Imaging Guidelines for Paediatric Brain Tumours 2

Response assessment in paediatric high-grade glioma: recommendations from the Response Assessment in Pediatric Neuro-Oncology (RAPNO) working group

Craig Erker, Benita Tamrazi*, Tina Y Poussaint, Sabine Mueller, Daddy Mata-Mbemba, Enrico Franceschi, Alba A Brandes, Arvind Rao, Kellie B Haworth, Patrick Y Wen, Stewart Goldman, Gilbert Vezina, Tobey J MacDonald, Ira J Dunkel, Paul S Morgan, Tim Jaspan, Michael D Prados†, Katherine E Warren†*

Response criteria for paediatric high-grade glioma vary historically and across different cooperative groups. The Response Assessment in Neuro-Oncology working group developed response criteria for adult high-grade glioma, but these were not created to meet the unique challenges in children with the disease. The Response Assessment in Pediatric Neuro-Oncology (RAPNO) working group, consisting of an international panel of paediatric and adult neuro-oncologists, clinicians, radiologists, radiation oncologists, and neurosurgeons, was established to address issues and unique challenges in assessing response in children with CNS tumours. We established a subcommittee to develop response assessment criteria for paediatric high-grade glioma. Current practice and literature were reviewed to identify major challenges in assessing the response of paediatric high-grade gliomas to various treatments. For areas in which scientific investigation was scarce, consensus was reached through an iterative process. RAPNO response assessment recommendations include the use of MRI of the brain and the spine, assessment of clinical status, and the use of corticosteroids or antiangiogenics. Imaging standards for brain and spine are defined. Compared with the recommendations for the management of adult high-grade glioma, for paediatrics there is inclusion of diffusion-weighted imaging and a higher reliance on T2-weighted fluid-attenuated inversion recovery. Consensus recommendations and response definitions have been established and, similar to other RAPNO recommendations, prospective validation in clinical trials is warranted.

Introduction

Paediatric high-grade gliomas account for 8–12% of CNS tumours in children, with the majority of tumours not located in the brainstem.[1,2] Paediatric high-grade gliomas are the leading cause of cancer-related death in children younger than 19 years and include various different WHO grade III and IV histological entities as well as H3 Lys27Met-mutant diffuse midline glioma.[3,4] This Series paper focuses on diffuse midline glioma and other paediatric high-grade glioma entities proven by biopsy, but excludes anaplastic ependymoma and diffuse intrinsic pontine glioma, whether or not proven by biopsy. Compared with non-pontine diffuse midline glioma, diffuse intrinsic pontine glioma is better correlated with pontine size and T2-weighted fluid-attenuated inversion recovery (T2-FLAIR) measurements. Diffuse intrinsic pontine glioma response assessment is, therefore, the focus of a separate Response Assessment in Pediatric Neuro-Oncology (RAPNO) working group and is discussed in the third paper of this Series.[5] For non-pontine diffuse midline glioma, it is unclear how to best assess their response; however, they are included in this consensus statement and not in the RAPNO diffuse intrinsic pontine glioma recommendations. In the future, it might become clearer whether or not diffuse midline glioma should be considered separately from other paediatric high-grade gliomas for response assessment purposes.

Excluding diffuse intrinsic pontine glioma, paediatric high-grade glioma has a 3-year event-free survival of 10% and a 3-year overall survival of 20%.[6] Substantial advances towards understanding the biology of paediatric high-grade gliomas have strongly influenced new clinical trial design and endpoints.[7,8] However, no specific criteria to unify response assessment for paediatric high-grade glioma across studies exists.

The Children's Oncology Group traditionally relies on MRI for objective response assessment, although clinical assessment and time from completion of radiotherapy are also considered when assessing progressive disease. The Pediatric Brain Tumor Consortium uses criteria similar to the Children's Oncology Group, but also incorporates neurological status, corticosteroid dosing, and durability of response. Several Société Internationale D'Oncologie Pédiatrique studies have defined response using radiographical assessment only.[9,10] The international multicentre study—the High-grade Glioma Efficacy and Tolerability Research of Bevacizumab in Young Children and Adolescents (HERBY) study—compared the addition of bevacizumab to radiotherapy plus temozolomide versus radiotherapy plus temozolomide alone in paediatric patients with high-grade glioma, and many findings have been reported in the last 5 years.[11–13] The HERBY study used the Response Assessment in Neuro-Oncology (RANO) assessment criteria and imaging review required a high adjudication rate.[14,11]

Lancet Oncol 2020; 21: e317–29

*Joint first authors

†Joint last authors

This is the second paper in a Series of three papers about imaging guidelines for paediatric brain tumours

Department of Pediatrics, Division of Pediatric Hematology/Oncology (C Erker MD), **and Department of Diagnostic Imaging** (D Mata-Mbemba MD), **Dalhousie University and IWK Health Centre, Halifax, NS, Canada; Department of Radiology, Keck School of Medicine, University of Southern California and Children's Hospital of Los Angeles, Los Angeles, CA, USA** (B Tamrazi MD); **Department of Radiology, Boston Children's Hospital, Boston, MA, USA** (Prof T Y Poussaint MD); **Department of Neurology** (S Mueller MD), **Department of Pediatrics** (S Mueller), **and Department of Neurosurgery** (S Mueller, Prof M D Prados MD), **University of California San Francisco, San Francisco, CA, USA; Department of Medical Oncology, Azienda USL, Bologna, Italy** (E Franceschi MD, A A Brandes MD); **IRCCS Institute of Neurological Sciences, Bologna, Italy** (E Franceschi, A A Brandes); **Departments of Computational Medicine and Bioinformatics and Radiation Oncology, University of Michigan, Ann Arbor, MI, USA** (A Rao PhD); **Division of Neuro-Oncology, Department of Oncology, St Jude Children's Research Hospital, Memphis, TN, USA** (K B Haworth MD); **Center For Neuro-Oncology, Dana-Farber Cancer Institute,**

Lancet Oncology, 21 (2020) e317-e329. doi:10.1016/S1470-2045(20)30173-X

Lancet Oncology, 21 (2020) e317-e329. doi:10.1016/S1470-2045(20)30173-X

Lancet Oncology, 21 (2020) e317-e329. doi:10.1016/S1470-2045(20)30173-X

Lancet Oncology, 21 (2020) e317-e329. doi:10.1016/S1470-2045(20)30173-X

Lancet Oncology, 21 (2020) e317-e329. doi:10.1016/S1470-2045(20)30173-X

Lancet Oncology, 21 (2020) e317-e329. doi:10.1016/S1470-2045(20)30173-X

Lancet Oncology, 21 (2020) e317-e329. doi:10.1016/S1470-2045(20)30173-X

Lancet Oncology, 21 (2020) e317-e329. doi:10.1016/S1470-2045(20)30173-X

Lancet Oncology, 21 (2020) e317-e329. doi:10.1016/S1470-2045(20)30173-X

Lancet Oncology, 21 (2020) e317-e329. doi:10.1016/S1470-2045(20)30173-X

Lancet Oncology, 21 (2020) e317-e329. doi:10.1016/S1470-2045(20)30173-X

Lancet Oncology, 21 (2020) e317-e329. doi:10.1016/S1470-2045(20)30173-X