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The role of diffusion-weighted imaging and ADC value in head and neck lesions

Zeliha Cosgun[1], Siddika Halicioglu[1], Aysu Kiyan[2], Emine Dagistan[1], Cetin Boran[3]

[1]*Department of Radiology, Bolu Abant Izzet Baysal University, Medical Faculty, Bolu, Türkiye*
[2]*Department of Public Health, Bolu Abant Izzet Baysal University, Medical Faculty, Bolu, Türkiye*
[3]*Department of Pathology, Bolu Abant Izzet Baysal University, Medical Faculty, Bolu, Türkiye*

ABSTRACT

Aim: To evaluate the contrast enhanced magnetic resonance imaging (MRI), diffusion weighted MRI findings of head and neck lesions in combination with histopathological diagnosis.

Method: Forty-two patients referred to our university, department of Radiology between July 2008 and June 2011 with a prediagnosis of head-neck lesion. Patients whom underwent contrast enhanced MRI, diffusion weighted MRI, and incisional or excisional biopsy, were included in the study. Patients, whose MRI examinations were suboptimal due to any artefacts, were excluded. After determination of MRI parameters, such as signal intensity, enhancement pattern, apparent diffusion coefficient (ADC) value, and contrast enhanced MRI and diffusion weighted MRI examinations were evaluated by a radiologist who had ten years of experience. Histopathological evaluation was made by a pathologist who had no information about patients' MRI findings.

Results: The mean ADC value of benign and malignant lesions were 0.128x10-3±0.053 mm²/sn and 0.100x10-3±0.026mm²/sn respectively. ADC value was found to be significantly higher in benign lesions compared to malignant ones (p=0.032). Conventional MRI criteria such as signal intensity, internal structure, presence of cystic space and enhancement were found to be insignificant in the differentiation of benign and malignant lesions.

Conclusion: Conventional MRI sequences are important in the diagnosis of head and neck lesions but not sufficient due to the overlapping findings. Diffusion weighted MRI, applied in addition to conventional MRI examination, is an efficient technique and has additional diagnostic value in determining nature of head and neck lesions in the preoperative period.

Keywords: Head and neck lesions, ADC value, diffusion weighted MRI, histopathology.

Dr. Zeliha Cosgun
Department of Radiology, Bolu Abant Izzet Baysal University, Medical Faculty, Bolu, Türkiye
E-mail: zeliha44@gmail.com
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Introduction

Conventional magnetic resonance imaging (MRI) sequences are valuable for identifying the location of head and neck lesions, lesion extension, and the composition of the lesions. However, it is not always possible to establish the diagnosis of head and neck lesions with conventional MRI alone. Fine-needle aspiration cytology, which is a cost-effective method for diagnosing head and neck lesions, is invasive, and specimens may be insufficient for a conclusive diagnosis [1]. Alternative diagnostic methods that enable a better preoperative evaluation of head and neck lesions have been sought. Diffusion-weighted (DW) MRI reflects levels of random molecular diffusion in tissues that are imaged, and the apparent diffusion coefficient (ADC) of head and neck lesions can be calculated with that modality. Head and neck lesions may differ in their ADC value, and those variations might help to establish a definitive diagnosis [2]. Several studies have found statistically significant differences in the ADC values of lymphomas, carcinomas, benign solid tumors and benign cystic lesions [2, 3]. We report the ADC values derived from DW-MRI for a series of head and neck lesions. Our aim was to determine whether the ADC calculation is valuable in the differential diagnosis of head and neck lesions.

Materials and methods

Forty two patients referred to Abant Izzet Baysal University, Faculty of Medicine, Department of Radiology between July 2008 and June 2011 with a pre-diagnosis of head-neck lesion, underwent contrast enhanced MRI and diffusion weighted MRI, and diagnosed as benign or malignant mass after incisional biopsy or operation, were included in this study. The project was approved by the ethics committee of our hospital (2011/83). Retrospective examined using a 1.5T MRI system with a phased-array head and neck coil system (Siemens Magnetom Symphony, Erlangen, Germany). The retrospective study involved 44 patients with head and neck lesions over a 4-year period. Two MRI examinations were excluded from the study due to artefacts.

Routine neck MRI imaging was performed with T1-weighted (T1W), T2-weighted (T2W) turbo spin-echo, and fat-suppressed T2-weighted images in the axial plane and T2-weighted turbo spin-echo images in the coronal plane with 5-mm slice thickness. DW-MRI was done using a 1.5T MR system, obtaining an echo-planar spin-echo sequence in the axial plane with b values of 0, 400, and 800 mm^2/s, following pre-contrast MRI examination. The ADC of each mass was calculated directly from the ADC maps using a circular region of interest (ROI) in 44 patients.

