REVIEW

Radiomics and deep learning approach to the differential diagnosis of parotid gland tumors

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Purpose of review
Advances in computer technology and growing expectations from computer-aided systems have led to the evolution of artificial intelligence into subsets, such as deep learning and radiomics, and the use of these systems is revolutionizing modern radiological diagnosis. In this review, artificial intelligence applications developed with radiomics and deep learning methods in the differential diagnosis of parotid gland tumors (PGTs) will be overviewed.

Recent findings
The development of artificial intelligence models has opened new scenarios owing to the possibility of assessing features of medical images that usually are not evaluated by physicians. Radiomics and deep learning models come to the forefront in computer-aided diagnosis of medical images, even though their applications in the differential diagnosis of PGTs have been limited because of the scarcity of data sets related to these rare neoplasms. Nevertheless, recent studies have shown that artificial intelligence tools can classify common PGTs with reasonable accuracy.

Summary
All studies aimed at the differential diagnosis of benign vs. malignant PGTs or the identification of the commonest PGT subtypes were identified, and five studies were found that focused on deep learning-based differential diagnosis of PGTs. Data sets were created in three of these studies with MRI and in two with computed tomography (CT). Additional seven studies were related to radiomics. Of these, four were on MRI-based radiomics, two on CT-based radiomics, and one compared MRI and CT-based radiomics in the same patients.

Keywords
artificial intelligence, deep learning, machine learning, parotid gland tumors, radiomics

INTRODUCTION

In the 1940s, the advent of programmable digital computers prompted scientists to ponder on the boundaries of what machines could do [1]. The idea led to the coining of the term 'artificial intelligence', defined differently depending on the source but based on the overall notion that a computer can replicate human cognitive capabilities. Advances in computer technology and growing expectations from computer-aided systems have led artificial intelligence to evolve into subsets, such as machine learning and deep learning [2]. The use of these systems in radiological diagnosis is revolutionizing the artificial intelligence field [3▪,4], with machine learning and deep learning in medical imaging ushering in an exciting era with re-engineered and re-imagined clinical and research capabilities [5].

An important driver of the emergence of artificial intelligence in medical imaging has been the enhancement of visual recognition to produce lower error rates than those attained among human observers [6,7]. Specific capabilities of artificial intelligence in medical imaging include, without being limited to, detection and classification of lesions, automated image segmentation, data analysis,

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Curr Opin Otolaryngol Head Neck Surg 2022, 30:107–113
DOI:10.1097/MOO.0000000000000782

KEY POINTS

- An important driver of the emergence of artificial intelligence in medical imaging has been the enhancement of visual recognition to produce lower error rates than those observed among human observers.
- The use of artificial intelligence tools, such as deep learning and radiomics analysis is revolutionizing computer-aided systems in medicine.
- Deep learning and radiomics applications in the differential diagnosis of parotid gland tumors (PGTs) have been limited because of the scarcity of data sets related to these neoplasms.
- Recent studies have shown that artificial intelligence applications can classify common PGTs with reasonable accuracy.
- Future developments of artificial intelligence applications will include greater integration in daily practice thanks to user-friendly graphical interfaces.

prioritizing reporting and study triage, and image reconstruction [5]. Additionally, artificial intelligence algorithms may be used to extract 'radiomics' information and features from pictures that are not visible to the naked eye, possibly enhancing the diagnostic and prognostic utility of image collections [8].

There are several applications of machine learning and deep learning that are of clinical interest for head and neck imaging, including delineation of organs/tissues at risk or primary tumor for radiation therapy, tumor segmentation, detection, and phenotyping, and precision oncology applications, such as prediction of histopathology or molecular phenotype, response to treatment, and survival [2,9–12]. In addition, machine learning and deep learning-based studies on specific organs of the head and neck, such as cervical lymph nodes, parotid, thyroid, and oral cavity, in which neoplasms can raise issues in the differentiation of benign vs. malignant lesions or in determining histotypes, are increasing. These studies have led to enthusiasm for the development of new noninvasive differential diagnostic methods for head and neck tumors using machine learning and deep learning models created with datasets consisting of clinical and radiological images.

