International Research Journal of Pharmacy and Medical Sciences
ISSN (Online): 2581-3277

Diffusion Weighted MRI in Differentiating Benign from Malignant Cervical Lymph Nodes

Ansam Moyaser Othman[1], Tara Farooq Kareem[2], Loban Fadhil Alwan Al-Hilli[3], Mohammed Al-Hilli[4]
[1]MBCHB CABMS, Radiology Department, Al Yarmouk Teaching Hospital, Baghdad, Iraq
[2]MBCHB, CABMS, Consultant Radiologist, Lecturer at College of medicine University of Baghdad
[3]MBCHB, CABMS, Radiology Department, Baghdad hospital, Medical city complex, Baghdad, Iraq
[4]Consultant Radiologist, M.B.Ch.B - F.I.B.M.S
Corresponding author: Tara Farooq Kareem, Email: tarafaroukkareem@gmail.com

Abstract*— *Background*: *The evaluation of cervical lymph nodes is essential for the diagnosis and staging of malignancies, as well as for treatment planning and monitoring. While ultrasound imaging, contrast-enhanced computed tomography, and contrast-enhanced MRI facilitate the identification of enlarged cervical lymphadenopathies, none of these modalities achieves optimal accuracy.* **Objectives:** *To evaluate the diagnostic efficacy of DWI in the assessment of cervical lymph nodes in a cohort of Iraqi patients, some of whom had head and neck cancer.* ***Methods: *A prospective study conducted at the Oncology Teaching Hospital, Medical City, involved a total of 39 patients with enlarged cervical lymph nodes. They were examined utilizing 1.5 T MRI. DWI was conducted with b values of 0 and 1,000 s/mm². The short axis diameter and ADC values (minimum, maximum, and mean) were assessed for benign and malignant neck lymph nodes, and the results were compared with histological findings obtained through either fine needle aspiration or excisional biopsy. The optimal ADC thresholds were assessed using receiver operating characteristic (ROC) curves to distinguish between cancer and benign neck lymph nodes.* ***Result:*** *The histopathological analysis of included cervical lymph nodes indicated that 56.4% (n=22) were benign, whereas 55% (n=44) were malignant neck lymph nodes, respectively. The ADC values of malignant cervical lymph nodes were significantly lower than those of benign cervical lymph nodes ($p < 0.001$); $0.6771 \pm 0.145 \times 10^{-3}$ mm²/s compared to $1.067 \pm 0.257 \times 10^{-3}$ mm²/s (mean ADC). The ideal mean ADC threshold was 0.965×10^{-3} for differentiating cancer from benign cervical lymph nodes, exhibiting a sensitivity of 95.5% and a specificity of 88.2%.* ***Conclusion:*** *MR diffusion imaging and ADC values serve as a non-invasive modality that significantly aids in the evaluation of cervical lymph nodes in head and neck cancer, exhibiting high sensitivity, specificity, and accuracy.*

***Keywords*— *DWI, MRI, neck lymph nodes, Head and neck cancer, metastasis.*

I. Introduction

Head and neck cancer ranks as the sixth most common malignancy globally, accounting for approximately 6% of all cancer diagnoses and 1–2% of cancer-related deaths (1). The evaluation of cervical nodes is essential for the diagnosis and staging of malignancies, as well as for treatment planning and monitoring. While ultrasound imaging, contrast-enhanced computed tomography, and contrast-enhanced MRI facilitate the identification of enlarged cervical lymphadenopathies, none of these modalities achieves optimal accuracy (2). Ultrasound-guided fine needle aspiration biopsy (US-FNAB) of lymph nodes is a precise method; nonetheless, it is invasive, operator-dependent, and associated with a significant incidence of false-negative results. Moreover, imaging metrics including shape, size, internal architecture, extranodal diffusion, and vascular characteristics have been demonstrated to be reliable (3). Single photon emission computed tomography (SPECT) and positron emission tomography (PET) are contemporary imaging modalities that provide functional information regarding blood flow and glucose metabolism; nevertheless, they entail higher radiation exposure, are costly, have limited availability, and possess relatively low spatial resolution (4, 5).

