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Racial differences in bone density variation in head and neck cancer patients with osteoradionecrosis: A pilot study

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Main Article

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Abstract

Objectives. This study aimed to assess pre- and post-radiation therapy mandibular bone densities in head and neck cancer patients with osteoradionecrosis and factors associated with decreased bone densities.

Methods. Retrospective pilot study (2007–2017) of osteoradionecrosis patients after 66- to 70-gray radiation therapy. Cortical and cancellous mandibular bone densities ipsilateral/contralateral to tumour were measured on pre-radiation therapy and at three-month and one-year post-radiation therapy positron emission tomography/computed tomography. Two-way analysis of variance and linear regression were used as exploratory analyses, given the pilot nature of the study.

Results. Sixteen of 67 head and neck cancer patients had osteoradionecrosis (41–67 years of age; nine African Americans, seven Caucasians). Bone density did not significantly change from baseline within either racial group. African Americans had higher bone densities than Caucasians (pre-radiation therapy ipsilateral cortical: 1044 ± 229.8 vs. 965.6± 278.7 Hounsfield units). At one year, African Americans had higher contralateral cortical (+35.5 per cent; $p = 0.008$) and cancellous (+109.4 per cent; $p = 0.028$) bone densities. Multivariable models showed lower contralateral cortical ($p = 0.039$) and cancellous ($p = 0.005$) bone densities in Caucasians.

Conclusion. In this small pilot study, mandibular bone densities appeared higher in African Americans, with a greater post-radiation therapy reduction observed in Caucasians; these findings are exploratory and require validation in larger cohorts.

Introduction

Approximately 50–60 per cent of head and neck cancer patients receive radiation therapy (RT). The current management of these malignancies relies on RT for advanced-stage disease and organ preservation strategies.[1] Osteoradionecrosis (ORN) of the mandible is one of the late and devastating side effects of head and neck RT.[2,3] Although the underlying cancer is eradicated, ORN causes long-term pain and may require additional surgeries with associated morbidity.[4] Medication-induced osteonecrosis of the jaw, specifically due to bisphosphonate use, has been primarily linked to the anti-angiogenic and bone-resorption–inhibiting properties of bisphosphonates.[5] Furthermore, the overall likelihood of developing osteonecrosis due to bisphosphonates rises with more frequent dosing, larger individual doses and prolonged treatment duration.[6]

Several other risk factors associated with the development of ORN include site and size of tumour, dentition status, the dosage and fractionation of RT, smoking and trauma.[1,4] Mechanistically, ORN is believed to be due to radiation-induced disruption of intra-osseous arteries.[5] Some studies have suggested that radiation may trigger a cascade of tissue changes marked by reduced cellularity, impaired vascularity and hypoxia that disrupt normal mucosal healing and ultimately lead to chronic non-healing wounds and osteonecrosis.[7] Our institutional data over 10 years revealed that of 2,323 patients diagnosed with jaw osteonecrosis, 65 per cent were Caucasian, suggesting a higher burden of disease in Caucasian patients compared to African-American patients at our institution. Similarly, Quispe *et al*. reported higher

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osteonecrosis rates in Caucasian compared to African Americans.[8] Regarding overall bone density (BD) differences between races, the National Health and Nutrition Examination Survey (NHANES) data demonstrated that African Americans exhibit femoral neck and total-site BD 6–11 per cent higher than Caucasians.[9,10] Furthermore, the trajectory of age-related bone loss in African Americans appears markedly attenuated, with annual hip BD decline roughly half that observed in Caucasians.[9] Therefore, we wanted to see if this racial difference in ORN prevalence could also be associated with differences in BD loss with radiation. Our study aimed to compare BDs of cancellous and cortical mandibular bone between African-American and Caucasian ORN patients in pre- and post-RT scenarios.

Materials and methods

Study design and population

This pilot study is an institutional review board (IRB) -approved retrospective chart review of ORN cases at our institution, limited to head and neck cancer patients treated with radiotherapy who developed ORN within five years and had sufficient positron emission/computed tomography (PET/CT) imaging available for analysis from 2007 to 2017.

Data collection

Data collected included patient demographics (age, gender and race/ethnicity), appropriate medical history (details about head and neck cancer subsite, treatment and follow-up) and relevant medical history (xerostomia, dental extractions and smoking).

Exposure and covariates

Imaging studies, including pre- and post-RT PET/CT scans, were performed. BDs were assessed by measuring Hounsfield units (HU) in predetermined areas of the mandible on the pre- and one-year post-RT PET/CT scans. Our method of using CT-derived HU as a validated surrogate measure of bone mineral density is well established in the literature, including for mandibular and craniofacial bone assessment in both implant and oncologic contexts.[11,12] The CT portion of each PET/CT scan was displayed in the bone window, and the BDs of the retromolar trigone and canine regions were measured bilaterally, both ipsilateral and contralateral to the tumour (Fig. 1). All PET/CT scans were acquired at a single institution using a consistent scanner platform and standardised acquisition and reconstruction protocols throughout the study period. BD measurements were performed by a single experienced radiologist to minimise inter-observer variability. The retromolar trigone and canine areas were chosen because these sites contain the densest cortical and cancellous bone, respectively.[11] BD of cortical and cancellous mandibular bone was compared between pre- and post-RT scans separately for the ipsilateral and contralateral sides of the tumour in both African-American and Caucasian patients. These cortical and cancellous BD measurements were performed at three different time points: (1) prior to initiation of RT, (2) three months following RT and (3) one year following RT. Other factors, including xerostomia, dental extractions, smoking and RT dosage for each patient, were also evaluated along with BD.

