Int. J. Radiation Oncology Biol. Phys., Vol. 56, No. 5, pp. 1488–1494, 2003

0360-3016/03/$–see front matter

doi:10.1016/S0360-3016(03)00440-1

PHYSICS CONTRIBUTION

CLINICAL IMPLEMENTATION OF AN AUTOMATED PLANNING SYSTEM FOR GAMMA KNIFE RADIOSURGERY

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Purpose: To evaluate an automated treatment planning system for gamma knife radiosurgery. This planning system was developed in our clinic and is now in routine clinical use. The system simultaneously optimizes the shot sizes, locations, and weights. It also guides the user in selecting the total number of radiation shots.
Methods and Materials: We assessed the clinical significance of the automated system by comparing an optimized plan with a manual plan for 10 consecutive patients treated at our gamma knife facility. Each treatment plan was analyzed using dose–volume histograms in conjunction with the conformity index, the minimum target dose, and the integral normal tissue dose.
Results: On average, the treatment plan produced by the inverse planning tool provided an improved conformity index, a higher minimum target dose, and a reduced volume of the 30% isodose line as compared to the corresponding plan developed by an experienced physician. An optimized treatment plan can typically be produced in 10 min or less.
Conclusions: The automated planning system consistently provides a high-quality treatment plan while reducing the time required for gamma knife treatment planning.

Gamma knife, Inverse treatment planning, Stereotactic radiosurgery.

INTRODUCTION

Gamma knife treatment plans are conventionally produced using a manual iterative approach (1, 2). In each iteration, the planner attempts to determine the following: (*1*) the number of shots, (*2*) the shot sizes, (*3*) the shot locations, and (*4*) the shot weights that would adequately cover the target and spare critical structures. For large or irregularly shaped treatment volumes, this process becomes rather tedious and time-consuming. Also, the quality of the plan produced often depends upon both the patience and the experience of the user. Consequently, a number of researchers have studied techniques for automating the gamma knife treatment planning process (3–20). One approach approximates each radiation shot as a sphere, thus reducing the problem to one of geometric coverage. A ball-packing approach (3, 4) can then be used to determine the shot locations and sizes. Other algorithms that have been tested include a modified Powell's method (10), simulated annealing (10, 12), and mixed integer programming (18).

We have developed a nonlinear programming approach for optimizing the gamma knife treatment plans. Our algorithm that was initially described in Ref. 17 simultaneously optimizes the shots sizes, locations, and weights. Numerous improvements to the inverse planning tool have been made since the publication of the original article:

1. The dose engine has been significantly improved (19) to minimize the discrepancy between the optimizer's dose calculation and the dose calculated by Elekta's GammaPlan software.
2. The algorithm now guides the planner in selecting the number of shots of radiation and the appropriate collimator helmet sizes.
3. A geometry-based heuristic is used to quickly obtain a high-quality starting point for the optimizer. This provides a significant reduction in the time required for each optimization (20).
4. The planning process has been made more flexible, with the ability to prescribe localized dose escalation and the ability to include dose constraints on sensitive structures.

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This research was partially supported by National Science Foundation Grant ACI-0113051.

Acknowledgments—The authors would like to thank all who contributed to this work, including Roger Ove, Lance Weems, and Lijun Ma.

Received Apr 1, 2002, and in revised form Mar 10, 2003. Accepted for publication Mar 11, 2003.

5. The tool is in routine clinical use.

In addition to describing these advances, this paper will analyze plans produced by the optimizer for 10 consecutive treatments at our gamma knife facility.

METHODS AND MATERIALS

Volume definition

The target and sensitive structures are outlined in Elekta's Gamma Knife treatment planning system (GammaPlan). The stereotactic coordinates of each volume are then extracted from the planning system using a routine provided by Elekta.

Defining the prescription

Before the optimization, the following prescription parameters must be defined: (*1*) the patient positioning (prone/supine), (*2*) the prescription isodose line, (*3*) the target conformity index, (*4*) the maximum number of shots, and (*5*) the allowable helmet sizes.

