The Gamma Knife Problem

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Abstract

Noninvasive gamma-knife radiosurgery treatment attacks brain tumors using spherical radiation dosages (shots). We develop methods to design optimized treatment plans using four fixed-diameter dosages. Our algorithms strictly adhere to the following rule: Shots cannot violate tumor boundaries or overlap each other.

From a mathematical perspective, the problem becomes a matter of filling an irregularly-shaped target volume with a conglomeration of spheres. We make no assumptions about the size and shape of the tumor; by maintaining complete generality, our algorithms are flexible and robust. The basic strategies of the algorithms are deepest-sphere placement, steepest descent, and adaptation.

We design representative 3D models to test our algorithms. We find that the most efficient packing strategy is an adaptive algorithm that uses steepest descent, with an average coverage percentage of 40% over 100 test cases while not threatening healthy tissue. One variation covered 56% of one test case but had a large standard deviation across 100 test cases. It also produced results four times as fast as the adaptive method.

Background

Brain Tumors

The average volume of a tumor operable by radiosurgery is about 15 cm^3 [Lee et al. 2002]. We generate 3D tumor models of approximately this volume with varying physical dimensions.

The Gamma Knife

The gamma knife unit consists of 201 individual cobalt-60 radiation sources situated in a helmet. The 201 beams converge at an isocenter creating a spherical

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dose distribution ("shot"). Four sizes of spheres are possible: 4, 8, 14, and 18 mm in diameter. A radiosurgery plan is used to map out shots to destroy the tumor without harming the patient. Following successful treatment, surviving cancer cells lose their ability to grow. In fact, many partially destroyed tumors shrink or even disappear in time [Kaye and Laws 1995].

The Problem

The plans should arrange radiation doses so that tumor destruction is maximized, healthy tissue is protected, and hot spots are avoided. Thus, the algorithms are subject to the following constraints:

- Prohibit shots from penetrating outside the target area.
- Prohibit overlap of shots, preventing hotspots.
- Maximize the percentage covered in the tumor, or target volume.
- Use a maximum of 15 shots.

Assumptions

- The tumor is homogeneous; it is equally productive to treat any part of it.
- The tumor is modeled discretely using a three-dimensional image.
- No assumptions are made about the shape of the tumor.
- Tumor cells are either been radiated or not; there are no partial dosages.

Problem Approach

We have divide the problem into three different pieces:

- create a variety of 3-dimensional brain tumor models,
- develop and refine sphere-packing algorithms, and
- test and compare algorithms using tumor models

Data Models

Our data consists of a $100 \times 100 \times 100$ array that represent a 1000 cm^3 space around the brain tumor. We refers to each element of the matrix as a *voxel* (three-dimensional pixel). Each voxel represents 1 mm^3 of brain tissue [Wagner 2000]. We use 1s to indicate tumor and 0s to represent healthy tissue, and we populate the arrays with tumor models as described below.

Sphere Tumor Model

Our first model is based on the simple equation for a sphere, $(x-x_0)^2+(y-y_0)^2+(z-z_0)^2=r^2$, where the center of the sphere is represented by (x_0, y_0, z_0) with radius r. We fill in the voxels representing the tumor by applying the inequality $(x-x_0)^2+(y-y_0)^2+(z-z_0)^2 \le r^2$ throughout the test volume.

Ellipsoid Tumor Model

The ellipsoid model uses the same principle as the spherical model. The inequality

$$\frac{(x-x_0)^2}{a^2}+\frac{(y-y_0)^2}{b^2}+\frac{(z-z_0)^2}{c^2} \le r^2$$

represents the interior of an ellipsoid. The spherical and ellipsoid models are a basis for the mutated sphere tumor model.

Mutated Spherical Tumor Model

Tumor shapes can be modeled by unions of ellipsoids [Asachenkov 1994]. Thus, our most accurate model is created by intersecting several ellipsoids at random locations. We start with a small spherical tumor. Then we create three discrete uniformly distributed random variables U_x, U_y, and U_z, where (U_x,U_y,U_z) represents a randomly chosen voxel within the sphere. This point becomes the center of an ellipsoid that is added to the tumor. The a, b, and c parameters that define the dimensions of the ellipsoid are defined by three other random variables U_a, U_b, and U_c, uniform continuous random variables over [5, 15].

