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# Physics and Imaging in Radiation Oncology

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Editorial

# Advanced treatment planning strategies to enhance quality and efficiency of radiotherapy

The radiotherapy (RT) process is becoming increasingly complex. Advances in RT delivery devices with all the flavors of intensity-modulation techniques, new approaches for in-room image-guidance including magnetic resonance imaging (MRI), and the increased complexity of the input data (from multi-modality imaging to the choice of optimization strategies) overall require an advanced level of management combined with sophisticated skills and tools. Several novel approaches have been proposed for coping with the treatment planning challenges [1–3]. In this editorial, important developments in treatment planning over the last few years are briefly summarized. In particular, the important contributions from recent papers in the present journal are discussed and placed in context.

One aim of automation of treatment planning in RT is harmonization and standardization, in order to reduce undesired inter-patient and inter-institution quality variations. Apart from reducing variations, another goal of automated planning may be the search for (on average) better plan quality than delivered by manual planners. The basic idea behind the latter approach is that solving the complex and large multi-objective planning problems could possibly be better performed by computers. Ideally the automatically generated plans are then both Pareto-optimal and clinically favourable. It is well recognized that large patient loads and often limited resources in the clinics for manual treatment planning may conflict with the quest for high-quality, individualized treatments. The potential for increased productivity is also an important driver for automation.

The current state-of-the-art in automated planning has been described in several recent review papers [1–3]. Basically, the solutions can be divided in i) knowledge-based planning (KBP), ii) protocol-based automatic iterative optimization, and iii) multi-criterial optimization (MCO) [1]. Various systems for knowledge-based planning (KBP) have been described [4–6]. The basic idea behind these systems is that similar anatomies can be treated with similar, intentionally high-quality, dose distributions. Machine learning is used to correlate anatomy with dose. Protocol-based automatic iterative optimization entails iterative heuristic adjustment of optimization objectives and constraints [7–9]. After each iteration, the system evaluates the dose distribution and establishes objectives and constraints for the next iteration, based on a pre-established protocol. There are two flavors of MCO; a posteriori MCO [10–12] and a priori MCO [13–15]. In a posteriori MCO, for each patient a series of plans is automatically generated and the final plan is then selected by a user, using Pareto navigation. In a priori MCO, for each patient only a single plan is automatically generated that is both clinically favourable and Pareto optimal. All of these strategies are (or are just becoming) commercially available (a priori MCO is currently being prepared by one vendor).

Several fully automated workflows for plan generation have been developed, including automatic segmentation of targets and organs at risk, automatic setup of beams with heuristic optimization of gantry and collimator angles, and automatic creation objective functions with ad-hoc tools [16,17].

A different approach to tackle some of the challenges of current treatment planning is real-time interactive planning (RTIP) [18,19]. The idea is that the real-time steering of the planning process based on a strong graphical user interface may result in fast generation of high-quality plans. RTIP does not require configuration (as for KBP, protocol-based automatic iterative optimization, and a priori MCO), or pre-computation of sets of Pareto-optimal plans (a posterior MCO).

The core of KBP consists of the development of mathematical models capable to predict achievable dose-volume and objective function constraints for new patients, based on their anatomy, i.e. a contoured planning CT-scan. Panettieri et al. [20] presented in this journal their results on a multi-centric investigation where a KBP model for prostate (based on commercial planning system) was developed, trained and validated by two centers and then distributed, re-validated according to local practice guidelines and then utilized clinically by six other institutions. The authors suggested the feasibility of developing and implementing at a multi-centric level an automated planning workflow. A general improvement in the quality of the dose distributions was observed. The results could be obtained even with the large heterogeneity in processes among the centers (particularly concerning contouring and planning protocols).

Roach et al. [21] investigated for another commercial auto-planning solution, the portability of system configurations through different centers. This was tested among three institutions. The study assessed also the level of adaptation of the pre-defined institutional configurations required to harmonize the results. The authors demonstrated the possibility to share automated planning configurations with simple adaptation of local protocols. Also this study was carried out on prostate patients.

In many published studies on automated treatment planning, the algorithm was trained with manually generated plans that were clinically delivered, while the training procedure had no or only minor drive to enhance quality in case of an, on average, inferior quality of the training plans. In these situations, also the automatically generated plans for future patients will in general not be optimal. Wheeler et al. [22] studied the use of Pareto navigation techniques in combination with clinical training plans to derive planning goals and weighting factors in association to 'protocol based' automated iterative optimization that utilizes dynamic objectives (to ensure trade-off balancing). They applied their methodology (implemented through a commercial system), again to prostate cancer cases. The results demonstrated the possibility to achieve clinically acceptable, well balanced treatment plans in a fully automated manner. Also in a priori MCO, the applied wish-list with constraints and prioritized objectives may be configured

with an explicit aim to improve on the training plans (see [1] and references therein).

Creemers et al. [23] retrospectively compared automated vs manually optimized volumetric modulated arc therapy plans for 25 patients with advanced stage non-small cell lung cancer. The study demonstrated that in about 50% of the cases, the plans were ready after the automated phase. In the remaining cases, some manual adjustment was needed. In conclusion, the automated plans were superior to the manual ones in terms of dose/volume endpoints for organs at risk while with equivalent coverage of the target volumes. There was a time gain of about a factor four in favor of the automated process.

Baker et al. [24] investigated the use of real-time interactive planning (RTIP) as inspired by the seminal work of Otto [19]. They applied retrospectively their method to 20 head and neck cases comparing the RTIP plans against the clinical plans (optimized without MCO or KBP). All their plans were found preferable by the majority of the five oncologists who blindly assessed the results.

Recently, many papers have appeared on the prediction of dose distributions with deep learning [25–27]. Calculation speed is a highly attractive feature of this approach; 3D dose distributions can be generated in seconds. On the other hand, only dose distributions are generated. Dose delivery needs subsequent establishment of appropriate treatment machine parameters, which costs time and may also result in quality loss. Training of the applied networks has no intrinsic mechanism to improve on the quality of the input plans. So inferior training plans will result in inferior plans for future patients. It therefore remains essential to continue development of planning approaches that will result in (near) Pareto-optimal and clinically favourable plans. In the end, such plans could be used for training of deep learning networks.

## Declaration of Competing Interest

L. Cozzi acts as Scientific Advisor to Varian Medical Systems and is Clinical Research Scientist at Humanitas Cancer Center. The Erasmus MC Cancer Institute has research collaborations with Accuray Inc and with Elekta AB.

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