The optimization algorithm is set up to minimize the underdosage in the target subject to a constraint on the conformity and on the maximum number of shots. This formulation can be easily modified, however, to add or remove various constraints (See Ref. 20).

Optimization methods

The optimization is performed in two steps. First, a geometry-based heuristic is used to produce a reasonable configuration of shot sizes and locations. Next, a dose-based optimization is used to produce the final treatment plan.

Geometry-based heuristic

The geometry-based heuristic is designed to quickly produce a reasonable configuration of shot sizes and locations. The resulting treatment plan serves as a high-quality starting point for the dose-based optimization that follows. The rationale is that a good initial guess helps to significantly reduce the overall optimization time.

In our geometry-based heuristic, each shot of radiation is modeled as a sphere, and the medial axis transform of the target volume is used to guide the placement of the shots (20–22). The medial axis transform, also known as the "skeleton," is frequently used in shape analysis and other related areas. The idea of using the skeleton to guide the placement of shots in radiosurgery was pioneered by Wu *et al*. (3), Wu and Bourland (4, 5, 7), and Wu (6). Our algorithm differs from this approach in that it uses a morphologic thinning approach to create the skeleton, as opposed to the Euclidean distance technique applied by Wu and Bourland (3, 4, 5, 7). In our case, a number of shots are placed along the skeleton of the target, and the algorithm modifies the configuration of shots to provide the best tumor coverage.

The geometry-based heuristic also serves to guide the user in selecting the number of shots and the most appropriate collimator helmets. This preliminary information assists the planner in striking the appropriate balance between plan quality and treatment efficiency. Often, the delivery time can be reduced if we can limit a treatment plan to one or two focusing helmets.

Table 1. Recommended number of shots with 2 focusing helmets

Helmet sizes	Number of shots
18 mm and 14 mm	7
18 mm and 8 mm	7
18 mm and 4 mm	7
14 mm and 8 mm	9
14 mm and 4 mm	10
8 mm and 4 mm	25

After the user selects the number of focusing helmets to be included in the treatment plan, the tool produces a list of the possible helmet combinations and a suggested number of shots for each (See Table 1). After reviewing the table, the user selects the helmet sizes and the number of shots to use for the dose-based optimization. The shot sizes, locations, and weights are then optimized, and the results are manually entered into Elekta's GammaPlan system. The final evaluation of the plan quality is performed in GammaPlan.

Dose-based optimization

We have developed a migrating shot technique for optimization of gamma knife treatment plans. This technique makes use of a limited number of shots, each of which is assigned five variables: the shot size, the *x* coordinate, the *y* coordinate, the *z* coordinate, and a relative weight. Nonlinear programming techniques are used to simultaneously optimize all of the variables.

Dose calculation

In gamma knife treatment planning, the complete dose distribution can be calculated as a sum of contributions from all of the individual shots of radiation. The dose for all (*i*, *j*, *k*) can be computed using Eq. 1:

$$Dose(i, j, k) = \sum_{(s,w)\in S\times W} t_{s,w} D_w(x_s, y_s, z_s, i, j, k), \tag{1}$$

where $D_w(x_s, y_s, z_s, i, j, k)$ is the dose delivered to voxel (*i*, *j*, *k*) by a shot of width *w* centered at (x_s, y_s, z_s) with a delivery time of $t_{s,w}$.

In previous work (17), our dose model was designed to match dose profiles for a single shot placed at the center of a spherical phantom. The dose cloud was approximated as a spherically symmetric distribution by averaging the profiles along the *x*, *y*, and *z* axes. The dose at a given distance from the shot center was then obtained from a single radial function.

In this work, we have improved the dose accuracy by accounting for the ellipsoidal nature of the dose falloff (19). The orientation of the patient (prone or supine) dictates the orientation of the principal axis of the ellipsoid. We therefore optimize in a rotated coordinate system where the axes lie along the ellipsoid's principal axes.

