Received:
23 June 2015

Revised:
5 October 2015

Accepted:
12 October 2015

doi: 10.1259/bjr.20150509

Cite this article as:

Falcinelli L, Palumbo I, Radicchia V, Arcidiacono F, Lancellotta V, Montesi G, et al. Prostate cancer: contouring target and organs at risk by kilovoltage and megavoltage CT and MRI in patients with and without hip prostheses. *Br J Radiol* 2015; **88**: 20150509.

SHORT COMMUNICATION

Prostate cancer: contouring target and organs at risk by kilovoltage and megavoltage CT and MRI in patients with and without hip prostheses

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Objective: In radiotherapy treatment, planning target volume and organs at risk are contoured on kilovoltage CT (kVCT) images. Unlike MR images, kVCT does not provide precise information on target volume extension. Since neither kVCT nor MRI may be suitable for contouring in patients with ferrous hip prostheses, this study evaluated whether megavoltage CT (MVCT) reduced interobserver variability.

Methods: Two patients without hip prostheses and one patient (Patient 3) with hip prostheses were enrolled. Six radiation oncologists contoured prostate, rectum and bladder on kVCT (Patients 1 and 3), MRI (Patient 2) and MVCT images (Patient 3). MVCT was acquired with fine, normal and coarse modalities. Interobserver variability for each organ was analysed using conformity index (CI) and coefficient of variation (CV).

Results: In patients without hip prostheses, CIs were higher in prostate contouring with MRI than with kVCT, indicating lower interobserver variability with MRI. Very slight variations were seen in rectum and bladder contouring. In the patient with hip prostheses (Patient 3), contouring on kVCT lowered CI and increased CV in the prostate, bladder and rectum. The differences were more marked in the prostate. Only fine modality MVCT reduced interobserver variability and only for the prostate.

Conclusion: Even though greater noise and less soft-tissue contrast increase contouring variability with MVCT than with kVCT, lack of artefacts on MVCT could provide better image definition by this modality in hip prosthesis patients in whom MRI is precluded.

Advances in knowledge: We recommend the fine modality MVCT for contouring hip prostheses patients.

INTRODUCTION

Either alone or associated with hormonal therapy, radiotherapy (RT) is commonly used as radical treatment for prostate carcinoma, the incidence of which has risen with population ageing. Since patients are usually elderly at diagnosis, they are often affected by comorbidities and may have hip prostheses.¹

Today, the standard RT approach is three-dimensional conformal RT, although advanced techniques such as intensity-modulated RT, volumetric RT, tomotherapy and image-guided RT² are becoming widespread, allowing protocols with dose escalation and hypofractionated schedules.³ With all these new techniques, treatment planning, which is

based on conventional kilovoltage CT (kVCT) images, requires precise definitions of target volumes and organs at risk (OARs) of toxicity. In areas such as the pelvis, however, relatively poor soft-tissue contrast prevents kVCT from providing precise definition of target volume extension. The consequent interobserver and intraobserver variations in delineation can be overcome by using MRI.⁴

Target volume definition with kVCT is even more difficult in patients with metallic hip prostheses because of the artefacts such as blurring and streaming which are caused by high-Z material. Although use of MRI would overcome the artefacts⁵ and provide better visualization of the prostate and other pelvic organs, MRI is precluded

Figure 1. Study design. kVCT, kilovoltage CT; MVCT, megavoltage CT.

in patients with ferrous prostheses because its static magnetic field may induce movement and its radio frequencies may overheat metallic prostheses. Indeed, Ebraheim *et al* even suggested replacing older prostheses with modern titanium in order to overcome the artefact issue.⁶ Ling *et al* and Wang *et al* proposed different image windowing techniques⁷ or algorithms⁸ to suppress data from the beam passing through the prosthesis and to reconstruct missing images by extrapolating data from other irradiated areas.⁸ Atlas-based autosegmentation techniques⁹ were developed to improve the definition of target organs and OARs. The use of megavoltage CT (MVCT) is another option in RT centres that are equipped with tomotherapy.¹⁰ Consequently, when tomotherapy units are available, volumes in patients with prostate tumours and hip prostheses are defined by means of integrated MVCT images.

To our knowledge, since no reports have compared kVCT, MRI and MVCT image quality and assessed the impact of MVCT on contouring in patients with bilateral hip prostheses, this study attempted to fill this gap.

Figure 2. Prostate contouring by six radiation oncologists. (a) Kilovoltage CT images of patients without hip prostheses; (b) MRI in patients without hip prostheses; (c) kilovoltage CT images of patients with hip prostheses; (d) fine megavoltage CT in patients with hip prostheses.

