Combination of MRI and dynamic FET PET for initial glioma grading

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Summary

Aim: MRI and PET with 18F-fluoro-ethyl-tyrosine (FET) have been increasingly used to evaluate patients with gliomas. Our purpose was to assess the additive value of MR spectroscopy (MRS), diffusion imaging and dynamic FET-PET for glioma grading.

Patients, methods: 38 patients (42 ± 15 aged, F/M: 0.46) with untreated histologically proven brain gliomas were included. All underwent conventional MRI, MRS, diffusion sequences, and FET-PET within 3±4 weeks. Performances of tumour FET time-activity-curve, early-to-middle SUVmax ratio, choline / creatine ratio and ADC histogram distribution pattern for gliomas grading were assessed, as compared to histology. Combination of these parameters and respective odds were also evaluated. Results: Tumour time-activity-curve reached the best accuracy (67%) when taken alone to distinguish between low and high-grade gliomas, followed by ADC histogram analysis (65%). Combination of time-activity-curve and ADC histogram analysis improved the sensitivity from 67% to 86% and the specificity from 63-67% to 100% (p < 0.008). On multivariate logistic regression analysis, negative slope of the tumour FET time-activity-curve however remains the best predictor of high-grade glioma (odds 7.6, SE 6.8, p = 0.022). Conclusion: Combination of dynamic FET-PET and diffusion MRI reached good performance for gliomas grading. The use of FET-PET/MRI may be highly relevant in the initial assessment of primary brain tumours.

Schlüsselwörter
MR, ADC-Histogramm, 18F-Fluorethyltyrosin, Gliom, Grading

Zusammenfassung


Primary brain tumours (PBT) represent 1–2% of adult cancers, the Central Brain Tumor Registry of the United States estimating that over 311,000 new patients with PBT or central nervous system tumour were newly diagnosed between 2005 and 2009 (5). Gliomas constitute the most frequent brain tumours and their histological differentiation and grading is predictive of aggressiveness and outcome (20).

They are currently divided in grade I and II tumours considered as low-grade with a prolonged evolution and in grade III (anaplastic glioma) and IV (glioblastoma) considered as high-grade lesions leading to death within weeks to months without treatment.

Magnetic resonance imaging (MRI) is currently used for the initial morphological assessment of suspected primary brain tumour. Its high spatial resolution allows tumour diagnosis and precise location, measurement of tumour size, and assessment of mass effect, oedema or haemorrhagic complications. It however does not allow the easy determination of tumour metabolism. Magnetic resonance spectroscopy (MRS) helps in the assessment of neuronal and membrane metabolites such as N-acetylaspartate, choline, creatine, inositol or lactates, but it is limited by poor spatial resolution and frequent artefacts due to cerebrospinal fluid or skull bone proximity. Glioma grading using conventional MRI sequences remains challenging and numerous studies aimed at determining the utility of MRS (19) or diffusion imaging with apparent diffusion coefficient (ADC) maps computation (1, 12, 15, 22, 29) in this setting.

Molecular imaging with positron-emission tomography (PET) provides information on tumour metabolism and helps in identifying zones of tumour with increased growth activity (17). $^{18}$F-fluorocholine or $^{18}$F-fluorodeoxyglucose ($^{18}$F-FDG) PET is used widely in oncology, particularly for the diagnosis of primary brain tumours and gliomas in a recent meta-analysis (6). Though FET-PET qualitative uptake analyses are not reliably linked to tumour grading, dynamic FET-PET analysis helps in differentiating high- from low-grade tumours (28).

As MRI and FET-PET combination improves the diagnostic accuracy of MRI (23) and MRS (8), the purpose of this report was to determine whether the combination of MRI, MRS and ADC maps with dynamic FET-PET could improve initial tumour grading in patients with newly diagnosed glioma, which could be of interest for simultaneous PET-MR.

Patients, material, methods

Study design

Between January 2006 and July 2012, forty-two patients (15 women, 27 men, aged 42±15 years) with suspected primary brain tumour on conventional MRI were prospectively enrolled in this study. Every patient underwent an MRI with MRS and ADC mapping followed by a FET-PET within 3±4 weeks (median 2 weeks). In 39 patients, subsequent surgical stereotactic tumour biopsy or tumour resection was performed and tumours were histologically classified according to the WHO classification of tumours of the central nervous system and the 3rd edition of the International Classification of Diseases for Oncology (ICD-O-3). Gliomas were defined by ICD-O-3 codes 9380–9384, 9391–9460 and 9480, the pathologist being blinded for imaging results. In three patients, biopsy or surgical resection could not be performed; in one patient, the lesion was characterized as a demyelinating, and in the two others, lesions not accessible for biopsy due to their location in the cerebral trunk were classified as low-grade tumours on absence of change on MRI follow-up at 3, 6 and 12 months.

