Biological reaction of alveolar bone to orthodontic tooth movement

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Abstract: Direct and indirect resorption are perceived as reactions to an applied force. This is in contrast to the view of orthopedic surgeons, who describe apposition as a reaction to loading of bone. A histomorphometric study of the circumalveolar bone reaction to a force system generating translation of premolars and molars of five *maccaca fascicularis* monkeys is described. Three force levels (100 cN, 200 cN, and 300 cN) were applied for a period of 11 weeks. Undecalcified serial sections were cut parallel to the occlusal plane, and a grid consisting of three concentric outlines of the root intersected by six radii was placed on each section. Areas anticipated to be submitted to different stress / strain distributions were isolated. A-posteriori tests were used in order to separate areas that differed with regard to parameters reflecting bone turnover. Based on these results, a new hypothesis regarding tissue reaction to orthodontic forces is suggested. Direct resorption could be perceived as a result of the lowering of the normal strain from the functioning PDL and as such, as a start of remodeling, in the bone biological sense of the word. Indirect remodeling could be perceived as a sterile inflammation attempting to remove ischemic bone under the hyalinized tissue. At a distance from the alveolus, dense woven bone was observed as a sign of a RAP (regional acceleratory phenomena). The apposition could, according to the new hypothesis, be perceived as a result of the bending of the alveolar wall produced by the pull from the Sharpey fibers. The above suggested interpretation of tissue reaction would be shared with bone biologists.

Key Words: Orthodontic tooth movement, Tissue reaction, Bone remodeling, Bone modeling, Histomorphometry, Orthopedics, Stress / strain distribution

Tissue reaction to orthodontic tooth movement is known to occur either through bone or with bone.[1,2] Tooth movement through bone is characterized by indirect resorption at a distance from the periodontal ligament, a so-called undermining resorption starting from the adjacent bone marrow.[3-6] During the period of undermining resorption, no formative activity takes place on the tension side, because only minor displacement of the tooth occurs. The periodontal ligament is compressed and cell-free hyalinized areas are often developed as a result of the localized ischemia. Hyalinization is caused by excessive compression of the periodontal ligament and results from too much stress (force per area). When the undermining resorption has reached the periodontal ligament and removed the hyalinized tissue, the tooth begins its displacement and becomes rather loose due to the widened periodontal ligament.[3] At this point, apposition can start at the tension side, followed by either renewed hyalinization or a continuation of the tooth movement through direct resorption of the alveolar wall.

When teeth are moved with bone, the resorption takes place directly on the wall of the alveolus from the periodontal ligament. If this is the case, the activity of the osteoclasts on the stress surface and the osteoblasts on the strain surface are synchronized as a remodeling cycle[7] identical to one seen in relation to physiological tooth movement. Corresponding to the resorption occurring on the alveolar wall in the direction of the force, apposition occurs at a certain distance within the alveolar process or on the external surface of the alveolus. Simultaneously, the periodontal ligament maintains its width through apposition on the alveolar wall opposing the force. In this way, the tooth can be moved into areas outside the outline of the original alveolar process, carrying its alveolus along with it.

Whether tooth movement occurs with or through bone depends on the

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Submitted: July 1997, **Revised and accepted:** March 1998
Angle Orthod 1999;69(2):151-158

stress/strain distribution in the periodontal ligament. The stress/strain distribution is determined by the following factors: force magnitude, bone area, and distribution of the force, which is the product of the type of tooth movement performed.[3,8,9] In tipping movements, the forces are concentrated in the marginal and apical parts of the alveolus, whereas translation results in more uniform force distribution along the alveolar wall.[10]

Orthodontists have traditionally related compression to resorption and tension to apposition. This is in contrast to orthopedic surgeons, who generally believe that mechanical compression stimulates bone formation and tension stimulates resorption.[11] This controversy was discussed in 1965 by Epker and Frost.[12] These authors showed that the change in the shape of the alveolar circumference resulting from stretching of the fibers across the periodontal ligament results in a decrease in the radius of the alveolar wall, i.e., a bending of the bone in the tension zone. Thus the apposition of the alveolar wall can be perceived as a reaction to bending, comparable to that of the long bones studied by the orthopedist.

