Optimizing Gamma Knife Radiosurgery Through Mathematical Morphology

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Abstract

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Abstract: In gamma knife radiosurgery, a large helmet is affixed to the patient's head, and 201 cobalt-60 sources within the helmet are focused at a given point within the skull in order to destroy tumor tissue. Planning a gamma knife treatment is a nontrivial process. Normal tissue outside the tumor must only receive a small fraction of the radiation, or, ideally, none at all. Shots should not overlap, and levels of radiation across the volume should be as even as possible. Finally, at least 90% of the target volume must be covered, and this must be done using as few shots as possible.

The treatment planning problem was described using a mathematical model, and algorithms were designed to plan and optimize treatments. Possible shot isocenters were identified using three-dimensional skeletonization and skeletal projection analysis. Algorithms were designed to build these into a set of possible treatments and to choose the one determined to be the most optimal, subject to limitations imposed by the equipment and the nature of the treatment. Through the use of surface fitting software, a formula was derived for selecting the most optimal treatment from the subset of all treatments affecting at least 90% of the target volume.

Optimizing Gamma Knife Radiosurgery Through Mathematical Morphology

Introduction

In gamma knife treatments, a large helmet is affixed to the patient's head, and 201 cobalt-60 sources within the helmet are focused at a given point within the skull in order to destroy tumor tissue. The sources emit beams of radiation that are 4, 8, 14, or 18mm in diameter, eliminating an approximately spherical area of the target volume. This process is usually repeated, possibly with beams of different diameters, until as much of the target volume as possible has been treated. Each iteration is referred to as a *shot*, and the target point is termed the *isocenter* of the treatment.

Planning a gamma knife treatment is a nontrivial process. Normal tissue outside the tumor must only receive a small fraction of the radiation, or, ideally, none at all. Shots should not overlap, since this would deliver an unnecessarily high dose of radiation to one area of the tumor. Levels of radiation across this volume should be as even as possible, eliminating the possibility of having sections of extreme radiation and others receiving almost no radiation. Finally, at least 90% of the target volume must be covered, and this must be done using as few shots as possible.

The gamma knife treatment problem can be restated as a sphere-packing problem: given a (possibly irregularly-shaped) volume, how can spheres of diameters 4, 8, 14, and 18 mm be arranged such that at least 90% of the volume is occupied, no spheres overlap, and no spheres protrude outside the target volume? Unfortunately, the "standard" sphere-packing solutions consider spheres of uniform size, often within a regularly-shaped volume. The gamma knife problem requires a more complicated solution.

Mathematical Morphology and Skeletonization

Mathematical morphology is a key component of computer vision, handwriting recognition, and many other areas of image processing; informally, it is the study of techniques used for the extraction of information from images (*Mathematical*). One important morphological operator is that of skeletonization, which reduces an image to a thin set of points that preserve its overall shape (*Skeletonization*). Figure 1 (displayed following page 1) shows several simple images and their skeletons (images from http://www.dai.ed.ac.uk/HIPR2/skeleton.htm). Although the implementation of skeletonization is fairly difficult, particularly in three dimensions, the concept is fairly simple and is the basis of our solution to the gamma knife problem.

Methodology

The solution presented is based on one designed by Wu and Bourland (Wu 2153-9). The tumor must first be modeled in three dimensions, either through direct three-dimensional input from radiographic imaging devices or from the composition of two-dimensional images of the sagittal, coronal, and transverse planes (identified in Figure 2, following page 1). The physician may, at his or her discretion, limit the treatment area to only a portion of the tumor; in this case, the area not to be treated should be removed from the model. Internally, the computer stores the three-dimensional model as a set of voxels, analogous to storing a two-dimensional image as a set of pixels. (It is assumed that the model is stored at a resolution of, minimally, several voxels per millimeter.)

First, the computer determines “critical points” in the model, identifying these as possible shot locations. This is done as follows. The model is first skeletonized (in three dimensions) using an algorithm such as one recently developed by Shahrokni, Soltanian-Zadeh, and Zoroofi.

