Research Article

Radiotherapy-Associated Changes in Mandibular Trabecular Microarchitecture and Radiographic Density: A Paired Fractal Dimension and Pixel Intensity Analysis

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Abstract

Background: Radiotherapy for head and neck cancer can adversely affect mandibular bone through vascular injury, cellular depletion, and impaired bone remodelling. These changes may precede clinically evident complications such as osteoradionecrosis and pathological fracture. Fractal dimension (FD) and pixel intensity (PI) derived from digital panoramic radiographs may provide a simple quantitative approach for detecting alterations in trabecular architecture and radiographic bone density.

Objective: To evaluate radiotherapy-associated changes in mandibular trabecular microarchitecture and radiographic density by comparing FD and PI values on paired digital panoramic radiographs obtained before and after three-dimensional conformal radiotherapy.

Materials and Methods: This retrospective observational study included 60 patients with head and neck cancer who underwent three-dimensional conformal radiotherapy between June 2023 and June 2026. A total of 120 digital panoramic radiographs, comprising one pre-radiotherapy and one post-radiotherapy image for each patient, were evaluated. Standardized bilateral regions of interest were selected in the mandibular body. Images were analysed using ImageJ 1.54p. Trabecular complexity was assessed using FD with a box-counting method following standardized image processing, while mean grayscale PI was used as a measure of relative radiographic density. Data distribution was assessed using the Shapiro–Wilk test, and paired pre- and post-radiotherapy measurements were compared at a significance level of $p < 0.05$.

Results: Mean PI decreased from 131.8 ± 30.6 before radiotherapy to 112.4 ± 31.8 after radiotherapy, with a mean reduction of 19.4 units ($p < 0.001$). Mean FD similarly decreased from 1.41 ± 0.09 to 1.31 ± 0.10, corresponding to a mean reduction of 0.10 ($p < 0.001$). The concurrent reduction in PI and FD indicated a measurable decline in radiographic density together with simplification of the mandibular trabecular pattern following radiotherapy.

Conclusion: Head and neck radiotherapy was associated with significant reductions in mandibular pixel intensity and fractal dimension, suggesting deterioration in both radiographic bone density and trabecular microarchitectural complexity. Quantitative analysis of routinely acquired panoramic radiographs may offer a practical, low-cost method for monitoring mandibular bone changes after radiotherapy. Further studies incorporating radiation dose, treatment field, and longer follow-up are required before FD and PI can be established as predictive markers of radiation-related mandibular complications.

Keywords: Radiotherapy; Mandible; Fractal dimension; Pixel intensity; Trabecular bone; Panoramic radiography; Head and neck cancer; Bone microarchitecture.

Introduction

Radiotherapy remains a central component of treatment for head and neck malignancies, either as definitive therapy or as part of multimodality care. Improvements in treatment planning and dose delivery have reduced exposure to normal tissues, yet the mandible remains vulnerable because it frequently lies within or close to high-dose treatment fields. Radiation-related injury to the jaws may impair healing, compromise dental rehabilitation, and, in its most severe form, culminate in osteoradionecrosis (ORN). Contemporary guidelines therefore emphasize prevention, dental optimization, and long-term surveillance of irradiated patients [1]. Although modern techniques have lowered the risk, ORN has not been eliminated [2,3]. A 2024 meta-analysis in patients with oral cavity cancer treated with intensity-modulated radiotherapy reported an overall ORN incidence of approximately 8%, with substantial variation across populations and treatment protocols [4].

Radiation injury to bone is not limited to established ORN. The process begins earlier and involves endothelial damage, microvascular compromise, altered bone-cell activity, impaired remodelling, and progressive fibroatrophic change [2,3]. The magnitude of injury is influenced by radiation dose and the volume of mandible exposed, as well as tumour site, dental status, surgery, smoking, and post-treatment trauma [5,6]. These biological changes may alter cortical integrity and trabecular organization before bone exposure or necrosis becomes clinically apparent. A recent systematic review and meta-analysis of imaging-based maxillomandibular changes after head and neck radiotherapy documented cortical thinning, altered trabecular density, sclerosis, osteolytic changes, and impaired healing, supporting the concept that radiation-induced bone injury exists along a spectrum [7].