Statistical analysis

Results were statistically analysed by utilising Graphpad PRISM software version 10.5.0. Descriptive statistics were calculated by computing the mean, median and range for continuous variables, while categorical variables were summarised using frequencies and percentages. Prior to two-way analysis of variance (ANOVA), normality was assessed using the Shapiro–Wilk test and homogeneity of variance was confirmed using Bartlett's test. Two-way ANOVA was employed to analyse BD, with race (African American vs. Caucasian) and time (pre-RT, three months post-RT and one year post-RT) specified as factors, thereby enabling assessment of intraracial changes over time (pre-RT vs. three months vs. one year within each race) and inter-racial differences at corresponding time points (African American vs. Caucasian at pre-RT, three months post-RT and one year post-RT). Non-parametric correlations were used to test for binary correlations between variables. Univariate and multivariate linear regression analysis were used to analyse the factors associated with BD variations, such as age, race and others.

Results

Patient characteristics

Out of 67 identified ORN cases, 16 were ultimately analysed due to limited pre-RT and post-RT scan availability. The mean age

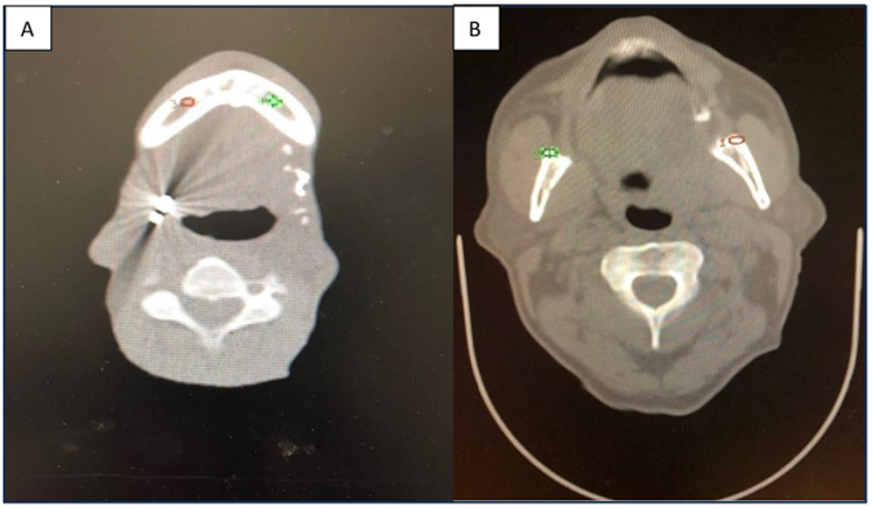


Figure 1. Axial CT images showing the regions of interest used for mandibular bone density measurements. (A) The canine region (cancellous bone density measurement sites). (B) The retromolar trigone region (cortical bone density measurement sites), bilaterally ipsilateral and contralateral to the tumour. These standardised sites were selected as they represent the regions of maximal cancellous and cortical bone density in the mandible, respectively. CT = computed tomography.

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Table 1. Patient distribution and demographics

Patient No	Age (years)	Gender	Race	Site	TNM	Stage	Treatment	Sides of RT	Smoking	Xero stomia	DM	Dental extraction	Treatment of ORN
1	56	M	AA	BOT	T3N2cM0	SCC IV	Surgery + RT	B/L	Y	N	N	N	Surgery
2	65	M	AA	Soft palate	T4bN2aM0	SCC IV	CRT	B/L	Y	N	N	N	Conservative
3	41	M	AA	Tonsil	T3N2bM0	SCC IV	Surgery + CRT	B/L	Y	N	N	Y	Surgery
4	66	M	AA	Tonsil	T3N1M0	SCC IV	CRT	B/L	N	Y	Y	N	Debridement
5	50	M	AA	Tonsil	T3N1M0	SCC IV	Surgery + CRT	B/L	Y	Y	N	N	Conservative
6	67	F	AA	BOT	T2N2cM0	SCC IV	Surgery + CRT	B/L	Y	Y	N	N	Surgery
7	55	M	C	Tonsil	T2N2bM0	SCC IV	Surgery + RT	B/L	Y	N	N	N	Conservative
8	52	M	AA	Tonsil	T4bN2cM0	SCC IV	CRT	B/L	N	N	N	N	Conservative
9	58	M	AA	Tonsil	T3N2bM0	SCC IV	CRT	B/L	Y	N	N	N	Debridement
10	62	M	C	Tonsil	T2N2bM0	SCC IV	Surgery + RT	B/L	Y	N	N	N	Debridement
11	55	M	AA	BOT	T3N2bM0	SCC IV	Surgery + RT	B/L	Y	N	N	N	Surgery
12	65	M	C	Tonsil	T1N2bM0	SCC IV	Surgery + CRT	B/L	N	Y	N	N	Debridement
13	57	M	C	Tonsil	T2N2bM0	SCC IV	Surgery + CRT	B/L	Y	Y	N	Y	Conservative
14	55	M	C	Tonsil	T1N2bM0	SCC IV	Surgery + RT	B/L	Y	N	N	N	Conservative
15	58	M	C	BOT	T4aN2cM0	SCC IV	CRT	B/L	Y	N	N	N	Conservative
16	62	M	C	BOT	T2N2bM0	SCC IV	CRT	B/L	N	N	N	N	Conservative

