ORIGINAL ARTICLE

Apparent diffusion coefficient of pituitary macroadenoma evaluated with line-scan diffusion-weighted imaging

Coefficient de diffusion apparent des macroadénomes hypophysaires évalué par imagerie de diffusion à balayage de lignes

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Abstract
Objective. — The goal of this study was to evaluate the consistency of pituitary macroadenoma using apparent diffusion coefficient (ADC) with line-scan diffusion-weighted imaging (LSDWI).

Methods. — Patients with pituitary macroadenoma (\(n=19\)) were studied prospectively. The LSDWI was performed using a maximum \(b\) factor of 1000 s/mm\(^2\). The consistency of macroadenoma was rated as soft, intermediate or hard at transsphenoidal surgery. The ADC values of tumors were compared with the tumor-consistency ratings.

Results. — A soft consistency was found at surgery in 13 patients (mean ADC: \(0.84 \pm 0.1 \times 10^{-3}\) mm\(^2\)/s); an intermediate consistency was observed in six patients (mean ADC: \(0.81 \pm 0.16 \times 10^{-3}\) mm\(^2\)/s). No tumors of hard consistency were found. There was no significant difference in ADC values between tumors of soft consistency compared with tumors of intermediate consistency (\(P = 0.37\)).

Conclusions. — A relationship between tumor consistency and the ADCs of soft and intermediate macroadenomas was not shown in this study using LSDWI.

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Introduction

Most pituitary macroadenomas can be removed adequately via the transsphenoidal route. However, a particularly firm, fibrous pituitary macroadenoma might indicate a transcra nial approach because very firm tumors cannot be sufficiently debulked by curettage and suction via the transsphenoidal approach. Therefore, knowledge of the macroadenoma consistency could help neurosurgeons to plan more appropriate surgical procedures.

Recently, it was reported that pituitary macroadenoma had been evaluated using echo-planar diffusion-weighted imaging (EPDWI) for detection of pituitary apoplexy or determination of macroadenoma consistency [4, 8, 9]. Pierallini et al. [8] reported that the apparent diffusion coefficient (ADC) using EPDWI could provide information on macroadenoma consistency: adenomas with a harder consistency using the transsphenoidal route. However, particularly in the pituitary region, EPDWI images may suffer considerably from susceptibility artifacts because of dental work and, particularly, the adjacent sphenoidal sinus air and bone [5]. For those reasons, DWI techniques that are not subject to susceptibility artifacts are more suitable for evaluating pituitary lesions.

Line-scan diffusion-weighted imaging (LSDWI) uses multiple diffusion-weighted spin-echo column excitations to form a two-dimensional image [1]. 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. This technique is advantageous because it is inherently insensitive to susceptibility artifacts [1, 5-7]. The purpose of this study was to evaluate the ADC of pituitary macroadenoma with respect to its consistency using LSDWI.

Materials and methods

Subjects

The LSDWI studies were performed prospectively for pituitary macroadenoma from July 2002 to November 2005, using a study protocol approved by the ethics committee at our institution. Informed consent was obtained from all patients. Pituitary adenoma was confirmed surgically in 19 patients (14 men and 5 women; mean age 55 years). Hormonal status was normal in 15 patients and markedly high in four patients (prolactin \( n = 2 \), growth hormone \( n = 1 \), growth hormone + prolactin \( n = 1 \)). These latter patients had received no treatment prior to the magnetic resonance (MR) studies. The mean maximum diameters of the tumors were 29 ± 13 mm (range 12-70 mm).

MR sequences

The MR study was performed using a 1.5-T MR imaging system (Signa CV/i; GE Medical Systems, Milwaukee, WI). All patients underwent conventional MR imaging including coronal T1-weighted spin-echo sequencing (416/11; repetition time (ms)/echo time (ms)) with and without contrast, and coronal T2-weighted fast-spin echo sequencing (4000/102; echo train length, 15). Other parameters included a field of view (FOV) of 16 × 16 cm, and a section thickness of 3 mm with a between-section gap of 0.5 mm.

The LSDWI method has been described elsewhere [1, 5-7]. Neither cardiac gating nor respiratory triggering was used for the LSDWI. We also used no antisusceptibility device to reduce artifacts. The LSDWI scans were acquired using the following parameters: TR = 3124 ms; TE = 56.5 ms; one excitation, matrix size of 128 × 128 columns, FOV of 20 × 20 cm; and section thickness of 3 mm with a between-section gap of 0.5 mm. The LSDWI images were...
obtained using two different $b$ values of 5 s/mm$^2$ and 1000 s/mm$^2$, with the maximum $b$ value applied along three orthogonal directions. The scan time per slice was 39 s: 3-5 slices were obtained in the coronal plane according to the lesion size.

