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Differentiation of Benign and Malignant Pathology in the Head and Neck Using 3T Apparent Diffusion Coefficient Values: Early Experience

A. Srinivasan, R. Dvorak, K. Perni, S. Rohrer and S.K. Mukherji

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ORIGINAL
RESEARCHA. Srinivasan
R. Dvorak
K. Perni
S. Rohrer
S.K. Mukherji**Differentiation of Benign and Malignant Pathology
in the Head and Neck Using 3T Apparent
Diffusion Coefficient Values: Early Experience****BACKGROUND AND PURPOSE:** The purpose of this work was to study differences in apparent diffusion coefficient (ADC) values between benign and malignant head and neck lesions at 3T field strength imaging.**MATERIALS AND METHODS:** Our study population in this retrospective study was derived from the patient population who had undergone routine neck 3T MR imaging (for clinical indications) from December 2005 to December 2006. There were 33 patients identified: 17 with benign and 16 with malignant pathologies. In all of the subjects, conventional MR imaging sequences were performed apart from diffusion-weighted sequences. The mean ADC values in the benign and malignant groups were compared using an unpaired *t* test with unequal variance with a *P* < 0.05 considered statistically significant.**RESULTS:** There was a statistically significant difference (*P* = .004) between the mean ADC values (in 10^{-3} mm²/s) in the benign and malignant lesions (1.505 ± 0.487 ; 95% confidence interval, 1.305–1.706, and 1.071 ± 0.293 ; 95% confidence interval, 0.864–1.277, respectively). There were 2 malignant lesions with ADC values higher than 1.3×10^{-3} mm²/s and 5 benign lesions with ADC values less than 1.3×10^{-3} mm²/s. The lack of overlap of ADC values within 95% confidence limits suggests that a 3T ADC value of 1.3×10^{-3} mm²/s may be the threshold value for differentiation between benign and malignant head and neck lesions.**CONCLUSION:** ADC values of benign and malignant neck pathologies are significantly different at 3T imaging, though larger studies are required to establish threshold ADC values that can be applied in daily clinical practice.

CT and conventional MR imaging (using spin-echo [SE] T1-weighted and T2-weighted images) are extensively used at present for evaluation of both palpable and nonpalpable neck lesions, as well as characterization of biologic behavior using imaging criteria, which include necrosis, invasion of adjacent structure, and perineural spread. However, it is not uncommon to encounter lesions that have indeterminate findings on cross-sectional imaging and necessitate further investigation.

Diffusion-weighted imaging (DWI) with calculation of apparent diffusion coefficient (ADC) values has been investigated in the past in an attempt to distinguish between benign and malignant head and neck lesions.¹⁻⁴ These previous studies have been performed at 1.5T strength.¹⁻⁴ 3T imaging with dedicated 16-channel head and neck coils results in substantially improved signal intensity to noise compared with 1.5T and has the potential to produce better quality DWI and ADC maps compared with conventional field strengths.

However, ADC values may vary with field strength, and some authors indicate that the quantitative ADC values obtained at 1.5T may not be transferable to 3T.⁵ The purpose of our study was to determine whether ADC mapping performed at 3T with a dedicated 16-channel head and neck coils can differentiate between benign and malignant pathologies of the head

and neck and to compare these findings with previously reported findings at 1.5T.

Materials and Methods

The retrospective study was approved by the institutional review board. Our study population was derived from the patient population who had undergone routine neck 3T MR imaging (for clinical indications), which included DWI, at our institution, from December 2005 to December 2006. All of the subjects had been scanned on a 3T MR scanner (Achieva 3T Quasar Dual; Philips, Best, the Netherlands). Review of the radiology reports identified 33 patients in this time period with either benign or malignant pathologies. Of these 33 patients, there were 17 patients with benign pathologies (Table 1) and 16 patients with malignant pathologies (Table 2). Twelve of the 17 patients with benign pathologies had pathologic confirmation of disease by tissue sampling. The remaining 6 patients either demonstrated benign features on conventional MR imaging and did not require tissue confirmation or were thought to have benign disease based on both clinical and imaging features. All 16 of the patients with malignant neck pathology had pathologic confirmation of disease by tissue sampling.

