Original Article

The Role of Diffusion-Weighted Magnetic Resonance Imaging (DWI) in Head and Neck Masses

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Objective: To differentiate between benign from malignant head and neck masses using diffusion-weighted imaging (DWI) and measured the cutoff point of apparent diffusion coefficient (ADC) value.

Materials and Methods: DWI and measured ADC value were performed in 24 patients with head and neck masses at Ramathibodi Hospital from May 2013 to September 2015. The 37 lesions in 24 patients were divided into benign and malignant head and neck masses.

Results: The 30 lesions were malignant and 7 lesions were benign head and neck masses. By visual inspection, DWI can differentiate benign from malignant head and neck masses by 93.3% of sensitivity, 85.5% of specificity, 91.8% of accuracy, 96.6% of PPV and 75% of NPV. Mean ADC values in benign and malignant head and neck masses were 1.126×10^{-3} mm^2/s and 0.973×10^{-3} mm^2/s, respectively, which was no statistical significant difference (*p*-value of 0.445). The cutoff point of mean ADC value was 1.200×10^{-3} mm^2/s for differentiation of benign and malignant head and neck masses.

Conclusion: DWI can differentiate benign from malignant head and neck masses qualitatively. It should be applied to MR protocol in the head and neck masses to enhance diagnostic accuracy.

Keywords: DWI (diffusion-weighted imaging), ADC (apparent diffusion coefficient)

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The DWI is a noninvasive magnetic resonance imaging (MRI) technique that depicts free molecular diffusion of the water protons within biological tissues, which is termed Brownian motion. The translational diffusion can be measured and expressed in apparent diffusion coefficient (ADC). DWI can reflect changes of tissue organization at cellular level. Microstructural changes affect the motion of water molecule and consequently alter the water diffusion properties and the MRI signal intensity. Therefore, the techniques can provide different information about tissue of different disease[1,2].

DWI has been proven useful for brain imaging in differentiation between infarcted tissue and other pathological processes[1,3,4]. In recent years, there are many reports of the potential utility of DWI for evaluation of extracranial disease[3]. In tissues with cytotoxic edema or in highly cellular regions, there is restricted diffusion, which can be measured both qualitatively and quantitatively[5]. Hypercellular tissue, such as malignant tumors will present restricted diffusion and low ADC values but vasogenic edema, inflammation, fibrosis and necrosis are not restricted diffusion and higher ADC values[6,7]. DWI seems to be safer and more affordable method considering the absence of radiation and to the higher cost of FDG-PET-CT[8-10].

The present cross-sectional study collected retrospective data. The purpose was to differentiate between benign from malignant head and neck masses by using DWI with measurement of the cutoff point of ADC values.

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Materials and Methods

Patient population

Twenty four patients with 37 lesions of head and neck masses who underwent contrast-enhanced MRI

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study with DWI and ADC at Ramathibodi Hospital from May 2013 to September 2015 were enrolled. The present was approved by the Ethics Committee on Human Experimentation of Faculty of Medicine Ramathibodi Hospital.

Demographic data

The demographic data included gender, age and clinical history (underlying disease of malignancy, prior to treatment).

Inclusion criteria:

1. The patients with head and neck masses underwent MRI study with DWI and ADC, and confirmation of diagnosis was needed by at least one of the following criteria:
   i) Pathological diagnosis of benign and primary malignant masses,
   ii) Pathological diagnosis of lymph nodes
   iii) Metastatic lymph nodes in proven primary malignant head and neck masses which were defined as pathologic radiologic criteria with first and second anatomical lymphatic drainage pathways.

Pathologic radiologic criteria for lymph nodes would be assumed to be suspicious for metastatic involvement if they showed one of the following features:

(i) Oval in shape with a maximum transverse diameter greater than 10 mm
(ii) Round shaped and exceeded 8 mm in diameter
(iii) Any size and shape with internal central or eccentric necrotic areas, and
(iv) Any size and shape with speculated or indistinct borders, and heterogeneous signal intensity (SI) on fat-suppressed T2-weighted (T2W) images[11,12].

