

Biomechanical investigation of osseointegration of loosely and overtightly placed titanium implants

Investigación biomecánica de la osteointegración de implantes de titanio colocados de forma suelta y demasiado apretada

Ozmen Istek¹ , Murat Tanrisever^{2*} , Erhan Cahit Ozcan³ , Umit Koray Can⁴ , Ali Yusuf Altunyuvu² ,
Serbest Demir⁵ , Serkan Dundar^{5,6} 

¹Mus Alparslan University, Faculty of Health Medicine, Department of Nursing. Mus, Türkiye.

²Firat University, Faculty of Veterinary Medicine, Department of Surgery. Elazig, Türkiye.

³Firat University, Faculty of Medicine, Department of Esthetic, Plastic and Reconstructive Surgery. Elazig, Türkiye.

⁴Turkish Jockey Club Elazig Racecourse Horse Hospital, Elazig, Türkiye.

⁵Firat University, Faculty of Dentistry, Department of Periodontology, Elazig, Türkiye.

⁶Firat University, Institute of Sciences, Department of Statistics, Doctorate Student. Elazig, Türkiye.

*Corresponding author: mtanrisever@Firat.edu.tr

ABSTRACT

The objective of this research was to biomechanically assess the osseointegration of implants placed in bone sites prepared with diameters smaller than, larger than, or equal to the implant diameter. Twenty-one 6-month-old female Sprague Dawley rats weighing between 250–300 g were used in the study. The rats were divided into three groups and titanium implants, 2.5 mm diameter and 4 mm length, were placed in the cortico-cancellous bone structure in the metaphyseal parts of the right tibia bones of all rats included in the study. The study groups were; the group in which a bone bed of 2.2 mm in diameter and 4 mm in length was prepared and the implants were placed very tightly (n=7), the group in which a bone bed of 2.8 mm in diameter and 4 mm in length was prepared and the implants were placed loosely (n=7), and the control group in which a bone bed of 2.5 mm in diameter and 4 mm in length was prepared and the implants were placed. The rats were sacrificed 15 days after the operation. The implants were then subjected to torque analysis to measure biomechanical osseointegration values. Data were analyzed using One-Way Anova and Tukey HSD tests. Statistical significance was accepted as $P<0.05$. Biomechanical osseointegration values ($N\cdot cm^{-1}$) of overly tightly placed implants (12.86 ± 3.09) and implants in the control group (12.56 ± 3.58) were found to be significantly higher than those of loosely placed implants (6.56 ± 1.43) ($P<0.05$). Although the biomechanical osseointegration values of overly tightly placed implants those of implants in the control group were numerically higher, no statistically significant difference was found ($P>0.05$). As a result of the study, it was determined that tightly implant placement increased biomechanical osseointegration values. Additionally, osseointegration can be achieved without initial placement tightness too.

Key words: Bone implantation; biomechanical measurement; osseointegration; rat; titanium implant

RESUMEN

El objetivo de este estudio fue evaluar biomecánicamente la osteointegración de implantes colocados en sitios óseos preparados con diámetros menores, mayores o iguales al diámetro del implante. Se utilizaron veintiún ratas Sprague Dawley hembras de 6 meses de edad, con un peso entre 250 y 300 g. Ratas incluidas en el estudio se dividieron en tres grupos y se colocaron implantes de titanio con un diámetro de 2,5 mm y una longitud de 4 mm en la estructura ósea corticoesponjosa de las área metáfisis de la tibia derecha de todas las ratas. En un grupo, se preparó un lecho óseo de 2,2 mm de diámetro y se colocaron los implantes muy ajustados (n=7), en un grupo se preparó un lecho óseo de 2,8 mm de diámetro y se colocaron los implantes de forma holgada (n=7) y el grupo control se preparó un lecho óseo de 2,5 mm de diámetro y se colocaron los implantes de forma rutinaria; todos los lechos óseos tuvieron una longitud de 4 mm. Las ratas fueron sacrificadas 15 días después de la colocación del implante. Posteriormente, los implantes fueron sometidos a un análisis de torque para medir sus valores de osteointegración biomecánica. Los datos se analizaron mediante ANOVA unidireccional y la prueba HSD de Tukey. La significación estadística se aceptó con un valor de $P<0,05$. Los valores de osteointegración biomecánica ($N\cdot cm^{-1}$) de los implantes con una colocación excesivamente apretada ($12,86 \pm 3,09$) y de los implantes del grupo control ($12,56 \pm 3,58$) fueron significativamente superiores a los de los implantes con una colocación más suelta ($6,56 \pm 1,43$) ($P<0,05$). Si bien los valores de osteointegración biomecánica de los implantes con una colocación excesivamente apretada fueron numéricamente superiores a los de los implantes del grupo control, no se observó una diferencia estadísticamente significativa ($P>0,05$). Como resultado del estudio, se determinó que la colocación apretada de los implantes aumentó los valores de osteointegración biomecánica. Además, se puede lograr la osteointegración sin necesidad de una colocación inicial rígida.

