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Abstract

# First Prospective Trial in LINAC-based 4pi Radiotherapy: Initial Results in Patients with Recurrent Glioblastoma

Tania Kaprealian [1], Angelia Tran [2], Victoria Y. Yu [3], Jean-Claude Rwigema [2], Dan Nguyen [2], Kaley Woods [2], Minsong Cao [4], Daniel A. Low [3], Michael L. Steinberg [4], Ke Sheng [2]

1. Radiation Oncology, UCLA 2. University of California Los Angeles 3. Department of Radiation Oncology, University of California, Los Angeles 4. Department of Radiation Oncology, University of California, Los Angeles, Los Angeles, USA

**Corresponding author:** Tania Kaprealian, tkaprealian@mednet.ucla.edu

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Objectives: It is hypothesized that non-coplanar beam orientation optimized 4pi radiotherapy is dosimetrically superior to manually created non-coplanar volumetric modulated arc therapy (VMAT) plans that are practical to deliver on existing C-arm linacs. We test the hypothesis in this prospective trial. The goal of the trial is to test the safety, patient tolerance, intrafractional motion and delivery efficiency of 4pi treatments.

Methods: Seven patients with recurrent glioblastoma (GBM) have enrolled in the ongoing trial. All patients received 60 Gy to their primary PTV on prior treatment. Both 4pi and non-coplanar VMAT plans were created and compared in dosimetric metrics, including target dose homogeneity and normal organ sparing. The 4pi plans were initially created using an in-house beam orientation optimization program and subsequently imported into the traditional treatment planning system for dose recalculation and creation of clinically deliverable plans. A machine and human 3D model were used to eliminate undeliverable beams. In the 4pi plans, 14-19 non-coplanar beams were used, and 3 full and partial arcs were used in VMAT plans. One of the seven patients was not treated due to near-maximum-tolerance dose to the brainstem from the prior treatment; another patient received VMAT because of undemanding dosimetry. Five patients received 4pi treatment of 25 Gy in 5 fractions (3) or 30 Gy in 10 fractions (2). Radiosurgical masks were used for immobilization. Patients were set up based on initial CBCT. Three additional 2D X-ray images were taken to determine the intrafractional motion. A patient survey was conducted after every fraction of treatment.

Results: Overall, 4pi plans showed either unchanged ($p>0.05$) or significant reductions in organs at risk (OAR) mean and max doses ($p<0.05$). The most clinically relevant dose improvement was a 38.4% reduction in the brainstem max dose. The 4pi treatment was well tolerated by the five treated patients. One patient experienced moderate discomfort with positioning on the last 3/10 fractions, but tolerated the treatment without incident. The total treatment time ranged from 26 minutes with remote couch rotation to 49 minutes with manual couch rotation. The intrafractional motion was less than 1 mm for all fractions of treatment.

Conclusions: We demonstrated the feasibility of delivering beam orientation and fluence optimized non-coplanar 4pi treatment, with minimal intrafractional motion. The treatments

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were well tolerated despite longer treatment times, which can be substantially reduced with automation. Due to improved dosimetry, 4pi allowed us to treat recurrent glioblastoma without compromising the target coverage yet sparing the surrounding critical structures, establishing the clinical feasibility and benefit of 4pi radiotherapy.