The study protocol was approved by the State of Vaud Ethics Committee and Federal Regulatory Agencies. Each participant gave written informed consent before inclusion.

MRI protocol

MR images were obtained with an 3-T imager and included sagittal T1-weighted spin-echo (repetition time 400 ms/echo time 3 ms; 3-mm section thickness, matrix size of 448×420), axial T2-weighted spin-echo (5000/85; 3-mm section thickness; 24 cm field-of-view; matrix size of 512×448), and contrast enhanced (gadoteric acid, Dotarem, Guerbet, Switzerland; 0.1 mmol/kg) axial T1-weighted spin-echo (400/3; 3-mm section thickness; matrix size of 448×380) sequences. Diffusion weighted imaging (DWI) or diffusion tensor imaging (DTI) images were also acquired. DWI was performed by using DWI pulse sequence (5000/85; 3–5 mm section thickness; 24-cm field-of-view; matrix size of 256×256) at b = 0 s/mm² and three orthogonal diffusion weighted acquisitions at b = 1000 sec/mm², ADCs being calculated from the trace images. DTI was performed by using 6–30 direction DTI sequence (5000/85; 3–5-mm section thickness; 24 cm field-of-view; matrix size of 256×256) at b = 0 s/mm² and b = 1000 s/mm² from which ADCs were calculated.

Single voxel spectroscopy was performed after gadolinium enhanced T1-weighted image acquisition using a 135-ms echo time. A standard 1-cm³ voxel was placed on the area of tumour that enhanced on post-gadolinium T1-weighted images as visually assessed on subtraction T1-weighted images or on the center of the tumour when there was no significant enhancement. The metabolite peaks were assigned as follows: choline 3.22 ppm; creatine 3.02 ppm; N-acetylaspartate 2.02 ppm. Tumour spectra and metabolite ratios were obtained by an experienced neuroradiologist (PM.) to ensure quality and consistency of spectroscopic data. Maximal choline / creatine ratio was collected for every patient. Using a previously described threshold of 1.56 to distinguish between low and high-grade gliomas patients were secondarily dichotomized based on choline / creatine ratios (19).

FET-PET protocol

FET-PET acquisitions were performed on PET/CT scanner (Discovery LS, GE Healthcare, Milwaukee, Michigan, USA). All patients fasted for at least 4 hours from any intake prior to FET injection as recommended by EANM guidelines (32). After
intravenous infusion of 203±26 MBq (median 203 MBq) of FET, PET images were acquired using a dynamic protocol over 60 minutes (12 frames of 5 min; 4.2-mm section thickness; 24 cm field-of-view, matrix size of 256 × 256). Raw data were corrected for attenuation by soft tissue and skull bone using an unenhanced cerebral CT (120 kV, 10 mAs) and normalized to the injected dose and body mass by calculation of the standardized uptake value (SUV).

MRI and FET-PET analyses

All images analyses were performed using dedicated PET/CT/MR software (PMOD 3.1, PMOD Technologies, Zurich, Switzerland). Observers were blinded to histological results. Region-of-interest (ROInt) around the tumour were manually delineated (V.D., M.N.L) on consecutive slices of averaged 50–60 min FET-PET images using fixed displayed window width (0.3–4.0 g/ml). Tumour volume-of-interest (VOIt) was defined as the sum of allROInt. This VOIt was used to measure tumour mean SUV (SUVmean) and maximum SUV (SUVmax). Another VOI was drawn on contralateral normal brain to measure SUVmean of the background (VOIb) in case of a lateralized lesion and on a nearby midline structure devoid of tumour for midline lesions. Maximal and mean target-to-background ratios (TBR) of the tumour were determined as the ratio of tumour SUVmax and SUVmean over background SUVmean. As previously reported by Calcagni et al. (4) early-to-middle (e-m) ratio was also calculated as the ratio between early frames (5–10 min) and middle frames (30–35 min) tumour SUVmax. Using previously described threshold of 0.93 to distinguish between low and high-grade gliomas patients were dichotomized based on e-m ratio. A 90% SUVmax isocontour threshold VOI was finally drawn within theVOI and applied on the whole dynamic acquisition (0–60 min) to determine tumour time-activity-curve (TAC), the tumour being subsequently dichotomized in increasing or decreasing TAC according to the curve slope calculated between early (5–10 min) and last frame (55–60min) (13).

