBCT scans showed accurate visualization of the trabecular network in the mandible.^{12,13} These morphometric bone parameters can be automatically and operator-independent calculated, and comprise relevant aspects for bone quality evaluation—namely quantity and structure—which are difficult to visually evaluate.

Therefore, the aim of the present study was to develop and validate an automatic method to assist bone quality classification at the implant site based on 3D morphometric characteristics of the trabecular bone. The efficiency of this computer-based classification was then compared with the traditional subjective evaluation performed by oral radiologists.

METHODS AND MATERIALS

Data acquisition

25 Caucasian adult human mandibles (16 males and 9 females) were obtained from the Anatomy Department of the University of Hasselt, Diepenbeek, Belgium and approved for research by the medical bioethics committee of the KU Leuven, Leuven, Belgium (s55619). Each mandible was scanned with a NewTom VGi evo CBCT (QR Verona, Verona, Italy) using a clinical scanning protocol (125 μ m) containing the entire mandible in the field of view (10 $\times$ 5 cm) and with the occlusal plane parallel to the floor. The tube voltage was fixed at 110 kV, while the tube current was modulated to reduce the dose yet maintain the image quality. Anatomical structures (tongue and skin) made from Mix-D were placed around the mandible to simulate soft tissue radiation attenuation.¹⁴

Image processing & quantification of morphometric parameters

The DICOM images with isotropic voxel size of 125 μ m were imported in CT-Analyser (Bruker, Kontich, Belgium) whereafter the posterior part of the mandible was divided per tooth position (premolar and molar region), resulting in a total of 100 bone regions with an average volume of 1507.7 $\pm$ 821.7 mm³. Within each region, the trabecular bone in the

consecutive slices was segmented using the computer-suggested bone threshold and morphometric parameters were calculated following a previously described methodology.^{12,13} Figure 1 shows an overview of the image processing steps prior morphometric analysis implemented in CT-Analyser. Routinely used morphometric indices were calculated following the recommendations of the American Society for Bone and Mineral Research.¹⁵ Bone volume fraction (BV/TV in %) is seen as the main parameter to evaluate bone quantity as it indicates the proportion of mineralized bone tissue. Bone surface density (BS/TV in mm²/mm³) and the ratio of bone surface to volume (BS/BV in mm²/mm³) are useful parameters for characterizing the complexity of bone structures. Parameters such as trabecular separation (Tb.Sp in mm), trabecular thickness (Tb.Th in mm) and trabecular number (Tb.N in mm⁻¹) provide information on the spatial distribution of the bone, which enables the contribution of microstructure to bone strength to be assessed.¹⁶ Connectivity density (Conn.Dn in mm⁻³) represents the trabeculae connections divided by the total volume. Trabecular pattern factor (Tb.Pf in mm⁻¹) calculates an index of relative connectivity or isolated disconnected structures of the total bone surface. Structure model index (SMI) indicates the relative prevalence of rod-like and plate-like trabeculae. An ideal trabecular plate, cylinder and sphere have SMI values of respectively 0, 3 and 4. Negative values indicate a more concave or closed structure; positive values indicate a more convex and open structure. Fractal dimension (FD) is an indicator of trabecular complexity. Higher the FD, the more the morphological complexity at the ultrastructural level.¹⁷ Degree of anisotropy (DA) describes the preferential alignment of the bone trabecular structure. Values higher than one represents a highly-oriented structure whereas equals to one represents an isotropic structure without a preferred orientation.¹⁸

Automatic trabecular bone classification

Three observers with expertise in oral implant and dentomaxillofacial radiology (LFPN, JVD and RJ) classified together the 100 bone regions in three classes: a sparse class was assigned to regions with very large medullar spaces containing few trabeculae (hollow bone); intermediate class was given to regions with medium to large trabecular spaces; and dense regions were characterized by very close trabecular spaces (Figure 2). Classifications were based on visualization of the full CBCT images of each tooth region, previously selected for image processing. The images were visualized in a dark room on a radiological screen Barco MDRC-2221 (Barco, Kortrijk, Belgium) with a 54 cm diagonally viewable size and 1600 $\times$ 1200 pixels. The experts were able to deliberately scroll through the slices until an overall consensus was reached. This joint classification served as reference standard to feed into a Linear Discriminant Analysis (LDA). This statistical model searches for a linear combination of morphometric parameters that best separates the trabecular bone in three types. The strength of the canonical correlation (cc) in the structure matrix was used to indicate the discriminatory power of each morphometric parameter for trabecular pattern classification. A repeated-measures analysis of variance was used to compare

