Shoot to Kill!

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Abstract

The goal of the model is to approximate a target volume by spherical doses (or shots) of radiation. The model that we provide satisfies several important constraints.

- The algorithm guarantees that no shot overlaps another; thus "hot spots" are eliminated.
- Each shot must also lie entirely within the target volume (to prevent harm to healthy tissue).
- The final shot arrangement is optimal in the sense that it is impossible to place an additional shot of any size without causing an overlap or breach of the target volume.

The algorithm's strength lies in deciding the best possible location for the placement of the initial shot. The remaining volume of the target area is filled by placing shots tangent to previous shots. The shots are placed in a way that guarantees as many large shots as possible are used before resorting to smaller shots, thereby minimizing the total number of doses. Our model's simplicity easily allows for adaptation when its features need to be modified to enhance its accuracy. The algorithm also is very efficient—even for an exceptionally large tumor, our program is bounded by just several million iterations, making it easily computable with any modern hardware.

We include a working computer program based on our algorithm. The software takes into account the need to protect healthy tissue while treating abnormal tissue. Our program uses digital images similar to those from MRI scans to define accurately the boundary around the target volume. This boundary then serves to prevent the normal tissues from receiving harmful levels of radiation.

We constructed data sets (sample tumors) to test our program. The performance of our algorithm on these data sets provides great confidence in its feasibility and practical effectiveness. In each case, every shot lies within the target volume without overlapping with another shot. The volume coverage had a high degree of success in each case, ranging between 86% and 91%.

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In summary, our model safely allows for strategic gamma knife planning. The algorithm approaches the final shot arrangement from a geometrical perspective. It provides an efficient and effective way of planning the treatment and guarantees that several important criteria are satisfied.

Analysis of the Problem

Our task is to approximate the shape of a target volume (the brain tumor) by spherical doses (shots) of radiation. Several conditions are desirable for this approximation:

- Prohibit shots from protruding outside the target in order to avoid harm to healthy areas of the brain.
- Prohibit shots from overlapping (to avoid hot spots).
- Cover the target volume with effective dosage as much as possible, with at least 90% of the target volume covered.
- Use as few shots as possible. This is to help reduce the total amount of radiation passing through the healthy portion of the brain.

Additionally, the algorithm should be efficient enough to avoid unreasonable waiting times.

We can view the problem of formulating the treatment plan in mathematical terms. The object then is to place the least number of shots in the target volume while filling at least 90% of the volume. From a theoretical perspective, this is a sphere-packing problem; that is, to fill as much of a volume as possible with spheres.

Unfortunately, the problem of packing unequal spheres into a given volume is NP-complete [Wang 1999], making an absolute optimal solution intractable for all but the smallest target volumes. Hence, we find not an optimal solution but a solution that satisfies all the requirements while remaining of reasonable complexity.

Assumptions

- The diagnostic images are acquired from MRI scans; we assume that the resolution is 1 mm $\times$ 1 mm$\times$ 1 mm. (The actual resolution is approximately 1 mm $\times$ 1 mm $\times$ 1.5 mm [Leventon 1998].) We assume that the image can be represented as a three-dimensional array of points such that the set of points in the tumor and the set of healthy points can easily be determined.
- The mean diameters of brain tumors range from 1 mm to 40 mm [New Jersey ... n.d.]. We assume that no tumors larger than 100 mm$\times$100 mm$\times$100 mm need to be considered. At the assumed resolution of 1 mm $\times$ 1 mm $\times$ 1 mm, this gives 10^6 data points, a reasonably small amount of data.

- Each shot volume contains 100% of its potency with no leakage to outside points.
- All shots have uniform radiation density.

The Algorithm

Overall Description

The basic idea is to construct each successive sphere based on the location of previous spheres. For this reason, the choice of the initial shot or shots is very important.

The first shot placed is the largest possible shot that fits inside the target volume. Heuristics and curvature measurements of the target volume can be used to determine the exact location of this shot. For example, the first sphere could be placed tangent to the surface of the target volume in a location in which the curvature of the volume and the sphere are in close correspondence. In general, the first sphere should be placed tangent to the surface of the target volume.

The algorithm then calculates the position of the next shot by determining the location of the largest possible shot tangent to the first one. This is repeated, placing new shots tangent to the first until no more shots of any radius can be placed.

To determine if a shot of given radius and position is possible, it suffices to check each point on the surface of the proposed shot to make sure that it is fully contained in the tumor and intersects no previously placed shot.

After the volume tangent to the first sphere is full, the program begins checking points tangent to the sphere placed second. The largest possible sphere tangent to the second sphere is then placed; this is again repeated until no more spheres can be placed.