Similarly, ADC maps were transferred to the same workstation and automatically realigned using MR-PET automatic coregistration based on mutual information with FET images. TheVOIt defined on FET-PET images was applied to the ADC images and tumour pixel-by-pixel ADC values expressed in units of 106 mm2/s were extracted, tumour ADCmin and ADCmean values being secondarily calculated. As reported by Pope et al. (25), ADCs calculated on a pixel-by-pixel basis were exported to Stata 12.1 software and used for histogram analysis. Univariate kernel density estimation was first performed to estimate the probability density function of ADC pixel values. As previously reported by Pope et al., a two-mixture normal distribution was subsequently used and ADC histograms were analyzed and divided into unimodal or bimodal pattern (25). ADCmean values for the upper and lower peak (ADCL, lower-curve mean, and ADCH, upper-curve mean) were collected and ADC histogram was classified as bimodal when ADCH > ADCL + 1.56.

Statistical analysis

All statistics were performed with Stata 12.1 (Stata College Station, Texas, USA) and a p value < 0.05 was considered as statistically significant. Dichotomized histological diagnosis (low-grade or high-grade glioma) according to the WHO classification of tumours of the central nervous system (20) and the 3rd edition of the International Classification of Diseases for Oncology (ICD-O-3) was used as the gold standard. ADCmean, ADCmin, SUVmax, SUVmean, TBRmax, TBRmean, e-m ratio and choline / creatine ratio values between low and high-grade tumours were compared by using Wilcoxon sum rank test. Sensitivity, specificity, accuracy, positive and negative predictive values and the respective 95% confidence intervals (CI) were calculated for each of the following diagnostic parameters: choline / creatine ratio (≤1.56 or >1.56), ADC histogram pattern (uni- or bimodal), early-to-middle SUVmax ratio (≤0.93 or >0.93), tumour FET uptake TAC pattern (increasing or decreasing) and in combination. Accuracy was estimated as follow: accuracy = (number of true positives + true negatives) / (number of true positives + false positives + true negatives + false negatives).

Mc Nemar test was used to compare the sensitivity and specificity of the different parameters. Subsequently, multivariate logistic regression analysis was carried out to

**Tab. 1**

<table>
<thead>
<tr>
<th>characteristics</th>
<th>low-grade</th>
<th>high-grade</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>16</td>
<td>22</td>
<td>0.3</td>
</tr>
<tr>
<td>age (years)</td>
<td>39±14</td>
<td>44±15</td>
<td>0.09</td>
</tr>
<tr>
<td>sex ratio (men:women)</td>
<td>11:5</td>
<td>15:7</td>
<td>0.7</td>
</tr>
<tr>
<td>SUV (g/ml)</td>
<td>max</td>
<td>2.8±1.7</td>
<td>0.7</td>
</tr>
<tr>
<td></td>
<td>mean</td>
<td>1.7±0.9</td>
<td>0.7</td>
</tr>
<tr>
<td>TBR</td>
<td>max</td>
<td>2.1±0.7</td>
<td>0.7</td>
</tr>
<tr>
<td></td>
<td>mean</td>
<td>1.3±0.3</td>
<td>0.8</td>
</tr>
<tr>
<td>early-to-middle</td>
<td>ratio &gt; 0.93</td>
<td>0.93±0.12</td>
<td>0.1</td>
</tr>
<tr>
<td>FET PET TAC</td>
<td>increasing/decreasing</td>
<td>10/5</td>
<td>7/14</td>
</tr>
<tr>
<td>ADC (10^6 mm^2/s)</td>
<td>mean</td>
<td>1174±277</td>
<td>0.2</td>
</tr>
<tr>
<td></td>
<td>min</td>
<td>276±222</td>
<td>1.0</td>
</tr>
<tr>
<td>choline / creatine</td>
<td>ratio</td>
<td>2.1±1.3</td>
<td>0.5</td>
</tr>
<tr>
<td></td>
<td>ratio &gt; 1.56</td>
<td>6/9</td>
<td>1.0</td>
</tr>
</tbody>
</table>
predict tumoural grade by including significant variables on univariate analysis (p < 0.1) as dependent variables to determine individual odds and their respective 95% CI.

