International Journal of Medical Imaging
2016; 4(1): 1-6
Published online February 19, 2016 (http://www.sciencepublishinggroup.com/j/ijmi)
doi: 10.11648/j.ijmi.20160401.11
ISSN: 2330-8303 (Print); ISSN: 2330-832X (Online)

Role of Diffusion Weighted Imaging in Differentiating Benign from Malignant Head and Neck Tumors

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To cite this article:
Haney Heneidy, Waled Yosef. Role of Diffusion Weighted Imaging in Differentiating Benign from Malignant Head and Neck Tumors. *International Journal of Medical Imaging.* Vol. 4, No. 1, 2016, pp. 1-6. doi: 10.11648/j.ijmi.20160401.11

Abstract: Head and neck mass is considered to be a relatively common finding in adult and pediatric patients and can present a difficult diagnostic challenge. Differentiation of benign head and neck tumors from malignant lesions are important for treatment strategy as well as for predicting prognosis of malignant tumors. The aim of this work is to review the role of diffusion MRI scan in differentiation between benign and malignant head and neck masses This study was performed on 72 patients (30 men and 42 women aged from 13 years to 85 years, mean age of 51 years) with head and neck mass, in the period from September 2012 until May 2014. We found that DWI is a reliable noninvasive imaging tool to help in differentiation between malignant and benign head and neck lesions and also to identify the tumor-free soft tissue in patients with head and neck neoplasms. It could be performed with conventional MR systems in few minutes time, Further studies on larger number of patients is required to assess if such a technique should be implemented routinely with conventional MRI scan.

Keywords: Head and Neck, Diffusion MRI, Tumors, Benign, Malignant

1. Introduction

Head and neck mass is a considered to be a relatively frequent pathology in adult and pediatric patients with the Head and neck squamous cell carcinoma as the fifth cancer worldwide to date. Getting an adequate demarcation between benign and malignant head and neck tumors is a fundamental requirement in proper management of those lesions and in estimating the future planes for them. Currently, Fine needle aspiration biopsy is the commonest diagnostic test for differentiating between benign and malignant head and neck lesions. Side effects of tissue sampling is invasive and may not be representative of the entire tumor and also carries the hazards of hemorrhage infection, and seeding along the needle tract [1, 2].

Routine T1 and T2 MR are not sufficient to diagnose reliably if the tumor is benign or malignant. In spite of the invasive nature of the biopsy and its false positive or negative results, it is commonly used to resolve that problem of benignity or malignancy as a decisive tools to differentiate head and neck lesions. [2, 3].

Different tissue characterization obtained by using diffusion-weighted magnetic resonance (MR) imaging is different from that attained by using conventional MR techniques. The diffusion technique involves the diffusion of water protons in the tissues, and this technique produces different contrast in different types of tissue. Therefore, the findings of the diffusion MR scan can provide different characterization about pathological tissues [4-6].

Diffusion-weighted imaging (DWI) measures diffusion of water molecules in the examined tissues. Water molecules visible on MRI scan at 1.5 T are located mainly in the extracellular space (ECS) and can be quantified and analyzed by measuring the apparent diffusion coefficient (ADC). Malignant lesions that have more cells packing tend to have more restricted diffusion with the resultant smaller ADC measurements, while cancer treatments with chemotherapy or radiotherapy causing malignant cells destruction and eventual death increase water diffusion with subsequent associated higher ADC values. Currently, DWI is still under evaluation in a wide range of cancers of the brain, head, neck and body, as well as for assessment of function in organs such as the kidneys, pancreas, and salivary glands [5, 6]. In the head and neck it has been almost documented that diffusion scan is able to differentiate malignant tissue from normal tissue. DWI has a successful role in the evaluation

and follow up of head and neck tumors treatment response, tissue differentiation of primary tumors from lymph nodes deposits, differentiation of recurrent tumor from post-therapeutic changes, the detection of post operative residual tumors, the evaluation of salivary gland functions and in the discrimination diagnosis of the cystic and/or necrotic head and neck lesions. [7-9].

One of the challenges that faced the implementation of diffusion weighted MR imaging in head and neck was the susceptibility artifacts with resultant image distortion, however with the enhancement of echoplanner technique, some studies showed that such application might be successful especially if it could be used when there was a contraindication to contrast medium administration [10].

