Session: Neuroradiology: Post-Treatment Brain Evaluation

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Highlights:

- Pseudoprogression is a common occurrence after treatment of high grade tumors with temozolomide and radiation therapy; a similar phenomenon is frequently seen after stereotactic radiosurgery for brain metastases.
- Perfusion and permeability imaging have been relatively widely studied for distinguishing true progression of tumor from pseudoprogression and/or radiation necrosis, and have shown relatively promising results.
- Further standardization of image acquisition and analysis techniques, and validation in multicenter trials will be needed before the promise of these techniques can be realized.

Title: The Post-Treatment Brain: Perfusion & Permeability

TARGET AUDIENCE – Radiologists, oncologists, physicists, scientists and technologists with an interest in dynamic imaging techniques such as dynamic susceptibility contrast-enhanced (DSC) and dynamic contrast-enhanced (DCE) MRI and their application to patients who have undergone treatment for brain tumors.

OUTCOME/OBJECTIVES – Attendees of this lecture will better understand the dilemmas faced by clinicians and radiologists attempting to interpret specific imaging findings (for example, the appearance of new enhancing lesions) in patients after treatment for neoplastic disease in the brain. Because the results of conventional MRI may be ambiguous, advanced imaging techniques are often employed in an attempt to more specifically characterize these findings. Attendees will become familiar with our evolving understanding of the pathophysiology underlying specific imaging findings, the reasons that perfusion and permeability techniques are promising to evaluate these conditions, and the barriers that need to be overcome before these techniques can become routinely used in clinical decision making.

PURPOSE – The purpose of this lecture is to review the four major scenarios presenting diagnostic challenges in patients under treatment for brain tumors: (1) Pseudoprogression vs. true progression in gliomas; (2) Radiation necrosis vs. recurrent tumor; (3) Pseudoresponse vs. true treatment response in gliomas; and (4) Interpretation of response of brain metastases to stereotactic radiation therapy. Based on the underlying pathophysiology of these imaging appearances, the rationale for use of perfusion and permeability dynamic MR imaging will be discussed.

METHODS – The MRI acquisition protocols and the image processing steps used to derive parameter maps such as cerebral blood volume (CBV) from DSC-MRI and the volumetric transfer coefficient from the plasma space to the extracellular extravascular space (K^{trans}) from DCE-MRI will be briefly reviewed.

RESULTS – There is a growing body of evidence that supports the potential of dynamic imaging

techniques for specific use cases in the post-therapeutic brain. When enhancing abnormalities appear after primary treatment of gliomas with radiation therapy and temozolomide, cases demonstrated to be pseudoprogression are associated with tumors that show O^6-methylguanine-DNA methyltransferase (MGMT) promoter methylation and are associated with improved survival. There are relatively consistent results across several reports showing that if DSC-MRI can be performed with proper correction for contrast agent leakage, the finding of high CBV can distinguish true progression from pseudoprogression. On DCE-MRI, a pattern of rapid wash-in and rapid washout of contrast agent may also be helpful for identifying true tumor progression. In a different scenario, similar findings on DSC-MRI and DCE-MRI may be helpful to diagnose true tumor progression as distinguished from radiation necrosis.

There has been comparatively less study of the use of advanced imaging for evaluating decrease or resolution of enhancing lesions in patients receiving anti-angiogenics for recurrent high grade glioma. This decrease could be due to true anti-tumoral cytotoxic effect of the treatment, repair of the blood-brain barrier without tumor regression (called "pseudoresponse"), or both. Because side effects from anti-angiogenic agents are not infrequent, an imaging technique that accurately identified true treatment responses could be clinically useful in order to help more accurately weigh the benefits and risks of treatment cessation in this group.

With more frequent use of stereotactic radiosurgery (SRS) for treatment of brain metastasis, note has been made that in approximately 60% of patients, MR imaging will show lesion growth at some time after treatment. Properly categorizing whether this lesion growth represents true progression or an inflammatory response due to radiation poses a diagnostic challenge in this situation. It has been noted that even pathology obtain by biopsy of these indeterminate lesions may be difficult to interpret. The potential of advanced imaging to contribute to accurate diagnosis of these lesions is considerable, but only now beginning to be studied.

DISCUSSION – In order to bring the potential benefits of perfusion and permeability imaging for post-treatment brain imaging into clinical practice, it will be important to validate these applications in a multicenter clinical trial. The lack of standardization of image acquisition and analysis strategies across centers, magnet field strengths and magnet manufacturers represents a significant barrier to the design of a clinical trial, but is being addressed by groups such as the Quantitative Imaging Biomarker Alliance (QIBA) of the RSNA and others. There is also a need for a better understanding of the repeatability and reproducibility of parameters derived from DCE-MRI and particularly DSC-MRI in order to help understand the meaning of any particular measurement for an individual patient.

CONCLUSION – Our understanding of how perfusion and permeability imaging may be useful for evaluation of patients treated for brain tumors continues to evolve. Although these techniques are already being used in many centers, efforts directed at increasing the precision of the quantitative metrics derived from DSC-MRI and DCE-MRI may be helpful to advance optimized techniques into clinical trials and, ultimately, to validate these techniques for widespread clinical use.

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