To set up the dose engine, we needed to determine a functional form for the dose delivered at a voxel (i, j, k) from the shot centered at (x_s, y_s, z_s). A sum of error functions has been noted in the literature to approximate this dose distribution (23). We therefore used the following functional form:

$$D_w(x_s, y_s, z_s, i, j, k) = \sum_{p=1}^{2} \lambda_p \left\{ 1 - erf \left[\frac{\sqrt{(i - x_s)^2 + \mu_p^y (j - y_s) + \mu_p^z (k - z_s)^2} - r_p^2}{o_p} \right] \right\},$$

where $erf(x)$ represents the integral of the standard normal distribution from $-\infty$ to x. For each shot size, the parameters $(\lambda_p, \mu_p^y, \mu_p^z, r_p,$ and $\sigma_p)$ were matched to the dose profiles extracted from GammaPlan via a least-squares fit. The parameters were optimized separately for each shot width. The resulting nonlinear optimization problem

$$\min_{\lambda, \mu, r, \sigma} \left\| \begin{pmatrix} \bar{D}_w^x(i) - \sum_{p=1}^{2} \lambda_p \left\{ 1 - erf\left[\frac{\sqrt{(i - x_s)^2} - r_p^2}{o_p} \right] \right\} \\ \bar{D}_w^y(i) - \sum_{p=1}^{2} \lambda_p \left\{ 1 - erf\left[\frac{\sqrt{(i - y_s)^2} - r_p^2}{o_p} \right] \right\} \\ \bar{D}_w^z(i) - \sum_{p=1}^{2} \lambda_p \left\{ 1 - erf\left[\frac{\sqrt{(i - z_s)^2} - r_p^2}{o_p} \right] \right\} \end{pmatrix} \right\|_2$$

was solved using CONOPT (24–26) and GAMS (27). The values of λ_p, μ_p^y, μ_p^z, r_p, and σ_p were then fixed and incorporated into the nonlinear models used throughout the remainder of this paper.

Final plan evaluation

After the optimization is complete, a list is printed with the optimized shot sizes, locations, and weights. These values are manually entered into the Leksell GammaPlan system, where the final dose calculation and treatment plan evaluation are performed.

RESULTS

Accuracy of the dose engine

The optimizer and GammaPlan use different methods of dose calculation. Consequently, there may be some degradation in the quality of the plan when it is evaluated in GammaPlan. In Fig. 1, a dose–volume histogram comparison is shown for one treatment. In this case, note that the target dose uniformity was actually improved when the plan was entered into the GammaPlan system. This difference may, in part, be attributable to differences in the dose–volume histogram algorithms.

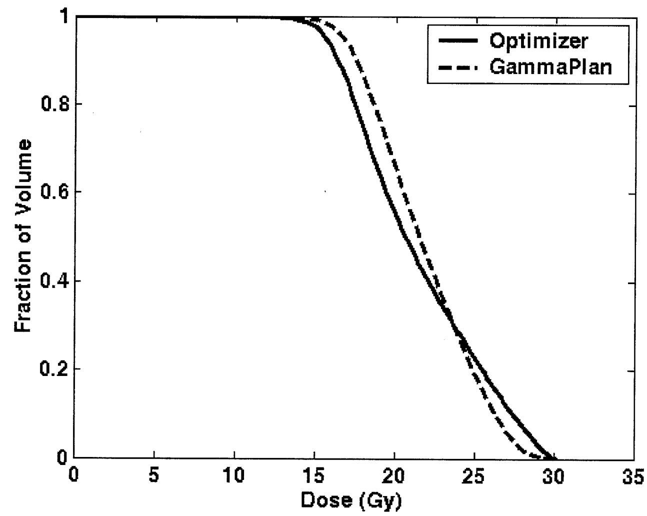

Fig. 1. A dose–volume histogram comparison for the same plan with the dose computed using the inverse planning tool and the final dose calculated in Elekta's GammaPlan.

