Journal of Radiotherapy in Practice

Journal of Radiotherapy in Practice 2001
2, 125–132

Original Article

Improving the accuracy of localisation in the radiotherapy treatment of head and neck, and brain cancer: some initial findings

M. J. McJury[1], R. Nakielny[2], D. Levy[3], J. Lilley[4], J. Conway[1], M.H. Robinson[5]

Departments of Radiotherapy Physics[1], Radiation Oncology[3], YCR Clinical Oncology[5], Weston Park Hospital, Whitham Road, Sheffield and Department of Radiology[2], Royal Hallamshire Hospital, Glossop Road, Sheffield and Department of Medical Physics[4], Cookridge Hospital, Leeds.

Abstract

Aims: To investigate the impact on localisation of utilising contrast enhanced computed tomography (CT) scans and the formal input of a radiologist in the radiotherapy planning process.

Method: Ten head and neck / brain patients had pre- and post-contrast CT scans in the treatment position. Over several months, their unenhanced and enhanced scans were re-contoured by the original oncologist, and a radiologist. These new contours were compared to the original unenhanced contours and differences in contour volume, geographical position and tolerance doses on the associated PTVs were evaluated.

Results: The use of contrast lead to significant differences in the size of GTVs. Mean differences in GTVs of 32.8 % were significant at p=0.01. No significant impact on the position of the contour centre was noted. The impact of the radiologist lead to large differences in GTV (mean 20.5 %), but large SDs meant this result was not statistically significant. The contouring precision of the oncologist showed no significant difference for GTVs and PTVs.

Conclusions: The use of contrast when planning the radiotherapy treatment for head and neck/ brain patients was found to lead to significant differences in GTV size, a lesser effect on PTV definition and little impact on the position of the contour centre. It may have important implications for multi-phase treatments where the GTV (rather than the PTV) is targeted for boost doses. Differences due to the input of a radiologist appear to be considerable and require further investigation when additional patient numbers have been acquired to improve precision.

INTRODUCTION

The goal of modern three-dimensional (3D) conformal radiotherapy is to accurately conform dose to the tumour target whilst minimising dose to nearby normal tissue. Failure of loco-regional tumour control is a major factor determining the quality and length of life in many patients undergoing radiotherapy, and is known to be due to biological and technical factors.[1] The first step in the treatment process is localisation of the tumour, usually using radiographic films and/or CT data. Tepper et al.[2] showed that performing a planning CT scan in addition to existing diagnostic information, enabled improvements in target localisation in 49% of patients. In the authors' oncology centre, intravenous (IV) contrast is used routinely in diagnostic CT scanning of patients with head and neck, and brain cancer, however, it is not used when acquiring CT scans for treatment planning purposes. The use of enhanced CT scans can offer improved tumour visibility in many cases and may enable improved localisation for planning.[3] Whilst seemingly obvious, improvements may be available in marking-up visible gross tumour volumes (GTVs), the overall impact on the target or planning target volume (PTV) and general plan quality is unknown. A limited amount of information has been reported on this topic[3,4] especially for head and neck/brain patients.

Correspondence to: Dr M McJury, Department of Radiotherapy Physics, Weston Park Hospital, Whitham Road, Sheffield, UK. Tel: 0114 226 5188; Fax: 0114 226 5521; E-mail: mark.mcjury@sth.nhs.uk

https://doi.org/10.1017/S1460396900000212 Published online by Cambridge University Press

When localising the tumour, the oncologist will mark the visible extent of the tumour, the gross tumour volume (GTV). To this volume, margins are then added to allow for non-visible tumour infiltration. To this volume, margins are then added to allow for non-visible tumour infiltration (resulting in clinical target volume (CTV)) patient movement and set-up inaccuracies, generating a final planning target volume (PTV) to be treated.[5] For this study, PTVs are not marked on directly, but are always generated by adding a uniform 2D margin to the initial GTV. Once generated, the initial PTV may be edited by the clinician to achieve a final PTV contour. This may be necessary, for example, if lesions are close to the skull. In this case, the software-generated PTV may initially extend beyond the skull and requires editing to enclose the contour by the skull. Although a radiologist is the recognised expert in the interpretation of medical images, in many centres (the authors' included) definition of the GTV is performed solely by the oncologist. By requiring the GTV to be defined by a radiologist and the remainder of the marking-up process (definition of the CTV and PTV) to be done by the oncologist, improvements in planning accuracy and outcome may be possible.

