Interest of diffusion-weighted and gadolinium-enhanced dynamic MR sequences for the diagnosis of parotid gland tumors

Intérêt des séquences de diffusion et de l’IRM dynamique pour le diagnostic des tumeurs parotidiennes

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Parotid gland; Benign and malignant tumors; MRI; Apparent diffusion coefficient; Gadolinium-enhanced dynamic MRI; Time—signal intensity curves

Summary
Purpose. — This study aimed to evaluate the value of diffusion-weighted imaging (DWI) and gadolinium-enhanced dynamic magnetic resonance imaging (MRI) for differentiating benign and malignant parotid gland tumors, and for characterizing the various histological types (pleomorphic adenoma, and Warthin’s and malignant tumors).

Patients and methods. — This retrospective study involved 60 patients with suspected parotid gland tumors (mean age: 59.4 years), and was carried out from April 2005 to February 2008. All had undergone pathological examination. All MRI examinations were performed using the Siemens Magnetom Avanto 1.5T MRI system. Non-enhanced T1-weighted (T1W), gadolinium-enhanced fat-suppressed T1W and T2-weighted (T2W) images were obtained for all 60 patients, with diffusion-weighted echoplanar imaging (DW-EPI) and apparent diffusion coefficient (ADC) evaluation in 59 patients, and gadolinium-enhanced dynamic MRI sequences in 51 patients. Interpretation was carried out by two experienced radiologists (the first evaluation used T1W, gadolinium-enhanced fat-suppressed T1W and T2W images; the second evaluation used T1W, T2W, DWI and dynamic MRI) and, for each case, the benign/malignant nature of the tumor and its histological type were determined.

Results. — After the second reading, increases were noted in sensitivity, specificity, malignant positive predictive value (PPV) and negative predictive value (NPV), as well as in accuracy (90—100% for the first observer, and 90—97% for the second observer). Interobserver reliability also showed a significant increase from the first to the second reading (kappa = 0.63 to 0.87, respectively).

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Introduction

Parotid gland tumor pathology is complex, as it includes a variety of different benign and malignant tumors that are difficult to differentiate clinically. The surgical approach, when necessary, depends on tumor histology, localization and size. The use of magnetic resonance imaging (MRI), with conventional spin-echo (SE) T1-weighted (T1W) and T2-weighted (T2W) sequences, is well established in the preoperative workup of parotid tumors (for evaluating the topography, or perineural or deep-face space infiltration), but its role in differentiating the pathological process in parotid tumors is more controversial [1–6]. The present study (n = 60) compared the performance of conventional SE sequences with that of diffusion-weighted echoplanar imaging (DW-EPI) combined with gadolinium-enhanced dynamic MRI for differentiating the various types of parotid tumor (pleomorphic adenoma, Warthin’s tumor and malignant tumors). On the basis of these 60 cases together with a review of the literature, it appears that the apparent diffusion coefficient (ADC) and analysis of dynamic tumor enhancement, using time–signal intensity curves (TIC), constitute a reliable, reproducible means of improving radiologists’ performance in the preoperative histological diagnosis of parotid gland tumors.

Patients and methods

Patient population

In the present study, 60 consecutive patients (28 women, 32 men; age range: 19–86 years; mean age: 59.4 years) with clinically suspected parotid tumors were examined between April 2005 and February 2008 (34 months). All tumors were within the parotid gland, and the diameter of the lesions ranged from 9 to 75 mm (average 25 mm). Three patients had multiple tumors of the same histology. In these cases, only the largest tumor diameter was recorded, thereby showing only one tumor per patient, as in the other cases. In 59 patients, tumor histology was based on a surgical specimen and, in the remaining case, by fine-needle aspiration cytology (FNAC) (Table 1).

Image acquisition

All patients were examined with a 1.5-Tesla MRI system (Magnetom Avanto Syngo MR 2004V; Siemens, Germany). Surface coils were used in addition to the head coil to improve spatial resolution, particularly during the diffusion-weighted imaging (DWI) sequences, as these are prone to producing artefacts in the skull base. The protocol was essentially the same for all patients: non-enhanced SE T1W images, gadolinium-enhanced fat-suppressed T1W images and turbo (T) SE T2W images for all patients (n = 60); DW-EPI MRI with ADC evaluation (n = 59); and gadolinium-enhanced dynamic MRI sequences (n = 51).