Imaging data analysis

Isotropic LSDWI scans with a $b$ factor of 1000 s/mm$^2$ were generated from the three diffusion directions assessed. Trace ADC maps were generated using the equation described by Stejskal and Tanner [11]: $S = S_0 e^{-bS}$, where $b$ is the diffusion-weighting factor, $S$ is the signal intensity of the diffusion trace for $b = 5$ s/mm$^2$. The ADC measurements were performed by one neuroradiologist from trace ADC maps by placing regions of interest (ROI) over the tumors. For ROI measurements in the tumor, particular care was taken to include the apparently solid parts of the tumors and to exclude obviously hemorrhagic or cystic areas, as shown in the corresponding T1-weighted, T2-weighted and contrast-enhanced MR images. The mean ROI size for tumors was $0.77 \pm 0.51$ cm$^2$. On T2-weighted images, T1-weighted enhanced MR images. The mean ROI size for tumors was the corresponding T1-weighted, T2-weighted and contrast-enhanced MR images. The mean ROI size for tumors was $0.77 \pm 0.51$ cm$^2$. On T2-weighted images, T1-weighted enhanced MR images. The mean ROI size for tumors was $0.77 \pm 0.51$ cm$^2$

Surgery

All patients with macroadenoma underwent surgical resection using the transsphenoidal approach, all performed by one neurosurgeon. At surgery, the neurosurgeon, who was blinded to the preoperative DWI study, evaluated the tumor consistency according to three classifications: soft (easily removable through suction); intermediate (removable with difficulty through suction); and hard (not removable through suction).

Statistical analysis

The Mann-Whitney $U$ test was used to detect significant differences for ADC values, and the SI ratio on T2-weighted, T1-weighted and DWI images, across the three degrees of tumor consistency. A $P$ value of less than 0.05 was considered a statistically significant difference.

Results

ADC values versus consistency of macroadenoma

Representative LSDWI scans and ADC maps are shown in Figs. 1-3. On surgery, 13 patients were considered to have a soft macroadenoma consistency, and 6 patients were deemed to have an intermediate macroadenoma consistency. A hard consistency was not found in the present cases. Regarding hormonal pituitary status, hormone-secreting adenomas ($n = 4$) showed a soft consistency in 3 patients and an intermediate consistency in 1 patient. Non-secreting adenomas ($n = 15$) showed a soft consistency in ten patients and an intermediate consistency in five patients.

Overall, the mean ADC value was $0.83 \pm 0.12 \times 10^{-3}$ mm$^2$/s for these pituitary macroadenomas ($n = 19$). The mean ADC value of those of soft consistency ($n = 13$) was $0.84 \pm 0.1 \times 10^{-3}$ mm$^2$/s (range: $0.7-1.03 \times 10^{-3}$ mm$^2$/s). The mean ADC value of those of an intermediate was $0.81 \pm 0.16 \times 10^{-3}$ mm$^2$/s (range: $0.67-1.12 \times 10^{-3}$ mm$^2$/s). The difference in ADC between soft and intermediate consistencies was not significant ($P = 0.37$) (Fig. 4a). In addition, the mean ADC value between hormone-secreting and non-secreting adenomas was also not significant ($P = 0.40$; $0.88 \pm 0.17$ versus $0.81 \pm 0.10 \times 10^{-3}$ mm$^2$/s).

SI ratio on T2-weighted images, T1-weighted images and DWI scans versus consistency of macroadenoma

The mean SI ratio on T2-weighted images in the soft-consistency group ($n = 13$) was $1.59 \pm 0.23$, and $1.89 \pm 0.09$ in the intermediate-consistency group ($n = 6$), with a statistically significant difference ($P = 0.011$) between the two (Fig. 4b). The mean SI ratio on T1-weighted images was $0.82 \pm 0.08$ in the soft consistency group ($n = 13$) and $0.76 \pm 0.05$ in the intermediate group ($n = 6$), but here the difference was not significant ($P = 0.08$) (Fig. 4c). The mean SI ratio on DWI scans was $1.20 \pm 0.16$ in the soft group ($n = 13$) and $1.36 \pm 0.25$ in the intermediate group ($n = 6$); here again, the difference was not statistically significant ($P = 0.13$) (Fig. 4d).

Discussion

The application of DWI techniques to sellar regions is challenging and rarely done. Rogg et al. [9] first reported that pituitary apoplexy can be detected early using EPDWI. More recently, Lomban et al. [4] also reported that EPDWI demonstrated increased signal intensity in the pituitary mass in a case of pituitary apoplexy. Both reports emphasized that a decreased ADC was found in pituitary apoplexy and that this measure might facilitate the early detection of pituitary apoplexy.

