Usefulness of advanced MR techniques in the differential diagnosis of sellar and parasellar tumours

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Aims and objectives

Sellar/parasellar tumors constitute 10 to 15% of all primary intracranial neoplasms and are the most common causes of pituitary dysfunction and field of view disturbance [1]. Therefore, early correct diagnosis and therapy of patients with sellar/parasellar tumors are of high importance in clinical practice. The most common pituitary tumors are adenomas, which on MR can present various enhancement patterns and other imaging features. Therefore pituitary adenomas may be mimicked by other tumors located in the sellar region, such as meningiomas, craniopharyngiomas, Rathke cleft cysts, metastases, gliomas, abscesses, as well as uncommon types of sellar/parasellar tumors like hemangioblastoma. The plain MR appearance of different sellar/parasellar lesions may be very similar (Fig.1, Fig.2), which often leads to misdiagnosis [1].

Since many intracranial tumors are indistinguishable using plain MRI, the advanced MR techniques, such as diffusion weighted imaging (DWI), perfusion weighted imaging (PWI) and magnetic resonance spectroscopy (MRS) can be applied to obtain more information useful in the differential diagnosis. Nevertheless, these techniques are rarely used in diagnosis of sellar/parasellar tumors. There are only a few reports concerning the contribution of DWI and MRS in sellar/parasellar tumors imaging, and most of them have been performed in small groups of subjects, and their results are often contradictory [2,3].

The aim of this study is to establish the imaging patterns, which are typical for different sellar/parasellar tumors, using the advanced MR techniques. Therefore this paper will be the first study concerning the contribution of both DWI and PWI in diagnostic imaging of pituitary and parasellar tumors. The results of this research will provide the noninvasive in vivo imaging biomarkers, which enable the differential diagnosis of sellar and parasellar tumors.
Fig. 1: Sellar tumors presenting very similar appearance on plain MR: post-contrast T1-weighted images (upper row) and T2-weighted images (bottom row). The histopathological examinations obtained after resection of these tumors revealed: adenoma (1), abscess (2) and Rathke cleft cyst (3).

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Fig. 2: Sellar tumors presenting very similar appearance on plain MR: T2-weighted images (upper row) and post-contrast T1-weighted images (bottom row). The histopathological examinations obtained after resection of these tumors revealed: adenoma (1) and hemangioblastoma (2).

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Methods and materials

Patients

Seventy-five patients (34 women and 41 men; mean age 58.9 yrs), with sellar/parasellar tumors were prospectively enrolled in the study. The histopathological examinations obtained after resection of these tumors revealed: 46 macroadenomas, 12 meningiomas (including 2 meningiomas in an intrasellar location and 10 meningiomas in a parasellar location), 10 craniopharyngiomas: 6 adamantinomatous type (4-intrasellar, 2-suprasellar), 4 squamous-papillary type (suprasellar), as well as 1 intrasellar hemangioblastoma, 3 intrasellar metastases, 2 suprasellar lymphomas and 1 suprasellar glioma. Among the adenomas there were: 8 prolactin-secreting adenomas, 1 growth hormone-secreting adenoma and 37 nonfunctioning adenomas.

The craniocaudal diameter of tumors included in our study ranged between 1.4 cm and 6.0 cm (mean 2.9 cm).

The study was conducted in accordance with the guidelines of the local University Ethics Committee for conducting research involving humans. Each patient provided his/her signed consent to participate in the examination.

Imaging protocol

Imaging was performed on a 1.5T Signa Hdx scanner (GE Healthcare, Medical System) using a 16-channel coil dedicated for head and spine imaging. Conventional sequences included: coronal and sagittal T1 FSE, coronal and sagittal T2 FSE, and post-contrast T1-weighted images in coronal and sagittal planes (slice thickness 3 mm). Additionally, axial T2-weighted images covering the whole brain were performed.

Axial DWI EPI (echo planar imaging) was performed with a b value of 0 and 1000; TR = 8000, TE = 81.5; FOV = 26x20,8; section thickness 4 mm (with no gap).

