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Usefulness Of Diffusion Weighted Mr-Imaging And Apparent Diffusion Coefficient Values In Evaluation Of Neck Masses

Samar M. Shehata, Asmaa A. Alshamy, Hanan A. Bahaaeldin

Department of Radiology, Faculty of Medicine, Zagazig University, Egypt
Corresponding author: Asmaa A. Alshamy

ABSTRACT

purpose: The aim of this study was to evaluate the role of DW- MRI & ADC value in characterization of neck masses as well as prediction of tumor response to therapy.

Patients and methods: This study included 110 pediatric patients (63 males and 47 females with a mean age of (40.46±17.93) years) with head and neck mass. Routine MR imaging and diffusion weighted MR imaging were done on a 1.5-T MR unit using a single-shot echo-planar imaging (EPI) with a b factor of 0, 500 and 1000 s mm−2. The ADC value was calculated. The mean ADC values of the malignant tumors and benign masses were calculated.

Results: there was highly statistical significant difference (P< 0.001**) between means of benign and malignant swellings on MRI with ADC findings, with mean ADC value of malignant tumors was 0.98±0.20 and that of benign tumors was 1.76±0.39.

Conclusion: DWI is a simple, noninvasive and not time consuming imaging modality that if added to conventional MR imaging can increase sensitivity and specificity in differentiating between benign and malignant neck masses.

Keywords: Usefulness Of Diffusion Weighted Mr-Imaging, Apparent Diffusion Coefficient Values, In Evaluation Of Neck Masses

Correspondence:
Asmaa A. Alshamy,
Department of Radiology, Faculty of Medicine,
Zagazig University, Egypt

*Corresponding author: Asmaa A. Alshamy

INTRODUCTION

The neck is a complex space with variant anatomic structures and the problem of having a neck mass is a relatively frequent pathology in adult and pediatric patients. Getting an adequate demarcation between benign and malignant neck tumors is a fundamental requirement in proper management of those lesions. **(1)**Imaging plays an important role in diagnosing lesions and also in differentiation of benign lesions from malignant lesions and staging of tumors that are important in determining the future planes for neck masses. While conventional imaging methods mainly evaluate morphological properties, their value is limited in recognizing prognostic characteristics such as benign-malignant differentiation of lesions. **(2)** Diffusion-weighted magnetic resonance imaging (DW-MRI) is a short sequence produced from EPI, FASE, SPLICE sequences. DW-MRI is sensitive to the randomized (Brownian) motion of water molecules at a microscopic level, so it provides functional information about tissues. **(3-5)**Malignant lesions with rapid growth and 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. DW-MRI was initially used to diagnose early stroke in the brain and to evaluate brain masses. **(3-5)** Currently, DWI is still under evaluation in a wide range of cancers of the head and neck as well as for assessment of function in organs such as the kidneys, pancreas, and salivary glands**. (6,7)** The aim of this study is to review the role of diffusion MRI scan in differentiation between benign and malignant neck masses and in detection of tumor response to radiotherapy by discrminating between tumor recurrence and post radiotherapy necrosis.

SUBJECTS AND METHODS

This study included 110 patients with neck lesions; 63 males and 47 females, their age ranged from 2.5 years to 66 years with a mean age of (40.46±17.93) years. Patients were referred from the Otorhinolaryngology (ENT) department, Radiotherapy department, Oncology center and Pediatric hospital to the Radiodiagnosis department; zagazig University Hospitals during the period from February 2016 to August 2019.All patients were subjected to the Clinical assessment and history of operation or radiotherapy and DWI MR examination. The patients excluded from this study included those with general contraindication to MRI or to Gadolinium administration. Ethical consideration had been approved by the ethical committee of faculty of medicine, zagazig university. An informed consent in Arabic was obtained from all participants. Finally, histopathological confirmation (94.5%) was obtained either by surgical biopsy or FNAC and compared to DW –MRI results and follow up (5.5%) in patients with suspected inflammatory LN.

MRI TECHNIQUE

All patients underwent MRI examination using 1.5 tesla superconductive magnet **(Philips Achieva)** using standard head and neck coil. Patients were instructed to avoid movement, coughing or swallowing. Our MR protocol included Axial T1WIs, T2WIs & STIR, coronal T1WIs, T2WIs (or STIR), Axial DWIs & ADC map, axial, coronal & sagittal T1WIs post contrast (with fat suppression). Then ADC value was measured within the lesion. Parameters of the conventional MRI sequences was included at

TABLE 1.