MRI, either independently or in conjunction with PET scans, offers multiple methodologies for evaluating tissue and intracellular properties in oncology, including PET imaging parameters, MRS, DTI, DKI, and DWI (ADC) (6). DWI, a non-invasive PET/MRI imaging modality, delineates tissues by the displacement motion of water molecules (Brownian motion) as determined by Apparent Diffusion Coefficient (ADC) values (7). The ADC map quantifies the extent of signal loss in biological tissue, attributable to the mobility of water molecules, which causes phase dispersion of the spin. As a result, the diffusion sequences undergo signal degradation. The ability to differentiate malignant from normal lesions using DWI/ADC in a clinical context is a recurring and significant inquiry. It has been established that benign lymph nodes display elevated ADC values compared to malignant lymph nodes. To aid clinicians in distinguishing between malignant and benign nodes, it is essential to define practical threshold values for daily application, regardless of the invasive procedures utilized to determine the nature of these nodes. The latest meta-analysis indicates that studies utilizing DWI/ADC to distinguish between benign and malignant nodes demonstrated a restricted efficacy owing to the broad spectrum of ADC thresholds and the limited sample size.

This study aimed to investigate the usefulness of DWI in cervical lymph nodes and cancer and to evaluate the diagnostic utility of ADC in identifying malignant lymph nodes by determining the cutoff value with the best sensitivity and specificity.

Ansam Moyaser Othman, Tara Farooq Kareem, Loban Fadhil Alwan Al-Hilli, and Mohammed Al-Hilli, “Diffusion Weighted MRI in Differentiating Benign from Malignant Cervical Lymph Nodes,” *International Research Journal of Pharmacy and Medical Sciences (IRJPMS)*, Volume 7, Issue 6, pp. 9-13, 2024.

II. METHODS

Patient selection

This was a prospective study conducted at the Oncology Teaching Hospital, Medical City complex, from January 2021 to January 2022. The research received approval from the ethical committees of Medical City Directorate and Oncology Teaching Hospital.

A total of 39 individuals were recruited. Inclusion criteria were patients with enlarged neck lymph nodes who either complained of neck discomfort or a palpable neck lump or were being followed routinely for a known head and neck cancer (whom post treatment base line imaging study was normal regarding neck lymphadenopathy). Exclusion criteria included patients with claustrophobia, patients with poor MR diffusion imaging quality and patients with no feedback results were all excluded from the study.

Neck MRI was performed on all patients who were either referred by their practitioner or volunteered for this study. Diffusion weighted sequence included in the examination and ADC value of each Lymph node was measured and correlated with the final result that was achieved either by Fine needle aspiration (FNA) or complementary excisional biopsy. The biggest or most suspicious LN was recommended as the target for FNA or surgical removal.

The procedure was explained to the patients before starting and an informed verbal consent was provided.

The MR imaging technique

An MRI was conducted utilizing a 1.5 Tesla Siemens system (Magnetom Aera; Siemens Healthineers, Erlangen, Germany) with a specialized head and neck coil. The MR sequences comprised: Turbo spin-echo T2-weighted imaging (TR/TE: 5610/80, FOV: 190 x 190 mm, slice thickness: 3 mm, intersection gap: 1 mm) in axial planes. Turbo spin-echo T2-weighted imaging (TR/TE: 3300/37, FOV: 240x240 mm, slice thickness: 3 mm, intersection gap: 1 mm) in coronal planes. Axial plane images acquired using T1-weighted parameters (TR/TE: 300/4.76, FOV: 200 x 200 mm, slice thickness: 3 mm, intersection gap: 1 mm). DWI was acquired in the axial plane using single-shot spin-echo echo-planar imaging (EPI) with b values of 50, 500, and 800 (TE: 72, TR: 6830, slice thickness: 5 mm with no interval between slices). Measured apparent diffusion coefficient (ADC) value of the relevant lymph node. The MRI variables taken for each lymph node were: 1-Long axis and short axis diameter (to measure the short to long axis ratio), 2-Presence of internal cystic changes (which may represent malignant necrosis or benign caseation), 3-Lymph node marginal irregularity ADC measurement:

After reviewing the MR images, the ADC value for each concerned lymph node was obtained in square millimeters per second by applying multiple circular regions of interest (ROIs) ranged in size from 5 to 20 mm2 on the lymph node avoiding the surrounding fatty tissue of the neck and the fatty hilum (if preserved) and avoiding any area of cystic changes by correlation the DW image with both T1WI and T2WI. The average of the mean ADC value for each lymph node was taken as a reference in our research and then compared with the final result.