Pattern of lymphatic drainage and metastatic spread of head and neck cancer was divided into four groups as follow [13]:

i) Main lymphatic pathway drainage initiating in the oral cavity, parotid nodes, or buccal nodes, proceeds to levels IA, IB or IIA and then to levels III and IV,
ii) The posterior accessory pathway drainage originates in the posterior scalp, postauricular and suboccipital regions and proceeds through levels IIB, VA and VB,
iii) The anterior lymphatic pathway drainage involved in anterior regions of the oral cavity, including the tip of the tongue, floor of the mouth, median part of the lower lip, and the anterior buccal and gingival areas, directs drainage to level IA to III or IV, and
iv) The superficial lateral pathway drainage begins with the suboccipital or retroauricular nodes, but instead proceeds along the superficial nodal group in level II and then merges with the nodal chain at level III.

Exclusion criteria:

1. Any patient who had undergone any prior treatment with surgery, radiotherapy or chemotherapy,
2. Any patient who had undergone biopsy before performing MRI study,
3. Incomplete patient information, i.e., no pathological report, and
4. Any MRI findings of the masses having hemorrhage or calcification.

MR imaging technique

MR imaging of nasopharynx, sinonasal regions, oropharynx, oral cavity, salivary glands, thyroid gland, larynx/hypopharynx and other neck spaces, were performed on a 1.5T MR (maximum gradient strength 45mTmin^{-1}, maximum slow rate 150 Tm^{-1}s^{-1}) (Signa LX 15.0_0947a, GE Medical Systems, Milwaukee, Wisconsin, USA). The 12-element neurovascular coils were placed to optimize the signal-to-noise ratio (SNR).

The DWI sequences were performed using a multislice axial single-shot spin-echo echo-planar sequences including background suppression with fat saturation and b-values of 0 and 500-1000 s/mm^2.

The other technical parameters were as follow:

i) Slice thickness 6 mm
ii) Intersection gap 2 mm
iii) Matrix 128x128
iv) Receiver bandwidth 1240 Hz/Pixel
v) Number of excitations 6
vi) ASSET 2

Diffusion weighting was achieved by applying pairs of sensitizing gradients before and after the 180^o radiofrequency pulse of the spin-echo T2-weighted sequence in three orthogonal directions (X, Y and Z). Trace images were synthesized for each b-value, and an ADC map was calculated by the MR unit from all diffusion weightings and directions on a voxel-by-

voxel basis.

Image processing was done on a GE workstation, Functool release 4.3 (Advantage windows, General Electric, Milwaukee, USA).

MRI findings analysis

The present study classified head and neck masses (primary tumors and lymph nodes) into benign and malignant groups. In case of proven primary tumor, metastatic lymph nodes were included in the study. The metastatic lymph nodes have been classified by radiographic criteria of pathologic lymph nodes with first and second cervical lymphatic drainage pathway from primary tumors.

In the malignant group, they were divided into 5 subgroups according to pathological diagnosis and anatomical regions; squamous cell carcinoma (SCC) of oral cavity and oropharynx, non-keratinizing carcinoma of nasopharynx, papillary thyroid carcinoma, metastatic carcinoma of lymph nodes and others (esthesioneuroblastoma, T-cell lymphoma, spindle cell sarcoma, malignant peripheral nerve sheath tumor, adenoid cystic carcinoma).

MRI were reviewed in the Picture Archiving and Communication System (PACS) and characterized masses by an 18-year MRI experienced radiology technician and a 3rd year radiology residency. DWI with b1000 images allowed easier identification of lesion borders compared to the ADC map. DWI was interpreted by visual analysis, and then divided into two groups: restricted diffusion and non-restricted diffusion. Restricted diffusion was defined as hyperintense signal intensity in DWI and hypointense signal intensity in ADC. Exception for this, there is non-restricted diffusion.

