Original Article

Screw-type device diameter and orthodontic loading influence adjacent bone remodeling

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ABSTRACT

Objective: To evaluate the effect of diameter and orthodontic loading of a screw-type implantable device on bone remodeling.

Materials and Methods: Screw-shaped devices of four distinct diameters, 1.6, 2, 3, and 3.75 mm, were placed into edentulous sites in five skeletally mature beagle dogs (n = 14/dog) following premolar extraction. Using a split-mouth design, devices on one side were loaded using calibrated 2N coil springs. Epifluorescent bone labels were administered intravenous prior to sacrifice. Bone-implant sections (~ 70 μm) were evaluated to quantify bone formation rate (BFR), and other histomorphometric variables were assessed in the implant supporting bone.

Results: The mean BFR ranged from 10.93 percent per year to 38.91 percent per year. BFR in the bone adjacent to the device was lower for the loaded 1.6-mm screws when compared with the nonloaded 1.6-mm screws ($P < .01$) and the loaded 2.0-, 3.0-, and 3.75-mm diameter screws ($P < .01$). No significant differences in BFR were noted, regardless of loading condition, between the 2.0-, 3.0-, and 3.75-mm diameter screws.

Conclusions: We detected a dramatic reduction in bone remodeling. Although orthodontic loading of 2N did not alter bone remodeling associated with screws with a 2.0-mm diameter or larger, it did decrease bone remodeling adjacent to a loaded 1.6-mm screw. The long-term effect of this diminished remodeling should be further investigated. (*Angle Orthod.* 2017;87:466–472)

KEY WORDS: Mini screws; Orthodontic force; Bone remodeling; Beagle dogs

INTRODUCTION

Utilization of temporary skeletal anchorage and specifically miniscrew implants is increasing in contemporary orthodontic practice.[1] Temporary anchorage devices are a broad category of biocompatible devices inserted into the bone for the purpose of supporting tooth movement and other orthodontic treatment applications.[2] Varying forms of these devices are currently in use, including dental implants, bone plates, and small-diameter (typically < 2 mm) screws that are also referred to as miniscrew implants (MSI). Some of the most frequently used skeletal anchors in contemporary orthodontics are MSI, typically 1.6 to 1.8 mm in diameter, which are placed in the monocortical plate of maxillary and mandibular alveolar bone.[3] The diameter of MSI anchors in orthodontics has been based on the ability to place the device in interradicular locations and thus smaller diameters (~1.6 mm) are very popular. However, with larger diameter extraalveolar anchorage becoming more common, it is reasonable to study diameter and dimensions not limited by intraalveolar anatomy.[4]

The purpose of this study was to evaluate the effects of screw diameter and orthodontic load on dynamic

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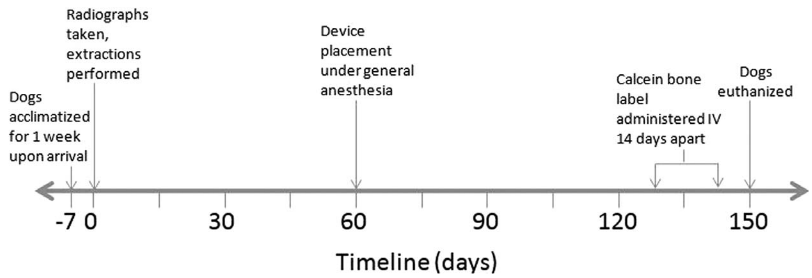

Figure 1. Timeline of experimental design.

bone parameters in supporting osseous tissue. Device diameter and loading alter the rigidity of implants and thereby could influence the bone–implant interface and the adjacent bone response.[5] Although primary stability depends on bone–implant contact and bone modeling near the screw surface,[6] remodeling in the implant-adjacent bone is critical to the secondary stability of a screw.[7–9] In this study, we analyzed osteonal remodeling in cortical bone supporting screw-type devices intended for skeletal anchorage. We hypothesized that both screw diameter and orthodontic loading alter device-adjacent bone remodeling in beagle dogs.

