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Value of diffusion MR imaging in differentiation of recurrent head and neck malignancies from post treatment changes

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ABSTRACT

Purpose: Role of diffusion-weighted (DW) MR imaging in differentiating residual or recurrent neck malignancies from postoperative/post-radiation changes with histopathological correlation and comparison with PET-CT.

Methods and materials: Prospective observational study for a period of 1 year in 62 post-radiation/post-operative patients suspected to have residual/recurrent tumors of neck with lesion diameter more than 5 mm measured on MRI.

Results: Mean ADC for recurrent/residual tumors: $1.008 \pm 0.220 \times 10^{-3}\,mm^2/s$ - significantly lower than mean ADC value for post-treatment changes of $1.69 \pm 0.40 \times 10^{-3}\,mm^2/s$ ($p < 0.0001$). The overall diagnostic accuracy, positive predictive value (PPV) and negative predictive value (NPV) of the qualitative assessment for the use of DWI in differentiating tumors recurrence from post-treatment changes were 96.6%, 96% and 83.3%, respectively. Upon quantitative analysis of the DW imaging data, a threshold ADC value of $1.3 \times 10^{-3}\,mm^2/s$ used for differentiating between post-treatment changes and recurrent cancers showed the highest combined sensitivity of 94%, specificity of 83.3%, accuracy of 93.6%, positive predictive value of 95.9%, and negative predictive value of 83.3%.

Conclusion: DW MRI is a promising non-invasive MRI technique used to differentiate recurrent/residual head and neck malignancies from posttreatment changes based on ADC values. DWI offers advantage as it has a short scanning time and can be safely added to standard MRI protocol with minimum patient discomfort. Complementary use of DWI and PET/CT imaging may increase diagnostic confidence for differentiating recurrent disease from radiation therapy-induced changes after 6–12 months in posttreatment cases.

Introduction

Head and neck cancers are amid the 10 most common cancers globally and are the most common cancers in developing countries. According to the Globocan fact sheet for Indian subcontinent 2018, carcinoma of oral cavity and lip has surpassed lung cancer and now is the second most common carcinoma responsible for deaths. Head and neck cancer also constitute a bulk of new cases only being surpassed by Breast cancer. Crucial risk factors allied with head and neck cancer include tobacco, alcohol consumption, human papilloma virus (HPV) infection and Epstein-Barr virus (EBV) infection (for nasopharyngeal cancer). The chronic exposure of the upper aero digestive tract to these carcinogenic factors can result in dysplastic or premalignant lesions in the oropharyngeal mucosa ultimately resulting in head and neck cancer.

Multidisciplinary treatment with surgery, radiation and chemotherapy improves patient survival and quality of life but complicates the interpretation of post treatment follow-up imaging studies due to altered anatomy and post radiation edema and fibrosis. Evaluation of post treatment head and neck cancer patient poses a challenge to the

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radiologist despite the availability of advanced imaging techniques. Most patients have a suboptimal clinical examination on account of pain and trismus, further compounding an already complex scenario. Post-treatment changes result in fibrosis, edema and at times, necrosis within the soft tissues, making it difficult for the radiologist to detect recurrent neoplastic disease within this distorted anatomy [1]. Some recurrent lesions do not enhance after contrast administration, making them indistinguishable from post treatment changes [2]. Imaging signs have been described in the literature that can help the radiologist differentiate post-treatment changes from recurrent tumor disease. However, these signs have limitations and most patients have to undergo histopathology.

Advances in the clinical applications of magnetic resonance imaging (MRI) and the cumulative availability of these techniques in everyday practice have resulted in early diagnosis and staging of head and neck cancers. Quantitative DWI studies have shown that the apparent diffusion coefficient (ADC) values of recurrent tumors are substantially lower than those of post-treatment changes. DWI is customarily performed in the same sitting along with anatomical MRI, without any considerable additional time or cost to the patient. ADC values are expected to vary according to the microstructures or pathophysiologic states of the tissues and they can be calculated by measuring signal intensities in a series of diffusion-weighted MR images by using different b-values [3].

In recent literature, post treatment imaging with PET -CT has been reported to be a sensitive technique for detection of recurrent head and neck cancer [4]. It relies on increased metabolic activity of malignant tissues. FDG-PET is also helpful in distinction of tissue necrosis from recurrent tumor. To reduce false-positive results, 18-F FDG-PET should be performed at 10–12 weeks after the end of treatment; this time point is also considered an optimal balance between clinical response evaluation and surgical management, if necessary [5]. This study was done to evaluate utility of diffusion parameters in differentiating post treatment changes from recurrent tumors in head and neck cancers and also its comparative analysis with PET-CT (see Fig. 1–5).

Methods

After scientific committee approval, prospective study over a period of one year including all post treated patients who were suspected to have recurrent tumor of the head and neck on clinical examination. Inclusion criteria incorporated patients who presented with clinical suspicion of recurrence or were symptomatic and had a history of chemo radiation given with a curative intent for head and neck carcinomas. The time frame of presentation had to be more than equal to 3 months and less than 3 years from point of completion of chemo radiation. Patients with any contra indication to MRI examination (Cardiac pacemaker, aneurysmal clip, metal prosthesis) and those lost to follow up were excluded from the study. 62(n = cohort) patients were included in the study who underwent routine MR Imaging and Histopathological follow up. Due to economical constrains on part of the patient only a subset of 33 patients (33/62) underwent FDG PET-CT examination (see Tables 1–4).

