Purpose:

The cell-kill-based uniform dose (cEUD) formula accounts for varying tumor volume and dose variability in the tumor, has been shown to be highly correlated with local control (LC) in head and neck (H&N) and non-small-cell lung (NSCLC) cancer datasets. However, previous fits resulted in high fitted surviving fractions at 2 Gy (SF2 ~0.8), which is not radiobiologically credible. The purpose of this work is to apply a modification to the cEUD equation to more realistically model the tumor volume effect, while obtaining radiobiologically meaningful estimates of SF2.

Methods:

We propose a modification of Niemierko's formula, such that SF2 increases linearly with tumor volume, normalized to an arbitrary reference tumor size: SF2(1+ k(VT/Vref)). The resulting proportionality constant was fitted using outcome data. We modeled two different datasets collected at Washington University in Saint Louis: (A) 56 NSCLC patients who received 3D conformal radiotherapy with a median prescription dose of 70 Gy (60-84 Gy) and a median follow-up of 32 months; (B) 80 H&N squamous cell carcinoma patients who received definitive IMRT, with a median prescription dose of 70 Gy (66-72 Gy) and a median follow-up of 19 months. We tested correlation with LC using the area under the receiver operating characteristic curve (AUC).

Results:

Using a proportionality constant of k=0.05, and Vref=10 cc, we obtained high correlations with outcome for both datasets (AUC_lung= 0.729; AUC_H&N= 0.758), while keeping SF2 at a meaningful value (<=0.5). However, AUC values did not significantly increase compared to the simpler model.

Conclusions:

Introducing this modification into SF2 to account for increasing radioresistance with increasing tumor volume, led to comparable correlations of cEUD with LC, while allowing for a more reasonable range of SF2 values. This modified model is expected to make more realistic predictions concerning the effects of cold-spots or hot-spots than the unmodified model.

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