Statistical analysis

Statistical analyses were performed using Statistical Package for Social Sciences for windows version 22 (IBM Corp., Armonk, N.Y., USA). Descriptive statistics presented as mean ± standard deviation (SD) and frequencies as percentages. Chi-square and Fisher's exact tests were used for categorical variables when appropriate. T- test was used for continuous variables. Sensitivity, specificity, accuracy and the ADC cut-off value were calculated to differentiate benign from malignant cervical lymph nodes using ROC curve. P-value of <0.05 was considered significant.

III. RESULTS

Study group characteristics

The study included 24 females and 15 males with a mean age of 42.46 ±10.62 ranging between 21 -59 years, more than half of them were older than 40 years. The majority (71.8%) were presented with a palpable neck mass. Patient with post malignancy follow up represented 5 (12.8 %), as shown in Table 1.

TABLE 1. study group characteristics

Variable	Frequency	Percent
Age		
≤ 30	6	15.4
31-40	9	23.1
41-50	15	38.4
> 50	9	23.1
Gender		
Male	15	38.5
Female	24	61.5
Clinical presentation		
Palpable mass	28	71.8
Tender/ discomfort	6	15.4
Asymptomatic / follow up	5	12.8

About half of the examined LN were at level II, only 5 (12.8%) were with irregular margins and 7 (17.9%) depicted internal cystic changes. The long axis of examined LNs ranged between 11-38 mm and the short axis range was 7-30 mm with a mean of 19.56 and 13.69 mm respectively, as shown in Table 2.

TABLE 2. MRI findings of examined Lymph nodes

MRI features	Frequency	Percent
Site		
Level I	6	15.4
Level II	21	53.8
Level III	4	10.3
Level IV	2	5.1
Level V	5	12.8
Level VI	1	2.6
Margins		
Smooth	34	87.2
Irregular	5	12.8
Internal cystic changes		
Absent	32	82.1
Present	7	17.9
Axis	**mean**	**± SD**
Long	19.56	7.32
Short	13.69	6.097
S/L axis	0.69	0.115

Ansam Moyaser Othman, Tara Farooq Kareem, Loban Fadhil Alwan Al-Hilli, and Mohammed Al-Hilli, "Diffusion Weighted MRI in Differentiating Benign from Malignant Cervical Lymph Nodes," *International Research Journal of Pharmacy and Medical Sciences (IRJPMS)*, Volume 7, Issue 6, pp. 9-13, 2024.

The final histopathological/ cytological diagnosis revealed 17 (44%) malignant LN; 11 (27.7%) were metastatic and 6 (15.4%) were lymphomas, as shown in (Figure 1).

