Biologically Guided Radiation Therapy for Glioblastoma Using Spectroscopic MRI and AI Course:

Glioblastoma (GBM) is the most aggressive primary brain tumor, with a median survival of approximately 16 months despite surgery, radiation therapy (RT), chemotherapy, and tumor-treating fields. A major challenge in GBM treatment is the inability of conventional MRI to accurately delineate infiltrative tumor or reliably distinguish viable tumor from edema and treatment-related changes. As a result, empiric geometric treatment margins may undertreat infiltrative disease or unnecessarily irradiate normal brain. Large randomized dose-escalation studies, including NRG BN001, have failed to demonstrate a survival benefit from simply increasing radiation dose, highlighting a fundamental principle of modern neuro-oncology: improving outcomes requires biologically accurate target definition rather than simply increasing radiation dose.

This course introduces the principles, clinical applications, technical foundations, and future directions of whole-brain three-dimensional spectroscopic MRI (sMRI) for biologically guided RT. The course will examine how sMRI maps tumor metabolism using the choline-to-N-acetylaspartate (Cho/NAA) ratio and how metabolically active tumor can be identified beyond conventional MRI abnormalities.

Our group developed whole-brain 3D sMRI and demonstrated its clinical feasibility in a prospective multicenter trial (NCT03137888), in which sMRI-guided RT was associated with a median overall survival of 23.0 months compared with historical outcomes of approximately 15–16 months. sMRI has subsequently been incorporated into the national ECOG-ACRIN EAF223 trial, reflecting increasing clinical acceptance.

The course will also address the remaining barriers to clinical implementation, including legacy research software, computationally intensive processing, lack of standardized quality control (QC), operator dependence, and the absence of a commercial platform for routine clinical use. Students will learn about the development of BrIM AI (Brain Imaging Metabolism AI), a Software-as-a-Medical-Device (SaMD) platform to transform raw whole-brain sMRI data into treatment-planning–ready metabolic maps.

Course Objectives

By the end of this course, learners will be able to:

1. Explain the biological and clinical challenges associated with defining the extent of GBM for radiation therapy.
2. Describe the limitations of conventional MRI for identifying infiltrative tumor and distinguishing tumor from treatment-related changes.
3. Explain the principles of whole-brain 3D spectroscopic MRI and the biological significance of the Cho/NAA ratio.
4. Describe how metabolic imaging can complement conventional anatomical MRI for radiation treatment planning.
5. Review the clinical evidence supporting sMRI-guided RT, including prospective and multicenter clinical trials.
6. Explain why radiation dose escalation alone has not substantially improved outcomes in GBM.
7. Describe the technical workflow required to convert raw sMRI data into clinically usable metabolic maps.

Case-Based Learning

Students will review representative GBM imaging cases and consider:

- Conventional MRI findings versus metabolic abnormalities
- Identification of metabolically active tumor beyond anatomical abnormalities
- Potential implications for RT target delineation
- Sources of uncertainty in sMRI interpretation
- How automated AI-based processing could improve reproducibility and clinical workflow

Overall Course Theme

The future of GBM radiation therapy is not simply delivering more radiation—it is identifying the right biological target. This course explores how whole-brain sMRI, AI, and high-performance computing can enable that transition from anatomy-based to biologically guided precision neuro-oncology.