ELSEVIER

Brachytherapy ■ (2017) ■

BRACHYTHERAPY

Initial clinical assessment of "center-specific" automated treatment plans for low-dose-rate prostate brachytherapy

Mustafa Ege Babadagli[1], John Doucette[1], Nawaid Usmani[2], John Amanie[2], Albert Murtha[2], Don Yee[2], Muhammad Jamaluddin[2], Ron S. Sloboda[2,*]

[1]*Department of Mechanical Engineering, Donadeo Innovation Centre for Engineering, University of Alberta, Edmonton, AB, Canada*
[2]*Department of Oncology, University of Alberta, Edmonton, AB, Canada, T6G 1Z2*

ABSTRACT

PURPOSE: To report results of an initial pilot study assessing iodine-125 prostate implant treatment plans created automatically by a new seed-placement method.

METHODS AND MATERIALS: A novel mixed-integer linear programming method incorporating spatial constraints on seed locations in addition to standard dose−volume constraints was used to place seeds. The approach, described in detail elsewhere, was used to create treatment plans fully automatically on a retrospective basis for 20 patients having a wide range of prostate sizes and shapes. Corresponding manual plans used for patient treatment at a single institution were combined with the automated plans, and all 40 plans were anonymized, randomized, and independently evaluated by five clinicians using a common scoring tool. Numerical and clinical features of the plans were extracted for comparison purposes.

RESULTS: A full 51% of the automated plans were deemed clinically acceptable without any modification by the five practitioners collectively versus 90% of the manual plans. Automated plan seed distributions were for the most part not substantially different from those for the manual plans. Two observed shortcomings of the automated plans were seed strands not intersecting the prostate and strands extending into the bladder. Both are amenable to remediation by adjusting existing spatial constraints.

CONCLUSIONS: After spatial and dose−volume constraints are set, the mixed-integer linear programming method is capable of creating prostate implant treatment plans fully automatically, with clinical acceptability sufficient to warrant further investigation. These plans, intended to be reviewed and refined as necessary by an expert planner, have the potential to both save planner time and enhance treatment plan consistency.

Keywords: Brachytherapy; Prostate; Low-dose-rate; Seed implant; Treatment planning

Introduction

According to figures recently published by the American Cancer Society in 2012, prostate cancer was the leading newly diagnosed malignancy and the third leading cause of death in men living in developed countries (1). Among commonly available treatment options for low- and intermediate-risk disease that include radical prostatectomy, radiation therapy, and watchful waiting (2), permanent prostate brachytherapy (PPB) is a well-established and well-accepted outpatient procedure (3) that has provided excellent long-term clinical outcomes (4) with comparatively low morbidity (5). Standard PPB technique involves placing I-125, Pd-103, or Cs-131 seeds at planned target locations in prostatic or periprostatic tissues using hollow needles guided by a fixed perineal template and transrectal ultrasound imaging. Delivering the prescribed dose of radiation to the full planning target volume (PTV) while concurrently limiting the dose received by the urethra, bladder, and rectum to clinically acceptable

Received 28 July 2017; received in revised form 12 October 2017; accepted 16 October 2017.
Financial disclosure: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.
* Corresponding author. Cross Cancer Institute, Room 0418, 11560 University Avenue, Edmonton, AB T6G 1Z2, Canada. Tel.: +1-780-432-8719.
E-mail address: rsloboda@ualberta.ca (R.S. Sloboda).

1538-4721/$ - see front matter
https://doi.org/10.1016/j.brachy.2017.10.012

levels is the primary goal of individualized treatment planning carried out for this technique.

