

# Use of Spherical Segmentation Radiomic Analysis for Differentiation of Odontogenic Keratocysts and Radicular Cysts

## Odontojenik Keratokistler ile Radiküler Kistlerin Ayırt Edilmesinde Küresel Segmentasyon Tekniği ile Elde Edilen Radyomik Özelliklerin Kullanımı

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### ABSTRACT

**INTRODUCTION:** The objective of this study was to investigate the potential of radiomics in distinguishing between odontogenic keratocyst, a developmental odontogenic cyst, and radicular cyst, an inflammatory odontogenic cyst.

**MATERIAL and METHODS:** This retrospective case-control study included 10 patients with odontogenic keratocysts who were admitted to the Department of Oral and Maxillofacial Radiology. The control group consisted of patients diagnosed with radicular cysts. Radiomic analysis was performed on the cone-beam computed tomography images of the lesions using a three-dimensional spherical segmentation centered on the lesion. From a total of 93 radiomic features, the most relevant features for lesion differentiation were selected using a Lasso regression model. Based on this analysis, four radiomic features were identified as most strongly associated with the differentiation of the two lesion types. Subsequently, a radiomic score for each patient was calculated as the linear combination of the coefficients of the selected features.

**RESULTS:** The calculated radiomic scores predicted radicular cysts with a sensitivity and specificity of 80%. The model correctly classified 80% of radicular cysts and 80% of odontogenic keratocysts. Additionally, radiomic scores were found to be higher in radicular cyst patients compared to odontogenic keratocyst patients (OR: 25.251;  $p = 0.018$ ).

**CONCLUSION:** Radiomic features enabled the differentiation between radicular cysts and odontogenic keratocysts. However, the findings of this study should be interpreted as preliminary, considering the sample size and study limitations. Nonetheless, the proposed approach has the potential to assist in the differential diagnosis between odontogenic keratocysts and radicular cysts, and to provide clinically valuable insights as a non-invasive virtual biopsy method prior to surgery.

**Keywords:** Radiomics, CBCT, Biopsy, Odontogenic Keratocyst, Radicular Cyst

### ÖZ

**GİRİŞ:** Bu çalışmanın amacı, gelişimsel bir odontojenik kist olan odontojenik keratokist ile iltihabi bir odontojenik kist olan radiküler kistin ayırt edilmesinde radyomik özelliklerin potansiyelini araştırmaktır.

**YÖNTEM ve GEREÇLER:** Bu retrospektif olgu-kontrol çalışmasında, Ağız, Diş ve Çene Radyolojisi Anabilim Dalına başvuran 10 odontojenik keratokist hastası incelenmiştir. Kontrol grubunu, radiküler kist tanılı hastalar oluşturmuştur. Lezyonların konik ışınli bilgisayarlı tomografi görüntüleri üzerinde, lezyonun merkez noktasından alınan alanlarda üç boyutlu küresel segmentasyon tekniği kullanılarak radyomik analiz gerçekleştirilmiştir. Radyomik analizden elde edilen 93 özellik arasında, lezyon ayırımında en ilişkili özellikleri seçmek amacıyla Lasso regresyon modeli uygulanmıştır. Sonuç olarak, bu lezyonların ayırımında en ilişkili dört radyomik özellik belirlenmiştir. Ardından, her hastanın radyomik skoru, seçilen özelliklerin katsayılarının lineer kombinasyonu alınarak hesaplanmıştır.

**BULGULAR:** Elde edilen radyomik skorlar, radiküler kistlerin öngörülmesinde %80 duyarlılık ve %80 özgüllük değerlerine sahip olmuştur. Model, radiküler kistleri %80, odontojenik keratokistleri ise %80 doğrulukla tespit etmiştir. Ayrıca, radyomik skor radiküler kist hastalarında, odontojenik keratokist hastalarına kıyasla daha yüksek bulunmuştur (OR: 25,251;  $p = 0,018$ ).

**SONUÇ:** Radyomik özellikler, radiküler kist ile odontojenik keratokistin ayırt edilmesini mümkün kılmıştır. Ancak, bu çalışmadan elde edilen bulguların, örneklem büyüklüğü ve çalışma sınırlılıkları göz önünde bulundurularak ön bulgular olarak değerlendirilmesi gerektiği unutulmamalıdır. Bununla birlikte, bu çalışmada geliştirilen yaklaşım, odontojenik keratokist ile radiküler kistin ayırıcı tanısında yardımcı olabilecek ve cerrahi öncesinde non-invaziv bir sanal biyopsi yöntemi olarak klinik açıdan önemli katkılar sağlayabilecek bir potansiyele sahiptir.

**Anahtar Kelimeler:** Radyomik, KİBT, Biyopsi, Odontojenik Keratokist, Radiküler Kistdir.

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## INTRODUCTION

The similar radiological appearances of many pathologies can make it challenging to distinguish between lesions in the maxilla and mandible during the evaluation of jaw lesions.<sup>1</sup> Among jaw lesions, radicular cysts are the most common, typically associated with inflammatory conditions. On radiographs, they commonly appear as radiolucent lesions surrounding the tooth root, frequently encased by a dense rim of cortical bone.<sup>2</sup> Although less common than radicular cysts, odontogenic keratocysts present greater challenges in management for both clinicians and patients due to their high recurrence rate, distinctive histological features, aggressive clinical behaviour, and potential association with nevoid basal cell carcinoma syndrome.<sup>2,3</sup>

A definitive diagnosis of these two lesions requires histopathological examination, even though their characteristic radiographic and clinical features may sometimes allow them to be distinguished from one another at the stage of differential diagnosis.<sup>4</sup> Surgical management strategies for odontogenic keratocysts differ markedly from those for radicular cysts, as odontogenic keratocysts are more prone to recurrence and display a more aggressive clinical course.<sup>5</sup> However, no non-invasive method has yet been established that can reliably distinguish these two lesions with certainty.