It is generally recognized that the reaction to stimulus is distributed regionally, apart from the effect directly adjacent to the stimulus. In the case of a trauma of any kind, the reaction seems to include a regional acceleratory phenomenon (RAP), which leads to increased bone turnover. Continuous mechanical stimulus can, on the other hand, also lead to increased density, a so-called SATMU (structural adaptation to a mechanical usage[13]).

The tissue reaction of the periodontal ligament has been the subject of numerous qualitative and few quantitative studies,[14,15] as has the reaction of the bone surface facing the periodontal ligament.[16] The reaction of the bone adjacent to the alveolus has, on the other hand, not been thoroughly analyzed.

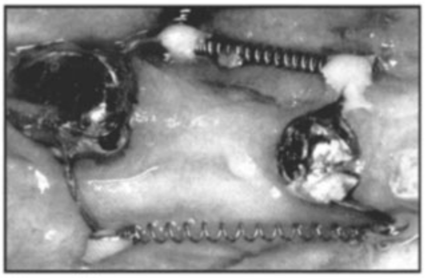

Figure 1A

The appliance delivering forces to the teeth. Sentalloy springs were added to the extension bucally and lingually

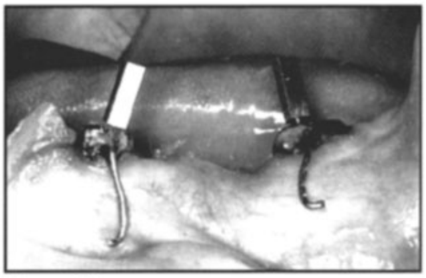

Figure 1B

The extension used for measurements

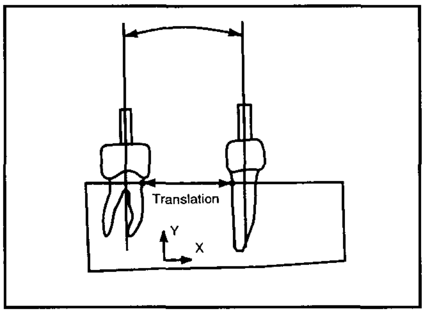

Figure 2

Schematic of the measurements performed, including the amount of translation and rotation

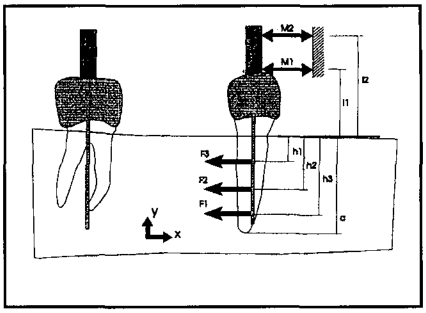

Figure 3

Schematic of the calculations carried out

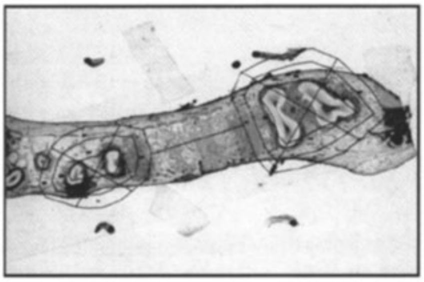

Figure 4

Example of a histological section including cross section of roots of two teeth. Grid used for histomorphometric evaluation is projected onto the section

The present study evaluates histomorphometrically the tissue reaction to a well defined orthodontic force system at various regions of the bone adjacent to the alveolus, excluding the alveolar wall.

Materials and methods

Six adult maccaca fascicularis monkeys were purchased from the National Bacteriological Laboratory, Stockholm, Sweden. They were acclimatized for at least 1 month, then their mandibular first and second molars were removed. Following a healing period of 4 months, the right mandibular second premolar and third molar were prepared for veneer crowns. Extensions were welded on the crowns buccally and lingually in such a way that orthodontic springs could be placed as close as possible to the estimated level of the center of resistance (Figure 1). To improve the measurement of tooth displacement, a screw hole was drilled in the occlusal of the crown (Figure 2) to accommodate a square extension having three notches at different levels. Immediately before the springs were inserted, the extensions were placed on the occlusal surface of the crowns and impressions of each segment were taken with President N (Coltêne/Whaledent Inc, New Jersey) using individual trays. The impressions were cast in red Velmix (Kerr Co, Orange, Calif) plaster. Two measurements were made using an electronic measurement device between a cast splint fitted to the anterior segment serving as anchorage and each tooth that was to be moved. One measurement was made between the notches close to the crown and the other between the notches close to the top of the extension (Figure 3). Measurements were made to the nearest 1/10 mm. On the basis of bone measurements, the type and magnitude of tooth movement in the sagittal plane of space could be calculated when the procedure was repeated at the end of the experiment.