This process is continued with each sphere until no more can be placed inside the target volume. The output is a list of the centers and radii of the shots.

Definitions

We are given digital images from the MRI scans, which are converted to three-dimensional arrays of data.

Let the data set D be defined as

$$D = \{p = (x, y, z) \,|\, x \in \{1, 2, \ldots, N_x\}, y \in \{1, 2, \ldots, N_y\}, z \in \{1, 2, \ldots, N_z\}\},$$

where N_x, N_y, and N_z are the resolution (in pixels) of x, y, and z, respectively.

We define a function $\delta : D \to \{0, 1\}$ by

$$\delta(p) = \begin{cases} 1, & \text{if point } p \text{ is part of the tumor;} \\ 0, & \text{otherwise.} \end{cases}$$

Hence, T is the set of points in the tumor denoted by

$$T = \{p \in D \,|\, \delta(p) = 1\}\,.$$

We say that a point $p = (x, y, z)$ borders $p' = (x', y', z')$ if

$$(x, y, z) = (x' + \Delta_1, y' + \Delta_2, z' + \Delta_3),$$

where $\Delta_i \in \{0, 1, -1\}$ for $i = 1, 2, 3$. It is also useful to determine the set of points on the surface of the tumor. We let this set of boundary points B be defined as

$$B = \{p \in D \,|\, \delta(p) = 1 \quad \text{and} \quad \exists p' \in D \text{ such that } \delta(p') = 0 \text{ and } p \text{ borders } p'\}\,.$$

We represent each shot by a set of points on a sphere. Let $S_{p,r}$ denote the surface of a sphere of radius r centered at p, i.e.

$$S_{p,r} = \{p' \,|\, \lfloor \Delta(p', p) \rfloor = r\}\,,$$

where $\Delta(p', p)$ is simply the distance between the two points and $\lfloor \cdot \rfloor$ is the floor function.

There is only a finite set R of possible radii of shots, corresponding to the set of collimator sizes. In this case,

$$R = \{9, 7, 4, 2\}\,.$$

Formal Specification of Algorithm

Input: The set D of data points and the function δ used to determine the target volume. From this, the set of target volume points T is determined, as well as the set of surface points B.

Output: The center and radius of each shot placed by the algorithm.

Notation:

C_i , for $i = 0, 1, 2, \ldots$, is the set representing the ith shot: $C_i = S_{p_i, r_i}$ for some point p_i and radius r_i;

n is the the number of shots placed; and i.e., $n = \max\{i \,|\, C_i \text{ is defined}\}$.

c is the index of the sphere to which new spheres will be placed tangent.

Algorithm:

1. Choose $C_0 = S_{p,r}$ such that $r \in R$ is the maximum possible and $C_0 \subseteq T$. (Details in next subsection.)

2. Let $c = 0$.

3. While $c < n$ do the following:

   (a) for every $r \in R$ (from largest to smallest) do the following:

      i. Let r' and p' be the radius and center of sphere C_c, i.e. $C_c = S_{p',r'}$.

      ii. Construct as many possible spheres $C_k = S_{p,r}$, where $r \in R$, $p \in S_{p',(r+r')}$, such that $C_k \subseteq T$ and $C_k \cap C_i = \emptyset$ for all $i \neq k$. (See details later.)

   (b) Let $c = c + 1$.

Placement of Initial Shot

Near the surface of the target volume is the most difficult area to encompass by doses of the gamma knife—hence, the first shot should be arranged to conform as closely as possible to the contour of the tumor. **Figure 1** gives an example of matching the contour.

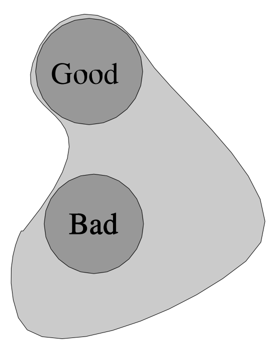

Figure 1. Placement of a good initial shot.

Measuring the curvature of the target volume is straightforward and could be used to fit the initial shot to an ideal position. Alternatively, the doctors could choose the initial position interactively based on their judgment.

A further alternative is the placement of multiple initial shots if the need arises. This could occur if the shape of the target is such that there is an obvious optimal configuration.

One additional method is the use of many runs of the algorithm with a random initial placement. The algorithm requires very little computation time, even with a large tumor size. Many runs could be made, after which the best configuration is selected. This method is also easily parallelized, allowing for a very large number of trials.

