

## Search Strategy

All searches were performed on 2018-03-29.

### Pubmed:

("Glioma"[Mesh] OR glioma\*[tiab] OR glioblastom\*[tiab] OR astrocytom\*[tiab] OR oligodendrogliom\*[tiab] OR oligoastrocytom\*[tiab] OR (glia\*[tiab] AND (tumor[tiab] OR tumour[tiab]))) AND ("Positron-Emission Tomography"[Mesh] OR PET[tiab] OR Positron emission[tiab]) AND ("Disease Progression"[Mesh] OR "Treatment Outcome"[Mesh:NoExp] OR "Radiation Injuries"[Mesh] OR "Dose-Response Relationship, Radiation"[Mesh] OR "radiation effects" [Subheading] OR treatment-induc\*[tiab] OR radiation induc\*[tiab] OR radiation associat\*[tiab] OR radiation chang\*[tiab] OR radiation effect\*[tiab] OR treatment effect\*[tiab] OR post treat\*[tiab] OR posttreat\*[tiab] OR posttherap\*[tiab] OR post therap\*[tiab] OR postsurg\*[tiab] OR post-surg\*[tiab] OR post irradiat\*[tiab] OR postirradiat\*[tiab] OR after irradiat\*[tiab] OR after rad\*[tiab] OR post radiat\*[tiab] OR postradiat\*[tiab] OR treatment outcome\*[tiab] OR radiation injur\*[tiab] OR pseudo progress\*[tiab] OR true progress\*[tiab] OR pseudoprogress\*[tiab] OR pseudorespon\*[tiab] OR radiation necro\*[tiab] OR radio necro\*[tiab] OR radionecros\*[tiab] OR disease progress\*[tiab] OR recurrent glio\*[tiab] OR true tumo\*[tiab] OR treatment-relat\*[tiab] OR residu\*[tiab] OR pseudo[tiab] OR ((recurr\*[tiab] OR progress\*[tiab]) AND (tumor\*[tiab] OR tumour\*[tiab]))) AND ( ( "2005/01/01"[PDat] : "3000/12/31"[PDat] ) )

Results: 661

**Web of Science:**

You searched for: TS=(glioma\* OR glioblastom\* OR astrocytom\* OR oligodendrogliom\* OR oligoastrocytom\* OR (glia\* AND (tumor OR tumour))) AND TS=(PET OR "Positron emission") AND (TS=(necro\* OR radionecro\* OR true OR residu\* OR pseudo\* OR posttreat\* OR posttherap\* OR postsurg\* OR postirradi\* OR postradiat\*) OR TS=(treatment NEAR/2 (induc\* OR effect OR effects OR relat\* OR outcome\* OR post)) OR TS=(radiation NEAR/2 (induc\* OR associat\* OR chang\* OR effect\* OR injur\*)) OR TS=((post OR after) NEAR/1 (treat\* OR surg\* OR therap\* OR irradiat\* OR radiat\*)) OR TS=(true NEAR/5 progress\*) OR TS=(disease NEAR/1 (course OR progress\*)) OR TS=(recurr\* NEAR/5 glio\*) OR TS=((recurr\* OR progress\*) AND (tumor\* OR tumour\*)))

**Refined by: PUBLICATION YEARS:** ( 2014 OR 2010 OR 2018 OR 2017 OR 2008 OR 2015 OR 2007 OR 2013 OR 2006 OR 2016 OR 2012 OR 2005 OR 2009 OR 2011 )

**Timespan:** All years. **Indexes:** SCI-EXPANDED, SSCI, A&HCI, ESCI.

Results: 1,145 (from Web of Science Core Collection)

## Embase:

((('glioma'/exp OR 'glioma' OR glioma\*:ab,ti OR glioblastom\*:ab,ti OR astrocytom\*:ab,ti OR oligodendrogliom\*:ab,ti OR oligoastrocytom\*:ab,ti OR (glia\*:ab,ti AND (tumor:ab,ti OR tumour:ab,ti))) AND ('positron emission tomography'/exp OR 'positron emission tomography' OR pet:ab,ti OR 'positron emission':ab,ti) AND ('disease exacerbation'/exp OR 'disease exacerbation' OR 'disease course'/exp OR 'disease course' OR 'treatment outcome'/exp OR 'treatment outcome' OR 'clinical outcome'/exp OR 'clinical outcome' OR 'radiation injury'/exp OR 'radiation injury' OR 'radiation response'/exp OR 'radiation response' OR 'minimal residual disease'/exp OR 'minimal residual disease' OR ((treatment NEAR/2 (induc\* OR effect OR effects OR relat\* OR outcome\* OR post)):ab,ti) OR ((radiation NEXT/2 (induc\* OR associat\* OR chang\* OR effect\* OR injur\*)):ab,ti) OR (((post OR after) NEXT/1 (treat\* OR surg\* OR therap\* OR irradiat\* OR radiat\*)):ab,ti) OR posttreat\*:ab,ti OR posttherap\*:ab,ti OR postsurg\*:ab,ti OR postirradiat\*:ab,ti OR postradiat\*:ab,ti OR ((true NEAR/5 progress\*):ab,ti) OR radionecros\*:ab,ti OR ((disease NEXT/1 (course OR progress\*)):ab,ti) OR ((recurr\* NEAR/5 glio\*):ab,ti) OR residu\*:ab,ti OR pseudo\*:ab,ti OR necro\*:ab,ti OR ((recurr\*:ab,ti OR progress\*:ab,ti) AND (tumor\*:ab,ti OR tumour\*:ab,ti)))) AND (2005:py OR 2006:py OR 2007:py OR 2008:py OR 2009:py OR 2010:py OR 2011:py OR 2012:py OR 2013:py OR 2014:py OR 2015:py OR 2016:py OR 2017:py OR 2018:py)