The (two-dimensional) sagittal, coronal, and transverse projections of the skeleton are then analyzed separately. In each projection, voxels with 0, 1, and 3 or more coplanar adjacent voxels are identified as isolated voxels, endpoints, and crosspoints, respectively, all of which are considered to be critical points. In one exceptional case (a spherical model after one reduction, described below), the skeleton may form a circle in all three projections, and no critical points will be found via the aforementioned criteria. In this case, a random skeletal point is chosen to be critical.

After critical points are identified, the computer determines whether a shot of each size (4, 8, 14, and 18 mm) would "fit" (i.e. not extend outside the model) at each critical point. For each shot that fits, the skeletonization/shot procedure is repeated on the same model with the sphere representing the shot removed. If a shot fits in this reduced model, another sphere is removed, and the procedure repeats for this further-reduced model. The procedure continues until the model is so small that no shots fit. Through the use of recursion, this procedure generates a set of treatments based on different combinations of shot sizes and critical points.

An optimal treatment must then be selected from the set of possible treatments. We consider only those treatments that affect 90% or more of the original model. For each treatment *T*, we calculate a value

$$\frac{0.7717657102 - 0.04046790807T_n + 0.2693164541T_p}{1 - 0.1580097209\ln(T_n) - 9.032235582\ln(T_p)} \tag{1}$$

where T_p is a decimal representing the percentage of the model affected by the treatment and T_n is the number of shots in the treatment. Our first instinct was to maximize the ratio T_p/T_n, that is, determine which treatment gives the greatest amount of coverage per shot. However, consider the case where there are three options: 10 shots covering 90% of the initial volume, 15 covering 91%, and 12 covering 95%. Obviously the second case is not ideal, but it is very likely that a doctor would recommend 12 shots instead of 10 in order to gain the extra 5% coverage. In other words, the ratio needs to reflect a preference for an increase in coverage even if it is not directly proportional to the increase in the number of shots. We devised several hypothetical sets of treatments and assigned a “preference value” to each treatment: 0.0 for unacceptable, 1.0 for ideal, and several discrete values in between for various intermediate levels of acceptability. (Please bear in mind that we are not physicians; others more knowledgeable about the treatment process and the individual cases being considered may not agree with our preferences.) Through the use of surface fitting software, we derived ratio (1) as being representative of our treatment preferences. Thus, our algorithm reflects this ratio; we select as optimal the treatment that maximizes it. (A graph of (1) is shown in Figure 3, following page 1.)

Variables, Assumptions, and Hypotheses

Before we present our algorithms in detail, we present, for reference, a table of all variables.

Symbol	Unit	Definition
c		Isocenter vector of a Shot
C		Set of critical voxels in skeleton
(c,s)		Ordered pair describing a shot
I		Set of Shots
M		Set of voxels that comprise a 3-dimensional Model
n_{opt}		Number of shots in optimal Treatment
P		Set of all possible Treatments
p_{opt}		Percentage of target volume affected by optimal Treatment
Q		Candidate set, i.e., set of Treatments that affect at least 90% of the original volume
r	mm	Radius of a sphere
s	mm	Beam diameter
S		A set of voxels approximating a sphere
T		A Treatment or set of Treatments (depending on context)
T_n		Number of shots in a Treatment T
T_{opt}		Optimal Treatment
T_p		A decimal representing the percentage of target volume affected by a Treatment T
V		Set of voxels that comprise the skeleton
v		A voxel within the skeleton V
V'		Planar projection of V (sagittal, coronal, or transverse)
V_M	mm^3	Volume of Model M

Our solution assumes that (1) a three-dimensional computer representation of a tumor is an accurate representation of the actual tumor, (2) shots are perfectly spherical, or the overlap of radiation from the use of non-spherical shots is negligible, and (3) the case is not exceptional. Exceptional cases would exhibit an unusually high preference for a small number of shots or for a maximal coverage of the area. In this case, the optimization procedure would need to be modified to fit that specific case.

We hypothesize that isolated, cross- and endpoints on a skeleton of the tumor will provide optimal shot isocenters. We also hypothesize that maximizing (1) is an effective method of choosing an optimal solution from a set.

Algorithms

Let *M* denote the 3-dimensional model (i.e., a set of voxels). Let *P* denote the set of all possible Treatments, where a Treatment is a set of Shots. A Shot is an ordered pair (*c,s*) where *c* is the isocenter vector of the shot and *s* is the beam diameter (4, 8, 14, or 18 millimeters). (The beam diameter is generally understood to encompass all area up to the 50% isodose line (IDL) (Wu 2152).)

