1	Effects of Buccal Thickness Augmentation on Bone Remodeling after Maxillary
2	Anterior Implantation
3	Keke Zheng ¹ , Nobuhiro Yoda ² , Junning Chen ³ , Zhipeng Liao ¹ , Jingxiao Zhong ¹ , Shigeto Kovama ⁴ Christopher Peck ⁵ Michael Swain ¹ Keiichi Sasaki ² and Qing Li ^{*,1}
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6 7	¹ School of Aerospace, Mechanical and Mechatronic Engineering, The University of Sydney, NSW 2006, Australia
8 9	 ² Division of Advanced Prosthetic Dentistry, Tohoku University Graduate School of Dentistry, 4-1, Seiryo-machi, Aoba-ku, Sendai, Miyagi, 9808575, Japan
10 11	³ College of Engineering, Mathematics, and Physical Sciences, University of Exeter, EX4 4QF United Kingdom
12 13	⁴ Maxillofacial Prosthetics Clinic, Tohoku University Hospital, 1-1, Seiryo-machi, Aoba-ku, Sendai, Miyagi, 9808575, Japan
14 15	⁵ Faculty of Dentistry, The University of Sydney, Sydney, NSW, 2006, Australia
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24 Abstract

25 The biomechanics associated with buccal bone thickness (BBT) augmentation remains 26 poorly understood, as there is no consistent agreement in the adequate BBT to avoid overloading resorption or over-augmenting surgical difficulty. This study utilizes longitudinal 27 28 clinical image data to establish a self-validating time-dependent finite element (FE) based 29 remodeling procedure to explore the effects of different buccal bone thicknesses on long-term 30 bone remodeling outcomes *in silico*. Based upon the clinical computed tomography (CT) scans, a patient-specific heterogeneous FE model was constructed to enable virtual BBT 31 32 augmentation at four different levels (0.5, 1.0, 1.5 and 2.0 mm), followed by investigation into 33 the bone remodeling behavior of the different case scenarios.

34 The findings indicated that although peri-implant bone resorption decreased with 35 increasing initial BBT from 0.5mm to 2mm, different levels of the reduction of bone loss was 36 associated with the amount of bone augmentation. In the case of 0.5 mm BBT, overloading 37 resorption was triggered during the first 18 months, but such bone resorption was delayed when the BBT increased to 1.5 mm. It was found that when the BBT reached a threshold thickness 38 39 of 1.5 mm, the bone volume can be better preserved. This finding agrees with the consensus in 40 dental clinic, in which 1.5mm BBT is considered clinically justifiable for surgical requirement 41 of bone graft. In conclusion, this study introduced a self-validating bone remodeling algorithm 42 in silico, and it divulged that the initial BBT affects the bone remodeling outcome significantly, 43 and a sufficient initial BBT is considered essential to assure long-term stability and success of 44 implant treatment.

45 Keywords: Bone remodeling validation, Overloading bone resorption, Buccal bone thickness
46 (BBT), Virtual surgery, Iterative finite element analysis (FEA).

48 **1. Introduction**

49 Along with the popularity of dental implants in prosthodontics, clinical expectation following implant treatment anticipates not only yielding initial stability but also preserving 50 51 long-term bone volume and maintaining a healthy status of peri-implant tissue. This becomes 52 particularly crucial in the case of implantation with significant anatomical restrictions, such as 53 insufficient bone volume and surgically unfavorable positions, which could potentially lead to 54 severe postoperative bone resorption. In the maxillary anterior region, for example, alignment 55 with native teeth is considered a major priority for implantation (1). However, this often leads 56 to unbalance of bone volume between the buccal and patatel sides of the implant (i.e. thinner 57 bone thickness on the buccal side than patatel region). When the initial bone volume is 58 insufficient, part of the buccal bone could gradually reduce as a result of over-loading 59 resorption over time, along with a further high-risk consequence of soft tissue recession (2). For this reason, the critical buccal bone morphology around an implant is widely considered to 60 61 be a primary factor to reduce peri-implant bone resorption (2-6). Although the recent clinical 62 studies (7, 8) reported high survival rates of implants inserted in the anterior maxillary bone 63 augmented with mandibular bone grafts, the actual effect of additional bone volume on the 64 long-term bone remodeling activity remains unclear; and there is limited information available 65 to estimate the minimal bone thickness required from the biomechanical perspective.