	T1	T2	STIR
TR	500 ms	3.0s	3.0s
TE	11 ms	100 ms	150 ms
Matrix	512×512	512×512	512×512
Slice Thickness	5mm	5mm	5mm
Field of view (FOV)	220mm	220mm	220mm
Slice Gap	1–2 mm	1–2 mm	1–2 mm

Table 1: parameters used in conventional mri sequences

DIFFUSION WEIGHTED MRI PROTOCOL

DWI was achieved at b factors of 0 ,500 and 1000 sec/mm2. Images were Carried out on the same MR imager **(Philips Achieva)** with gradient strength of 33 mT/m. Single-Shot Echo-planar diffusion sensitized sequences (TR 3.4s, TE 99ms, matrix 512×512, slice-thickness 3mm with an interslice gap of 1mm and FOV 230 mm) were acquired on the axial plane. Trace ADC maps (automatically constructed by software of MR unit). Evaluation of the quality of diffusion weighted images and ADC map was performed. We excluded non acceptable examination with images distortion or ghosting artifact.

STATISTICAL ANALYSIS

The collected data were coded, entered, presented, and analyzed by computer using a data base software program, Statistical Package for Social Science (SPSS) version 20. Optimum cut off value of ADC values with highest accuracy were estimated using region operator characteristic (ROC) curve and The results were considered statistically significant and highly statistical significant when the significant probability (P value) was **< 0.05*** and **<0.001**** respectively.

RESULTS

The distribution & mean ADC values of the lesions according to histopathology findings are showen in table 2 for malignant lesions & table 3 for benign lesions.

Histopathology findings (Malignant Lesions)	**No**	Mean± SD
Squmaous cell carcinoma of neck origin (primary) involving: ▪ SCC of nasopharynx ▪ SCC of tongue ▪ SCC of epiglottis ▪ SCC of larynx	28 16 6 3 3	1.05±0.65
Lymphoma	8	0.8±0.35
Thyroid carcinoma	4	1.04±0.45
Metastatic lymph nodes	4	1.07±0.56
Rhabdomyosarcoma	3	1.03±0.21
Adenoid Cystic Carcinoma	3	1.04±0.46
Mucoepidermoid carcinoma	2	1.05±0.76

Table 2 shows the distribution & mean ADC values of the malignant lesions according to histopathology

Histopathology findings (Benign lesions)	**No**	Mean± SD
Pleomorphic adenoma involving: ▪ Parotid gland ▪ Minor salivary gland	21 16 5	1.68±0.55
Benign inflammatory lymphadenopathy	11	1.48 ±0.48
Oncocytoma	3	1.43±0.34
Schwannoma	3	1.97±0.65
Ranula	3	2.31±0.66
Thyroglossal duct cyst	3	2.24±0.73
Aggressive fibromatosis	3	1.61±0.45
Post-operative changes	2	1.53±0.30
Haemangioma	2	1.89±0.42
Warthin tumor	2	0.86±0.57
Abscess	2	1.019±0.62
Amelobalstoma of mandible	1	1.09 ±0.54
Thornwaldt's cyst	1	2.21±0.53
Spindle cell fibroma	1	1.06±0.34

Table 3 shows the distribution & mean ADC values of the benign lesions according to histopathology

The mean ADC value of the malignant tumors and benign lesions were 0.98±0.20and 1.76±0.39×10-3 mm2/s, respectively. There was highly significant difference between ADC value of benign and malignant lesions (P < 0.001).

ROC analysis was used to detect the cutoff value differentiating malignant from benign lesions (Fig. 1). The area under the curve was 0.954. When 1.25 ×10-3 mm2/s was used as the cutoff ADC to distinguish between benign and malignant lesions, sensitivity was calculated as 98.07% and specificity as 93.1%.

