RESEARCH ARTICLE

Differentiation of benign and malignant lesions of the tongue by using diffusion-weighted MRI at 3.0 T

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Objectives: Diffusion-weighted MRI (DWI) has been introduced in head and neck lesions and adds important information to the findings obtained through conventional MRI. The purpose of this study was to assess the role of DWI in differentiating benign and malignant lesions of the tongue at 3.0-T field strength imaging.

Methods: 78 patients with 78 lingual lesions underwent conventional MRI and DWI with b-values of 0 and $1000 \, \mathrm{s \, mm^{-2}}$ before therapy. The apparent diffusion coefficient (ADC) maps were reconstructed, and the ADC values of the lingual lesions were calculated and compared between benign and malignant lesions of the tongue.

Results: The mean ADC values of the malignant tumours, benign solid lesions and cystic lesions were $(1.08 \pm 0.16) \times 10^{-3}$, $(1.68 \pm 0.33) \times 10^{-3}$ and $(2.21 \pm 0.35) \times 10^{-3} \, \mathrm{mm^2 \, s^{-1}}$, respectively. The mean ADC values of malignant tumours were significantly lower ($p < 0.001$) than those of benign solid lesions, and the mean ADC values of benign solid lesions were significantly lower ($p < 0.001$) than those of cystic lesions. Receiver operating characteristic analysis showed that when an ADC value $< 1.31 \times 10^{-3} \, \mathrm{mm^2 \, s^{-1}}$ was used for predicting malignancy, the highest accuracy of 95.3%, sensitivity of 92.6% and specificity of 97.3% were obtained.

Conclusions: ADC values of benign and malignant lesions are significantly different at 3.0-T imaging. DWI can be applied as a complementary tool in the differentiation of benign and malignant lesions of the tongue.

Introduction

An early and accurate differentiation of malignant tumours of the tongue from benign lesions is critical for treatment planning and prognosis.[1–3] Since location of the tongue is superficial, the pathological biopsy is commonly used for the pre-operative diagnosis. However, the biopsy is invasive, and the results are not always conclusive.[4] Therefore, pre-operative imaging plays an important role in treatment selection and surgical planning. CT and conventional MRI are used to localize lingual masses and delineate their extent.[5,6] However, accurate diagnosis and differentiating malignant from benign pathologies are likely to be difficult because of unspecific and overlapping imaging findings.[7]

Recently, diffusion-weighted MRI (DWI) has been introduced in the differentiation of head and neck tumours as a relatively new technique that depicts molecular diffusion, which is the random motion of water protons in biological a tissues. The random motion, classically called Brownian motion, is affected by cellular packing, intracellular elements, cell membranes and macromolecules present in various tissue compartments. The extent of molecular diffusion can be quantified in terms of the apparent diffusion coefficient (ADC). The

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ADC values reflect the microstructure or pathophysiological state of a tissue and are inversely correlated with tissue cellularity.[8–10] Some studies reported the application of DWI with calculation of ADC in the differentiation between benign and malignant head and neck masses.[11–15] However, most studies used 1.5-T field strength. To our knowledge, there is only one report on using ADC measurements for differentiating malignant from benign lesions of the tongue at 1.5-T MR.[16] However, it is reported that the quantitative ADC values obtained at 1.5 T may not be transferable to 3.0 T.[17]

The purpose of our study was to investigate the diagnostic value of the ADCs calculated from DWI in distinguishing between benign and malignant lesions of the tongue at 3.0-T field strength imaging.

Methods and materials

This retrospective study was performed on 87 consecutive patients with lingual lesions from May 2012 to August 2014. All patients underwent conventional MRI and DWI at The First Affiliated Hospital of Zhengzhou University (Henan, China) without previous biopsy, surgery or treatment. Nine subjects were excluded from the study owing to lesions <1 cm on MR images ($n = 4$), obvious susceptibility artefacts ($n = 4$) or motion artefacts ($n = 1$). The final diagnoses were made histologically by using either surgery ($n = 67$) or biopsy ($n = 9$), and two inflammatory lesions were established with follow-up studies that revealed disappearance or remarkable regression of the lesions after antibacterial therapy. One patient had two lesions with different image characteristics, and the lesion that was the cause of the patient's chief complaint was selected for ADC analysis. Thus, 78 patients with 78 lingual lesions were enrolled in this study. This study was approved by the local institutional ethics committee, and informed consent was waived because this was a retrospective study.