As observed by Butler *et al.* (6) in 2000, most PPB programs make use of seed-placement strategies implemented by manual planners that can be broadly classified as either modified uniform, nonuniform, or peripheral. Multiinstitutional analyses of PPB treatment planning practices among expert practitioners has revealed, not entirely unexpectedly, that there is substantial variability regarding PTV definition, seed strength, and extracapsular seed placement despite the existence of professional guidelines (7, 8). Yet notwithstanding such variability, clinical outcomes at the participating institutions were consistently excellent and not significantly different, suggesting that seed-placement strategy is to a large extent a matter of style, with different approaches evidently leading to similar outcomes in capable hands. This perspective is consistent with a clinical observation made by Bowes and Crook (9), who in their review of the long-term impact of PPB emphasize that implant quality (and not seed-placement strategy) is a key determinant of outcome. They note that ''programs with strict quality assurance and consistent high quality are reporting 7−10 year biochemical no evidence of disease rates 20% higher than series in which quality assurance is lacking and poor quality predominates''. The perspective is also consistent with the scientific observation that PPB treatment planning is an underconstrained problem, meaning that there are several ways to satisfy the anatomical structure dose−volume constraints recommended in societal practice guidelines (10, 11).

An attractive alternative to manual planning from a conceptual standpoint is computer-automated seed placement, in that it has the potential to save human resources while producing plans of high quality and consistency. This has motivated several investigators to attempt to solve the PPB planning problem algorithmically. Notable examples include Yu *et al.* (12) making use of genetic algorithms, Pouliot *et al.* (13) adopting simulated annealing, D'Souza *et al.* (14) developing a sequential solution method used in conjunction with the branch-and-bound algorithm, Lee and Zaider (15) presenting matrix reduction schemes and a penalty-based primal heuristic, Yoo *et al.* (16) using adjoint functions to drive a greedy heuristic, and Guthier *et al.* (17) formulating a matching pursuit-inspired algorithm. In all of these approaches, the primary focus was on finding solutions to the seed-placement problem that satisfy specified dose−volume constraints. Apart from incorporation of a limited number of additional constraints such as blocking certain needle locations or restricting the number of consecutive seeds loaded into a needle, clinical requirements and preferences were not considered and accommodated in an in-depth manner. As a consequence, the computer-generated plans produced tend to be characterized by their own unique features, which are rooted in the particular algorithmic approach taken (12, 13), and thus deviate to a greater or lesser extent from the traditional planning styles described by Butler *et al.* (6). Some of the automated planning algorithms have found their way into commercial software (18, 19) and permit the user to input some spatial constraints; however, none of the algorithms does so in a comprehensive, fully integrated, and easy-to-use manner.

In an effort to bridge the gap that exists between the too-often unintuitive solutions that current automated planning software offers and the traditional, clinically familiar results that many brachytherapy teams desire, this article makes use of an automated planning method specifically designed with the expressed needs of end users in mind. After consultation with expert planners and implant practitioners at one cancer center, desirable treatment plan characteristics were identified with the goal of designing an automated seed-placement method that (*1*) is highly intuitive and easy to use in a fast-paced clinical setting, (*2*) offers a comprehensive set of customizable clinical parameters that accommodate various expert planning styles, and (*3*) produces high-quality plans that require minimal modification by experts. The overarching objective integrating these three goals is to produce automated treatment plans that clinicians will find familiar in style to manual plans created at their respective cancer clinics and will therefore be comfortable in using for the treatment of their patients. The proposed automated planning approach is not meant to replace an expert planner; instead, the aim is to provide substantial time-saving computational assistance to expert planners in producing seed-implant plans characterized by a high level of seed distribution and dose distribution consistency from plan to plan. The capabilities of the presented method are unique in that it can create plans fully automatically in any one of a number of styles. It accomplishes this by working directly with a set of explicit constraints that are selected by the user and *in toto* serves to define the planning style. Hence, unlike other approaches to automated planning, tuning the algorithm (e.g., by specifying weighting factors in an objective function) or training the algorithm (e.g., by having it reference a database of treatment plans having desired properties) is unnecessary.

This article provides an overview of the key features of the proposed automated planning method, including its philosophical and technical differences from the general trends observed in current automated brachytherapy treatment planning. A full description of the method and its software implementation are reported elsewhere. The overview is followed by the details of an initial retrospective pilot study conducted at the Cross Cancer Institute (CCI) to assess the clinical quality of automated plans produced by this new approach using a single fixed set of constraints in comparison to manual plans produced by expert planners. The dosimetric and geometric features of the plans created in the pilot study are subsequently analyzed. In the discussion section, readers are oriented with regard to the current capability of the automated planning approach implemented to capture expert planning style and its potential clinical utility. This work represents the first phase of testing of the automated planning method;