Assessment of nasal and paranasal sinus masses by diffusion-weighted MR imaging

Étude des masses nasales et paranasales par IRM de diffusion

A.A.K.A. Razek*, S. Sieza, B. Maha

Diagnostic radiology department, Mansoura faculty of medicine, 62, ElNokrasi street, Meet Hadr, 53312 Mansoura, Egypt

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SUMMARY

Purpose. — To assess nasal and paranasal sinus masses by diffusion-weighted echoplanar magnetic resonance imaging (MRI).

Patients and methods. — This prospective study included 55 consecutive patients (34 males, 21 females; aged 14–64 years, mean 39 years) with nasal and paranasal sinus masses. All underwent diffusion-weighted MRI using single-shot echoplanar imaging (EPI) with a b factor of 0.500 and 1000s/mm². Apparent diffusion coefficient (ADC) maps were constructed, allowing ADC values of the mass to be calculated and correlated with histopathological findings.

Results. — The mean ADC value of nasal and paranasal sinus malignant lesions (1.10 ± 0.25 × 10⁻³ mm²/s) was significantly different (P = 0.001) from that of benign lesions (1.78 ± 0.41 × 10⁻³ mm²/s). Also, there was a significant ADC difference between carcinoma and sarcoma (P = 0.01) as well as between well differentiated and poorly differentiated malignancies (P = 0.005). Using an ADC value of 1.53 × 10⁻³ mm²/s as the threshold value for differentiating malignant from benign lesions, the best result obtained had an accuracy of 93%, sensitivity of 94%, specificity of 92%, a positive predictive value of 92% and negative predictive value of 94%. However, the use of 0.97 × 10⁻³ mm²/s and 1.16 × 10⁻³ mm²/s as threshold values to differentiate carcinomas from sarcomas and poorly differentiated malignancy, respectively, gave the best results.

Conclusion. — The ADC value is a non-invasive imaging parameter that can be used to assess nasal and paranasal sinus masses, as it can help in the differentiation of malignant tumors from benign lesions, and in the characterization and grading of malignancies.

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* Corresponding author.
E-mail address: arazek@mans.eun.eg (A.A.K.A. Razek).

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High-resolution computed tomography (CT) scans help to reveal bony erosion in critical areas, and magnetic resonance imaging (MRI) studies provide excellent delineation of sinonasal tumor from surrounding inflamed soft tissue and secretions, making both of these technologies useful for disease staging and surgical planning. Differentiating malignant nasal and paranasal sinus tumors from benign lesions, characterizing malignant tumors and grading the malignancy are essential for treatment planning as well as determining the patient's prognosis. However, the appearances of nasal masses on routine CT and MRI are not pathognomonic. Some malignant tumors may be as slow-growing as benign lesions, while some benign lesions extend into adjacent structures, mimicking malignancies. Also, routine imaging of nasal masses does not allow pathological grading or distinguish between the various pathological types of tumors [1–8].

Diffusion-weighted MRI imaging (DWI) offers better characterization of tissues and their physiological processes because it reflects the random motion of water protons, which is disturbed by the intracellular organelles and macromolecules located in tissues. Thus, the apparent diffusion coefficient (ADC) values of tissues vary according to their pathology and cellularity [9–12]. DWI has been used to differentiate benign and malignant head-and-neck masses, to characterize cervical lymph nodes, parotid tumors and thyroid nodules, and to evaluate pediatric neck and nasal masses [11–19].

The aim of the present study was to assess nasal and paranasal sinus masses using echoplanar DWI.

Patients and methods

This prospective study included 55 consecutive patients (43 men and 12 women, aged 14–64 years [mean 39 years]) presenting with nasal mass (n = 37), nasal obstruction (n = 30), epistaxis (n = 25), facial swelling (n = 15) or cranial nerve palsies (n = 7). The criteria for inclusion were the presence of a nasal and/or paranasal mass greater than 1 cm that had not undergone biopsy or treatment with radio- or chemotherapy prior to MRI. Five patients were excluded from the study because of poor image quality: there were susceptibility artifacts due to small mass size (<1 cm) in the maxillary sinus in three cases; and claustrophobia in two. The study was approved by the relevant institution’s ethics committee, and all participating patients gave their informed consent.

