Original Article

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Radiology Section

Role of Apparent Diffusion Coefficient in Characterisation of Neck Masses-A Cross-sectional Study

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ABSTRACT

Introduction: Neck masses are frequently encountered in clinical practice and differential diagnoses of a patient presenting with a neck mass is wide. Diffusion-Weighted Magnetic Resonance Imaging (DW-MRI) is an imaging technique based on molecular diffusion. It is a very helpful complementary technique in distinguishing neoplastic from non neoplastic tissue and has numerous applications in the evaluation of head and neck masses especially in head and neck lymphadenopathy.

Aim: To evaluate the accuracy of Apparent Diffusion Coefficient (ADC) in differentiating benign and malignant neck masses.

Materials and Methods: A single-centre cross-sectional study comprising of 50 patients of all age groups with clinical suspicion of neck swelling was conducted in Department of Radiodiagnosis at Sri Guru Ram Das Institute of Medical Sciences and Research, Amritsar, Punjab, India from March 2018 to February 2020. All patients included were subjected to general physical and detailed local examination. MRI was carried out on 1.5 Tesla Unit On Philips Intera Achieva using Sense Body Coil with b factor of 0 and 1000 s/mm² and ADC maps were generated and the results were compared with histopathological results and/or follow-up. Statistical assessment was carried out using Statistical Package for the Social Sciences (SPSS) version 24.0. Qualitative data were compared using the Chi-square test.

Results: The most common cause of neck mass was lymph nodal masses (18%) with highest numbers of patients in age group 40-60 years (34%). When a cut-off ADC value of 1.1×10^{-3} s/mm² was used, sensitivity of 95.23% and specificity of 89.65% were obtained for characterisation of malignant lesions which was statistically significant. There was a strong agreement (k value=0.838) in diagnosing the nature of lesion using ADC value on MRI with histopathological findings.

Conclusion: Diffusion Weighted Imaging (DWI) and ADC values are new promising aspect of MRI and can help in differentiating the nature of the neck lesions. DWI can readily differentiate between benign and malignant lesions of neck with good efficacy and reproducibility.

Keywords: Hodgkins lymphoma, Ludwig's angina, Mesenchymal tumour, Plunging ranula

INTRODUCTION

Neck masses are frequently encountered in clinical practice and can present a diagnostic dilemma for the clinician's involvement [1]. The differential diagnoses of a patient presenting with a neck mass is wide. The role of clinical assessment is to identify and ensure prompt onward referral. Careful clinical examination of all lymph node groups in the neck, the salivary glands and the thyroid gland is important, as well as the examination of the oral cavity, tongue and oropharynx [2].

There are various means by which neck masses can be subdivided and classified, such as by age of presentation, anatomical location including compartments and fascia of the neck, their classical imaging appearance, or by aetiology. Various imaging modalities including radiography, gray-scale and Doppler ultrasonography, computed tomography, Magnetic Resonance Imaging (MRI) and Magnetic Resonance (MR) angiography have been suggested for the evaluation of these lesions, and each has its own advantages and limitations [3].

The role of imaging is to characterise these lesions in order to better determine which lesions can be expectantly managed and which require immediate intervention. DW-MRI is an imaging technique based on molecular diffusion. Cell size, density and integrity are the factors influencing the signal intensity on DWI. It is a very helpful complementary technique in distinguishing neoplastic from non-neoplastic tissue and has numerous applications in the evaluation of head and neck masses especially in head and neck lymphadenopathy [4]. DWI characterises tissues based on differences in water mobility. Hypercellular tissues, such as those present within malignant tumours, will show low ADC values. Non-neoplastic tissue changes such as oedema, inflammation, necrosis and fibrosis are expected to have low cellularity as compared to a viable tumour. This results in high ADC values. Although DWI-MRI is an integral part of brain imaging and has been used for some time for brain evaluation, applications of DW-MRI in imaging of other body parts are gaining importance. As DWI is able to differentiate between inflammatory and neoplastic tissues, another possible utilisation could be the monitoring of tumour response to radiotherapy: this could have prognostic significance and possibly help in the management of the patient [5].

Clinical, pathologic, and radiologic differentiation of neck masses is often challenging because they frequently manifest as painless, enlarging masses and share many histologic and MRI features. Nevertheless, characterisation of the lesions into benign and malignant is essential as the prognosis and treatment varies according to the lesion. Various previous studies have been done to characterise these masses. However, the cut-off and mean ADC values need to be researched further [5-7].

