Dynamic susceptibility contrast-enhanced MRI evaluation of cerebral intraventricular tumors: Preliminary results

Introduction. — The aims of the present study were to determine the perfusion characteristics of several types of intraventricular tumors and to evaluate the usefulness of dynamic contrast-enhanced MRI in making the differential diagnosis.

Methods. — A total of 28 patients with intraventricular tumors (five meningiomas, five papillomas, three ependymomas, four subependymomas, seven central neurocytomas, two subependymal giant cell astrocytomas and two metastases) underwent conventional and dynamic susceptibility contrast-enhanced MRI. Cerebral blood volume (CBV) maps were obtained and the relative CBV (rCBV) calculated for each tumor. Mean rCBV_max values were compared across the different types of tumors (ANOVA, \( P = 0.05 \)).

Results. — Intraventricular tumors presented with three different patterns of vascularization: highly vascularized tumors (mean rCBV_max > 3), including papillomas, meningiomas and renal carcinoma metastases; poorly vascularized tumors (mean rCBV_max < 2), including ependymomas and subependymomas; and intermediately vascularized tumors (mean rCBV_max > 2 but < 3), including central neurocytomas and lung metastases. There was a significant difference between the highly vascularized (papillomas, meningiomas) and poorly vascularized (subependymomas) tumors. In cases of suspected meningioma, papilloma or neurocytoma, low rCBV values (< 3) point to a diagnosis of neurocytoma rather than either of the other tumor types.

KEYWORDS
Intraventricular tumors;
Magnetic resonance imaging;
Perfusion imaging

Summary
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Introduction

Intraventricular tumors are uncommon, representing only 1–10% of all intracranial neoplasms [1–6]. Intraventricular tumors can arise directly from tissue present in the ventricles such as the choroid plexus (choroid plexus papilloma, choroid plexus carcinoma) [7,8], and in the walls of the ventricles (ependymoma, subependymoma, subependymal giant cell astrocytoma, central neurocytoma) and septum pellucidum (central neurocytoma), or from arachnoidial cap cells trapped within the ventricles (intraventricular meningioma). Cavernous hemangioma and hemangioblastoma (associated or not with von Hippel–Lindau disease or metastases) can also be found in the ventricles [9–12]. Although these tumors present with specific radiological features [13] and can often be differentiated by conventional magnetic resonance imaging (MRI), in some cases, the differential diagnosis remains difficult, and more sophisticated MRI techniques, such as dynamic susceptibility contrast-enhanced MR perfusion imaging (DSC-MRI), can provide additional information on tumor vascularization that may help in making the differential diagnosis [14–19].

DSC-MRI is a technique based on the transient signal reduction induced by the first pass of a gadolinium chelate through the brain vessels [16,20]. The technique involves calculation of cerebral blood volume (CBV) maps and the subsequent correlation of tumor vascularity with histological grades of malignancy [21–23]. Calculation of CBV maps and determination of the relative CBV (rCBV; the ratio between the CBV in the tumor and in normal tissue) provide information that is not available with conventional MRI. Indeed, such information has so far proved to be invaluable for improving the differentiation of various types of tumors such as high-grade glioma and renal carcinoma metastases [24,25] from low-grade glioma [26,27] and lymphoma [25,28,29].

However, to our knowledge, no data are as yet available on the vascularization of intraventricular tumors and the usefulness of DSC-MRI in the differential diagnosis of cerebral intraventricular tumors. For this reason, the purposes of the present study were first, to determine the perfusion characteristics of the various intraventricular tumors and, second, to evaluate the usefulness of DSC-MRI in establishing the differential diagnosis.

Subjects and methods

Subjects

Altogether, 28 patients (15 men, 13 women; age: 43.7 ± 15 years) with cerebral intraventricular tumors (five meningiomas, three choroid-plexus papillomas, three ependymomas [grade 2], four subependymomas, seven central neurocytomas, two subependymal giant cell astrocytomas and two metastases) were evaluated between January 2003 and January 2007. All patients underwent conventional MRI and DSC-MRI before surgical biopsy or tumor excision. None of the patients had undergone a major therapeutic procedure prior to MRI examination. Samples of each tumor were examined by a neuropathologist and graded according to the World Health Organization (WHO) classification system of tumors of the central nervous system [30].

MRI examination

MRI was performed using a 1.5-Tesla imager (Twin-speed, GE Medical Systems; Milwaukee, WI, USA) and an eight-channel headcoil. After inserting a 20-gauge catheter into an antecubital vein, unenhanced axial T1-weighted (TR/TE = 600/11 ms) and sagittal T2-weighted (TR/TE = 4520/100 ms) spin-echo (SE) MRI scans were acquired.

