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Value of diffusion weighted and ADC value - magnetic resonance imaging in differentiation between benign and malignant solid parotid gland masses

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Abstract
Background: magnetic resonance imaging (MRI) is becoming an essential tool for assessment of parotid gland pathology. Diffusion weighted imaging (DWI) provides quantitative and qualitative information reflecting the changes in tissue cellularity and integrity of cell membranes.
Objective: To evaluate the diagnostic accuracy of diffusion weighted -MRI in the differentiation between benign and malignant solid parotid gland masses using 1.5 Tesla MRI scanner and to obtain the best cutoff value of apparent diffusion coefficient (ADC) to differentiate between benign and malignant masses.
Patients and methods: prospective cross-sectional analytic study was conducted in Al Imamein Al Kadhumein Medical City, at the period between January 2019 and January 2020, 50 patients were included in the study. DWI was acquired at following b-values [50, 1000 millimeter (mm) 2/second (sec)], in this study the results were obtained and depending on b-value 1000 mm2/sec.
Results: The mean level of ADC value of malignant masses (0.599 ± 0.117 SD x 10-3 mm2/sec), while for benign masses (1.590 ± 0.363 SD x10-3 mm2/sec); According to Receiver operating characteristic (ROC) curve the optimal cutoff point of ADC value was (0.914x10-3 mm2/sec) with sensitivity 100%, specificity 97%. The association between MRI diagnosis and histopathological diagnosis was significant (P value< 0.001).
Conclusion: Diffusion weighted- MRI and ADC values are highly sensitive and specific to differentiate between benign and malignant solid parotid gland masses and the best ADC cut off value was (0.914x10-3 mm2/sec).

Keywords: Diffusion weighted imaging, magnetic resonance imaging, benign and malignant solid parotid gland masses

Introduction

Characterization of parotid gland masses is important for preoperative treatment planning, the clinical symptoms do not correlate well with histopathology, most of the patients with parotid gland masses present with slowly growing lump in the parotid space either benign or malignant, the facial nerve palsy which is considered strong sign of malignancy usually occurs late; therefore, the clinical examination is not so helpful in determination of the lesion nature [1]. Surgical management plan in case of parotid mass depends mainly on the histologic type of the lesion (benign or malignant), the local excision and superficial parotidectomy are usually suitable for benign tumor, while malignant tumors usually indicate total parotidectomy, with potential hazard to the facial nerve injury [2, 3]. Whereas the risk for local recurrence in pleomorphic adenoma and Warthin tumors (both are the commonest benign parotid gland tumors) are 50% and 2% respectively, also about 25% of pleomorphic adenoma undergo malignant transformation, the corresponding rate is about 1% in Warthin tumor therefore to reduce these risk, should remove with its capsule [4]. Fine needle aspiration cytology (FNAC) is widely used in the preoperative diagnosis of parotid gland masses; However, the result of cytology may be inconclusive or even false, owing to insufficient samples and small mass size; Also this method is limited with deep lobe (DL); In addition, if FNAC is not performed correctly, it may cause spread of cancer or infection [2, 3]. Therefore, preoperative imaging is mandatory and has assumed a major role in surgical planning for assessing the location and preventing treatment delay in case of malignancy tumor, helpful in assessing and establishing a policy toward lymph node dissection,

avoiding surgery for inflammatory disease and inform the patient more appropriately as to the treatment options and the possible risk of facial nerve injury [4, 5]. Conventional MRI and MRI-based advanced techniques such as DWI have become the preferred diagnostic tools for differential diagnosis of parotid masses, because of their excellent soft tissue resolution, non-invasive multiplanar imaging, and absence of ionizing radiation [6, 7]. MRI specifies the DL or superficial lobe (SL) location of the parotid gland mass, as well as any additional mass; That cannot be determined by physical examination, mass extension, contour, signal features, and the relation between the mass and the facial nerve [8]. The DWI provides functional information related to random water diffusion of the masses, the ADC value calculated from DWI data provide additional quantitative information related to random diffusion of water molecules in tissues and functionally complement conventional MRI and has been reported as helpful for narrowing the different diagnosis of parotid gland masses [9].