PWI was performed with a dynamic susceptibility-weighted contrast-enhanced (DSC) method, using a gradient-recalled T2*-weighted echo-planar imaging sequence. Parameters used were as follows: TR/TE = 1900/80 ms, flip angle = 80°, NEX = 1.0, matrix size = 192 × 128, and slice thickness = 5 mm (with no gap). Perfusion images were obtained in axial slices parallel to anterior comissure - posterior commissure (AC-PC) line. During the first 10 seconds images were acquired before starting the contrast agent injection to establish a pre-contrast baseline. Ten seconds after the start of image acquisition, 0.2 mmol/kg of body weight gadopentetate dimeglumine was injected with a power injector (Medrad) at a rate of 5 mL/s through an intravenous catheter placed in the antecubital vein. This was immediately followed by a bolus injection of saline (total of 20 mL at 5 mL/s). Total duration of acquisition was 1 minute and 24 seconds.
**Image post-processing**

Post-processing of perfusion data and perfusion measurements was performed using the commercial GE Healthcare workstation (ADW 4.4).

**Diffusion Measurements**

Regions of interest (ROIs) were drawn on the grey-scale ADC maps. Multiple ROIs (size 30-40 mm²) were placed over several dark spots, and the minimum ADC values of all ROIs were chosen. Additionally for each transaxial section, the aligned imaging data set was used to manually draw a single ROI around the entire region of tumor. Mean ADC values for each transaxial section of tumor were calculated. For normalization, another ROI with a size of approximately 30-50 mm² was placed in the contralateral normal-appearing white matter, carefully excluding gray matter. The rADC ratio was then obtained by dividing the lesion ADC by the values obtained from the contralateral normal-appearing white matter.

**Perfusion Measurements**

To obtain relative (normalised) values, all perfusion measurements from the lesions were divided by values from the normal appearing white matter in the right hemisphere.

*Measurements of cerebral blood volume (CBV)*

To obtain mean CBV from the whole tumor we used irregular hand drawn regions of interest (ROIs) outlining the tumors margins on each axial section. The mean tumor CBV was calculated as the mean value from all those ROIs. On the other hand, to obtain maximum CBV values, several small round ROIs (size 30-40 mm²) were used. These ROIs were placed over several hot spots on color-coded CBV maps and the ROI with the highest CBV value was chosen as the maximum CBV. T1- and T2-weighted images and raw data of perfusion images were used to ensure that regions of interest did not include any hemorrhage or apparent blood vessels. For the best tumor localization we also used CBV maps overlaid on post-contrast T1 images. In craniopharyngiomas only regions without calcifications were evaluated. Due to large, diffused calcifications in one craniopharyngioma to assess CBV measurements, only a small ROI method was applied. In this case mean values from the whole tumor were not possible to assess because of artifacts distorting mathematical measurements and perfusion curves.

*Measurements of percentage of signal intensity recovery (PSR) and peak height (PH)*

The T2*-weighted signal-intensity curves obtained for the ROIs with max. CBV and mean CBV were analyzed. For each perfusion curve 3 major points were established: $S_0$ - a baseline T2*-weighted signal intensity before contrast arrival, $S_{min}$ - the highest drop in T2*-weighted signal intensity after contrast arrival (minimum T2*-weighted signal intensity), $S_1$ - T2*-weighted signal intensity recovery after 24 seconds. The PSR was
calculated using the following equation: \( \text{PSR} = \frac{(S_1 - S_{\text{min}})}{(S_0 - S_{\text{min}})} \), while PH was calculated with the following equation: \( \text{PH} = S_0 - S_{\text{min}} \) (Fig.3).

**Statistical analysis**

Perfusion measurements: relative cerebral blood volume (rCBV), relative peak height (rPH), relative percentage of signal intensity recovery (rPSR) from adenomas and meningiomas were compared using the Student T-test. Additionally sensitivity and specificity of PWI in distinguishing adenomas from meningiomas were assessed for fixed cut off values of the perfusion parameters showing the most significant differences between these two groups of tumors. Statistical computations were performed using the Statistica PL software package version 10.0, and the \( p < 0.05 \) was set as a significant level.

Due to the small number of other tumor types statistical analysis between them was not possible.
Fig. 3: Representative T2*-weighted signal intensity-time curve. PH is calculated with the following equation: PH = S0-Smin, where S0 is a baseline T2*-weighted signal intensity before contrast arrival, Smin is the highest drop in T2*-weighted signal intensity after contrast arrival (minimum T2*-weighted signal intensity). PSR is calculated with the following equation: PSR = (S1-Smin)/(S0-Smin), where S1 is post-contrast T2*-weighted signal intensity recovery after 24 seconds.

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Results

Perfusion Measurements

The mean and maximum values of rCBV, rPH and rPSR, calculated for different types of examined sellar/parasellar tumors are demonstrated in table 1.