Imaging may therefore have a role not only in diagnosing advanced complications but also in identifying earlier structural deterioration. Panoramic radiography is routinely used in dental assessment because it is accessible, inexpensive, and provides broad visualization of the jaws. A systematic review of post-radiotherapy dentomaxillofacial findings confirmed that hard-tissue alterations can be detected on panoramic radiographs [8]. However, subtle changes in trabecular architecture may be difficult to judge visually, and subjective interpretation may overlook early or slowly progressive changes. Quantitative image analysis can extract additional information from radiographs already available in clinical records.

Fractal dimension (FD) and pixel intensity (PI) are two such quantitative measures. FD numerically describes the complexity of trabecular patterns, whereas PI represents grayscale information within a defined region of interest and can be used as an indirect indicator of relative radiographic density rather than a direct measurement of bone mineral density. Palma et al. demonstrated significant post-radiotherapy reductions in both FD and PI in the mandibular angle region [9]. More recently, Duman Tepe et al. reported persistent reductions in mandibular fractal values up to 36 months after radiotherapy [10], while a 2026 study found significant decreases in both FD and PI in the mandibular condylar process after three-dimensional conformal radiotherapy [11]. These findings suggest that quantitative panoramic analysis can capture structural effects of irradiation that may not be obvious on visual inspection.

Despite growing interest, the evidence remains heterogeneous in relation to tumour site, radiation technique, region of interest, follow-up interval, and imaging outcome [7,12]. Current recommendations continue to emphasize preventive follow-up and earlier recognition of radiation-related jaw injury [13–15]. There is therefore a need for paired, standardized assessment of the mandibular body using complementary measures of trabecular complexity and radiographic density. The present study aimed to compare pre- and post-radiotherapy FD and PI values on digital panoramic radiographs in patients with head and neck cancer treated with three-dimensional conformal radiotherapy, with the hypothesis that both parameters would decrease following treatment.

Materials And Methods

Study design and setting

This retrospective paired radiographic study was conducted in the Department of Oral Medicine and Radiology, Saveetha Dental College and Hospitals, Chennai, India. Digital clinical and radiographic records of patients treated for head and neck malignancies between June 2023 and June 2026 were reviewed. The study was designed to assess longitudinal changes in mandibular trabecular architecture and radiographic density by comparing digital panoramic radiographs obtained before radiotherapy and six months after completion of radiotherapy. The study was conducted in accordance with the principles of the Declaration of Helsinki. Institutional ethical approval was obtained before retrieval and analysis of patient records. As the study involved retrospective evaluation of previously acquired radiographs, no additional radiation exposure was required for research purposes.

Study population

Patients with histopathologically confirmed head and neck malignancies who had undergone surgical management followed by postoperative three-dimensional conformal radiotherapy (3D-CRT) were screened for eligibility. A total of 60 patients fulfilling the predefined selection criteria were included in the final analysis. Each patient contributed two digital panoramic radiographs: one obtained before initiation of radiotherapy and a second obtained approximately six months after completion of treatment. Thus, a total of 120 panoramic radiographs were evaluated. All patients received postoperative external-beam radiotherapy using a 3D conformal technique, with a total prescribed dose ranging from 60 to 66 Gy according to the individual oncological treatment plan.

Eligibility criteria

Patients were included when they:

- had a confirmed diagnosis of head and neck malignancy;
- had undergone surgical treatment followed by 3D conformal radiotherapy;
- received a total radiation dose of 60–66 Gy;
- had an acceptable-quality digital panoramic radiograph obtained before radiotherapy;
- had a corresponding post-radiotherapy panoramic radiograph obtained approximately six months after treatment; and
- demonstrated adequate visualization of the mandibular body bilaterally for quantitative analysis.

Patients were excluded when the panoramic radiographs showed marked positioning errors, motion artefacts, severe image distortion or inadequate visualization of the proposed region of interest. Images demonstrating mandibular fractures, extensive local bone destruction, previous mandibular reconstruction, focal osseous pathology, or other conditions that could substantially alter the trabecular pattern within the selected region were also excluded.