2. Aim

The aim of this work is to review the role of diffusion MRI scan in differentiation between benign and malignant head and neck masses with a special concern to those who are considered to be suspicious lesions.

3. Subjects and Methods

Seventy-two patients complaining from head and neck masses who came to our hospital between September 2012 and May 2014. All patients underwent routine sequence MRI with DWI. Thirty patients were males and forty-two were females with a mean age 51 years (table 1). The youngest was 13 years while the eldest was 85 years. Among the seventy-two patients there were seventy-five lesions. All patients had lesions larger than 1 cm in the greatest minimal transverse diameter on MR images and had undergone biopsy and some of them treatment with radiation therapy. When the patients had multiple lesions with the same histologic diagnosis, only the largest one was used for calculation of ADCs. The final diagnosis was done by FNA for cystic lesion (no= 11) or surgery (no=52). The inflammatory lymph node showed disappearance in 3 of them and remarkable decrease in size in the other 3. Almost all the children under 8 years old required anesthesia or sedation and were evaluated by anesthesiologist.

Table 1. *Shows the number and sex of patients.*

Patient character	Value
No. Of patient	72
Sex	M-30
	F-42
Age	Mean (51)
	Range (13-85)
No. of lesions	75

3.1. MRI Technique

MRI was done for all patients with 1.5 Tiesla Phillips machine using head and neck circular coil. Conventional MR was performed by using T2 weighted and T1 weighted images before and after contrast medium intravenous bolus injection of 0.2 ml kg−1 of body weight of gadopentate, dimeglumine, with slice thickness of 4 mm interslice gap of 0.5 mm. All patients underwent T1 weighted images (TR/TE of 523/15 ms) and T2 (TR/TE 4200/102 ms) fast spin echo.

Diffusion weighted images were done for all the patients. Field of view was 250x203 cm, matrix 156x104 with TR/TE 5000/84. In patients with cystic lesions the ROI encircled the whole cyst while in multiple lesions with the same pathology, we measured the apparent diffusion coefficient (ADC) of the largest one. An average of 20-25 slices was obtained in the axial plane covering the area of interest.

We asked the patient not to swallow as possible during imaging, together with minimizing acquisition time to 1 minute to reduce motion artifact. A qualitative analysis of the apparent diffusion coefficient map was done. The region of interest (ROI) was drawn using an electronic cursor delineating the margin of the solid components in different lesions trying to skip the cystic portions to avoid false positive results.

3.2. Statistical Analysis

Statistical analysis was done with the p value was considered significant when it was ≤0.05. We used the Statistical Package for Social Science for assessing the results and to perform data analysis for significant values. The Mann–Whitney U test were used to compare the results of pathology and ADC measurements of head and neck lesions and normal areas.

Table 2. *Shows the number and mean ADC value of different head and neck pathologies.*

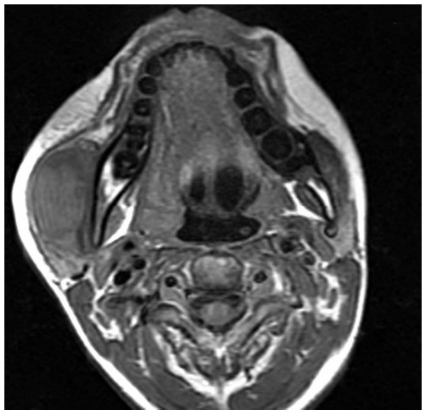
Diagnosis	Pathology	Number	Mean ADC ($10^{-3}mm^2/s$)
Malignant(no.=26)	Squamous Cell carcinoma of the oral cavity	15	0.89±0.09
	Malignant lymphoma	7	0.92±0.08
	Mucoepidermoid carcinoma	2	1.22±0.07
	Rhabdomyosarcome of the cheek	2	0.97±0.06
Benign(no.=30)	Haemangioma	14	1.73±0.11
	Inflammatory node	6	1.60±0.12
	Pleomorphic adenoma of the parotid	5	1.71±0.14
	TB lymph node	3	1.42±0.09
	Neurofibroma	2	1.62±0.13
Cyst(no.=16)	Retention cyst	4	2.4±0.11
	Thyroglossal cyst	4	2.08±0.11
	Ranula	3	2.2±0.06
	Dermoid	3	1.91±0.12
	Thornwald's cyst	2	2.00±0.13