Conventional and diffusion-weighted MRI studies were performed with a Siemens 1.5 Avanto MRI scanner by using a head and neck circular polarization surface coil. All of the patients underwent diffusion-weighted images by using a multisection spin-echo single-shot echo-planar imaging (EPI) sequence. An average of 15 sections was obtained in the axial plane covering the area of interest. Imaging parameters were as follows: TR/TE of 10,000/108 ms, FOV of 23 × 23 cm, an acquisition matrix of 128 × 128, and section thickness of 5 mm with an intersection gap of 1–2 mm. Diffusion-probing gradients were applied in the 3 orthogonal directions (X, Y, and Z) with the same strength. Diffusion- weighted MR images were acquired with diffusion-weighted factor, factor b of 0, 400 and 800 s/mm^2. The quality of the diffusion-weighted MR images was evaluated by two radiologists and it was determined by consensus whether they were acceptable for further analysis. Special attention was paid to image distortion by susceptibility artifacts. A qualitative and quantitative analysis of the diffusion-weighted MR images was made. A region of interest (ROI) was placed in the darkest region on ADC map, corresponding to diffusion restriction and the ADC value was measured. The proper choice of areas of sampling for calculation of ADC values was a very important factor to reduce false results. Hence we took precautions during ADC measurement, like excluding areas of gross necrosis from the sample (ROI), and plotting a freehand-drawn ROI.

Finally, post contrast T1WIs (TR/TE of 800/15 ms) were obtained after an intravenous bolus injection of 0.2 mL/kg of body weight of gadolinium based contrast in all of the patients. The Renal function parameters were checked for all patients before administration of contrast and consent was acquired.

Characteristics signs suggestive of recurrence on routine MR imaging were proximity to the tumor site; areas of T2 prolongation that may represent variable degrees of edema, fibrous-inflammatory reaction, or neoplasm; enhancement after the administration of gadolinium and variable degrees of mass effect. Areas of abnormal enhancement are considered predominantly worrisome for recurrent tumors.

As per institution protocol, 18F-FDG PET-CT was performed following MR Imaging on same day. PET-CT was done at a single centre and performed on a dedicated conventional full ring high resolution dedicated PET-CT machine (Siemens Biograph 40 True Point PET-CT scanner). All patients were prepared with standard guidelines with 4–6 h of fasting. Patients were injected with 4–5 MBq/kg body weight 18FFDG. A low dose CT was done along with PET for generating attenuation map and anatomical localization. All images were reconstructed in triaxis using standard method. Factory-fitted software was used to generate region of interest and standardized uptake values (SUVmax) normalized to injected dose and the patient's weight was calculated.

The final diagnosis in our study was histology in all of the patients. The selection of the site was sought from findings on diffusion imaging and PET- CT.

Sensitivity, specificity, positive predictive value and negative predictive value will be calculated, followed by use of Chi Square test. t-Test for two independent variables has been used to calculate the significance (p value) between post treatment recurrent cases and inflammatory changes. P values < 0.05 were considered statistically significant. We determined a threshold of ADC value, with which the highest accuracy was obtained for discriminating residual or recurrent head and neck tumors from postoperative or post radiation changes. Statistical analysis was done using IBM software SPSS (Version 23.0).

Results

The mean age of total population was 49.5 years. Mean age of patients with recurrent disease was 49.5 years and of patients with inflammatory/post treatment changes was 49.6 years. The male to female ratio in total population was 11.4.

In the present study, Carcinoma of buccal mucosa was the commonest tumor accounting for 34% of the cases. Next in order is Carcinoma of tongue and alveolus contributing 21 and 16% respectively.

In the present study the 81% (50/62) cases were recurrent neoplasm with inflammatory/post treatment changes cases accounting for 19% (12/62). 50 lesions out of 62 showed significant restricted diffusion. 48 of these (96%) were found to be a recurrent malignancy on histology. 2 lesions (4%) showing restricted diffusion were confirmed as post-treatment inflammatory changes on histology. 12 lesions out of 62 did not show diffusion restriction and demonstrated a loss of signal intensity on the DWI MRI images with high signal intensity on the ADC maps. 10 lesions (83.3%) were found to be due to post-treatment changes. 2 lesions (16.6%), which did not show restricted diffusion, were found to be malignant confirmed by histology.

