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Original Article

Optimising the use of virtual and conventional simulation: a clinical and economic analysis

M. McJury[1], B. Foran[2], J. Conway[1], S. Dixon[3], K. Wilcock[4], G. Brown[4], M.H. Robinson[4]

[1]*Department of Radiotherapy Physics, Weston Park Hospital, Sheffield, UK,* [2]*Department of Radiation Oncology, Weston Park Hospital, Sheffield, UK,* [3]*School of Health and Related Research (ScHARR), University of Sheffield, UK,* [4]*YCR Department of Clinical Oncology, Weston Park Hospital, Sheffield, UK*

Abstract

Background and purpose: Currently, optimal use of virtual simulation for all treatment sites is not entirely clear. This study presents data to identify specific patient groups for whom conventional simulation may be completely eliminated and replaced by virtual simulation.

Sampling and method: Two hundred and sixty patients were recruited from four treatment sites (head and neck, breast, pelvis, and thorax). Patients were randomly assigned to be treated using the usual treatment process involving conventional simulation, or a treatment process differing only in the replacement of conventional plan verification with virtual verification. Data were collected on set-up accuracy at verification, and the number of unsatisfactory verifications requiring a return to the conventional simulator. A micro-economic costing analysis was also undertaken, whereby data for each treatment process episode were also collected: number and grade of staff present, and the time for each treatment episode.

Results: The study shows no statistically significant difference in the number of returns to the conventional simulator for each site and study arm. Image registration data show similar quality of verification for each study arm. The micro-costing data show no statistical difference between the virtual and conventional simulation processes.

Conclusions: At our institution, virtual simulation including virtual verification for the sites investigated presents no disadvantage compared to conventional simulation.

Keywords

CT; imaging; radiotherapy; virtual simulation

INTRODUCTION

Virtual simulation (VS) in radiotherapy is a process in which acquired computed tomography (CT) localisation data (used alone, or as part of a registered multi-modality image dataset) are used to construct a 'virtual' patient. The target and organs at risk (OAR) can then be marked up, beam portals can be applied and the data sent to a treatment planning system (TPS) for further planning aspects such as dose calculation. VS can be used to its full potential, when

Correspondence to: Mark McJury, Department of Medical Physics, Northern Ireland Cancer Centre, Belfast City Hospital Trust, Lisburn Road, Belfast, Northern Ireland BT9 7AB, UK. E-mail: mark.mcjury@mpa.n-i.nhs.uk

the planning data are returned to the system for virtual verification: the treatment plan is verified by generating high-quality DRRs (digitally reconstructed radiographs) of beam portals and comparing these with portal images acquired at or prior to the first treatment fraction.[1–4] This virtual verification may also be performed on systems other than the virtual simulator, for example some record and verify systems such as VARiS (Varian Medical Systems, Palo Alto).

Virtual patient verification offers a number of potential advantages, both from a patient and departmental point of view. It offers the possibility of immediately eliminating an entire patient visit, with associated savings in terms of staff time and cost, transport costs, equipment use and consumables. Additionally, in many radiotherapy centres, patients can be treated on one of a number of linacs, which are supplied by a single conventional simulator, which must verify all patients, potentially creating an organisational 'bottle-neck' at the simulator. This issue can be resolved with VS being done with portal imaging on the linac set in question for each patient, and therefore has potential for shortening waiting times (the time delay to the start of first treatment). In terms of set-up accuracy, it also eliminates an additional setup on the conventional simulator couch, instead verifying on the treatment couch to be used throughout the patients' treatment. If used as the sole means of simulation (i.e. without any conventional simulation (CS)), it offers a process with fewer transfer errors (systematic differences between setup at verification and setup at treatment).[5]

Some authors have reported no loss of set-up accuracy when switching from conventional to VS.[4,6,7] In fact, VS can result in the increased accuracy of target definition, and in the case of simulator-planned patients, smaller fields being marked up by clinicians for the treatment for certain sites.[8] Another advantage of VS and CT planning is the ability to produce dose–volume histograms to define the dose received to various structures, including OAR and the planning target volume. Previous work has shown that there is very little difference in the cost of CS and VS. (Dixon S., personal communication, 2000).

