Pruning Radiotherapy Treatment Plans

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Faculty Development Proposal, Summer 2003
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Overview

Over the last few years, radiation oncologists and medical physicists have included mathematical programmers in their research groups. The reason for this is that today's technology is capable of treating patients in an extremely complicated manner, and designing treatment procedures that take optimal advantage of the new technology is beyond the scope of human consciousness. Since mathematical programmers have the required skills to model and optimize the design process, they have been actively sought to help design sophisticated treatment procedures.

The problem addressed in this proposal is that of Intensity Modulated Radiotherapy Treatment (IMRT) design. IMRT is the treatment of cancerous tissues with beams of radiation, and IMRT design is the process of selecting how the beams of radiation will travel through a patient. The basic idea is to select a collection of beams that deposit a sufficient amount of radiation into the cancerous tissue, and at the same time, spare any critical structures, like the liver, heart, lung, etc..., from receiving a detrimental amount of radiation. To illustrate the complexity of the design process, we note that a small optimization model has over $10,000$ variables, and deciding a value for each of these variables surpasses a human's capabilities. So, asking a single person to **optimize** a treatment procedure is preposterous.

Fortunately, mathematical programmers have been able to develop optimization models and clever solution procedures that aid IMRT design. The best news is that some of the mathematical advances are starting to appear in planning software. Rarely does the academic literature have such an immediate impact on peoples lives, and this transcending of information demonstrates the importance of these mathematical results.

The investigator of this proposal has been working on IMRT design for the last four years, and over this time he has singly authored three papers on the subject [**?**, **?**, **?**] ([**?**] is to appear in *Health Care and Management Science*, vol. 6, 2003, and [**?**] is to appear in the *Handbook of Operations Research/Management Science Applications in Health Care*). The paper *Designing Radiotherapy Plans with Elastic Constraints and Interior Point Methods* was awarded the 2000 William B. Pierskalla prize, which annually recognizes the best optimization paper addressing the health care profession. Moreover, the investigator is going to guest edit a special edition of *Optimization and Engineering* on IMRT design. The investigator also administers the *Operations Research & Radiation Oncology* web site, which contains a database of researchers and a depository of

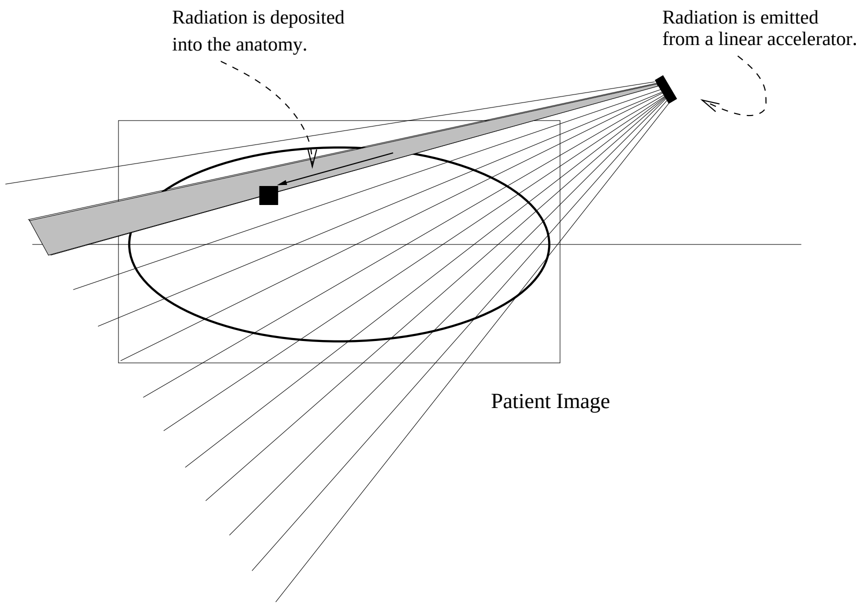

Figure 1: The 2-dimensional geometry of treating a patient

technical reports. Support of this proposal will help continue the investigators involvement in this area and will bring further recognition to Trinity.