MATERIALS AND METHODS

All protocols were approved by the University of Kentucky Institutional Animal Care and Use Committee. A total of five skeletally mature, approximately 1-year-old, male beagle dogs were purchased from Ridglan Farms (Mount Horeb, Wis) and acclimatized for 1 week prior to beginning the study. Canines serve as an established animal model for implant studies.[10] Male animals are not influenced by estrus cycles. Briefly, after the acclimatization period, the animals were sedated, anesthetized, intubated, and maintained on isoflurane as has been previously described.[6] Maxillary second and third premolars and mandibular third and fourth premolars were surgically extracted to allow for uniform bone stock for screws. Extraction sites were allowed to heal for 60 days prior to screw placement (Figure 1). Custom-machined, titanium alloy (Ti6Al4V) screws were designed specifically for this study. The screws were identical (7-mm length, symmetric threads, surface preparation) except for the diameters (1.6, 2.0, 3.0, and 3.75 mm). A sample of five dogs with approximately six treated implants per dog had 80% power to detect an effect size of 2.3 or larger when compared adjacent to distant sites at the $.05/3 = .017$ level of significance.[6] Prior to screw placement, pilot holes were made into the buccal plate of the maxilla and mandible, with a final drill size 0.5-mm smaller than the intended screw diameter. Screws were placed ($n = 14$/dog) bilaterally in a split-mouth design, with the screws on one randomly determined side of the mouth being loaded immediately with 2N force using calibrated coil springs (Figure 2). No external load was applied to the screws on the contralateral side. Screw location within each quadrant was rotated between dogs to ensure the equal distribution of all diameter screws.

Intravital bone labels were administered intravenously. Calcein (5 mg/kg) was given 21 and 7 days prior to sacrifice using a typical labeling schedule.[6] Dogs were euthanized 90 days after screw placement. At sacrifice, maxillary and mandibular bone blocks were obtained. The bone blocks were prepared for microscopic analysis using undecalcified methods. The bone specimens were dehydrated in ascending alco-

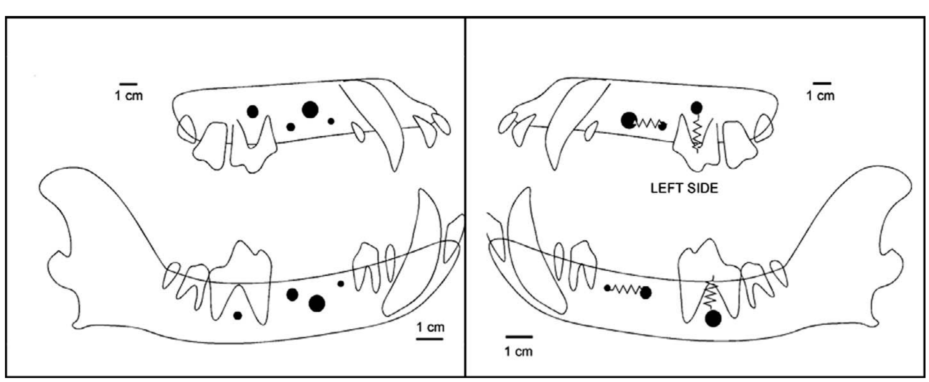

Figure 2. Schematic of device distribution in split mouth design. (a) Nonloaded. (b) Loaded. Screws were placed in a staggered array with adequate space (5 mm) between screws.