Panoramic radiographic acquisition

Digital panoramic radiographs were retrieved from the institutional imaging archive. Images had been acquired using a Carestream Dental digital panoramic imaging system as part of routine clinical care. Because the study was retrospective and involved images obtained over several years, the exact panoramic unit model was not consistently documented in the archived records.

Radiographs were obtained according to the standardized positioning and exposure protocol followed by the Department of Oral Medicine and Radiology. Only diagnostically acceptable images were included. Images with substantial differences in positioning, magnification, contrast, or visible technical artefacts that could interfere with quantitative measurements were excluded. The original digital images were exported in a lossless format wherever available and analysed without additional enhancement intended to alter trabecular appearance.

Selection of the region of interest

Quantitative analysis was performed bilaterally in the mandibular body. A standardized region of interest (ROI) of identical dimensions was selected on each side of the mandible. The ROI was positioned within cancellous bone and was chosen to contain a representative trabecular pattern while avoiding structures that could influence grayscale or fractal measurements. Care was taken to exclude the inferior cortical border of the mandible, tooth roots, periodontal structures, mandibular canal, mental foramen, areas of focal pathology, metallic restorations, superimposed structures and obvious radiographic artefacts. For each patient, the anatomical position and dimensions of the ROI selected on the pre-radiotherapy image were reproduced as closely as possible on the corresponding six-month post-radiotherapy radiograph. Anatomical landmarks were used as reference points to maintain consistency between paired images. Measurements obtained from the right and left mandibular body were recorded using the same image-processing protocol.

Image analysis

All quantitative measurements were performed using ImageJ version 1.54p (National Institutes of Health, Bethesda, MD, USA). Two radiographic parameters were evaluated: pixel intensity and fractal dimension.

Pixel intensity analysis

Pixel intensity was used as an indicator of relative radiographic density within the selected mandibular ROI. It was not interpreted as a direct measurement of bone mineral density. For analysis, each standardized ROI was opened in ImageJ and converted to an 8-bit grayscale image when required. The mean grayscale value of all pixels within the ROI was calculated using the ImageJ measurement function. Higher values represented greater relative radiographic intensity, whereas lower values represented reduced grayscale intensity within the analysed region. The same ROI dimensions and measurement procedure were used for pre- and post-radiotherapy images to minimize variability related to region selection. Mean pixel intensity values were subsequently compared between the two time points.

Fractal dimension analysis

Fractal dimension was used to quantitatively characterize the complexity of the mandibular trabecular pattern. A standardized image-processing sequence was applied to each ROI before calculation of FD. The selected ROI was duplicated and converted into an 8-bit grayscale image. A Gaussian blur was applied to the duplicated image to suppress large-scale variations in brightness.

The blurred image was then subtracted from the original ROI, and a constant grayscale value of 128 was added to normalize the resulting image. The image was subsequently converted into a binary representation. Morphological processing, including erosion and dilation, was performed to reduce noise and improve delineation of the trabecular pattern. The image was then inverted and skeletonized so that the remaining trabeculae were represented as single-pixel-wide structures. Fractal dimension was calculated using the box-counting method available in ImageJ. The algorithm superimposes grids of progressively changing box sizes over the skeletonized image and evaluates the relationship between box size and the number of boxes containing trabecular structures.

The resulting FD value represents the degree of structural complexity within the ROI; comparatively lower values indicate a simpler and less complex trabecular pattern. The same processing sequence was used for every pre- and post-radiotherapy image to maintain methodological consistency.

Observer calibration and reproducibility

All radiographic measurements were performed under standardized viewing conditions by an examiner trained in ROI placement and ImageJ-based quantitative analysis. To evaluate measurement reproducibility, 20% of the study images were selected for repeat assessment. The selected radiographs were re-evaluated without reference to the initial measurements. Reproducibility of

FD and PI measurements was assessed using the intraclass correlation coefficient (ICC). Agreement was interpreted using conventional ICC thresholds, with values approaching 1.0 indicating greater measurement reliability. The final ICC estimates should be reported with their 95% confidence intervals once the original reproducibility output is retrieved.