MR examinations were performed on a 3.0-T whole-body MR unit (MAGNETOM® Skyra®; Siemens Healthcare, Erlangen, Germany) with an integrated 20-channel head and neck coil. Sedation was routinely achieved in children under 10 years old using oral chloral hydrate (70–80 mg kg^{-1} body weight) in 11 patients. Before DWI, T_1 weighted spin echo images [repetition time/echo time (TR/TE) of 2000/9 ms], T_2 weighted turbo spin echo images (TR/TE of 3800/92 ms) and T_2 weighted turbo spin echo images with fat suppression (TR/TE of 7440/125 ms) were obtained in the transverse plane, with a section thickness of 5 mm, an intersection gap of 1 mm, a field of view of 24×24 cm and an acquisition matrix of 256×256. 24 transverse images of each sequence covered the lesions and areas of drainage from the regional lymph nodes. T_2 weighted images with fat suppression (TR/TE of 4000/94 ms) were obtained in the coronal plane, with the same pulse sequence parameters.

DWI was obtained at the same section position as the axial T_1 weighted images by using the spin echo single-shot echo-planar sequence. The parameters were as follows: TR/TE of 3200/70 ms, field of view of 24×24 cm, an acquisition matrix of 192×192, 24 sections and section thickness of 5 mm with an intersection gap of 1 mm. Diffusion-probing gradients were used in the x-, y-, and z-directions with b-values of 0 and 1000 s mm^{-2}. ADC maps were automatically generated by the manufacturer software built into the MR unit (Syngo® REVEAL; Siemens Healthcare). Acquisition time for DWI was 48 s. After intravenous bolus injection of 0.1 mmol kg^{-1} gadopentetate dimeglumine (Magnevist®; Bayer Schering Pharma AG, Berlin, Germany), enhanced T_1 weighted images (TR/TE of 884/6.8 ms) were obtained with or without fat suppression.

The quantitative analysis of the ADC map was made by one radiologist (15 years' experience in head and neck MRI) who was blinded to the clinical information and histopathological results. The region of interest was drawn within the centre of the lesions (avoiding the peripheral 2-mm internal to the circumference) on the ADC maps using an electronic cursor at the Siemens MMWP workstation (Syngo multimodality workplaces; Siemens Healthcare). In measuring the ADCs, region of interests were placed on the solid-appearing areas for the solid masses (avoiding cystic or necrotic portion) and on the cystic parts for the cystic lesions using both DWI and conventional MRI as reference images, including T_1 weighted, T_2 weighted or contrast-enhanced T_1 weighted images. The mean ± standard deviation of the ADC values for the lingual lesions was calculated.

Statistical analyses were performed by using SPSS® v. 11.0 software (SPSS Inc., Chicago, IL). The Kolmogorov–Smirnov (K–S) test was used for diagnosis normality of data distribution. As all data were revealed to be parametric with normal distribution, an independent samples t-test was used to compare between the two groups. To compare more than two groups, one-way analysis of variance was used. Receiver operating characteristic curve analysis was used to determine the cut-off point with highest accuracy and sensitivity as the optimal ADC threshold value to differentiate between benign and malignant lesions. The area under the receiver operating characteristic curve was also calculated. A probability p-value < 0.05 indicated a statistically significant difference.

Results

There were 37 patients with malignant tumours (age range, 11–81 years; mean age, 52.71 ± 16.11 years; male : female ratio, 28 : 9), including 24 squamous cell carcinomas, 6 adenoid cystic carcinomas, 4 non-Hodgkin's lymphomas, 1 mucoepidermoid carcinoma, 1 epi-myo-epi carcinoma and 1 metastasis. 27 patients (age range, 2–84 years; mean age, 31.75 ± 27.88 years; male : female ratio, 12 : 15) had benign solid masses that consisted of 18 cases of vascular malformation, 6 inflammatory

lesions, 1 schwannoma, 1 hamartoma and 1 lingual thyroid. 14 patients (age range, 1–74 years; mean age, 21.46 ± 23.07 years; male : female ratio, 9 : 5) had cysts.

Table 1 displays the mean ADC values of the malignant and benign histological diagnoses. Figure 1 shows the distribution of ADC values. The mean ADC values of the malignant tumours, benign solid lesions and cystic lesions were $(1.08 \pm 0.16) \times 10^{-3}$, $(1.68 \pm 0.33) \times 10^{-3}$ and $(2.21 \pm 0.35) \times 10^{-3} \, \text{mm}^2 \, \text{s}^{-1}$, respectively (Figures 2–4). A statistically significant difference was found among the three groups ($p < 0.001$). The mean ADC values of the malignant tumours were significantly lower ($p < 0.001$) than those of the benign solid masses, and the mean ADC values of the benign solid masses were significantly lower ($p < 0.001$) than those of the benign cystic lesions.