66 Clinical CT-based three-dimensional (3D) finite element (FE) models have exhibited 67 compelling advantages in the biomechanical analysis, which allow fairly precisely capturing 68 anatomical features of an individual subject in terms of patient-specific bone morphology and 69 site-dependent heterogeneity of material properties (9, 10). Further, various mechanobiology-70 based bone remodeling algorithms have been proposed for dental implantology, enabling to 71 understand, predict and manipulate bone adaptation associated with a range of clinical 72 scenarios (11-15). Although few FE-based remodeling studies (15, 16) have investigated how 73 peri-implant tissue responds to different insertion angles and loading directions of implants in 74 the anterior maxillary region, none of them has genuinely considered the influence of grafted 75 buccal bone thickness (BBT). In addition, validation of the remodeling prediction against 76 clinical follow-up is largely missing in the previous remodeling studies, though few recent 77 studies have enabled to validate their simulated remodeling results by generating virtual X-Ray 78 against the clinical X-ray images measured at the same time points (11, 12, 17). Note that in 79 comparison with X-ray imaging, computed tomography (CT) imaging is more sophisticated by 80 featuring its 3D nature that provides more thorough non-invasive longitudinal data for 81 validating the simulated bone remodeling process in silico.

82 Considering the above challenges, this study aimed to (1) establish a finite element based bone remodeling procedure to associate the mechanobiological stimulus modeled in silico with 83 84 the change of bone density measured in clinical follow-up in vivo; and (2) explore the effects 85 of different buccal bone thicknesses (BBTs) on long-term outcome of bone remodeling. It is 86 hypothesized that increase of BBT would improve bone remodeling and preservation thanks to 87 alleviation of over-loading resorption. This study demonstrates that the combined in-vivo 88 clinical follow-up and *in-silico* FE remodeling algorithm establishes an effective framework to 89 examine and predict time-dependent activities of bone turnover subject to different clinical 90 options in maxilla, thereby evaluating and enabling surgical planning for the minimal buccal 91 bone required, thus ensuring stability and longevity of implantation treatment.

- 92 **2. Materials and Methods**
- 93 **2.1. Clinical data acquisition and analysis**

In this study, a 52-year-old female was recruited, following the treatment of maxillary right
 incisor fracture in Tohoku University Hospital in Japan. A titanium implant (Osseospeed TX)

96 3.5S, DENTSPLY Implants, Mölndal, Sweden), with a 3.5mm diameter and 13.0mm length, 97 was inserted after a healing period of 8 weeks. The cone-beam (CB) CT scan (3D Accuitomo, 98 MORITA Corp., Kyoto, Japan) was performed at a standardized exposure of 90 kV and 35 mA 99 at 0 month (T0), 6 months (T1), 12 months (T2) and 18 months (T3) after implantation. An 100 initial buccal bone thickness (BBT) was measured and found to be 0.25mm. It is noted that 101 direct loading in the implant region was avoided over the first six months. Since this study 102 focused on biomechanically-driven bone remodeling following the initial healing process, the 103 starting time point (T1) was selected to be month six after implantation. Besides, there was no 104 sign of infection observed around the implant in this experimental course, which allows us to 105 restrict our attention to the biomechanical aspect behind in this study.

106 3D image registration was carried out to quantify the longitudinal changes of bone surface 107 profile and mineral density by using Amira 2016.22 (Zuse Institute Berlin (ZIB), Berlin, 108 Germany). The implant was selected to be the reference geometry because of its rigidity and 109 high contrast. As shown in Fig. 1, the region of interest (ROI) around the implant was divided 110 into four sectors (namely SegB, SegM, SegP, and SegD), starting from the position that is 45° 111 away from either x or y-axis, which prescribed its origin in the center of mass of the implant 112 (Fig. 1b). In each set of CTs, 52 slices that cover the implant region were selected, and thereby 208 ROIs were generated for a specific time point. To characterize the variation in bone mineral 113 114 density (BMD) in the peri-implant area along the axial direction of implant, the variation of 115 greyscale in the ROIs was measured with respect to the distance from the implant neck to the 116 apex. The average voxel intensity (i.e., greyscale) was calculated in the cortical bone region of 117 each slice (at a regular spacing of 0.25 mm along the coronal axis), enabling us to plot the 118 change of pixel value in the axial direction.



120 Fig. 1 Procedure for identification of the region of interest (ROI) and illustration of the orientation in this study: 121 The peri-implant region was covered in the 52 slices (a), four sectors were divided in each slice to represent 122 ROIs in the different directions (b), based upon the coordinates generally accepted in dental clinics.