AA = African American; BOT = base of tongue; C = Caucasian; CRT = chemoradiation; F = female; M = male; N = no; ORN = osteoradionecrosis; RT = radiation therapy; SCC = squamous cell carcinoma; Y = yes.

of these patients was 57.75 (SD = 6.59) years, ranging from 41 to 67 years, and there were 15 males and one female. Of the 16 patients, 10 (62.5 per cent) had tonsillar cancer, five (31.3 per cent) had base of tongue cancer and one (6.2 per cent) had soft palate cancer. Nine patients were African Americans, and seven were Caucasians. All patients in both groups had Stage IV squamous cell carcinoma and received bilateral radiotherapy at a minimum dose of 66 Gy. Five of the African-American and five of the Caucasian patients underwent surgical management (Table 1). Twelve out of 16 were smokers, five suffered from xerostomia, one was diabetic and two underwent post-RT dental extraction. Mean age was similar between African-American and Caucasian patients (56.7 vs. 59.1 years; $p = 0.67$). Both groups were predominantly male (89 per cent vs. 100 per cent; $p = 0.99$). Smoking rates were comparable (78 per cent vs. 71 per cent; $p = 0.99$), as were rates of xerostomia (33 per cent vs. 29 per cent; $p = 1.000$), dental extraction (11 per cent vs. 14 per cent; $p = 0.99$) and diabetes (11 per cent vs. 0 per cent; $p = 0.99$) (Table 2).

Table 2. Baseline demographic and clinical characteristics by race

Variable	African American ($n = 9$)	Caucasian ($n = 7$)	p-Value
Mean age, years (range)	56.7 (41–67)	59.1 (55–65)	0.670[a]
Gender, M/F	8/1	7/0	0.99[b]
Smoking, n (%)	7 (78%)	5 (71%)	0.99[b]
Xerostomia, n (%)	3 (33%)	2 (29%)	0.99[b]
Diabetes, n (%)	1 (11%)	0 (0%)	0.99[b]
Dental extraction, n (%)	1 (11%)	1 (14%)	0.99[b]
Stage IV, n (%)	9 (100%)	7 (100%)	NA
Bilateral RT, n (%)	9 (100%)	7 (100%)	NA
RT dose ≥66 Gy, n (%)	9 (100%)	7 (100%)	NA
Surgical ORN management, n (%)	5 (56%)	5 (71%)	0.633[b]

[a]Mann–Whitney U-test.
[b]Fisher's exact test. No statistically significant between-group differences were identified for any baseline variable (all $p > 0.05$).
F = female; M = male; NA = not applicable; ORN = osteoradionecrosis; RT = radiotherapy.

Pre- vs. post-RT mandibular BD analysis for Caucasians

In Caucasian patients, mandibular BD remained statistically stable from pre-RT through the one-year post-RT follow-up. On the ipsilateral side of the tumour, neither cortical nor cancellous BD changed significantly across any pairwise comparison, pre-RT versus three months, three months versus one year or pre-RT versus

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Table 3. Mean mandibular bone density (HU) by time point within each racial group, with within-group pairwise comparisons

Race	Side	Bone	Pre-RT (HU)	3 mo (HU)	1 yr (HU)	*p* (pre vs. 3 mo)	*p* (3 mo vs. 1 yr)	*p* (pre vs. 1 yr)
Caucasian	Ipsilateral	Cortical	965.6	1009.0	929.8	0.99	0.93	0.98
Caucasian	Ipsilateral	Cancellous	268.8	262.6	269.8	0.99	0.99	0.99
Caucasian	Contralateral	Cortical	1043.0	960.0	890.1	0.91	0.94	0.53
Caucasian	Contralateral	Cancellous	247.3	222.4	195.3	0.99	0.99	0.94
African American	Ipsilateral	Cortical	1044.0	1049.0	983.8	0.99	0.92	0.93
African American	Ipsilateral	Cancellous	320.8	287.3	353.3	0.95	0.75	0.95
African American	Contralateral	Cortical	1118.0	1197.0	1206.0	0.85	0.99	0.77
African American	Contralateral	Cancellous	384.1	374.6	409.0	0.99	0.97	0.98

Note: All within-group comparisons were non-significant ($p > 0.05$).
HU = Hounsfield units; RT = radiotherapy.

Table 4. Inter-racial comparison of mean mandibular bone density (HU); difference expressed as African American relative to Caucasian

Time point	Side	Bone	African American (HU)	Caucasian (HU)	Difference	*p*-Value
Pre-RT	Ipsilateral	Cortical	1044.0	965.6	+8.1%	0.51
Pre-RT	Ipsilateral	Cancellous	320.0	268.8	+19.3%	0.50
Pre-RT	Contralateral	Cortical	1118.0	1043.0	+7.2%	0.51
Pre-RT	Contralateral	Cancellous	384.0	247.3	+55.3%	0.17
3 months	Ipsilateral	Cortical	1049.0	1009.0	+4.0%	0.78
3 months	Ipsilateral	Cancellous	287.3	262.6	+9.4%	0.79
3 months	Contralateral	Cortical	1197.0	960.0	+24.6%	0.08
3 months	Contralateral	Cancellous	374.6	222.4	+68.4%	0.20
1 year	Ipsilateral	Cortical	983.8	929.8	+5.8%	0.65
1 year	Ipsilateral	Cancellous	353.3	269.8	+30.9%	0.26
1 year	Contralateral	Cortical	1206.0	890.1	**+35.5%**	**0.008**
1 year	Contralateral	Cancellous	409.0	195.3	**+109.4%**	**0.028**