There were also statistically significant differences between ADC values of different malignant tumours of the tongue ($p < 0.001$). Non-Hodgkin lymphomas $[(0.73 \pm 0.08) \times 10^{-3} \, \text{mm}^2 \, \text{s}^{-1}]$ revealed significantly lower ADC values than squamous cell carcinomas $[(1.12 \pm 0.11) \times 10^{-3} \, \text{mm}^2 \, \text{s}^{-1}]$ ($p < 0.001$) and adenoid cystic carcinomas $[(1.14 \pm 0.10) \times 10^{-3} \, \text{mm}^2 \, \text{s}^{-1}]$ ($p < 0.001$). There was no significant difference in the ADC values between squamous cell carcinomas and adenoid cystic carcinomas ($p = 1.000$). Within different benign solid lesions, the highest ADC value was detected in patients with vascular malformation, and the ADC values of inflammatory lesions $[(1.35 \pm 0.23) \times 10^{-3} \, \text{mm}^2 \, \text{s}^{-1}]$ were significantly lower than those of vascular malformation $[(1.80 \pm 0.29) \times 10^{-3} \, \text{mm}^2 \, \text{s}^{-1}]$ ($p = 0.005$). There was significant difference in the ADC values between malignant tumours and inflammatory lesions ($p = 0.001$).

Receiver operating characteristic analysis showed that when the optimal threshold for the ADC was $1.31 \times 10^{-3} \, \text{mm}^2 \, \text{s}^{-1}$, the best result for distinguishing between benign solid lesions and malignant tumours of the tongue was obtained with a sensitivity of 92.6%, a specificity of 97.3%, an accuracy of 95.3% and the area under the curve of 0.963 (Figure 5).

Discussion

The results of this study demonstrated that the mean ADC values of malignant tumours were significantly lower than those of benign solid and cystic lesions. The lower ADC values of malignant tumours were attributed to the pathophysiological status (hypercellularity and enlarged nuclei). Hypercellularity reduces the extracellular matrix and the diffusion space of water protons in the extracellular compartment, and enlarged nuclei decreases the intracellular dimensions, both resulting in decreased ADC values.[11–13]

The findings of this study are in concordance with prior studies. Srinivasan et al[12] demonstrated a significant difference in ADC values between benign and malignant lesions in the head and neck at 3.0-T imaging. They established an optimal ADC threshold of $1.3 \times 10^{-3} \, \text{mm}^2 \, \text{s}^{-1}$ for differentiating malignant from benign tumours. The ADC threshold of our study is very similar to Srinivasan's. In a study by Wang et al,[11] the researchers found that the ADC values of solid benign masses were significantly higher than those of malignant tumours in the head and neck, and the ADC values of cystic lesions were significantly higher than those of solid benign masses. These results were also supported by Abdel Razek et al.[14] To our knowledge, there is only one previous report on DWI in the diagnosis of the tongue tumours by Ai et al.[16] Their results indicated that malignant tumours exhibited significantly lower ADC values (using *b*-values of 500 and 1000 s mm^{-2}) than those of benign lesions at 1.5-T imaging, and the ADC$_{b=500}$ value was $< 1.43 \times 10^{-3} \, \text{mm}^2 \, \text{s}^{-1}$ for predicting malignancy. Their ADC threshold was greater than ours. This variation can be explained by multiple factors including the use of different *b*-values, field strength and also by the variation in histology of included lesions. Within the benign lesions, Ai et al[16] included cystic lesions and they had no inflammatory lesions, whereas our study had solid lesions (including inflammatory lesions) and cystic lesions as two groups, resulting in a lower mean ADC value.

Table 1 Mean apparent diffusion coefficient (ADC) values of malignant tumours, benign solid and cystic lesions of the tongue ($\times 10^{-3} \, \text{mm}^2 \, \text{s}^{-1}$)

