Purpose: We have analyzed recent clinical data obtained from chemoradiation of unresectable, locally advanced pancreatic cancer in order to examine possible benefits from radiotherapy (RT) dose escalation as well as to propose possible dose escalated fractionation schemes.

Methods: A modified linear quadratic (LQ) model was used to fit clinical tumor response data from chemoradiation treatments using different fractionations. Biophysical radiosensitivity parameters, $\alpha$ and $\alpha/\beta$, tumor potential doubling time, $T_d$, and delay time for tumor doubling during treatment, $T_k$, were extracted from the fits and were used to calculate feasible fractionation schemes for dose escalations.

Results: Examination of published data from 20 institutions showed no clear indication of improved survival with raised radiation dose. However, an enhancement in tumor response was observed for higher irradiation doses, an important and promising clinical result with respect to palliation and quality of life. The radiobiological parameter estimates obtained from the analysis are: $\hat{\alpha} = 0.010 \pm 0.003 \text{ Gy}^{-1}$, $\hat{T}_d = 56 \pm 5 \text{ days}$ and $\hat{T}_k = 7 \pm 2 \text{ days}$. Possible dose escalation schemes are proposed based on the calculation of the biologically equivalent dose (BED) required for a 50% tumor response rate.

Conclusions: From the point of view of tumor response, escalation of the administered radiation dose leads to a potential clinical benefit, which when combined with normal tissue complication analyses may result in improved treatments for certain patients with advanced pancreatic cancer. Based on this analysis, a dose escalation trial with 2.25 Gy/fraction up to 69.75 Gy is being initiated for unresectable pancreatic cancer at our institution.

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