Radiomics is an analytical approach that extracts high-dimensional data at the pixel/voxel level.<sup>6</sup> This analytical framework offers the revolutionary potential to enable differential diagnosis between neoplasms, establish correlations with molecular biology and genomics, predict survival, and evaluate treatment response.<sup>7</sup> Although widely applied in oncology and many other medical fields, the literature remains limited in dentistry.<sup>1</sup> Therefore, there is still a need for further studies and new methodological approaches in the literature regarding its use for differentiating jaw lesions.

The primary objective of this investigation was to assess the capability of radiomics in distinguishing between odontogenic keratocyst, characterized by aggressive clinical behaviour and a heightened recurrence rate, and radicular cyst, an inflammatory odontogenic cyst. Additionally, this study employed an experimental spherical segmentation technique, strategically designed to unveil the inherent characteristics of the lesions under scrutiny. The null and alternative hypotheses of this study are as follows:

H<sub>0</sub>: Radiomic features extracted from lesions using spherical segmentation do not enable differentiation between odontogenic keratocysts and radicular cysts.

H<sub>1</sub>: Radiomic features extracted from lesions using spherical segmentation enable differentiation between odontogenic keratocysts and radicular cysts.

## MATERIAL AND METHODS

The non-interventional Clinical Research Ethical Committee of Kocaeli University approved the study protocol (decision no. KÜ GOKAEK-2024/09.21). The study was conducted in accordance with the principles of the Declaration of Helsinki.

### Study Population

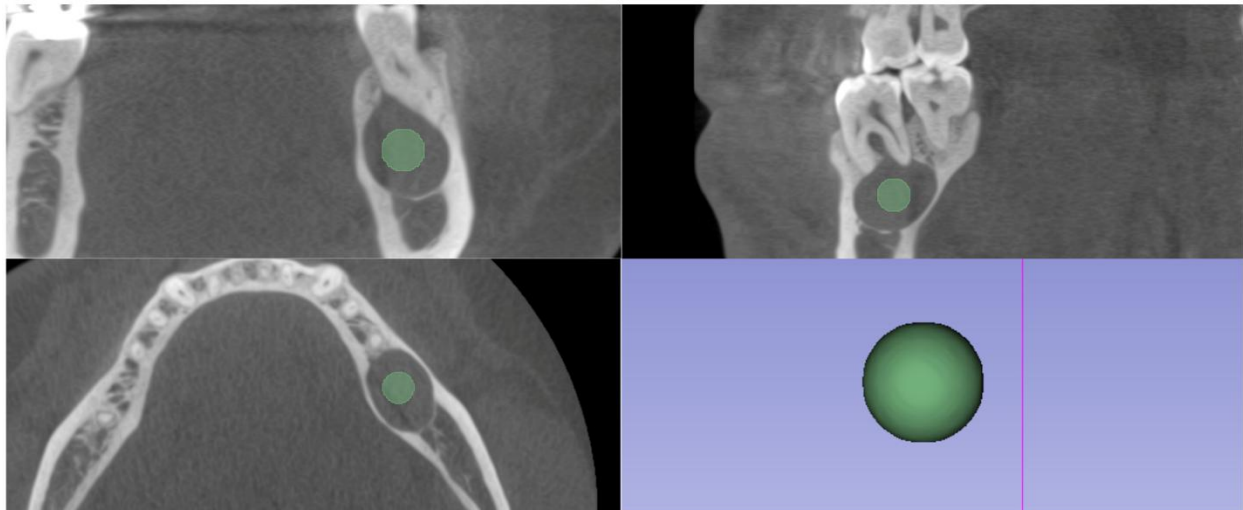
This retrospective group comparative research evaluated histopathologically verified cases of odontogenic keratocysts and radicular cysts which were retrieved from archives of the Department of Oral and Maxillofacial Radiology at Kocaeli University Faculty of Dentistry. Cone-beam computed tomography (CBCT) data of OKC and RC cases were retrospectively analysed. Cases possessing lesions with intact osseous boundaries and with no evidence of any perforation were included in the study. Exclusion criteria were applied rigorously to filter out artifacts that could hinder radiomic analysis, and to cases with images which that did not meet ideal standards.

### Acquisition of CBCT Volumes

The scans were acquired using a Planmeca Promax 3D Max CBCT device (Planmeca Oy, Helsinki, Finland) with a field of view (FOV) of 13 × 9 cm and 0.2 mm voxel size at 96 kVp, 5.6 mA, and 12 s exposure time.

### Segmentation Process and Radiomic Analysis

The obtained DICOM files of the study group were transferred to the 3D Slicer software program for the radiomic analysis.<sup>8</sup> All segmentations were performed by a blinded researcher who was unaware of the histopathological diagnoses of the lesions. For each case, an experimental spherical segmentation was formed and placed in the epicentre of the lesion after orienting the data in axial, coronal and sagittal planes (Figure 1). The rationale for selecting the spherical segmentation technique lies in the biological growth pattern of cystic lesions: as cysts expand, they tend to draw fluid from surrounding tissues and exert equal pressure on their walls, resulting in a generally symmetrical growth from the center.<sup>9,10</sup> Based on this fundamental characteristic, it was hypothesized that the central region of the lesion may contain specific radiomic features capable of distinguishing between different cyst types. Therefore, this experimental approach was adopted in the present study.



