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Multiple Objective Linear Programming in Radiotherapy Treatment Planning

A thesis submitted in partial fulfilment of the requirements

for the degree of Doctor of Philosophy

Lizhen Shao

Supervised by Assoc. Prof. Matthias Ehrgott

and Prof. David Ryan

Department of Engineering Science

School of Engineering

The University of Auckland

New Zealand

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Abstract

The aim of intensity modulated radiation therapy (IMRT) is to kill tumor cells while at the same time protecting the surrounding tissue and organs from the damaging effect of radiation. To achieve these goals computerized inverse planning systems are used. Given the number of beams and beam directions, beam intensity profiles that yield the best dose distribution under consideration of clinical and physical constraints are calculated. This is called beam intensity optimization problem.

In this thesis, we first review existing mathematical models and computation methods for the beam intensity optimization problem. Next, we formulate the beam intensity optimization problem as a multiobjective linear programme (MOLP) with three objectives. For clinical cases this optimization problem involves thousands of variables and tens of thousands of constraints and existing methods such as multiobjective simplex methods can not handle it. The rest of the thesis is dedicated to developing methods to solve this large MOLP efficiently and to the application in the beam intensity optimization problem.

Benson (1998c) argues that solving an MOLP in objective space needs less computation time than solving it in decision space if the number of objectives of the MOLP is much smaller than the number of variables. Moreover, the constraint matrix of the problem relies on the calculation of dose deposited in tissue. Since this calculation is always imprecise solving the MOLP exactly is not necessary in practice. This motivates us to develop algorithms for solving an MOLP in objective space approximately.

We summarize Benson's outer approximation algorithm for solving MOLPs in objective space and propose some small changes to improve computational per-

formance. Then in order to approximate the true nondominated set we propose a modification of Benson's algorithm which is called an approximation version of Benson's algorithm. Our approximation algorithm computes an inner and an outer approximation of the nondominated set. We prove that the inner approximation provides a set of ε-nondominated points.

The geometric duality theory of Heyde and Löhne (2006) defines a dual to an MOLP and it assures us to be able to find the nondominated set of the primal MOLP by solving its dual MOLP. Based on this we develop a dual variant of Benson's outer approximation algorithm to solve the dual MOLP in objective space. We prove that solving the dual provides a weight set decomposition. We compare the primal algorithm and the dual algorithm on small illustrative and on radiotherapy examples. Furthermore, we propose an algorithm to solve the dual MOLP approximately but within specified tolerance. This approximate solution set can be used to calculate an approximation of the nondominated set of the primal MOLP. We show that this set is an ε-nondominated set of the original primal MOLP and provide numerical evidence that this approach can be faster than solving the primal MOLP approximately.

Considering that the set of nondominated points is infinite, it is not very useful from the planners' point of view. We address the problem of finding well distributed nondominated points for an MOLP. We propose a method which combines the global shooting and normal boundary intersection methods. By doing so, we overcome the limitation of normal boundary intersection method that parts of the nondominated set may be missed. Discrepancy analysis of the nondominated points from a geometry point of view shows that this method produces evenly distributed nondominated points. Moreover, the coverage error and the uniformity level can be measured.

Finally, we apply the algorithms developed to the beam intensity optimization problem of 3D clinical cases with voxel size of 5mm and 3mm. A technique of reducing the resolution in normal tissue has been used to reduce the computation time. The results clearly illustrate the advantages of our methods.

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Table of Abbreviations

AD5	abdomen (5mm) problem
AN	acoustic neuroma problem
AN3	acoustic neuroma (3mm) problem
AN5	acoustic neuroma (5mm) problem
AVM	arterial veinous malformation problem
BAO	beam angle optimization
CHIM	convex hull of individual minima
CPU	central processing unit
3DCRT	three dimensional conformal radiation therapy
CT	computed tomography
CUB	critical organ upper bounds
DM	decision maker
DNA	deoxyribonucleic acid
DVH	dose-volume histogram
DVC	dose-volume constraint
EUD	equivalent uniform dose
FMO	fluence map optimization
gEUD	generalized equivalent uniform dose
IMB	intensity modulated beam
IMRT	intensity modulated radiation therapy
ITP	intersection points
LG5	lung (5mm) problem
LP	linear programme

MATLAB	MATrix LABoratory
MIP	mixed-integer programme
MLC	multi-leaf collimator
MO	multiple objective
MOP	multiobjective programme
MOLP	multiobjective linear programme
MONP	multiobjective nonlinear programme
MRI	magnetic resonance imaging
NC	normal constraint
NBI	normal boundary intersection
NDP	nondominated points
NTCP	normal tissue complication probability
NUB	normal tissue upper bounds
OAR	organ at risk
PL	pancreatic lesion problem
PR	prostate problem
PTV	planning target volume
PET	positron emission tomography
RFP	reference points
SA	simulated annealing
TCP	tumor control probability
TLB	tumor lower bounds
TUB	tumor upper bounds
GA	genetic algorithm