The diagnostic value of combined dynamic contrast-enhanced MRI (DCE-MRI) and diffusion-weighted imaging (DWI) in characterization of parotid gland tumors

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Abstract

**Background:** MRI is considered to be the imaging modality of choice in preoperative diagnosis of parotid gland tumors and differentiating benign from malignant ones. Recently, functional MR imaging sequences including dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) and diffusion-weighted imaging (DWI) have significantly contributed to the diagnosis of head and neck masses. The purpose of this study was to evaluate the diagnostic value of combined DCE-MRI and DWI in characterization of parotid gland tumors.

**Results:** There was significant difference between benign and malignant parotid gland tumors as regard the type of time intensity curve (TIC) \((P < 0.001)\). There was significant difference between pleomorphic adenoma (PMA) and malignant parotid gland tumors (MT) as regard mean ADC value \((P = 0.046)\) and TTP \((P = 0.002)\). There was no significant difference between Warthin’s tumor (WT) and malignant parotid gland tumors as regard the ADC value and TTP \((P > 0.5)\); on the other hand, WT usually have high WI when compared with MT \((P = 0.004)\). Combined use of DCE-MRI and DWI had 100% sensitivity, 90.5% specificity, and 93.3% accuracy in differentiating benign from malignant parotid gland tumors.

**Conclusion:** Combined use of DCE-MRI and DWI could result in high sensitivity, specificity, and diagnostic accuracy in characterization of parotid gland tumors.

**Keywords:** Parotid gland, MRI, DWI, DCE-MRI

**Background**

Salivary gland tumors (SGTs) account for nearly 3% of tumors that occur in the head and facial region; about 80% of all SGTs are found in the parotid gland with an incidence of malignancy within the parotid gland tumors about 20%. Proper preoperative diagnosis of these tumors is essential for adequate surgical planning [1]. Clinical assessment has a limited role in diagnosing malignant parotid tumors. In addition, fine needle aspiration biopsy (FNAB) is sometimes inconclusive and insufficient [2].

Several imaging modalities such as ultrasonography and computed tomography (CT) may aid in diagnosis of parotid gland tumors, but now magnetic resonance imaging (MRI) is considered to be the imaging modality of choice in preoperative diagnosis of parotid gland tumors and differentiating benign from malignant ones [1]. MRI gives information on the exact location, extent of the lesion, relation to the surrounding structures, and allows assessment of perineural spread and bone invasion. However, it was reported that both benign and malignant parotid gland tumors show considerable overlap with regard to imaging appearance such as tumor margins, homogeneity, and signal intensity [3].
In recent years, functional MR imaging sequences including dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) and diffusion-weighted imaging (DWI) have significantly contributed to the diagnosis of head and neck tumors [4]. They provide more information about tumor cellularity, microstructure, and vascularity so they help in differentiating benign from malignant parotid gland tumors [5].

**Aim of the study**
The purpose of this study was to evaluate the diagnostic value of combined DCE-MRI and DWI in characterization of parotid gland tumors.

**Methods**

**Patient’s demographic data**
This prospective study was carried out during the period from September 2017 till January 2020. Approval from our institution’s ethics committee was obtained and informed consents were obtained from all patients before inclusion in this study. Forty-five patients with clinically palpable parotid swelling were included in this study. Out of the 45 patients, 8 patients were lost and their pathological diagnosis were not available so they were excluded from the study, 4 patients with improper imaging technique (motion artifact) were also excluded from the study, and 3 patients with impaired renal function were also excluded from the study as injection of contrast media was contraindicated in these patients. Finally, this study included 30 patients (16 males (53.3%) and 14 females (46.7%)) with clinically palpable parotid swellings. Their ages ranged from 18 to 67 years with a mean age of 47 years. The results of histopathological examination were our standard of reference; it was obtained 1–2 weeks after performing MRI examinations.

**MRI technique**

MRI was performed on a 1.5-T MRI scanner (Philips, Inginia) using dedicated multichannel head and neck coil.

