Endosseous Implant Anchorage Is Critically Dependent on Mechnostructural Determinants of Peri-Implant Bone Trabeculae

Yankel Gabet,1 David Kohavi,2 Romain Voide,3 Thomas L. Mueller,3 Ralph Müller,3 and Itai Bab1

1Bone Laboratory, Institute of Dental Sciences, Hebrew University–Hadassah Faculty of Dental Medicine, Jerusalem, Israel
2Oral Implant Center, Hebrew University–Hadassah Faculty of Dental Medicine, Jerusalem, Israel
3Institute for Biomechanics, ETH Zürich, Switzerland

ABSTRACT
Low bone mass is highly prevalent among patients receiving endosseous implants. In turn, the implantation prognosis in low-density skeletal sites is poor. However, little is known about the mechanostuctural determinants of implant anchorage. Using metabolic manipulations that lead to low bone density and to its rescue, we show here that anchorage is critically dependent on the peri-implant bone (PIB). Titanium implants were inserted horizontally into the proximal tibial metaphysis of adult rats 6 weeks after orchiectomy (ORX) or sham ORX. Systemic intermittent administration of human parathyroid hormone (1–34) [iαhPTH(1–34)] or vehicle commenced immediately thereafter for 6 weeks. The bone-implant apparatus was then subjected to image-guided failure assessment, which assesses biomechanical properties and microstructural deformation concomitantly. Anchorage failure occurred mainly in PIB trabeculae, 0.5 to 1.0 mm away from the implant. Mechanically, the anchorage performed poorly in ORX-induced low-density bone, attributable mainly to decreased trabecular number. iαhPTH(1–34) rescued the PIB density and implant mechanical function by augmenting trabecular thickness (Tb.Th). However, implant biomechanical properties in low-density bone were relatively insensitive to implant surface treatment that affected only the osseointegration (%bone-implant contact). These results support a model wherein anchorage failure involves buckling of the weakest trabecular struts followed by sequential failure of the stronger trabeculae. Treatment with iαhPTH(1–34) induced thicker struts, which were able to delay and even prevent failure of individual elements, thus implicating trabecular thickness as a prime target for enhancing implant anchorage by systemic bone anabolic therapy. © 2010 American Society for Bone and Mineral Research.

KEY WORDS: ENDOSSEOUS IMPLANTS; ORCHIECTOMY-INDUCED TRABECULAR BONE LOSS; IMAGE-GUIDED FAILURE ASSESSMENT; PARATHYROID HORMONE; PERI-IMPLANT BONE

Introduction

Endosseous implantology is a leading skeletal reconstructive discipline, with millions of procedures carried out annually in developed societies. Uncemented titanium implants are currently the most widely used prostheses1,2 mainly because titanium has the unique property of inducing osseointegration, namely, a firm bonding with the surrounding bone, even in the complete absence of exogenously administered mediators such as bonding materials or enhancers of bone formation. Low bone density jeopardizes the prognosis of implantation procedures clinically3,4 and in experimental animals.5,6 Because of incomplete understanding of the biomechanical apparatus that provides implant anchorage, the means to support endosseous implantation in low-density bone are rather limited.

The implant anchorage apparatus has two structural components: the bone-implant bonding (osseointegration (OI)) and peri-implant trabecular bone (PIB). The OI is formed with trabecular struts that are integrated into the PIB, which, in turn, bridges the implant with the bony cortex, thus forming a structural unity between the implant and the skeleton.7,8

Intermittently administered human parathyroid hormone 1–34 [iαhPTH(1–34)] is the only clinically approved bone anabolic therapy for osteoporotic patients. It rescues bone loss in humans and in experimental animals.9–12 Of more relevance to the present article, we have recently reported that iαhPTH(1–34) markedly enhances implant anchorage in a rat model of gonadectomy-induced low-density trabecular bone.13