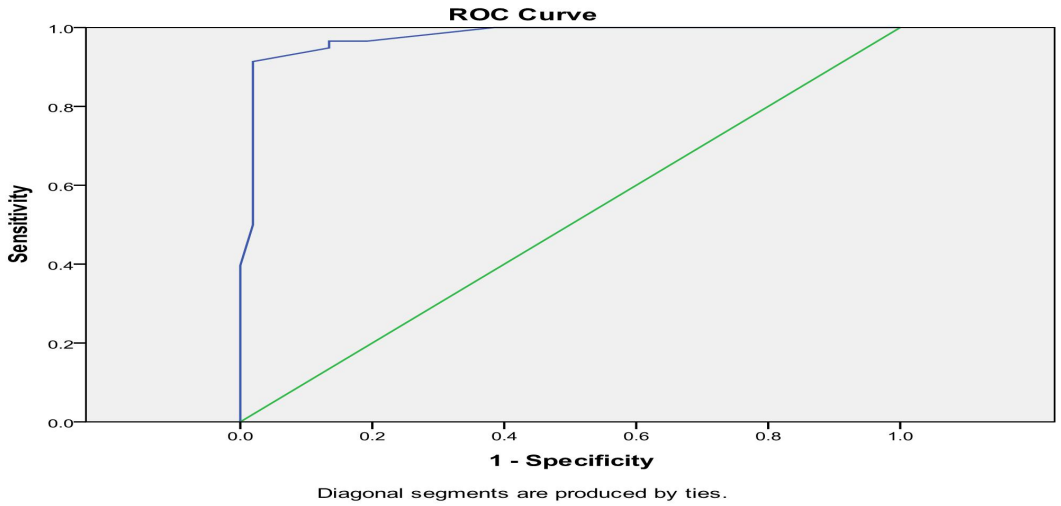
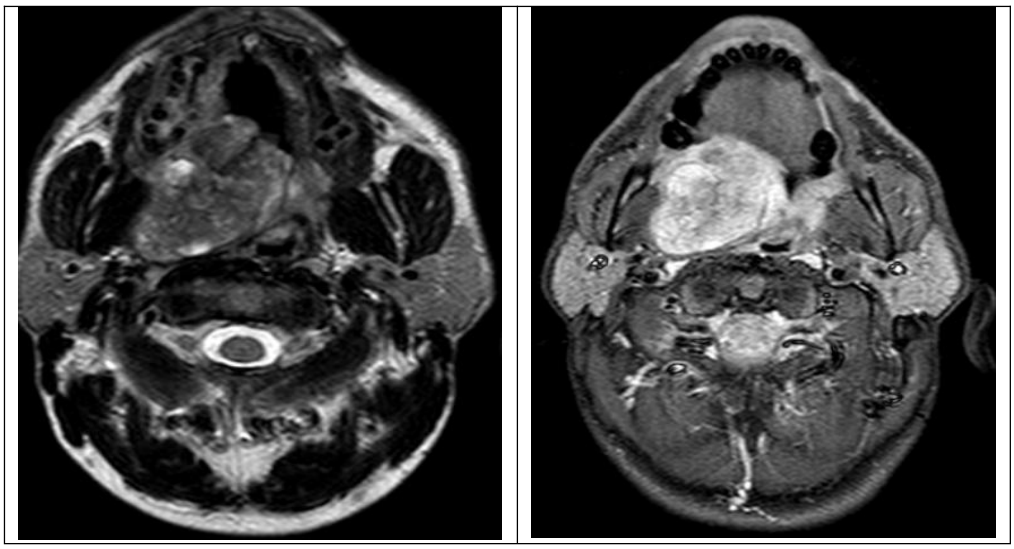


Fig.1: Roc curve showing accuracy of ADC as a screening test for malignancy.

In 58 benign lesions, 15 lesions (22.4%) were of inflammatory nature (3 cases of inflammatory lymphadenopathy,8 cases of reactive lymphadenopathy ,2 cases of abscess and 2 cases with post-operative changes), while 43 lesions (77.6%) were non-inflammatory (tumoral lesions and benign non-inflammatory cysts).There was no statically significant difference (P value 0.0084) between ADC value of benign inflammatory (1.78 ± 0.43 $x10^{-3}$ mm^2/sec) and benign non-inflammatory lesions (1.76 ± 0.50 $x10^{-3}$ mm^2/sec).In 52 malignant lesions, 28 were diagnosed by histopathology as squamous cell carcinoma and the remaining 30 cases were of non-squamous cell origin. There was no significant difference between ADC value of squamous cell carcinoma and non-squamous cell carcinoma (NSCC) with mean ADC value for SCC about 1.0043±0.155×10-3 gmm2/s and mean ADC value for NSCC about 0.95±0.26×10-3 mm2/s (P value 0.00214) and lymphomas had the lowest ADC value among malignant lesions (0.9±0.35).



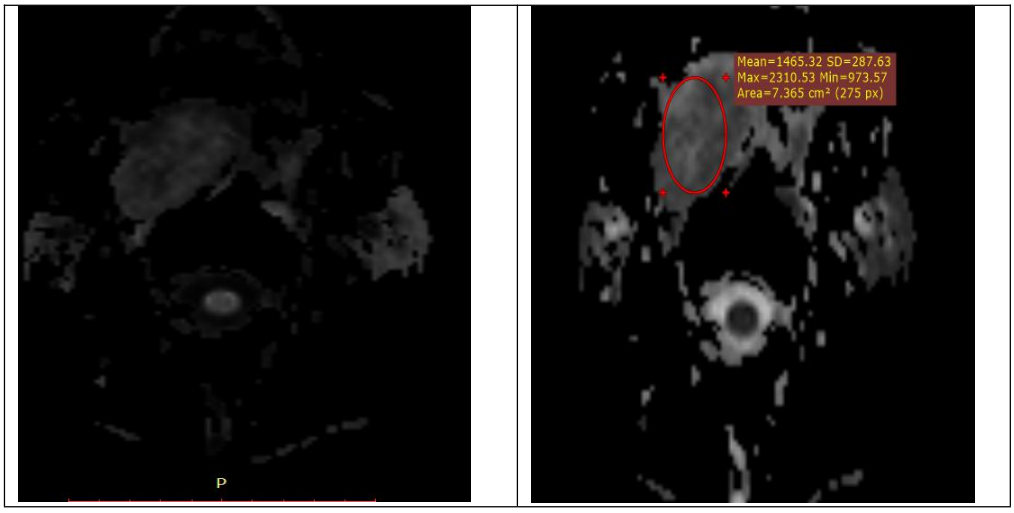


Fig. (2):40-year-old male patient with painless swelling in the upper right palatal region ago MRI examination demonstrated a large ovoid soft tissue mass with clear margins originating from the posterior soft palate A) Axial T2WI shows that the mass has heterogeneous signal intensity. B) Axial STIR image shows the mass has hyperintense signal. C) DWI show hypointense signal of the mass & D) ADC map show hyperintense signal with ADC value about 1.42x $10^{-3} mm2/sec$ .....denoting facilitated diffusion. Histopathological diagnosis confirmed__Pleomorphic adenoma of the minor salivary glands of the palate