First, we present a utility algorithm that builds a set of possible Treatments for a given Model. Pseudocode for this algorithm is given following page 1. Two parameters are passed to it: the model *M* and a set of Shots, *I*. The algorithm is recursive; in the initial call, *I* is equal to the empty set. The Model is analyzed and possible Shots are determined. For each possible Shot, the sphere affected by that Shot is removed from the Model, and the procedure recurses for the reduced Model. In the recursive case, *I* equals the set of Shots that, when subtracted from the original Model, produced the one passed as an argument. The recursion stops when the remaining bits of tissue (if any) are too small to be removed by additional Shots; in this case, *I* constitutes an entire Treatment.

Next, we present our primary algorithm, which accepts a Model of the volume to be treated and returns a Treatment (i.e., a set of Shots) determined to be optimal for that model. (Again, pseudocode is given following page 1.) It begins by calling the `Build_Treatments` procedure described previously, storing the set *P* of all possible Treatments. It then determines the number of shots in each Treatment and the percentage of the original model affected by each Treatment. Treatments affecting at least 90% of the original volume are stored (along with the number of shots and affected percentage) in a set *Q* of candidates for optimization. As described previously, the Treatment *T* in *Q* that maximizes (1) is selected as the optimal Treatment.

As given above, these algorithms expect the availability of three other procedures: `Volume(M)`, `Sphere(c,r)` and `Skeletonize(M)`. The first simply returns a numerical representation of the volume of a model *M*. Since a Model is simply a set of voxels, this may be either the order of the set or a real-world volume (e.g. a measurement is μm^3). The second is expected to return a set of voxels approximating a sphere with center *c* and radius *r*, i.e., a Model of a sphere. The third should return the set of voxels forming the three-dimensional skeleton of *M*. We will not describe these algorithms in detail, as the first is implementation-dependent and the latter two are very complicated. Fortunately, implementations of sphere-generation and skeletonization algorithms are widely discussed in computer graphics and mathematical morphology literature, respectively. For the skeletonization procedure, we recommend an algorithm developed by Shahrokni, Soltanian-Zadeh, and Zoroofi, which is based on the work of Zhou and Toga. Three-dimensional skeletonization is still an active area of research, and this is, to the best of our knowledge, the fastest such algorithm presently known.

Effectiveness Analysis

Through our 90% coverage requirement and skeletal preferences for corners, edges, and other areas of the target volume that might otherwise be ignored, radiation doses will be approximately uniform throughout the target volume. Towards the edges of shots, the overlapping of slight rings of falloff radiation further minimizes the variance in shot dosage.

The skeletal preference for edges further guarantees that the solution is fit to the target volume rather than the volume being fit to a known solution. Since tumors are generally not perfect cubes or spheres, it is absolutely critical that a solution adapt to any shape, no matter how irregular it is. Skeletonization allows our solution to do this. Furthermore, a center-working-outward approach would be much more likely to leave many bits of tissue around the edges untreated. It is preferable for untreated tissue to be confined to a single small area, such as at the center of the original tumor, since this provides for easier elimination should a second treatment be required. This is also accomplished through the use of skeletonization, thanks again to its preference for edges and corners.

Our algorithm does not even consider treatments where shots overlap or extend outside into normal tissue outside the target. This simultaneously prevents “hot spots” (points of excessive radiation) and guarantees that normal tissue will receive only miniscule amounts of falloff radiation. The dose of radiation at the edge of a shot is 50% of that in at the isocenter, and, because of the rapidity of falloff, the radiation received immediately outside a shot is virtually zero (Wu 2152).

Finally, our algorithm selects what we believe to be an effective compromise between number of shots and area covered. The returned treatment is guaranteed to cover at least 90% of the target volume. From all plans that meet the 90% requirement, the maximization of (1) minimizes, within reason, the number of shots while simultaneously maximizing the coverage volume.

