The British Journal of Radiology, 84 (2011), 819–825

Preliminary experience of a predictive model to define rectal volume and rectal dose during the treatment of prostate cancer

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Objectives: The aim of this study was to define a method to evaluate the total dose delivered to the rectum during the whole treatment course in six patients undergoing irradiation for prostate cancer using an offline definition of organ motion with images from a cone beam CT (CBCT) scanner available on a commercial linear accelerator.
Methods: Patient set-up was verified using a volumetric three-dimensional CBCT scanner; 9–14 CBCT scans were obtained for each patient. Images were transferred to a commercial treatment planning system for offline organ motion analysis. The shape of the rectums were used to obtain a mean dose–volume histogram (<DVH>), which was the average of the DVHs of the rectums as they appeared in each verification CBCT. A geometric model of an average rectum (AR) was produced using the rectal contours delineated on the CBCT scans (DVH_{AR}). To check whether the first week of treatment was representative of the whole treatment course, we evaluated the DVHs related to only the first five CBCT scans (<DVH5> and DVH_{AR5}). Finally, the influence of a dietary protocol on the goodness of our results was considered.
Results: In all six patients the original rectal DVH for the planning CT scan showed higher values than all DVHs.
Conclusion: Although the application of the model to a larger set of patients is necessary to confirm this trend, reconstruction of a representative volume of the rectum throughout the entire treatment course seems feasible.

Received 24 February 2010
Revised 27 April 2010
Accepted 6 May 2010

DOI: 10.1259/bjr/25741415

Commercially available cone beam CT (CBCT) image-guided radiotherapy (IGRT) [1, 2] offers the opportunity of online verification of the set-up treatment position and offline correction as adaptive radiotherapy (ART) for prostate cancer. Imaging information from the first treatment fractions may be used to reoptimise the treatment plan to include systematic errors and organ motion [3–7]. This improvement in delivery accuracy may increase the probability of disease control with a consistent dose to the organs at risk [8–11].

Assessing the dose actually delivered to any portion of an organ during the treatment course is admittedly difficult. On the one hand, there are known problems, with no widely accepted solution, in performing reliable dose calculations on a CBCT scan. On the other hand, even assuming that the aforementioned problems can be overcome and a reliable dose distribution can be made available on each treatment session CBCT scan, we are still left with the difficult task of identifying the same volume element of a given organ in all the different scans so that the doses received by that volume element in the treatment sessions can be totalled. The strategy most often chosen to fulfil this task involves deformable registrations [12–15]. Indeed, once a registration map is found that matches voxels in all the treatment session CBCT scans to their corresponding voxel in the planning CT scan, this same map can drag along the dose matrices (supposedly) calculated on the CBCT scans, so that they can be totalled up in the planning CT and compared with the dose distribution of the original treatment plan. A different approach entails the construction, in the planning CT scan, of a volume representative of the average position and shape of a chosen organ for the whole treatment course. The projection of the planning dose matrix on this "average" volume can be taken as representative of the dose received by that organ during the treatment course. Therefore, in our investigation, we evaluated the possibility of developing a method to calculate the dose delivered to the rectum throughout the whole course of treatment using the information derived from the offline definition of organ volumes in each treatment session using a commercially available CBCT scanner with a beam modulator (Linac Elekta Synergy S; Elekta, Crawley, UK). Set-up errors were corrected before treatment using the image registration algorithm of the X-ray volume imaging (XVI) software that manages the CBCT scanner. The algorithm performance in detecting translational and rotational set-up errors has been previously tested [16]. In our investigation we defined

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the "average rectum" as the volume obtained by three-dimensional (3D) interpolation of elliptical contours delineated in each CBCT scan after registration with the planning CT. For each patient, the dose–volume histogram (DVH) of the AR was compared with the DVH resulting from averaging the DVHs of the rectums as they appeared in each verification CBCT scan. This comparison allowed us to assess the relevance of the well-known loss of spatial information in DVHs, which usually prevents their summation and/or averaging. The construction of the AR was repeated for the first five CBCT scans to check whether they were representative of the rectum shape and position throughout the whole treatment course. These DVHs were compared with the DVH of the rectum in the planning CT scans. To ensure reproducibility of this method, we instructed patients to follow a dietary protocol to reduce the shape and distension of the rectum during the whole treatment course.