Salivary gland tumors constitute 3–12% of head and neck neoplasms of which 80% originate from the parotid [13]. Preoperative tumor localization, differential diagnosis, and ensuing choice of the most adequate treatment are clearly important in parotid gland tumors (PGTs). However, the relative rarity of such neoplasms and the high dispersion of their possible histotypes in the latest WHO Classification [13] create the unmet need of having subtle differential diagnosis of such neoplastic lesions based upon preoperative radiomics. In fact, clinical features alone make it challenging to diagnose malignant PGTs as early symptoms, such as pain and palpable lesions are nonspecific [14,15]. Although the diagnostic strategy may greatly vary, medical imaging, such as ultrasonography, computed tomography (CT), MRI, and fine needle aspiration cytology (FNAC) are frequently used [16,17]. In particular, the latter has an accuracy in discriminating benign vs. malignant tumors from 85 to 97% [18–20]. However, because of the difficulty of sampling, especially in deep lobe tumors, and the heterogeneity of the tumor itself, FNAC is sometimes inadequate and not representative of the true nature of the lesion [21▪]. Additionally, it may result in tumor cell spread, increasing the likelihood of local recurrence, and, in rare cases, risk of infection [22]. In addition to FNAC, preoperative imaging plays an important role in evaluating the location and nature of the tumor for adequate surgical planning. Ultrasonography and CT are common imaging modalities for differential diagnosis of PGTs, but both have significant limitations [23]. MRI is generally the preferred imaging modality for parotid masses because of its well known capability of providing high resolution of soft tissues, showing tumors located in the deep lobe clearly, distinguishing perineural and surrounding soft tissues invasion, and providing better information about the nature and anatomical localization of the PGT [24,25]. It is essential that imaging methods performed are evaluated by an expert head and neck radiologist, and that a fast and accurate result is reached. In this review, artificial intelligence applications developed within the field of radiomics and deep learning methods used in the differential diagnosis of PGTs will be emphasized.

RADIOMICS AND DEEP LEARNING IN MEDICAL IMAGING

The majority of artificial intelligence applications in head and neck imaging are in their infancy; however, widespread use and integration into healthcare are not far off. A working knowledge of fundamental words and ideas enables improved interpretation of the medical literature, cooperation with data scientists, and involvement in the decision-making processes that is necessary prior to workflow integration [2]. Artificial intelligence is a broad concept that covers several techniques to make machines think like humans [26] and encompasses two major fields: machine learning and deep learning. Machine learning can be described as a collection of data-driven methodologies and algorithms to predict or infer new situations from historical data [26,27]. There are several machine learning algorithms in use, such as neural networks, support vector machine, and k-nearest neighbor. In particular, neural networks are composed of layers, that is, functions that are linked in the same way that human neurons are and perform in parallel. Neural networks with several hidden layers are classified as 'deep'. Deep learning is based on a network of interconnected multilevel algorithms that resembles a neural network. In other words, deep learning is a set of complicated routines that discovers connections in raw data automatically. Higher abstraction is extracted from the data to produce this collection. Deep learning uses a structure that mimics that of a human brain and can extract features like radiomics from medical images without requiring human intervention [28]. Radiomics is a frequently used method of mining objective and quantitative features, such as shape, intensity, and energy of regions of interest from medical images (e.g. gray-level co-occurrence matrix and run length matrix features), describing the relationships between image voxels far beyond the traditional visual features that can be obtained, and thus reflecting the underlying genetic and biological variability of the tissue analyzed, which can promote accurate diagnosis and individualize cancer treatment [29].

RADIOMICS AND DEEP LEARNING APPLICATIONS IN DIFFERENTIAL DIAGNOSIS OF PAROTID GLAND TUMORS

The development of artificial intelligence models has opened new scenarios owing to the possibility of noninvasively assessing features of medical images that are not evaluated by physicians [30]. PGTs are rare tumors of the head and neck; however, because of important adjacent anatomical structures, their precise preoperative classification can help to guide the surgical plan correctly and prevent avoidable complications as well as overtreatments or undertreatments. deep learning and radiomics applications in the differential diagnosis of PGTs have so far been limited because of the scarcity of data sets related to these lesions. In this review, the concepts relevant to the search terms were defined as 'Deep Learning', 'Radiomics', 'Parotid Gland Tumors' and 'Medical Imaging'. Table 1 summarizes the 12 articles retrieved by the search terms. Five articles are focused on deep learning-based PGTs differential diagnosis. The remaining seven articles are related to radiomics-based PGTs differential diagnosis. The data sets consist of MRI images in seven manuscripts and CT images in four. In one study, the data set was created with both MRI and CT imaging techniques. All studies aimed at the differential diagnosis of benign vs. malignant PGTs or between the commonest histotypes of PGTs.