Unfortunately, no model and no solution come without limitations. Although we treat shots as spheres, in practice, their shape is slightly distorted (Wu 2152). Additionally, although falloff is quite rapid, tiny doses of radiation do extend beyond the spheres targeted. Although the falloff area is, again, very small, it is still possible for very small volumes between shots to receive, cumulatively, an effective dose of radiation, even if the model indicates that they receive no radiation at all. Finally, while not really a deficiency, our choice of (1) as an optimization formula is based on our opinion of what is desirable in a treatment; this is simply a suggestion and will vary between physicians and among individual cases.

Further Study

Given appropriate resources, the given solution could be simulated entirely on computer with "tumors" of randomly-generated shape and size. However, a better analysis would be to input models of actual tumors and compare the computer's recommendation to that of experienced professionals. Alternately, experienced professionals could choose their own optimal treatment from the candidate set (Q); with the addition of artificial intelligence, the computer could, over time, learn the preferences of the associated physician(s) and begin to select as optimal the treatment most like the ones the same physician previously selected as optimal.

Conclusion

We have presented a model and associated algorithms for determining, in a reasonable, finite amount of time, an optimal gamma knife treatment for a given target volume, based primarily on the morphological concept of skeletonization. The given solution meets all the requirements of a successful treatment while working within the limitations imposed by radiosurgery and the equipment involved.

Figures

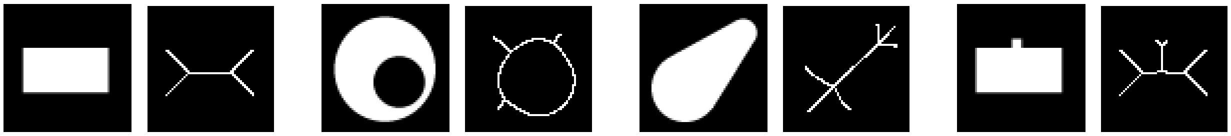

Figure 1: Examples of Skeletonization

http://www.dai.ed.ac.uk/HIPR2/skeleton.htm

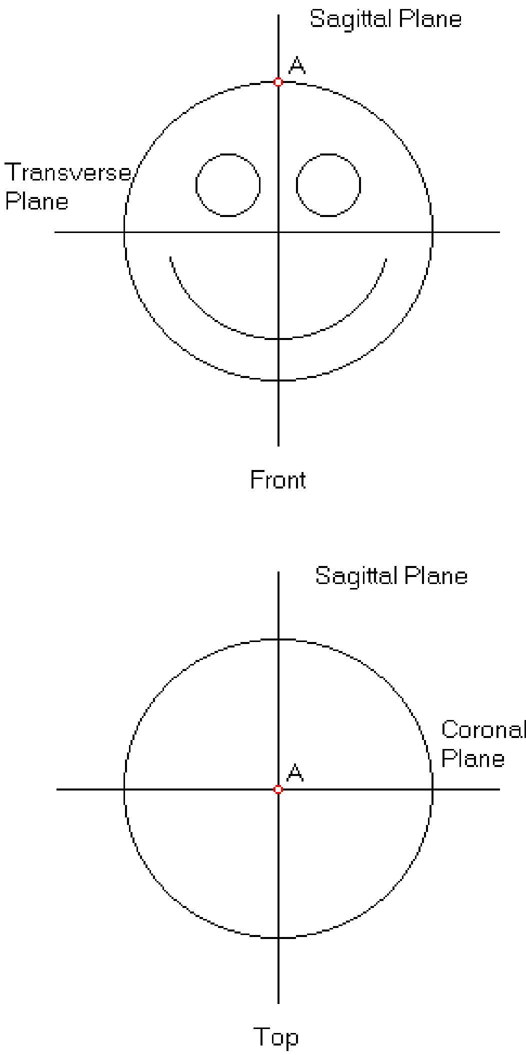

Figure 2: Planes of Section

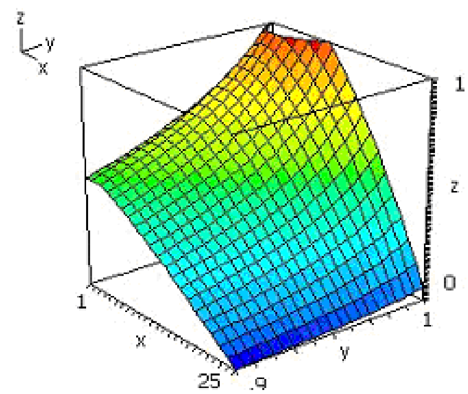

Figure 3

$$z = \frac{0.7717657102 - 0.04046790807x + 0.2693164541y}{1 - 0.1580097209 \ln x - 9.032235582 \ln y}$$

