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REVIEW ARTICLE

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The use of artificial intelligence in the diagnosis of odontogenic cysts and tumors

Abstract:

The application of artificial intelligence (AI) in healthcare has garnered growing interest, particularly for its ability to improve diagnostic accuracy and streamline clinical workflows. This literature review examines the latest advancements and ongoing challenges in the use of AI for diagnosing odontogenic cysts and tumors. These lesions, originating from odontogenic epithelium or ectomesenchyme, present with a wide range of clinical and radiographic features that often overlap, complicating accurate diagnosis. AI, particularly through machine learning (ML) and deep learning (DL) models, offers promising solutions to these challenges by enhancing automation and precision in diagnostic processes. Numerous studies have highlighted the potential of AI algorithms to analyze various imaging modalities, such as radiographs, computed tomography (CT), and histopathological slides, achieving diagnostic outcomes comparable to those of expert clinicians. These AI systems have been designed to identify key radiological and histopathological characteristics, enabling earlier and more accurate detection of odontogenic lesions. Despite these promising results, significant challenges persist, such as the need for larger, more diverse datasets, the establishment of standardized protocols, and the seamless integration of AI tools into existing clinical practices.

Keywords: Artificial intelligence; Machine learning; Deep learning; Odontogenic cysts; Tumors.

INTRODUCTION

Odontogenic cyst (OC) and tumor (OT) represent a significant subset of lesions affecting the oral and maxillofacial region[1]. OC are relatively common in clinical practice, accounting for 7–17% of all oral biopsies processed by oral pathology services, with an incidence estimated at 3–4 cases per 100,000 individuals annually[2]. In contrast, OTs are considerably rarer, constituting less than 1% of tumors affecting the human body. Globally, the incidence of OT is reported to be around 1–2 cases per 1 million people every year[1]. The prevalence and distribution of specific OTs, such as odontomas and ameloblastomas, varies geographically, with benign tumors being more frequent than malignant tumors[3]. These epidemiological variations underline the importance of regional studies to fully understand the impact of these lesions on public health[3,4].

Statement of Clinical Significance
AI offers significant potential for improving the diagnosis of odontogenic cysts and tumors, which often present overlapping features that complicate detection. By enhancing diagnostic accuracy and enabling earlier identification, AI-driven tools can optimize patient outcomes and streamline workflows. Addressing challenges like dataset diversity and protocol standardization is essential for clinical integration.

Integrating artificial intelligence (AI) into oral pathology and medicine has introduced new possibilities for enhancing the accuracy and efficiency of detecting OCs and OTs[5]. AI addresses critical gaps in the diagnosis of OCs and OTs by reducing variability in interpretation and overcoming challenges posed by overlapping clinical and radiographic features. Furthermore, it streamlines workflows by automating complex data analyses, it may provide clinicians with a reliable decision-support tool to improve diagnostic accuracy and

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efficiency. These lesions, which often present overlapping clinical and radiographic features, pose diagnostic challenges that can benefit from AI's ability to improve precision. Machine learning (ML) and deep learning (DL) models have shown significant promise in medical imaging by automating the analysis of complex data and identifying patterns that may elude the human eye[6]. In the case of OCs and OTs, AI has been successfully applied to radiographs, CBCT, and histopathological slides, where it aids in detecting and differentiating between specific lesions[7].

The potential of AI to transform diagnostic practices is especially valuable given the relative rarity of some OTs and the need for early intervention[8,9]. By reducing variability in interpretation and offering clinicians a reliable decision-support tool, AI can contribute to more timely and accurate diagnoses[10]. Despite these promising advancements, there remain challenges to overcome, such as the need for larger, more diverse datasets, standardization of AI protocols, and seamless integration of AI technologies into existing clinical workflows. This review explores the current state of AI applications in diagnosing OC and OT, examining the progress made, the challenges faced, and the potential for further integration of AI into routine clinical practice.