4. Results

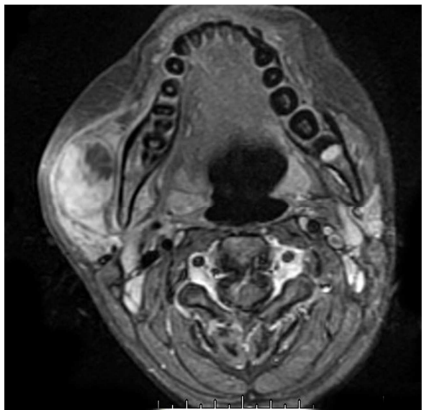
This study was performed on 72 patients (30 men and 42 women aged from 13 years to 85 years, mean age of 51 years) with head and neck mass, in the period from September 2012 until May 2014. They presented with swelling (n=72) and or pain (n=24). skin changes and discolorations were seen in 15 patients. The histopathologic diagnosis of the 26 malignant lesions was 16 Squamous cell carcinoma, 7 malignant lymphoma and 3 mucoepidermoid carcinoma. The number of benign lesions were 30, of which 14 were haemangioma, 6 were inflammatory nodes, 5 were pleomorphic parotid adenoma, 3 were TB lymph nodes and 2 were neurofibroma. There were 16 cystic lesions in the study; retention cysts were 4, Thyroglossal cyst were 4 and both Ranula and Thryoglossal cysts were 3 and 2 were Thornwaldt's cyst.

The mean ADC value for malignant lesions was 0.95±52 $x10^{-3}$, benign lesions was 1.65±61$x10^{-3}$ and cystic lesions was 2.13±0.41$x10^{-3.}$ There was significant difference in the mean ADC among the three categories ($P < 0.00$). The mean ADC value of cysts was significantly higher than that of both benign and malignant tumors.

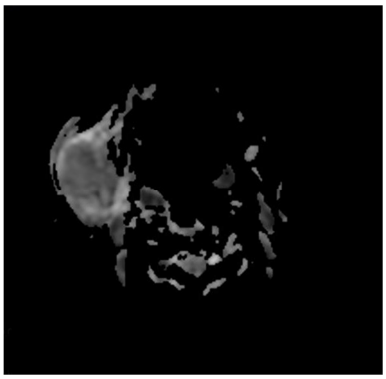
In this study there were 10 lymph nodes diagnosed as metastatic from other primary, 7 associated with malignant lymphoma, 3 with TB lymphadenopathy and 6 diagnosed as benign inflammatory lymph adenopathy.



1-a



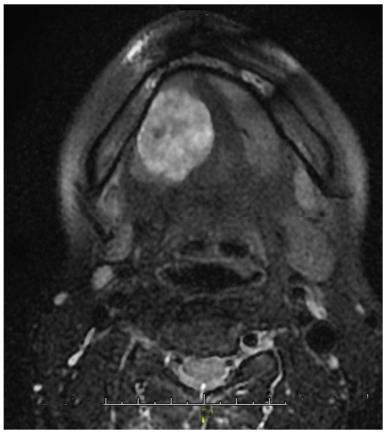
1-b



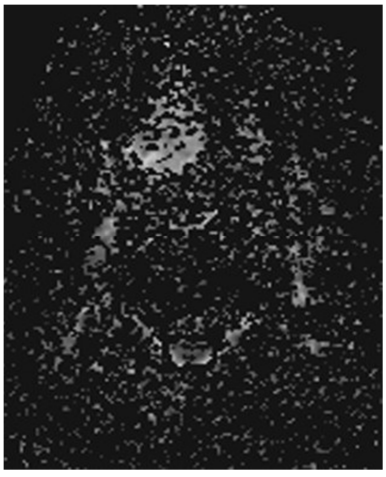
1-c

Figure 1. *Rhabdomyosarcoma.*

a. T1W non contrast image of the RT cheek showing intermediate signal lesion.
b. Contrast enhanced T1WI shows the hetergenous enhancement pattern of the lesion.
c. ADC shows diffusion restriction of the lesion.