Methods and materials

Six consecutive patients who were referred to the Radiation Oncology Unit of the University of Rome, Tor Vergata, with clinical Stage I or II carcinoma of the prostate were included in the present evaluation. The patients underwent only radiotherapy using 15 MV photons produced by a commercially available linear accelerator, the Elekta Synergy S. Planning CT (pCT) scans were always obtained in the supine position with a 2.5 mm slice thickness and an average total number of slices ranging between 70 and 80. The prostate, seminal vesicles (SVs) and outer rectal wall were always delineated by the same radiation oncologist. The rectal circumference was delineated between the superior and inferior limits of the planning target volume (PTV) plus two axial slices on each side in the craniocaudal direction (rectum within PTV) [17, 18]. All of the patients received a dose of 76 Gy in 38 fractions (66 Gy to the prostate plus SVs (CTV1) and 10 Gy to the prostate only (CTV2)) using a 6-field 3D conformal technique with 15 MV photons. The CTV1 to PTV1 margins were chosen to be 4 mm in the direction of the rectum and 6 mm in all other directions, reducing the conventional margins, usually found in the literature, after a CBCT set-up error analysis. The same margins were used to define the PTV2. Treatment plans were developed using Pinnacle 8.0m (Philips Medical Systems, Cleveland, OH). With regard to the dose to the rectum, our treatment constraints were that less than 40% of the rectal volume had to receive 60 Gy; less than 50% of the rectal volume had to receive 50 Gy; and less than 25% had to receive a maximum dose of 70 Gy.

The Elekta Synergy S with a beam modulator combines a micro multileaf collimator linear accelerator and a kilovolt (kV) imaging system. The system allows the acquisition of planar projections and the creation of 3D X-ray volume images (CBCT scans) using the management software XVI. The tube and flat panel of the imaging system are mounted on retractable arms that extend from the accelerator's drum structure. The kV system is mounted in an orthogonal direction to the MV beam, sharing a common axis of rotation. Transmission images are acquired during a 360° single rotation of the gantry. Reconstruction is performed by the management software using an Intel Xeon 3.06 GHz processor personal computer processing approximately 625 planar images (projections).

According to some reports [10, 12, 19], one of the most important causes of prostate intrafraction motion may be the result of differing bowel contents. We instructed patients to prepare their bowel before the pCT scan and any single treatment session throughout the therapy course. Bowel preparation consisted of dietary advice to reduce intestinal gas and to ensure that the rectum was empty. The diet was prescribed in combination with a daily mild laxative (1000 mg magnesium oxide) every night before sleeping.

For each patient a CBCT scan was acquired before each of the first five consecutive treatment sessions and once weekly over the entire treatment course. Acquisition parameters were 120 kV, 25 mA and 40 ms per projection. Approximately 625 planar images were acquired during 1 full revolution of the gantry in a total time of 113 s. The complete reconstruction of the volume scan took approximately 60 s. An appropriate clip-box was chosen to co-register the CBCT scan and the pCT scan using the pelvic bone anatomy excluding the femoral heads. In this way, the planning isocentre (isoplan) was matched to the machine isocentre. The registration was performed automatically by the XVI software using a 3D chamfer matching algorithm [12], verified and, if necessary, corrected by the radiation oncologist. Only translational set-up errors were considered and corrected online before treatment, as our treatment couch cannot be rotated. However, we always repositioned the patient whenever rotational set-up errors were 1° or greater.

No additional CBCT scans were acquired at the end of each single session. The image set obtained before each treatment session was transferred to the treatment planning system (TPS) for offline organ motion analysis.