Setting of spin-echo sequences

The SE T1W sequence used the following protocol: TR/TE: 584 ms/12 ms; slice number: 30; slice thickness: 2 mm; transverse plane; matrix: 384 × 345; field of view (FOV): 220 mm (voxel size: 0.6 × 0.6 × 2.0 mm); excitation number: 2; acquisition number: 1; and acquisition time: 3 minutes 45 seconds.

The gadolinium-enhanced SE T1W sequence used the following protocol: TR/TE: 651 ms/13 ms; slice number: 30; slice thickness: 2.2 mm; matrix: 384 × 325; FOV: 220 mm (voxel size: 0.7 × 0.6 × 2.2 mm); excitation number: 2; number of acquisitions: 1; fat saturation by water excitation; and acquisition time: 5 minutes 23 seconds.

The TSE T2W sequence used the following protocol: TR/TE: 3860 ms/10 ms; turbo factor: 25; slice number: 30; slice thickness: 2 mm; transverse plane; matrix: 384 × 384; FOV: 230 mm (voxel size: 0.6 × 0.6 × 2.0 mm); excitation number: 2; acquisition number: 2; and acquisition time: 3 minutes 45 seconds.

Setting of DWI sequences

The DWI sequences used the following protocol: TR/TE: 4700 ms/86 ms; EPI factor: 128; slice number: 30; slice thickness: 2.2 mm; transverse plane; matrix: 128 × 128; FOV: 210 mm (voxel size: 1.6 × 1.6 × 2.2 mm); excitation number: 2; acquisition number: 1; selective fat suppression; acquisition time: 1 minute 12 seconds; and b factors: 0, 500 and 1000 s/mm².

Setting of dynamic contrast-enhanced sequences

An ultrafast 3D fat-suppressed gradient-echo T1W (GE T1W) sequence with spoilers was used (3D-VIBE: volume interpolated breath-hold examination; Siemens). A set of eight images was obtained before, and every 6 seconds after, intravenous injection of gadodiamide (Omniscan; Amer- sham Health, Ireland; dose: 0.2 mL/kg body weight) at a rate of 2.0 mL/s, followed by a 20-mL saline flush (TR/TE: 8.84 ms/3.0 ms; number of slices per series: 8; slice thickness: 4 mm; matrix: 256 × 192; FOV: 220 mm (voxel size: 1.1 × 0.9 × 4.0 mm); excitation number: 1; number of acquisitions: 1; fat suppression by selective saturation; and acquisition time: 10 minutes).

Conclusion. — Gadolinium-enhanced dynamic MRI and DW-EPI with ADC evaluation improved the performance of MRI in distinguishing between benign and malignant parotid gland tumors, and characterizing the different histological types of benign tumors (pleomorphic adenoma and Warthin’s), thus leading to greater consensus in interpretation of the images.
Table 1  Postoperative histological diagnosis of the studied parotid tumors.

<table>
<thead>
<tr>
<th>Parotid gland tumor histology</th>
<th>Number of lesions (n = 60)</th>
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<tbody>
<tr>
<td><strong>Benign tumors</strong></td>
<td></td>
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<tr>
<td>Pleomorphic adenoma</td>
<td>n = 44</td>
</tr>
<tr>
<td>Warthin’s tumor</td>
<td>n = 30</td>
</tr>
<tr>
<td>Cystic lesions</td>
<td>n = 12</td>
</tr>
<tr>
<td>Salivary cyst, n = 1; lymphoepithelial cyst</td>
<td>n = 1</td>
</tr>
<tr>
<td><strong>Malignant tumors</strong></td>
<td></td>
</tr>
<tr>
<td>Malignant lymphoma</td>
<td>n = 16</td>
</tr>
<tr>
<td>Adenoid cystic carcinoma</td>
<td>n = 3</td>
</tr>
<tr>
<td>High-grade mucoepidermoid carcinoma</td>
<td>n = 2</td>
</tr>
<tr>
<td>Epidermoid carcinoma</td>
<td>n = 1</td>
</tr>
<tr>
<td>Poorly differentiated high-grade carcinosarcoma</td>
<td>n = 1</td>
</tr>
<tr>
<td>Low-grade carcinosarcoma</td>
<td>n = 2</td>
</tr>
<tr>
<td>Salivary duct carcinoma</td>
<td>n = 1</td>
</tr>
<tr>
<td>Carcinoma (FNAC)</td>
<td>n = 1</td>
</tr>
<tr>
<td><strong>Metastasis</strong></td>
<td></td>
</tr>
<tr>
<td>Pulmonary, n = 1; squamous cell carcinoma</td>
<td>n = 2</td>
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</table>

