

# Evidence-Based PET for Brain Tumours

# 3

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## 3.1 Background

Positron emission tomography (PET) using different radiotracers evaluating different metabolic patterns is able to early detect pathophysiological changes in oncological patients, including those with brain tumours. These functional changes usually occur before the development of morphological changes detected by conventional radiological imaging techniques such as computed tomography (CT) and magnetic resonance imaging (MRI) [1]. MRI is the standard neuroimaging method used for diagnosis of brain tumours, for performing stereotactic biopsy and surgical planning in neuro-oncology [2]. Currently, hybrid

imaging techniques as PET/CT and PET/MRI, providing a combination of both functional and morphological information, may be useful methods for early diagnosis of brain tumours [1, 2].

Different PET radiotracers have been used to evaluate brain tumours including fluorine-18 fluorodeoxyglucose ( $^{18}\text{F}$ -FDG), carbon-11 methionine ( $^{11}\text{C}$ -methionine), fluorine-18 fluoroethyltyrosine ( $^{18}\text{F}$ -FET), fluorine-18 fluorodihydroxyphenylalanine ( $^{18}\text{F}$ -FDOPA), fluorine-18 fluorothymidine ( $^{18}\text{F}$ -FLT) and radiolabelled choline ( $^{11}\text{C}$ -choline or  $^{18}\text{F}$ -choline).

Enough literature data already exist about the diagnostic performance and prognostic value of PET with different tracers in brain tumours. In particular, 24 meta-analyses on the use of PET or PET/CT with different tracers in brain tumours, published from 2012, were selected through a comprehensive computer literature search [3–26]. The findings of the selected meta-analyses on the diagnostic performance are presented in Table 3.1. Here below we have summarized the main findings of meta-analytic studies based on the different clinical indications of PET or PET/CT.

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## 3.2 Evaluation of Suspicious Primary Brain Tumour

Four meta-analyses have assessed the diagnostic performance of PET or PET/CT with different tracers in patients for whom primary brain tumours are suspected [3, 20, 23, 26].

**Table 3.1** Characteristics and main findings of included meta-analyses on the diagnostic performance of PET or PET/CT with different tracers in patients with brain tumours

| Indication                                    | Tracer                     | Authors                    | Sensitivity (95%CI)                       | Specificity (95%CI)                       | LR+ (95%CI)    | LR- (95%CI)      | DOR (95%CI)         |
|---|----------------------------|----------------------------|---|---|----------------|------------------|---------------------|
| Evaluation of suspicious primary brain tumour | <sup>18</sup> F-FDG        | Zhao et al. [23]           | 43% (28–59)                               | 74% (49–90)                               | 1.7 (0.6–4.8)  | 0.77 (0.48–1.24) | NR                  |
|   |                            | Dunet et al. [20]          | 38% (27–50)                               | 86% (31–99)                               | 2.7 (0.3–27.8) | 0.72 (0.47–1.11) | 4 (0–58)            |
|   | <sup>11</sup> C-methionine | Zhao et al. [23]           | 95% (85–98)                               | 83% (65–93)                               | 5.5 (2.5–12.2) | 0.07 (0.02–0.2)  | NR                  |
|   | <sup>18</sup> F-FET        | Dunet et al. [26]          | 82% (74–88)                               | 76% (44–92)                               | 3.4 (1.2–9.5)  | 0.24 (0.14–0.39) | 14 (3–60)           |
|   |                            | Dunet et al. [20]          | 94% (79–98)                               | 88% (37–99)                               | 8.1 (0.8–80.6) | 0.07 (0.02–0.30) | 113 (4–2975)        |
|   | <sup>18</sup> F-FDOPA      | Xiao et al. [3]            | 71% (54–85)                               | 86% (42–100)                              | 3.7 (0.9–15.8) | 0.36 (0.19–0.68) | 10.88 (1.57–75.31)  |
| Glioma grading                                | <sup>18</sup> F-FDG        | Dunet et al. [20]          | 60% (mean TBR ≥1.4)<br>72% (max TBR ≥1.8) | 91% (mean TBR ≥1.4)<br>73% (max TBR ≥1.8) | NR             | NR               | NR                  |
|   |                            | Katsanos et al. [6]        | 63% (51–74)                               | 89% (73–95)                               | 5.2 (2.1–13)   | 0.42 (0.29–0.6)  | 12.4 (3.86–39.8)    |
|   | <sup>11</sup> C-methionine | Falk Delgado et al. [14]   | 80% (66–88)                               | 72% (62–81)                               | NR             | NR               | NR                  |
|   |                            | Katsanos et al. [6]        | 94% (79–98)                               | 55% (32–77)                               | 2.1 (1.25–3.5) | 0.11 (0.03–0.37) | 18.25 (4.73–70.5)   |
|   | <sup>18</sup> F-FET        | Dunet et al. [20]          | 88% (mean TBR ≥2)<br>80% (max TBR ≥3)     | 73% (mean TBR ≥2)<br>82% (max TBR ≥3)     | NR             | NR               | NR                  |
|   |                            | Katsanos et al. [6]        | 88% (82–93)                               | 57% (40–73)                               | 2.1 (1.4–3.15) | 0.2 (0.11–0.37)  | 10.16 (3.9–26.5)    |
|   | <sup>18</sup> F-FDOPA      | Xiao et al. [3]            | 88% (81–93)                               | 73 (64–81)                                | 2.9 (2.2–3.85) | 0.16 (0.08–0.36) | 25.87 (10.53–63.54) |
|   | Glioma delineation         | <sup>11</sup> C-methionine | Verburg et al. [16]                       | [HGG]<br>93.7%                            | [HGG]<br>61.3% | NR               | NR                  |

