Influence of Implant Positions and Occlusal Forces on Peri-Implant Bone Stress in Mandibular Two-Implant Overdentures: A 3-Dimensional Finite Element Analysis

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The aim of this study was to evaluate and compare the bone stress around implants in mandibular 2-implant overdentures depending on the implant location and different loading conditions. Four 3-dimensional finite element models simulating a mandibular 2-implant overdenture and a Locator attachment system were designed. The implants were located at the lateral incisor, canine, second premolar, and crossed-implant levels. A 150 N unilateral and bilateral vertical load of different location was applied, as was 40 N when combined with midline load. Data for von Mises stress were produced numerically, color coded, and compared between the models for peri-implant bone and loading conditions. With unilateral loading, in all 4 models much higher peri-implant bone stress values were recorded on the load side compared with the no-load side, while with bilateral occlusal loading, the stress distribution was similar on both sides. In all models, the posterior unilateral load showed the highest stress, which decreased as the load was applied more mesially. In general, the best biomechanical environment in the peri-implant bone was found in the model with implants at premolar level. In the crossed-implant model, the load side greatly altered the biomechanical environment. Overall, the overdenture with implants at second premolar level should be the chosen design, regardless of where the load is applied. The occlusal loading application site influences the bone stress around the implant. Bilateral occlusal loading distributes the peri-implant bone stress symmetrically, while unilateral loading increases it greatly on the load side, no matter where the implants are located.

Key Words: overdenture, mandible, implants, locator attachments, bone stress, occlusal load

INTRODUCTION

Prosthetic rehabilitation of a totally edentulous mandible has always been a major challenge for dentists. Edentulous patients, with more or less severe mandibular alveolar bone resorption, often relate functional and psychosocial problems with the use of a conventional denture associated with a lack of stability and denture retention. Currently, the high predictability and survival of dental implants solve these problems, meaning the treatment of a fully edentulous mandible using an implant-retained overdenture has become a routine therapy. Thus, an overdenture retained by 2 or more implants is a highly predictable treatment with implant success and survival rates above 95.5%.1,2 This method also provides high levels of satisfaction, comfort, and quality of life for patients compared with a complete conventional denture.3–6 Furthermore, the old debate about how many implants are necessary to retain mandibular overdentures seems to have been solved. The McGill and York international consensus established that 2 interforaminal location implants are sufficient and are the minimum option to retain an overdenture with a good degree of stability and masticatory function.7,8 The dental literature in recent years has supported this option, with an overwhelming majority of studies supporting the proposal that the 2-implant overdenture has become the preferred choice of treatment for the edentulous mandible.9–15 Most clinical and biomechanical studies choose the interforaminal region, especially at the canine level, as the preferred location for the 2 implants. However, other implant distributions are possible. Bone availability factors may require the clinician to place the implants near the mandibular symphysis (at the lateral incisor level); biomechanical considerations related to the stress transferred to the peri-implant bone and implant/attachment complex during overdenture movements may make it necessary to place implants more distally, at the premolar level, or to combine one anterior and another contralateral posterior. At present there is insufficient scientific evidence available regarding the effect of any of these locations on the...
distribution of stress around implants. The lowest stress is reported when implants are inserted in lateral incisor areas, and this position is recommended, while other studies have found lower stress levels with the implants at the first premolar site compared with lateral incisor and canine sites. This question requires clarification.

