Clinical Paper
Head and Neck Oncology

Correlation of apparent diffusion coefficient with histopathological parameters of salivary gland cancer

A. A. KhalekAbdel Razek[1],
S. M. Elkhamary[1], N. Nada[2]
[1]Department of Diagnostic Radiology, Mansoura Faculty of Medicine, Mansoura, Egypt; [2]Department of Pathology, Mansoura Faculty of Medicine, Mansoura, Egypt

A. A. Khalek Abdel Razek, S. M. Elkhamary, N. Nada: Correlation of apparent diffusion coefficient with histopathological parameters of salivary gland cancer. Int. J. Oral Maxillofac. Surg. 2019; 48: 995–1000. © 2019 International Association of Oral and Maxillofacial Surgeons. Published by Elsevier Ltd. All rights reserved.

Abstract. The aim of this study was to correlate the apparent diffusion coefficient (ADC) with histopathological parameters of salivary gland cancer. A retrospective analysis of 44 patients with salivary gland cancer who underwent diffusion-weighted magnetic resonance imaging of salivary glands was performed. The ADC of salivary gland cancer was correlated with pathological tumour type and grade, stage (T stage and N stage), and morphological (perineural spread and location) prognostic parameters. There was a significant difference in ADC values between low–intermediate- and high-grade tumours (P = 0.024), lower T stages (T1, T2) versus higher T stages (T3, T4) (P = 0.001), lower N stages (N0, N1) versus higher N stages (N2, N3) (P = 0.001), and the presence versus absence of perineural spread (P = 0.001). The cut-off ADC values to predict higher-grade, higher T stage, nodal spread, and perineural spread were 0.94, 0.92, 0.94, and 0.98×10^{-3} mm^2/s, with area under the curve of 0.847, 0.858, 0.900, and 0.798 and accuracy of 75.0%, 75.0%, 75.0%, and 77.3%, respectively. The ADC value is a non-invasive imaging parameter that correlates with histopathological parameters of salivary gland cancer.

Salivary gland cancer is rare and represents 3–5% of all head and neck cancer. Salivary gland tumours are heterogeneous in histology and behaviour. Current guidelines recommend surgery, with adjuvant radiotherapy for high tumour grades and stages[1,2]. Most patients with salivary gland cancer tend to present at an advanced stage due to its deep location and vague symptoms. The prognosis of salivary gland cancer depends on the histopathological subtype, its grade, T stage, N stage, and location, and the presence of perineural spread[2–4].

Diffusion-weighted magnetic resonance imaging (MRI) has a growing role in the evaluation of head and neck cancer[5–10]. It has been used to differentiate benign salivary gland tumours from malignancy[11–14], to characterize metastatic cervical lymph nodes, and to differentiate recurrent tumours from post-radiation changes[6,11]. Only a few studies have discussed the correlation between the apparent diffusion co-

efficient (ADC) and prognostic parameters of head and neck cancer[15], nasopharyngeal cancer[16–18], and retinoblastoma[19], as well as positron emission tomography–computed tomography (PET–CT) correlations with histopathological parameters of salivary gland cancers[20]. There appears to have been no previous study reported in the English literature on the correlation between the ADC and histopathological parameters of salivary gland cancer.

The aim of this study was to correlate the ADC with histopathological parameters of salivary gland cancer.

Materials and methods

Patients

Institutional review board approval was obtained and the need for informed consent was waived because of the retrospective nature of the study. This retrospective analysis included 47 consecutive patients with salivary gland cancer who underwent diffusion MRI during the period June 2001 to July 2017. The inclusion criteria were patients with salivary gland cancer who underwent diffusion-weighted MRI. Three patients were excluded: two because of poor image quality due to motion artefacts and one because a biopsy was not available. Thus, a total of 44 patients were included, 24 female and 20 male, ranging in age from 39 to 78 years (mean age of 59 years). These patients with salivary gland cancer presented with facial swelling (n = 44), facial palsy (n = 25), and/or a neck mass (n = 22).