Routine MRI was performed on all patients, using a 1.5-Tesla MRI scanner (Magnetom Symphony; Siemens Medical Systems, Erlangen, Germany) and a circular, head-mounted, polarization surface coil. All patients underwent T1-weighted imaging (TR/TE of 800/15 ms) and T2-weighted fast spin-echo imaging (TR/TE of 4500/80 s) with a section thickness of 5 mm, an interslice gap of 1–2 mm, a field of view (FOV) of 20 × 25 cm and an acquisition matrix of 256 × 256. The images were obtained in the transverse plane.

DWI was carried out using a multislice, spin-echo, single-shot echoplanar imaging (EPI) sequence. Imaging parameters were a TR/TE of 10,000/108 ms, FOV of 20 × 25 cm, acquisition matrix of 256 × 128 and section thickness of 5 mm, with an interslice gap of 1–2 mm. Diffusion-probing gradients were applied in the three orthogonal directions (x, y and z) with the same strength. Images were acquired with a diffusion-weighted b factor of 0.500 and 1000 s/mm² to obtain a precise ADC map. ADC maps were generated for all images. The DWI data-acquisition time was 1 min. Finally, enhanced T1-weighted images (TR/TE of 800/15 ms) were obtained from 47 patients after intravenous bolus injection of 0.2 mL/Kg body weight of gadopentate dimeglumine.

Quantitative analysis of the ADC map was carried out. The region of interest (ROI) was drawn by two radiologists in consensus, using the electronic cursor to follow the margin of the solid part of the mass while avoiding the cystic parts as much as possible, as these can lead to falsely elevated ADC values.

The final diagnosis of nasal and paranasal sinus masses was confirmed by pathological examination after either excision (n = 34) or biopsy (n = 16). Biopsy was performed following MRI after a time interval of 10–17 days. The histological results were correlated with the ADC values.

Data are expressed as means ± standard deviation (SD). The Kolmogorov–Smirnov (K–S) test was used to determine the normality of data distribution. All data were found to be parametric with normal distribution. Data analyses to test statistical significant differences were also performed, using Student’s t test for between-group comparisons. To compare more than two groups, a one-way ANOVA test was used. Receiver operating curves (ROC) were used to determine the cutoff points with the highest accuracy and sensitivity to differentiate malignant from benign tumors, carcinomas from sarcomas, and low-grade from high-grade malignancy. The P value was considered significant if it was inferior or equal to 0.05 with a 95% confidence interval (CI). Statistical analyses were carried out using Microsoft Excel and Statistical Package for Social Science (SPSS) version 10 software.

Results

The histopathological findings of nasal and paranasal masses were malignant tumors (n = 38) and benign lesions (n = 12), and the sizes of the masses were 15–120 mm in diameter (mean: 71 mm). They were seen in one or more of the paranasal sinuses, and located in the nasal cavity (n = 22), maxillary sinus (n = 19), ethmoid sinus (n = 12) or frontal sinus (n = 7). The malignant tumors (n = 27) comprised squamous cell carcinoma (n = 20), undifferentiated carcinoma (n = 3), mucoepidermoid carcinoma (n = 3) and adenoid cystic carcinoma (n = 1), while sarcomas (n = 11) comprised non-Hodgkin’s lymphoma (n = 4), rhabdomyosarcoma (n = 3), olfactory neuroblastoma (n = 2), chondrosarcoma (n = 1) and osteosarcoma (n = 1). The malignant tumors were well differentiated (n = 13), or poorly differentiated or undifferentiated (n = 25). The benign tumors (n = 12) included juvenile angiofibroma (n = 4), inverted papilloma (n = 3), inflammatory polyps (n = 3), ossifying fibroma (n = 1) and aneurysmal bone cyst (n = 1).

The mean ADC value for malignant tumors was 1.10 ± 0.25 × 10−3 mm²/s and, for benign lesions, 1.78 ± 0.41 × 10−3 mm²/s. There was a statistically significant
difference in ADC values between malignant tumors and benign lesions ($P = 0.001$; Fig. 1; Table 1). Using an ADC value of $1.53 \times 10^{-3}$ mm$^2$/s as the threshold value for differentiating malignant from benign lesions gave the best results, with 94% sensitivity, 92% specificity, 93% accuracy, positive predictive value (PPV) of 92%, negative predictive value (NPV) of 94% and an area under the curve (AUC) of 0.89 (Fig. 2).