**Table 3.1** (continued)

| Indication                          | Tracer                     | Authors             | Sensitivity<br>(95%CI)  | Specificity<br>(95%CI)   | LR+<br>(95%CI)               | LR-<br>(95%CI)               | DOR<br>(95%CI)         |
|-------------------------------------|----------------------------|---------------------|-------------------------|--------------------------|------------------------------|------------------------------|------------------------|
| Diagnosis of recurrent brain tumour | <sup>18</sup> F-FDG        | Nihashi et al. [25] | 77%<br>(66–85)          | 78%<br>(54–91)           | 3.4<br>(1.6–7.5)             | 0.3<br>(0.21–0.43)           | NR                     |
|                                     |                            | Zhao et al. [23]    | 75%<br>(67–81)          | 79%<br>(66–88)           | 3.5<br>(2.2–5.7)             | 0.32<br>(0.25–0.41)          | NR                     |
|                                     |                            | Li et al. [21]      | 78%<br>(69–85)          | 77%<br>(66–85)           | 3.3<br>(2.2–5)               | 0.29<br>(0.20–0.42)          | 12<br>(6–22)           |
|                                     |                            | Wang et al. [22]    | 70%<br>(64–75%)         | 88%<br>(80–93%)          | 4<br>(2.1–7.5)               | 0.38<br>(0.29–0.51)          | NR                     |
|                                     |                            | Furuse et al. [7]   | 81%<br>(67–90)          | 72%<br>(64–79)           | NR                           | NR                           | NR                     |
|                                     | <sup>11</sup> C-methionine | Nihashi et al. [25] | [HGG]<br>70%<br>(50–84) | [HGG]<br>93%<br>(44–100) | [HGG]<br>10.3<br>(0.8–139.4) | [HGG]<br>0.32<br>(0.18–0.57) | NR                     |
|                                     |                            | Deng et al. [24]    | 87%<br>(81–91.8)        | 81.3%<br>(71.5–88.8)     | 4.35<br>(2.8–6.8)            | 0.19<br>(0.13–0.29)          | 21.86<br>(10.7–44.5)   |
|                                     |                            | Zhao et al. [23]    | 92%<br>(83–97)          | 87%<br>(75–93)           | 6.8<br>(3.4–13.7)            | 0.09<br>(0.04–0.21)          | NR                     |
|                                     |                            | Wang et al. [22]    | 85%<br>(76–91%)         | 83%<br>(71–92%)          | 4.4<br>(2.5–7.7)             | 0.22<br>(0.13–0.35)          | NR                     |
|                                     |                            | Xu et al. [13]      | 88%<br>(85–91%)         | 85%<br>(80–89)           | 5.3<br>(3.3–8.7)             | 0.16<br>(0.11–0.23)          | 35.3<br>(22.9–54.4)    |
|                                     |                            | Furuse et al. [7]   | 81%<br>(73–87)          | 81%<br>(74–87)           | NR                           | NR                           | NR                     |
|                                     | <sup>18</sup> F-FET        | Yu et al. [11]      | 82%<br>(79–84)          | 80%<br>(76–83)           | 3.9<br>(3.0–5.1)             | 0.21<br>(0.17–0.27)          | 23.03<br>(14.42–36.77) |
|                                     |                            | Furuse et al. [7]   | 91%<br>(79–97)          | 95%<br>(61–99)           | NR                           | NR                           | NR                     |
|                                     | <sup>18</sup> F-FDOPA      | Yu et al. [11]      | 85%<br>(81–88)          | 77%<br>(74–81)           | 3.4<br>(2.8–4.3)             | 0.21<br>(0.16–0.29)          | 21.7<br>(12.61–37.33)  |