**Figure 1.** Three-dimensional spherical segmentation was performed in planes using the 3D Slicer program.

In 3D Slicer software, a total of 93 radiomic features were extracted using the SlicerRadiomics plugin for the segmented area of the lesions. One month after the initial segmentations, the same researcher who performed the original annotations re-segmented the entire dataset to assess the reproducibility of the segmentations. Radiomics analysis was then performed again on these new segmentations, and the resulting values were compared with the radiomics values obtained from the initial segmentations using the Intraclass Correlation Coefficient (ICC). This comparison yielded an ICC value of 0.99.

#### *Statistical Analysis*

Data were analysed using IBM SPSS and R Project software. For Lasso logistic regression, the “glmnet” package in R Project was used. To select the features most associated with lesions from 93 radiomic features, the optimal tuning parameter was determined using 100 repetitions and 5-fold cross-validation with the minimum criterion for the best model fit. Features with non-zero coefficients at this parameter were selected. A linear combination of the selected radiomic feature coefficients was calculated to obtain a radiomic score for each patient. ROC analysis was performed to determine the cutoff values for the radiomic score. The effect of the radiomic score on lesions was evaluated using a multinomial

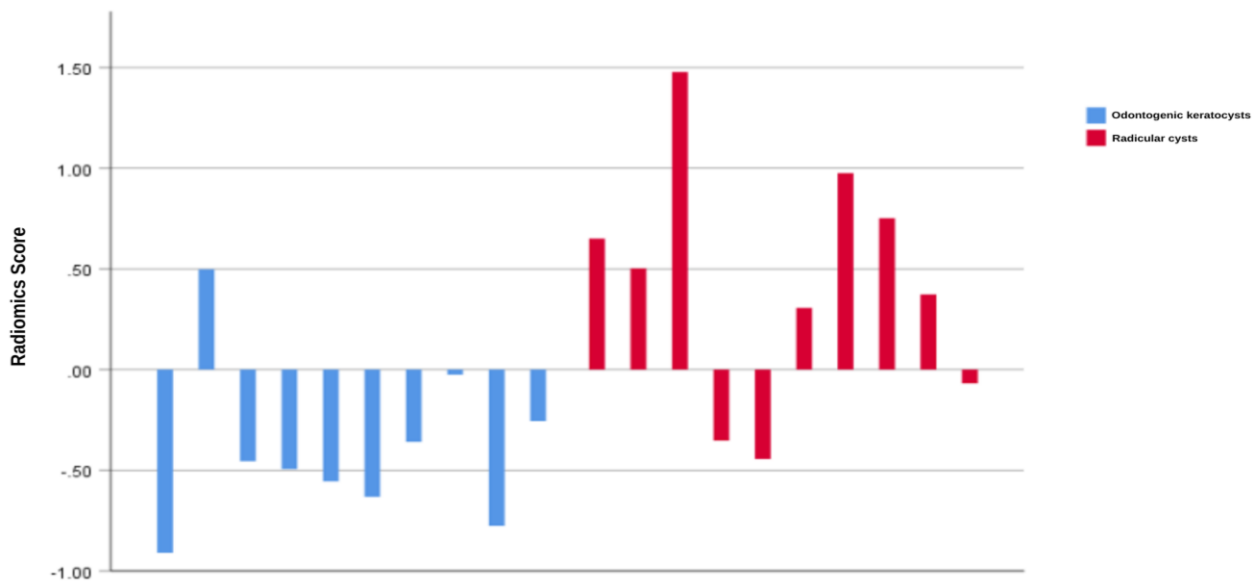
regression model. Results are presented as mean  $\pm$  standard deviation. A significance level of 0.05 was used.

#### **RESULTS**

The CBCT data of a total of 10 OKC and 10 RC cases were analysed. The optimal tuning parameter was established at  $\lambda = 0.1489713$ , indicative of the regression model's optimal alignment with the dataset for the purpose of feature selection among 93 available radiomic features. Under this specified parameter, four non-zero radiomics features were selected and are comprehensively presented in Table 1. The radiomics score was calculated for each patient by obtaining a linear combination of the coefficients of the selected radiomics features (Figure 2).

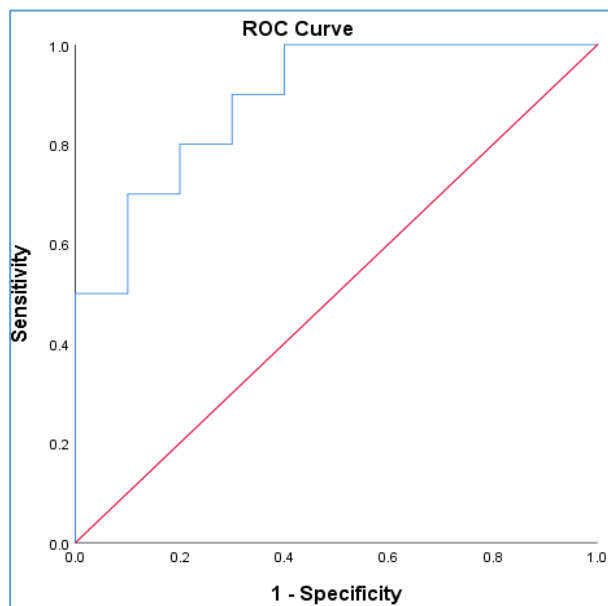
**Table 1.** Radiomics features selected by Lasso Regression

	Coefficients
Constant	-0.2109634
LargeDependenceHighGrayLevelEmphasis	-0.00009815968
SizeZoneNonUniformity	0.002049544
SizeZoneNonUniformityNormalized	0.2070987
ZonePercentage	13.66912



**Figure 2.** Distribution of radiomics scores of datasets based on lesion groups. Blue bars represent the radiomic scores associated with odontogenic keratocyst cases, whereas red bars correspond to radicular cyst cases. Overall, radicular cysts exhibit generally higher radiomic scores compared to odontogenic keratocysts, indicating a discernible distinction between the two lesion types based on the evaluated radiomic features.

$$\text{Radiomics Score} = -0.211 - (0.0001) \times \text{LargeDependenceHighGrayLevelEmphasis} + (0.002) \times \text{SizeZoneNonUniformity} + (0.207) \times \text{SizeZoneNonUniformityNormalized} + (13.669) \times \text{ZonePercentage}$$



**Figure 3.** Receiver Operating Characteristic (ROC) curve of the radiomic score used to differentiate odontogenic keratocysts from radicular cysts (AUC = 0.890).

