

Ex vivo means that which takes place outside an organism. In science, ex vivo refers to experimentation or measurements done in or on tissue from an organism in an external environment with minimal alteration of natural conditions.

Gliomas are composed of multiple clones of tumor cells. This intratumor heterogeneity contributes to the ability of gliomas to resist treatment. It is vital that gliomas are fully characterized at a molecular level when a diagnosis is made to maximize treatment effectiveness.

Kirby et al. collected ultrasonic tissue fragments during glioma surgery. Large tissue fragments were separated in the operating theater and bathed continuously in oxygenated **artificial cerebrospinal fluid** to keep them alive. The ex vivo tissue fragments were transferred to a laboratory and incubated in 5-aminolevulinic acid (5-ALA). 5-ALA is metabolized to Protoporphyrin IX (PpIX), which accumulates in glioma cells and makes them fluorescent. The molecular and neuropathological features of the PpIX fluorescent ultrasonic tissue fragments were studied.

They showed that PpIX fluorescence can rapidly identify tissue fragments infiltrated by glioma in the laboratory. Ultrasonic tissue fragments from the tumor core provided molecular and neuropathological information about the glioma that was comparable to the surgical biopsy. We characterized the heterogeneity within individual gliomas by studying ultrasonic tissue fragments from different parts of the tumor. We found that gliomas exhibit a power relationship between cellular proliferation and tumor infiltration. Tissue fragments that deviate from this relationship may contain foci of more malignant glioma. The methylation status of the O 6-methylguanine DNA methyltransferase gene promoter varied within each glioma.

Ex vivo ultrasonic tissue fragments can be rapidly screened for glioma infiltration. They offer a viable platform to characterize heterogeneity within individual gliomas, thereby enhancing their diagnosis and treatment ¹⁾.

¹⁾

Kirby AJ, Lavrador JP, Bodi I, Vergani F, Bhangoo R, Ashkan K, Finnerty GT. Ex vivo ultrasonic samples of human brain tumors in the molecular era. *Neurooncol Adv.* 2020 Feb 8;2(1):vdad014. doi: 10.1093/noajnl/vdad014. PubMed PMID: 32226940; PubMed Central PMCID: PMC7099933.

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