Figure 1. Overview of the image processing steps for each class of trabecular pattern. Only the trabecular bone, excluding teeth root and alveolar canal, was selected in the coronal view (second column) and saved as a volume of interest (third column). Trabecular bone was segmented based on histogram selection (fifth column). The computer-suggested threshold value was visually reassessed in order to give a perfect overlap with the original image. The segmented images were subsequently smoothed using a Gaussian filter with a radius size of one voxel ($125\ \mu\text{m}^3$) (sixth column). ROI, region of interest; VOI, volume of interest.

morphometric indices between the three classes. Mean and standard deviations of each parameter for the three trabecular pattern classes were reported. Leave-one-out cross-validation was used to assess model prediction performance and how the results of LDA will generalize to an independent data set. All statistical tests were performed in IBM SPSS Statistics (IBM corp., New York, USA).

Subjective trabecular bone classification

After reading a printed instruction, four observers with 4 to 6 years' experience in dentomaxillofacial radiology visually classified the trabecular pattern using the same methodology

described for the experts. Additionally, five randomly selected scans were duplicated to assess misclassification of the same region. Evaluators were able to use the CBCT scan as much as necessary to make a conclusive decision. One month later, trabecular pattern classification was repeated and the Cohen's κ was calculated for each observer to assess the general test-retest reliability. The inter-rater reliability was assessed by Fleiss κ and the validity of the subjective classification for each examiner was assessed by comparing them with the reference standard classification. Finally, their ratings were compared with the computer-based classification.

Figure 2. Three-dimensional models of three classes of trabecular pattern in the posterior regions of the mandible.

RESULTS

Automatic trabecular bone classification

The overall correct classification was 83% for quantity-, 86% for structure-related parameters and 84% for the parameters combined (Table 1). The highest accuracy was achieved for the sparse bone class (100%), followed by the intermediate (92%) and dense bone (74%). Cross-validation showed a 79% model prediction accuracy. Morphometric parameters were ranked according to distinctive importance: BV/TV ($cc = 0.74$), Tb.N ($cc = 0.71$), Tb.Pf ($cc = -0.65$), FD ($cc = 0.65$), Tb.Sp ($cc = 0.61$),

SMI ($cc = 0.60$), BS/TV ($cc = -0.59$), Conn.Dn ($cc = -0.27$), BS/BV ($cc = 0.15$), Tb.Th ($cc = -0.07$) and DA ($cc = -0.04$). Variables with stronger canonical correlations can be considered more important for the performance of the given discriminant model. BV/TV accounted for 100% of variance within the quantity-related model. Figure 3 shows differentiating bone type limits with 95% confidence intervals. There were statistically significant differences ($p < 0.05$) between the three classes for all bone parameters, except for Tb.Th and DA. These cut-off values differentiated between visual distinctive sparse, intermediate and dense bone regions. Sparse bone regions were associated with a lower bone volume density ($\downarrow$ BV/TV) a lower bone surface density ($\downarrow$ BS/TV) but higher specific surface ($\uparrow$ BS/BV), described by a decreased trabecular complexity ($\uparrow$ SMI; $\downarrow$ FD), wide-spaced ($\uparrow$ Tb.Sp; $\downarrow$ Tb.N) and less connected trabeculae ($\uparrow$ Tb.Pf; $\downarrow$ Conn.Dn), while for dense bone it was the exact opposite for all parameters.

Subjective trabecular bone classification

The interobserver agreement between the four observers was 0.25 (fair), while the test-retest agreement was 0.46 (ranging from fair 0.21 to moderate 0.57). In comparison with the reference standard, the overall agreement was 0.44 (ranging from fair 0.24 to moderate 0.60).

DISCUSSION

Although multiple subjective classification schemes and analytical methods exist to evaluate bone quality prior to implant surgery, none of these methods provide a standardized follow-up nor are they validated as prognostic test.^{7,19,20} In the present study, an automatic computer-aided method was used to assist classification of trabecular bone pattern based on 3D morphometric parameters derived from CBCT images of alveolar regions. This computer-based process showed a twofold higher accuracy in predicting trabecular bone pattern compared to a visual classification performed by oral radiologists. Computer-aided

Table 1. Prediction results of the trabecular pattern classification using linear discriminant analysis