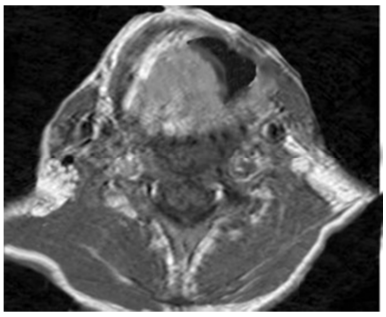
2-a



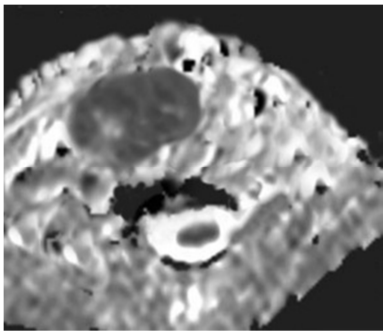
2-b

Figure 2. *Ranula.*

a. MRI T2 weighted image showing high signal intensity lesion in the floor of the mouth
b. ADC map and c, Diffusion scan showing high signal intensity of that lesion denoting no appreciable diffusion restriction.



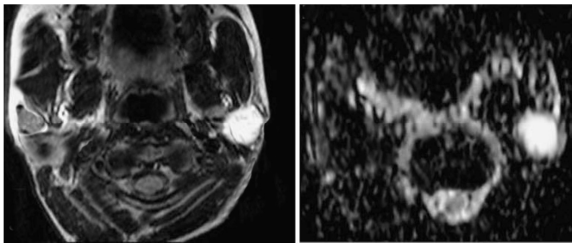
3-a



3-b

Figure 3. *Hypopharynx tumor.*

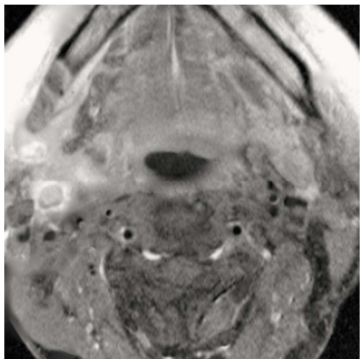
a. MRI Axial T1-weighted post-contrast MRI showing a primary hypopharyngeal enhancing tumor.
b. ADC map showing the tumor as a low signal clearly marginated from the surrounding tissue denoting apparent diffusion restriction



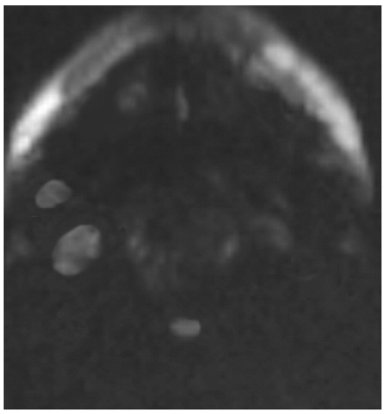
4-a 4-b

Figure 4. *Pleomorphic adenoma.*

a. Axial T2-weighted image shows mass of high signal intensity is seen in the left parotid gland
b. ADC map shows high signal intensity of the mass with high ADC value.(1.62Å~10–3 mm2 s−1)



5-a



5-b

Figure 5. *Squamous cell carcinoma of the oral cavity in 45 yeas old man showing.*

a. Axial T1-weighted contrast-enhanced with fat-saturation showing marginally enhancing two metastatic lymph adenopathy.
b. Diffusion scan showing high signal of the lymph nodes suggesting its metastatic nature. Histopathology examination revealed metastasis from primary squamous cell carcinoma.

5. Discussion

Diffusion of water protons in biologic tissues derives from the diffusion of extracellular water protons, transport of water protons through the cell membranes, and diffusion of intracellular water Protons. Measuring the ADC evaluate the random motion of water molecules and the microcirculations of the blood in the capillary network, in biologic tissues. It is clear that water molecules can move more freely in fluid than in solid tissues, it is generally accepted that the ADC value of cystic lesions is higher than that of solid lesions, hence, ADC value estimation is useful in definition of normal and pathological tissue, therefore, It is no surprise that the mean ADC values in benign nodules are higher due to the increased mobility of water proton. [11, 12].