Aims of the Study

To evaluate diagnostic accuracy of DW-MRI in the differentiation between benign and malignant solid parotid masses using 1.5 Tesla MRI scanner and to obtain the best cut-off ADC value between benign and malignant solid parotid masses.

Patients and Methods

Study design: This prospective cross-sectional analytic study was conducted in MRI unite of Al Imamein Al Kadhumein Medical City/ Baghdad/ Iraq, at the period between January 2019 and January 2020; Fifty patients with clinical diagnosis of parotid gland masses were included in the study, their ages ranged from 9 to 72 years (mean 42 ± 16.6) years; 35 were male and 15 were female. The patients were referred to the Radiology Department of Al Imamein Al-Kadhimein Medical city by facio-maxillary, ENT, and general surgeons. All patients were examined by ultrasound using linear array 7.5 MHz probe to confirm clinical diagnosis and insure solid consistency of the parotid mass.

Inclusion criteria: Patients with clinical and ultrasound diagnosis of solid parotid gland mass.

Exclusion criteria: totally cystic parotid lesion, patients with previous history of parotid surgery, patients in whom histopathological diagnosis were unavailable or non-conclusive, and patients with general contraindication for MRI.

Ethical consideration: The approval was taken from scientific committee of diagnostic radiology in the Iraqi board of medical specialization; an oral informed consent was taken from all patients included in this study.

MRI protocol: All patients underwent MRI examination using 1.5 Tesla MRI Unit (MAGNETUM AERA, Siemens medical system, Germany); all patients were examined in the supine position, utilizing 20 channel head and neck phased array surface coil. The following imaging sequences were done: Coronal T1 spin echo WI (slice thickness 3mm, field of view (FOV) 240x240mm, intersection gap 1mm, TE 10ms, TR 420ms, flip angle 90 degree, matrix size 256 mm), Sagittal T1 spin echo WI (slice thickness 3mm, FOV240x240mm, intersection gap1mm, TE 10ms, TR 633ms, flip angle 90 degree, matrix size 256 mm), Axial T1 fat suppression WI (slice thickness 3mm, FOV240x240mm, intersection gap1mm, TE 36ms, TR 1220ms, flip angle 150 degree, matrix size 256mm), Coronal T2 spin-echo WI (slice thickness 3mm, FOV 240x240mm, intersection gap 1mm, TE 96ms, TR 6480ms, flip angle 90 degree, matrix size 256 mm), Axial T2 fat suppression WI (slice thickness 3mm, FOV 220x220mm, intersection gap 1mm, TE 36ms, TR 3800ms, flip angle 150 degree, matrix size 256mm), DWI: a multisection spin echo single-shot echoplanar sequence was used, sensitizing diffusion gradients were applied sequentially in the x, y, and z directions with b-values of 50, and 1000 mm2/sec and the results were obtained and depending on b- value 1000 mm2/sec The parameters for DWI were as follows (TR 5560 ms; TE 74 ms, FOV: 277x190mm, slice thickness 5mm; intersection gap 0mm and matrix size 128 mm), ADC measurement were done on the ADC map which were automatically generated from the DWI sequences; The ADC values were measured manually by placing ROI of 0.50 –0.70 cm2 over the lesion. At least three measurements (according to the size of the lesion) were taken for each lesion and the mean value was calculated and recorded. The measurements were performed in the most homogenous solid parts of the lesions with restricted or not restricted on DWI and for heterogeneous lesions if there were no parts restricted diffusion the solid enhanced part of each lesion was considered for measurement; Cystic, necrotic and hemorrhagic parts of the lesions were not included in the measurements. Finally Axial T1 gat suppresion WI with IV contrast, the IV agent used for MRI study was GADODIAMIDE injected by using infusion pump at dose of 0.1 milli-mole/kg of body weight at flow rate of 2ml/ sec followed by flushing 25ml of saline.

