Evaluation of radiomorphometric indices and bone findings on panoramic images in patients with scleroderma

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Objectives. The aim of this study was to make radiomorphometric measurements on panoramic images and evaluate the radiologic findings of bones and teeth in patients with scleroderma.

Study Design. Panoramic images of 49 patients with scleroderma and 51 healthy controls were assessed. Mandibular radiomorphometric indices, including mandibular cortical index (MCI), mental index (MI), panoramic mandibular index (PMI), gonial index (GI), and antegonial index (AI), were determined. Furthermore, mandibular osteolysis, changes of periodontal ligament (PDL) space and changes in the lamina dura were recorded for the scleroderma group.

Results. Statistically significant differences were found for MCI ($P = .003$), MI ($P = .001$), and PMI ($P < .001$) between the scleroderma and control groups, but not for GI or AI ($P > .05$). Widening of the PDL space (79.6%), thickening of the lamina dura (44.9%), limited mouth opening (71.4%), and osseous resorption of the mandible (8%) were detected in the scleroderma group.

Conclusions. The radiomorphometric indices determined in the present study can be used on panoramic images to identify the existence of a porous structure in the mandibular cortical bone in patients with scleroderma. The most common prevalent oral radiographic manifestations of scleroderma were widening of the PDL space and of the lamina dura. (Oral Surg Oral Med Oral Pathol Oral Radiol 2019;127:e23–e30)

Scleroderma is a chronic, autoimmune, inflammatory disease of connective tissue, with a partially unknown etiology, and its clinical course includes fibrosis, inflammation, and vascular changes. The incidence of scleroderma is 19.3 cases per million. There is a female-to-male ratio of 8:1, and the disease is seen most frequently in those 30 to 50 years of age.[1] Histologically, there is a common accumulation of dense collagen within and around normal healthy tissues. This abnormal collagen replaces normal tissue and destroys it, resulting in loss of function in normal tissues.[2,3] According to the features presented, 2 different clinical pictures have been defined: (1) localized scleroderma (morphea and linear scleroderma), which is characterized only by skin thickening; and (2) systemic scleroderma (including limited cutaneous scleroderma, acrosclerosis, CREST [calcinosis, Raynaud phenomenon, esophageal involvement, sclerodactyly, telangiectasia] syndrome, and diffuse cutaneous scleroderma), which can involve both skin and the pulmonary, cardiac, gastrointestinal, and renal systems.[3]

Oral and perioral tissues are commonly affected in scleroderma. The most common clinical findings are thickening of the skin of the face and of the tongue and thinning of the lips.[4] In addition, other clinical signs, such as limited mouth opening, microstomia, xerophthalmia, oral mucosal and facial telangiectasia, xerostomia, oral ulcerations caused by gastroesophageal reflux, dental caries, periodontal disease, widening of the periodontal ligament (PDL) space, and osseous resorption of the mandible, may be encountered.[2,5] A characteristic smooth and tense mask-like face ("Mona Lisa face") is formed as a result of the accumulation of subcutaneous collagen in the face, constriction of the eyes, and loss of skin folds around the mouth. A face with tightened nose, referred to as "mouse face," also results as a consequence of atrophy of the nose wings.[3]

The most common oral radiographic sign of systemic scleroderma is widening of the PDL space, seen in two-thirds of patients (Figure 1).[2,5] This widening is seen in both anterior and posterior teeth but is more prominent in posterior teeth.[6,7] In spite of the widening of the PDL space, the lamina dura may remain intact, and teeth are often not mobile, so the gingival

Statement of Clinical Relevance

Radiomorphometric indices can be used to determine the existence of a porous structure in the mandible on panoramic images of patients who have scleroderma and may have a high risk for osteoporosis; widening of the periodontal ligament space and thickening of the lamina dura can be seen on radiographs.