At this point, it is not clear whether current technology allows CS to be completely replaced by VS for all tumour sites. Some authors report positive experiences with virtual-only simulation, but report only on one or two sites.[7,9,10] Others remain unconvinced and recommend proceeding with caution.[11] VS and CS are very different in how they work and the images and quality they produce. CS will generate high-contrast diagnostic energy verification images, and of course allows for the opportunity to screen during patient breathing, enabling a clinician to assess target/organ motion and adjust margins accordingly. CS is poor at visualising certain critical structures, for example, nodes in the chest compared with VS. VS will involve the use of comparatively low-contrast MV energy portal images for verification, although currently the use of amorphous silicon flat-panel imagers does enable the acquisition of significantly higher quality portal images. DRR quality is dependent on, among other parameters, the slice thickness of the source CT data. Successful verification will require the acquisition of high-quality DRRs, with narrow slice thickness, preferably $\leq$5 mm. With the advent of the current generation of multi-slice CT scanners, this is possible in acceptable scan times, and current processing power has little problems with reconstruction and processing high resolution DRRs. Localisation using standard helical scanning protocols, however, are less useful for assessing motion due to breathing, for example, and data tend to represent images acquired randomly throughout the breathing cycle. Currently, there are increasing options to optimise scan protocols, such as breath-hold imaging, physiologically/respiratory-gated scanning, and others such as slow scanning where 'blurring-out' the effects of breathing hopes to show the maximal extend of organ motion.[12]

At Weston Park Hospital, although VS has been part of the treatment process for many years, all patients return to the conventional simulator for plan verification, which obviously requires the use of both virtual and conventional simulator equipment and processes. This study was undertaken to identify patient groups for whom CS may be completely eliminated and replaced by VS, to optimise the use of CS and VS. The study recruited patients from the

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major radical treatment sites (breast, head and neck, pelvis and thorax), and the patients were randomly assigned to be treated using the usual treatment process involving CS, or a treatment process differing only in the replacement of CS with VS. Current practice at Weston Park Hospital is to include a CS episode for all patient treatments. Data were collected on set-up accuracy at verification, numbers of unsatisfactory verifications, and time and motion data for each treatment process episode for each study arm. The study highlights differences between CS- and VS-only treatment processes in terms of accuracy, and impact on departmental workload and work processes for the four major tumour sites.

METHOD

Patients undergoing radical radiotherapy with CT planning were recruited by consent to this randomised prospective trial. Two hundred and sixty patients were recruited into the study. During the study, 36 patients withdrew from the study and 8 had significant missing data. The trial includes the four most common sites treated at the hospital: head and neck (76), thorax (39), pelvis (55) and breast (46). Patient selection criteria: all patients having radical external beam treatment with CT planning were considered. They must be physically able to undergo CT scanning (weight and girth can result in some exclusions) and be able to consent. Patients undergoing head and neck treatments with bilateral anterior neck fields were excluded as this technique is currently marked up by the clinician at the time of verification of the planned fields in the conventional simulator. The study protocol was approved by the local research ethics committee and voluntary informed consent was obtained from all patients before inclusion in the study.