Image analysis: Image analysis was performed by two independent radiologists, before getting the result of histopathology. All the images were evaluated on the workstation, each lesion was identified in T1 spin echo WI, T2 spin echo WI, T1 fat suppression WI, T2 fat suppression WI, T1 spin echo WI post intravenous contrast, T1 fat suppression WI post intravenous contrast, DWI and ADC map.

MRI diagnosis: Round or lobulated solid mass, well-defined contour, low intense rim (representing a capsule), homogeneous hyperintense SI (when the signal intensity brighter than the adjacent muscle) on T2 WI and homogenous enhancement, not restricted on diffusion with ADC values greater than 0.914 x10-3mm2/sec, the masses matching these criteria were diagnosed as benign masses. The masses showing focal signal voids were diagnosed as hemangioma. Irregular mass margin, invasion into adjacent structures, heterogeneous hypointense SI (when the signal intensity lower than the adjacent muscle) on T2 WI, heterogeneous enhancement, perineural and lymphatic spread, also showed restricted diffusion and ADC values lower than 0.914x10-3mm2/sec were accepted as malignant mass features. The Final histopathological diagnosis was obtained by FNAC in 23 patients and excisional biopsy in 27 patients.

Statistical analysis: Statistical analysis was done using

SPSS version 22. Mean, SD, frequency and percentage were used for descriptive analysis. Chi-square and Fisher's Exact Test were used for correlation for analysis categorical variable association between variables; ROC curve used for determine most sensitive and specific cutoff point. P-value of <0.05 was considered statistically significant.

Results

This prospective study included 50 patients with solid parotid gland masses, their ages ranged from 9-72 years with mean of (42±16.6) years, 35 (70%) of them were male and 15 (30%) female with male: female ratio of 2.3:1. The final histopathological diagnosis showed 35 (70%) benign masses and 15 (30%) malignant masses. The MRI diagnosis showed 37 (74%) benign masses and 13 (26%) malignant masses as shown in figure (3-3). DWI distribution showed that 14 (28%) was restricted and 36 (72%) was not restricted.

The mean age of patients with malignant masses were significantly higher than that of benign masses, this results was statistically significant (P-value 0.0001); No significant difference was observed between benign and malignant masses regarding gender distribution (p-value 0.5).

The mean ADC value for malignant masses was (0.599±0.117 x 10-3 mm2/ sec), and for benign masses was (1.590± 0.362 x 10-3 mm2/ sec) this difference in mean ADC vale was statistically significant (P value < 0.0001), as shown in table (1).

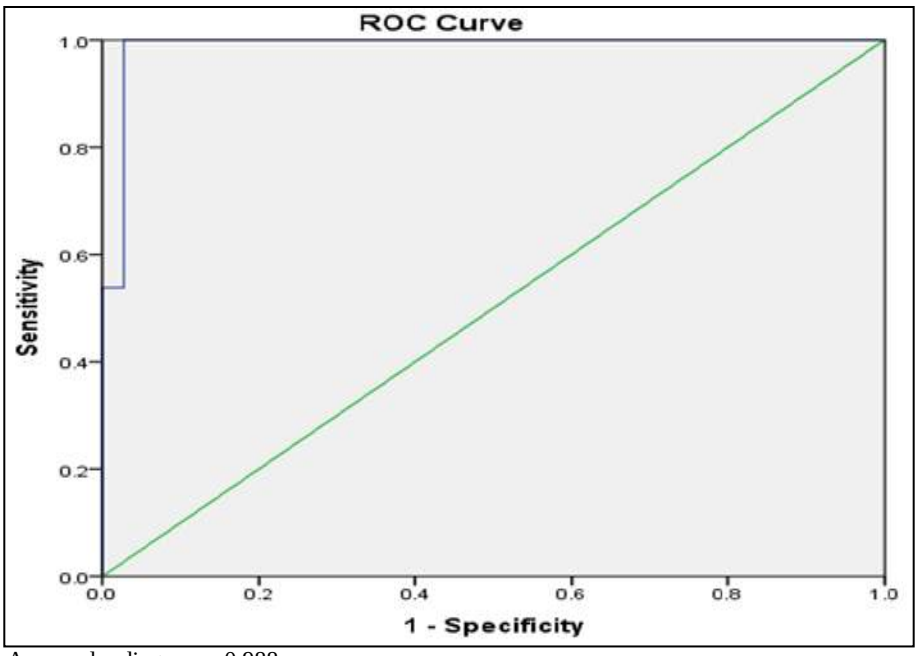
Table 1: ADC value of benign and malignant parotid masses