An unresolved issue related to the implant anchorage apparatus is the differential contribution of OI and PIB parameters to its
biomechanical properties in the normal skeleton as well as in untreated low-density bone and following bone anabolic therapy. We hypothesized that like the OI, the integrity of the PIB is critical for anchorage. Furthermore, once OI is attained, the PIB properties become the primary determinant of anchorage strength. Testing this hypothesis is of key importance in determining the enhancers used to stimulate implant anchorage, for example, modification of the implant surface, which preferentially affects the OI versus systemically administered bone anabolic agents capable of augmenting the PIB mass by increasing the trabecular number or thickness. To address this issue, we used a combined experimental approach in rats consisting of (1) time-lapsed image-guided failure assessment (IGFA) allowing concomitant assessment of biomechanical properties and microstructural deformation using micro-computed tomography (μCT) and biomechanical pullout testing, (2) low-density bone induced in rats by orchietomy (ORX), and (3) rescue of the ORX-induced low-density bone by iahPTH(1−34). We also assessed the structural and biomechanical consequences of implant surface modification. This approach revealed a critical role for the PIB in implant anchorage, demonstrating that the processes leading to functionally compatible mechaanostructural properties of the anchorage apparatus are related to the metabolic state of the skeleton.

**Materials and Methods**

**Animals**

The experimental protocol was approved by the Institutional Animal Care and Use Committee of the Hebrew University-Hadassah Medical Center. Thirteen-week-old male Sprague-Dawley rats were purchased from Harlan Laboratories (Jerusalem, Israel) and maintained at the animal research facility of the Hebrew University-Hadassah Medical Center. Animals were fed standard rat chow and water ad libitum throughout the experiment. The rats were divided randomly into two groups of bilateral ORX animals and one group of sham ORX animals. Six weeks were then allowed to pass prior to implantation to permit significant bone loss to occur in the ORX animals. At this time, titanium implants were inserted into the proximal metaphysis of the right tibia in each animal, as described recently. Human PTH(1−34) was chemically synthesized and purified by HPLC as previously reported. Daily subcutaneous injections (5 days a week) of 1,250 μg/kg of human PTH(1−34) or vehicle only (saline containing 0.001 N HCl and 2% heat-inactivated rat serum) were then administered to the ORX/PTH and ORX/VEH groups, respectively. The 25 μg/kg per day dose has an optimal effect on implant anchorage in this model. The animals were sacrificed 6 weeks after implant insertion and the tibiae separated. Tibial specimens with postoperative swelling, skin ulceration, or excessive bone formation around the extracortical part of the implant were excluded from the study. The remaining specimens were prescanned by μCT, and the distance of the implant longitudinal axis from the tibial proximal primary spongiosa was determined. Because of the critical importance of the implant position along the metaphyseal trabecular bone gradient, only implants positioned 1680 ± 480 μm distal of the primary spongiosa were further selected for IGFA, leaving a sample of four specimens per group with very similar implant positions (p > .32).

**Image-guided failure assessment (IGFA)**

Immediately after separation, the specimens were kept for 48 hours in phosphate-buffered formalin and further maintained in 70% ethanol. Twenty-four hours prior to analysis, they were rehydrated in PBS. A micro loading device (MLD) was designed in which a jig devised for pullout testing of rat tibial implants is housed in a μCT specimen holder and activated essentially as described previously for an IGFA compression testing device. The specimen was kept in a wet environment enclosed in a polystyrene film wrapping. All the MLD components present in the μCT scanning window are made of Torlon 4203, which is both radiolucent and stiff. For a detailed qualitative and quantitative 3D evaluation throughout the IGFA, the proximal 15 mm of the tibia in MLD was examined by a μCT imaging system (μCT 40, Scanco Medical AG, Geneva, Switzerland) at 15 μm resolution, as described recently. Beam-hardening artifacts were corrected automatically during image reconstruction using software included in the μCT package provided by the manufacturer. Scattering artifacts projecting from the titanium implant were corrected in the CT images by scanning a reference implant in saline and then subtracting this image from the images of the implantation specimens. The titanium and mineralized tissue then can be segmented from each other and from the bone marrow by applying a multilevel thresholding procedure. The accuracy of this procedure has been confirmed visually in three 200 to 250 μm spaced CT slices from each specimen. This validation is based on an established correlation demonstrating that bone-implant contact areas can be visualized in μCT slices at the same precision as in histologic sections. The %OI was calculated as the ratio between bone and total voxels in contact with the implant. The PIB volume of interest included the entire trabecular compartment between the cross-sectional planes 0.9 mm proximally and 0.9 mm distally from the implant longitudinal axis. Trabecular bone volume density (BV/TV), trabecular thickness (Tb.Th), trabecular number (Tb.N), and trabecular connectivity density (Conn.D) were calculated in the PIB.

