Results of positron emission tomography guidance and reassessment of the utility of and indications for stereotactic biopsy in children with infiltrative brainstem tumors

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Object. Most intrinsic infiltrative brainstem lesions diagnosed in children are gliomas, and these carry a very bad prognosis. Although the utility and risk of stereotactically guided biopsy procedures in intrinsic infiltrative brainstem lesions have been widely questioned, the neuroimaging diagnosis may be inaccurate in approximately 25% of cases, and the consequences of empirical therapy should not be underestimated. Stereotactic biopsy sampling is still performed in many centers, but the reported diagnostic yield ranges from 83 to 96%. The authors integrated positron emission tomography (PET) images into the planning for stereotactic biopsy procedures to direct the biopsy needle’s trajectory to hypermetabolic foci of intrinsic infiltrative brainstem lesions. Their aim was to assess the benefit of the technique in terms of target selection and diagnostic yield.

Methods. Twenty children with newly diagnosed infiltrative brainstem lesions underwent a PET-guided stereotactic biopsy procedure. The PET tracer was 18F-2-fluoro-2-deoxy-D-glucose (FDG) in six cases, 11C-methionine in eight, and both agents were used in six. A single biopsy target was selected in the area of highest PET tracer uptake in all cases. The PET data were compared with diagnoses and outcome.

Results. Use of PET guidance improved target selection and provided tumor diagnosis in all trajectories and in all children (high-grade glioma was diagnosed in 10, low-grade glioma in five, and nonglial tumor in five). The PET-guided trajectories provided a higher diagnostic yield than those guided by magnetic resonance imaging alone, which allowed the sampling to be reduced to a single trajectory. The PET data might also carry a prognostic value that could be useful for oncological management.

Conclusions. These data support the suggestion that PET guidance improves the diagnostic yield of stereotactic biopsy sampling, allows the practitioner to reduce the number of sampling procedures, and might lead to a reassessment of the utility of and indications for stereotactic biopsy in children with intrinsic infiltrative brainstem lesions.

(DOI: 10.3171/PED-07/11/392)

KEY WORDS • brainstem lesion • children • diagnostic yield • pediatric neurosurgery • positron emission tomography • stereotactic biopsy

In the past decade, the utility and risk of stereotactic biopsy procedures and indications for their use in intrinsic infiltrative lesions of the brainstem in children have been widely questioned. These questions have arisen due to the following factors: 1) most of these lesions are gliomas; 2) approximately 90% of children will die within 2 years of diagnosis; 3) advances in MR imaging technology have allowed better classification of brainstem lesions; 4) a typical MR presentation (diffuse pontine tumor engulfing the basilar artery with rapidly evolving abducens nerve palsy) has a higher diagnostic value than histological findings; 5) the diagnostic yield of stereotactic biopsy sampling based on MR imaging is not optimal, ranging from 83 to 96%; and 6) conventional fractionated radiotherapy remains the standard treatment, whatever the tumor malignancy grade.

Therefore, the management of these lesions requires careful consideration of the risk related to serial biopsy trajectories and the level of radiological diagnostic certainty.

It is common, however, to encounter intrinsic infiltrative brainstem lesions that cannot be diagnosed on the basis of imaging studies alone; the preoperative neuroimaging diagnosis may not be accurate for tumor type in approximately

Abbreviations used in this paper: AA = anaplastic astrocytoma; FDG = 18F-2-fluoro-2-deoxy-D-glucose; MET = 11C-methionine; MR = magnetic resonance; PET = positron emission tomography; PNET = primitive neuroectodermal tumor; WHO = World Health Organization.
Use of PET-guided biopsy of intrinsic brainstem tumors

25%, and up to 13% of such lesions are nonneoplastic ones.\textsuperscript{13-27,24} Therefore, the consequences of empirical therapy should not be underestimated before making appropriate treatment recommendations. Actually, in many centers a stereotactic biopsy procedure is still performed whenever possible, with estimates of low and acceptable combined surgical morbidity/mortality rates of 0.7 to 3% and 3 to 5%, respectively.\textsuperscript{10,21,25,26,28}