Reconstructed images of the CBCT scans were exported via digital imaging and communications in medicine (DICOM) to the Pinnacle TPS and imported as secondary fusion data sets into the patient's treatment plan using the Syntegra image fusion module. Registration of the CBCT scans with the pCT scan was performed using a script that was developed in house that aligns the centre of the CBCT scan (isocentre) with the isoplan. Translations performed online during patient set-up to correct positioning errors were manually reported within Syntegra using the utility "Parameter registration". The accuracy of this procedure has been established and verified elsewhere [16]. The correct treatment position of the patient was obtained in the Pinnacle co-ordinate system. The same radiation oncologist who approved the treatment and verified the set-up errors during the XVI registration delineated, on each of the CBCT scans, the shape of the rectum as it appeared before each treatment session. These contours were projected onto the reference CT scan and its associated dose matrix. An average of the different shapes of the rectum on different treatment days was then obtained. For a given CT slice, the co-ordinates of the sides of the rectangle bounding the contour of the rectum were determined. This was repeated for each axial slice of each CBCT scan. The co-ordinates of each side were averaged to obtain an average bounding rectangle. An ellipsoidal curve tangential to this rectangle was determined and drawn on the pCT scan in the chosen slice. The procedure

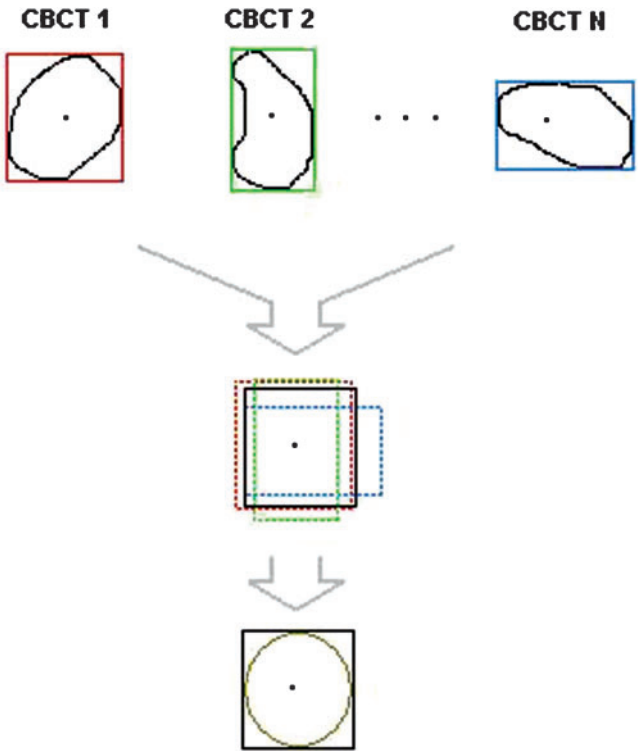


Figure 1. Schematic diagram of the steps involved in the construction of the average rectum shape. Rectum contours, taken at a given value of the craniocaudal co-ordinate, of co-registered cone beam CT scans acquired on different days are shown along with their bounding rectangles. An average bounding rectangle is then obtained by taking the arithmetic means of the co-ordinates of the sides of the "daily" rectangles. Finally, an elliptical contour is drawn within the average bounding rectangle. The whole sequence is repeated for every slice.

was repeated for each slice in which rectum contours were present (Figure 1). The volume obtained by 3D interpolation of the elliptical contours is referred to as the AR. The same procedure, when applied to the first five CBCT scans only, yielded the volume defined as the AR5. We defined the DVH_{AR} as the DVH of the AR and <DVH> as the DVH obtained by averaging the DVHs of the rectal volumes as they appeared in the verification CBCT scans. The same calculations were repeated for the first five CBCT scans only, producing DVH_{AR5} and <DVH5>, respectively. Figure 2 shows a screenshot of the registration module showing transaxial, sagittal and coronal sections of delineated rectal volumes on different treatment days for one patient.

