Non-invasive grading of oligodendrogliomas: correlations between in vivo metabolic pattern and histopathology

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Abstract. Several studies have shown that the prognosis of oligodendrogliomas is dependent on their histological grade. In order to identify a non-invasive method for the primary diagnosis and follow-up of these tumours, we investigated the relationship between their in vivo metabolism, assessed by positron emission tomography (PET), and their histological grade assessed at the same time. Forty-seven patients with histologically confirmed oligodendrogliomas were investigated. Conventional neuroradiological assessment by computed tomography and magnetic resonance imaging (MRI) was performed in all the patients. All the histology slices were reviewed by the same pathologist after referral from various pathology laboratories. The PET investigation included a carbon-11 methionine (^{11}C-MET) uptake study and, in the majority of cases, a fluorine-18 fluorodeoxyglucose (^{18}F-FDG) uptake study, in order to investigate at the same time both amino acid metabolism and glycolysis. The sampled tumour region of interest (ROI) was defined from the T1-weighted 3D MR scan matched with the PET scan. Tracer concentration in each voxel of the tumour ROI was divided by the mean concentration in an ROI of the same size located in the healthy brain tissue. For each tumour and each tracer, we characterized the metabolic pattern on the basis of the mean and the maximum tumour to healthy tissue concentration ratio, and also the standard deviation and range of the ratios, which indicate the degree of metabolic heterogeneity of the tumour. The histological criteria for differentiating between high- and low-grade tumours were those of the WHO and, partially, of the Sainte-Anne–Daumas-Duport classification. Highly significant differences between high- and low-grade oligodendrogliomas (Mann-Whitney test: $P<0.0001$) were observed for all the assessed parameters of ^{11}C-MET uptake. On the other hand, the pattern of ^{18}F-FDG uptake showed only moderate differences between the two tumour groups.

Key words: Positron emission tomography – Brain tumour – Oligodendroglioma

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Introduction

Oligodendrogliomas are relatively infrequent tumours (accounting for 4%–10% of all primary intracranial tumours) which occur essentially in adulthood and in supratentorial locations. Although their histological features have now been well characterized for 70 years [1], there has long been controversy over the relevance of different grading systems to the prognosis in individual cases. The most recent works consider that there are only two prognostic histological grades: low-grade oligodendrogliomas, which correspond to grade II of the WHO classification, and anaplastic oligodendrogliomas, which correspond to grade III. These two groups exhibit a dramatic prognostic difference, with a median survival of about 10 years for low-grade tumours and 3 years for anaplastic tumours. However, the criteria for allocating individual cases to one of these categories are still under debate. Moreover, the tissue sample on which histological assessment is based is often obtained from a stereotactic biopsy, and therefore represents only a very small part of an often very large tumour. There is thus some fear that such assessment may underestimate the true growth potential of the lesion. Lastly, there are no specific neuroradiological features which can differentiate be-

tween oligodendrogliomas and astrocytomas or mixed gliomas, or between low-grade and anaplastic oligodendrogliomas, even if the occurrence of CT contrast (or gadolinium) uptake is strongly suggestive of anaplastic lesions.

Recently it has been shown that oligodendrogliomas are chemosensitive tumours. There is accordingly a need for a non-invasive tool that can be used repeatedly during the course of the disease to clarify their response to chemotherapy, as well as to radiation therapy and surgical resection. Such a tool is also needed to address the main practical issues facing the neuro-oncologist, such as: (a) the true grading of a large tumour of which only a small sample has been established to be of low grade; (b) clarification of whether there is progression toward an anaplastic form during the follow-up of a low-grade oligodendroglioma that is enlarging (progression towards anaplasia is encountered in about one-third of low-grade oligodendrogliomas); (c) differentiation between recurrence and necrosis of a previously irradiated tumour; (d) prediction of the late clinical and anatomical response to chemotherapy or radiotherapy from the assessment of the early modifications of functional parameters.

In a previous study [2], we have shown that positron emission tomography (PET) using fluorine-18 fluorodeoxyglucose (^{18}F-FDG) and carbon-11 L-methyl-methionine (^{11}C-MET) can differentiate on a functional basis between low-grade astrocytomas and oligodendrogliomas, two tumour categories which are difficult to distinguish on the basis of purely anatomical imaging data. We therefore decided to investigate whether PET can help to distinguish low-grade from high-grade oligodendrogliomas, using the same imaging methods as were employed in the aforementioned preliminary work.

Materials and methods

Clinical, radiological and histopathological data

We assessed 27 patients with supratentorial low-grade oligodendrogliomas and 20 patients with supratentorial high-grade (or anaplastic) oligodendrogliomas. Brief clinical data regarding each population are presented in Table 1. The main neuroradiological features addressed were the presence or absence of (a) calcifications and (b) CT contrast (or gadolinium) uptake – the former being considered to strongly favour the diagnosis of oligodendroglioma, and the latter as indicative of anaplasia.

