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3 **Beam selection for stereotactic ablative radiotherapy using**

4 **Cyberknife with multileaf collimation**

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6 **James L Bedford, Peter Ziegenhein, Simeon Nill and Uwe Oelfke**

7 Joint Department of Physics, The Institute of Cancer Research and The Royal
8 Marsden NHS Foundation Trust, London, SM2 5PT, UK.

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10 Corresponding author:

11 James Bedford

12 james.bedford@icr.ac.uk

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14 **Abstract.** The Cyberknife system (Accuray Inc., Sunnyvale, CA) enables radiotherapy using
15 stereotactic ablative body radiotherapy (SABR) with a large number of non-coplanar beam
16 orientations. Recently, a multileaf collimator has also been available to allow flexibility in
17 field shaping. This work aims to evaluate the quality of treatment plans obtainable with the
18 multileaf collimator. Specifically, the aim is to find a subset of beam orientations from a
19 predetermined set of candidate directions, such that the treatment quality is maintained but the
20 treatment time is reduced. An evolutionary algorithm is used to successively refine a
21 randomly selected starting set of beam orientations. By using an efficient computational
22 framework, clinically useful solutions can be found in several hours. It is found that 15 beam
23 orientations are able to provide treatment quality which approaches that of the candidate beam
24 set of 110 beam orientations, but with approximately half of the estimated treatment time.
25 Choice of an efficient subset of beam orientations offers the possibility to improve the patient
26 experience and maximise the number of patients treated.

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28 **Highlights:**

- 29
- 30 • A fast optimisation framework is used to create IMRT SABR plans for Cyberknife.
 - 31 • The value of the Cyberknife multileaf collimator is investigated.
 - 32 • A beam selection algorithm is used to determine a subset of beam orientations.
 - 33 • Fifteen selected beams are sufficient to create high-quality treatment plans.
 - 34 • Treatment time is minimised using this approach.

35 **Keywords:** Cyberknife, multileaf collimator, beam-orientation selection, IMRT, inverse
36 planning.

37

38 **Abbreviations**

39	BOS	Beam orientation selection
40	CT	Computed tomography
41	IMRT	Intensity-modulated radiotherapy
42	L-BFGS	Limited-memory Broyden-Fletcher-Goldfarb-Shanno
43	MLC	Multileaf collimator
44	PTV	Planning target volume
45	SABR	Stereotactic ablative body radiotherapy

46 **1. Introduction**

47 The Cyberknife system (Accuray Inc., Sunnyvale, CA) includes a multileaf collimator
48 (MLC), which allows maximal flexibility in field shaping and fewer monitor units in stereotactic
49 radiosurgery than with a cone collimator [1, 2]. The MLC consists of 26 leaf pairs, each of width
50 3.85mm, giving a maximum field size of 115 mm \times 100 mm at a nominal source-axis distance of 800
51 mm.

52 The standard beam set for a Cyberknife stereotactic ablative body radiotherapy (SABR)
53 treatment uses 110 beams, referred to as nodes. These are typically non-isocentric and non-coplanar,
54 and are chosen so as to provide a collision-free path for the delivery robot around the patient [1].
55 However, such a large number of beams is unlikely to be necessary for many, if not all, treatment
56 sites, and may lead to an excessive treatment delivery time without much benefit [3]. This work
57 therefore aims to determine an optimal subset of beams for each patient, such that the treatment
58 quality approaches that of the full node set. This is accomplished firstly by examining predetermined
59 beam subsets defined by the manufacturer, and secondly by applying a beam selection technique.

60 A number of approaches have previously been used for beam orientation selection in
61 radiotherapy. As well as the implementation of methods for conformal radiotherapy [4], the more
62 complex problem of determining beam orientations and fluence maps for intensity-modulated
63 radiotherapy (IMRT) has been approached by beam's eye view score methods [5, 6], combination of
64 individually selected beams [7], successive addition of beams to a pool [8-10], angle perturbation [11-
65 13] and cluster analysis [14]. Other methods have also been reported [15-21]. All of these methods
66 benefit from fast optimisation methods [22, 23] and comparisons of methods have helped to clarify
67 the benefits of these approaches [24, 25].

68 Some of the recent work on trajectory optimisation for arc therapy can also be applied
69 usefully to the question of beam orientation selection for Cyberknife. For example, Smyth *et al.* [26,
70 27] find the least cost path through a cost function map based on individual beam metrics. Wild *et al.*
71 [28] also use a path connection algorithm to find the shortest path between desirable orientations.
72 Locke and Bush [29] also use a path search algorithm, but take into account the connectedness of the
73 areas of the beam's eye view which are useful for beam delivery.

74 Several methods have focused specifically on the Cyberknife device. For example, Kearney
75 *et al.* [30] describe a method for producing arc trajectories for Cyberknife. A subset of optimal beams
76 is selected from a complete library of beams, and then these beams are joined using a path selection
77 method, and formed into a continuous arc.

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81 **2. Methods and materials**

82 *2.1. Patients and treatment plans*

83 Four patient cases were considered in this study, with tumour sites of prostate and base of
 84 seminal vesicles, lung, liver and partial breast. The prostate case was planned with two distinct
 85 techniques, as described below, leading to a total of five types of treatment plan. All treatment plans
 86 used a SABR technique, with hypofractionated dose prescriptions of 3-5 fractions (see Table 1).

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88 Table 1. Fractionation schemes used in this study.

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CASE	TOTAL DOSE (Gy)	FRACTIONS	PROTOCOL
Prostate A	36.25	5	RTOG 0938
Prostate B	38.00	4	Fuller <i>et al.</i> [31, 32]
Lung	50.00	5	RTOG 0813
Liver	42.75	3	Vautravers-Dewas <i>et al.</i> [33]
Partial breast	35.00	5	RTOG 0413

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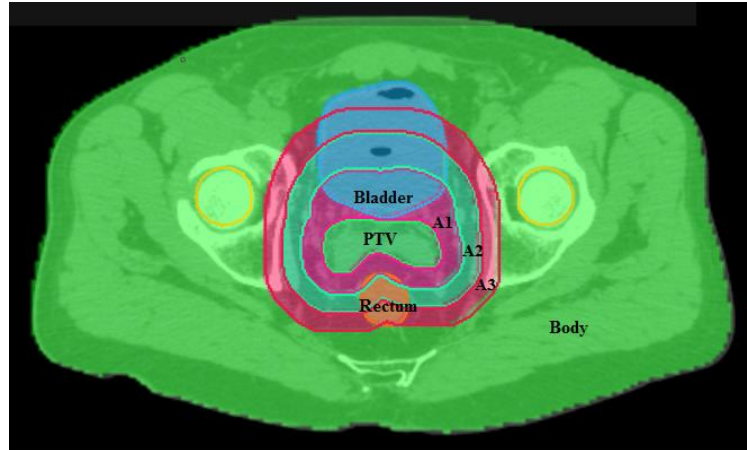
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92 Patient cases were imported into the in-house treatment planning system DynaPlan and dose
 93 was calculated using a standalone dose calculation module supplied by Accuray Inc., so as to
 94 accurately represent dose delivered by the Cyberknife system. The computational framework
 95 required that appropriate priorities were assigned to the different anatomical structures outlined on the
 96 CT images so that the optimizer would work correctly in the case of overlap (see Figure 1). Each
 97 voxel in the volume was assigned to one structure only.

