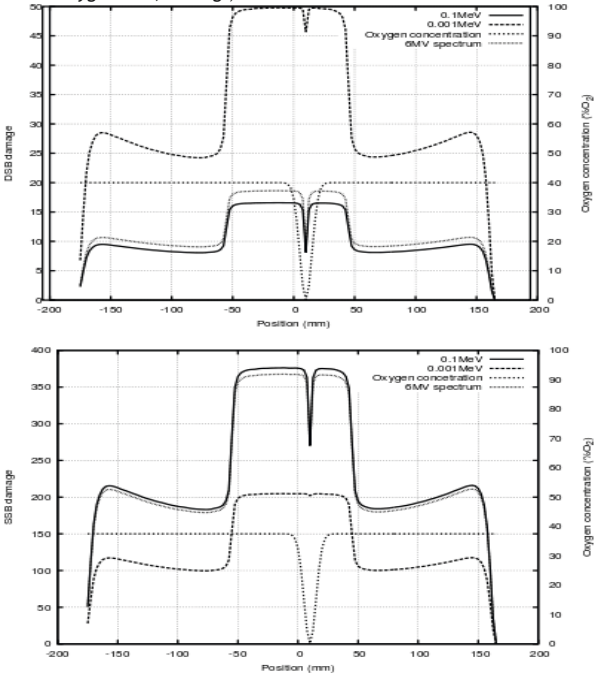
$$M_s = \frac{\int_0^{E_{max}} \Psi(E)(\mathbf{D} \circ F_s(\mathbf{P}', E))dE}{\int_0^{E_{max}} \Psi(E)dE}$$

with ° denoting the Hadamard or element-wise matrix product, F_s denotes the parameterization.

3) In the realistic beam setup an effort is made to compensate for the lack of damage, introducing *iso-malic* treatments. This is attempted by quantifying the needed increase in localized dose. Alternatively, changing the dose depositing electron energy spectrum by introducing gold nano-particles is investigated.

Results: 1) For electrons, absolute standard deviations of SSB: 0.24, DSB: 0.15 (in number of strand breaks) led to relative errors of the order of resp. 0.0005 and 0.003 for 2Gy. For protons SSB:0.34 and DSB: 0.041, was found.

2) In both DSB and SSB damage maps the results are consistent with the clinical experience that lowered oxygen levels imply lower damage levels. Even for electrons high LET effects showing reduced dependency on oxygenation at very low energies is observed. DSB damage levels in the low oxygenated environment for realistic beams are of the order of those obtained outside the treated volume (which is well oxygenated, see fig.).



3) Using dose escalation to obtain iso-malic treatment proved to be difficult. To obtain the same damage in DSB a dose increase of 40% was needed while for SSB an increase of100%. In the spectral approach the damage difference between regular and gold enhanced spectra, resulted in damage increases which were lower than the accuracy of our models, making it ineffective at accelerator energies.

Conclusions: We have introduced a methodology to represent microscopic effects in clinical radiation treatment plans, yielding plans that provide uniform damage throughout the treated volume.

PO-0840

Use of equivalent uniform dose objectives in inverse planning to reduce bladder toxicity in high dose prostate IMRT

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Purpose/Objective: EUD-based Normal Tissue Complication Probability (NTCP) models have been shown to significantly predict late bladder toxicity *(J. Zhu, ESTRO 2011)*. *The goal of* this study was to assess the benefit of using bladder EUD objectives in intensity-modulated radiotherapy (IMRT) inverse optimization to reduce bladder toxicity, while keeping the same PTV coverage for prostate cancer.

Materials and Methods: Using Pinnacle treatment planning system, two IMRT plans were generated for 53 prostate cancer patients, to deliver 80Gy to the prostate PTV (V95>95%). The bladder wall was obtained by a negative expansion of 7 mm from the external manually delineated wall. In addition, the bladder wall was separated into two parts: the inner-bladder-wall (bla-in), which represented the portion of the bladder wall that intersected the PTV (10 mm from the prostate and the seminal vesicles) and the external-bladder-wall (bla-ex), which represented the remaining part of the wall (outside the PTV). IMRT plans fit the French 'GETUG' group recommendations (D_{max} (1.8cc) $\leq$ 80 Gy and $V_{70} \leq$ 50 %). The dose-volume objective for bladder wall was replaced with two 'maximum EUD' objectives: choosing 'a'=10.0 (*J. Zhu, ESTRO 2011*) for bla-in and 'a'=2.3 (*Dirscherl, IFMBE 2009*) for bla-ex from the EUD definition (where 'a'=1/n). If the rectum wall dose exceeded the GETUG recommendations, a new objective 'maximum EUD' for the rectum wall was added with 'a'=5 (*R. De Crevoisier, ESTRO 2011*). The two plans (without EUD vs. with EUD use in the inverse planning) were compared in terms of DVH and 5-year bladder NTCP (≥ Grade2 SOMA/LENT toxicity estimated with the Källman model). A non parametric test (Wilcoxon) was used to compare the DVH, EUD and NTCP values of the two plans.

Results:

- Concerning the prostate PTV: D_{95}, D_{98}, D_2, and $D_{mean,}$, no significant differences were found between the two plans (hypothesis of the work).
- With respect to the bladder: the use of bladder EUD objectives increased significantly the conformal index (0.73±0.04 vs. 0.93±0.02) and decreased both the doses in the bladder wall (full wall, bla-in, bla-ex) and the bladder wall NTCP values (Table).
- The use of bladder EUD objectives, although slightly decreased the dose to the rectum wall increased the dose to the femoral heads (Table).

Organ at risk	Parameters	without EUD objectives	with EUD objectives	**p value
rectum wall	*D_{max}	75.19±1.08 Gy	75.05±1.16 Gy	0.05
	V_{72}	12.95±3.67 %	12.72±3.57 %	0.06
total bladder wall	*D_{max}	79.70±0.45 Gy	79.45±0.49 Gy	0.01
	V_{70}	22.66±11.85 %	18.88±10.63 %	0.01
	5 year NTCP§	20.15±6.61 %	17.75±6.27 %	0.01
bladder-wall-external	EUD	77.05±0.86 Gy	76.25±0.98 Gy	0.01
bladder-wall-external	EUD	34.57±8.16 Gy		
femoral heads	V_{55}	0.04±0.20 %	0.21±0.60 %	0.02

* D_{max}: maximum dose in 1.8cc,
** Wilcoxon test,
§Källman model parameters: $TD_{50}(1)$=77.14Gy, s=1.50, γ=2.54 at 5 years

Conclusions: Separating bladder wall into two parts with appropriate model parameters, bladder EUD objectives can be advantageously used in the inverse optimization in order to reduce bladder toxicity probability without significant reduction of the dose to the prostate.