The radiological assessment was carried out in two stages by a radiologist with ten years of experience. The lesion signal intensity, internal structure, cystic area content, macroscopic fat content, mass effect, invasion to neighboring structures were evaluated in contrast-enhanced neck MRI examinations (Figure 1). Diffusion-weighted images were transferred to workstation (Leonardo, Software Version 2.0; Siemens; Germany) to perform ADC measurements. ROI (region of interest) were placed inside each lesion, the diameter of which was set to be at least half of the mass diameter and manually adjusted by the radiologist, and ADC measurements were performed. In the presence of cystic-necrotic contents, ROI was placed in the solid component of the lesion

Histopathological evaluation was made by a pathologist who had no knowledge about the ADC value. In histopathological evaluation, the nature of the lesion (benign-malignant), stroma type, cellularity, nucleus-cytoplasm ratio, matrix, tumor-matrix ratio were evaluated.

Statistics

Descriptive data are presented as number (percentages) or median and interquartile ranges (25^{th}-75^{th} percentiles) or mean ± standard deviation. Independent samples t-tests or non-parametric Mann-Whitney U-tests were used for the comparison of continuous variables between two groups. The analyses were performed using the Statistical Package for Social Sciences (SPSS 15.0, version 15.0). The results were considered to be significant at a level of $p < 0.05$.