Aim of this study was to evaluate the accuracy of ADC in differentiating benign and malignant neck masses. MRI findings and ADC values were then compared with histopathological findings.

MATERIALS AND METHODS

A single-centre cross-sectional study comprising of 50 patients of all age groups with clinical suspicion of neck swelling was conducted in Department of Radiodiagnosis at Sri Guru Ram Das Institute of Medical Sciences and Research, Amritsar, Punjab, India from March 2018 to February 2020 after obtaining approval from the Institutional Ethics Committee with ethical approval number of BFUHS/2K16p-TH/11769. An informed consent was taken from all the patients.

Inclusion criteria: Patients presenting with neck swelling on self-examination or clinical examination were included.

Exclusion criteria: Patients having any prior history of any surgical treatment or having contraindications to MRI were excluded which are as follows: Electronically, magnetically and mechanically activated implants like cardiac pacemaker, Ferro-magnetic or electronically operated stapedial implants, other pacemakers like for carotid sinus, insulin pumps, nerve stimulators, lead wires or similar wires, non-ferro-magnetic stapedial implants, cochlear implants or prosthetic heart valves.

Study Procedure

The clinical history and detailed local examination of all the patients was recorded. Examination for the swelling size, location, shape, consistency, fluctuance, trans-illumination, pulsatility, temperature, overlying skin changes, relation to underlying/overlying tissue, auscultation, bimanual examination, movement with deglutination, movement with protrusion of tongue and laryngeal crepitus were done. Patients underwent MRI neck. Only 28 out of the 50 patients underwent surgery. Rest of the patients underwent conservative treatment. Histopathological examination {Fine Needle Aspiration Cytology (FNAC)/biopsy} was done in all cases.

The MRI was carried out on 1.5 Tesla Unit on Philips Intera Achieva using sense body coil. [Table/Fig-1] shows the MRI protocol followed for the evaluation of the neck masses. DW-MRI were obtained using a multislice single-shot spin-echo, echo-planar sequence with b-factor of 0 and 1000 s/mm^2, and ADC maps were generated. A Region Of Interest (ROI) was drawn using a circle and mean ADC value was calculated. The final diagnosis was made by histopathological examination.

Sequence	FOV (mm)	RFV (mm)	Matrix	Thickness (mm)	GAP (mm)	NSA	TR (ms)	TE (ms)
MRI protocols								
STIR COR	250	75	272×512	3.0	1.3	3	4000-4500	10-15
T1W COR	250	75	352×512	3.0	1.3	4	400-500	110-15
T2W FS TRA	250	80	352×512	4.0	0.4	3	2200-2700	60-100
STIR SAG	250	75	272×512	3.0	1.3	3	4000-4500	10-15
T1W FS TRA	250	80	352×512	4.0	0.4	4	500-700	10-15
T1 AXIAL	250	80	352×512	4.0	0.4	4	400-500	10-15
Diffusion Axial	230	80	112×80	5.0	0.5	4	400-500	10-15
Post contrast								
T1W FS AXIAL	250	80	352/512	4.0	0.4	4	500-700	10-15
T1W FS COR	250	80	352/512	3.0	1.3	3	400-500	10-15
T1W FS SAG	250	80	352/512	4	0.4	4	500-600	10-15

[Table/Fig-1]: MRI protocol and post contrast MRI for the evaluation of the neck masses.
FOV: Field of view; RFV: Restricted field of view; NSA: Number of signals averaged; TR: Repetition time; TE: Echo time; COR: Coronal; TRA: Transverse; SAG: Sagittal; FS: Fat suppressed

STATISTICAL ANALYSIS

Statistical assessment was carried out using Statistical Package for the Social Sciences (SPSS) version 24.0. Qualitative data were compared using the Chi-square test. Mean ADC value for all benign and malignant lesions was calculated and compared with cut-off ADC value (1.1×10^{-3} mm^2/s) [6]. Sensitivity, specificity and p-value was calculated this cut-off ADC value in differentiating malignant from benign lesions. The value of p-value <0.05 was considered statistically significant at a 95% confidence level. The observations found on MR and DWI was correlated with histopathological examination using kappa index.

RESULTS

There was a strong agreement in diagnosing the nature of lesion using ADC value on MRI with histopathological findings with kappa value of 0.838.