The mean ADC for sarcomas ($0.89 \pm 0.18 \times 10^{-3}$ mm$^2$/s) was significantly different ($P = 0.01$) from that for carcinomas ($1.18 \pm 0.24 \times 10^{-3}$ mm$^2$/s; Fig. 1B). The mean ADC value was $1.15 \pm 0.6 \times 10^{-3}$ mm$^2$/s (squamous cell carcinoma; Fig. 3). The highest ADC value ($1.73 \times 10^{-3}$ mm$^2$/s) was seen in a patient with an adenoid cystic carcinoma that was mistaken for a benign lesion, whereas the lowest ADC value ($0.72 \times 10^{-3}$ mm$^2$/s) was seen in non-Hodgkin’s lymphoma (Fig. 4). There were non-significant differences in ADC values for the different types of sarcomas as well as the different types of carcinomas. The ADC used to differentiate carcinomas from sarcomas was $0.97 \times 10^{-3}$ mm$^2$/s, which had 92% sensitivity, 82% specificity, 87% accuracy, PPV of 84%, NPV of 91% and AUC of 0.83 (Fig. 2B).

The mean ADC value for well-to-moderately differentiated malignancies ($1.29 \pm 0.29 \times 10^{-3}$ mm$^2$/s) was significantly different ($P = 0.005$) from that for poorly differentiated and undifferentiated malignancies ($1.00 \pm 0.17 \times 10^{-3}$ mm$^2$/s; Fig. 1C). The ADC value used to differentiate low- from high-grade malignancy was $1.16 \times 10^{-3}$ mm$^2$/s, which had 80% sensitivity, 77% specificity, 79% accuracy, PPV of 78%, NPV of 79% and AUC of 0.76 (Fig. 2C).

The mean ADC value for benign lesions was $1.78 \pm 0.41 \times 10^{-3}$ mm$^2$/s. Benign vascular lesions such as juvenile angiofibroma had higher ADC values than that of the other benign solid tumors, including inverted papilloma and angiomatous polyps (Fig. 5). There was an insignificant difference in ADC value across the various benign lesions. The highest ADC value was seen in a patient with

Figure 1  Box and plot of the ADC value. A. The mean ADC value for malignant tumors ($1.10 \pm 0.25 \times 10^{-3}$ mm$^2$/s) is significantly lower ($P = 0.001$) than that for benign lesions ($1.78 \pm 0.41 \times 10^{-3}$ mm$^2$/s). B. The mean ADC value for carcinoma ($1.18 \pm 0.24 \times 10^{-3}$ mm$^2$/s) is significantly different ($P = 0.01$) from that for sarcoma ($0.89 \pm 0.18 \times 10^{-3}$ mm$^2$/s). C. The ADC value in low-grade malignancy ($1.29 \pm 0.29 \times 10^{-3}$ mm$^2$/s) is significantly different ($P = 0.005$) from that in high-grade malignancy ($1.00 \pm 0.17 \times 10^{-3}$ mm$^2$/s).

Figure 2  Receiver operating characteristic (ROC) curve. A. The cutoff ADC value used to differentiate malignant from benign lesions was $1.53 \times 10^{-3}$ mm$^2$/s. The area under the curve (AUC) was 0.89 with 94% sensitivity, 92% specificity and 93% accuracy. B. The ADC value used to differentiate carcinoma from sarcoma was $0.97 \times 10^{-3}$ mm$^2$/s. The AUC was 0.83 with 92% sensitivity, 82% specificity and 87% accuracy. C. To separate high-grade from low-grade malignancy, the AUC was 0.76, with sensitivity of 80%, specificity of 77% and accuracy of 79%.
Figure 3  Squamous cell carcinoma. A. Coronal contrast T1-weighted image shows a right nasal mass with marked contrast enhancement associated with retained secretions in the right maxillary sinus. B. axial ADC map shows a low ADC value in the mass ($1.11 \times 10^{-3} \text{mm}^2/\text{s}$) with a high ADC value in the retained fluid ($2.2 \times 10^{-3} \text{mm}^2/\text{s}$).

Figure 4  Non-Hodgkin’s lymphoma. A. axial T2-weighted image shows a mass with intermediate signal intensity in both maxillary antra and nasal cavities associated with retained secretions in the right maxillary antrum. B. axial ADC map shows a low ADC value in the mass ($0.72 \times 10^{-3} \text{mm}^2/\text{s}$) and a high ADC value in the retained fluid ($1.98 \times 10^{-3} \text{mm}^2/\text{s}$).