Note: Shaded rows and bold values indicate statistically significant differences ($p < 0.05$).
HU = Hounsfield units; RT = radiotherapy.

one year (all $p > 0.05$; Table 3). Ipsilateral cortical BD rose modestly three months before returning toward baseline by one year, while ipsilateral cancellous BD was essentially unchanged throughout. On the contralateral side, both cortical and cancellous BD showed a consistent downward trend across follow-up, declining by 14.6 per cent and 21.0 per cent, respectively, from baseline to one year. Despite this directional decrease, none of the contralateral changes reached statistical significance. Overall, mandibular BD did not change significantly before versus after RT for Caucasian patients on either side.

Pre- vs. post-RT mandibular BD analysis for African Americans

A similar pattern of statistical stability was observed in African-American patients. On the ipsilateral side, neither cortical nor cancellous BD changed significantly across any time-point comparison (all $p > 0.05$; Table 3). Ipsilateral cancellous BD dipped at three months and then recovered to above baseline by one year, but these shifts were not significant. On the contralateral side, both cortical and cancellous BD remained stable or trended slightly upward over follow-up, in contrast to the downward contralateral trend seen in Caucasian patients. As in the Caucasian group, mandibular BD in African-American patients did not change significantly on either side from pre-RT to post-RT.

Pre-RT baseline mandibular BD inter-racial analysis

At baseline, mean mandibular BD was higher in African-American than in Caucasian patients at all four measurement sites (Table 4). The differences were modest for cortical bone (+8.1 per cent ipsilateral; +7.2 per cent contralateral) but more pronounced for cancellous bone, particularly on the contralateral side, where African-American patients had 55.3 per cent higher BD than Caucasian patients. Although African-American patients had consistently higher mean baseline BD on both sides, none of these inter-racial differences reached statistical significance (all $p > 0.05$).

Post-RT mandibular BD inter-racial analysis

The higher mean BD observed in African-American patients persisted through follow-up. At three months, African-American patients had higher mean BD than Caucasian patients at every site, with the largest differences again in the contralateral mandible (+24.6 per cent cortical; +68.4 per cent cancellous); however, these differences remained non-significant (Table 4). At one year,

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the inter-racial difference became statistically significant in the contralateral mandible: African-American patients had markedly higher contralateral cortical BD (1206.0 vs. 890.1 HU; +35.5 per cent; $p = 0.008$) and contralateral cancellous BD (409.0 vs. 195.3 HU; +109.4 per cent; $p = 0.028$) than Caucasian patients. Ipsilateral differences, while still favouring African-American patients, did not reach significance at either time point. Figure 2 illustrates these inter-racial comparisons across follow-up.

We further evaluated factors associated with reduced BD. On univariate linear regression analysis, we found that there was a statistically significant reduction of contralateral cortical BD in Caucasians ($\beta = -316.3$; $p = 0.03$) (Table 5). Similarly, multivariate analysis of contralateral cortical BD showed a significant reduction of contralateral cortical BD in Caucasians ($\beta = -310.5$; $p = 0.039$) (Table 6). On univariate analysis of contralateral cancellous bone, we found there was a statistically significant reduction of contralateral cancellous BD with Caucasians ($\beta = -213.7$; $p = 0.02$) (Table 7). This association was also reported in multivariate linear regression ($\beta = -284.6$; $p = 0.005$) (Table 8).

Discussion

Most patients with head and neck cancer receive RT with or without chemotherapy in a definitive or adjuvant setting. Patients receiving RT have short-term and long-term complications. ORN is one of the serious long-term complications of ionising radiation in the craniofacial region.[13] The risk factors commonly associated with the development of ORN are age, sex, medical comorbidities, type of dentoalveolar surgery, trauma and dosage of RT.[14] ORN commonly occurs in the mandible due to its sparse blood supply, as opposed to other bones like the maxilla, which has an abundant blood supply.

Although ORN constitutes one of the common long-term complications, there has been reduction of ORN due to improved dental care, better radiation techniques like intensity-modulated radiation therapy (IMRT) and three-dimensional conformal radiation therapy (3D-CRT) and the advent of megavoltage radiation.[4] Although there are known risk factors for osteonecrosis, we have institutional data that supports Caucasians are more prone to developing osteonecrosis. In line with this, the literature also reports trends in higher jaw osteonecrosis rates in Caucasians on bisphosphonate therapy.[8,15] Quispe *et al.* reported in their cohort that Caucasian patients receiving bisphosphonates had a significantly higher incidence of jaw osteonecrosis (15 per cent) compared to African-American patients (2 per cent).[8] Multiple studies have also consistently shown that African-American women have approximately half the risk of fractures compared to their Caucasian counterparts.[16–18] All these findings add further focus to determine the jaw BD variation in ORN between Caucasians and the African-American population. In our study, both Caucasian and African-American ORN patients exhibited a comparable decrease in mean BD on the ipsilateral (direct radiation) side compared to their pre-RT baselines. However, on the contralateral side, African-American patients showed minimal to no reduction in mean BD, whereas Caucasian patients demonstrated a notable decrease relative to their pre-radiation measurements. Hence, the true difference on the contralateral side appears to be an increased susceptibility to radiation-induced BD loss in Caucasians. It is well known that radiation affects the bone primarily by reducing the number of structural units rather than the size. Local high-dose radiation has been associated with atrophy of trabecular bone, which can lead to spontaneous fractures. Studies have shown that the irradiation causes reduced blood flow to the mature bone and decreased bone mineral density.[19] Radiation also increases vascular permeability, causing haemorrhage and fibrosis. Furthermore, it has been observed that osteoblast and osteoclast activity is directly impacted by radiation, leading to increased bone resorption.[20]