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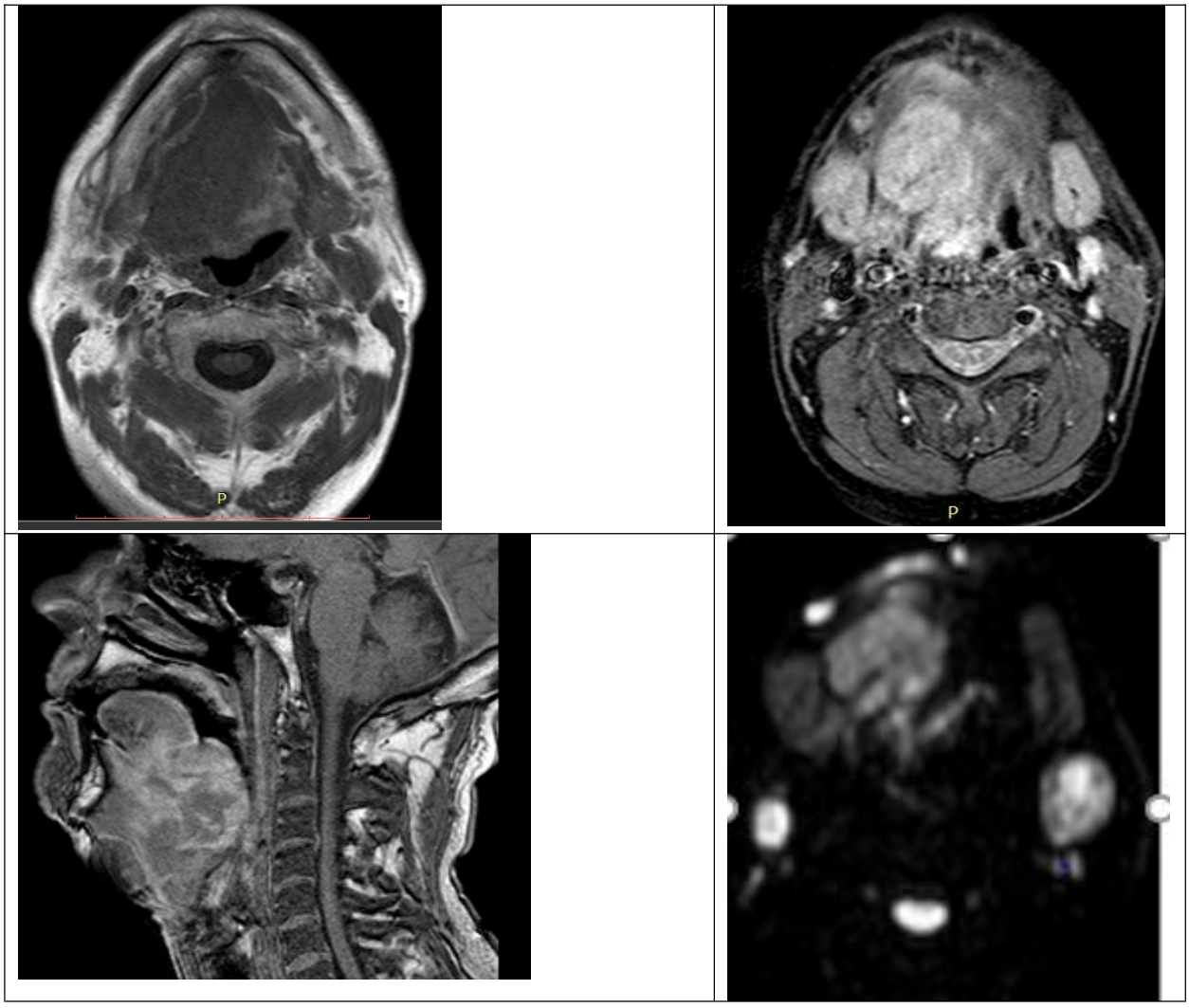