Outcome measures

The primary outcomes were:

1. change in mean mandibular pixel intensity between the pre-radiotherapy and six-month post-radiotherapy panoramic radiographs; and
2. change in mandibular fractal dimension over the same period.

Pixel intensity was interpreted as a quantitative measure of relative radiographic density, whereas fractal dimension represented trabecular microarchitectural complexity.

Statistical analysis

Data were entered into Microsoft Excel and analysed using IBM SPSS Statistics for Windows, version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were summarized using mean and standard deviation for approximately normally distributed data and median and range where appropriate. Normality of quantitative variables and paired differences was assessed using the Shapiro–Wilk test together with visual inspection of their distributions. Pre- and post-radiotherapy measurements represented repeated observations from the same patients and were therefore analysed as paired data. The paired-samples Student's t-test was used when the distributional assumptions for parametric analysis were satisfied. For variables that did not meet these assumptions, the Wilcoxon signed-rank test was considered appropriate. Changes in pixel intensity and fractal dimension from baseline to the six-month post-radiotherapy assessment were calculated for each patient. All statistical tests were two-sided, and a p-value <0.05 was considered statistically significant.

Table 1. Study and treatment characteristics

CHARACTERISTIC	STUDY DATA
Patients included	60
Panoramic radiographs analysed	120
Radiographs per patient	2
Treatment sequence	Surgery → postoperative radiotherapy
Radiotherapy technique	3D conformal radiotherapy
Total radiation dose	60–66 Gy
Baseline imaging	Pre-radiotherapy OPG
Follow-up imaging	6 months post-radiotherapy
Region analysed	Bilateral mandibular body
Quantitative parameters	Pixel intensity and fractal dimension
Image-analysis software	ImageJ 1.54p

RESULTS

Study sample

A total of 60 patients with head and neck malignancies who underwent surgical treatment followed by three-dimensional conformal radiotherapy were included in the study. Each patient had an eligible digital panoramic radiograph obtained before radiotherapy and a corresponding radiograph obtained six months after treatment, yielding 120 radiographs for paired analysis. All patients received a total radiation dose of 60–66 Gy.

Changes in pixel intensity

A clear reduction in mandibular pixel intensity was observed at the six-month post-radiotherapy assessment. Mean pixel intensity decreased from 131.8 ± 30.6 before radiotherapy to 112.4 ± 31.8 after radiotherapy. The mean absolute change was −19.4 grayscale units, corresponding to an approximately 14.7% reduction from the baseline group mean. The paired difference was statistically significant ($p < 0.001$). The distributional findings were consistent with the mean-based analysis. Median pixel intensity decreased from 133.5 before radiotherapy to 113.0 after treatment. Pre-radiotherapy values ranged from 68.4 to 184.2, whereas post-radiotherapy values ranged from 55.8 to 169.6. Thus, both measures of central tendency demonstrated a shift toward lower radiographic intensity six months after radiotherapy.

Changes in fractal dimension

Fractal dimension also showed a significant reduction following radiotherapy. Mean FD decreased from 1.41 ± 0.09 at baseline to 1.31 ± 0.10 at the six-month follow-up. The mean absolute change was −0.10, representing an approximately 7.1% reduction relative to the baseline group mean. This difference was statistically significant ($p < 0.001$). Median FD showed a similar pattern, decreasing from 1.42 before radiotherapy to 1.31 after radiotherapy. Values ranged from 1.21–1.56 at baseline and 1.12–1.49 at the post-radiotherapy assessment. The reduction in FD indicates a measurable simplification of the mandibular trabecular pattern following radiation exposure.

Table 2. Pre- and post-radiotherapy quantitative mandibular changes

Parameter	Pre-RT	6-month post-RT	Absolute change	Relative change*	p value
Pixel intensity	131.8 ± 30.6	112.4 ± 31.8	**−19.4**	**−14.7%**	**<0.001**
Fractal dimension	1.41 ± 0.09	1.31 ± 0.10	**−0.10**	**−7.1%**	**<0.001**

Figure 1. Individual patient trajectories in mandibular pixel intensity and fractal dimension before and 6 months after radiotherapy (n = 60).