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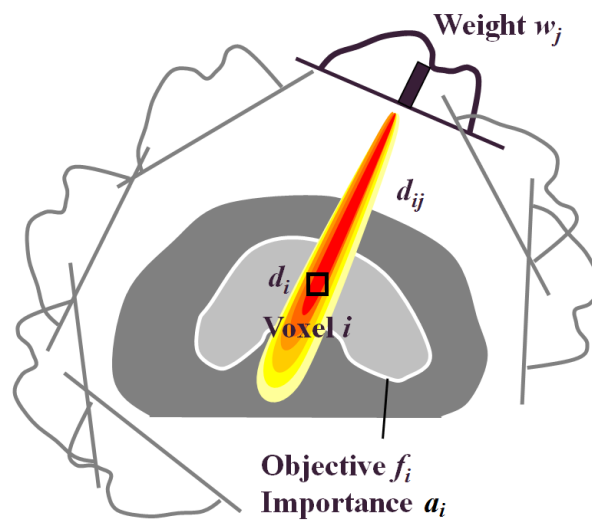
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Figure 1. Overlap and priorities. Planning target volume (PTV) has the highest priority, followed by critical structures such as rectum and bladder. Three annular structures, (A1, A2, A3) with width 10 mm then follow, and the remainder of the body then has the lowest priority.

The inverse planning method required the dose, d_i , at voxel i to be calculated as [28]:

$$d_i = \sum_j d_{ij} w_j, \quad (1)$$

where d_{ij} was the dose at voxel i due to fluence w_j at element j of the intensity matrices (Figure 2).



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Figure 2. Dose model.

116 Accordingly, the dose-influence matrix d_{ij} was determined by calculating dose distributions for fields
 117 of one intensity bixel in size. This was an approximation as the dose due to a single large field was
 118 not exactly equal to the sum of doses delivered by a sum of individual bixels, but was considered
 119 accurate enough for this study. In all cases, the fluence bixel size was $2 \times$ MLC leaf width by 5 mm
 120 and the fluence grid approximately covered the beam's eye view of the PTV with a 5 mm margin. In
 121 some regions of some of the beams, the fluence grid was greater in extent than the PTV, and in others,
 122 it was less. This imperfection was not found to have a significant impact on the results. The
 123 calculation voxel size was $2 \times$ CT pixel width by $2 \times$ CT pixel height \times CT slice spacing. A lower
 124 dose threshold of $1/60000$ of the maximum dose of each d_{ij} component was used, which in practice
 125 meant that all scattered dose was incorporated into the inverse planning. The d_{ij} matrices covered the
 126 entire patient, so that the components relating to each beam totalled approximately 1 GB in size. All
 127 dose voxels were used in structures for which optimisation objectives were specified.

128 Each treatment plan consisted of 110 beam orientations, using an average of two apertures per
 129 beam orientation (node). Treatment plans were optimized using an objective function, F , summed
 130 over a number of volumes, i , each with individual objective value f_i :

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$$132 \quad F = \sum_i f_i, \quad (2)$$

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134 with f_i defined as:

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$$136 \quad f_i = a_i \left[d_i^{\min} - d_i \right]_{\geq 0}^p + a_i \left[d_i - d_i^{\max} \right]_{\geq 0}^p \quad (3)$$

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138 where a_i was a structure-specific importance factor. Both the minimum and maximum terms were
 139 used for targets, while only the maximum term was used for normal tissues. A number of iterations,
 140 x , of an iterative gradient descent method were then used to reach a solution for the intensity values in
 141 the fluence matrix:

142

$$143 \quad w_j^{x+1} = \left[w_j^x - \alpha p_j^x \right]_{\geq 0}. \quad (4)$$

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145 where α was a relaxation parameter. The direction vector p^x was *in principle* given as:

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$$147 \quad p^x = \left[\nabla^2 F(w^x) \right]^{-1} \nabla F(w^x). \quad (5)$$

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149 However, the low-memory Broyden-Fletcher-Goldfarb-Shanno (L-BFGS) method was used to avoid
 150 the memory-intensive calculation of the inverse Hessian matrix $[\nabla^2 F(w^x)]^{-1}$. In this scheme, the
 151 direction vectors were obtained by a recursion relation [28]:

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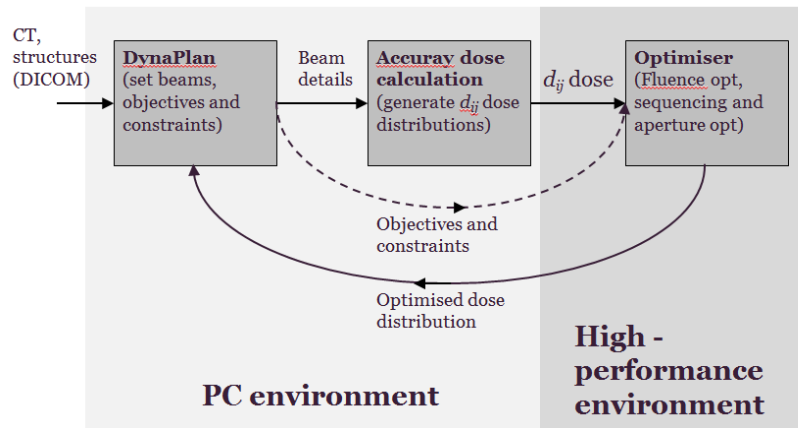
$$153 \quad p^{x+1} = p^x + B(F, \nabla F). \quad (6)$$

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155 Following fluence optimisation, sequencing was carried out using a standard sequencing
 156 method [34], and aperture optimisation was then carried out, also using a gradient descent method
 157 [28, 35]. This method converted the aperture optimisation problems into a fluence optimisation
 158 problem, so that the same L-BFGS method could be used for aperture optimisation as for fluence
 159 optimisation. No attempt was made to optimise the numbers of beam directions, apertures or monitor
 160 units (MU) in the final plan.