Pituitary macroadenomas revealed high values of the rCBV parameter. The maximum rCBV values for adenomas ranged between 2.42 and 7.55 (mean max. rCBV= 5.18).

Sellar meningiomas, similarly to adenomas, showed high values of rCBV (ranging 2.99 and 12.18, mean max. rCBV= 8.22). Both pituitary adenomas and sellar meningiomas revealed signal-intensity curves with little or no return to the baseline levels characterized by high values of PH and low values of PSR (table 1). Comparing adenomas and meningiomas we found a statistically significant difference in mean and maximum rCBV values (p= 0.026 and p= 0.019, respectively), but not in rPH and rPSR values. When a cut off value for maximum rCBV was fixed at > 7.14, the sensitivity and specificity of PWI in distinguishing adenomas from meningiomas was 63% and 91%, respectively. When a cut off value for mean rCBV was fixed at >5.74, the sensitivity and specificity reached 38% and 100%, respectively.

Apart from adenomas and meningiomas, the other sellar/parasellar tumors demonstrating high perfusion values (maximum rCBV>2) were: metastases, glioma, hemangioblastoma and squamous-papillary type of craniopharyngioma. These tumors did not differ significantly in rCBV values, but they showed different signal-intensity curves with variable rPH and rPSR values. Hemangioblastoma and glioma revealed high rPH values, craniopharyngiomas showed intermediate rPH, and metastases - low rPH value. On the other hand, glioma and metastases demonstrated intermediate rPSR values, while hemangioblastoma presented a very low rPSR value (rPSR<0.00) with characteristic descending signal-intensity curve. rPSR values of squamous-papillary type craniopharyngiomas were higher, compared to hemangioblastoma, but lower than rPSR values of glioma and metastasis.

The low perfusion (maximum rCBV<2) sellar/parasellar tumors included adamantinomatous type of craniopharyngiomas as well as lymphomas. These tumors showed low values of rCBV (maximum rCBV= 1.12 and rCBV= 1.08, respectively), as well as low rPH value. They presented a very high rPSR value (rPSR>1.00) with a characteristic ascending signal-intensity curve.

Diffusion Measurements

The mean and minimum values of ADC and rADC, calculated for different types of examined sellar/parasellar tumors are demonstrated in table 2.
There were no significant differences in ADC values between adenomas and meningiomas (p>0.05), while other tumors revealed significantly different values of ADC, compared to pituitary adenomas. Hemangioblastoma and craniopharyngiomas (both types) showed high ADC values, while metastases and lymphomas presented very low ADC values (table 2). Glioma revealed intermediate ADC values compared to other sellar/parasellar lesions.
Table 1: The mean and maximum values of rCBV, rPH and rPSR parameters.

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<table>
<thead>
<tr>
<th>Type of tumor (number of cases)</th>
<th>ADC</th>
<th>rADC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (range)</td>
<td>Minimum (range)</td>
</tr>
<tr>
<td>Adenomas (n= 46)</td>
<td>0.89 (0.65-1.37)</td>
<td>0.58 (0.35-0.97)</td>
</tr>
<tr>
<td>Meningiomas (n= 12)</td>
<td>0.95 (0.70-1.37)</td>
<td>0.73 (0.28-0.96)</td>
</tr>
<tr>
<td>Glioma (n= 1)</td>
<td>1.60</td>
<td>0.67</td>
</tr>
<tr>
<td>Hemangioblastoma (n= 1)</td>
<td>1.92</td>
<td>1.70</td>
</tr>
<tr>
<td>Metastases (n= 3)</td>
<td>0.65 (0.61-0.68)</td>
<td>0.39 (0.28-0.50)</td>
</tr>
<tr>
<td>Craniopharyngiomas: squamous-papillary type (n= 4)</td>
<td>1.57 (1.56-1.58)</td>
<td>1.09 (1.06-1.11)</td>
</tr>
<tr>
<td>Craniopharyngiomas: adamantinomatous type (n= 6)</td>
<td>2.21 (1.73-2.47)</td>
<td>1.39 (0.82-1.42)</td>
</tr>
<tr>
<td>Lymphomas (n=2)</td>
<td>0.63 (0.60-0.67)</td>
<td>0.52 (0.48-0.55)</td>
</tr>
</tbody>
</table>

Table 2: The mean and minimum values of ADC and rADC parameters.

