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Optimization for high-dose-rate brachytherapy of cervical cancer with adaptive simulated annealing and gradient descent

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ABSTRACT

PURPOSE: To validate an in-house optimization program that uses adaptive simulated annealing (ASA) and gradient descent (GD) algorithms and investigate features of physical dose and generalized equivalent uniform dose (gEUD)−based objective functions in high-dose-rate (HDR) brachytherapy for cervical cancer.

METHODS: Eight Syed/Neblett template-based cervical cancer HDR interstitial brachytherapy cases were used for this study. Brachytherapy treatment plans were first generated using inverse planning simulated annealing (IPSA). Using the same dwell positions designated in IPSA, plans were then optimized with both physical dose and gEUD-based objective functions, using both ASA and GD algorithms. Comparisons were made between plans both qualitatively and based on dose−volume parameters, evaluating each optimization method and objective function. A hybrid objective function was also designed and implemented in the in-house program.

RESULTS: The ASA plans are higher on bladder $V_{75\%}$ and D_{2cc} ($p = 0.034$) and lower on rectum $V_{75\%}$ and D_{2cc} ($p = 0.034$) than the IPSA plans. The ASA and GD plans are not significantly different. The gEUD-based plans have higher homogeneity index ($p = 0.034$), lower overdose index ($p = 0.005$), and lower rectum gEUD and normal tissue complication probability ($p = 0.005$) than the physical dose-based plans. The hybrid function can produce a plan with dosimetric parameters between the physical dose-based and gEUD-based plans. The optimized plans with the same objective value and dose−volume histogram could have different dose distributions.

CONCLUSIONS: Our optimization program based on ASA and GD algorithms is flexible on objective functions, optimization parameters, and can generate optimized plans comparable with IPSA.

Keywords: Adaptive simulated annealing; HDR; Volumetric brachytherapy; Optimization; Equivalent uniform dose

Introduction

High-dose-rate (HDR) volume-based brachytherapy is an effective approach to cervical cancer treatment (1−3). With increased availability of CT, MRI, and positron emission tomography, it is possible to visualize and identify target volumes in three dimensions and optimize a set of dwell times for the radioactive source to deliver a highly conformal dose distribution. In computational optimization, dwell times are determined by minimizing an objective function, which parameterizes treatment goals. Optimization is complicated because objective functions are usually nonlinear and present multiple local extrema, ''trapping'' simple optimizers. Stochastic optimization methods such as simulated annealing (SA) have the advantage of hill climbing to escape from local extrema and improve the quality of HDR treatment plan at the cost of calculation time (4).

Adaptive simulated annealing (ASA), originally called very fast simulated re-annealing, was developed by L. Ingber in 1989 and has been previously used in radiation therapy treatment optimization (5, 6). It is an SA algorithm variant and is more efficient and less sensitive to user-defined parameters. The main advantage of ASA compared with other varieties of SA algorithm is that the annealing schedule decreases exponentially with the annealing-time step, which is faster than fast simulated annealing (7) and

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much faster than Boltzmann annealing. Exponentially decreasing the cooling schedule allows solutions more rapidly converge to the global optimum. ASA also performs periodic re-annealing to remove sensitivity to initial conditions. One study evaluated the performances of Boltzmann annealing, fast simulated annealing, and ASA (8). Only ASA regularly attained the global minimum.

Gradient descent (GD) is a first-order optimization algorithm, which finds a local minimum for any n-dimensional continuous function. In brief, the gradient at some starting point is calculated and followed until a new minimum is reached. This is repeated recursively until user-defined cutoff criteria are achieved. GD-based algorithms tend to be fast but sensitive to the shape of the function and initial state. We implemented the golden line search algorithm as described in *Numerical Recipes in C* (9) as a simple fast technique to compare with the more complex ASA optimization.

Common constraints for HDR plan optimization are minimum and maximum doses for the target and maximum doses for normal structures, each associated with a penalty factor. Lessard *et al.* developed an anatomy-based dose optimization algorithm where dwell times are optimized using an inverse planning simulated annealing (IPSA) algorithm (10), which is used in the Oncentra planning system (Nucletron, an Elekta company, Elekta AB, Stockholm, Sweden). The objective function is based on physical doses to target and organs at risk (OARs) with penalty factors. An alternative technique is to use equivalent uniform dose (EUD) −based constraints. EUD is a homogeneous dose inside an organ that has the same cell killing effect as a heterogeneous dose distribution. The original definition of EUD was derived for tumor on the basis of linear-quadratic cell survival model (11). Niemierko later suggested a generalized form of EUD (gEUD) for both tumor and normal tissues (12). The concept of gEUD incorporates radiobiologic factors into the optimization algorithm. It has shown potential of improved sparing of OARs in intensity modulated radiation therapy (13) and HDR brachytherapy (14) optimization.

The purpose of this study was to evaluate an in-house volumetric HDR brachytherapy optimization program and explore the effectiveness of ASA and GD optimization on several objective functions. The program was developed on Windows platform using C# language. Using eight cervical cancer cases, the program was validated against a well-established commercial IPSA algorithm. We also explored the use of a hybrid objective function that combined the requirements from gEUD and physical dose-based constraints.

Methods and materials

Patient data sets

Eight previously treated squamous cell carcinoma cervical cancer cases (Stage IB2-IVA) were used in this study. The Syed/Neblett interstitial gynecologic template system (Best Medical International, Inc., Springfield, VA) was used for catheter insertion. CT scans with slice thickness of 2 mm were acquired and imported into the Oncentra treatment planning system (version 4.2 SP2, Elekta) and the clinical target volume (CTV), bladder and rectum were outlined by a radiation oncologist. Dwell positions within 5 mm of CTV border were activated in IPSA with a step size of 5 mm. The number of catheters and dwell positions varied with CTV volume are listed in Table 1. Plans were generated using Oncentra (Elekta) and IPSA, after which the regions of interest (ROIs) including CTV, bladder, rectum, and dwell positions were exported into our program for optimization. The preset dwell positions in IPSA were used for optimization. The in-house program regenerated an orthotropic dose grid with 4 mm spacing, with extra sampling points every 4 mm along each ROI surface contour. An Ir-192 source of air kerma strength 39.87 kU was used for dose calculation. The prescribed dose for this study was 35 Gy in five fractions to CTV from HDR brachytherapy after an assumed uniform 45 Gy in 25 fractions to each ROI from external beam radiation.

Dose calculation

The dose rate to a given dose point i from a dwell position j, denoted by d_{ij} was calculated using the TG-43 formalism (15). The dose D_i at a dose calculation point i from all n dwell positions is given by

$$D_i = \sum_{j=1}^{n} d_{ij}.t_j \tag{1}$$

where t_j is the dwell time at dwell position j.

Objective functions

Optimized plans were generated using a physical dose-based and a gEUD-based objective functions with both ASA and GD algorithms. The physical dose-based objective function used in this study is similar to that suggested by Lessard *et al.* (10). The objective function is

$$F_{PHY} = \sum^{k} \frac{w_{i,k}}{N_k} \tag{2}$$

Table 1
Clinical target volume and dwell positions generated using inverse planning simulated annealing in Oncentra

Patient	CTV (cm^3)	Catheters	Dwell positions
1	63.4	16	108
2	99.1	26	228
3	74.3	17	172
4	94.7	20	212
5	68.7	22	154
6	32.6	17	98
7	98.3	22	208
8	93.3	20	230

CTV = clinical target volume.