Image processing

ADC evaluation

The ADC was measured using an ADC map, generated by a pixel-by-pixel calculation according to the equation: \( \text{ADC} = \log(S\text{I}_{1}/S\text{I}_{2})/(b_2 - b_1) \), wherein \( b_1 \) and \( b_2 \) are gradient factors of sequences \( S_1 \) and \( S_2 \) (\( b_1 = 500 \text{s/mm}^2; b_2 = 1000 \text{s/mm}^2 \)), and \( S\text{I}_1 \) and \( S\text{I}_2 \) are signal intensities in the \( S_1 \) and \( S_2 \) sequences, respectively. Image quality was considered sufficient for analysis of the pathological area in every study case. In each case, a circular, 12-pixel, region of interest (ROI) was placed manually by the radiologist over the tumor area. Where the lesion showed heterogeneous signal intensity on routine sequences (SE T1W, TSE T2W and contrast-enhanced SE T1W), particular care was taken on placing the ROI to avoid cystic or calcified areas (Fig. 1).

Time—signal intensity curves

The TICs were obtained using the dedicated Siemens software for dynamic curves, which involves careful placing of the ROI over the lesion to avoid cystic or calcified areas — which, by definition, are not enhanced by contrast injection — and blood vessels. The ROI size varied on average by 3 to 4 mm (Fig. 2).

In accordance with previous studies by Takashima et al. [7] and Yabuushi et al. [8], the time to peak enhancement (\( T_{\text{peak}} \)) was determined from the TICs and the washout ratio (WR) calculated, using the equation \( ([S\text{I}_{\text{max}} - S\text{I}_{10\text{min}}]/[S\text{I}_{\text{pre}}]) \times 100 \%) \) for each case, wherein \( S\text{I}_{10\text{min}} \) refers to the signal intensity at 10 minutes after the administration of contrast. The TICs were then divided into four groups: type A (gradual enhancement with \( T_{\text{peak}} > 120 \text{ seconds} \), \( \text{WR} = 0 \)); type B (early enhancement with \( T_{\text{peak}} < 120 \text{ seconds} \), \( \text{WR} > 30\% \)); type C (early enhancement with \( T_{\text{peak}} < 120 \text{ seconds} \), \( \text{WR} < 30\% \)); and type D (a flat curve). These four curve types were considered by Yabuushi et al. [8] to be characteristic of pleomorphic adenoma, Warthin’s tumor, malignant tumors and cystic lesions, respectively (Figs. 3–6). Nevertheless, in the present study, the healthy parotid gland was moderately enhanced early, with a rapid washout. To our knowledge, this observation has never been published before.

Interpretation and analysis

Image analysis

Two experienced radiologists (S.R. and F.V.) independently read the 60 cases twice. The first evaluation — called...
Figure 2  Time versus signal intensity curve (Warthin’s tumor), with the ROI placed on the gadolinium-enhanced dynamic images (dynamic curves software, Siemens).

"morphological" — was based on tumor shape and signal analysis of the conventional sequences (SE T1W and FSE T2W). For the second evaluation — called "functional" — both readers combined the ADC and TIC of the tumor with the morphological data.

Histopathological analysis
All surgical specimens were examined by an experienced pathologist, who was well versed in parotid lesions, but unaware of the MRI findings. The specimens were analyzed at various magnifications (×2, ×4, ×20 and ×40) after hematoxylin and eosin (H&E) staining.

Statistical analysis
The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of the first and second interpretations for differentiating benign from malignant tumors were evaluated, with malignancy

Figures. 3–6  The time–signal intensity curves (TIC) for each tumor classification (according to Yabuuchi et al. [14]): (Fig. 3) type A (pleomorphic adenoma), $T_{\text{peak}} > 120$ seconds, washout ratio (WR) = 0; (Fig. 4) type B (Warthin’s tumor), $T_{\text{peak}} < 120$ seconds, WR > 30%; (Fig. 5) type C (malignant tumors), $T_{\text{peak}} < 120$ seconds, WR < 30%; and (Fig. 6) type D, no enhancement.
considered a positive result. Interobserver reliability was also determined by calculating the kappa coefficient for each set of readings.