The patients followed a treatment process comprising four episodes: CT scanning (Picker PQS CT) and mark up by an oncologist for tumour localisation (performed on the Philips AcQSIM workstation), 3D conformal treatment planning (Varian Eclipse TPS), treatment verification by set-up comparison with DRRs generated from the planned beam portals (DRRs generated in AcQSIM) and delivery of external beam treatment (Varian Clinacs 600 and 2100 with either 6 or 6 + 10 MV photons). The treatment techniques used were those standardised at our institution. Our standard practice is to verify all patients on the conventional simulator (Varian Ximatron or Acuity) with clinicians comparing the DRR image with an acquired simulator image (generally an anterior and/or lateral beam). Our tolerances for an acceptable setup are a deviation of $\leq$5 mm for immobilised patients, and $\leq$10 mm for unimmobilised patients. Standard anterior/posterior, lateral films and beam's-eye-views are acquired for ongoing comparisons. Over the duration of the study, a newer Acuity simulator replaced the Ximatron, and is fitted with an amorphous silicon (aSi) detector panel.

Following recruitment to the study, patients were randomised to be verified with either virtual or CS. The process for each trial arm was identical, except for the verification episode: in the CS trial arm, verification was undertaken on the conventional simulator; in the VS arm, it was performed on the treatment set prior to the first fraction of treatment. To assess financial and workload implications of each process, the duration and staff present at each episode of the treatment process was recorded. In the VS trial arm, failures at verification on the treatment set were returned to the CS for set-up checks and all details of changes made were recorded. Failure of set-up at verification might occur for one of two reasons: the set-up is found to be out of tolerance, or the acquired images are of insufficient quality to enable the clinician to have confidence in the accuracy of patient setup. If the setup is altered, the acquired simulator image will then replace the planning DRR as the gold standard for comparison henceforward. Weekly portal images were acquired, and were registered with reference images (conventional simulator films or DRRs) to enable the assessment of the accuracy of each trial arm.

Failure at verification can happen due to inadequate visualisation of fixed bony landmarks rendering the confident acceptance of an accurate patient setup impossible. This is a more likely occurrence for patients on the VS trial arm

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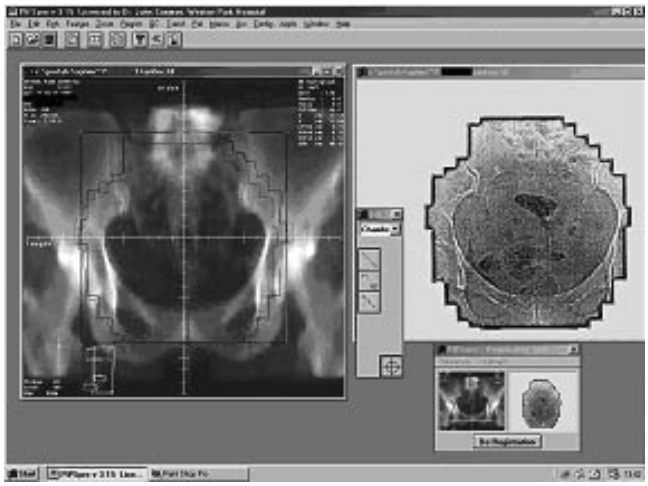

Figure 1. Workspace of the PIPSpro (Standard Imaging) 2D image registration package. The treatment image on the right is an amorphous silicon portal image (Varian PortalVision), registered to a planned beam portal shown as a digitally reconstructed radiograph on the left (AcQSIM). Field outlines and anatomy have been defined by the user.

having verification involving portal images. Portal images routinely used are either standard hardcopy films (Kodak XV) or digital images acquired using the Varian PortalVision system. The clinician accepts or rejects the verification by comparing the acquired verification image and DRR/sim film by eye on a standard lightbox. This was used as an endpoint in the study, but additionally, retrospective quantitative 2D image registration was also performed using the PIPSpro package, see Figure 1 (Standard Imaging Inc.). DRRs were imported from the VARiS/Vision database and simulator films digitised on a VIDAR scanner (Vidar Systems Corp.) and imported. When the user had defined the field edges and fixed anatomical landmarks, either manually or automatically using an edge-detection tool (using manually positioned fiducial marking points or manually drawn lines/curves following bony anatomy) PIPSpro automatically registered the images using a chamfer matching algorithm. PIPSpro gives results in the form of the deviation of the isocentres of the two fields in terms of 2D x and y distances in mm, and will also output the consequent areas of overlap of the two fields in terms of over- and under-coverage of the reference 'target' field.