| Pathology	Number	ADC (mean ± standard deviation)	ADC (minimum)	ADC (maximum)
Malignant	37	1.08 ± 0.16	0.68	1.32
Squamous cell carcinoma	24	1.12 ± 0.11	0.94	1.32
Adenoid cystic carcinoma	6	1.14 ± 0.10	1.04	1.29
Non-Hodgkin's lymphoma	4	0.73 ± 0.08	0.85	0.68
Mucoepidermoid carcinoma	1	1.00	–	–
Epi-myo-epi carcinoma	1	1.15	–	–
Metastasis	1	1.27	–	–
Benign	27	1.68 ± 0.33	0.98	2.43
Vascular malformation	18	1.80 ± 0.29	1.34	2.43
Inflammatory lesions	6	1.35 ± 0.23	0.98	1.67
Schwannoma	1	1.33	–	–
Hamartoma	1	1.82	–	–
Lingual thyroid	1	1.63	–	–
Cyst	14	2.21 ± 0.35	1.16	2.63
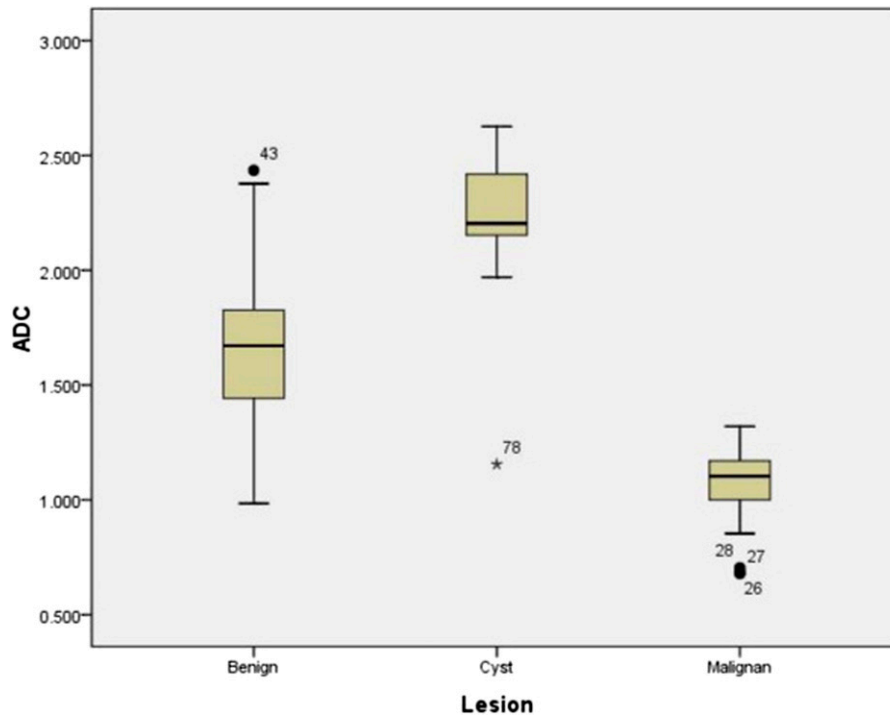
Figure 1 Box and whisker plot of apparent diffusion coefficient (ADC) values of lingual lesions at 3.0-T strength. Malignant tumours (Malignan) showed lower ADC values than benign solid masses and cystic lesions (Cyst).

Although the result of this study demonstrated significant difference in ADC values between benign and malignant lesions, there was variability in ADC values within each group. Within the malignant tumours, lymphomas have more cellularity, and larger nuclei, resulting in less extracellular or intracellular space. The ADC values of lymphomas were lower than those of squamous cell carcinomas ($p < 0.001$) and adenoid cystic carcinomas ($p < 0.001$), and this finding is similar to prior studies.[18,19] In addition, the present study found that there was no significant difference in ADC values between squamous cell carcinomas and adenoid cystic carcinomas ($p = 1.00$). Although inflammatory lesions showed lower ADC values in benign lesions of the tongue, they were still higher than those of malignant tumours ($p = 0.001$). This result may be associated with hypercellularity and enlarged nuclei in malignant tumours and varying properties of secretions in inflammatory lesions. The prior studies on the difference between inflammation and malignant tumours on DWI had reached no agreement. Wang et al[20] found there was no significant difference in the ADC values between inflammatory and malignant masticator
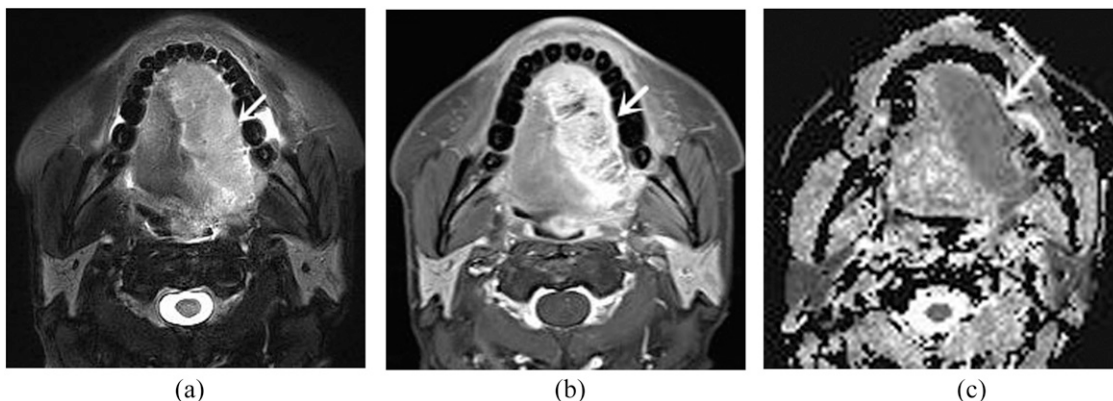