The radiomics score obtained had a cut-off point of  $\geq -0.07$ . The AUC (95% CI) value was 0.890 (0.500 - 1.000), with a sensitivity and specificity of 80% each in predicting radicular cyst lesions (**Figure 3**). The radiomics score correctly detected 80% of radicular cyst lesions and 80% of odontogenic keratocyst lesions (**Table 2**).

Logistic regression analysis revealed a significant effect of the radiomics score in predicting the lesion. The average radiomic score for patients with keratocyst lesions was -0.4, whereas it was 0.42 for those with radicular cyst lesions (**Table 3**).

It was observed that radicular cysts had a higher radiomics score than odontogenic keratocysts (OR: 25.251;  $p=0.018$ ). As shown in **Figure 4**, the red line represents the cutoff value of the radiomic score. Lesions with radiomic scores above this cutoff were more likely to be radicular cysts, whereas those below the cutoff were mostly odontogenic keratocysts. The model achieved a correct classification rate of 75%. The Nagelkerke R<sup>2</sup>, which is one of the measures of goodness of fit, indicated that the model could explain 53.5% of the lesion.

**Table 2.** ROC curve analysis showing the discriminative performance of radiomic scores between odontogenic keratocyst and radicular cyst cases.

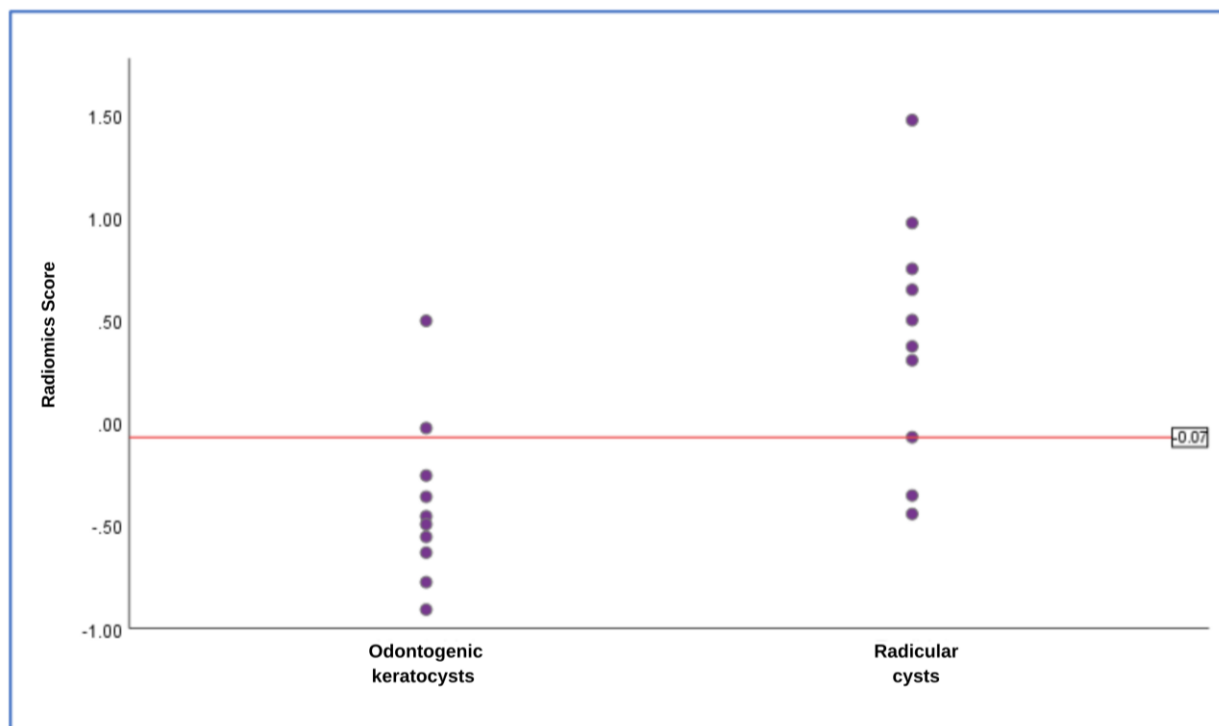
	AUC (95% CI)	Cut-off value	Sensitivity	Specificity	p
Radiomics Score	0.890 (0.500 - 1.000)	-0.07	80%	80%	<b>0.003</b>

AUC: Area Under the Curve, CI: Confidence interval

**Table 3.** Results of logistic regression analysis

	Radiomics Score
<b>Lesion</b>	
Odontogenic keratocysts	-0.4 ± 0.4
Radicular cysts	0.42 ± 0.6
<b>OR</b>	25.251
<b>95% CI</b>	1.752 - 364.007
<b>p</b>	<b>0.018</b>

Mean ± SD, OR: Odds ratio, CI: Confidence Interval, Accuracy = 0.750



**Figure 4.** Scatter plot graph of the radiomics score in differentiating lesions. Radiomic scores above the established cutoff value of -0.07 indicate a higher likelihood that the lesion is a radicular cyst, whereas scores below this threshold suggest a greater probability of an odontogenic keratocyst.