161 This method was implemented in a fast multi-threaded planning framework [35]. This
 162 enabled a solution for 110 nodes to be obtained in less than 15 minutes for 40 fluence iterations and
 163 40 iterations of direct aperture optimisation (see Figure 3). The optimisation itself was implemented
 164 in a high-performance environment, which was a dual Intel Xeon E5-2650 with 128 GB RAM.

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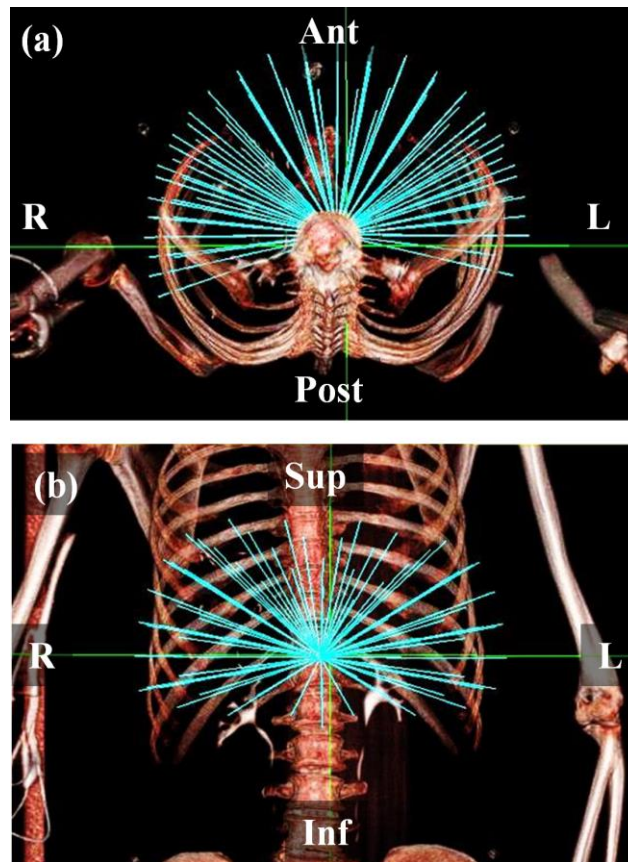
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Figure 3. Computational system.

169 The starting point for comparisons was to use an Accuray-supplied body nodeset with 110
 170 nodes (Figure 4), with a variable number of apertures being specified to the optimizer. This number
 171 was 2 for the prostate cases, 1 for liver and breast cases, and 3 for the lung case, reflecting the degree
 172 of intricacy required in the solution. An Accuray-supplied subset of the body nodeset, containing 36
 173 nodes spaced evenly over the same total solid angle, was also used. This approach was similar to the
 174 standardised bouquet determined by Yuan *et al.* [36].



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Figure 4. The body nodeset from which the beams were selected. (a) transaxial view, (b) coronal view.

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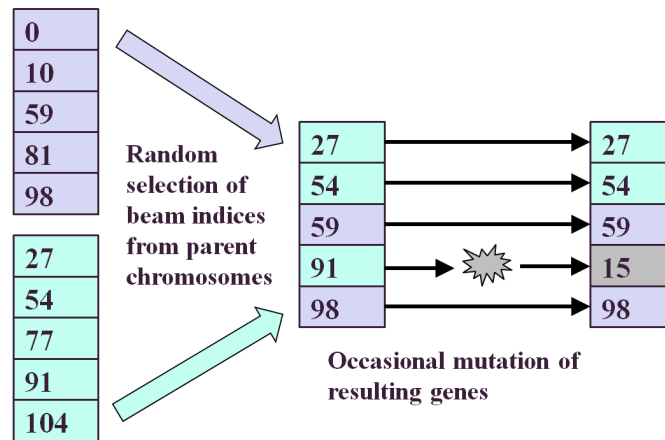
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Beam selection was carried out using a variation of the the evolutionary algorithm of Li *et al.* [37], which was also similar to the approach of Hou *et al.* [38], who used an evolutionary algorithm for orientation selection and a simulated annealing algorithm for intensity calculation. The concept of nesting an intensity calculation inside a beam orientation loop was also used by Rowbottom *et al.* [39]. Using this method, 15 beams were selected from the 110-node body nodeset. Other numbers of beams were investigated and 15 beams were found to be the practical minimum that allowed for production of a high-quality dose distribution. For all orientation-selected cases, five segments per beam were allowed, except for the liver case, where the relative simplicity of the planning target volume (PTV) required only three segments per beam to be used. The method is summarised in figure 5.



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Figure 5. Concepts involved in the evolutionary algorithm used in this work. The two left-hand lists represent two node sets in a population, the numbers representing node indices. The offspring has features of both of these two individuals, with occasional mutations.

A population of 20 plans was used in this work, representing a collection of plans whose properties were to be successively improved by the evolutionary algorithm. The beam orientations for each plan were chosen initially by randomly selecting beam indices from the candidate node set of 110 beams. This population of individual treatment plans, or individuals, then underwent 20 iterations, or generations. The generation was defined as the population at a given phase in the optimisation process. At each iteration, 20 new individuals were generated from the current 20 individuals, to form the next generation. In this way, the population was maintained at 20 throughout the scheme. The genetic encoding consisted of a list of beam indices used by each individual or treatment plan. Note that the fitness function was taken to be the objective function, F , as defined in equation (2), with lower values representing greater fitness.

To generate a new individual, the fittest tenth of the current population was identified according to objective function value, and these two individuals were combined. Each gene, i.e. each beam index, of the new individual was determined by randomly using a beam index from either of the parent genes. In this crossover or recombination operation, the probability of using a beam index from one parent was 0.4 and the probability of using a beam index from the other was 0.6, following empirical tests. If the new beam index was identical to a beam index already existing in the new individual, another attempt was made to generate that particular beam index, and if this also matched an existing beam index, it was accepted anyway. This new beam index then underwent mutation, with a probability of 0.05. This involved replacing it with another beam index from the set of

218 candidate beam indices. As there was no simple relationship between beam index and beam
219 orientation, (i.e. beams with adjacent indices did not necessarily have adjacent beam orientations), no
220 attempt was made to select similar indices or orientations. Mutation therefore involved a change of
221 index and orientation that could be considerable.

222 The end result of this process was that each randomly selected pair of individuals gave rise
223 to an offspring. After 20 of such offspring were generated, they replaced the original individuals, so
224 that a new generation of 20 plans was produced. Each of these plans was then optimised using 20
225 fluence iterations, sequencing, and 20 iterations of direct aperture optimisation. The whole process
226 was then repeated for 20 iterations. In the implementation of Li *et al.* [37], the optimal plan was taken
227 as the fittest individual in the final generation. However, in our implementation, the optimal plan was
228 taken as the fittest individual to be found in any of the generations. This was used to provide a similar
229 effect to elitism, in which the fittest individuals are retained for subsequent generations.