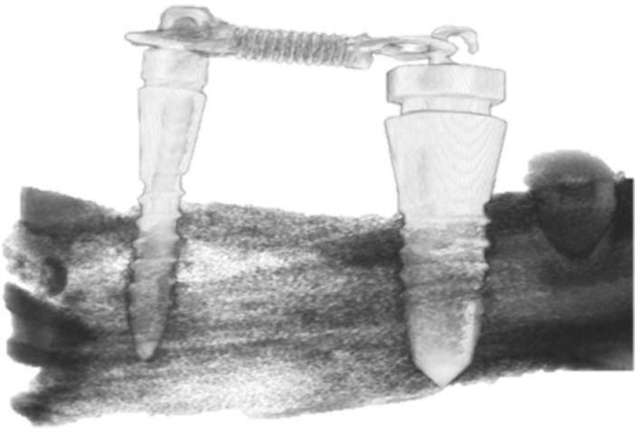

Figure 3. Micro-computed tomography image of devices loaded with 2N forces with calibrated coil springs. These images assisted in sectioning the screws along the long axis in the desired orientation.

holic solutions and infiltrated with Technovit 7200 VLC (Exakt Technologies, Inc., Oklahoma City, Okla). Micro-computed tomography images (Scanco Medical, Bruttisellen, Switzerland) were made for each bone block to assist with alignment during sectioning (Figure 3). The infiltrated bone blocks were cut down to approximately 70 μm sections using the Exakt Technologies, Inc. cutting and grinding system to reliably obtain sections through the widest and thereby central portion of the screw.

Histomorphometry (Figure 4) of screw-supporting bone sections was performed using computer microscopic imaging software (Bioquant Osteo, Nashville, Tenn). All measurements were made at 40× magnification by a single trained and blinded histomorphometrist. Cortical bone remodeling[11] was analyzed both within 1 mm (adjacent region) and 1 mm to 3 mm

