

The volume effect for suspected subclinical disease is investigated. A dose-response model including the kinetics of micrometastatic foci establishment and development is constructed. Although radiobiological parameter values and precise model assumptions are uncertain, some qualitative conclusions based on model results can be drawn: a) Subclinical disease control probability model results consistently show, for a wide range of plausible radiobiological parameters, that TCP models applied to regions of suspected subclinical disease probably overestimate the detrimental effect of volumes of depressed dose ('cold spots'). b) Nevertheless, any cold spot with dose less than about 50-60 Gy degrades the expected level of subclinical disease control. c) Increasing dose to greater than about 50-60 Gy shows a greatly diminished return on disease control per unit dose for regions of suspected subclinical disease compared to gross disease. And d) Comparison of treatment plans which include tradeoffs between the quality of the radiation dose distribution to the gross disease and the quality of the radiation dose distribution to regions of suspected subclinical disease cannot be reliably ranked solely using TCP models developed for gross disease. Cold spots are expected to affect local control less for sites of suspected subclinical disease compared to gross disease for two reasons: there is some probability that the cold spot will not contain any metastatic foci, even if foci are present elsewhere, and also many micrometastatic foci will have very small numbers of clonogens, which are controlled even with relatively low doses.