230 The parameters described above were chosen following empirical tests to determine the
231 optimum settings. To demonstrate that the selected values were optimum, the values were perturbed
232 and the progress of the beam orientation selection (BOS) was evaluated for the prostate B case and the
233 liver case. Several different combinations of the crossover proportions and the mutation rate were
234 evaluated. Furthermore, to evaluate the statistical accuracy of the evolutionary algorithm, these cases
235 were recalculated 25 times using different seed values in the random number generator. The
236 adequacy of the number of plans and number of generations was also assessed for the prostate B case
237 by recalculating using 100 plans in 100 generations.

238 Sometimes the importance factors were adjusted during production of the plans using BOS.
239 This was mainly to reduce the surface dose when using relatively few beam orientations. This meant
240 that the objective values were different for the BOS plan and the reference plan produced from the
241 body or even path, even for identical dose distributions. Consequently, where objective values were
242 compared, the BOS objective value was compared against that for a re-optimised plan using the body
243 or preset short path but with the same importance factors as used in the BOS plan.

244 Plans were compared using dose statistics and conformity index, which was defined as the
245 volume receiving the prescribed dose divided by the volume of the planning target volume.
246 Treatment times were estimated according to a vendor-supplied algorithm incorporating initial patient
247 setup, beam-on, MLC reshaping between apertures, robot traversal between nodes and imaging.

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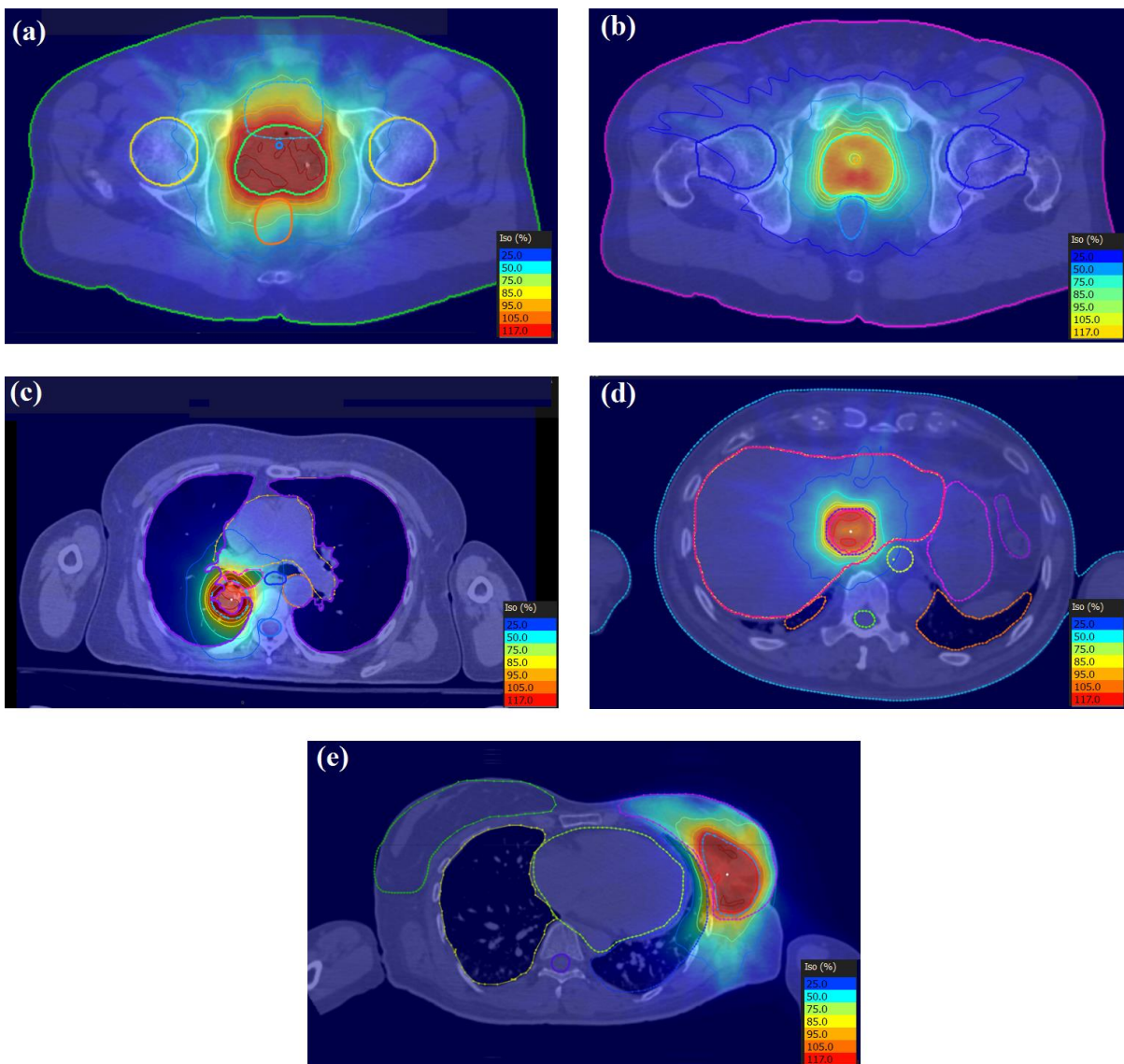
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253 **3. Results**

254 The transaxial dose distributions are shown in Figure 6 for the five cases with the 110-node
 255 body node set. The dose distributions shown are for the d_{ij} -based dose distribution output from the
 256 optimiser, without recalculation of the apertures as complete beams. It can be seen that the dose
 257 distributions are conformal in nature, with appropriate sparing of organs at risk near to the PTV. A
 258 summary of results over the five patients for the body path, the preset short path and BOS path are
 259 shown in Table 2.

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264 **Figure 6.** Transaxial dose distributions for (a) prostate A, (b) prostate B, (c) lung, (d) liver and (e) partial breast
 265 cases. The dose levels as a percentage of the prescription dose are shown in each case.

266 **Table 2.** Plan statistics for the five patient cases.

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	BODY PATH	PRESET SHORT PATH	ORIENTATION SELECTED PATH
Number of nodes	110	36	15
Inverse planning time per run (mins)	10	5	120
Median apertures	310	158	165
Median MU per Gy	1575	1881	1499
Median conformality index	1.03	1.05	1.06
Median estimated treatment time (mins)	51	37	34

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270 The orientation selection takes longer for inverse planning than the other techniques due to the
 271 number of plan optimisations required. The number of apertures approximately follows the number
 272 of nodes in the plan for the body path and the preset short path, although there is a similar number of
 273 apertures for the BOS path as with the preset short path, for rather fewer beams. The estimated
 274 treatment time follows accordingly. The monitor units per gray and conformality index are
 275 approximately constant for all three of the types of treatment plan.

