

Purpose: The microenvironment varies throughout a tumor and is known to affect radiotherapy treatment response. In this study, impact of various microenvironmental conditions (currently thought to be critical to treatment response) was evaluated, based on the development of a compartmental TCP model.

Methods: The model has three theoretical compartments based on two main microenvironmental factors, proliferation and hypoxia. The model focuses on small ‘tumorlets’ that are assumed to respond independently. The basic assumption is that each tumorlet has a limited capacity to supply cells with oxygen or glucose. The treatment response to the RT was estimated for head and neck cancer using relevant parameter values based on published sources. The tumor dose required for a TCP of 50% (TD50) was numerically derived for various growth fractions (GF's), and the effect of alternating fractionation was also evaluated.

Results: Generally, the TD50 decreased as the GF increased, with fewer cells in the hypoxic compartments. Due to the tradeoff between repopulation and reoxygenation, there typically exists an optimal fraction size having the lowest TD50 for a given GF. Smaller conventional fraction sizes (2~3 Gy/fx) were shown to be more effective for GF's in the range of 5~15%, which is thought to be the biologically relevant range. The effective reoxygenation time was evaluated for a given GF and showed decreasing tendency as GF increases. The effect of overall treatment time on the TD50 was also evaluated and the extra dose required to overcome the longer schedule was estimated to be 0.43 Gy/day using published parameters.

Conclusions: In spite of the simplicity of the model, the model reproduces the loss of local control with prolonged treatment time. The model suggests the optimal fractionation schedules may exist which have not been explored.