Maximum number of patients presented with clinical suspicion of neck mass was in the age group of 40-60 years i.e., 17 patients (34%) as shown in [Table/Fig-2]. The youngest patient in the present series was two-month-old whereas the oldest patient was 79-year-old. On analysing the gender distribution of patients with neck mass in the present study, it was found that there were more male patients (32) than female (18).

Age group in years	No. of patients	Percentage
<20	11	22
21-40	11	22
41-60	17	34
>60	11	22
Total	50	100

[Table/Fig-2]: Age of incidence.

The most common site for neck mass was anterior triangle of neck on left-side i.e., in 20% of patients, followed by anterior triangle of neck on right side i.e., in 16% of patients as shown in [Table/Fig-3]. The least common sites were nape of neck and midline as they were seen only in one patient each (i.e., 2%). Out of 50 cases studied, 29 cases (58%) had benign lesions and 21 (42%) cases had malignant lesions.

Site	Number of patients	Percentage (%)
Left anterior triangle of neck	10	20
Right anterior triangle of neck	8	16
Right parotid space	4	8
Sublingual region	2	4
Left parotid space	5	10
Midline	1	2
Right submandibular space	4	8
Nape of neck	1	2
Left submandibular space	2	4
Left angle of mandible	6	12
Bilateral parotid space	4	8
Right angle of mandible	3	6
Total	50	100

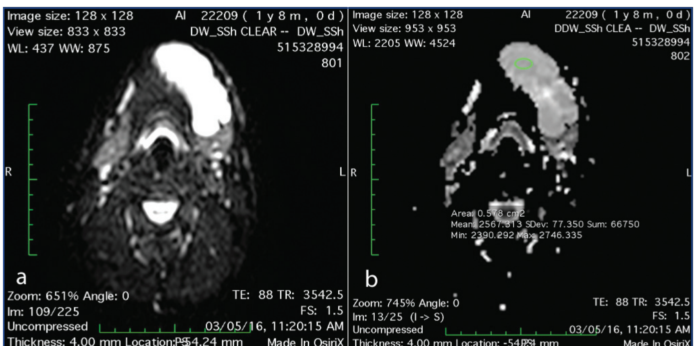
[Table/Fig-3]: Incidence of individual neck masses at various subsites.

Out of fifty patients, maximum number of patients presented with lymph nodal mass i.e., 18% (nine patients). The mean ADC value was 1.56±0.4×10^{-3} mm^2/s in benign neck lymph nodes and 0.8±0.15×10^{-3} mm^2/s in case of malignant lymph nodes. Second most common pathology was of parotid malignancies (12%). Pleomorphic adenoma was seen involving both parotid (mainly deep lobe) and submandibular glands and was seen in 8% of patients. Three cases were seen in parotid gland and one in submandibular gland. Most of the parotid tumours were iso to hyperintense on T2W sequences and had ill-defined borders with inhomogeneous glandular architecture with infiltration of surrounding structures with associated lymphadenopathy. The mean ADC value of malignant parotid tumours was 0.78×10^{-3} mm^2/s and that of benign tumours was 1.8×10^{-3} mm^2/s. One case of Warthin tumour was seen which had a low ADC value (0.82×10^{-3} mm^2/s) because of the presence of lymphoid tissue within the tumour. The mean ADC value of malignant parotid tumours was 0.78×10^{-3} mm^2/s and that of benign tumours was 1.8×10^{-3} mm^2/s.

Soft tissue vascular malformation i.e., both lymphangioma and venous malformations were seen in 6% of patients each. Soft tissue vascular malformations showed high ADC value with mean ADC value of 1.9×10^{-3} mm^2/s. Three cases (6%) of carcinoma involving the thyroid gland were seen. There was a significant difference in ADC value of benign and malignant thyroid nodules. The mean ADC value of benign nodules ($1.7\pm0.13\times10^{-3}$ mm^2/s) was higher than malignant ones ($0.78\pm0.14\times10^{-3}$ mm^2/s). Two case of parotitis were seen. Both cases were seen in paediatric age group. Two cases of sjogren's syndrome were seen and both were female patients with long standing history of bilateral parotid swelling with dryness of eyes and mouth as presenting complaint. Mesenchymal tumour was diagnosed in two patients one in each male and female patient. Two cases of each haemangioma, goitre, dermoid cyst, second branchial cleft cyst and carcinoma involving the submandibular gland were seen. One case (2%) each of plunging ranula, epidermoid cyst, carcinoma post cricoid region, thyroglossal duct cyst, submandibular sialadenitis and Ludwig angina were seen [Table/Fig-4]. All the cystic lesions and mesenchymal tumour had higher ADC values with mean ADC value of 1.5×10^{-3} mm^2/s. Ranulas are rare, benign, acquired, cystic lesions that occur at the floor of the mouth as sublingual or minor salivary gland retention cysts. The extension to the typical submandibular space favours the diagnosis of plunging ranula [Table/Fig-5a,b].