AI main terms

In AI, key concepts include data science, which involves gathering and analyzing large datasets to extract insights that inform decision-making[9,11]. AI focuses on creating systems capable of tasks requiring human-like intelligence, such as learning and pattern recognition[9,12]. Machine learning (ML), a subset of AI, enables systems to learn from data and improve without explicit programming, often using algorithms like decision trees and linear regression[11,12]. For more complex data relationships, non-linear algorithms are applied[12]. Deep learning (DL), an advanced branch of ML, uses artificial neural networks to tackle intricate tasks[9,11], and convolutional neural networks (CNNs) are particularly effective in analyzing visual data, excelling in tasks like image recognition[11,12].

In the context of image pre-processing, classification and segmentation are important in diagnosing OCs and OTs. Classification aids in differentiating odontogenic cysts and tumors by leveraging AI models to analyze radiographic and histopathological data. For instance, convolutional neural networks (CNNs) applied to panoramic radiographs can differentiate between ameloblastomas and odontogenic keratocysts based on radiographic features like multilocular radiolucency and cortical expansion. Similarly, in histopathology, classification models can help distinguish benign lesions such as dentigerous cysts from more aggressive lesions like ameloblastomas by recognizing key cellular and structural patterns[9,13]. Segmentation plays a crucial role in lesion margin assessment, particularly in histopathology. For example, deep learning-based segmentation models, such as U-Net, can accurately delineate tumor margins in hematoxylin and eosin (H&E)-stained slides, which is critical for surgical planning. In CBCT imaging, segmentation models can isolate periapical cysts from surrounding bone structures, aiding in precise lesion measurement and treatment decision-making[13].

AI-assisted diagnosis based on radiomics

A wide range of ML techniques have been applied in recent studies to improve the diagnosis of OC and OT, demonstrating promising results. For example, logistic regression (LR) analysis on CT and panoramic radiographs has been used for the classification of ameloblastoma and odontogenic keratocyst (OKC), identifying bone expansion and the number of locules as key diagnostic features. Similarly, a hybrid framework combining Contourlet and Spherical Harmonics (SPHARM) features with support vector machines (SVM) and sparse discriminant analysis significantly improved the classification of radicular cysts, dentigerous cysts, and OKC using CBCT[14].

Among other approaches, SVM demonstrated superior accuracy in distinguishing periapical cysts from OKC using CBCT images[15]. Meanwhile, CNN models such as VGG-16 were used for the classification of ameloblastomas and OKC in panoramic radiographs, achieving diagnostic accuracy comparable to that of oral and maxillofacial surgeons, but with significantly reduced diagnostic time[16].

More advanced CNN models have been employed for object detection and classification. For instance, DetectNet successfully detected and classified various radiolucent lesions, including ameloblastomas, OKC, dentigerous cysts, radicular cysts, and simple bone cysts in panoramic radiographs, with particularly strong performance for dentigerous cysts[17]. DL models such as Inception V3, when applied to CBCT images, outperformed traditional methods in the classification of OKC and ameloblastomas, delivering higher diagnostic accuracy[18].

Furthermore, modified You Only Look Once architectures (YOLO) (YOLOv3 and YOLO v2) have shown significant potential in object detection and classification of lesions such as dentigerous cysts, periapical cysts, OKC, and ameloblastomas from panoramic radiographs, achieving real-time classification with high precision. Similarly, CNN models like Inception V3 and DenseNet121 demonstrated excellent performance in the classification of Stafne's bone cavity, dentigerous cysts, OKC, and ameloblastomas using multidetector CT and panoramic radiographs[19].

In the classification of ameloblastomas and OKC using panoramic radiographs, CNN models such as VGG-19 and ResNet-50 significantly improved diagnostic accuracy. DetectNet has further been used for object detection to accurately identify and differentiate between radicular cysts, nasopalatine duct cysts, OKC, dentigerous cysts, ameloblastomas, and other OT in panoramic radiographs[8].

A random forest (RF) classifier applied to panoramic radiographs for the detection and classification of odontogenic and non-OCs, as well as control cases, demonstrated results comparable or superior to dental professionals. For the classification of dental anomalies, AlexNet applied to panoramic radiographs successfully identified supernumerary teeth, odontomas, and other conditions[20].