Results

In Figure 3 the 11 CBCT DVHs of the rectal volumes of the same patient reported in Figure 2 are displayed as they appeared in the verification CBCT scans on different treatment days, together with the pCT scan rectum DVH, the <DVH> and the DVH_{AR}. In Figure 3, the DVH_{AR} (violet line) is fairly coincident with the <DVH> (blue line), although the curves are distributed over a wide range. Both DVHs are lower than the pCT DVH. A similar trend can be observed for the remaining five patients analysed, whose results are reported in Table 1, which shows the percentage of the rectal volumes receiving progressively increasing doses between 40 Gy and 70 Gy. Column 1 in Table 1 shows the rectal volumes as calculated on the pCT scan. In all the patients, the constraints established for the treatment plan were maintained with the exception of patient 5 at 40 Gy and 50 Gy, when a larger percentage of the rectum received these

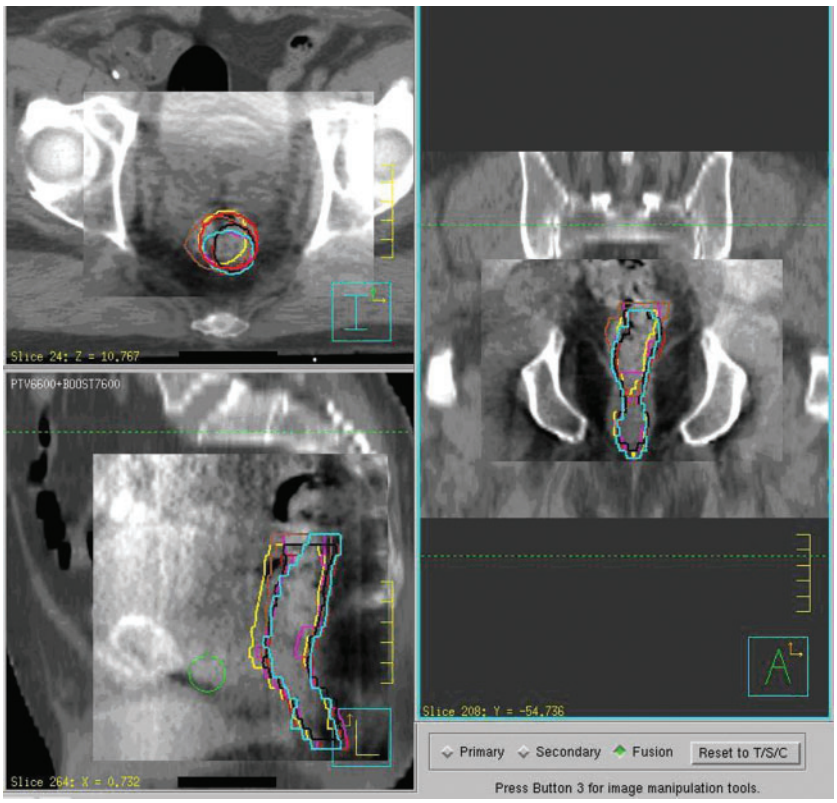


Figure 2. Screenshot of the Syntegra registration module showing transaxial, sagittal and coronal sections of rectum contours on different treatment days for one patient.