Histological data were obtained either from stereotactic biopsy (performed 11 times in low-grade lesions and twice in high-grade lesions) or from large pieces of tumour tissue obtained during open surgery (16 times in low-grade lesions and 18 times in high-grade lesions). Some patients first had a biopsy and then surgical sampling: in such cases only the histology drawn from the latter study was considered. Practically all histological samples, initially referred from seven different laboratories, were reviewed by the same pathologist (F.C.), who was not aware of the PET patterns of the lesions. When there was doubt about the correct grade, the tissue blocks were resliced for further assessment. In most cases, in addition to pure morphological classification, immunocytochemistry was performed for identification of an astrocytic cell component [glial fibrillary acidic protein (GFAP) expression] and assessment of the growth fraction (MIB1 expression). Only pure oligodendrogliomas were considered, i.e. mixed gliomas were not included in the present series. Classification of the tumour specimens as low grade or high grade (anaplastic) was based on the WHO brain tumour classification [3] and partially on the most recent Sainte-Anne–Daumas-Duport grading system [4, 5], as follows:

- Low-grade oligodendroglioma: cell density is variable but may sometimes be high; nuclear pleomorphism may or may not be present; there are few mitoses if any; there is no endothelial hyperplasia or proliferation and no necrosis; the MIB1 index is less than 1.
- High-grade oligodendroglioma: cell density is high at least in part of the sample; nuclear pleomorphism is consistently present; there are obvious mitoses which can be rapid and numerous; there are areas of endothelial hyperplasia or proliferation, and sometimes necrosis is present; the MIB1 index may exceed 1.

PET data

All patients underwent ^{11}C-MET studies, and most of them also had an ^{18}F-FDG study on the same day or 24 h apart. All patients gave informed consent to the procedure. Between 1991 and 1996, all measurements were obtained with a high transaxial resolution time-of-flight PET camera (LETI TTV03, Grenoble, France), providing seven slices with a spatial resolution of 5.5 mm in plane and a slice thickness of 9 mm. Patients were carefully positioned in a stereotactic headholder to ensure correct and reproducible positioning by use of a method based on the glabella–inion line determined on a lateral cranial X-ray [6]. The PET camera was then tilted to obtain seven planes parallel to this line. Attenuation correction was performed by means of a germanium-68 transmission

Table 1. Clinical and demographic data

	Low-grade oligodendrogliomas (n=27)	High-grade oligodendrogliomas (n=20)	P values
Mean age (SD)	44 (±14)	42 (±14)	0.7
Sex (M/F)	16/11	12/8	0.9
Type of tumour (primary[a]/recurrent)	25/2	13/7	<0.05
Symptoms (epilepsy[b]/others)	25/2	15/5	<0.05

[a] Tumour assessed by PET before any treatment (some patients, however, had a stereotactic biopsy before the PET investigation)

[b] Sometimes associated with other symptoms

scan. Since June 1996, some patients have been investigated with an ECAT HR+ (Siemens/CTI, Knoxville, Tenn., USA) after careful orientation of the patient's orbitomeatal line parallel to the gantry, imaging 63 planes simultaneously over an axial length of 15.5 cm. Almost isotropic, the spatial resolution was 4.6 mm full-width at half-maximum. Before injection, transmission scanning using three ^{68}Ge rod sources was performed for attenuation correction. AIR Software allowed magnetic resonance imaging (MRI) data acquired in three dimensions to be sliced according to the PET images.

Conventional three-dimensional MRI was performed at the time of the PET study (GE Advantage, 1.5 T; General Electric, Buc, France). Software enabled the MRI data acquired in three dimensions to be subsequently sliced according to the PET coordinates with respect to the glabella–inion line landmarks, which have known relationships with the anterior commissure–posterior commissure reference points [6].

^{11}C-MET studies. ^{11}C-MET uptake was evaluated during 40- to 60-min acquisition periods after an intravenous bolus injection of 11.38±2.03 mCi (mean ± standard deviation) of ^{11}C-MET. The time course of the brain activity concentration after intravenous administration of ^{11}C-MET has been reported elsewhere [7], based on dynamic PET measurements in healthy subjects. The time-activity function, which includes physical decay of ^{11}C-MET, seems to show a better equilibrium of the tracer at 40–60 min time points after injection than at 20–60 min time points. Nevertheless, we performed a within-subject comparison of ratio values between 20–60 min and 40–60 min time points. Results acquired on eight new, randomly selected patients showed a very small decrease (2.6% on average) between 20–60 min and 40–60 min ratio values. To our knowledge, this relative difference will not invalidate our results. Raw data were normalized as a percentage of injected dose (percent injected dose per millilitre).

^{18}F-FDG studies. Cerebral metabolic rate of glucose (CMR-Glu) values (mg 100 g^{-1} min^{-1}) were calculated according to PET data obtained 50–60 min after bolus intravenous injection of 5.76±2.10 mCi (mean ± standard deviation) of ^{18}F-FDG, using the autoradiographic method and including the k_4 value [8, 9]. Arterial blood sampling was obtained through a radial artery catheter.

