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Dose optimization in high-dose-rate brachytherapy: A literature review of quantitative models from 1990 to 2010

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ABSTRACT

High-dose-rate brachytherapy is a form of internal radiotherapy, in which a tumor receives a temporary high dose of radiation. The treatment is commonly used in clinical practice. We discuss the literature based on the following topics: scope (interstitial or intracavitary), planning method (forward or inverse planning), objectives (in order to guarantee the right dose for the target area, critical organs and normal tissue), decision process (a priori, a posteriori or interactive), optimization techniques (exact, deterministic heuristic or stochastic heuristic method) and evaluation criteria (to measure the performance of the model results). The review serves three goals. First, we provide an overview of recent developments in the literature regarding the application of quantitative models for high-dose-rate dose optimization. Second, the classification allows to indicate recent developments in relation to each criterion and as such, provides an effective overview for researchers who are interested in a particular perspective. Finally, we want to explore opportunities for these quantitative models. We end the paper by revealing the main shortcomings in the current models: a better adaptation of clinical requirements to the mathematical model formulation, and a focus on probabilistic planning.

1. Introduction

Every year, 12.7 million people worldwide are diagnosed with cancer [1]. Cancer can be treated in different ways. Radiotherapy is one of the most common methods of treating cancer, together with surgery and chemotherapy. It is a local treatment with ionizing radiation to kill cancer cells. Each radiation treatment method aims to give the required dose to the tumor while minimizing the dose to the surrounding tissues [2]. The radiation can take place externally or internally. In external radiotherapy, the tumor is irradiated from different directions outside the body. In internal radiation therapy or brachytherapy, the tumor is irradiated using radioactive sources inside the body. This internal therapy has the advantage of reducing the dose outside the target volume [3].

High-dose-rate (HDR) brachytherapy is a form of internal radiotherapy, where the tumor is temporarily exposed to high-dose-rate radiation. To this end, catheters are placed into the body of the patient, in or adjacent to target tissues. A radioactive source is then sent through these catheters by an afterloader device with remote source control. The source is usually made of the isotope iridium-192. The source will stay for short time periods in predefined locations in the catheters, in order to deliver an accurately defined amount of radiation dose to the tumor. These time periods are defined as "dwell times" whereas the locations are called "dwell locations". Through the precision of this therapy, the dose to the surrounding organs is minimized. After the treatment, the catheters are removed from the body. A video illustrating this HDR brachytherapy treatment and its jargon can be found in [4,5].

Other common brachytherapy techniques are low-dose-rate (LDR) and pulse-dose-rate (PDR) brachytherapy. The treatments differ in dose rate. The dose rate is expressed in Gray per hour (Gy/h), depending on the strength of the radioactive source. HDR is done only with afterloading devices and uses a high dose rate (> 12 Gy/h). In HDR, the irradiation takes place in multiple sessions. The treatment takes only a few minutes per session. In LDR, a low dose rate is used (0.4–2 Gy/h). LDR is a procedure where the source is implanted for a few days or permanently (see, e.g., [6]). Finally, in PDR brachytherapy, the same total dose and time as LDR are prescribed but the dose is administered over a large number of small fractions every one to four hours [3].

In this study, we focus only on HDR brachytherapy. HDR still has great promise because of its well-known advantages (e.g., it eliminates radiation exposure, it has short treatment times,

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…) [7]. This treatment is used either as a boost treatment after an external beam radiation therapy series, and as monotherapy. HDR brachytherapy is applied for gynecological tumors such as uterine cancer, and for breast, bronchus, lung, esophagus or prostate cancer [8]. Compared to LDR, HDR brachytherapy offers many advantages. Besides the dosimetric advantage due to the stepping source, there are also practical and economic benefits: the hospital staff are no longer exposed to radioactivity, there is only one source, the patient requires no isolation between the various sessions and the short treatment time of a session is less a burden than the long LDR treatment [3].

The traditional problem with radiotherapy is that not only cancer cells but also healthy cells are damaged. The development of an accurate treatment plan, resulting in an individualized dose distribution for each patient, is therefore extremely important for a successful outcome. Such dose distributions are calculated by treatment planning systems, computerized systems to display the patient anatomy, the tumor and organs at risk, together with the dose distribution. Quantitative models implemented in HDR planning systems seek to optimize this dose distribution. This (planning) problem can thus be represented as a mathematical optimization problem. More particularly, it is a combinatorial optimization problem aiming at the optimal combination of dwell times. Varying the dwell times throughout the applicators makes it possible to give certain areas more radiation than others. However, trade-offs should be made. E.g., increasing the dose in the tumor volume might also increase the dose in healthy tissues and/or critical organs (i.e., depending on the catheter positioning and patient geometry) [9]. Whereas the increase of the dose in the tumor volume might be positive, the latter increase might harm healthy tissue and/or critical organs.