Standardized intraoral radiographs were likewise taken at the beginning and end of the experiment. These were used as controls for measuring tooth movement and were later subject to subtraction analysis.

Following the registrations, Sentalloy (GAC, Central Islip, NY) springs[3] extending from the anterior premolar to the posterior molar were added to the power arms buccally and lingually. In one monkey, Sentalloy springs delivering 50 cN were used corresponding to a total of 100 cN. In three monkeys the force level was 100 cN per side, i.e., a total of 200 cN to each tooth. In one monkey the force delivered by the spring was 150 cN per side, corresponding to 300 cN per tooth. One monkey served as a control. The appliance was adjusted and calibrated every 2 weeks for a period of 11 weeks, corresponding to the total observation period.

At the end of the experiment the monkeys were anaesthetized with Ketalar and sacrificed by perfusion with buffered neutral formalin. The alveolar process of the mandible corresponding to the premolar region was excised, and fixation was continued by immersion of the tissue blocks in formalin at 4°C for 1 week. The tissue blocks were immersed in 1% basic fuchsin in absolute ethanol[17] and embedded in a mixture of glycol methacrylate and the Kulzer Extract embedding medium (Technovit 7,200 VLC). Polymerization was obtained in two steps using light having a 45 µ wave length.

Using a special procedure, 15 to 20 parallel horizontal sections between the marginal bone level and the apex of the teeth were cut with a diamond band saw. The sections were polished in an exact microgrinding system to a thickness of approximately 60 µm,[18] then stained with fast green. This procedure allows for the exact measurement of the section thickness and determination of the level of the tissue block to which the section corresponds. The latter could be crucial in evaluating the relationship between bone reaction and induced tooth movement, which was calculated by measurements performed on casts. Before microscopy, specially produced grids consisting of three concentric outlines of the root cross section intersected by six equidistant radii were placed so that the center of each grid coincided with the center of the tooth being studied, which had been loaded. The distance between the circles was monitored so that the areas limited by the concentric circles and the radii were identical (Figure 4).

Evaluation was performed in eight areas, four within the inner and middle circles, and four within the middle and outer circles. The sections were studied in an Olympus microscope equipped with a Zeiss II integrating reticle with equidistant parallel test lines. The microscopic fields were chosen in equidistant steps parallel to the concentric circles. Orientation of the test specimens was changed through random rotation of the reticle between fields.

The following parameters were measured (M x 160, Figure 5A-B):

Fractional resorption surface Sfract(r) m2/ m2: the extent of resorption lacunae as a fraction of the total trabecular bone surface. Resorption lacunae were identified as scalloped defects in the trabecular surface showing distinct erosion of the lamellar system in polarized light.

Fractional formation surfaces Sfract(f) m2/ m2: the extent of osteoid-covered surfaces as a fraction of the total trabecular surface.

Fractional resting surface was calculated as 100%—fraction recorded as resorptional or appositional. In addition, bone density was evaluated according to Gundersen et al.[19] in the areas mesial and distal to the third molars and second premolar.

Statistics

The relationship between force level and amount of tooth movement recorded at the bony margin was evaluated by means of an analysis of correlation, as was the relationship between the force level and the type of tooth movement.

The results of the histomorphometric analysis were expressed as a percentage of the measured surface. Eight areas around each tooth were evaluated. The results obtained from the corresponding areas at different heights were compared by means of an analysis of variance, comparing the variation and the corresponding areas of different height. Because no significant differences could be detected, the results of the corresponding areas at different levels were summarized for each tooth.