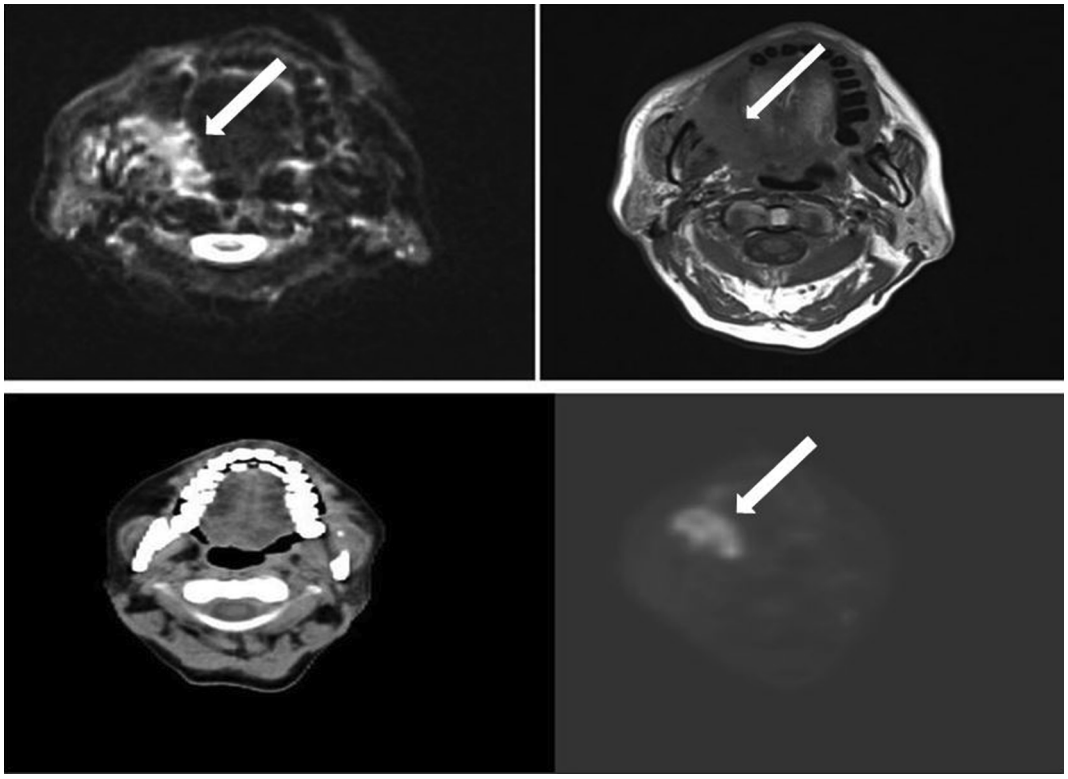

Fig. 1. CASE I- Case of Carcinoma tongue, post op/RT/CT with induration on right side of tongue. Right buccal mucosa region shows diffusion restriction in the premolar - molar region involving right RMT posteriorly and extending up to the right lateral wall of the oropharynx. PET-CT showed metabolic activity at the same site. Histology was suggestive of invasive squamous cell carcinoma consistent with recurrence.

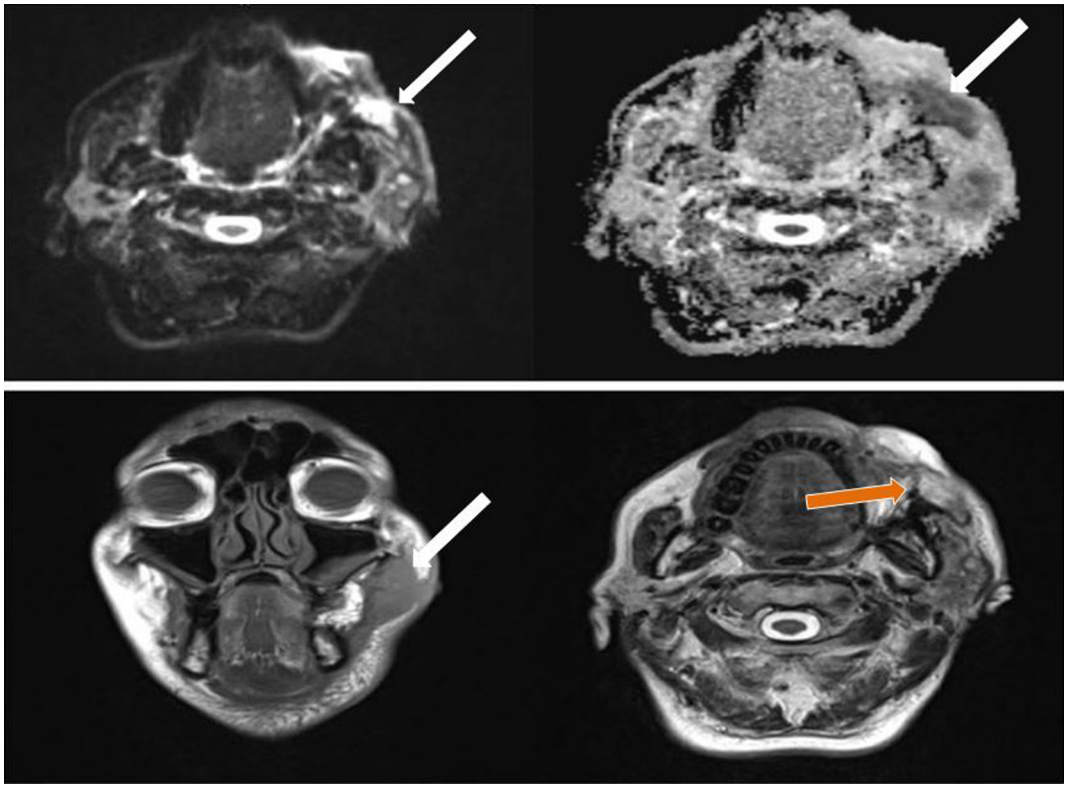

Fig. 2. CASE II - Case of Carcinoma left buccal mucosa, post op/RT/CT with clinical swelling at site of flap. Altered signal intensity lesion showing diffusion restriction on lateral aspect of flap extending left masticator space. Results confirmed on Histology: squamous cell carcinoma consistent with recurrence.