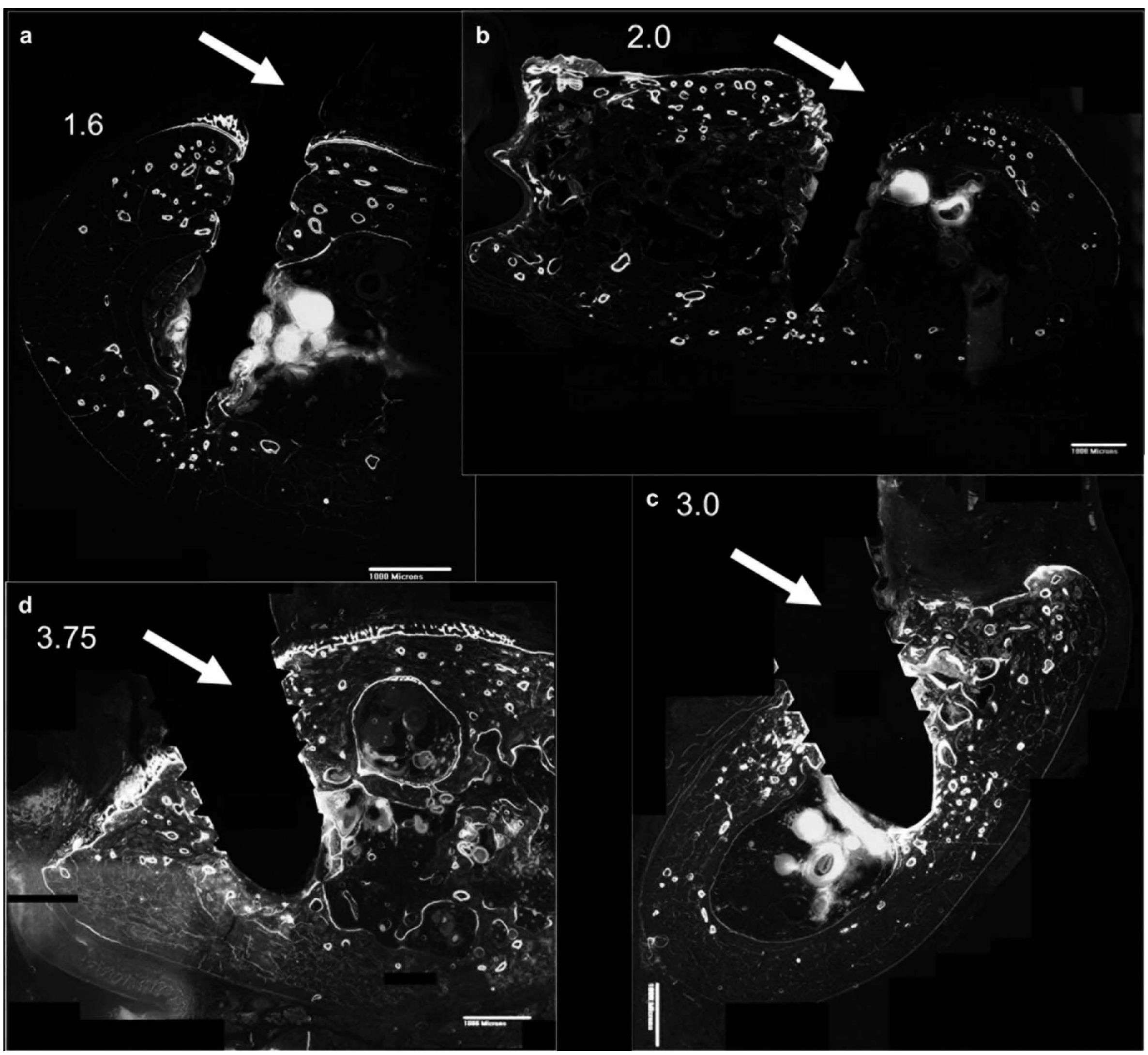

Figure 4. Longitudinal sections of (a) 1.6-mm, (b) 2.0-mm, (c) 3.0-mm, and (d) 3.75-mm diameter screws and supporting bone under fluorescent light. The bone in these sections was examined to assess various histomorphometric measurements.

Table 1. Descriptive Statistics (Means and Standard Deviations) of Histomorphometric Variables (BV/TV, MAR, and BFR[a]) Subdivided by Key Variables (Jaw, Diameter, and Loading)

			BV/TV, %				MAR, μm/day				BFR, %/year					
			Adjacent		Distant		Adjacent		Distant		Adjacent		Distant		Combined	
Variable	Subset	n	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Jaw	Maxillary	31	75.20	13.46	75.67	14.59	1.75	0.41	1.68	0.30	25.43	12.79	17.94	14.40	20.14	12.50
	Mandibular	30	83.57	12.85	85.08	11.74	1.74	0.31	1.74	0.29	35.77	19.48	26.67	13.97	30.09	15.08
Diameter	1.60 mm	15	74.01	15.01	75.00	13.91	1.66	0.38	1.74	0.30	21.77	18.92	18.46	14.70	19.37	14.37
	2.00 mm	18	79.79	15.75	79.77	14.83	1.72	0.29	1.65	0.28	31.04	13.08	23.17	14.96	25.74	13.26
	3.00 mm	14	78.39	12.12	80.52	13.67	1.79	0.39	1.71	0.16	30.83	12.43	21.26	10.93	24.24	11.00
	3.75 mm	14	85.32	9.06	86.45	12.08	1.80	0.40	1.73	0.42	38.91	20.51	26.04	18.00	30.96	18.28
Loading	None	34	79.78	13.61	81.26	13.23	1.76	0.40	1.70	0.22	32.96	18.50	24.23	16.22	26.90	16.12
	2N	27	78.73	14.09	79.10	15.05	1.72	0.30	1.71	0.38	27.45	14.92	19.73	12.50	22.67	12.31

[a] BFR, bone formation rate; BV/TV, bone volume/total volume; MAR, mineral apposition rate.