Before the treatment planner creates a treatment plan, the positions of the catheters and the patient anatomy are mapped through imaging. Then the major regions of interest are drawn on the images of the patient. These include the target volume, organs at risk and the normal tissue. The target volume consists of the main tumor mass expanded by a margin of typically one to two cm to cover tumor extensions. Organs at risk are organs adjacent to the target volume that could receive high doses in areas near to the target volume. To achieve the desired dose distribution, dose points can be generated in relation to the target volume. Then, the treatment planner prescribes the desired dose at these points. The actual dose in a dose point equals the sum of the dose contributions of each dwell location in which the source emits radiation [10]. Optimization algorithms are used to find the optimal dwell locations and dwell times such that the resulting dose distribution matches the prescribed one as close as possible.

Over the past 20 years, much literature has appeared on dose optimization in HDR brachytherapy. Many quantitative models have been developed to meet this planning problem. Each model uses a unique method of minimizing the difference between the desired dose and the actual dose over the target volume and regions at interest, using specific constraints and parameters. These quantitative models are now the research topic of this study. The purpose is threefold. Firstly, we want to provide an overview of recent developments in the literature regarding the application of quantitative models for HDR dose optimization. Here, we focus on the literature that explicitly includes dose optimization as a subject. We disregard the literature on factors that affect optimization, but does not have it as their main subject. Secondly, we want to organize this literature from multiple perspectives (see Section 2) to obtain an effective overview for researchers who are interested in a particular perspective. Thirdly, we want to explore opportunities for these quantitative models. We wish to reveal the shortcomings or gaps in the current models proposed in the literature.

Table 1
The number of research contributions as part of the literature, according to publication type and publication year.

	1990–1999	2000–2010	Total
Journal papers	6	38	44
Conference papers	0	11	11
Ph.D. dissertation/master thesis	0	2	2
Book chapter	4	0	4
Conference abstract	0	4	4
Total	10	55	65

2. Methodology

The research is mainly carried out on the basis of a literature review. This was the best method for indicating the latest thinking concerning HDR dose optimization. We have searched for relevant studies on optimizing the dose distribution for HDR brachytherapy in the following databases: Web of Science, Current Contents Connect, Inspec and PubMed. The references in these publications were also analyzed. During the search process the keywords "HDR", "brachytherapy" and "optimization" were used. Only English-written studies were included. This has led to a set of 65 research contributions. Table 1 represents the number of research contributions as part of the literature, according to publication type and publication year. It is clear from Table 1 that papers in scientific journals constitute the main contribution. We also see that the interest of researchers in this field has grown significantly over the past decade. In the period 2000–2010, there appeared far more studies of HDR dose optimization as compared to the period 1990–1999.

Following the review by Cardoen et al. [11] about the planning of operating rooms, we have structured the literature according to different topics. Each topic covers a different perspective. We distinguish the following six topics:

- scope (Section 3): the kind of HDR brachytherapy that is applied (interstitial or intracavitary) and for which region of the body such as the prostate, breast, etc.;
- planning method (Section 4): the type of planning (forward planning or inverse planning);
- objectives (Section 5): how is an adequate dose for the target area and/or a minimum dose for critical organs and normal tissue guaranteed;
- decision process (Section 6): when does the decision of the physicist take place as compared to the optimization process (a priori, a posteriori or interactive);
- optimization techniques (Section 7): the type of optimization technique (exact, deterministic heuristic or stochastic heuristic method);
- evaluation criteria (Section 8): the criteria used to get an idea of the performance of different models, such as the quality of the treatment plan, the computation time, etc.

In what follows, each of the above topics is discussed in detail in a separate section. Table 2 provides an overview of all these sections and subsections. Each section provides a table representing the different items compromising each topic. The table is then followed by a discussion of these various items based on a selected set of studies. A list of acronyms used throughout the text and their meaning can be found in Table 3. By studying the literature, we are able to reflect on the shortcomings in the quantitative models for dose optimization in HDR brachytherapy (see Section 9).