

# Evidence Discussion (ONC 2.1-2.5 and 2.10)

---

## Primary Central Nervous System Tumors- Background. General Considerations

### Background

Primary Central nervous system tumors account for 1.4% of all new cancer diagnoses in the United States and 2.7% of deaths due to cancer. Primary central nervous system tumors develop within any region of the brain. Utilizing the WHO classification of tumors, Low grade tumors (WHO I, II) are the most common primary brain tumors. (71.7% of all tumors). High grade tumors (WHO III/IV) account for 28.3% of all tumors. Meningioma is the most common low grade tumor accounting for 39.7% of all tumors... Glioblastoma is the most common malignant glioma accounting for 15.4% of all tumors. The most recent classification of these tumors is based on histology and on molecular diagnostics.

Evicore guidelines align with NCCN guidelines. Evicore ONC 2.1-2.10 guidelines address primary central nervous system tumors in adults. Metastatic brain cancer is discussed elsewhere in ONC 31.3 and in disease specific sections.

### General Considerations-Imaging

The primary imaging modality for the evaluation of primary brain tumors is a MRI brain and spine (with and without contrast). The standard MRI protocol minimally includes T1 and T2, fluid-attenuated inversion recovery (FLAIR), gradient-echo/susceptibility, diffusion-weighted imaging, and post contrast T1-weighted images to characterize the tumor. MRI provides much better characterization of intracranial parenchymal tumors in comparison to CT. MRI is more sensitive in detecting lesions in the posterior fossa and in evaluation of leptomeningeal spread of tumor. CT imaging (with and/or without contrast) is valuable in the emergent scenario to assist in initial description of the disease. CT imaging of brain and spine should be used in patients with a contraindication for use of MRI (those with metallic implants or those who experience claustrophobia). If there is bone involvement, CT imaging may be included with MRI for disease assessment.

Advanced imaging modalities may be included to complement standard imaging to further characterize tumors and assist in treatment decisions. MRI perfusion measures blood flow in the tumor and can be useful in differentiating viable tumor versus radiation necrosis, in determining tumor grade and in determining optimal site for biopsy. MR Spectroscopy involves analysis of the levels of certain chemicals in pre-selected voxels

(small regions) on an MRI scan done at the same time. MR spectroscopy may be useful in defining grade of tumor or differentiate viable tumor from radiation necrosis. The use of MR spectroscopy is limited to specific histologies based on peer-reviewed literature. A major limitation of both modalities is the added imaging time. Brain FDG-PET imaging may also be considered to differentiate viable tumor versus radiation necrosis, to determine optimal biopsy site and to determine tumor grade. The use of Brain FDG-PET imaging is limited to specific histologies based on peer-reviewed literature.

## References

Mabray, M.C.; Barajas, R.F., Jr.; Cha, S. Modern brain tumor imaging. *Brain Tumor Res. Treat.* 2015, 3, 8–23

Nabors LB, Portnow J *et al.* Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Central Nervous System Cancers. Version 1.2024-May 31, 2024. All rights reserved. Accessed [June 26, 2024]. To view the most recent and complete version of the guideline, go online to NCCN.org

Ostrom QT, Price M, Neff C *et al.* CBTRUS Statistical Report: Primary Brain and Other Central Nervous System Tumors Diagnosed in the United States in 2015-2019. *Neuro Oncol.* 2022;24(Suppl 5):v1.

American College of Radiology. ACR–ASNR–SPR practice parameter for the performance of intracranial magnetic resonance perfusion imaging. 2017; Available at: <https://www.acr.org/-/media/ACR/Files/PracticeParameters/MR-Perfusion.pdf?la=en>.