Sphere-Packing Algorithms

In practice, tumors are usually represented as a 3D image obtained from MRI (magnetic resonance imaging). We discretize the tumor and the removal spheres for processing. We explore four different methods:

- first-deepest,

- steepest descent,
- improved steepest descent, and
- adaptive.

Grassfire Algorithm

All of our sphere-packing methods employ the *grassfire algorithm* [Wagner 2000]. The grassfire method progressively marks the layers of the tumor from the outside in, analogous to a fire burning away an object one layer at a time.

For each 1-valued voxel, all surrounding voxels are surveyed. If any are 0-valued (outside the tumor), the current voxel is set to a depth of 2, which represents the boundary of the tumor. This process is repeated for every voxel in the 3D test volume, with layer numbers progressively increasing until all of the 1s in the array have been consumed. In other words, the grassfire method calculates an approximate measure of depth for each voxel in the tumor. Doing so gives an easy measure of the largest sphere that can be placed at any given point without violating the tumor boundary. If the voxel is at depth 8 or 9, then a 7-mm sphere should be used, and so on.

The basic operation of grassfire (shown in two dimensions) is shown in **Figure 1**, which shows the effect of grassfire on a circle. For readability, the boundary layer has been left at a value of 1 and the data arrays represent a much smaller area than the plots. Depth is indicated by shade; darker is deeper. The arrows show progression through initial grassfiring to the removal of a small circle from the center (just as spheres are removed from the tumor). Notice that when grassfire is applied after removal, the maximum depth is smaller than that of the original circle.

Although it is simple, grassfire provides the foundation for all of our sphere-packing algorithms.

Sphere Placement Methodology

After grassfiring the tumor model, the deepest point in the tumor is easily found. Reasonably, the deeper the point in the tumor, the more likely it is that a large radius sphere can be placed without harming normal tissue. Large (particularly 9-mm) spheres being placed in the tumor increases the coverage of the solution. Conversely, the smallest sphere (2-mm radius) is the least efficient in eradicating cancerous tissue. For the average tumor size, the 2-mm sphere removes less than 1% of the volume. Therefore, we place as many large spheres as possible before placing smaller spheres.