For the actual analysis, the initial μCT scanning was carried out after applying a 2 N preload to ensure firm specimen alignment in the MLD. Following the preload scan, the MLD was transferred to a material testing and data-acquisition system operated in tension to pull out the implant at a displacement rate of 1 mm/minute. A total of four loading and subsequent scanning cycles were performed, namely, preload, 130 μm displacement, additional 130 μm displacement, and further displacement to failure. Ultimate force, stiffness, and toughness were calculated from the individual force-displacement curves obtained in each cycle (Fig. 2), as reported previously.

**Modulation of implant surface**

All implants used for IGFA had a turned surface and were designated type 1 implants. To specifically affect OI, the anchorage apparatus of type 1 implants was assessed in ORX rats.
separately by μCT and biomechanical testing 6 weeks after implantation as compared with type 2 implants prepared by further sand blasting and acid etching. The atomic force microscopy characteristics of these implant surfaces were analyzed using a 20 nm probe on three areas of 5 × 5 μm on the screw head (flat surface). The root-mean-square (rms), average roughness (Ra), and Z range are 17.8 ± 2.5, 13.2 ± 2.1, and 167.7 ± 13.4 nm, respectively, for type 1 implants and 486.9 ± 31.6, 372.7 ± 14.3, and 2375.3 ± 108.8 nm, respectively, for type 2 implants (data are mean ± SE obtained in three implants per type). Only implants positioned 2085 ± 390 μm distal of the primary spongiosa were selected for further analysis, leaving a sample of four to six specimens per group with very similar implant positions (p = .89).

Statistical analysis
SigmaStat software (SPSS, Chicago, IL, USA) was used throughout. Differences in morphometric and biomechanical parameters were analyzed by Student’s t test for comparisons involving two groups and analysis of variance (ANOVA) for multiple group comparisons. When significant differences were indicated by ANOVA, group means were compared using the Student-Newman-Keuls method for multiple comparisons. Pearson correlation coefficients were calculated to assess the relationship between biomechanical and structural μCT measurements.

Results
Metabolic manipulations affect load-induced strain distribution in implant anchorage apparatus
Using IGFA, we identified axial load-induced critical strains in OI and PIB at high resolution (Fig. 1). Small distortions were observed already after the first loading step (data not shown). Regardless of the metabolic state of the skeleton, the distortions induced by the first loading step were small and apparently within the elastic range because they were confined to the linear part of the displacement curve (Fig. 2). In 10 of the 12 specimens analyzed, the nonthreaded part of the implant shank moved in relation to the cortical bone already during the second loading step, which preceded failure of the trabecular anchorage apparatus. Of the remaining two specimens with no such detectable movement, one belonged to the vehicle-treated ORX animal (ORX/VEH) group and the other to the iahPTH (1–34)-treated ORX (ORX/PTH) group. At this stage, a few scattered OI and PIB failure sites were noticed only in the ORX/VEH group (data not shown). In addition, in all specimens, including those from ORX/VEH animals, the displacement curve showed increasing reactive force even during the third loading step (Fig. 2). Taken together, these observations suggest that the contribution of the cortex-implant bonding is negligible compared with the trabecular anchorage.