American College of Radiology. ACR–ASNR–SPR practice parameter for the performance and interpretation of magnetic resonance spectroscopy of the central nervous system. [www.acr.org/-/media/ACR/Files/Practice-Parameters/mr-spectroscopy.pdf?la=en](https://www.acr.org/-/media/ACR/Files/Practice-Parameters/mr-spectroscopy.pdf?la=en)

Brain tumours (primary) and brain metastases in adults. London: National Institute for Health and Care Excellence (NICE); 2021 Jan 29. (NICE Guideline, No. 99.) Available from: <https://www.ncbi.nlm.nih.gov/books/NBK544711/>

WHO Classification of Tumors Editorial Board (2021) Central nervous system tumours, 5th edn. International Agency for Research on Cancer, Lyon

## Evidence Summary for Low Grade Gliomas ONC 2.2

Evicore guidelines align with NCCN guidelines.

The primary brain tumors classified as low grade gliomas are listed in the guideline. Initial staging in low grade glioma includes both MRI brain as well as MRI whole spine. Whole spine MRI imaging is indicated for initial staging as the finding of spinal metastases, leptomeningeal disease will impact prognosis, and treatment approaches. MRI Studies should be completed both without and with gadolinium contrast. However, MRI spine with contrast only can be approved if being performed immediately following a contrast-enhanced MRI brain for patient centricity to limit time in the MRI machine if requested, since the non-contrast component is less essential for the evaluation of spine. MRI imaging is completed after initial resection or radiation to establish a new baseline for disease monitoring. If intracranial or intraspinal recurrence is suspected or documented, MRI imaging that was completed for initial staging is repeated.

In patients undergoing active therapy, MRI imaging may be repeated after every 2 cycles of therapy for disease assessment. If there is spine involvement, MRI spine of the involved spinal region can be included on this same schedule.

Advanced imaging modalities such as MRI perfusion imaging, MR spectroscopy and/or PET Brain Metabolic Imaging used in conjunction with standard MRI imaging can be performed to characterize non-invasively changes in the tumor not noted on standard MRI or as problem solving tools with inconclusive findings on MRI imaging... Results of these advanced imaging modalities may be the basis to pursue additional treatment and/or surgical intervention; to define transition of the tumor to a higher grade or to distinguish between radiation-induced radiation necrosis and progressive disease within 18 months of completing radiation therapy.

Surveillance imaging is conducted at a frequency and interval based on published standards noted in the NCCN guidelines. More frequent imaging may be done as clinically indicated by the treating physician, in the event of clinical changes such as development of seizures or neurologic deterioration that are suspicious for disease progression.

## References

Forst DA, Nahed BV et al. Low-Grade Gliomas. Oncologist. 2014 Apr; 19(4): 403–413.

Mabray MC, Soonmee C. Current Clinical Brain Tumor Imaging. *Neurosurgery* 81:397–415, 2017

Nabors LB, Portnow J et al. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Central Nervous System Cancers. Version 1.2024-May 31, 2024. All rights reserved. Accessed [June 26, 2024]. To view the most recent and complete version of the guideline, go online to NCCN.org

Ostrom QT, Price M, Neff C et al. CBTRUS Statistical Report: Primary Brain and Other Central Nervous System Tumors Diagnosed in the United States in 2015-2019. Neuro Oncol. 2022;24(Suppl 5):v1.

American College of Radiology. ACR–ASNR–SPR practice parameter for the performance of intracranial magnetic resonance perfusion imaging. 2017; Available at: <https://www.acr.org/-/media/ACR/Files/PracticeParameters/MR-Perfusion.pdf?la=en>.

American College of Radiology. ACR–ASNR–SPR practice parameter for the performance and interpretation of magnetic resonance spectroscopy of the central nervous system. [www.acr.org/-/media/ACR/Files/PracticeParameters/mr-spectroscopy.pdf?la=en](https://www.acr.org/-/media/ACR/Files/PracticeParameters/mr-spectroscopy.pdf?la=en)

Brain tumours (primary) and brain metastases in adults. London: National Institute for Health and Care Excellence (NICE); 2021 Jan 29. (NICE Guideline, No. 99.) Available from: <https://www.ncbi.nlm.nih.gov/books/NBK544711/>

Wen PY, Macdonald DR, Reardon DA, et al. Updated response assessment for high-grade gliomas: Response assessment in neuro-oncology working group. J Clin Oncol 2010;28:1963-1972.