**Results**

**Size, margins, T1W and T2W MRI signal intensity, and histopathological correlations for each parotid-tumor type studied**

**Pleomorphic adenoma**
The present series included 30 cases of pleomorphic adenoma that had maximum diameters ranging from 9 to 63 mm (mean: 21 mm). A further three cases were located within the deep parotid lobe. All 30 cases showed regular margins that, in 11 cases, were lobulated. Typical MRI findings were seen in 27 cases (90%) with a low T1W signal and a bright T2W signal [9]. Histopathology showed large stromal components of a predominantly myxoid nature [10,11]. Three other cases (10%) showed atypical low signals on both T1W and T2W imaging. Histology of these three lesions revealed a predominantly hypercellular epithelial component with a second fibrous component (n = 1), a predominantly myoepithelial component (n = 1) and an almost exclusively myoepithelial component (n = 1). (There is some histopathological doubt between a monomorphic adenoma, such as myoepithelioma, and pleomorphic adenoma of exclusively myoepithelial composition). In all 30 cases, relatively homogeneous and significant contrast-enhancement patterns were observed.

**Warthin’s tumor**
Of the 12 cases of Warthin’s tumor, the maximum diameter ranged from 15 to 38 mm (mean: 27 mm), and all were within the superficial lobe and had regular margins. In two cases, there were multiple and bilateral localizations. In eight cases (66.6%), the tumors showed heterogeneous hypo-intense signals on T1W and T2W imaging. Histopathological correlation showed a predominantly oncocytic epithelial component. In three cases (25%), there was a heterogeneous hypo-intense signal on T1W and T2W imaging, with high-signal areas on T2W sequences. Important macro- and microcystic changes were found on microscopy in these cases. The different composition of these cysts can explain the wide variation in signals [10–12]. In one case (8%), the tumor appeared hypo-intense with small hyperintense inclusions on T1W, and was hypo-intense with very hypo-intense inclusions on T2W. Hemorrhagic areas were found on histology in this case. In all these cases, however, enhancement was moderate and, in particular, highly heterogeneous.

**Cystic tumors**
Our series included two pseudotumors, the diameters of which were 20 and 24 mm, respectively (mean: 22 mm). Both were in the superficial lobe. The former lesion had smooth, regular margins, was clearly hypo-intense on T1W and hyper-intense on T2W imaging, and showed no contrast uptake; a simple salivary cyst was found on histology. The latter lesion had ill-defined margins, was moderately hypo-intense on T1W, and was heterogeneous and hypo-intense on T2W, with high-signal areas. Moderate peripheral contrast uptake was also observed. Histological analyses concluded that this was a lympho-epithelial cyst with thick secretions within a fibrous, inflammatory parenchyma.

**Malignant tumors**
The present series also included 16 malignant tumors, with diameters that ranged from 13 to 75 mm (mean: 33 mm). Irregular margins were found in 12 cases (75%) and regular margins in the remaining four (25%). In six cases (37.5%), extensive tumor infiltration of the entire gland was found. Another case (6%) showed extensive invasion of the lateropharyngeal space, while three cases (18.7%) had suspected perineural infiltration, two of which were subsequently confirmed by histology.

Five of the malignant tumors (31%) were homogeneously and markedly hypo-intense on T1W and T2W imaging. On histology, these proved to be epidermoid carcinoma (n = 1), metastasis of squamous cell carcinoma (n = 1), high-grade (n = 1) and low-grade (n = 1) poorly differentiated carcinosarcoma with spindle cells, and carcinoma (n = 1, on FNAC). Nine cases (56%) had low T1W signals and a highly heterogeneous appearance on T2W, with bright areas. Histology of these cases revealed high-grade mucoepidermoid carcinoma (n = 1), pulmonary adenocarcinoma metastasis (n = 1), squamous cell carcinoma metastasis (n = 1), solid and cribriform adenoid cystic carcinoma (n = 1), salivary duct carcinoma (n = 2) and malignant lymphoma (n = 3). In all of these cases, the hyperintense T2W areas corresponded to cystic changes or tumor necrosis. One lesion (6.2%) was hypo-intense on T1W and had a homogeneous hyperintense appearance on T2W, which proved to be a cribriform adenoid cystic carcinoma on histology. Finally, only one case showed hypointense signals on T1W and a bright signal on T2W imaging similar to those seen in pleomorphic adenoma, with a small hypo-intense walled nodule; this proved to be a mucoepidermoid carcinoma (n = 1). In all of these malignant tumors, intense heterogeneous contrast enhancement was evident.