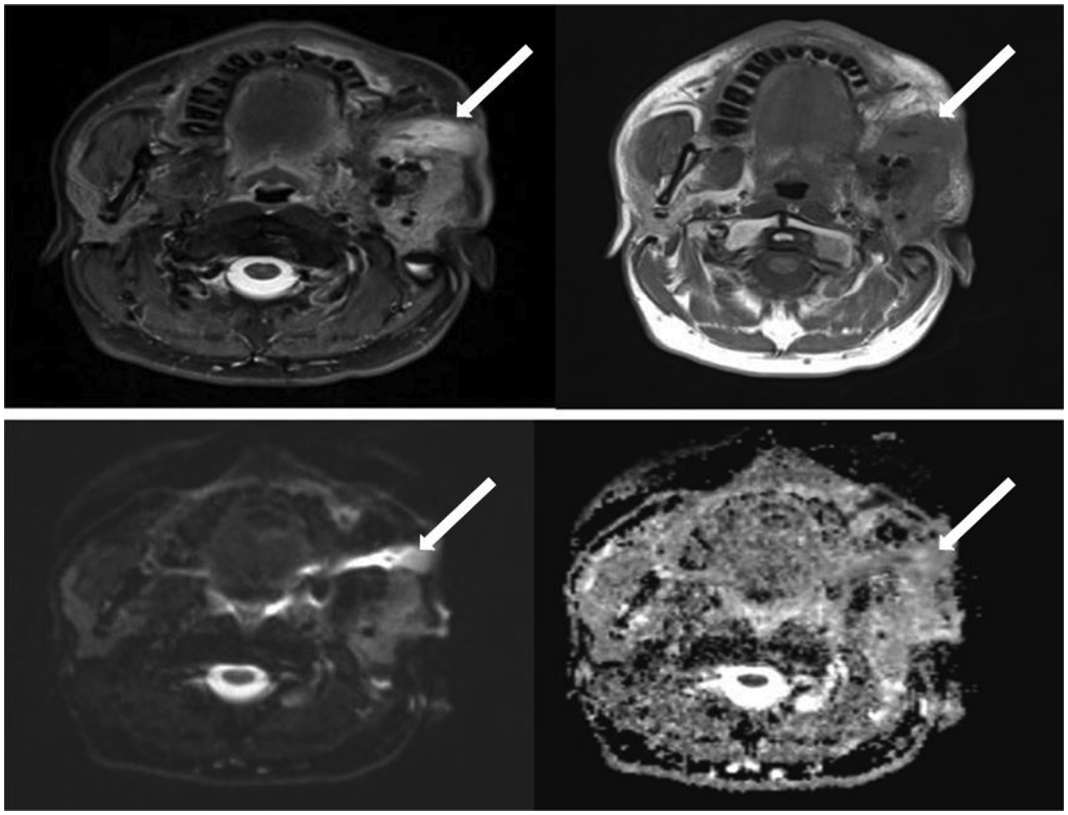

Fig. 3. CASE III - Case of Carcinoma left Retromolar trigone, post op/RT/CT with clinical swelling at site of flap. Altered signal intensity area on superomedial part of flap, appearing hyper intense on DWI with no evidence of restriction on ADC sequence. Histology suggestive of no evidence of malignancy/dysplasia.

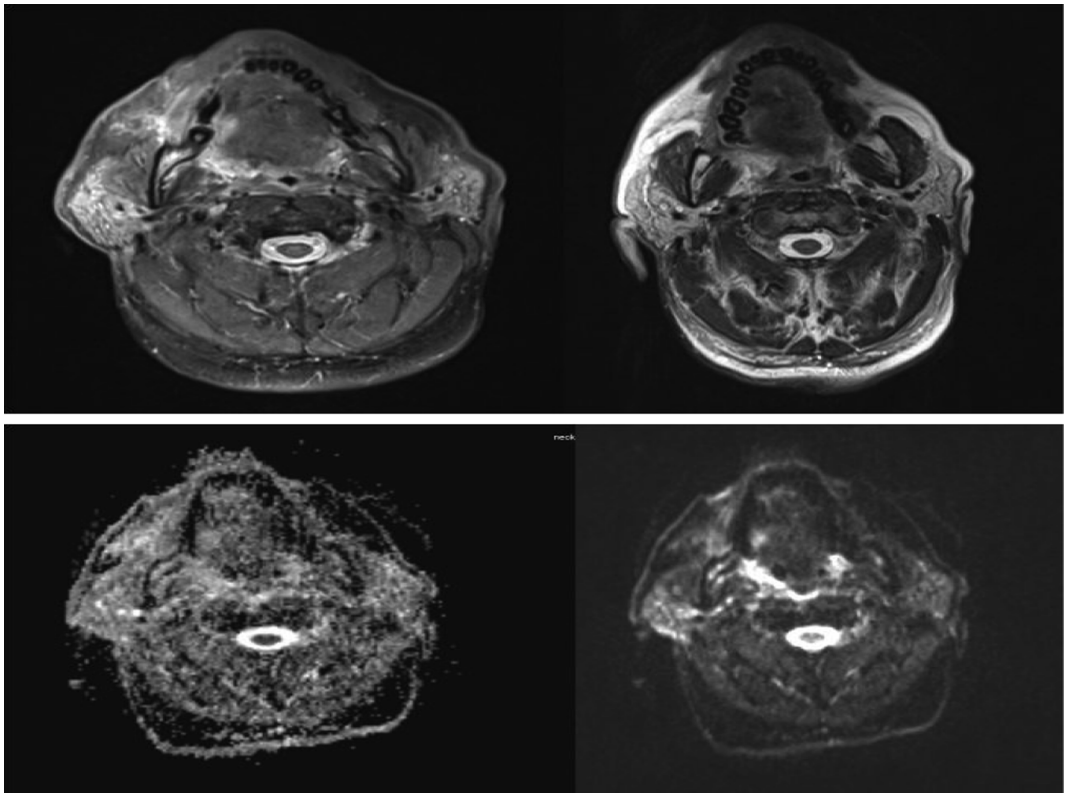

Fig. 4. CASE IV - Case of Carcinoma right tongue, post op/RT/CT. Right lateral border of tongue shows altered signal intensity lesion in posterior half with no diffusion restriction on ADC s/o post RX changes. Histology: confirmed granulation tissue.