This study consists of 25 patients with head and neck or brain tumours of which this is an interim report on 10 cases. It addresses two main questions: (i) Does the use of IV contrast during the acquisition of CT data for treatment planning significantly improve the accuracy of tumour localisation? and (ii) Does the input of a radiologist in marking-up the tumour GTV significantly alter the accuracy of localisation?

The study also aims to address the more general problems facing clinicians involved in the marking-up process. The process of defining tumour targets which may be poorly visible on images, and which entails a clinician combining non-imaging information in the form of medical notes, physical observation/examination and images from more than one modality often acquired in non-treatment set-up, is a subtle and complex task. The study hopes to highlight the impact of these factors on the accuracy and reproducibility (or precision) of localisation.

METHODS

A group of 10 head and neck, and brain patients undergoing CT planning gave informed consent to enter the study. They had pre- and post-contrast CT scans carried out in the treatment position. After administering contrast, the couch was returned to the original position without any patient movement, enabling both scans (unenhanced and enhanced) to be acquired with identical scanner co-ordinates.

GTV and PTV contours were marked-up using the AcQSIM™ virtual simulator (Marconi Medical) on the unenhanced scan and the patients treated based on this scan. After a gap of several weeks, each patient's unenhanced *and* enhanced scans were then retrospectively re-contoured by (i) the original oncologist (A) (to generate data on intra-observer precision), (ii) a second oncologist (B) (to generate inter-observer precision), and (iii) a radiologist. In this way several sets of GTVs and PTVs were generated for each patient (see Table 1). At each contouring session, all previous contours were turned off so the clinician was blinded to all previous work. Any diagnostic films/images and patient notes were made available to the clinician marking-up at each contouring session.

The enhanced studies were registered with the unenhanced, such that contours marked on the enhanced image would be automatically transferred and stored with all previous others already marked on the unenhanced study (Fig. 1). For data sets with identical scanner co-ordinates, image registration was performed automatically by the AcQSIM™ software. The accuracy of this registration is dependent on negligible patient

*Table 1. Contouring timetable. Contours marked with * denote PTVs generated by the oncologist using GTVs defined by a radiologist.*

Doctor	Type	Contour set	Week
Oncologist (A)	Unenhanced	GTV(1)+PTV(1)	1
Oncologist (A)	Unenhanced	GTV(2)+PTV(2)	7
Oncologist (A)	Enhanced	GTV(3)+PTV(3)	13
Oncologist (A)	Enhanced	GTV(4)+PTV(4)	19
Radiologist	Unehnanced	GTV(5) +PTV(5)*	25
Radiologist	Unenhanced	GTV(6) +PTV(6)*	31
Radiologist	Enhanced	GTV(7) +PTV(7)*	37
Radiologist	Enhanced	GTV(8) +PTV(8)*	43
Oncologist (B)	Unenhanced	GTV(9)+PTV(9)	49

https://doi.org/10.1017/S1460396900000212 Published online by Cambridge University Press

movement during scanning. All contours were stored on the unenhanced data set and analysis performed on this data set. As it takes several months to complete the contouring for each patient, for this interim report, a limited set of three contour pairs for each patient will be presented.

The contour data sets have three procedures performed for comparison and presentation in this paper:

To investigate the influence of contrast: a comparison of unenhanced and enhanced contours marked-up by oncologist (A); changes in contour data (volume, tolerance dose and contour centre displacement) are represented as $DGTV_C$, and ΔPTV_C;

To investigate the influence of the radiologist: a comparison of unenhanced contours marked-up by oncologist (A) and the radiologist; changes in contour data are represented as ΔGTV_R, and ΔPTV_R;

To investigate the precision of marking-up by the oncologist: a comparison of the original unenhanced scan contours and the re-contour; changes in contour data are represented as ΔGTV_p, and ΔPTV_p;

In comparing the pairs of contours, three indexes were used.

