REVIEW

Usefulness of diffusion-weighted imaging and the apparent diffusion coefficient in the assessment of head and neck tumors

Apport de l’imagerie de diffusion et du coefficient de diffusion apparent pour l’étude des tumeurs de la tête et du cou

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Tumor;
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**Summary** The aim of this review was to determine the usefulness of diffusion-weighted imaging (DWI) and the apparent diffusion coefficient (ADC) in the assessment of head and neck tumors. DWI and the ADC can help in the differential diagnosis of particular disorders (such as carcinomas vs lymphomas, or necrosis vs abscess) of the head and neck. The ADC can also provide further information to help differentiate benign from malignant tumors, as ADC values are usually lower in cases of malignancy. However, the ADC is itself influenced by various complex factors such as the cellularity and matrix of tumors and there is also some overlap between certain benign and malignant tumors of the salivary glands.

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**MOTS CLÉS**
Imagerie de diffusion ;
Imagerie par résonance magnétique ;
Coefficient de diffusion apparent ;
Tumeur ;
Tête et cou

**Résumé** L’objectif de cette revue est de montrer l’intérêt de l’imagerie de diffusion (DWI) et du coefficient de diffusion apparent (ADC) pour l’étude des tumeurs de la tête et du cou. DWI et ADC sont utiles pour le diagnostic différentiel de certaines entités (carcinomes vs lymphomes, nécrose vs abcès) de la tête et du cou. L’ADC peut également apporter des informations sur la différenciation entre tumeurs bénignes et malignes, les valeurs d’ADC étant généralement plus basses en cas de tumeurs malignes. Cependant, l’ADC est influencé par plusieurs paramètres complexes tels que la cellularity et la matrice tumorale et des chevauchements existant entre certaines tumeurs bénignes et malignes des glandes salivaires.

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Introduction

Diffusion-weighted imaging (DWI) is used to evaluate the rate of microscopic water diffusion within tissues. Although DWI is known to be of great value in stroke, this method has also been used to evaluate tumors of the central nervous system [1—4]. Indeed, the results of studies comparing the apparent diffusion coefficient (ADC) to histopathological findings in tumors have strongly suggested that greater cellularity is associated with a more restricted diffusivity [3,4]. More recently, DWI has been applied to the head and neck regions [5—23]. Reportedly, DWI may be useful for characterizing head and neck tumors and help to differentiate among particular tumors and between benign and malignant ones, based on ADC assessment [5,8,9,16—18]. We have proposed the application of line-scan DWI (LSDWI) in the head and neck because this technique has proven to be relatively free of susceptibility artifacts [15,21,22,24—29]. In this article, we describe the LSDWI method and review the usefulness of DWI scans and the ADC for characterization of head and neck tumors.

DWI techniques for head and neck lesions

Several DWI techniques have been proposed for the evaluation of head and neck lesions. Echoplanar DWI (EPDWI) has generally been used despite its susceptibility to artifacts in the head and neck regions [5—14,16—20,23]. According to some investigators, 16% of their cases showed local distortions that affected the lesions on single-shot EPDWI scans obtained with a b factor of 1000 s/mm²; their ADC maps were also suboptimal because of susceptibility artifacts [5]. More recently, a parallel-imaging technique has been used to avoid susceptibility artifacts on EPDWI images, resulting in acceptable EPDWI and ADC images of lesions close to the airways [20]. Another DWI technique is the application of line-scan DWI (LSDWI) [15,21,22]. As this technique is inherently insensitive to susceptibility artifacts, it appears to be eminently suitable for the evaluation of diffusivity of head and neck lesions (Fig. 1).

Principles and methods of line-scan DWI

To create a two-dimensional image, LSDWI uses multiple diffusion-weighted spin-echo column excitations. Fig. 2 shows that the basic sequence comprises spatially selective 90° and 180° pulses. The LSDWI image comprises a series of one-dimensional magnitude profiles obtained from parallel columns lying in the image plane. Each column is formed by the intersection of two slices that are selected by the two-slice selective radio frequency (RF) pulses. This excitation scheme (Fig. 3) allows rapid repetition of the excitation without spin saturation. The fundamental principle of the scheme is to avoid alignment of the slices excited by the selective pulses with the imaging plane. The selected planes are positioned such that the volume at their intersection forms the column of interest in the imaging plane. For optimal coverage, the columns overlap slightly and column

Figure 1  In a 64-year-old woman with malignant melanoma: A: T2-weighted fat-suppression image shows a tumor in the right maxillary sinus (arrow); B: echoplanar DWI (b = 1000 s/mm²) shows a prominent susceptibility artifact (arrow), resulting in image degradation; C: line-scan DWI (b = 1000 s/mm²) reveals the tumor without susceptibility artifacts (arrow); D: the ADC map shows values within the tumor (arrow) to be lower (mean: 0.98 × 10⁻³ mm²/s) than those of adjacent structures.