Table 1. Kilovoltage CT in Patient 1 without prosthesis

Organs (volumes in cm ³)	Operator 1	Operator 2	Operator 3	Operator 4	Operator 5	Operator 6	Average	SD	CI	CV
Prostate	55.17	49.50	47.64	53.80	48.71	49.05	50.65	3.07	0.59	6.06
Rectum	63.77	67.41	73.05	55.76	67.49	57.11	64.10	6.65	0.84	10.37
Bladder	293.18	287.06	277.05	288.40	300.88	297.12	290.62	8.44	0.56	2.90

CI, conformity index; CV, coefficient of variation; SD, standard deviation.

Table 2. MRI in Patient 2 without prosthesis

Organs (volumes in cm ³)	Operator 1	Operator 2	Operator 3	Operator 4	Operator 5	Operator 6	Average	SD	CI	CV
Prostate	48.97	49.98	53.09	55.03	51.97	48.29	51.22	2.60	0.78	5.08
Rectum	78.87	62.36	65.17	60.66	61.85	73.24	67.03	7.37	0.87	11.00
Bladder	249.73	242.15	240.37	242.30	243.28	246.25	244.01	3.40	0.64	1.39

CI, conformity index; CV, coefficient of variation; SD, standard deviation.

METHODS AND MATERIALS

This study recruited three patients with a histologically confirmed diagnosis of low-risk intracapsular prostate carcinoma who were candidates for RT alone. Disease was staged by a transrectal ultrasound scan in all three patients and by MRI with surface coil in Patients 1 and 2. As the Roach formula indicated a low risk of seminal vesicle involvement (<15%) in all patients, no seminal vesicle treatment was needed. Patients 1 and 2 did not have a prosthesis and served as controls. They were randomly selected as they were referred to us in the same time period as Patient 3 who had bilateral hip prostheses.

The impact of kVCT, MRI and MVCT images on contouring was analysed by interobserver variability in three regions of interest (ROIs): prostate, rectum and bladder. Contouring was carried out on kVCT images in Patient 1, on MRI images in Patient 2 and on kVCT and MVCT images in Patient 3. The study design is reported in Figure 1. Treatment planning steps were as follows.

Image acquisition

30 min before image acquisition, all patients drank 1 l of water to ensure that they had a full bladder; they were then placed in the supine position and immobilized by knee and foot supports (Combifix®; Novater Unipersonale, Italy). Urethrography identified the prostatic apex in each patient.

The kVCT scan (Aquilion® OKS16; Toshiba Medical Systems Corporation, Otawarashi, Japan) was performed without contrast medium (5-mm slice thickness and step). MRI (Achieva® 3.0 T; Philips Healthcare) was performed without contrast medium using a T_2 sequence. MVCT images were acquired in three different scans: fine (2-mm), normal (4-mm) and coarse (6-mm) slice thicknesses. Bladder filling and rectal dilation were checked on all images. If filling was inadequate or dilation excessive owing to air or faeces, scans were repeated after the patient had drunk more water or undergone an enema. A rectal balloon was never used.

For each MVCT scan, a cylindrical solid water phantom, aligned along the tomography central axis, was used to estimate the patient's absorbed dose. The dose to the phantom was measured in the phantom's central axis by an ionizing camera (Standard Imaging A1SL; Standard Imaging Inc., Middleton, WI).

Images were transferred to a treatment planning system (TPS Pinnacle3 v. 9.0; Philips Medical Systems, Fitchburg, WI) for contouring.

Contouring

All ROIs (prostate, rectum and bladder) were contoured on kVCT (Patient 1, no prosthesis and Patient 3 with prostheses), MRI (Patient 2, no prosthesis) and MVCT (Patient 3 with prostheses) by six radiation oncologists (LE, IP, FA, VL, GM, FM) who had all worked in pelvic area contouring for several years (range: 4–15 years). They were blinded to the staging images and their colleagues' contouring plans. Figure 2 illustrates the prostate as contoured by the six radiation oncologists using the various imaging modalities in patients with and without hip prostheses. The entire rectum with its internal air is contoured.

Statistical analysis

The conformity index (CI) and the coefficient of variation (CV) assessed the impact that the image had on interobserver variability. The CI, which expresses agreement between contoured volumes, is derived from the relationship between intersection of segmented volumes and their union ($V_1 \cap V_2 \cap V_n / V_1 \cup V_2 \cup V_n$).¹¹ A high CI indicates good agreement and consequently low interobserver variability. The CV, which measures error, derives from the standard deviation expressed as a percentage of the mean.¹¹ A high CV indicates strong disagreement and consequently high interobserver variability. The Friedman test followed by Conover *post hoc* analysis compared kVCT volumes with each of the MVCT slice modalities (fine, normal and coarse).