Palabras clave: Implante óseo; medición biomecánica; osteointegración; rata; implante de titanio

INTRODUCTION

The term osseointegration was first used in the literature as a subject heading in an article written by Brånemark *et al.* [1], but it has not been explained conceptually much. Osseointegration is a fundamental determinant of implant stability and long-term functionality. It refers to the direct structural bond formed between the implant surface and surrounding bone tissue, without the interposition of any non-bony connective tissue. Additionally implant and tissue integration can be defined as a more complex structural and functional association between differentiated, adequately remodeled biological tissues and more permanent, conducted the specific clinical functions, and precisely defined and controlled components that do not initiate rejection mechanisms, continuing in a symbiotic manner [2, 3].

The functional aspect is that a biomechanically based bony connection resistant to shear and tensile forces is emphasized [4]. Brånemark, who was introduced to metallic implants at the University of Gothenburg in the early 1960s [5]. 'Direct contact between living bone tissue and the Ti implant, without any intervening connective tissue, observed with light microscope magnification' is the most concise and up-to-date scientific definition of osseointegration [6]. The initial insertion tightness of titanium implants has been reported to be a significant parameter directly related to implant success and function. Initial placement tightness in other words, primary stabilization, is the tight placement achieved during the placement of the implant into the bone.

The connection of the implant with the bone is the combination of biomechanical tightness, which occurs with the compression of the bone holding the implant, and biological tightness, which occurs with the accumulation of new bone during osseointegration. Following surgical implant placement, mechanical (primary stabilisation) tightness is usually high; however, it decreases with the resorption of the recipient bone during the healing process. Biological (secondary) tightness also increases over time with the formation and accumulation of new bone tissue around the implant. So biomechanical tightness is replaced by biological strength.

Osseointegration is the sum of connection of whole periimplant bone and whole implant surface; osseointegration is a living process and therefore does not remain constant [7, 8]. The initial firmness achieved during implant placement is the stability achieved when the implant is first placed in the bone and in contact with the surrounding bone tissue. It is necessary for successful osseointegration during the initial placement of the implant in the bone. If the implant does not have optimum firmness during placement in the bone socket, the fusion process with the bone may be adversely affected and connective tissue formation may occur in the bone tissue around the implant. This connective tissue formation may disrupt osseointegration and lead to clinical failure of the implant [9].

During implant surgery, factors such as the quality of the host bone, the dimensions of the implant site, the surgical technique used for socket preparation, and the implant's geometry can all influence the primary stability at the time of placement. Apart from these factors, two basic elements affect the initial tightness of the implant during the surgical placement phase. The first of these is the total surface area of the implant placed in the bone that is in contact with the bone. It has been shown that implants

placed in dense marbled bone are tighter than implants placed in cancellous trabecular bone [10].

The second is the pressure and compression forces at the bone-implant interface. When an implant is placed in a bone bed prepared smaller than the implant diameter, a significant amount of pressure is created in the surrounding bone tissue and hoop stresses occur. Hoop stresses are environmental stresses resulting from internal or external pressure in cylindrical structures. Hoop stresses can be beneficial in increasing the initial tightness, but when they reach high amounts, they can cause regional blood supply disruption and local bone death in the bone tissue around the implant [11].

To characterize the osteogenic process occurring in the peri-implant bone tissue, the presence and organization of both cortical and cancellous components within mature lamellar bone play a critical role. Woven bone is caused by rapid growth resulting from embryonic development or healing during fracture healing rather than remodeling during the formation of lamellar bone. Although lamellar and woven bone show some differences in terms of microarchitecture, the histodynamic features in the formation process of these two bone tissues are quite similar [12].

New bone forms occur on the surfaces of the bone tissue that is destroyed during remodeling. This phenomenon may suggest that osteoblasts in the surrounding bone tissue of implants placed in the bone may form new bone on the old bone and implant surfaces. These two phenomena (distance and contact osteogenesis) were defined by Osborn and Newesley and they stated that the bone may come together on the surface of the implant [13].

