PULSE LOW DOSE RATE RADIATION THERAPY FOR RE-TREATMENT OF THE SAME DISEASE SITE WHICH NORMAL TISSUE TOLERANCES ARE AT OR NEARLY REACHED

Robert Gleason, Department of Radiation Oncology, Fox Chase Cancer Center, Philadelphia, PA

Introduction

With the emergence of new technologies and targeted therapies, cancer patients are able to live longer. However, as they live longer there is a growing number of patients that need re-treatment of cancer at or near the same disease site. The re-treatment of patients at the same disease site is an arduous task because usually the surrounding normal tissue structures are nearing their radiation dose tolerances. Pulse low dose rate therapy is a technique that has shown to be effective in the re-treatment of patients to the same disease site that would previously not be possible.

Methods

Research has shown that cells can repair themselves at low dose rates and are most pronounced at rates of 1-100cGy. There is a hypersensitivity to radiation at doses <0.3Gy. We know from studies that repair is triggered at a higher dose in tumor cells than it is in normal tissue cells. This can be achieved by dividing the number of radiation beams into pulses with each individual beam dose receiving less than the tumor transition dose but greater than the normal tissue transition dose so that the radiation repair is activated in normal tissues but not in tumor cells.

Planning and Treatment

PLDR can be done using IMRT, VMAT, or 3D. A PTV target must be contoured in order to ensure that the PLDR constraints are met. When planning PLDR each individual beam must deliver <40cGy to the PTV in order to not illicit the tumor cell's repair mechanism. Our normal prescription dose for treatment of re-irradiation of the same disease site is 200cGy per fraction to 3000cGy-6000cGy depending on physician preference. We maintain a 180/200cGy daily dose in order to achieve the PLDR hypersensitivity. When beginning the planning process, start with two beams and a prescription of 40cGy daily dose and a dose rate of 100cGy. Adjust the fractions to meet the correct total dose initially. Counterintuitively, do not put any constraints on the normal tissue structures when inverse planning, as this often will cause the plan to exceed PLDR constraints. When planning, try using beams that avoid the critical structure in question. This is not always possible however, and so it is not absolutely necessary when planning. After calculation, check that each of the two beams do not contribute more than 40cGy to the PTV. If the dose is over 40cGy for either beam, then you must change a parameter and try again. Once the PLDR criteria is met, the beams are copied to equal 10 beams and the prescription is adjusted with the correct dose and fractionation. Each beam is to be delivered with a 3-minute interval between beams to allow for repair.

DOSE RATE EFFECT

- Cells can repair themselves at low dose rates and are most pronounced at rates of 1-100cGy
- There is a hypersensitivity to radiation at doses <0.3Gy