	Benign	Malignant	P value
Mean	1.590	0.599	*P*< 0.0001
SD	0.362	0.117	
Min.	0.933	0.477	
Max.	2.100	0.899	

According to ROC curve the best cutoff ADC value to differentiate between benign and malignant parotid masses was (0.914 x 10-3 mm2/ sec) with sensitivity of 100% and specificity of 97%, as show in table 2 and figure 1.

Table 2: ADC value cutoff point to differentiate between benign and malignant parotid masses (x 10-3 mm2/ sec)

Mean ADC cut off point	Sensitivity	Specificity	PPV	NPV
0.796	92%	97%		
0.914	100%	97%	92.8%	100%
0.960	100%	46%		



Area under diagram = 0.988

Fig 1: ROC comparative diagnostic values of quantitative ADC value for discriminating between benign and malignant solid parotid masses.

The association between MRI diagnosis and histopathological diagnosis was significant, MRI diagnosis was 80% sensitive and 97% Specific when comparing with histopathological results, 12 (80%) patients diagnosed as malignancy by MRI also diagnosed malignancy by histopathology, 34 (79.1%) patients diagnosed as benign by MRI also diagnosed benign by histopathology, only 1(2.9%) patient diagnosed as malignancy by MRI had diagnosed benign by histopathology while 3 (20%) patients diagnosed as benign by MRI had diagnosed malignancy by histopathology, p-value 0.0001, as shown by table 3. Figures 2, 3 and 4 show images of 3 patients included in the study.

Table 3: Association between MRI diagnosis and histopathological diagnosis in solid parotid masses.

MRI diagnosis	Histopathological diagnosis			P value
	Malignant	Benign	Total	
Malignant	12 (80%)	1 (2.9%)	13(26%)	**0.0001***
Benign	3 (20%)	34 (97.1%)	37(74%)	
Total	15 (100%)	35 (100%)	50 (100%)	

Fisher's Exact Test= 32.477, DF=1. P-value= 0.0001 (significant).

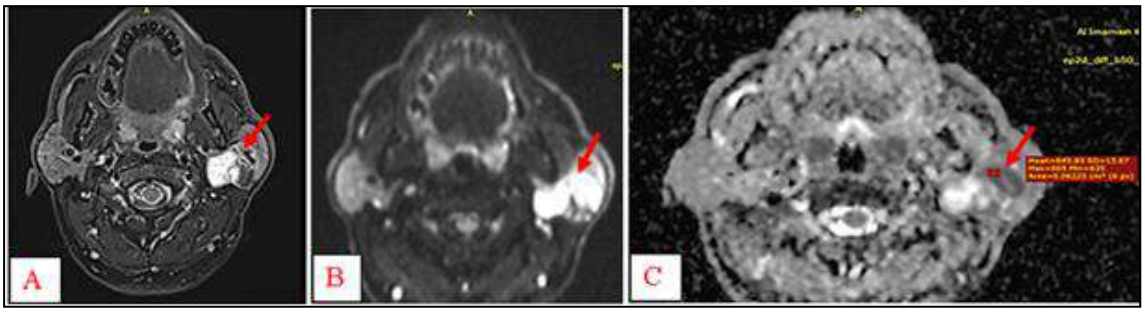


Fig 2: 70 years old male presented with left side painful parotid swelling with left side facial palsy, A: axial T2 fat suppression image show heterogeneous SI mass (red arrow) involved both superficial and deep lobes, B: the mass show hypersintense SI on DWI, C: on the corresponding ADC map, part of the mass show resticted diffusion and the mean ADC values are 0.645 x10-3mm2/sec, the histopathology proved to be mucoepidermoid carcinoma.

