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CLINICAL INVESTIGATION **Prostate**

WHAT CTV-TO-PTV MARGINS SHOULD BE APPLIED FOR PROSTATE IRRADIATION? FOUR-DIMENSIONAL QUANTITATIVE ASSESSMENT USING MODEL-BASED DEFORMABLE IMAGE REGISTRATION TECHNIQUES

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Purpose: To quantify adequate anisotropic clinical target volume (CTV)-to-planning target volume (PTV) margins for three different setup strategies used during prostate irradiation: *(1)* no setup corrections, *(2)* on-line corrections determined from bony anatomy, and *(3)* on-line corrections determined from gold markers.

Method and Materials: Three radiation oncologists independently delineated the CTV on computed tomography images of 30 prostate cancer patients. Eight repeat scans were acquired to allow simulation of the delivered dose distributions in changing geometry. Different registration approaches were taken to mimic the different setup strategies. A surface model–based deformable image registration system was used to warp the delivered dose distributions back to the dose in the planning computed tomography scan. On the basis of the geometric extent of the underdosed areas, a set of anisotropic margins was derived to ensure a minimal dose to the CTV of 95% for 90% of the patients.

Results: Without setup correction, margins of approximately 11 mm for the corpus of the prostate and 15 mm for the seminal vesicles were required. These margins could be reduced to 8 and 13 mm when aligning the patient to the bony anatomy and to 3 and 8 mm aligning the patient to implanted gold markers. A larger margin at the apex was required to account for the significant observer variability and steep dose gradients at this location (11 mm using skin marker registration, 9 mm using bony anatomy registration, and 6 mm using gold marker registration).

Conclusions: Novel voxel tracking techniques have enabled us to calculate accumulated dose distributions and design accurate three-dimensional CTV-to-PTV margins for prostate irradiation.

Prostate, Margins, Image-guided radiotherapy, IGRT, Deformable registration, Dose accumulation.

INTRODUCTION

The planning target volume (PTV) is a geometric concept that takes into consideration the net effect of all possible geometric variations and is used to ensure that the clinical target volume (CTV) receives the prescribed dose. These geometric uncertainties include organ delineation, setup errors, and organ motion that occur throughout the planning and treatment process. In the past decade, many treatment strategies have been explored to reduce these uncertainties to maximize the benefits of conformal therapy and intensity-modulated radiotherapy (IMRT).

For external beam radiotherapy of the prostate, one of the first setup and correction strategies was based on the comparison of bony anatomy, visual on portal images, with reference simulation film or digitally reconstructed radiographs (1, 2). More recently, implanted fiducial markers have been used to visualize motion of the prostate itself (3, 4). Using that method, not only setup errors, but also internal motion of the prostate relative to the bony anatomy, can be identified (4, 5).

Both on-line and off-line approaches have been proposed and implemented for both bony anatomy registration and marker registration (1, 2, 6, 7). Although off-line correction protocols aim at reducing systematic errors, on-line correction protocols have the potential to reduce both systematic and random errors, but at the expense of increasing the treatment time per fraction considerably.

Although these setup correction protocols can reduce geometric treatment uncertainties, it is not straight forward to derive appropriate CTV-to-PTV margins. Stroom *et al.* (8) and

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van Herk *et al.* (9) derived recipes expressing the margin as a function of the systematic and random errors:

$$M = \alpha\Sigma + \beta\sigma \quad (1)$$

where Σ is the standard deviation of the overall systematic error, and σ, the standard deviation of the overall random error; both errors were assumed to be normally distributed. On the basis of a coverage probability simulation, Stroom *et al.* (8) concluded that an α of 2.0 and β of 0.7 would result in a margin to cover 99% of the CTV with a dose of 95%. These values are comparable to a simplified outcome of the margin recipe using dose population statistics by van Herk *et al.* (α = 2.5 and β = 0.7), yielding a minimal dose to the CTV of 95% for 90% of the patient population.

An important shortcoming of these margin recipes is their lack of adequately incorporating both rotational and morphologic errors. It is just these errors that become essential after eliminating the translational errors and, for this reason, margin recipes might have only limited validity when trying to establish adequate CTV-to-PTV margins when using setup correction protocols.