**DISCUSSION**

This study investigated two of the most common jaw lesions, radicular cysts and odontogenic keratocysts, which cannot be reliably distinguished without histopathological confirmation. The results showed that radiomic features extracted from segmented regions within the lesions on CBCT images can differentiate between these two types with high sensitivity and specificity values of approximately 80%. An experimental data extraction method was applied, in

which radiomic features were obtained from regions marked using spherical segmentation centered on the lesion’s midpoint. This approach was designed as a virtual incisional biopsy, based on the knowledge that cysts expand from their center. It differs from the conventional approach frequently described in the literature, where the entire lesion volume is segmented to extract radiomic data. The study has two main outcomes. The primary outcome of this study is that radiomic features demonstrated a strong potential in differentiating radicular cysts from odontogenic keratocysts on CBCT

images. The secondary outcome is that the experimental spherical segmentation method employed for lesion differentiation showed potential as an effective analytical tool.

In this study, among the 93 extracted radiomic features, only four were found to be significantly associated with the differentiation between odontogenic keratocysts and radicular cysts, and these were subsequently used in the formulation of the radiomic score. The first of these, *Large Dependence High Gray Level Emphasis*, belongs to the GLDM (Gray Level Dependence Matrix) family, while the other three are derived from the GLSZM (Gray Level Size Zone Matrix) family. GLDM represents the gray-level dependence matrix, in which a gray-level dependence is defined as the number of neighboring voxels within a given distance that depend on the central voxel. The *Large Dependence High Gray Level Emphasis* feature quantifies the joint occurrence of large homogeneous regions with higher gray-level values. A higher value indicates that the image contains broader areas with similar high-intensity gray levels.<sup>11</sup> In this study, this feature showed higher mean values in odontogenic keratocysts (mean: 6260.32, min: 2803.97, max: 10372.09) compared to radicular cysts (mean: 4503.36, min: 3633.05, max: 5157.91). This finding suggests a distinct difference between the internal contents of the two lesions, reflecting more uniform high-intensity regions in odontogenic keratocysts. Furthermore, this radiomic feature has been previously reported to be associated with lesion heterogeneity in studies on liver fibrosis.<sup>12</sup> Although the biological nature of the two conditions differs substantially, the current results also point to a possible difference in lesion homogeneity between these cyst types.

In addition, three GLSZM-derived radiomic features were also found to be important in differentiating the lesions. The GLSZM quantifies zones of connected voxels that share the same gray-level intensity within an image. A higher number of such zones results in higher corresponding GLSZM values, while larger and more homogeneous zones lead to lower values.<sup>11</sup> Among these features, *Size Zone NonUniformity* and its normalized form, *Size Zone NonUniformity Normalized*, describe the variability in the size of homogeneous gray-level zones within the image. Higher values of these features are generally associated with greater tissue heterogeneity.<sup>13</sup> In our study, odontogenic keratocysts demonstrated lower *Size Zone NonUniformity* values (mean: 56.23, min: 15.32, max: 180.14) compared with radicular cysts (mean: 233.39, min: 16.29, max: 561.31). A similar trend was observed for *Size Zone NonUniformity Normalized*, where odontogenic keratocysts exhibited lower mean values (mean: 0.15, min: 0.10, max: 0.24) than radicular cysts (mean: 0.21, min: 0.12, max: 0.26).

The fourth feature, *Zone Percentage*, represents the ratio of the total number of zones to the total number of

voxels within the region of interest. Higher values indicate a greater number of smaller, more fragmented zones, corresponding to finer texture patterns, whereas lower values reflect larger, coarser structural patterns.<sup>14</sup> In this study, odontogenic keratocysts exhibited lower *Zone Percentage* values (mean: 0.02, min: 0.01, max: 0.04) than radicular cysts (mean: 0.04, min: 0.01, max: 0.07), suggesting that the tissue structure of odontogenic keratocysts may be less fragmented and more uniform. Although direct comparison with previous studies is limited due to the scarcity of similar research and the absence of histopathological correlation analysis in this study, these findings provide valuable insight into the subtle, non-visible grayscale characteristics of these lesions. The results also highlight the potential of radiomic analysis as a foundation for future studies aimed at exploring the microstructural and diagnostic properties of odontogenic cystic lesions.

Although studies using radiomics with CBCT are less common in the literature compared to imaging modalities frequently used in medical radiology, such as MRI and CT, there are a few investigations focusing on lesion differentiation. In one study, Yılmaz et al.<sup>15</sup> aimed to distinguish radicular cysts from odontogenic keratocysts in a total of 50 CBCT images. Order statistics (median, standard deviation, skewness, kurtosis, entropy) and 3D Haralick features were calculated from pixel intensities in each CBCT dataset and used for binary classification experiments. After segmenting the entire lesion in three dimensions, the researchers developed several machine learning models using these features. In their study, they reported that the Support Vector Machine (SVM) classifier, combined with a ten-fold cross-validation method and an advanced feature selection algorithm, achieved the best classification performance with 100% accuracy and a 100% F1-score. In the present study, the entire lesion was not segmented; instead, radiomic features were extracted from a small, defined region within the lesion. Therefore, the regression model developed in this study may have achieved lower performance compared to the 100% accuracy reported by Yılmaz et al.<sup>15</sup> Additionally, our study included a total of 20 patients, with 10 in each group, whereas Yılmaz et al.<sup>15</sup> used 50 CBCT scans. The smaller sample size in our study may have limited the model's predictive performance. Furthermore, while Yılmaz et al.<sup>15</sup> employed a machine learning approach, regression-based analysis was used in the present study, which may also account for the relatively lower performance observed. Nevertheless, despite these methodological limitations, the success of the experimental segmentation approach proposed in this study should not be overlooked. This methodological innovation may provide a valuable direction for future research, as lesion segmentation in radiomics remains a complex and often non-reproducible process. Determining the precise boundaries of lesions can be particularly challenging, potentially influencing

the extracted radiomic values. Therefore, although the performance achieved in our study did not match that of Yılmaz et al.,<sup>15</sup> the results demonstrate that the proposed innovative methodology is both functional and promising.