Fibers and intracellular molecules in the tissues alter the motion. Since the water protons in each portion in the tissue behave differently to the diffusion of the tissue, any structural changes in the tissue, including the change in the proportion of intracellular to extracellular water protons, will alter the diffusion coefficient of the tissue Thus, signal intensity of DWI and ADCs of the tissues varies according to the microstructure and physiologic state of the tissues. In general condensed cellular malignancy have more restricted diffusion resulting in lower ADC values, while chemotherapy or radiotherapy malignancy treatments result in cell death with increase water diffusion leading to up rise value in ADC. [7, 13-15].

In this study, the ADC value of cyst (mean 2.13×10^{-3} mm^2/s) was significantly higher than that in malignant tumors (mean 2.13×10^{-3} mm^2/s and $P<0.004$) and benign tumor (mean value was $1.65x10^{-3}$ mm^2/s), this could be explained by the free mobility of water in fluid more than other tissue. This is matching with previous study done by Thoeny et al [4] who stated that results from DW imaging investigations have shown that there is a significant

difference in mean ADCs of these three groups of tumors, namely cysts, benign tumors and malignant tumors. Initially promising results in which ADC thresholds were used to help differentiate benign from malignant parotid gland lesions.

Diffusion scan was diagnostic for cyst with the sensitivity, specificity, accuracy, PPV, and NPV were 94%, 88%, 90%, 71%, and 98%, respectively. The benefit of this is to skip the administration of CM if there was contraindication. [16]

The results of this study demonstrated that benign vascular lesions as hemangiomas (mean 1.73) show higher ADC values than that of the other benign solid tumors such as neurofibroma (mean 1.62) and TB lymph node (1.42) due to excess extracellular spaces with free diffusion within the vascular lesions however, this was not statistically significant. TB lymph nodes (mean 1.42) showed statistically insignificant difference with lower ADC values than that of inflammatory nodes (mean 1.60) probably due to caseous material in granulomatous nodes with subsequent restricted diffusion. This was in concordance with Razek et al [2] who stated that, the mean ADC value of malignant pediatric head and neck tumors was significantly lower than that of benign solid and cystic lesions. This is explained by difference in histopathology characteristics of the benign and malignant neoplasms. Malignant tumors have prominent size and stain of its nuclei and curvature of nuclear margin, and they show increased cellularity. These histological characteristics reduce the extracellular component and the diffusion of protons in the extracellular and intracellular fields with a subsequent decrease in ADCs, furthermore they stated that poorly differentiated malignant tumors showed lower ADC values than those of well differentiated malignancy mostly due to greater cellularity of poorly differentiated tumors. In this study, the ADC of 7 malignant lesion showed significant lower value of ADC than rest of malignant lesion, and all the 7 were of low differentiated malignant nature, however a larger scale study on dedicated poorly differentiated malignant lesions is recommended in a trial to figure out a range value for highly malignant poorly differentiated malignant lesions.

In this study there were 10 lymph nodes diagnosed as metastatic from other primary, 7 associated with malignant lymphoma, 3 with TB lymphadenopathy and 6 diagnosed as benign inflammatory lymph adenopathy. Our results showed those with necrotic center were associated with malignancy rather than benign conditions. Koç O et al [8] reached almost to a comparable result and stated that necrotic lymph adenopathy is seen in malignant and TB lymphadenopathy. Central nodal necrosis is important nodal characteristic of metastatic nodes from head and neck primary cancers but they cannot differentiate them from the abscess and lymphadenitis by conventional MRI.

6. Conclusion

DWI is a reliable quantitative assessment-imaging tool to help in differentiation between malignant and benign head and neck lesions and also to identify the tumor-free soft tissue in patients with head and neck neoplasms. It could be performed with conventional MR systems in few minutes time as a fast sequence not requiring a contrast agent, Further studies on larger number of patients is required to assess if such a technique should be implemented routinely with conventional MRI scan. The advantages of DW-MRI in this aspect are entire tumor coverage and safety in the assessment performed.

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