DWI was performed on a 16-channel head and neck coil from the skull base up to the thoracic inlet using a single-shot spin-echo (SE) echo-planar imaging sequence (and eddy current correction) with the following parameters: 1) axial plane using a 2454-ms TR, 45-ms TE, 90° flip angle, 4-mm section thickness, 240-mm FOV, and b-values of 0 and 800 s/mm²; and 2) sagittal plane using a 2468-ms TR, 49 ms TE, 90° flip angle, 4-mm section thickness, 260-mm FOV, and b-values of 0 and 1000 s/mm². In all of the subjects, SE axial T1-weighted, turbo SE axial T2-weighted, and post-gadolinium SE axial T1-weighted (with and without fat satu-

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From the Department of Radiology, Division of Neuroradiology, University of Michigan Health System, Ann Arbor, Mich.

Please address correspondence to Ashok Srinivasan, Department of Radiology, Division of Neuroradiology, University of Michigan Health System, 1500 E Medical Center Dr, Ann Arbor, MI 48109; e-mail: ashoks@med.umich.edu

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Table 1: 3T ADC values in benign neck lesions

Age, y/Sex	Lesion	ADC, $\times 10^{-3}$ mm ² /s
89/F	Lipomatous hemangiopericytoma	1.611 \pm 0.167
45/F	Fibrous dysplasia (F/U-15 y)*	0.949 \pm 0.070
22/F	Masseteric hemangioma	1.842 \pm 0.075
57/F	Orbital apex aspergillosis	1.576 \pm 0.214
77/F	Clival mass stable for 7 y*	1.915 \pm 0.221
37/M	Schwannoma (vestibular)	0.739 \pm 0.079
34/F	Schwannoma (vestibular)	1.566 \pm 0.237
36/F	Schwannoma (vestibular)	1.742 \pm 0.181
58/M	Schwannoma (vestibular)	1.922 \pm 0.186
66/M	Schwannoma (jugular foramen)	2.080 \pm 0.332
39/F	Schwannoma (mandibular nerve)	2.033 \pm 0.521
33/M	Oncocytoma (parotid)	2.150 \pm 0.004
62/M	Meningioma (cavernous sinus) (F/U of 2 y)*	1.041 \pm 0.158
58/M	Meningioma (cavernous sinus) (F/U of 3 y)*	1.512 \pm 0.462
29/F	Meningioma (jugular foramen)	0.669 \pm 0.128
41/F	Glomus jugulare	1.379 \pm 0.144
31/F	Sarcoidosis (right cerebellopontine angle mass) (F/U 3 y)*	0.863 \pm 0.151

Note:—F/U indicates follow-up duration; ADC, apparent diffusion coefficient; F, female; M, male.
*No tissue confirmation was obtained.

ration) sequences were performed in addition to axial and sagittal DWI sequences.

All of the ADC measurements were made by 1 neuroradiologist at an Advantage Windows workstation 4.1 (2006; GE Healthcare, Milwaukee, Wis) by placing freehand regions of interest (ROIs) over the pathology on the ADC map. The neuroradiologist was blinded to the histologic diagnosis. ROIs were placed carefully within the center of the lesions (avoiding the peripheral 2 mm internal to the circumference) to avoid any volume averaging, with the average ADC calculated from a minimum of 3 ROIs within each lesion. If there were regions within the lesion that varied in signal intensity on conventional imaging (like cystic changes or necrosis), separate measurements from these distinct areas were obtained. The mean ADC values in the benign and malignant groups were compared using an unpaired *t* test with unequal variance with a *P* < .05 considered statistically significant.

Results

The mean age of the patients with benign disease in the head and neck was 47.8 \pm 18.5 years, and those with malignant

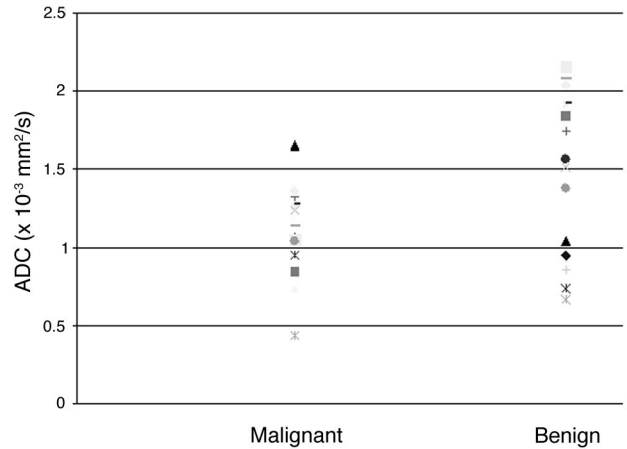


Fig 1. Scatter plot of ADC values in benign and malignant head and neck lesions at 3T strength.

disease was 61.1 \pm 14.8 years. There were 17 benign lesions and 16 malignant lesions, tabulated in Tables 1 and 2, respectively.