For ADC, quantification could be done by drawing regions of interest (ROI) over the tissue of interest in software of GE MRI by an 18-year MRI experienced radiology technician and a 3rd year radiologic residency. Both of them were blinded to clinical data and pathological diagnosis.

A region of interest (ROI) was drawn using an electronic cursor around the margin of solid part of the masses, avoiding cystic or necrotic parts, because cystic or liquefactive necrosis parts could overestimate the mean ADC value[3]. Small ROI area was about 25 mm^2 or greater. Multiple small regions of interest (ROI) were drawn freehand over entire mass volume in all tumor slice section. ADC value was obtained for each small ROI and averaged to calculate the mean ADC value of the whole tumor volume.

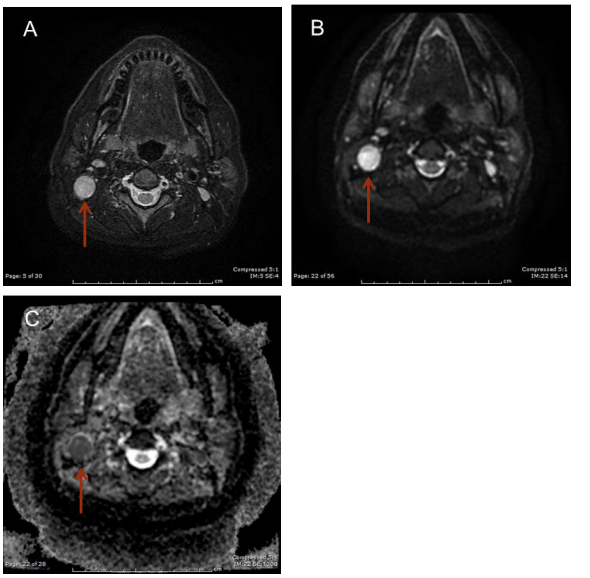

Figure 1. A 55-year-old man with history of nasopharyngeal cancer and right cervical nodal metastasis (arrows). The right cervical node level II shows restricted diffusion seen as hyperintense-T2W (A), hyperintense in DWI (B) and hypointense in ADC (C).

Statistical analysis

The baseline demographic data, continuous variables (age) were presented as mean ± standard deviation (SD). Statistical presentation and analysis of the study used the mean and standard deviation by PASW statistics 18.0. DWI and mean ADC value between benign and malignant groups were determined as the significant difference by using *t*-test. A p-value < 0.05 is considered to be significant difference.

When any difference was detected, the authors tried to determine the cut-off point of the ADC value for differentiation between benign and malignant groups. Receiver-operating-characteristic (ROC) curve analysis was used to investigate the discriminatory capability of the ADC in differentiating benign and malignant groups. The area under the ROC curve was calculated to show sensitivity, specificity, accuracy, positive predictive value (PPV) and negative predictive value (NPV) and to find the optimal cut-off point of ADC value.

Results

There were 37 lesions in 24 patients (Table 1). The mean age of the patients with benign group in the head and neck was 39.8 ± 15.8 years, and those with malignant group was 49.9 ± 13.5 years. These lesions consisted of 14 lesions of lymph nodes and 23 lesions

of primary tumors. The primary tumors were located in different anatomical head and neck regions (Table 2). Pathological diagnosis of each anatomical region was shown in Table 3.

DWI was obtained with a *b* factor of 0 and 500 – 1,000 sec/mm^2. Most of the malignant tumors had by qualitative study restricted diffusion with 28 lesions of the total 30 lesions. Two non-restricted diffusion lesions were esthesioneuroblastoma at the nasal cavity and spindle cell sarcoma of the maxillary sinus. Most of the benign tumors had non-restricted diffusion with 6 lesions of total 7 lesions. One restricted diffusion lesion was Warthin's tumor. DWI was used for discriminating benign and malignant masses with 93.3% of sensitivity, 85.7% of specificity, 96.6% of positive predictive value (PPV), 75% of negative predictive value (NPV) and 91.8% of accuracy.

