TITLE: Quantitative Blood Oxygenation Level Dependent (qBOLD) MR Imaging of Glioblastoma Multiforme for Assessment of Tumour Hypoxia

SUMMARY OF PROGRESS AND CURRENT STATUS

This midterm progress report covers the period of October 2014 through March 2016. During this time, project activities focused on acquiring approval for the Toronto Academic Health Science Network Research Ethics Board of Record (TAHSN BoR) model; obtaining TAHSN BoR and Health Canada approval for study improvements/amendments; satisfying Clinical Trial Services requirements for site activation; enrolling and activating St. Michael's Hospital (SMH) as an additional institution; patient recruitment; improving patient flow at SMH; and image processing pipeline refinement. Currently, Sunnybrook is actively recruiting patients and we are finalizing the last steps of patient flow at SMH.

Thus far, we have successfully completed the following milestones:

1) Enrolling and activating SMH as a secondary site for patient recruitment.

We experienced delays in patient recruitment due to lower-than-projected GBM cases presented at Sunnybrook. The study was active for 8 months without any potential candidates. To remedy this dilemma, we recruited two more neurosurgeons at our primary site and enlisted SMH as a secondary site. In collaborating with SMH, we transitioned over to the TAHSN BoR model to expedite approval by allowing us to consolidate requirements in the site enrolment process at SMH. Implementing the TAHSN BoR model, with Sunnybrook REB as the Board of Record in a multi-centre study, also allowed us to achieve a more fluid transition.

2) Received final approval from Health Canada and TAHSN BoR in April and August 2015, respectively, with Site Initiation and Activation approval from Clinical Trial Services in early 2016.

While we enlisted SMH as a secondary site to increase patient recruitment, a number of additional requirements had to be fulfilled prior to site activation at SMH, resulting in a delay of 5 months:

- **i.** Establishing a legal collaboration contract between Sunnybrook and SMH;
- **ii.** Procuring approval and acquiring individual agreements with SMH's phlebotomy laboratory, MRI Committee and nursing support;
- **iii.** Revising the logistics of study implementation to accommodate differences in hospital procedure and layout;
- **iv.** Training new study members;
- **v.** SMH Site Initiation Visit and Site Activation Approval by Clinical Trial Services.

Currently, we have received approval from all governing bodies with no further items pending. We are actively working on improving patient flow and logistics at both sites.

3) To date, our study has 2 active sites, and we have recruited and screened 5 patients: 4 from Sunnybrook and 1 from SMH. Of those patients, we successfully enrolled 4 and omitted 1 due to ineligibility. We anticipate a sample size of 27 participants.

Preliminary data of the 4 patients screened so far supports the use of our qBOLD technique in accurately and non-invasively identifying hypoxic regions in GBM, which could be used for personalized and targeted treatment. We continue to be hopeful that this technique will lead to better patient outcomes compared to the standard therapeutic techniques currently in place.

While we have overcome several hurtles to reach this point, we are actively still trying to optimize patient flow at SMH. One area that could be greatly improved is nursing support, which we are in the last stages of optimizing. While SMH was approved and an active site by early January 2016, we were only recently (late March/early April) able to establish a Memorandum of Agreement with their nursing union. At the moment, we are working on finding a suitable applicant pool of nurses with the appropriate skills to assist with the study. We expect to complete this task and work out remaining logistical issues within the month. Moving forward, we expect much better patient recruitment rates at both sites.

Given the aforementioned delays our study has encountered, we estimate a study completion date of July 2018 which requires a 24-month extension to our current July 2016 deadline. We continue to appreciate your generosity and thank you in advance for your time. It is only with your contribution and support that we will achieve our goal of improving future treatment by demonstrating that qBOLD imaging can accurately and non-invasively assess tumour hypoxia in GBM, and correlates with invasive measurements of tissue oxygenation and histological markers of tissue hypoxia.