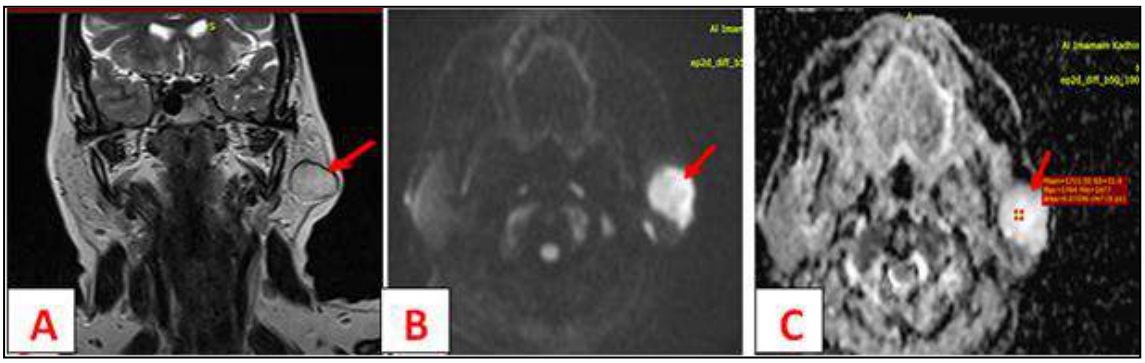


Fig 3: A 52 years old female presented with left side painless parotid swelling, A: coronal T2 spin echo image showed well defined hyper intense SI mass seen in superficial lobe (red arrow). B: the lesion show mild hyperintense SI on DWI. C: on the ADC map the lesion is not restricted and the mean ADC values are 1.711 x10-3mm2 /sec, the histopathology proved to be pleomorphic adenoma.

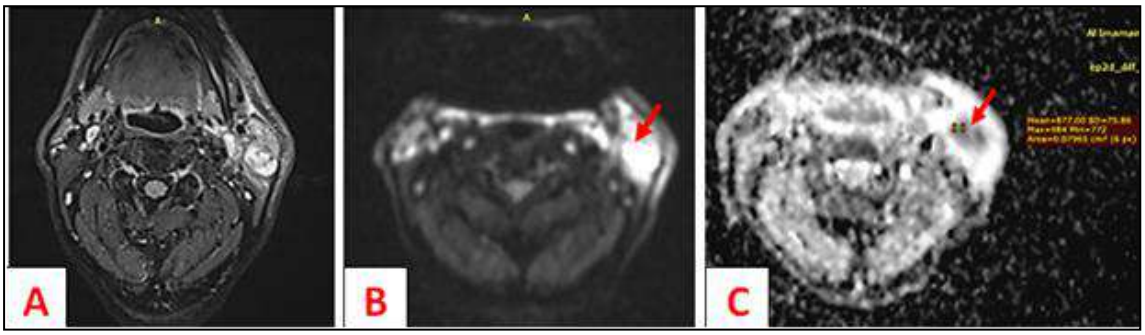


Fig 4: 69 years old male presented with left side painful parotid swelling. A: axial T2 fat suppression image showed heterogeneous SI mass (red arrow) involved both superficial and deep lobes. B: the mass show hyperintense SI on DWI. C: on the corresponding ADC map the mass showed restricted diffusion and the mean ADC values are 0.577 x10-3mm2/sec, the histopathology proved to be tuberculosis of parotid gland.

Discussion

Pre-operative diagnosis of the parotid mass can help the surgeon to determine the most suitable surgical procedure. MRI provides morphological information of the mass and DWI provides functional information related to the random water diffusion of the mass. The ADC of a parotid gland mass can be calculated quantitatively from DWI data. The ADC calculation has been reported as helpful for narrowing the differential diagnosis of parotid masses [10]. FNAC has some shortcomings in the exact diagnosis of parotid masses, so different pre-operative imaging approaches have an important role in the evaluation of these lesions [11].