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2.2 Finite element (FE) modeling

124 The 3D FE models were created for this specific patient based upon the CT scan data obtained at time point T1. ScanIP Ver. 4.3 (Simpleware Ltd, Exeter, UK) was used for 125 segmentation and Rhinoceros 4.0 (Robert McNeel & Associates, Seattle, USA) was used for 126 127 parametrization of the reconstructed models with non-uniform rational B-spline (NURBS) representation. Following the development of the maxilla model with detailed dentition, the 128 129 implant with abutment and screw was modeled in SolidWorks 2015 (SolidWorks Corp, 130 Waltham, MA, USA), as shown in Fig. 2a. In the peri-implant region, the cylindrical ROI 131 described in the previous section was created (Fig. 2b).

132 Using virtual morphological modification in ScanIP, four different buccal bone thicknesses were created by augmenting from the baseline model (T1) to replicate the extent of bone 133

grafting in the buccal bone region, with an increment of 0.5 mm in Rhinoceros. The specific
buccal bone region was determined as the rectangular area covered by the length of the dental
implant and the breadth of the intra-implant-tooth distance (the green square-shaped area in
Fig. 2e).

In this study, site-dependent material heterogeneity was assigned to model the maxillary bone by characterizing the bone density as per localized Hounsfield Unit (HU). This allowed to more precisely capture the anatomic variation of bone density and modulus, which could considerably affect biomechanical responses (Fig. 2c) (9, 11). Teeth and dental implants were assumed to be linear elastic. All the material properties adopted in this study are summarized in Table 1.

A masticatory force was set to be 38.3 N. This value was obtained from the measured force *in vivo* by crushing a peanut through a single implant-supported crown at the maxillary incisor region (18). The load transfer angle was set to be 65° to the long axis of the implant, as measured between the upper and the lower incisor tooth axes in the cast model of the patient (Fig. 2b). Full constraints were prescribed on the sectioned regions that were considered remote from the loading point (Fig. 2d).

Table 1. Material properties adopted in FE models (Yoda et al 2017)

Materials	Young's Modulus (MPa)	Poisson's ratio
Bone	Heterogeneous	0.30
Bone Graft	14,000	0.3
Periodontal ligament (PDL)	Hyperelastic (Marlow)	0.45
Teeth (enamel and dentine)	20,000	0.20

Titanium (Implant, abutment, screw)	110,000	0.35
Ceramic crown	140,000	0.28

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Fig. 2 Procedure for FE model construction: (a) solid models of the maxilla and implant; (b) region of interests (ROIs) in the peri-implant and loading condition: F = 38.3 N, $\alpha = 65$ degrees; (c) site-specific material properties of osseous tissues assigned in terms of Hounsfield Unit (HU) values obtained from the clinical CBCT data through a FORTRAN subroutine in ABAQUS; (d) kinematic boundary conditions; and (e) virtual bone grafting region

158 The final assemblies were exported to ABAQUS 6.13.1 (Dassault Systèmes, Tokyo, Japan) for the FE analysis. An adaptive mesh was generated, and a mesh convergence test was 159 160 conducted to ensure numerical accuracy. The final model comprised of 301,108 10-node 161 quadratic tetrahedral elements, with 9,033,240 degrees of freedoms (DoF). An assumption of complete bone - implant contact (BIC), implying full osseointegration status, was assigned (14, 162 163 19, 20). The implant components, including implant body, screw, abutment, and superstructure 164 were assumed to be perfectly bonded for simplification, as the micromotions between these 165 components were not the primary interest of this study.

166 **2.3. Bone remodeling algorithm**

The FE-based bone remodeling prediction requires the biomechanical responses of sitedependent units (e.g., elements) within the bone by determining the mechanical stimuli generated by external loads. Once the mechanical stimulus deviates to a certain extent from the specific homeostatic level, the bone will respond by adapting its morphology (21, 22). In the literature, the strain energy density (SED) per unit apparent density has been widely accepted as an appropriate mechanical stimulus for bone remodeling of dental bones (22-24), which is defined by

174
$$\Xi = \frac{U}{\rho} \tag{1}$$

where parameters U, ρ and Ξ are the SED (J/cm³), local bone density (g/cm³) and mechanical stimulus (J/g), respectively.