In distance osteogenesis, new bone is generated from the surface of the existing bone bed surrounding the implanted material. Over time, this newly formed bone progressively encases the implant, without the presence of any intervening non-osseous tissues, such as connective tissue. The bone surface around the implant creates a new bone tissue matrix and allows osteogenic cells, which will provide bone formation, to accumulate here [14].

During the preparation of the implant socket, tissue death occurs in the cortical bone around the implant as a result of the disruption of vascularization and nutrition in the bone cortex, and since it is known that osteoclast invasion from the medullary part under the cortex causes gradual remodeling, distance osteogenesis can be observed during the healing process of the marbled bone tissue [15].

In another form of peri-implant bone formation, contact osteogenesis, the new bone tissue that will surround the implant begins to form directly on the surface of the implant. In the absence of pre-existing bone tissue on the implant surface, the implant material becomes directly encircled by osteoblasts responsible for new bone formation. Peri-implant ossification of this nature is typically observed in regions of bone undergoing remodeling, where old bone is resorbed and the implant surface becomes lined with osteogenic cells prior to the deposition of new bone tissue. The common factor that relates the physiological remodeling process to contact osteogenesis is that the osteogenic cells of the bone differentiate and form bone for the first time in the appropriate place. This bone is called *de novo* bone tissue [12].

While distance osteogenesis enables the surrounding bone tissue to gradually grow toward the implant surface, contact osteogenesis facilitates the direct formation of new bone on the implant surface itself. Although it is physiological for both distance osteogenesis and contact osteogenesis to occur in every bone where intraosseous healing region is seen, these two different healing types are important in terms of revealing the importance of implant surface properties, implant design and bone type in osseointegration. In weak bone tissues, it is important to optimize osteogenesis by improving implant surface properties in order to obtain initial firmness [12, 16]. This study aims to biomechanically evaluate the osseointegration of implants placed in bone sockets prepared with diameters smaller than, larger than, or equal to that of the implant itself.

MATERIAL AND METHODS

Experimental design

The experimental procedures involving animal subjects were carried out at the Firat University Experimental Research Center. The rats (*Rattus norvegicus*) included in the study were provided by the Firat University Experimental Research Center. All surgical procedures were performed on twenty-one female Sprague Dawley rats, aged six months and weighing between 250 and 350 g (WL, Shimadzu, Japan). This study was approved by the Firat University Local Ethics Committee for Animal Experiments. (Approval Number: 21838, Date: February, 02, 2024).

During the experimental applications, the rules of the Helsinki Declaration regarding studies conducted with experimental animals were adhered to. In all *in vivo* experimental stages, the rats were housed in plastic cages with 12 hours (h) of darkness and 12 h of light. The rats were allowed to have free access to food and water throughout the entire experimental setup. In addition, in order to ensure standardization in the experimental setup, care was taken to ensure that all rats included in the study were in the same estrus period by performing vaginal smears.

TiAl₆V₄ implants (2.5 mm diameter of and 4 mm length) were inserted into the corticocancellous bone tissue in the metaphyseal region of the right tibia of all rats involved in the study. The rats were divided into 3 groups, each consisting of 7 rats in the experimental phase. The first group was defined as the rats in which the titanium implant was placed very tightly into a bone bed with a diameter of 2.2 mm and a length of 4 mm (n=7). The second group was defined as the titanium implant group in which a bone bed larger than the diameter of the implant with a diameter of 2.8 mm and a length of 4 mm was created and placed loosely into the socket (n=7), and the last group was defined as the control group (n=7) in which titanium implants with a diameter of 2.5 mm and a length of 4 mm were placed into the bone bed and a bone bed with the same diameter and length as the implant diameter and length was formed.

Surgical procedures

The rats to be operated on due to surgical procedures were fasted for 8 h prior to the operation. In order to perform the operations under general anesthesia, 10 mg·kg⁻¹ Xylazine (Rompun, Bayer, Germany) and 50 mg·kg⁻¹ Ketamine hydrochloride (Ketasol, Richter Pharma AG, Wels, Austria) were administered intraperitoneally.

Afterwards, the surgical intervention area was shaved and washed with Povidone iodine (Batikon, Detro Healthcare, Istanbul, Türkiye). After the disinfection process, a surgical incision of approximately 1.5 cm in length was made by taking bone contact from the crestal part of the right tibia bones of all rats using a number 15 scalpel.