MRI

MRI studies were performed with a 1.5 Tesla MRI unit (Magnetom Symphony; Siemens Medical Systems, Erlangen, Germany). All patients underwent axial T1-weighted (repetition time (TR)/echo time (TE) = 800/20 ms) and T2-weighted imaging (TR/TE = 8000/80 ms), with section thickness = 4 mm, inter-slice gap = 1 mm, field of view (FOV) = 20–30 cm, and acquisition matrix = 256 × 224. Diffusion-weighted images were obtained using a multi-slice, spin-echo, echo-planar image sequence. A set of multiple axial scans of the head and neck were obtained. The imaging parameters were as follows: TR/TE = 10,000/100 ms, number of excitations (NEX) = 12, bandwidth = 300 kHz, matrix = 256 × 128, FOV = 20–30 cm, section thickness = 5 mm, inter-slice gap = 1 mm, and b-factor of 0, 500, and 1000 mm^2/s. The ADC maps were reconstructed.

Image analysis

Image analysis was done by one radiologist (AAKAR), an expert in MRI for 22 years, who was blinded to the clinical data and pathology results. A standard round region of interest (ROI) was drawn on the ADC map using the electronic cursor. The ROI was drawn on the section that showed the largest solid part of the tumour without cystic parts and the ADC value of the tumour was then calculated (Fig. 1).

Pathology

The final diagnosis of salivary gland cancer was made by one pathologist (NN), an expert in pathology for 30 years, who was blinded to the clinical data and imaging findings. The pathological type of salivary gland cancer was classified according to the World Health Organization (WHO) classification[21]. The pathological grade of the malignancy was classified as low–intermediate or high grade. The criteria that were used to assess the differentiation were subjective. The final diagnoses of nodal metastasis and perineural spread were made by histopathological analysis.

Statistical analysis

The statistical analysis of data was done using IBM SPSS Statistics version 20.0 (IBM Corp., Armonk, NY, USA). The mean and standard deviation (SD) ADC values were calculated for the histopathological parameters. The data analysis was done to test for a statistically significant difference. The Student t-test was used to study the difference in ADC between two groups, and one-way analysis of variance (ANOVA) was used to assess differences between more than two groups. The cut-off ADC value used to differentiate between the different degrees of the prognostic parameters was determined by calculation of the area under the receiver operating characteristics curve (AUC), accuracy, sensitivity, and specificity. The P-value was considered significant if less than 0.05 at a confidence interval of 95%.

Results

Table 1 reports the mean ± SD, minimum and maximum ADC values of the pathological subtypes of salivary gland cancer. The most common salivary gland cancer was mucoepidermoid carcinoma (n = 10), followed by adenoid cystic carcinoma (n = 9). The lowest ADC value (0.75 × 10^{-3} mm^2/s) was seen in high-grade mucoepidermoid carcinoma and the highest ADC value in oncocytic carcinoma (1.17 × 10^{-3} mm^2/s). The higher-grade subtypes of salivary gland cancer, including small cell carcinoma, squamous cell carcinoma, myoepithelial carcinoma, carcinoma ex pleomorphic adenoma, and adenoid cystic carcinoma, had ADC values of 0.92 × 10^{-3} mm^2/s or less; however, the difference in ADC values between the pathological subtypes of salivary gland cancer was non-significant (P = 0.06).

Table 2 shows the ADC values in relation to tumour grade, T stage, N stage, presence/absence of perineural spread, and location of the salivary gland cancer. Table 3 shows the receiver operating characteristics curve results for ADC values in relation to prognostic parameters of salivary gland cancer.

The mean ADC of low–intermediate-grade salivary gland cancer (n = 29) was 0.98 ± 0.13 × 10^{-3} mm^2/s and for high-
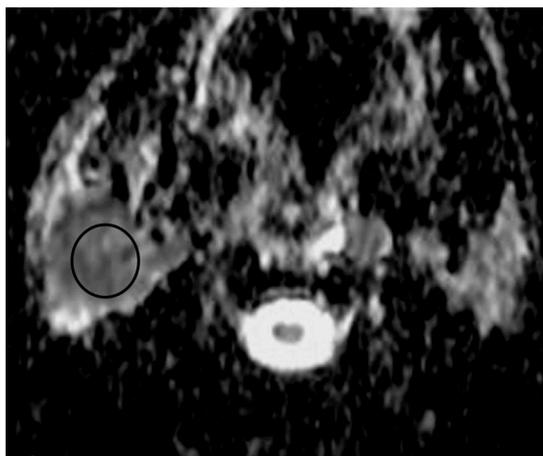

Fig. 1. Region of interest localization: axial image showing the standard round region of interest drawn on the ADC map using an electronic cursor in the solid part of the tumour.