For each of the parameters reflecting bone turnover, the next step in the data reduction process was an analysis of variance comparing the variation within each area with the variation between different areas, the interarea variation. Finally, the difference between different teeth was evaluated. Only the variation accounted for by areas was significant. Finally, an a-posteriori SNK test was applied in order to analyze whether the data could be identified as subsets of data related to their loading history based on clinical data, i.e., whether the areas were submitted to compression, tension, or shearing.

Using correlation analysis, the parameters reflecting turnover expressing bone density in the areas submitted to compression and tension zones were also evaluated in relationship to the force level applied to the teeth.

Results

Two teeth were lost due to periapical problems related to crown preparation. Loading of the other tooth in the region was continued with an implant inserted as anchorage near the lost tooth. In many cases, the buccolingual areas could not be evaluated due to the small dimension of the alveolar process. A total of 640 areas were included in the statistical analysis.

The type of tooth movement registered varied from translation to controlled tipping around a center localized at varying distances above the tooth apex. The amount of tooth movement varied between .21 mm and .9 mm per month, measured at the bone margin. No relationship between force magnitude, type of tooth movement, and amount of displacement could be verified (Table 1A-B).

Due to the variation in clinical behavior of the individual teeth, the histological results were analyzed separately for each area of each tooth. All parameters demonstrated a marked variation on all levels of the analysis, between sections within corresponding areas, between teeth within corresponding areas, and between different areas. But because no significant difference could be established between corresponding areas of different sections, the results obtained from identical areas from sections at different heights were pooled during the following data reduction procedure. Based on the analysis of variance comparing inter- and intratooth variance, it was further concluded that data from corresponding areas from different teeth could be pooled.

However, when evaluating the histomorphometric parameters in relation to area, it was obvious that the all-bone parameters reflecting turnover, i.e., resorption and formation, were influenced by the change in the stress/strain distribution produced by the applied force system (Figure 5A-C, Tables 2A-B). In all parameters of all areas, the test teeth deviated markedly from the corresponding variables for the controls. There was an increase in the relative extension of resorption from 3% to 5% observed in the specimens of the control animals to 7% to 13% of the total trabecular surfaces around the loaded teeth. Likewise, there was an increase in the extension of appositional surfaces from 15% to 20% in the controls to 35% to 49% around the loaded teeth. A corresponding reduction in the extension of resting surfaces was observed in bone surrounding the loaded teeth. Although there was a marked variation, this could not be related to the quantity of displacement of individual teeth. However, based on the a-posteriori SNK-tests, different subsets of areas could be defined.

The subsets were clearly related to the stress/strain distribution. Increased stress was reflected in increased activity compared with the strain zone, where the increase in activity was limited, although increased when compared with the control teeth, which exhibited a uniform pattern of bone turnover (Table 3A-C).

Three subsets could be defined with respect to the relative extent of resorption. The least relative extent of resorption was seen lingually and buccally to the teeth being displaced and corresponding to the area where shearing could be anticipated (Figures 4 and 5C). The areas submitted to compression exhibited the highest resorption activity. Based on the relative extent of apposition, no subsets could be distinguished. On the other hand, the relative extent of resting surface gave ground for the separation of four subsets. The greatest activity reflected by the least extent of resting zones was observed in the areas submitted to compression, and was greatest close to the alveolus. Less activity was seen corresponding to the tension zone, again greatest close to the alveolus. The least activity was observed in the shearing zones.

Most spectacular was the variation in density between the areas subject to loading and those subject to strain transferred from the periodontal ligament during loading. These parameters were influenced by both site and loading. Relative to the control teeth, density in the direction of tooth movement was increased by a factor of two to three, most pronounced at force level 200-300cN (Table 4). In the

Table 1A
Displacement per month

	Premolar		Molar		
Monkey	mm	degree	mm	degree	cN
432	1.34	6	1.08	6	100
431	1.72	3	1.27	3.5	200
433	2.14	6.5	0.90	1	200
434	1.92	17	1.85	17	200
435	1.19	4.4	1.50	8	300

Table 1B
Correlation coefficient between displacement per month cN

Premolar displacement		Molar displacement	
0.47 mm	0.24 degree	0.22 mm	0.30 degree