After determination of the tumor site from the T2-weighted images, DSC-MRI was performed, using a T2-weighted SE echo-planar imaging (EPI) sequence (TR/TE = 2400/80 ms; FOV = 240 × 240 mm; 192 f × 128 p; slice thickness = 5 mm; 17 axial slices parallel to the intercomissural line; no inter-slice gap). The SE technique was used because it has been shown to be more sensitive to signal changes from paramagnetic contrast material passing through small vessels, which are more representative of tumor neovascularization, than through large vessels such as cortical veins [31,32]. Imaging was performed during the first pass of a dose of gadobenate dimeglumine (0.1 mmol/kg body weight; MultiHance; Bracco Imaging SpA, Milan, Italy), followed by a saline bolus (30 mL), both administered by a power injector (MEDRAD Inc, Indiana, PA, USA) at a rate of 8 mL/s. The injection was started simultaneously with image acquisition to establish a precontrast baseline (the first acquisitions were performed before the contrast agent reached the cerebral circulation).

As T2-weighted SE EPI sequences are less sensitive to susceptibility effects induced by the first pass of a gadolinium chelate bolus through the cerebral circulation than are gradient-echo (GE)-weighted sequences, a higher injection rate associated with a high-relaxivity contrast agent (such as gadobenate dimeglumine) was used [33].

Conventional contrast-enhanced axial T1-weighted (TR/TE = 600/11 ms) SE images and coronal 3D T1-weighted GE (TR/TE = 20/8 ms, flip angle = 35°) images were then acquired after the dynamic perfusion series.

Postprocessing

The DSC-images were subsequently processed using a dedicated image workstation and software (Advantage Windows Workstation 4.3, FuncTool software; GE Medical Systems, Milwaukee, WI, USA). The rCBV maps were generated from the DSC-images, using the methodology well
described elsewhere in the literature [14,31,34]. Changes in the R2* relaxation rate (ΔR2*) were measured pixel by pixel from signal intensity, according to the equation ΔR2*(t) = −ln[S(t)/S(0)]/TE, where S(t) is the signal intensity at time t, S(0) is the baseline signal intensity and TE is the echo time.

Previous studies have demonstrated that ΔR2* is proportional to the concentration of contrast agent in the tissue, and that CBV is proportional to the area under the curve (AUC) ΔR2*(t) [35]. This AUC can be calculated by fitting a gamma-variate function to the measured ΔR2* curve.

To quantify CBV, values obtained from the tissue concentration–time curve were deconvoluted, using the arterial input function (AIF). To determine the AIF, a region of interest (ROI) map was manually positioned by one of the present authors over the left middle cerebral artery (M2 portion). Although, theoretically, AIF determination allows quantitative evaluation of CBV, we normalized CBV values after comparison against an internal reference, which allowed calculation of rCBV values while avoiding inaccuracies induced by AIF measurement errors. In the present study, the internal reference was the CBV of the normal contralateral white matter (CBVn). The rCBV was then calculated as rCBV = CBVp/CBVn, where CBVp is the value in pathological tissue [36].

We defined several ROIs (average size: 50 mm²) in the tumor on the CBV maps. However, because intraventricular neoplasms are often lying close to the choroid plexus, which is highly vascularized, great care was taken to not place the ROI in the choroid plexus to avoid the possibility of tumor CBV overestimation.

The ROI with the maximum CBV was identified independently by three neuroradiologists (S.K., S.G., A.H.), with a majority ruling in cases of disagreement. A reference ROI was then defined in the contralateral white matter for supratentorial tumors and in the white matter of the cerebellum for tumors of the posterior fossa. The maximum rCBV (rCBVmax = maximum CBV of tumor/CBV of contralateral hemisphere) was considered representative of the lesion. The mean rCBVmax in each group of tumors was compared using non-parametric analysis of variance (ANOVA) at a level of significance of P = 0.05.

**Results**

Significant differences were found between the rCBVmax values in subependymomas (1.8 ± 1.7, range: 0.6—4.4; Fig. 1) compared with the rCBVmax values in both papillomas (4.6 ± 0.7, range: 3.5—5.4; P = 0.0004; Fig. 2) and meningiomas (4.6 ± 1.6, range: 3.0—7.2, P = 0.002). However, no difference was found between the rCBVmax values of papillomas and meningiomas (P = 0.99), or between the rCBVmax values of these tumors and the rCBVmax value of central neurocytomas (2.9 ± 1.1, range: 1.5—5.1; P = 0.0556 and P = 0.210, respectively; Fig. 3). Similarly, no significant difference was found between the rCBVmax values of central neurocytomas and subependymomas (P = 0.184).