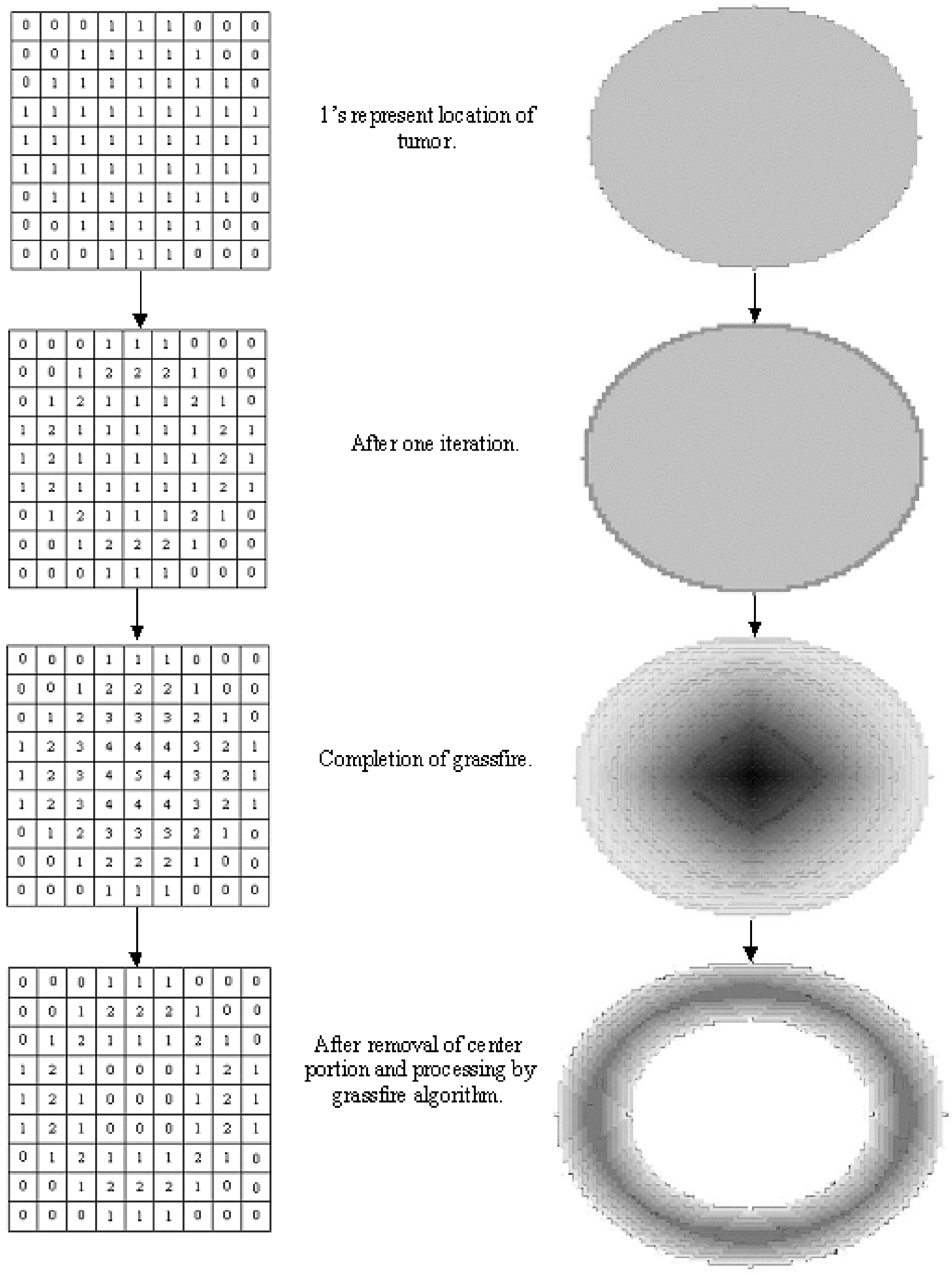

Figure 1. Grassfire algorithm flowchart.

First-Deepest Method

The first-deepest method begins by applying the grassfire algorithm to the tumor data. We generate a list of the deepest voxels (nearly all volumes will have multiple "deepest" points after the layering process). This method simply takes the first voxel off that list and places the removal sphere at that location; the radius of the sphere used is determined from the depth value at that voxel. For example, if a voxel is 8 layers deep (and thus 8 mm deep), then a 7-mm radius sphere can be removed from that location without harming healthy tissue.

Step-by-Step

1. Grassfire the tumor data.
2. Grab one of the points at the deepest level.
3. Calculate the equation for the sphere centered at that point with the largest acceptable radius.
4. Set all voxels within the radius of the sphere to zero (effectively removing a spherical portion of tumor).
5. Reset all nonzero voxels to 1s (resetting the tumor for another grassfire run).
6. Return to step 1.

This method is very robust; when a sphere is removed, it is simply seen as a new tumor boundary, so any of the variables such as shot size, number of shots, or tumor shape can change and the algorithm still works.

Variations

We try to improve the method by looking down the list of the deepest voxels to find a more appropriate sphere center. We accomplish this by giving each voxel a score based on the depths of its neighboring points. Essentially, the algorithm tries to place the sphere at the greatest possible average depth. But doing this does not improve the total coverage; in fact, this algorithm is inferior to the first-deepest method. Placing the sphere as deep as possible reduces the depth of the next iteration, preventing more large spheres from being placed. A better strategy would be placing the sphere as shallow as possible (see **Figure 2** for a 2D example), in an effort to leave room for more large spheres.

Steepest Descent Method

The method of steepest descent tries to place the largest possible sphere (as determined by grassfire) close to the tumor boundary. The steepest descent uses a scoring function to find the best location for the biggest sphere.