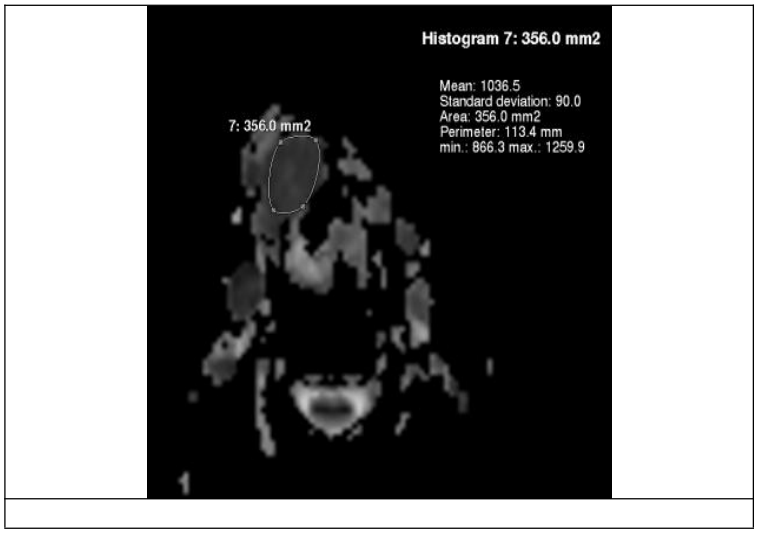

Fig.3:52-year-old Male patient, with enlargement of the tongue.Contrast enhanced MRI & DWI was done revealing large ill-defined infiltrative soft tissue mass centered on the epiglottis displaying low SI on axial T1WI **(A),** high SI on T2WI **(B),** heterogeneous post contrast enhancement on post contrast study **(C).** On **D)**DWI it shows high SI of the mass **&E)** ADC map shows the mass is hypointense (restricted diffusion) with ADC value = 1.03x $10^{-3}mm2/sec$ .Histopathological diagnosis:Epiglottic squamous cell carcinoma.

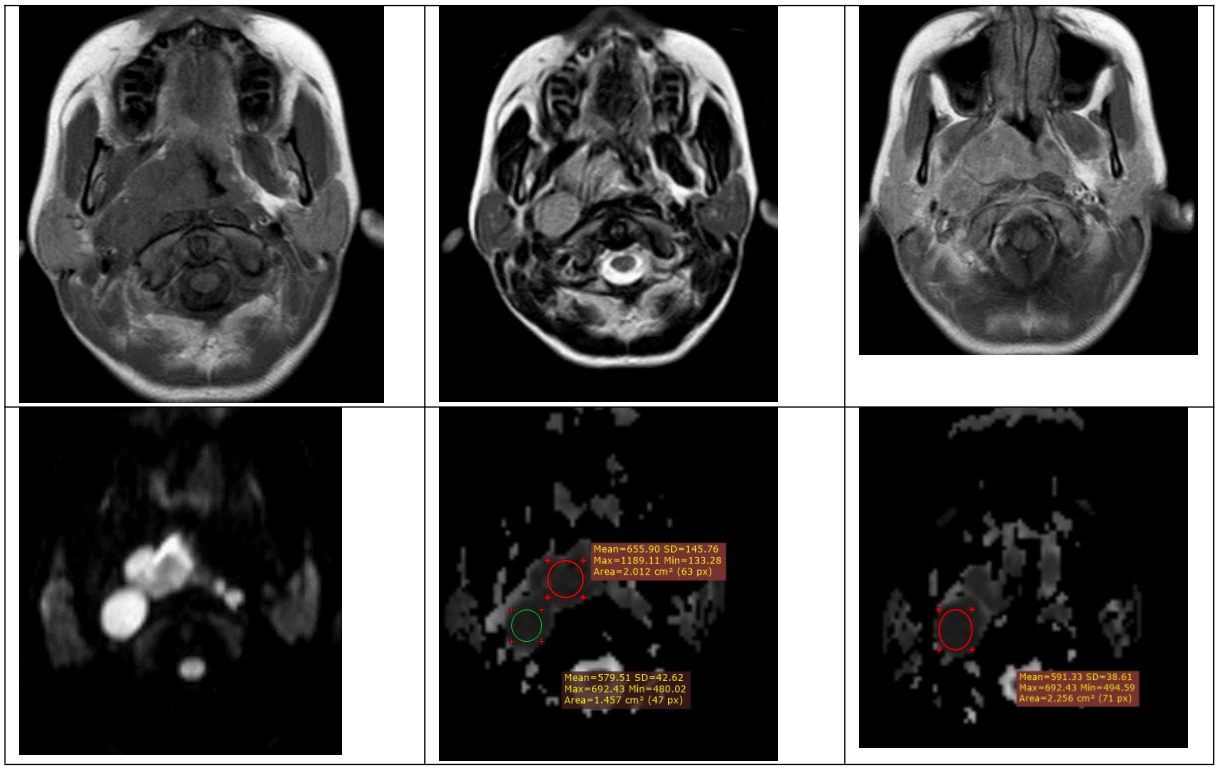

Fig.4: 9 years old boy with history of multiple neck swellings. A) Axial T1WI show large RT nasopharyngeal mass obliterating the related airways, it shows low SI associated with multiple bilateral upper and lower deep cervical lymph nodes more on the RT side. B) Axial T2WI show the mass and LNs of intermediate to high SI. C) Axial T1WI post contrast demonstrate heterogenous enhancement of both the mass and LN.D) DWI show high SI of the mass and LN matched with low SI of the mass and LN on ADC map (E& F) with ADC value (0.665x $10^{-3}mm2/sec$ for the mass) & (0.591x $10^{-3}mm^2/sec$ for the LN) denoting restricted diffusion.Histopathological diagnosis:Non- Hodgkin lymphoma.