The three metabolic states studied show distinct load-displacement curves. By comparison with sham ORX animals, the yield point (elastic-to-plastic transition) and failure in the ORX/VEH group appear earlier (Fig. 2A, B). The ORX/PTH animals showed a very short plastic range, with the yield and failure almost coinciding (Fig. 2C). These results suggest that in the sham ORX and, in particular the ORX/VEH rats, a substantial permanent plastic deformation of the anchorage apparatus precedes its complete collapse during the biomechanical testing. Thus, in low-density bone sites, the failure process of the anchorage apparatus is apparently dominated by a chain reaction involving the PIB and/or OI. This reaction is triggered by buckling of the weakest trabeculae and escalates as the stronger trabeculae yield to the increasing load. These displacement curves further suggest that the vastly increased resistance to loading featured by the ORX/PTH specimens is associated with fewer but thicker struts that delay and even prevent failure of individual elements, thus improving both the elastic and ultimate failure behavior of the treated specimens.

Most failure sites in the trabecular compartment were observed in the PIB, 0.5 to 1.0 mm away from the implant surface at the thinnest locus of individual trabeculae (Fig. 1). The mode of distortion at these loci suggests that the failure was due mainly to bending forces. Failure at the tip of the implant occurred at the bone-implant interface because of the axial direction of the pullout load at these sites and/or the proximity of the tip to the cortex, where trabeculae are thicker and more resistant to failure (see Fig. 1). Progression of the trabecular deformation and eventual failure with the increasing pullout force exhibit distinct trends related to the metabolic state of the animals. ORX/VEH animals show a net decrease in Tb.N and BV/TV (Fig. 3A, C), with the failure occurring mainly within the PIB, even in the tip region (Fig. 1B). By contrast, treatment with iahPTH(1–34) markedly reverses the decrease in BV/TV by increasing Tb.Th (Fig. 3D), with no effect on Tb.N (Fig. 3O). The percent implant surface in contact with bone (%OI) is also markedly stimulated by the iahPTH(1–34) administration (Fig. 3B). However, relatively more failures are observed at the bone-implant interface (Figs. 1C and 4C).

Figure 4 shows data consistent with respective OI-to-PIB and PIB-to-OI shifts in critical strains (strains associated with pullout to failure) in the implant anchorage apparatus induced by ORX and iahPTH(1–34) treatment. The loss of bone-implant contacts resulting from these strains is represented by the difference between the %OI before the first loading step and after failure (ΔOI). Likewise, the difference between preloading and postfailure connectivity densities (ΔConn.D) represents the PIB failure because the connectivity is impaired consequent to trabecular rupture. Although statistically insignificant, the ORX- and ORX/iahPTH(1–34)-induced alterations in ΔOI and ΔConn.D demonstrate mirrored trends (Fig. 4A, B). Specifically, of the three treatment groups, the ORX/VEH animals exhibit the lowest ΔOI and highest ΔConn.D, whereas ORX/PTH and sham ORX groups show similar levels. To enhance the sensitivity of this analysis and achieve statistical significance, we further calculated the ΔOI/ΔConn.D ratio, which reflects the relative durability of OI versus PIB. Indeed, this ratio shows a significant threefold increase in the ORX/PTH over the ORX/VEH group with an intermediate value in the sham ORX rats (Fig. 4C), suggesting that ORX and iahPTH(1–34) lead to respective OI-to-PIB and PIB-to-OI shifts in critical strains generated by axial loading in the implant anchorage apparatus.
Fig. 1. Patterns of pullout-induced failure in implant anchorage apparatus. Representative specimens were obtained from (A) sham ORX, (B) ORX, and (C) iahPTH(1–34)-treated ORX animals. Gray lines on implants are reference landmarks demonstrating implant displacement; solid black line is a skeletal reference landmark; dashed black lines are arbitrary reference landmarks to assist evaluation of implant displacement and trabecular distortion.
Increased trabecular thickness mechanically compensates for loss of PIB trabeculae