Results

Study population

42 patients were included in this study. Three patients did not have biopsy or tumour resection and were thus excluded from further analyses. For one patient histological analysis reveals medulloblastoma. 38 patients with histological diagnosis of gliomas were finally retained (mean age 42±15 y; sex ratio F : M= 0.46). Of these patients, 16 had low-grade gliomas (41%): astrocytoma (n = 8), oligoastrocytome (n = 6), oligodendroglome (n = 2). 22 had high-grade gliomas (59%): anaplastic (n = 16) and glioblastoma (n = 6). Contrast enhancement was present in 9 of 22 patients with high-grade glioma and in 6 of 16 patients with low-grade glioma. In this population, contrast enhancement had thus poor sensitivity, specificity and accuracy of 41%, 60% and 49% to distinguish between low and high-grade glioma. Patient characteristics as well as MR and FET-PET results for low- and high-grade gliomas are summarized (▶Tab. 1).

Spectroscopy and ADC histogram analyses

Out of the 38 included patients, 33 (87%) had MRS of sufficient quality to provide choline / creatine ratio. For five patients MRS results could not be used due to proximity of bone or cerebrospinal fluid. Choline / creatine ratio was not significantly different between low-grade and high-grade gliomas (p = 0.5) (▶Tab. 1). Using previously described threshold for choline / creatine ratio of 1.56, MRS reached sensitivity, specificity and accuracy of 56%, 40% and 48% respectively (▶Tab. 2) (19).

37 (97%) MR examinations had analysable ADC maps, one having patient motion artefacts. ADC histogram was bimodal in 6 of 16 patients (38%) with low-grade gliomas (▶Fig. 1a) while ADC histogram was of 62%, 53% and 58% to identify high-grade gliomas (▶Tab. 2). Moreover, patients with high-grade gliomas mostly had a decreasing TAC (▶Fig. 1b, 1c), this latter having thus a very good positive predictive value of 74% (▶Tab. 2).

Combination of MRI and FET-PET

According to criteria of dichotomization described above for choline / creatine ratio and ADC histogram results, combination of MRS and diffusion imaging reached a sensitivity, specificity and accuracy of 77%, 31% and 58% to distinguish between low and high-grade gliomas. There was only moderate concordance of 63% between both imaging modalities.

<table>
<thead>
<tr>
<th>parameter</th>
<th>sensitivity</th>
<th>specificity</th>
<th>accuracy</th>
<th>PPV</th>
<th>NPV</th>
<th>LR+</th>
<th>LR−</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 early-to-middle ratio &gt; 0.93</td>
<td>62 [38–81]</td>
<td>53 [27–78]</td>
<td>58 [38–79]</td>
<td>65 [41–84]</td>
<td>50 [26–74]</td>
<td>1.3 [0.7–2.5]</td>
<td>0.7 [0.4–1.4]</td>
</tr>
<tr>
<td>2 decreasing TAC</td>
<td>67 [43–85]</td>
<td>67 [39–87]</td>
<td>67 [47–86]</td>
<td>74 [49–90]</td>
<td>59 [33–81]</td>
<td>2.0 [0.9–4.3]</td>
<td>0.5 [0.3–1.0]</td>
</tr>
<tr>
<td>3 bimodal ADC histogram</td>
<td>67 [43–85]</td>
<td>63 [36–84]</td>
<td>65 [45–85]</td>
<td>70 [46–87]</td>
<td>59 [33–81]</td>
<td>1.8 [0.9–3.6]</td>
<td>0.5 [0.3–1.1]</td>
</tr>
<tr>
<td>4 choline / creatine &gt; 1.56</td>
<td>56 [31–78]</td>
<td>40 [17–67]</td>
<td>48 [27–70]</td>
<td>53 [29–75]</td>
<td>43 [19–70]</td>
<td>0.9 [0.5–1.7]</td>
<td>1.1 [0.5–2.3]</td>
</tr>
<tr>
<td>5 2 or 3</td>
<td>86 [64–96]</td>
<td>31 [12–59]</td>
<td>63 [44–83]</td>
<td>63 [44–79]</td>
<td>63 [26–90]</td>
<td>1.3 [0.9–1.8]</td>
<td>0.4 [0.1–1.6]</td>
</tr>
<tr>
<td>6 3 or 4</td>
<td>77 [54–91]</td>
<td>31 [12–59]</td>
<td>58 [38–78]</td>
<td>61 [41–78]</td>
<td>50 [20–80]</td>
<td>0.5 [0.2–0.8]</td>
<td>0.5 [0.2–0.8]</td>
</tr>
<tr>
<td>7 2 and 3</td>
<td>41 [21–63]</td>
<td>100 [76–100]</td>
<td>66 [47–85]</td>
<td>100 [63–100]</td>
<td>55 [36–73]</td>
<td>∞</td>
<td>0.6 [0.4–0.8]</td>
</tr>
</tbody>
</table>