Geometry-based heuristic

In Fig. 2, we illustrate the capabilities of the medial axis transform algorithm with the help of a simple two-dimensional bean-shaped target. Figure 2b shows the corresponding skeleton of the target volume. With each shot modeled as a rigid sphere, the algorithm uses the skeleton as a guide for shot placement. The resulting 6-shot dose distribution is shown in Fig. 2c, along with the corresponding shot locations. The prescription isodose line (50%) is plotted as a dashed line.

Although the plan provides a rapid falloff in dose outside of the target, the prescription isodose line can be seen to miss a portion of the target. The geometry-based heuristic provides, nevertheless, a high-quality starting point for the subsequent dose-based optimization. Figure 2d plots the final plan after the dose-based optimization. The optimizer required only 40 iterations, indicating that the geometry-based heuristic provides a good starting point for the dose-based optimization. When supplied with a random starting point, the dose-based optimization required over 600 iterations to reach convergence. Therefore, the geometry-based heuristic can significantly reduce the overall optimization time. Even for tumor volumes as large as 35 cm^3, the geometry-based optimizer was able to produce a treatment plan within 7 seconds.

The geometry-based heuristic has proven also to be a useful tool for assisting in the selection of the appropriate number of shots and helmet sizes. For example, axial,

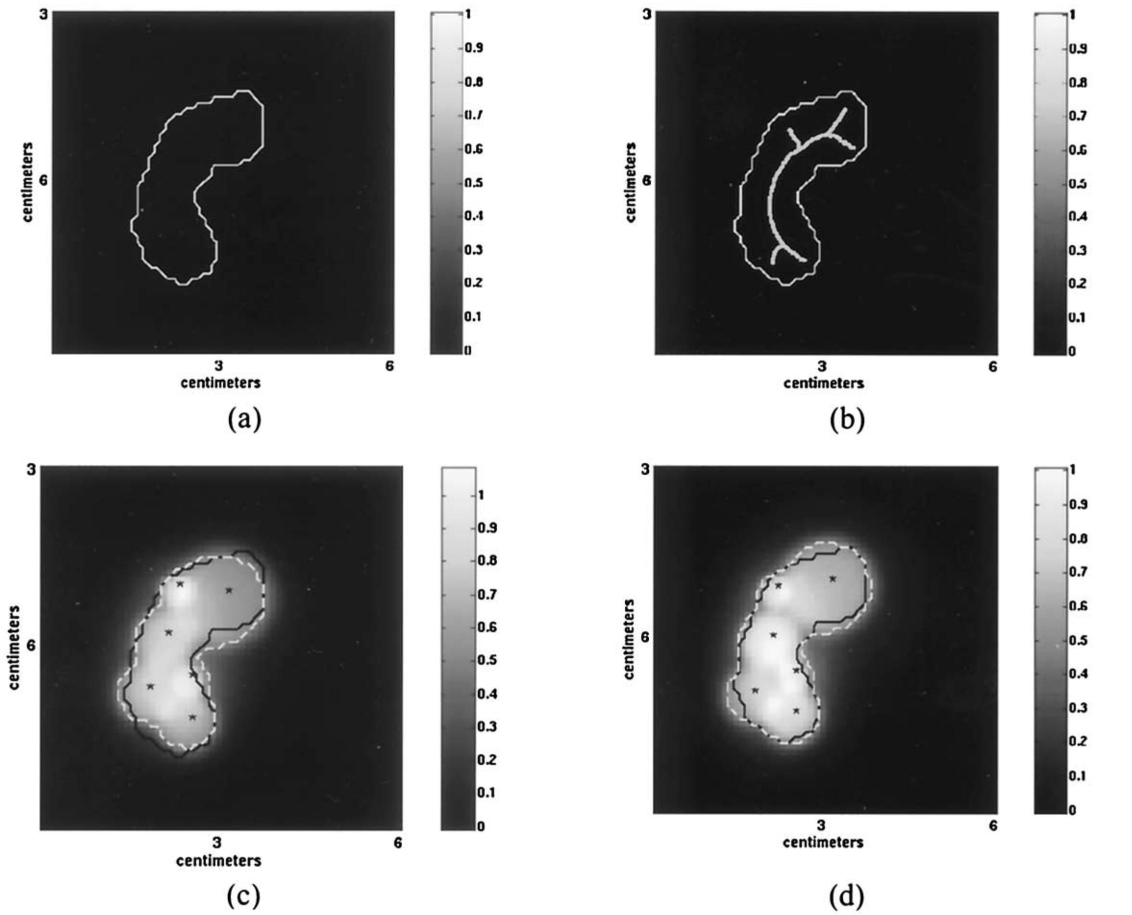

Fig. 2. (a) A simple two-dimensional bean-shaped target. (b) The skeleton of the tumor volume is plotted. (c) Dose distribution produced using the skeleton to guide a geometry-based optimization. The prescription isodose line (50%) is plotted as a dashed line. (d) Solution from the dose-based optimization.