The remodeling algorithm relates the changing rate of the apparent bone density to the differences between mechanical stimulus and physiological threshold K (23). As the mechanical stimulus increases, three phases of remodeling outcomes can be resulted namely; underloading bone resorption, bone equilibrium, bone apposition (25, 26). Note that the greater 181 the mechanical stimulus, the higher the rate of density change, which does not necessarily 182 correlate to the clinical scenarios where severe damage can be caused if loading is excessively 183 higher than a critical value for physiological self-repair in the bone. Therefore, a quadratic term 184 was introduced to the bone apposition phase once the mechanical stimulus exceeds a specific 185 level (24). In summary, the density increment ($\Delta \rho$) over a time interval (Δt) can be calculated 186 as,

$$187 \qquad \Delta \rho = \begin{cases} C_{ap}[\Xi - K(1+s)]\Delta t - C_{or}[\Xi - K(1+s)]^2 \Delta t; & if \ \Xi > K(1+s) \\ 0; & if \ K(1-s) \le \Xi \le K(1+s) \\ C_{ur}[\Xi - K(1-s)]\Delta t; & if \ \Xi < K(1-s) \end{cases}$$
(2)

188 where the reference stimulus K = 0.00036 (J/g) (Lin et al. 2010c) and 2s = 0.2 is the width of the lazy zone doe the dental bones (Rungsiyakull et al. 2011). C_{ap} , C_{or} and C_{ur} are the rate 189 190 constants for bone apposition, overloading resorption and underloading resorption, respectively. 191 All these rate constants were determined by using an inverse identification approach during the 192 model validation against the longitudinal historic data acquired from clinical follow-up, the 193 details of which will be described in the following section. The minimum and maximum densities of bone were set to be 0.7 g/cm³ and 1.9 g/cm³, respectively (Lin et al. 2010c). The 194 195 time step in this study represented 1 month, thereby 48 iterations were set in total here.

The remodeling procedure was implemented through a FOTRAN subroutine (UMAT) in ABAQUS, where the material properties of bone in each element were evaluated as per the user-defined constitutive models. A flowchart that presents the bone remodeling procedure is depicted in Fig. 3. To more appropriately quantify the variations in bone density and mechanical stimulus within each ROIs, their volume average was calculated as:

201
$$\rho = \frac{1}{v} \int_{V} \rho dV \cong \frac{\sum_{e=1}^{n} \rho_{e} v_{e}}{\sum_{e=1}^{n} v_{e}}$$

202
$$\Xi = \frac{1}{V} \int_{V} \Xi dV \cong \frac{\sum_{e=1}^{n} \Xi_{e} V_{e}}{\sum_{e=1}^{n} V_{e}}$$
(3)



Fig. 3 Flowchart of the FE-based bone remodeling algorithm and the procedure of correlation with clinical follow up

208 2.4. Bone remodeling validation

To validate the remodeling outcome, the FE-based virtual CT images were generated from the simulated densities at the time points T1, T2, and T3, respectively. A python program, namely pxyCT was used to convert the simulated results into virtual CTs (12), which were correlated with the clinical follow-up in a quantitative fashion. As aforementioned, the virtual CT stacks were aligned with the corresponding clinical CT images at the same time point. As such, the virtual *in-silico* simulated CTs and real *in-vivo* clinical CTs were compared in the identical ROIs. At each time point, these 208 ROIs were correlated (Fig. 4).

The time-dependent changes of mean grayscale values in these ROIs were calculated based
upon both virtual CT and clinical CT using MATLAB (MathWorks, Inc., Massachusetts, USA).

218 A linear regression analysis was performed by using Graph-Pad Prism 7 (GraphPad Software, Inc. CA,USA) to evaluate the coefficients of determination (R^2) , coefficients of correlation (R)219 and p-values. The R² and R were calculated for assessing the correlation between the simulated 220 221 and clinical data, in terms of the changes in the bone grayscale values in all ROIs at different time points. The *p* values were calculated to test the null hypothesis that the overall slope of 222 223 the fitted line is zero. It should be noted that the linear regression was implemented for any two time periods, e.g., T12 (i.e. from time point T1 to time point T2) and T13 (from T1 to T3), for 224 225 a better clinical relevance (27).

By regulating the bone resorption and apposition rates, one set of remodeling parameters in Eq. (2), which provides the best possible correlation between the grayscale value in the simulated remodeling results and clinical data in all the ROIs, was finally selected. Specifically, C_{ap} , C_{or} and C_{ur} were set to be 5.1 month g/cm⁵, 6000 month³ g/cm⁷ and 5.1 month g/cm⁵, respectively.



