Supplementary material for Lindblom E, et al. Survival and tumour control probability in tumours with heterogeneous oxygenation: A comparison between the linear-quadratic and the universal survival curve models for high doses. Acta Oncol 2014;53:1035–40.

Supplementary Appendix

Calculation of tumour control probability

The tumour response was assessed as the tumour control probability (TCP) calculated with a Poisson Equation 1.

$$\text{TCP} = \exp \left\{ - \sum_{i=1}^{N_{\text{vox}}} N_i [\text{SF}(d, p\text{O}_{2i})]^n \right\} \quad (1)$$

where n is the number of fractions, N_{vox} is the total number of voxels, d is the dose, N_i is the number of cells in each voxel i and $p\text{O}_{2i}$ is the oxygen tension in voxel i . The total number of clonogenic cells in the tumour was set to 10^8 .

Uniform dose delivery employing fractionation schemes of 1, 2, 3, 5, 8 and 10 fractions were simulated for the tumours in Supplementary Figures 1 and 2 and dose-response curves were fitted to the resulting TCP data using a logit expression [14]:

$$\text{TCP} = 100 \cdot \frac{1}{1 + \left(\frac{D_{50}}{D} \right)^{4\gamma}} \quad (2)$$

where D_{50} is the total dose required for a tumour control probability of 50% and γ is the slope of the curve at 50% TCP.

Supplementary Table I. Values of D_{50} for the dose-response curves presented in Figure 3 and Supplementary Figure 3.

HF	Survival model	D_{50} (Gy)					
		1 fx	2 fx	3 fx	5 fx	8 fx	10 fx
1%	LQ	37.6	48.2	54.8	63.4	70.7	74.1
	USC	43.0	50.0	55.0	63.1	70.8	74.0
11%	LQ	40.6	52.3	59.7	69.2	77.8	81.3
	USC	50.1	55.1	60.1	69.2	77.8	81.3

Supplementary Table II. Values of γ_{50} for the dose-response curves presented in Figure 3 and Supplementary Figure 3.

HF	Survival model	γ_{50}					
		1 fx	2 fx	3 fx	5 fx	8 fx	10 fx
1%	LQ	6.5	6.2	5.8	5.6	5.6	4.8
	USC	4.7	5.2	5.6	5.6	5.6	4.8
11%	LQ	7.3	6.9	6.7	6.3	6.1	5.6
	USC	5.2	5.7	6.1	6.4	6.2	5.5

Supplementary Figure 1. Realistic models of heterogeneous tumour oxygenation: (a) moderately hypoxic tumour with $\text{HF} \approx 1.1\%$, (b) hypoxic tumour with $\text{HF} \approx 11.1\%$.

Supplementary Figure 2. Realistic models of heterogeneous tumour oxygenation with decreasing hypoxic fraction: (a) after the first reoxygenation, $HF \approx 10.5\%$, (b) after the second reoxygenation, $HF \approx 9.3\%$, (c) after the third reoxygenation, $HF \approx 8.1\%$, (d) after the fourth reoxygenation, $HF \approx 7.4\%$.

Supplementary Figure 3. Dose-response curves for the various fractionation schedules as a function of total dose delivered to a tumour with 11.1% hypoxic fraction. Calculations have been done based on both the LQ model (solid curves) and the USC model (dashed curves).

Supplementary Figure 4. Dose-response curves for the 10-fraction schedule as a function of total dose delivered to a tumour with 11.1% hypoxic fraction with and without reoxygenation (green and blue curves respectively). Calculations have been done based on both the LQ model (solid curves) and the USC model (dashed curves).