With PET, a functional imaging technique, investigators can record independent information helpful in the understanding and management of brain tumors, especially with two radiotracers: FDG, which assays glucose metabolism, and MET, which assays amino acid transport and protein metabolism.\textsuperscript{1,3-5,9,15-18,22-24,29} These PET tracers have a much higher sensitivity and specificity than MR signals in tumor and anaplastic tissue detection. We have developed a technique allowing routine integration of stereotactic PET images into the planning of MR-guided stereotactic biopsy sampling: this is used to direct biopsy trajectories to hypermetabolic foci of brain tumors.\textsuperscript{15} We have shown that this technique significantly increased the diagnostic yield of stereotactic biopsy procedures\textsuperscript{15,17,22} and secondarily allowed us to reduce the number of sampling procedures performed.\textsuperscript{18,22}

Herein, we analyzed the contribution of PET-guided stereotactic biopsy in the management of disease in 20 children with intrinsic infiltrative brainstem lesions.

Clinical Material and Methods

Patient Population

Twenty children with intrinsic infiltrative brainstem lesions that were newly diagnosed on MR imaging between 1995 and 2006 were selected for this study. Data related with age, sex, and tumor location/presentation on MR imaging are summarized in Table 1. Fourteen lesions were located in the pons as follows: eight were symmetrical (heterogeneous MR signal and enhancement in three), four were lateralized, one also involved the tegmentum, and one was subependymal. Three lesions were mesencephalic and three others were located in the medulla oblongata. Selection criteria consisted of the following: 1) the lesion’s atypical appearance on MR imaging, which resulted in diagnostic uncertainty for a diffuse glioma on the part of the neuroradiologists (lesions were either strongly enhanced by contrast or lateralized, suggesting a nonglial tumor or a nontumoral lesion); or 2) a difficult selection of the biopsy target (either in areas of MR contrast enhancement [12 cases] or in areas of highest fluid-attenuated inversion recovery or T2-weighted MR signal [eight cases]) that would increase the need for multiple biopsy trajectories to avoid nondiagnostic samples. Parents gave informed consent in all cases and the procedure was performed in accordance with the ethical guidelines of our institution.

During the same period, nine children harboring an intrinsic brainstem lesion were treated without PET imaging. The reasons were as follows: 1) limited accessibility to PET imaging within the 10 days after admission (one patient); 2) the lesion’s appearance was estimated as typical of a glioma by the neuroradiologists (five patients); and 3) the lesion was homogeneous and the target selection on MR imaging was straightforward (three patients). In four of the children in the second group, no biopsy sampling was performed because of rapid clinical evolution of the disease and poor clinical status in three children, and because the parents refused to allow the biopsy procedure in the fourth child.

Stereotactic PET Imaging Acquisition

All children underwent MR and PET imaging studies. To integrate PET data into the planning of stereotactic biopsy procedure and to allow accurate correlation between PET- and MR-generated images, both PET and MR imaging data were acquired in stereotactic conditions, as described elsewhere.\textsuperscript{15,24} The MR images were acquired first and were followed by the PET image acquisition. The MR-compatible carbon fiber base head ring (ZD Neurosurgical Localizing Unit, F. L. Fischer) was secured after induction of local anesthesia. In four children younger than 6 years of age, general anesthesia with endotracheal intubation was induced. For the PET tracer we used either MET (eight patients), FDG (six), or both tracers successively (six). Each child was injected intravenously with 10 to 15 mCi of MET or 6 to 9 mCi of FDG (specific activity > 2 Ci/μmol). Images were acquired between 20 and 40 minutes after MET injection and between 40 and 60 minutes after contrast addition for FDG. When both tracers were used, MET-PET imaging was performed first and FDG was injected 80 minutes later.\textsuperscript{18} The characteristics of intrinsic infiltrative brainstem lesions on MR and PET imaging studies are summarized in Table 1.

The spatial resolution of PET images has evolved with time in this study. Originally we used a Siemens/CTI ECAT 933 tomograph (CPS Innovations), allowing simultaneous acquisition of 15 slices approximately 6.5 mm thick, with a full width at half-maximum resolution of approximately 6 mm. Later in the study (since 2001), PET images were acquired with the Siemens/CTI ECAT 962 (HR+) 2D and 3D tomograph (CPS Innovations), allowing the simultaneous acquisition of 63 planes with a slice thickness of 2.4 mm, with a full width at half-maximum resolution of approximately 4.5 mm.