On the other hand, after loading and during masticatory functional activities and parafunctional clenching and grinding, complex occlusal forces of different intensity, location, and direction occur. These forces are transmitted to the overdenture, attachment/implant complex, and peri-implant bone. When the stress/strain, transferred to the peri-implant bone as a consequence of the occlusal forces, exceeds the physiological adaptation limits, bone remodeling and resorption processes are initiated, leading to bone loss around the implant. The taking into consideration of the application site, direction, and intensity of the occlusal force required to avoid overload and bone loss becomes a matter of prime consideration for the dentist when carrying out occlusal adjustment of an overdenture. Although under discussion, the bilateral balanced occlusion criteria are normally the recommended occlusal scheme for overdentures. However, empirical clinical practice shows that this is not the case, with a large number of dentists completing a patient’s treatment with an overdenture using other occlusal criteria or random occlusal contact distribution that leads to the predominance of guides or unilateral contacts. Such behavior can change the bone stress/strain distribution and concentration around implants, resulting in bone loss. Several biomechanical studies have tested the effect on peri-implant bone stress of different attachment designs, implant location, and unilateral or bilateral occlusal load characteristics of a mandible overdenture. Most of these studies, with unilateral load, relate higher peri-implant bone stress on the load side compared with the contralateral side and a more balanced distribution with bilateral load. However, this information is not conclusive. With the exception of one study that applies bilateral and unilateral posterior load in 3 different implant positions, there is no single study with sufficient data to clarify and compare the effect on bone stress of unilateral and bilateral loads applied at different points for 2 implants in different positions. More information is needed to provide practitioners with information about the implant and occlusal load locations that favor the best biomechanical environment and thus enable them to make appropriate clinical decisions. In agreement with the aforementioned, the aim of this study was to evaluate and compare the effect on bone stress around implants in mandibular 2-implant overdentures depending on the implant location and occlusal load application sites and to give dentists a comparative insight into the influence of these factors.

**Materials and Methods**

*Finite element models design*

Three-dimensional (3D) finite element models were created to evaluate the bone stress distribution around implants in a mandibular 2-implant overdenture retained by a self-aligning attachment system. An arch structure was modeled to simulate the symphysis and body of a fully edentulous mandible with the following dimensions: 60 mm mandibular body length from the middle line, 20 mm inferosuperior height, and 12 mm buccolingual width. Bone quality type 2 was assumed in the symphysis and type 3 in the mandibular body according to the Lekholm and Zarb classification and 2 mm thick cortical bone surrounding the cancellous bone. In addition, a threaded implant was modeled, using as a reference the geometry of a Stark D Active internal connection implant (Sweden & Martina, Due Carrere, Italy), 4.2 mm body diameter, and 10 mm length. Furthermore, a self-aligning attachment brand Locator (Zest Anchor Inc, Escondido, Calif) was modeled, with abutment (matrix) of 4 mm gingival height and metallic cap with nylon insert (patrix). The matrix was screwed to the implant and the patrix was attached to the overdenture.

The overdenture was a superstructure made of acrylic resin, 10.7 mm high and similar in shape, width, and length to the jaw bone. Four different finite element models were created. The Implants at Laterals model simulated an overdenture retained by 2 implants placed at the lateral incisor level and with a center-to-center separation of 15 mm. In the Implants at Canines model, the centers of the 2 implants were separated by 27 mm. In the Implants at Second Premolars model, the distance between centers was 53 mm (26.5 mm from the mandibular midline). In the Crossed Implants model, one implant was placed on the left side, 13.5 mm from the midline (canine level), and the other in the contralateral arcade, 26.5 mm from the midline (second premolar level).

*Material properties and interface conditions*

The jaw bone and all the materials used in these models were considered to be linearly elastic, homogeneous, and isotropic. Values for elastic moduli and Poisson ratio of the bone and different materials were taken from published data (Table 1). A continuous bone-implant interface, flawless and with 100% osseointegration, was assumed. All other interfaces between the rest of the different materials and structures were also assumed to be continuous (matrix-implant, patrix-matrix, and patrix-overdenture). Moreover, a passive fit without friction was assumed between the overdenture and the jaw bone, without gingival mucosa interface.

*Loading and boundary conditions*

In the 4 models, a vertical occlusal bilateral or unilateral static load of 150 N was applied under 6 different loading conditions. The unilateral single load (150 N) was applied at midline, at the left canine level, at the first left molar (10 mm from the distal implant) and combined at midline (40 N) and first molar level (150 N). The bilateral load was applied at the level of the first molars (75 N on each side) and also combined with 40 N at midline. The data for von Mises stresses were produced numerically, and the stresses in the finite element analysis were color coded to allow comparison of the biomechanical differences between models.