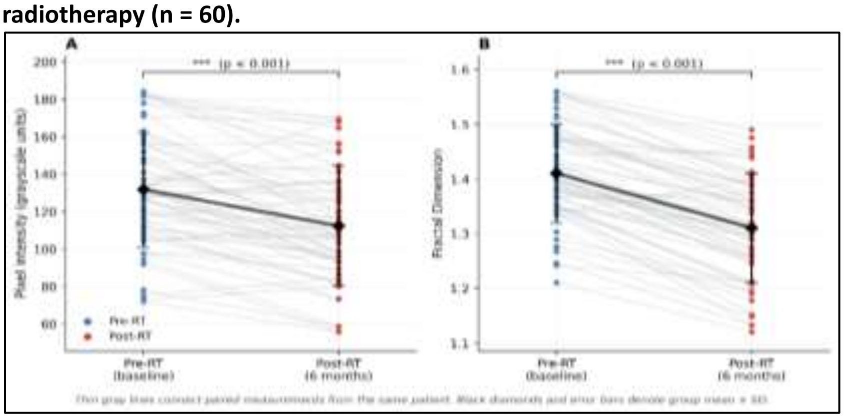
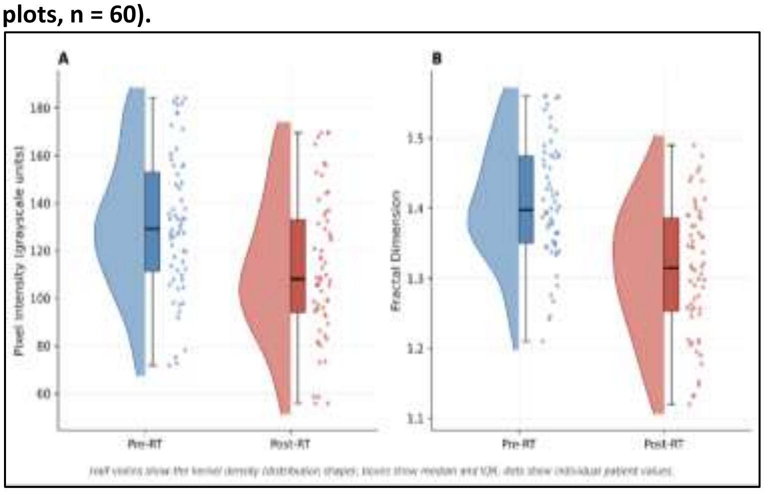


Figure 2. Distribution of mandibular pixel intensity and fractal dimension before and 6 months after radiotherapy (raincloud plots, n = 60).



Combined radiographic response

Both quantitative radiographic measures changed in the same overall direction. Pixel intensity demonstrated a larger relative reduction of 14.7%, while fractal dimension decreased by 7.1% over the six-month observation period. The simultaneous decline in these two independent image-derived parameters suggests that post-radiotherapy mandibular alterations involve both a reduction in relative radiographic density and loss of trabecular microarchitectural complexity. Taken together, the findings demonstrate a significant quantitative alteration of the mandibular body within six months of postoperative radiotherapy. These results support subsequent evaluation of PI and FD as complementary radiographic markers rather than interchangeable measurements of the same bone characteristic.

Table 3. Distribution of PI and FD before and after radiotherapy

Parameter	Pre-RT median	Post-RT median	Pre-RT range	Post-RT range
Pixel intensity	133.5	113.0	68.4–184.2	55.8–169.6
Fractal dimension	1.42	1.31	1.21–1.56	1.12–1.49

Figure 3. Relationship between radiographic density loss (ΔPI) and trabecular microarchitectural simplification (ΔFD) (n = 60).

