The radiobiology of prostate cancer including new aspects of fractionated radiotherapy.

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Abstract

Total radiation dose is not a reliable measure of biological effect when dose-per-fraction or dose-rate is changed. Large differences in biological effectiveness (per gray) are seen between the 2 Gy doses of external beam radiotherapy and the large boost doses given at high dose-rate from afterloading sources. The effects are profoundly different in rapidly or slowly proliferating tissues, that is for most tumors versus late complications. These differences work the opposite way round for prostate tumors versus late complications compared with most other types of tumor. Using the Linear-Quadratic formula it is aimed to explain these differences, especially for treatments of prostate cancer. The unusually slow growth rate of prostate cancers is associated with their high sensitivity to increased fraction size, so a large number of small fractions, such as 35 or 40 "daily" doses of 2 Gy, is not an optimum treatment. Theoretical modeling shows a stronger enhancement of tumor effect than of late complications for larger (and fewer) fractions, in prostate tumors uniquely. Biologically Effective Doses and Normalized Total Doses (in 2 Gy fraction equivalents) are given for prostate tumor, late rectal reactions, and--a new development--acute rectal mucosa. Tables showing the change of fraction-size sensitivity (the alpha/beta ratio) with proliferation rates of tissues lead to the association of slow cell doubling times in prostate
tumors with small alpha/beta ratios. Clinical evidence to confirm this biological expectation is reviewed. The alpha/beta ratios of prostate tumors appear to be as low as 1.5 Gy (95% confidence interval 1.3-1.8 Gy), in contrast with the value of about 10 Gy for most other types of tumor. The important point is that alpha/beta =1.5 Gy appears to be significantly less than the alpha/beta =3 Gy for late complications in rectal tissues. Such differences are also emerging from recent clinical results. From this important difference stems the superior schedules of, for example, 20 fractions of 3 Gy, or 10 fractions of 4.7 Gy, or 5 fractions of 7 Gy, which can all give tumor results equivalent to 80-90 Gy in 2 Gy fractions, while keeping late complications equivalent to only 72 Gy in 2 Gy fractions. Combination treatments of external beam (EBRT) and brachytherapy boost doses (25F x 2 Gy plus 2 x 10 Gy) can give higher biological tumor effects than any EBRT using daily 2 Gy doses, and with acceptable late complications. Monotherapy by brachytherapy for low-risk cancer prostate using two to four fractions in a few days can give even higher biological effects on the tumors.