Simulation Framework for Vascular Radiation Damage

Final Report for Storage Allocation (wdsims01)

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Background and Significance:

Increasing patient survival rates following cancer treatment have brought more attention to the long-term effects of radiation therapy, which can detrimentally affect the patient's quality of life. Radiation-induced necrosis of the brain has received increased attention in the literature due to the difficulty of diagnosis, its severe and potentially deadly impact on the patient's quality of life, and concerns over its relation to proton and heavy ion therapies. Researchers have demonstrated a correlation between vascular network damage and necrosis induction. The long term goal of this project is to investigate the mechanisms linking vascular damage to radiation induced necrosis through simulation and small animal models.

Radiation damage to cells in vascular tissue can cause changes to a blood vessel's geometry, i.e. radius and length, and possibly lead to vessel death through rupture or occlusion. This radiation-induced vascular damage can cause local and non-local changes in blood flow through vascular remodeling and redistribution of blood flow, possibly leading to hypoxic regions in healthy tissue. Figure 1 shows a possible series of events that could connect radiation damage in vascular cells to radiation-induced necrosis.

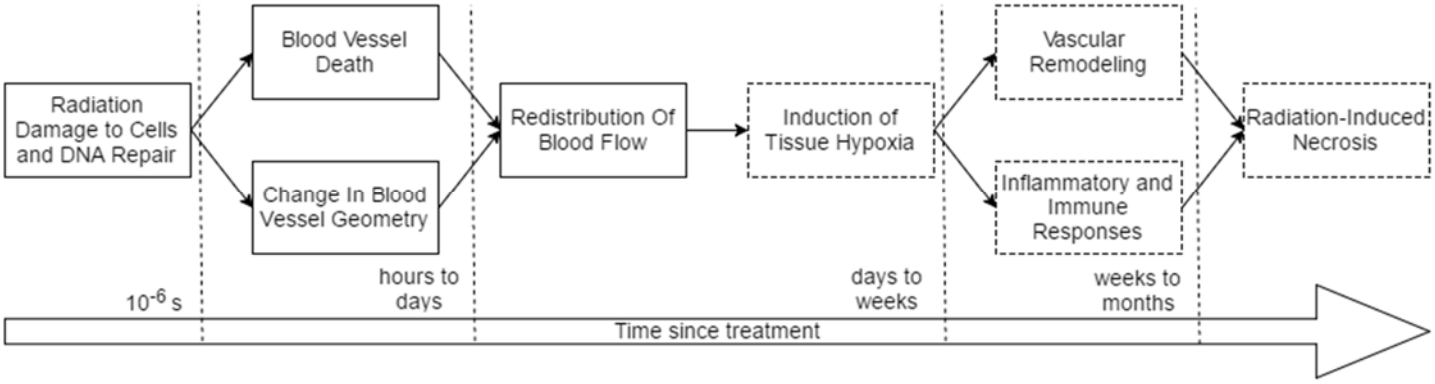

Figure 1: A diagram of some of the possible connections between radiation damage to cells and vascular tissues and radiation necrosis. The dashed boxes represent aspects of the hypothesis that are not the focus of the work described in this proposal.

Vascular networks in an organ, such as the brain, contain billions of vessels with dimensional scales spanning four orders of magnitude. The calculation of dose to large multi-scale geometries is computationally difficult and time consuming. Recent improvements in the modeling of vascular network geometry and radiation track structure lend themselves to the investigation of multi-scaled damage in vascular networks of a human brain. However, the computational requirement such a model

for the whole brain poses one of the biggest challenges. The goal of this project is to develop a computational framework for simulating vascular radiation damage, and to show that it is computationally feasible to perform these calculations for the whole brain.

To investigate the role of multi-scale vascular damage in radiation-induced necrosis, we will develop a computational framework to simulate radiation damage on whole-organ vascular networks. Using this framework, we will test the following hypothesis: *It is computationally feasible to simulate multi-scale radiation-induced changes with 10% statistical uncertainty in a 3 billion vessel network, mimicking the human brain, within 3 million CPU-h using less than 4000 CPUs.*

We propose to the test this hypothesis by performing the following specific aims:

Specific Aim 1: Evaluate a computational figure-of-merit (composite of accuracy, speed, and efficiency) for multi-scale dose calculations of proton tracks incident on a vascular network, while limiting simulation time to 2 million CPU-h ($FOM \geq 5\times10^{-5}$).

Specific Aim 2: Determine if multi-scale simulations of vasculature shrinkage caused by radiation-induced DNA damage can be completed in 800,000 CPU-h for the entire brain vascular network.

Specific Aim 3: Determine if changes in blood flow through the whole-brain vascular network can be computed using steady state Poiseuille equations within 200,000 CPU-h using less than 512 GB electronic memory.

Summary of work performed:

With the help of this allocation we were successfully able to develop a network generation algorithm and begin work on the blood flow computation component. The results from the network generation algorithm demonstrated that it is computationally feasible to generate networks containing the number of vessels in the human body. The preliminary work on the blood flow modeling was held up due to algorithmic errors in some libraries. This is currently under investigation on SuperMike. The research received a new allocation to work on the SuperMIC cluster focusing on Aims 1 & 2.

Applications of work:

The results of the research conducted under this allocation can have a wide-reaching effect in the medical community. While the current work used simplistic models of vasculature, which are suitable for computational feasibility studies, the techniques used here could be expanded to generate more realistic vascular networks. These networks could be used to study the impacts of blunt trauma injuries in the brain, pharmacokinetics, or tumor oxygenation and metastasis. Using advanced vascular models will enable researchers in the biomedical sciences to look at local and non-local changes in blood flow due to injury and design more accurate simulations of blood flow and oxygenation.

Associated Publications with this allocation:

Donahue, W. & Newhauser, W.D. Towards a Computational Model of the Vasculature of the Whole Human Brain (In Preparation)