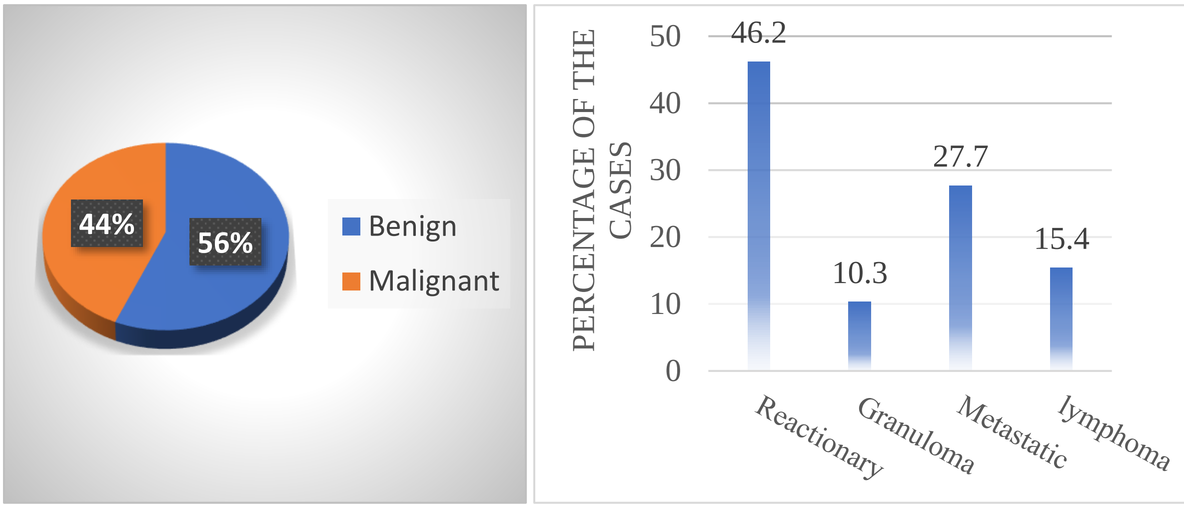


Figure 1. Histopathology/ cytology final diagnosis of the examined lymph nodes

TABLE 3. The comparison between benign and malignant LN in terms of parameters under investigation

Parameters	Benign (n=22)	Malignant (n=17)	P value
Age mean (±SD)	38.41 (12.2)	47.71 (4.6)	0.005
Gender No (%) Male Female	6 (27.3) 16 (72.7)	9 (52.9) 8 (47.1)	0.097
ADC value mean (±SD)	1.07 (0.26)	0.68 (0.15)	<0.001
Long axis mean (±SD)	15. 95 (3.0)	24.23 (8.61)	<0.001
Short axis mean (±SD)	10.45 (2.36)	17.88 (6.90)	<0.001
S/L Axis ratio mean (±SD)	0.66 (0.09)	0.74 (0.13)	0.022
Margins No (%) Smooth Irregular	22 (100) 0	12 (70.6) 5 (29.4)	0.01
Internal cystic areas No (%) Absent Present	22 (100) 0	10 (58.8) 7 (41.2)	0.001

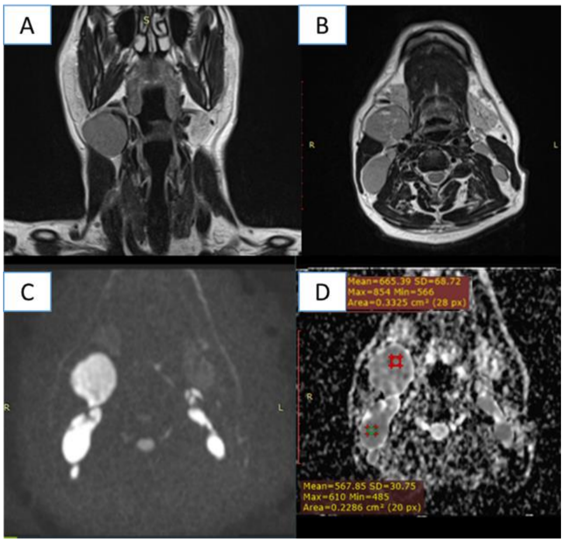


Figure 2. A 43-year-old male presented with bilateral palpable neck lymph nodes. A) Coronal view T2WI with B) Axial views MRI T1WI, C) DWI 1000 and D) ADC image showed multiple enlarged lymph nodes. The mean ADC value of the largest one measured 0.67 x 10^{-3} mm^2/s. Excisional biopsy revealed non-Hodgkin lymphoma.

MRI features in benign and malignant cervical LN

When the MRI features of benign and malignant cervical LN were compared; mean ADC was significantly lower in malignant LN (0.68, ± 0.15 mm^2/s) compared to benign LN (1.07, ± 0.26 mm^2/s), P<0.001. Other parameters such as higher S/L axis ratio, irregular margins and presence of internal cystic area were also significantly higher in malignant LN, as detailed in Table 3, and shown in Figures 2-4.

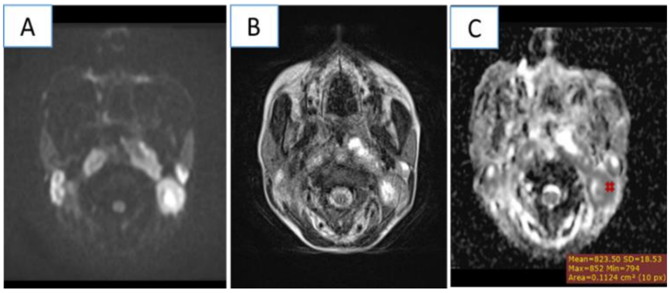


Figure 3. A 45-year-old female presented with bilateral neck lymphadenopathy. Axial views MRI A) T1WI, B) DWI 1000 and C) ADC images showed multiple enlarged lymph nodes with some showed central necrosis. The mean ADC value of the largest suspicious measured 0.824 x 10^{-3} mm^2/s. Excisional biopsy revealed metastatic squamous cell CA