The mean ADC values in the benign and malignant lesions were $1.505 \times 10^{-3} \pm 0.487 \times 10^{-3}$ mm²/s (95% confidence interval, 1.305×10^{-3} to 1.706×10^{-3}) and $1.071 \times 10^{-3} \pm 0.293 \times 10^{-3}$ mm²/s (95% confidence interval, 0.864×10^{-3} to 1.277×10^{-3}), respectively. There was a statistically significant difference in ADC values in the 2 groups using the independent samples *t* test with a *P* = .004. The scatter plot of ADC values in the benign and malignant groups is illustrated in Fig 1. Although there is some overlap of ADC values between the benign and malignant lesions, the 95% confidence limits do not show any overlap (Figs 2 and 3). These preliminary findings suggest that ADC value of 1.3×10^{-3} mm²/s on 3T imaging may prove to be the threshold value (cutoff point) for differentiation between benign and malignant head and neck lesions. This number will, however, have to be substantiated by future studies with larger numbers of subjects. In our study, there were only 2 malignant lesions that demonstrated ADC values higher than 1.3×10^{-3} mm²/s: 1 nasopharyngeal cancer (1.319×10^{-3}) and 1 adenosquamous cell cancer (Fig 4) of the skull base (1.649×10^{-3}). The latter lesion demonstrated

Table 2: 3T ADC values in malignant neck lesions

Age, y/Sex	Lesion	Stage	ADC, $\times 10^{-3}$ mm ² /s
65/M	Sinonasal undifferentiated SCC (P)	T4N0M0	0.719 \pm 0.157
35/M	Sinonasal undifferentiated SCC (P)	T4N0M0	1.042 \pm 0.068
51/F	SCC Parotid (P)	T4N2M1	1.064 \pm 0.162
61/M	SCC palatine tonsil (P)	T4N2BM0	0.847 \pm 0.083
62/M	SCC palatine tonsil (P)	T4N3M1	0.733 \pm 0.055
62/M	SCC palatine tonsil (MD)	T3N1M0	1.261 \pm 0.168
59/M	SCC base of tongue (P)	T2N3M0	0.955 \pm 0.095
65/F	SCC soft palate (P)	T1N3M0	1.033 \pm 0.183
78/F	SCC nasopharynx (W)	T4N0M0	1.319 \pm 0.194
58/M	SCC supraglottis (MD)	T4N2BM0	1.278 \pm 0.070
83/M	SCC supraglottis (MD)	T4N0M0	1.138 \pm 0.148
43/M	SCC oropharynx (MD)	T4N1M0	1.359 \pm 0.087
90/F	SCC orbit (W)	T4N1M1	1.055 \pm 0.047
40/F	Adenosquamous cell carcinoma skull base	T4N0M0	1.649 \pm 0.229
57/F	Carcinoma ex pleomorphic adenoma (parotid)	T2N1M0	1.241 \pm 0.194
69/M	Orbital B-cell lymphoma	3A	0.438 \pm 0.099

Note:—SCC indicates squamous cell carcinoma; W, well-differentiated; MD, moderately differentiated; P, poorly differentiated; F, female; M, male; ADC, apparent diffusion coefficient.