### **Evidence Summary for High Grade Gliomas ONC 2.3**

Evicore guidelines align with NCCN guidelines.

The primary brain tumors classified as high grade gliomas are listed in the guideline. Initial staging in high grade glioma includes both MRI brain as well as MRI whole spine. Whole spine MRI imaging is indicated for initial staging as the finding of spinal metastases and leptomeningeal disease will impact prognosis and treatment approaches. MRI Studies should be completed both without and with gadolinium contrast. However, MRI spine with contrast only can be approved if being performed immediately following a contrast-enhanced MRI brain for patient centricity to limit time in the MRI machine if requested, since the non-contrast component is less essential for the evaluation of spine. MRI imaging is indicated after initial resection or radiation to establish a new baseline for disease monitoring. If intracranial or intraspinal recurrence is suspected or documented, MRI imaging that was completed for initial staging is repeated.

In patients undergoing active therapy, MRI imaging may be repeated after every 2 cycles of therapy for disease assessment. If there is spine involvement, MRI spine of the involved spinal region can be included on this same schedule.

Advanced imaging modalities such as MRI perfusion imaging, MR spectroscopy and/or PET Brain Metabolic Imaging used in conjunction with standard MRI imaging can be performed as problem solving tools to characterize non-invasively changes in the tumor noted on standard MRI. Results of these advanced imaging modalities may be the basis to pursue additional treatment and/or surgical intervention; to distinguish low-grade from

high-grade gliomas; to distinguish between radiation-induced radiation necrosis and progressive disease within 18 months of completing radiation therapy.

Surveillance imaging is conducted at a frequency and interval based on published standards noted in the NCCN guidelines. More frequent imaging may be done as clinically indicated by the treating physician, in the event of a clinical change such as development of seizures or neurologic deterioration that is suspicious for disease progression.

## References

Nabors LB, Portnow J *et al.* Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Central Nervous System Cancers. Version 1.2024-May 31, 2024. All rights reserved. Accessed [June 26, 2024]. To view the most recent and complete version of the guideline, go online to NCCN.org

Mabray MC, Soonmee C. Current Clinical Brain Tumor Imaging. *Neurosurgery* 81:397–415, 2017.

American College of Radiology. ACR–ASNR–SPR practice parameter for the performance of intracranial magnetic resonance perfusion imaging. 2017; Available at: <https://www.acr.org/-/media/ACR/Files/PracticeParameters/MR-Perfusion.pdf?la=en>.

American College of Radiology. ACR–ASNR–SPR practice parameter for the performance and interpretation of magnetic resonance spectroscopy of the central nervous system. [www.acr.org/-/media/ACR/Files/Practice-Parameters/mr-spectroscopy.pdf?la=en](https://www.acr.org/-/media/ACR/Files/Practice-Parameters/mr-spectroscopy.pdf?la=en)

Brain tumours (primary) and brain metastases in adults. London: National Institute for Health and Care Excellence (NICE); 2021 Jan 29. (NICE Guideline, No. 99.) Available from: <https://www.ncbi.nlm.nih.gov/books/NBK544711>

Wen PY, Macdonald DR, Reardon DA, *et al.* Updated response assessment for high-grade gliomas: Response assessment in neuro-oncology working group. *J Clin Oncol* 2010;28:1963-1972.

## **Evidence Summary for Medulloblastoma and Supratentorial Primitive Neuroectodermal Tumors (sPNET) ONC 2.4**

Evicore guidelines align with NCCN guidelines. Medulloblastoma and other embryonal tumors (supratentorial primitive neuroectodermal tumors and pineoblastoma) are much more common in pediatric patients than in adults. The imaging indications in adult individuals are identical to those for pediatric patients (PEDONC 4.4 Medulloblastoma (MDB), Other CNS Embryonal Tumors, and Pineoblastoma).