The technical considerations related to PET tracer dosimetry and image magnification in children have been detailed elsewhere.\textsuperscript{24} There is no age limit for PET studies. Indeed, the major limitation for PET guidance is the stability of the stereotactic frame in children younger than 1 year of age, which corresponds to a limitation in the biopsy procedure itself.

Planning for Stereotactic Biopsy Sampling

We combined PET and MR imaging data in the stereotactic biopsy planning by using a methodology previously described in detail.\textsuperscript{15,22-24} Before 2000, we performed two biopsy trajectories whenever possible according to a standard protocol used in brain tumors.\textsuperscript{15,24} As shown in Fig. 1, a first biopsy target was selected in the area of highest PET tracer uptake in the tumor (PET-guided trajectory). The level of PET tracer uptake was expressed as high (Figs. 1 and 2), moderate (Fig. 3), or absent, and was measured by semi-quantitative methods as superior, equivalent, or inferior to its uptake in the neighboring gray matter. The extent of PET tracer uptake was expressed as focal or extended.\textsuperscript{15,22} Coordinates of the target were subsequently projected onto the corresponding MR slice to verify that the target was safe and that it projected into the lesion. A second target outside of
the area of increased PET tracer uptake was then selected on MR images (MR-guided trajectory; Fig. 1). After 2000, the high diagnostic yield of PET-guided stereotactic biopsy samples observed in series reported in adults led us to reduce the number of samples taken to a single PET-guided biopsy trajectory in the last 12 children (Figs. 2 and 3).

**Biopsy Procedure and Data Analysis**

The biopsy procedure was performed after induction of general anesthesia in all cases. Serial sampling was performed every 10 mm along each trajectory by using a side-cutting Sedan needle. All biopsy specimens were formalin-fixed and analyzed after staining with H & E, Masson trichrome, and immunostains. Glial tumors were classified according to the 2000 WHO criteria.

**TABLE 1**

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs), Sex</th>
<th>MR Presentation &amp; Tumor Location†</th>
<th>PET Presentation</th>
<th>Combined MR- &amp; PET-Guided Stereotactic Biopsy</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3, F</td>
<td>pons symmetrical; heterogeneous</td>
<td>FDG mod, focal</td>
<td>transcerebellar</td>
<td>none</td>
</tr>
<tr>
<td>2</td>
<td>11, F</td>
<td>pons symmetrical; heterogeneous</td>
<td>FDG high, extended</td>
<td>transcerebellar</td>
<td>none</td>
</tr>
<tr>
<td>3</td>
<td>13, M</td>
<td>pons symmetrical; heterogeneous</td>
<td>FDG mod, focal</td>
<td>transcerebellar</td>
<td>none</td>
</tr>
<tr>
<td>4</td>
<td>6, M</td>
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<td>MET high, extended</td>
<td>transcerebellar</td>
<td>none</td>
</tr>
<tr>
<td>5</td>
<td>5, M</td>
<td>pons symmetrical</td>
<td>FDG high, focal</td>
<td>transcerebellar</td>
<td>none</td>
</tr>
<tr>
<td>6</td>
<td>13, M</td>
<td>pons symmetrical</td>
<td>MET high, focal</td>
<td>transcerebellar</td>
<td>none</td>
</tr>
<tr>
<td>7</td>
<td>12, M</td>
<td>pons subependymal</td>
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<td>transcerebellar</td>
<td>none</td>
</tr>
<tr>
<td>8</td>
<td>10, M</td>
<td>pons lateral</td>
<td>MET mod, focal</td>
<td>transcerebellar</td>
<td>none</td>
</tr>
<tr>
<td>9</td>
<td>1, F</td>
<td>MET high, focal</td>
<td>MET high, focal</td>
<td>transcerebellar</td>
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</tr>
<tr>
<td>10</td>
<td>13, F</td>
<td>pons lateral</td>
<td>MET high, focal</td>
<td>transcerebellar</td>
<td>none</td>
</tr>
<tr>
<td>11</td>
<td>6, F</td>
<td>pons lateral</td>
<td>MET mod, focal</td>
<td>transcerebellar</td>
<td>none</td>
</tr>
<tr>
<td>12</td>
<td>7, M</td>
<td>pons symmetrical</td>
<td>MET high, focal</td>
<td>transcerebellar</td>
<td>none</td>
</tr>
<tr>
<td>13</td>
<td>3, M</td>
<td>pons symmetrical</td>
<td>MET high, focal</td>
<td>transcerebellar</td>
<td>none</td>
</tr>
<tr>
<td>14</td>
<td>6, M</td>
<td>tectum, pineal region; heterogeneous</td>
<td>FDG high, focal</td>
<td>transfrontal</td>
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</tr>
<tr>
<td>15</td>
<td>12, F</td>
<td>tegmentum; heterogeneous</td>
<td>FDG high, focal</td>
<td>transfrontal</td>
<td>none</td>
</tr>
<tr>
<td>16</td>
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<td>tectum; infiltrative</td>
<td>FDG mod, focal</td>
<td>transfrontal</td>
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<tr>
<td>17</td>
<td>11, M</td>
<td>pons–tegmentum</td>
<td>MET high, focal</td>
<td>transcerebellar</td>
<td>none</td>
</tr>
<tr>
<td>18</td>
<td>6, M</td>
<td>medulla oblongata</td>
<td>MET high, focal</td>
<td>transcerebellar</td>
<td>none</td>
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<tr>
<td>19</td>
<td>13, M</td>
<td>medulla oblongata</td>
<td>MET high, focal</td>
<td>transcerebellar</td>
<td>none</td>
</tr>
<tr>
<td>20</td>
<td>6, F</td>
<td>medulla oblongata</td>
<td>MET high, focal</td>
<td>transcerebellar</td>
<td>none</td>
</tr>
</tbody>
</table>