	Predicted group membership (%)		
	Sparse ($n = 11$)	Intermediate ($n = 51$)	Dense ($n = 38$)
Quantity-related parameters			
Sparse	90.9	9.1	0
Intermediate	2.0	93.7	4.3
Dense	0	36.8	63.2
Structure-related parameters			
Sparse	100.0	0	0
Intermediate	3.9	92.2	3.9
Dense	0	26.3	73.7
All parameters combined			
Sparse	90.9	9.1	0
Intermediate	3.9	90.2	5.9
Dense	0	26.3	73.7

Figure 3. Mean and standard deviations of quantity- and structure-related morphometric parameters for the three trabecular pattern classes. The classes were statistically significant different for all parameters besides Tb.Th and DA. S, sparse; I, intermediate, D, dense.

applications of structural pattern recognition are already often used in clinical radiological applications, such as screening for cervical cancer, breast tumors and cardiovascular diseases.^{21–23} Pairing machine learning expertise with a radiologist, whether it is through an imaging platform, could help prediction of bone quality, augment the consenting process with higher expected implant treatment outcome, and reduce the cost of multiple expert diagnostic opinions.

Evidence concerning accuracy of currently used radiographic methods for bone quality assessment is scarce. Previous studies

have classified bone in two, three or four bone types suggesting that there is no overall consensus in how many classes bone quality should be distinguished in order to help predicting implant survival.^{7,24} From a clinical point of view, oral implant surgeons want to avoid extremities. Sparse bone may hamper primary stability,²⁵ while compact bone with reduction of trabecular spaces may show impaired vascularization.²⁶ The ideal bone for implant placement lies somewhere in between these two types. This intermediate type is, however, more difficult to visually differentiate,^{8,27,28} especially if trabecular bone structure is not homogeneous in a particular dental implant site. In this context, Lindh et al.¹⁹ showed that 2D radiographic assessment of trabecular pattern in the jaw bone was more reliable when using a classification with three classes than with four classes from Lekholm & Zarb index, which is based on schematic drawings of homogeneous trabecular network.¹⁹ This complexity becomes even higher when the bone structure is analyzed in 3D. Differently from 2D images, 3D visualization may display an association of more than one trabecular pattern in a particular implant region that will decrease pattern recognition and variable interaction. Consequently, our subjective evaluation showed lower reliability when compared with traditional 2D evaluation.¹⁹

Since clinical quantification of morphometric parameters became feasible with an adequate CBCT scanner and protocol,^{12,13,29} the 3D information of the trabecular bone structure could help objective classification of bone type. The present results indicate that the trabecular regions could be automatically categorized by specific morphometric parameters. Structural parameters (Tb.N, Tb.Sp, FD, Tb.Pf, SMI, Conn.Dn, DA, BS/BV) showed to be as important as quantity-related parameters (BV/TV, BS/TV, Tb.Th) for the bone type prediction.¹² However, the classification of sparse bone type reached 100% when considering structure-related parameters alone. The most difficult class to predict was dense bone, even quantity-related parameters (63%) were not able to estimate it better the correct class compared to structure-related parameters (74%). Still, all parameters combined did not performed better than structural parameters alone. Although more parameters give more information about the data, a complex model with more parameters can cause overfitting due to high variance of the parameters.³⁰

BV/TV accounted for 100% of the variance within the prediction model. This can be explained by the fact that Tb.Th was not different between the bone types (Figure 3) and BS/TV that is closely linked with BV/TV.³¹ Also some structural-related parameters contributed little to the class prediction, including Conn.Dn, BS/BV and DA. Interestingly, these parameters have been shown to be closely related to mechanical bone properties,^{32–34} which may indicate that more sparse structures are not always associated with poor mechanical properties and vice-versa. This is in agreement with previous studies on *in vivo* and *ex vivo* jaw bone biopsies that found a dependency of bone quality on BV/TV, Tb.Pf, Tb.N Tb.Sp and SMI and a less influence from Tb.Th.^{35,36}

Computer algorithms make use of the various parameters to find high dimensional interactions between multiple data points, that can provide the optimal solution.³⁷ These algorithms work as statistical models recognizing subgroups with same patterns in the full data (clustering) or using a specific clinical information to make predictions (supervised learning).³⁸ The LDA belongs to the latter and builds a predictive model based on linear combinations of features of a known dataset that will be used to maximize separation between classes. Among other classification methods, such as logistic regression, LDA is more robust because requires continuous and normally distributed data, while performing better with small sample sizes.