**ADC values**
The ADC (mean ± standard deviation, SD) was measured in 59 patients (Table 2). The ADC of malignant tumors is significantly lower than that of benign tumors (Student’s t test, P < 0.001), whereas the ADC of pleomorphic adenoma (1.87 ± 0.38 × 10⁻³ mm²/s) is significantly higher than that of Warthin’s tumor (0.84 ± 0.18 × 10⁻³ mm²/s) (P < 0.001). However, no significant difference was found between the ADCs of pleomorphic adenoma and cystic lesions, nor was there any significant difference between the ADC val-

<table>
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<th>Table 2</th>
<th>Apparent diffusion coefficient (ADC) values in the studied parotid tumors.</th>
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<tr>
<td>Tumor type</td>
<td>n</td>
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<tr>
<td>Pleomorphic adenoma</td>
<td>30</td>
</tr>
<tr>
<td>Warthin’s tumor</td>
<td>12</td>
</tr>
<tr>
<td>Cystic lesions</td>
<td>2</td>
</tr>
<tr>
<td>Malignant tumors</td>
<td>15</td>
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</tbody>
</table>
ues of malignant \((0.83 \pm 0.16 \times 10^{-3} \text{mm}^2/\text{s})\) and Warthin’s tumors.

**Time versus signal intensity curves**

Gadolinium-enhanced dynamic MRI was also performed \((n = 51)\). In five cases, the curves were considered incoherent and were therefore rejected. In 22 of the 23 cases of pleomorphic adenoma (95.6%), there was a type A curve, while one case (4.3%) showed a type B curve. The latter was the case with the doubtful differential diagnosis (either a benign myoepithelial tumor or a pleomorphic adenoma with an exclusively myoepithelial component). Most \((n = 11)\) of the Warthin’s tumors in our study had type B dynamic curves, while one cystic lesion included in the dynamic curve analysis showed a type D curve and all \((n = 16)\) of the included malignant tumors showed a type C curve.

**Results for the two evaluations**

The sensitivity, specificity, PPV, NPV and accuracy were all increased in the second readings by both radiologists (Table 3). In particular, there was improvement in the NPV of malignancy, which reached 100% for both readers when using the complete protocol. A histogram of the results (Fig. 7) shows the homogeneity of the results of the two readers in the second reading session. This increase in reliability was statistically significant: in the differentiation of benign and malignant lesions, the kappa coefficient \((K)\) was 0.63 for the first reading and 0.87 for the second — a progression from good to excellent for both readers. As for the preoperative histological diagnosis, \(K\) was 0.56 for the first reading and 0.88 for the second — a progression from satisfactory to excellent for both readers. For the first reader, the correct histological typing progressed from 79.5 to 100% from the first to the second reading for benign tumors, but remained low for malignant tumors. The second observer improved from 90 to 95.5% in the analysis of benign tumors, but remained low for the histological diagnosis of malignant tumors. The most reliably recognized tumor was pleomorphic adenoma (86 and 100% for both readings by the first reader, and 100% for both by the second reader). Warthin’s tumor was the least recognized tumor, and was correctly identified in only 58% of cases in the first evaluation, but increased to 100% of cases in the second evaluation by one reader. Of the malignant tumors, only metastases (in a known cancer patient) and mucoepidermoid cancer were correctly identified.

**Synthesis**

**Pleomorphic adenoma**

In the present series, pleomorphic adenoma was seen in 90% \((n = 27)\) of cases as a mass with regular, though frequently polylobulated, margins, and with a low signal on T1W and a characteristic bright signal on T2W imaging, with fine hypo-intense septa. On DWI, the tumor appears bright because of the T2W shine-through effect. The ADC was high \((1.87 \pm 0.38 \times 10^{-3} \text{mm}^2/\text{s})\). A dynamic type A curve was found in 90% of cases (progressive enhancement with a late \(T_{\text{peak}}\) due to poor tumor vascularity, and a lack of washout due to the fact that the low cellular myxoid stroma of the tumor reportedly retains contrast material) \([8,13]\). In 10% \((n = 3)\) of cases, the adenoma showed a lower signal on T2W and DWI, and the ADC was lower than in the other cases \((1.33 \pm 0.16 \times 10^{-3} \text{mm}^2/\text{s})\). Two of these three cases had a type A curve, and the histopathology showed an atypical mixed tumor containing a hypercellular epithelial component and fibrous stroma \((n = 1)\), and a mixed tumor with predominantly myoepithelial components \((n = 1)\) (Fig. 8). The third case had a type B curve with an early \(T_{\text{peak}}\) and a marked washout effect, and proved to be an atypical adenoma with an almost exclusively myoepithelial component (making it a doubtful diagnosis of either a benign myoepithelial tumor or a pleomorphic adenoma with an almost exclusively myoepithelial component).