Regarding the consistency of pituitary macroadenoma in comparison to ADC values, Pierallini et al. [8] found that the ADC increased with the hardness of the tumor. They reported that adenomas characterized as hard at surgery were more fibrous and displayed higher ADCs, whereas adenomas with a soft consistency showed higher cellularity, scant fibrous stroma and considerably lower ADC values. In their results, cases with an intermediate consistency showed higher ADCs than those with a soft consistency, with some overlapping between the two groups.

However, our results do not accord with those results. In the present study, the mean ADC of the intermediate-consistency group was slightly lower than that of the soft
Figure 1  Pituitary macroadenoma in a 43-year-old man. Tumor consistency was judged as soft at surgery. (a) Coronal T1-weighted imaging shows a hemorrhagic component within the tumor (arrow). (b) Coronal T2-weighted imaging shows a high-intensity mass. (c) LSDWI imaging shows an isointense signal from the tumor compared with normal brain tissue. (d) ADC map shows a heterogeneous signal from the tumor. The region of decreased diffusion corresponds to the hemorrhagic component of the tumor (arrow). The ADC of the mass, excluding the hemorrhage, is $1.03 \times 10^{-3}$ mm$^2$/s. (e) Photomicrograph shows hypercellularity of the tumor tissue (blue) with scant fibrous stroma (red). Foci of small hemorrhages are present (arrows).

Figure 1  Macroadénome hypophysaire chez un homme âgé de 43 ans. La consistance tumorale a été jugée molle à l'intervention. (a) L'image coronale pondérée T1 montre une composante hémorragique au sein de la tumeur (flèche). (b) L'image pondérée T2 montre une masse de signal hyperintense. (c) L'image en diffusion à balayage de lignes montre un signal iso-intense de la tumeur comparé au parenchyme cérébral. (d) La cartographie ADC montre une hétérogénéité de signal de la tumeur. La zone de diffusion restreinte correspond à la composante hémorragique de la tumeur (flèche). L'ADC en zone tumorale non hémorragique est mesurée à $1.03 \times 10^{-3}$ mm$^2$/s. (e) La photomicrographie montre une hypercellularité du tissu tumoral (bleu) avec un stroma fibreux peu abondant (rouge). Des foyers de microhémorragies sont retrouvés (flèches).
Figure 2  Pituitary macroadenoma in a 47-year-old man. Tumor consistency was judged as intermediate at surgery. (a) Coronal T2-weighted imaging shows high signal intensity from the tumor involving the entire sphenoidal sinus. (b) Contrast-enhanced T1-weighted imaging shows tumor heterogeneity. (c) LSDWI scan shows a slightly hyperintense signal from the tumor compared with normal brain tissue. (d) The ADC map shows lower diffusion of the tumor than in normal brain tissue. The tumor ADC is $0.67 \times 10^{-3}$ $\text{mm}^2/\text{s}$. (e) Photomicrograph shows small cells (blue) with conspicuous fibrous stroma (red).

**Figure 2** Macroadénome hypophysaire chez un homme âgé de 47 ans. La consistance tumorale a été jugée intermédiaire à l’intervention. (a) L’image coronale pondérée T2 montre un signal élevé de la tumeur qui envahit la totalité du sinus sphénoïdal. (b) L’image pondérée T1 après injection montre un rehaussement hétérogène de la tumeur. (c) L’image en diffusion à balayage de lignes montre un signal discrètement hyperintense de la tumeur comparé au tissu cérébral normal. (d) La cartographie ADC montre une diffusion plus basse de la tumeur comparée au tissu cérébral normal. (e) La photomicrographie montre des cellules de petite taille (bleu) avec un stroma fibreux important (rouge).
Figure 3  Macroadénome hypophysaire chez un homme âgé de 40 ans. La consistance tumorale a été jugée comme intermédiaire à l’intervention. (a) L’image coronale pondérée T2 montre un signal élevé de la tumeur qui s’étend dans le sinus sphénoïdal (flèche). (b) L’image coronale pondérée T1 après injection montre un rehaussement modéré de la tumeur. (c) L’image en diffusion à balayage de lignes montre un signal iso-intense de la tumeur comparé au tissu cérébral normal. (d) La cartographie ADC montre une diffusion plus élevée de la tumeur que le tissu cérébral normal. L’ADC de la tumeur est $1,12 \times 10^{-3}$ mm²/s. (e) La photomicrographie montre un stroma fibreux abondant (rouge) avec une cellularité peu abondante (bleu).
group, but the between-group ADCs were not significantly different.

Pierallini et al. [8] also suggested that an ADC value of $1.0 \times 10^{-3} \text{mm}^2/\text{s}$ is useful as a cut-off value to designate tumors that are amenable to aspiration. However, in the present study, we found two tumors (one soft and one intermediate) that had ADC values greater than $1.0 \times 10^{-3} \text{mm}^2/\text{s}$. The reasons why our data do not concur with the Pierallini findings are unknown. The different DWI techniques (LSDWI vs. EPDWI) used and the small numbers of adenoma cases in both our study and theirs (soft, $n = 13$; intermediate, $n = 6$, and soft, $n = 12$; intermediate, $n = 6$, respectively) may be a partial explanation.

