

Orthotopic Brain Tumors in Mice

Orthotopic tumors models are created by directly injecting tumor cells or small tissue fragments into the organ of interest in mice. For brain tumors, this involves implanting cancerous cells directly into the brain parenchyma, allowing the tumor to grow within its natural environment (Figure 1). This is critical for studying brain cancers like glioblastomas, as the brain's unique architecture and immune environment cannot be accurately replicated in non-brain tissues. These models are also widely used in preclinical testing for therapeutic interventions, such as chemotherapy, radiation, and immunotherapy.

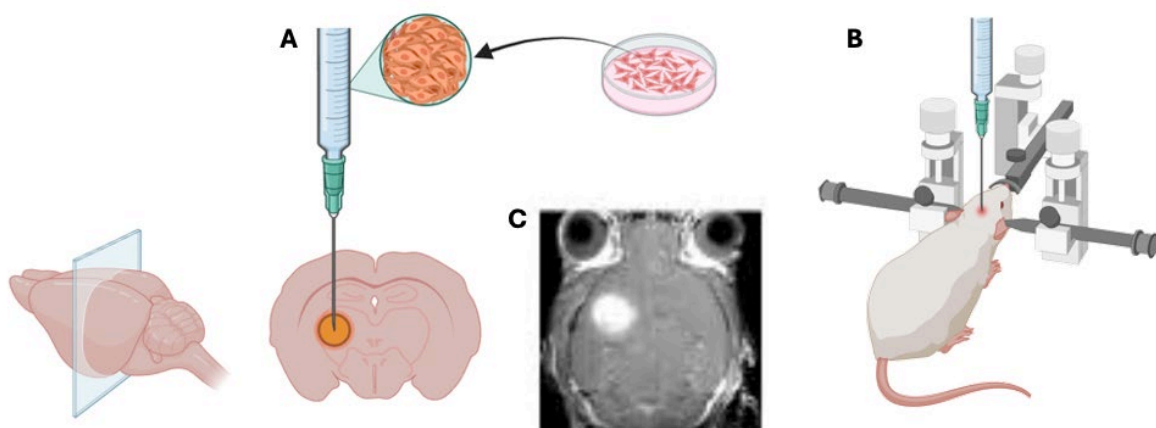


Figure 1. Schematic Representation of the Process of Generating an Orthotopic Model in the Brain of a Mouse, starting from cell culture to the localization of the injection site **(A)** using a stereotactic injection system, precisely targeting an exact location within the brain parenchyma **(B)**. The effectiveness of the process can be monitored using methods such as Magnetic Resonance Imaging **(C)**. *These images were created using BioRender.com.*

Brain orthotopic tumor models are particularly useful in investigating the molecular and cellular dynamics of **tumor progression** and **metastasis** in the brain. They allow us to examine how tumors invade surrounding brain tissues, interact with the immune system, and respond to hypoxia ¹⁻³. Several studies have shown the effectiveness of the **Precision X-Ray, Inc.** systems in

accurately targeting brain orthotopic tumors. For example, *Salzillo et al. (2021)* measured the metabolic evolution of glioblastoma during tumor development, regression, and recurrence in tumor-bearing mice undergoing radiotherapy. On Days 25 and 27, the mice were both imaged and treated with 5 Gy whole-brain irradiation using the **SmART+ (Small Animal RadioTherapy)** Irradiator (Precision X-ray, Inc., Madison, CT) (Figure 2)⁴.

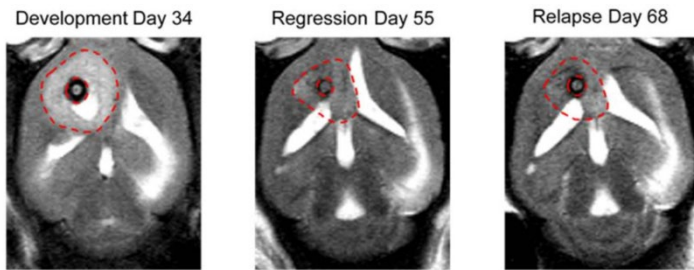


Figure 2. Anatomic and metabolic imaging of tumor-bearing mice over time. Tumor volume (A), imaged with T2-weighted MRI is displayed at the end of tumor development (Day 34), end of tumor regression (Day 55), and at the point of relapse (Day 68) in the same mouse. Adapted from (4).

Brain orthotopic models provide valuable insights into the mechanisms of radioresistance and the potential for combination therapies, such as radiosensitizers or immune-modulating agents. *Watson et al. (2024)* analyzed the microenvironmental response to radiation therapy in a preclinical glioblastoma model, comparing it with a **mouse model of breast-to-brain metastasis** (Figure 3)⁵. In this study, female C57BL6 mice were intracranially injected with a breast-to-brain metastasis cell line at matched ages and cranial coordinates to initiate tumor growth. A single, targeted whole-brain dose of ionizing radiation (10-15 Gy) was administered using the **Precision X-Ray SmART+** irradiator to assess the effects of radiation.

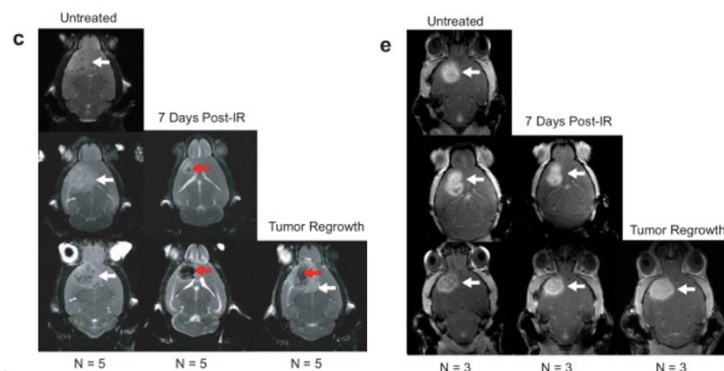


Figure 3. Single whole-brain focalized dose of ionizing radiation using the Precision X-Ray, Inc. SmART+ irradiator. Irradiation Treatment Sample Collection and Antibody Panel. Biweekly MRI monitoring tracked the process of regression and recurrence for each mouse following IR for (c) PDGfp (10 Gy) and (e) BrM tumors (15 Gy). White arrows indicate the tumor in both tumor types, red arrows indicate post-IR lesion in PDGfp tumors. Adapted from (5).

Conclusion

Orthotopic brain tumor models in mice are essential tools for advancing our understanding of brain cancer, as they closely replicate the unique environment in which brain tumors develop and interact with surrounding tissues. These models are invaluable for assessing the efficacy of different therapeutic strategies, including X-radiation therapy, which is commonly used alone or in combination with chemotherapy or immunotherapy, in the clinical treatment of brain tumors like glioblastoma.

References

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