Despite the clear advantage of computer-aided classifications, there are however also a number of limitations. First, LDA techniques require a gold-standard set of predictor variables to accurately classify groups. Currently, no objective ground truth in bone quality type exists. We have opted for a classification generated by experts' combined responses, which may serve as reasonable reference standard.^{39,40} Secondly, the groups were unequal in sample size, of the 100 bone regions only 11 sparse zones were found. LDA priors were therefore based on group sizes instead of equal groups. Future studies with larger sample sizes may help overcome this problem. Thirdly, bone mineral density is also an important parameter to determine bone strength and quality. This index could not

be taken into account, as grey values on CBCT do not correspond with multislice CT derived Hounsfield units needed to predict bone mineral density.^{41,42} Lastly, although several variables related to bone structure and quantity appeared as significant predictors in LDA model, future work is needed to establish their direct clinical impact in implant treatment outcome.

The present method was able to remove the subjectivity in evaluating trabecular pattern using computer-aided image processing and categorization using morphometric bone parameters. This could be a step forward in the development of a more predictable and standardized bone quality evaluation techniques, which eventually could be incorporated in implant planning software's and in the computer-aided design and manufacture of implant prosthetics.

ACKNOWLEDGMENT

This research was supported by Coordination for the Improvement of Higher Education Personnel (CAPES) program Science without borders from the Brazilian government (BEX 9419/13-6). Jeroen Van Dessel is a Research Foundation Flanders (FWO) research fellow (11.ZU.117N). The authors are thankful to Omar El Mahraoui, Dr Yan Huang, Dr Mariana Quirino Silveira Soares and Dr Karla de Faria Vasconcelos for their help with the subjective observations.

REFERENCES

1. Davies JE. Understanding peri-implant endosseous healing. *J Dent Educ* 2003; **67**: 932–49.
2. Laroche M. Intraosseous circulation from physiology to disease. *Joint Bone Spine* 2002; **69**: 262–9. doi: [https://doi.org/10.1016/S1297-319X\(02\)00391-3](https://doi.org/10.1016/S1297-319X(02)00391-3)
3. Quirynen M, Gijbels F, Jacobs R. An infected jawbone site compromising successful osseointegration. *Periodontol* 2000 2003; **33**: 129–44. doi: <https://doi.org/10.1046/j.0906-6713.2002.03311.x>
4. Madrid C, Sanz M. What impact do systemically administrated bisphosphonates have on oral implant therapy? A systematic review. *Clin Oral Implants Res* 2009; **20**(Suppl 4): 87–95. doi: <https://doi.org/10.1111/j.1600-0501.2009.01772.x>
5. Trisi P, Berardini M, Falco A, Podaliri Vulpiani M, Perfetti G. Insufficient irrigation induces peri-implant bone resorption: an in vivo histologic analysis in sheep. *Clin Oral Implants Res* 2014; **25**: 696–701. doi: <https://doi.org/10.1111/clr.12127>
6. Simons WF, De Smit M, Duyck J, Coucke W, Quirynen M. The proportion of cancellous bone as predictive factor for early marginal bone loss around implants in the posterior part of the mandible. *Clin Oral Implants Res* 2015; **26**: 1051–9. doi: <https://doi.org/10.1111/clr.12398>
7. Ribeiro-Rotta RF, Lindh C, Pereira AC, Rohlin M. Ambiguity in bone tissue characteristics as presented in studies on dental implant planning and placement: a systematic review. *Clin Oral Implants Res* 2011; **22**: 789–801. doi: <https://doi.org/10.1111/j.1600-0501.2010.02041.x>
8. Fu MW, Fu E, Lin FG, Chang WJ, Hsieh YD, Shen EC. Correlation Between Resonance Frequency Analysis and Bone Quality Assessments at Dental Implant Recipient Sites. *Int J Oral Maxillofac Implants* 2017; **32**: 180–7.
9. Bouxsein ML, Boyd SK, Christiansen BA, Guldberg RE, Jepsen KJ, Müller R. Guidelines for assessment of bone microstructure in rodents using micro-computed tomography. *J Bone Miner Res* 2010; **25**: 1468–86. doi: <https://doi.org/10.1002/jbmr.141>
10. Huang Y, Dessel JV, Depypere M, EzEldeen M, Iliescu AA, Santos ED, Van Dessel J, Dos SE, et al. Validating cone-beam computed tomography for peri-implant bone morphometric analysis. *Bone Res* 2014; **2**: 14010. doi: <https://doi.org/10.1038/boneres.2014.10>
11. Kim JE, Yi WJ, Heo MS, Lee SS, Choi SC, Huh KH. Three-dimensional evaluation of human jaw bone microarchitecture: correlation between the microarchitectural parameters of cone beam computed tomography and micro-computer tomography. *Oral Surg Oral Med Oral Pathol Oral Radiol* 2015; **120**: 762–70. doi: <https://doi.org/10.1016/j.oooo.2015.08.022>
12. Van Dessel J, Nicolielo LF, Huang Y, Slagmolen P, Politis C, Lambrichts I, et al. Quantification of bone quality using different cone beam computed tomography devices: Accuracy assessment for edentulous human mandibles. *Eur J Oral Implantol* 2016; **9**: 411–24.
13. Van Dessel J, Nicolielo LF, Huang Y, Coudyzer W, Salmon B, Lambrichts I, et al. Accuracy and reliability of different cone beam computed tomography (CBCT) devices for structural analysis of alveolar bone in comparison with multislice CT and micro-CT. *Eur J Oral Implantol* 2017; **10**: 95–105.
14. Oenning AC, Salmon B, Vasconcelos KdeF, Pinheiro Nicolielo LF, Lambrichts I,