Chang *et al.* proposed an automatic approach to diagnose PGTs from MRI and classify them by using deep learning architecture. In this study, two-dimensional convolutional neural network, called U-Net, was employed to accomplish a fully automatic system. The authors constructed the data set with pleomorphic adenoma (PMA), Warthin tumors, and malignant tumors from 85 patients using five MRI sequences, namely conventional T1-weighted (T1W) with contrast enhancement, T2-weighted (T2W), diffusion-weighted b0, b1000, and Apparent Diffusion Coefficient (ADC) maps. The results showed that diffusion weighted sequences-based deep learning models have better performance than conventional MRI sequences. The deep learning model with diffusion weighted images yielded accuracy of 0.81, 0.76, and 0.71, sensitivity of 0.83, 0.63, and 0.33, and specificity of 0.80, 0.84, and 0.87 for Warthin tumors, PMA, and malignant tumors, respectively [31▪].

In another deep learning study on MRI, Xia *et al.* evaluated 123 patients by T1W, T1W with contrast enhancement, and T2W imaging series. A total of 3791 parotid gland region images were cropped and labeled as PMA, Warthin tumors, malignant tumors or tumor-free based on histological results. The ResNet18 DL architecture was modified to classify these images. The accuracy of the architecture in the test set to correctly diagnose and classify PGTs was 82.18%, and the micro-AUC was 0.93 [21▪].

In another study, the authors stated that with their proposed anomaly detection and VGG16-based deep learning method, the classification of benign and malignant PGTs could also be successful in a small amount of imbalanced distributed data [3▪]. They used nonmedical images obtained from the CUReT data set [32] to reduce the overfitting caused by the small number of images and facilitate the removal of general visual models of the PGT. According to the histopathological results, T1W and T2W conventional MRI images containing 190 benign and 55 malignant PGTs were cropped to obtain input data for the VGG16 DL model. They evaluated the diagnostic accuracy of the proposed method and compared it with a board-certified radiologist's results. According to the diagnostic performance observed, the proposed methods outperformed radiologists. Although the model's ROC-AUC was 0.86 and PR-ROC was 0.77, the radiologist's ROC-AUC was 0.74 and PR-ROC 0.51.

Table 1. Summary of radiomics and deep learning related works on differential diagnosis of parotid gland tumors