A radiomics-based ML model demonstrated strong predictive capabilities in distinguishing ameloblastomas with and without BRAF-V600E mutations using CBCT, with the RF model performing exceptionally well[21]. Similarly, a study utilizing CBCT and the OCL-Net model, an adaptation of U-Net, effectively segmented radicular cysts, dentigerous cysts, OKCs, and ameloblastomas with high accuracy[22].

In another example, ML models such as EfficientDet-D3, Faster R-CNN, and YOLO v5 were applied to panoramic radiographs for detecting and classifying nasopalatine duct cysts and periapical cysts, with EfficientDet-D3 emerging as the most accurate. Additionally, a modified U-Net applied to CBCT images was able to classify and segment jaw lesions, including ameloblastomas, OKC, dentigerous cysts, periapical cysts, and osteomyelitis, with high efficiency[23].

Meanwhile, Inception-ResNet-V2 demonstrated reliable performance in differentiating OKC from simple bone cysts in panoramic radiographs. Finally, XGBoost and other ML models, including LR and RF, were effectively used to differentiate ameloblastomas from OKC in CBCT images[24] (Table 1).

AI-assisted diagnosis based on histopathology

ML was applied to hematoxylin and eosin (H&E) slides to improve segmentation and classification of various OCs and OTs. In particular, the graph cuts algorithm successfully segmented epithelial tissue in H&E-stained images in numerous OCs including dentigerous cysts, OKC, lateral periodontal cysts, and glandular odontogenic cysts, demonstrating the effectiveness of segmentation techniques for these different cyst types. Additionally, SVM and bagging with LR were shown to classify these four OCs with high accuracy[25].

Further advancements were made using Bouligand-Minkowski Fractal Descriptors and linear discriminant analysis, which improved classification accuracy, particularly in distinguishing sporadic OKCs, syndromic OKCs, and radicular cysts. For radicular cysts, the classification-guided segmentation algorithm using ResNet34 combined with a neural conditional random field significantly improved segmentation performance. In terms of classification tasks, DenseNet-169 effectively classified OKCs, dentigerous cysts, and radicular cysts from H&E slides, with high accuracy. The use of Inception-ResNet-V3 demonstrated excellent performance in predicting the recurrence of OKCs from biopsy images. For more complex lesions, ResNet50 outperformed other models in differentiating between ameloblastoma and ameloblastic carcinoma, although issues of overfitting and instability were noted during model training and validation[26].

Additionally, the use of CNN (P-C-ReliefF) allowed for accurate classification of OKCs versus non-keratocystic lesions, with reduced computational costs due to parameter reduction. The attention-based image sequence analyzer (ABISA) model, which incorporates multi-head self-attention mechanisms and long short-term memory (LSTM), further enhanced the automation of risk stratification for recurring OKCs[27].

In the case of orthokeratinized odontogenic cysts and Gorlin syndrome-associated OKCs, AI models including SVM, RF, XGBoost, and multilayer perceptrons (MLP) demonstrated excellent diagnostic performance, with multi-slide models providing better predictive power compared to single-slide models. Lastly, innovative applications like Bayesian-based systems and ChatGPT-4 showed potential as supportive diagnostic tools for OT (i.e. ameloblastoma) and OKCs, but human oversight remains critical to ensure accurate diagnoses[28] (Table 1).

AI-assisted diagnosis based on biomarkers

ML and statistical approaches have been applied to the classification and biomarker identification of OCs and OTs. For instance, gene expression analysis was utilized to classify radicular cysts and periapical granulomas using a MLP neural network, offering insights into the molecular mechanisms underlying these conditions. For OKCs and healthy controls, untargeted metabolomics on serum samples combined with Least Absolute Shrinkage and Selection Operator (LASSO) regression enabled the successful identification of key metabolic biomarkers, resulting in a diagnostic model with perfect sensitivity and specificity[29].