* Roman numerals in parentheses denote the WHO grade. Abbreviations: LGA = low-grade astrocytoma; mod = moderate; ND = nondiagnostic; — = not done.
† Cases 14, 15, and 16 were included in the study because the MR presentation demonstrated tumors infiltrating the brainstem (tectum or tegmentum) and did not suggest a pineal origin to the neuroradiologists.

**Results**

**Acquisition of PET Data and PET Guidance**

The acquisition of PET and MR images was uneventful in all cases. The MET uptake was increased in 14 of 14 cases (high in 11, moderate in three; focal in nine, extended in five). The FDG uptake was increased in 10 of 12 cases (high in seven, moderate in three; focal in eight, extended in two). In all cases, PET provided a target for biopsy sampling, either a focal area of increased FDG uptake (Cases 1, 3, 5, 6, 10, 12, 15, and 16; Figs. 1 and 2); the center of an extended area of increased FDG uptake (Cases 2 and 11; 10 FDG-PET–guided biopsy procedures); a focal area of increased MET uptake (Cases 7–9, 13, and 17–20; Fig. 3); or the center of an extended area of increased MET uptake (Cases 4 and 14; 10 MET-PET–guided biopsy procedures). The two children with no FDG uptake showed increased MET uptake, which was used as a biopsy target. In patients with increased uptake of both PET tracers (Cases 1–3 and 15), the area of highest FDG uptake corresponded with the
area of highest MET uptake. Tracer uptake within the tumor was heterogeneous in 16 patients (Cases 1, 3, 5–10, 12, 13, and 15–20).

**Diagnostic Yield per Trajectory**

A tumor diagnosis was established in all cases (Table 1); 25% were nonglial tumors. All PET-guided trajectories yielded tumor tissue, whereas MR-guided trajectories yielded two nondiagnostic samples. In the eight cases in which biopsy specimens were obtained using two trajectories, the histological findings yielded by the tissue obtained in each of the trajectories were different in six (Cases 1–3, 5, 6, and 8). The PET-guided trajectory always yielded samples with equivalent or higher malignancy grades than those obtained with the MR-guided one. A biopsy procedure performed without PET guidance in these six patients could have led to inaccurate diagnosis in two or incorrect grading in four cases. Moreover, PET guidance yielded a tumor diagnosis in all cases in which biopsy specimens were obtained with a single PET-guided trajectory. In summary, PET guidance improved biopsy target selection in all but two of the eight cases (Cases 4 and 7, in which diagnoses of tissue obtained in both trajectories were identical).