In a separate study, we measured the tumour to tissue ratios with either ^{18}F-FDG or ^{11}C-MET in seven patients, both on the LETI TTV03 and then on the Siemens HR+ camera, after one injection of tracer. It appeared that differences between ratio values obtained with each camera were close to zero (Wilcoxon signed-rank test P value = 0.99) and did not affect the reliability and reproducibility of measurements according to the type of camera used.

Data analysis

Regions of interest (ROIs). In each case, the anatomical images (T1-weighted MR images) were transferred to a work station. The limits of the tumour image (Tum ROI) were manually drawn by the observer and then automatically copied onto the same FDG-PET slice. Accurate repositioning of the images was performed by superimposing the contours of the brain obtained from both the anatomical and the FDG-PET slices by the isodensity method. Thereafter, the contours of the brain and tumour were copied onto the MET-PET image and adjusted, if necessary, to allow accurate superimposition of the images. The symmetrical contralateral ROI of the tumour was then determined, and thereafter both ROIs were copied from the FDG-PET image onto the MET-PET image, thus providing a healthy tissue reference ROI (Ref ROI) of the same size as the Tum ROI for each slice. When the tumour was not strictly unilateral, the Ref ROI was displaced anteriorly or posteriorly in order to sample only anatomically normal tissue. This method of delineating tumour ROIs is likely to be reliable in primary lesions, before any therapeutic modification due to either surgery or radiotherapy. In those patients who had previously undergone only surgery, we excluded from the tumour ROI the residual cavity of the resection, which was easily delineated from the MR scan. In those patients who had received radiotherapy (after or without previous surgery), it was clear that part of the abnormal MRI signal could have been due to necrosis and not to tumour. However, as our method of data analysis takes into account not only the mean ratio values but also the maximum values, and as there is no a priori method to define a PET data threshold of what is tumour and what is not, we chose to include the whole morphologically abnormal lesion in the so-called tumour ROI.

Parametric measurements. Software was used to divide each Tum ROI (together with its contralateral counterpart, the symmetrical Ref ROI) into large pixels, each containing a matrix of 8×8 pixels. The same software was used to compute the mean concentration of the tracer in the whole Ref ROI and then the concentration in each large pixel of the Tum ROI, and to subsequently provide the concentration ratio between each such large pixel and the healthy ROI area. The following data were obtained for each patient: mean ratio of tumour to healthy tissue concentration for ^{11}C-MET and ^{18}F-FDG, maximum and minimum ratios recorded from all slices, standard deviation for the ratio values, and total volume of the integrated ROIs for the different slices. Moreover, a histogram indicated for each tracer the percentage of all tumour pixels belonging to each of two ratio categories, i.e. below and above 1, 1 being the value defining "normality".

Statistical analyses

Results were expressed as mean ± SD or as proportions. Since several metabolic parameters had a very skewed distribution and the between-groups differences in variability were statistically significant, the non-parametric Mann-Whitney rank sum test was used to compare low- and high-grade oligodendroglioma groups. For those subjects who underwent both PET scans, the Spearman rank correlation test was used to study the direct relationship between ^{11}C-MET and ^{18}F-FDG mean ratios. A survival analysis using the Kaplan-Meier method was then performed on the time to death for each group of patients. In order to compare the survivor functions across groups, the Mantel-Haenszel test was performed on the subgroup estimates. All P values were two-tailed and were considered significant when less than 0.05.

Results

Correlations between histological and clinical data

These correlations are displayed in the Kaplan-Meier cumulative survival function for duration of follow-up (Fig. 1), which shows a highly significant prognostic difference between the two tumour grades, confirming the relevance of the histological criteria which were used.

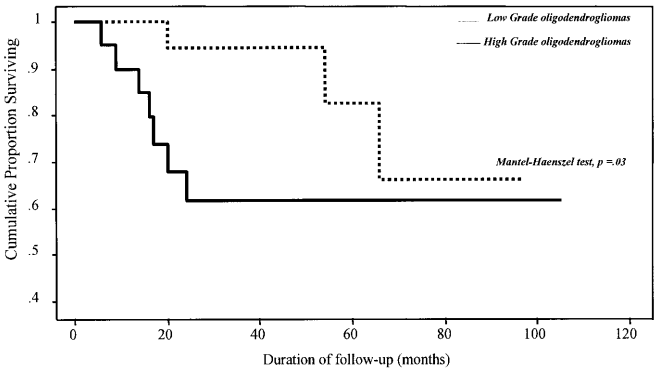

Fig. 1. Cumulative proportion of patients surviving in each group (low-grade vs high-grade oligodendrogliomas) in relation to duration of follow-up. Note that survival probability at each time point is significantly higher in the low-grade group than in the high-grade group (Mantel-Haenszel test, P=0.03)