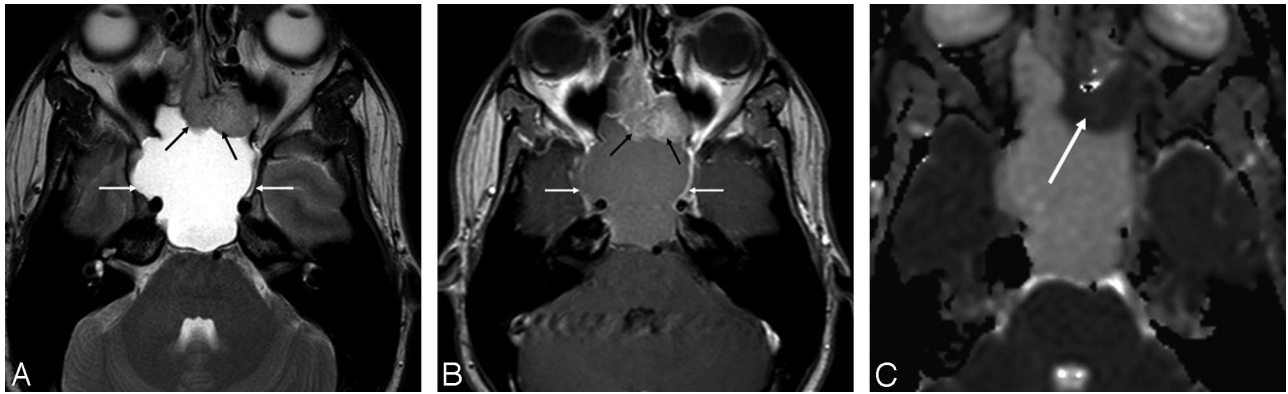


Fig 2. A, T2-weighted axial image in a 35-year-old male patient with pathologically proved sinonasal undifferentiated carcinoma reveals a mass lesion in the left ethmoidal region (*black arrows*) with resultant sphenoidal mucocele (*white arrows*). B, The mass demonstrates heterogeneous enhancement (*black arrows*) on the post-gadolinium axial T1 image with no enhancement within the mucocele (*white arrows*). C, The ADC in the lesion averaged $1.042 \times 10^{-3} \text{ mm}^2/\text{s}$.

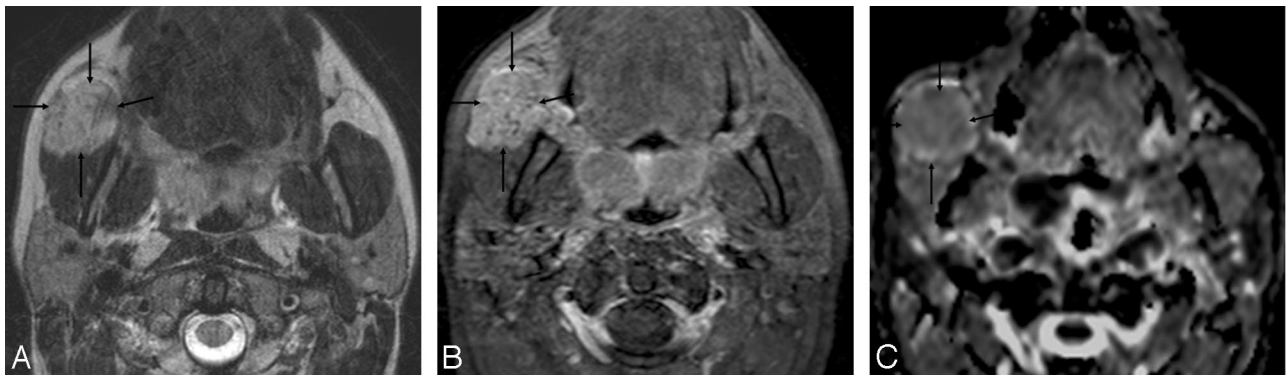


Fig 3. Axial T2-weighted (A) and postcontrast T1-weighted (B) images in a 22-year-old female patient demonstrate a T2 hyperintense lesion with intense contrast enhancement within the right masseter (*black arrows*), which was a biopsy-proven hemangioma. C, The ADC within the lesion measured $1.842 \times 10^{-3} \text{ mm}^2/\text{s}$.

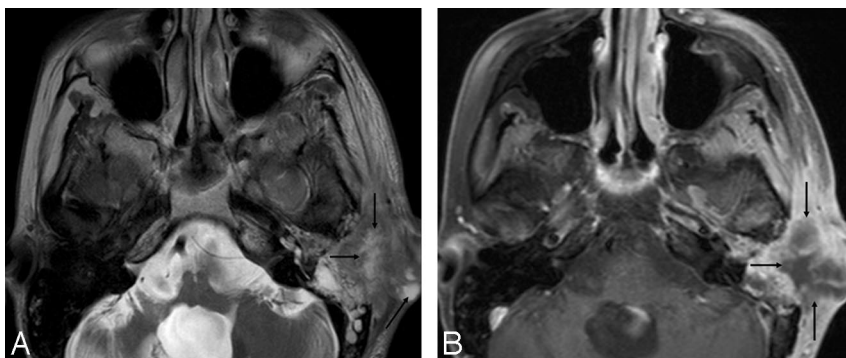


Fig 4. Axial T2-weighted (A) and postcontrast T1-weighted (B) images in a 40-year-old female patient demonstrate a destructive left skull base pathology with heterogenous hyperintensity and cystic areas on T2-weighted images (*black arrows*) and nonenhancing portions on the postcontrast images (*black arrows*). This was a biopsy-proven adenosquamous cell carcinoma with an increased ADC value averaging $1.649 \times 10^{-3} \text{ mm}^2/\text{s}$, probably due to the necrotic areas within the tumor.