According to Park *et al.*, the thickness and density of the mandible increase from anterior to posterior. When measurements were taken at the sites of maximal BD, cortical BD was consistently greatest in the retromolar region, whereas cancellous BD was greatest in the canine region.[11] BD measurements contralateral to the tumour may be more representative, as measurements made on the ipsilateral side could be skewed due to local tumour erosion. Our key finding is that mandibular BD did not change statistically within each racial group from pre-RT to post-RT. However, when comparing between races, BD loss at the one-year post-RT time point was statistically significantly greater in Caucasian patients than in African-American patients, especially in the contralateral mandible. On CT, ORN of the mandible typically demonstrates a heterogeneous mixture of destructive and reparative changes rather than a uniform loss of bone. Reported findings include cortical defects, osteolysis, alteration of the trabecular architecture, lingual and buccal cortical thinning or disruption, pathological fractures, sequestrum formation and areas of dense bone sclerosis, often with loss of normal cancellous trabeculae and bicortical involvement. Many of these components have opposing effects on CT-based BD measurements: cortical defects and osteolysis tend to lower HU values, whereas bone sclerosis, sequestra and healing fractures can increase local HU.

In the absence of ORN, radiation alone is expected to produce a more uniform decline in BD due to demineralisation and microstructural damage, and this pattern was more evident on the contralateral, non-ORN side in our cohort. In contrast, on the ipsilateral side, where ORN and tumour bed changes are more common, the BD change likely reflects an admixture of both destructive and sclerotic processes within the same region of interest. The presence of sclerotic foci and sequestra may partially offset the HU-lowering effects of osteolysis and cortical disruption, resulting in a smaller net reduction in measured BD on the ipsilateral side despite clinically significant radiation-related injury. This complex balance between bone loss and reactive sclerosis provides a plausible explanation for the relatively attenuated decrease in BD observed ipsilaterally compared with the contralateral mandible. This radiographic pattern is well supported in existing literature. Patil *et al.* reported that, at the time ORN was clinically suspected, CT commonly demonstrated mandibular resorption and cortical erosions in all cases, along with sclerosis in 86 per cent and fragmentation in 83 per cent.[21] On subsequent imaging, sclerosis became even more prominent, occurring in 92 per cent of cases, while erosive changes continued to progress in 77 per cent. Miyamoto *et al.* further suggested that sclerosis and resorption may reflect successive bone responses to radiation-induced injury, rather than mutually exclusive findings.[22] In line with these observations, the ISOO-MASCC-ASCO guideline defines ORN radiographically as a lytic or mixed sclerotic bone lesion, thereby recognising that osteolytic destruction and sclerosis may coexist within the same disease process.[23] The difference in the contralateral BD before and after radiation was statistically significant between African Americans and Caucasians, showing a considerably higher decrease in BD after RT in Caucasians. It is important to acknowledge that race is a self-identified, socially constructed category rather than a direct biological variable,[24,25] and the observed BD differences likely