Authors	Methods	Imaging technique	Datasets *n* and *i* denote patients and images number, respectively	Classes	Accuracy (%)/AUROC
Chang *et al.* [31■]	Two-dimensional CNN	MRI	WT ($n=27$) PMA ($n=33$) MT ($n=25$)	WT, PMA, MT	Acc: 81% Acc: 76% Acc: 71%
Xia *et al.* [21■]	ResNet18	MRI	WT ($i=594$), PMA ($i=771$) MT ($i=954$) Free of tumors ($i=991$)	PMA vs. WT vs. MT vs Free of tumor	Acc: 82.18% (overall)
Matsuo *et al.* [3■]	VGG16, Anomaly detection	MRI	Benign tumors ($n=190$) MT ($n=55$) CUReT texture database	BT vs. MT vs. CUReT Radiologist	AUROC (AI) 0.86 (overall) AUROC (radiologist): 0.74
Zhang *et al.* [33■]	Improved CNN model, VGG16, InceptionV3, ResNet and DenseNet	CT	BT ($n=139$) MT ($n=91$)	BT vs. MT	Acc (improved CNN model): 97.78% (overall)
Yuan *et al.* [34]	ResNet50 DL model	CT	PMA ($n=101$) MT ($n=51$)	PMA vs. MT	Acc: 90%
Gabelloni *et al.* [35■]	Radiomics features + SVM	MRI	PMA ($n=32$) WT ($n=23$) Oncocytomas ($n=6$) MT ($n=14$)	PMA vs. WT, PMA vs. MT	Acc: 89.09% Acc: 80.43%
Zheng *et al.* [36■]	Radiomics features	MRI	PMA ($n=69$) WT ($n=58$)	PMA vs. WT	AUROC: 0.918
Zheng *et al.* [37■]	Radiomics features	MRI	BT ($n=60$) MT ($n=55$)	BT vs. MT	AUROC: 0.938
Piludu *et al.* [38■]	Radiomics features + SVM	MRI	BT ($n=24$) WT ($n=13$) MT ($n=32$)	WT vs. MT BT vs. WT BT vs. MT	Acc: 86.7% Acc: 91.9% Acc: 80.4%
Xu *et al.* [39■]	Radiomics features + SVM	CT	125 PGTs patients	SVM model Radiomics signature Location Lymph nodes status	Acc: 83.5% Acc: 77.1% Acc: 65.3% Acc: 60.8%
Zhang *et al.* [40■]	Radiomics features	CT	Low-grade MEC ($n=9$) High-grade MEC ($n=9$)	Low-grade MEC vs. high-grade MEC	AUROC: 0.802
Liu *et al.* [41■]	Radiomics features	MRI and CT	626 PGTs patients (PMA and WT)	MRI-based radiomics (PMA vs. WT) vs. CT-based radiomics (PMA vs. WT)	MRI: 0.716 (border index AUROC) CT: 0.608 (border index AUROC)

AUROC, area under the receiver operating characteristic; BT, benign tumors; CNN, convolutional neural networks; CT, computed tomography; DL, deep learning; MEC, mucoepidermoid carcinoma; MT, malignant tumors; PGTs, parotid gland tumors; PMA, pleomorphic adenoma; SVM, support vector machines; WT, Warthin tumor.

Although MRI is preferred in PGT evaluation because of its superior soft tissues resolution, CT is another widespread imaging method, frequently used for its more favorable cost-effectiveness profile and quicker examination time. Zhang *et al.* used five deep learning models trained with CT images of 230 PGTs (139 benign and 91 malignant). In their study, the four pretraining models of VGG16, InceptionV3, ResNet, and DenseNet using transfer learning methods and an improved convolutional neural network model were used. The results show that the improved neural network model achieved an accuracy of 97.78%, and its classification performance for PGTs was better than those of the other four transfer learning methods [33■].

In another deep learning model trained with CT images, Yuan *et al.* aimed to make the differential diagnosis of PMA and malignant tumors automatically and with high accuracy. They used data sets of CT images containing 101 PMA and 51 malignant tumors and the ResNet50 model. The authors obtained that the accuracy of the test set merges to 90% when the model was iterated 1000 times, and stated that this study has practical importance and application value for the auxiliary differential diagnosis of PGTs and other head and neck tumors [34].

Another way of image analysis with artificial intelligence is radiomics as previously mentioned. Gabelloni *et al.* studied MRI radiomics analysis to differentiate PGTs. Seventy-five T2W images of parotid gland lesions, namely 32 PMA, 23 Warthin tumors, 6 oncocytomas, and 14 malignant tumors, were included in the study. The most discriminative radiomics features were used to train a support vector machine classifier. The best classification performance was the differentiation between PMA and Warthin tumors with a sensitivity, specificity and diagnostic accuracy of 0.8695, 0.9062, and 0.8909, respectively. The second-best classification performance was obtained by comparing PMA with malignant tumors, with sensitivity, specificity, and diagnostic accuracy of 0.6666, 0.8709, and 0.8043, respectively. The authors stated that radiomics features of conventional T2W MRI images based on a histogram and gray-level co-occurrence matrix can help to differentiate PMA from Warthin tumors and malignant tumors with high sensitivity, specificity, and diagnostic accuracy [35▪].