Table 1. ADCs of histopathological subtypes of salivary gland cancer; mean ± standard deviation (range) values.

Pathology	ADC ($\times 10^{-3}$ mm^2/s)
Mucoepidermoid carcinoma ($n=10$)	0.97 ± 0.16 (0.75–1.14)
Adenoid cystic carcinoma ($n=9$)	0.92 ± 0.08 (0.83–1.05)
Acinic cell carcinoma ($n=3$)	1.00 ± 0.06 (0.93–1.05)
Adenocarcinoma ($n=3$)	1.01 ± 0.10 (0.89–1.08)
Carcinoma ex pleomorphic adenoma ($n=3$)	0.83 ± 0.09 (0.75–0.93)
Lymphocarcinoma ($n=2$)	1.00 ± 0.09 (0.93–1.07)
Myoepithelial carcinoma ($n=2$)	0.91 ± 0.03 (0.89–0.93)
Oncocytic carcinoma ($n=2$)	0.99 ± 0.25 (0.82–1.17)
Salivary duct carcinoma ($n=6$)	0.95 ± 0.12 (0.82–1.12)
Small cell carcinoma ($n=2$)	0.83 ± 0.01 (0.82–0.84)
Squamous cell carcinoma ($n=2$)	0.91 ± 0.06 (0.87–0.95)

ADC, apparent diffusion coefficient.

Table 2. ADCs in relation to histopathological parameters of salivary gland cancer.

Histopathological parameter	ADC ($\times 10^{-3}$ mm^2/s)	P-value
Tumour grade		
Low–intermediate grade ($n=29$)	0.98 ± 0.13 (0.82–1.17)	0.024
High grade ($n=15$)	0.89 ± 0.09 (0.75–0.95)	
T stage		
T1 and T2 ($n=23$)	1.02 ± 0.09 (0.82–1.17)	0.001
T3 and T4 ($n=21$)	0.86 ± 0.08 (0.75–1.05)	
N stage		
N0 and N1 ($n=29$)	0.99 ± 0.09 (0.83–1.17)	0.001
N2 and N3 ($n=15$)	0.84 ± 0.07 (0.75–0.95)	
Perineural spread		
Present ($n=22$)	0.88 ± 0.08 (0.75–1.05)	0.001
Absent ($n=22$)	1.01 ± 0.11 (0.82–1.17)	
Location		
Parotid gland ($n=32$)	0.96 ± 0.11 (0.75–1.17)	0.15
Submandibular and sublingual glands ($n=12$)	0.90 ± 0.12 (0.75–1.12)	

ADC, apparent diffusion coefficient.

Table 3. ROC curve results of ADCs of salivary gland cancer in relation to histopathological parameters.

	AUC	Cut-off[a]	Sensitivity	Specificity	Accuracy
Low grade vs. high grade	0.847	0.94	88.2%	66.7%	75.0%
Low T stage vs. high T stage	0.858	0.92	73.7%	76.0%	75.0%
Low N stage vs. high N stage	0.900	0.94	93.3%	65.6%	75.0%
Perineural spread	0.798	0.98	90.9%	63.6%	77.3%

AUC, area under the ROC curve; ADC, apparent diffusion coefficient; ROC, receiver operating characteristics.

[a] ADC ($\times 10^{-3}$ mm^2/s).

grade salivary gland cancer (n = 15) was 0.89 ± 0.09 × 10^{-3} mm^2/s. The ADC of low–intermediate-grade salivary gland cancer tumours was significantly higher than the ADC of high-grade tumours (P = 0.024). The cut-off ADC for high-grade salivary gland cancer was 0.94 × 10^{-3} mm^2/s, with AUC of 0.847, sensitivity of 88.2%, specificity of 66.7%, and accuracy of 75.0% (Fig. 2A).

The mean ADC of lower T stage (T1, 2) salivary gland cancer (n = 23) was 1.02 ± 0.09 × 10^{-3} mm^2/s and of higher T stage (T3, 4) salivary gland cancer (n = 21) was 0.86 ± 0.08 × 10^{-3} mm^2/s. The ADC differed significantly between the lower and higher T stages of salivary gland cancer (P = 0.001). The cut-off ADC for suspected higher T stages of salivary gland cancer was 0.92 × 10^{-3} mm^2/s, with AUC of 0.858, sensitivity of 73.7%, specificity of 76.0%, and accuracy of 75.0% (Fig. 2B).