Geographical changes

Pairs of GTVs were compared to identify any geographical shift of the re-marked contours from the position of the original GTV. On the virtual simulator, shifts between the centres of the GTV contours were measured in three orthogonal axes,

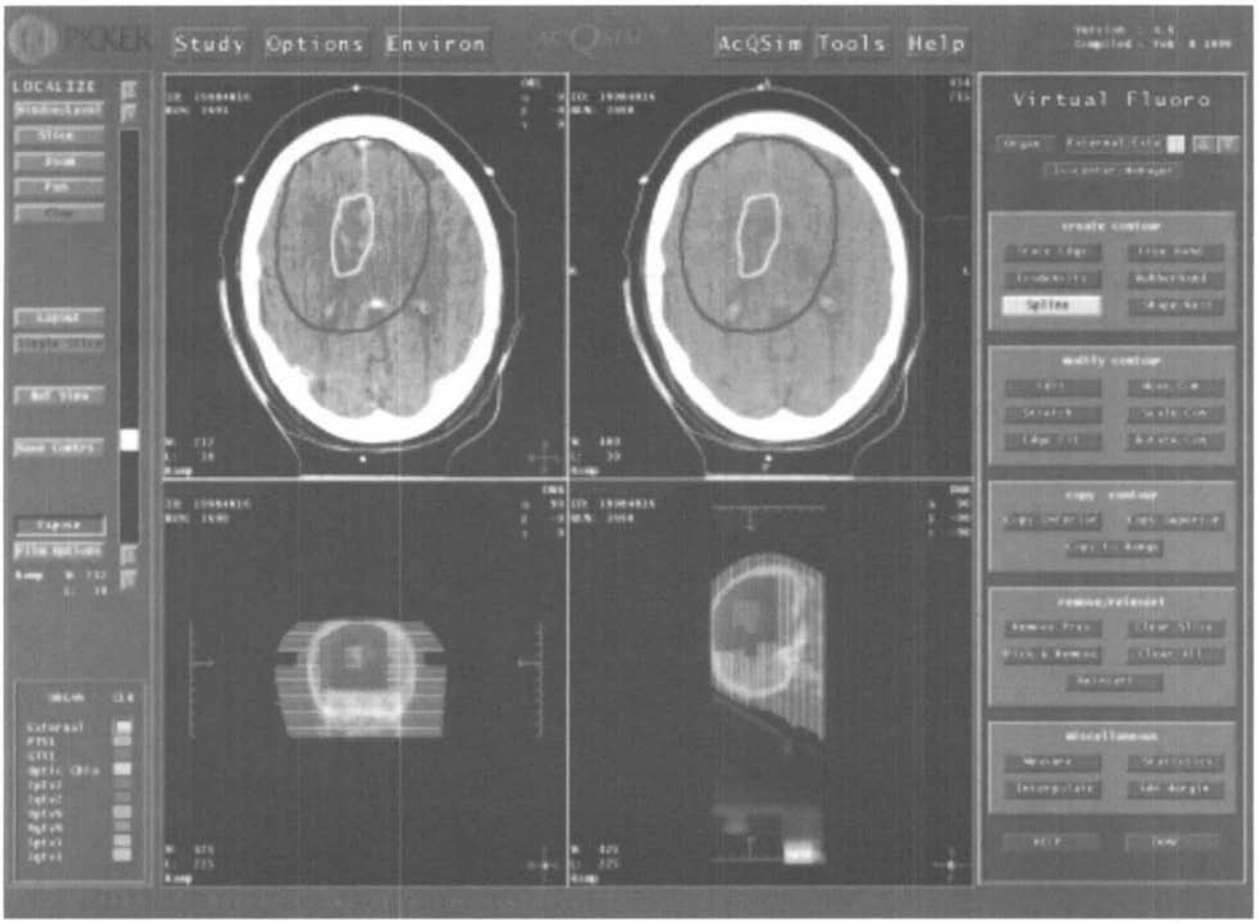

Figure 1. The image fusion workspace showing marked-up contours. If the CT co-ordinates are the same for both scans, enhanced CT data on the left can be automatically fused to the unenhanced data on the right. Contours marked-up on the enhanced scan are then automatically transferred to the unenhanced scan for storage with previous contours. Contours shown are PTV_{unenh} (dark line) and GTV_{unenh} (light line).

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defined as lateral (L), anterior/posterior (A/P) and sup./inf. (S/I) shift. Using the Isocentre Manager on the virtual simulator workstation, the centre of gravity of each GTV was identified automatically. Shifts between centres of GTVs under comparison were then simply found by subtraction of the co-ordinates in the orthogonal axes.

Volume changes

Contour pairs were analysed to identify any changes in the volume of the GTV or PTV contours. All unenhanced patient scans and contours were imported into the CADPLAN™ (Dosetek and Varian Medical Systems) treatment planning system (TPS) and dose volume histograms (DVHs) were generated to yield values for GTVs and PTVs.