Causes	No of patients	Percentage (%)
Lymph nodal	9	18
Pleomorphic adenoma	4	8
Parotitis	2	4
Plunging ranula	1	2
Lymphangioma	3	6
Epidermoid cyst	1	2
Sjogren's syndrome	2	4
Parotid gland malignancies	6	12
Mesenchymal tumour	2	4
Ca post cricoid region	1	2
Goitre	2	4
Thyroid malignancies	3	6
Dermoid cyst	2	4
Second branchial cleft cyst	2	4
Thyroglossal duct cyst	1	2
Venous malformations	3	6
Haemangioma	2	4
Sailadenitis	1	2
Ludwig's angina	1	2
Submandibular gland malignancies	2	4

[Table/Fig-4]: Various causes of neck masses as diagnosed on histopathology.



[Table/Fig-5]: Histopathologically confirmed case of plunging ranula. a) DWI; b) Corresponding ADC maps showing no significant restriction with mean ADC value of 2.5×10^{-3} mm^2/s.

The nature of lesions according to ADC values and its comparison with histopathology is shown in [Table/Fig-6]. The mean ADC value of benign lesions was 1.62×10^{-3} mm^2/s, while that of malignant lesions was 0.88×10^{-3} mm^2/s and the difference was statistically

Sr. No.	ADC value ($\times 10^{-3}$ s/mm^2)	Nature of lesion according to ADC value	Histopathology
1.	1.7	Benign	Benign
2.	1.05	Malignant	Benign
3.	2.5	Benign	Benign
4.	1.6	Benign	Benign
5.	0.98	Malignant	Benign
6.	1.2	Benign	Benign
7.	1.7	Benign	Benign
8.	1.65	Benign	Benign
9.	0.99	Malignant	Malignant
10.	1.5	Benign	Benign
11.	0.89	Malignant	Malignant
12.	1.8	Benign	Benign
13.	0.76	Malignant	Malignant
14.	1.6	Benign	Malignant
15.	1.8	Benign	Benign
16.	0.49	Malignant	Malignant
17.	0.99	Malignant	Malignant
18.	1.53	Benign	Benign
19.	1.22	Benign	Benign
20.	0.55	Malignant	Malignant
21.	1.9	Benign	Benign
22.	2.1	Benign	Benign
23.	1.4	Benign	Benign
24.	1.01	Malignant	Malignant
25.	1.44	Benign	Benign
26.	1.56	Benign	Benign
27.	2.1	Benign	Benign
28.	1.8	Benign	Benign
29.	2.9	Benign	Benign
30.	2.1	Benign	Benign
31.	0.77	Malignant	Malignant
32.	0.98	Malignant	Benign
33.	0.98	Malignant	Malignant
34.	1.9	Benign	Benign
35.	1.22	Benign	Benign
36.	1.5	Benign	Benign
37.	0.88	Malignant	Malignant
38.	1.4	Benign	Benign
39.	1.01	Malignant	Malignant
40.	1.23	Benign	Benign
41.	0.65	Malignant	Malignant
42.	1.3	Benign	Benign
43.	0.9	Malignant	Malignant
44.	0.88	Malignant	Malignant
45.	0.97	Malignant	Malignant
46.	0.64	Malignant	Malignant
47.	0.78	Malignant	Malignant
48.	0.81	Malignant	Malignant
49.	0.87	Malignant	Malignant
50.	1.1	Malignant	Malignant

[Table/Fig-6]: Nature of lesion according to ADC value and its comparison with histopathology.

significant (p-value<0.05). When a cut-off ADC value of 1.1×10^{-3} mm²/s was used, sensitivity of 95.23% and specificity of 89.65% were obtained for characterisation of malignant lesions, which was statistically significant [Table/Fig-7].

Pathology	n	%	Mean ADC value	Cut-off ADC value	Sensitivity	Specificity	p-value
Benign	29	58	1.62×10^{-3} mm²/s	$>1.1\times10^{-3}$ mm²/s	89.65%	95.23%	<0.05
Malignant	21	42	0.88×10^{-3} mm²/s	$<1.1\times10^{-3}$ mm²/s	95.23%	89.65%	<0.05

[Table/Fig-7]: Mean ADC value, cut-off ADC value, sensitivity, specificity and p-value for benign and malignant lesions.