MRI exam included the following sequences: axial T1 turbo spin echo (TSE) with and without Fat suppression, axial T2 Turbo-spin echo without fat suppression, and coronal T1 sequence with fat suppression. They were obtained using the following parameters: axial T1WI fat suppressed (TR/TE: 4000/90), coronal T2 sequence with fat suppression, and axial T2 Turbo-spin echo (TSE) with and without Fat suppression, and coronal T1 sequence with fat suppression. They were obtained using the following parameters: axial T1-weighted image (TR/TE: 600/20) and T2-weighted image (TR/TE: 4000/90). Field of view: 18 cm, matrix: 256 × 256, section thickness: 2 mm, and section gap: 1 mm; images were obtained before the administration of contrast agent.

DWI were obtained by “High” repetition time (TR) 1700 ms, “short” echo time (TE) 100 ms, “Coarse” matrix, 192 × 144, slice numbers: 30, slice thickness: 5 mm, interslice gap: 2.5 mm, field of view (FOV): 25 cm, and acquisition time of approximately 1 min 45 s. “Three b-factors” were used including 0, 500, and 1000 s/mm² in the axial plane. An apparent diffusion coefficient (ADC) map was automatically constructed. Mean ADC value was measured by placing circular region of interest (ROI) (1–2 cm) within the solid parts of the parotid masses.

DCE-MRI was obtained during injecting a bolus (0.1 mmol/kg) of contrast agent (gadopentetate dimeglumine) (GD-DTPA) (Magnevist) at a rate of 2.5 ml/S given intravenously via an automatic injector followed by 20 ml saline flush. It was obtained using dynamic 2D (axial T1WI fat suppressed) fast spoiled gradient recalled sequence with the following imaging parameters (TR/TE: 10.4/2.3, flip angle: 30°, field of view: 18 cm, matrix: 256 × 128, slice thickness: 4 mm, interslice gap: 1 mm, and total acquisition time of 300 s). Sequential images were obtained through the lesion in axial plane and at different time intervals (at 10, 30, 60, 90, 120, and 180 s). Following dynamic acquisition, conventional post contrast MR images were obtained in the axial, sagittal, and coronal planes.

Multiphase dynamic images were analyzed using Philips extended work space (EWS) release 2.6 workstation. We placed a region of interest within an area of 10 mm² of the tumor that showed the greatest degree of early enhancement on the dynamic images (cystic parts, vessels, necrosis, calcifications, and hemorrhages were avoided). Time signal intensity curve (TIC) in the ROI of each examination was plotted. TIC parameters include time of peak enhancement (TTP) and washout ratio (WR) were obtained.

**Image interpretation**
MR images were analyzed by an expert radiologist (15 years’ experience in head and neck imaging) who was blinded to the results of histopathological examination.

Regarding diffusion images, there were two methods for analysis: (a) qualitative analysis of DWI was performed by a combined visual assessment of the high b value DWI (b 1000) and the corresponding ADC maps. Lesion is considered restricted on diffusion when it showed high signal intensity (SI) on DWI and low SI on ADC map; lesion is considered free on diffusion when it showed low SI on DWI and high SI on ADC map. (b) Quantitative analysis of DWI was performed by measuring the mean ADC value of the lesion.

Regarding DCE-MR images, there were also two methods for analysis: (a) semiquantitative method based on assessment of the type of TIC. According to Yabuuchi et al. [6], TIC was classified into four types: type A: time to peak is more than 120 s with ascending plateau (this is considered to be a gradual enhancement); type B: time to peak is 120 s or less, with high washout ratio (≥30%) (this is considered to be as early enhancement and
high washout); type C: time to peak is 120 s or less, with low washout ratio (<30%) (a parotid gland tumor with this pattern is considered to have early enhancement and low washout); and type D: flat (tumor of this type is considered to be markedly cystic). (b) Quantitative method based on measurement of TTP and WR.
Fig. 2 (See legend on next page.)
Statistical analysis

Data were analyzed using the Statistical Package of Social Science (SPSS) program for Windows (Standard version 21). The normality of data was first tested with one-sample Kolmogorov-Smirnov test. Qualitative data were described using number and percent. Association between categorical variables was tested using Chi-square test while Fisher exact test and Monte Carlo test were used when expected cell count less than 5. Continuous variables were presented as mean ± SD (standard deviation) for parametric data. ANOVA test was used to compare more than two means. Sensitivity and specificity were tested at different cutoff points by receiver operating characteristic curve. For all abovementioned statistical tests, the threshold of significance is fixed at 5% level (p value). The results was considered non-significant when the probability of error is more than 5% (P > 0.05), and significant when the probability of error is less than 5% (P ≤ 0.05).