**Number of Trajectories, Morbidity, and Outcome**

One child suffered a permanent complication from the biopsy (increased abducent nerve palsy), and another experienced a transient increase in a preexisting hemiparesis (Table 1). All seven children with high FDG uptake had a malignant tumor and died within 5, 7, 7, 9, 9, and 20 months, whereas the five with moderate or absent FDG uptake died at 14 and 18 months or still survived at 28, 53, and 60 months. More precisely, the four patients with glioblastomas marked by a high FDG uptake survived for 5, 6, 7, and 9 months (mean survival 6.75 months), whereas the two with glioblastomas marked by a moderate FDG uptake

![Figure 1](image1.png)

**Fig. 1.** Case 5. Planning PET (A) and MR (B) images obtained in a patient with a glioblastoma (WHO Grade IV) in which two trajectories were performed in two tumor areas that enhanced after addition of contrast material. The diagnosis of a brainstem abscess had been suggested. The only trajectory yielding the tumor diagnosis was that guided toward the focus of increased FDG uptake (see panel A). The second trajectory yielded abnormal tissue but was nondiagnostic.

![Figure 2](image2.png)

**Fig. 2.** Case 12. Planning neuroimages obtained in a patient with a pontine glioblastoma (WHO Grade IV), in which combined stereotactic MR and FDG-PET images (A–C) allowed us to define a single biopsy trajectory toward the focus (small green circles) of highest FDG uptake within the lesion (D).
survived for 14 and 18 months. Contrast enhancement on MR images did not correlate with the level of FDG uptake. A moderate MET uptake was found in two low-grade astrocytomas and in one AA. A high MET uptake was found in three glioblastomas, three AAs, one low-grade astrocytoma, two pilocytic astrocytomas, one teratoma, and one germ cell (Table 1).

**Discussion**

These data support the suggestion that PET guidance improves the benefit/risk ratio of stereotactic biopsy procedures and provides several reasons to reconsider the usefulness of stereotactic biopsy in children with intrinsic infiltrative brainstem lesions. Indeed, PET imaging of intrinsic infiltrative brainstem lesions yielded the following benefits: 1) it recorded functional data independent of and complementary to those obtained using MR imaging; 2) it provided information that contributed to the biopsy planning; 3) it improved the biopsy target selection; 4) it increased the diagnostic yield of the biopsy procedure; 5) it allowed us to reduce the sampling to one trajectory; and 6) it confirmed that the intratumoral histological heterogeneity of brainstem gliomas in children detracts from the accuracy of tissue diagnosis. Moreover, PET scanning might provide additional prognostic information that would be useful for predicting disease worsening and for adapting therapeutic strategies. Different steps, as discussed in the sections that follow, have led to the application of the present technique in children.

**Limitations of MR Imaging Guidance in Brainstem Tumors**

Advances in MR imaging allow us to visualize brainstem lesions precisely, and these improvements provide sufficient diagnostic certainty of glioma in typical pontine intrinsic infiltrative brainstem lesions. When MR imaging is used for stereotactic biopsy sampling of these lesions, however, the biopsy diagnostic yield ranges from 83 to 96%. This means that biopsy target selection based on combined MR signals from different sequences (T1-weighted, T2-weighted, fluid-attenuated inversion recovery, and T1-weighted with gadolinium enhancement sequences) does not yield representative tumor tissue in all cases. Some samples con-

![Fig. 3. Case 8. Planning neuroimages obtained in a patient with an AA (WHO Grade III), on which a moderate but significantly increased MET uptake (C, E, and F) was observed (A and B) in an area located at the border of the lesion’s hyposignal contour on T1-weighted sequences (D and G). Two transcerebellar trajectories were defined (red lines, F) based on fusion of stereotactic MR and PET images: one PET-guided trajectory targeting the area of hypermetabolism and one MR-guided trajectory were defined. The PET-guided trajectory was the only one to yield the diagnosis of AA.](image-url)
Use of PET-guided biopsy of intrinsic brainstem tumors

Another cause of inaccuracy in MR-guided stereotactic biopsy samples with MR imaging characteristics, investigators have calculated that the sensitivity and specificity of combined MR sequences in detecting tumor tissue were 96 and 53%, respectively, and that the sensitivity and specificity for detecting tumor grade were 72 and 65%, respectively. Another cause of inaccuracy in MR-guided stereotactic biopsy sampling of brainstem tumors lies in intratumoral variations of the malignancy grade according to location; such variations are frequently observed in gliomas. That histological heterogeneity, which is not distinguished on MR images even with contrast injection, may be responsible for inaccurate diagnosis or grading. Information provided by functional imaging modalities such as MR spectroscopy or PET scanning might improve the accuracy of tumor tissue targeting in the brainstem.