As ependymomas (Fig. 4), subependymal giant cell astrocytomas and metastases constituted fewer than four cases, they were not included in the statistical analysis.

In 70% of meningiomas, the first-pass curve did not return to baseline but, instead, increased very slowly. In the other tumors, the first-pass curve analyses did not present any peculiarities.

The mean rCBVmax value in each group of tumors is presented in Table 1, together with ranges and values of standard deviation.

**Discussion**

The present study results suggest that intraventricular tumors present three different patterns of vascularization: highly vascularized tumors (mean rCBVmax > 3), including choroid papillomas, meningiomas and renal carcinoma metastases (Fig. 2); poorly vascularized tumors (mean rCBVmax < 2), including ependymomas and subependymomas (Fig. 4); and intermediately vascularized tumors (mean rCBVmax > 2 but < 3), including central neurocytomas and lung metastases (Fig. 3).

Radiological presentations of subependymoma, ependymoma and subependymal giant cell astrocytoma usually help to make the differential diagnosis of papilloma, meningioma and neurocytoma [4]. DSC-MRI brings additional information concerning tumor vascularization to confirm the differentiation of papilloma from meningioma, which is highly vascularized, and subependymoma, which is a tumor of low vascularization. These results are in agreement with histological data showing that subependymomas are avascular tumors [37].

However, the radiological differential diagnosis between papilloma and meningioma and between these two entities and neurocytoma can sometimes be difficult [4]. In these cases, DSC-MRI does not appear to offer any additional information to help make the differential diagnosis, as no significant differences have been found between these different tumor types. In addition, the vascular appearance of central neurocytoma is highly variable, with reports ranging from avascularity to a vascular blush [38]. These reports are in agreement with the data from the present study, in which rCBV values ranged from 1.5 to 5.1 (mean: 2.9 ± 1.1). For meningioma and papilloma, rCBV values less than 3 were never found in our study. Moreover, the statistical compari-
Figure 2  Post-contrast (A), T2-weighted MRI (B) and cerebral blood volume (CBV) map (C) of papilloma: MRI shows a vividly enhancing mass in the lowermost portion of the fourth ventricle, which also shows dilatation. The whole of the tumor shows a high relative CBV (rCBV$_{\text{max}}$) of 3.25, so this is a highly vascularized tumor (rCBV$_{\text{max}}$ > 3). The radiological presentation of this tumor and the rCBV$_{\text{max}}$ (> 3) suggest a diagnosis of papilloma or meningioma.

Figure 3  Post-contrast (A), T2-weighted MRI (B) and cerebral blood volume (CBV) map (C) of central neurocytoma: the tumor has developed in the left lateral ventricle attached to the septum pellucidum, and shows a characteristic 'bubbly' appearance. The tumor also shows an relative CBV (rCBV$_{\text{max}}$) of 2.8, so this is an intermediately vascularized tumor (rCBV$_{\text{max}}$ > 2 but < 3). The radiological presentation of this tumor and the rCBV$_{\text{max}}$ (< 3) point to a diagnosis of central neurocytoma rather than meningioma or papilloma.

Table 1  Distribution of maximum relative cerebral blood volume in each studied group of lesions.

<table>
<thead>
<tr>
<th>Pathological lesions</th>
<th>M ± S.D.</th>
<th>Range</th>
<th>Patients (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Papilloma</td>
<td>4.6 ± 0.7</td>
<td>3.5—5.4</td>
<td>5</td>
</tr>
<tr>
<td>Meningioma</td>
<td>4.6 ± 1.6</td>
<td>3.0—7.2</td>
<td>5</td>
</tr>
<tr>
<td>Central neurocytoma</td>
<td>2.9 ± 1.1</td>
<td>1.5—5.1</td>
<td>7</td>
</tr>
<tr>
<td>Subependymoma</td>
<td>1.8 ± 1.7</td>
<td>0.6—4.4</td>
<td>4</td>
</tr>
<tr>
<td>Ependymoma</td>
<td>1.0 ± 0.3</td>
<td>0.8—1.4</td>
<td>3</td>
</tr>
<tr>
<td>Subependymal giant cell astrocytoma</td>
<td>1.65 ± 1.9</td>
<td>0.3—3.3</td>
<td>2</td>
</tr>
</tbody>
</table>

Data are expressed as means ± standard deviation (M ± S.D.).
Perfusion MRI for the evaluation of intraventricular tumors