Dose changes

In the TPS, the original treatment plan was applied to all sets of contours. Pairs of PTVs (original and re-marked) were then compared in terms of tolerance volumes (TV), i.e. the percentage of the target which is either below 90% prescribed dose (target under-dosing) or above 105% prescribed dose (target overdosing). If, for example, the enhanced target contour is assumed to be the 'true' target, the amount of under- or overdosing the 'true' target will experience can be measured, the original treatment plan (based on the unenhanced target contour) having been applied.

RESULTS AND DISCUSSION

The results are summarised in Figures 2–5. Figure 2 shows the changes in volume for both GTVs and PTVs. It can be seen that the GTV contours experience a greater change in volume than PTVs. Values of ΔGTV_P and ΔPTV_P have mean values of 23.9% and 8.4 % respectively, while ΔGTV_C and ΔPTV_C have mean values of 32.8% and 0.9% respectively. Absolute volume changes show greater differences, with ΔGTV_C having mean 47.7% SD 18.8. These changes due to marking-up on the enhanced images are significant at $p<0.05$ (Wilcoxon signed rank test, two-tailed). GTVs are comparatively small volumes and usually defined over a small number of CT slices. Simply adding one extra slice at the top and/or bottom of the extent of the tumour (where it is often very difficult decide on the final extend of the volume) can alter the volume of the GTV by a considerable percentage. This process will have a much smaller effect on the volume of the much larger PTV (note that the PTVs are defined over approximately 30 slices, while the GTVs are defined over approximately 10 slices). Figure 3 shows these differences more clearly. Here, enhanced studies (left-hand side) are shown fused to unenhanced studies

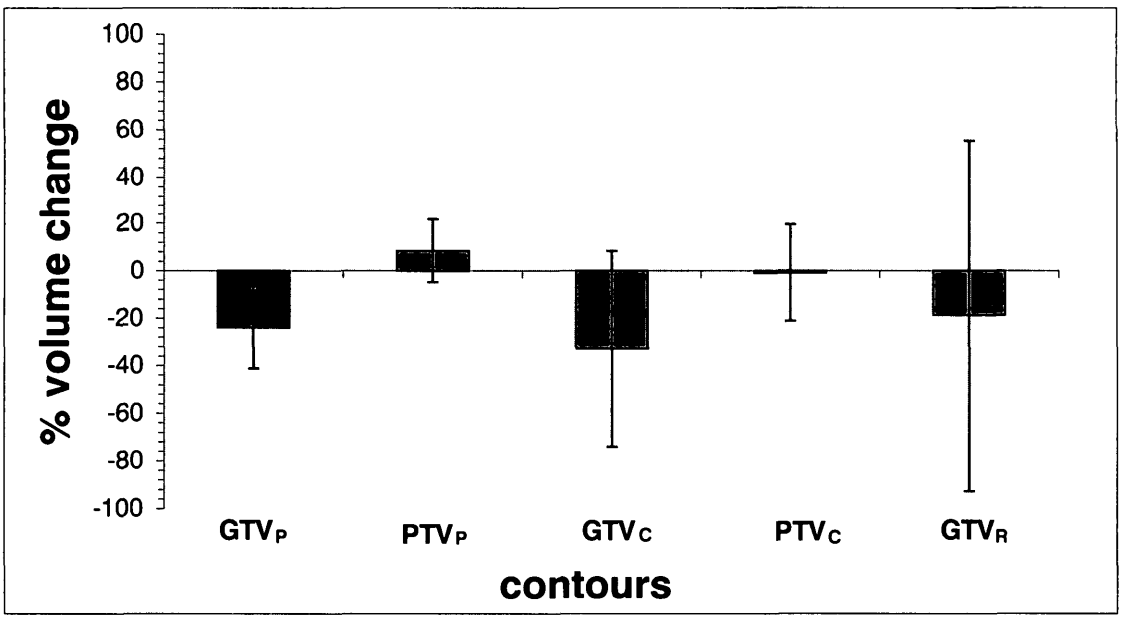

Figure 2. The differences in volume between original contours and those later re-marked.

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(right-hand side). The top two images show the original GTV_{unenh} (light line) and GTV_{enh} (dark line). In the lower images, PTV_{unenh} (light line) and PTV_{enh} (dark line) are shown. It is easy to note the larger differences to GTV values than PTV values.