Figure 5  Inverted papilloma. A. Axial T2-weighted image shows a small well-defined mass in the ethmoidal air cells on the right side. B. axial ADC map shows high signal intensity with a high ADC value in the mass ($1.79 \times 10^{-3} \text{mm}^2/\text{s}$).

Discussion

A variety of malignant tumors and benign lesions are seen in the sinusal region, and distinguishing malignant...
from benign lesions as well as grading and characterizing malignant tumors is crucial in the therapeutic strategy-planning process. Different MRI pulse sequences and CT scans are useful for the evaluation of tumor extent. However, they cannot accurately differentiate malignant tumors from benign lesions in some cases [1–5,19].

In the present study, the mean ADC value for malignant sinonasal tumors was significantly lower ($P < 0.001$) than that for benign lesions. This is explained by differences in the histopathological features of these tumors. Malignant tumors show enlarged nuclei, hyperchromatism, angulation of nuclear contour and hypercellularity. These histological characteristics reduce the extracellular matrix and the diffusion space of water protons both extracellularly and intracellularly, leading to decreases in ADC [9,10,20]. White et al. [19] found a statistically significant difference ($P = 0.05$) in the ADC values between benign and malignant lesions. They also added that the lower the ADC value of a lesion, the greater the likelihood that it is malignant, and that, to some extent, ADC analysis is promising in helping to separate benign from malignant lesions.

DWI has been used in the characterization of brain and head-and-neck tumors. Guo et al. [21] reported that ADC values were significantly lower in lymphomas than in high-grade gliomas, whereas cellularity was significantly greater in lymphomas than in high-grade gliomas. Maeda et al. [22] found a statistically significant difference in the ADC values ($P < 0.001$) of carcinomas vs lymphomas in the head and neck. Sumi et al. [23] reported that the ADC value of pharyngeal lymphoma was significantly lower than that of carcinoma, and King et al. [24] were able to differentiate metastatic from lymphomatous nodes in the head and neck using DWI. The present study findings suggest that ADC measurements can differentiate between carcinomas and sarcomas in the nasal and paranasal sinus masses. The mean ADC value for carcinoma is significantly higher than that for lymphoma, which may be attributable to the small foci of necrosis in carcinoma (not identifiable on MRI). In addition, lymphoma cells have relatively high nuclear-to-cytoplasm ratios and are densely packed [10,21–23].

The grade of a malignant tumor gives an idea of the tumor’s prognosis [1–4]. Sumi et al. [23] reported that the ADCs of poorly differentiated and undifferentiated carcinomas ($0.691 \pm 0.149 \times 10^{-3}$ mm$^2$/s) were significantly lower than those of moderately differentiated and well-differentiated carcinomas ($0.971 \pm 0.221 \times 10^{-3}$ mm$^2$/s) of the pharynx. Abdel Razek et al. [18] reported that the mean ADC value of poorly differentiated malignant tumors was lower than that of well-differentiated malignant pediatric head-and-neck tumors ($P < 0.03$). In the present study, poorly differentiated and undifferentiated malignant tumors had significantly lower ADC values ($P = 0.01$) than those in well-differentiated malignant lesions. This is explained by the fact that poorly and undifferentiated tumors show greater cellularity and, subsequently, restricted diffusion. In poorly differentiated or undifferentiated carcinomas, the tumor cells often appear to be overlapping. In the highly and moderately differentiated subtypes, tumor cells are often smaller and the nuclear-to-cytoplasm ratio is lower. Highly differentiated tumor cells often exhibit a plexiform pattern of growth that is associated with richly stromal areas, tissue components that are considered to have better water-diffusing characteristics [9,10,22].

The present study also shows that benign vascular lesions, such as juvenile angiofibroma, have higher ADC values than other benign solid tumors, such as inverted papilloma. This is due to the excess extracellular spaces and free diffusion within vascular lesions [18]. In addition, the perfusion of blood flow and susceptibility effects brought about by hemosiderin deposition may also affect ADC values [25].

In our study, there was overlapping of ADC values between benign and malignant lesions. Indeed, one benign fibroma exhibiting a low ADC value on ADC mapping was misdiagnosed as a malignant tumor. This was attributed to the excess fibrous tissue, typical of fibroma, leading to subsequent restriction of diffusion [26]. Also, one patient with adenoid cystic carcinoma showed a high ADC value. This can be explained by the prominent myxoid stroma in such carcinomas that offers fewer impediments to the movement of water molecules, thus giving rise to higher ADC values [19].