central necrosis on conventional images, which is probably responsible for the increased ADC value. There were 5 benign lesions that revealed ADC values less than $1.3 \times 10^{-3} \text{ mm}^2/\text{s}$: fibrous dysplasia (0.949×10^{-3}), acoustic schwannoma (0.739×10^{-3}), cavernous sinus meningioma (1.041×10^{-3}), jugular fossa meningioma (0.669×10^{-3} ; Fig 5), and a neurosarcoidosis mass (0.863×10^{-3}). We think that the hypercellular nature of some benign tumors, like meningiomas, may be responsible for the decreased ADC values observed in the benign category.

Discussion

The results of our study demonstrate a significant difference in ADC values between benign and malignant lesions in the head and neck. This suggests that the addition of diffusion-

weighted MR to routine MR neck protocols may increase the accuracy of imaging in distinguishing benign and malignant neck pathologies. Reductions in both the extracellular matrix and the diffusion space of water protons in the extracellular and intracellular dimensions (due to an increased nuclear-to-cytoplasmic ratio and hypercellularity) have been described as potential reasons for the decreased ADC values within malignant lesions compared with nonmalignant tissue.^{1,6-8}

Although we found significant differences in ADC values between benign and malignant lesions, there was variability in ADC values within each group. Benign lesions like vestibular schwannomas and meningiomas demonstrated a wide range of ADC values that could be because of difference in internal architecture between lesions. For example, one vestibular schwannoma revealed low signal intensity on T2-weighted

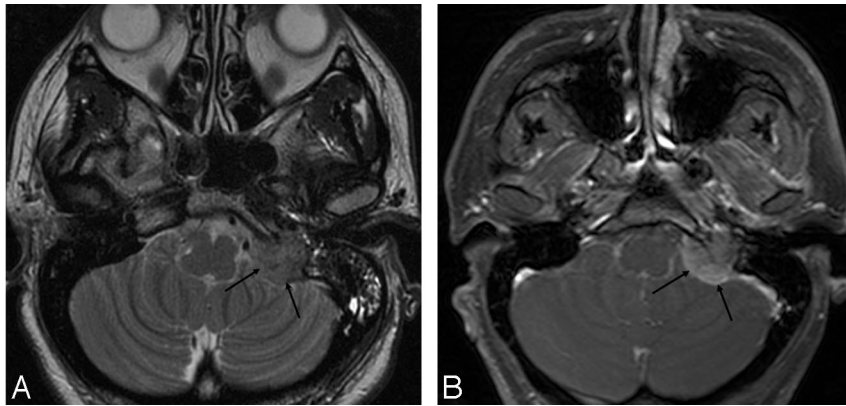


Fig 5. Axial MR images in a 29-year-old woman reveal a left jugular foramen mass that is hypointense on T2-weighted (A) images and enhances with contrast (B). This was a biopsy-proven meningioma with a decreased ADC value of $0.669 \times 10^{-3} \text{ mm}^2/\text{s}$, which may be due to hypercellularity within the benign tumor.

images (suggesting hypercellularity) and an ADC value of $0.739 (\times 10^{-3} \text{ mm}^2/\text{s})$, whereas other vestibular schwannomas that demonstrated cystic changes showed higher ADC values. Although the numbers are limited, there was no trend identified in the relationship of ADC values with degree of differentiation among malignant lesions. One feature of note that we observed with these small numbers was that when the threshold ADC of $1.3 \times 10^{-3} \text{ mm}^2/\text{s}$ was applied in our population, there were 5 outliers (of 17) in the benign category but only 2 outliers (of 16) in the malignant category. In all 5 of the outliers in the benign category, conventional imaging features favored benignancy over malignancy.

Although the difference in ADC values between benign and malignant processes has been demonstrated by other authors, to the best of our knowledge, these have been performed on 1.5T magnets. In addition, it is unclear (and probably controversial) how ADC values vary between different field strengths. A recent study by Huisman et al⁵ demonstrated significant differences in ADC and fractional anisotropy values measured in brain gray and white matter between 1.5T and 3T scanning. Therefore, it is prudent to investigate whether the differences in ADC values between benign and malignant neck lesions that exist at 1.5T prove to be true with higher field strength. This assumes even more importance if we consider the fact that an increasing number of imaging centers is evaluating patients with higher field strength magnets.