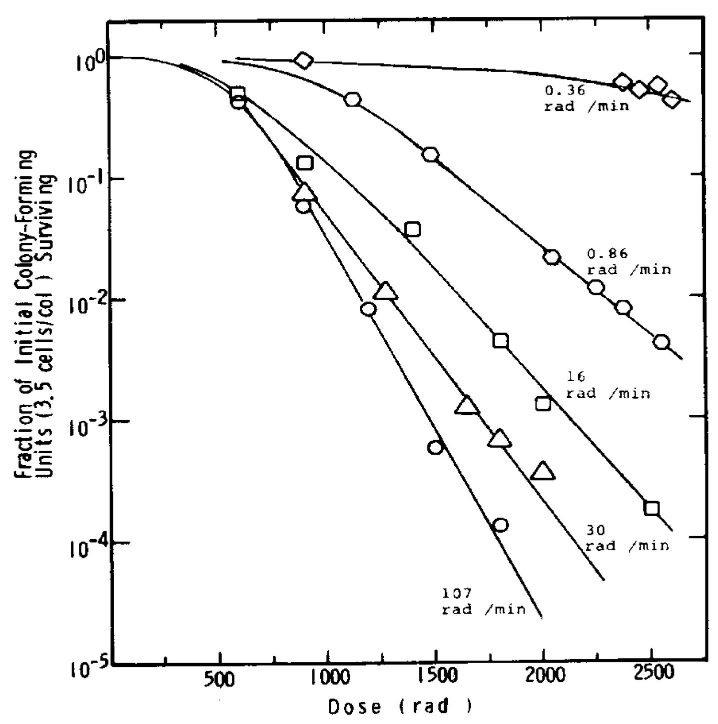
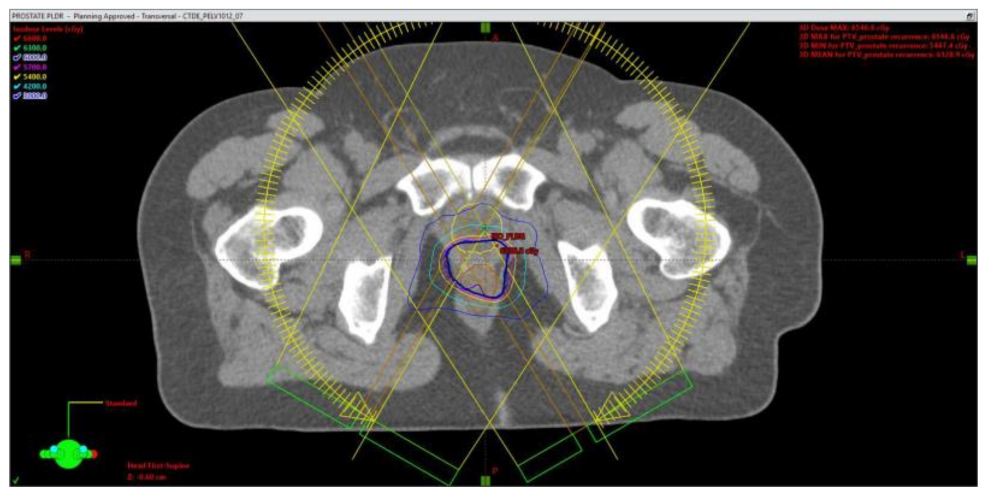


Figure 5.10. Dose–response curves for Chinese hamster cells (CHL-F line) grown *in vitro* and exposed to cobalt-60 γ-rays at various dose rates. At high doses a substantial dose-rate effect is evident even among 1.07, 0.3, and 0.16 Gy/min (107, 30, and 16 rad/min). The decrease in cell killing becomes even more dramatic as the dose rate is reduced further. (From Bedford JS, Mitchell JB: Dose rate effects in synchronous mammalian cells in culture. Radiat Res 54:316–327, 1973, with permission.)

Hall, E.J. and A.J. Giaccia, Radiobiology for the radiologist. 6th ed. 2006, Philadelphia: Lippincott Williams & Wilkins. ix, 546 p.

VMAT PLDR (Prostate Re-Treatment)



10 field VMAT 60Gy in 30 Fractions 100cGy Dose Rate treat each Beam 3 minutes apart

LOW DOSE HYPERSENSITIVITY

- There is a hypersensitivity to radiation at doses <0.3Gy
- From ~ 0.3-0.6 Gy there is a more radio-resistant response to radiation. The transition associated with overcoming hyper-radiosensitivity (HRS) is termed increased radioresistance (IRR)