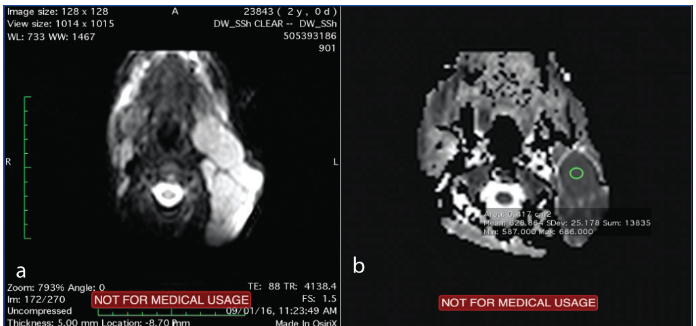
DISCUSSION

Neck masses have a wide array of differential diagnosis. Although most of these masses are usually benign inflammatory lymph nodes, an asymptomatic neck mass is usually the most common presentation of head and neck malignancies. Cystic lesions are more often than not vascular malformations or pharyngeal cleft remnants, whereas solid lesions are usually either inflammatory or neoplastic aetiology. While the history and the physical examination are first and the most important parts of the evaluation of neck masses in any age group, histopathological examination may be necessary to reach the final diagnosis.

As in most of the applications of DWI, a tumour in which tumour cells are densely packed and more number of cell membranes presents a greater resistance to movement of water molecules and, consequently, a lower ADC. On the other hand, a tumour, which has less number of cells, a cystic tumour, or has necrosis, has a less of a resistance to diffusion and a consequently higher ADC value. Therefore, by using this information a solid tumour can easily be detected by analysis of high b-value images (i.e., b-value of 1000), including the corresponding ADC maps. However, comparison of conventional MR findings and ADC measurement was needed for further lesion characterisation [Table/Fig-6] [7].

Nodal masses were the most common masses encountered in the present study accounting to 18%. Most of the lymph nodal masses were of malignant aetiology with metastasis representing the major portion. Metastasis was suspected when shortest dimension of lymph node was greater than 1.5 cm in maximum diameter either in the jugulodigastric region (level II) or in the submandibular triangle (level I) or, when a node was greater than 10 mm (1 cm) in greatest diameter elsewhere in the neck [8]. These findings were in concordance with study done by Mathur R et al., [9].

The mean ADC value was $1.56\pm0.4\times10^{-3}$ mm²/s in benign neck lymph nodes and $0.8\pm0.15\times10^{-3}$ mm²/s in case of malignant lymph nodes. These findings were in concordance with study done by Taha Ali T, in which best threshold for differentiating malignant from benign lymph nodes was 1.15×10^{-3} mm²/s [Table/Fig-8a,b] [10]. De Bondt R et al., have also reported that ADC is useful in the assessment of lymph nodes with metastatic lymph nodes having a significantly lower ADC values when compared with benign lymph nodes [11].



[Table/Fig-8]: a) DWI; b) Corresponding ADC maps showing significant restriction with mean ADC value of 0.62×10^{-3} mm²/s.
Histopathologically confirmed case of Hodgkin's lymphoma

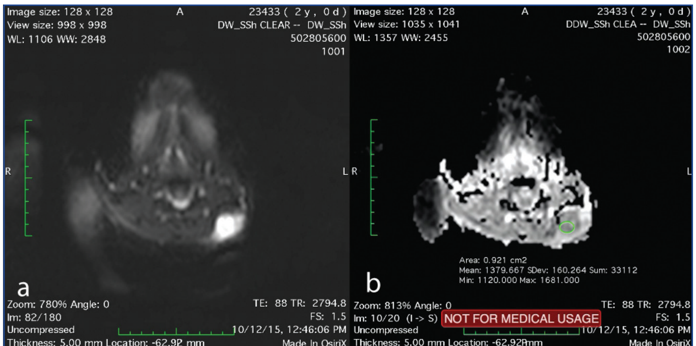
Most of the parotid tumours were iso to hyperintense on T2W sequences. This finding of hyperintensity on T2W sequences was not in concordance with study done by Christe A et al., in which most of the tumours were hypointense on T2W sequences [12].