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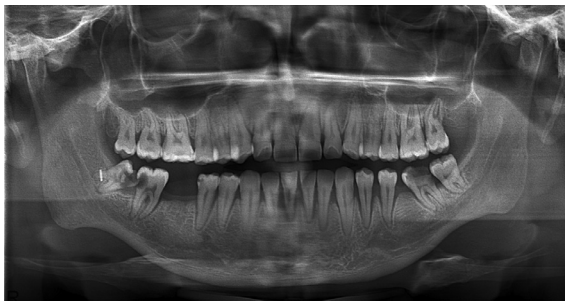

Fig. 1. In the panoramic view of a 28-year-old male patient who was diagnosed with scleroderma 8 years ago, widening of the periodontal ligament (PDL) space in most teeth and thickening of the lamina dura in some areas are seen.

attachment is stable.[2,8] Radiographically observed thickening of the lamina dura has also been reported.[7,9-11] Bone resorption is rare but has been suggested to be an expected complication in patients with long-term systemic scleroderma.[12] Resorption is generally seen in the angulus mandible region and is most often bilateral. Other, less frequent sites of involvement are the condyle, coronoid process, and posterior border of the ramus.[5,7,11,13,14] The etiology of osteolysis is not fully understood. However, 3 theories have been proposed: Bone loss in the mandible can occur as a result of (1) pressure from the tightening of the facial skin; (2) a decrease in mandibular blood flow, resulting in vasculopathy that can cause ischemia; or (3) atrophy of the muscles of mastication.[15] The blunting of the angulus mandible, as seen on a panoramic radiograph, causes a "whale's tail" appearance (Figure 2).[4]

Mandibular radiomorphometric indices are used to assess bone quality and the quantity of the mandible on panoramic radiographs or images.[16] The indices are based on 5 different regional measurement systems; mandibular cortical index (MCI), mental index (MI), panoramic mandibular index (PMI), gonial index (GI), and antegonial index (AI).[17,18] In studies performing morphometric measurements of the mandible, the measurements were generally used for evaluation of osteoporosis. To the best of our knowledge, there are no reports in the literature on the application of radiomorphometric indices for scleroderma. The aim of this study was to perform morphometric measurements on panoramic images from patients with scleroderma and then to compare them with the same measurements on images from healthy individuals. We also evaluated the radiologic findings of the mandible and teeth.

Fig. 2. A panoramic view of a 47-year-old woman with scleroderma shows that resorption of the bilateral angulus mandible produces an image similar to a typical "whale's tail."

MATERIALS AND METHODS

Study group

The study protocol was approved by the Hacettepe University Ethical Committee for Non-Interventional Clinical Investigations (Project no. GO13/380-16). The study included 49 patients with scleroderma (43 females and 6 males; ages 26−74 years; mean age 50 ± 12.3 years), diagnosed by the Department of Rheumatology, Faculty of Medicine, Hacettepe University, and 51 healthy individuals (44 females and 7 males; ages 18−75 years; mean age 47 ± 15 years), who had applied to the dentistry clinic for any reason and had been admitted in the Dentomaxillofacial Radiology department. Study patients who had not completed bone development or had existing metabolic bone diseases and those who were taking medications affecting bone metabolism were excluded. An exception was made for drugs used for the treatment of scleroderma, for example, steroids, because almost all patients with scleroderma use steroids. A total of 100 panoramic images of the patients were obtained from the Veraview IC5 HD (Morita Corporation, Osaka, Japan) device by the same radiologist, with the following standard positioning and exposure parameters: 65 kVp, 7 mA, and a 10-second scan time. The panoramic images in which the complete mandible, condyle, mental foramen, and cortical borders were observed and showed no artifacts were selected for measurement. Two panoramic images in the scleroderma group were excluded from the study because they did not fulfill the criteria. Calibration was performed in each patient for the reliability of the study and standardization of the images. For calibration, a 0.88-mm-thick orthodontic wire was affixed with a transparent tape (to avoid the field of view) to the cheek close to the angulus region. In this program, measurements were started after the orthodontic wire was detected as 0.88 mm thick on each image before starting the measurements, and thus standardization was achieved. Panoramic images were acquired by the TurcaSoft system and exported in TIFF (Tag Image File Format) without data compression. Image processing and analysis were performed by using Image J software (Image J 1.48u; NIH, Maryland, MD).

Panoramic measurements and evaluations

Radiomorphometric measurements on digital panoramic views were performed separately for the right and left sides of the mandible by 2 oral radiologists. Means of the measurements of both sides were calculated, and the data obtained were recorded after applying a magnification correction of 1:3. The drawings made for the mandibular radiomorphometric indices on the panoramic image are shown in Figure 3. We also investigated possible changes in the width of the PDL space, the continuity or dimensional change of the lamina dura, and the presence of osteolysis in the mandible in panoramic images from patients with scleroderma.