coronal, and sagittal slices from a gamma knife patient are shown in Figs. 3a–c. It can be difficult to predict the appropriate number of shots and helmet sizes if the geometry-based heuristic is not used. In this case, the user constrained the optimizer to use only two focusing helmets. In less than a minute, the optimizer listed the recommended number of shots for each possible helmet combination (See Table 1). Note that more shots are required to obtain adequate coverage if smaller shot sizes are used. The user selected a combination of 18-mm and 14-mm shots with a total of 7 shots, as recommended by the optimizer. The corresponding isodose plots are shown in Figs. 3d–f.

Comparison with experienced planner

For 10 consecutive patient cases, both a manual plan and an optimized treatment plan were produced. In each case, a neurosurgeon and a radiation oncologist produced the manual plan. This team has over 7 years of gamma knife experience, including more than 1,000 gamma knife treatments. This study excluded targets requiring only one or two shots of radiation, because inverse planning is not justified in such simple cases.

In Table 2, the manual and optimized treatment plans for 10 consecutive patients are compared on the basis of the number of shots, the conformity index, the volume of the 30% isodose line, and the minimum target dose. These indices were chosen based upon the radiosurgery guidelines of the Radiation Therapy Oncology Group (RTOG) (28). The RTOG guidelines specify that a case is per protocol if the target is encompassed by 90% of the prescription isodose. The conformity index is defined as the volume of the prescription isodose divided by the target volume. The RTOG considers a case to be per protocol if this ratio falls between 1.0 and 2.0.

On average, the treatment plan produced by the inverse planning tool provided an improved conformity index, a higher minimum target dose, and a reduced volume of the 30% isodose line as compared to the corresponding plan developed by an experienced physician.

For a number of the patients shown in Table 2, the selection of the preferable plan is not clear-cut. This stems from the need to balance the conflicting goals of dose conformity and target coverage. To illustrate this point, we ran five optimizations for a single patient case. For each optimization, the only parameter