A micro-costing study was undertaken, whereby the time of each treatment episode was recorded together with number and grade of staff present. Four different types of care episode were identified; CT scanning, planning, verification and treatment.

Unit cost data were requested from Weston Park Hospital, and cost per minute were calculated for consultants/registrars, MTOs (various grades), radiographers (various grades) and different types of machines. These costs (at 2004/5 price levels) include allowances for support staff and other Trust overheads. Although the costs are around 2 years old, our comparisons made using these costs remain valid.

Once the mean costs and the associated distributions were known for each episode type, the full cost of treatment for a 30 fraction schedule was modelled probabilistically, incorporating the passbacks (return to conventional simulator for setup check) from the main clinical study. Any passback required the addition of a conventional verification to the treatment schedule.

RESULTS

Table 1 shows the number of cases returned to the conventional simulator following unsatisfactory verification, for each study arm. The VS

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Table 1. *Rates of patient returns to simulator (passbacks) for setup check, following unsuccessful verifications. The data show ratios of returns out of the total number of cases, with the corresponding percentages*

	Head and Neck	Breast	Thorax	Pelvis
Conventional simulation	2/38 (5.2%)	2/23 (8.7%)	1/20 (5.0%)	0/28 (0%)
Virtual simulation	8/39 (20.5%)	1/23 (4.3%)	4/19 (21.1%)	2/27 (7.4%)

Table 2. *The results of image registration of verification images and reference planned images (DRRs or simulator films)*

	Conventional Simulation		Virtual Simulation	
	Mean (mm)	SD	Mean (mm)	SD
	($n = 38$)		($n = 38$)	
Head and neck				
Right/left	1.6	2.1	0.8	2.9
Superior/inferior	−0.5	1.2	−0.4	2.1
Rot. (°)	0.5	1.9	0.1	1.7
	($n = 23$)		($n = 23$)	
Breast				
Right/left	0.5	3.8	−1.8	3.3
Superior/inferior	−0.4	3.0	−0.9	2.6
Rot. (°)	0.0	2.2	0.0	5.1
	($n = 20$)		($n = 19$)	
Thorax				
Right/left	−0.1	2.0	−0.5	3.4
Superior/inferior	−0.4	3.1	−0.5	2.3
Rot. (°)	0.0	2.8	0.0	1.5
	($n = 28$)		($n = 27$)	
Pelvis				
Right/left	−0.2	2.8	−0.9	8.1
Superior/inferior	0.5	2.9	−2.5	6.8
Rot. (°)	0.0	1.5	1.0	1.7

DRR = digitally reconstructed radiographs; SD = standard deviation.
Note: Shown are the deviations in millimetre along the horizontal or vertical image axis on anterior/posterior images corresponding to right/left and superior/inferior axes respectively. Any image rotation (Rot.) deviation in degrees is also shown.

study arm shows raised numbers of returns to the simulator for the majority of sites (excluding breast). As expected perhaps, these differences are larger for some sites (head and neck, thorax), than for others (breast, pelvis). However, for each site these differences are not statistically significant (Fisher Exact test) showing the virtual simulator to be statistically as accurate in setup as the conventional simulator.

Results from the image registration of verification images with planned reference images are shown in Table 2. Data are shown for the deviation between the isocentres of the pairs of images along the two orthogonal axes, and for any rotation of the verification images with respect to the reference planned image. Only anterior/posterior images have been included in this analysis, so deviations are along the right/left or superior/inferior directions. For the head and neck, breast and thorax (Table 2) sites, image registration data show all image verifications well within our setup tolerances. There is also no statistical difference between

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Table 3. *Time analysis data*

	Head and neck		Breast		Thorax		Pelvis	
	Time (min)	SD	Time (min)	SD	Time (min)	SD	Time (min)	SD
Conventional simulation	16.8	3.9	15.6	5.1	16.1	5.0	14.3	3.8
Virtual simulation	17.4	6.4	17.8	4.9	18.1	6.6	19.9	7.5

SD = standard deviation.
Note: Time for the verification episodes for each study arm and site. Case numbers remain the same as for Table 2.