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Conclusion

In our study we found the pituitary adenomas to appear in PWI as hyperperfused tumors (Fig.4) with elevated rCBV values and maximum rCBV ranging between 2.42 and 7.55 (mean max. rCBV = 5.18) (table 1).

In gliomas, the CBV parameter has been reported to correlate positively with the vascular endothelial growth factor (VEGF) [4], which is also expressed in the normal pituitary gland and pituitary adenomas. Moreover, increased concentrations of VEGF and of VEGF receptor 1 (VEGF-R1) were found in non-functioning pituitary adenomas when compared to normal pituitaries, suggesting that VEGF and VEGF-R1 expression may be related to pituitary tumor growth and vascularization [5]. These findings coincide with our preliminary results and support our conclusions that pituitary adenomas are highly vascular tumors.

In our study, apart from high rCBV values, pituitary adenomas showed characteristic time-intensity curves with little or no return to the baseline (mean value of max. rPSR = 0.36).

Meningiomas of the sellar region (cavernous sinus, planum sphenoidale, diaphragm sellae and clinoid process) account for about 15% of nonadenomatous sellar masses and for 20-30% of all intracranial meningiomas [1]. In our study meningiomas (Fig.5) showed perfusion patterns and time-intensity curves identical to meningiomas in other intracranial locations reported in the literature [1].

Moreover, both adenomas and meningiomas showed very similar perfusion curves with reduced values of rPSR. This pattern of time-intensity curve is caused by the absence of blood-brain barrier in neovessels of these tumors and thus the high rate of extracapillary leakage of contrast agent [6]. In our study the mean values of maximum rPSR were as follows: adenomas - 0.36; meningiomas - 0.33. Furthermore, adenomas as well as meningiomas demonstrated similar mean values of maximum rPH parameter (adenomas - 4.07; meningiomas - 3.57).

There were statistically significant differences between adenomas and meningiomas in the mean and maximum values of rCBV. Furthermore, in our opinion, the usage of fixed cut off values such as 7.14 for max. rCBV and 5.74 for mean rCBV showing high specificity (91% and 100%, respectively) and sensitivity (63% and 38%, respectively) with the analysis of the shape of the time-intensity curve may be very useful in differentiation between intrasellar meningiomas and pituitary adenomas. Values of max. rCBV exceeding 7.14 and mean rCBV above 5.74 with a time-intensity curve not returning to the baseline level are very suggestive of the diagnosis of meningioma.

Craniopharyngiomas are the most common suprasellar lesions. They account for approximately 3% of all intracranial neoplasms and 8% of sellar/parasellar tumors [1]. In plain MR craniopharyngiomas (especially in an intrasellar location and with enhancing
the solid part of a tumor), may be easily misdiagnosed as pituitary adenomas. Two different clinicopathologically types of craniopharyngiomas can be distinguished: the adamantinous and the squamous-papillary variants [7]. In our study these two types of craniopharyngiomas showed different perfusion patterns. The squamous-papillary type of craniopharyngiomas (Fig.6) presented high rCBV values (maximum rCBV= 5.95), intermediate PH, as well as PSR values, while measurements from enhancing parts of the adamantinomatous type of craniopharyngiomas (Fig.7) revealed low values of rCBV parameter (maximum rCBV = 0.75). Additionally, these tumors showed high value of rPSR (rPSR= 1.39) with the characteristic signal-intensity curve, returning and even exceeding the baseline level (Fig.7c).

This is partially in accordance with Holscher et al. who reported craniopharyngiomas to be hypoperfused tumors in transcranial duplex sonography, but the author did not indicate the type of craniopharyngioma [8].

We do believe that the different perfusion patterns can be explained by the different tumor development. According to the hypothesis concerning tumor development, the adamantinomatous craniopharyngioma arises from embryonic remnants of the craniopharyngeal duct and the squamous-papillary type from the squamous cell nests of the pars tuberalis of the adenohypophysis [7]. This hypothesis agrees with our preliminary results and may explain the different clinicopathological presentation, as well as different perfusion patterns of these craniopharyngioma variants. The squamous-papillary craniopharyngiomas are hyperperfused tumors similarly to adenomas, because both neoplasms arise from the adenohypophysis [7] and thus may resemble adenomas in perfusion examination.

In our opinion perfusion studies allow us to differentiate not only various types of craniopharyngiomas but also hypoperfused adamantinomatous craniopharyngiomas from hyperperfused adenomas. This fact is of high importance in everyday clinical practice, because it enables the correct differential diagnosis, despite the similar appearance of contrast enhanced intrasellar lesions in the conventional MR sequences.