Figure 2 A 55-year-old male with squamous cell carcinoma. (a) Axial T_2 weighted image with fat suppression shows a homogeneously hyperintense mass (arrow) at the right lateral aspect of the tongue, which extends across the midline. (b) Axial contrast-enhanced T_1 weighted MR image with fat suppression demonstrates heterogeneous enhancement (arrow). (c) Apparent diffusion coefficient (ADC) map reveals a hypointense mass (arrow). The ADC value is $1.17 \times 10^{-3}\,\mathrm{mm^2\,s^{-1}}$.
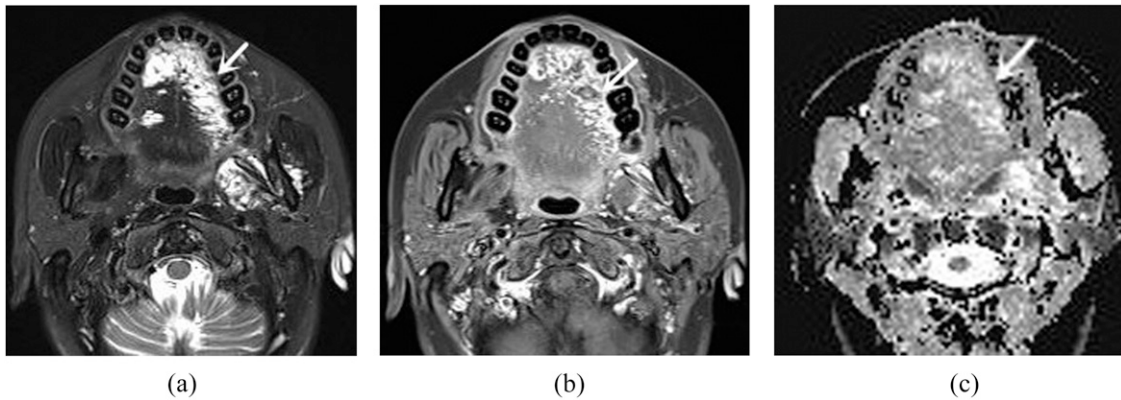
Figure 3 A 43-year-old female with vascular malformation. (a) Axial T_2 weighted image with fat suppression shows multiple heterogeneously hyperintense lesions (arrow) in the tongue dorsum. (b) Axial contrast-enhanced T_1 weighted MR image with fat suppression demonstrates heterogeneous enhancement (arrow). (c) Apparent diffusion coefficient (ADC) map reveals heterogeneously hyperintense lesions (arrow). The ADC value is $1.51 \times 10^{-3}\,\mathrm{mm^2\,s^{-1}}$.

space lesions. However, Abdel Razek and Nada[21] reported that the ADC value of masticator space malignancy was significantly lower than that of masticator space infection. Sasaki et al[18] also demonstrated that DWI could differentiate inflammatory from malignant tumours in the sinonasal area. The different results may be owing to different pathologies of patients as well as different data acquisitions. However, it is obvious that the ADC values of benign cystic lesions in this study was higher than those of the other two categories of lesions owing to the relatively freer mobility of water protons in the fluid than in other tissues.

In the present study, the ADC threshold value was $1.31 \times 10^{-3}\,\mathrm{mm^2\,s^{-1}}$, resulting in the highest sensitivity of 97.3%, a specificity of 92.6% and an accuracy of 95.3%. One patient with squamous cell carcinoma ($1.32 \times 10^{-3}\,\mathrm{mm^2\,s^{-1}}$) was misdiagnosed with a benign lesion. The small foci of liquefactive necrosis in the tumour may explain the slightly high ADC value of squamous cell carcinoma. Two inflammatory lesions exhibited low ADC values (1.24×10^{-3} and $0.98 \times 10^{-3}\,\mathrm{mm^2\,s^{-1}}$) and were falsely diagnosed as malignant lesions. A large

amount of inflammatory cells with abundant exudation of protein would limit the motion of the water protons in the extracellular compartment and may be the reason for the low ADC value of the inflammatory lesion. Another inflammatory lesion showed low ADC value because of squamous cell hyperplasia in the pathological analyses. One dermoid cyst revealed a lower ADC value ($1.16 \times 10^{-3}\,\mathrm{mm^2\,s^{-1}}$) among cystic lesions owing to higher protein component in the fluid that increased the viscosity and decreased the water proton mobility.[11]