|                                     |                            | Xiao et al. [3]     | 92%<br>(88–95)          | 76%<br>(66–85)           | 2.9<br>(2–4.1)               | 0.13<br>(0.07–0.23)          | 29.65<br>(13.09–67.15) |
|                                     | AA*                        | Kim et al. [4]      | 89%<br>(82–94)          | 88%<br>(76–94)           | 7.3<br>(3.6–14.7)            | 0.12<br>(0.07–0.21)          | 60<br>(23–152)         |
|                                     | <sup>18</sup> F-FLT        | Li et al. [21]      | 82%<br>(51–95)          | 76%<br>(50–91)           | 3.5<br>(1.6–7.7)             | 0.24<br>(0.08–0.70)          | 15<br>(4–56)           |
|                                     | <sup>11</sup> C-choline    | Gao et al. [9]      | 87%<br>(78–93)          | 82%<br>(69–91)           | 4.9<br>(2.6–9.1)             | 0.16<br>(0.09–0.29)          | 35.5<br>(11.7–107.7)   |

(continued)

**Table 3.1** (continued)

| Indication                              | Tracer                     | Authors           | Sensitivity (95%CI) | Specificity (95%CI) | LR+ (95%CI)       | LR- (95%CI)      | DOR (95%CI)       |
|---|----------------------------|-------------------|---------------------|---------------------|-------------------|------------------|-------------------|
| Diagnosis of brain metastases           | <sup>18</sup> F-FDG        | Li et al. [19]    | 21% (13–32)         | 100% (99–100)       | 184.7 (24.8–1374) | 0.79 (0.70–0.89) | 235 (31–1799)     |
| Diagnosis of recurrent brain metastases | <sup>18</sup> F-FDG        | Li et al. [12]    | 85% (77–94)         | 90% (83–96)         | NR                | NR               | NR                |
|   |                            | Suh et al. [8]    | 83% (74–92)         | 88% (81–95)         | NR                | NR               | NR                |
|   |                            | Furuse et al. [7] | 91% (73–97)         | 80% (60–91)         | NR                | NR               | NR                |
|   | <sup>11</sup> C-methionine | Li et al. [12]    | 86% (74–97)         | 79% (66–93)         | NR                | NR               | NR                |
|   |                            | Furuse et al. [7] | 79% (67–87)         | 76% (61–87)         | NR                | NR               | NR                |
|   | <sup>18</sup> F-FET        | Li et al. [12]    | 83% (76–91)         | 89% (83–95)         | NR                | NR               | NR                |
|   |                            | Yu et al. [11]    | 80% (76–84)         | 79% (75–83)         | 3.9               | 0.24             | 19                |
|   | <sup>18</sup> F-FDOPA      | Li et al. [12]    | 86% (74–97)         | 88% (79–97)         | NR                | NR               | NR                |
| Yu et al. [11]                          |                            | 78% (73–82)       | 75% (71–89%)        | 3                   | 0.31              | 11               |                   |
| AA*                                     | Suh et al. [8]             | 84% (79–90)       | 85% (80–91)         | NR                  | NR                | NR               |                   |
| Diagnosis of PCNSL                      | <sup>18</sup> F-FDG        | Zhou et al. [17]  | 88% (80–94)         | 86 (73–94)          | 4 (2.3–6.9)       | 0.11 (0.04–0.32) | 33.4 (10.4–107.3) |
|   |                            | Yang et al. [18]  | NR                  | NR                  | NR                | NR               | NR                |