The mean ADC value of salivary gland cancer with nodal N0 and N1 (n = 29) was 0.99 ± 0.09 × 10^{-3} mm^2/s and in patients with nodal N2 and N3 (n = 15) was 0.84 ± 0.07 × 10^{-3} mm^2/s (n = 15). There was a significant difference in ADC between patients with N0/N1 and those with N2/N3 (P = 0.001). The cut-off ADC for suspected higher N stage of salivary gland cancer was 0.94 × 10^{-3} mm^2/s, with AUC of 0.900, sensitivity of 93.3%, specificity of 65.6%, and accuracy of 75.0% (Fig. 2C).

Perineural spread was reported in 22 patients with salivary gland cancer. The ADC of salivary gland cancer with perineural spread (0.88 ± 0.08 × 10^{-3} mm^2/s) was significantly lower (P = 0.001) than the ADC for cancer without perineural spread (1.01 ± 0.11 × 10^{-3} mm^2/s). The cut-off ADC for suspected perineural spread in salivary gland cancer was 0.98 × 10^{-3} mm^2/s, with AUC of 0.798, sensitivity of 90.9%, specificity of 63.6%, and accuracy of 77.3% (Fig. 2D).

The salivary gland cancer was located in the parotid (n = 32), submandibular (n = 11), and sublingual (n = 1) glands. The ADC of parotid cancer (0.96 ± 0.11 × 10^{-3} mm^2/s) was higher than the ADC of submandibular and sublingual cancer (0.90 ± 0.12 × 10^{-3} mm^2/s), but the difference did not reach a significant level (P = 0.15).

Discussion

The main study finding was the correlation between the ADC of salivary gland cancer and tumour grade, T stage, N stage, and perineural spread. In this study of salivary gland cancer, lower ADC values were found for higher tumour grade, higher T stage, higher N stage, and suspected perineural spread. The tumours with a higher T stage, nodal metastases, or perineural tumour spread were demonstrated to have statistically lower ADC values that correlated with tumour grade.

