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<p>Introduction</p>	<p>Glioblastoma (GBM) is the most aggressive and fatal human brain tumor, with a median survival of 14 months. GBM is characterized by uncontrolled proliferation, massive angiogenesis, high genomic instability, and resistance to radio and chemotherapy. This resistance to therapies as well as the high frequency of relapse is due to a subset of tumorigenic stem-like cells called glioblastoma stem cells (GSCs) which are self-renewing and multipotent. Previous studies suggest that microgravity may influence negatively the rate at which tumor mass progresses. In particular, microgravity simulations on GBM cell lines performed by specific tools, as 3-D clinostat, showed a decrease in cell proliferation and an increase in sensitivity to chemotherapies, demonstrating that GBM is particularly sensitive to the environmental conditions on spacecraft.</p>
<p>Method</p>	<p>Primary GSCs will be inoculated into mice brain to create an in vivo model. Subsequently, mice with GBM and healthy mice will be sent on the International Space Station (ISS). Following the same injection protocol, mice with GBM and healthy mice will be maintained in our laboratories for the corresponding on-ground experiments. Procedures involving animals will be conducted in accordance with the international guidelines of the National Institutes of Health Guide (NIH). On board the ISS, mice will be kept in special cages and they will be monitored 24/7 thanks to internal cams. Cages will be equipped with automatized systems to provide food and water, hygiene and adjust sleep/wake cycles.</p>
<p>Results</p>	<p>At the end of the mission, mice will be examined with behavioural tests through our specifically projected maze to evaluate their cognitive abilities and Magnetic Resonance Imaging will be exploited to rate the variation in dimension and vascularization of the tumor mass. Furthermore, tumor mass will be explanted and studied at morphological, cellular, molecular, and genetic levels. We expect to assist to a decrease in GSC viability and an increase in sensitivity to chemotherapies, in order to demonstrate that GBM is particularly sensitive to the environmental conditions on spacecraft and to improve the current therapy through the translation of results obtained on the GBM management.</p>
<p>Discussion</p>	<p>Cells exposed to microgravity may be profoundly affected by the physical changes that occur in the ISS unique environment, which include the loss of gravity-dependent convection, hydrodynamic shear, and lack of sedimentation. Our study intends to investigate microgravity and ionizing radiation effect on tumor mass, in order to improve our knowledge of GBM biological mechanisms. Data collected from this research will help us to develop new therapeutic strategies and improve GBM clinical outcome.</p>
<p>Learning Objectives</p>	<ul style="list-style-type: none"> ■ Analyse the effects of microgravity and ionizing radiations on GBM ■ Use the results obtained in the ISS to improve the current therapy on-ground