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See the letter by Chamberlain, on pages 1296.

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Does early identification of low-grade glioma growth impact outcome?

Dr Pallud and colleagues represent a vanguard research team in understanding glioma growth by serial anatomic MRI and the use of their novel radiographic methodology, that is, the determination of the velocity of diametric expansion (VDE) by ellipsoid approximation.[1] Several issues, however, temper enthusiasm for the incorporation of this radiographic method of low-grade glioma (LGG) growth into routine clinical practice as the authors suggest.

Firstly this method has never been assessed and validated in a prospective clinical trial, requirements that for example have been fulfilled for response assessment of high-grade gliomas using the Macdonald and RANO criteria.[2,3] If treatment of LGG is to be determined by a VDE analysis, a prospective trial showing the benefit of this approach is relevant compared with the current standard practice of altering therapy at time of radiographic enhancement and presumed glioma de-differentiation to a higher grade or enlargement of the tumor by >25% as assessed by fluid attenuated inversion recovery or T2-weighted MRI.[4]

Secondly, routine clinical practice, at least in the United States, only rarely after radiographic demonstration of a presumed LGG follows patients with serial MRI. Rather these patients more often undergo resective surgery and after pathological and molecular assessment are considered for further therapy, most often radiotherapy (RT), particularly in the high risk LGG subgroup.[5] The recently reported and data-mature RTOG 9802 trial demonstrated a significant survival benefit in patients studied defined as high risk (age >40 y or incompletely resected LGG) with the combined use of RT and PCV (procarbazine, lomustine, and vincristine) chemotherapy.[6] This practice-changing RTOG study suggests that the majority of patients with LGG benefit from combined modality treatment in the up-front setting, a marked contrast to the watch and wait serial MRI assessment of Pallud et al.

Thirdly, this author is unaware of any data that indicate that treating radiographic progressive disease or a so-called more growth-aggressive LGG as defined by Pallud et al (VDE > 8 mm/y by serial MRI) results in an improved outcome with respect to either survival (overall or progression free) or quality of life. Clearly the intent is to introduce more aggressive therapy (RT or chemotherapy) to alter outcome in a clinically meaningful manner, but it is uncertain if earlier treatment affects overall outcome in progressive LGG. Any benefit of earlier treatment may arguably be explained by a lead-time bias.

Pallud and colleagues are to be congratulated for continuing their efforts to define LGG based upon radiological growth characteristics and I look forward to their further research in this regard.

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