The ADC value is not only dependent on the extent of molecular diffusion but also varies with the underlying chosen b-values. At lower b-values, an additional effect of microperfusion is introduced, leading to stronger signal decay and higher ADC values. At The First Affiliated Hospital of Zhengzhou University, we opted to use a maximum b-value of $1000\,\mathrm{s\,mm^{-2}}$, which was consistent with most clinical studies.[9] The use of higher b-values results in ADC values that are much lower and better approximate the true diffusion of the tissue. To the best of our knowledge, it is still controversial how ADC values vary between different field strengths. While significant
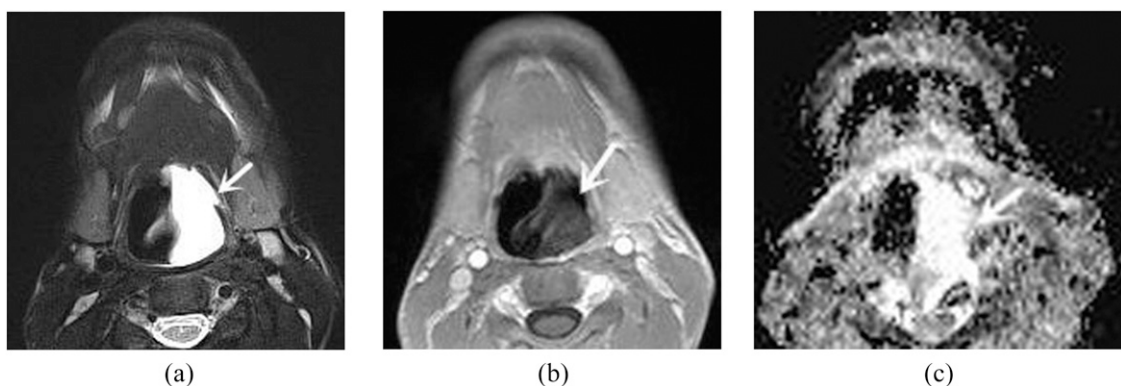

Figure 4 A 17-year-old male with cyst. (a) Axial T_2 weighted image with fat suppression shows a homogeneously hyperintense lesion (arrow) in the tongue root. (b) Axial contrast-enhanced T_1 weighted MR image demonstrates heterogeneously peripheral enhancement (arrow). (c) Apparent diffusion coefficient (ADC) map reveals a hyperintense lesion (arrow). The ADC value is $2.17 \times 10^{-3}\,\mathrm{mm^2\,s^{-1}}$.
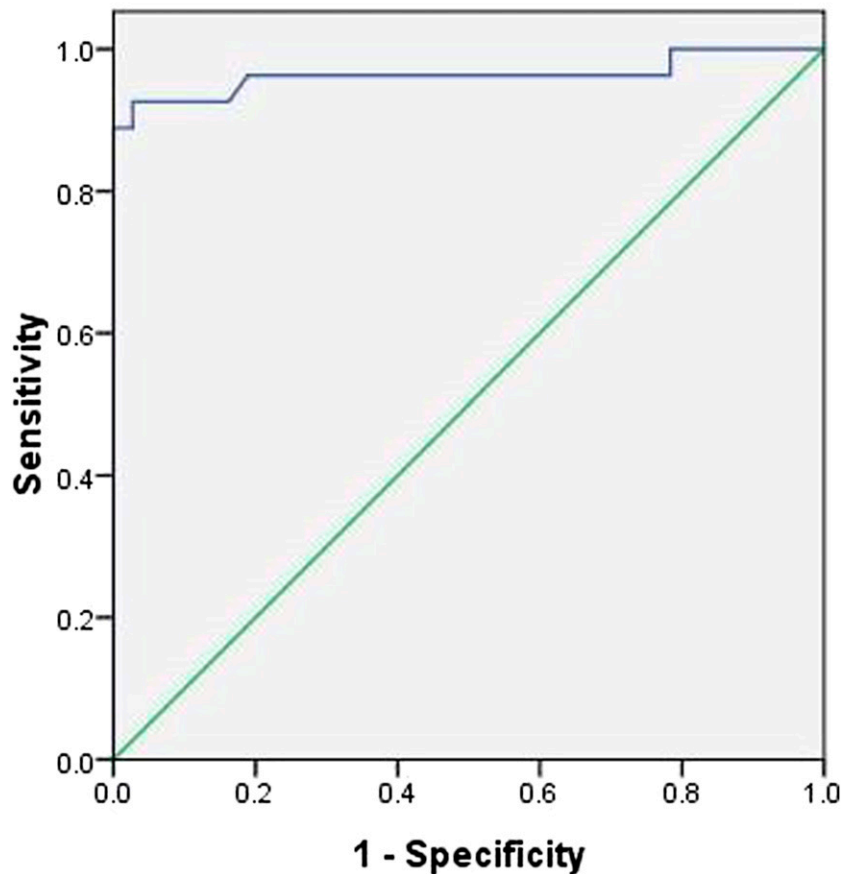
ROC Curve