Table 4. *Cost of each type of care episode by treatment group*

	Cost of technician time Mean (£)	Cost of radiographer time Mean (£)	Cost of doctor time Mean (£)	Cost of equipment Mean (£)	Total cost Mean (£)
Virtual simulation					
CT	11.33	23.00	0.94	24.71	59.98
Planning	52.31	0.00	0.13	0.00	52.44
Verification and fraction	7.88	31.67	3.01	43.34	85.89
Fraction	0.00	13.98	0.00	22.98	36.97
Conventional simulation					
CT	12.27	23.85	0.12	25.47	61.72
Planning	52.27	0.14	0.00	0.00	52.90
Verification	10.44	24.28	6.98	21.74	63.33
Fraction	0.00	13.34	0.00	23.64	37.98

CS and VS study arms for these sites. The pelvic site (Table 2) does, however, show a statistical difference between CS and VS image registration along the superior/inferior direction ($p = 0.05$, Wilcoxon rank sum test, two tailed). It is unclear why there should be a significant difference for this particular site and orientation and this may relate to insufficient cases Though differences are shown, the deviation for the VS pelvis patients is still well within the setup tolerance limit (10 mm for unimmobilised patients).

Table 3 shows the time analysis data for each site. There is a large range in the mean time for the verification episode (13.6–23.7 min). The standard deviations similarly show a sizeable range, evidence that some sites are widely variable in terms of verification time on a patient-to-patient basis compared with others. There is, however, no statistical difference between each arm of the study in terms of verification episode time.

The micro-costing study used episode data from 211 patients (5 patients had incomplete costing data), covering 871 episodes of care ($n = 463$ VS group, $n = 408$ CS group). When considering the number of staff, staff grades and staff time, there appeared to be little difference between the two techniques, except perhaps for a small increase in radiographer time associated with VS. This is reflected in the estimated costs of each type of care episode (Table 4). When the full treatment schedule of 30 fractions is modelled using the estimated care costs (Table 4) and passback rates (Table 1), this produces total costs of £1,320 and £1,316 for conventional and VS, respectively; a mean difference of £4 (95% CI: −£1,070 to +£1,043) (see Appendix). This reflects practice as part of the trial, where VS and the first fraction were undertaken at separate patient visits. VS has the potential to be undertaken at the same time as the first treatment fraction, thereby reducing costs further. This can be approximated by calculating the cost of a 29 fraction schedule of VS, which produces a cost of £1,279 and a mean cost reduction of £41 (95% CI: −£950 to +£1,170) (see Appendix). This represents a potential cost saving for VS. The cost of a CS episode was calculated at a value

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of £63, so the VS cost saving represents a significant fraction of this, and may be a larger fraction once VS is an established departmental process.

DISCUSSION

This work has presented results of a comparison of virtual and CS based on 216 patients from four treatment sites, to enable the optimisation of the use of VS in the radiotherapy treatment process. Virtual simulation appears to offer no disadvantage in terms of a satisfactory verification – based on accuracy, image quality and time to perform.

Verification accuracy is similar for both study arms, having been confirmed by quantitative image registration results. Both study arms also recorded similar numbers of successful verifications (based on number of returns to the CS for checks). Obviously, this is dependent on the quality of portal imaging available. At Weston Park Hospital, amorphous silicon (aSi) portal imagers, which have been suggested as having replaced film as the gold standard for portal imaging[13] are available on four of five of the linacs. In Table 1, differences in passback rates for each arm of the study, reach 16.1%. Although not small, they are not found to be statistically significant. These non-negligible differences in rates, and retention of the null hypothesis may relate to small case numbers.