In another study, Bayesian network meta-analysis was employed to classify conventional ameloblastomas, unicystic ameloblastomas, and peripheral ameloblastomas based on BRAF mutations. The study found that BRAF mutations were more frequent in younger patients, tumors located in the mandible, and in the unicystic variant. Molecular tests and immunohistochemistry (IHC) showed a high level of concordance, making them valuable tools for confirming BRAF mutations in ameloblastomas[28,29] (Table 1).

DISCUSSION

The application of AI-assisted diagnostic tools based on radiomics has led to significant advancements in the diagnosis of OCs and OTs. By incorporating ML models into the analysis of imaging modalities such as CT, CBCT, and panoramic radiographs, researchers have demonstrated improved diagnostic accuracy and efficiency. Studies using models like LR, SVMs and CNNs have shown promising results in classifying various lesions, including ameloblastomas, OKCs, and radicular cysts[14,15]. In addition, the main findings of the present review are summarized in Supplementary Table 1 and Supplement 1.

DL models, particularly CNNs such as DetectNet, Inception V3, VGG-19, and ResNet-50, have proven highly effective in object detection and classification tasks. These models not only reduce diagnostic time but also achieve accuracy levels that are on par with, or even surpass, those of expert clinicians[16,18]. Hybrid models like YOLO and EfficientDet-D3 have further enhanced real-time detection and classification of lesions such as nasopalatine duct cysts and periapical cysts in panoramic radiographs, offering a level of precision that is invaluable in clinical settings[18].

A particularly promising area of development is the use of deep learning models for segmentation tasks. U-Net-based architectures, such as OCL-Net, have shown great success in accurately segmenting odontogenic cystic lesions from CBCT images, providing more detailed and reliable assessments that are critical for diagnosis and treatment planning. For instance, segmentation models applied to histopathological slides of OKC help delineate epithelial boundaries, which is essential for evaluating invasive potential and recurrence risk. Similarly, classification models have been instrumental in differentiating between benign and malignant odontogenic lesions. Studies have demonstrated that CNN-based classifiers trained on panoramic radiographs can distinguish between odontogenic tumors, such as ameloblastomas and odontogenic myxomas, with high accuracy[22]. Furthermore, histopathology-based classifiers can predict the risk of malignancy in ameloblastic carcinoma by analyzing nuclear pleomorphism and mitotic activity, providing valuable prognostic insights for clinicians[23,24].

AI-assisted diagnosis based on histopathological analysis has also seen considerable progress. Segmentation algorithms like graph cuts and classification models such as SVM and CNNs have significantly improved the detection and classification of various OCs and tumors in hematoxylin and eosin (H&E) slides[25]. Advanced AI techniques, including ABISA and multi-head self-attention mechanisms combined with LSTM, have further optimized risk stratification for recurring OKCs, enhancing the ability to predict patient outcomes and recurrence risk[27].

In addition to imaging and histopathology, AI has been instrumental in biomarker identification for OCs and OTs. Gene expression analysis using neural networks, such as MLP, has provided insights into the molecular mechanisms of radicular cysts and periapical granulomas, leading to improved classification[49]. Furthermore, the application of untargeted metabolomics combined with LASSO regression has successfully identified metabolic biomarkers for OKCs, resulting in diagnostic models with perfect sensitivity and specificity. Studies using Bayesian network meta-analysis have also been effective in classifying BRAF mutations in ameloblastomas, demonstrating the value of combining molecular tests and IHC to improve diagnostic accuracy[29].

The integration of multi-omics data with AI models represents a significant advancement in the early detection and classification of OC and OT. By leveraging AI-driven analytical techniques, particularly deep learning and machine learning algorithms, it becomes possible to identify intricate molecular patterns that may elude conventional diagnostic methods. The synergistic use of diverse biological data layers enhances diagnostic precision, enables more accurate differentiation between tumor subtypes, and improves the prediction of disease progression. Furthermore, multi-omics integration improves a deeper understanding of tumor biology, leading to the identification of novel biomarkers with potential applications in early detection and targeted therapies. This approach is in accordance with the principles of precision medicine, offering more individualized and effective treatment strategies. However, challenges such as data standardization, variability in sample quality, and the computational complexity of multi-omics analysis must be addressed to maximize the clinical utility of AI in this field. Overcoming these barriers will be essential to fully harness the potential of AI-driven multi-omics research in improving patient outcomes[30].

