Tumor control, probability of cure, and all that.

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In current practice *tumor control* (TC) is taken to mean the extinction of clonogenic tumor cells at the end of treatment, a sufficient but not necessary condition for cure. In contrast, patients undergoing radiation therapy are concerned with the *probability of cure* (long term recurrence-free survival, meaning the absence of a detectable or symptomatic tumor). Tumor control thus defined has significant deficiencies, viz. it is an unobservable event, and elimination of *all* malignant clonogenic cells is in some cases unnecessary. As well, many primary cancers, such as breast and prostate cancer, are not lethal per se; they kill through metastases and, consequently, an object of tumor control in such cases should be the prevention of metastatic spread of the disease.

I shall argue that full information about the long-term treatment outcome is contained in the distribution, $P_m(T)$, of the number of malignant cells m that remain clonogenic at the end of treatment and the birth (b) and death rates (d) of surviving tumor cells after treatment. Accordingly, plausible definitions of tumor control are invariably traceable to $P_m(T)$. Specifically, I shall explain the link between survival time – where the events of interest are local recurrence or distant (metastatic) failure (cancer-free survival) or death (cancer-specific survival) – and the distribution, $P_m(T)$; and show how to link $P_m(T)$ to treatment planning (modality, total dose and schedule of radiation) and tumor-specific parameters (initial number of clonogens, birth and spontaneous death rates during the treatment period, parameters of the dose-response function).

Learning Objectives: (1) understand (and appreciate) the difference between tumor control and cure probability, (2) become familiar with the mathematical tools available for describing these quantities, (3) link $P_m(t)$ to treatment planning algorithms, and (4) become aware of many important factors that determine tumor response to radiation (cell cycling, interaction with the immune system, selection effects, spatial heterogeneity of the tumor and its capillary network, etc) that have not been taken into account. As a bonus you'll learn why the ubiquitous Poisson expression of tumor control probability is wrong and should be avoided.

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