
Focused Ultrasound and Microbubbles for Controlled Release of Circulating Cancer Biomarkers for Retinoblastoma: A Safety and Feasibility Assessment

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Introduction: Retinoblastoma (RB) is the most common pediatric eye cancer, affecting approximately 9,000 children globally each year. Tumour cell-free DNA (cfDNA) is commonly extracted by sampling the aqueous humor (AH); however, we suspect that AH cfDNA underrepresents the heterogeneous tumor clones in the posterior eye. Therefore, this project proposes focused ultrasound (FUS) as a technology to facilitate the release of tumor cfDNA from the intraocular environment into the bloodstream.

Methods: An animal use protocol (AUP) was developed by sourcing methods from the work of collaborators and relevant scientific literature, consulting with UHN's histopathology and imaging labs, and seeking advice from leads at UHN's animal facility. Feedback on the AUP and feasibility of the study were obtained from collaborators of the project.

Results: The protocol outlines two phases for this study. The first phase involves iterative changes to up to 6 groups of wild-type (WT) mice to determine FUS and MB parameters that increase BRB permeability. Magnetic resonance images will assess signs of contrast leakage and edema, while histology will assess local tissue damage. The most optimal parameters will be applied to the second phase of the study, using RB transgenic mice. In addition to MRI and histology, blood will be exsanguinated and assessed for tumor cfDNA and extravasation.

Conclusion: This will be the first proof-of-concept study utilizing FUS and MBs to disrupt the BRB and enrich circulating tumor cfDNA. If successful, these results will open the door to the feasibility of collecting liquid biopsies for biomarker comparisons in RB patients and promoting the potential for liquid biopsy in personalized cancer care.