



## Proton Magnetic Spectroscopic Assess Metabolic Changes of Glioma Tumor of a Patient under Intranasal Perillyl Alcohol-Based Therapy

Gisele M. Marques<sup>1,2</sup>, Giselle M Faria <sup>1</sup>, Alair S. dos Santo <sup>3</sup>, Clovis O. da Fonseca<sup>3</sup>,  
Thereza Quirico-Santos <sup>1\*</sup>

<sup>1</sup> Instituto de Biologia, Universidade Federal Fluminense, Brasil.

<sup>2</sup> Instituto Nacional de Cancer, RJ, Brasil;

<sup>3</sup> Faculdade de Medicina, Universidade Federal Fluminense, Niteroi, Rio de Janeiro, Brasil 24020-141

\* Corresponding author: [tquirico@id.uff.br](mailto:tquirico@id.uff.br)

### Abstract

Glioblastoma (GBM) is the primary brain tumor most common and aggressive in adults, characterized by intense cellular proliferation and accumulation of deleterious genetic changes which contribute to the aggressive behavior, low survival, resistance to chemotherapy and tumor recurrence. Tumor cells shows specific metabolic alteration, such as increased choline (Cho) which is characteristic of highly proliferative tumor cells, reduced N-acetyl-aspartate (NAA) a marker for neuronal density and viability and phosphocreatine (Cr) peak serves as a marker for energy-dependent systems. Metabolic information within the tumor microenvironment can be detected by proton magnetic spectroscopy (<sup>1</sup>H MRS) considered a noninvasive procedure that also provides anatomical and functional image data for diagnosis and patient follow-up. Perillyl alcohol (POH), a naturally occurring monoterpene has recognized antitumor effect inhibits tumor proliferation and increase survival of GBM patients under intranasal POH-based therapy.

To assess by H MRS metabolic changes within the tumor microenvironment and survival rate up to 8 months of a patient with GBM after intranasal administration of the monoterpene perillyl alcohol.

The present study was approved by CONEP (number 2.218.551); UFF Ethics Committee (UFFCAAE: 14613313.8.0000.5243) and was carried out at the Hospital Universitário Antonio Pedro, UFF. This case report covers a 60 years-old male GBM patient who had failed current standard treatment (surgery, radio and chemotherapy) for malignant glioma and was at terminal stage under palliative care. The patient signed a written informed consent prior to enroll in this clinical trial to assess the therapeutic efficacy (BR Patent Number PI 0107262-5) of POH (55 mg; 0.3% v/v) daily inhalation 4 times per day totaling 266.8 mg/day. MRS image and brain metabolism data (NAA/Cr; NAA/Cho, Cho/Cr ratios) were collected at the time of protocol inclusion and after 1, 5 and 8 months of POH-based treatment.

One month after POH based-therapy it was observed a marked increase of NAA/Cr and NAA/Cho ratios 23.7 and 33.5 fold respectively. Such metabolic ratios maintained a sustained increase with ongoing POH treatment (5 and 8 months). Conversely it was observed a gradual and consistent reduction of Cho/Cr ratio. During the period of this study the patient showed no image of recrudescence and was considered with partial response with reduction of the lesion size.

The present findings corroborate the already described therapeutic efficacy of POH inhalation for recurrent GBM patients due to its anti-inflammatory, antiangiogenic and antiproliferative properties. It is also highlighted the importance of including H MRS metabolic data evaluation as a monitoring tool for these patients follow up, considering the expected increment of NAA/Cr and NAA/Cho as well as the decrease of Cho/Cr.

### Keywords:

Glioblastoma,  
Perillyl Alcohol,  
Proton Magnetic Spectroscopy,  
Tumor Metabolic Indicators..