According to the current study the ages ranged from 9 to 72 years,the mean and SD of (42 ± 16.6) years, the final diagnosis by histopathology showed 35 (70%) benign and 15 (30%) malignant, 35(70%) of them were male and 15(30%) female, These results were approximately similar to that of Al-Kheshen *et al*. study [12], they stated that 40 patients (24 male and 16 female), 16 patients had malignant lesions and 24 had benign lesions. Other studies done by Salama *et al.* [13], Yologlu Z *et al.* [14], Eida S *et al.* [15], and Balçık *et al.* [16] also showed similar results.

In this study the mean age of malignant masses were significantly higher than benign (P value = 0.0001), these results were similar to that of Balcik *et al.* [16] who stated that the mean age of malignant lesions was significantly higher than benign lesions (P value=0.038), Reinheimer *et al.* [17] showed patients with benign tumors generally were younger (mean 41.3 years) than patients with malignant tumors (mean 54.3 years).

In this study No significant difference was observed between benign and malignant masses regarding gender distribution (p-value 0.5), Similar results were observed by Balcik *et al.* [16] and Yuan *et al.* [18].

In the current study the mean ADC value of malignant parotid masses were significantly lower than the mean ADC

value of benign parotid masses with cutoff point of ADC value level for MRI diagnosis of parotid gland malignancy was (0.914 x 10-3 mm2/sec), P value =0.0001; with sensitivity 100%, specificity 97%.

Al-Kheshen *et al.* [12] show similar results where the absolute ADC value of lesions were significantly different between benign and malignant salivary gland tumors (P value<0.001) with cutoff ADC value is below 0.85×10−3 mm2/sec, had high probability that the mass will be malignant with sensitivity of 93.7% and specificity of 95.8%. Salama *et al.* [13] also show similar results and stated that the mean ADC value for malignant lesions were 0.65±0.21×10−3mm2/sec. Balçık *et al.* [16] showed that the mean ADC value of benign parotid lesions were significantly higher than malignant lesions (P value=0.006). Eida *et al.* [15] showed high ADC values with significant statistical differences in the differentiation of benign and malignant lesions (ADC values were high in benign while low in malignant). Several studies have calculated cutoff points for benign and malignant masses: Wang *et al.* [19], Srinivasan *et al.* [20], and Inci *et al.* [21], the cutoff points calculated to be 1.22 x10-3 mm2 /sec, 1.3 x10-3 mm2 /sec and 1.3 x 10-3 mm2 /sec, respectively. These cutoff points, obtained with a b value of 1000 mm2 /sec, were slightly higher than the results of the current study (cutoff point 0.914 x 10-3 mm2/sec), and this difference can be attributed to the low number and non-homogeneity of malignant tumors in the current. On the other hand Matsushima *et al.* [22] found no significant differences between benign and malignant lesions on the basis of ADC values and stated that mean ADC values increased with the degree of extracellular components. They concluded that ADC levels alone were not enough to differentiate benign and malignant parotid tumors. Sakamoto *et al.* [23] study also stated that there was no significant difference between the ADC values of benign and malignant tumors (P value =0.246). Habermann *et al.* [8] study stated that mucoepidermoid carcinomas, acinic cell carcinomas, and basal cell adenocarcinomas cannot differentiable from Warthin tumors on the basis of ADC values solely. These differences might be attributed to different sample size, different inclusion and exclusion criteria, difference in obtaining the measurement ROI and technical difference such as using 3 Tesla and 1.5 Tesla and difference in MRI protocols and parameters.

Conclusions

Diffusion weighted- MRI and ADC values are highly sensitive and specific to differentiate between benign and malignant solid parotid gland masses. The best ADC cut off value was (0.914 x 10-3 mm2/ sec).

No conflicts of interest

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