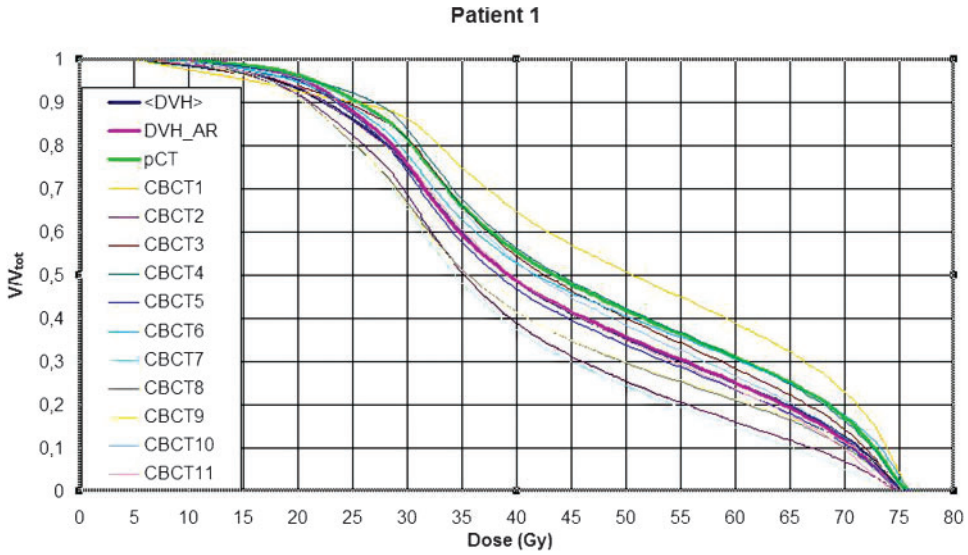


Figure 3. Dose–volume histograms (DVHs) of the cone beam CT (CBCT) scans throughout the whole treatment course (same patient as shown in Figure 2) together with the planning CT rectal DVH (green; pCT), average rectum DVH (violet; DVH_{AR}) and the average of the DVHs of the rectal volumes as they appeared in the verification CBCT scans on different treatment days (blue; <DVH>) superimposed on the DVH_{AR}.

doses. At higher doses (⩾60 Gy and ⩾70 Gy), on the contrary, all the constraints were maintained.

Columns 2 and 3 in Table 1 show the values of <DVH5> and <DVH>, respectively, and columns 4 and 5 show the values of DVH_{AR5} and DVH_{AR}, respectively. All the reported values are lower than those in column 1 (pCT), ensuring that the percentage of the rectal volumes receiving progressively increasing doses were within the limits of the constraints established for this organ throughout the whole treatment session. Even patient 5, who showed, in most of the CBCT scans, a larger rectal volume than the other patients, remained within the constraints of the plan.

Figure 4 shows the complete DVHs for two patients whose rectums had average reconstructed shapes which gave DVHs the closest (4a) and the farthest (4b) from the arithmetic mean of the DVHs, respectively. In Figure 4a,b, the pCT DVH is compared with the DVH_{AR} (after the first five CBCTs only or after the end of the treatment) and with the <DVHs> of the rectal contours as they appeared on the verification CBCT scans after the first five CBCTs only or after the end of the treatment. The DVH_{AR} and <DVH> curves are always lower than the pCT DVH obtained to develop the treatment plan. The same trend is evident for DVH_{AR5} and <DVH5>.

Discussion

Different studies have shown that dose escalation in prostate cancer improves the clinical outcome [4, 8, 20, 21]. However, increasing the dose to the prostate may produce an increased risk of rectal toxicity, as was demonstrated in a randomised trial comparing 68 Gy with 78 Gy with the prostate [22].

Different solutions have been suggested to prevent late rectal bleeding. The dose to the rectum may be decreased by using different delivery modalities, such as intensity-modulated radiotherapy, and/or introducing smaller planning target volume margins. In spite of these efforts, the dose to the anterior rectal wall and the position of the prostate and SVs are determined by the rectal contents. Control of the physiological changes in these organs may reduce the uncertainties and the systematic and/or random errors in dose delivery to the target. Verification of the relationship between pelvic organs may be obtained using kilovoltage CBCT scans, which allow for soft-tissue registration immediately before and/or after treatment. With CBCT scans one should be able to verify the position of the pelvic organs and obtain data to assess the dose distribution truly delivered during the treatment to the target and to the organs at risk, reducing systematic and/or random errors.

ART for prostate cancer was first suggested by Yan et al [23] and Martinez et al [4], who used information from the first treatment sessions to reoptimise the treatment plan. They described a method to increase the dose to the prostate while maintaining acceptable doses to the organs at risk, but in their studies they did not consider the variations in rectal shape. A similar experience was described by Remeijer et al [24] and Hoogeman et al [14], who included changes in rectal volume and shape. The first four scans were used in combination with the pCT scan to create an average prostate position and rectal shape. The systematic error for the rectal wall position was reduced by 43%, on average, and with this improved estimate of the rectal shape a better prediction of rectal dose could be obtained. Some efforts have been made to introduce methods such as dietary control and bowel preparation using mild laxatives to minimise prostate motion. Several reports have mentioned the use of protocols to achieve an empty rectum during the course of radiotherapy [25, 26] or advocated the administration of mild laxatives before acquisition of the pCT scan in order to reduce rectal contents [27]. A recent publication [28] demonstrated that a dietary protocol significantly decreased the incidence of faeces and moving gas from 55% and 61% to 31% and 47% of scans in the non-diet and diet groups, respectively. These authors concluded

