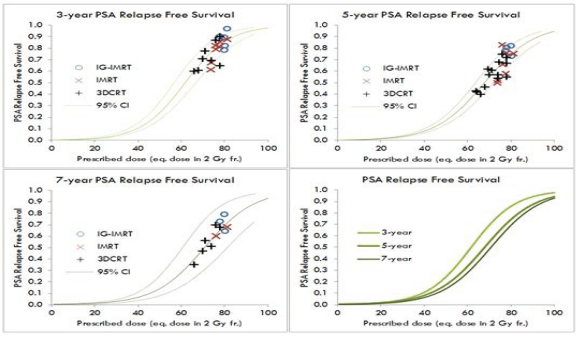
(D_{50}) were fitting parameters and studies were weighted using inverse variance (see Eq. 1).

$PRFS=1/(1+\exp(4\cdot\gamma_{50}\cdot(1-D/D_{50})))$ [Eq.1]

Results: A total of ca 4000 publications were reviewed of which 15 met the acceptance criteria, providing a total of 28 dose level outcome data at 1-4 time points. A total of 6/28 were using IG-IMRT, 7/28 IMRT, 15/28 3DCRT and 6/28 were randomized trials. IG, IMRT and radiation dose were associated with improved PRFS at 5 years (Table 1), while randomized trials (yes/no), the frequency of use or duration of ADT were not.Only the radiation dose remained significant in a multivariate analysis, indicating that a pooled analysis of all studies was reasonable. The gradient of the dose response curve (γ_{50}) was ca 1.5% at 3-7 years, and the dose required to obtain 50% PRFS (D_{50}) was significantly different at 3 vs. 5 and 7 years ($p<0.001$) (Fig. 1.). A reduction of 6% in PRFS per year was estimated for year 3-5 post RT. Increased treatment margin tended to improve PRFS independent of IGRT use. No publication bias was evident.

Univariate analysis	PRFS (3yrs) Rs	PRFS (3yrs) p-value	PRFS (5yrs) Rs	PRFS (5yrs) p-value
Equivalent dose in 2 Gy/fr.	*0.712*	*0.000*	*0.752*	*0.000*
Posterior PTV margin (mm)	-0.161	0.486	-0.159	0.437
Daily IGRT	*0.540*	*0.012*	*0.526*	*0.006*
IMRT	0.421	0.057	*0.504*	*0.009*
Androgen DT (%)	0.238	0.300	0.174	0.395
Med duration of ADT (time, yrs)	0.184	0.425	0.355	0.075
Randomized trial	-0.240	0.294	-0.353	0.077

Multivariate analysis	PRFS (3yrs) Coefficient	PRFS (3yrs) p-value	PRFS (5yrs) Coefficient	PRFS (5yrs) p-value
Equivalent dose in 2 Gy/fr.	*0.020*	*0.000*	*0.021*	*0.000*
Posterior PTV margin (mm)	0.007	0.114	0.005	0.307
Daily IGRT	0.040	0.369	0.083	0.082
IMRT	-0.013	0.780	0.019	0.634
Androgen DT (%)	-0.036	0.563	0.017	0.760
Med duration of ADT (time, yrs)	0.003	0.869	0.023	0.247
Randomized trial	-0.029	0.527	-0.039	0.319



Conclusions: High-dose IG-IMRT was associated with superior PRFS vs. low-dose RT for high-risk PCa. PRFS at 3 years can potentially be used to predict outcome at 4-7 years. The possibility of a minor effect on PRFS by reducing the treatment margin could be discerned. By extrapolation of our model, RT to ca 85-95 Gy in equivalent dose in 2-Gy fractions is predicted to improve PRFS for high-risk PCa, after which the local control plateaus and the benefit diminishes.

