Electronic Appendix

Wish-list generation for prostate SBRT

For each patient, Erasmus–iCycle automatically generates a Pareto optimal plan with clinically favourable trade–offs between treatment objectives. Input for Erasmus–iCycle plan generation is a contoured CT–scan and a wish–list.

A wish–list contains the hard constraints, which always need to be fulfilled in plan generation, and treatment objectives with assigned priorities. Objectives are planning aims that need to be met as closely as possible (or superseded, if possible). Starting with the highest priority, the objectives in the wish–list are sequentially minimized, each time followed by adding the attained objective value as a novel constraint for the next optimization problem to ensure that high priority goal values will not be deteriorated in the minimization of lower priority objective functions ([1] and [2] for more details). The wish–list is generated in an iterative procedure, starting with a first 'guess' of the wish–list by an experienced planner. This wish–list is then used for automated plan generation for a small group of (5-10) patients, followed by plan evaluation to update the wish–list for plan generation in a next iteration. This process with repeated wish–list updates stops if no further enhancement of plan quality is feasible. For groups of patients (e.g. all prostate patients treated with SBRT) this list is fixed, i.e. for all patients in the group the plan is fully automatically generated with the same wish–list.

As described in more details in the Material and Methods section, in this study, two versions of Erasmus–iCycle were used, one for non–coplanar plan generation for a robotic system equipped with a variable aperture collimator, the other for VMAT pre–optimization for an Elekta linac with MLC. Using the above described iterative procedure in parallel for the two Erasmus–iCycle versions, a single wish–list was generated for both robotic and VMAT pre–optimization.

Table A shows the wish–list used for all robotic and VMAT automated plan generations. All applied constraint and objective convex functions were used for the automated multi–criterial plan generation. These functions were selected to generate plans in line with the (not always convex) clinical planning aims (see Plan Evaluation comparison in M&M). The SE function (Sum of Exponentials) defined by Eq. is basically a sum of exponentials of differences between attained voxel doses d_j and D_c, a user–defined critical dose.

$$\mathrm{SE} = \frac{1}{m}\sum_{j=1}^{m} \exp^{\alpha(d_j - D_c)} \qquad \text{(A)}$$

where m is the number of voxels in the structure and α is the sensitivity parameter. For tumors, the parameter α is positive, and SE is equal to the Logarithmic Tumor Control (LTCP), as introduced by Alber & Reemtsen [3], with D_c equal to the prescribed tumor dose. The attractive characteristic of SE is that tumor underdosage is heavily penalized, while overdose has a relatively low impact on the function value. In Table A, SE is used in priorities 1 and 2 to obtain clinically favourable PTV dose distributions. To limit for each patient both positive and negative deviations from the clinically requested 95% PTV coverage ($V_{100\%}$=95%), the goal value for SE in priority 1 is set automatically (Table A). To this purpose, for priority 1, two plans are first generated with relatively small and large goal values, respectively. For both plans, the PTV coverage is then calculated and the final goal value for SE is determined by exponential interpolation. The aim of SE in priority 2 is creating a large dose inhomogeneity in the PTV like in HDR brachytherapy.

For prostate SBRT, it is extremely important that especially the high doses in rectum and bladder are avoided as much as possible. To this purpose, a SE function with negative α is used in priorities 4 and 5, highly favouring avoidance of doses higher than the defined critical values D_c (Table A).

Table A: Applied wish-list for all study patients.

Constraints

Structure	Type	Limit	Parameter
PTV_{opt} [a]	maximum	61.5 Gy	
Rectum	maximum	36.5[b] Gy	
Rectum	gEUD[c]	28	a = 20
Rectal Mucosa	maximum	27 Gy	
Overlap(Rectum,PTV+3mm)	maximum	38 Gy	
Bladder	maximum	39.5 Gy	
Bladder	gEUD	30.7	a = 20
Overlap(Bladder,PTV+3mm)	maximum	41.8 Gy	
Urethra	maximum	50 Gy	
Urethra	gEUD	39 Gy	a = 3
Penis Scrotum	maximum	1.5 Gy	
Shell 3 mm from PTV	maximum	38 Gy	
Shell 3 cm from PTV	maximum	20 Gy	
Entrance dose[d]	maximum	20 Gy	

Objectives

Priority	Structure	Type	Goal	Parameters
1	PTV_{opt}	SE [e]	optimized[f]	D_c = 37 Gy, α = 0.9, sufficient = as goal
2	PTV_{opt}	SE	2.2	D_c = 57 Gy, α = 0.07, sufficient = 2.2
3	CTV	minimum	34 Gy	sufficient = 34 Gy
4	Rectum	SE	0 Gy	D_c = 28 Gy, α = -0.3
5	Bladder	SE	0 Gy	D_c = 34 Gy, α = -0.1
6	Rectum	mean	0 Gy	
7	Bladder	mean	0 Gy	
8	Urethra	mean	0 Gy	
9	Dose bath[g]	maximum	15 Gy	
10	Left Femur head	maximum	24 Gy	
10	Right Femur head	maximum	24 Gy	

[a]PTV_{opt} is the PTV excluding overlaps with rectum, bladder and urethra.

[b]Maximum dose constraints were set lower than clinical requirements to account for voxel sampling for the optimizations.

[c]Generalized Equivalent Uniform Dose [4].

[d]Dose in 2 cm thick layer inside the body contour.

[e]SE (Sum of Exponentials), defined in Eq. .

[f]Values are automatically set to ensure a PTV coverage of 95%, if feasible within the constraints, see text

[g]Dose in patient volume in between shells at 3 cm from the PTV and 2 cm from the body contour.

[1] Breedveld S, Storchi P, and Heijmen B. The equivalence of multi-criteria methods for radiotherapy plan optimization. Phys. Med. Biol. 2009;54:7199-7209.

[2] Breedveld S, Storchi P, Voet P, and et. al. iCycle: Integrated, multi-criterial beam angle, and profile optimization for generation of coplanar and non-coplanar IMRT plans. Med. Phys. 2012;39:951-963.

[3] Alber M, and Reemtsen R. Intensity modulated radiotherapy treatment planning by use of a barrier-penalty multiplier method, Optim. Methods Softw. 2007;22:391-411.

[4] Niemierko A. A generalized concept of equivalent uniform dose (EUD), Med. Phys. 1999;26:1100.