Figure 4  Post-contrast (A), T2-weighted MRI (B) and cerebral blood volume (CBV) map (C) of ependymoma: MRI shows a lobular enhancing mass in the fourth ventricle extending through the left foramen of Luschka into the left cerebellopontine angle. The tumor has a low relative CBV (rCBV)max of 0.9, so this is a poorly vascularized tumor (rCBVmax < 2). The radiological presentation of this tumor and the rCBVmax (< 2) point to a diagnosis of ependymoma.

son of mean rCBVmax values of neurocytomas and papillomas (4.6 ± 0.7, range: 3.5–5.4) are the near the significance level \(P = 0.556\). It may be hypothesized that a low rCBVmax (< 3) suggests a diagnosis of central neurocytoma rather than meningioma or papilloma.

Thus, while papilloma and meningioma remain difficult in some cases to distinguish from each other on conventional MRI, DSC-MRI does not appear to bring any further information, as they are both highly vascularized tumors. These results are in agreement with those of previous studies, which have shown that enlargement of the choroidal artery is a common feature on both cross-sectional and angiographic images in papilloma [39]. Choroid-plexus tumors located in the lateral ventricle are typically supplied by the anterior choroidal artery, and the lateral and medial posterior choroidal arteries [40]. On the other hand, tumors of the fourth ventricular choroid plexus are usually supplied by choroidal branches of the posterior inferior cerebellar artery [40].

On angiographic studies, intraventricular meningioma is also a highly vascularized tumor [41]. However, we found values that are lower than those previously published for extra-axial meningioma (mean rCBVmax values: 4.6 ± 1.6, range: 3.0–7.2 versus 9.1 ± 4.4, range: 4.1–16.8, respectively) [25]. This difference could arise from the meningeal arterial supply from the external carotid artery in the case of extra-axial meningioma compared with the choroidal arterial supply arising from the internal carotid artery and cerebral posterior artery in the case of intraventricular meningioma. Another explanation could be that intraventricular meningioma is usually fibromatous, which, as a rule, is less vascular than other types of meningioma [41].

The curve after the first pass is of particular interest only in the case of meningioma, where the curve typically increases very slowly after the first pass [17]. The rCBV values of intracerebral metastases depend on the primary tumor. Renal and thyroid carcinomas, and melanoma metastases are all highly vascularized compared with other metastases, which are intermediate vascularized [24,25], and intraventricular metastases appear to have similar features. Thus, in the present study, renal carcinoma metastases were highly vascularized tumors while lung carcinoma metastases were immediately vascularized.

The present study had three main limitations. The first is that the number of tumors in each subgroup was comparatively small, thus requiring the use of a non-parametric test (ANOVA) to analyze the data. Also, in cases of subependymal giant cell astrocytoma and ependymoma, the tumor population was too small to allow any definite conclusions to be drawn regarding CBV. However, ependymoma can be classified as low-grade (WHO grade 2) tumors and high-grade tumors or anaplastic ependymoma (WHO grade 3): the former are tumors of low vascularity compared with high-grade tumors, which present with endothelial proliferation [42]. These data are in agreement with our results, which showed low rCBV values in three low-grade ependymomas (1.0 ± 0.3, range: 0.8–1.4).

Another limitation is that other important intraventricular tumors, such as hemangioblastoma, cavernous hemangioma and choroid plexus carcinoma, were missing from our study population [9–11].

The final limitation, inherent with any dynamic perfusion MRI study of intraventricular lesions, is the risk of overestimation of the CBV as a result of the proximity of such neoplasms to the choroid plexus. Although great care was taken in the present study to avoid placing an ROI in the choroid plexus, the risk of CBV overestimation cannot be totally dismissed.

Conclusion

Conventional MRI provides important information on the location, number, signals and contrast enhancement of lesions, all of which help to make the differential diagnosis of intraventricular tumors. Based on our present findings, the use of DSC-MRI may provide additional information on the vascularization of intraventricular cerebral tumors that is not available with conventional MRI. Such further findings may allow confirmation of the differential diagnosis between subependymoma and highly vascularized tumors such as meningioma and papilloma. However, the differential diagnosis of papilloma, meningioma and neurocytoma remains difficult and, in cases of low rCBV values, DSC-MRI could point to a diagnosis of neurocytoma rather than either of the other two tumor types. Further research involving a
larger cohort of patients is needed to confirm these preliminary findings and to better establish their clinical value. Moreover, MR spectroscopy [43], cerebral computed tomography (CT) perfusion [44] and pulsed arterial spin-labelling [45] in association with DSC-MRI may further increase its diagnostic value.

Conflict of interest statement

None.

References