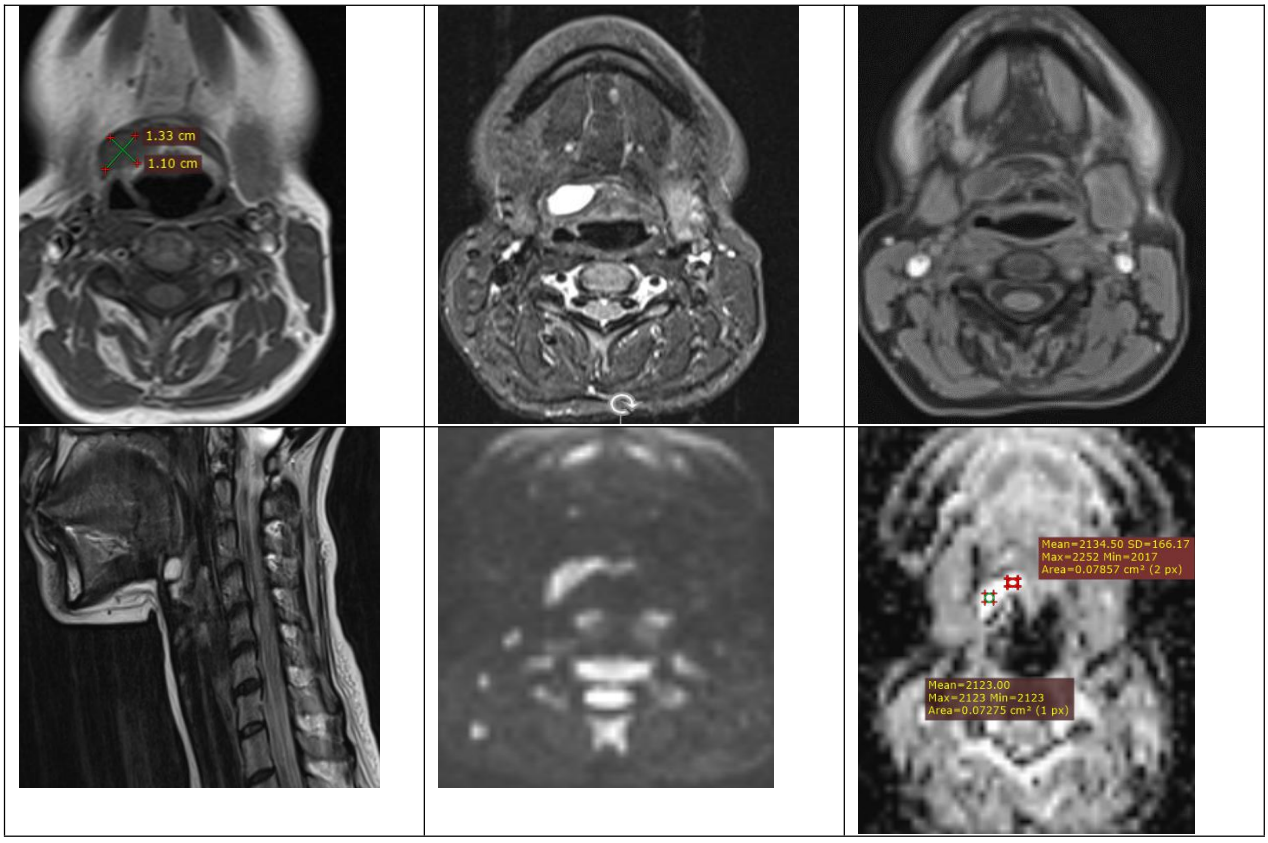

Fig.5:14 years old female patient presented with painful small swelling at the neck. **A)** Axial T1-WI & **B)** Axial T2 with fat suppression show well defined pear shaped cystic lesion, intimately related to the right aspect of the hyoid bone displaying low to intermediate signal intensity on T1 & high T2 signal with no surrounding reactive changes.**C)** Axial T1 post contrast fat saturated image shows peripheral enhancement. **D)** sagittal T2WI confirm the intimate relation of the lesion to the hyoid bone. **E)** DWI show low SI of the lesion matched with high SI on ADC map **F)**with high ADC value (2.13x $10^{-3} mm^2/sec$)...facilitated diffusion.**Histopathological_diagnosis:_**Thyroglossal duct Cyst

