Radiobiological modeling of hyperthermia combined with Gamma-Knife radiosurgery in pediatric brain cancer

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Introduction

Assessment of the synergistic effect of radiotherapy (RT) and hyperthermia (HT) in clinical settings is crucial for further expansion of hyperthermia. The radiobiological modeling using an extended version of the LQ model with temperature-dependent radiosensitivity parameters, has been suggested for combination with external beam radiotherapy in previous studies. This study investigates the radiobiological effect of intracranial hyperthermia combined with stereotactic radiosurgery (SRS) in pediatric brain cancers.

Materials & Methods

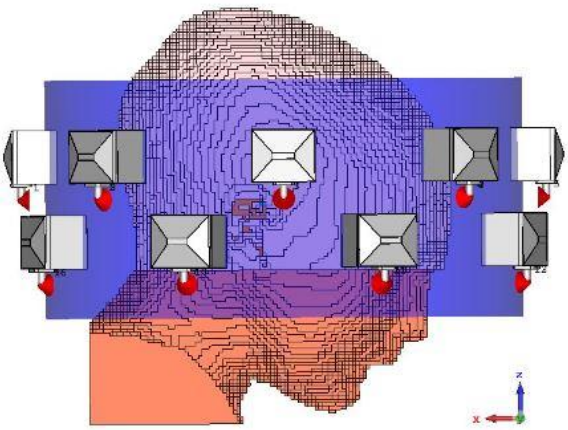
We expanded the established radiobiological LQ model by incorporating oxygenation effects to assess the effect of molecular oxygen on the irradiated tissue. The oxygen modification factor (OMF) is defined and incorporated in the linear and quadratic parameters of the model. The quantitative metrics of biologically effective dose (BED) and tumor control probability (TCP) are used in the brain model to assess the efficacy of the combined plan in a pediatric patient with Medulloblastoma. The hyperthermia treatment plan was achieved with an elliptical applicator working at 400 MHz which is recently developed by our group and the specific absorption rate (SAR) optimization procedures. The radiotherapy plan was created by the treatment planning software of Leksell Gamma Knife® Icon™.

Results

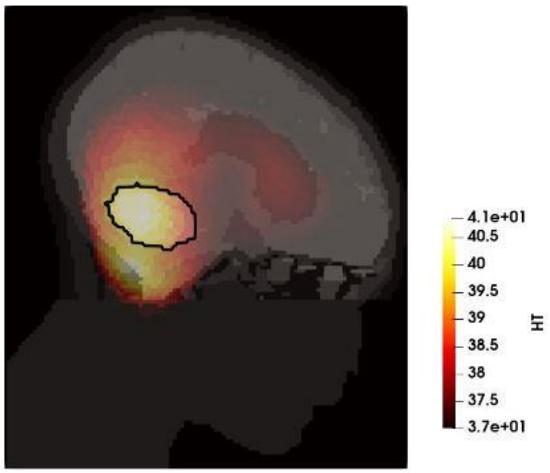
The hyperthermia treatment plan resulted in a hotspot-tumor-quotient (HTQ) value of 1.57 and the tumor coverage of TC_{25} = 97% and TC_{50} = 78%. The achieved T_{90} = 38.57 ^{o}C, T_{50} = 39.79 ^{o}C and T_{10} = 40.77 ^{o}C indicate adequate tumor coverage by the thermal dose. The Gamma Knife treatment plan with prescribed dose of 15 Gy resulted in 99.4% coverage and BED of 37.5 Gy when delivered in a single fraction. Although the results suggest a noticeable increase in the BED values for all levels of oxygenation, the administration of HT directly after RT, i.e. T_{int} = 0, yields a higher boost for each oxygenation level.

Conclusion

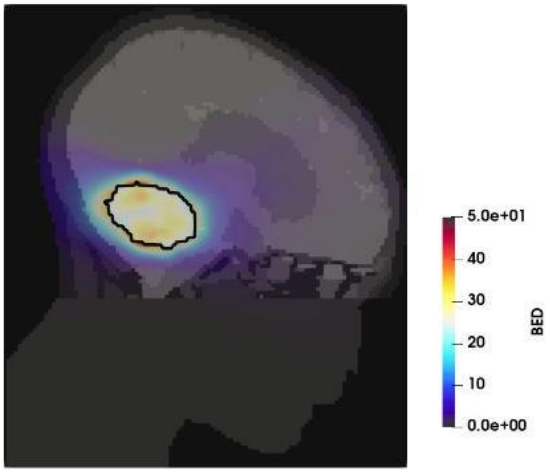
The results presented in terms of clinically relevant parameters, BED in target and surrounding healthy tissue and TCP of the optimized plan, indicate that the focused intracranial heating yields a considerable boost regardless of the time interval. The different oxygenation levels of the tumor prove the coherence of the results. This study is the first of its kind to advocate a combination of SRS with focused heating and motivates future developments.



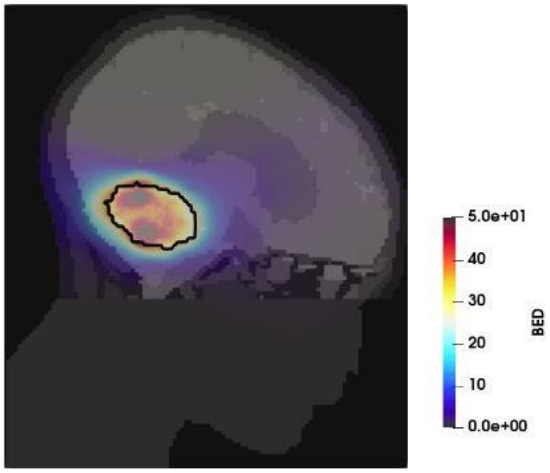
(a) Child model & the applicator



(b) Hyperthermia Temperature (°C)



(c) BED of RT-Alone (Gy)



(d) BED, Oxic, $T_{int} = 0$