Results

This prospective study included 30 patients [16 males (53.3%), and 14 females (46.7%)], with an age range from 18 to 67 years (mean ± SD = 47.20 ± 13.19). In 21 cases, the lesions were found on the right parotid gland; in 12 cases, the lesions were on the left parotid gland; and only on 2 cases the lesions were bilateral (bilateral Warthin’s tumor). According to results of histopathology, we had 21 benign cases and 9 malignant cases. Out of the 21 benign cases, we had 15 cases with pleomorphic adenoma (mean ± SD = 1.08 ± 0.13) and 6 cases with Warthin’s tumor (Fig. 2). Out of 9 malignant cases, we had 7 cases with mucoepidermoid carcinoma and 2 cases with acinic cell carcinoma (Fig. 3).

Study of TIC type on DCE-MRI showed that 15 benign parotid gland tumors (pleomorphic adenoma) had type A TIC, and 6 benign tumors (Warthin’s tumor) had type C TIC. On the other hand, most malignant parotid gland tumors (66.7%) had type C TIC, 22.2% had type B TIC, and only 11.1% (1 case) had type A TIC. There was statistically significant difference as regard the type of TIC between benign and malignant parotid gland tumors (P < 0.0001) (Table 1). When considering that type A and B TIC denote benign lesions and type C TIC denote malignant lesions, we found that TIC type had 100% sensitivity, 87.5% specificity, 66.6% positive predictive value (PPV), 100% negative predictive value (NPV), and 90% accuracy (Table 4).

Pleomorphic adenomas showed higher TTP (mean ± SD = 165 ± 87.2 S) when compared with malignant parotid gland tumors (mean ± SD = 77.78 ± 33.8 S) (P = 0.002). Although there was no significant difference as regard the TTP of Warthin’s tumor (mean ± SD = 70.73 ± 42.5 S) and malignant parotid gland tumors (mean ± SD = 77.78 ± 33.8 S) (P > 0.05), however, Warthin’s tumor had higher WR (mean SD = 42 ± 5.24%) when compared with malignant parotid gland tumors (mean ± SD = 28.57 ± 8.02%) (P = 0.004) (Table 2).

Analysis of receiver operating curve showed that cut off TTP value of < 85 s could predict malignant parotid gland tumors with 88.8% sensitivity, 85.7% specificity, and 86.7% accuracy (Fig. 4). Cut off WR of < 35.5% could predict malignant parotid gland tumors with 87.5% sensitivity, 85.7% specificity, and 86.7% accuracy (Fig. 5).

A regard the measured ADC value, we found that there was statistically significant difference between the mean ADC value of pleomorphic adenoma (mean ± SD = 1.08 ± 0.42) and malignant parotid gland tumors (mean ± SD = 1.08 ± 0.13) (P = 0.046). However, there was no significant difference between the measured ADC value of Warthin’s tumor (mean ± SD = 0.94 ± 0.1) and malignant parotid gland tumors (mean ± SD = 1.08 ± 0.13) (P > 0.5) (Table 3).

Analysis of receiver operating curve showed that a cut off mean ADC value of 1.3 × 10⁻³ mm²/s could differentiate pleomorphic adenoma from malignant parotid gland tumors with 88.8% sensitivity, 93.3% specificity, 88.8% PPV, 93.3% NPV, and 91.6% accuracy (Fig. 4).

The combined use of DCE-MRI and DWI had sensitivity of 100%, specificity of 90.5%, and accuracy of 93.3% in differentiating benign from malignant parotid gland tumors (Table 4).

Discussion

Differentiating benign from malignant parotid gland tumors is essential for adequate surgical planning. MRI is considered to be the best non-invasive method for diagnosis of parotid gland tumors. However, there is still overlap between benign and malignant tumors in terms of imaging appearance on conventional MRI. In the last years, the role of functional MRI (DWI and DCE-MRI) have been assessed in head and neck neoplasms to overcome the overlap in imaging appearance of benign and malignant tumors on conventional MRI [1].
The main findings in this study are that combined use of DCE-MRI and DWI had high sensitivity and specificity in differentiating benign from malignant parotid gland tumors. Analysis of TIC had high sensitivity and specificity in differentiating benign from malignant parotid gland tumors. Pleomorphic adenoma could be easily
differentiated from malignant parotid gland tumors on basis of measured ADC and TTP values. On the other hand, there is still overlap between Warthin’s tumor and malignant parotid gland tumors as regard the measured ADC value and TTP value. In this study, the only way to differentiate between Warthin’s tumor and malignant parotid gland tumors is the WR.