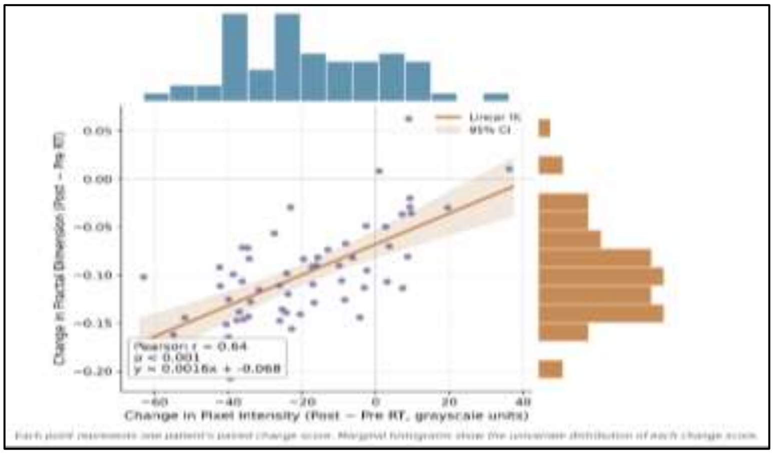
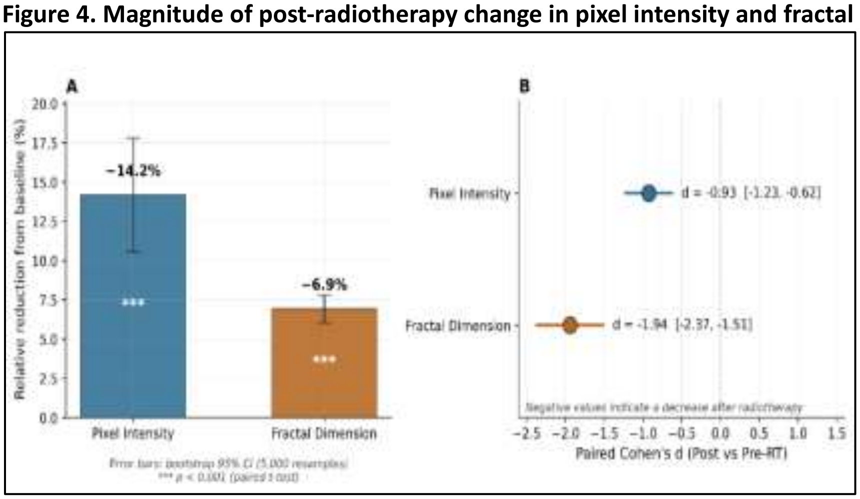


Figure 4. Magnitude of post-radiotherapy change in pixel intensity and fractal dimension (n = 60).



Discussion

The present study demonstrated measurable alterations in mandibular bone six months after postoperative radiotherapy. Pixel intensity decreased by approximately 14.7%, while fractal dimension decreased by 7.1%, indicating that changes occurred in both relative radiographic density and trabecular organization. The paired design is particularly relevant because each patient served as their own baseline, reducing the influence of inter-individual differences in mandibular morphology. Importantly, the reduction in PI should not be interpreted as a direct measure of mineral loss; rather, it reflects a shift in grayscale characteristics within a standardized region. The accompanying reduction in FD strengthens the observation by showing that the internal trabecular pattern also became less complex.

These radiographic changes are biologically plausible. Examination of irradiated human mandibular bone has demonstrated increased osteocyte loss, marrow adiposity and impaired osteogenic potential, suggesting that radiation disturbs normal bone homeostasis even in the absence of established necrosis [16]. Ultrastructural evaluation has similarly shown reductions in osteons, osteocytes and osteocytic processes in irradiated mandibular specimens, supporting progressive deterioration in bone quality and microarchitecture [17]. Such cellular and structural injury provides a reasonable biological basis for the lower PI and FD observed in the present cohort.

Radiation exposure, however, is unlikely to affect the mandible uniformly. Contemporary dosimetric studies indicate that local dose distribution and the volume of mandible receiving intermediate-to-high doses may be more informative than the prescribed total dose alone [18,19]. This is particularly relevant to our patients, who received 60–66 Gy. In postoperative oral cavity cancer cohorts, increasing mandibular V60 has been associated with greater ORN risk [20], while other work has identified V44 and V58 as potentially important volumetric constraints [21]. Mapping radiation dose to individual tooth-bearing mandibular sectors has also demonstrated considerable regional variation in exposure [22]. These observations suggest that future FD and PI studies should correlate the exact ROI with three-dimensional dose maps rather than relying solely on the total prescribed dose.