With EPI, a pulse sequence is the sequence of choice for a quantitative study of diffusion, as the diffusion and relaxation effects contribute separately to the MRI signal intensity and, so, are easily separated. Furthermore, EPI is a very fast technique that allows data acquisition with different $b$ values within a reasonably short period of time [18]. However, with DWI of the nasal cavity, the paranasal sinuses are prone to susceptibility artifacts, which are considerably minimized when the tumors are greater than $3$ cm in size [19]. Diffusion-weighted spin-echo sequences such as split acquisition of fast spin-echo signals (SPLICE), line scans and fast asymmetrical spin-echo (FASE) have been used in the evaluation of head-and-neck lesions, but they all have long

### Table 1

<table>
<thead>
<tr>
<th>Pathology</th>
<th>ADC value (minimum–maximum)</th>
</tr>
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<tbody>
<tr>
<td>Squamous cell carcinoma ($n = 20$)</td>
<td>$1.15 \pm 0.6$ (1.01–1.27)</td>
</tr>
<tr>
<td>Adenoid cystic carcinoma ($n = 1$)</td>
<td>1.73</td>
</tr>
<tr>
<td>Mucoepidermoid carcinoma ($n = 3$)</td>
<td>$1.35 \pm 0.58$ (1.13–1.42)</td>
</tr>
<tr>
<td>Undifferentiated carcinoma ($n = 3$)</td>
<td>$1.35 \pm 0.05$ (1.01–1.99)</td>
</tr>
<tr>
<td>Non-Hodgkin’s lymphoma ($n = 4$)</td>
<td>$0.72 \pm 0.66$ (0.67–0.82)</td>
</tr>
<tr>
<td>Rhabdomyosarcoma ($n = 3$)</td>
<td>$0.85 \pm 0.60$ (0.78–0.89)</td>
</tr>
<tr>
<td>Olfactory neuroblastoma ($n = 2$)</td>
<td>$0.92 \pm 0.14$ (0.91–0.93)</td>
</tr>
<tr>
<td>Osteosarcoma ($n = 1$)</td>
<td>0.78</td>
</tr>
<tr>
<td>Chondrosarcoma ($n = 1$)</td>
<td>0.93</td>
</tr>
<tr>
<td>Juvenile angiofibroma ($n = 4$)</td>
<td>$1.88 \pm 0.86$ (1.77–1.97)</td>
</tr>
<tr>
<td>Inverted papilloma ($n = 3$)</td>
<td>$1.72 \pm 0.70$ (1.65–1.79)</td>
</tr>
<tr>
<td>Inflammatory polyps ($n = 3$)</td>
<td>$1.95 \pm 0.01$ (1.83–2.03)</td>
</tr>
<tr>
<td>Ossifying fibroma ($n = 1$)</td>
<td>0.57</td>
</tr>
<tr>
<td>Aneurysmal bone cyst ($n = 1$)</td>
<td>2.27</td>
</tr>
</tbody>
</table>
examination times, albeit with fewer susceptibility artifacts [25,27]. As echoplanar DWI is limited by notable susceptibility artifacts in the head and neck due to the presence of dental work as well as the adjacent air and bone, it may be of interest to use PROPELLER EPI and parallel imaging to improve image quality [28,29].

The present study has a few limitations, including the heterogeneity and small number of pathological types of lesions. Further studies of squamous cell carcinoma are recommended, as this is the most common type of tumor seen in the nasal cavity, and larger studies are required to confirm the results, given the wide variety of benign and malignant tumors observed in the sinonasal region. In addition, the ROI for measuring ADC values could not be correlated with histological specimens on a site-to-site basis, and there was no correlation between the ADC value and tumor cellularity. Finally, there was no comparison between the ADC value and standard MRI in the differentiation of malignant and benign sinonasal tumors. Further studies comparing the ADC value in sinonasal squamous cell carcinoma with standard MRI findings are recommended.

We conclude that the ADC value is a quantitative parameter that provides useful information for the differentiation of malignant and benign nasal and paranasal sinus tumors. It may also help in the differentiation of carcinoma from sarcoma as well as in the grading of malignant tumors. For this reason, it is recommended that diffusion-weighted MRI be added to routine MRI studies in patients with nasal and paranasal sinus tumors.

References