Several previous studies had investigated the role of DCE-MRI in evaluation of parotid gland tumors and found that analysis of TIC could reveal physiological characterizations of different tissues using blood flow in them so it may help in differentiation between benign and malignant parotid gland tumors [7–10].

Zheng et al. [7] evaluated salivary gland tumors based on the TIC classification by Yabuuchi et al. [6] and found that most cases of pleomorphic adenomas (88.9%) had type A TIC; all cases of Warthin’s tumor had type B TIC; regarding malignant parotid gland tumors, most of them (81.8%) had type C TIC, and only 18.2% had type B TIC. Lam et al. [8] also studied TIC in differentiation between benign and malignant parotid gland tumors and found that 96.2% of pleomorphic adenomas had type A TIC; type C TIC was observed in all cases of malignant parotid gland tumors except lymphoma. They concluded that TIC had 79% sensitivity, 95% specificity, and 91% accuracy. This matches with our results where all cases of pleomorphic adenomas in our study had type A TIC, and all cases of Warthin’s tumor had type B TIC and most cases of malignant parotid gland tumors (66.7%) had type C TIC. In this study, analysis of TIC type had 100% sensitivity, 87.5% specificity, and 90% accuracy in differentiating benign from malignant parotid gland tumors.

Regarding WR values of Warthin’s tumor and malignant parotid gland tumor, Zheng et al. [7] stated that WR of Warthin’s tumor (57.5 ± 8.1%) was significantly higher than that of malignant parotid gland tumors (17.2 ± 13.2%). Gokce [5] performed analysis of several previous studies in literature and concluded that WR value of Warthin’s tumor was significantly higher than that of malignant parotid gland tumors. This matches with our results where we found that the WR was the most important predictor to differentiate between Warthin’s tumor and malignant parotid gland tumors (high WR of WT when compared with MT).

Mikaszewski et al. [11] stated that TTP < 120 s and WR < 30% could diagnose malignant parotid gland tumors with 89.5% sensitivity, 100% specificity, and 97.7% diagnostic accuracy. Tao et al. [12] found that TTP < 58 s and WR < 22% had 78.7% sensitivity, 84.2% specificity, and 82.4% accuracy in diagnosis of malignant parotid gland tumors. Ogawa et al. [13] stated that TTP < 105 s and WR < 30% had 73.1% sensitivity, 94% specificity, and 88.2% accuracy in diagnosis of malignant parotid gland tumors. This is in agreement with our results where we found that TTP of < 85 s could predict malignant parotid gland tumors with 88.9% sensitivity, 78.9% specificity, and 82.1% accuracy. WR of < 35.5% could predict malignant parotid gland tumors with 87.5% sensitivity, 85.7% specificity, and 86.7% accuracy.

Regarding the measured mean ADC value, we found that there was significant difference between the mean ADC value of pleomorphic adenoma and malignant parotid gland tumors (P = 0.046) and this in agreement with several previous studies. Mikaszewski et al. [11] stated that pleomorphic adenomas had high mean ADC value (1.862 × 10−3 mm²/s) when compared with malignant parotid gland tumors (1.059 × 10−3 mm²/s). Tao et al. [12] found that mean ADC value of pleomorphic

### Table 1: Type of TIC among benign and malignant cases included in this study

| Variables | Malignant lesions (n = 9) | Benign lesions (n = 21) | P value |
|-----------|--------------------------|------------------------|---------|
| A         | 1 (11.1%)                | 15 (71.4%)             | < 0.001 |
| B         | 2 (22.2%)                | 6 (28.6%)              |         |
| C         | 6 (66.7%)                | 0 (0.0%)               |         |