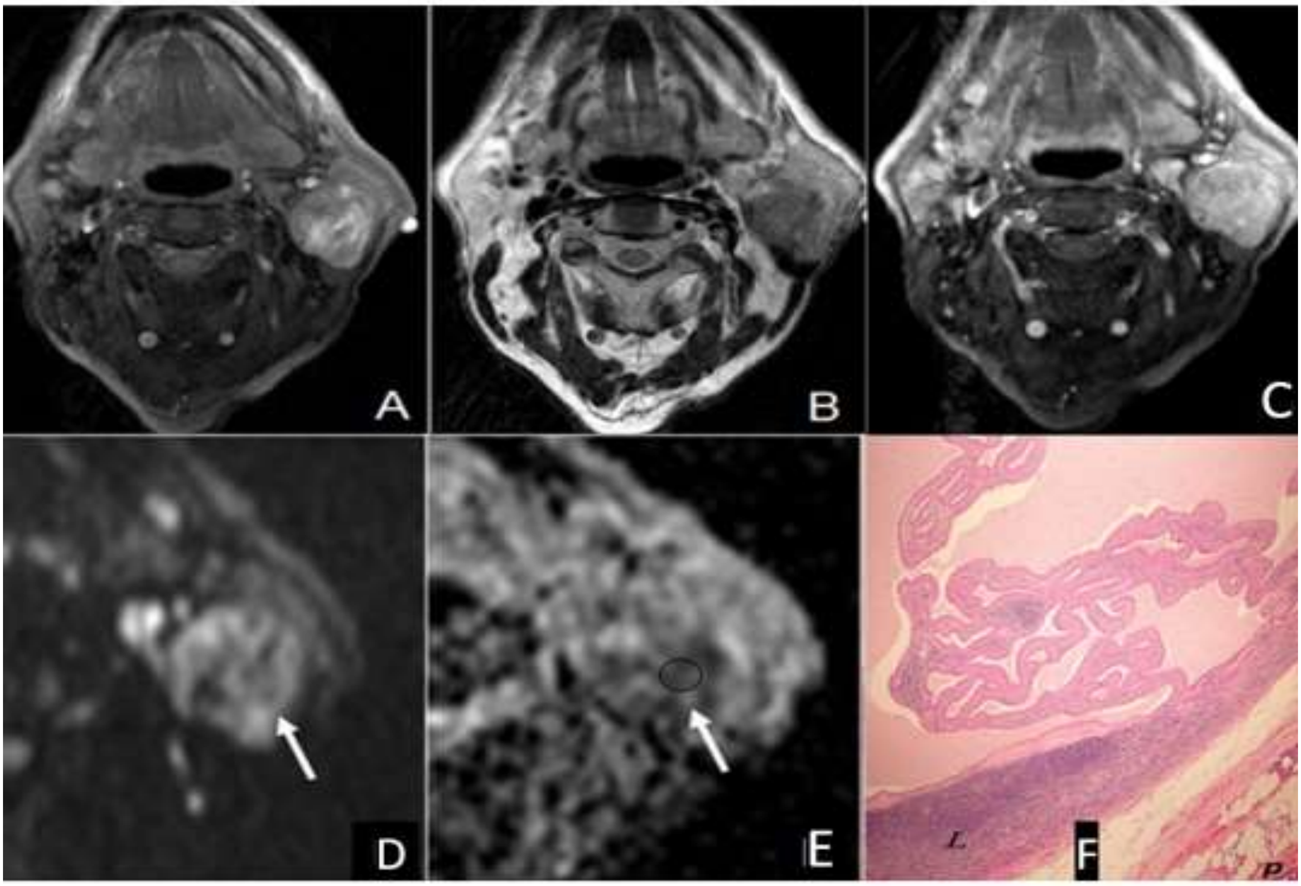

Figure 1: 66-year-old male patient complaining of swelling on the left side of the neck, Hyperintense and contrast enhancing mass on T1 W, T2W and postcontrast T1W images (A,B,C) in the left parotid gland, the mass is heterogeneous hyperintense in DW-MRI (D) and hypointense in ADC mapping(E), ADC value is $0.085x10^{-3}$, Histopathological examination of the mass (F) reported as a Warthin tumor shows dense lymphoid tissue (*L*)

Results

The retrospective study involved 44 patients with head and neck lesions (25 men and 19 women, mean age 46 years, range 5–85 years) over a 4-year period. Two MRI examinations were excluded from the study due to artefacts. Forty-two masses were detected in 42 patients. Of the 42 masses 25 were benign and 17 were malignant. Benign and malignant tumor subtypes are given in detail in table 1.

The signal intensity patterns of masses on T1- and T2- weighted MR images are shown in Table 2, 3). Due to the insufficient number of patients, a comparison between the T1A and T2A signaling intensities of benign and malignant lesions could not be made statistically. The lesions were divided into two groups as homogeneous and heterogeneous in terms of their internal structure. There was no statistically significant difference between benign and malignant lesions and their internal structures (p=0.66).

The mean ADC value for the benign head and neck lesions ($0.128x10^{-3}\pm0.053$ mm²/sec) was significantly higher than the corresponding value for the malignant tumors ($0.100x10^{-3}\pm0.026$ mm²/sec) (p=0.032) (Table 4, Graph 1).

The relationship between the nucleus cytoplasm ratio and our other pathogenic findings and the ADC values could not be compared due to the decency of the number of cases between the subgroups. In squamous cell

Table 1. Histopathological diagnosis and the mean apparent diffusion coefficients (ADCs, x 10^{-3} mm²/sec) for head and neck lesions.

Histopathology		Number of patients (n=42)	ADC value ($x10^{-3}$ mm² /sec)
Malign (n=17)	Adenoid cystic carcinoma	1	0.158
	Basosquamous cell carcinoma	1	0.080
	Diffuse large B-cell lymphoma	1	0.084
	Undifferentiated tumor infiltration	1	0.078
	Malignant epithelial tumor	2	0.083
	Infiltration of malignant melanoma	2	0.071
	Plasmacytoma	1	0.116
	Squamous cell carcinoma	8	0.105±24
Benign (n=25)	Branchial cyst	2	0.098
	Dentigerous cyst	1	0.105
	Inflammatory myofibroblastic tumor	1	0.160
	Epidermal cysts	1	0.072
	Chronic pharyngitis	3	0.133
	Cavernous hemangioma	1	0.168
	Lipoma	1	0.021
	Hyperplasia of lymphoid tissue	3	0.097
	Colloidal nodular goiter	1	0.124
	Pleomorphic adenoma	6	0.184±42
	Schwannoma	1	0.177
	Thornwaldt cyst	1	0.096
	Warthin's tumor	2	0.083
	Inflammatory granulation tissue with foreign body giant cells	1	0.121

Table 2. The signal intensity features of head and neck lesions on conventional sequences, T1-weighted images.

Pathology	**The signal intensity features**		
	Isointense	**Hypointense**	**Hyperintense**
Benign	11	0	14
Malign	8	2	7
Total	19	2	21

Table 3. The signal intensity features of head and neck lesions on conventional sequences, T2-weighted images.

Pathology	**The signal intensity features**		
	Isointense	**Hypointense**	**Hyperintense**
Benign	1	0	24
Malign	0	0	17
Total	1	0	41

Table 4. The mean apparent diffusion coefficients (ADCs, x 10^{-3} mm² /sec) for head and neck lesions.