- Sanderink G, et al. DIMITRA paediatric skull phantoms: development of age-specific paediatric models for dentomaxillofacial radiology research. *Dentomaxillofac Radiol* 2018; **118**: 20170285. doi: <https://doi.org/10.1259/dmfr.20170285>
15. Dempster DW, Compston JE, Drezner MK, Glorieux FH, Kanis JA, Malluche H, et al. Standardized nomenclature, symbols, and units for bone histomorphometry: a 2012 update of the report of the ASBMR Histomorphometry Nomenclature Committee. *J Bone Miner Res* 2013; **28**: 2–17. doi: <https://doi.org/10.1002/jbmr.1805>
 16. Klintström E, Klintström B, Pahr D, Brismar TB, Smedby Ö, Moreno R. Direct estimation of human trabecular bone stiffness using cone beam computed tomography. *Oral Surg Oral Med Oral Pathol Oral Radiol* 2018; **126**: 72–82. doi: <https://doi.org/10.1016/j.oooo.2018.03.014>
 17. Zeytinoglu M, İlhan B, Dünder N, Boyacıoglu H. Fractal analysis for the assessment of trabecular peri-implant alveolar bone using panoramic radiographs. *Clin Oral Investig* 2015; **19**: 519–24. doi: <https://doi.org/10.1007/s00784-014-1245-y>
 18. Bruker-MicroCT. Bruker Micro - Ct AcademyBruker Micro-CT Academy. *Bruker Micro-CT Acad* 2015; **2**: 1–2.
 19. Lindh C, Petersson A, Rohlin M. Assessment of the trabecular pattern before endosseous implant treatment: diagnostic outcome of periapical radiography in the mandible. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1996; **82**: 335–43.
 20. Ribeiro-Rotta RF, Lindh C, Rohlin M. Efficacy of clinical methods to assess jawbone tissue prior to and during endosseous dental implant placement: a systematic literature review. *Int J Oral Maxillofac Implants* 2007; **22**: 289–300.
 21. Yassin NIR, Omran S, El Houbay EMF, Allam H. Machine learning techniques for breast cancer computer aided diagnosis using different image modalities: A systematic review. *Comput Methods Programs Biomed* 2018; **156**: 25–45. doi: <https://doi.org/10.1016/j.cmpb.2017.12.012>
 22. Torheim T, Malinen E, Hole KH, Lund KV, Indahl UG, Lyng H, et al. Autodelineation of cervical cancers using multiparametric magnetic resonance imaging and machine learning. *Acta Oncol* 2017; **56**: 806–12. doi: <https://doi.org/10.1080/0284186X.2017.1285499>
 23. Shameer K, Johnson KW, Glicksberg BS, Dudley JT, Sengupta PP. Machine learning in cardiovascular medicine: are we there yet? *Heart* 2018; **104**: 1156–64. doi: <https://doi.org/10.1136/heartjnl-2017-311198>
 24. Lindh C, Oliveira GH, Leles CR, do Carmo Matias Freire M, Ribeiro-Rotta RF. Bone quality assessment in routine dental implant treatment among Brazilian and Swedish specialists. *Clin Oral Implants Res* 2014; **25**: 1004–9. doi: <https://doi.org/10.1111/clr.12221>
 25. Merheb J, Temmerman A, Rasmusson L, Kübler 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; **18**: 253–60. doi: <https://doi.org/10.1111/cid.12290>
 26. Mikami T, Miake Y, Bologna-Molina R, Takeda Y. Ultrastructural analyses of alveolar bone in a patient with osteomyelitis secondary to osteopetrosis: a review of the literature. *J Oral Maxillofac Surg* 2016; **74**: 1584–95. doi: <https://doi.org/10.1016/j.joms.2016.02.016>
 27. Trisi P, Rao W. Bone classification: clinical-histomorphometric comparison. *Clin Oral Implants Res* 1999; **10**: 1–7.