DISCUSSION

Differentiation of malignant head and neck tumors from benign lesions and accurate definite diagnosis are essential for treatment planning as well as for prognosis of malignant tumors. Conventional MRI is often nonspecific for the distinction between most tumors in the head and neck, **(8)** Moreover, post-treatment changes can be difficult to separate from tumor recurrence, as both entities may present with similar imaging features. Advanced MR imaging techniques provide information regarding the metabolic, molecular and pathophysiological aspects of a tumor. These techniques include the use of proton and phosphorous MR spectroscopy, dynamic contrast-enhanced MR imaging and diffusion-weighted imaging in initial diagnostic characterization of head and neck cancers. **(9)** Diffusion-weighted echo-planar MR imaging is a technique for evaluating the rate of microscopic random water diffusion in tissues. The degree of translational diffusion of different molecules measured in the human body is known as the ADC. The ADC is expected to vary according to the cellular density of the lesion. **(10)** The aim of this study was to evaluate the role of DWI and ADC value measurement in the characterization of different neck lesions.Our study indicates that quantitative ADC mapping instead of qualitative DWI imaging, can provide valuable information in differentiating benign and malignant lesions, with a significant difference between mean ADC of solid malignant lesions versus mean ADC of solid benign lesions (p = 0.001).**Our study agrees with** most studies in the literature with a statistically significant difference between the ADC values of benign and malignant (P< 0.001**) as the mean calculated ADC value for benign lesions was 1.76±0.39x 10−3 mm2/sec and the mean calculated ADC value for malignant lesions was 0.98±0.2x 10−3 mm2/sec. This is explained by the difference in histopathologic features of the benign and malignant tumors.This is matching with results of similar study by **EL-Shahat et al., 2013(11),** who found that the mean ADC value of malignant tumors was (1.02 ± 0.22) and the mean ADC value of benign tumors was (1.62 ± 0.27). Also, a study by **Heneidy and Yosef, 2016(12),** showed that the mean ADC value for malignant lesions was 0.95±52 x10-3, benign lesions was 1.65±61x10-3 and cystic lesions was 2.13±0.41x10-3. 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. Similar results were found in our study, as the ADC value of benign cystic lesions (mean 2.03±0.43 × 10−3 mm2/s) was significantly higher than that in malignant tumors and benign solid tumors, this could be explained by the free mobility of water in fluid more than other tissue.Upon ROC curve analysis we found that the ADC value 1.25x10−3 mm2/s can be used as cut off value for differentiating between benign

and malignant neck lesions with an accuracy of 95.4%, sensitivity of 98.07%, specificity of 93.1%, positive predictive value of 92.7% and negative predictive value of 98.2%. ROC curve analysis of similar study by **El Shahat et al,2013, (11)** revealed that the threshold ADC value (1.2) x 10-3 mm2/s used for differentiating between benign and malignant head and neck lesions had an accuracy of 94%, sensitivity of 95%, specificity of 92%, positive predictive value of 92% and negative predictive value of 94%. Similarly, **Abdel Razek et al., 2009, (1)** found1.25×10-3 mm2/s ADC value had a sensitivity of 94% and a specificity of 91% for benign-malignant mass differentiation in a study of head and neck masses in pediatric patients. However, **Sakamoto et al., 2009, (13)** used a threshold ADC value of 1.61×10-3 mm2/s and contrary to the previous literature they found that there was no statistical difference between the ADC values of benign and malignant masses. This was linked to the wide range of variations in ADC values due to tumor cellularity, cystic or necrotic component and presence of fibrosis. On the other hand, a study by **Vandecaveye & De Keyzer ,2013**, **(14)** stated that it is unlikely that a generalized use of ADC with a single determined threshold is feasible for lesion differentiation in the head and neck region, he attributed this to the broad range of both malignant and benign histological entities in the head and neck.Our study showed no statically significant difference (P value 0.0084) between ADC value of benign inflammatory (1.78 ± 0.43 x10^{-3} mm^2/sec) and benign non-inflammatory lesions (1.76 ± 0.50 x10^{-3} mm^2/sec). **This was in agreement with Şerifoğlu et al., 2015, (15) they** stated that in benign lesions, the median ADC value of inflammatory and non-inflammatory lesions were 1.13×10-3 mm2/s (range, 0.85–2.38×10-3 mm2/s) and 1.27×10-3 mm2/s, (range, 0.52–2.33×10-3 mm2/s), respectively. So, the ADC value of inflammatory lesions did not significantly differ from those of non-inflammatory benign lesions (P = 0.910). However, in disagreement with a study done by **Kito et al., 2006, (16)** conducted that it is possible to distinguish inflammatory and non-inflammatory tissues using DW-MRI, without contrast material. The median ADC value of inflammatory lesions (1.13×10-3 mm2/s) was lower than the median ADC value of non-inflammatory benign lesions (1.26×10-3 mm2/s), but there was no statistically significant difference between the ADC values of the two groups. **Şerifoğlu et al., 2015 (15)** concluded that this may be because benign mass lesions are regarded as non-inflammatory in our study un like previous studies in which normal tissues are regarded as non-inflammatory. As a result, the wide histopathological variety among non-inflammatory benign lesions affected our results.In our study, there was no significant difference between ADC value of squamous cell carcinoma and non-squamous cell carcinoma (NSCC) with mean ADC value for SCC about 1.0043±0.155×10-3 gmm2/s and mean ADC value for NSCC about 0.95±0.26×10-3 mm2/s (P value 0.00214).This was similar to the study by **Şerifoğlu et al., 2015**, **(15)** who found that when carcinomas of head and neck were divided into SCC and non-SCC groups, the median ADC value of non SCC group tumors was 0.74×10-3 mm2/s (range, 0.63–1.51×10-3 mm2/s). There was no significant difference between ADC value of these tumors (P = 0.799)