Figure 1  Mélanome malin chez une femme âgée de 64 ans : A : l’image pondérée T2 avec suppression de graisse montre une tumeur du sinus maxillaire droit (flèche) ; B : l’imagerie de diffusion échoplanar (b = 1000 s/mm²) montre un artéfact de susceptibilité (flèche) responsable d’une dégradation de l’image ; C : l’imagerie de diffusion à balayage de lignes (b = 1000 s/mm²) montre la tumeur sans artéfacts (flèche) ; D : la cartographie ADC montre des valeurs d’ADC de la tumeur plus basses (flèche) que celles des structures adjacentes. La valeur moyenne de l’ADC du mélanome est 0,98 × 10⁻³ mm² par seconde.
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acquisition is interleaved to avoid column cross-talk caused by saturation.

The methods used in LSDWI have been previously described [15,21,22,24–29]. Neither cardiac gating nor respiratory triggering was employed and no antisusceptibility devices were used to reduce susceptibility artifacts. The LSDWI images of the head and neck were acquired using the following scan parameters: TR = 3168–4048 ms; TE = 57.1–70.7 ms; one excitation = FOV of 20–24 cm; matrix size of 128 × 128 columns. The effective section thickness was set to 3–5 mm with a between-section gap of 1 mm. The LSDWI images were obtained using two different b values, with the maximum b value applied along three orthogonal directions: one with a low diffusion-weighting (b) factor of 5 s/mm² and the other with a high (maximum) b factor of 1000 s/mm². The scan time per slice was 37 to 49 s; in all, three to five slices were obtained according to the lesion size. Isotropic diffusion images with a b factor of 1000 s/mm² were generated from the three diffusion directions that were assessed. Trace ADC maps were generated using the equation described by Stejskal and Tanner [30]:

\[ S = S_0 e^{-bADC} \]

in which b is the diffusion-weighting factor, S is the signal intensity of the diffusion trace for b at maximum and S₀ is the signal intensity for b at 5 s/mm².

Clinical applications in head and neck tumors

ADC and tumor cellularity

Experimental studies have reported that tumor cellularity strongly influences the ADC [31]. Clinical data of brain tumors present a clear inverse relationship between the ADC values and cellularity of tumors [3,4]. The data suggest that greater cellularity is associated with more restricted diffusivity. Similarly, it appears that such a relationship may also apply to head and neck tumors [17] (Fig. 4). Densely-packed tissue structures with a high nucleus-to-cytoplasm ratio might reflect lower ADC values of the lesions.

Figure 4 In a six-month-old girl with recurrent retinoblastoma: A: T2-weighted fat-suppression image shows a mass in the left orbit (arrow); B: contrast-enhanced T1-weighted image shows the mass to be moderately enhanced (arrow); C: line-scan DWI (b = 1000 s/mm²) shows that the tumor is hyperintense relative to the normal brain tissue (arrow); D: ADC map shows remarkably reduced values within the tumor (arrow), with a mean value of 0.42 × 10⁻³ mm²/s; E: photomicrograph shows that the tumor is remarkably hypercellular with a high nucleus-to-cytoplasm ratio.

The ADC appears to be useful for differentiating malignant tumors of the head and neck. Squamous cell carcinoma (SCC) is the most common malignant tumor of the head and neck, but lymphoma is also commonly found in this region. In many cases, the clinical symptoms and pattern of growth are so characteristic that distinction between the two tumors is possible. However, the MR characteristics of the two tumor types, such as signal intensities and contrast-enhancement patterns, are sometimes indistinguishable [32]. It can, therefore, be a challenge to distinguish between SCC and lymphoma using the ADC. The ADC was found to be significantly lower in lymphoma (0.65 ± 0.09 × 10⁻³ mm²/s) than in SCC (0.96 ± 0.11 × 10⁻³ mm²/s) using LSDWI [15] (Figs. 5 and 6). Accuracy was 98% when an ADC of 0.76 × 10⁻³ mm²/s was used to distinguish between SCC and lymphoma [15]. Other investigators have also reported that, with EPDWI, the ADC of lymphomas (0.454 ± 0.075 × 10⁻³ mm²/s) was significantly lower than
Figure 5 In a 55-year-old man with squamous cell carcinoma: A: T2-weighted fat-suppression image shows a tumor in the left oropharynx (arrow); B: contrast-enhanced T1-weighted image shows that the tumor is moderately enhanced (arrow); C: line-scan DWI \((b = 1000 \text{s/mm}^2)\) shows a slight hyperintensity of the tumor (arrow); D: mean ADC value of the tumor is \(0.98 \times 10^{-3} \text{mm}^2/\text{s}\) on the ADC map (arrow); E: photomicrograph shows squamous cell carcinoma.