Figure 5 Receiver operating characteristic (ROC) curve of apparent diffusion coefficient value used for differentiating malignant tumours from benign solid lesions of the tongue. The optimal threshold was $1.31 \times 10^{-3}\,mm^2\,s^{-1}$ with a sensitivity of 92.6%, a specificity of 97.3% and an accuracy of 95.3%.

differences in ADC values measured in the brain's gray and white matter regions have been reported between 1.5- and 3.0-T field strengths,[17] no such studies have been performed in head and neck tumours. Therefore, the present study attempted to investigate whether the differences in ADC values between benign and malignant lesions of the tongue are reproducible towards 3.0 T.

The present study is a retrospective study, which includes patients suspected or at risk of a specific diagnosis. The design of this study is appropriate to evaluate diagnostic accuracy and is comparable to daily practice, compared with a case–control design, which introduces a bias in patient selection and risks the chance of overestimation of the diagnostic accuracy.[22] In addition, the quantitative analysis of the ADC map and region-of-interest delineation of this study were made by one radiologist who may have a bias in ADC values measurement. In the study by Ai et al,[16] two radiologists in consensus obtained the ADC values measurement, and the ADC threshold ($1.43 \times 10^{-3}\,mm^2\,s^{-1}$) was greater than that of ours ($1.31 \times 10^{-3}\,mm^2\,s^{-1}$). Except for the use of different

b-values, field strength and the variation in pathological types, delineation methods can be other possible factors that affect ADC values.

In this study, the group of patients was heterogeneous with different pathological entities and different age groups of adults and children. Further investigations are recommended in a larger number of cases on certain pathological lesions in adults or children. One limitation of the echo-planar sequence of the tongue is image degradation caused by motion and susceptibility artefacts. We noted that five patients were excluded because of bad image quality in this work. It is reported that artefact volumes were lower with a 3.0-T MRI scanner than with a 1.5-T machine.[23] We expect a thinner section, and parallel imaging can be performed for better image contrast in the future studies.[8] Another shortcoming of this study is that ADC values between some benign lesions and malignant tumours overlap, and this could result in misdiagnosis. Thus, future studies of multiparametric MRI may be helpful to improve the diagnostic accuracy of differentiating malignant from benign lesions.[24]

In conclusion, DWI is useful in differentiating benign lesions from malignant tumours of the tongue at 3.0 T. The ADC values are lower in malignant tumours than in benign lesions of the tongue. An ADC value $<1.31 \times 10^{-3}\,\mathrm{mm^2\,s^{-1}}$ can be used for predicting malignant tumours of the tongue.

References

1. Lim YC, Lee JS, Koo BS, Kim SH, Kim YH, Choi EC. Treatment of contralateral N0 neck in early squamous cell carcinoma of the oral tongue: elective neck dissection versus observation. *Laryngoscope* 2006; **116**: 461–5. doi: 10.1097/01.mlg.0000195366.91395.9b

2. Johnson PL, Eckard DA, Brecheisen MA, Girod DA, Tsue TT. Percutaneous ethanol sclerotherapy of venous malformations of the tongue. *AJNR Am J Neuroradiol* 2002; **23**: 779–82.

3. Williams JD, Sclafani AP, Slupchinskij O, Douge C. Evaluation and management of the lingual thyroid gland. *Ann Otol Rhinol Laryngol* 1996; **105**: 312–16. doi: 10.1177/000348949610500414

4. Zbären P, Nuyens M, Loosli H, Stauffer E. Diagnostic accuracy of fine-needle aspiration cytology and frozen section in primary parotid carcinoma. *Cancer* 2004; **100**: 1876–83.

5. Ong CK, Chong VF. Imaging of tongue carcinoma. *Cancer Imaging* 2006; **6**: 186–93. doi: 10.1102/1470-7330.2006.0029

6. Lwin CT, Hanlon R, Lowe D, Brown JS, Woolgar JA, Triantafyllou A, et al. Accuracy of MRI in prediction of tumour thickness and nodal stage in oral squamous cell carcinoma. *Oral Oncol* 2012; **48**: 149–54. doi: 10.1016/j.oraloncology.2011.11.002

7. Alberico RA, Husain SH, Sirotkin I. Imaging in head and neck oncology. *Surg Oncol Clin N Am* 2004; **13**: 13–35. doi: 10.1016/S1055-3207(03)00124-8