Contribution of PET Scanning in Diagnosing Brain Tumors

The PET data are very helpful in the management of brain tumors, especially with the addition of FDG and MET, and might provide benefits in the management of intrinsic infiltrative brainstem lesions in children. The type of information obtained with PET studies depends mostly on the radiotracer used. Malignant tumors are characterized by an increased FDG uptake, so that the clinical interest in FDG-PET scanning resides in the information related to the differential diagnosis, the degree of malignancy, the prognosis, and the persistence or recurrence of malignant tissue. The FDG uptake is significantly correlated with the presence of anaplasia and is a more accurate reflection of tumor grade than MR contrast enhancement. The accumulation of MET in tissues is influenced by cellular needs for protein synthesis precursors, and correlates with tissue proliferation and malignancy. Protein metabolism is much higher in the tumor than in the brain tissue, and MET-PET sensitivity and specificity to detect tumor tissue are both approximately 90%. We studied the usefulness of PET guidance in stereotactic biopsy sampling of brainstem lesions in adults. The literature on PET imaging of pediatric brain tumors remains scarce. Both FDG and MET uptake levels seem to be associated with the malignancy grade, as in adults.

Usefulness of Stereotactic PET Guidance

Using PET guidance for stereotactic biopsy sampling in adult brain tumors showed that: 1) the FDG uptake in gliomas is anatomically heterogeneous and correlates regionally with the presence of anaplasia; 2) FDG-PET guidance increases the diagnostic yield of stereotactic biopsy samples by reducing the incidence of nondiagnostic trajectories; 3) comparing FDG and MET in the same patients, we found that MET was a better choice than FDG for PET guidance because it was more specific for tumor tissue, it targeted anaplasia as well as FDG did, and it avoided the risk of low FDG uptake; 4) the areas of highest FDG and MET uptake are correlated with each other and with the presence of anaplasia in gliomas; and 5) PET guidance allows a reduction in the number of samples taken to one trajectory in eloquent brain areas.

The technique was straightforward when used in children, with no additional morbidity, and the spatial resolution of the PET camera, which improved after 2001 (used in Cases 11–20), allowed us to study small brainstem lesions accurately. Indeed, after 2001, no false-negative PET finding was observed in brain lesions smaller than 10 mm, and the size of tumor lesions or anaplastic foci detected with the addition of MET were much beyond the precision required for the biopsy procedure.

Specific adaptations to the pediatric population have been described elsewhere.

Contribution of PET Data in Brainstem Tumors

The PET data contributed to the surgical planning and improved biopsy target selection in all cases in this series. Indeed, we made the following observations: 1) MET uptake was always increased (at a high level and relatively focal in the majority of cases); 2) FDG uptake was increased in all but two cases, in which MET offered useful information; 3) PET provided a focal target for biopsy sampling in all cases within a diffuse and ill-defined lesion on MR images (either an FDG-PET–guided target [generally a focal area of increased FDG uptake], or an MET-PET–guided target [generally a focal area of increased MET uptake]); and 4) FDG-MET PET offered a more focal target than MET-PET (that is, when both PET tracers were increased), and their highest uptake spots corresponded spatially. These data are in accordance with our previous findings in adult and pediatric brain tumors. We also confirmed the following findings in the present series: 1) the high sensitivity of MET in tumor tissue detection (all tumors had an increased MET uptake); 2) the intratumoral metabolic heterogeneity of brainstem tumors (illustrated in 16 of 20 cases—either focally increased FDG uptake within a larger lesion on MR imaging or an extended area of increased MET uptake); and 3) the existence of intratumoral histological heterogeneity in pediatric brainstem gliomas (illustrated in six cases, in which each trajectory yielded a different diagnosis), which has never been shown before.