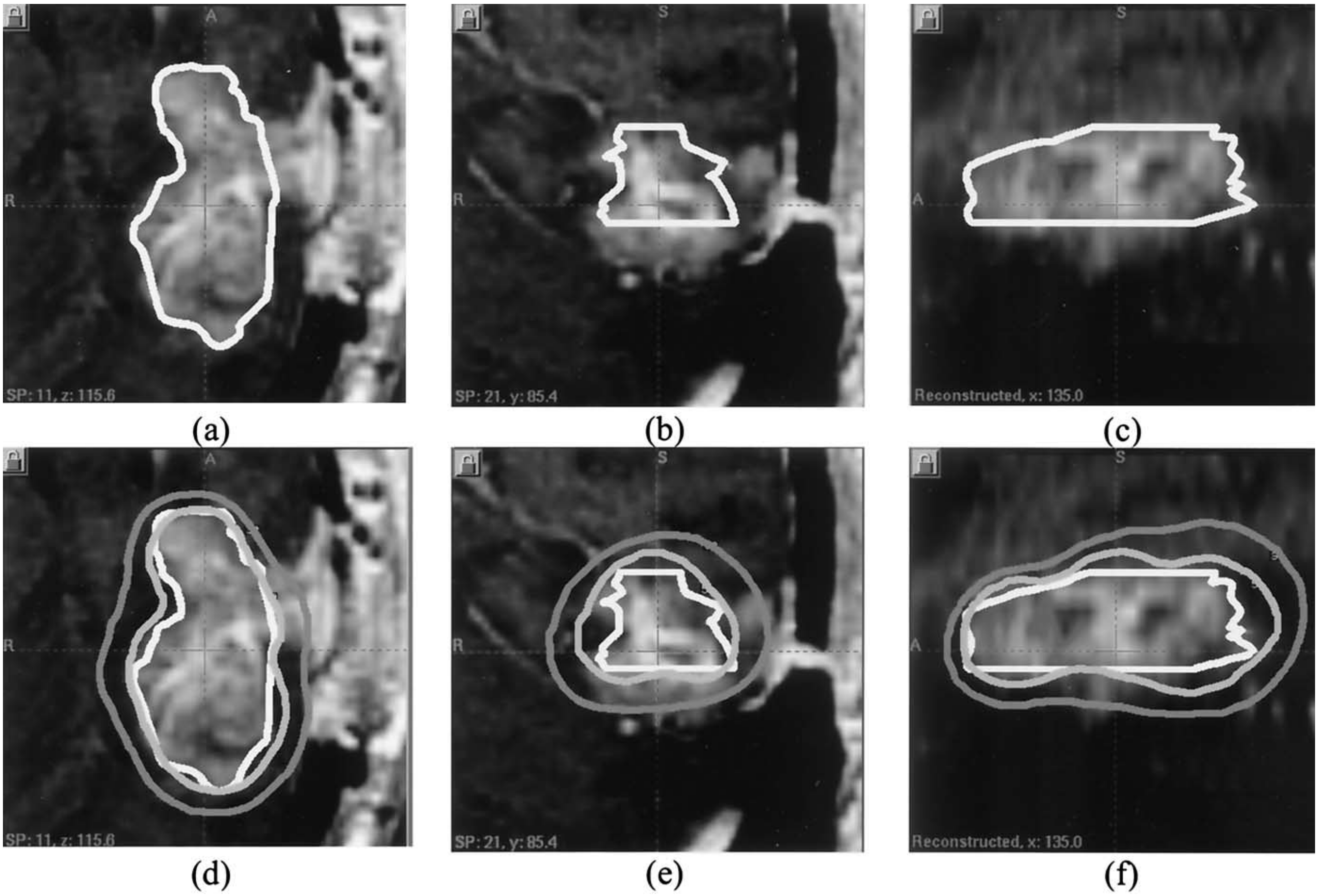

Fig. 3. (a–c) An axial, coronal, and sagittal slice of tumor volume. The geometry-based optimization routine was used to predict that 7 shots were needed using the 14-mm and 18-mm focusing helmets. (d–f) The optimized dose distribution using 7 shots. The 50% isodose line is plotted in light gray, and the 30% isodose line is plotted in dark gray.

in the prescription that was changed was the required conformity. The results shown in Table 3 illustrate that the optimizer is able to provide a range of conformity indices for the same patient. However, as the conformity improves, sacrifices must be made in the target dose coverage. It should be noted, however, that each of these optimizations took less than 2 min to perform. One can therefore run a series of optimizations to find the plan that best satisfies the physician-specific and patient-specific goals.