Verification on the linac appears to take no longer than conventional verification episodes on the conventional simulator (some departments have indeed reported time savings with VS episodes[14,15]).

Although intuitively one might expect some tumour sites to have comparatively higher rates of unsatisfactory verification, for example thorax, where breathing motion can degrade image quality, this study shows in fact that all sites investigated (head and neck, breast, pelvis and thorax) can achieve satisfactory routine VS verification and indeed VS represents an opportunity to miss out on an additional patient setup and inclusion of a potential additional setup error. Several technical developments over the last few years have perhaps aided in achieving more confidence in on-set verifications. New aSi flat-panel portal imagers offer significantly improved the quality of megavoltage images. Current VS systems offer increased DRR quality, with sophistications such as ultrasound-style depth-control of reconstructed tissue, and user-defined tissue weighting for optimising contrast of tissue and bone. The current generation of multi-slice CT scanners also enable the acquisition of large volumes of high resolution source data (for high-quality DRRs) in clinically acceptable times.

Very little difference in staffing was identified between the different stages of treatment between the two groups. The biggest differences in cost are higher capital costs for VS (£43 vs £22, Table 4); however, this is more than offset by an effective reduction of one visit for treatment (£37, Table 4). The differential passback rates have little effect at the levels seen in the trial. Overall, the total cost of treatment was £4 less in the VS group, with the potential to reduce costs further, although this was associated with very wide confidence intervals. Additionally, for staff involved, VS verification was a newly introduced process, which would entail initial presence of more senior staff and slightly longer episodes. This would result in higher initial costs for VS patients and costs would be expected to drop once the technique had become established.

CONCLUSION

Results are presented on a study of 216 patients, comparing the use of conventional and VS. For the treatment sites assessed (head and neck, breast, thorax and pelvis), there were no statistically significant differences in the quality of plan verification, based on rates of passback to the simulator for a setup check. An assessment of the verification quality, based on a comparison of image registration errors (deviation between planed reference image and verification image), also show equal accuracy for both study arms. Micro-costing shows no economic disadvantage and in fact a potential advantage for a treatment process involving virtual-only simulation.

At our institution, VS including virtual verification for the sites investigated offers a similar

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quality of verification to CS currently employed. It is therefore possible to omit a conventional simulator verification appointment for these patients.