Fig. 4 Procedure of validating bone remodeling algorithm against clinical follow-up: firstly, a python program called pxyCT was used to convert the simulated density model (right upper) to a stack of virtual CT images (right lower). To be noted, since only one bone region was focused on, other anatomical structures such as teeth and PDLs, were excluded in this process. Secondly, the same ROIs dividing process (as illustrated in Fig. 1) was

performed on both sets of images in Matlab, to quantify the volume-averaged densities for correlation between
 the real clinical CT (left) and virtual simulated CT images.

238 **3. Results**

3.1. Bone remodeling validation



Fig. 5 Linear regression analysis between the timeframe changes of ROI grayscale in the real clinical CT and
virtual simulated CT, for (a) T12 (T1 to T2) and (b) T13 (T1 to T3).

The correlations between the clinical CT and FE virtual CT images at the two time periods (i.e. T1 to T2 and T1 to T3, respectively) are shown in Fig. 5. As described, the linear regressions between the density changes (%) in ROIs were carried out in both the images sets. Specifically, the R^2 values from the multi-stage remodeling procedure were evaluated to be 0.619 and 0.634 for T12 and T13, respectively, with the *p* values less than 0.001. Therefore, a proper correlation was obtained between the simulated bone remodeling *in silico* and the clinical follow-up *in vivo* (28).

250 **3.2. Images based assessment of bone mineral density**

The contours of simulated bone resorption were compared with the surface model generated from the clinical CT images at time points T1, T2 and T3 (Fig. 6 a-b). By regulating 253 the remodeling parameters for matching the clinical follow-up data, a similar trend of bone 254 resorption was observed between these two sets of data, in which the buccal bone covering the 255 implant neck was seen to resorb from time T2 and continued until almost one-third of the 256 implant was directly exposed at time point T3. More specifically, from the clinical CT results it is observed and quantified that bone resorption started from the neck region then propagated 257 258 towards the apical area of the implant along the axial direction of the implant (Fig. 6c-f). By 259 looking at the buccal and palatal regions of the implant, sector SegB underwent more severe 260 resorption than sector SegP. The buccal bone line (SegB) moved towards the implant apex by 261 1.75mm and 4 mm at T2 and T3, respectively; whereas this movement was only 0.5mm and 262 2mm in the palatal region (SegP). Meanwhile, in the medial (SegM) and distal (SegD) regions, 263 the extent of bone resorption was less than that in SegB and SegP.

264 In contrast to the neck region, bone remodeling around the implant from the body to apex 265 is far milder. Interestingly, the shape of the density variation curve in SegB differs with the 266 others that all have an evident drop in the density. This is due to the fact that the implant was 267 inserted into the position required to align it with the other native teeth, which necessitated the 268 implant to be placed close to the buccal side, making the region SegB mostly cortical bone. In 269 the other regions, the average bone density drops in the cancellous regions (Fig. 6 d-f). The 270 overall distributions of bone density at the different time points exhibit fairly close resemblance 271 between the real clinical CT images and simulated virtual CT images in all these four regions, 272 except that there is a certain delay of the bone resorption rate. In region SegB, the simulated 273 bone resorption progressed to 1.5mm and 3.5mm from the implant neck region at time points 274 T2 and T3, respectively, which differed by around 0.25mm and 0.5mm from the clinical CT 275 data. Considering the overall correlation of the density distributions between the FE virtual CT 276 and clinical CT data, such errors are at an acceptable level.



Fig. 6 Illustrative and quantitative comparison on bone remodeling at the three time points (i.e. T1, T2 and T3)
for both clinical CT and simulated results: the illustrative comparison of the three time points has been conducted
for (a) surface models generated from clinical CT images and (b) contours of density distribution from the

simulated models. Afterward, a quantitative comparison on the bone density distribution curves along the implant
axis was performed in the four specific regions, such as (c) SegB, (d) SegM, (e) SegP and (f) SegD. In each region,
the density distribution around the implant from the neck towards the apex were quantified from the both clinical
(right) and simulated (left) data.