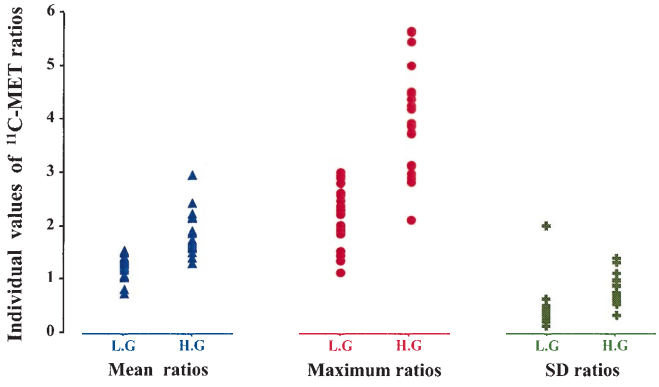

Fig. 2. Individual values of ^{11}C-MET ratios in low-grade and high-grade oligodendrogliomas. L.G., Low grade oligodendrogliomas, H.G., High grade oligodendrogliomas

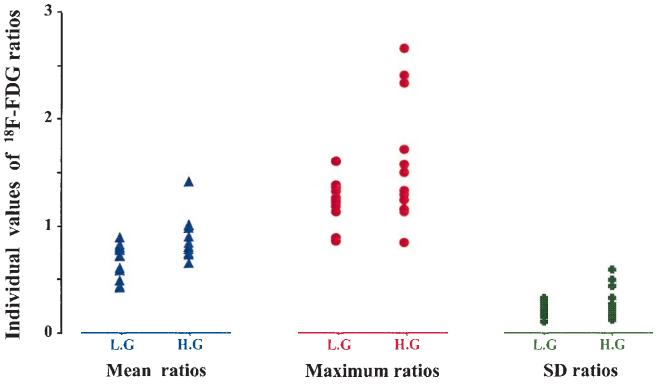

Fig. 3. Individual values of ^{18}F-FDG ratios in low-grade and high-grade oligodendrogliomas

Correlations between histological and neuroradiological data

It is clear from our series that *calcifications* were not a consistent feature of oligodendrogliomas, since they were present in only 6 out of 19 (31%) patients with low-grade tumours in whom a CT scan was performed, and in 5 out of 12 (41%) patients with high-grade tumours. The occurrence of *CT contrast uptake* was observed in 6 out of 12 high-grade tumours, but in none of 19 low-grade lesions. *Gadolinium uptake* was observed more frequently, in 13 out of the 20 patients with high-grade tumours in whom an MRI study was performed, but also in 10 out of the 27 patients with low-grade tumours.

Correlations between histological and metabolic data

PET data for ^{11}C-MET and ^{18}FDG studies are presented in Figs. 2 and 3, respectively, for both low-grade and high-grade tumours, and examples are illustrated in Figs. 4 and 5. Results of statistical analyses are shown in Figs. 6, 7 and 8 and are summarized in Table 2. There was a significant difference between ^{18}F-FDG uptake by low-grade and high-grade tumours, as assessed with mean and maximum ratios (Fig. 7). However, on all parameters the differences were much more dramatic and significant with respect to ^{11}C-MET uptake (Fig. 6). Amino acid metabolism of the latter group was much more heterogeneous than that of the former, as illustrated by the results for SD ratios and range ratios. With ^{11}C-MET studies, the overlap between the metabolic pattern of the different populations was very limited.

With both tracers, the anaplastic oligodendrogliomas exhibited a higher metabolism than the low-grade oligodendrogliomas.

The mean ratios for ^{11}C-MET were approximately twice as high as those obtained with ^{18}F-FDG in the same subjects (Fig. 8).

Discussion

Ever since the classification of gliomas by Bailey and Cushing in 1926 [1] and the subsequent development of a grading scale by Kernohan [10], the practical management of low-grade lesions has been similar for astrocytomas, oligodendrogliomas and mixed gliomas. For most of the intervening period they were considered slowly growing lesions with a relatively favourable prognosis and an infiltrative nature which in most cases precluded their radical surgical removal. Conservative treatment – with or without biopsy – was held to be the best solution when patients had only seizures, and it was felt safe to delay aggressive therapy (surgery or radiotherapy) until focal disorders or high intracranial pressure developed [1, 10]. The histological grade of the lesion was, of course, a relevant parameter when it could be ascer-