In another study, Jiang et al.<sup>16</sup> investigated whether radiomic features could be useful for the preoperative differentiation of odontogenic keratocysts from simple bone cysts. Similar to the study by Yılmaz et al.,<sup>15</sup> the researchers segmented the entire lesion and extracted a total of 10,323 radiomic features per case. In their analysis, they employed a sequence forward selection method to statistically identify the most significant radiomic features for differentiating between the two lesion types. However, unlike both our study and that of Yılmaz et al.,<sup>15</sup> they subsequently applied a correlation-based method to select the radiomic features that most effectively distinguished between the two lesions. Due to this methodological difference, the statistical results of their study are not directly comparable to ours. Nevertheless, their analysis revealed that the 25 selected features demonstrated statistically significant correlations, with correlation coefficients ranging from  $-0.487$  to  $0.775$ .

In a different study, Song et al.<sup>17</sup> aimed to differentiate between ameloblastoma and odontogenic keratocyst, which are radiologically very difficult to distinguish. They used radiomic features extracted from CBCT images of these lesions. Their study included 152 cases of ameloblastoma and 174 cases of odontogenic keratocyst. Similar to other studies in the literature, the entire lesion was segmented in this study, and 2,084 radiomic parameters were extracted for each lesion. The researchers employed a data reduction approach comparable to that used in the present study, applying Lasso regression to select the 348 most significant parameters for distinguishing between the two lesion types. However, unlike our study, these selected features were subsequently used to develop several machine learning models, among which the XGBoost model demonstrated the best performance, achieving an AUC value of  $0.872$  in differentiating the two lesions. In contrast, the present study focused on distinguishing odontogenic keratocysts from radicular cysts rather than ameloblastomas, as examined by Song et al. Despite using a smaller dataset, our regression model achieved an AUC of  $0.890$ . The fact that comparable results were obtained using radiomic features extracted solely from the lesion's center underscores the methodological value of our approach. Furthermore, the researchers compared the diagnostic performance of their model with that of radiologists and found that their model outperformed human experts in differentiating the lesions. In our study, such a comparison was not conducted. Nonetheless, incorporating this methodological approach in future research could provide a more scientifically robust comparison by evaluating the diagnostic power of radiomic data alongside clinicians' diagnostic capabilities.

In another study on jaw lesions, Yomtako et al.<sup>18</sup> evaluated the performance of texture analysis rather than comprehensive radiomic features in distinguishing radicular cysts from periapical granulomas. Unlike other studies, they used CT instead of CBCT images. A total of 131 lesions (28 radicular cysts and 103 periapical granulomas) were fully segmented, yielding 43 texture features. Using these features, the researchers developed SVM and decision tree models, which achieved AUC values of  $0.829$  and  $0.803$  in the training dataset and  $0.727$  and  $0.701$  in the validation dataset, respectively. In comparison, a model developed using conventional radiological features achieved lower AUC values in the training dataset ( $0.579$  for the decision tree and  $0.566$  for the SVM), underscoring the superiority of radiomic analysis. Similarly, although the present study did not directly compare the diagnostic performance of radiomic and conventional radiological features, the results indicated that even radiomic features extracted solely from the central region of the lesion may provide sufficient discriminatory power for lesion differentiation.

Sha et al.,<sup>19</sup> in another CBCT-based study, sought to differentiate conventional ameloblastoma from unicystic ameloblastoma using radiomic features. In 100 cases of ameloblastoma, complete segmentation of the lesions yielded 1,781 radiomic features. A two-step feature selection process was applied: first, features with the highest scores were identified using ANOVA; second, optimal features with the highest average accuracy were selected using SVM. Five different machine learning models were developed, and among them, the logistic regression model performed best, achieving an AUC of  $0.936$  in the training cohort and  $0.929$  in the validation cohort. One of the most recent studies on the use of radiomic features in differentiating jaw lesions was conducted by İçöz et al.,<sup>20</sup> who analysed CBCT images of 161 odontogenic lesions (55 radicular cysts, 53 dentigerous cysts, and 53 odontogenic keratocysts). The entire lesions were segmented, and radiomic features were analysed using ANOVA without developing regression or machine learning models. The authors found significant differences in shape-based, first-order, and textural features.

The primary distinction of our study from those in the literature is that, instead of segmenting the entire lesion, we used a spherical region taken only from the center of the cyst. Our findings indicate that, although these lesions appear radiolucent on CBCT images, they may contain differences at the voxel level that are imperceptible to the human eye. These differences likely stem from variations in lesion content and histopathological characteristics and can be detected through radiomic analysis. The findings obtained in this study support the potential use of radiomic data as a virtual biopsy. In the future, integrating the advantages offered by omics technologies along with more detailed clinical and individual patient data could enable the use of algorithms generated by

machine learning models to provide clinicians with enhanced insights into the characteristic features of lesions prior to performing a biopsy. This approach may allow clinicians to approach lesions with greater precision and informed decision-making during procedures, ultimately facilitating more accurate and effective patient treatment.

