

Pseudoprogession, recurrence and radiation necrosis

Pia C Sundgren, MD PhD

Increased enhancement has been used as a surrogate for measuring tumor progression as part of the standard MacDonald criteria in response assessment of GBM (1). However recent studies have clearly indicated that increased gadolinium enhancement due to a disrupted blood-brain barrier may be influenced by a number of factors, including acute changes immediately after surgery or radiation therapy, corticosteroids, radiation necrosis or injury and effects to the vasculature (2,3). New treatment strategies for glioblastoma multiforme (GBM) have prolonged survival. For example the combination of temozolomide and radiation significantly prolongs survival compared with radiation alone and has become standard treatment for GBM (4). However treatment response assessment of GBM might be difficult as a result of the frequent occurrence of early imaging changes that are indistinguishable from tumor progression so called pseudoprogession (5-7) but also by delayed changes in form of radiation injury or necrosis (8). The incidence of pseudoprogession after concurrent chemotherapy and radiation is 15% to 30%. It has been suggested that the increased contrast enhancement seen in pseudoprogession may result from transient radiation effects on the vasculature, leading to vasodilatation, edema, and increased capillary permeability.

While pseudoprogession occurs early during ongoing treatment, radiation injury or necrosis might be seen much later during follow up scanning and remains a diagnostic dilemma (9, 10).

Different MR imaging methods are used such as for example MR spectroscopy, Dynamic susceptibility contrast enhanced MRI imaging and also new imaging analyzing methods like functional parametric response maps (11) are used in attempt to separate pseudoprogession from progressive tumor, or radiation necrosis from tumor recurrence. Also CT perfusion has shown some promising results (12,13) in this field.

The present presentation will focus on imaging findings of pseudoprogession and radiation injury and discuss if it is possible to distinguish these entities from progressive or recurrent brain tumor by the use of advanced imaging techniques and analyzing methods.

References:

- 1 Macdonald DR, Cascino TL, Schold SC Jr *et al.* Response criteria for phase II studies of supratentorial malignant glioma. *J Clin Oncol* 1990;8:1277–1280
2. Clarke JL, Chang S. Pseudoprogression and pseudoresponse: Challenges in brain tumor imaging. *Curr Neurol Neurosci Rep* 2009; 9:241–246.
3. Sorensen AG, Batchelor T, Wein Patrick Y. Response criteria for glioma. *Nat Clin Pract Oncol* 2008;5:634–644.
4. Stupp R, Heigi MP, Mason WP *et al.* Effects of radiotherapy with concomitant and adjuvant temozolomide versus radiotherapy alone on survival in glioblastoma in a randomised phase III study: 5-year analysis of the EORTC-NCIC trial. *Lancet Oncol* 2009;10:459–466.
5. De Wit MC, de Bruin HG, Eijekboom W *et al.* Immediate post-radiotherapy changes in malignant glioma can mimic tumor progression. *Neurology* 2004;63:535–537
6. Brandsma D, Stalpers L, Taal W *et al.* Clinical features, mechanisms, and management of pseudoprogression in malignant gliomas. *Lancet Oncol* 2008;9:453–461
7. Taal W, Brandsma D, de Bruin HG *et al.* Incidence of early pseudoprogression in a cohort of malignant glioma patients treated with chemoradiation with temozolomide. *Cancer* 2008;113:405–410
8. Sundgren PC, Cao Y. Brain irradiation effects on normal brain parenchyma and radiation injury *Neuroimaging Clin N Am.* 2009 Nov;19(4):657-68.
9. Sundgren PC. MR Spectroscopy in radiation injury *AJNR Am J Neuroradiol* 2009; 30(8):1469-76
10. Jain R, Narang J, Sundgren PM, *et al.* Treatment induced necrosis versus recurrent/progressing brain tumor: going beyond the boundaries of conventional morphologic imaging. *J Neurooncol* 2010 Oct;100(1):17-29.

11. Galbán CJ, Chenevert TL, Meyer CR *et al.* The parametric response map is an imaging biomarker for early cancer treatment outcome Nat Med 2009;May;15(5):572-6.
12. Jain R. Perfusion CT imaging of brain tumors. An overview AJNR Am J Neuroradiol 2010 E-publ. Nov 24, 2010.
13. Jain R, Ellika SK, Scarpace L, *et al.* Quantitative estimation of permeability surface-area product in astroglial brain tumors using perfusion CT and correlation with histopathologic grade. AJNR Am J Neuroradiol. 2008 Apr;29(4):694-700