All elements were modeled with Pro/Engineer Wildfire v4.0 (Parametric Technology Corp, Needham, Mass) software of computer-aided design. The finite element models were created and meshed using Ansys 11.0, a commercial 3D finite
element software (Ansys Inc, Canonsburg, Pa). In order to generate the meshes, the following 4 different kinds of elements were employed: 3D 10-node tetrahedral structural solid, 3D 20-node structural solid, 3D 8-node surface-to-surface contact, and 3D target segment. As a result, the smallest model has 844,000 nodes and 97,003 elements while the largest has 964,132 nodes and 108,802 elements.

RESULTS

Table 2 shows the von Mises stress in the bone around implants for each model and occlusal load application site. In all models, when a unilateral load (at the canine level or first molar location) or combined load (combination of unilateral first molar and midline load) was applied, the highest peri-implant bone stress values were recorded around the load-side implant, with values that increased the peri-implant stress of the contralateral implant between 2 and 6 times. However, a symmetrical stress distribution on both sides was recorded with midline unilateral load or bilateral first molar load or combined bilateral first molar and midline position loads. In general, of all the models, the best peri-implant bone biomechanical environment was found in the premolar implant model, including the crossed-implant model when applying the load on the side of the implant placed at second premolar level. Even with this model and loading site, with some exceptions, the stress values were lower compared with the second premolar level implant model. However, this crossed-implant model revealed the worst biomechanical environment when occlusal load was applied on the most mesial implant side at canine level. Lateral incisor and canine level implant models revealed the next worst biomechanical environment, with slight differences for each occlusal load application site. On the load side and in all models, unilateral load, except for midline load, showed the highest peri-implant bone stress values compared with bilateral posterior load alone or combined with midline load. With certain exceptions, the data also showed a progressive decrease in stress on the load side as the unilateral load was applied more mesially. However, the combined unilateral midline and posterior (first molar) load caused similar stress values to those recorded with unilateral posterior load. In each and every model, bilateral posterior load not only distributed stress symmetrically but also generally revealed lower stress values than in the case of unilateral load at any location, except when applied at midline.

In general, regardless of the model and the load application site, unilateral load on the bone was located in the peri-implant crestal bone area of both implants, but with greater stress concentration in the load-side implants, toward the distal/distolingual implant area. This stress extended and was dissipated toward the neck and first threads of the implant body as well as to the alveolar bone located distally to the implant. In the bone surrounding the implant apex, stress was also recorded, especially in the load-side implants and in the canine-level and crossed-implant models (Figures 1 through 4). In all models, the midline load also showed stress in the most distal areas of the support alveolar ridge bone. No significant differences have been found in the stress distribution and location with bilateral posterior load alone or combined with midline. With the exception of the crossed-implant model,

<table>
<thead>
<tr>
<th>Material</th>
<th>Structure</th>
<th>Young’s Modulus (GPa)</th>
<th>Poisson Ratio</th>
<th>References</th>
</tr>
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<tr>
<td>Titanium Ti6Al4V</td>
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<td>135.00</td>
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<td>Daas et al 28</td>
</tr>
<tr>
<td>Titanium grade 4</td>
<td>Abutment and metallic cap attachment</td>
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<td>Daas et al 28</td>
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<tr>
<td>Acrylic resin</td>
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<td>Hong et al 29</td>
</tr>
<tr>
<td>Cortical bone</td>
<td>Peri-implant bone</td>
<td>13.70</td>
<td>0.30</td>
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<tr>
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<td>1.37</td>
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<td>Daas et al 28</td>
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</table>

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<th>TABLE 2</th>
<th>Von Mises stress (MPa) on the peri-implant bone stress for each overdenture model and occlusal load application site</th>
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<tr>
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<td>Right Side</td>
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<td>Unilateral posterior (first molar)</td>
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<tr>
<td>Unilateral canine right side</td>
<td>11.12</td>
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<tr>
<td>Unilateral anterior midline</td>
<td>11.10</td>
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<tr>
<td>Unilateral posterior and midline</td>
<td>26.38</td>
</tr>
<tr>
<td>Unilateral posterior and midline right side</td>
<td>27.14</td>
</tr>
</tbody>
</table>
which showed the highest stress concentration in the most mesial implant at canine level, in all other models stress was located symmetrically in the peri-implant crestal bone area of both implants, with the highest concentration toward the distolingual area. This bone stress spread and dissipated, as with the unilateral load, to the implant neck, a coronal third of the implant body, and the alveolar bone located distally to the 2 implants, except in the case of the premolar model, which did not show this distal stress extension. With this load, the bone surrounding the implant apex also registered stress (Figures 1 through 4).