As for the former issue, it is reported that the ADC values of normal brain parenchyma are not significantly different with LSDWI and EPDWI [7]. However, pituitary adenomas can be highly susceptible to artifacts because of the surrounding air sinuses and bone. This means that the ADCs of evaluated pituitary adenomas could vary with the different DWI techniques. However, we have no data with which to clarify this speculation. It has been hypothesized that the ADC of macroadenomas may simply be influenced by the cellularity of tumors as well as the fraction of extracellular fibrosis [8]. However, other factors may also be involved. For those reasons, further investigations including a greater number of cases and using different DWI techniques may be necessary to elucidate the relationship between tumor consistency and ADCs.

In this study, macroadenomas with a soft consistency showed a lower SI ratio on T2-weighted imaging than did those with an intermediate consistency. On the other hand, the SI ratio on T1-weighted images and DWI scans showed no significant differences between the two types of consistency. Previous reports have described that the low signal intensities of tumors seen on T2-weighted images provide useful information in terms of tumor consistency—they represent firm and fibrous tumors [3,10]. However, low signal intensities on T2-weighted images are not exclusively attributable to dense collagen fiber in macroadenomas [2]. A high cellularity with a high nucleus-to-cytoplasm

**Figure 4** Box plots show median, interquartile ranges, and extreme ADC values (a) and signal-intensity ratios (tumor to white matter) on T2-weighted images (b), T1-weighted images (c) and DWI scans (d) in the group with soft tumors ($n = 13$) and in those with intermediate tumors ($n = 6$). No statistically significant differences were found in ADC values between macroadenomas with soft and intermediate consistencies ($P = 0.37$), nor in the between-group signal-intensity ratios of T1-weighted images ($P = 0.08$) or DWI scans ($P = 0.13$). However, a significant difference was found in signal-intensity ratios on T2-weighted imaging between the two tumor groups ($P = 0.011$).

**Figure 4** Graphiques montrant la médiane, l’étendue de la distribution (intervalle interquartile) et les extrêmes des valeurs d’ADC (a) et des ratios d’intensité de signal (tumeur/substance blanche) sur les images pondérées T2 (b), les images pondérées T1 (c) et les images de diffusion (d) dans le groupe de tumeurs de consistance molle ($n = 13$) et dans le groupe de tumeurs de consistance intermédiaire ($n = 6$). Il n’a pas été retrouvé de différence significative dans les valeurs d’ADC entre les consistances molles et intermédiaires ($p = 0.37$). Une différence significative était retrouvée entre les deux groupes dans les ratios d’intensité de signal sur les images pondérées T2 ($p = 0.0011$). Il n’a pas été retrouvé de différence significative entre les deux groupes des ratios d’intensité de signal des images pondérées T1 ($p = 0.08$) et celles pondérées en diffusion ($p = 0.13$).
ratio could produce a decrease in SI, whereas abundant extracellular spaces combined with scattered collagen fiber could cause a sufficient increase in SI on T2-weighted images. These pathological findings can contribute independently to SI on T2-weighted images. Some investigators have also reported that the amounts of fibrous tissue, amyloid and iron seen in adenomas on histological analyses bear little relationship with hypointensity on T2-weighted images [2]. Indeed, T2-weighted images may be of limited value for estimating the fraction of fibrosis in adenomas.

The present study had some limitations. First, regarding consistency, we encountered no cases of hard tumors. As several large series suggest that pituitary macroadenomas with a hard consistency occur in only 5-8% of patients [10], it may be difficult to collect a sufficient number of such tumors. Second, in our study, we did not quantitatively analyze the degree of fibrosis in the adenoma specimens. Although fibrosis appeared more conspicuously in tumors of intermediate rather than soft consistency in Fig. 1e, Fig. 2e and Fig. 3e, these samples represent only a small fraction of the tumor volume. We were unable to assess precisely what proportion of tumor was fibrous. Tumor removal by suction makes it difficult to preserve the tissue architecture intact. This fact convinced us that assessing the degree of fibrosis histologically was not worthwhile. Finally, objective quantitative measurements (such as ADC values) were compared to subjective assessments (by a neurosurgeon) of tumor consistency. Thus, different neurosurgeons may have rated the tumor consistencies differently.

Conclusions

Although our cases were limited to soft and intermediate consistencies, no relationship was apparent between consistency and ADC values of pituitary macroadenomas using LSDWI. However, this was a small-scale study. For that reason, we believe that further investigations with larger patient populations are necessary to better evaluate the potential usefulness of the ADC in the preoperative assessment of pituitary macroadenomas.

References