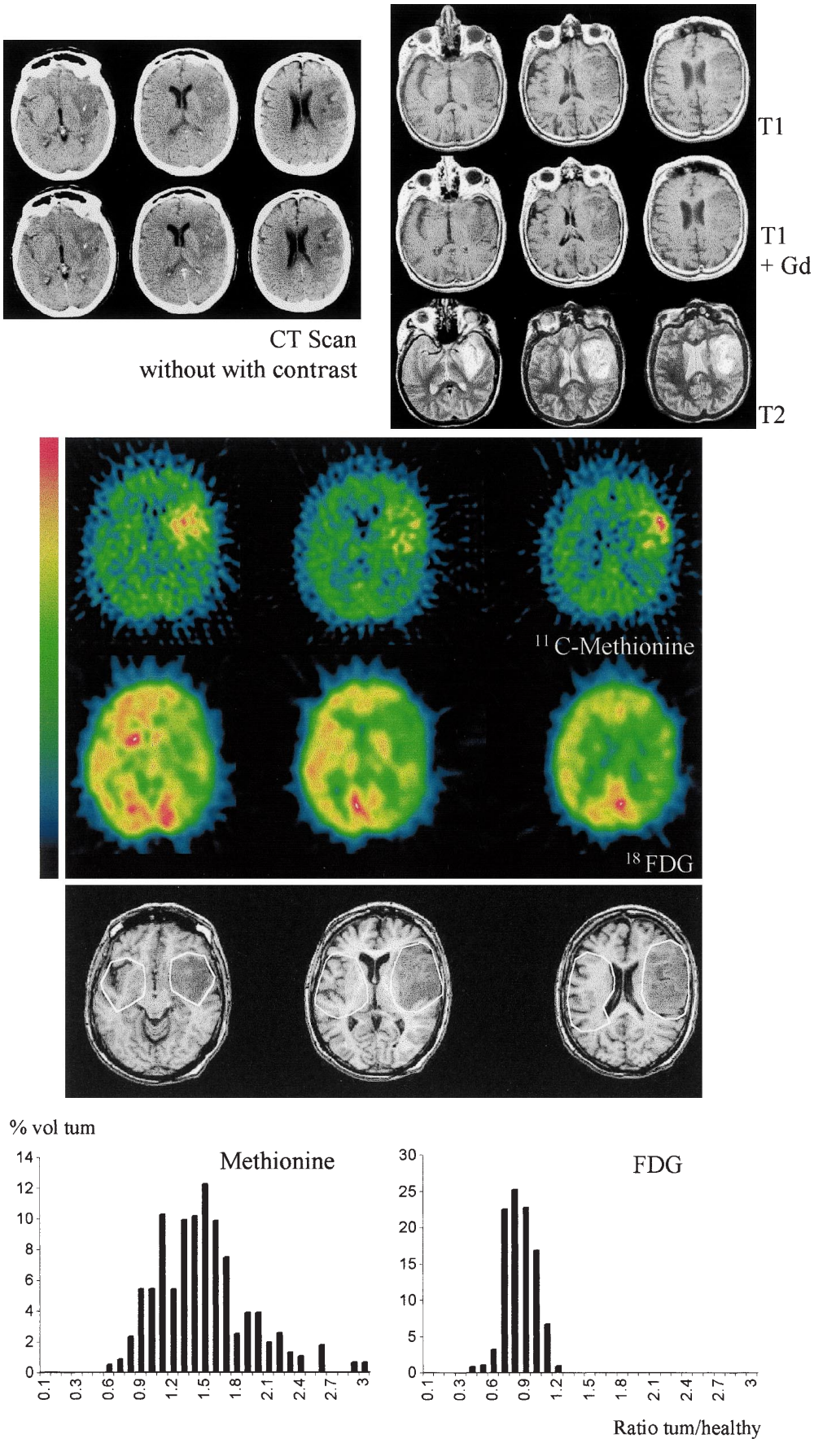

Fig. 4. A 60-year-old woman presented with a low-grade left temporo-insular oligodendroglioma and seizures. The CT scan (*top row:* images obtained without contrast; *bottom row:* images obtained with contrast) shows small calcifications, but no contrast uptake. On MRI, there is no gadolinium uptake. The PET pattern showed a slightly decreased glucose metabolism of the tumour relative to healthy tissue, and a definite methionine hypermetabolism in some parts of the tumour ROI