By the two groups: 30 in malignant masses and 7 in benign masses, the mean ADC values in the benign masses were 1.126 x 10^{-3}±0.451 x 10^{-3} mm^2/s (0.542 x 10^{-3}-2.216 x 10^{-3} mm^2/s). The mean ADC values in the malignant masses were 0.973 x 10^{-3}±0.385 x 10^{-3} mm^2/s (0.639 x 10^{-3}-1.846 x 10^{-3} mm^2/s). There was no statistically significant difference in mean ADC values between benign and malignant masses, using *t*-test with a *p*-value = 0.445. There was no significant difference of mean ADC measurement between the 3rd year radiology residency and the 18-year MRI experienced radiology technician, using paired *t*-test with a *p*-value = 0.014.

In subgroups of malignancy, mean ADC values of squamous cell carcinoma (SCC) were 1.060 x 10^{-3}±0.447 x 10^{-3} mm^2/s. There was no significant difference between benign group and SCC subgroup with *p*-value of 0.78. Mean ADC value of non-keratinizing carcinoma of nasopharynx was 0.754 x 10^{-3}±0.054 x 10^{-3} mm^2/s, which was no significant difference between benign group and non-keratinizing carcinoma of nasopharynx subgroup with *p*-value of 0.072. Mean ADC values of metastatic carcinoma of lymph nodes were 0.645 x 10^{-3}±0.076 x 10^{-3} mm^2/s. There was no significant difference between benign group and metastatic carcinoma of lymph nodes

Table 1. Demographic Data

Parameters	Benign	Malignant	Total No.
No. of patients	7	17	24
Male	3	8	11
Female	4	9	13
Lesions	7	30	37
Mean age (year)	39.8±15.8	49.9±13.5	48±14.32

Table 2. Anatomical regions of head and neck tumors

Parameters	Male	Female	Total No.
No. of patients	11	13	24
No. of lesions	7	30	37
Anatomical location			
lymph nodes	4	10	14
primary tumors			
- nasopharynx	2	0	2
- sinonasal regions	0	2	2
- oropharynx	2	3	5
- oral cavity	2	1	3
- larynx	1	0	1
- salivary glands	1	1	2
- thyroid gland	0	4	4
- other neck spaces	2	2	4
Total	14	23	37

Table 3. Pathological diagnosis of each anatomical region

Region	Pathological diagnosis	Number
Primary tumor		
- nasopharynx	Non-keratinizing carcinoma	2
- sinonasal regions	Esthesioneuroblastoma	1
	Spindle cell sarcoma	1
- oropharynx	Squamous cell carcinoma, well differentiation	2
	Squamous cell carcinoma, moderate differentiation	1
	T cell lymphoma	1
	Adenoid cystic carcinoma	1
- oral cavity	Squamous cell carcinoma, moderate differentiation	2
	Microinvasive squamous cell carcinoma	1
- larynx/hypopharynx	Squamous cell carcinoma, moderate differentiation	1
- salivary gland	Chronic inflammation	1
	Warthin's tumor	1
- thyroid gland	Papillary thyroid carcinoma	2
	Thyroglossal duct cyst	1
	Adenomatous goiter	1
- other neck spaces	Malignant peripheral nerve sheath tumor	1
	Lipoma	1
	Nerve sheath tumor	1
	Vascular malformation	1
Lymph nodes	Metastatic carcinoma	14
Total		37

subgroup with *p*-value of 0.114. Mean ADC values of papillary thyroid cancer subgroup were 1.054 x 10^{-3}±0.027 x 10^{-3} mm^2/s. There was no significant difference between benign thyroid lesions and papillary thyroid cancer with *p*-value of 0.838. Mean ADC values of other subgroups were 1.126 x 10^{-3}±0.438 x 10^{-3} mm^2/s. There was no significant difference between benign group and other subgroups with *p*-value of 0.99.