Figure 5 Carcinome à cellules squameuses chez un homme âgé de 55 ans : A : l’image pondérée T2 avec suppression de graisse montre une tumeur de l’oropharynx latéralisée à gauche (flèche) ; B : l’image pondérée T1 après injection de gadolinium montre un rehaussement modéré de la tumeur (flèche) ; C : l’image de diffusion à balayage de lignes \((b = 1000 \text{s/mm}^2)\) montre un signal discrètement hyperintense de la tumeur (flèche) ; D : la valeur moyenne de l’ADC est \(0.98 \times 10^{-3} \text{mm}^2/\text{s}\) sur la cartographie ADC (flèche) ; E : photomicrographie du carcinome à cellules squameuses.

Figure 6 In a four-year-old boy with malignant lymphoma: A: T2-weighted image shows a mass in the left maxillary sinus (arrow); B: line-scan DWI \((b = 1000 \text{s/mm}^2)\) shows a hyperintense mass compared with the brain (arrow); C: ADC map shows restricted diffusion of the mass (arrow), with a mean ADC value of the tumor of \(0.65 \times 10^{-3} \text{mm}^2/\text{s}\); D: photomicrograph shows prominent hypercellularity and the high nucleus-to-cytoplasm ratio of the tumor.

Figure 6 Lymphome malin chez un garçon âgé de quatre ans : A : l’image pondérée T2 montre une masse dans le sinus maxillaire gauche (flèche) ; B : l’image de diffusion à balayage de lignes \((b = 1000 \text{s/mm}^2)\) montre une masse de signal plus élevé que le parenchyme cérébral (flèche) ; C : la cartographie ADC montre une diffusion restreinte de la tumeur (flèche). La valeur moyenne de l’ADC est \(0,65 \times 10^{-3} \text{mm}^2\) par seconde ; D : la photomicrographie montre une hypercellularité marquée et un rapport nucléocytoplasmique élevé de la tumeur.

those of carcinomas \((0.863 \pm 0.238 \times 10^{-3} \text{mm}^2/\text{s})\) [20]. The greatest accuracy achieved was 96% when an ADC lower than \(0.560 \times 10^{-3} \text{mm}^2/\text{s}\) was used for predicting lymphomas [20]. The ADC can also discriminate between malignant lymphoma \((0.51 \pm 0.06 \times 10^{-3} \text{mm}^2/\text{s})\) and carcinoma \((0.99 \pm 0.08 \times 10^{-3} \text{mm}^2/\text{s})\) in the cavernous sinus [27]. Thus, the ADC provides useful information related to the differential diagnosis at anatomical locations where a biopsy is difficult to obtain. The observed differences in ADC values appear to be attributable to differences in tumor cellularity, with lymphoma having greater cellularity than SCC (Figs. 5E and 6D).

**ADC and bulk tumor necrosis/cystic degeneration and epidermal cysts**

In general, bulk necrosis and cystic degeneration of head and neck tumors will increase diffusivity \([5,8,19,20]\) (Fig. 7). This finding may explain the free movement of water molecules within these histological changes. A frequent observation, particularly in head and neck malignant tumors, is that the necrotic parts of the tumor contain material that is less viscous, resembling a serous fluid. For this reason, special care should be taken to include the solid-appearing portions of the tumors and to exclude obviously necrotic or cystic regions in T2-weighted and contrast-enhanced MR images when determining the ADC for characterization of tumors.

However, unlike bulk necrosis, small foci of necrosis scattered across the tumor tissue may not contribute significantly to a higher tumor ADC [15]. Lyng et al. [31] reported that the fraction of mass necrosis might be correlated to the ADC values, but not the fraction of small necrotic foci because such foci may be smaller than the voxel size of MR images.