**Warthin’s tumor**

In the present series, Warthin’s tumor was seen in 91.7% \((n = 11)\) of cases as a sometimes multiple tumor with regular margins, and distinctively low signals on T1W imaging and highly heterogeneous T2W signals. Histopathological correlation revealed a variable amount of oncocytic epithelial component, and extensive micro- and macrocystic changes. The wide variability of the cystic contents composition explains the wide variability of signals. On DWI, the high signals reflect the high tumor cellularity, and vary according to the size and extent of the cystic elements. The ADC was low in all of these cases \((0.84 \pm 0.18 \times 10^{-3} \text{mm}^2/\text{s})\), and all showed a type B curve (early \(T_{\text{peak}} < 120\) s, indicating high tumor vascularity, and the high WR > 30%, reflecting the high stroma cellularity) \([8]\). In one case (8.3%), the tumor had slightly blurred margins, with small high-signal T1W areas and low-signal T2W areas, which corresponded to hemorrhagic foci on histology (Fig. 9).

**Cystic tumors**

In the two cases of cystic lesions, the T2W shine-through effect resulted in a high signal on DWI; the ADC was also high.

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Diagnostic performance with the two different MRI protocols for the two readers in the study.</th>
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<tbody>
<tr>
<td>Reader 1</td>
<td>1st evaluation</td>
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<tr>
<td>Reader 2</td>
<td>2nd evaluation</td>
</tr>
<tr>
<td>Reader 1</td>
<td>2nd evaluation</td>
</tr>
<tr>
<td>Reader 2</td>
<td>2nd evaluation</td>
</tr>
</tbody>
</table>

Data are expressed as % (95% confidence intervals); PPV: positive predictive value; NPV: negative predictive value.
Pleomorphic adenoma with an almost exclusively myoepithelial component, as seen on (A) T1-weighted (T1W), (B) T2-weighted (T2W) and (C) diffusion-weighted (DW) imaging; the tumor does not present with its characteristic bright signal because of the lack of myxoid component; the ADC was $1.39 \times 10^{-3} \text{mm}^2/\text{s}$; (D) TIC shows the gradual enhancement pattern (type A); (E) microscopy [hematoxylin and eosin (H&E) stain, original magnification $\times 2$] shows the high tumor cellularity (*) and the lack of myxoid matrix (arrow); (F) microscopy (H&E stain, original magnification $\times 0$) shows the widespread myoepithelial cell proliferation; the ADC and enhancement pattern allowed the diagnosis of atypical pleomorphic adenoma.

(1.90 ± 0.85 $\times 10^{-3} \text{mm}^2/\text{s}$). One lesion had regular smooth margins, a distinctively low signal on T1W and a high signal on T2W imaging, and no contrast enhancement; on histology, this proved to be a simple salivary cyst. The other lesion had irregular margins, a moderately low T1W signal and a heterogeneous low signal on T2WI with high-signal inclusions. Moderate peripheral enhancement was noted after contrast administration. Histology showed a lymphoepithelial cyst with thick secretory contents that had developed within fibrous, inflammatory parotid gland tissue.
Warthin’s tumor: (A) T1W imaging shows high-signal areas in a low-signal lesion, and the tumor margins are slightly blurred; (B) low-signal areas are seen on T2W imaging; (C) on DWI, the ADC was $0.66 \times 10^{-3}$ mm²/s; (D) areas are not enhanced on gadolinium-enhanced fat-suppressed SE T1W imaging; (E) type B TIC; (F) microscopy (H&E stain, original magnification × 4) shows hemorrhagic foci (arrow) corresponding to high-signal T1W areas, typical proliferation of eosinophilic cells in the cyst wall and lymphoid follicle formation (*); the pattern of enhancement allowed the diagnosis of malignancy to be eliminated.