Initial staging in these tumors includes both MRI brain as well as MRI whole spine. This group of tumors has a tendency for leptomeningeal dissemination in the brain, but also seeding metastases along the spinal axis. Whole spine MRI imaging is indicated for initial staging as the finding of spinal metastases and leptomeningeal disease will impact prognosis and treatment approaches. MRI Studies should be completed both without and with gadolinium contrast. However, MRI spine with contrast only can be approved if being performed immediately following a contrast-enhanced MRI brain for patient centricity to limit time in the MRI machine if requested, since the non-contrast component is less essential for the evaluation of spine.

Postoperative MRI imaging of brain (within 48 hours of surgery) is indicated to quantify residual tumor volume. A second resection may be considered based on the initial postoperative disease volume noted on MRI in an attempt to obtain a gross total resection. Pre-operative MRI of the whole spine is preferred; otherwise, this imaging is to be completed within 28 days post-operatively. At that point, post-surgical changes may mask the presence of leptomeningeal spread of tumor.

Both MRI Brain as well as MRI whole spine are to be completed after radiation therapy. In patients undergoing active therapy, MRI brain as well as whole spine may be repeated after every 2 cycles of therapy for disease assessment. If signs or symptoms of recurrence or progression develop, MRI brain and whole spine are to be completed.

Advanced imaging including PET Brain Metabolic Imaging and MR spectroscopy may be pursued to further non-invasively characterize findings on standard MRI. PET Brain Metabolic Imaging may be useful: 1) to distinguish radiation-induced tumor necrosis from progressive disease within 18 months of completing radiotherapy; 2) to evaluate inconclusive MRI findings when the PET findings will be used to determine need for biopsy or change in therapy, including a change from active therapy to surveillance or 3) to evaluate a brain lesion of indeterminate nature when the PET findings will be used to determine whether biopsy/resection can be safely postponed. MR spectroscopy may be useful to evaluate a brain lesion of indeterminate nature when the MRS findings will be used to determine whether biopsy/resection can be, safely postponed. MR Spectroscopy and PET Brain Metabolic imaging are not indicated for routine surveillance.

CT imaging without contrast is indicated for rapid assessment of acute neurologic changes, evaluation of intracranial hemorrhage, assessment of ventriculomegaly or evaluation of shunt malfunction.

Surveillance imaging is conducted at a frequency and interval based on published standards and as noted in the NCCN guidelines. More frequent imaging may be done as clinically indicated by the treating physician, in the event of clinical changes such as development of seizures or neurologic deterioration that are suspicious for disease progression.

## References

Francesschi E, Giannini C et al. Adult Medulloblastoma: Updates on Current Management and Future Perspectives. *Cancers (Basel)*. 2022 Aug; 14(15): 3708.

Mabray MC, Soonmee C. Current Clinical Brain Tumor Imaging. *Neurosurgery* 81:397–415, 2017.

Nabors LB, Portnow J et al. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Central Nervous System Cancers. Version 1.2024-May 31, 2024. All rights reserved. Accessed [June 26, 2024]. To view the most recent and complete version of the guideline, go online to NCCN.org

Nikam RM, YUE X et al. Advanced Neuroimaging Approaches to Pediatric Brain Tumors. *Cancers (Basel)*. 2022 Jul; 14(14): 3401.

American College of Radiology. ACR–ASNR–SPR practice parameter for the performance and interpretation of magnetic resonance spectroscopy of the central nervous system. [www.acr.org/-/media/ACR/Files/Practice-Parameters/mr-spectroscopy.pdf?la=en](http://www.acr.org/-/media/ACR/Files/Practice-Parameters/mr-spectroscopy.pdf?la=en)

Brain tumours (primary) and brain metastases in adults. London: National Institute for Health and Care Excellence (NICE); 2021 Jan 29. (NICE Guideline, No. 99.) Available from: <https://www.ncbi.nlm.nih.gov/books/NBK544711>.