LR+ positive likelihood ratio; LR- negative likelihood ratio; DOR diagnostic odds ratio; 95%CI 95% confidence interval; AA\* radiolabelled amino acid PET including radiolabelled methionine, fluoroethyltyrosine and fluorodihydroxy-phenylalanine; NR not reported; HGG high-grade gliomas only; PCNSL primary central nervous system lymphoma; mean TBR mean tumour-to-background uptake ratio; max TBR maximum tumour-to-background uptake ratio

### 3.2.1 <sup>18</sup>F-FDG

A meta-analysis including patients with suspicious primary brain tumours showed that <sup>18</sup>F-FDG PET or PET/CT has a moderate sensitivity and specificity for differentiating brain tumours from non-tumour lesions. False-positive findings were often due to inflammatory lesions or other non-tumour tissues; on the other hand, reduced <sup>18</sup>F-FDG uptake in brain tumours is usually influenced by the high physiological glucose metabolism in surrounding normal brain tissue, leading to a decreased sensitivity [23]. Another meta-analysis also demonstrated that <sup>18</sup>F-FDG PET or PET/CT has a moderate diagnostic performance in distinguishing between tumour and non-tumour lesions in the brain, lower than amino acid PET [20].

### 3.2.2 <sup>11</sup>C-Methionine

A meta-analysis by Zhao et al. demonstrated a good diagnostic performance of <sup>11</sup>C-methionine PET or PET/CT in detecting brain tumours (pooled sensitivity and specificity were of 95% and 83%, respectively) with higher diagnostic accuracy values compared to <sup>18</sup>F-FDG PET or PET/CT, likely due to the higher <sup>11</sup>C-methionine uptake in brain tumours and lower accumulation in normal brain tissue [23].

### 3.2.3 <sup>18</sup>F-FET

For initial assessment of patients with a newly diagnosed brain lesion, <sup>18</sup>F-FET PET or PET/CT demonstrated a good performance in the diagno-

sis of a brain tumour with a pooled sensitivity and specificity of 82% and 76%, respectively. A mean tumour-to-background uptake ratio (TBR) threshold of at least 1.6 and a maximum TBR of at least 2.1 had the best diagnostic value for differentiating brain tumours from non-tumour brain lesions. For the diagnosis of glioma versus non-glioma brain lesions,  $^{18}\text{F}$ -FET PET or PET/CT demonstrated a good sensitivity (84%) but a not adequate specificity (62%) [26]. In a head-to-head comparative meta-analysis, the diagnostic performance of  $^{18}\text{F}$ -FET PET or PET/CT in distinguishing between tumour and non-tumour lesions in the brain was found significantly higher compared to that of  $^{18}\text{F}$ -FDG PET or PET/CT performed in the same patients [20].

### 3.2.4 $^{18}\text{F}$ -FDOPA

$^{18}\text{F}$ -FDOPA PET or PET/CT revealed a moderate sensitivity (71%) and a good specificity (86%) in detecting newly diagnosed gliomas [3].