Malignant tumors
The morphology and signals in malignant tumors are highly variable, depending on the histological nature of the tumor, as described above. DWI showed a variable high signal, depending on the presence and size of the cystic and/or necrotic components. The calculated ADC was low in all cases ($0.83 \pm 0.16 \times 10^{-3}$ mm²/s), and a type C curve (early $T_{peak} < 120$ s, reflecting neovascularization, and a low WR < 30%, reflecting low stromal cellularity) was found in all our analyzed cases. In 75% of cases ($n = 12$), the malignant diagnosis was easily made because of the irregular margins and invasive characteristics of the tumor. In 25% of cases
Figure 9  High-grade carcinosarcoma with spindle cells: (A) T1W, (B) T2W and (D) gadolinium-enhanced images show a well-defined, low-signal encapsulated tumor, with homogeneous and moderate enhancement; (C) on DWI, the ADC was $0.67 \times 10^{-3}$ mm$^2$/s; (E) TIC depicts the typical “plateau” appearance of malignant tumors; (F) microscopy (H&E stain, original magnification x 20) shows spindle cell proliferation (*) and the fibrous capsule (arrow); the pattern of enhancement eliminated a benign diagnosis, including Warthin’s tumor.

(n = 4), however, the diagnosis of malignancy was made for a lesion with regular margins based solely on low ADC values and the dynamic enhancement pattern (Figs. 10 and 11).

Discussion

The role of MRI in establishing the precise extent and site of a parotid gland lesion is well established, but its performance in providing an indication of its pathological nature is still controversial. However, it is of major importance to determine whether or not a tumor is benign or malignant, as this will have a strong influence on the choice of surgical procedure and can help to avoid perioperative difficulties. The aim of the present study was to compare a conventional MRI study (using T1W and T2W imaging) with a more complete protocol, including DWI and dynamic
parameters, in predicting the benign or malignant nature of parotid masses. There are few reports in the literature on the use of DWI and/or dynamic MRI [7,8,13–20] and, to our knowledge, no one has yet established whether or not these new techniques can improve diagnostic performance in everyday clinical practice. Many teams do not use these "new" sequences routinely, and a number of reasons may explain their reluctance to do so: these sequences extend the overall examination time as well as the time needed by the radiologist for post-processing which, if done by the physician him/herself, will greatly improve the quality of the examination; positioning of the ROI to
measure the ADC and TIC is only reliable provided that the tumor is large enough (about 1 cm) and that the DWI does not show too many artefacts. In our study, the ADC values of the malignant tumors (0.83 ± 0.16 × 10⁻³ mm²/s) were significantly lower (P < 0.001) than those of benign tumors (1.58 ± 0.47 × 10⁻³ mm²/s), whereas the ADC values of pleomorphic adenoma (1.87 ± 0.18 × 10⁻³ mm²/s) were significantly higher (P < 0.001) than those of Warthin’s tumor (0.84 ± 0.18 × 10⁻³ mm²/s). However, there was no significant difference between the ADC values of pleomorphic adenoma and cystic lesions (1.9 ± 0.85 × 10⁻³ mm²/s), nor between malignant tumors and Warthin’s tumors. Our results are in agreement with those previously published except in the case of malignant tumors, for which our ADC values were lower (1.19 ± 0.19 × 10⁻³ mm²/s) for Ikeda et al. [14], and 1.13 ± 0.43 × 10⁻³ mm²/s for Wang et al. [15]. We believe that these differences may be explained by, on the one hand, the high grade of malignancy in our series (three malignant lymphomas, one high-grade sarcomatoid carcinoma, one poorly differentiated carcinoma and one solid-type adenoid cystic carcinoma) and, on the other hand, the absence of tumor necrosis in 10 cases. However, according to Wang et al. [15], an ADC value less than 1.22 × 10⁻³ mm²/s is suggestive of malignancy. Yet, in our study and in agreement with others [13,14], the benign tumors (pleomorphic adenoma and Warthin’s tumors) all had an ADC below that level, and one malignant mass had an ADC higher than that level. For this reason, we believe that using the various ranges of ADC values described in literature for the different tumor types, rather than an absolute threshold, is more reliable when analyzing a parotid mass.

The present study also confirms the place of MRI as the best first examination in the workup of a parotid mass, as it led to a high level of accuracy in differentiating between benign and malignant masses, even at the first reading for both of our readers (90%). Adding the ADC (n = 59) and TICs (n = 51) confirmed the initial diagnoses in 50 cases for the first reader and in 53 cases for the second reader, and led to a change in the diagnosis in 10 and seven cases, respectively. Overall, five tumors were correctly reclassified into the malignant group (two malignant lymphomas, two undifferentiated carcinoma with regular margins and one mucoepidermoid carcinoma) and four into the benign group (one pleomorphic adenoma with cystic changes, two Warthin’s tumors and one inflammatory cyst), while 12 changes in the histological diagnosis were made (mainly between pleomorphic adenoma with a mostly epithelial component and Warthin’s tumor). These modifications mostly involved tumors with atypical appearances on conventional MRI sequences.