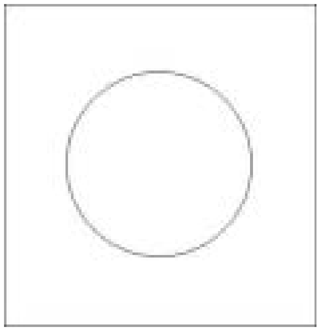

Figure 2a. A single large circle in the center prevents placement of any more large circles.

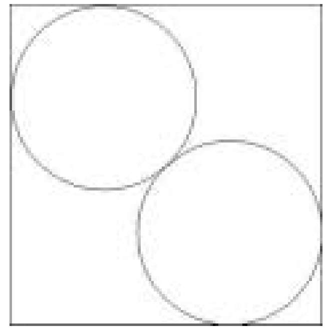

Figure 2b. If the first circle is placed far from the center, a second large circle can fit.

Starting from the deepest voxel, we calculate the gradient of the score function and proceed along the steepest path until a local max is reached, and this point is used as a sphere isocenter. This is implemented as follows:

1. Calculate the score of the deepest voxel.
2. Calculate the score of all surrounding voxels.
3. If the original voxel has the highest score, it becomes an isocenter, otherwise move to the highest scoring voxel and go back to step 1.

Scoring Function

This method is only as good as the scoring function. We have two factors, W_1 and W_2, that figure into the score of a given voxel.

The W_1 factor measures the depth of any nearby voxels; more specifically, it is an estimation of the depth-density of a sphere centered at that voxel. More rigorously defined, we estimate the W_1 at voxel (x_0, y_0, z_0):

$$W_1 \approx \frac{\iiint_{S(x,y,z)} D(x,y,z)\,dxdydz}{\text{total volume of sphere}},$$

where $S(x_0, y_0, z_0)$ is a sphere centered at (x_0, y_0, z_0).

$D(x,y,z)$ is the depth at (x,y,z), so effectively W_1 represents the average depth throughout the sphere's volume. To speed up the scoring function, we estimate this volume integral by averaging the depth values for a cube surrounding the point. The sphere is inscribed within our cube of estimation; and given that the scoring function will only be a basis of relative comparison, the level of error is tolerable.

The W_2 factor is used to make sure that normal tissue is not contained in the shot. Given the sphere size that will be used for the potential shot, we have

$$W_2 = \begin{cases} 1, & \text{if depth } (x_0, y_0, z_0) > \text{shot radius;} \\ 0, & \text{if depth } (x_0, y_0, z_0) \leq \text{shot radius.} \end{cases}$$

This is another place where our decision to prohibit destroying healthy tissue becomes a central part our solution. Total coverage of the tumor could be improved at the expense of healthy tissue by implementing a continuous scoring function for the W_2 weight.

Finally, the total score is given by W_2/W_1. This scoring function rewards the shot for being at a closer distance to the tumor edge (or a removed sphere, since this looks like an edge to our algorithms) while still being entirely contained within the tumor.

Improved Steepest Descent Method

The improvement on steepest descent is to allow spheres to be placed closer to the tumor boundary. The only changes lie in how the W_1 and W_2 weights are calculated in the score function.

Altered Score Function

The improved scoring function calculates the W_2 score factor in a more rigorous manner. Before, we used the depth (determined by grassfire) to determine if the shot would fit or not. The grassfire depth is actually a conservative depth estimate—there can be more distance between the voxel and the boundary than it indicates. To fit a sphere more tightly, we construct a list of the points on the boundary and consult it each time W_2 is calculated. Now,

$$W_2 = \begin{cases} 1, & \text{if any shot voxels are in } \{(x, y, z) | (x, y, z) \text{ is on tumor boundary}\}\ ; \\ 0, & \text{else.} \end{cases}$$

Adaptive Method

The adaptive method generates an initial sequence of shots using steepest descent (coverage could be improved by using improved steepest descent, but the simulations would run an order of magnitude slower). The initial sequence is then changed one sphere at a time and repacked until each shot in the sequence has been changed once. Theoretically, taking this action allows for the exchange of a large sphere for many smaller spheres, which may be more effective. It follows the idea that perhaps some spheres need to be placed poorly initially in order to allow smarter shots to be placed down the line.

