A Novel Radiosurgery Software for Treating Multiple Brain Metastases Simultaneously in a Single Fraction: First Clinical Experience

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Purpose/Objective(s): To evaluate a new, automated brain metastases planning software designed to treat up to ten brain metastases simultaneously.

Materials/Methods: Between August 2014 and February 2015 we treated 21 patients with multiple brain metastases using the novel Elements software. Patients had a minimum of 2 and a maximum of 10 metastases (median 6) ranging from 0.01cc to 8.64 cc in volume. Dose prescription was 18-24 Gy depending on histology, size, and location of the metastasis. In this software dose is prescribed to the tumor margin. Plans are normalized to give between 95% and 99% of the dose prescription to 100% of the tumor volume delivered with a maximum of 5 non-coplanar arcs using a single isocenter at the center of mass of all metastases. The number of arcs and their lengths are optimization parameters. The high degree of automation shortens the planning time to 15-20 minutes per patient. For comparison we planned 9 of the patients (46 metastases) using volumetric modulated arc therapy. We used two coplanar arcs so as to keep planning times as short as possible, and comparable to the BL planning times. Optimization objectives were applied as in the Elements software. We compared the Paddick conformity index CI = (TV/PV)^2/(TVxPV), where TV is the tumor volume, PV the prescription isodose, and TVxPV the volume of PTV receiving at least the prescription dose. We also compared the volume of brain receiving over 12 Gy (V12) in the BL and RA plans. The Mann-Whitney Rank-Sum test was used to determine statistical significance of differences between BL and RA plans.

Results: All BL and RA plans were judged clinically acceptable. CI values were not significantly different between planning systems. Median V12 of all the patients was 1.43 and 1.77cc in BL and RA respectively (p<0.005). The average number of monitor units was 6863 in RA plans, compared to 6507 in BL plans, not significantly different. RA plans took a minimum of twice as long to plan. Delivery times for BL plans were on average threefold longer than RA plans, 30 minutes is a significant improvement over conventional radiosurgery techniques.

Conclusion: The CI in both RA and BL plans was similar, although V12 was significantly larger in the RA plans. The clinical significance of this finding is unclear, as these volumes are a very small percentage of the whole brain. Due to the high level of automation, planning times for BL were much shorter than for RA. While treatment times for the new BL software plans were on average threefold longer than RA plans, 30 minutes is a significant improvement over conventional radiosurgery techniques where each metastasis is treated individually and delivery times to 10 metastases are typically over 200 minutes. Elements are a novel software allowing fast, automated planning and efficient radiosurgical irradiation of multiple brain metastases with minimal dose to the healthy brain.


Prediction of Long-term Clinical Dose Response for Early-Stage Breast Cancer Using a Dual-Compartment Mathematical Model

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Purpose/Objective(s): Growing evidence from recent cancer cell research and clinical data supports the existence of cancer stem cells (CSCs) within solid tumors. Solid tumors including breast, lung, brain, etc. may comprise a small population of distinct heterogeneous population of CSCs, which exhibit more radioresistant than the differentiated tumor cancer cells (TCs). The objectives are to analyze the pooled published clinical outcome data from adjuvant breast radiation therapy, using a dual-compartment mathematical model to account for the heterogeneous radiosensitivity.

Materials/Methods: A Poisson probability model based on a dual-compartment cell survival model was developed to calculate local disease-free survival rate (LDFSR) at follow-up times of 5- and 8-years. Clinical LDFSR data from a series of randomized clinical trials of early-stage breast radiation therapy (7806 pts) were included, including Whelan et al (1234 pts, Owen et al (1410 pts, two large randomized trials in the United Kingdom Standardization of Breast Radiation therapy (UK START) trial A (2236 patients). 9) and trial B (2215 pts). The prescription doses were between 39 and 50 Gy in 13-25 fractions. The evaluation cohorts using hypofractionation regimen of 32.5 Gy in 5 fractions (265 pts), including Ortolan et al and Courdi et al were used to validate the model prediction power. The fraction of breast CSCs (f) in total tumor cells and its radiosensitivity (a_{BCSC}) were determined using the least square metric.

Results: The model derived fitting parameters for breast cancer stem cells (BCSCs) using the dual-compartment model are a_{BCSC}=0.04 ±0.03 Gy^{-1}, \beta_{BCSC} = 0, with the fraction of BCSCs f = 0.008 ±0.04, compared to the derived parameters for breast tumor cells (BTCs) using the single-compartment model: a_{BTC}=0.11 ±0.03 Gy^{-1}, f/\beta (BTC) =4.89 ±0.02 Gy. The dual-compartment model consistently yielded a small yet finite fraction of BCSCs, suggesting the existence of BCSCs after breast conservative surgery for early stage breast cancer patients. Both single- and dual-compartment model predictions agreed with the clinical dose-response points for patient cohorts receiving doses of 40 Gy or higher at 5- and 8-year follow-up time. Dual-compartment model more accurately predicted the testing cohorts receiving doses of <39 Gy than the single-compartment model, which underestimated the LDFSR.

Conclusion: A dual-compartment radiobiological model, accounting for the level and radiosensitivity of the heterogeneous cancer stem cells, better predicted the pooled clinical outcome data than the standard single-compartment model. The result suggests the importance of separate modeling the cancer stem cells in the dose response study.


Feature Based Deformable Registration of Three-Dimensional Medical Images for Automated Quantitative Analysis and Adaptive Image Guidance

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Purpose/Objective(s): Highly robust, automated deformable registration is requisite for real-time adaptive image guidance. We investigate the feasibility of a fully automated feature-based deformable registration algorithm that mimics and extends aspects of the human visual pathway in three dimensions to reliably register and deform computed tomographic (CT) and cone beam CT (CBCT) images for planning, patient setup, or image guidance purposes.

Materials/Methods: A state-of-the-art algorithm, which automatically annotates and registers scale- and rotation-invariant landmarks robustly to small and large displacements, was developed and evaluated systematically by recovering known random fields of deformations of varying severity which were artificially introduced to a clinical planning CT. Displacements and residual errors were evaluated for all voxels excepting those near the image borders, in air or in the treatment table. To simulate daily patient setup, large random translational shifts ranging up to 80mm were incorporated in addition to the random deformation fields. Automatic CBCT registrations were evaluated subjectively and compared against manually-directed deformable registrations.