Editorial

Observations on the role of brain stereotactic radiosurgery

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As a research paradigAs a research paradigm (1) evaluated measures of animal performance correlated with markers of microglia activation and inflammation as they sought to see the effects of more focused radiation in two-month-old male athymic nude rats. The authors used intensity modulated radiation therapy (IMRT) and volumetric modulated arc therapy (VMAT) to irradiate the hippocampus either unilaterally or bilaterally. Treatment plans delivered a total dose of 10 Gy to either one or both hemispheres of the rat brain. Their data suggests that specific behavioral tasks could be reduced by focused radiation delivered to the hippocampus, and in unilaterally treated animals, the contralateral brain seemed to up-regulate repair mechanisms. This report provides additional information relative to the mechanisms of radiobiological effect using targeted radiation.

In general, the evidence that animal cognitive function may be affected by selective irradiation of one hemisphere with potentially compensatory mechanisms being increased (more neurogenesis) in the contralateral brain suggests that repair mechanisms remain when the radiation is confined to a smaller brain volume.

Stereotactic radiosurgery, defined as delivery of a small but intensely focused field of radiation to a limited volume in a single procedure, has revolutionized the concept of radiation delivery. For almost a century, radiation therapy was delivered to wide anatomic areas with the hope that targeted neoplastic tissue would have a differential sensitivity because of more rapidly dividing cells. Normal anatomy, especially the brain, was thought to be late responding tissue that could withstand the deleterious effect of the radiation therapy when given in small incremental or cumulative amounts. Because of the inability to adequately image the target prior to the development of computed tomography and magnet resonance imaging, the alternative was simply using wide-field radiation therapy in a fractionated mode. This approach was couched a means to exploit the differential sensitivity of neoplastic compared to non-neoplastic tissue. In reality, fractionation was developed to reduce collateral damage. The revolution created by stereotactic radiosurgery was based on the development of adequate imaging tools to recognize the limitation of disease and enabled by technologies that could truly focus radiation on small volumes. Because of the severe collateral damage created, the use of whole brain fractionated radiation therapy has been gradually abandoned.

Similarly, in recent years, increasing evidence has changed the management of metastatic disease to the brain. This usually later clinical problem in the context of systemic cancer has increased in frequency over the last 20 years. Since a high-definition MRI scan can pinpoint the number of tumors earlier in the course of disease, reliance on whole brain radiation therapy as a shotgun approach has waned. The long-term morbidity of whole brain radiation becomes strikingly evident in patients who live longer than one year. Instead, radiosurgery done for each individual tumor limits this collateral damage. The mechanism for CNS injury continues to be defined. Cytokine mediated inflammatory cell activation leads to reactive brain edema which can be refractory. The oligodendroglia that maintain white matter myelin sheaths in the brain are especially sensitive. Whole brain radiation therapy also destroys the germinal matrix centers of the periventricular regions of the brain, thereby inactivating reparative neurogenesis. Specific, targeted radiation delivery by radiosurgical technique selectively treats the tumor, reduces the risks of widespread cytokine release, prevents damage to normal brain and preserves function in those brain regions. It is likely that the same

repair mechanisms noted in animal models are also present in the human brain.

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