The difference in ADC values between the pathological subtypes of salivary gland cancer seen in this study was non-significant. Determination of the pathological subtype of salivary gland cancer is important for the prognosis and for treatment planning. Previous studies have reported an overlap in the ADCs for the subtypes of salivary gland cancer that reflect the pathological nature of these tumours[1]. The ADC value of mucoepidermoid carcinoma varies according to the tumour grade. The finding of a high ADC value for low-grade mucoepidermoid carcinoma may be attributed to the presence of microcysts and macrocysts, which cause the squamous and intermediate cells to be less densely packed, leading to unrestricted diffusion. In contrast, the finding of a low ADC value for high-grade mucoepidermoid carcinoma may be related to the more densely packed cells and reduced extracellular spaces, leading to restricted diffusion. The high ADC value of low-grade onco-
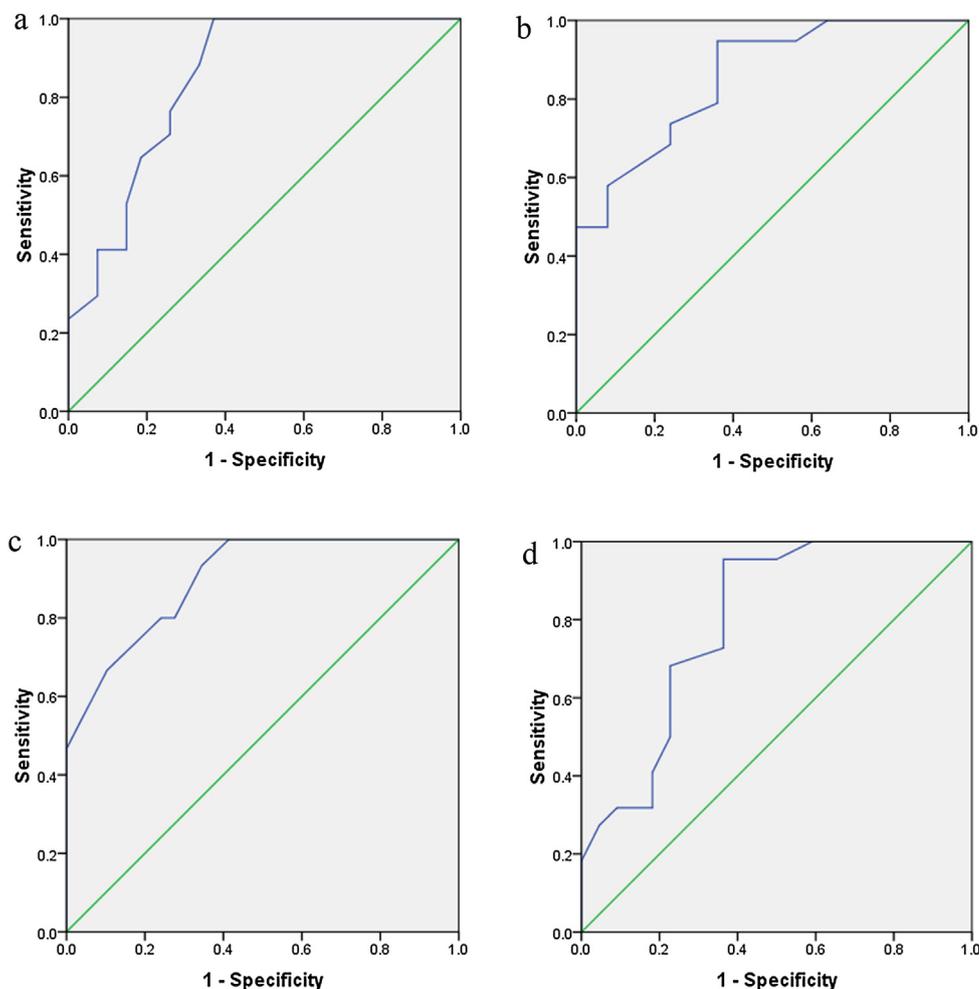
Fig. 2. Receiver operating characteristic (ROC) curves. (A) The cut-off ADC for high-grade salivary gland cancer was 0.94×10^{-3} mm^2/s, with AUC of 0.847, sensitivity of 88.2%, and accuracy of 75.0%. (B) The cut-off ADC for suspected higher T stages of salivary gland cancer was 0.92×10^{-3} mm^2/s, with AUC of 0.858, sensitivity of 73.7%, and accuracy of 75.0%. (C) The cut-off ADC for suspected higher N stages of salivary gland cancer was 0.94×10^{-3} mm^2/s, with AUC of 0.900, sensitivity of 93.3%, and accuracy of 75.0%. (D) The cut-off ADC for suspected perineural spread in salivary gland cancer was 0.98×10^{-3} mm^2/s, with AUC of 0.798, sensitivity of 90.9%, and accuracy of 77.3%.

cytic carcinoma may be attributed to the presence of fewer cellular oncocytes, abundant cytoplasm, and wide interstitial spaces, which are associated with unrestricted diffusion[5–11].

Histological grade is the most important factor for predicting the prognosis of those with salivary gland cancer. Salivary gland cancers are generally classified into low-grade, intermediate-grade, and high-grade categories. High-grade salivary gland cancer has a 5-year survival of roughly 40%, whereas low and intermediate-grade tumours have a 5-year survival of 85% to 90%[1–4]. The most common low-grade salivary gland cancer is low-grade mucoepidermoid carcinoma, and the most common high-grade salivary gland cancer is high-grade mucoepidermoid carcinoma[9,10].

In this study, a significant difference in the ADC value was found between low–

intermediate-grade and high-grade salivary gland cancer. Few studies have discussed the correlation between the ADC value and the degree of tumour differentiation, and these have reported an inverse correlation between the ADC value and the degree of tumour cellularity in head and neck cancer, including squamous cell carcinoma, nasopharyngeal cancer, and retinoblastoma[16,19,27]. In this study, high-grade malignancies were found to have lower ADCs than low–intermediate-grade malignancies. This could be attributed to the increased cellular density of high-grade malignancies, resulting in lower ADCs[22–27].