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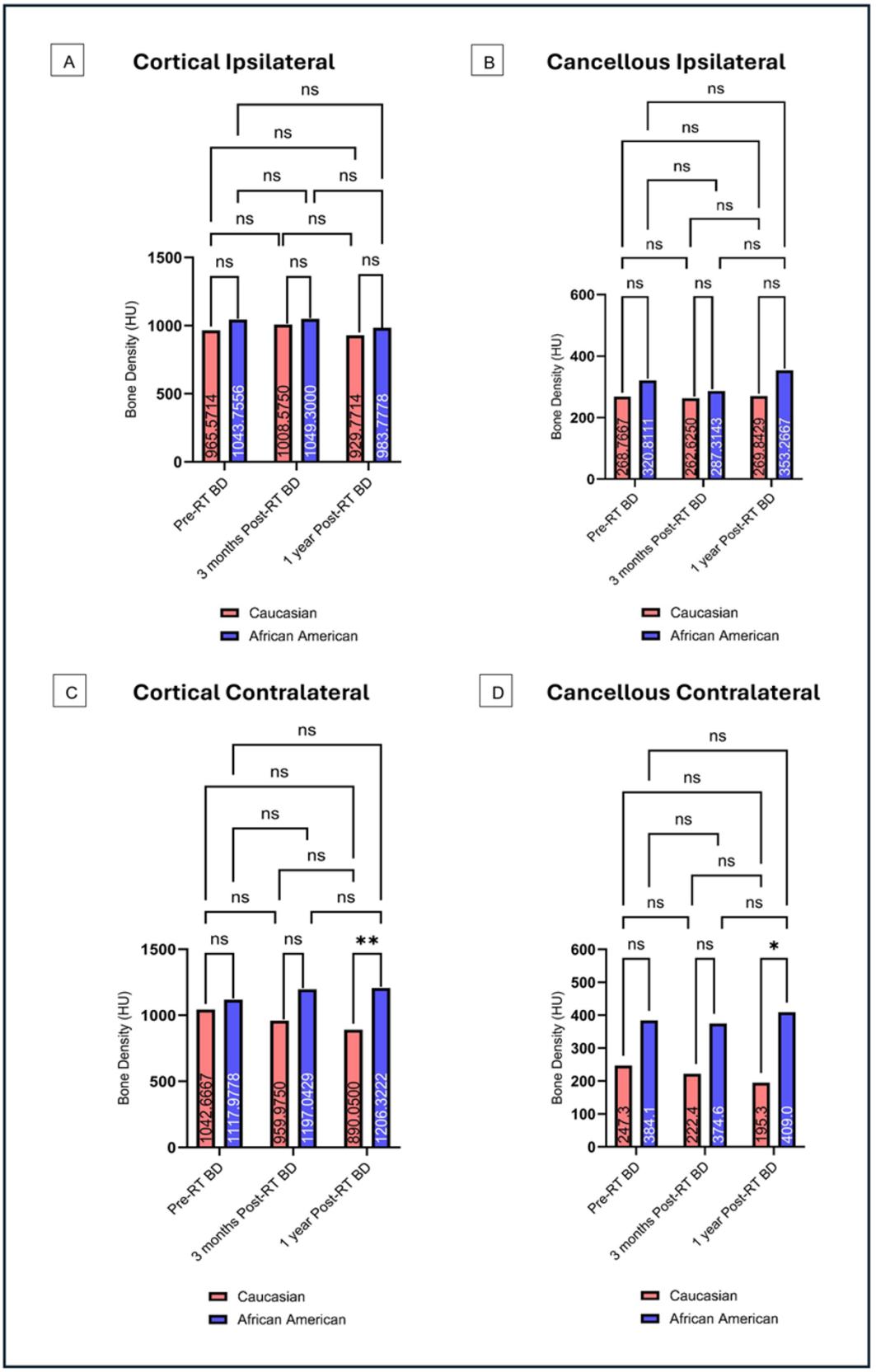


Figure 2. Intraracial and inter-racial comparisons of mandibular bone density by race and time in (A) cortical ipsilateral, (B) cancellous ipsilateral, (C) cortical contralateral and (D) cancellous contralateral bone. Within each racial group, bone density did not change significantly across any time point (all $p > 0.05$). Key finding: At one-year post-RT, African-American patients had significantly higher contralateral cortical (**$p = 0.008$) and cancellous (*$p = 0.028$) bone density compared to Caucasians, reflecting greater radiation-induced bone density loss in Caucasian patients. **$p < 0.01$; *$p < 0.05$. ns = not significant; AA = African American; RT = radiotherapy.

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Table 5. Univariate linear regression analysis of factors associated with contralateral cortical Bone density change in the ORN patients

Variables	Estimate	(95% CI)	*p*-Value
Age	−6.956	−31.02 to 17.11	0.54
Sex			
Female (ref)	-	-	-
Male	−280.9	−925.8 to 364.0	0.36
Subsite			
BOT (ref)	-	-	-
Soft palate	383.1	−330.9 to 1097	0.26
Tonsil	120.6	−257.3 to 498.4	0.50
Race			
African American (ref)	-	-	-
Caucasian	−316.3	−597.8 to −34.75	**0.03**

Note: Bold value indicates statistically significant differences ($p < 0.05$).
BOT = base of tongue; CI = confidence interval; ORN = osteoradionecrosis; ref = reference.

Table 6. Multivariate linear regression analysis of factors associated with contralateral cortical bone density change in the ORN patients

Variables	Estimate	(95% CI)	*p*-Value
Sex			
Female (ref)	-	-	-
Male	−387.3	−995.8 to 221.2	0.19
Subsite			
BOT (ref)	-	-	-
Soft palate	402.3	−206.2 to 1011	0.17
Tonsil	295.0	−50.87 to 640.9	0.08
Race			
African American (ref)	-	-	-
Caucasian	−310.5	−602.8 to −18.16	**0.039**

Note: Bold value indicates statistically significant differences ($p < 0.05$).
BOT = base of tongue; CI = confidence interval; ORN = osteoradionecrosis; ref = reference.

Table 7. Univariate linear regression analysis of factors associated with contralateral cancellous bone density change in the ORN patients

Variables	Estimate	(95% CI)	*p*-Value
Age	4.57	−11.32 to 20.46	0.54
Sex			
Female (ref)	-	-	-
Male	−172.1	−599.4 to 255.1	0.40
Subsite			
BOT (ref)	-	-	-
Soft Palate	0.1400	−483.7 to 484.0	0.99
Tonsil	37.36	−204.6 to 279.3	0.74
Race			
African American (ref)	-	-	-
Caucasian	−213.7	−389.2 to −38.3	**0.02**

Note: Bold value indicates statistically significant differences ($p < 0.05$).
BOT = base of tongue; CI = confidence interval; ORN = osteoradionecrosis; ref = reference.