Zheng *et al.* established an MRI-based radiomics nomogram for preoperative differential diagnosis between Warthin tumors and PMA. A total of 127 patients with histological diagnosis of Warthin tumors or PMA were enrolled in a training set of 34 Warthin tumors and 41 PMA, and an external test set of 24 Warthin tumors and 28 PMA. Radiomics features were extracted from axial T1W and T2W sequences. The authors found that the radiomics signature had a notable predictive value in differentiating parotid Warthin tumors from PMA, with an AUC of 0.953 and 0.918 for the training and test sets, respectively [36▪]. In another study, Zheng *et al.* [37▪] applied clinical factors and radiomics signatures to logistic regression analysis for differential diagnosis of 60 benign and 55 malignant PGTs by T1W and T2W MRI sequences. The authors obtained an AUC value of 0.952 in the training set and 0.938 in the validation set [37▪].

Piludi *et al.* extracted MRI-based radiomics features from T2W images and diffusion-weighted ADC maps. The created model for discriminating between Warthin tumors vs. malignant tumors, benign vs. Warthin tumors, and benign vs. malignant tumors had an accuracy of 86.7, 91.9, and 80.4%, respectively [38▪].

In the diagnosis of PGTs, CT is used less frequently as it provides limited information about soft tissues [24]. However, while some information might not be properly evaluated by physicians through the naked eye, they can possibly be extracted from CT through radiomics features. With this thought in mind, Xu *et al.* aimed to develop a prediction model based on clinical–radiological data and CT-based radiomics to discriminate between benign vs. malignant PGTs. In their work, 378 radiomics features were extracted from CT images and dimensionality reduction used to obtain a radiomics signature. Location, lymph nodes metastases, and rad-score were found to be independent predictors of tumor malignancy in an analysis of variance and multivariable logistic regression analysis [39▪].

Zhang *et al.* determined if CT-radiomics features of mucoepidermoid carcinomas (MECs) can differentiate low-grade tumors from high-grade tumors. The authors collected a data set of 18 MECs whose 9 were low-grade and the rest high-grade. After manual segmentation of tumors, radiomics features were compared between low-grade and high-grade MECs. The authors found no significant individual radiomics features that could differentiate low-grade and high-grade MECs. However, a logistic regression model including surface regularity and two gray-level co-occurrence matrix features (energy and information measure II of correlation) was able to predict high-grade MECs with a sensitivity of 89% and a specificity of 68%. The AUC was 0.802. Thus, the authors concluded that high-grade MECs tend to have a low energy, high correlation texture, as well as surface irregularity [40▪].

In another interesting study on radiomics and PGT, MRI and CT-based radiomics were compared in terms of differential diagnosis of PMA and Warthin tumors. The authors extracted 123 radiomics features from MRI and CT images of 626 PGTs, and found a diagnostic performance of rad-score and border index AUC for MRI of 0.911 and 0.716, respectively, whereas those of CT were 0.876 and 0.608, respectively. MRI and CT-based rad-score of both modalities showed no statistically significant differences but tumor border index and tumor margin examination properties on MRI had superior diagnostic performance over CT [41▪].

CONCLUSION

The studies reviewed in this article have shown that artificial intelligence applications can classify common PGTs with reasonable accuracy. Artificial intelligence models that are able to make more detailed classifications will be developed when larger data sets including images of rare PGTs will be obtained. In fact, histological grading of these tumors can be made more sensitive thanks to the appropriate radiomics analysis.

Artificial intelligence applications for medical images have received the necessary attention in recent years and will offer solutions to more complex problems with future developments in computer technology. Although the studies reviewed herein are still in their infancy and do not offer a general benefit for the physician, over time artificial intelligence applications will undoubtedly be more integrated in medical practice thanks to user-friendly graphical interfaces. Potentially, with artificial intelligence models integrated with the Picture Archiving and Communication Systems (PACS), it will be possible to obtain real-time diagnostic reports in only minutes after medical images are taken. In addition, recurrence detection could become possible with deep learning models analyzing postoperative radiological images.

Future deep learning models will enable facial nerve mapping and navigation prior to parotid gland surgery, and this will potentially help avoiding a number of nerve-related complications. By combining virtual reality devices and 'metaverse' research with artificial intelligence models, the complex anatomy of the parotid region will be hopefully visualized with an unparalleled degree of accuracy, thus contributing to surgical training.

Acknowledgements

None.

Financial support and sponsorship

None.

Conflicts of interest

There are no conflicts of interest.

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This study is special because of its comparison of MRI-based and CT-based radiomics results on the same data.