The following indices were used for radiomorphometric measurements:

1. MCI was assessed according to the Klemetti[19] classification: C1—the endosteal margin of the cortex is even and sharp. C2—the endosteal margin shows semilunar defects or 1 to 34 cortical residues. C3—the cortical layer includes many endosteal cortical residues and appears porous. MCI was determined visually from both sides, and the more deteriorated cortex was used to diagnose the cortical shape.
2. MI is the thickness of the mandibular cortex at the mental foramen region and was assessed according to the technique described by Ledgerton et al.[16]
3. GI is the width of the inferior cortical border of the mandible at the gonial angle.[20] The bisector of the gonial angle was determined, and the cortical thickness corresponding to the line defining this bisector was measured.
4. AI is the cortical width in the region of the anterior gonion.[16] We measured the cortical thickness at the site defined by the straight line extending tangentially from the anterior border of the ascending ramus to the lower border of the mandible.
5. PMI is the ratio of the mandibular cortical thickness at the mental foramen region to the distance between the mental foramen and the lower cortical border.[17] PMI can be calculated in 2 ways, on the basis of the upper or the lower border of the mental foramen. In the present study, PMI was calculated on the basis of the upper border of mental foramen.

Fig. 3. The drawings made for measurements for the mandibular radiomorphometric indices are shown in the panoramic view.

Reliability

Reliability was evaluated by using repeated measurements. The morphometric measurements were performed on 100 panoramic images by 2 oral radiologists, and interobserver reliability was assessed by using a subset of 24 patients, including 12 controls and 12 with scleroderma. Measurements were repeated one week apart.

Statistical analysis

Statistical analyses were performed by using SPSS version 11.5 (SPSS Inc., Chicago, IL). Intraclass correlation coefficients for MI, GI, AI, PMI, and weighted κ-statistics for MCI were used to evaluate intraobserver and interobserver reliability. The correlation between the radiomorphometric indices and categorical variables was evaluated by using χ^2 analysis. To compare the results from patients with scleroderma and healthy controls, the Mann-Whitney U test was used for qualitative data (MI, GI, AI, and PMI), and the χ^2 test was used for quantitative data (MCI), with a significance level set at 5% ($P < .05$). The effect of age on the MI, GI, AI, and PMI measurements of both groups was examined with Pearson's correlation. To determine the effect of age on MCI values in the group with scleroderma, 1-way analysis of variance (ANOVA) was used. The effect of gender on the mandibular radiomorphometric indices could not be evaluated statistically, because the number of the male patients in the group with scleroderma was insufficient.

RESULTS

The average duration of scleroderma in our patients was 12 $\pm$ 7.4 years. Interobserver agreement was found to be excellent (0.79 for MCI, 0.89 for MI, 0.77 for GI, 0.96 for AI, and 0.87 for PMI). Intraobserver agreement values demonstrated high reproducibility for the 2 observers (intraclass correlation coefficient$\geq$ 0.75). The second observer was accepted as the main observer after the agreement was confirmed as adequate. On the basis of the measurements and evaluations of the main observer, comparisons with the control group were made. There was a significant difference between the scleroderma group and the control group with regard to MCI variability ($P = .003$). According to the MCI classification, a high rate of C2 was found in both groups. The MCI values of patients with scleroderma revealed a more porous structure. The C3 rate was 20.4% in the scleroderma group,

Table I. Frequency distribution of MCI values in scleroderma cases and controls

	MCI			
Group	*C1*	*C2*	*C3*	*Total*
Scleroderma n (%)	11 (22.4)	28 (57.1)	10 (20.4)	49 (49)
Control n (%)	13 (25.5)	38 (74.5)	0 (0)	51 (51)
Total	24 (24)	66 (66)	10 (10)	100 (100)

$P = .003$.
MCI, mandibular cortical index.