276 The impact of the parameters used in the evolutionary algorithm on the median final objective
 277 value for the BOS result in the prostate B case is shown in Table 3. Run 1, the standard case, is
 278 shown to be competitive with the other runs using different parameters. Only run 7 has a median final
 279 objective value which is appreciably lower than that of run 1, but takes many hours to achieve the
 280 result. Figure 7 shows the objective values for 20 iterations of the BOS scheme for the prostate B
 281 case, corresponding to run 1 of Table 3. The optimisation rapidly reaches convergence to a fit
 282 population of treatment plans. The minimum objective value encountered is better than that of the
 283 preset short path and approaching that of the body path. It can be seen that there is scope to reduce
 284 the number of iterations, as the global solution is found relatively rapidly. Figure 8 shows the results
 285 of the evolutionary algorithm for the same case when the BOS scheme is repeated 25 times (run 6).
 286 The same pattern of convergence is seen as with the single run, and the small range of the median
 287 objective function values shows that the algorithm is statistically stable. Note that Figure 7 shows the

288 objective values of the individuals, whereas Figure 8 shows the median objective values of various
 289 runs.

290 Similar results are also seen in Figure 9 for the case of 100 individuals in 100 generations (run
 291 7). Although there is a large range in the objective function values at each generation, the median
 292 objective value reaches a constant value after around 20 iterations. The objective value reaches a
 293 slightly smaller value than in Figure 7, showing that there is a small additional benefit in the larger
 294 population size. However, the benefit is not large, and the use of 20 individuals in 20 generations is
 295 considered to be adequate for the purposes of providing good quality dose distributions.

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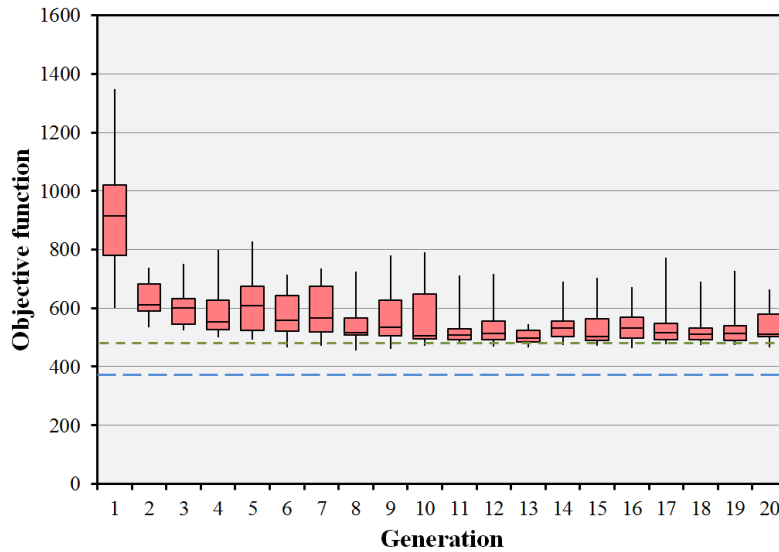
299 **Table 3.** Impact of varying the parameters of the evolutionary algorithm in the prostate B case. The
 300 pertinent changes in parameter values are shown in bold type. Note that the median and range final objective
 301 values for run 6 relate to the median value attained by the population at each of multiple runs rather than the
 302 value attained by the individuals at a single run.

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PARAMETER	RUN 1	RUN 2	RUN 3	RUN 4	RUN 5	RUN 6	RUN 7
Population size (plans)	20	20	20	20	20	20	100
Generations	20	20	20	20	20	20	100
Statistical repeats	1	1	1	1	1	25	1
Crossover ratio	0.4	0.3	0.5	0.4	0.4	0.4	0.4
Mutation probability	0.05	0.05	0.05	0.01	0.1	0.05	0.05
Final objective median	512	509	515	518	526	536	493
Final objective range	466-664	483-659	461-568	482-594	489-849	512-555	432-945
Lowest objective found	456	481	457	482	485	447	418

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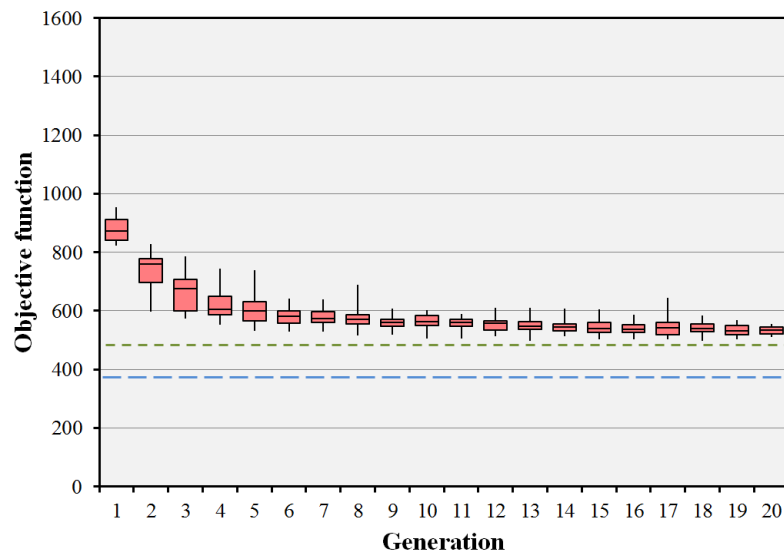


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307 **Figure 7.** Convergence of the objective function for the prostate B case with 15 beams selected from 110
 308 candidate beams. The boxes represent the median and the 25th and 75th percentiles of the 20 individual objective
 309 function values at each generation. The error bars represent the range of these 20 objective values. The green
 310 dotted line shows the objective value for the preset short path and the blue dashed line shows the objective value
 311 for the body path.