To further investigate the differential role of structural determinants in the implant anchorage apparatus, we carried out a correlative analysis between structural and biomechanical parameters. This analysis shows that the ORX-induced loss of PIB trabeculae (Fig. 3C) and decrease in BV/TV (Fig. 3A) are associated with impaired mechanical properties, in particular toughness (Fig. 5). It should be reiterated that ORX does not affect the Tb.Th (Fig. 3D) and that iahPTH(1–34) reverses the ORX-induced decreases in the PIB BV/TV to a level higher than that recorded in the sham ORX rats only by increasing Tb.Th (Fig. 3A, C). Importantly, the nearly 30% iahPTH(1–34)-induced increase in Tb.Th was associated with 34% higher %OI (Fig. 3B) and translated into respective approximately three-, two-, and fourfold increases in ultimate force, stiffness, and toughness (Fig. 5). However, the relation of Tb.Th with biomechanical parameters is particularly strong, whereas the correlation with the %OI is substantially weaker or even insignificant (Table 1). Hence, in the PIB, Tb.Th appears as the predominant structural variable determining the differences in the anchorage biomechanical properties among normal, weakened, and iahPTH(1–34)-treated bone. The relative strength of the OI over PIB in the low-density bone is reduced following iahPTH(1–34) treatment, which leads to thicker trabeculae and hence shifting of critical strains to the bone-implant contacts. In further support of such shifting is the observation that most failures at the implant tip occur in its interface with bone, where trabeculae are especially thick because of their proximity to the cortex (Fig. 1).

That in the weakened skeleton the OI is relatively resistant to loading suggests that substantial changes in %OI in low-density bone would have a limited effect on the biomechanical properties. Indeed, implant surface modulations, which specifically affect OI,(14,15) result in a significant 29% decrease in %OI, with the PIB and biomechanical parameters remaining unchanged (Fig. 6). These findings further support the notion that the critical strains induced by pullout loads in the low-density bone occur primarily in the PIB, highlighting the importance of trabecular thickness.

Discussion

Although the distinction between OI and PIB has been recognized for quite a while now(15,28,29) so far their differential contribution to the load-bearing capacity of endosseous implants had been unclear. This issue is especially relevant for the enhanced understanding and consequent reduction of the high failure rate of implantation procedures in low-density bone sites. Using IGFA to analyze the structure-function relationship of the implant anchorage apparatus, we show here distinct failure patterns in normal, gonadectomized, and iahPTH(1–34)-rescued gonadectomized animals. A comparative assessment of these patterns assigns a critical role for the PIB, in particular the trabecular strut thickness, in implant anchorage. The basal level of titanium-induced bone-implant bonding is such that alterations in its extent over the implant surface seem to have a relatively minor effect on the anchorage apparatus. These considerations assume that changes in hormonal status have little effect on the material properties of the mineralized matrix and of the actual bone-implant bonding.(30–32)

In line with previous experimental studies addressing endosseous implantation, the present results confirm weakening of the anchorage apparatus in low-density bone.(16,33) This weakening does not result from impaired OI because the ORX/VEH rats display a low ∆OI/∆Conn.D ratio (i.e., OI-to-PIB shift of...
critical strains) and decreased biomechanical properties that are associated with structural changes restricted to the PIB. This conclusion is further supported by the generally high correlation coefficients between biomechanical and PIB structural parameters. Likewise, the involvement of changes in %OI in the iahPTH(1–34)-induced improvement in anchorage biomechanical properties appears substantially smaller than the impact of changes in the PIB. It may be considered an important finding that Tb.Th explains most of the mechanical variability in implant failure. Interestingly, although ORX reduced the amount of bone by decreasing the Tb.N, this did not result in reduced stiffness nor ultimate force because the process did not involve a change in the average Tb.Th. Nevertheless, ORX influenced the postyield behavior, resulting in reduced toughness. It can be concluded from the correlative analysis that toughness is equally influenced by changes in BV/TV (through a decrease in Tb.N) as by changes in Tb.Th. A corollary of this conclusion is that the initial linear and yield behaviors of the implants are mostly influenced by Tb.Th. Once yielding occurs and individual struts have already started to buckle and bend, it is also the total amount of bone available that influences the postyield behavior of the implants. Treatment with iahPTH(1–34) improves both Tb.Th and BV/TV and consequently the mechanical resistance and failure behavior in a synergistic fashion.