Lower ADC values were found for higher T stages of salivary gland cancer in this study. Most previous studies have reported that there is a good correlation between T staging and the prognosis of salivary gland cancer, and that higher T

stages of salivary gland cancer are associated with a poor prognosis[28]. Another study found that there was a significant difference in the ADC values of different tumour stages of breast cancer[29].

In this work, the ADC values of salivary gland cancer of N stage N2 and N3 were lower than those of N0 and N1 stage cancer. This may be attributed to cancer with a higher N stage usually being seen in the presence of a higher grade of malignancy. Nodal metastases of parotid cancer are seen in 10–15% of patients at presentation, but are more common (>30%) in high-grade than in low-grade parotid cancer. The incidence of nodal metastasis is 7–16% in lower T stages. The status of the regional lymph nodes in parotid cancer has tremendous prognostic significance, so the cervical lymph nodes must be assessed for each patient with parotid cancer[30–35].

Low ADC values were revealed for salivary gland cancer with perineural spread in this study. The perineural spread of salivary gland cancer dramatically alters the treatment and prognosis. Perineural spread is characteristic of adenoid cystic carcinoma, but is also reported in other high-grade malignancies such as adenocarcinoma and squamous cell carcinoma. Polymorphous adenocarcinoma has the highest percentage of perineural invasion, yet this does not affect its prognosis and it is mostly regarded as a low-grade tumour. Perineural spread does not correlate with the clinical prognosis for all salivary tumours, and perineural spread is poor prognostically for adenoid cystic carcinoma and squamous cell carcinoma, but not for polymorphous low-grade adenocarcinoma[34,35]. Perineural spread in salivary gland cancer can predict a worse prognosis. The most commonly involved nerves in perineural spread of salivary gland cancer are the facial and trigeminal nerves, which are closest to the salivary glands[35,36].

In this study, the ADC values of parotid cancer were higher than the ADC values of submandibular and sublingual cancer; however, the difference did not reach statistical significance. A previous study reported that more than half of salivary gland cancers originate in the parotid gland, one third arise from the minor glands, and submandibular carcinomas make up about 20%[1]. Tumours of the submandibular gland area are associated with higher rates of malignancy and less favourable prognoses compared with other salivary gland malignancies[1–4]. Another study added that there is an insignificant difference in the ADC values according to the subsite of origin of head and neck squamous cell carcinoma[15].

This study has a few limitations. First, it included a small number of patients without a follow-up study after therapy, and there was no clinical information regarding survival, recurrence, or follow-up. Multicenter studies on a larger number of patients are required, with the correlation of ADC values with treatment outcomes and monitoring of patients after therapy. Second, this study applied routine diffusion-weighted MRI. Further studies applying multi-parameter imaging with dynamic contrast MRI, proton MR spectroscopy, diffusion tensor imaging, and arterial spin labelling will improve the results[37–43]. Third, analysis of the images was performed by one radiologist. Further studies should be performed with analysis of imaging performed by more than one reader and with inter-observer reliability assessed.

In conclusion, the ADC is a non-invasive imaging parameter that correlates with histopathological parameters of salivary gland cancer.

Funding

None.

Competing interests

None declared.

Ethical approval

Patient consent

Not required.