For instance, consider an initial sequence of length N that starts with the following shots: $\{$ 9 mm, 4 mm, 4 mm, $\ldots$ $\}$. Using the same initial tumor, the adaptive method runs the steepest descent method, but the new sequence *must* change the first sphere, so it starts with a 7-mm sphere. On the second iteration, the new sequence keeps the leading 9-mm sphere but must change the second element to a 2-mm sphere. The third iteration starts with a 9-mm sphere, followed by a 4-mm sphere, and then changes the third sphere to a 2-mm sphere. This continues until all $N-1$ sequences have been generated. We seek and use the sequence with maximum coverage.

Quantitative Results

Table 1.
Comparison of methods.

Method	Timing		% Coverage			
	Avg. (s)	Relative speed	Mean	SD	Min.	Max.
First-deepest	83	1	34	5.2	20	45
Steepest descent	104	1.25	38	2.9	32	45
Improved steepest descent	229	2.8	37	6.2	28	56
Adaptive	1025	12.3	40	2.5	35	44

We ran each method on the same suite of 100 test cases, except for the adaptive method, for which, because of its longer runtime we used a subset of 20 cases. **Table 1** contains a summary of the results. The maximum coverage that we could achieve was 56% (**Figure 3**).

Our algorithms work on tumors of arbitrary shape, even disjoint tumors. The result of one such pack is shown in **Figure 4**.

Qualitative Results

First-Deepest Method

As expected, this algorithm's performance is quantitatively the weakest. The maximum coverage of 45% is actually slightly better than the other methods. However, the minimum value of 20%, as well as the average of 34% are quite low compared with other methods. It also exhibits large random variations in coverage, meaning that the algorithm is equally likely to fill in a low percentage as it is to fill in a relatively high percentage of a tumor.

The method is inconsistent, yields the lowest average coverage of all methods, but it is the fastest.

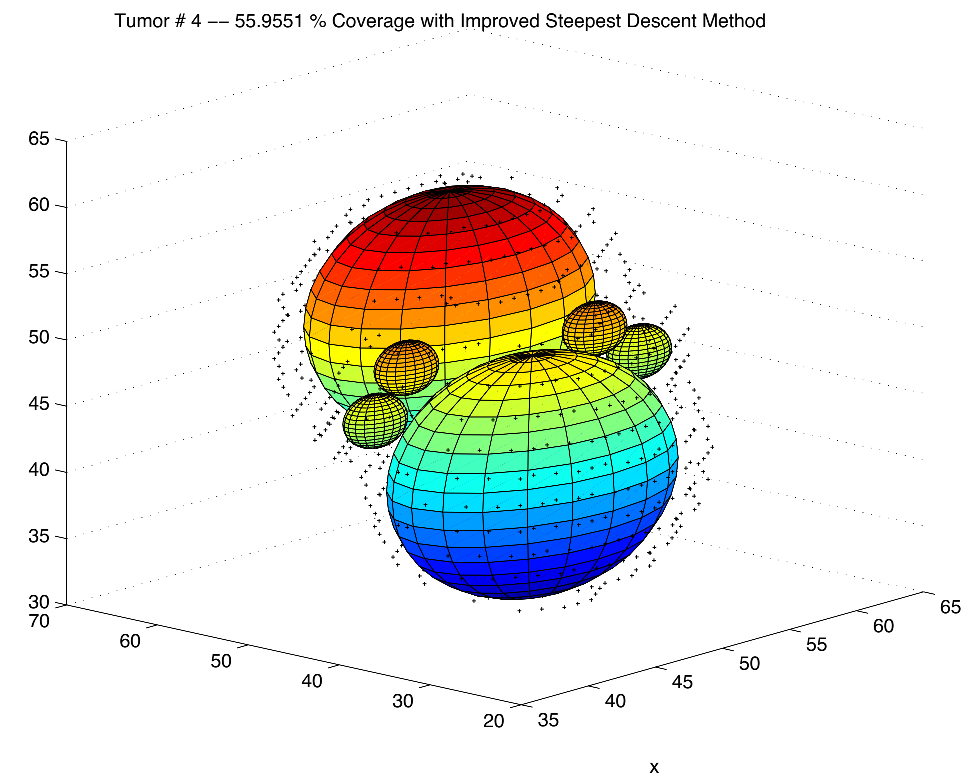

Figure 3. Our best result: 56% coverage.