Algorithm 1: Build_Treatments

```
// Procedure: Build_Treatments(M, I)
// Inputs:
//    M, a Model of a target region (tumor or portion thereof)
//    I, the set of Shots that, when subtracted from the original Model,
//       formed this Model (empty set on initial call; set on recursion)
// Returns: P, a set of possible Treatments for the given Model

Procedure Build_Treatments(M, I)

   P := {}                     // P: Set of Treatments for this Model
   V := Skeletonize(M)         // V: Set of voxels of the skeleton
   C := {}                     // C: Set of critical voxels in skeleton

   // Collect isolated, endpoint, and crosspoint voxels as critical voxels
   For each v in V
      For each planar projection V’ of V in {sagittal, coronal, transverse}
         If there are 0 voxels adjacent to v in V’
            Or if there is 1 voxel adjacent to v in V’
            Or if there are ≥3 voxels adjacent to v in V’
            C := C ∪ {v}       // v is critical
         End If
      Next V’
   Next v

   // If there are no critical voxels, we are in an exceptional case
   // (a sphere after one reduction).  Select a random voxel as critical.
   If C = {} Then C := { One Randomly-chosen Element from V }

   // Try all four shot sizes at each critical voxel
   Did_Recurse := False
   For each c in C
      For each s in {4, 8, 14, 18}        // For each shot size s
         S := Sphere(c, s/2)              // S: A sphere with radius s/2
                                          //    S is also a set of voxels
         If S – (S ∩ M) = {} Then         // Shot won’t extend beyond model
            // Recurse with this Shot removed from the model
            Did_Recurse := True
            P := P ∪ Skeletonize(
                        M – (Sphere at c with radius s/2),
                        I ∪ {(c,s)})
         End If
      Next s
   Next c

   // If we did not successfully recurse for any “critical” voxel,
   // we are at our base case; I constitutes an entire Treatment.
   If Not Did_Recurse Then
      P := P ∪ {I}
   End If

   Return P

End Procedure
```

Algorithm 2: Select_Optimal_Treatment

```
// Procedure: Select_Optimal_Treatment(M)
// Inputs:
//    M, a model of a target region (tumor or portion thereof)
// Returns: The optimal treatment T or Null if a suitable Treatment
//    could not be found

Procedure Select_Optimal_Treatment(M)

   // Store the volume of the original Model
   v_M := Volume(M)

   // Determine all Treatments for this Model
   P := Build_Treatments(M, {})

   // For each Treatment, determine the number of Shots and
   // percentage of Model affected and add to Q iff the Treatment
   // affects 90% or more of the volume of the original Model
   Q := {}                    // Set of ordered triples (T,n,p)
                              // where T is a Treatment, n is the
                              // number of shots, and p is the
                              // percentage of the tumor affected
                              // by the Treatment
   For each T in P
      n := 0                  // Number of Shots for this Treatment
      v := 0                  // Volume affected by all Shots in T
      For each (c,s) in T
         n := n + 1
         v := v + Volume(Sphere(c, s/2))  // Volume affected by Shot
      Next T
      If v/v_M ≥ 0.9 Then Q := Q ∪ {(T, n, v/v_M)}
   Next T

   // Be sure that at least one Treatment worked
   If Q = {} Then Return Null

   // Using the elements in Q, determine which Treatment has the greatest
   // modified-affected-volume-per-shot and select that as being optimal
   T_opt := Null
   n_opt := 999
   p_opt := 0
   For each (T,n,p) in Q
      If (0.7717657102-0.04046790807*n+0.2693164541*p)/
         (1-0.1580097209*ln(n)-9.032235582*ln(p)) >
         (0.7717657102-0.04046790807* n_opt +0.2693164541*p_opt)/
         (1-0.1580097209*ln(n_opt)-9.032235582*ln(p_opt)) Then
         T_opt := T
         p_opt := p
         n_opt := n
      End If
   Next (T,n,p)

   Return T_opt

End Procedure
```

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