Purpose:
A patient-specific method to optimize IMRT treatment of incurable disease by maximizing tumor cell death and minimizing dose to normal tissue is proposed.

Methods:
A multiobjective evolutionary algorithm was used to optimize IMRT dose distributions on an example patient throughout treatment using a published patient-specific 4D mathematical model of glioblastoma proliferation and invasion [Rockne 2010] to calculate the distribution of diffusely invaded tumor cells, hypoxia, and radiosensitivity and recalculate distributions after each week of treatment. Each optimized IMRT plan was designed to maximize EUD for tumor cells while holding constant the EUD for normal tissue. Dose distributions were scaled such that the EUD delivered to the normal tissue for each fraction was equal to the EUD delivered from one fraction using the current clinical protocol of 1.8 Gy to the frank tumor with a 2.5 cm margin.

Results:
The mathematical model predicted that the total volume of tumor was reduced by 41.0% after one week and 72.5% after two weeks of treatment using the proposed protocol. The current clinical protocol was shown to reduce volume by only 5.5% after one week and 11.2% after two weeks for the same EUD delivered to normal tissue. After 7 weeks of treatment using the clinical protocol and 250% higher normal tissue EUD, the tumor burden was only reduced by 40.4%.

Conclusions:
A patient-specific mathematical model showed that a 4D treatment plan that maximizes tumor cell killing while sparing normal tissue reduces the tumor volume more in one week than in seven weeks using current clinical protocol for the same EUD delivered to normal tissue. This approach has the potential to optimize and tailor IMRT treatment planning to individual patient’s disease through an iterative dialog between a mathematical model for disease and response to therapy with objective-based treatment optimization.