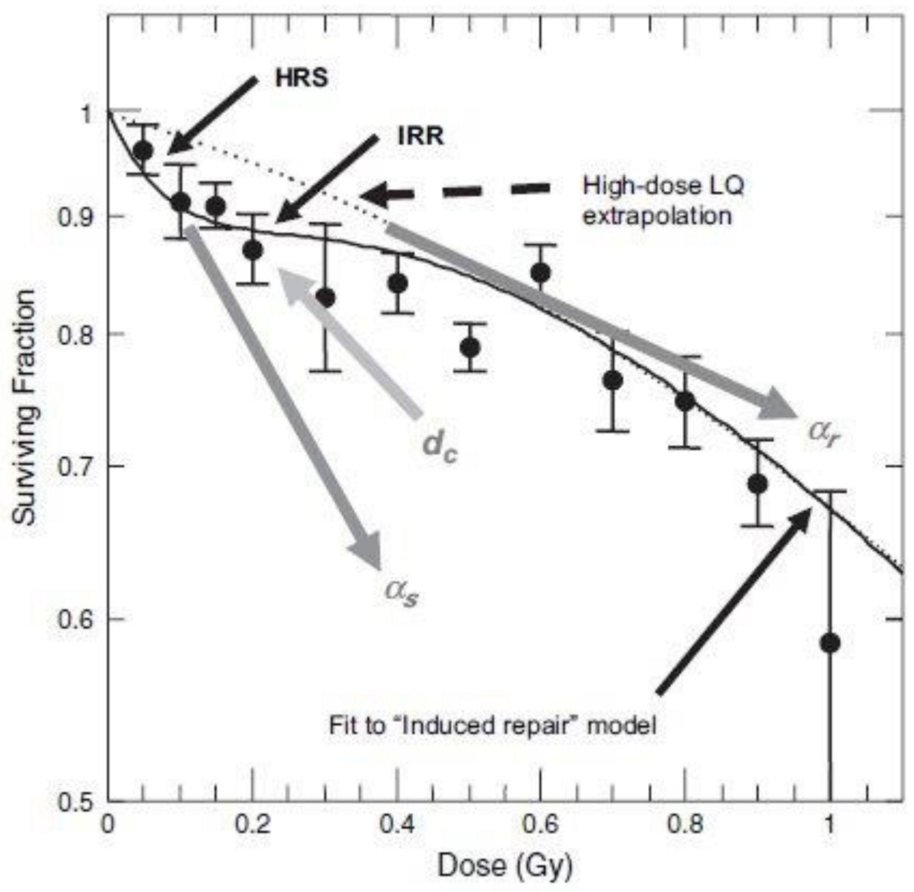
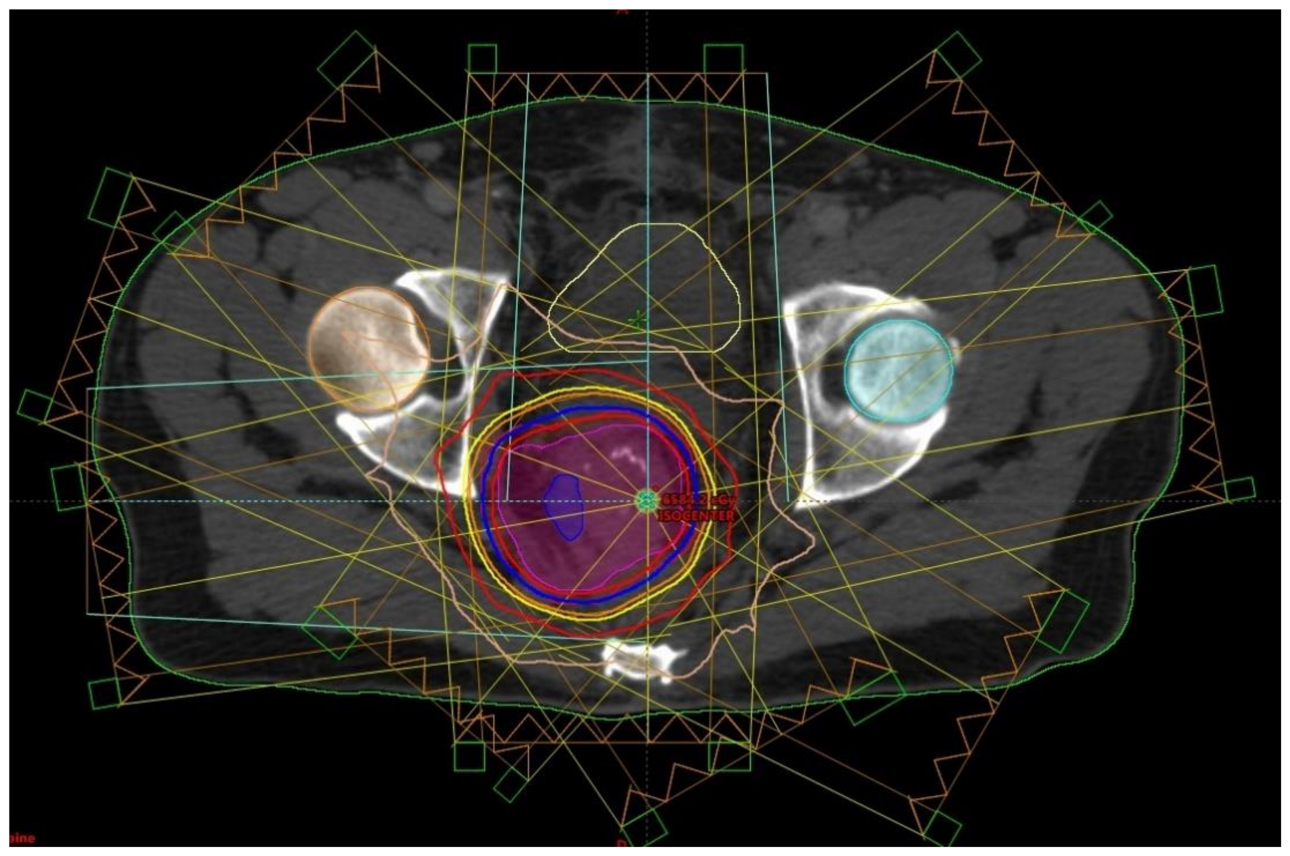