References

1. Seethala RR. Salivary gland tumors: current concepts and controversies. *Surg Pathol Clin* 2017;**10**:155–76.
2. Becker C, Dahlem KKK, Pfeiffer J. Prognostic value of comorbidities in patients with carcinoma of the major salivary glands. *Eur Arch Otorhinolaryngol* 2017;**274**:1651–7.
3. Seethala RR, Griffith CC. Molecular pathology: predictive, prognostic, and diagnostic markers in salivary gland tumors. *Surg Pathol Clin* 2016;**9**:339–52.
4. Gutschenritter T, Machiorlatti M, Vesely S, Ahmad B, Razaq W, Razaq M. Outcomes and prognostic factors of resected salivary gland malignancies: examining a single institution's 12-year experience. *Anticancer Res* 2017;**37**:5019–25.
5. Abdel Razek AAK, Mukherji SK. State-of-the-art imaging of salivary gland tumors. *Neuroimaging Clin N Am* 2018;**28**:303–17.
6. Bhatt N, Gupta N, Soni N, Hooda K, Sapire JM, Kumar Y. Role of diffusion-weighted imaging in head and neck lesions: pictorial review. *Neuroradiol J* 2017;**30**:356–69.
7. Razek AA. Diffusion-weighted magnetic resonance imaging of head and neck. *J Comput Assist Tomogr* 2010;**34**:808–15.
8. Connolly M, Srinivasan A. Diffusion-weighted imaging in head and neck cancer: technique, limitations, and applications. *Magn Reson Imaging Clin N Am* 2018;**26**:121–33.
9. Abdel Razek AAK. Routine and advanced diffusion imaging modules of the salivary glands. *Neuroimaging Clin N Am* 2018;**28**:245–54.
10. Thoeny HC, De Keyzer F, King AD. Diffusion-weighted MR imaging in the head and neck. *Radiology* 2012;**263**:19–32.
11. Razek AAKA. Prediction of malignancy of submandibular gland tumors with apparent diffusion coefficient. *Oral Radiol* 2019;**35**:11–5.
12. Attyé A, Troprès I, Rouchy RC, Righini C, Espinoza S, Kastler A, Krainik A. Diffusion MRI: literature review in salivary gland tumors. *Oral Dis* 2017;**23**:572–5.
13. Abdel Razek AA, Samir S, Ashmalla GA. Characterization of parotid tumors with dynamic susceptibility contrast perfusion-weighted magnetic resonance imaging and diffusion-weighted MR imaging. *J Comput Assist Tomogr* 2017;**41**:131–6.
14. Milad P, Elbegiermy M, Shokry T, Mahmoud H, Kamal I, Taha MS, Keriakos N. The added value of pretreatment DW MRI in characterization of salivary glands pathologies. *Am J Otolaryngol* 2017;**38**:13–20.
15. Razek AA, Nada N. Correlation of choline/creatine and apparent diffusion coefficient values with the prognostic parameters of head and neck squamous cell carcinoma. *NMR Biomed* 2016;**29**:483–9.
16. Lai V, Li X, Lee VH, Lam KO, Fong DY, Huang B, Chan Q, Khong PL. Nasopharyngeal carcinoma: comparison of diffusion and perfusion characteristics between different tumour stages using intravoxel incoherent motion MR imaging. *Eur Radiol* 2014;**24**:176–83.
17. Abdel Razek AA, Kamal E. Nasopharyngeal carcinoma: correlation of apparent diffusion coefficient value with prognostic parameters. *Radiol Med* 2013;**118**:534–9.
18. Xu XQ, Ma G, Wang YJ, Hu H, Su GY, Shi HB, Wu FY. Histogram analysis of diffusion kurtosis imaging of nasopharyngeal carcinoma: correlation between quantitative parameters and clinical stage. *Oncotarget* 2017;**8**:47230–8.
19. Abdel Razek AA, Elkhamary S, Al-Mesfer S, Alkatan HM. Correlation of apparent diffusion coefficient at 3T with prognostic parameters of retinoblastoma. *AJNR Am J Neuroradiol* 2012;**33**:944–8.
20. Park MJ, Oh JS, Roh JL, Kim JS, Lee JH, Nam SY, Kim SY. 18F-FDG PET/CT versus contrast-enhanced CT for staging and prognostic prediction in patients with salivary gland carcinomas. *Clin Nucl Med* 2017;**42**:e149–56.
21. Seethala RR, Stenman G. Update from the 4th edition of the world health organization classification of head and neck tumours: tumors of the salivary gland. *Head Neck Pathol* 2017;**11**:55–67.
22. Sumi M, Nakamura T. Head and neck tumours: combined MRI assessment based on IVIM and TIC analyses for the differentiation of tumors of different histological types. *Eur Radiol* 2014;**24**:223–31.
23. Rayess HM, Dezube A, Bawab I, Raza SN, Yoo GH, Lin HS, Jacobs JR. Tumor differentiation as a prognostic factor for major salivary gland malignancies. *Otolaryngol Head Neck Surg* 2017;**157**:454–61.
24. Yun TJ, Kim JH, Kim KH, Sohn CH, Park SW. Head and neck squamous cell carcino-

ma: differentiation of histologic grade with standard- and high-b-value diffusion-weighted MRI. *Head Neck* 2013;**35**:626–31.

25. Razek AAKA. Assessment of masses of the external ear with diffusion-weighted MR imaging. *Otol Neurotol* 2018;**39**:227–31.