Additional applications

With our tool, the treatment volume can be divided so that each section of the tumor can be assigned a separate set of treatment goals. For example, the nodular regions

Table 2. Manual vs. optimized plans: 10 consecutive patients

Patient number	Target volume (cm^3)	Number of shots		Conformity index		Volume of 30%		Minimum target dose	
		Manual	Optimized	Manual	Optimized	Manual	Optimized	Manual	Optimized
1	12.1	6	6	1.67	1.61	44.4	41.9	48%	47%
2	3.4	4	4	1.35	1.47	12.4	13.0	46%	45%
3	3.9	7	7	1.46	1.43	14.3	13.3	45%	47%
4	11.4	6	6	1.19	1.34	34.7	35.8	45%	49%
5	7.6	8	8	1.76	1.39	33.6	24.2	49%	46%
6	6.7	6	6	1.62	1.60	28.0	27.4	52%	52%
7	9.0	5	5	1.64	1.56	35.4	31.9	47%	48%
8	37.1	12	12	1.56	1.32	132.2	108.4	45%	45%
9	7.2	6	6	1.51	1.29	30.2	25.3	49%	48%
10	3.8	9	9	1.29	1.53	13.3	13.7	45%	48%
Average	10.2	6.9	6.9	1.51	1.45	37.9	33.5	47.1	47.5

Table 3. Results for 5 optimized plans with increasing conformity requirements

Conformity index	Volume of 30%	Percent coverage 90%	Minimum target dose
1.75	16.8	100	52
1.58	14.5	100	48
1.50	13.6	99	46
1.35	12.0	99	43
1.1	9.9	96	30

of a tumor can be outlined separately from the surrounding edema. A higher isodose coverage level can then be specified for the nodular regions.

Figure 4 shows an axial and a coronal slice from a treatment plan in which the optimizer was used to provide a simultaneous boost at the time of delivery. The tumor volume is outlined in white, and the boost volume is outlined in black. In this case, the tumor volume was prescribed to the 50% isodose line (shown in gray), and the boost volume was prescribed to 70% of the maximum dose. The cumulative dose–volume histogram shown in Fig. 5 demonstrates that the optimizer achieved both of these treatment goals without sacrificing the overall conformity of the plan. In this case, the conformity index was 1.70. This type of precise placement of a hot spot within the target volume is very difficult to achieve with manual planning.