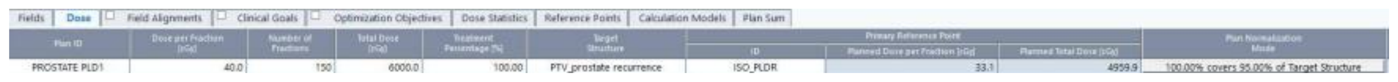
Fig. 1. Typical cell survival curve with evidence of hyper-radiosensitivity (HRS). Broken line shows low-dose extrapolation from linear quadratic (LQ) model applied to high-dose survival data. Solid line shows Induced Repair fit. Derivation of α_s, α_r, and d_c parameters are shown in Eqn. 1.

Joiner, M.C., et al., *Low-dose hypersensitivity: current status and possible mechanisms.* Int J Radiat Oncol Biol Phys, 2001. **49**(2): p. 379-89.
Gridley D.S., W.J.R., and Slater, M., Low-dose/low-dose-rate radiation: A feasible strategy to improve cancer radiotherapy. Cancer Therapy, 2005. 3: p. 105-130.
Lin, P.S. and A. Wu, Not all 2 Gray radiation prescriptions are equivalent: Cytotoxic effect depends on delivery sequences of partial fractionated doses. Int J Radiat Oncol Biol Phys, 2005. 63(2): p. 536-44.