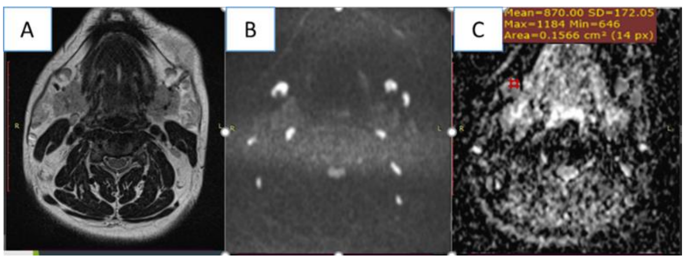
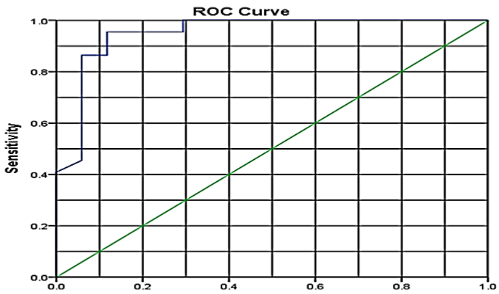


Figure 4. MRI images of case 4. A 24-year-old Male exhibited a painful, palpable upper cervical lymph node on the right side. Axial MRI images A)

T1-weighted imaging, B) diffusion-weighted imaging at 1000, and C) apparent diffusion coefficient image revealed bilateral level I lymph nodes with a mean ADC value of 0.87 x 10^-3 mm²/s. The fine needle aspiration (FNA) yielded benign results, and a follow-up ultrasound after two months indicated a reduction in size.

The diagnostic utility of ADC in cervical LN

The ROC curve was utilized to assess the efficiency of ADC as a diagnostic tool. ADC values effectively distinguished malignant lymph nodes from benign ones, achieving an area under the curve of 0.951, P<0.001, and a 95% confidence interval of (0.879-1.00), as illustrated in Figure 5.



ADC value

Area under the curve	Std. Error	P-vlaue	Asymptotic 95% Confidence Interval Lower Bound	Asymptotic 95% Confidence Interval Upper Bound
0.951	.036	<0.001	0.879	1.000

Figure 5. ROC curve examining the utility of ADC value in predicting malignant cervical lymph nodes with table showing the associated calculations.

ADC cut off values 0.965 10^{-3} mm^2/s showed the best sensitivity 95.45% and specificity 88.24% with an overall accuracy of 92.31% as shown in Table 4.

TABLE 4. Validity calculation of ADC cutoff 0.965 x 10^{-3} mm^2/s.

Statistic	Value
Sensitivity	95.45%
Specificity	88.24%
Positive Predictive Value	91.30%
Negative Predictive Value	93.75%
Accuracy	92.31%

IV. Discussion

Magnetic Resonance with diffusion-weighted imaging is a noninvasive technique that quantifies the movement of water in the extracellular environment. Numerous studies indicate that metastatic nodes exhibit diminished diffusion, attributable to hypercellularity, an elevated nuclear-to-cytoplasmic ratio, and perfusion (8). This is especially applicable in instances of lymphoma, where metastatic lymph nodes have restricted diffusion, appearing as hyperintense regions on diffusion pictures with a low ADC value (4, 5).

The present study assessed 22 patients with benign cervical lymph nodes and 17 patients with malignant cervical lymph nodes. The average ADCs of normal and cancerous nodes are compared. The average ADC value for malignant lymph nodes, whether metastatic or lymphoma, was 0.678 × 10−3 mm²/s, which is lower than that of benign lymph nodes at 1.067 × 10^{-3} mm²/s (P < 0.001). The optimal ADC threshold for distinguishing benign from malignant nodes was 0.965 × 10^{-3} mm²/s, exhibiting a sensitivity of 95.5% and a specificity of 88.24%.