After the incision, the soft tissues and periosteum were removed using a periosteal elevator and the corticocancellous bone part of the metaphyseal part of the tibia bone was reached. The sockets for titanium implants were prepared using a drill (NSK, Japan) under physiological serum perfusion (FIG. 1). While preparing the bone sockets of tightly placed implants, first a point drill, then 1.8 mm diameter and 2.2 mm diameter burs were used. In loosely placed implants, the milling operations were performed using point drill, 1.8, 2.2, 2.5 and 2.8 mm diameter drills, respectively.



FIGURE 1. After the skin incision was made to reach the tibia where the implant was placed, the socket was opened with the help of a drill

When implants were placed in the control group, the bone socket was prepared with other drills without using a 2.8 mm diameter drill (FIG. 2). All drilling operations were performed at 500 rpm with physiodispenser.



FIGURE 2. Image of the implant placed after the bone socket was opened with a drill in the tibia

Then, the fascia, subcutaneous tissue and skin were closed with 4–0 polyglactin suture. In the postoperative period, each subject was injected with antibiotics (Penidro, 50 mg·kg⁻¹ Penicillin, Pi Farma İlaç Sanayi ve Ticaret AŞ, İstanbul, Türkiye) and analgesics (Contramal, 0.1 mg·kg⁻¹ Tramadol hydrochloride, Abdi İbrahim İlaç Sanayi ve Tic AŞ, İstanbul, Türkiye) intramuscularly for 3 d to prevent pain and infection. All surgical procedures were performed with atraumatic methods (making small incisions, avoiding unnecessary tissue dissection, rinsing with saline during bone drilling). All rats were euthanized after two weeks of experimental setup. After the implants and surrounding tissues were freed from soft tissues, reverse torque analysis was performed to measure biomechanical bone implant union values.

Biomechanical analysis

A reverse torque test was conducted to assess the osseointegration of titanium implants placed in bone sockets of varying sizes: small, large, and equal to the implant diameter. The samples were kept in 10% buffered formalin (Kimya Grup, İstanbul, Türkiye) and evaluated without waiting to prevent possible dehydration in the samples. All implants taken as samples were placed in polymethylmethacrylate (SIGMA–Aldrich, Germany) blocks for analysis and a digital torque device (Mark 10, NY, USA) was fixed for each implant (FIG. 3).



FIGURE 3. Biomechanical reverse torque device (Mark 10, NY, USA)

In the biomechanical osseointegration evaluation, the reverse torque device was gradually applied manually in the counterclockwise direction, which is the direction of implant insertion. The reverse torque was completed when the implant made its first rotational movement in the bone. The force value obtained for each implant was recorded.

Statistical analysis

SPSS 23.0 for Windows program (IBM SPSS Statistics for Windows, Armonk, NY, USA) software program was used for statistical analysis. The mean and standard deviation of the data were calculated. Data for each group were expressed as mean ± standard deviation. The conformity of the data to normal distribution was evaluated with Shapiro Wilk and Kolmogorov Smirnov tests and it was determined that the data showed normal distribution. One Way Anova and Tukey HSD tests were used to evaluate the distribution of the data and statistical significance was accepted as $P < 0.05$. Parameter data were expressed as mean and standard deviation.

RESULTS AND DISCUSSION

In the experimental stages of the study applied on rats, the healing processes in all animals were completed without any complications

and no infection or death was detected in any animal. After the experiment, the implants removed from the surrounding soft tissues and the biomechanical torque analyses were performed and the osseointegration ($\text{N}\cdot\text{cm}^{-1}$) values of the samples obtained from the study are shown in TABLE I. According to this results, it was seen that the osseointegration values of the implants placed excessively tightly and the implants in the control group were statistically significantly higher than the implants placed loosely ($P < 0.05$). Upon examining the osseointegration values of implants placed with excessive tightness and those in the control group, numerical differences were observed between the two groups; however, no statistically significant difference was found ($P > 0.05$).