In our study we also included several other types of sellar/parasellar tumors. The high perfusion sellar/parasellar tumors were: intrasellar hemangioblastoma, intrasellar prostate cancer metastasis and suprasellar glioma. All these lesions showed elevated rCBV values (max. rCBV>2), but they demonstrated different signal-intensity curves (with different rPH and rPSR values). Hemangioblastoma and glioma presented a higher rPH compared to metastasis. However, our case of intrasellar hemangioblastoma, strongly mimicking adenoma in plain MR, showed a characteristic descending signal-intensity curve with very low rPSR values (rPSR below 0), which was completely different from perfusions curves of other hyperperfused sellar/parasellar tumors, including adenomas. This was our first patient enrolled in the study and initially misdiagnosed as macroadenoma on the basis of conventional MR examination (at that time the perfusion results were not routinely included in the decision making process because of a lack of knowledge and experience). This patient underwent a huge life-threatening hemorrhage,
and almost died during transsphenoidal surgery, which should have not been performed in this case.

Finally, the low perfusion sellar/parasellar tumors also included lymphomas, which presented low values of rCBV parameter (maximum rCBV = 1.08). Additionally, these tumors showed high value of rPSR (mean rPSR= 1.38) with the characteristic signal-intensity curve, returning and even exceeding the baseline level. Our findings coincide with other papers reporting that CNS lymphomas are low perfusion tumors [9,10].

We also evaluated the ADC values of sellar/parasellar tumors. Mahmoud et al. claimed that calculation of the ADC values can help to differentiate between various sellar and parasellar lesions, especially hemorrhagic pituitary adenomas and non-hemorrhagic lesions with similar structural MR appearance (non-hemorrhagic pituitary adenomas, Rathke cleft cysts, and craniopharyngiomas). ADC was also useful for differentiating between pituitary adenomas vs. meningiomas and craniopharyngiomas vs. Rathke cleft cysts [2].

In our study there were no significant differences in ADC values between adenomas and meningiomas, while other tumors revealed significantly different values of ADC, compared to pituitary adenomas. Hemangioblastoma and both types of craniopharyngiomas showed high ADC values. On the other hand, metastases and lymphomas presented very low ADC values.

Sellar/parasellar tumors present with different diffusion and perfusion patterns. The values of ADC, as well as of rCBV, rPH and rPSR could be noninvasive in vivo imaging biomarkers of tumor cellularity (ADC) and neoangiogenesis (rCBV, rPH, rPSR). In our opinion PWI and DWI seem to be very useful in the differential diagnosis of sellar/parasellar tumors, which may be of high importance in clinical practice, especially in the proper choice of tumor treatment.
**Fig. 4:** Pituitary adenoma. A. Post-contrast T1-weighted axial image. B. Color-coded map of Cerebral Blood Volume. C. T2*-weighted signal intensity-time curves of: 1- adenoma (purple curve), 2- normal appearing white matter (green curve). Pituitary adenoma shows elevated rCBV value (red coloring) and characteristic time-intensity curve with little return to the baseline.

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**Fig. 5:** Sellar meningioma. A. Post-contrast T1-weighted axial image. B. Color-coded map of Cerebral Blood Volume. C. T2*-weighted signal intensity-time curves of: 1- meningiomas (purple curve), 2- normal appearing white matter (green curve). Meningioma demonstrates high rCBV value (red coloring) and typical time-intensity curve with little return to the baseline.

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**Fig. 6:** Suprasellar craniopharyngioma (squamous-papillary type). A. Post-contrast T1-weighted coronal image. B. Color-coded map of Cerebral Blood Volume. C. T2*-weighted signal intensity-time curves of: 1- craniopharyngioma (purple curve), 2- normal appearing white matter (green curve). Squamous-papillary type of craniopharyngioma shows high rCBV value (red coloring) and intermediate rPSR value.

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**Fig. 7:** Intrasellar craniopharyngioma (adamantinomatous type). A. Post-contrast T1-weighted coronal image. B. Color-coded map of Cerebral Blood Volume. C. T2*-weighted signal intensity-time curves of: 1- craniopharyngioma (purple curve), 2- normal appearing white matter (green curve). Adamantinomatous type of craniopharyngioma presents low rCBV value (blue coloring) and characteristic ascending signal-intensity curve, returning and exceeding the baseline level (rPSR>1).

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References