Placement of Tangent Shots

The placement of each shot following the initial sphere continues in a similar manner. The volume should be placed in contact with as many tangent points as possible in order to minimize lost volume. More specifically, choose the new $C_k = S_{p,r}$ to maximize the number of tangent points

$$t = \left| \left\{ q \in \bigcup_{i=1}^{n} C_i \bigcup B \mid q \text{ borders some element } q' \in C_k \right\} \right|.$$

Other methods may be employed, including random placement and multiple runs (similar to those mentioned above). The number of shots placed is proportional to the size of the tumor.

Analysis of Model

Worst Case Analysis

We establish a bound on the total number of points that must be checked by our algorithm. We assume a resolution of 1 mm $\times$ 1 mm $\times$ 1 mm.

For each shot S_{p_2,r_2} placed tangent to S_{p_1,r_1}, at most all of the points on the sphere $S_{p_2,(r_1+r_2)}$ must be examined. To confirm placement of the sphere S_{p_2,r_2}, each point on its surface must be checked for penetration of the boundary or intersection with other shots. We can estimate the number of points on the surface of a digitally represented sphere by its area (in mm^2). If all possible radii must be checked when placing the new sphere, then the placement requires

$$P_2 \leq \sum_{i=1}^{|R|} A(S_{p_2,r_i}) A(S_{p_2,(r_1+r_i)})$$

examinations of points, where $A(S)$ is the area of sphere S in mm^2 (rounded up to nearest integer), and $|R|$ is the number of possible radii.

We are given that the target volume is usually filled by fewer than 15 shots. Hence, we assume that 30 shots is a reasonable bound. Since 9 mm is the maximum radius and $|R| = 4$, the total number of checks necessary after placement of the initial sphere is

$$P \leq 30 P_2 \leq 30 \left(4 A(S_{p_2,9}) A(S_{p_2,(9+9)})\right) = 30(4)(4\pi)(9^2 18^2) < 4 \times 10^7.$$

The number of checks required to place the initial sphere is assumed to be negligible, as it is bounded by the resolution of the digital image. The 4×10^7 data point examinations is also trivial for modern computers. Hence, our algorithm, even in the worst case, requires minimal computing time.

Other Strengths

- By design, this model conforms to the constraints of gamma knife treatments. That is, the model prohibits shots from protruding outside the target volume, while avoiding overlapping shots within the target volume. By placing as many shots of large radii as possible before placing smaller shots, the algorithm guarantees a minimal number of shots. In a sample implementation, our algorithm shows a coverage of nearly 90%.
- The main strength of our model is its simplicity and realistic application.
- In the model, the tumor image is transformed to a set of points, where each point represents a pixel from the MRI image. We address the boundary set to position our initial shot. The algorithm places each successive shot along contours of the target volume.
- In the final shot arrangement determined by the algorithm, overlapping shots are prohibited.
- While the shot configuration is not guaranteed to be optimal, the configuration is optimal in the sense that no shots can be added to the final configuration without overlap.
- While we assumed 0% shot gradient, our model's design addresses this issue by allowing for different shot gradients to be added easily. In short, the model can be adjusted continuously for different shot gradients at each iteration.

Limitations

- The final shot arrangement is not guaranteed to be absolutely optimal.
- A nonuniform dosage within each shot is not accounted for; however, if information is known, our program should be adapted accordingly.
- The algorithm considers only the local configuration of shots rather than the entire volume of the tumor. However, by examining only the volume tangent to a given sphere, the complexity is reduced dramatically. In practice, this limitation should affect only exceptional target volume shapes.

A Sample 2D Implementation

We create a working implementation of our algorithm in two dimensions to test its effectiveness.

The input is shown on the left in **Figure 2** as a black-and-white image describing the shape of the target volume. This image can be thought of as a two-dimensional analog of an MRI image and is assumed to have approximately the same resolution (1 mm $\times$ 1 mm). The output of the algorithm is shown on the right in **Figure 2**, with each circle representing a shot. (Any visible overlapping of shots is only a result of roundoff error in scaling the image.)

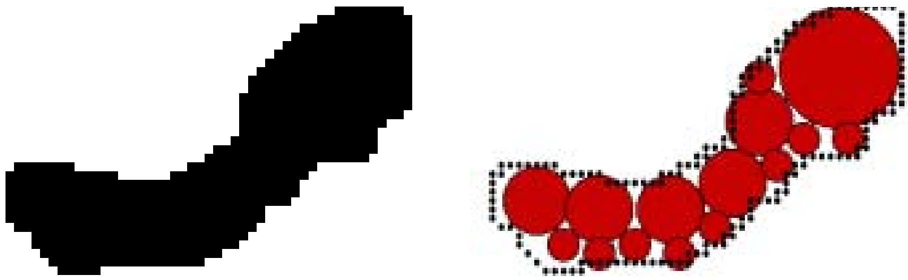

Figure 2. Sample target area and placement of 15 shots.