Indeed, DWI and dynamic MRI — despite some overlap between confidence intervals — increased the sensitivity, specificity, PPV, NPV and global accuracy (100 and 97%, respectively) in the diagnosis of malignancy for both our study readers, and the preoperative histological diagnosis was also greatly improved. This was especially true for benign lesions — and Warthin’s tumor in particular — which have highly variable appearances on conventional SE sequences and do not always require surgery, particularly in elderly or frail patients. However, we observed no improvement in the differentiation of malignant tumors, particularly lymphomas, which should not be treated surgically. Nevertheless, the complementarity of DWI and dynamic imaging needs to be emphasized: in the present study as well as in those in the literature, the ADC values overlapped across the various histologies. This was particularly true for malignant tumors and Warthin’s tumors, both of which have low ADCs, but which can be easily identified thanks to their TICs (slow washout in the former, rapid washout in the latter). This is why we believe it is necessary to always include both ADC values and dynamic sequences. In six of our cases, the qualitative analysis of the washout was insufficient to classify TICs correctly, and it was necessary to calculate the quantitative WR.

In addition, in the present study, interobserver reliability progressed from good to excellent in correctly differentiating benign from malignant tumors, and from satisfactory to excellent in the preoperative histological diagnosis. The systematic use of ADCs and dynamic contrast studies appears to result in more homogeneous interpretations by physicians, even when their levels of experience are varied, making their assessments less subjective.

However, the main limitation of the present study is the small number of included cases, due to the relative scarcity of parotid tumor pathology and the only recent systematic use of the complete protocol within the department. Indeed, our observations need to be tested in larger study populations to obtain statistically significant results. The role of preoperative cytolology and pathology (FNAC and cutting-needle biopsy) in the management of parotid neoplasms should also be mentioned. Some centers systematically perform these to ensure the preoperative histological diagnosis. However, many surgical teams disapprove of such techniques because of the risk of incising the tumor capsule and, thus, seeding neoplastic cells. Such a risk has been widely described in the literature along with other possible complications such as bleeding, neurovegetative
symptoms, and damage to the facial nerve and its branches [21,22]. Biopsies can also modify tumor structure (necrosis, hemorrhage, fibrosis, squamous metaplasia), thereby making the subsequent histological evaluation more difficult [23,24].

In addition to these technical risks, the reliability of biopsy samples in distinguishing benign from malignant masses is also highly variable in the literature. Evidently, it very much depends on the quality of the sample (quantity of tissue, avoidance of non-specific areas such as cystic changes or necrosis) and the pathologist’s experience [25]. The published false-negative rate with FNAC ranges from 40 to 50% [26–29], and is particularly high for lymphomas, which most series fail to identify. The results with core-needle biopsies are better, with a sensitivity and specificity of almost 100% for both [21,30,31], although this is a more invasive procedure that usually requires local anesthesia and computed tomographic or ultrasonographic guidance [32], making this procedure more expensive and time-consuming. For preoperative histological diagnoses, FNAC only rarely differentiates between the different malignant tumor types and may also not correctly diagnose the various benign types, especially Warthin’s tumor [33]. In a study of 180 cases, Paris et al. [34] compared FNAC with a conventional MRI protocol in the prediction of malignancy in parotid tumors. The sensitivity, specificity and accuracy of the two methods were similar (81, 95 and 92% vs 87, 94 and 93% respectively), although the authors emphasized that MRI alone offered important additional morphological information (such as size, location and extent).

We believe that a complete MRI study including DWI and gadolinium-enhanced dynamic MRI is the most useful, most reliable and most reproducible preoperative investigation available for preoperative parotid gland tumor assessment. Such a protocol provides a detailed morphological study of the tumor and its surroundings, and improves the performance of MRI in differentiating between benign and malignant tumors, and in the histological typing of benign tumors.

Conclusion

Gadolinium-enhanced dynamic MRI and DW-EPI MRI with ADC evaluation can improve the performance of MRI in both distinguishing between benign and malignant parotid gland tumors, and characterizing the different histological types of benign tumors (pleomorphic adenoma and Warthin’s tumor) and, thus, can lead to more consistent and accurate interpretations.

Conflicts of interest

No potential conflicts of interest relevant to this article are reported.

References