Results: 2,518

## **Methodological Quality of Included Studies**

In the first domain regarding patient selection, one out of 39 studies (3%) was considered to be of high risk of bias (19), since patients who demonstrated significant tumor growth were excluded from the analysis. This might have induced a selection bias. Furthermore, 17 studies (44%) were considered to be of unclear risk of bias since it was not specified whether their patient selection was random or consecutive (18,21,24–26,31–33,37–39,41–43,46,47,51). The remaining 21 studies (54%) were considered to be of low risk of bias (7,16,17,20,22,23,27–30,34–36,40,44,45,48–50,52,53).

In the index test domain 20 studies (51%) were considered to be of high risk of bias, 19 of which because they did not pre-specify the PET threshold or cut-off value (7,17,18,21,22,28–32,35,38–43,46,51), and one study due to awareness of the evaluating physician of the results of the reference test (16). In an additional 9 studies (23%) it was not assured that the results of the reviewed PET technique were interpreted without knowledge of the results of the reference standard (23,25,26,33,36,47–49,53). Hence, we considered them to be of unclear risk of bias. We considered the 10 remaining studies (26%) to be of low risk of bias (19,20,24,27,34,37,44,45,50,52).

In the domain of the reference standard, four studies (10%) were considered to be of high risk; one of these studies used a too high pathologic cut-off for tumor progression (20% viable tumor in the pathologic specimen) (51), whereas in the other three studies the reference standard results were interpreted without blinding to the PET results (7,30,49). All 35 other studies (90%) were considered to be of unclear risk of bias as it was not specified if the reference standard results were interpreted without knowledge of the PET results (16–29,31–48,50,52,53). Moreover, in four of these studies, the reference standard itself was too imprecisely described (16,24,28,33).

Finally, in the flow and timing domain, 30 studies (77%) were considered to be of high risk of bias, because not all patients received the same reference standard (7,17–23,25–29,31,32,34–38,43–46,48–51,53) or because not all patients were included in the analysis (30). Five other studies (13%) were considered to be of unclear risk of bias, as it was unknown if all patients received the same reference

standard (16,24,33) or the interval between the PET and the reference standard was not specified (42,47). The remaining four studies (10%) were considered to be of low risk of bias (39–41,52).

All studies showed high risk of bias in at least one of the four domains with the exception of four studies (24,33,47,52). However, none of the studies showed low risk of bias in all domains. Overall, study quality can be regarded as moderate.

Regarding the applicability assessment, we had concerns that the included patients and setting matched our review question in one study (3%), as not all high-grade glioma patients received treatment according to Stupp (49). In 19 other studies (49%), there were limited patient applicability concerns (16,21,22,24–27,31–34,36,37,41,42,44,45,47,50); in 18 of these studies, there were limited concerns if all patients were treated according to the Stupp protocol (16,21,25–27,31–34,36,41,42,44,45,47,50) and/or if there were no patients <18 years included (24–26,31,34,37,45,47,50). In one study, it was not explicitly stated that all patients were high-grade glioma patients (22). In the 19 remaining studies, there were no concerns regarding patient applicability (7,17–20,23,28–30,35,38–40,43,46,48,51–53). In two studies (5%), there were applicability concerns regarding the PET conduct and interpretation (39,42) that might not be feasible in clinical practice. In one study, a relatively complicated cluster analysis was performed (39). In the other study, a modified  $^{11}\text{C}$ -MET PET was used (exclusion of vascular factors from a normal  $^{11}\text{C}$ -MET PET) (42). There were no concerns in any of the other studies regarding applicability of index test. Moreover, there were no concerns that the reference standard did not match our review question in any of the studies. In conclusion, we had no applicability concern for 18 out of the 39 included studies (7,17–20,23,28–30,35,38,40,43,46,48,51–53).