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## 3.3 Glioma Grading

Gliomas are the most frequent primary brain tumours. High-grade gliomas like glioblastomas are the most common gliomas in adults, with a poor prognosis with any current therapy. Conversely, low-grade gliomas, the second most common type of gliomas, are potentially curable with appropriate treatment. Several meta-analyses have evaluated the role of PET or PET/CT with different tracers in differentiating between high-grade and low-grade gliomas [3, 6, 14, 20].

### 3.3.1 $^{18}\text{F}$ -FDG

$^{18}\text{F}$ -FDG uptake is significantly higher in high-grade gliomas compared with low-grade gliomas. According to the meta-analysis of Dunet et al., a mean TBR of at least 1.4 and a maximum TBR of at least 1.8 at  $^{18}\text{F}$ -FDG PET had

the best value to distinguish between low- and high-grade gliomas, with a sensitivity, specificity and accuracy of 60%, 91% and 74%, respectively, for mean TBR and 72%, 73% and 72%, respectively, for maximum TBR [20]. A recent meta-analysis demonstrated a lower sensitivity of  $^{18}\text{F}$ -FDG PET or PET/CT in differentiating between high-grade and low-grade gliomas compared to radiolabelled amino acid PET ( $^{11}\text{C}$ -methionine and  $^{18}\text{F}$ -FET) but with higher specificity [6].

### 3.3.2 $^{11}\text{C}$ -Methionine

$^{11}\text{C}$ -methionine PET or PET/CT had a moderate diagnostic accuracy in differentiating between high-grade and low-grade gliomas, according to data provided by a recent meta-analysis (pooled sensitivity and specificity of 80% and 72%, respectively) [14]. Another meta-analysis demonstrated that  $^{11}\text{C}$ -methionine PET or PET/CT has a higher sensitivity compared to  $^{18}\text{F}$ -FDG PET or PET/CT in differentiating between high-grade and low-grade gliomas but with lower specificity; diagnostic performance values were similar to those of  $^{18}\text{F}$ -FET PET or PET/CT in this setting [6].

### 3.3.3 $^{18}\text{F}$ -FET

$^{18}\text{F}$ -FET uptake is significantly higher in high-grade gliomas compared with low-grade gliomas. Dunet et al. reported that a mean TBR of at least 2.0 and a maximum TBR of at least 3.0 at  $^{18}\text{F}$ -FET PET reached a sensitivity, specificity and accuracy of 88%, 73% and 81%, respectively, for mean TBR, and 80%, 82% and 81%, respectively, for maximum TBR [20]. A recent meta-analysis demonstrated that  $^{18}\text{F}$ -FET PET or PET/CT has a higher sensitivity compared to  $^{18}\text{F}$ -FDG PET or PET/CT in differentiating between high-grade and low-grade gliomas but with lower specificity; diagnostic performance values were similar to those of  $^{11}\text{C}$ -methionine PET or PET/CT in this setting [6].

### 3.3.4 <sup>18</sup>F-FDOPA

For differentiating high-grade from low-grade gliomas, <sup>18</sup>F-FDOPA PET or PET/CT showed a pooled sensitivity of 88% and a pooled specificity of 73% [3].

## 3.4 Delineation of Gliomas

For surgical and radiation therapy planning in patients with glioma, a correct delineation of the target volume is needed. A recent evidence-based article suggested that radiolabelled amino acid PET may ameliorate the delineation of high-grade gliomas compared to standard MRI [16].

## 3.5 Diagnosis of Recurrent Brain Tumours

Distinguishing recurrent brain tumours from non-tumour lesions after radiation therapy and/or chemotherapy is a crucial clinical issue, because the different diagnosis will lead to divergent treatments. Several meta-analyses have assessed the diagnostic performance of PET with different tracers in this setting [3, 4, 7, 9, 11, 13, 21–25].

