Purpose: To investigate optimal fractionations to achieve high tumor control probabilities (TCPs) while maintaining acceptable normal-tissue complication probability (NTCP) using radiobiological models with new parameters derived from recent clinical data for hypofractionated liver-cancer patients.

Methods and Materials: Biological parameters for the Marsden TCP model were derived from reported outcomes of a multi-institutional Phase I/II trial. TCP and NTCP (using the LKB model with Dawson's parameters) were calculated for 8 liver cancer patients treated with different hypofractionation regimens. The correlation between tumor size, the normal liver volume receiving at least 15 Gy and NTCP were examined. Using the BioSuite software, we determined the range of fractionation regimens that achieve high TCP for 5% NTCP.

Results: The TCP parameters for liver tumors are: alpha = 0.217 Gy-1, alpha spread is 0.067 Gy-1, assuming alpha/beta = 10 Gy and 107 tumor clonogens cm-3. For any given fractionation we have found that NTCP is not correlated with the absolute liver volume receiving at least 15 Gy, nor with the dose received by the hottest 700-cc of the normal liver; these constraints are widely used in liver hypofractionation treatment planning. Instead, the parameter which correlates best with NTCP is the percentage liver volume receiving at least 15 Gy. For 5 of the 8 patients, no more than 3 fractions were required to achieve a TCP over 96%; for 2 patients TCP increased gradually with number of fractions (from 3 to 10) to 95.2% and 92.2% respectively. The remaining patient had a small liver and larger target volume which resulted in high NTCP for any fractionation.

Conclusions: A range of different hypofractionated regimens from 3x12 Gy to 5x12 Gy is found to ensure excellent outcomes. However, the commonly used dose-volume metrics for normal liver do not correlate well with NTCP. A new metric is proposed in this study.