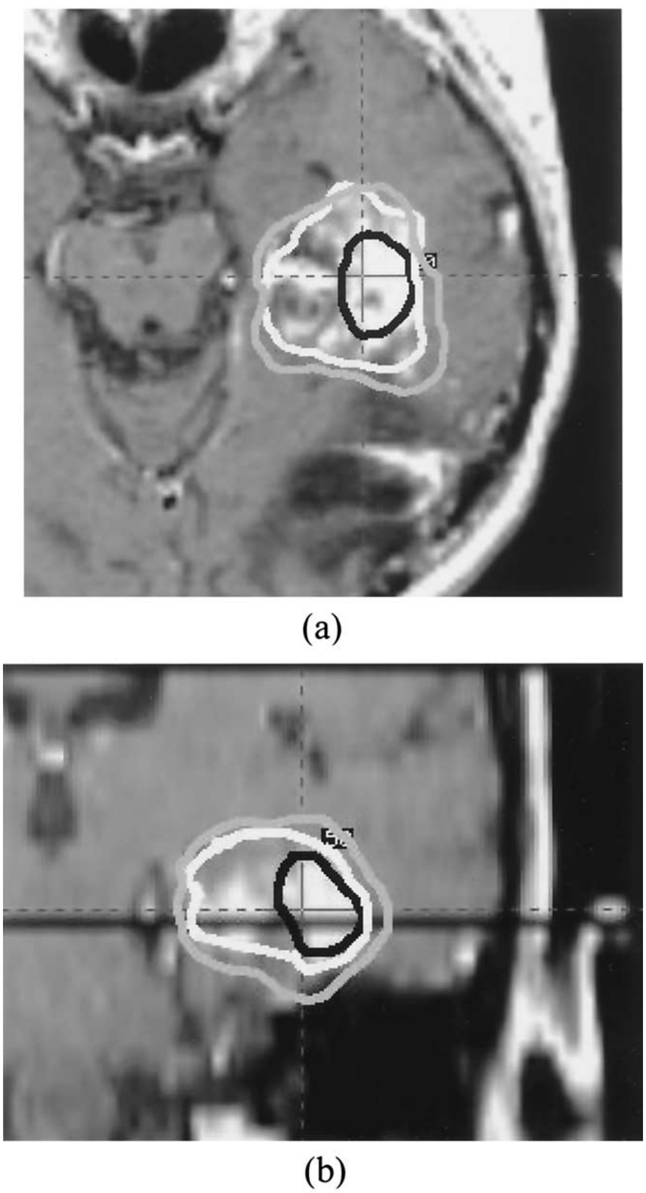

Fig. 4. (a) Axial and (b) coronal slice showing the gross tumor volume in white and the boost volume in black. The 50% isodose line is plotted in gray.

Speed

The dose-based optimization can typically produce an optimized treatment plan in less than 10 min on an 800-MHz PC.

DISCUSSION

An inverse planning system has been developed for gamma knife radiosurgery. The tool first guides the planner in selecting the number of shots and which focusing helmets are best suited for each particular case. Based on the choice of the planner, the tool simultaneously optimizes the shots

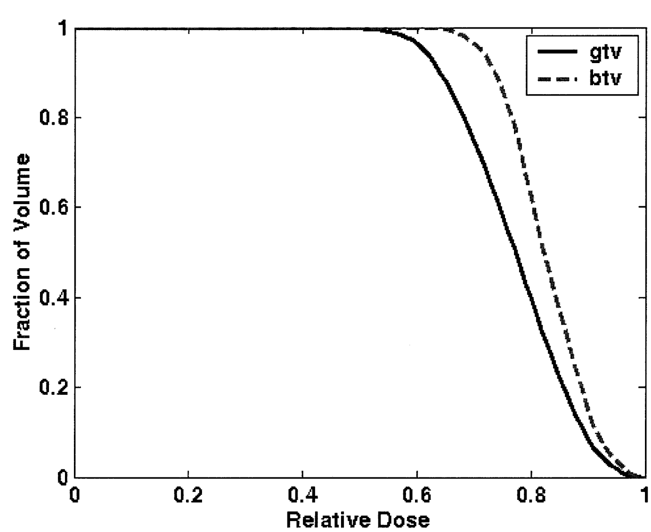

Fig. 5. The cumulative dose–volume histogram for the case shown in Fig. 4. Note that the boost volume has been raised to a higher dose level than the gross tumor volume.

sizes, locations, and weights. The tool provides additional features, such as the ability to simultaneously boost a portion of the tumor and the ability to place an upper limit on the dose to any nearby sensitive structures. For 10 consecutive patients, the optimizer was run head-to-head against an experienced neurosurgeon. On average, the treatment plan produced by the inverse planning tool provided an improved conformity index, a higher minimum target dose, and a reduced volume of the 30% isodose line as compared to the manual plan. This tool is now in routine clinical use.

One of the major benefits of this tool is that it saves time. The optimizer typically takes between 1 and 10 min to optimize. During this time, the user is free to complete other work. The need for a tedious trial-and-error approach to treatment planning is therefore eliminated. This is particularly beneficial for tumors that are large or irregularly shaped, in which case manual treatment planning can take an hour or more.

A second benefit to this tool is consistency. Because of the large number of variables and the complicated nature of gamma knife treatment planning, the quality of each treatment plan can be strongly dependent upon the experience and patience of the treatment planner. With this tool, user-to-user variability can be virtually eliminated. With minimal training, anyone can create high-quality gamma knife treatment plans. This would be particularly beneficial for new gamma knife sites and physicians or physicists who are less experienced with the gamma knife.

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