## Evidence Summary for Ependymoma ONC 2.5

Evicore guidelines align with NCCN guidelines. Ependymoma imaging indications in adult individuals are identical to those for pediatric patients (PEDONC 4.8 Ependymal Tumors (Ependymoma))

Initial staging in these tumors includes both MRI brain as well as MRI whole spine. This group of tumors has a tendency for leptomeningeal dissemination in the brain, but also seeding metastases along the spinal axis. Whole spine MRI imaging is indicated for initial staging as the finding of spinal metastases and leptomeningeal disease will impact prognosis and treatment approaches. MRI Studies should be completed both without and with gadolinium contrast. However, MRI spine with contrast only can be approved if being performed immediately following a contrast-enhanced MRI brain for patient centricity to limit time in the MRI machine if requested, since the non-contrast component is less essential for the evaluation of spine.

Postoperative MRI imaging of brain (within 48 hours of surgery) to quantify residual tumor volume. A second resection may be considered based on the initial postoperative disease volume in an attempt to obtain a gross total resection. Pre-operative MRI of the whole spine is preferred; otherwise, this imaging is to be completed within 28 days post-operatively. At that point, post-surgical changes may mask the presence of leptomeningeal spread of tumor.

Both MRI Brain as well as MRI whole spine are to be completed after radiation therapy. In patients undergoing active therapy, MRI brain as well as whole spine may be repeated after every 2 cycles of therapy for disease assessment. If signs or symptoms of recurrence or progression develop, MRI brain and whole spine are to be completed.

Advanced imaging including PET Brain Metabolic Imaging and MR spectroscopy may be pursued to further non-invasively characterize findings on standard MRI. PET Brain Metabolic Imaging may be useful: 1) to distinguish radiation-induced tumor necrosis from progressive disease within 18 months of completing radiotherapy; 2) to evaluate inconclusive MRI findings when the PET findings will be used to determine need for biopsy or change in therapy, including a change from active therapy to surveillance or 3) to evaluate a brain lesion of indeterminate nature when the PET findings will be used to determine whether biopsy/resection can be safely postponed. MR spectroscopy may be useful to evaluate a brain lesion of indeterminate nature when the MRS findings will be used to determine whether biopsy/resection can be safely postponed. MR Spectroscopy and PET Brain Metabolic are not indicated for routine surveillance

CT imaging without contrast is indicated for rapid assessment of acute neurologic changes, evaluation of intracranial hemorrhage, assessment of ventriculomegaly or evaluation of shunt malfunction.

Surveillance imaging is conducted at a frequency and interval based on published standards and as noted in the NCCN guidelines. More frequent imaging may be done as clinically indicated by the treating physician, in the event of clinical changes such as development of seizures or neurologic deterioration that are suspicious for disease progression.

Based on evidenced based study, PET Brain Metabolic imaging does not have a defined role in the evaluation of ependymal tumors MR Spectroscopy is not indicated for routine surveillance.

## References

Mabray MC, Soonmee C. Current Clinical Brain Tumor Imaging. *Neurosurgery* 81:397–415, 2017.

Nikam RM, YUE X et al. Advanced Neuroimaging Approaches to Pediatric Brain Tumors. *Cancers (Basel)*. 2022 Jul; 14(14): 3401.

Nabors LB, Portnow J et al. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Central Nervous System Cancers. Version 1.2024-May 31, 2024. All rights reserved. Accessed [June 26, 2024]. To view the most recent and complete version of the guideline, go online to NCCN.org

Wu J, Armstrong TS, Gilbert MR. Biology and management of ependymomas *Neuro Oncol*. 2016 Jul;18(7):902-13. doi: 10.1093/neuonc/now016. Epub 2016 Mar 28.