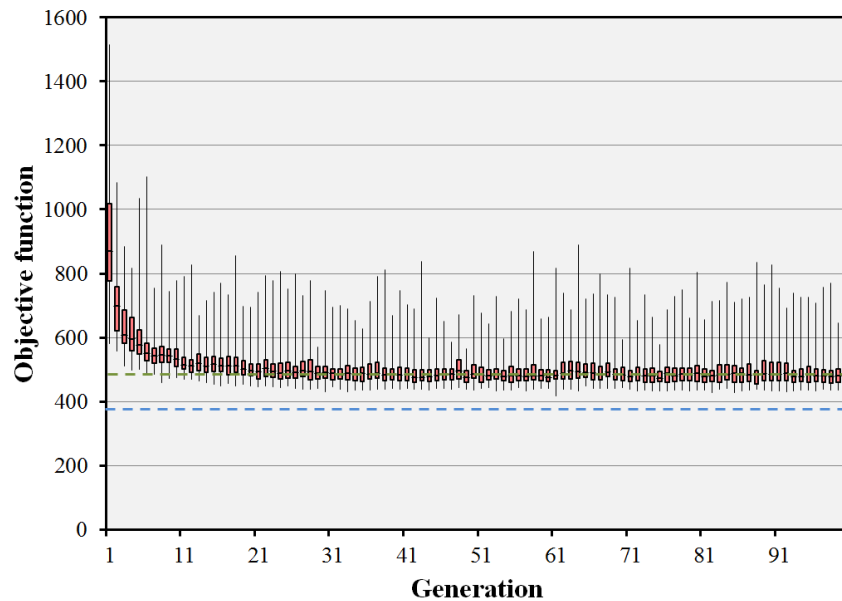
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315 **Figure 8.** Statistical performance of the evolutionary algorithm for the prostate B case. The algorithm has been
 316 run 25 times and the median objective value of the population of 20 individuals recorded for each run. The
 317 boxes represent the median and the 25th and 75th percentiles of the 25 median objective function values at each
 318 generation. The error bars represent the range of these 25 median objective values. The green dotted line shows
 319 the objective value for the preset short path and the blue dashed line shows the objective value for the body path.



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322 **Figure 9.** Convergence of the objective function for the prostate B case with 15 beams selected from 110
323 candidate beams. In this run, 100 individuals in 100 generations are used. The boxes represent the median and
324 the 25th and 75th percentiles of the 100 individual objective function values at each generation. The error bars
325 represent the range of these 100 objective values. The green dotted line shows the objective value for the preset
326 short path and the blue dashed line shows the objective value for the body path.

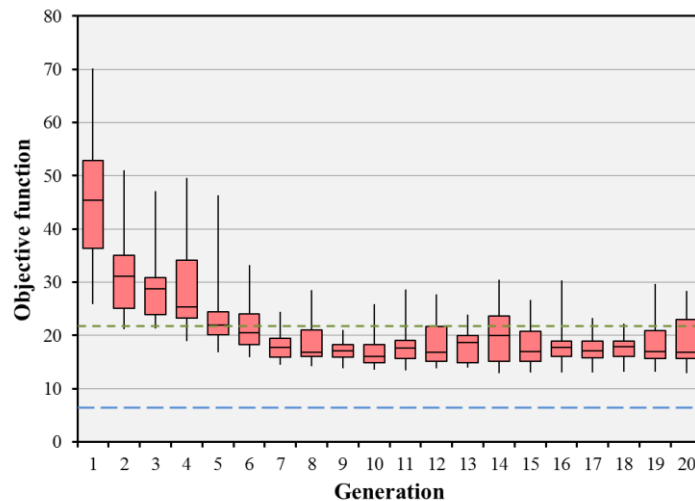
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331 The impact of the parameters used in the evolutionary algorithm on the median final objective
332 value for the BOS result in the liver case is shown in Table 4. As with the prostate B case, the
333 standard run (run 1), is shown to produce final objective values which are competitive with the other
334 runs. The difference in magnitude of the objective function values, compared to the prostate B case,
335 is a reflection of the different anatomical structures and importance factors used for the two cases, and
336 comparison of these values between the cases is therefore not meaningful. Figure 10 shows the
337 objective values for 20 iterations of the BOS scheme for the liver case, corresponding to run 1 of
338 Table 4. The optimisation rapidly reaches convergence to a fit population of treatment plans. The
339 final objective value is better than that of the preset short path and approaching that of the body path.
340 Figure 11 shows the results of the evolutionary algorithm for the same case when the BOS scheme is
341 repeated 25 times (run 6). Again, the small range of the median objective function values shows that
342 the algorithm is statistically stable.

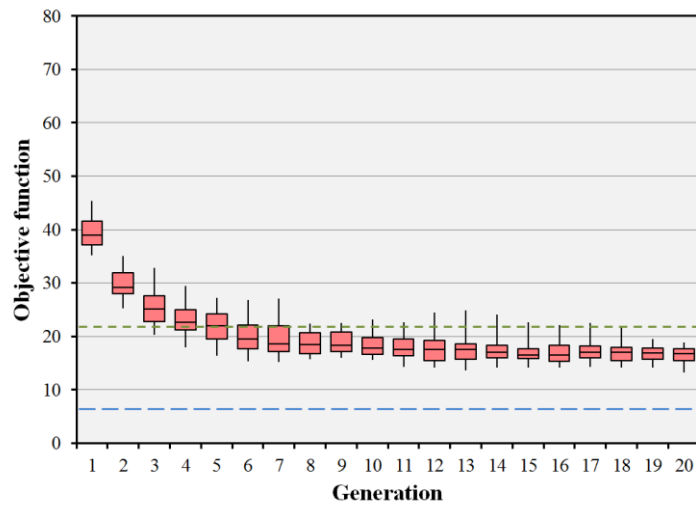
343 **Table 4.** Impact of varying the parameters of the evolutionary algorithm in the liver case. The
 344 pertinent changes in parameter values are shown in bold type. Note that the median and range final objective
 345 values for run 6 relate to the median value attained by the population at each of multiple runs rather than the
 346 value attained by the individuals at a single run.
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PARAMETER	RUN 1	RUN 2	RUN 3	RUN 4	RUN 5	RUN 6
Population size (plans)	20	20	20	20	20	20
Generations	20	20	20	20	20	20
Statistical repeats	1	1	1	1	1	25
Crossover ratio	0.4	0.3	0.5	0.4	0.4	0.4
Mutation probability	0.05	0.05	0.05	0.01	0.1	0.05
Final objective median	16.8	17.7	19.3	15.1	18.9	16.7
Final objective range	12.9-28.3	14.6-28.2	14.0-25.8	13.1-18.0	14.7-27.1	13.3-18.8
Lowest objective found	12.9	14.0	14.0	13.0	11.9	11.0

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 353 **Figure 10.** Convergence of the objective function for the liver case with 15 beams selected from 110 candidate
 354 beams. The boxes represent the median and the 25th and 75th percentiles of the 20 individual objective function
 355 values at each generation. The error bars represent the range of these 20 objective values. The green dotted line
 356 shows the objective value for the preset short path and the blue dashed line shows the objective value for the
 357 body path.