26. Surov A, Meyer HJ, Wienke A. Correlation between apparent diffusion coefficient (ADC) and cellularity is different in several tumors: a meta-analysis. *Oncotarget* 2017;**8**:59492–9.

27. Driessen JP, Caldas-Magalhaes J, Janssen LM, Pameijer FA, Kooij N, Terhaard CH, Grolman W, Philippens ME. Diffusion-weighted MR imaging in laryngeal and hypopharyngeal carcinoma: association between apparent diffusion coefficient and histologic findings. *Radiology* 2014;**272**:456–63.

28. Schmitt NC, Sharma A, Gilbert MR, Kim S. Early T stage salivary duct carcinoma: outcomes and implications for patient counseling. *Otolaryngol Head Neck Surg* 2015;**153**:795–8.

29. Razek AA, Gaballa G, Denewer A, Nada N. Invasive ductal carcinoma: correlation of apparent diffusion coefficient value with pathological prognostic factors. *NMR Biomed* 2010;**23**:619–23.

30. Hong HR, Roh JL, Cho KJ, Choi SH, Nam SY, Kim SY. Prognostic value of lymph node density in high-grade salivary gland cancers. *J Surg Oncol* 2015;**111**:784–9.

31. Abdel Razek AA, Soliman NY, Elkhamary S, Alsharaway MK, Tawfik A. Role of diffusion-weighted MR imaging in cervical lymphadenopathy. *Eur Radiol* 2006;**16**:1468–77.

32. Shinomiya H, Otsuki N, Yamashita D, Nibu K. Patterns of lymph node metastasis of parotid cancer. *Auris Nasus Larynx* 2016;**43**:446–50.

33. Abdel Razek AA, Gaballa G. Role of perfusion magnetic resonance imaging in cervical lymphadenopathy. *J Comput Assist Tomogr* 2011;**35**:21–5.

34. Abdel Razek AAK, Mukherji SK. Imaging of posttreatment salivary gland tumors. *Neuroimaging Clin N Am* 2018;**28**:199–208.

35. Dantas AN, Morais EF, Macedo RA, Tinôco JM, Morais Mde L. Clinicopathological characteristics and perineural invasion in adenoid cystic carcinoma: a systematic review. *Braz J Otorhinolaryngol* 2015;**81**:329–35.

36. Abdel Razek AAK, Mukherji SK. Imaging of minor salivary glands. *Neuroimaging Clin N Am* 2018;**28**:295–302.

37. Marzi S, Piludu F, Forina C, Sanguineti G, Covello R, Spriano G, Vidiri A. Correlation study between intravoxel incoherent motion MRI and dynamic contrast-enhanced MRI in head and neck squamous cell carcinoma: evaluation in primary tumors and metastatic nodes. *Magn Reson Imaging* 2017;**37**:1–8.

38. Khalek Abdel Razek AA. Characterization of salivary gland tumours with diffusion tensor imaging. *Dentomaxillofac Radiol* 2018;**47**:20170343.

39. Abdel Razek AA, Poptani H. MR spectroscopy of head and neck cancer. *Eur J Radiol* 2013;**82**:982–9.

40. Razek AA, Elsorogy LG, Soliman NY, Nada N. Dynamic susceptibility contrast perfusion MR imaging in distinguishing malignant from benign head and neck tumors: a pilot study. *Eur J Radiol* 2011;**77**:73–9.

41. Abdel Razek AAK, Nada N. Arterial spin labeling perfusion-weighted MR imaging: correlation of tumor blood flow with pathological degree of tumor differentiation, clinical stage and nodal metastasis of head and neck squamous cell carcinoma. *Eur Arch Otorhinolaryngol* 2018;**275**:1301–7.

42. Razek AA. Diffusion magnetic resonance imaging of chest tumors. *Cancer Imaging* 2012;**12**:452–63.

43. Abdel Razek AA, Gaballa G, Denewer A, Tawakol I. Diffusion weighted MR imaging of the breast. *Acad Radiol* 2010;**17**:382–6.

Address:
Ahmed Abdel Khalek Abdel Razek
Department of Diagnostic Radiology
Mansoura Faculty of Medicine
Mansoura
Egypt
Tel: +20 161948567
E-mail: arazek@mans.edu.eg