There have been several studies investigating the ability of ADC values to differentiate between benign and malignant neck lesions at 1.5T but not at 3T. Wang et al¹ demonstrated that ADC threshold values ($1.22 \times 10^{-3} \text{ mm}^2/\text{s}$) could be used with high accuracy (86%) for predicting malignancy in the neck. This is quite similar to the threshold value of $1.3 \times 10^{-3} \text{ mm}^2/\text{s}$ at 3T imaging in our study. In their study, the ADC values in lymphomas were found to be significantly lower than ADCs in carcinomas, which were, in turn, significantly lower than ADCs of benign solid tumors.¹ These results were also supported by Maeda et al,⁹ who demonstrated significantly lower ADC values in lymphomas compared with squamous cell carcinomas.

A study of parotid tumors by Habermann et al³ revealed ADC values of $2.14^{-3} \pm 0.11^{-3} \text{ mm}^2/\text{s}$, $0.85^{-3} \pm 0.1^{-3} \text{ mm}^2/\text{s}$, and $1.04^{-3} \pm 0.3^{-3} \text{ mm}^2/\text{s}$ in pleomorphic adenomas, Warthin tumors, and mucoepidermoid carcinomas, respectively, with statistically significant different ADC values in comparison with all other evaluated tumors ($P = .001$) and

also among each other ($P < .001$). There was no statistical difference ($P = .18$ to 1.00) in ADC values among all of the other primary malignant parotid gland tumors.

In a study by Sumi et al,² the authors found significantly greater ADC values in metastatic lymph nodes than in benign lymphadenopathy, with nodal lymphomas showing even lower ADC levels. The ADC from metastatic nodes from highly or moderately differentiated cancers was significantly greater than that from poorly differentiated cancers. The findings of this study suggest that DWI could be useful for discrimination of metastatic nodes. Although threshold ADC values were helpful for discriminating benign from metastatic nodes in a study by Abdel Razek et al,⁴ the mean ADC values of both metastatic and lymphomatous nodes were significantly lower than those of benign nodes. This was in contrast to the study by Sumi et al,² where metastatic nodes had higher ADC values than benign nodes. The reason for the discrepancy between the 2 studies is unclear, but it suffices to say that further studies in this regard with larger sample size may help clarify the issue.

ADC values may not only be useful for differentiation for benign and malignant pathologies in their pretherapeutic state but they also hold promise for identification of recurrent tumors after therapy that can potentially alter anatomy enough to make identification by routine imaging challenging. In a study by Vandecaveye et al,¹⁰ the authors investigated the value of diffusion-weighted MR performed at 1.5T in differentiating persistent or recurrent head and neck squamous cell carcinoma from nontumoral postradiotherapeutic alterations. They found the signal intensity on native B0 images to be significantly lower for squamous cell carcinoma than for nontumoral postradiotherapeutic tissue ($P < .0001$) and the signal intensity on native B1000 images to be significantly higher for carcinomas than for nontumoral tissue ($P < .0001$). ADC values were significantly lower for squamous cell carcinomas than for nontumoral tissue ($P < .0001$), resulting in a sensitivity of 94.6%, specificity of 95.9%, and accuracy of 95.5% and supporting the application of diffusion-weighted MR in posttherapeutic imaging. Vandecaveye et al¹¹ also demonstrated in another study that the ADC values were able to differentiate tumor tissue from radiation therapy-induced tissue alterations in 4 patients with laryngeal squamous cell carcinomas.

The present study not only demonstrates that ADC values are different between benign and malignant neck pathologies but also shows that 3T diffusion in the neck can be performed

without degradation of the images by susceptibility artifact. By using 4-mm sections, shorter echo times (45-ms axial plane; 49-ms sagittal plane), and a smaller in-plane voxel size (128×99 axial matrix; 128×101 sagittal matrix), we were able to decrease susceptibility artifacts on a 16-channel head and neck coil with parallel imaging.¹²

In conclusion, we have demonstrated that the ADC values of benign and malignant neck pathologies are significantly different performed at 3T, and our findings are similar to previously reported results performed at 1.5T. These findings are probably due to inherent differences in internal architecture between tissue containing benign and malignant cells. Although our study suggests that an ADC value of 1.3×10^{-3} mm²/s may be the threshold value for distinguishing benign from malignant head and neck pathologies on 3T imaging when conventional imaging is indeterminate, larger studies are required to confirm our results, as well as to establish threshold ADC values that can be applied in daily clinical practice.

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