CONCLUSION

The addition of DWI to MRI protocols in the evaluation of head and neck malignancies increases lesion detection and helps the differentiation process between both solid and cystic lesions and benign from malignant lesions es at anatomical locations where a biopsy is difficult to obtain.DWI does not require administration of a contrast agent and thus, is completely noninvasive and the DWI data is acquired with a relatively short acquisition time .Finally data processing tools required to compute ADC maps are generally available on clinical scanners. Thus, the DWI sequence can be easily implemented in routine clinical protocol for neck MRI.

REFERENCES

1. Abdel Razek AAK, Gaballa G, Elhawarey G, Megahed AS, Hafez M, Nada N. Characterization of pediatric head and neck masses with diffusion-weighted MR imaging. Eur Radiol. 2009; 19: 201-208.
2. Driessen JP, van Kempen PM, van der Heijden GJ, et al. Diffusion-weighted imaging in head and neck squamous cell carcinomas: A systematic review. Head Neck 2015; 37:440–448.
3. Kim YJ, Chang KH, Song IC, et al. Brain abscess and necrotic or cystic brain tumor: discrimination with signal intensity on diffusion-weighted MR imaging. AJR Am J Roentgenol 1998; 171:1487–1490. [CrossRef]
4. Schaefer PW. Applications of DWI in clinical neurology. J Neurol Sci 2001; 186:S25–S35. [CrossRef]
5. Moseley ME, Kucharczyk J, Mintorovitch J, et al. Diffusion-weighted MR imaging of acute stroke: correlation with T2-weighted and magnetic susceptibility-enhanced MR imaging in cats. AJNR Am J Neuroradiol 1990; 11:423–429.
6. Hatakenaka M, Nakamura K, Yabuuchi H, et al. Pretreatment apparent diffusion coefficient of the primary lesion correlates with local failure in head-and-neck cancer treated with chemoradiotherapy or radiotherapy. Int J Radiat Oncol Biol Phys 2011; 81(2): 339–345.
7. King AD, Mo FK, Yu KH, et al. Squamous cell carcinoma of the head and neck: diffusion weighted MR imaging for prediction and monitoring of treatment response. Eur Radiol 2010; 20(9): 2213–2220.
8. Rodriguez I., Martín T., Luna A. (2012). Role of DWI in the Evaluation of Tumors of the Head and Neck and in the Assessment of Lymph Nodes.In: Diffusion MRI Outside the Brain. Springer, Berlin, Heidelberg. pp 307-338.
9. Chawla S, Kim S, Wang S, et al. Diffusion-weighted imaging in head and neck cancers. Future Oncol 2009;5(7):959–75.
10. Koh D, Collins D. Diffusion-weighted MRI in the body: applications and challenges in oncology. AJR 2007;188(6): 1622–35.
11. El Shahat H.M., Fahmy H. S., Gouhar G. K. (2013). Characterization of head and neck lesions with diffusion-weighted MR imaging and the apparent diffusion coefficient values.The Egyptian Journal of Radiology and Nuclear Medicine 44, 791–798.

12. Heneidy H. and Yosef W. (2016). Role of Diffusion Weighted Imaging in Differentiating Benign from Malignant Head and Neck Tumors.International Journal of Medical Imaging. Vol. 4, No. 1, pp. 1-6.
13. Sakamoto J, Yoshino N, Okochi K, et al. (2009): Tissue characterization of head and neck lesions using diffusion-weighted MR imaging with SPLICE. Eur J Radiol; 69:260–268.
14. Vandecaveye, V. and De Keyzer, F., (2013). Diffusion-weighted MRI in head and neck cancer: experience to date and future potential. Imaging in Medicine, 5(4), pp.319-331.
15. Şerifoğlu I, İlker I, Damar M, et al (2015). Diffusion-weighted imaging in the head and neck region: usefulness of apparent diffusion coefficient values for characterization of lesions. Diagn Interv Radiol, Turkish Society of Radiology.
16. Kito S, Morimoto Y, Tanaka T, et al. (2006): Utility of diffusion-weighted images using fast asymmetric spin-echo sequences for detection of abscess formation in the head and neck region. Oral Surg Oral Med Oral Pathol Oral Radiol Endod; 101:231– 238.