The integration of AI into clinical practice offers significant potential to enhance the diagnosis of OCs and OTs by improving accuracy and efficiency in radiographic and histopathological assessments. AI models can assist clinicians in detecting subtle patterns, reducing diagnostic uncertainty, and supporting evidence-based decision-making. However, several challenges hinder its routine adoption. The lack of standardized, high-quality datasets limits the generalizability of AI models, while concerns regarding interpretability and reliability make clinicians hesitant to rely on automated predictions. Additionally, integrating AI into existing diagnostic workflows requires technological adaptation and professional training, ensuring that these tools complement, rather than replace, clinical expertise. Ethical and regulatory issues, including data privacy, bias, and external validation, further complicate its implementation. To overcome these barriers, multidisciplinary collaboration is essential, alongside efforts to improve AI transparency, data standardization, and regulatory frameworks, ultimately fostering a responsible and effective transition of AI into routine oral and maxillofacial pathology[5].

While AI has advanced odontogenic cyst and tumor diagnosis, key challenges remain. Overfitting limits model generalizability, especially with small datasets that reduce robustness[26]. The lack of external validation hinders performance consistency across different populations and imaging protocols. Dataset imbalance further skews predictions, favoring common lesions while underrepresenting rarer ones. Addressing these issues requires larger, diverse datasets, standardized evaluation metrics, and explainability techniques to ensure reliable, unbiased AI applications[26,30].

CONCLUSION

In conclusion, this review highlights the remarkable potential of AI in transforming the diagnosis of OCs and OTs. The advancements made so far demonstrate AI's ability to enhance diagnostic precision and efficiency by identifying subtle patterns in imaging and histopathological data that might otherwise go unnoticed. The integration of multi-omics data has further broadened the possibilities, opening doors to the discovery of novel biomarkers and paving the way for more personalized approaches to treatment.

Despite these achievements, several challenges need to be addressed before AI can become a routine part of clinical practice. The lack of standardized, high-quality datasets limits the applicability of AI models across diverse patient populations, while the complexity and opacity of many AI systems can make them difficult for clinicians to fully trust or understand. Ethical and regulatory issues, such as ensuring data privacy, minimizing algorithmic bias, and validating AI systems in real-world settings, add further complexity to their adoption.

Moving forward, collaboration between researchers, clinicians, and policymakers will be essential to overcome these hurdles. By addressing these challenges and refining AI tools to better integrate into clinical workflows, there is immense potential to revolutionize the diagnostic landscape for OCs and OTs. Ultimately, this progress will lead to improved patient care, more efficient diagnostics, and a deeper understanding of these conditions, ensuring AI's role as a valuable partner in oral and maxillofacial pathology.

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AUTHOR CONTRIBUTIONS

LLS: conceptualization, data curation, formal analysis, investigation, methodology, validation, visualization, writing – original draft, writing – review & editing. ALOCR: conceptualization, data curation, formal analysis, investigation, methodology, validation, visualization, writing – original draft, writing – review & editing. DGR: conceptualization, data curation, formal analysis, investigation, methodology, validation, visualization, writing – original draft, writing – review & editing. IJCN: conceptualization, data curation, formal analysis, investigation, methodology, validation, visualization, writing – original draft, writing – review & editing. MAL: conceptualization, data curation, formal analysis, methodology, validation, visualization, writing – original draft, writing – review & editing.

SAK: conceptualization, data curation, formal analysis, methodology, validation, visualization, writing – original draft, writing – review & editing. PAV: conceptualization, data curation, formal analysis, funding acquisition, investigaton, methodology, Project administration, resources, supervision, validation, visualization, writing – original draft, writing – review & editing.

CONFLICT OF INTEREST STATEMENT

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Ethics approval: This study is a literature review and does not involve human participants, animal subjects, or the use of confidential data. Therefore, approval from an ethics committee was not required.

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