8. Chawla S, Kim S, Wang S, Poptani H. Diffusion-weighted imaging in head and neck cancers. *Future Oncol* 2009; **5**: 959–75. doi: 10.2217/fon.09.77

9. Thoeny HC, De Keyzer F, King AD. Diffusion-weighted MR imaging in the head and neck. *Radiology* 2012; **263**: 19–32. doi: 10.1148/radiol.11101821

10. 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**: 134–46. doi: 10.1148/radiol.2511080128

11. Wang J, Takashima S, Takayama F, Kawakami S, Saito A, Matsushita T, et al. Head and neck lesions: characterization with diffusion-weighted echo-planar MR imaging. *Radiology* 2001; **220**: 621–30. doi: 10.1148/radiol.2202010063

12. Srinivasan A, Dvorak R, Perni K, Rohrer S, Mukherji SK. Differentiation of benign and malignant pathology in the head and neck using 3T apparent diffusion coefficient values: early experience. *AJNR Am J Neuroradiol* 2008; **29**: 40–4. doi: 10.3174/ajnr.A0743

13. Sakamoto J, Yoshino N, Okochi K, Imaizumi A, Tetsumura A, Kurohara K, et al. Tissue characterization of head and neck lesions using diffusion-weighted MR imaging with SPLICE. *Eur J Radiol* 2009; **69**: 260–8. doi: 10.1016/j.ejrad.2007.10.008

14. Abdel Razek AA, Gaballa G, Elhawarey G, Megahed AS, Hafez M, Nada N. Characterization of pediatric head and neck masses with diffusion-weighted MR imaging. *Eur Radiol* 2009; **19**: 201–8. doi: 10.1007/s00330-008-1123-6

15. Schakel T, Hoogduin JM, Terhaard CH, Philippens ME. Diffusion weighted MRI in head-and-neck cancer: geometrical accuracy. *Radiother Oncol* 2013; **109**: 394–7. doi: 10.1016/j.radonc.2013.10.004

16. Ai S, Zhu W, Liu Y, Wang P, Yu Q, Dai K. Combined DCE- and DW-MRI in the diagnosis of benign and malignant tumors of the tongue. *Front Biosci (Landmark Ed)* 2013; **18**: 1098–111.

17. Huisman TA, Loenneker T, Barta G, Bellemann ME, Hennig J, Fischer JE, et al. Quantitative diffusion tensor MR imaging of the brain: field strength related variance of apparent diffusion coefficient (ADC) and fractional anisotropy (FA) scalars. *Eur Radiol* 2006; **16**: 1651–8.

18. Sasaki M, Eida S, Sumi M, Nakamura T. Apparent diffusion coefficient mapping for sinonasal diseases: differentiation of benign and malignant lesions. *AJNR Am J Neuroradiol* 2011; **32**: 1100–6. doi: 10.3174/ajnr.A2434

19. Fong D, Bhatia KS, Yeung D, King AD. Diagnostic accuracy of diffusion-weighted MR imaging for nasopharyngeal carcinoma, head and neck lymphoma and squamous cell carcinoma at the primary site. *Oral Oncol* 2010; **46**: 603–6. doi: 10.1016/j.oraloncology.2010.05.004

20. Wang P, Yang J, Yu Q, Ai S, Zhu W. Evaluation of solid lesions affecting masticator space with diffusion-weighted MR imaging. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2010; **109**: 900–7. doi: 10.1016/j.tripleo.2010.01.005

21. Abdel Razek AA, Nada N. Role of diffusion-weighted MRI in differentiation of masticator space malignancy from infection. *Dentomaxillofac Radiol* 2013; **42**: 20120183. doi: 10.1259/dmfr.20120183.

22. Driessen JP, van Kempen PM, van der Heijden GJ, Philippens ME, Pameijer FA, Stegeman I, et al. Diffusion-weighted imaging in head and neck squamous cell carcinomas: a systematic review. *Head Neck* 2015; **37**: 440–8. doi: 10.1002/hed.23575

23. Rylander S, Thörnqvist S, Haack S, Pedersen EM, Muren LP. Intensity profile based measurement of prostate gold markers influence on 1.5 and 3T diffusion-weighted MR images. *Acta Oncol* 2011; **50**: 866–72. doi: 10.3109/0284186X.2011.590523

24. Sasaki M, Sumi M, Eida S, Ichikawa Y, Sumi T, Yamada T, et al. Multiparametric MR imaging of sinonasal diseases: time-signal intensity curve- and apparent diffusion coefficient-based differentiation between benign and malignant lesions. *AJNR Am J Neuroradiol* 2011; **32**: 2154–9. doi: 10.3174/ajnr.A2675