**FIGURE 1.** Peri-implant bone stress location in second premolar level implant overdenture model according to the application load site. (a–c) Left posterior unilateral load. (d–f) Unilateral midline load. (g–i) Unilateral load at left canine level.

**DISCUSSION**

Using 3D-Finite Element Analysis, this study evaluated bone stress distribution around implants in mandibular overdentures retained by 2 implants at different locations, applying unilateral or bilateral occlusal load in several places. When dentists plan a mandibular overdenture design, the choice of the number and position of implants in the mandible is an important decision that can limit the survival of the restoration. The question of whether there is an optimal number of implants for retaining a mandibular overdenture has been under discussion for many years. Recent clinical literature reviews show that there is overwhelming evidence to support the McGill and York consensus proposals, which state that 2 implants should become the first choice of treatment. Furthermore, randomized controlled trial results evaluated by means of meta-analyses show minimal differences in implant loss risk and average peri-implant bone loss between the use of 2 or 4 implants, although none of these trials used the Locator attachment system. These data may lead the dentist to choose 2 implants. However, the location of the 2 implants in the mandible that provide the best biomechanical environment and survival is still an unresolved question.
In a fully edentulous patient, the anterior mandible tends to have substantial residual alveolar bone; thus, it is the most favorable site for implants. Despite the heterogeneity of different clinical studies, placing 2 implants in the canine area is common. Although other options are possible, no clinical and very few biomechanical studies have as yet reported data comparing clinical outcomes or stress/strain distribution related to 2 implants in different positions for mandibular overdentures. This makes it more difficult for dentists to decide. In the present study, for most applied loads, the worst biomechanical environment was found with the lateral incisor and the crossed-implant overdenture models with maximum peri-implant bone stress levels of 38.65 MPa and 43.89 MPa, respectively. Although these stress values (equivalent to approximately 1850 and 2200 microstrains, assuming that 1 MPa equals to 50 microstrains) are below the physiological tolerance threshold of bone, clinicians should not risk placing the 2 implants in the incisal area. However, this is a controversial issue. Data from other biomechanical studies have support the advantage of placing implants in the lateral incisor areas, as they show less peri-implant bone stress compared with 2 implants placed more posteriorly. Additionally, anatomical features related to a higher trabecular bone ratio and thickened cortical bone and recommendations related to mechanical advantages of lower posterior rotation and greater area of denture/mucosa contact that reduce implant stress have been reported to support this option. However, taking into account the data from the present study on stress distribution, the position of the 2 implants in the mandible is an important variable; the second premolar level is the best biomechanical environment site, worsening as the implants become more mesial, whether bilateral or unilateral load is applied. The exception is when the load is applied at the midline, perhaps due to a greater length of the lever arm and increase in the bending moment. While this trend does not agree with findings of other
biomechanical studies, the results support the placement of 2 implants in the premolar area to retain a mandibular overdenture.

At the same time, the main causes of bone loss around implants are mechanical factors (occlusal overload), biological/infectious events (peri-implantitis), or a combination of both. During chewing, complex force patterns of varying magnitude, direction, and application site occur, transferring stress to the overdenture, attachment/implant/bone system, and alveolar ridge without the dampening effect of the periodontal ligament. Moreover, as found in patients, the overdenture moves and rotates around one or more rotation axes that can change, causing lever arms and bending moments that may increase the stress around implants. Clinicians should pay attention to occlusal harmony control to prevent overload and excessive movement of the denture and so minimize the peri-implant bone stress. This study supports the balanced occlusal scheme for the 2-implant supported mandibular overdentures. Data show that the bilateral posterior loading and unilateral loading at the incisor level transfer at similar relatively low peri-implant bone stress levels to each implant, whereas the unilateral load exhibits high peri-implant bone stress levels in the load-side implants and substantial stress differences with respect to the no-load side. This is a constant reported in numerous different biomechanical designs of 2-implant supported mandibular overdentures, and it provides another argument for recommending that dentists use an occlusal adjustment with the bilateral balanced occlusion scheme and patients chew on both sides simultaneously. When a unilateral load is applied, an overdenture anchored by