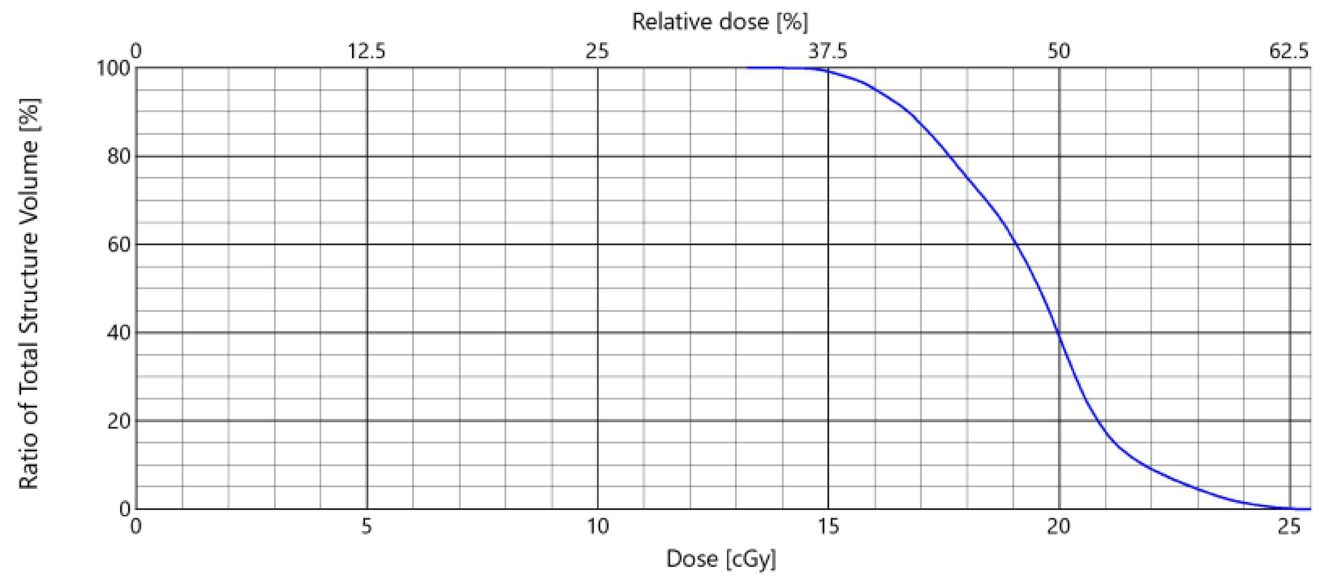
FCCC PLDR PRACTICE



60 Gy in 30 fx.. 10-field IMRT. 100 MU/min. Treat each beam within 3-minute intervals

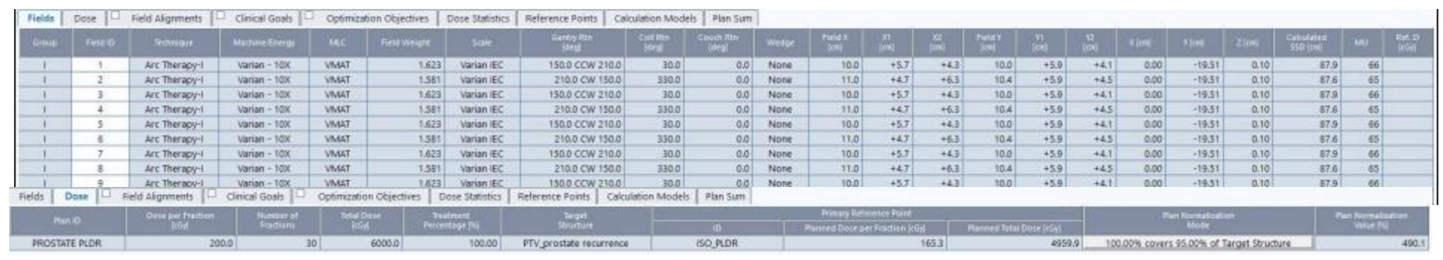


Start with two beams and a dose of 40cGy, copy to ten once PLDR criteria is met



DVH	Structure	Structure Status	Coverage [%/%]	Volume	Min Dose	Max Dose	Mean Dose	Modal Dose	Median Dose	Std Dev
	PTV prostate recurrence	Approved	100.0 / 100.0	38.1 cm³	13.2 cGy	25.5 cGy	19.4 cGy	19.9 cGy	19.6 cGy	2.0 cGy

DVH criteria: PTV <40cGy for each Beam



PLDR with 10 beams 200 cGy in 30 Fractions treating each field in 3-minute intervals

Conclusions

As cancer patients live longer with cancer there becomes an increased potential for the patient to need re-treatment of the same disease site with radiation. Treatment with Pulse Low Dose Radiation (PLDR) by taking advantage of the hypersensitivity of cells below 0.3Gy and delivering radiation in pulses to allow repair of the normal tissue structures is a good way to safely irradiate the re-treatment area and not cause the potential adverse radiation side effect from the associated normal tissue structure that would now be considered over tolerance.