285

3.3. BBT effects on remodeling outcome

286 Since bone grafting allows the surgeon to generate a range of buccal bone thicknesses 287 (BBTs) before implantation, four different BBTs (named as BBT05, BBT10, BBT15, and 288 BBT20, representing 0.5, 1.0, 1.5 and 2.0mm buccal bone thicknesses) were modeled in this 289 study (upper row in Fig. 7a). A palatal-buccal sectional view was selected for comparing the 290 mechanical stimulus and density contours of the buccal and palatal bone areas for these 291 different BBTs. Strain energy density (SED) distributions are provided in the lower row of Fig. 292 7a as an example of mechanical stimuli. From the contour of BBT05 (thickness = 0.5mm), it 293 can be seen that the buccal side generated substantially higher SED than the palatal side, which 294 was associated with the direction of the occlusal force and amount of the bone volume for 295 bearing the occlusal load. As BBT increased, nevertheless, the concentration of SED on the 296 crestal bone region decreased.

297 As shown in Fig. 7b, the density contours as the simulated results of bone remodeling at 298 the four-time points (i.e., months 12, 24, 36 and 48) are presented for the different BBTs. Note 299 that month 6 (T1) was selected to be the initial time point for the remodeling simulation, as the 300 direct loading started only from this time point. For clearer observation of the bone resorption, 301 density was considered to be zero when it fell below 0.1g/cm³ and was displayed in dark gray 302 area. In the original model (BBT05), evident resorption started on the buccal bone in the neck 303 region and propagated along the implant axis direction. However, the resorption plateaued in 304 the both regions after month 24. Meanwhile, the bone resorption on the palatal side appeared 305 to be slower in comparison with the other side from month 24 to month 48. Whilst bone

- 306 apposition was observed in the buccal bone region around the implant body, from month 36 to
- 307 month 48.



309 Fig. 7 The mechanical stimuli in a buccal bone area with different BBTs. (a) FE models (upper row) and the 310 examples of SED distribution (lower row) based upon the simulated bone grafting strategy; (b) cross-sectional 311 images of buccal bone on the implant for investigating the distribution of density in different BBTs.

312 When BBT increased, the overall density contour retained a similar pattern, except for the 313 local area around the implant neck, where a decrease of the resorption rate can be observed on 314 the both buccal and palatal sides in the course from month 6 to month 48. When the BBT was 315 set to be 1.5mm (BBT15), the bone resorption that initiated from the bone-implant contact 316 (BIC) area was restricted from extending to the buccal bone surface. Comparison between 317 BBT05, BBT10 and BBT15, exhibited a similar pattern, but in a larger magnitude, of bone apposition from month 24 to month 48. Interestingly, bone apposition was not seen in BBT20. 318 319 This is due to the fact that the buccal bone region was too thick, and the bone surface is too far 320 away from the loading point, meaning that the load and associated strain energy may not be 321 uniformly distributed across such a thick bone section. Apart from the buccal side, the bone 322 resorption on the palatal side decreased as the BBT increased. Interestingly, it is found that in 323 the regions where bone resorption plateaued, bone apposition was still observed, acting as a 324 barrier to prevent bone resorption from further progression.



Fig. 8 Remodeling progress of (a) SegB, and (b) SegP region over the 48 months.

328 The collective quantification of bone remodeling in regions SegB and SegP are compared 329 for the different BBTs in Fig. 8, because the buccal and palatal regions of the implant attracts the most attention in clinic (27). For the SegB region, the simulated remodeling process developed relatively faster from 6 to 16 months; but such a process appears to become stable in the following months. It is interesting to note that after month 21, the overall density progressively increased till month 48 while the resorption in the SegP region progressed continuously from month 6 to month 21 until the remodeling process was leveled off.

335 Regarding the effect of BBT variation, overall density was seen to substantially increase 336 on the buccal side (SegB) when the BBT increased from 0.5mm to 1.5 mm. However, when 337 BBT reached 2.0 mm, the density decreased. On the opposite side (SegP), the overall density 338 increased as the BBT increased, but no noticeable difference can be seen between BBT15 and 339 BBT20. In other words, an increase in BBT from 0.5mm to 1.5mm successfully decelerated 340 the resorption rate for both the regions; but an increase from 1.5 mm to 2.0 mm led to almost 341 the same trend of remodeling, meaning that there was no significant difference of remodeling 342 progression between BBT15 and BBT20, except that BBT15 has more density increase on the 343 buccal side after month 18. On the opposite region (SegP), a similar trend of bone remodeling 344 was observed to that in SegB, except for the relatively small variation between the different 345 BBTs. In this region, the overall density decreased from BBT05 to BBT15 and became stable 346 without further change between BBT15 and BBT20.