(distant region) from the device–bone interface. Bone formation rate (BFR, % per year) was calculated from calcein labeled secondary osteonal bone turnover. BFR values were also calculated for the combined regions (0–3mm from the device interface). All measurements and calculations followed the standard nomenclature and formulae described by Parfitt et al.[12]

Both static and dynamic histomorphometric indices were measured. Static measurements included (1) bone volume, (2) void volume, and (3) bone volume/total volume. By administering intravital labels at two time points, the dynamic histomorphometric parameters were calculated by the measurement of (1) single-label surfaces, (2) double-label surfaces, (3) interlabial width, (4) mineral apposition rate (measure of rate of bone matrix deposition [MAR], μm/day), and (5) the BFR. The detailed formulas have been described previously.[6]

Data were analyzed for each variable (BV/TV, MAR, and BFR) using a repeated-measure analysis of variance. In this study, the repeated measures included jaw (maxilla or mandible), screw diameter (1.6, 2, 3, and 3.75 mm), presence or absence of external loading, and all interactions among these factors. Random effects were dogs and all interactions among the fixed effects and their interactions with dogs. The unit of randomization (choice of loading and diameter) was the implant and the unit of analysis was the site (adjacent or distant) surrounding the tooth. Post hoc comparison of means were analyzed using Fisher's protected least significant procedure with statistical significance set at $P < .05$. There was no evidence of any outliers influencing the results.

Table 2. Significant Main Effects and Interactions Obtained From the Mixed-Model Analyses for the Histomorphometric Variables

Variable[a]	Region	Comparison	*P* Value
BV/TV		Main effects	
	Adjacent	Jaw: maxilla vs mandible	.0100
	Distant	Jaw: maxilla vs mandible	.0074
BFR		Main effects	
		Region: adjacent vs distant	<.0001
	Adjacent	Jaw: maxilla vs mandible	.0120
	Combined	Jaw: maxilla vs mandible	.0046
	Adjacent	Diameter	.0350
		Interaction	
	Adjacent	Diameter × Loading	.0398

[a] BFR, bone formation rate; BV/TV, bone volume/total volume.

RESULTS

All animals remained healthy through the entire duration of the study. At, or prior to, sacrifice, 6 of 70 total screws demonstrated clinical mobility. In addition, three screws were excluded because of difficulties in sectioning, tooth-root proximity, or inadequate adjacent alveolar bone, which would have compromised valid histomorphometric measurements.

Descriptive statistics (means and standard deviations) for the histomorphometric variables are summarized in Table 1. The results for BFR in the adjacent, distant, and combined regions with screws separated by jaw, diameter, and external load are also detailed in Table 1. Statistically significant differences from the analysis of variance of fixed effects and significant interactions are reported in Table 2.

Histomorphometric Measurements

BV/TV. This measurement quantifies the bone porosity in regions of interest surrounding the screw-type device. The means (SD) for the BV/TV for the adjacent and distant regions for the maxillary devices were 75.2% (±13.5%) and 75.7% (±14.6%), respectively. In the mandible, the mean BV/TV for the adjacent and distant regions were 83.6% (±12.9%) and 85.1% (±11.7%), respectively. BV/TV was significantly different ($P = .01$) between jaws, whereas the differences between adjacent and distant regions in each jaw (maxillary $P > .85$, mandibular $P > .45$) were not significant.

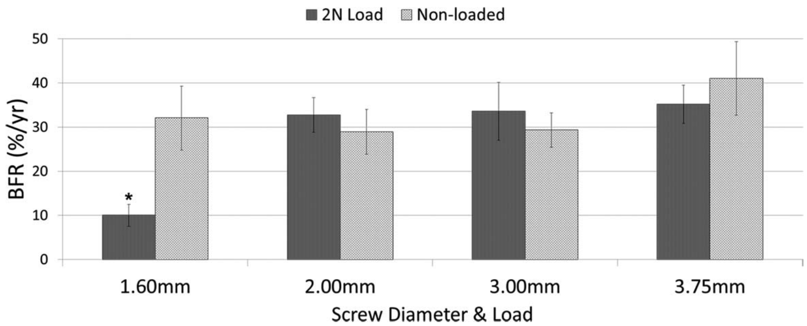

Figure 5. Bone remodeling rates (mean BFR, % per year, ± SE) adjacent to varying diameter screws and loading conditions. By separating screw-type devices by both diameter and loading condition, significantly decreased adjacent bone remodeling was noted adjacent to loaded 1.6-mm screws ($P < .005$). No difference was detected in the nonloaded screws of varying diameter.