Volume changes ΔGTV_C and ΔGTV_R are noted as being considerably larger than changes due to the precision of marking-up. The mean of ΔGTV_R, due to marking-up by the radiologist, has a mean of 20.4%, but due to large SD is not statistically significant. Absolute changes in volume show a mean 57.3 % SD 46.1. The precision of the oncologist marking up unenhanced contours also shows a high SD (SD 13.3–17.2), due not only to low case numbers, but perhaps also emphasising the difficulty of the task in many cases.

Figure 4 shows the comparisons in terms of geographical shifts between the centres of the

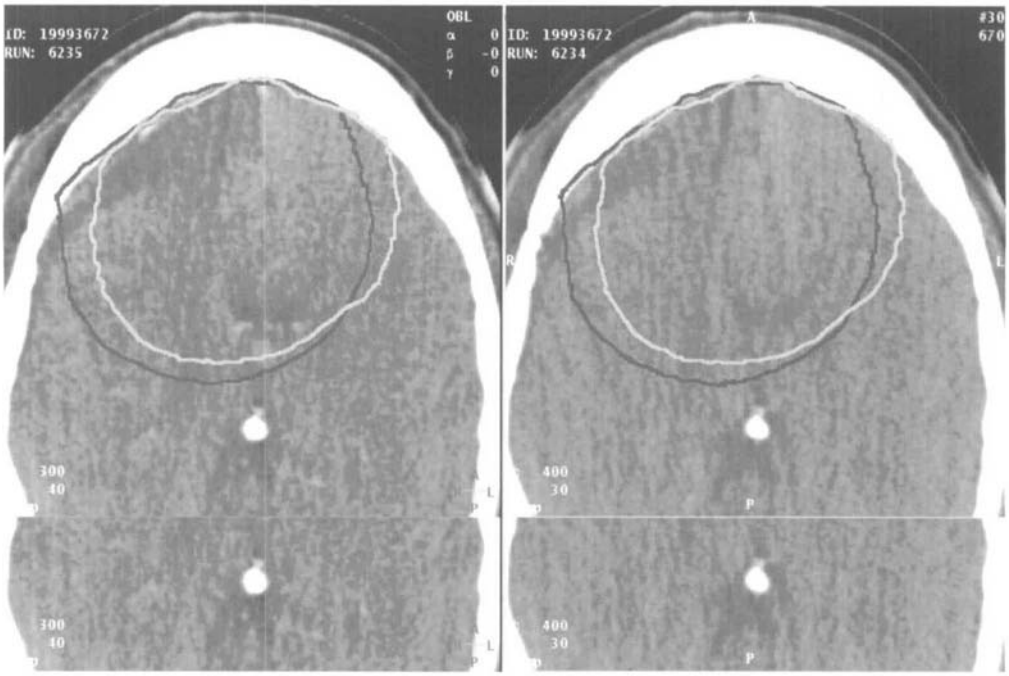

Figure 3. Images showing enhanced studies (left-hand side) fused to unenhanced studies (right-hand side). The two images at the top show GTV_{enh} (dark line) and GTV_{unenh} (light line), while the images on the bottom show PTV_{enh} (dark line) and PTV_{unenh} (light line).

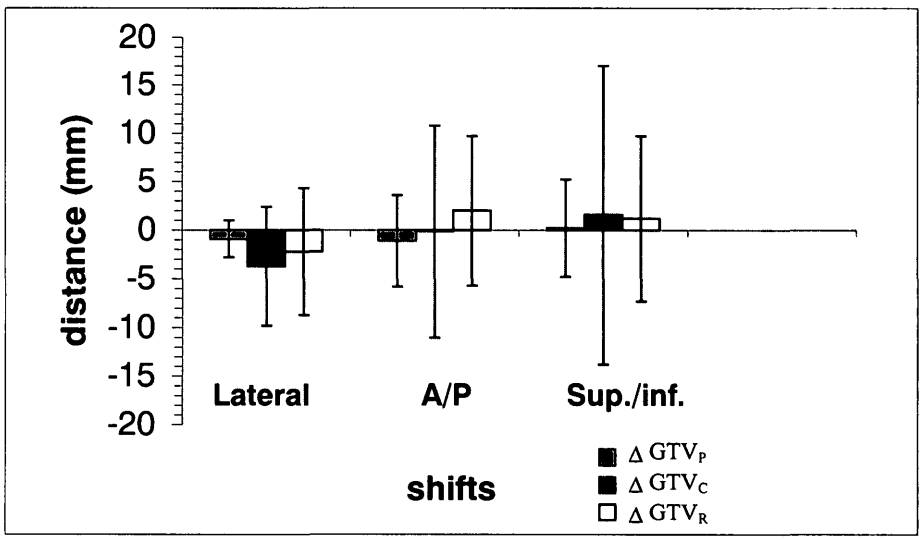

Figure 4. The geographical shifts between original contours and those later re-marked.