The clinical meaning of reduced FD also requires careful interpretation. Barcelos et al. found no statistically significant difference in FD between irradiated patients with and without established ORN, despite potentially meaningful effect sizes [23]. Thus, FD should presently be viewed as a marker of altered trabecular architecture rather than a stand-alone diagnostic marker for ORN. This distinction is important when translating the current findings into clinical practice. More advanced quantitative approaches are already showing promise; CT-based radiomics has recently differentiated ORN from unaffected mandibular bone with high discriminatory performance [24].

Panoramic PI and FD therefore occupy a practical position between subjective radiographic assessment and resource-intensive three-dimensional imaging. Their main value may lie in inexpensive longitudinal surveillance using radiographs already obtained during routine dental care. Future studies combining serial panoramic features with patient characteristics and spatial radiation-dose information may provide more clinically useful risk models, an approach increasingly supported by multimodal toxicity-modelling research [25].

Limitations

Several limitations should be considered when interpreting these findings. The retrospective, single-centre design and relatively modest sample may limit generalizability. Panoramic radiography is inherently two-dimensional and is affected by magnification, positioning and acquisition-related variability. Recent evidence shows that differences in panoramic acquisition and digitization can significantly influence FD measurements, emphasizing the importance of image standardization [26]. ROI placement is another potential source of variability, as even differences in ROI orientation can alter calculated FD values [27]. The study also lacked patient-specific mandibular dose–volume mapping; therefore, the observed changes cannot be directly related to the radiation dose received by each ROI. PI should additionally be regarded as relative radiographic density rather than a direct measure of bone mineral density.

Future Implications

Future prospective multicentre studies should include larger cohorts, serial follow-up beyond six months, standardized image acquisition, and spatial correlation between FD/PI measurements and mandibular dose–volume parameters. Clinical and dosimetric modelling has already demonstrated the value of combining mandibular radiation exposure with patient-specific risk factors for predicting ORN [28]. Integration of panoramic biomarkers with CT-based dose mapping, automated segmentation and longitudinal clinical outcomes could further improve individualized surveillance. Emerging deep-learning approaches capable of segmenting mandibular subregions and individual teeth may eventually permit precise regional correlation between radiation exposure and subsequent bone alteration [29].

Conclusion

This study demonstrates that postoperative head and neck radiotherapy is associated with measurable alterations in the mandibular body within six months of treatment. Both pixel intensity and fractal dimension showed significant reductions after radiotherapy, indicating a concurrent decline in relative radiographic density and simplification of trabecular microarchitecture.

The paired pre- and post-radiotherapy design strengthens these observations by allowing each patient to serve as their own baseline and reducing the effect of inter-individual anatomical variability.

Pixel intensity and fractal dimension should be regarded as complementary rather than interchangeable parameters. Pixel intensity reflects changes in grayscale characteristics and relative radiographic density, whereas fractal dimension provides information on the structural complexity of the trabecular pattern. Their simultaneous reduction suggests that radiation-related mandibular injury may involve both qualitative and quantitative alterations in bone architecture before overt clinical complications become evident.

Digital panoramic radiography is routinely available, relatively inexpensive, and commonly used during dental evaluation of patients with head and neck cancer. When combined with standardized ImageJ-based quantitative analysis, it may therefore provide a practical approach for longitudinal assessment of mandibular changes without the need for additional advanced imaging at every follow-up visit. However, these measurements should not be interpreted as direct measures of bone mineral density or as independent diagnostic markers for osteoradionecrosis.

Further prospective, multicentre studies with larger samples, longer follow-up, standardized radiographic protocols, and patient-specific dose-volume correlation are required to validate these findings. Integration of radiographic parameters with clinical risk factors, radiation dosimetry, and three-dimensional imaging may help clarify their future role in identifying patients at greater risk of radiation-related mandibular complications and in guiding personalized post-radiotherapy surveillance.

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