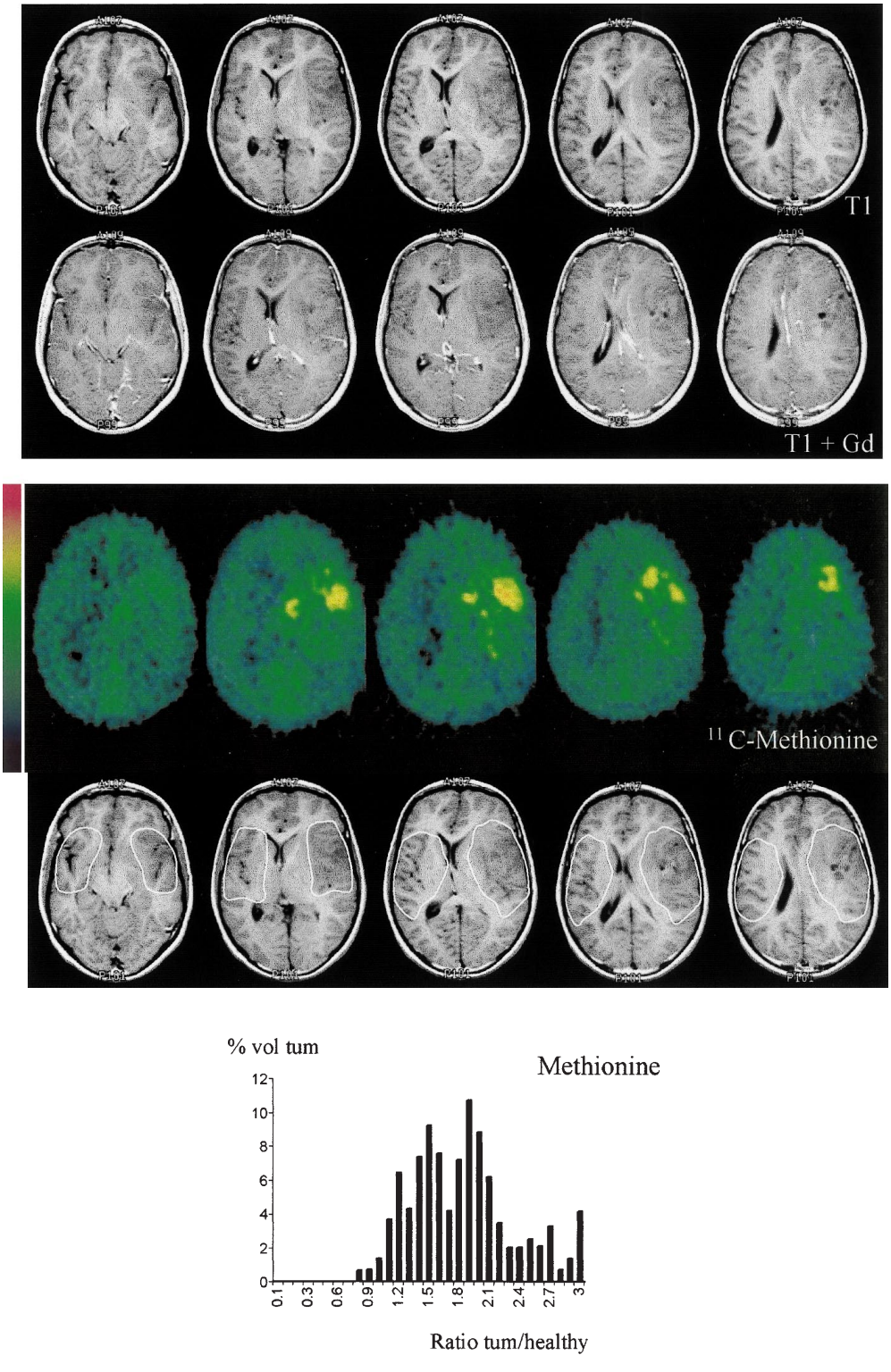

Fig. 5. A 15-year-old boy presented with a large left fronto-insular tumour, without gadolinium uptake. The diagnosis obtained from biopsy was that of an anaplastic oligodendroglioma. The ^{11}C-MET pattern is that of an extremely hypermetabolic and heterogeneous lesion. The patient died 6 months after the PET study, despite radiotherapy and chemotherapy

tained, but such was not the case when purely conservative treatment was chosen.

Moreover, if there was good agreement about the reliability of grading classifications – either from Kernohan [10], Sainte-Anne–Mayo Clinic [5] or WHO [3] – in the case of astrocytic tumours, there was much controversy regarding the grading of oligodendrogliomas. In the classification proposed by Smith et al. [11], Bruner et al. [12] and Ludwig et al. [13], four histological groups were defined (from A to D) according to the number of observed parameters from among a battery of five criteria of anaplasia: nuclear atypia and a high nucleocyto-