Table 1. Rectal volumes receiving progressively increasing doses between 40 Gy and 70 Gy in the 6 evaluated patients

	40 Gy dose rectal volume (%)				
Patient no.	pCT	<DVH5>	<DVH>	DVH_{AR5}	DVH_{AR}
1	55.40	52.20	48.76	50.50	48.76
2	52.50	42.50	41.40	41.49	40.60
3	51.90	41.35	47.00	42.57	48.50
4	57.50	45.05	50.80	46.70	53.20
5	73.00	58.60	54.50	63.40	58.10
6	58.90	46.75	45.80	48.07	47.20
	50 Gy dose rectal volume (%)				
Patient no.	pCT	<DVH5>	<DVH>	DVH_{AR5}	DVH_{AR}
1	41.80	38.40	35.40	37.80	35.70
2	38.00	31.25	29.90	29.90	29.00
3	37.40	29.04	35.40	30.20	36.10
4	43.50	33.20	38.80	34.41	40.30
5	54.50	43.30	37.90	45.10	39.50
6	43.70	29.76	30.20	30.48	30.50
	60 Gy dose rectal volume (%)				
Patient no.	pCT	<DVH5>	<DVH>	DVH_{AR5}	DVH_{AR}
1	31.00	27.50	25.10	27.40	25.10
2	24.40	21.70	20.30	20.40	19.40
3	26.70	19.77	26.30	20.60	26.20
4	33.60	24.60	29.40	25.29	30.20
5	40.60	31.30	26.00	32.16	26.90
6	32.40	17.92	19.70	17.97	18.90
	70 Gy dose rectal volume (%)				
Patient no.	pCT	<DVH5>	<DVH>	DVH_{AR5}	DVH_{AR}
1	17.00	14.20	12.40	14.00	11.70
2	10.40	12.30	10.60	10.50	0.90
3	15.50	10.30	15.80	10.10	14.70
4	22.10	14.60	18.20	14.10	17.60
5	23.50	15.50	11.40	15.30	11.30
6	20.70	8.00	10.00	7.70	8.40

pCT, planning CT rectal dose–volume histogram; <DVH5>, dose–volume histogram obtained by averaging the first five cone beam CT scans only; <DVH>, average of the dose–volume histograms of the rectal volumes as they appeared in the verification cone beam CT scans on different treatment days; DVH_{AR5}, dose–volume histogram of the average rectum with reference to the model of the first five CBCT scans only; DVH_{AR}, dose–volume histogram of the average rectum.

that using a dietary protocol is advisable with and without CBCT-based image guidance.

In our preliminary experience we evaluated the dose delivered to the rectum in six consecutive patients, calculating the DVHs of the rectum as it appeared on the reference scan, on a rectum obtained as the average of the first five CBCT scans, during the first week of treatment (<DVH5>), throughout the course of the irradiation (<DVH>) (Table 1, columns 2–3) and on the AR obtained as the 3D interpolation of the elliptical contours obtained from all of the CBCT slices in which rectal contours were present (DVH_{AR5} and DVH_{AR}) (Table 1, columns 4–5).