In addition to these considerations, the segmentation method developed in our study has the potential to provide significant benefits in addressing the current limitations of radiomics analysis. In radiomics studies, one of the first steps in the analysis workflow is to determine the Region of Interest (ROI) from which radiomic features will be extracted. Depending on the study design, this involves either manual or automated segmentation of the entire lesion or the relevant anatomical region of interest. Manual segmentation is typically performed by experienced specialists in the field. However, as segmentation is one of the upstream steps in the radiomics workflow, uncertainties at this stage are particularly critical and inevitably influence all downstream processes.<sup>21</sup> Previous studies have demonstrated that interobserver variability affects the stability and reproducibility of radiomic features.<sup>22–26</sup> Among the studies employing radiomics analysis for lesion differentiation, only İcöz et al.,<sup>20</sup> calculated the ICC to evaluate interobserver agreement. In their study, the authors included only those radiomic features with ICC values above 0.850, obtained from repeated lesion segmentations. However, since this value is not perfect, it still carries the potential to influence radiomic measurements, primarily due to the difficulty of marking the entire lesion accurately in different times. In our study, the near-perfect ICC value we achieved was obtained as a result of the segmentation technique we implemented. Moreover, while aggressive jaw lesions such as odontogenic keratocysts and ameloblastomas frequently cause bone perforations, radicular cysts can also cause perforations, albeit rarely.<sup>27–29</sup> Although CBCT devices provide high-resolution bone imaging, they offer limited visualization in soft tissue windows.<sup>30</sup> Consequently, when bone perforation is present, delineating the lesion boundaries becomes more challenging, which can naturally reduce segmentation reproducibility. In this study, only lesions without any perforation were included. This was primarily to ensure that all odontogenic keratocyst and radicular cyst lesions had well-defined boundaries without perforation, thereby preventing potential alteration of their characteristic features due to bone perforation. Nevertheless, with the

segmentation method proposed in our study, it can be suggested that even in lesions with bone perforation the radiomic features extracted from a central spherical ROI could still offer potential for differentiation between lesions. However, it should be noted that the high ICC value obtained in our study may be partly due to the relatively small sample size of only 20 CBCT images and the fact that all segmentations were performed by a single researcher.

One of the most significant limitations of our study is the relatively small dataset. Our dataset consisted of only 10 radicular cyst and 10 odontogenic keratocyst cases, which may limit the generalizability of our findings. Furthermore, our study focused on differentiating between two lesion types that are often distinguishable by their radiological features, which may be considered another potential limitation. As another limitation, the radiomic score calculation formula derived from the regression model developed in this study was not tested on an external dataset. Nonetheless, the results obtained are highly promising. Therefore, we believe that future radiomics studies designed with larger and multicenter datasets, and aimed at differentiating a broader spectrum of jaw lesions, could contribute to the development of clinically applicable diagnostic algorithms. Moreover, incorporating automated segmentation algorithms into such study designs may further facilitate the development of fully automated, clinician-assisting diagnostic tools and help reduce workload.

## CONCLUSION

In this preliminary study, the differentiation between radicular cysts and odontogenic keratocysts was explored using radiomic features derived from CBCT images, with four specific radiomic parameters identified through spherical segmentation. These findings suggest that radiomics may have potential utility in providing additional insights into lesions with similar radiologic appearances prior to surgical intervention. However, the results should be interpreted with caution due to the limited sample size and the experimental nature of the segmentation approach. Further studies with larger cohorts and standardized methodologies are warranted to validate these preliminary observations and to clarify the clinical applicability of radiomic analysis in distinguishing between radicular cysts and odontogenic keratocysts.