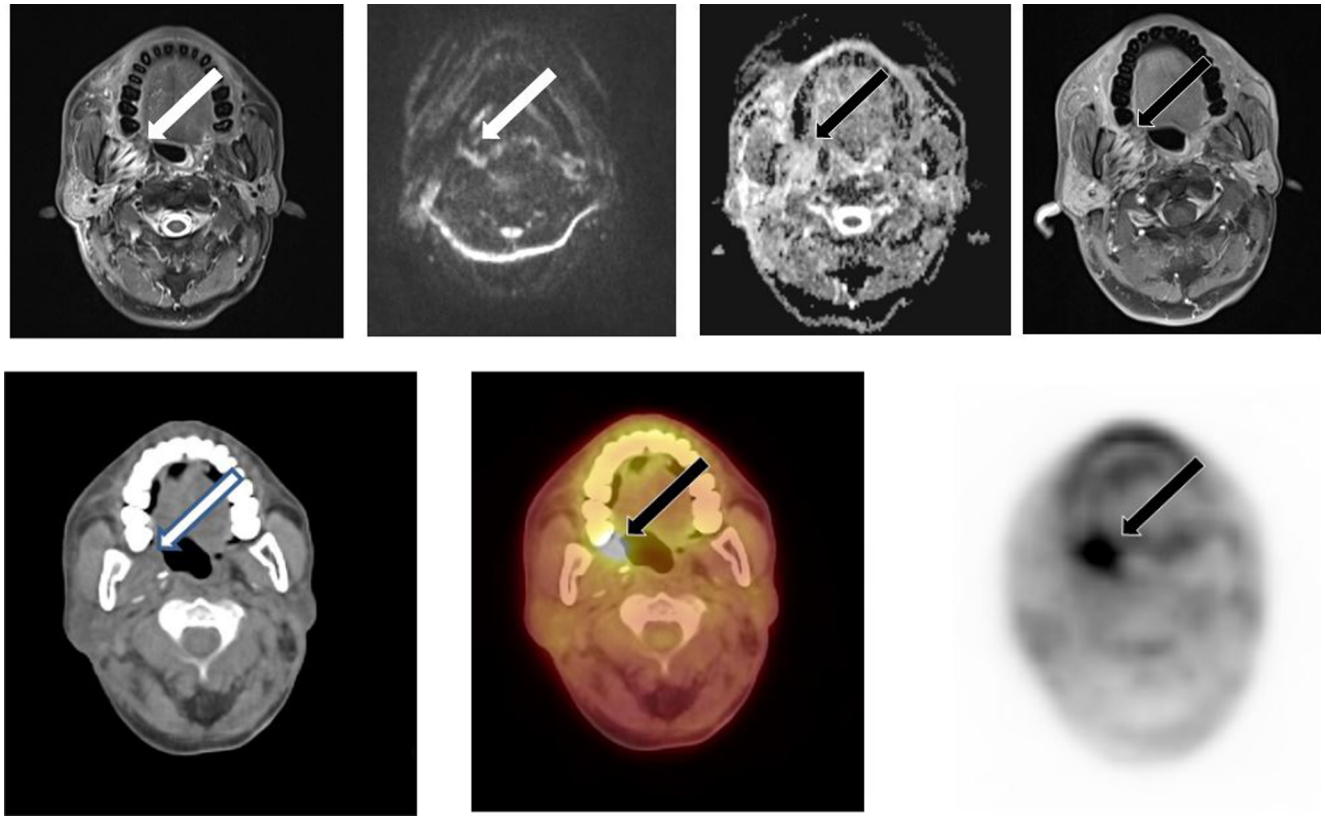

Fig. 5. Case V: Case of Carcinoma of right tonsil. Post TORS radical tonsillectomy/Post CT/RT. Complains of swelling right side of neck. Altered signal intensity lesion showing no significant diffusion restriction in right tonsillar region. Fusion PET –CT images show heterogeneous tracer uptake in right tonsillar fossa with postop changes. Results confirmed on Histology: squamous cell carcinoma consistent with recurrence.

Table 1
The Patient Characteristics: Mean age and Age group.

Age (years)	Inflammatory/Post treatment changes	Recurrence
0–29	0	4
30–59	11	32
60–89	1	14
> 90	0	0

Table 3
Method of treatment.

Treatment	Number of patients
Surgery and Radiotherapy	30
Radiotherapy and Chemotherapy	12
Surgery, Radiotherapy and Chemotherapy	16
Radiotherapy	4

Quantitative analysis

ADC values of recurrent tumors ranged from $0.65 \times 10^{-3}\,mm^2/s$ to $1.4 \times 10^{-3}\,mm^2/s$ with mean of $1.008 \pm 0.220 \times 10^{-3}\,mm^2/s$. The ADC values of lesions due to post treatment changes ranged from $1.3 \times 10^{-3}\,mm^2/s$ to $2.3 \times 10^{-3}\,mm^2/s$ with a mean of $1.69 \pm 0.40 \times 10^{-3}\,mm^2/s$. There was a statistically significant difference in the ADC values between malignant and post treatment lesions ($p < 0.0001$) consistent with previous imaging studies. The diffusion parameters correlated with the qualitative analysis in all 62 lesions with the exception of two false positive and two false negative cases. An ADC value of $1.3 \times 10^{-3}\,mm^2/s$ (Refer supplementary data) to differentiate tumor recurrence from post treatment changes provides us best results with an overall sensitivity of 94%, specificity of 83.3%, positive predictive value of 95.9%, and negative predictive value of 83.3% and accuracy of 93.6%. Since the true positive cases were same

Table 2
Distribution of diseases.

Disease	Number of cases	Percentage
Ca Vocal cord + Orolaryngopharynx + PFS**	2 + 2 + 1 = 5	8%
Ca Buccal mucosa	21	34%
Ca Lip + GBS* + RMT# + Maxilla + Tonsil + Soft palate	2 + 2 + 2 + 3 + 1 + 1 = 10	16%
Ca Tongue	13	21%
Ca Alveolus	10	16%
Ca Nasopharynx	2	3%
Ca Thyroid	1	2%

** Pyriform sinus.
* Gingivo buccal sulcus.
# Retromolar trigone.

Table 4
Tabulated data of imaging (restriction) and histology.

IMAGING	HISTOLOGY		
	Malignant	Benign	Total
Bright DWI + dark ADC (restricted diffusion)	48 (96%)	2 (4%)	50(80.6%)
No restricted diffusion	2 (16.6%)	10 (83.3%)	12 (19.4%)
Total	50 (100%)	12(100%)	62 (100%)

(Refer Table 5), we can safely assume that sensitivity of detecting tumor recurrence of Diffusion weighted MRI and PET- CT is comparable.

Statistical evaluation with a 2 × 2 contingency table of both MRI and PET-CT for recurrence in accordance with histology findings reveals the following output (Refer supplementary data for 2 × 2 contingency table). Diffusion parameters in MR imaging revealed a sensitivity of 96%, specificity of 83.3%, positive predictive value of 96%, and negative predictive value of 83.3% and accuracy of 96.6% in differentiating recurrent disease from post treatment inflammatory changes keeping histological findings as gold standard. PET-CT reported a high sensitivity (100%), positive predictive value (90.3%) and negative predictive value (100%). However, specificity (40%) is low. This could be attributed to less number patients taken for PET-CT (see Table 6).