American College of Radiology. ACR–ASNR–SPR practice parameter for the performance and interpretation of magnetic resonance spectroscopy of the central nervous system. [www.acr.org/-/media/ACR/Files/Practice-Parameters/mr-spectroscopy.pdf?la=en](http://www.acr.org/-/media/ACR/Files/Practice-Parameters/mr-spectroscopy.pdf?la=en)

Brain tumours (primary) and brain metastases in adults. London: National Institute for Health and Care Excellence (NICE); 2021 Jan 29. (NICE Guideline, No. 99.) Available from: <https://www.ncbi.nlm.nih.gov/books/NBK544711>.

## Evidence Summary for Choroid Plexus Tumors (ONC-2.10)

Choroid Plexus tumors arise within the ventricular system in the brain and account for less than 1 % of primary brain tumors. This group of tumors include choroid plexus papilloma, atypical choroid plexus papilloma and choroid plexus carcinoma. These tumors arise within the central nervous system ventricular system and present with hydrocephalus and clinical signs and symptoms of increased intracranial pressure. Choroid plexus papilloma (WHO Grade II tumor) is the most common of the group. These tumors rarely metastasize and recurrence is rare after surgical resection. Choroid plexus carcinoma (WHO Grade III tumor) is an aggressive tumor with a high rate of central nervous system metastases. Gross total resection is potentially curative. There is a role for radiation therapy and chemotherapy in choroid plexus carcinoma. However, overall survival rates range 35-40%. Atypical choroid plexus papilloma has features midway in the malignant spectrum between papilloma and carcinoma. Recurrence in this group is rare after surgical resection.

MRI is the standard imaging modality for these tumors. The guideline for imaging in this group of tumors is based on the guidelines established in children as these tumors are much more common in the pediatric age group and have similar patterns. MRI brain is indicated at diagnosis and after surgical resection to assess for residual disease. MRI whole spine is indicated in both atypical choroid plexus papilloma and choroid plexus carcinoma due to risk for spinal cord metastases. Subsequent imaging in choroid plexus papilloma and atypical choroid plexus papilloma is supported with clinical signs/symptoms suspicious for recurrence of hydrocephalus or based on CT imaging evidence of hydrocephalus. Surveillance imaging with MRI brain and spine is supported for choroid plexus carcinoma. Advanced imaging using MR Spectroscopy is supported in evaluation of a brain lesion of indeterminate nature when MRS findings will be used to determine whether biopsy/resection can be safely postponed.

Wolff JEA, Sajedi M, Brant et al. Choroid Plexus tumors. *British Journal of Cancer* (2002) 87, 1086-1091

Bahar, M., Hashem, H., Tekautz, T. et al. Choroid plexus tumors in adult and pediatric populations: the Cleveland Clinic and University Hospitals experience. *J Neurooncol* **132**, 427–432 (2017). <https://doi.org/10.1007/s11060-017-2384-1>

Jung AY. Basics for Pediatric Brain Tumor Imaging: Techniques and Protocol Recommendations *BrainTumor Res Treat* 2004. 12: 1-13

Jaju A, Li Y, Dahmouch et al. Imaging of pediatric brain tumors: A COG Diagnostic Imaging Committee/SPRONcology Committee/ASPNR White Paper. *Pediatr Blood Cancer*. 2023;70(Suppl. 4):e30147. <https://doi.org/10.1002/pbc.30147>

American College of Radiology. ACR–ASNR–SPR practice parameter for the performance and interpretation of magnetic resonance spectroscopy of the central nervous system. [www.acr.org/-/media/ACR/Files/Practice-Parameters/mr-spectroscopy.pdf?la=en](http://www.acr.org/-/media/ACR/Files/Practice-Parameters/mr-spectroscopy.pdf?la=en)