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References

1. Aird E, Conway J. CT simulation for radiotherapy treatment planning. Br J Radiol 2002;75:937–949.
2. Conway J, Robinson MH. CT virtual simulation. Br J Radiol, 1997;70:S106–S118.
3. Perez CA, Purdy JA, Harms W, et al. Design of a fully integrated three-dimensional computed tomography simulator and preliminary clinical evaluation, Int J Radiat Oncol Biol Phys 1994;30(4):887–897.
4. Buchali A, Dinges S, Koswig S, Rosenthal P, Salk S, Harder C, Schlenger L, Budach V. Virtual simulation. First clinical results in patients with prostate cancer. Strahlenther Onkol, 1998;174(2):88–91.
5. Bel A, Bartelink H, Vijlbrief RE, Lebesque JV. Transfer errors of planning CT to simulator: A possible source of setup inaccuracies? Radiother Oncol 1994;31:176–180.
6. Butker EK, Helton DJ, Keller JW, Hughes LL, Crenshaw T, Davis LW. A totally integrated simulation technique for three-field breast treatment using a CT-simulator. Med Phys 1996;23(10):1809–1815.
7. Valicenti RK, Waterman FM, Corn BW, Curran WJ Jr. A prospective randomized study addressing the need for conventional simulation following virtual simulation. Int J Radiat Oncol Biol Phys 1997;39(5):1131–1135.
8. McJury MJ, Fisher PM, Pledge S, Brown G, Anthony C, Hatton MQ, Conway J, Robinson MH. The impact of virtual simulation in palliative radiotherapy for non-small lung cancer. Radiother Oncol 2001;59:311–318.
9. Bollet MA, McNair HA, Hansen VN, Norman A, O'Doherty U, Taylor H, Rose M, Mukherjee R, Huddart R. Can digitally reconstructed radiographs (DRRs) replace simulation films in prostate cancer conformal radiotherapy? Int J Radiat Oncol Biol Phys 2003;57(4):1122–1130.
10. Van Sornsen de Koste JR, de Boer HC, Schuchhard-Schipper RHS, Heijmen BJ. Procedures for high precision setup verification and correction of lung cancer patients using CT-simulation and digitally reconstructed radiographs (DRRs). Int J Radiat Oncol Biol Phys 2003; 55(3):804–810.
11. Schuller P, Bruns F, Hesselmann S, Horn K, Panke JE, Schuck A, Schafer U, Micke O, Willich N. Simulator verification of the accuracy of patient repositioning after virtual simulation. Is physical simulation still needed? Strahlenther Onkol 2002;178(12):715–721.
12. Lagerwaard FJ, Van Sornsen de Koste JR, Nijssen-Visser MR, Schuchhard-Schipper RH, Oei SS, Munne A, Senan S. Multiple 'slow' CT scans for incorporating lung tumor mobility in radiotherapy planning. Int J Radiat Biol Phys 2001;51(4):932–937.
13. Kruse JJ, Herman MG, Hagness CR, Davis BJ, Garces YI, Haddock MG, Olivier KR, Stafford SL, Pisansky TM. Electronic and film portal images: a comparison of landmark visibility and review accuracy. Int J Radiat Oncol Biol Phys 2002;54(2):584–591.
14. Buchali A, Geismar D, Hinkelbein M, Schlenger L, Zinner K, Budach V. Virtual simulation in patients with breast cancer. Radiother Oncol 2001;59(3): 267–272.
15. Mah K, Danjoux CE, Manship S, Makhani N, Cardoso M, Sixel KE. Computed tomographic simulation of craniospinal fields in pediatric patients: improved treatment accuracy and patient comfort. Int J Radiat Oncol Biol Phys 1998;41(5):997–1003.

Appendix

Incremental cost of virtual simulation over conventional simulation = total cost of treatment incorporating virtual simulation (TC_{virt}) minus total cost of treatment incorporating conventional simulation (TC_{conv}).

$$TC_{virt} = CT_{virt} + Planning_{virt} + Verification_{virt} + (Passback\ Rate \times Simulation_{conv}) + (30 \times Fraction_{virt})$$

$$TC_{virt} = 59.98 + 52.44 + 85.89 + (0.14 \times 63.33) + (30 \times 36.97) = 1{,}316$$

$$TC_{conv} = CT_{conv} + Planning_{conv} + Verification_{conv} + (Passback\ Rate \times Simulation_{conv}) + (30 \times Fraction_{conv})$$

$$TC_{conv} = 61.72 + 52.90 + 63.33 + (0.05 \times 63.33) + (30 \times 37.98) = 1{,}320$$

Incremental cost of virtual simulation over conventional simulation = 1,316 − 1,320 = −4.

For the scenario where the first fraction is given at the same time as VS, incremental cost is calculated in the same way. However, TC_{virt}

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is calculated using only 29 treatment-only fractions. Therefore:

$$TC_{virt} = CT_{virt} + Planning_{virt} + Verification_{virt} + (Passback\ Rate \times Simulation_{conv}) + (29 \times Fraction_{virt})$$

$$TC_{virt} = 59.98 + 52.44 + 85.89 + (0.14 \times 63.33) + (29 \times 36.97) = 1{,}279$$

Incremental cost of virtual simulation over conventional simulation = 1,279 − 1,320 = −41.

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