 28. Norton MR, Gamble C. Bone classification: an objective scale of bone density using the computerized tomography scan. *Clin Oral Implants Res* 2001; **12**: 79–84. doi: <https://doi.org/10.1034/j.1600-0501.2001.012001079.x>
 29. Panmekiate S, Ngonphloy N, Charoenkarn T, Faruangsang T, Pauwels R. Comparison of mandibular bone microarchitecture between micro-CT and CBCT images. *Dentomaxillofac Radiol*. 2015; **44**.
 30. Claeskens G, Hjort NL. Model selection and model averaging. *J App Stat* 2008; **37**: 1419–20.
 31. Parkinson IH, Fazzalari NL. Interrelationships between structural parameters of cancellous bone reveal accelerated structural change at low bone volume. *J Bone Miner Res* 2003; **18**: 2200–5. doi: <https://doi.org/10.1359/jbmr.2003.18.12.2200>
 32. Oravec D, Kim W, Flynn MJ, Yeni YN. The relationship of whole human vertebral body creep to geometric, microstructural, and material properties. *J Biomech* 2018; **73**: 92–8. doi: <https://doi.org/10.1016/j.jbiomech.2018.03.021>
 33. Kim DG, Shertok D, Ching Tee B, Yeni YN. Variability of tissue mineral density can determine physiological creep of human vertebral cancellous bone. *J Biomech* 2011; **44**: 1660–5. doi: <https://doi.org/10.1016/j.jbiomech.2011.03.025>
 34. Kersh ME, Zysset PK, Pahr DH, Wolfram U, Larsson D, Pandy MG. Measurement of structural anisotropy in femoral trabecular bone using clinical-resolution CT images. *J Biomech* 2013; **46**: 2659–66. doi: <https://doi.org/10.1016/j.jbiomech.2013.07.047>
 35. Ribeiro-Rotta RF, de Oliveira RC, Dias DR, Lindh C, Leles CR. Bone tissue microarchitectural characteristics at dental implant sites part 2: correlation with bone classification and primary stability. *Clin Oral Implants Res* 2014; **25**: e47–. doi: <https://doi.org/10.1111/clr.12046>
 36. Lee JH, Kim HJ, Yun JH. Three-dimensional microstructure of human alveolar trabecular bone: a micro-computed tomography study. *J Periodontal Implant Sci* 2017; **47**: 20–9. doi: <https://doi.org/10.5051/jpis.2017.47.1.20>
 37. Murphy KP. What and why? In: Murphy K. P, ed. *Machine learning: a probabilistic perspective*. Cambridge, UK: MIT Press; 2012. pp. 1–3.
 38. Wang S, Summers RM. Machine learning and radiology. *Med Image Anal* 2012; **16**: 933–51. doi: <https://doi.org/10.1016/j.media.2012.02.005>
 39. Hripcsak G, Wilcox A, Standards R. Judges, and Comparison Subjects. *J Am Med Informatics Assoc* 2002; **9**: 1–15.
 40. Alonso MB, Vasconcelos TV, Lopes LJ, Watanabe PC, Freitas DQ. Validation of cone-beam computed tomography as a predictor of osteoporosis using the Klemetti classification. *Braz Oral Res* 2016; **30**. doi: <https://doi.org/10.1590/1807-3107BOR-2016.vol30.0073>
 41. Pauwels R, Nackaerts O, Bellaiche N, Stamatakis H, Tsiklakis K, et al. Variability of dental cone beam CT grey values for density estimations. *Br J Radiol* 2013; **86**: 20120135. doi: <https://doi.org/10.1259/bjr.20120135>
 42. Nackaerts O, Maes F, Yan H, Couto Souza P, Pauwels R, Jacobs R. Analysis of intensity variability in multislice and cone beam computed tomography. *Clin Oral Implants Res* 2011; **22**: 873–9. doi: <https://doi.org/10.1111/j.1600-0501.2010.02076.x>