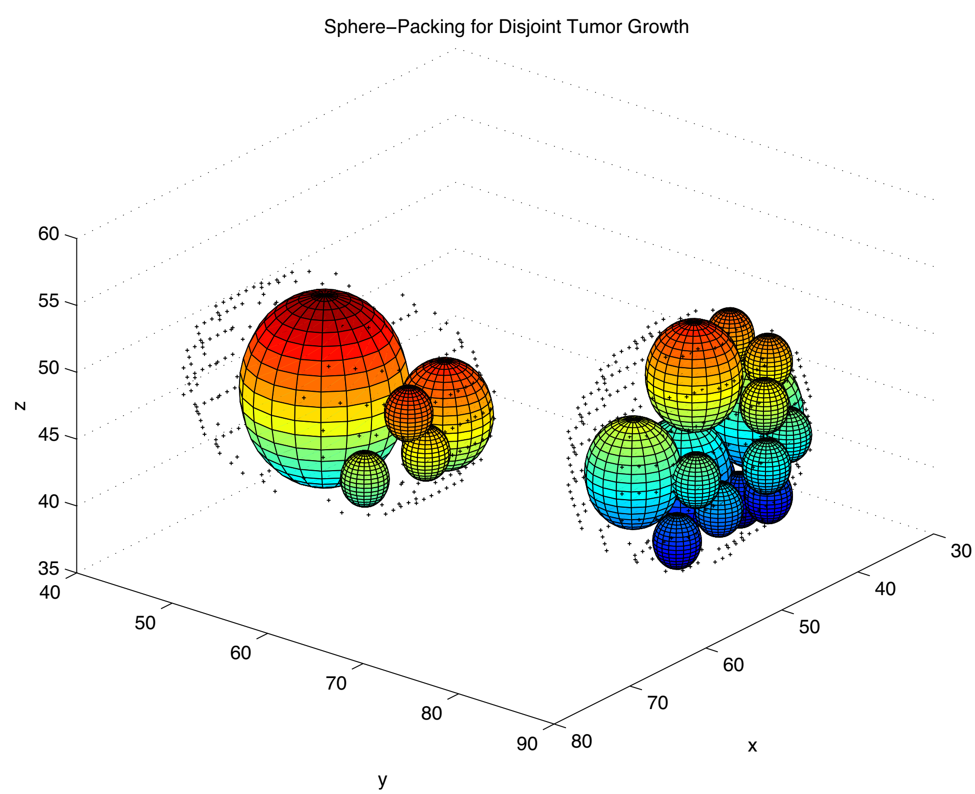

Figure 4. Sphere packing into two disjoint tumors.

Steepest Descent

The minimum and average coverages are significantly better than for first-deepest, and the method is much more consistent. This makes sense, because this method adapts to variations in tumor size and shape rather than using the first available isocenter for each sphere. It is fast compared to the improved steepest descent and adaptive methods.

Improved Steepest Descent

This algorithm is similar to steepest descent, except for the ability to pack spheres closer to edges and other spheres. This method does poorly on average, worse than steepest descent and the adaptive method. But it yields the best coverages—over 50% on four different test cases. Also, this method has the highest deviation of all our methods.

Adaptive Method

The average coverage of approximately 40% is the best of all four algorithms, and this method also has the lowest standard deviation. But it is the slowest and most complicated algorithm.

Conclusions

All of our algorithms have strengths and weaknesses. The first-deepest method is fast, while steepest descent is consistent in coverage. Improved steepest descent yields some of the best results in terms of coverage, while the adaptive algorithm maintains the highest average coverage and smallest standard deviation.

Weaknesses

Prohibition of hot spots and radiating healthy brain tissue prevents our algorithms from covering much of the tumor.

Strengths

Our algorithms can process any possible tumor. They are "patient-friendly"—they don't destroy anything outside of the tumor, nor do they produce spheres that intersect each other. They are also simple and robust.

Future Work

It would be nice to merge the adaptive algorithm with steepest descent to try to build up the coverage.

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