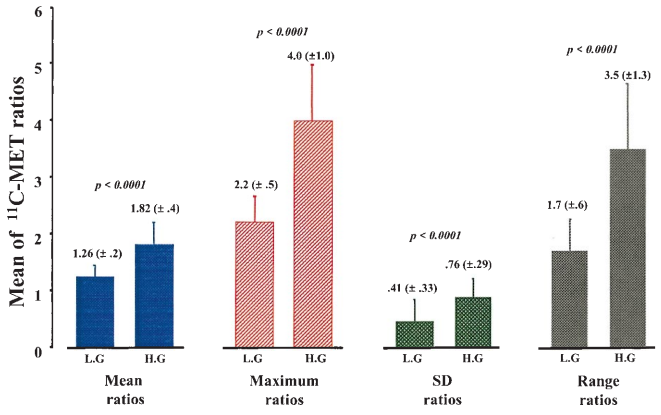

Fig. 6. In vivo ^{11}C-MET pattern of oligodendrogliomas

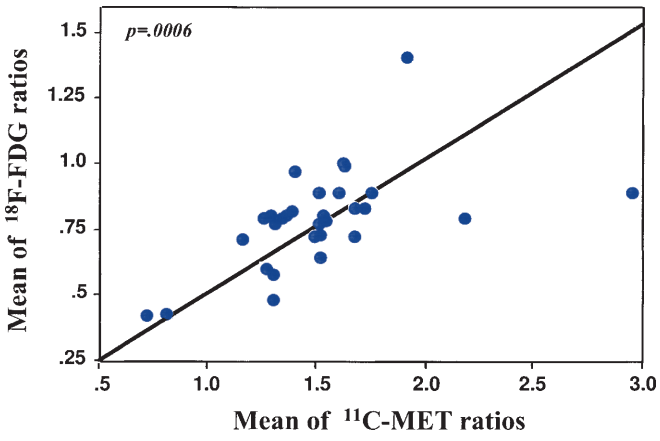

Fig. 8. Within-subject correlation of ^{18}F-FDG and ^{11}C-MET outcome measures

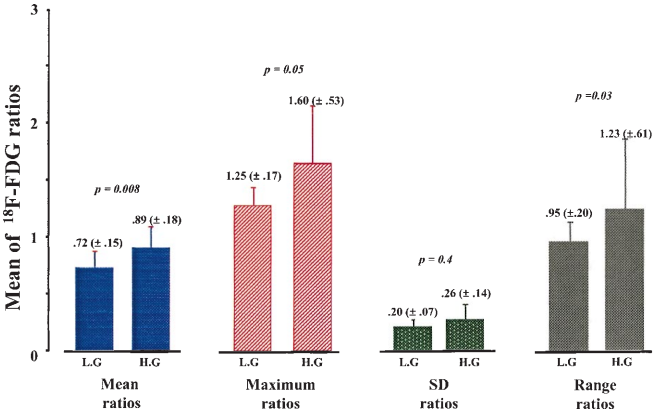

Fig. 7. In vivo ^{18}F-FDG pattern of oligodendrogliomas

plasmic ratio, high cell density, endothelial proliferation, necrosis and pleomorphism. However, it appeared from the study by Ludwig et al. in a series of 323 patients [13] that very few patients fall into group A and that the prognosis is almost the same in groups B and C (and significantly different from that in group D). This suggests that, from a practical point of view, only three histoprognostic groups can be identified with this classification. This was also the conclusion drawn from a study by Mork et al. [14], and then by Daumas-Duport in an analysis of the Mayo Clinic series. However, the WHO classification developed by Kleihues [3] has further simplified the classification into two groups: low grade and high grade (or anaplastic). Such a simplification has been corroborated by the last study by Daumas-Duport [4, 5], who showed a significant prognostic difference between low-

Table 2. Results with regard to ^{11}C-MET and ^{18}F-FDG uptake by low-grade and high-grade tumours

Parameter	^{11}C-MET		*P* values
	Low-grade oligodendrogliomas (*n*=27)	High-grade oligodendrogliomas (*n*=20)	
Mean ratios	1.26±0.2	1.82±0.4	<0.0001
Maximum ratios	2.20±0.5	4.00±1.0	<0.0001
SD ratios	0.41±0.3	0.76±0.3	<0.0001
Range ratios	1.70±0.6	3.50±1.3	<0.0001

Parameter	^{18}F-FDG		*P* values
	Low-grade oligodendrogliomas (*n*=17)	High-grade oligodendrogliomas (*n*=14)	
Mean ratios	0.72±0.15	0.89±0.18	0.008
Maximum ratios	1.25±0.17	1.60±0.53	0.05
SD ratios	0.20±0.07	0.26±0.14	0.4
Range ratios	0.95±0.20	1.23±0.61	0.03

grade and high-grade lesions, with a median survival of 10 years for the former group and 2.9 years for the latter group. The main histological criterion for ascribing patients to one or the other grade was, in this study, the occurrence of endothelial hyperplasia or proliferation. The problem is that this classification was not founded only on histological parameters but rather also took into account morphological neuroradiology, namely the presence or absence of CT contrast and/or gadolinium uptake. As we have seen in our Results section, there is no consistent correlation between such uptake and endothelial abnormalities. This is the reason why we considered only pure histological criteria, which were applied in many cases on large surgical tissue samples – such was not the case for the series of Daumas-Duport.

During the past decade, many works have renewed the interest of neuro-oncologists in oligodendrogliomas. One of the main advances has been the demonstration of a chemosensitivity of these tumours that is unique among the gliomas, and is especially marked when lesions are aggressive and fast growing [15, 16]. Another salient point is the development of new surgical techniques allowing resection of tumours located near functionally eloquent brain areas [17, 18, 19, 20]. For these reasons, the differential diagnosis between oligodendrogliomas and other glial tumours is no longer purely contemplative, but may have very practical consequences in terms of management and therapy. This also holds true for the differential diagnosis between slowly growing and aggressive forms of these tumours. As repetition of biopsies is problematic (given that they are invasive and in any case sometimes fail to yield a diagnosis), and as anatomical imaging does not provide sufficiently specific data for differential diagnostic purposes, functional and metabolic imaging, namely PET, may represent an important source of support.

Among the many studies that have used PET to assess in vivo metabolism in gliomas, most have been dedicated to astrocytic tumours and have used ^{18}F-FDG as the tracer of choice. These studies have shown a good correlation between uptake of ^{18}F-FDG and histological grade [21, 22] and between uptake of ^{18}F-FDG and prognosis [23, 24, 25, 26]. They have also demonstrated the usefulness of this tracer during the follow-up of patients insofar as it permits the diagnosis of progression towards a more anaplastic grade [27] and the differential diagnosis between tumour recurrence and radiation necrosis.