Project Details

Optimization models are appropriate for IMRT design because of the way radiation is deposited into the anatomy. Consider Figure 1, where several beams of radiation are being emitted through a patient image. This figure depicts how the beams from a single angle radiate as they travel through a patient. The amount of radiation that is transmitted along each of these beams can be controlled, and the design problem is to find the amount of radiation to transmit along each of these beams so that the radiation is focused on the cancerous tissue and not on the healthy tissue. The diagram only depicts a single angle, but typically there is an angle for each degree, and each of these angles contains a minimum of 32 beams (this amounts to $360 \times 32 = 11,520$ beams).

Medical physicists have experimentally discovered that the process of taking radiation from a linear accelerator and depositing it into the anatomy is linear. The linearity is important because if we allow x_i to be the amount of radiation that is transmitted along beam i (these are the decision variables that we want to find), then there are matrices A_T, A_C, and A_N such that

$A_T x$ is the radiation deposited into the tumor,
$A_C x$ is the radiation deposited into the critical structures, and
$A_N x$ is the radiation deposited into the normal, healthy tissue.

So, the vector x contains the amount of radiation for each beam as it leaves the linear accelerator, and the products $A_T x$, $A_C x$, and $A_N x$ contain the amounts of radiation that are deposited into the anatomy —i.e. the physical process of depositing radiation into the anatomy is mathematically represented by the products $A_T x$, $A_C x$, and $A_N x$.

The linearity is important to mathematical programmers because it means that the design problem is a linear program, and there are extremely efficient algorithms to solve this type of problem. We briefly describe the linear program developed in [**?**]. An oncologist provides a *prescription* that bounds the amount of radiation received by the tumor, the critical structures, and the normal, healthy tissue. These bounds are represented by

- TUB - a vector of upper bounds for the tumor,
- TLB - a vector of lower bounds for the tumor,
- CUB - a vector of upper bounds for the the critical structures, and
- NUB - a vector of upper bounds for the normal, healthy tissue.

These vectors represent the desires of the oncologist. For example, the oncologist is asking that the tumor receives at least TLB units of radiation and no more than TUB units of radiation. Since $A_T x$ is the amount of radiation deposited into the tumor, the mathematical inequality that represents this desire is $TLB \leq A_T x \leq TUB$ —i.e. find the amount of radiation to transmit along each beam (find x) such that the tumor receives an adequate amount of radiation. Similarly, we do not want any critical structure to receive more than CUB units of radiation. The inequality describing this desire is $A_C x \leq CUB$. In a like fashion, we have for the normal, healthy tissue that $A_N x \leq NUB$. So to satisfy the oncologist's desires, we need to find a treatment plan x that satisfies

$$TLB \leq A_T x \leq TUB, \ \ A_C x \leq CUB, \text{ and } \ A_N x \leq NUB.$$

Unfortunately, the oncologist's desires are often overly stringent, and there is no way to simultaneously satisfy these inequalities. The optimization model in [**?**] uses these inequalities to minimize the amount that the cancerous tissue is under its prescribed dose and minimize the amount that the critical and normal tissues are over their prescribed limits.

This optimization model has been implemented in the academic software $\mathcal{R}$adiotherapy optim$\mathcal{A}$l $\mathcal{D}$esign ($\mathcal{RAD}$), and this software makes it easy for a physician to highlight regions and form a prescription. Figures 2 through 5 illustrate two examples, with Figures 2 and 4 depicting both the geometry of the problem and the oncologist's desires. Figures 3 and 5 show how the beams of radiation travel through the image. The red regions are the ones that receive the highest amounts of radiation. Notice that these regions cover the tumor and do not intersect the critical structures. This indicates that the tumor is receiving a high dose and that the critical structures are not. A similar behavior is shown in Figure 5, although in this case the highest amount of radiation is between the two critical structures near the bottom of the diagram. Unfortunately, this region must receive a high dose to adequately treat the tumor.