PD-0136

Hypoxia biomarkers for prognostic evaluation and the prediction of outcome following prostate radiotherapy

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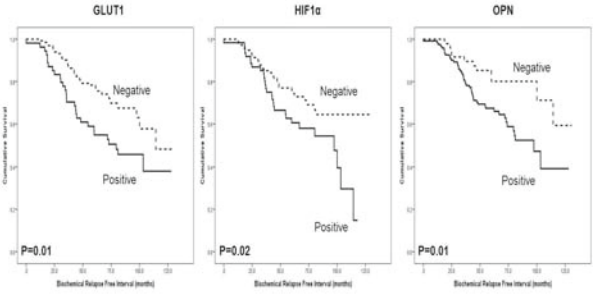
Purpose/Objective: The dose-response relationship for prostate radiotherapy has been demonstrated in several clinical trials with an advantage for high dose treatments. Established prognostic factors; including tumour stage, Gleason score, and PSA explain only a moderate proportion of the variation in outcome following prostate radiotherapy. There are no reliable predictors to determine which patients are likely to benefit from the extra dose. Prostate cancer exhibits regions of hypoxia with oxygen partial pressures that are likely to have radiobiological significance. The concept of the oxygen enhancement ratio is well established and it is possible that hypoxia biomarkers may predict which patients require dose escalation. We aimed to study the predictive value of intrinsic biomarkers of tumour hypoxia (GLUT1, HIF1α and osteopontin (OPN)) in patients treated with radiotherapy for localised prostate cancer.

Materials and Methods: Paraffin embedded prostate biopsies were collected from patients enrolled into a trial of external beam radiotherapy (EBRT) versus combined EBRT followed by a high dose rate (HDR) brachytherapy boost.

Immunohistochemical staining was performed for GLUT1, HIF1αand OPN using monoclonal antibodies. Tumours were assessed for biomarker expression by two independent investigators, blinded to patient outcome and scored as negative or positive depending upon the proportion of cells staining for the marker in question. Biochemical relapse free interval for all patients was determined using the Kaplan-Meier method.

Results: 191 samples were included in the analysis. Hif1α, Glut1 and OPN expression were all significantly associated with a shorter biochemical relapse free interval (see figure and table). High dose radiotherapy (EBRT plus HDR boost) was advantageous over conventional dose radiotherapy (EBRT alone) for patients that exhibited OPN expression (p=0.017) but not for patients with negative OPN staining (p=0.349). Conversely, for GLUT1, high dose radiotherapy was only advantageous over conventional dose radiotherapy for patients that lacked GLUT1 expression (p=0.006).

		Mean BRFI estimate (months)	Median BRFI estimate (months)	p-value for overall significance	p-value stratified for the different RT arms
Statistical Method		*Kaplan-Meier*	*Kaplan-Meier*	*Log-Rank*	*Log-Rank*
Glut 1	Neg	98.7	114.4	0.005	0.006
	Pos	78.5	79.5		0.460
HIF1α	Neg	100.7	Not Reached	0.019	0.010
	Pos	77.7	97.4		0.084
Osteopontin	Neg	107.8	Not Reached	0.012	0.349
	Pos	85.3	97.4		0.017



Conclusions: Overall, expression of OPN, HIF1α or GLUT1 confers a poorer prognosis for patients receiving prostate radiotherapy compared to those that do not express these hypoxia biomarkers. Furthermore, these data generate the following hypothesis: OPN becomes positive in the presence of mild/moderate hypoxia, GLUT1 only becomes positive under conditions of severe hypoxia. Therefore, If both OPN and GLUT1 are negative (i.e. minimal hypoxia), there is no benefit from dose escalation. If OPN is positive and GLUT1 is negative (moderate hypoxia), there is a benefit for dose escalation. However, If GLUT1 is positive (severe hypoxia), there is no benefit from dose escalation because patients will do badly despite very high doses of radiotherapy. Further evaluation using an independent data set is ongoing.

PD-0137

Generation of geometrically adaptable IMAT plans for prostate cancer treatment

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Purpose/Objective: Daily location of the target volume has become a usual clinical practice after introduction of portal imaging devices. The actual information on the day of treatment is used to relocate the patient to maximize target coverage. However, relocation is not capable to account for large deformations of structures of interest, and the therapeutic ratio remains lower then desired. We propose a method of generating triple-arc IMAT plans to treat prostate cancer