ADC value (x 10^{-3} mm² /sec)	Mean	Minimum	Maximum	Standard Deviation
Benign lesions	0.128	0.021	0.232	0.053
Malign lesions	0.100	0.071	0.158	0.026
***P* value**	0.032			

carcinomas, the nucleus cytoplasm ratio varies between 0.25-2, in schwannoma 0.25, plasmocytoma 0.5-0.6, lipoma 0.01, malignant epithelial tumor 2, malignant melanoma infiltration 2-5, malignant tumor infiltration 1.5-2.3, and diffuse large cell B lymphoma 3-4, bas decuamous carcinoma it was rated as 2. The tumor stroma ratio was between 1.5 and 4 in squamous cell carcinoma. In Warthin's tumor, the stroma was quite dense. Only 20 of the 42 patients could be evaluated for the presence and rate of necrosis. Necrosis was not detected in 14 patients, and there was mild necrosis in three patients, moderate necrosis in one patient, and significant necrosis in two patients. The ratio of myxoid-decondroid matrix-epithelium ranged from 0.5-4 in pleomorphic adenomas.

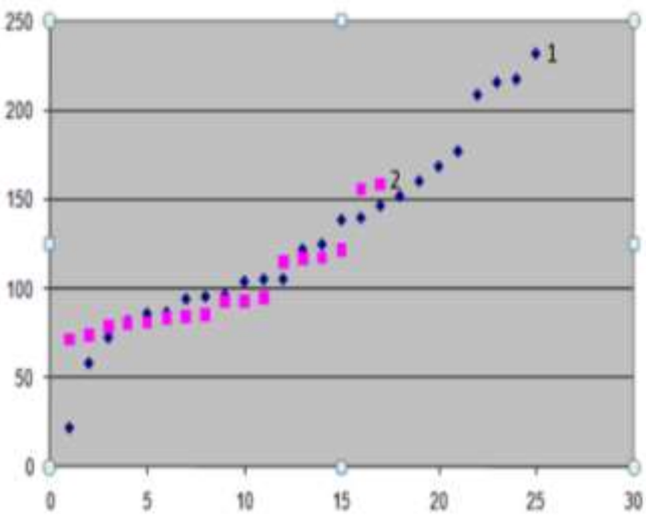

Figure 2. Distribution of head and neck masses of ADC value.

(1: Benign head and neck lesions, 2: Malignant tumors)

Discussion

Our aim in this study is to make an evaluation of contrasted neck MRI, DW-MRI and histopathologic examination results on head and neck lesions. For this purpose, we have retrospectively examined contrasted MRI, DW-MRI findings, ADC values and histopathologic specifications of 42 patients who have been diagnosed to have lesions in their head and neck area and who have been pathologically diagnosed too. We have found that although MRI sequences are important to define localization of the lesion, lesion extension and relation of the lesion with neighboring tissues; MRI findings like signal specifications, inner characterization, being of a cystic area, contrasting specifications are not enough to define benign and malign differentiation and ADC values are meaningfully higher in benign lesions with respect to malignant lesions.