whereas the same value was 0% in the control group (Table I). There was a significant difference in the correlation of MCI values with age in the scleroderma group ($P = .041$). When the correlation of MCI subgroups according to age was evaluated, a significant difference was found only between C1 and C3 ($P = .013$). Mean age at which C1 appeared was 45 years, whereas mean age at which C3 was observed was 58 years (Table II). There were significant statistical differences between the group with scleroderma and the control group in terms of MI and PMI variables ($P = .001$ and $P < .001$, respectively), but no significant difference was observed among the groups for GI and AI parameters ($P = .408$ and $P = .168$, respectively) (Table III). For the correlations of MI, GI, AI, and PMI measurements in the group with scleroderma by age, no significant statistical difference was detected ($P > .05$). In the control group, the correlations of MI, AI, and PMI measurements by age were not significant ($P > .05$), but a significant negative correlation was determined between the GI measurement and age ($P < .05$). The mouth-opening distance in individuals with scleroderma was correlated with the measurements for the mandibular radiomorphometric indices, and there was a significant difference only between GI and mouth-opening distance ($P = .036$). No significant correlation was found between the values of the mandibular radiomorphometric indices and the duration of the disease ($P > .05$). The descriptive statistics of the group with scleroderma are shown in Table III.

Thirty-nine (79.6%) of 49 patients with scleroderma had widening of the PDL space involving at least 1 tooth in more than 1 quadrant, 22 (44.9%) had thickening of the lamina dura involving at least 1 tooth, 35 (71.4%) had limitation of mouth opening, and 4 (8%) had at least 1 site where mandibular resorption was detected. Widening of the PDL space was seen in both anterior and posterior teeth in more than 1 quadrant; but it was more prominent in posterior teeth. Teeth were often not mobile, so the gingival attachment was stable. In 2 patients, mandibular resorption was identified in the angulus region, and the other 2 patients were found to have destruction of the posterior border of the descending part of the ramus. The small number of cases was not amenable to statistical analysis.

Table II. Mean age of MCI values in scleroderma cases per MCI category

MCI	*Mean age*	*MCI*	*P*
C1	44.90 ± 12.83	C2	0.235
		C3	0.013*
C2	49.92 ± 12.07	C1	0.235
		C3	0.062
C3	58.20 ± 9.10	C1	0.013*
		C2	0.062

*$P < .05$.
MCI, mandibular cortical index.

DISCUSSION

Several previous studies have been carried out on the dental and maxillofacial radiographic correlates of scleroderma, such as PDL space enlargement and mandibular resorption, but we have not found any studies evaluating panoramic mandibular radiomorphometric indices of patients with scleroderma.

Previous research has emphasized the need for measurements to be performed by 2 investigators to ensure the reliability of radiologic measurements. Schulze et al.[21] stated that differences in the determination of the reference point affected the measurement results negatively and led to incorrect results. In our study, interobserver consistency and intraobserver consistency were statistically assessed to evaluate individual differences, and consistency rates were satisfactory.

The MCI has been shown as having the best panoramic radiographic parameters for predicting osteoporosis.[19,20,22,23] Yaşar and Akgünlü[23] stated that MCI, which is easy to apply, may be a useful method in diagnosing osteoporosis, and those authors found a significant difference in MCI evaluation between patients with osteoporosis and healthy individuals. There was also a significant statistical difference between the scleroderma and control groups according to the MCI values in our study. The occurrence of C3 in the scleroderma group was 20.4%, whereas the value was 0% in the control group. This result demonstrates that the possibility of resorption in the mandible is high in patients with scleroderma. Henriques et al.[24] found MCI to be more porous in patients with chronic renal failure, which was similar to our results.

Table III. Descriptive statistics of GI, AI, PMI, and MI in scleroderma cases and controls

	P	*Group*	*Mean ± SD*	*Median*	*Minimum*	*Maximum*
MI	.001*	**Control**	2.31 ± 0.36	2.35	1.58	3.13
		Scleroderma	2.70 ± 0.65	2.65	1.30	3.94
		Total	2.50 ± 0.55	2.40	1.30	3.94
PMI	.0*	**Control**	0.22 ± 0.04	0.21	0.14	0.35
		Scleroderma	0.26 ± 0.06	0.26	0.13	0.52
		Total	0.24 ± 0.05	0.23	0.13	0.52
GI	.408	**Control**	0.75 ± 0.18	0.75	0.37	1.47
		Scleroderma	0.87 ± 0.83	0.66	0.00	5.38
		Total	0.81 ± 0.59	0.71	0.00	5.38
AI	.168	**Control**	1.71 ± 0.44	1.76	0.80	3.00
		Scleroderma	1.64 ± 0.84	1.64	0.00	5.30
		Total	1.67 ± 0.66	1.70	0.00	5.30

*$P < .05$.
AI, antegonial index; *GI,* gonial index; *MI,* mental index; *PMI,* panoramic mandibular index.