Numerous writers examined the capacity of DWI to distinguish among various etiologies of enlarged cervical lymph nodes. In agreement with our findings, Suh et al. demonstrated that all ADC values obtained from metastatic lymph nodes were significantly lower than those from benign lymph nodes (9). Perrone et al. showed that metastatic and lymphomatous nodes exhibited hyperintensity on DWI (b = 1000 mm²/s) and hypo intensity on ADC maps. In contrast, inflammatory nodes exhibited hypo intensity (b = 1000 mm/s) and hyperintensity on ADC maps (10).

The optimal ADC threshold reported by different studies ranged between 0.965-1.03 x 10-3 mm2/s (11) (12) (13) (10) (9) as detailed in summary table 5. The proposed threshold by Suh et al. (9) and Alamolhoda et al. (14) were in agreement to ours, however the sensitivity and specificity of the current study was higher.

TABLE 5. The summary table showing the results of current study versus previous studies

	ADC cutoff value×10−3mm2/s,	Sensitivity	Specificity
This study	0.96	95%	88.2%
Suh et al (9)	0.965	90%	88%
Alamolhoda et al (13)	0.996	80.5 %	77.2 %
Perrone et al (10)	1.03	100%	92.9%
de Bondt et al (11)	1.0	92.3%;	83.9%
Vandecaveye (12)	0.94	84%	94%

In studies focusing solely on metastatic lymph nodes, Vandecaveye and colleagues identified a statistically significant difference (p < 0.0001) between the mean ADC values of benign cervical lymph nodes (1.19 × 10−3 ± 0.22 × 10−3 mm²/s) and HNSCC nodal metastases (0.85 × 10−3 ± 0.27 × 10−3 mm²/s). They propose a threshold value of 0.94 × 10−3 mm²/s, which is similar to ours but exhibits lower sensitivity and specificity, as detailed in Table 5, with an overall accuracy of 91%. In smaller study more heterogenous cohort included 32 patients Perrone et al. found that 1.03×$10^{−3}$ mm^2/s cut off has a 100% sensitivity and 92.9%.

In an earlier study in 2003, however, Sumi et al. reported a controversial finding. They found in cohort of 25 benign, 25metastatic and 5 lymphoma that mean ADC value was significantly higher in malignant nodes, followed by benign then lymphoma 0.410 ± 0.105 x 10^{-3}, 0.302 +/- 0.062 x 10^{-3}, 0.223 +/- 0.056 x 10^{-3} mm^2/s respectively (15).

The discrepancies in ADC values between these investigations can be ascribed to other factors. The selection of b values is paramount: lower b values enhance the signal-to-noise ratio but diminish sensitivity to diffusion.

The identification of the region of interest on ADC maps and the use of sequences that minimize artifacts to enhance the accuracy of measurements in the designated area.

The sample size and inclusion criteria also contributed to the variation of the findings.

In head and neck primary malignant tumors, nodal necrosis is the most valued sign of metastatic involvement. In this study

Ansam Moyaser Othman, Tara Farooq Kareem, Loban Fadhil Alwan Al-Hilli, and Mohammed Al-Hilli, "Diffusion Weighted MRI in Differentiating Benign from Malignant Cervical Lymph Nodes," *International Research Journal of Pharmacy and Medical Sciences (IRJPMS)*, Volume 7, Issue 6, pp. 9-13, 2024.

about 7 cases out of 17 malignant cases show necrotic changes, while none the benign lymph nodes showed necrosis (P= 0.001). This agrees with King et al findings, who calculated the predictive values of internal necrosis and found a 93% sensitivity and 89% (16).

A further known criterion for distinguishing between benign and malignant lymph nodes evaluated in this study was marginal irregularity; a normal lymph node often exhibits a reniform shape with smooth, well-defined borders. Metastatic illness can modify the morphology of the node by infiltrating nodal tissue and distending the nodal capsule. Consequently, rounder nodes, as opposed to oval ones, are deemed suspect. As the disease advances, the capsule fails to enclose the node; indistinct irregular edges in a lymph node indicate malignancy and may signify extracapsular tumor dissemination. In the present investigation, approximately 5 out of 17 malignant instances exhibit marginal irregularity, whereas none of the benign lymph nodes displayed such characteristics.

This study has some limitations, including a limited sample size and a small number of lymphomatous patients. Another issue was the limited spatial resolution of echoplanar imaging, which is exacerbated when large b values (b = 1000s/mm2) are used to increase the sensitivity of diffusion imaging. As a result, nodes with a diameter less than 9mm are difficult to spot on ADC maps.