Discussion

Our study showed mean ADC for recurrent/residual tumors of $1.008 \pm 0.220 \times 10^{-3}\,mm^2/s$ and it was significantly lower than mean ADC value for post treatment changes of $1.69 \pm 0.40 \times 10^{-3}\,mm^2/s$ ($p < 0.0001$). These findings were consistent with other studies. Abdel Razek et al. [12] reported that the mean ADC value of the viable and necrotic part of the head and neck tumor are $1.17 \pm 0.33 \times 10^{-3}\,mm^2/s$ and $2.11 \pm 0.58 \times 10^{-3}\,mm^2/s$ respectively. The differences in ADC values reflect the distinct difference in the histopathological features and post treatment soft tissue changes due to water proton distribution of tumors. Malignant tumors have enlarged nuclei, hyperchromatism and show hypercellularity. These histological characteristics reduce the diffusion space of water protons in both the extracellular and intracellular dimensions with a consequential decrease in the ADCs. On the other hand, tissues with post treatment changes show relatively low cellularity associated with variable degrees of edema and inflammatory reaction that are characterized by an increase of the interstitial water content, where fewer barriers for diffusion exist, with a subsequent increase in their ADCs.

The overall diagnostic accuracy, positive predictive value (PPV) and negative predictive value (NPV) of the qualitative assessment for the use of DWI in differentiating tumor recurrence from post treatment changes were 96.6%, 96% and 83.3%, respectively. Upon quantitative analysis of the DW imaging data, a threshold ADC value of $1.3 \times 10^{-3}\,mm^2/s$ used for differentiating between post-treatment changes and recurrent cancers showed the highest combined sensitivity of 94%, specificity of 83.3%, accuracy of 93.6%, positive predictive value of 95.9%, negative predictive value of 83.3%. These figures were compared to earlier existing comparable studies conducted by different groups.

The present findings and threshold ADC value of $1.3 \times 10^{-3}\,mm^2/s$ used for differentiating between post-treatment changes and recurrent cancers reinforces and corroborates the findings of most previously conducted studies. The lower threshold values proposed by Desouky et al. [7] may lead to a significant number of recurrent tumors being misdiagnosed as post treatment changes, which would have a negative outcome.

False-negative and false-positive results were seen in 4 (6.4%) of our cases. False negative results were seen in 2 cases after treatment. These lesions showed mixed signal intensity on DW images and ADC maps with borderline/high ADC measurements and hence were diagnosed as post-treatment changes. However, histology revealed evidence of recurrent tumor disease, necessitating further aggressive therapy. A likely cause for the misdiagnosis could be due to marked focal edema and small areas of tissue liquefaction induced by radiation. Matzek et al. [13] reported a statistically significant increase in the ADC value of squamous cell carcinoma of the oropharynx 10 days after radiation therapy ($0.71 \pm 0.19 \times 10^{-3}\,mm^2/s$ before treatment versus $2.05 \pm 0.43 \times 10^{-3}\,mm^2/s$ after treatment). They attributed this increase to areas of micro necrosis and edema developing within the tumor. False-positive results from DWI were recorded in two lesions treated using radiation and/chemotherapy therapy, which exhibited restricted diffusion on DWI images and had a low signal on the ADC maps associated with low ADC values. These lesions were falsely interpreted on DWI as a recurrence of malignancy. One of these lesions was confirmed as an abscess upon histological examination, which further was due to Tubercular etiology confirmed by culture. Tuberculosis is widespread and endemic disease in Indian subcontinent. During the initial 6 months following radiation therapy, the prevailing changes include edema, active fibrous-inflammatory reaction and increased vascular permeability due to endothelial damage. Later (6–24 months subsequent to radiation), these changes demonstrate gradual regression to be dominated by an attenuated fibrous reaction with restriction of water diffusion, proposed by Nomayr et al. [22]. It was envisaged that a study determining contributions of different components such as necrosis, fibrous scar tissue and granulation tissue to the ADC after therapy have not been determined thus far in absolute values. This could possibly serve as an explanation for variability of ADCs found in 2 patients with post treatment changes who demonstrated a relatively low ADC value.

Accuracy of PET in detecting recurrent disease at the primary site after treatment

In our study, out of 62 cases PET-CT was done in 33 cases. 29 of 33 patients had a proven recurrence. A negative predictive value of 100% gives clinical confidence that a false-negative result is unlikely. In our study, positive predictive value, negative predictive value, sensitivity and specificity of differentiating tumor recurrence from post treatment changes was 90.6%, 100%, 100% and 40%. Low specificity in our study could be due to less number of cases taken for PET-CT. PET-CT has high sensitivity (80–100%) for the detection of residual or recurrent disease at the primary site after treatment. Specificities are less reliable,

Table 5
Comparison of ADC and PET findings.

	Diffusion restriction (ADC values 10 mm^2/s)	PET-CT	Histology
Recurrent tumors (positive)	29 28 (True positive) 1 (False positive)	31 28 (True positive) 3 (False positive)	28
Inflammatory/post treatment changes (Negative)	3 (True negative) 1 (False negative)	2 (True negative) 0 (False negative)	5
Total	33	33	33

Table 6
Accuracy of Diffusion weighted MRI.

