

AbstractID: 6967 Title: Hypofractionated RT: Biological basis and clinical application in the prostate and lung

Hypo-fractionation, the delivery of radiation therapy with a dose per fraction >2.0 Gy, was introduced in curative radiotherapy in many centers all over the World in the period from WWII to the mid-1970's, mainly for health economics reasons. Clinical studies published in the late 70's and early 80's showed that these schedules were often associated with excessive late toxicity compared to standard fractionation schedules, and hypo-fractionation was abandoned in most centers. In hindsight, this negative experience largely resulted from the over-estimation of tolerance doses in hypo-fractionated schedules arising from the Ellis NSD formula. Logically, this historical clinical experience does not exclude that hypo-fractionation can be acceptable or even advantageous under certain defined circumstances.

The current status of the linear-quadratic bio-effect model in clinical practice is reviewed. Two clinical settings, where hypo-fractionation is considered, are presented and discussed: (1) definitive radiotherapy for non-small cell lung cancer (NSCLC); (2) definitive radiotherapy for prostate cancer.

For both NSCLC and prostate cancer the current interest in the development and clinical testing of safe hypo-fractionation regimens springs partly from the improved physical dose distribution achievable with 3D conformal radiotherapy or IMRT. This provides a window of opportunity for escalating dose per fraction. But there is also a biological rationale for hypo-fractionation in these two tumor types – and a slightly different one in the two cases! For NSCLC there is strong evidence that shortening the overall treatment time creates a favorable efficacy:toxicity ratio with respect to late toxicity: hypo-fractionation is a convenient way of delivering accelerated radiotherapy. In other words, we are trading in time for dose per fraction. For prostate cancer, there are no good reasons to believe that there is a strong time factor. However, there is increasingly convincing evidence that the α/β ratio for this tumor type is low, perhaps even lower than for the dose-limiting rectal side-effects. This alone creates a case for exploring hypo-fractionation in this disease.

Hypo-fractionation schedules are being tested in controlled clinical trials in several tumor types at the moment. These schedules should not be introduced in the clinic without appropriate evidence that they are safe and effective. However, based on our improved knowledge of clinical radiobiology, it appears that hypo-fractionation schedules may yield a beneficial therapeutic ratio and/or a superior cost-effectiveness in some clinical indications.

Learning objectives:

After this session the participants should be able to:

1. Recognize the limitations of the traditional linear-quadratic model
2. Summarize the changes in biological understanding of dose fractionation that have occurred over the last 10-15 years
3. Explain the rationale behind the current interest in hypo-fractionation in NSCLC and prostate cancer