### 3.5.1 <sup>18</sup>F-FDG

A meta-analysis of Zhao et al. demonstrated a moderate diagnostic accuracy of <sup>18</sup>F-FDG PET or PET/CT in detecting brain tumour recurrence [23]. This finding was confirmed by another meta-analysis which showed a pooled sensitivity and specificity of 78% and 77%, respectively [21]. Furuse et al. showed that the diagnostic performance of <sup>18</sup>F-FDG PET or PET/CT in detecting recurrent brain tumours was lower compared to that of radiolabelled amino acid PET or PET/CT [7]. Nihashi et al. showed that, when considering both low- and high-grade gliomas, pooled sensitivity and specificity of <sup>18</sup>F-FDG PET or PET/CT in detecting glioma recurrence were 77% and 78%, respectively. In subgroup analyses limited to high-grade gliomas, pooled sensitivity

and specificity were 79% and 70%, respectively [25]. Wang et al. reported a moderate sensitivity (70%) but a good specificity (88%) of <sup>18</sup>F-FDG PET or PET/CT in detecting recurrent glioma; however, the diagnostic accuracy was lower compared to that of <sup>11</sup>C-methionine PET or PET/CT and magnetic resonance spectroscopy in this setting [22]. Another meta-analysis demonstrated that the diagnostic performance of <sup>18</sup>F-FDG PET or PET/CT in detecting recurrent glioma is not optimal, in particular if compared with other available neuroimaging methods [7].

### 3.5.2 <sup>11</sup>C-Methionine

<sup>11</sup>C-methionine PET or PET/CT demonstrated good diagnostic performance in detecting brain tumour recurrence (pooled sensitivity and specificity of 92% and 87%, respectively), with higher values compared to <sup>18</sup>F-FDG PET or PET/CT [23]. For high-grade gliomas, pooled sensitivity and specificity of <sup>11</sup>C-methionine PET or PET/CT in detecting glioma recurrence were 70% and 93%, respectively [25]. Compared to dynamic susceptibility contrast-enhanced MRI, <sup>11</sup>C-methionine PET or PET/CT demonstrated comparable pooled sensitivity and specificity in detecting glioma recurrence, with pooled values of 87% and 81.3%, respectively [24]. Similar values of sensitivity and specificity (85% and 83%, respectively) were described by Wang et al., which demonstrated that the diagnostic performance of <sup>11</sup>C-methionine PET or PET/CT in detecting glioma recurrence was similar to that of magnetic resonance spectroscopy [22]. A large meta-analysis including 29 studies confirmed the good diagnostic performance of <sup>11</sup>C-methionine PET or PET/CT in this setting with a pooled sensitivity and specificity of 88% and 85%, respectively [13].

### 3.5.3 <sup>18</sup>F-FET

A recent meta-analysis demonstrated that <sup>18</sup>F-FET PET or PET/CT has a good diagnostic accuracy in differentiating between brain tumour

recurrence and radiation necrosis after treatment, with pooled sensitivity and specificity values of 82% and 80%, respectively. In the subgroup of patients with suspicious glioma recurrence, sensitivity and specificity of  $^{18}\text{F}$ -FET PET or PET/CT were 83% and 81%, respectively [11]. The good diagnostic performance of  $^{18}\text{F}$ -FET PET or PET/CT in this setting was also confirmed by Furuse et al. who reported increased diagnostic performance of  $^{18}\text{F}$ -FET PET or PET/CT compared to  $^{18}\text{F}$ -FDG and  $^{11}\text{C}$ -methionine PET or PET/CT [7]. Kim et al. found that amino acid PET or PET/CT, including  $^{18}\text{F}$ -FET PET, has a good diagnostic performance in differentiating residual or recurrent brain tumour from treatment-related changes (pseudoprogression) in patients with high-grade gliomas [4].

### 3.5.4 $^{18}\text{F}$ -FDOPA

A recent meta-analysis indicated that  $^{18}\text{F}$ -FDOPA PET or PET/CT has a good diagnostic accuracy in differentiating between brain tumour recurrence and radiation necrosis after treatment, with pooled sensitivity and specificity values of 85% and 77%, respectively. In the subgroup of patients with suspicious glioma recurrence, sensitivity and specificity of  $^{18}\text{F}$ -FDOPA PET or PET/CT were 94% and 89%, respectively [11]. Xiao et al. reported a good sensitivity of  $^{18}\text{F}$ -FDOPA PET and PET/CT in detecting recurrent glioma (92%) and a moderate specificity (76%) [3].