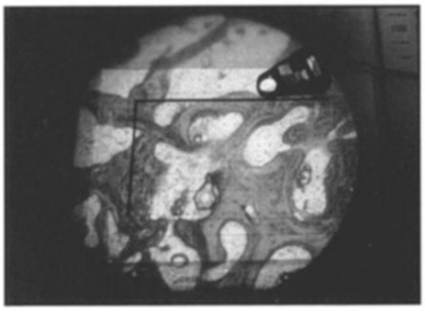

Figure 5A
Histological section of cross section of loaded tooth. Note root resorption (a), direct resorption (b), and dense woven bone in the direction of movement (c)

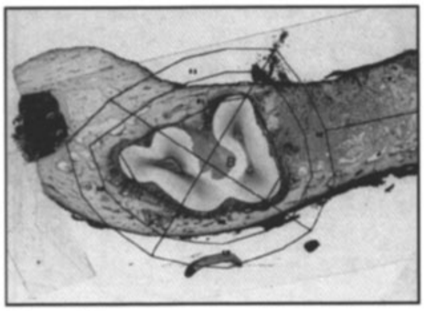

Figure 5B
Detail of trabecular bone onto which a grid used for the determination of bone density is projected

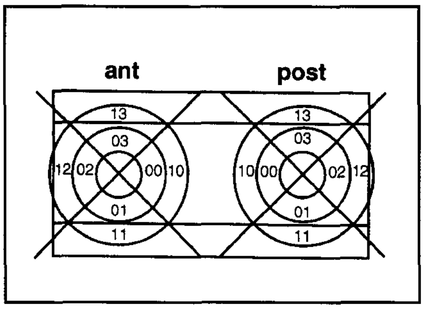

Figure 5C
Schematic illustration of the area evaluated histomorphometrically. The numbers are referred to in the tables

Table 2A
Resting surfaces

Area	Mean %	SD
0	42	15
1	44	19
2	43	17
3	51	15
10	50	17
11	57	19
12	53	16
13	63	20
Total	49	18

Table 2B
Appositional surfaces

Area	Mean %	SD
0	44	14
1	42	16
2	44	15
3	38	13
10	40	15
11	36	16
12	37	12
13	29	17
Total	39	15

Table 2C
Resorptional surfaces

Area	Mean %	SD
0	14	7
1	14	9
2	13	7
3	11	6
10	11	6
11	7	5
12	10	8
13	8	6
Total	11	8

Table 3A
SNK for resting surfaces in PCT

	Subset			
Area	1	2	3	4
0	42			
2	43	43		
1	44	44		
10	50	50	50	
3		51	51	
12			53	
11			57	57
13				63
Sig.	.09	.09	.09	.06

Table 3B
SNK for appositional surfaces in PCT

Area	Subset
13	
11	36
12	37
3	38
10	40
1	42
2	44
0	44

Table 3C
SNK for resorptional surfaces in PCT

	Subset		
Area	1	2	3
11	7		
13	8	8	
12		10	10
10		10	11
3		11	11
2			13
1			14
0			9

case of this parameter, however, there was also a marked variation within the group.

Discussion

According to Frost,[20] any regional noxious stimulus of sufficient magnitude can evoke a RAP. The extent of the affected region and the intensity of response vary directly with the magnitude and nature of the stimulus. In the present study, the nature of the stimulus was a controlled orthodontic force. The strain did vary in magnitude, due both to the difference in forces and to biological variation related to root size and structure of the bone surrounding the teeth.[21] When the RAP includes bone, the reaction seems to span from the cellular to the organ level. In the present study, the most conspicuous result was the increase in both activation frequency and density of the bone subjected to compression in the direction of tooth movement.