An epidermal cyst is a common, benign mass that occurs frequently in head and neck regions. The mass contents are not fluid, but keratinous debris. MRI characteristics include
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Figure 7 In a 36-year-old man with a rhabdomyosarcoma: A: T2-weighted fat-suppression image shows a mass in the oropharynx (arrows); B: contrast-enhanced T1-weighted image shows massive necrosis within the tumor (arrow); C: line-scan DWI ($b = 1000$ s/mm$^2$) shows hypointensity in the necrotic parts (long arrow) and hyperintensity in the viable parts (small arrows) of the tumor; D: ADC map shows increased values in the necrotic parts (long arrow, $1.74 \times 10^{-3}$ mm$^2$/s) and decreased values in the viable parts (small arrows, $0.67 \times 10^{-3}$ mm$^2$/s) of the tumor.

Figure 8 In a 56-year-old man with an epidermal cyst: A: T1-weighted image shows a mass in the right parotid gland (arrow) that is isointense in relation to the adjacent muscle; B: T2-weighted fat-suppression image shows a markedly high-signal mass (arrow) resembling a fluid-filled cyst; C: line-scan DWI ($b = 1000$ s/mm$^2$) shows hyperintensity of the mass (arrow); D: the ADC map shows low values (mean: $0.88 \times 10^{-3}$ mm$^2$/s) in the mass (arrow).

A well-circumscribed margin, bright signals on T2-weighted images and no contrast enhancement with the cyst—rather like a fluid signal [33]. Epidermal cysts and intracranial epidermoid cysts are pathologically identical [22]. In these cases, ADCs can provide useful information on tissue characterization of the mass [22], as epidermal cysts generally have low ADC values ($0.81 \pm 0.14 \times 10^{-3}$ mm$^2$/s) (Fig. 8).

DWI signal intensity and infectious necrosis

Water diffusion is known to be restricted in brain abscesses [34], perhaps because of the organization of the abscess environment, which contains microorganisms, protein complexes and inflammatory cells [35]. In addition, water molecules in the abscess bind with the carboxy, hydroxyl and amino groups on the macromolecules, which will limit their random movements. These factors probably explain the reduced ADCs of infectious necrotic lesions. Nevertheless, differentiation between central necrosis of metastatic nodes and infectious necrotic nodes can be difficult with conventional MRI. Head and neck infectious necrotic lesions, such as abscesses and necrotic lymphadenitis, appear hyperintense on DWI (Fig. 9), whereas necrotic tumor and necrotic nodal metastases appear hypointense (Fig. 7). Therefore, DWI appears to be useful for differentiating necrotic tumor lesions from infectious necrosis [19].
Figure 9  In a 32-year-old man with an abscess: A: T2-weighted fat-suppression image shows a hyperintense mass in the left submandibular region (arrow); B: contrast-enhanced T1-weighted image shows no enhancement within the mass (arrow); C: linescan DWI ($b = 1000$ s/mm$^2$) shows hyperintensity of the abscess (arrow); D: the ADC map shows low values (mean: $0.75 \times 10^{-3}$ mm$^2$/s) in the abscess (arrow).

Figure 9  Abcès chez un homme âgé de 32 ans : A : l’image pondérée T2 avec saturation de graisse montre une masse hyperintense de la région sous-mandibulaire gauche ; B : l’image pondérée T1 après injection de gadolinium ne montre pas de rehaussement au sein de la masse ; C : l’image de diffusion à balayage de lignes ($b = 1000$ s/mm$^2$) montre un signal hyperintense de l’abcès (flèche) ; D : la cartographie ADC montre des valeurs d’ADC basses (flèche). La valeur d’ADC moyenne est $0.75 \times 10^{-3}$ mm$^2$ par seconde.

Figure 10  In a 59-year-old woman with a pleomorphic adenoma: A: T2-weighted image shows the hyperintense mass in the left parotid gland (arrow); B: contrast-enhanced T1-weighted image shows mild enhancement of the tumor (arrow); C: ADC map shows increased values (mean: $1.72 \times 10^{-3}$ mm$^2$/s) in the tumor (arrow); D: photomicrograph shows an abundant myxoid matrix (arrow).

Figure 10  Adénome pléomorphe chez une femme âgée de 59 ans : A : l’image pondérée T2 montre une masse hyperintense de la glande parotide gauche (flèche) ; B : l’image pondérée T1 après injection de gadolinium montre un discret rehaussement de la tumeur (flèche) ; C : la cartographie ADC montre des valeurs d’ADC élevées de la tumeur (flèche). La valeur d’ADC moyenne de la tumeur est $1.72 \times 10^{-3}$ mm$^2$ par seconde ; D : la photomicrographie montre une matrice myxoïde abondante (flèche).