347 **4. Discussion**

Recently, there has been an increasing concern on progressive resorption on the buccal bone above the implant in the anterior maxilla (1, 29-31). Clinically, this consequence may lead to insufficient bone volume for maintaining functionality and esthetics following implantation treatment. In contrast to the other efforts dedicated to investigation specifically into the influence of implant inclinations, little attention has been paid to the effects of buccal bone resorption (BBT) on consequent changes in bone volume and density around an implant so far. Therefore, in this study, a clinically validated bone remodeling algorithm was first
developed for evaluating the long-term remodeling process in a patient-specific fashion by
involving the effects of different BBTs.

357 **4.1. Remodeling outcome**

Although various mechanobiology-driven bone remodeling algorithms have been proposed and utilized for dental implantation analysis (22), the remodeling parameters, especially the rate constants that regulate the overall remodeling progress, vary widely within the literature as they have been derived from different human tissues, patient groups and research methodologies. Therefore, a proper correlation between the remodeling simulation results and corresponding clinical follow-up data is required for validating the bone remodeling algorithm to ensure reliable prediction results.

Compared with the previous studies that focused on specific regions (e.g. the regions with clinical significance) for correlating with clinical data (11, 12), ROIs used in this study were generated by dividing the entire peri-implant region into four representative segments with a specific number of image slices. Considering a slice interval of 0.25mm, 208 ROIs were generated in this study to cover the bone around the whole implant (13mm), which provided more thorough spatial quantification of the remodeling information.

It is noted that in this specific case, buccal bone resorption started from the onset of the remodeling process (Fig. 8a) but decelerated overtime during the remodeling process. In general, two types of bone resorption can be specified, which are associated with underloading or overloading resorptions respectively (24). Crupi et al (2004) found that excessive marginal bone loss correlated well with the presence of overload. Other studies indicated that bone remodeling can be driven by micro-damage induced by a certain level of loading (32). It is noteworthy noting that excessive load generated around implants can impair osseointegration (33), thus decreasing peri-implant bone density and leading to the occurrence of crater-likedefects (34).

According to Eq. (2), underloading resorption initiates when mechanical stimulus Ξ is below the lower threshold K(1 - s), and apposition is triggered when Ξ passes the upper threshold K(1 + s); whereas when Ξ passes a critical upper limit, overloading resorption may take place. As the resorption was originated from the crestal bone region around the screw threads, where the highest SED appeared, the risk of the overloading resorption was high. For this specific case, the initial buccal bone volume was considered insufficient for achieving a proper long-term survivorship of implantation.

387 As shown in Fig. 8, although dramatic bone resorption was observed during the first few 388 months of loading and the resorption rate decreased as time passed. Furthermore, at month 18, 389 bone resorption plateaued, and was followed by bone apposition till month 48. This is due to the fact that when the bone density decreased to a level below 0.1 g/cm³, such region was 390 391 unable to provide mechanical support to the occlusal load. As a consequence, the loading region 392 in buccal bone that withstood the maximum loading from the implant was shifted from the neck 393 to the middle region under the same loading condition; this lower SED was accumulated in the 394 supporting region. Therefore, in this case, the resorption rate decreased as a result of the bone resorption progressed. 395

On the other hand, the bone resorption progressed faster on the buccal side than that on the palatal side, which agrees well with the relevant clinical studies reported in literature (35). The possible causes are attributable to the direction of the applied occlusal load (36) and different initial bone volume available to support the implant. Due to the asymmetry of the bone around the implant axis, the buccal side has less bone in comparison with the palatal side. Thus, the SED distributions in the buccal and palatal regions are asymmetric. Specifically, the buccal region exhibits a higher SED in response to the transverse loading as a result of its lower 403 bone volume relative to the palatal region (Fig. 8a). This is due to the fact that there was less404 bone volume on the buccal side for bearing mechanical loading.

Since SED was considered to be the mechanical stimulus for driving remodeling simulation, the higher SED distributed on the buccal bone due to its less supporting bone volume and the inherent direction of occlusal loading (i.e. towards to the buccal side), faster resorption rate was observed than the other side. Also, such finding directs more attention to the consequence of changing BBTs on remodeling outcomes.