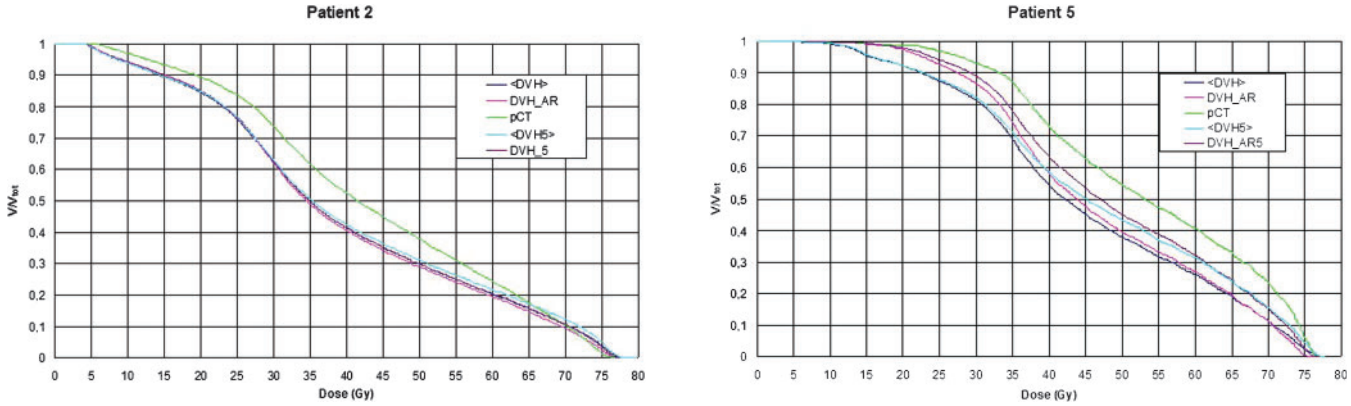
In all of the patients reported, the reference DVH shows values which are higher than those calculated for the geometrically averaged shape and for the simple arithmetic mean of the DVH curves. The instructions we gave to the patients for bowel preparation were repeated frequently during the course of the treatment and helped to have a clean bowel at the time of irradiation, aiding rectal sparing. The treatments were always delivered between 10 a.m. and 12 a.m. to ensure similar bowel conditions throughout the whole course of irradiation.

These preliminary data allow a few cautious comments:

- Bowel preparation with simple instructions given to the patients ensures that the prostate area is treated with an empty rectum throughout the whole 7–8 weeks of treatment. This separates the rectum from the prostate, improving the DVH values.
- The reference DVH (pCT) appeared in all of the patients to be slightly higher than the other DVHs, and this may be interpreted as a need to assess the diet and bowel cleaning, which is probably not yet "optimal".
- The arithmetic means of the DVHs calculated in the first five CBCTs or on all of the acquired scans at the end of the treatment are very similar, indicating that the information on the total dose to the rectum calculated after 1 week of irradiation may be reliable. Given a reliable patient we can predict, after the first five sessions, the total dose to any point of the rectum at the end of the course of irradiation.
- The same conclusions may be drawn about the geometrically averaged shape of the rectum after the first week and at the end of irradiation with respect to the simple arithmetic means of the DVHs; given the time necessary to elaborate the data and to obtain the model, we suggest that the arithmetic mean may be used as a reliable indication of the total rectal dose.
- Smitsmans et al [28] concluded that using a dietary protocol is advisable with and without CBCT-based image guidance; we believe, based on our preliminary experience, that a dietary protocol is, of course, advisable given reliable patients. More experience is necessary on this topic before we can rely only on diet and bowel preparation. For conventional treatments with relatively low doses, we can rely on a limited number of CBCTs during the first week of treatment, but we believe that this must be more carefully monitored throughout dose-escalating programmes and high-dose (>80 Gy) protocols.

Conclusions

The satisfactory agreement between the rectal volumes receiving specified doses as measured on the "geometrically" averaged rectal shape and on the simple arithmetic mean of the DVH curves is shown by the data in Table 1, which indicate that the latter is a reliable representation of the behaviour of the rectal shape throughout the course of the treatment. These data also show that the values obtained from the arithmetic mean of the first five CBCT scans and those obtained from the mean of all the CBCT scans are approximately equal



(a) (b)

Figure 4. Complete dose–volume histograms (DVHs) for the two patients whose rectums had average reconstructed shapes (DVH_{AR} and DVH_{AR5}; violet and dark violet, respectively), which gave DVHs the closest (a) and the farthest (b) from the arithmetic mean of the DVHs (<DVH> and <DVH5>; blue and cyan, respectively).

(within 5% with a few exceptions) (Table 1). The first five CBCT scans seem to be fairly representative of the whole treatment course, although the application of the model to a larger number of patients is necessary to confirm this trend.

Previous data have demonstrated that a dietary protocol significantly decreases the incidence of faeces and moving gas, suggesting the relevance of dietary protocols, which may be verified using CBCT image guidance, as has been shown by our preliminary experience.

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