MAR. This measurement quantifies the tissue-level activity of the osteoblasts. Mean MAR for all the regions of interest around all screws was 1.7 μm/day. No significant differences in MAR values were identified when the data were compared by screw diameter, loading, or jaw.

BFR. This is a product of mineral apposition rate and the number of sites of active bone formation within a designated volume of bone. A statistically significant ($P < .001$) higher remodeling rate (30.5% per year) was identified in the bone of the adjacent region when compared with the distant region (22.2% per year) for all devices combined. Significantly greater turnover ($P < .01$) was also noted in the mandible, with an average mandibular BFR of 30.1% per year when compared with 20.1% per year in the maxilla.

The 1.6-mm diameter screws exhibited a significantly ($P = .035$) lower remodeling rate (21.8% per year) in the bone-adjacent region when compared with 2.0 mm (31.0% per year), 3.0 mm (30.8% per year), and 3.75 mm (38.9% per year) screws. Screw diameter was not statistically significant when both the adjacent and distant regions (ie, 0–3 mm) were combined ($P = .156$).

No statistically significant difference in BFR was found between the loaded (2N) and nonloaded groups for all of the devices combined. In the adjacent region, bone around loaded screws on average demonstrated a nonsignificant ($P = .194$) lower remodeling rate of 27.5% per year when compared with 33.0% per year adjacent to nonloaded screws. However, a significant interaction between diameter and loading was identified in the adjacent region ($P < .04$). Considering only 1.6-mm diameter screws, the bone adjacent to the loaded screws exhibited a 10.0% per year remodeling rate that was significantly lower ($P = .004$) than the bone remodeling rate of 32.1% per year around nonloaded 1.6-mm diameter screws (Figure 5). Furthermore, when only loaded screws were considered, the diameter had a statistically significant ($P < .002$) effect. Bone adjacent to loaded 1.6-mm diameter screws demonstrated a lower remodeling rate (10.0% per year) than bone adjacent to loaded 2.0-mm (32.7% per year), 3.0-mm (33.6% per year), and 3.75-mm (35.2% per year) diameter screws. When only nonloaded screws were considered, no significant difference ($P = .198$) in remodeling rate was seen by diameter (Figure 5).

DISCUSSION

The purpose of this study was to determine the effects of both screw diameter and orthodontic loading on the adjacent bone response. The most striking finding of this study was the significantly decreased bone remodeling rate adjacent to the 2N loaded 1.6-mm diameter screws. This remodeling rate was approximately threefold lower than both the bone adjacent to the 1.6-mm diameter nonloaded screws as well as the loaded screws of larger diameters.

Bone remodeling is critical to maintaining a long-term, vital bone-implant interface.[7] However, this type of remodeling is certainly not the only indicator of miniscrew stability or success as other mechanical parameters are also important.[13] After the initial stages of healing, it is thought that implant-adjacent bone remodeling is elevated as a response to increased stress.[14] This elevated bone turnover could prevent microdamage from accumulating by providing a compliant layer of bone.[15] In this study, increased osteonal remodeling was noted in the region adjacent to the screw-type device relative to the distant region. This localized increase also confirms similar findings in previously published studies performed in various animals and humans.[6–8]

Ideally the development and recommendation of skeletal anchorage modalities in orthodontics should be guided by biologically driven scientific evidence. This animal study allowed for the control of multiple factors that are not possible in humans. This provided a valid comparison of diameter and loading and included screw diameters as narrow as typical miniscrews and as wide as traditional endosseous implants.

