Supplementary material

Lyman–Kutcher–Burman model

According to this model, NTCP is described by three equations,

$$NTCP = \Phi(t) = 1/\sqrt{2\pi}\int_{-\infty}^{t} \exp(\frac{-x^2}{2})dx$$

$$t = \left(D - TD_{50}(v)\right) / \left(m \cdot TD_{50}(v)\right)$$

$$V_{effi} = \sum_j \upsilon_{ij} d_{ij}^{1/n}$$

Where D is the dose that, if given if given uniformly to the entire volume, will lead to the same NTCP as the actual non-uniform dose distribution. TD50 is the uniform dose given to the entire organ volume that results in 50% complication risk, m is a measure of the slope of the sigmoid curve represented by the integral of the normal distribution, n is a parameter which describes the magnitude of the volume effect and (di, vi) are the bins of a differential dose-volume histogram.

The dose associated with a 50% risk of complication (TD50i), related to Veff for patient i is then as follows:

$$TD_{50_i} = TD_{50}(1) \cdot V_{effi}^{-n}$$

$TD_{50}(v)$ represents the risk doses associated with a 50% risk of complications for a HBV reactivation. $TD_{50i}(v)$ is related to the whole HBV reactivation tolerance(v =1) through the power law relationship for patient I in this study. $TD_{50i}(1)$ represents the tolerance of the whole liver to irradiation for patients with no HBV reactivation, the parameter “m” characterizes the steepness of the dose response at $TD_{50i}(v)$, and “n” is the volume effect parameter, which correlates the tolerance doses of a uniform whole organ irradiation with a uniform partial organ irradiation. When n is close to 1, the volume effect is large whereas the volume effect is small when it is close to 0.

For each patient i, let the vectors di and vi be the normalized DVH, when the components of vi summed to 1 and the components of di were divided by the uniform

dose Di, so that the maximum component of di equals, or is very close to 1. Let the components of di and mi be dij and vij, respectively, where 'j' represents the number of dose-volume bins for each patient's DVH (range of j approximately 50–150). Let Ri=1 if the patient i experienced HBV reactivation, otherwise Ri = 0.

The log-likelihood for the entire data set, was then maximized over all feasible values of TD50(1), m and n using Quasi-Newton and genetic algorithm implemented in Matlab software (The MathWorks, Inc.). The log-likelihood formula was,

$$L\left(m,n,TD_{50}\left(1\right)\right)=\sum_{i}\left(\log\left(N_{i}\right)^{Ri}+\log\left(1-N_{i}\right)^{1-Ri}\right)$$