ADC: apparent diffusion coefficient; LR: likelihood ratio; P(N)PV: positive (negative) predictive value; TAC: time activity curve

FET-PET

FET-PET tumour e-m ratio and TAC were reliably obtained in thirty-six of thirty-eight patients (95%) due to patient motion during the acquisition. Early-to-middle ratio was not significantly different between low-grade and high-grade gliomas (p = 0.1). Using previously described threshold of 0.93 for distinguishing between low and high-grade gliomas, e-m ratio sensitivity, specificity and accuracy was of 62%, 53% and 58% to identify high-grade gliomas (▶Tab. 2). Moreover, patients with high-grade gliomas mostly had a decreasing TAC (▶Fig. 1b, 1c), this latter having thus a very good positive predictive value of 74% (▶Tab. 2).

Tab. 2 Performances of MRI and FET-PET parameters for glioma grading (values [95%CI])
The combination of dynamic FET-PET with diffusion imaging presented the best performances in univariate analysis and their combination was secondarily assessed. When considering decreasing TAC or bimodal ADC histogram as indicative of high-grade glioma, the combination of both modalities had a significant higher sensitivity (p = 0.005) than any modality alone (▶ Tab. 2), however with a poor specificity. TAC analyses were concordant with ADC analyses in only 17 of 38 patients (46%) (▶ Fig. 1a, 1b) and discordant in 21 of 38 patients (54%) (▶ Fig. 1c). TAC analyses were concordant with MRS analyses in 18 of 38 patients (48%). Inversely, when considering only tumours that had both decreasing TAC and bimodal ADC histogram distribution as positive results for identifying high-grade gliomas, we reached a perfect specificity of 100% (p = 0.008).

Multivariate logistic regression analysis revealed that a decreasing TAC was the best predictor of high-grade glioma (odds ratio 7.6; 95% CI: 1.3–44; p = 0.022) followed by a bimodal ADC histogram distribution (odds 6.3; 95% CI: 1.1–36; p = 0.038) (▶ Tab. 3).

Discussion

This study suggests that combining MRI and FET-PET parameters has good performance for the initial grading of untreated gliomas. For identifying high-grade gliomas, a decreasing tumour FET uptake TAC had the best positive predictive value. However, when combining the latter with ADC histogram analysis, we demonstrated that a good sensitivity to predict high-grade glioma could be reached (decreased TAC OR bimodal ADC histogram). Moreover, these two criteria can be combined to reach an excellent specificity (decreased TAC AND bimodal ADC histogram).

Owing to the need for better identifying brain tumour with high metabolic activity for better patient management, FET was developed in the past decade. FET-PET was demonstrated to be helpful in distinguishing between non-tumour and proliferative tumour lesion (31, 34), between infectious and tumour lesion (30), or between radionecrosis and recurrent tumour (31).

Fig. 1 Imaging of primary brain tumours (ADC: apparent diffusion coefficient; FET: 18F-fluoro-ethyl-tyrosine; PET: positron emission tomography; SUV: standard uptake value)

a) WHO grade I pilocytic astrocytoma:
A. T2-weighted image showing a hyperintense left cerebellar hemisphere lesion. B. ADC maps showing no diffusion restriction C. ADC histogram showing a unimodal distribution. D. Post-gadolinium T1-weighted image showing no enhancement. E. Corresponding 50–60 min PET image showing high FET uptake (SUV\textsubscript{max} = 4.0 g/ml). F. Time-activity-curve with increasing slope pattern.