Uysal et al.[25] found that MCI was affected by gender and age, and more porosity with increasing age was observed in the mandibular cortex of women. In the present study, there was a significant correlation between age and MCI in the group with scleroderma. Furthermore, a statistically significant difference was found only between C1 and C3 in the scleroderma group when the MCI subgroups were correlated with each other by age. Mean age at which C1 appeared was 45 years, whereas mean age at which the C3 was observed was 58 years. It is thought that C3 may be linked to osteoporosis and to age.

There was a correlation of GI, AI, MI, and PMI measurements with age in the study groups, and only a statistically significant negative correlation was found in the GI measurements of the control group. According to this result, the GI measurement values may decrease with advancing age, and it could be the result of osteoporosis caused by aging. Despite these data from the control group, there was no correlation between GI and age in the scleroderma group. This could be explained by sclerotic changes in connective tissue.

The MI is a quantitative parameter for assessing the osteoporosis status of patients. When previous studies on MI values are examined, Leite et al.,[22] Gülşahı et al.,[26] and Devlin et al.[27] found MI of 3.0, 3.15, and 3.5 mm, respectively, at the reference values in osteoporosis. Gülşahı et al.[28] established MI less than 3 mm and PMI less than 0.30 mm in their other studies and asserted that this poses a high risk for osteoporosis. Mean values of MI and PMI in the scleroderma group in the present study was found to be 2.70 mm and 0.26 mm, respectively. Furthermore, gonial cortical bone thickness (GI) less than 1 mm was a radiographic sign of metabolic bone disease.[24] The mean value of GI in the scleroderma group was found to be 0.87 mm in our study. In line with these results, it is considered that patients with scleroderma may be at high risk for osteoporosis. For MI, there was a statistically significant difference between cases and controls in this study. Interestingly, median value of MI was found to be higher in the scleroderma group than in the control group, at 10% and 25% intervals. This result is lower than the MI reference values obtained in osteoporosis studies and suggests that scleroderma can affect bone quality and quantity. As the MI value of the scleroderma group was higher than that of the control group, we concluded that the proportion of women in the control group who were in active menopause could have affected the results. In contrast to our study, Nagi et al.[29] confirmed that postmenopausal women have lower MI values compared with normal individuals. In the present study, mandibular indices according to gender were not examined statistically because of the inadequate number of male cases.

Michiwaki et al.[30] suggested that as the level of the parathyroid hormone increases in patients with chronic renal failure, the MI value tends to decrease. Henriques et al.[24] indicated that as the level of the parathyroid hormone increases, mandibular cortex resorption tends to increase. On the basis of these results, MI and MCI have been reported to be important parameters in the evaluation of patients with chronic renal failure. It is thought that parathyroid hormone level is also important in patients with scleroderma and kidney involvement because MCI and MI values are similar to these studies in our study. Neves et al.[31] performed panoramic radiomorphometric analysis of patients with sickle cell anemia, especially of those in older age groups, and found that PMI and MI values decreased and MCI classification tended toward C2. In our study, there was no statistically significant difference in the correlation of MI, PMI, and MCI measurements according to age, and the C2 ratio was high in the group with scleroderma. Dagistan et al.[32] found no statistically significant

alterations in the MI, PMI, and AI of male patients with chronic renal failure except in MCI. Güngör et al.[33] compared the PMI upper and lower measurement values of 2 observers, and they found that the PMI upper value was 2-fold more consistent for both observers. In our study, the evaluations were made on the basis of PMI upper measurement values, and we found a significant difference between case and control PMI values. Although the range between minimum and maximum values was small, the median values were higher in the scleroderma group. Because the MI value, in the numerator of PMI, was higher in the group with scleroderma, the PMI value can be detected at a higher value than that in the control group.