### 3.5.5 $^{18}\text{F}$ -FLT

$^{18}\text{F}$ -FLT PET or PET/CT demonstrated a similar diagnostic performance in detecting brain tumour recurrence compared to  $^{18}\text{F}$ -FDG PET or PET/CT with pooled sensitivity and specificity of 82% and 76%, respectively [21].

### 3.5.6 $^{18}\text{C}$ -Choline

A recent meta-analysis indicated that  $^{11}\text{C}$ -choline PET or PET/CT has a good diagnostic accuracy

for differentiating glioma recurrence from radiation induced necrosis after treatment, with a pooled sensitivity and specificity of 87% and 82%, respectively [9].

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## 3.6 Diagnosis of Brain Metastases

The reliability of PET or PET/CT with different tracers in detecting brain metastases has been evaluated to a less extent compared to primary brain tumours. A meta-analysis demonstrated that the pooled sensitivity and specificity of  $^{18}\text{F}$ -FDG PET or PET/CT in detecting brain metastases in patients with lung cancer were 21% and 100%, respectively. In particular, the sensitivity of this method is lower compared to that of contrast-enhanced MRI [19].

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## 3.7 Diagnosis of Recurrent Brain Metastases

The meta-analysis of Li et al., focused on the use of PET or PET/CT with different tracers in differentiating recurrent brain metastasis from radionecrosis after radiation therapy, demonstrated a good diagnostic accuracy of PET or PET/CT with both  $^{18}\text{F}$ -FDG and radiolabelled amino acid tracers ( $^{11}\text{C}$ -methionine,  $^{18}\text{F}$ -FET,  $^{18}\text{F}$ -FDOPA) in this setting [12]. MRI and PET with different tracers showed similar diagnostic performance for the detection of recurrent brain metastasis after stereotactic radiosurgery; nevertheless, advanced MRI methods showed a significantly higher diagnostic performance in this setting compared to PET [8].

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## 3.8 Diagnosis of Primary Central Nervous System Lymphoma (PCNSL)

$^{18}\text{F}$ -FDG PET and PET/CT showed considerable accuracy in identifying PCNSL among various brain lesions in immunocompetent patients (pooled sensitivity and specificity of 88% and

86%, respectively), therefore,  $^{18}\text{F}$ -FDG PET/CT could be a valuable diagnostic imaging method in this setting [17]. High diagnostic accuracy of  $^{18}\text{F}$ -FDG PET and PET/CT has also been demonstrated in identifying PCNSL among various brain lesions in patients with human immunodeficiency virus (HIV) infection [18].

### 3.9 Prognostic Value in Patients with Glioma

Beyond the diagnostic accuracy, PET/CT parameters, and particularly the TBR, may be significant prognostic factors in patients with glioma. A recent meta-analysis demonstrated that increased TBR at  $^{18}\text{F}$ -FDG PET,  $^{11}\text{C}$ -methionine PET and  $^{18}\text{F}$ -FET PET could indicate poor overall survival (pooled hazard ratios were 3.05 for  $^{18}\text{F}$ -FDG PET, 1.59 for  $^{11}\text{C}$ -methionine PET and 1.15 for  $^{18}\text{F}$ -FET PET) [5]. Another meta-analysis showed that the TBR and metabolic tumour volume at  $^{11}\text{C}$ -methionine PET are significant prognostic parameters for patients with gliomas. Patients with a high TBR have a higher risk of death, and patients with a high metabolic tumour volume have a higher risk of adverse events or death [10].

### 3.10 Conclusions

Evidence-based data demonstrated good diagnostic performance of PET with different tracers in detecting brain tumours, in particular radiolabelled amino acid tracers showed the highest diagnostic performance values. All the PET tracers evaluated had significant prognostic value in patients with glioma [27].

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