410 **4.2. Effect of BBT on the mechanical stimuli**

411 Since resorption occurred after initial occlusal loading, the presence of sufficient buccal 412 bone volume at implant placement is considered to be one of the essential factors for preventing 413 bone resorption under loading. According to the simulated results, the apportion rate was seen 414 to decrease on the buccal side. This arises because as buccal bone volume increases, the SED 415 concentration decreases as more bone volume is available for withstanding occlusal loads. As 416 a result, the mechanical stimuli in the peri-implant region were found to be lower in the thicker 417 BBT (Fig. 8a), suggesting a significant role played by BBT on redeploying mechanical stimuli 418 in the peri-implant regions. However, from BBT15 to BBT20, bone resorption rates showed 419 the minimal difference in the first 15 months (Fig. 8a). This can be explained by the reduction 420 of the SED magnitude when the BBT reached a certain amount, where the extra bone volume 421 has limited benefit to the alleviation of the SED concentration.

Interestingly, from month 18 onwards, all the four models with the different BBTs experienced bone apposition for the remainder of the period. As shown in Fig. 8b, except for BBT20, evident bone appositions can be seen in the buccal bone above the mid-region of the implant at month 36 and month 48. As the bone apposition started from the buccal surface, a possible explanation can be that the stress caused by the bending moment from the occlusal 427 force was concentrated in this region. Unlike the other three models, BBT20 has an extra bone 428 volume on the buccal side which provided sufficient bending support from the occlusal force. 429 In other words, more bone volume there to withstand stress under the same loading condition 430 reduced the overall stress concentration at the "bending spot", i.e., the region substances major 431 load under bending. Thus, no significant bone apposition occurred for that specific region. In 432 general, when BBT reached 1.5mm, remodeling outcomes were substantially improved in 433 comparison with the original stage, in terms of both bone resorption reduction and bone 434 apposition.

435 **4.3.** Clinical implication and limitations

436 As a pilot study of using a time-dependent FEA procedure to investigate the long-term 437 effect of BBT on the bone remodeling, the present findings were in good agreement with the 438 clinical data available in literature. Through a clinical CBCT analysis of an anterior maxillary 439 implant, Veltri et al. showed that buccal bone resorption occurred in the neck region of the 440 implant (i.e., thin bone area) in most cases (1). They also found that the implant with the 441 greatest bone resorption was associated with a smaller buccal bone volume in the coronal 442 portion and thinner bone, both buccally and marginally. Needless to say, a thicker bone is more 443 ideal for implantation. Clinically, it is well accepted that 1.5mm is a sufficient thickness for the 444 bone augmentation (27). If the native BBT is more than 1.5 mm, the implant placement can be 445 carried out without bone augmentation. Otherwise, it is necessary to perform bone grafting 446 before implantation. The findings in the present study are in good agreement with current 447 clinical consensus that BBT of 1.5 mm appears to be a threshold value for determining the pre-448 surgical bone thickness.

There are some inherent limitations in this patient-based study. First, while the specific patient was modeled to establish a conceptual assessment framework accounting for buccal 451 bone responses, all the interfaces between different tissue/materials were assumed to be fully 452 bonded and osseointegrated completely after a 6 month healing period. This assumption will 453 affect the transfer of occlusal load to the bone around an implant. There is a need to develop a 454 proper algorithm to model the bone-implant contact (BIC) interaction in a time-dependent manner. Second, further follow-up observations and data collection of this patient are still 455 456 needed to obtain more detailed longer-term results of the bone remodeling. Third, the 457 remodeling parameters were obtained for this specific patient and a larger number of patient 458 samples is certainly required to gain broader popularity and confidence on this topic. 459 Nevertheless, these abovementioned factors were beyond the scope of the present paper, further 460 research will help clarify the biomechanical responses induced by implant treatment more 461 realistically.

462 **5.** Conclusions

463 This study developed a computational procedure to assess the effects of buccal bone 464 thickness (BBT) on the bone remodeling outcome in a time-dependent fashion by correlating 465 simulated remodelling *in silico* with the clinical follow-up *in vivo*. The simulated remodeling 466 results of apparent bone density were converted into virtual CT image data and then 467 quantitatively correlated with the corresponding clinical CT data over one and half year 468 duration of clinical follow-up. The strong correlation provided sufficient confidence and 469 credibility for the proposed FE based remodeling algorithm. Importantly, this patient-specific 470 validation approach provided us with a procedural tool to explore individualized bone 471 remodeling outcome for surgical planning. For this particular patient, the simulated results 472 revealed that increasing the initial BBT could decrease the bone resorption in the peri-implant region, and when BBT reached 1.5mm, it is considered to achieve a safe condition for 473 474 implantation surgeries.

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480	
481	Conflict of interest
482	Authors have no conflict of interest concerning the present manuscript.
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