Investigation of amino acid uptake in glial tumours [28, 29, 30, 31] has also shown a correlation between tumour metabolism and histological grading. Some studies have investigated several parameters simultaneously [32, 33, 34, 35] and concluded that different tracers, such as ^{18}F-FDG and ^{11}C-MET, can provide different and complementary information in individual cases. However, most of these studies have addressed tumours of various cell types and have consequently failed to accrue a sufficient number of cases in each tumour group, such as astrocytomas, oligodendrogliomas or mixed gliomas. Moreover, the ROIs for metabolic sampling of tumours or healthy tissue were usually determined by purely visual analysis of the PET images. Therefore, they may have included too much or too little of the whole lesion, and were especially difficult to use in cases where the tumour metabolism was only slightly different (higher or lower) from that of the normal brain tissue.

Starting from these considerations (the need for accurate histology and a reproducible way to determine ROIs), we focussed on low-grade gliomas, a group of tumours for which the diagnosis and prognosis can be difficult to establish from clinical, neuroradiological and sometimes even histological data. In a previous study [2], using an original method to define tumour and reference ROIs from a superimposed three-dimensional MR scan (see the Materials and methods section), we were able to demonstrate a highly significant difference between low-grade astrocytomas and low-grade oligodendrogliomas in terms of ^{11}C-MET uptake but only a modest difference with regard to ^{18}F-FDG uptake. Clearly, oligodendrogliomas had a much higher amino acid uptake than did astrocytomas. This difference was striking given that no clinical or neuroradiological feature (except the occurrence of calcifications, which were more frequent in patients with oligodendrogliomas) could distinguish one population from the other.

We therefore started a second study, looking for any metabolic differences between low-grade and high-grade (anaplastic) oligodendrogliomas. In this study, we again took extreme care over histological analysis and case selection, excluding from the series every case for which there was not perfect agreement between the diagnosis of the referring pathology laboratory and that of the pathologist at our own institution (F.C.), who reviewed all the data. In particular, we excluded all cases in which there was an astrocytic tumour component. Grading was established only on the basis of histological analysis, and was performed blind to the findings of neuroradiology and PET. Our results showed that while ^{18}F-FDG can discriminate only rather weakly between the two grades, ^{11}C-MET is a very powerful tool for this purpose. In fact, anaplastic tumours not only had a considerably increased metabolism, both mean and maximum, but also appeared to be extremely heterogeneous (as expressed by the SD and the range of the ratio values) compared with the low-grade tumours.

We have not yet started to look for an independent univariate correlation between methionine metabolism and survival or time to recurrence because the mean length of follow-up of our patients is too short compared with the expected lifespan of patients with oligodendrogliomas, at least in the low-grade category. However, it is clear from the actuarial survival curve that the prognosis of the two populations is markedly different.

To our knowledge, this series of oligodendrogliomas assessed with PET is unique. It is therefore difficult to

compare our results with the small number of cases reported in earlier works, either from case reports [36, 37] or from larger series of gliomas [34, 35]. The fact that Kaschten et al. [34] found decreased ^{11}C-MET uptake in two high-grade oligodendrogliomas compared with two low-grade ones is striking and difficult to understand, unless one takes into consideration the fact that their way of defining ROIs and expressing results was totally different from our own.

The *practical usefulness* of PET investigation in the management of oligodendrogliomas will be addressed on the basis of our data in another study. To date we have been able to identify two major applications. The first is in the initial evaluation of a brain glioma, before or after histological diagnosis has been established. Prior to any invasive procedure, PET can help in making a choice between stereotactic biopsy – when the metabolic pattern is indicative of a slowly growing lesion – and open surgery. Of course, this choice will also be determined by the location of the lesion, i.e. whether it is near eloquent functional areas or not. After a biopsy providing a diagnosis of a low-grade lesion, PET can modify this initial result if the metabolic pattern is that of an aggressive lesion. This was the case for several patients in our series, in whom we moved to open surgery because PET was not in good agreement with needle biopsy diagnosis. This explains why a greater number of pathology specimens were obtained from open surgery in primary high-grade than in low-grade tumours.

The second practical application is in the assessment of residual tumour after surgical removal, in order to assist in the decision as to the appropriate adjuvant therapy. PET appears to be a strong tool for differentiating between scar or gliotic tissue on the one hand, and tumour tissue on the other.

There is a third potential application that has not been a central focus in the present work but is very important and will be addressed in another study. This is the use of PET during follow-up in order to ascertain whether there is progression towards an anaplastic grade when a known low-grade oligodendroglioma is clearly recurring or growing. In the present study, two patients of the low-grade cohort and six patients of the high-grade cohort (who were known to have previously had a low-grade lesion) illustrated such an application. One patient was investigated twice, and was re-operated on after the second investigation, displaying the good correlation between metabolic pattern modification and change in histological grade.

Further potential applications are for the differential diagnosis between radiation necrosis and recurrence, and for the early assessment of response to treatment (radiotherapy or chemotherapy).

In conclusion: In vivo metabolic imaging with PET, when using fusion techniques with anatomical imaging, provides accurate and reproducible data which are very well correlated with the histopathology of oligodendrogliomas. ^{11}C-MET appears to be a more powerful tracer than ^{18}F-FDG for this category of tumours. The potential applications of these methods for the management of oligodendrogliomas seem important, taking account of recent developments in therapy.

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