Table 8. Multivariate linear regression analysis of factors associated with contralateral cancellous bone density change in the ORN patients

Variables	Estimate	(95% CI)	*p*-Value
Age	13.14	−1.025 to 27.31	0.06
Subsite			
BOT (ref)	-	-	-
Soft palate	−184.7	−565.7 to 196.3	0.31
Tonsil	111.8	−77.97 to 301.6	0.22
Race			
African American (ref)	-	-	-
Caucasian	−284.6	−464.7 to −104.4	**0.005**

Note: Bold value indicates statistically significant differences ($p < 0.05$).
BOT = base of tongue; CI = confidence interval; ORN = osteoradionecrosis; ref = reference

reflect a complex interplay of factors co-varying with race, including skeletal biology, vitamin D metabolism, socioeconomic status and healthcare access.[26] African Americans are known to have higher baseline bone mineral density and lower osteoporosis rates compared to Caucasians, attributed to a combination of genetic, hormonal and mechanical factors rather than race.[18,27] While our findings are consistent with this literature, they should not be interpreted as evidence that race is a direct biological determinant of radiation response. Rather, race likely serves as a proxy for underlying factors that future studies should aim to measure and adjust for directly, and the observed differences should be regarded as exploratory associations pending further mechanistic investigation.[25] This was true for both cortical and cancellous bone and may indicate that Caucasians are more susceptible to ORN. While we did not observe a statistically significant reduction in contralateral cancellous BD in Caucasians (vs. African Americans) in the difference analysis, both univariate and multivariate linear regression models demonstrated a significant decrease. With a larger sample size in future studies, this difference is likely to become more pronounced.

Considering that African Americans have a lower prevalence of osteoporosis,[28] efforts were made to correlate BD and ORN. Although precautions are needed to avoid ORN in all cases, additional care concerning dentition, prevention of xerostomia and smoking cessation will help Caucasian patients. This pilot study is limited by its small sample size ($n = 16$), which restricts statistical power and generalisability. The multivariable regression findings carry a risk of overfitting and should be considered exploratory and hypothesis-generating. Larger sample size studies would be required to validate the outcomes of this multivariate analysis. Of 67 identified ORN cases over 10 years, only 16 had adequate serial PET/CT imaging, reflecting the rarity of ORN and the stringent imaging requirements. The exclusion of the remaining 51 out of 67 initial ORN cases was solely due to the absence of adequate pre- and post-RT PET/CT imaging, rather than any systematic clinical or demographic differences, minimising the likelihood of clinically driven selection bias. Key clinical variables, including smoking, xerostomia, dental extractions and diabetes, were collected but could not be simultaneously adjusted in the regression models due to the small sample size. Race remained a significant predictor of contralateral BD change after adjustment for sex and tumour subsite; however, residual confounding from these variables cannot

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be excluded and represents an important limitation. Future larger studies should prospectively adjust for these covariates to better isolate the independent effect of race on radiation-induced BD loss. Larger sample size studies are needed to enhance the validity of our pilot findings of racial differences in contralateral side BD and explore further potential differences on the ipsilateral radiation side, allowing for a more robust evaluation and the inclusion of additional covariates to assess independent risk factors for BD variation. Future prospective studies should also focus on comparing BD changes between patients who develop ORN and those who do not following radiotherapy, to better understand the potential association between lower BD and the increased prevalence of ORN in Caucasian patients.

- Mandibular osteoradionecrosis (ORN) is a major late complication after high-dose head and neck radiotherapy (RT)
- Bone quality/density is relevant to ORN risk, but longitudinal mandibular bone density tracking is not routinely reported
- Racial differences in baseline bone density are recognised in general populations, but mandibular patterns after radiotherapy in ORN patients are not well defined
- Uses positron emission tomography/computed tomography (PET/CT) - derived Hounsfield units to track cortical and cancellous mandibular bone density pre-RT, three months and one year post-RT in ORN patients
- Shows mandibular bone density remained broadly stable over time within each racial group
- Finds African-American patients had higher mandibular bone density than Caucasian patients at baseline and at one year, with greater relative reduction in Caucasian patients, suggesting race may be an important factor to consider in ORN-related bone density variation

Conclusion

Our pilot study shows that cortical and cancellous mandibular BDs are higher in African Americans compared to Caucasians, and the percent decrease in BD post-RT is greater in Caucasians. Caucasians have an increased association of BD loss in the contralateral mandible compared to African-American ORN patients. This may be associated with why Caucasians are at a higher risk for osteonecrosis and possibly ORN. Further study with a larger sample size and multi-institutional data will confirm these findings.