Scleroderma is 8 times more common in females than in males and is most commonly reported in those 30 to 50 years of age.[1] In the present study, the female-to-male ratio was 7:2, and mean age was 50 years; these results are compatible with those reported in the literature. Widening of the PDL space in patients with scleroderma was first described by Stafne and Austin,[6] and the incidence was reported to be 7%. White et al.[7] found this rate to be greater than 37%, and Vincent and Agard[34] found it to be 33%. In the present study, widening of the PDL space was detected in 79.6% of patients with scleroderma. In accordance with these results and the literature, it can be said that widening of the PDL space is a common oral finding in patients with scleroderma, and it is more prominent in posterior teeth.

Auluck[35] and Haers and Sailer[13] reported that the increased amount of collagen causes hypertrophy in muscles and induces widening of the PDL space resulting from traumatic occlusion. Rout et al.[36] did not accept the idea of hypertrophy in the chewing muscles because this condition does not occur in all patients. Mehra[37] also disagreed with this hypothesis and suggested that increased fibrosis and atrophy in the chewing muscles and related blood vessels might cause ischemia, thus eliminating the possibility of traumatic occlusion. According to Mehra, there is a likelihood of an increase in collagen synthesis in these patients to explain the etiology of widening of the PDL space. However, in this hypothesis, it is difficult to explain why widening of the PDL space is not seen in all patients with systemic scleroderma and why it is often seen in posterior teeth.[2] We consider that because scleroderma is a disease with a variable course in each patient, muscles of mastication might atrophy if vasculopathy predominates, whereas muscles could become hypertrophic if fibrosis is more prevalent.

Studies have reported different opinions on the changes in the lamina dura in patients with scleroderma. There are ~~a~~ few studies indicating that the lamina dura is thickened in patients with scleroderma.[7,9-11] In contrast, Anbiaee and Tafakhori[2] and White and Pharoah[8] stated that there was no change in the lamina dura in patients with scleroderma. In the present study, 44.9% of the patients with scleroderma had thickening of the lamina dura. This result is compatible with the findings of other studies that reported thickening of the lamina dura.

Bone resorption in scleroderma was first described in 1959 by Taversa in the posteroinferior ramus.[7] Auluck et al.,[14] Vincent et al.,[34] Haers and Sailer,[13] and Rout et al.[36] reported resorption in the mandible in 10%, 7%, 20% to 33%, and 10% of the patients with scleroderma, respectively. In the present study, resorption in the mandible was detected in 4 cases (8%). We identified that in 2 of these cases, resorptions were in the angulus mandible, whereas the other 2 showed destruction of the posterior border of the ascending ramus.

Significant reduction in interincisal distance is observed in patients with scleroderma. Mean interincisal distance in these individuals was reported to be approximately 33 mm.[38] In the present study, mean interincisal distance in patients with scleroderma was found to be 33.77 mm in accordance with the literature. A statistically significant positive correlation was found between GI and mouth opening in the patients with scleroderma in this study. On the basis of this result, we consider that gonial angle value and mouth opening distance are increased with respect to the spatial geometry principal, depending on the increase in GI measurement.

A limitation of this study is that scleroderma being an autoimmune disease, almost all of the patients with scleroderma included in the study were using steroids. Steroid-induced osteoporosis is the most prevalent form of drug-induced osteoporosis because steroids suppress osteoblastic activity. Therefore, in this study, we could not determine whether bone resorption was caused by steroid-induced osteoporosis or by scleroderma. However, our results could not be directly compared because a similar study on this subject could not be found in the literature. Another limitation of the study was inclusion of only a few males in the study population. Therefore, further studies with higher number of samples are needed. Because the MI and PMI values of the scleroderma group are higher than those of the control group, we concluded that the proportion of women in the control group who are in active menopause affected our statistical results. We propose that menopausal status of female participants in the control group be taken into account in future radiomorphometric bone studies.

CONCLUSIONS

The radiomorphometric indices determined in the present study can be used on panoramic images to determine the existence of a porous structure in the mandibular cortical bone in patients with scleroderma. Statistically significant differences were found for MCI ($P = .003$), MI ($P = .001$), and PMI ($P < .001$) between the scleroderma group and the control group, but not for GI and AI ($P > .05$). We consider that patients with scleroderma may have a high risk for osteoporosis because of their use of steroid medications, and MCI may indicate the effects of scleroderma on the mandibular cortical bone. The most common oral radiographic manifestations of scleroderma are widening of the PDL space and thickening of the lamina dura. Future studies could investigate whether or not steroid therapy causes bone resorption in patients with scleroderma or if it is only a contributing factor.

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