Frost[20] graphically illustrated the relationship between strain and net balance of bone turnover (Figure 6). In the case of low strain values, a net loss of bone occurs as a consequence of increased remodeling space. With increasing strain, modeling is initiated and a positive balance is achieved. Where the strain curve crosses the neutral line, resorption and apposition are in balance and the newly formed bone consists of lamellar bone, in contrast to the woven bone formed as a result of an even greater strain. Still higher strain will result in a negative balance because repair cannot keep up with the occurrence of micro fractures.[22] The border between a noxa, i.e., a traumatic stimulus, and a mechanical stimulus resulting in an increased bone mass has not yet been established, but it is likely that the present model evokes strain values perceived as trauma as well as strain values perceived as mechanical usage provoking a structural adaptation to mechanical usage (SATMU).[20] Frost[23] listed the threshold strain values for lamellar bone fibrous tissue. A typical MES seems to be 1500-3000 μE for lamellar bone to start modeling; if the strain is below 100-300 μ, remodeling is activated as a result of inactivity. Based on the loading of bone transferred from implants to trabecular bone, the values recorded for trabecular bone seem to be slightly higher.[21] A large body of evidence of structural adaptation to changes in strain has been generated experimentally and has confirmed the hypothesis forwarded by Frost[23] without, however, taking histomorphometric changes into account.[24-27] The histomorphometric studies do contribute to an understanding of the reaction, since the same net result may be the outcome of a wide range of various changes.

The observation of this study, that loading induces increased density and the generation of woven bone, is in general agreement with SATMU[13] and with the findings of adaptation to increased loading of rat diaphysis reported by Jee et al.[28] Burr et al.[29] performed a histomorphometric study of the effect of altered strain on the radius of dogs in which one front leg was subjected to ulnar osteotomy with and without a fixation plate. They measured strain by means of rosette strain gauges and demonstrated that the activity of individual cells was not influenced, but that the findings could be ascribed to increased activation frequency. Their study also permitted them to separate transitional from sustained responses. As a short-term response, the RAP could be observed, whereas the sustained response was characterized by increased formation of lamellar bone modeling. Parameters reflecting the dynamics of bone indicated that an increase in activation frequency took place in relation to both remodeling and modeling, but the balance was altered only in relation to modeling in the direction of more bone formation. The same group[28,29] also verified that the response to increased mechanical strain may be the formation of woven bone, if the strain is intense enough. Frost[30] described the presence of woven bone as a response seen when the stimulus exceeded a certain value, below which lamellar bone was formed. Wolff[31] likewise considered woven bone a pathophysiological response to overloading and an indication of healing.

When studying the reaction to the loading of bone, the time factor is a considerable problem; most studies present only the modeling response because the true remodeling response would require a much longer observation period. Long-term studies are necessary in order to distinguish between transitional responses and permanent adaptation. The model used in the present study does not allow an observation period long enough to reach a new steady state, as teeth are continuously displaced until they have reached contact. In addition, healing following the extraction of two teeth had surely not reached a steady state when the experiment was initiated. The difference between bone surrounding the control teeth and that surrounding loaded teeth can indeed give information about alveolar bone reaction to orthodontic forces. The findings presented reflect the response to ongoing loading of a tooth into bone undergoing long-term healing following extraction.

Table 4
Bone density at a distance of 20 mm from the alveolus

Force level	N	Mean (tooth)	Range (tissue)
Control	4	20.8 %	12.5-26.5 %
100 cN	3	48.6 %	20.5-65.0 %
200 cN	11	61.5 %	40.0-78.5 %
300 cN	4	63.2 %	38.0-82.5 %

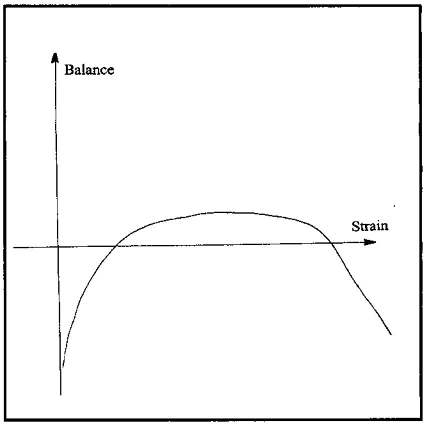

Figure 6
Schematic by Frost illustrating the relationship between strain and bone balance. At very low strain values, the bone is in a negative balance due to active remodeling. At higher strain values, modelling is turned on resulting in a positive balance. At even higher strain values, the balance will again be negative due to repair of microfractures.