b) WHO grade III anaplastic oligodendroglioma:
A. T2-weighted image showing a hyperintense lesion of the right thalamus and posterior limb of the internal capsule. B. ADC maps showing focal diffusion restriction. C. ADC histogram showing a bimodal distribution. D. Post-gadolinium T1-weighted image showing little enhancement. E. Corresponding 50–60 min PET image showing high FET uptake (SUV\textsubscript{max} = 2.5 g/ml). F. Time-activity-curve with a decreasing slope pattern.
Following these early studies in tumour recurrence (26), several human studies assessed FET-PET performances in the initial evaluation of isolated brain tumour. A recent meta-analysis confirmed that FET-PET is highly relevant for the initial diagnosis of primary brain tumour and gliomas (6). However, gliomas constitute a large spectrum of disease and tumour grading is critical to determine patient prognosis and first line therapy. Qualitative FET-PET uptake is not directly linked to glioma grading. The uptake mechanism of this artificial amino acid involves Na⁺-independent system L and ubiquitous Na⁺-dependent system, similarly to the natural amino-acid C-methionine. While both tracers are taken up into upregulated neoplastic cells, FET is not incorporated into proteins. Several studies aimed at determining whether FET uptake quantitation is of value in grading gliomas. Though low-grade gliomas had significantly lower TBRmean (1.7±0.7 vs. 2.6±1.0, p < 0.001) and TBRmax (2.4±1.0 vs. 3.0±1.1, p < 0.001) than high-grade gliomas in the meta-analysis by Dunet et al., the overlap does not allow using this parameter at the patient level (6).

Using dynamic PET acquisition, a recent study by Calcagni et al. (4) reported accurate distinction between low-grade and high-grade gliomas by using the early-to-middle uptake ratio and a threshold of 0.93. When using the same methodology and e-m ratio threshold, we were not discriminant however. This might be due to the presence in their study population of one third of recurrent tumours that could exhibit modified amino-acid metabolism and transport. Other studies reported tumour time-activity-curves pattern as a relevant indicator for grading glioma (13, 28) or for detecting recurrence (27). In comparison with these results, we demonstrated a good positive predictive value but moderate accuracy of a decreasing TAC to indentify anaplastic glioma or glioblastoma. It could be due to the higher proportion of glioma with oligodendroglial components in our study population, which influences TAC-based uptake ratio rather depends on cellular type in normal brain and in gliomas (10).

In the study by Pauleit et al. (23), PET-MR fusion increased specificity from 53% for MRI alone to 94% to guide diagnostic biopsy. Similarly, Floeth et al. (8) reported that the combination of MRI with MRS and FET-PET yielded an accuracy of 97% for the diagnosis of primary brain tumour. Extending these observations, we further found that combining MRS and diffusion imaging increased our ability to correctly identify tumour grade. Moreover, by using histogram analysis of ADC maps and dynamic FET-PET results, we demonstrated that diffusion MRI and dynamic FET-PET combination...
could provide better performances for grading gliomas, with a good sensitivity of 86% and a high specificity of 100%. The combination of FET-PET and ADC mapping may non-invasively assess both tumour metabolism and cell density. By integrating an indirect measure of cell density with ADC maps (7) and an indirect measure of cell amino acid transport with dynamic FET-PET, both cell density and metabolism may be evaluated to determine tumour aggressiveness potential. Consequently, we do believe that, by improving initial assessment of primary brain tumour, FET-PET/MR can be used for better selecting patients who can benefit from aggressive first line therapy.

Further investigations including larger population while applying the recommended standardization for FET-PET acquisition as well as determining optimal PET-MR protocol are now needed (11, 18, 32). The ability of dynamic FET-PET and diffusion MRI combination for diagnosing tumour recurrence, assessing response to therapy and patients prognosis should be also evaluated. Finally, the usefulness of images acquisition on latest PET/MR imagers as compared to PET-MR on different machines should be investigated in order to both improve cost effectiveness and accelerate patients’ management.

Conclusion

Our results indicate that the combination of dynamic FET-PET and diffusion MRI may achieve a high diagnostic value for grading of gliomas. The use of combined modalities with optimized standardized acquisition protocol and analysis, potentially on latest PET/MR imagers should be highly relevant for the management of patients with primary brain tumours.

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Conflict of interest

The authors do not declare any conflict of interest

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References