Case Study:
Novel Application for Monitoring Interstitial Fluid Pressure in Glioblastoma Mouse Model

Introduction

Cancer remains the second leading cause of death worldwide. Glioblastoma (GBM), the most common primary brain tumor, develops as a solid tumor(s) and is considered the most aggressive type of brain cancer, with an average life expectancy between 12-15 months. Many factors contribute to the increased difficulty in treating brain tumors, including the blood brain barrier and increased interstitial fluid pressure (IFP). While the blood brain barrier limits the types of compounds able to cross into the brain, increased pressure in the interstitial fluid surrounding GBM and other types of solid tumors has been found to decrease the uptake of anti-tumor treatments. Academic researchers wanted to evaluate the effects of administering the protein Antisecretory Factor (AF) in mouse models with GBM. AF has been shown to decrease excessive fluid secretion and inflammation in mammals when induced endogenously and/or given exogenously. Pressure measurements must be taken before, during, and after administration to be certain of AF's effect on tumor IFP. This study investigates a novel application of using continuous telemetry implants in a conscious, freely moving mouse model to obtain IFP during tumor progression of Glioblastoma.

The Challenge

Previous methodologies to measure IFP required animals to be anesthetized while collecting data. In addition, they often could not be used simultaneously with imaging machines, which provide valuable data on tumor growth. Researchers searched for an approach which would allow them to monitor real-time pressure changes in a model mimicking the human condition, as well as the ability to use imaging during tumor development.

The Solution

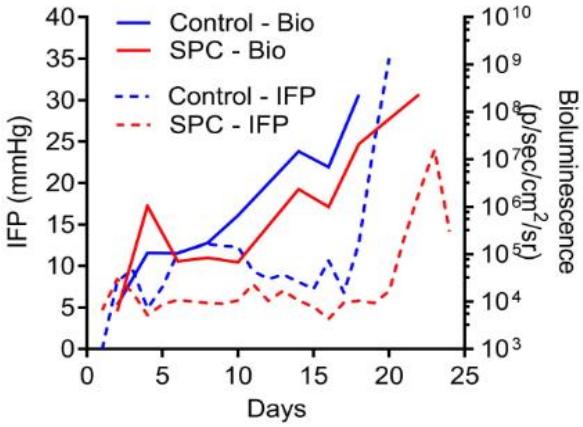
The researchers deployed the use of wireless telemetry implants, which allows pressure to be measured wirelessly and continuously in freely-moving animals. In addition, the implants are compatible with imaging techniques, such as magnetic resonance imaging (MRI).

The Study

Telemetry implants (PA-C10, Data Sciences International, St. Paul, MN USA) were calibrated, sterilized, and implanted in 4-6 week old nude mice. The pressure sensor was placed within the intercranial injections of GBM xenografts and was fixated. The mice were given chow designed to stimulate the production of AF protein and exogenous oral and nasal doses of AF peptide. They also received doses of temozolomide, the most commonly given chemotherapy for GBM. Data was collected from each mouse for at least two hours, at the same time each day. Tumor growth measurements were taken in concurrence with pressure measurements using bioluminescence every second day.

Results and Successes

During tumor progression, the data showed that IFP levels corresponded with tumor growth rates, showing decreases in the AF treatment group. This decrease showed increased uptake of chemotherapy in the patient derived xenograft mouse model. Approximately 40% of the xenografts showed reduced volume with increases in apoptotic activity after administration. The study conclusions indicate AF, in conjuction with oral chemotherapy, decreases IFP leading to increased drug uptake and improved outcomes of GBM.



This case study demonstrates the ability of DSI's pressure telemetry solution to provide real-time, continuous data of tumor IFP and researchers were able to correlate it with treatment administration. long-term

DSI

Data Sciences International (DSI) has been committed to life science research for over 30 years and is the proven leader in preclinical physiological monitoring. DSI offers complete systems that sense, transmit, acquire and report physiological data. Each system is engineered with quality and performance you can trust. The DSI team ensures that researchers are equipped and prepared from the first minute of their study to the last; because your research is everything.

References:

Sabelstrom H, Iikhanizadeh S, Miroshnikova YA, Frantz A, Zhu W, Idilli A, Quigley D, Fenster T, Yuan E, Saxena S, Mouw JK, Burdick JA, Magnitsky S, Berger MS, Arosio D, Sun D, Weaver VM, Weiss WA, Persson AI. (2017). "Exth-23. Antisecretory Factor-Mediated Lowering Of Interstitial Fluid Pressure Produces Anti-Tumor Activity In Glioblastoma". Neuro-Oncology. 19(Suppl_6); Vi77-Vi77.