Resorption of the alveolus in the direction of the force is a necessary precondition for tooth movement. Resorption of the alveolus wall was also a consistent finding in all cases. Most of the teeth studied exhibited significant root resorption. Brudvik and Rygh[32-34] described initial root resorption related to hyalinization. This would indicate that resorption had started as a reaction to the hyalinization and thus as an indirect or undermining effect. However, the present study showed that the applied force system caused a pronounced formation of woven bone in rapid remodeling of the trabecular, ahead of the alveolus in the direction of the tooth movement. According to Meikle,[35] the first cells to react to orthodontic forces are the preosteoblasts, the helper-osteoblasts, that through the synthesis of cytokines, pass on the necessary message for the differentiation of resorbing cells. It is, however, also likely that the ischemia generated in the periodontal ligament may lead to local necrosis of the bony trabeculae beneath the hyalinized zone, where lining cells on the bone—in this case the alveolar surface necessary for intercellular communication[36] and thus the vitality of the bone—have disappeared. The indirect resorption is probably an attempt to remove necrotic bone. The development of osteoclasts is thus not a reaction to the force but to the ischemia of the tissue, a phenomenon parallel to that of the PDL, where clasts are recruited for the removal of the hyalinized zone.[33-35] During the period of removal of hyalinized tissues, the teeth are not being displaced but forces are transferred to the bone in the direction of the tooth movement, obviously resulting in a dramatic increase in density.

Activity of the bone in that region was related to mechanical loading. Discrimination of the areas according to stress/strain distribution could be done with respect to the extent of resting and resorption surfaces, but not with respect to appositional surfaces. This could be explained when the total reaction is considered in light of the sequence of remodeling ARF (activation, resorption, apposition), as described by Frost.[37] The duration of the resorption period is short in relation to that of the apposition period.[38] It is thus easier to differentiate bone reaction on the basis of this parameter than in relation to apposition. The extension of resting surfaces indirectly reflected the total activity, and it was also possible to distinguish between four subsets of data with respect to this parameter.

At the time of sacrifice, direct resorption of the alveolar wall was occurring in the direction of the force, with a corresponding apposition in the region of tension; the PDL was only slightly deformed. Analyzed in relation to the model introduced by Epker and Frost,[12] the apposition can be explained by an increase in the concavity of the alveolar wall, when the tooth is displaced as a consequence of the stretching of the periodontal ligament fibers that are oriented toward the center of the tooth. Evidence of apposition following bending of an alveolar wall was presented in 1961 by Basset et al.[39] Vignery and Baron,[7] on the other hand, perceived the tooth movement with bone as a model of the BSU (bony structural units),[40] and the resorption and apposition thus coupled by a mechanism that is not yet fully understood. Resorption of the alveolar wall may not, in this context, be directly related to the formation of woven bone in the direction of the tooth movement, which is most likely the response to the initial loading. Direct resorption could occur as part of the macro BSU and actually be a response to the relaxation of the periodontal ligament fibers, resulting in a loading below the limit for minimum effective strain (MES),[13] whereby remodeling starts with resorption. Whether the marked formation of woven bone is directly related to the present resorption of the alveolar wall cannot be clarified in this study. However, since the woven bone both in and around the alveolus had not healed completely almost 7 months after extraction, it constitutes an obstacle to ongoing tooth movement because the dense bone with a high extension of osteoid will be resorbed less easily than trabecular bone with only few osteoid seams. This may increase the risk of root resorption. The effect of a loading large enough to generate hyalinization and increased bone density in the direction of the tooth movement may thus increase the risk of root resorption, both initially during removal of the hyalinized tissue and later, when the woven bone has to be passed.

Conclusions

This paper is based on a series of experimental tooth movements in monkeys. It discusses the tissue reaction related to tooth movement from an osteological point of view, as opposed to the orthodontist's traditional point of view. A new hypothesis regarding the initial tissue reaction is presented and an explanation of apparent controversy between orthopedists (who generate bone with compression) and orthodontists (who resorb bone with compression) is suggested. The direct resorption can be perceived as an activation of remodeling and the undermining resorption as a repair to a trauma. The apposition can be taken as a reaction to a bending of the alveolar wall.

Acknowledgments

This study was supported by the Dannin Foundation, Denmark, and Aarhus University Research Foundation, Denmark.

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