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References

1 Rivero JA, Shamji O, Kolokythas A. Osteoradionecrosis: a review of pathophysiology, prevention and pharmacologic management using pentoxifylline, α-tocopherol, and clodronate. *Oral Surg Oral Med Oral Pathol Oral Radiol* 2017;**124**:464–71
2 Singh A, Kitpanit S, Neal B, Yorke E, White, C, Yom SK, *et al.* Osteoradionecrosis of the jaw following proton radiation therapy for patients with head and neck cancer. *JAMA Otolaryngol Head Neck Surg* 2023;**149**:151–9
3 Vasudevan SS, Candelo E, Sharifi A, Ma DJ, Patel SH, Routman DM, *et al.* Survival, tumor control, and safety outcomes of proton therapy in sinonasal cancer population: a systematic review and meta-analysis. *Head Neck* 2025;**47**:1291–1305
4 Chronopoulos A, Zarra T, Ehrenfeld M, Otto S. Osteoradionecrosis of the jaws: definition, epidemiology, staging and clinical and radiological findings. A concise review. *Int Dent J* 2018;**68**:22–30
5 Kün-Darbois J-D, Fauvel F. Medication-related osteonecrosis and osteoradionecrosis of the jaws: update and current management. *Morphologie* 2021;**105**:170–87
6 Otto S, Pautke C, Van den Wyngaert T, Niepel D, Schiødt M. Medication-related osteonecrosis of the jaw: prevention, diagnosis and management in patients with cancer and bone metastases. *Cancer Treat Rev* 2018;**69**:177–87
7 Marx RE. Osteoradionecrosis: a new concept of its pathophysiology. *J Oral Maxillofac Surg* 1983;**41**:283–8
8 Quispe D, Shi R, Burton G. Osteonecrosis of the jaw in patients with metastatic breast cancer: ethnic and socio-economic aspects. *Breast J* 2011;**17**:510–13
9 Noel SE, Santos MP, Wright NC. Racial and ethnic disparities in bone health and outcomes in the United States. *J Bone Miner Res* 2021;**36**:1881–905
10 Perry HM III, Horowitz M, Morley JE, Fleming S, Jensen J, Caaccione P, *et al.* Aging and bone metabolism in African American and Caucasian women. *J Clin Endocrinol Metab* 1996;**81**:1108–17
11 Park H-S, Lee Y-J, Jeong S-H, Kwon T-G. Density of the alveolar and basal bones of the maxilla and the mandible. *Am J Orthod Dentofacial Orthop* 2008;**133**:30–7
12 Shapurian T, Damoulis PD, Reiser GM, Griffin TJ, Rand WM. Quantitative evaluation of bone density using the Hounsfield index. *Int J Oral Maxillofac Implants* 2006;**21**:290–7
13 Sathasivam HP, Davies GR, Boyd NM. Predictive factors for osteoradionecrosis of the jaws: a retrospective study. *Head Neck* 2018;**40**:46–54
14 Raguse J-D, Hossamo J, Tinhofer I, Hoffmeister B, Budach V, Jamil B, *et al.* Patient and treatment-related risk factors for osteoradionecrosis of the jaw in patients with head and neck cancer. *Oral Surg Oral Med Oral Pathol Oral Radiol* 2016;**121**:215–21.e1
15 Villa A, Castiglioni S, Peretti A, Omodei M, Ferrieri GB, Abati S. Osteoporosis and bisphosphonate-related osteonecrosis of the jaw bone. *ISRN Rheumatol* 2011;**2011**:654027
16 Griffin MR, Ray WA, Fought RL, Melton LJ III. Black-white differences in fracture rates. *Am J Epidemiol* 1992;**136**:1378–85
17 Baron JA, Barrett J, Malenka D, Fisher E, Kniffin W, Bubolz T, *et al.* Racial differences in fracture risk. *Epidemiology* 1994;**5**:42–7
18 Barrett-Connor E, Siris ES, Wehren LE, Miller PD, Abbott TA, Berger ML, *et al.* Osteoporosis and fracture risk in women of different ethnic groups. *J Bone Miner Res* 2005;**20**:185–94
19 Hopewell JW. Radiation-therapy effects on bone density. *Med Pediatr Oncol* 2003;**41**:208–11
20 Pacheco R, Stock H. Effects of radiation on bone. *Curr Osteoporos Rep* 2013;**11**:299–304
21 Patil V, Shah P, Mahajan A, Sable N, Shukla A, Bornak G, *et al.* Decoding osteoradionecrosis of the jaw: radiological progression and a novel CT-based grading system. *Cancers (Basel)* 2026;**18**:187
22 Miyamoto I, Tanaka R, Kogi S, Yamaya G, Kawai T, Ohashi Y, *et al.* Clinical diagnostic imaging study of osteoradionecrosis of the jaw: a retrospective study. *J Clin Med* 2021;**10**:4704
23 Peterson DE, Koyfman SA, Yarom N, Lynggaard CD, Ismaila N, Forner LE, *et al.* Prevention and management of osteoradionecrosis in patients with head and neck cancer treated with radiation therapy: ISOO-MASCC-ASCO Guideline. *J Clin Oncol* 2024;**42**:1975–96
24 Kaplan JB, Bennett T. Use of race and ethnicity in biomedical publication. *JAMA* 2003;**289**:2709–16
25 Bonham VL, Green ED, Pérez-Stable EJ. Examining how race, ethnicity, and ancestry data are used in biomedical research. *JAMA* 2018;**320**:1533–4

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26 Williams DR, Sternthal M. Understanding racial-ethnic disparities in health: sociological contributions. *J Health Soc Behav* 2010;**51**:S15–27
27 Ettinger B, Sidney S, Cummings SR, Libanati C, Bikle DD, Tekawa IS, *et al.* Racial differences in bone density between young adult black and white subjects persist after adjustment for anthropometric, lifestyle, and biochemical differences. *J Clin Endocrinol Metab* 1997;**82**:429–34
28 Aloia JF. African Americans, 25-hydroxyvitamin D, and osteoporosis: a paradox. *Am J Clin Nutr* 2008;**88**:545S–50S

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