Figure 11  In a 60-year-old man with Warthin’s tumor: A: T2-weighted fat-suppression image shows a mildly hyperintense mass arising in the deep lobe of the right parotid gland (arrow); B: contrast-enhanced T1-weighted image shows mild enhancement of the tumor (arrow); C: ADC map shows decreased values (mean: $0.80 \times 10^{-3}$ mm$^2$/s) in the tumor (arrow); D: photomicrograph shows a hypercellular matrix composed of lymphoid tissue (arrows).

Figure 11  Tumeur de Warthin chez un homme âgé de 60 ans : A : l’image pondérée T2 avec suppression de graisse montre une masse discrètement hyperintense intéressant le lobe profond de la glande parotide droite (flèche) ; B : l’image pondérée T1 après injection de gadolinium montre un discret rehaussement de la tumeur (flèche) ; C : la cartographie ADC montre des valeurs d’ADC diminuées de la tumeur (flèche). La valeur d’ADC moyenne est $0.80 \times 10^{-3}$ mm$^2$ par seconde.
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ADC and types of tumor matrix

The tumor matrix appears to influence the ADC greatly. There are various kinds of tumor matrices, including collagen fibers and myxoid and lymphoid tissues. Pleomorphic adenomas frequently have a myxoid matrix [9,18,21], which includes an abundance of free water molecules and, because of this, the ADC of pleomorphic adenomas is high [9,18,21] (Fig. 10). The mean ADCs of pleomorphic adenomas are ranged from 1.52 × 10⁻³ mm²/s to 1.74 × 10⁻³ mm²/s [9,21,23]. Warthin’s tumor is generally regarded as the second most common benign tumor of the parotid gland after pleomorphic adenoma. Ikeda et al. [10] reported that the mean ADC value for 19 Warthin’s tumors (0.96 ± 0.13 × 10⁻³ mm²/s) was significantly lower than that of 17 malignant parotid tumors (1.19 ± 0.19 × 10⁻³ mm²/s). Matsushima et al. [21] also reported that the mean ADC values in their study, including four Warthin’s tumors (0.89 ± 0.18 × 10⁻³ mm²/s) and 15 malignant salivary gland tumors (1.09 ± 0.34 × 10⁻³ mm²/s), were similar to those of Ikeda et al. However, no significant difference was found between the two studies in terms of results (p = 0.25), probably because of the low numbers of Warthin’s tumors [21]. Based on analyses of the pathological findings, the low ADC of Warthin’s tumors is due to proliferation of the epithelial component and intense lymphoid accumulation in the stroma [10,21] (Fig. 11).

Differentiation of benign and malignant tumors using ADC

Several studies have shown that the ADCs of malignant tumors of the head and neck are significantly lower than those of benign tumors [5,17,18]. Wang et al. [5] reported that their highest (86%) accuracy with 84% sensitivity and 91% specificity was obtained when an ADC lower than 1.22 × 10⁻³ mm²/s was used for predicting malignancy. White et al. [17] reported that ADCs were significantly lower in malignant tumors than in benign lesions and were inversely correlated with tumor cellularity. Eida et al. [18] reported that areas with high ADCs (> 1.8 × 10⁻³ mm²/s) were significantly more frequently found in benign salivary gland tumors than in malignant tumors. However, there may be considerable overlap between the two types of tumor, so ADC values alone may not be enough to differentiate benign from malignant salivary gland tumors [21]. In fact, the lower ADC values of Warthin’s tumor (0.89 ± 0.18 × 10⁻³ mm²/s) compared with other benign salivary gland tumors may also overlap with those of malignant salivary gland tumors such as malignant lymphoma and carcinomas (1.04 ± 0.27 × 10⁻³ mm²/s). Likewise, the ADCs of adenoid cystic carcinoma (1.41 ± 0.13 × 10⁻³ mm²/s) may overlap with those of pleomorphic adenomas (1.54 ± 0.35 × 10⁻³ mm²/s) (Fig. 12). These results suggest that the ADC is associated not only with tumor cellularity, but also with the type of tumor matrix. For this reason, particular care must be taken when assessing the ADC of salivary gland tumors.

Conclusion

The application of DWI in the head and neck regions has been increasingly explored over the past several years. In particular, it has been found that LSDWI produces minimal susceptibility artifacts, resulting in excellent DWI scans and precise ADC measurements. DWI and the ADC both offer clues for the differential diagnosis of the various disease entities found in the head and neck. The ADC may also provide insight into the differentiation of benign and malignant tumors in these regions. Nevertheless, it should be borne in mind that the ADC is itself influenced by several complex factors, such as the cellularity and matrix of the tumor. For this reason, there may be some overlapping of benign and malignant tumors, particularly among those of the salivary glands.

References