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 359 **Figure 11.** Statistical performance of the evolutionary algorithm for the liver case. The algorithm has been run
 360 25 times and the median objective value of the population of 20 individuals recorded for each run. The boxes
 361 represent the median and the 25th and 75th percentiles of the 25 median objective function values at each
 362 generation. The error bars represent the range of these 25 median objective values. The green dotted line shows
 363 the objective value for the preset short path and the blue dashed line shows the objective value for the body path.

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366 In terms of the clinical quality of the treatment plans, the clinical constraints are met in most
 367 cases where a solution is feasible. There are several cases, notably prostate PTV overlapping the
 368 rectum, and lung PTV overlapping with the proximal bronchial tree, where a solution is infeasible for
 369 certain beam arrangements. In addition, there are several other instances where the constraints are not
 370 met due to the PTV overlapping with a critical structure, which is difficult to handle due to the
 371 requirement in the computational framework to have only one structure defined at each location (see
 372 figure 1). The PTV is always set to the highest priority, so it is difficult to control the dose in the
 373 regions where a critical structure overlaps with the PTV. However, in general, clinical constraints are
 374 met in the cases presented.

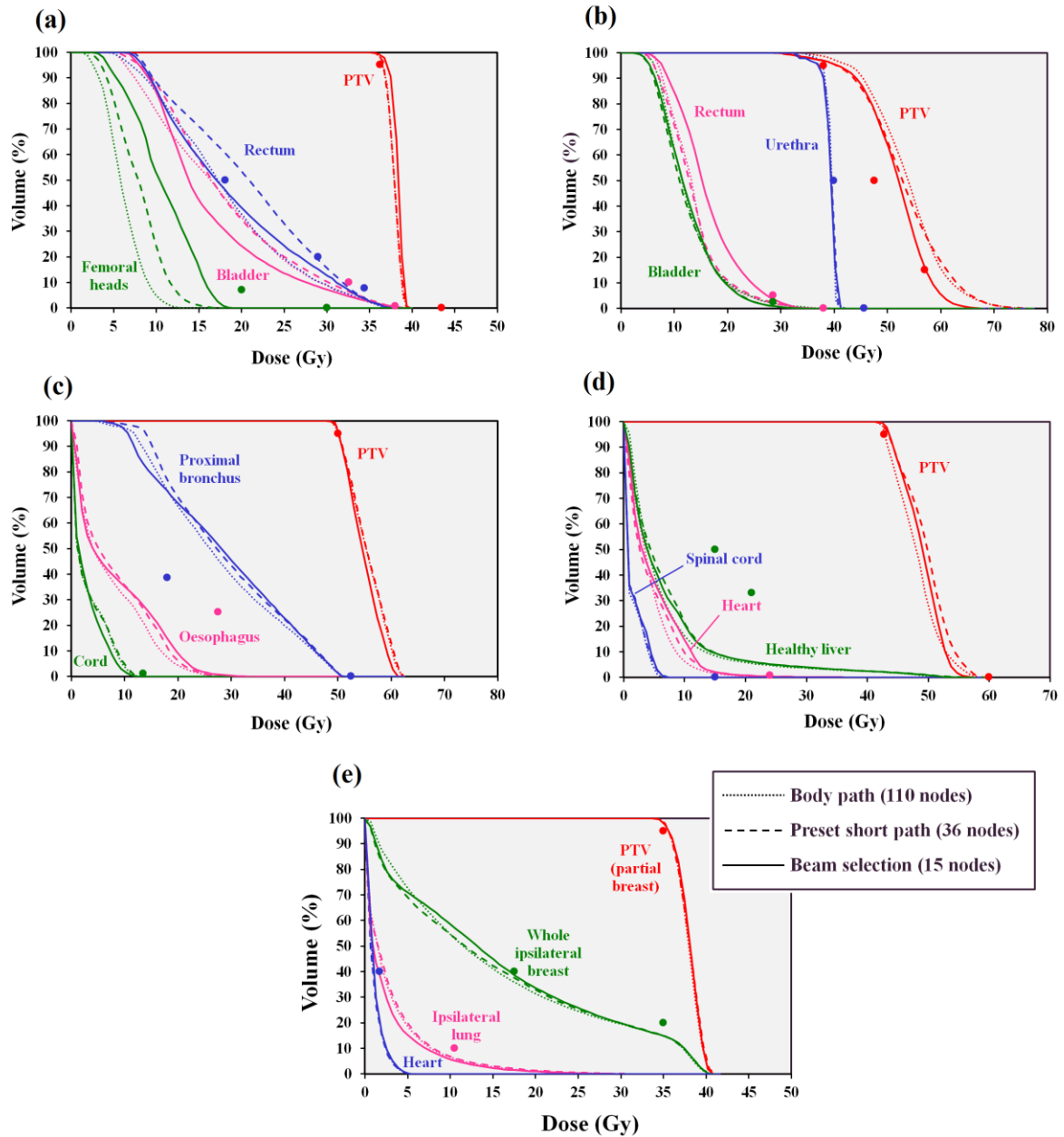
375 Dose-volume histograms comparing the body path, the preset short path and the BOS path are
 376 shown in Figure 12. For the prostate A case, the PTV receives a similar dose with the body path, the
 377 preset short path and the BOS path. The rectal dose passes the 18.12 Gy at 50% volume constraint
 378 with the full path and the BOS path but fails with the preset short path. Meanwhile the bladder dose is
 379 lower with BOS than with the body path and the femoral head dose is higher than with the body path.
 380 However, these doses are within tolerance (principally 18.12 Gy at 50% for the bladder and 20 Gy
 381 maximum dose for the femoral heads) for all of the techniques.

382 For the prostate B case, the PTV dose for the preset short path is similar to that for the body
 383 path, while the dose with BOS is slightly less, which in the context of this brachtherapy-like boost

384 protocol, represents a reduction in plan quality. However, all techniques give PTV dose which meets
385 the constraints (at least 38.00 Gy at 95%, at least 47.50 Gy at 50% and at least 57.00 Gy at 15%). The
386 urethra dose is similar with all techniques and within the tolerance of 39.90 Gy at 50%. Rectum dose
387 is slightly higher with BOS than with the body path or the preset short path, but again within tolerance
388 (principally 28.50 Gy at 2 cm³) for all techniques.

389 For the lung case, the plan with the preset short path is slightly lower in quality than the plan
390 with the body path, and the plan with BOS is slightly lower in quality still, particularly in terms of
391 proximal bronchus and oesophagus dose, but this is a very minor effect. All dose constraints are met,
392 except for the proximal bronchus (18.00 Gy at 4 cm³), which is not met by any of the three plans, due
393 to overlap with the PTV.