MC Monte Carlo test

### Table 2: TTP and WR values among benign and malignant cases included in this study

| Variables          | TTP         | WR          |
|--------------------|-------------|-------------|
| Pleomorphic adenoma (PMA) (n = 15) | 165 ± 87.2 | –           |
| Warthin’s tumor (WT) (n = 6)      | 70.73 ± 42.5 | 42.50 ± 5.24 |
| Malignant tumors (MT) (n = 9)     | 77.78 ± 33.8 | 28.57 ± 8.02 |
| PMA and MT           | P value = 0.002 | –           |
| WT and MT            | P value > 0.5 | P value = 0.004 |
Adenoma was $1.43 \times 10^{-3}$ mm$^2$/s and mean ADC value of malignant parotid tumors was $0.91 \times 10^{-3}$ mm$^2$/s. Abdel Razek et al. [14] stated that mean ADC values of pleomorphic adenoma and malignant parotid gland tumors was $1.35 \times 10^{-3}$ mm$^2$/s and $0.94 \times 10^{-3}$ mm$^2$/s respectively. Zang et al. [15] found that mean ADC value of pleomorphic adenoma and malignant parotid gland tumors was $1.57 \times 10^{-3}$ mm$^2$/s and $1.16 \times 10^{-3}$ mm$^2$/s respectively. This is in agreement with our results where the mean ADC value for pleomorphic adenoma was $1.38 \times 10^{-3}$ mm$^2$/s versus $1.08 \times 10^{-3}$ mm$^2$/s for malignant parotid gland tumors ($P = 0.046$).

In this work, we found that cut off mean ADC value of $1.3 \times 10^{-3}$ mm$^2$/s could differentiate pleomorphic adenoma from malignant parotid gland tumors with 88.8% sensitivity, 93.3% specificity, 88.8% PPV, 93.3% NPV, 91.6% accuracy, and 0.606 AUC.

![ROC curve for prediction of malignant lesions by ADC and TTP. At cut off ADC value of $1.3 \times 10^{-3}$ mm$^2$/s PMA could be differentiated from MT with 88.8% sensitivity, 93.3% specificity, 88.8% PPV, 93.3% NPV, 91.6% accuracy, and 0.606 AUC. TTP of < 85 s could predict malignant parotid gland tumors with 88.9% sensitivity, 78.9% specificity, 66.7% PPV, 93.7% NPV, 82.1% accuracy, and 0.833 AUC.](image1)

 ![ROC curve for prediction of malignant tumor by WR. WR < 35.5% could predict malignant parotid gland tumors with 87.5% sensitivity, 85.7% specificity, 87.5% PPV, 85.7% NPV, 86.7% accuracy, and 0.973 AUC.](image2)
Table 3 Mean ADC value among benign and malignant cases included in this study.

| ADC value (mean ± SD) | Value | P value |
|-----------------------|-------|---------|
| Pleomorphic adenoma (PMA) | 1.38 ± 0.42 | 0.046 |
| Warthin’s tumor (WT) | 0.94 ± 0.1 | 1.08 ± 0.13 |
| Malignant parotid gland tumor (MT) | 1.25 ± 0.34 | >0.5 |

Abbreviations
SD: Standard deviation; MRI: Magnetic resonance imaging; DCE-MRI: Dynamic contrast-enhanced magnetic resonance imaging; DWI: Diffusion-weighted image; ADC: Apparent diffusion coefficient; PPV: Positive predictive value; NPV: Negative predictive value; SGTs: Salivary gland tumors; FNAB: Fine needle aspiration biopsy; CT: Computed tomography; TSE: Turbo spin echo; TR: Repetition time; TE: Echo time; FOV: Field of view; ROI: Region of interest; EWS: Extended work space; TIC: Time signal intensity curve; TTP: Time to peak; WR: Washout ratio; SI: Signal intensity; PMA: Pleomorphic adenoma; WT: Warthin’s tumor; MT: Malignant parotid gland tumors; AUC: Area under curve; S: Second

Acknowledgements
Not applicable.

Authors’ contributions
AE revised the collected data and the manuscript. DM and ME analyzed the MRI images of all patients. DM wrote the manuscript. ME performed the statistical analysis. All authors read and approved the final manuscript.

Funding
No funding resources.

Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate
The study was approved by our institution’s ethics committee (Mansoura University of Medical Research Board) (ethics committee reference number: MS/16.09.15) and all patients gave their written informed consent before inclusion in the study.

Consent for publication
All patients included in this research gave written informed consent to publish the data contained within this study. If the patient was less than 16 years old, deceased, or unconscious when consent for publication was requested, written informed consent for the publication of this data was given by their parent or legal guardian.

Competing interests
The authors declare that they have no competing interests.

Received: 1 May 2020 Accepted: 26 June 2020
Published online: 13 July 2020

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