ROC curve analysis was used to detect the cut-off point of ADC value for differentiating benign from malignant lesions (Fig.2). The area under curve was 0.655. Mean ADC value of benign lesion was 1.126 x 10^{-3} mm^2/s (0.193 x 10^{-3} - 6.54 x 10^{-3} mm^2/s). Mean ADC value of malignant lesion was 0.973 x 10^{-3} mm^2/s (0.126 x 10^{-3} - 9.78 x 10^{-3} mm^2/s). The cut-off point of ADC value to differentiating benign from malignant lesion was 1.200 x 10^{-3} mm^2/s with 76.7% of sensitivity, 57.1% of specificity, 72.9% of accuracy, 88.5% of positive predictive value (PPV) and 36.4% of negative predictive value (NPV), (Table 4).

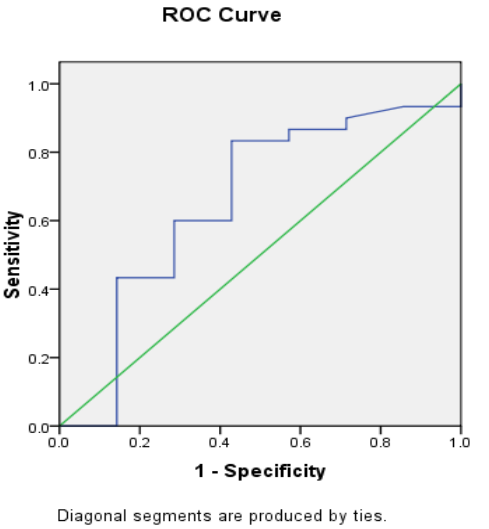

Figure 2. Receiver Operating Characteristic (ROC) curve

Discussion

In head and neck cancers, squamous cell carcinoma (SCC) is the most common malignant tumor. It originates from the epithelial lining of the upper aerodigestive tract. Accurate diagnosis is needed for treatment planning and for predicted prognosis of the tumor. Ultrasound, conventional CT and MRI are the first imaging modalities for evaluating head and neck cancers, but they are low sensitivity and accuracy. Advanced MR imaging techniques provide more information including the metabolic, molecular and pathophysiological aspects of a tumor. These are MR spectroscopy, dynamic contrast-enhanced MRI and DWI[14].

DWI is MR technique for evaluating rate of microscopic random water diffusion in tissues. The ADC is expected variation of cellular density of the lesion.

The present study demonstrated role of DWI that increased accuracy of MRI in differentiation between benign and malignant head and neck masses.

Several studies have shown that the ADC values of malignant tumors of the head and neck are significant lower than those of benign masses[15,16]. Wang et al. reported the lower ADC value than 1.22 x 10^{-3} mm^2/s for predicting malignancy[17,18]. The cut-off point ADC value in the present study was lower than 1.20 x 10^{-3} mm^2/s for predicting malignant head and neck masses similar to the prior study.

When the authors apply the cutoff point of mean ADC value at 1.20 x 10^{-3} mm^2/s for malignant mass, two malignant masses (esthesioneuroblastoma and spindle cell sarcoma) showed higher mean ADC value than the cutoff point of ADC value. Three benign lesions/masses with chronic inflammation of the parotid gland, Warthin's tumor and lipoma had lower mean ADC value than the cutoff point of ADC value.

In thyroid tumors, several studies reported variable mean ADC value in benign and malignant thyroid masses[5,19,20]. In the present study, there were two papillary thyroid carcinomas, one thyroglossal duct cyst and one adenomatous thyroid goiter. So, they influence a wider range of mean ADC values in benign

Table 4. ADC value with sensitivity, specificity, accuracy, PPV, NPV and area under ROC curve

Threshold of ADC Value (x10^{-3} mm^2/sec)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Positive Predictive Value (%)	Negative Predictive Value (%)	Area under ROC curve at 95% confidence interval
1.150	73.3(22/30)	57.1(4/7)	70.2(26/37)	88.0(22/25)	33.3(4/12)	0.652
1.200	76.7(23/30)	57.1(4/7)	72.9(27/37)	88.5(23/26)	36.4(4/11)	0.655
1.250	86.7(26/30)	42.9(3/7)	72.9(27/37)	86.7(26/30)	42.9(3/7)	0.648

and malignant groups, causing overlap of mean ADC values between benign and malignant groups. Either lower mean ADC value in benign group or higher mean ADC value in malignant group cause no significant difference of mean ADC value between benign and malignant groups.