In head and neck lesion characterization of routine contrasted MRI examinations; lesion signal, edge specification, cystic-necrotic area, hemorrhage or macroscopic fat and relation with neighboring tissues are used as parameters for fore sighting. According to this; circular sharp edged, well-capsulated tumors are evaluated to be benign in MRI and irregular, infiltrative bad-edged tumors are evaluated to be malignant; capsulated masses showing lobulation strongly advise for pleomorphic adenoma in especially in parotid gland. Many of malignant lesions, especially low degree tumors have relaxation times like elongated T1 and T2 relaxation times of benign masses. In T1-weighted MR sequences they are seen to be close the muscles and low intensity, in T2-weighted MR images they are seen to be hyperintense. Aggressive malignant tumors are more likely to give low signal in T1- and T2-weighted MR sequences [3]. This situation is related to rational decrease of water and increasing cellularity as a result of increasing mitotic activity. Structure of malignant mass can be homogeneous even though it is heterogeneous in most of the cases. Necrosis areas and cystic constituents which are strengthening findings in definition of malignant tumors are screened to be hypointense in before and after contrast T1-weighted MR images; high signal in T2-weighted MR images. When necrosis is found, inflammatory lesions should also be taken in consideration [4]. Even though edge irregularity and bad edging make malignity possible, they are not trustable findings for generalization. Especially, low valued mucoepidermoid tumors which are most common parotid gland malignity are visioned to have good edged and homogeneous masses at surface parotid lobs [3]. Even though conventional MRI findings are important they cannot let us make benign-malignant lesion differentiation by themselves. In this thesis, we have found in line with the literature findings that in the routine MRI of neck there is no meaningful difference in benign-malignant lesion differentiation except dynamic contrasting and in line with above mentioned parameters. It has been experimentally shown and clinically proven that ADC value is affected from tumor morphology to include nucleus cytoplasm ratio and cellular density and ADC value has a reverse relation with tumor cellularity [5, 6]. Examinations where ADC values and histopathological results are compared it has been strongly shown that more dense cellularity is highly related with diffusion limitations. But, in addition to cellularity, specifications of extracellular components has an effect on ADC values. It has been known specifically, that salivary gland tumors show widespread histologic spectrum. As a result, tumor tissue contrast has been widely affected from level of tumor cell differentiation, presence or absence of necrotic tissue and cist presence, myxomatous differentiation and variety of percentages on tumor tissue components. Whereas the aggressive tumors are screened to be hyperintense in DW-MRI in relation to limitation of diffusion; necrosis fields in tumors are differentiated to be hypointense in DW-MRI and hyperintense (high ADC value) in ADC mapping. Tissues that are not tumoral like edema, inflammation, fibrosis and necrosis are expected to screen low cellularity. This will result in high ADC value. Solid areas with ADC values of 1.80x10-3 mm^2/sec and high are informed to be more in benign tumors with respect to malignant tumors by the Eida and friends [7]. Average ADC value has been measured to be meaningfully higher in benign lesions with respect to malignant lesions in our thesis too (p=0.032). In our thesis highest fact number have been measured to be squamous cell carcinoma in malignant group and pleomorphic adenoma in benign group with average ADC values measured in line 0.105+/-24x10-3 mm^2/sec and 0.184+/-4x10-3mm^2/sec and to be in accordance with literature. In the squamous cell carcinoma events Nucleus-cytoplasm ratio with 0.25-2 and tumor-stroma ratio between 1.5-4 were showing a widespread diffusion, necrosis was either there with different levels or not existent. Myxoid/chondroid matrix-epithelium ratio on Pleomorphic adenomas was changing between 0.5-4.

Pleomorphic adenoma frequently show myxoid and/or chondroid matrix specifications [8]. Myxoid and chondroid matrixes of these tumors shows large amount of free liquid. For this reason, this histopathologic finding specific to salivary glands is seen to be related with ADC values. Motoori and friends represent the importance of differentiation of myxomatous tissue with MRI on differentiation between pleomorphic adenoma and malignant tumors in a different thesis of them they have informed that high ADC values in pleomorphic adenoma is related with myxoid and/or chondroid matrix specifications [9]. In our thesis, we had 6 cases of pleomorphic adenoma and average ADC values were measured to be 0.184x10-3mm^2/sec +/- 42. As the patient number was low in other salivary gland tumor subgroups which prevented us to make a comparison, the average value was 0.083x10-3mm^2/sec in 2 cases with Warthin's tumor we had.

We have defined 8 malignant and 14 benign to make 14 total histopathologic finding. Despite the number of different finding, as total number of cases for each group was too low, we could not get meaningful statistical results. Even though this is the case, in the squamous celled carcinoma events, which has the highest repeating number; Nucleus-cytoplasm ratio with 0.25-2 and tumor-stroma ratio between 1.5-4 were showing a widespread diffusion, necrosis was either there with different levels or not existent. In the same direction, Myxoid/chondroid matrix-epithelium ratio on pleomorphic adenoma as the most common in benign group, was changing between 0.5-4. By this way, we have shown that even in one histopathologic type there can be a wide differentiation of parameters. The effect of this widespread differentiation on ADC values can only worked with larger series.

The main limitation for our work was the retrospective design and inefficiency of the number of cases in each sub-groups and in total. With this in mind, meaningful difference in average ADC values showed that DW-MRI supplies an additional advantage in MRI examination of neck.

MRI is an indispensable screening method for advanced examination of soft tissue lesions because of high contrast resolution. In addition to conventional examinations advanced technical methods to define the nature of lesion like DW-MRI is needed. Even though, DW-MRI by the way of measuring ADC values as a reflection of the changes in the microenvironment of the live tissue helps to characterization of the lesion, it is not apparent yet how much it is affected from a number of variables.

Conclusion

In conclusion, we have shown that with routine contrasted MRI parameters differentiation of benign-malign cannot be made and there is statistically significant difference in average ADC values of DW-MRI between benign-malignant lesions. However in diagnostic algorithm DW-MRI and MRI findings should be evaluated together not on their own. Histopathologic correlation with DW-MRI should be worked in larger number of series for each anatomic structure and lesion type thus this will help to define threshold ADC values and role of tissue parts affecting the diffusion values.

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