It could be advocated that after experience with PET imaging is gained, PET data will contribute to a better approach to the diagnosis, and the need for a biopsy might be questioned. For example, in some of the children with a glioblastoma (Cases 1–3, 5, 6, and 12), the high PET tracer uptake, which occurs in malignant tissue, might have allowed them to avoid a biopsy procedure. We believe that this might be true in typical tumor presentations on MR imaging. This issue is indeed highly dependent on the initial MR presentation of the lesion, which might be atypical and suggest a nonglial tumor such as those defined by the selection criteria used in this series. On the other hand, for the patients in this series in whom the MR presentation suggested a glioblastoma (Cases 8–11), the final diagnoses were AA and pilocytic astrocytoma (one each), and PNET (two patients).

Improved Diagnostic Yield of Stereotactic Biopsy Sampling in Brainstem Tumors

Using PET guidance significantly improved the diagnostic yield of stereotactic biopsy sampling. Indeed, a total of
28 stereotactic trajectories were performed and the analysis of diagnoses showed that: 1) some intrinsic infiltrative brainstem lesions were nongliarial tumors and all glial tumors were not glioblastomas; 2) PET-guided trajectories never yielded nondiagnostic samples; 3) nondiagnostic samples were obtained in areas of enhanced MR signal after contrast injection but out of the area of increased FDG uptake (Fig. 1); and 4) PET-guided trajectories always provided tumor samples with equivalent or higher malignancy grades than those obtained with MR-guided trajectories. These data show that, with MR guidance alone, stereotactic biopsy sampling could have led to inaccurate diagnosis or grading, and confirm that histologically identified heterogeneity can impede the diagnostic accuracy of the biopsy procedure in pediatric brain tumors. In this study we also confirm, as we found earlier in adults, that in terms of a single-tracer PET-guided procedure, MET is a better choice than FDG because it avoids the risk of low or absent FDG uptake. Moreover, it also appears in this study that for this reason, the preference for the PET tracer changed from FDG to MET with time and experience (Table 1).

**Sampling Reduced to One Trajectory**

Use of PET guidance allowed us to reduce the number of samples taken to one trajectory. Usually, to improve the accuracy and the pertinence of the established diagnosis, multiple serial biopsies procedures and/or trajectories are performed, which increases the risk of complication. Failures may still occur, however, due to inadequate targeting. In our study, PET guidance improved the diagnostic yield of the biopsy sampling by reducing the incidence of noncontributive trajectories without increasing the number of samples taken. After 2000, we decided that this observation justified the performance of a single trajectory. In the 12 children who underwent the procedure after that date, the reduced sampling did not result in biopsy failure. The size of our series did not allow us to detect any reduction in biopsy-related morbidity. However, the two minor complications occurred in patients in whom two trajectories were used to obtain specimens.

**Additional Prognostic Information**

In addition to what was expected, PET provided additional information that allowed us to understand better the outcome in some children (Table 1). Indeed, all tumors with high FDG uptake were malignant and associated with a shorter survival time than those with absent or moderate FDG uptake. This preliminary finding confirms that high FDG uptake level or extent. The MET uptake level and the distribution of the spots with highest uptake were correlated with the level of FDG uptake, as expected from previous studies. We believe that brainstem tumors represent the area of neurooncology to which functional data from PET imaging might offer the highest benefit.

**Adapting Targeted Therapies**

Finally, it is highly probable that conventional fractionated radiotherapy will not remain the only efficient treatment in intrinsic infiltrative brainstem lesions in the next decades. Indeed, radiosurgery and new chemo-, gene, or immunotherapies will certainly, separately or in combination, succeed to improve these children’s outcome. These therapies will undoubtedly require tissue sampling for diagnostic confirmation and grading of tumors, for molecular marker studies, or for immunological purposes prior to adapting targeted therapies. Practitioners will also need to integrate functional imaging modalities for targeting, assessing, mapping, or providing follow-up care for these patients. The PET imaging modality is already used for guiding radiosurgical dosimetry planning (PET-guided radiosurgery) as well as for monitoring brain tumor response and recurrence.

**Conclusions**

These data support the suggestion that integration of PET metabolic information in the planning of stereotactic biopsy sampling may contribute to the improved management of intrinsic infiltrative brainstem lesions in children. Use of PET guidance significantly improves the diagnostic yield of the biopsy sampling and may therefore reduce the risk of complications from the procedure. This raises several good reasons to continue to perform biopsy sampling in these lesions.

**References**


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