In this study, the effect of screw diameter and its interaction with orthodontic external loading were evaluated by their effects on the level of device-adjacent bone remodeling. We identified a significant effect of diameter on the adjacent bone response, with the narrowest screw-type device tested (1.6-mm diameter) demonstrating the lowest adjacent bone remodeling rate. When all of the screws were considered independent of diameter, an external load of 2N had no significant effect on BFR. However, a statistically significant interaction between screw diameter and external load was identified. The further separation of screws by both diameter and loading conditions indicated that the overall effect of screw diameter is explained by the marked decrease in device-adjacent BFR of the loaded, 1.6-mm screws. Interestingly, BFR adjacent to nonloaded, 1.6-mm diameter screws was no different than BFR adjacent to larger diameter, nonloaded screws. This suggests that it is a loaded screw of this 1.6-mm diameter that experienced diminished bone turnover. In addition, device-adjacent BFR for 2.0-, 3.0-, and 3.75-mm diameter screws was not altered by the presence of a 2N load. These data suggest that in monocortical alveolar bone, 1.6-mm screws under a typical orthodontic load are less likely to maintain a vital, compliant bone–implant interface than wider screws. With time it is likely that the decreased remodeling would not sustain a successful device interface; this has to be substantiated experimentally. In animals receiving high-dose bisphosphonates, the bone remodeling rate is suppressed, and this is thought to lead in the long term to the failure of the implant.[16] Future studies should be designed to provide insight into if and when that difference in tissue-level response at the bone–implant/device interface may translate into failure or other complications such as drift.[17] The BV/TV would not account for differences between the various implant diameters or loading.

Controlling a number of variables that could influence our outcomes was important in the experimental design. The canine model and specifically beagles have been documented to be a valid animal model for implant research that allows for the comparison to numerous previously performed studies.[6,7,10,16–18] A loss of screws is not uncommon[18] and could have been related to gnawing by the animals even though Elizabethan collars were installed. The focus of this study was to measure histomorphometric variables and evaluate the biologic response and not to quantify the survival of individual MSI, for which a clinical study would be more appropriate. Last, the duration of the study allowed for a full bone-remodeling cycle following screw placement and minimized the influence of lingering "regional acceleratory phenomenon" on the data.[7]

Extrapolation of results from animal studies to humans is a concern and can be challenging with any model. As with many animal studies, large animal husbandry limits the duration of experiment to mimic long-term clinical use. As previously mentioned, placing screws in the alveolar cortical bone was advantageous; however, space constraints of that region limited the number of screws that could be placed in the extraction sites. External load in this study was low (2N) as commonly used for various orthodontic movements. It is plausible that a larger force, perhaps 5N as used for en masse retraction, may demonstrate more profound effects on adjacent bone turnover and needs to be investigated further. For example, with large orthodontic loads, even the larger diameter devices may have altered the bone-remodeling response in the adjacent region. To exploit the full spectrum of loading conditions used in clinical practice, the effect of orthopedic (eg, 10N) forces on larger diameter devices should be investigated. Finally, bone remodeling is only one of many current methods for evaluating osseointegration, and optimal levels of bone turnover for screw retention during clinical use is still unclear. Although adjacent bone remodeling likely plays a significant role, soft tissue considerations, force application, regional inflammation, and many other factors likely contribute to the clinical success or failure of miniscrews in orthodontic practice.

In summary, an important biologic variable, rate of bone turnover, was identified as being different between various diameter implants. To the best of our knowledge, there are no other data that have quantitatively measured histomorphometric variables and identified a dramatic reduction of a critical biologic parameter, bone remodeling, in a controlled experimental design.

CONCLUSIONS

- This study compared screw-type orthodontic anchorage devices of different diameters to determine the effect of diameter and orthodontic loading on the adjacent bone response.
- The results of this study indicate that adjacent bone remodeling was markedly decreased adjacent to 1.6-mm diameter screws under a typical (2N) orthodontic load. This may indicate that 2.0-mm diameter and wider screws are better supported by monocortical alveolar bone to withstand orthodontic forces from a biologic perspective.
- Eventually evidence-based guidelines and device recommendations should be created to make skeletal anchorage more predictably successful for orthodontic patients.

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