The aim of this study was to assess the appropriate CTV-to-PTV margins for 90% of the patient population by quantitatively simulating the total treatment dose using anatomic data obtained from repeat computed tomography (CT) scans during the course of therapy. The accumulated dose distribution was calculated using a surface-based deformable image registration method (10). By aligning the repeat CT data sets either to the external markers, the bony anatomy, or the internal markers, three different setup strategies were simulated. Furthermore, intensity-modulated radiotherapy (IMRT) plans were generated and evaluated for independent CTV delineations to assess the effect of interobserver variability in target delineation. The approach has two fundamental advantages. First, the use of a deformable dose accumulation algorithm fully accounts for translational, rotational, and morphologic variations. Second, in contrast to existing attempts, no Gaussian distributions need to be assumed to model geometric uncertainties, because the actual data in the repeat scans will be real samples in the treatment simulation.

METHODS AND MATERIALS

CT data

A total of 30 prostate cancer patients with four implanted gold markers were used in this simulation study. For each patient, nine CT scans of the pelvic region (one treatment planning and eight repeat CT scans) were acquired with a 16-slice helical scanner (Brilliance Big Bore CT Scanner, Philips Medical Systems, Cleveland, OH) using a slice thickness of 1.5 mm. The repeat scans were acquired immediately before eight treatment sessions regularly spread over the entire treatment course. The patients were instructed to void their bladder 1 h before treatment (and before the CT scan) and drink 300 mL afterward.

Delineation of CTV and organs at risk

Three experienced radiation oncologists independently delineated the CTV in a three-dimensional (3D) manner. In this procedure, we assumed only microscopic tumor involvement in the first 2 cm of the seminal vesicles corresponding to the pathologic features of intermediate-risk tumors (11, 12). First, two spheres with a radius of 2 cm were centered at the central part of the interfaces between the prostate and each of the seminal vesicles. Second, the CTVs were delineated slice by slice by each observer. In this process, the spheres were used as a guideline to indicate the boundaries of the seminal vesicles. Finally, a template CTV mesh with 962 nodes (or vertices) was automatically fit to the delineated contours. This template mesh was constructed from the CTV contours of an arbitrary patient with a left–right symmetric CTV and average-size seminal vesicles. In the fitting process, care was taken that the nodes were evenly distributed over the CTV and that each cluster of nodes always represented the same particular surface area of the CTV (Fig. 1). This enabled us to perform population statistics because the mesh of each prostate of each patient and observer had the same topology.

A similar procedure was used to generate a mesh of the rectum. First, the rectum was delineated by a single observer at the transverse slices of the CT scan. Second, a template rectum mesh was fit around the contours.

IMRT planning

Initially, the five-field IMRT plans were generated with no CTV-to-PTV margin for each delineated CTV. The aim was to generate a very conformal dose distribution. In a standard prostate IMRT plan, a high-dose gradient is often mainly desired at the prostate interface with the rectum; however, in this study, it was important to

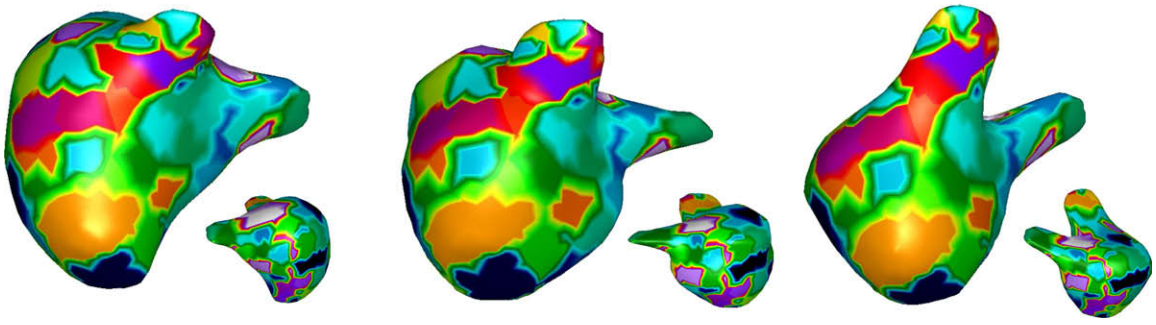

Fig. 1. "Patchwork" clinical target volume meshes of prostate and seminal vesicles for 3 patients, in which surface patches (*i.e.,* spatially connected regions of mesh nodes) were encoded with one color. Graph qualitatively illustrates that each node corresponds to approximately same surface location from one organ to another, allowing us to perform population statistics on a node-by-node basis.