For a different sample area, **Figure 3** illustrates the order in which our algorithm places the shots.

The shot placement algorithm is implemented as stated but no optimizations are made in the selection process. That is, the shots are chosen by searching systematically for a satisfactory point. Nevertheless, the outcomes are successful. Over 21 samples, the minimum volume percentage achieved was 87%, the mean was 89%, and the maximum was 91%.

Although the example is only for two dimensions, the procedure is essentially the same for three—in fact, in actual implementation only the array used to represent the tumor and the definition of a sphere need to be changed.

Conclusion

The gamma knife procedure is a highly tested and extremely effective treatment for a variety of brain abnormalities. Our model works to improve the placement of the shots; we believe that with the inclusion of our model, the treatment's efficiency will increase greatly.

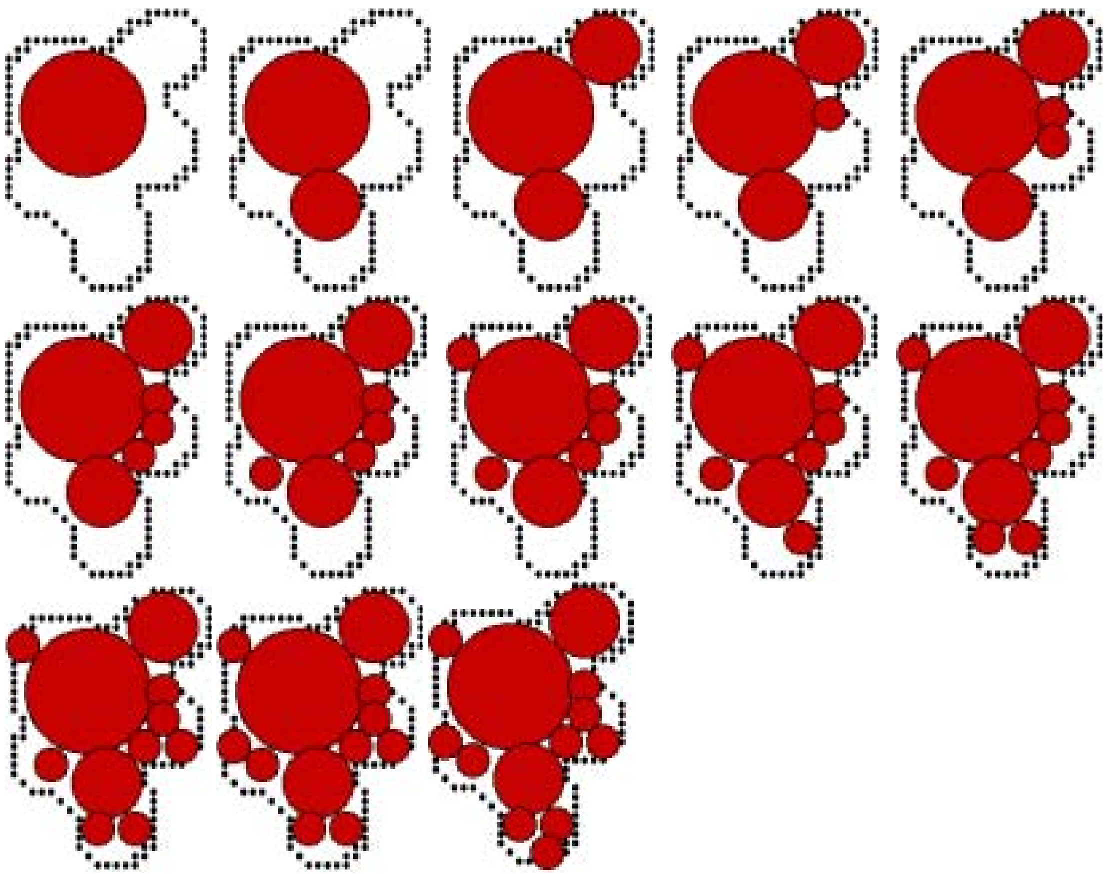

Figure 3. Sample shot sequence (13 shots).

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Receiving the MAA Award at MathFest 2003 in Boulder, Colorado: Team advisor Angela Spalsbury with the team members, who are all now graduate students: Sarah Grove (applied mathematics, North Carolina State). Joel Lepak (mathematics, Michigan), Chris Jones (mathematics, Pittsburgh). (Photo courtesy of J. Douglas Faires.).