Author	Year	Place of study	Sensiti vity (%)	Specif icity (%)	Positive predictiv e value (%)	Negative predictiv e value (%)	Acc urac y (%)	ADC value cut off ($10^{-3}mm^2/s$)
Current	2016	India	94	83.3	95.9	83.3	93.6	1.3
Vaid et al. [6]	2016	India	90.13	82.5	84.4	88.9	86.4	1.2
Desouky et al. [7]	2015	Egypt	100	74.2	70.4	100	84	0.9667
Hwang et al. [8]	2013	Korea	85	84.6	89.5	78.6	84.8	1.46
Gouhar et al. [9]	2011	Egypt	85	88	92	78	86	1.16
Abdel Razek et al. [10]	2007	Egypt	84	90	94	76	87	1.3
Wang et al. [11]	2001	Japan	84	91	93	78	87	1.22

Table 7
Comparison of accuracy of PET.

Author	Year	Place	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	Accuracy (%)
Current	2016	India	100	40	90.6	100	90.9
Horiuchi et al. [17]	2008	Japan	66.7	80	44.4	90.9	77.4
Ronan Abgral et al. [18]	2008	France	100	85	77	100	90
Gandhi et al. [19]	2005	United states	100	50	64.3	100	73.7
Goerres et al. [20]	2004	Switzerland	90.9	93.3	90.9	93.3	92.3
Kubota et al. [21]	2004	Japan	87.5	77.8	70	91.3	81.4
McCollum et al. [14]	2004	USA	100	65	27.3	100	69.2

varying from 50% to 100%, reflecting the prevalence of false positive results (Refer Table 7). The US National Comprehensive Cancer Network (NCCN) does not include specific guidelines for working up recurrent disease. The NCCN recommendations merely relate to standard follow-up with imaging of the primary tumor site within six months of completing treatment using PET/CT or CT and/or MRI with contrast. Further reimaging is indicated based on symptomatology. In our study, 3 patients showed positive results on PET-CT despite the absence of recurrent disease. These patients probably had local inflammation which is known to cause false- positive results. Concerning the optimal time point for follow-up imaging, it is hypothesized that PET scans done later than 12 wk after the end of therapy will not be helpful to surgeons attempting to judge the need for a neck dissection. Although these later scans may still provide clinically useful information (e.g., in the surveillance of high-risk patients or in the detection of early recurrence), they do not qualify as a tool for response assessment [27].

Comparison of PET-CT with DW- MRI

In our study, PET-CT was performed only after 3 months of treatment. Sensitivity of PET-CT and Diffusion weighted MRI was comparable and specificity was comparatively low.

Mc Collum et al. [14] showed that, although FDG PET-CT holds promise in the detection of recurrent SCC of the head and neck, it leads to more false positive results owing to inflammatory changes within the first 4 months after radiation therapy. We reported 3 false positive cases using PET-CT as opposed to 1 false positive using ADC. The ADC maps exhibit a high sensitivity, specificity and accuracy in the discrimination of tumoral and non tumoral tissues. Post contrast administration enhancement may be misleading as all recurrent tumors fail to enhance [23–25]. A morphological MRI assessment may not always be able to locate the accurate site of histology procurement and sometimes histological confirmation may not be feasible in all cases due to complications causing co-morbidities in the patient [26]. This necessitates the advent of a non invasive study like diffusion imaging for the early detection of recurrence in post treatment cases.

Some of the studies showed better sensitivity of PET-CT than DW MRI in early post treatment period (< 4 months). Ghaooni et al. [15] proved that the performance of 18F-FDG PET/CT and MRI are similar on follow up imaging, except for a higher sensitivity of 18F-FDG PET/CT at 4 months. Mukandan et al. [16] also showed similar results stating comparable results of PET-CT and MRI in follow up imaging after 4 months with better sensitivity of PET-CT when evaluation was done earlier.

Strengths of the study

Our cohort selection was uniform as compared to most of earlier studies. Most of the studies done earlier fail to mention a specific time frame of the patients included. Also we carefully measured ADC values using free hand ROI. Unlike most studies done earlier we have evaluated diffusion on both qualitative and quantitative fronts. A head to head comparison between MRI and PET-CT was done in subset of substantial patients who underwent PET-CT.

Conclusion

Diffusion MRI is a potential non-invasive MRI technique which can be used to differentiate recurrent head and neck malignancies from post treatment changes based on ADC values. This technique has very short scanning time and can be safely added to standard MRI protocol in order to achieve better diagnostic criteria with minimum patient discomfort. We postulate an ADC value of 1.3x 10–3 mm^2/s to differentiate tumor recurrence from post treatment changes, yielding an overall 94% sensitivity, 83.3% specificity, 95.9% positive predictive value and 83.3% negative predictive value and 93.6% accuracy. Our study concludes that PET-CT may have better sensitivity than DW MRI in post treatment evaluation period but has low specificity and positive predictive value, which makes us believe that ADC parameters may serve as better biological marker of early disease recurrence in post treatment period, as compared to PET-CT. Use of ADC also saves us from various hassles and radiation involved with use of FDG PET-CT. This study further opens up possibilities for future larger trials for comparison between PET-CT and MRI during early surveillance period for commenting on loco regional status. For distant sites it has been advocated in various studies that PET is a better modality.

Ethical statement

The author(s) declare that Ethics Committee approval was acquired.

The study encompasses MRI & PET-CT study both of which are done routinely in our institute.

Consent was taken prior to MRI examination, before administration of gadolinium based contrast and also before histopathology procedure.

Declaration of Competing Interest

The authors declare that there are no known conflicts of interest.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.oraloncology.2019.06.037.