In salivary gland tumor, Maeda et al[3] reported the lower ADC values in malignancy and ADC value are influenced by various complex factors such as the cellularity and matrix of tumors. They also reported lower ADC value in Warthin's tumor and higher ADC value in adenoid cystic carcinoma. In the present study, there was one Warthin's tumor and one adenoid cystic carcinoma, causing overlap of the mean ADC value between benign and malignant groups. They also caused no significant difference of mean ADC value between benign and malignant groups.

In squamous cell carcinoma, Srinivasan et al[21] reported a significant lower ADC value in extracranial squamous cell carcinomas (SCCs) with mean ADC value of $1.101\pm0.214 \times 10^{-3}$ mm^2/s. In the present study, mean ADC values of SCCs were $1.060 \times 10^{-3}\pm0.447 \times 10^{-3}$ mm^2/s, and they were similar mean ADC values to the prior study [22,23]. Chawla et al[15] reported the higher mean ADC value in well or moderately differentiated SCC than those of poorly differentiated SCC. In the present study, all squamous cell carcinoma were well or moderately differentiated, causing higher ADC range in the malignant group.

In nasopharyngeal tumor, Zheng et al. [24] reported that the mean ADC value of benign and malignant nasopharyngeal lesions was $0.913\pm0.168 \times 10^{-3}$ mm^2/s and $0.78\pm0.158 \times 10^{-3}$ mm^2/s, respectively. In the present study, the mean ADC values of non-keratinizing carcinoma of nasopharynx were $0.754 \times 10^{-3}\pm0.054 \times 10^{-3}$ mm^2/s, were similar to the prior study[25].

Limitation of the present study was too small sample size, which may not represent actual result of head and neck masses. Comparison between benign group and malignant subgroup is also limited, because small number of benign subgroup to compare with malignant subgroup, region by region.

Conclusion

The DWI is one of MR techniques used to differentiate benign from malignant head and neck masses. The technique should be applied to MR protocol of head and neck masses to enhance accuracy for diagnosis qualitatively. However, with the limitation in the present study, there was no statistically significant difference of mean ADC value between benign and malignant head and neck masses, which was different from the other recent studies. They have been reported a significant difference of ADC value between benign from malignant head and neck masses. The authors suggest for a further study on the role of ADC measurement with cut-off point mean or minimum ADC value to differentiate benign and malignant head and neck masses.

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What is already known on this topic?

There are many reports of the potential utility of DWI for evaluation of extra cranial disease.

What is this study adds?

1. By qualitative study, most of the malignant tumors had restricted diffusion. Two non-restricted diffusion malignant lesions were esthesioneuroblastoma at the nasal cavity and spindle cell sarcoma of the maxillary sinus. Most of the benign tumors had no restricted diffusion. One restricted diffusion lesion was Warthin's tumor. DWI was used for discriminating benign from malignant masses with 93.3% of sensitivity, 85.7% of specificity, 96.6% of positive predictive value (PPV), 75% of negative predictive value (NPV) and 91.8% of accuracy.
2. By quantitative study, the mean ADC values in the benign masses were $1.126 \times 10^{-3} \pm 0.451 \times 10^{-3}$ mm^2/s (0.542×10^{-3}-2.216×10^{-3} mm^2/s). The mean ADC values in the malignant masses were $0.973 \times 10^{-3} \pm 0.385 \times 10^{-3}$ mm^2/s (0.639×10^{-3}-1.846×10^{-3} mm^2/s). There was no statistically significant difference in mean ADC values between benign and malignant masses, using *t*-test with *p*-value = 0.445.

Potential conflicts of interest

The authors declare no conflict of interest.

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