TABLE I
Biomechanical BIC ($\text{N}\cdot\text{cm}^{-1}$) levels of the group after torque analysis

Groups	N	Mean (BIC) ($\text{N}\cdot\text{cm}^{-1}$)	Std. Deviation	P*
PS + ^{a1}	7	12.56	3.58	< 0.05
PS -	7	6.56	1.43	
PS ++ ^{a2}	7	12.86	3.09	

*P: 0.001 (One-Way ANOVA). ^{a1}, ^{a2}: Tukey HSD test. Statistically significantly different when compared to the PS - group, ^{a1}: 0.002, ^{a2}: 0.003. BIC: Bone Implant Connection. N: Newton

In osseointegration studies, the rat tibia model is generally preferred in terms of ease of application in bone implant integration. In addition, the fact that the tibial bone structure is surrounded by thick and well-vascularized muscles may also be considered as a factor in this preference. When such experimental studies are examined, it is seen that rats are often preferred in terms of skeletal change, maturity, bone metabolism and healing physiology [17, 18]. For these reasons, we also based the experimental structure of our study on this fact.

In this study, sockets were drilled since it was necessary to prepare implant beds in bone sockets of different diameters in the placement of titanium implants to ensure osseointegration in the bone. Since the area where the procedure was performed had a hard structure, it was necessary to use a high-speed drill for the drilling procedure. During this procedure, physiological saline solution was used to prevent deformations due to heating in the bone. Eriksson and Albrektsson [19], reported that bone healing was impaired when the friction temperature during drilling exceeded 47°C; therefore, low-speed drilling with irrigation was very important. To overcome this limitation, bone sockets were prepared prior to implant placement in areas where bone reconstruction had been performed. De Santis *et al.* [20] reported that bone implant connection was superior when performed simultaneously with implantation. They suggested that this would provide superior predictability of implant placement after bone reconstruction, in areas with large bone defects, and emphasized that for long-term implant success, the support of the bone tissue around the implant is very important.

Torque tests applied for the evaluation of bone implant osseointegration were first introduced by Johansson and Albrektsson [21], and when implant stability in osseointegration was examined from a biomechanical point of view with different methodologies such as biomechanical insertion or removal torque,

it was stated that different surgical protocols and processes were effective [22, 23, 24]. It has been reported that the surgical technique is especially related to implant insertion torque. When low insertion torque is compared to very high insertion torque, it is stated that high insertion torque provides much better stability in implants compared to low insertion torque, however, it can cause delay in the biological process of osseointegration [25]. In this study, reverse torque test was applied to determine the osseointegration levels of implants. It has been reported that reverse torque test is used in the analysis of bone implant stability and osseointegration studies conducted on experimental animals in laboratory environment [26, 27]. Thus, reverse torque osseointegration analysis of implants helps to provide an indirect measurement of the force required to separate the bone-implant interface.

This method is considered an objective criterion for the evaluation of different bone healing conditions with implants of different designs and surface properties. It has been reported that this analysis method is an application that allows the evaluation of all bone tissue around the implant [26, 27].

In the evaluation of osseointegration of titanium implants placed in bone sockets using the reverse torque method, as part of the biomechanical analysis outlined in this study, it was observed that the biomechanical osseointegration values for the control group and implants placed with excessive tightness were statistically higher compared to those of the loosely placed implants, as shown in TABLE I. Coelho *et al.* [22] in their study on beagle dogs created bone sockets with diameters of 3.2, 3.5 and 3.8 mm, respectively, in which they placed implants with a diameter of 4 mm and a length of 10 mm. The researchers reported that the removal torque values of the implants placed in the 3.2 mm diameter bone socket were statistically lower than the insertion torque values [22].

Duyck *et al.* [25], reported that osseointegration occurred with de novo bone formation in implants placed with loose torque in rabbit tibias. This bone neoformation may enable implants placed with low torque to reach the same level of osseointegration as implants placed with high torque, even in the early osseointegration stage. Duyck *et al.* [25] also did not report any negative effect of the peri-implant stress environment accompanying high insertion torque on the biological process of osseointegration at the tissue level. In this study, similarly, osseointegration occurred in loosely placed implants, although at a statistically significantly lower level than tightly placed implants. In addition, and similar to the results obtained of Duyck *et al.* [25], no osseointegration loss was observed in tightly placed implants.

CONCLUSION

In weak bone types, bone-implant connection levels may not be at the desired levels. In addition, bone-implant connection may fail in excessively hard bones. Based on the limited results of this study, it can be stated that osseointegration can be achieved without initial tightness. On the other hand, according to the data of this study, excessively tight placement may not cause problems in terms of osseointegration. It is thought that the data obtained in this study will provide new perspectives on implant-bone fusion and can be a reference for subsequent studies in the field.

Conflict of Interests

The authors have no conflict of interests to declare concerning the authorship or publication of this article.

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