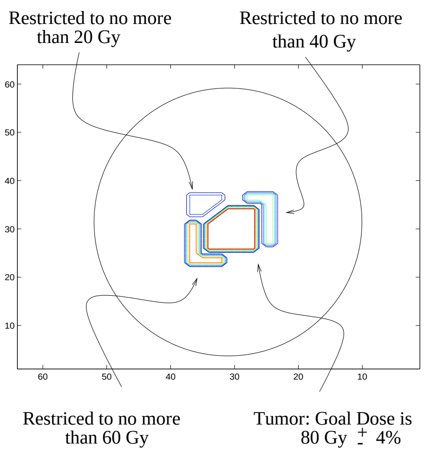

Figure 2: A tumor surrounded by three critical structures.

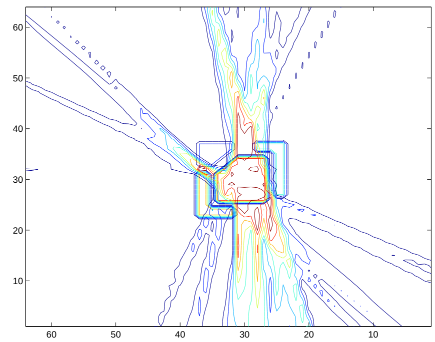

Figure 3: An illustration of an optimal treatment plan.

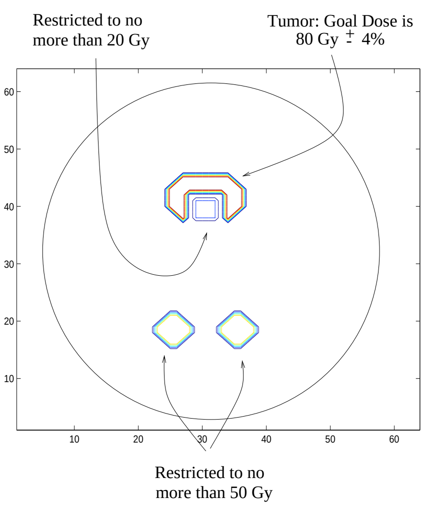

Figure 4: A tumor that has grown around a critical structure.

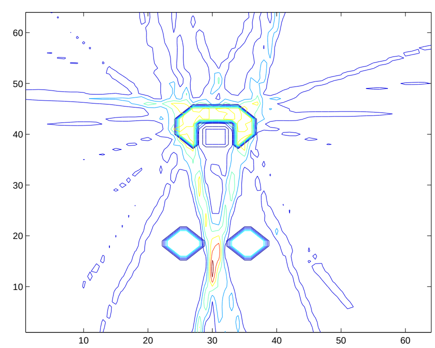

Figure 5: An illustration of an optimal treatment plan.

These treatment plans are optimal in the sense that there are no other plans that deliver less radiation to the critical structures and a sufficient amount of radiation to the cancerous tissue. A key observation about these plans is that they use several beams, and in fact, these treatment plans use so many beams that it is not possible to treat a patient with either of them. The problem is that the time needed to move the linear accelerator from angle to angle is non-trivial, and a normal treatment lasts only about 15 minutes. To be treated with one of these plans would take several hours. Because of the 15 minute time restriction, the vast majority of plans designed in a clinic have no more than 5 to 7 beams. However, the optimization routines typically design plans with hundreds of beams. Treatment plans designed by an optimization routine are desirable because they take advantage of the advanced technology in a way that a human can not perceive, but because it is not possible to implement these plans, clinicians often disregard optimal plans. This leads to the principal research question of this proposal.

Research Question: Is it possible to prune a treatment plan that was designed with an optimization routine to one that is implementable. Moreover, is it possible to do this pruning so that the advantages of the optimal plan are retained in the pruned plan?

As an example of the type of mathematical results that we hope to obtain, one of our goals is to identify the beams that are not used in any optimal plan (note that there may be several alternative optimal plans). This is a significant mathematical problem. There is also some exciting new work being done with Bergman projections by Censor and Herman (not yet published), and it appears that we may be able to use these operators to identify a collection of beams to prune. None of these research questions have been addressed, and they are important to answer if the state-of-the-art academic work is going to translate into realistic advantages for cancer patients.