Table 3. Kilovoltage CT in Patient 3 with hip prostheses

Organs (volumes in cm ³)	Operator 1	Operator 2	Operator 3	Operator 4	Operator 5	Operator 6	Average	SD	CI	CV
Prostate	39.52	23.22	33.93	61.81	35.80	43.39	39.61	12.83	0.24	32.39
Rectum	130.91	174.04	128.29	123.39	112.77	82.23	125.27	29.77	0.54	23.76
Bladder	184.55	199.66	143.00	142.11	203.88	175.83	174.84	26.98	0.35	15.43

CI, conformity index; CV, coefficient of variation; SD, standard deviation.

Table 4. Fine (2-mm) megavoltage CT in Patient 3 with hip prostheses

Organs (volumes in cm ³)	Operator 1	Operator 2	Operator 3	Operator 4	Operator 5	Operator 6	Average	SD	CI	CV
Prostate	25.16	22.03	16.89	20.11	20.72	24.35	21.54	3.02	0.34	14.02
Rectum	95.43	175.92	80.87	89.77	125.40	77.44	107.47	37.62	0.54	35.01
Bladder	153.80	136.05	105.25	153.59	163.96	150.74	143.90	20.96	0.35	14.57

CI, conformity index; CV, coefficient of variation; SD, standard deviation.

RESULTS

Tables 1 and 2 report volumes expressed in cubic centimetres, as contoured by the six radiation oncologists, as well as CI and CV in Patients 1 and 2 without hip prosthesis (controls). Contouring was performed on kVCT images in Patient 1 (Table 1) and on MRI in Patient 2 (Table 2). Prostate and bladder CIs were higher and CVs were lower in MRI than in kVCT contouring, suggesting interobserver variability was less with MRI images. No variations were seen in rectal contouring.

Table 3 reports volumes, CI and CV for prostate, rectum and bladder in Patient 3 with hip prostheses as contoured by six radiation oncologists on kVCT. Compared with kVCT contouring in Patient 1, the CI was lower and the CV was higher in all ROIs (prostate, rectum and bladder). The differences were more marked in the prostate, indicating increased interobserver variability.

Tables 4–6 show prostate, rectum and bladder contouring on MVCT, CI and CV in Patient 3 with prostheses according to the three MVCT modalities (fine, Table 4; normal, Table 5; coarse, Table 6). Compared with kVCT contouring on the same patient, interobserver variability was reduced only for prostate delineation with the fine modality, as shown by the higher CI.

Figure 3 illustrates CI and CV patterns in each organ according to each imaging modality (a: prostate; b: rectum; c: bladder). As the CI rises, the CV drops because low interobserver variability is expressed by high CI and low CV values.

When kVCT volumes were compared with each of the MVCT slice modalities (fine, normal and coarse) in Patient 3, significant differences emerged for each slice thickness (fine MV, $p = 0.0009$; normal MV, $p = 0.0017$; coarse MV, $p = 0.0416$).

Finally, the absorbed dose in MVCT images acquired for contouring in Patient 3 with hip prostheses was <2.5 cGy with the fine modality, <1.5 cGy with the normal modality and <1 cGy with the coarse modality.

DISCUSSION

The present study was designed because a patient with hip prostheses who was a candidate for radical RT for prostate cancer was referred to the Radiation Oncology Division of Perugia General Hospital for radiation treatment. As a tomotherapy unit is available, we evaluated the impact of different imaging modalities on the definitions of target volume and OAR in this patient.

Since our first step was to assess interobserver variability, six radiation oncologists in our institution contoured the prostate, rectum and bladder on kVCT and MRI images (which are recognized as producing best definition images¹²) in patients with prostate cancer without prosthesis who were also candidates for RT (Patients 1 and 2). Contouring on Patients 1 and 2 prevented our team of radiation oncologists from being influenced by repeat contouring on the same patient.

Contouring on kVCT in a patient without prosthesis (Patient 1) showed interobserver variability for prostate volume, which was slightly higher than that previously reported¹³ probably because only one patient was contoured. MRI, as used in Patient 2, reduced interobserver variability (MRI: CI and CV 78% and 5.08, respectively, vs kVCT: 59% and 6.06, respectively) because it overcomes the limitations of similar electronic densities in the prostate¹⁴ and surrounding pelvic organs and tissues.¹⁵ The advantages of MRI were less marked with rectum and bladder contouring. Confirming other observations,¹³ interobserver variability did not drop with bladder contouring because variability is, in any case, very low as a large bladder volume minimizes differences.

