AbstractID: 6982 Title: Application of hypofractionation in the prostate

Prostate cancer exhibits slow growth with a potential doubling time ranging from weeks to months (median 42 days). From these data emerged a hypothesis that adenocarcinoma of the prostate may behave more like a late reacting tissue. Brenner and colleagues (1) used data from prostate low dose rate permanent seed implants and external beam radiotherapy series and derived an α/β of approximately 1.5. Many other groups have also calculated the α/β ratio to be in the < 3.0 range; yet, ***hyper***fractionation does not seem to compromise outcome after radiotherapy (2). There are many potential pitfalls of these analyses and some investigators have concluded that the α/β for prostate cancer is closer to that for late effects of the surrounding normal tissues (>3).

Understanding the α/β ratio for prostate cancer is key to designing clinical trials that maximize the efficacy of radiotherapy. If the α/β for prostate cancer is lower than the surrounding normal tissues, hypofractionation will afford an advantage in terms of greater sensitivity of prostate cancer to this strategy, as compared to the bladder and rectum. Brenner et al (3) have estimated the α/β for the rectum to be over 5.0. Recently, Fiorino and Valdagni (4) have argued that these estimates may be inaccurate because of variation in, and dependence of toxicity on, the proportion of rectum receiving higher radiation doses.

Clinical results in the PSA/IMRT era using hypofractionation show that this strategy is well tolerated by the surrounding normal tissues, with outcomes consistent with a low α/β. Kupelian et al. (5) have treated a large series of men to 70 Gy at 2.5 Gy per fraction with excellent results. As an offshoot of this strategy, RTOG 04-15 contrasts this hypofractionation regimen with 73.8 Gy in 1.8 Gy fractions.

The Cleveland Clinic data also prompted us at Fox Chase Cancer Center to devise a randomized hypofractionation trial comparing 76 Gy at 2.0 Gy per fraction to 70.2 Gy at 2.7 Gy/Fx. The latter hypofractionation regimen is equivalent to 84.4 Gy at 2.0 Gy/Fx, assuming an α/β of 1.5. A total of 307 patients were entered from 2002 to 2006. The trial has completed accrual. Acute toxicity in the first 100 men entered shows minor differences between the two treatment groups (6). Analysis of late toxicity during the first year of follow-up also is revealing little difference. The encouraging results thus far with hypofractionation suggest that more significant hypofractionation (e.g., stereotactic radiotherapy) might be cost-effective and potentially advantageous.

1. Brenner DJ, *et al. Int J Radiat Oncol Biol Phys* 1999;43:1095-1101.
2. Valdagni R, *et al. Radiother Oncol* 2005;75:74-82.
3. Brenner DJ. *Int J Radiat Oncol Biol Phys* 2004;60:1013-1015.
4. Fiorino C, *et al. Int J Radiat Oncol Biol Phys* 2005;62:289-290; author reply 290-281.
5. Kupelian PA, *et al. Int J Radiat Oncol Biol Phys* 2005;63:1463-1468.
6. Pollack A, *et al. Int J Radiat Oncol Biol Phys* 2006;64:518-526.

Objectives

1) To understand the alpha/beta ratio for prostate cancer
2) To appreciate the efficacy of hypofractionation and resultant toxicity.