**Figure 3.** Peri-implant bone stress location in canine-level implant overdenture model according to the application load site. (a–c) Left posterior unilateral load. (d–f) Unilateral midline load. (g–i) Unilateral load at left canine level.
2 implants rotated over the implant from one side to another, bending randomly to the load side and away from the no-load side, causing bending moments in the implant/bone complex with the bending plane orientation varying according to the load situation, all of which increases the stress on the load side. Furthermore, when a vertical unilateral load is applied in mandibular posterior areas, it might cause a denture base mesial movement that could result in greater bone stress/strain throughout the distal area of the load-side implant. In any case, the resilient configuration of the Locator attachment could dampen this excess stress for any unilateral load location, causing a rocking motion in the lower denture base. In addition, a greater vertical displacement occurs, leading to greater contact surface compression between denture and mucosa, thus decreasing the implant/bone system stress. The special dual-retention mechanism of these self-aligning attachments, compared with other resilient ball-type attachments, would favor the phenomena described.

Since the loading site is an important factor that affects the stress distribution throughout the system, the behavior in this study of the midline load that would simulate the action of cutting food with incisor teeth requires some clarification. With this load, the data show low stress values compared with any other unilateral or bilateral applied load, and they further show symmetrical stress distribution on both sides for any implant location, especially those placed in canine and lateral areas. Although this result suggests a better biomechanical environment with incisal level load with implants placed at lateral incisor or canine levels and could influence the clinical decision to promote contacts in the anterior teeth during occlusal adjustment, it must be taken with caution. With design differences, meaning the data are not exactly comparable, several biomechanical studies report similar results, while others show greater peri-implant bone stress with anterior midline load compared with unilateral and bilateral load at a more posterior location.

As reported in all biomechanical studies, regardless of independent variables of the design, this study also found that
the peri-implant stress location and distribution in the crestal bone surrounding the neck and first threads of the implant is a constant for any type of load and model. This fact is explained by the complex beam analysis mechanical principle, which says that when 2 bodies with very different moduli of elasticity (eg, bone/implant titanium) come into contact, the highest stress is located at the beginning of the contact surface. It is widely known that the pattern of resorption and peri-implant bone loss reported in clinical studies matches the aforementioned biomechanical stress concentration location. In this study the distal or distolingual peri-implant areas were the main sites of compressive or tension stress concentration, making them the most likely areas for bone loss. This is similar to what has been reported in other biomechanical studies regarding overdentures with different designs and attachments. However, other different locations are cited for buccal or lingual, depending on the compressive or tensile stress nature or for mesial with Locator attachments and 2 anterior-level implants. As in previous studies, stress is also recorded in the implant apex bone, more often on the load side and with greater concentration in implants in the canine area. This can be explained by a fulcrum effect in the attachment/implant system caused by a load applied near the attachment, which tends to compress the apical area. In any case, apical stress can induce bone resorption or alter vascular apical flow, thereby affecting the modeling and remodeling bone processes, even leading to bone necrosis.

Furthermore, knowing the stress distribution pattern on the alveolar ridge becomes an important issue, given that just over half (63%) of the posterior bilateral load (simulating mastication) in an overdenture is transferred to the mucosa/alveolar bone. added to the fact that resilient attachments, such as the Locator, can occupy a greater denture/mucosa contact area than rigid ones can. All of this favors less peri-implant bone stress. In this study, regardless of the bone stress around implants, the highest alveolar ridge bone stress concentration and extent were found in the posterior mandible regions, more frequently with unilateral load in all models but especially in lateral and canine level implant models. Although this result shows a possible reduced risk of peri-implant bone loss through an increase in the denture/alveolar bone contact area, based on the remaining data this implant and load position cannot be recommended as that of the lowest biomechanical risk for a mandibular overdenture. This is also supported by the fact that similar stress distribution has been reported with different occlusal loading conditions or different stress location in the anterior alveolar ridge between the 2 attachments.