## REFERENCES

1. Santos GNM, da Silva HEC, Ossege FEL, et al. Radiomics in bone pathology of the jaws. *Dentomaxillofac Radiol.* 2023;52(1):20220225. doi:10.1259/dmfr.20220225
2. Soluk-Tekkesin M, Wright JM. The World Health Organization Classification of Odontogenic Lesions: A Summary of the Changes of the 2022 (5th) Edition. *Turk J Pathol.* 38(2):168-184. doi:10.5146/tjpath.2022.01573
3. Dioguardi M, Quarta C, Sovereto D, et al. Factors and management techniques in odontogenic keratocysts: a systematic review. *Eur J Med Res.* 2024;29(1):287. doi:10.1186/s40001-024-01854-z
4. Brown SJ, Conn BI. Odontogenic cysts: classification, histological features and a practical approach to common diagnostic problems. *Diagn Histopathol.* 2022;28(5):253-266. doi:10.1016/j.mpdhp.2022.02.007
5. Kshirsagar RA, Bhende RC, Raut PH, Mahajan V, Tapadiya VJ, Singh V. Odontogenic Keratocyst: Developing a Protocol for Surgical Intervention. *Ann Maxillofac Surg.* 2019;9(1):152-157. doi:10.4103/ams.ams\_137\_18
6. Gillies RJ, Kinahan PE, Hricak H. Radiomics: Images Are More than Pictures, They Are Data. *Radiology.* 2016;278(2):563-577. doi:10.1148/radiol.2015151169
7. Park JE, Kim D, Kim HS, et al. Quality of science and reporting of radiomics in oncologic studies: room for improvement according to radiomics quality score and TRIPOD statement. *Eur Radiol.* 2020;30(1):523-536. doi:10.1007/s00330-019-06360-z
8. Fedorov A, Beichel R, Kalpathy-Cramer J, et al. 3D Slicer as an image computing platform for the Quantitative Imaging Network. *Magn Reson Imaging.* 2012;30(9):1323-1341. doi:10.1016/j.mri.2012.05.001
9. Omami G, Yeoh M. Cysts and Benign Odontogenic Tumors of the Jaws. *Dent Clin North Am.* 2024;68(2):277-295. doi:10.1016/j.cden.2023.09.004
10. Chisci G, Chisci D, Chisci E, Chisci V, Stumpo M, Chisci E. The Management of a Geriatric Patient Using Dabigatran Therapy on Dentigerous Cyst with Oral Bleeding. *J Clin Med.* 2024;13(5):1499. doi:10.3390/jcm13051499
11. Zwanenburg A, Vallières M, Abdalah MA, et al. The Image Biomarker Standardization Initiative: Standardized Quantitative Radiomics for High-Throughput Image-based Phenotyping. *Radiology.* 2020;295(2):328-338. doi:10.1148/radiol.2020191145
12. Guo R, Zhong H, Xing F, et al. Magnetic susceptibility and R2\*-based texture analysis for evaluating liver fibrosis in chronic liver disease. *Eur J Radiol.* 2023;169. doi:10.1016/j.ejrad.2023.111155
13. Bicci E, Calamandrei L, Di Finizio A, et al. Predicting Response to Exclusive Combined Radio-Chemotherapy in Naso-Oropharyngeal Cancer: The Role of Texture Analysis. *Diagnostics.* 2024;14(10):1036. doi:10.3390/diagnostics14101036
14. De Bernardi E, Buda A, Guerra L, et al. Radiomics of the primary tumour as a tool to improve 18F-FDG-PET sensitivity in detecting nodal metastases in endometrial cancer. *EJNMMI Res.* 2018;8(1):86. doi:10.1186/s13550-018-0441-1
15. Yilmaz E, Kayikcioglu T, Kayipmaz S. Computer-aided diagnosis of periapical cyst and keratocystic odontogenic tumor on cone beam computed tomography. *Comput Methods Programs Biomed.* 2017;146:91-100. doi:10.1016/j.cmpb.2017.05.012
16. Jiang ZY, Lan TJ, Cai WX, Tao Q. Primary clinical study of radiomics for diagnosing simple bone cyst of the jaw. *Dentomaxillofac Radiol.* 2021;50(7):20200384. doi:10.1259/dmfr.20200384
17. Song Y, Ma S, Mao B, et al. Application of machine learning in the preoperative radiomic diagnosis of ameloblastoma and odontogenic keratocyst based on cone-beam CT. *Dentomaxillofac Radiol.* 2024;53(5):316-324. doi:10.1093/dmfr/twae016
18. Yomtako S, Watanabe H, Kuribayashi A, Sakamoto J, Miura M. Differentiation of radicular cysts and radicular granulomas via texture analysis of multi-slice computed tomography images. *Dentomaxillofac Radiol.* 2024;53(5):281-288. doi:10.1093/dmfr/twae011
19. Sha X, Wang C, Qi S, Yuan X, Zhang H, Yang J. The efficacy of CBCT-based radiomics techniques in differentiating between conventional and unicystic ameloblastoma. *Oral Surg Oral Med Oral Pathol Oral Radiol.* 2024;138(5):656-665. doi:10.1016/j.oooo.2024.06.010
20. İçöz D, Çetin B, Dinç K. Application of radiomics features in differential diagnosis of odontogenic cysts. *Dentomaxillofac Radiol.* 2025;54(3):180-187. doi:10.1093/dmfr/twae064
21. Wong J, Baine M, Wisnoskie S, et al. Effects of interobserver and interdisciplinary segmentation variabilities on CT-based radiomics for pancreatic cancer. *Sci Rep.* 2021;11(1):16328. doi:10.1038/s41598-021-95152-x

22. Granzier RWY, Verbakel NMH, Ibrahim A, et al. MRI-based radiomics in breast cancer: feature robustness with respect to inter-observer segmentation variability. *Sci Rep.* 2020;10(1):14163. doi:10.1038/s41598-020-70940-z
23. Homayounieh F, Singh R, Nitiwarangkul C, et al. Semiautomatic Segmentation and Radiomics for Dual-Energy CT: A Pilot Study to Differentiate Benign and Malignant Hepatic Lesions. *AJR Am J Roentgenol.* 2020;215(2):398-405. doi:10.2214/AJR.19.22164
24. Haarbuerger C, Müller-Franzes G, Weninger L, Kuhl C, Truhn D, Merhof D. Radiomics feature reproducibility under inter-rater variability in segmentations of CT images. *Sci Rep.* 2020;10(1):12688. doi:10.1038/s41598-020-69534-6
25. Belli ML, Mori M, Broggi S, et al. Quantifying the robustness of [18F]FDG-PET/CT radiomic features with respect to tumor delineation in head and neck and pancreatic cancer patients. *Phys Medica PM Int J Devoted Appl Phys Med Biol Off J Ital Assoc Biomed Phys AIFB.* 2018;49:105-111. doi:10.1016/j.ejmp.2018.05.013
26. Traverso A, Kazmierski M, Welch ML, et al. Sensitivity of radiomic features to inter-observer variability and image pre-processing in Apparent Diffusion Coefficient (ADC) maps of cervix cancer patients. *Radiother Oncol J Eur Soc Ther Radiol Oncol.* 2020;143:88-94. doi:10.1016/j.radonc.2019.08.008
27. Pesántez Alvarado JM, Lafebre Carrasco MF. A Radicular Cyst With Extensive Bone Loss Requires Surgical and Endodontic Management: Case Presentation and Literature Review. *Case Rep Dent.* 2025;2025:9977128. doi:10.1155/crid/9977128
28. Suma MS, Sundaresh KJ, Shruthy R, Mallikarjuna R. Ameloblastoma: an aggressive lesion of the mandible. *BMJ Case Rep.* 2013;2013:bcr2013200483. doi:10.1136/bcr-2013-200483
29. Acar G, Adiloğlu S, Aktaş A. TREATMENT OF A LARGE ODONTOGENIC KERATOCYST: A 5-YEAR FOLLOW-UP. *ADO Klin Bilim Derg.* 2024;13(1):161-166. doi:10.54617/adoklinikbilimler.1380700
30. Scarfe WC, Farman AG. What is cone-beam CT and how does it work? *Dent Clin North Am.* 2008;52(4):707-730, v. doi:10.1016/j.cden.2008.05.005