References

[1] Mukherji SK, Wolf GT. Evaluation of head and neck squamous cell carcinoma after treatment. AJNR Am J Neuroradiol 2003;24(9):1743–6.
[2] Hein P, Eskey C, Dunn J. Diffusion-weighted imaging in the follow-up of treated high- grade gliomas: tumour recurrence versus radiation injury. AJNR Am J Neuroradiol 2004;25(2):201–9.
[3] Kim T, Murakami T, Takahashi S, et al. Diffusion-weighted single-shot echo- planar MR imaging for liver disease. AJR Am J Roentgenol 1999;173:393–8.
[4] Subramaniam RM, Truong M, Peller P, Sakai O, Mercier G. Fluorodeoxyglucose-positron-emission tomography imaging of head and neck squamous cell cancer. AJNR Am J Neuroradiol 2010;31(4):598–604.
[5] De Bree R, van der Putten L, Brouwer J, Castelijns JA, Hoekstra OS, Leemans CR. Detection of locoregional recurrent head and neck cancer after (chemo)radiotherapy using modern imaging. Oral Oncol 2009;45(4–5):386–93.
[6] Vaid S, Chandorkar A, Atre A, Shah D, Vaid N. Differentiating recurrent tumours from post treatment changes in head and neck cancers: does diffusion-weighted MRI solve the eternal dilemma? Clin Radiol 2017;72:74–83.
[7] Desouky SE, AboSeif S, Shama S, et al. Role of dynamic contrast enhanced and diffusion weighted MRI in the differentiation between post treatment changes and recurrent laryngeal cancers. Egypt J Radiol Nucl Med 2015;46:379e89.
[8] Hwang I, Choi SH, Kim YJ, et al. Differentiation of recurrent tumour and post treatment changes in head and neck squamous cell carcinoma: application of high b-value diffusion weighted imaging. AJNR Am J Neuroradiol 2013;34(12):2343e8.
[9] Gouhar GK, El-Hariri MA. Feasibility of diffusion weighted MR imaging in differentiating recurrent laryngeal carcinoma from radionecrosis. Egypt J Radiol Nuclear Med 2011;42(2):169–75.
[10] Abdel Razek AA, Kandeel AY, Soliman N, et al. Role of diffusion-weighted echo-planar MR imaging in differentiation of residual or recurrent head and neck tumors and posttreatment changes. AJNR Am J Neuroradiol 2007;28(6):1146–52.
[11] Wang J, Takashima S, Takayama F, et al. Head and neck lesions: characterization with diffusion–weighted echo-planar MR imaging. Radiology 2001;220:621–30.
[12] Razek AAKA, Megahed AS, Denewer A, Motamed A, Tawfik A, Nada N. Role of diffusion weighted magnetic resonance imaging in differentiation between the viable and necrotic parts of head and neck tumors. Acta Radiol 2008;49(3):364–70.
[13] Matzek W, Czerny C, Krestan C, et al. Non-invasive therapy monitoring with diffusion weighted imaging: evaluation of effect of radiochemotherapy in squamous cell carcinoma of the oropharynx. Paper presented at: XVI International Congress of Head & Neck Radiology, September 2003; Frankfurt/Main, Germany.
[14] Mccollum AD, Burrell SC, Haddad RI, Norris CM, Tishler RB, Case MA, et al. Positron emission tomography with18F-fluorodeoxyglucose to predict pathologic response after induction chemotherapy and definitive chemoradiotherapy in head and neck cancer. Head Neck 2004;26(10):890–6.
[15] Hanooni R, Delpierre I, Magremanne M, et al. 18F-FDG PET/CT and MRI in the follow-up of head and neck squamous cell carcinoma. Contrast Media Mol Imag 2011;6:260e266.
[16] Mukundan H, Sarin A, Gill B, Neelakantan A. MRI and PET–CT: comparison in post-treatment evaluation of head and neck squamous cell carcinomas. Med J Armed Forces India 2014;70(2):111–5.
[17] Horiuchi C, Taguchi T, Yoshida T, Nishimura G, Kawakami M, Tanigaki Y, et al. Early assessment of clinical response to concurrent chemoradiotherapy in head and neck carcinoma using fluoro-2-deoxy-d-glucose positron emission tomography. Auris Nasus Larynx 2008;35(1):103–8.
[18] Abgral R, Querellou S, Potard G, et al. Does 18F-FDG PET/ CT improve the detection of post treatment recurrence of head and neck squamous cell carcinoma in patients negative for disease on clinical follow-up? J Nucl Med 2009;50(1):24–9.
[19] Gandhi D, Falen S, Mccartney W, Shockley W, Weissler M, Wrenn S, et al. Value of 2-[18F] fluoro-2-deoxy-D-glucose imaging with dual-head gamma camera in coincidence mode. J Comput Assist Tomogr 2005;29(4):513–9.
[20] Goerres GW, Schmid DT, Bandhauer F, Huguenin PU, Schulthess GKV, Schmid S, et al. Positron emission tomography in the early follow-up of advanced head and neck cancer. Arch Otolaryngol-Head Neck Surg 2004;130(1):105.
[21] Kubota K, Yokoyama J, Yamaguchi K, Ono S, Qureshy A, Itoh M, et al. FDG-PET delayed imaging for the detection of head and neck cancer recurrence after radiochemotherapy: comparison with MRI/CT. Eur J Nucl Med Mol Imag 2004 Jan;31(4):590–5.
[22] Nomayr A, Lell M, Sweeney R, et al. MRI appearance of radiation-induced changes of normal cervical tissues. Eur Radiol 2001;11:1807–17.
[23] Hein P, Eskey C, Dunn J, et al. Diffusion-weighted imaging in the follow up of treated high-grade gliomas: tumour recurrence versus radiation injury. AJNR Am J Neuroradiol 2004;25:201e9.
[24] Nomayr A, Lell M, Sweeney R, et al. MRI appearance of radiation-induced changes of normal cervical tissues. EurRadiol 2001;11:1807e17.
[25] Baba Y, Yamashita Y, Onomichi M, et al. Dynamic magnetic resonance imaging of head and neck lesions. Top Magn Reson Imag 1999;10:125e9.
[26] Srinivasan A, Mohan S, Mukherji SK. Biologic imaging of head and neck cancer: the present and the future. AJNR Am J Neuroradiol 2012;33:586e94.
[27] Schoder H, Fury M, Lee N, Kraus D. PET monitoring of therapy response in head and neck squamous cell carcinoma. J Nucl Med 2009;50(Suppl. 1):74se88s.