Five patients presented with focal thyroid swelling, out of which two patients had follicular adenoma, two had papillary carcinoma and one patient had medullary carcinoma of thyroid. There was a significant difference in ADC value of benign and malignant thyroid nodules. This was in agreement with study done by Salem F et al., which proved that the mean ADC of the malignant lesions was $(0.699+0.267\times10^{-3}$ mm²/s) while that of the benign lesions was $(1.879+0.751\times10^{-3}$ mm²/s) [13].

Six cases of vascular malformations were included in this study, which consisted of three cases venous malformations and lymphangioma each. Two cases of haemangioma were also seen. All the lesions showed high ADC value with mean ADC value of 1.9×10^{-3} mm²/s. This was in accordance with the study done by Kanmaz L and Karavas E. [6].

Mittal M et al., in their study on cystic masses of neck reviewed that epidermoid cysts manifest earlier in life, with most lesions evident during infancy. According to their study epidermoid cysts were seen as well-defined anechoic masses with posterior enhancement in the midline of neck. These may show homogenous internal echoes. Heterogeneous appearance could also be seen due to the presence of echogenic fat, osseous, or dental elements [14]. A single case of epidermoid cyst was seen in the present study. However, it was seen in a 45-year-old male patient which was not in concordance with study by Mittal M et al., [14].

Many lesions presented as cystic lesions, which included second branchial cleft cyst, thyroglossal cyst, dermoid cyst, epidermoid cyst and plunging ranula. All the cystic lesions and mesenchymal tumour had high ADC values [Table/Fig-9a,b]. It was in concordance in study done by Kanmaz L and Karavas E, who proved that the mean ADC value of the cystic masses $(1.98\times10^{-3}$ mm²/s) was higher than that of other benign solid masses [6]. In a study done by Thakkar DK et al., the most common congenital lesion was thyroglossal cyst followed by branchial cyst [15]. However, in our study, there was only a single case of thyroglossal cyst. A single case of Ludwig angina was there in our study. It was seen as a well-defined fluid collection with rim like enhancement on post contrast images and restriction on DW-MRI, a finding that represents an abscess. These were in concordance with study done by La'Porte S et al., Serour DK et al., Abou Khadrah RS et al., on imaging of neck masses [16-18].



[Table/Fig-9]: a) DWI; b) Corresponding ADC maps showing no significant foci of diffusion restriction with mean ADC value of 1.37×10^{-3} mm²/s.
Histopathologically confirmed case of Hodgkin's lymphoma

A single case of carcinoma of post cricoid region with associated diverticula formation was seen in the present study. Ultrasound was not able to make any definite diagnosis because of the associated diverticula. However, on MRI the growth was seen involving the post cricoid region and associated diverticula was seen. Connor S saw similar findings in his study which showed that the cross-sectional imaging provides excellent information about tumour detection with its extension across the laryngeal ventricle and infiltration of pharynx, paraglottic, pre-epiglottic and extralaryngeal spaces, which influence the probability for voice conserving partial laryngectomies and their response to radiotherapy [19].

When a cut-off ADC value of 1.1×10^{-3} mm^2/s was used, sensitivity of 95.23% and specificity of 89.65% were obtained for characterisation of malignant lesions, which were in concordance with study done by Elsaid NAE et al., (sensitivity of 100%), Kanmaz L and Karavas E, (sensitivity and specificity of 93.33% and 82.35, respectively), Taha Ali T, (sensitivity and specificity of 96% and 88.9, respectively), and Serour DK et al., (sensitivity of 90%) [5,6,10,17]. Lower specificity values were reported by Elsaid NAE et al., (62.5%) and Serour DK et al., (75%) [5,17].

Limitation(s)

In the present study, the patient groups were diverse with different histopathological entities. A limited number of cases were in each of the benign or malignant group. Further investigations with a larger sample size and a specific group of the same pathological diagnosis are necessary.

CONCLUSION(S)

The DWI and ADC values are new promising aspect of MR imaging and can help in differentiating the nature of the neck lesions. When a cut-off ADC value of 1.1×10^{-3} mm^2/s was used, sensitivity of 95.23% and specificity of 89.65% were obtained for characterisation of malignant lesions, which was statistically significant. DWI can readily differentiate between benign and malignant lesions of neck with good efficacy and reproducibility. It should be incorporated as routine sequence in head and neck imaging for differentiating neck masses.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Mar 20, 2021
- Manual Googling: Mar 24, 2021
- iThenticate Software: Jun 25, 2021 (22%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

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