

Purpose: It is well known that the overall Tumor Control Probability (TCP) can be strongly influenced by localized cold spots in the underlying dose distribution. To evaluate the clinical significance of cold spots, we propose two new indices which are derived from TCP, but which depend on spatial location and can be overlaid as isolines on the patient's anatomy.

Methods and Materials: The cumulative TCP index is calculated as a product of tcp_i

values which are locally computed at each voxel: $TCP = \prod_{i=1}^{i=n} tcp_i$. Assuming that the

treatment planner sets a cumulative TCP target, we argue that the goal of the treatment planning can be re-formulated as follows: *to maintain a uniform distribution of locally computed tcp_i throughout the treatment volume*. The re-formulation allows us to calculate *maximum local density of clonogenic cells that is consistent with the treatment objective of the cumulative TCP*. The logarithm of this density can be overlaid on the patient's anatomy as isolines, thus quantifying the change in the effectiveness of the treatment in areas of in-homogenous dose.

Results: The Clonogen Density Index (CDI) is defined as $c_i = \frac{\alpha(BED_i) + \ln[-\frac{\ln(TCP)}{V_{tgt}}]}{\ln(10)}$

, where V_{tgt} is the target volume, and the TCP is the desired Tumor Control Probability.

The Differential Clonogen Density Index (dCDI), is defined as: $\partial c_i = \frac{\alpha(BED_i - BED_{ref})}{\ln(10)}$

where BED_{ref} is derived from the dose prescription. The dCDI index quantifies voxel-to-voxel change in the maximum clonogen density, relative to a reference value.

Conclusion: We introduce two new indices which measure maximum clonogen density that can be supported by the treatment, given the treatment objective of a cumulative TCP. These indices can be used to evaluate plans with significant regions of dose inhomogeneities. They should be seen as complementary to the TCP index.