V. Conclusion

Cervical lymph nodes may be more accurately and sensitively assessed using non-invasive magnetic resonance imaging diffusion imaging and ADC values in the context of head and neck cancer.

References

1. Gatta G, Botta L, Rossi S, Aareleid T, Bielska-Lasota M, Clavel J, et al. Childhood cancer survival in Europe 1999–2007: results of EUROCARE-5—a population-based study. The lancet oncology. 2014;15(1):35-47.
2. Esen G. Ultrasound of superficial lymph nodes. European journal of radiology. 2006;58(3):345-59.
3. Castelijns JA, van den Brekel MW. Detection of lymph node metastases in the neck: radiologic criteria. Am Soc Neuroradiology; 2001. p. 3-4.
4. Yamazaki Y, Saitoh M, Notani K-i, Tei K, Totsuka Y, Takinami S-i, et al. Assessment of cervical lymph node metastases using FDG-PET in patients with head and neck cancer. Annals of nuclear medicine. 2008;22(3):177-84.
5. Kotani J, Kawabe J, Higashiyama S, Kawamura E, Oe A, Hayashi T, et al. Evaluation of diagnostic abilities of Ga-SPECT for head and neck lesions. Annals of nuclear medicine. 2008;22(4):297-300.
6. Razek AAKA. Routine and advanced diffusion imaging modules of the salivary glands. Neuroimaging Clinics. 2018;28(2):245-54.
7. Ali TFT. Neck lymph nodes: characterization with diffusion-weighted MRI. The Egyptian Journal of Radiology and Nuclear Medicine. 2012;43(2):173-81.
8. Sumi M, Van Cauteren M, Nakamura T. MR microimaging of benign and malignant nodes in the neck. American Journal of Roentgenology. 2006;186(3):749-57.
9. Suh C, Choi Y, Baek J, Lee J. The diagnostic value of diffusion-weighted imaging in differentiating metastatic lymph nodes of head and neck squamous cell carcinoma: a systematic review and meta-analysis. American Journal of Neuroradiology. 2018;39(10):1889-95.
10. Perrone A, Guerrisi P, Izzo L, D'Angeli I, Sassi S, Mele LL, et al. Diffusion-weighted MRI in cervical lymph nodes: differentiation between benign and malignant lesions. European journal of radiology. 2011;77(2):281-6.
11. De Bondt R, Hoeberigs M, Nelemans P, Deserno W, Peutz-Kootstra C, Kremer B, et al. Diagnostic accuracy and additional value of diffusion-weighted imaging for discrimination of malignant cervical lymph nodes in head and neck squamous cell carcinoma. Neuroradiology. 2009;51(3):183-92.
12. Vandecaveye V, De Keyzer F, Vander Poorten V, Dirix P, Verbeken E, Nuyts S, et al. Head and neck squamous cell carcinoma: value of diffusion-weighted MR imaging for nodal staging. Radiology. 2009;251(1):134-46.
13. Alamolhoda F, Faeghi F, Bakhshandeh M, Ahmadi A, Taheri MS, Abbasi S. Diagnostic value of diffusion weighted magnetic resonance imaging in evaluation of metastatic neck lymph nodes in head and neck cancer: a sample of Iranian patient. Asian Pacific journal of cancer prevention: APJCP. 2019;20(6):1789.
14. Alam F, Naito K, Horiguchi J, Fukuda H, Tachikake T, Ito K. Accuracy of sonographic elastography in the differential diagnosis of enlarged cervical lymph nodes: comparison with conventional B-mode sonography. American journal of roentgenology. 2008;191(2):604-10.
15. Sumi M, Sakihama N, Sumi T, Morikawa M, Uetani M, Kabasawa H, et al. Discrimination of metastatic cervical lymph nodes with diffusion-weighted MR imaging in patients with head and neck cancer. AJNR American journal of neuroradiology. 2003;24(8):1627-34.
16. King AD, Tse GM, Ahuja AT, Yuen EH, Vlantis AC, To EW, et al. Necrosis in metastatic neck nodes: diagnostic accuracy of CT, MR imaging, and US. Radiology. 2004;230(3):720-6.