Implant surface roughening has been the subject of intensive investigation.(34,35) Although a small number of studies claim that optimal roughening increases the %OI,(36–40) other articles report conflicting data ranging from no effect to even an impairment of implant anchorage.(41–43) It should be pointed out that in this study we have not investigated the potential benefit or harm resulting from implant surface roughening; we rather used this approach as a means to modulate the %OI. Indeed, using implant surface modulations that selectively target the bone-implant contact, we demonstrate here significant changes in %OI, with no effect on the biomechanical properties.

It is well established that gonadectomy-induced trabecular bone loss results mainly from a reduction in trabecular number, whereas its reversal by iahPTH(1–34) is due primarily to increased trabecular thickness, especially in the adult and aging skeleton.(12,44,45) Although finite-element analyses suggest that the load-bearing capacity of trabecular bone depends mainly on intact trabecular number with a lesser contribution by trabecular strut thickness,(46,47) biomechanical studies in compression demonstrate that iahPTH(1–34)-induced reversal of trabecular bone loss is accompanied by improved skeletal load-bearing properties even beyond normal levels.(48–51) The present IGFA suggests that the vast majority of PIB individual trabecular failures induced by the implant pullout results from bending stresses transmitted to the trabeculae, implying a preferential role of strut thickness over strut number. As in the case of testing in compression, the rescue of gonadectomy-induced PIB loss by iahPTH(1–34), herein and previously, leads to superior biomechanical properties of the anchorage apparatus by improving the PIB response to these bending forces.(13,16) The iahPTH(1–34) enhancement of the trabecular bone biomechanical function is independent of the loading mode. This is a major consideration for implant surgery because in real life vectors applied to the anchorage apparatus have multiple directions. Taken together, our data suggest that the mechanism leading to failure of implant anchorage, particularly in low-density bone, involves buckling of the thinnest struts followed by fractures of thicker trabeculae and complete PIB failure. The combination of a low trabecular number and increased strut thickness in the iahPTH(1–34)-treated animals explains the very small plastic

---

**Fig. 4.** Metabolically related OI-to-PIB and PIB-to-OI shifts in critical strains in implant anchorage apparatus induced by pullout to failure. (A) Percent decrease in %OI between pre- and postfailure values (ΔOI). (B) Percent decrease in Conn.D between pre- and postfailure values (ΔConn.D). (C) Ratio between failure at the bone-implant interface and intratrabecular failure (ΔOI/ΔConn.D). Black bars = sham ORX; gray bars = ORX/VEH; white bars = ORX/PTH. Data are mean ± SE. *Versus ORX; p < .05.

---

**Fig. 5.** Metabolically related changes in biomechanical parameters of implant anchorage. (A) Ultimate force. (B) Stiffness. (C) Toughness. Black bars = sham ORX; gray bars = ORX/VEH; white bars = ORX/PTH. Data are mean ± SE. (a) Versus ORX/VEH. (b) Versus sham ORX; p < 0.05.
range of the load-displacement changes, suggesting that the fewer thick struts collapse simultaneously rather than sequentially.

We used here a rather small sample of animals because of the logistic limitations inherent to IGFA. Nevertheless, the magnitude of the effects of ORX and iahPTH(1–34) and precision of the experimental methods employed lead to statistically significant results portraying the feasibility of systemic bone anabolic therapy using agents such as iahPTH(1–34) for the enhancement of endosseous implant anchorage. We have previously assessed the effect of iahPTH(1–34) dose dependently in the same endosseous implantation model in osteoporotic rats and found an optimal effect administering 25 µg/kg per day.\(^\text{(13)}\) This therapeutic window of iahPTH(1–34) is well within the range of 10 to 80 µg/kg per day reported for the rescue of gonadectomy-induced bone loss in rodents.\(^\text{(12,52–57)}\) An even lower range, 5 to 10 µg/kg per day, is reportedly sufficient to stimulate fracture healing.\(^\text{(58,59)}\) However, these studies were done in nongonadectomized animals. Also, unlike peri-implant healing, where only osteoblasts are targeted by PTH, the fracture callus contains chondrocytes, which express receptors for PTH\(^\text{(60)}\) and may affect the overall efficacy. Importantly, the effective iahPTH(1–34) doses in rodents are five- to tenfold higher than those used clinically.\(^\text{(10,61)}\) However, the clinical practice is influenced by considerations such as cancer risk and other side effects of iahPTH(1–34),\(^\text{(62)}\) which do not apply to most animal studies. Hence it remains to be tested clinically whether the approved dosage range for humans is sufficiently high to stimulate endosseous implant anchorage.