When kVCT was used in the patient with hip prostheses (Patient 3), interobserver variability was great for all contoured volumes. It was greatest in the prostate, probably because hip-related artefacts were concentrated in the prostate anatomic space between the left and right prostheses. MVCT reduced interobserver variability only for the prostate volume and only when “fine” mode was used. Normal and coarse acquisition did

Table 5. Normal (4-mm) megavoltage CT in Patient 3 with hip prostheses

Organs (volumes in cm ³)	Operator 1	Operator 2	Operator 3	Operator 4	Operator 5	Operator 6	Average	SD	CI	CV
Prostate	18.81	23.82	19.29	24.41	18.49	18.99	20.64	2.71	0.18	13.13
Rectum	98.75	181.20	95.79	106.66	105.51	113.92	116.97	32.10	0.58	27.44
Bladder	169.75	165.86	133.92	173.50	175.95	166.68	164.28	15.37	0.31	9.36

CI, conformity index; CV, coefficient of variation; SD, standard deviation.

Table 6. Coarse (6-mm) megavoltage CT in Patient 3 with hip prostheses

Organs (volumes in cm ³)	Operator 1	Operator 2	Operator 3	Operator 4	Operator 5	Operator 6	Average	SD	CI	CV
Prostate	25.81	21.97	24.93	24.73	28.16	32.06	26.28	3.46	0.11	13.17
Rectum	119.63	211.37	128.47	131.22	129.30	197.07	152.84	40.25	0.58	26.33
Bladder	202.34	213.96	158.41	202.62	222.26	213.19	202.13	22.71	0.38	11.24

CI, conformity index; CV, coefficient of variation; SD, standard deviation.

not impact upon interobserver variability, probably because thicker slices produced less detailed images, particularly for the craniocaudal volume extensions. MVCT has already been

Figure 3. Pattern of conformity index (CI) and coefficient of variation (CV) in each organ according to each imaging modality (a: prostate; b: rectum; c: bladder). Numbers in abscissa represent patients as follow: (1) Patient 1 without hip prostheses subjected to kilovoltage CT (kVCT); (2) Patient 2 without hip prostheses subjected to MRI; (3) Patient 3 with hip prostheses subjected to kVCT; (4) Patient 3 with hip prostheses subjected to megavoltage CT (MVCT) “fine”; (5) Patient 3 with hip prostheses subjected to MVCT “normal”; (6) Patient 3 with hip prostheses subjected to MVCT “coarse”.

recognized as providing the best images of pelvic ROI in patients with hip prostheses.¹⁶

How MV and kV X-rays interact differently with matter may account for present findings. MV X-rays interact predominantly through the Compton scatter mechanism which depends on mass density rather than atomic number Z , whereas the predominantly photoelectric kV X-ray interactions are strongly linked to the atomic number Z .³ Consequently, MVCT images are less able to differentiate small changes in Z but are not susceptible to the high- Z streaking artefacts, such as hip prosthesis.

Therefore, although contouring variability with MVCT images is greater than with kVCT images because of increased noise and reduced soft-tissue contrast,¹⁷ lack of artefacts provided better image definition and a smaller margin of error¹⁰ in a patient with hip prosthesis. Even though dose distribution calculations were beyond the scope of this article, it is worth noting that MVCT also reduced the margin of error by up to 70% in the Hounsfield unit calculations.^{10,18}

When MVCT is calibrated by means of the “CT to density table”, it provides a more accurate dose calculation than kVCT with artefacts as artefacts need to be contoured and their density values assigned before proceeding with kVCT dose calculation.^{19,20}

CONCLUSION

To our knowledge, this is the only study which investigated interobserver variability with kVCT, MRI and MVCT and established whether MVCT slice thickness impacted upon it. Since fine modality MVCT reduced interobserver variability in prostate contouring in the patient with hip prostheses, we recommend this approach in this subset of patients. No clear advantage emerged with any modality for rectum and bladder contouring. The main limitation of the present study is that results refer to only three patients and need to be validated in a larger number of patients. Patients with prostheses could be prospectively enrolled in a multicentre study that shares MVCT and kVCT images in order to assess interobserver variability more accurately. It would also be interesting to compare interobserver variability in the presence of bilateral and unilateral prostheses.

Any new study will need to use the MVCT v. 2.0 software (TomoTherapy Inc., Madison, WI) which offers a 1-mm slice interval for fine acquisition that might improve the longitudinal display resolution, with no impact on scan time or patient dose. It remains to be seen whether it improves image quality and reduces interobserver variability.

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