On the other hand, the variability in biomechanical studies regarding the intensity, angle and position of the occlusal load, location and inclination of the implants, type and height of attachments, and overdenture and mandible designs makes it difficult to compare data between such studies in a way that allows us to choose the implant and load position offering the lowest biomechanical risk. It is therefore necessary to standardize these factors.

Finite element analysis is a widely employed method in dentistry to estimate the stress/strain distribution in peri-implant bone, prostheses and prosthetic components in many diverse situations. However, with a mathematical and computational model it is not possible to model and simulate all prosthetic restoration, ground support, masticatory function, and oral environment design features and responses. It is necessary, therefore, to assume a number of simplifications related to material properties, geometry, interface, load, and contour conditions, which are limitations that mean the data obtained do not correspond exactly to the clinical results, they are only an approach to the clinical situations. So when this method is used, a qualitative comparison between models and variables is recommended rather than a focus on quantitative data. Material properties and structure geometries have a great influence on the stress/strain distribution, but as in similar studies, it was assumed that all materials were homogeneous and linearly isotropic. It was also assumed that the interfaces between different materials and structures were continuous and had a passive fit without any friction; in clinical reality this is not so and can be a limitation.

A curved overdenture of uniform height and thickness was modeled, as was a jaw of similar uniform morphology but different dimensions, without gingival mucosa interface, condylar anchorage, or other restrictions on movement; although these factors may be a limitation, they will not influence the attachment stress distribution because these structures remained constant for all models and loading. In accordance with Liu, the plastic insert of the matrix was made of nylon (polyamide); polymethylmethacrylate was used in another study. Although the elastic properties are not very different, the differences in stiffness between the 2 materials may influence the attachment/implant/bone system stress distribution. Several different studies show how plastic matrices of different stiffness influence the stress transfer to the attachment/implant/bone system or residual ridge. This may be a limitation and should be taken into consideration. During chewing, complex force patterns of variable magnitude and direction take place, from one area of the mouth to another and between subjects, which is impossible to mathematically reproduce and simulate. In this study, a 150 N vertical force was applied, which is considered an occlusal load very close to masticatory forces and similar to that used other overdenture finite element analysis studies. Also, since contacts between all teeth are established during mastication and an overdenture can combine straight and angled implants or abutments, a strictly vertical load design of unilateral or bilateral posterior location may be a limitation that the clinician should consider when comparing and discussing the clinical implications of a finite element analysis. Although unilateral and bilateral occlusal load combinations are cited in some studies, the dental literature concerning overdenture and finite element analysis reports a great variability in the direction, application site, and magnitude of occlusal loads, which per se is a limitation for the comparison of results; it is therefore necessary to standardize these factors.

**Conclusions**

In accordance with the results and within the limitations of a finite element analysis, the following conclusions may be drawn. (1) Overall, the worst biomechanical environment in the
bone around implants was registered in the overdenture model with implants at lateral incisor level, which means this model cannot be recommended. (2) Overall, the second premolar level implant overdenture should be the chosen design, regardless of the load application site. (3) If a crossed-implant overdenture model is chosen, this must be used together with occlusal load on the most distal implant side to provide a better environment compared with other models. (4) Since the application load site influences the stress, when occlusal adjustment of an overdenture is made, clinicians should be aware that bilateral occlusal load distributes the peri-implant bone stress symmetrically while the one-side load increases it greatly on the loaded side, whatever the implant situation.

**ABBREVIATIONS**

3D: 3-dimensional

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**NOTE**

The authors declare that they have no proprietary, financial, professional, or other personal interest of any kind in any product, service, and/or company that could be construed as influencing the position presented in the manuscript.

**REFERENCES**