Generally, the present results advocate bone anabolic agents to support implant anchorage in instances of generalized osteoporotic bone loss as well as in cases exhibiting low bone density locally at the implantation site. The specific use of iahPTH(1–34) in this context should be carefully evaluated in view of a recent report that the response to teriparatide is attenuated when it is readministered after an initial treatment period.\(^\text{(63)}\) In addition, this study was performed early in the stages of gonadectomy, whereas many orthopedic patients are long past menopause and may not be as responsive. Recently, a clinical study suggested that systemically administered bisphosphonates improve the clinical outcome of endosseous implantation procedures.\(^\text{(64)}\) Hence a combined antinflammatory-anabolic therapy may constitute a useful strategy to enhance implant anchorage in low-density bone.

In conclusion, this study supports a model wherein anchorage failure involves buckling and ultimately breakdown of the weakest trabecular struts followed by a sequential failure of stronger trabeculae. Treatment with iahPTH(1–34) induced thicker struts that were able to delay and even avoid failure of individual elements, thus implicating trabecular thickness as a

---

**Table 1. Correlation Coefficients Between Structural and Biomechanical Parameters of Implant Anchorage Apparatus in Sham ORX, ORX, and iahPTH(1–34)-Treated ORX Animals**

<table>
<thead>
<tr>
<th>Structural</th>
<th>%OI</th>
<th>BV/TV</th>
<th>Tb.Th</th>
<th>Tb.N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ultimate force</td>
<td>(r^2 = 0.592)</td>
<td>(r^2 = 0.744)</td>
<td>(r^2 = 0.862)</td>
<td>(r^2 = 0.041)</td>
</tr>
<tr>
<td>Stiffness</td>
<td>(r^2 = 0.331)</td>
<td>(r^2 = 0.543)</td>
<td>(r^2 = 0.823)</td>
<td>(r^2 = 0.044)</td>
</tr>
<tr>
<td>Toughness</td>
<td>(r^2 = 0.583)</td>
<td>(r^2 = 0.711)</td>
<td>(r^2 = 0.737)</td>
<td>(r^2 = 0.003)</td>
</tr>
</tbody>
</table>

\(n = 12\); N.S. = not significant.
prime target for enhancing implant anchorage using systemically administered bone anabolic agents.

Disclosures

DK, RM, and IB codirected the project. The authors state that they have no conflicts of interest.

Acknowledgments

This work was supported by a grant from the Julius Oppenheimer Fund (to IB and DK) and by the professorship in bioengineering from the Swiss National Science Foundation (Grant No. PP-104317/1).

References

32. Lane NE, Yao W, Kinney JH, Modin G, Balooch M, Wronska TJ. Both hPTH(1–34) and bFGF increase trabecular bone mass in osteopenic rats but they have different effects on trabecular bone architecture. J Bone Miner Res. 2003;18:2105–2115.


50. Iwaniuc UT, Mosekilde L, Mitova-Caneva NG, Thomsen JS, Wronski TJ. Sequential treatment with basic fibroblast growth factor and PTH is more efficacious than treatment with PTH alone for increasing vertebral bone mass and strength in osteopenic ovariectomized rats. Endocrinology. 2002;143:2515–2526.

51. Wronski TJ, Yen CF, Qi H, Dann LM. Parathyroid hormone is more effective than estrogen or bisphosphonates for restoration of lost bone mass in ovariectomized rats. Endocrinology. 1993;132:823–831.