394 For the liver case, there is little difference dosimetrically between the three types of plan
395 shown in the DVHs. The PTV constraints (principally 42.75 Gy at 95%) and the normal liver
396 constraints (principally 15 Gy at 50%) are met by all plans. Similarly, with the partial breast case, the
397 techniques are dosimetrically very similar and meet the PTV constraint (35.00 Gy at 95%) and the
398 constraint on the whole ipsilateral breast (17.50 Gy at 40%).
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402 **Figure 12.** Dose-volume histograms for (a) prostate A, (b) prostate B, (c) lung, (d) liver and (e) partial breast

403 cases. Dotted lines: body path (110 nodes), dashed lines: preset short path (36 nodes), solid lines: BOS path (15

404 nodes). The principal dose constraints are shown as points. The PTV constraints in (b) are all minimum dose

405

constraints.

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408 4. Discussion

409 These results show that our fast optimisation scheme is able to produce plans of a clinical
410 standard for predefined beam arrangements such as the body path and the preset short path, within a
411 very practical timeframe. Both the treatment time and the treatment planning time can be reduced
412 significantly by using a preset short path, as both are approximately proportional to the number of
413 beams. The benefit of this type of approach has been shown by a study of standardized beam
414 bouquets for lung planning [36]. The treatment plans in that study contain around six coplanar beams,
415 whereas 36 non-coplanar beams are used in the present study, but the similarity in outcome is clear:
416 carefully chosen standardized beams can produce good quality treatment plans.

417 However, the greatest benefit in treatment time is expected to be achieved with a BOS path.
418 In this case, as few as 15 beams can be used for the treatment, with plan quality which is almost as
419 high as with the 110-node body path. The BOS path has the shortest treatment time, although as there
420 are similar monitor units and number of apertures for the BOS path compared to the preset short path,
421 the beam-on time and the aperture reshaping times are similar for both paths, and the reduction in
422 treatment time with the BOS path is due to the reduction in robot traversal time. The treatment
423 planning time is much longer with this BOS algorithm, but there are a number of adjustments to the
424 method which would enable it to be used in a much shorter time in a clinical environment, such as
425 limiting the number of iterations for the optimisation at each fixed beam arrangement, and limiting the
426 low-dose extent of the d_{ij} matrices. Furthermore, it may be possible to use the information gained
427 from this study to design better class solutions without requiring the BOS algorithm to be run for each
428 patient in the clinical environment.

429 The results of this study are similar to those of Rossi *et al.* [3] for Cyberknife treatment of
430 prostate with a brachytherapy-like SABR protocol. That study investigates candidate beam sets
431 consisting of a full body path, a coplanar path and three extended body paths consisting of 180 – 500
432 nodes. Between 10 and 30 nodes are then selected from these node sets. They find that selecting
433 beams from the largest set of candidate directions favours plan quality. In their study, increasing the
434 number of selected beams from 10 to 30 has little effect on PTV coverage due to the design of the
435 study, but gradually improves the mean dose to the bladder and the irradiated volume of urethra. The
436 impact of increasing the beam number levels off between 15 and 20 beams. The mean dose to the
437 rectum and the rectal irradiated volume also decrease with increasing number of beams, with most of
438 the effect seen with beam numbers up to 20. The finding of the present study that around 15 beams is
439 sufficient to produce good quality plans is in accord with these results. Rossi *et al.* [3] report
440 optimisation times of up to 45 h, whereas the present work allows an optimisation time of an order of
441 magnitude shorter.

442 Much of the experience with a C-arm linear accelerator can also be compared with the present
443 study, such as the work of Woudstra *et al.* [4], Vaitheeswaran *et al.* [19], Breedveld *et al.* [8], Amit *et*
444 *al.* [20] and Bangert and Unkelbach [23]. Most recently, Liu *et al.* [21] report on selecting eight
445 beams from either 18 coplanar or 56 non-coplanar candidate orientations for prostate, head and neck,
446 or liver. They find that a sparse optimisation which approximates the exact BOS problem, thereby
447 allowing the use of a gradient method, can provide good quality plans with improved computational
448 efficiency.

449 To produce such high-quality treatment plans, a series of annular structures around the PTV
450 have been used in the present study. These provide dose distributions evenly balanced around the
451 area treated. The biggest challenge in producing non-coplanar plans with few beams by orientation
452 selection is to ensure that the surface dose is distributed around sufficiently. It has been found that 15
453 beams are sufficient for this, with 20 beams more than adequate. However, there are some practical
454 limitations to this study. In particular, the method of sequencing the fluence profiles into deliverable
455 segments [34] yields many small segments, with the effect that the total monitor units required are
456 very high. This effect could be overcome by using a more conformal segmentation algorithm.
457 Moreover, no attempt has been made to optimize the monitor units as part of the objective function,
458 but this should be possible. Another limitation is that dose components have been calculated from a
459 small field and the total dose due to a larger field has been calculated as a summation of these
460 elemental doses. It is well known that this is not a very accurate method of calculating the dose in a
461 large field. This could possibly be overcome by applying a segment weight optimisation in a post
462 processing step.

463 This study begins with candidate beam orientations chosen to avoid collisions. This is similar
464 to the work of Breedveld *et al.* [8] and Bangert *et al.* [25]. The present study uses an evolutionary
465 algorithm to select beam orientations, with a fluence optimisation, segmentation and aperture
466 optimisation for each plan at each iteration. However, use of fluence optimisation and aperture
467 optimisation at each iteration may ultimately not be necessary, as fluence optimisation alone may give
468 the required result. As the aperture optimisation problem is posed in this work as a special case of
469 fluence optimisation, so that its speed of execution is approximately the same as the speed of fluence
470 optimisation, removing the aperture optimisation would have the effect of reducing the optimisation
471 time by approximately half. This is also the approach taken by Rowbottom *et al.* [39] and Hou *et al.*
472 [38]. Further work is needed to establish what simplifications of the inverse planning can be achieved
473 for the same quality of plan.

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477 **5. Conclusion**

478 The gradient descent method implemented in a multiple-core computation environment offers
479 the possibility of fast optimisation for MLC-based delivery on the large number of nodes encountered
480 in the Cyberknife system. The number of delivery nodes can be reduced by using a preset short path,
481 but the greatest time saving is achieved by beam orientation selection. The beam selection method
482 takes much longer to run than the standard optimisation method using a fixed set of nodes. However,
483 evolutionary computing produces results which are almost as good in quality as those using the body
484 path. The main advantage of the fewer nodes is expected to be a reduction in treatment time.

485

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493 This study was retrospective, using patient images, for the use of which informed consent was
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