Glioblastoma

To The Editor: We are very interested in the laboratory investigation by Ju et al.1 (Ju H, Li X, Li H, et al: Mediation of multiple pathways regulating cell proliferation, migration, and apoptosis in the human malignant glioma cell line U87MG via unphosphorylated STAT1. Laboratory investigation. J Neurosurg 118:1239–1247, June 2013).

Glioblastomas multiforme are characterized by high invasiveness, rapid proliferation, and resistance to apoptosis. Therefore, the investigation of a novel therapy is very important. Ju et al.1 explored the effect of overexpression of the signal transducer and activator of transcription 1 (STAT1) protein on apoptosis, migration, and proliferation of the U87 glioma cell line. They concluded that STAT1-transfected U87 glioma cells decreased proliferation, suppressed migration, and increased apoptosis.

First, they did not show a fundamental result of the STAT1 band in the Western blot analysis in Fig. 2C to convince readers that the STAT1 was really well transfected into U87 glioma cells. To address this point, we suggest they could put the result of STAT1 Western blot analysis in their response to this letter. Moreover, as shown in the left panel of Fig. 2C, the expression level of cleaved caspase-3 seems not significantly higher in STAT1-transfected U87 glioma cells than in the mock or vector control groups in the Western blot analysis.

Despite these minor limitations, their findings raised the possibility of an important role of STAT1 in glioblastoma, suggesting that STAT1 overexpression is one of the therapeutic targets in human gliomas. Further studies performed using in vivo stereotactic orthotopic xenografts to investigate the effect of STAT1 overexpression on survival and tumor size are warranted.

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Disclosure
The authors report no conflict of interest.

Reference

Gamma Knife surgery

To The Editor: We read with interest the recently published article by Salvetti et al.2 (Salvetti DJ, Nagaraja TG, McNeill IT, et al: Gamma Knife surgery for the treatment of 5 to 15 metastases to the brain. Clinical article. J Neurosurg 118:1250–1257, June 2013). We were surprised that the authors omitted reference to our earlier work in the management of multiple brain metastases using Gamma Knife surgery (GKS), which was published in the Journal of Neurosurgery in 2002.1 In that paper we reported on 72 patients with more than 10 brain metastases from different primaries, including but not limited to lung cancer, breast cancer, melanoma, and renal carcinoma treated with GKS. A total of 147 treatment sessions were required to treat 1304 sites in the 72 patients. The mean tumor volume was 1.7 cm³. The median number of tumor sites during the first treatment session was 11. We noted in a multivariate survival analysis that the most significant prognostic factors for improved survival were 1) female sex, 2) total tumor volume < 30 cm³, and 3) Karnofsky Performance Scale score higher than 70. The origin of the primary neoplasm, patient age, radiosurgical dose, and previous whole-brain radiation therapy were not significant. The total intracranial tumor volume treated was of greater prognostic significance than the absolute number of metastases treated. In our previously published study2 of 22 patients with brain metastases from renal cell carcinoma, in which we treated with GKS an average of 6 lesions per patient, we achieved local control in 20 patients. In another previously published series of 68 women with breast cancer metastatic to the brain, we treated 26 patients with 1–3 lesions, 18 patients with 4–7 lesions, and 24 patients with 8 or more lesions.3

On a somewhat related note, in the editorial for Salvetti and colleagues’ article,4 the observation that the current payment paradigms limit reimbursement at 5 tumors is not valid in the state of Florida. In our state, Gamma Knife procedures are not reimbursed by the number of lesions treated, but instead by the number of treatment sessions performed.

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RESPONSE: No response was received from the authors of the original article.

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The authors report no conflict of interest.

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RESPONSE: We thank Drs. Wolf and Amendola for their interest in the article on 5–15 brain metastases and the accompanying editorials. Their early research in the field along with others, including the pioneering work of Dr. Yamamoto and colleagues, helped to expand indications for stereotactic radiosurgery. In their study published in a supplement to the Journal of Neurosurgery, it is important to note that most patients had stereotactic radiosurgery in 2 or more sessions and that the number of metastases managed in the first radiosurgery ranged from 1 to 30. The timing of initial and subsequent radiosurgeries was not specified in this publication. The current study reflects contemporary practice using the Gamma Knife to treat all brain metastases visible on MRI (5 or more) in a single session. As the indications for radiosurgery expand, the reimbursement will also need to be commensurate. After all, if one does two craniotomies in a single patient at one sitting, the neurosurgeon is reimbursed for both procedures. At radiosurgery, each tumor in a different location can have different clinical manifestations and ramifications, require a different preoperative discussion related to potential outcomes and risks, involve more work during the radiosurgery, and entail separate medicolegal risks. Gamma Knife surgery, particularly with the Perfexion unit, allows for robotics-assisted radiosurgery for a nearly limitless number of brain metastases in one session. However, current professional neurological codes for stereotactic radiosurgery (SRS) allow for reimbursement of up to 5 cranial lesions at one time using primary codes 61796 or 61798 along with add-on codes of 61797 or 61799. Since the SRS code changes in 2009, the reimbursement per lesion up to 5 has been the standard approach utilized by the Centers for Medicare & Medicaid Services and private payers (Dr. R. Patrick Jacobs, chair of the AANS & CNS Coding & Reimbursement Committee, personal communications). The choice of a number like 5 is an arbitrary one that is not relevant to outcome. We hope that the current work and other recent publications lead to expanded recognition of the role of radiosurgery for patients with 5 or more brain metastases and reimbursement commensurate with the effort to treat these challenging patients using single-session radiosurgery.©AANS, 2013

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Barrow Ruptured Aneurysm Trial: 3-year results

To The Editor: We would like to elaborate on some of the issues that have been brought forward in the Journal of Neurosurgery following the recent publication of the 3-year Barrow Ruptured Aneurysm Trial (BRAT) results. (Spetzler RF, McDougall CG, Albuquerque FC, et al: The Barrow Ruptured Aneurysm Trial: 3-year results. Clinical article. J Neurosurg 119:146–157, July 2013), as well as the editorial comments and response that followed. The first point we would like to emphasize is that if dialogue on the meaning of trial results in terms of impact on clinical practice is necessary, it would be naïve to believe that everything about ruptured aneurysms can now be settled by argumentation. The ongoing controversy indicates that more hard work is ahead: as proposed by the BRAT team, other trials are needed, and their design...