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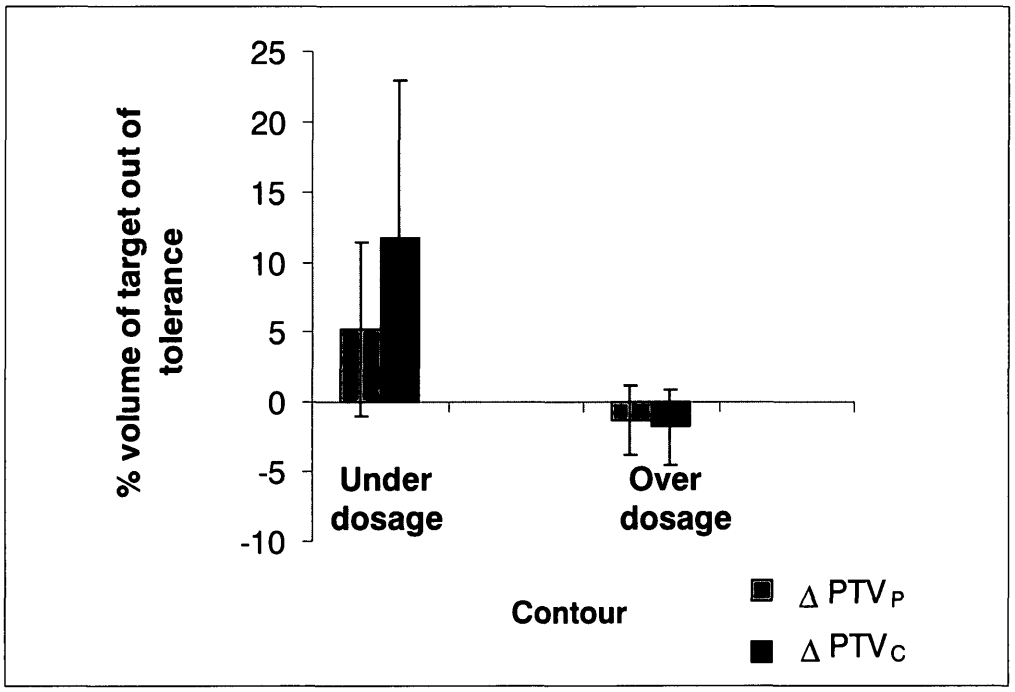

Figure 5. The difference in tolerance doses between original contours and re-marked. Target underdosing and overdosing are defined as <95% and >105% of the prescribed dose.

contours. Again, large SDs are apparent. The mean shifts in all directions are small (average –0.6, –0.7 and 0.3 mm for ΔGTV_P, ΔGTV_C and ΔGTV_R respectively) and are not significant, suggesting the re-marked contours are in the same geographical position as the original. Although the volume may change, the contours are being marked-up in the same anatomical position regardless of the use of contrast or the person marking-up. This interim finding is in keeping with Valcenti et al.[3] who have also reported that the use of enhanced scans has little effect on the definition of the contour centre.

Tolerance dose results are shown in Figure 5. Using dose-volume histograms, the volume of target receiving less than 90% (defined as target underdosing) and more than 105% (defined as target over-dosing) of the required dose were calculated for each PTV. The data in figure 5 show the differences in tolerance doses between the original unenhanced PTV, and the later re-contoured PTVs. In effect, this is equivalent to subtracting the re-contoured target ΔV_H from the original target ΔV_H and categorising the results into under- or over-dosing as defined above. For this section, only data on the precision of oncologist (A) and the influence of contrast are presented.

The use of contrast shows negligible difference in target volume over-dosing (mean difference 1.8%, SD 2.8) but a larger change in target underdosing (mean 11.7% SD 11.2) which is significant at $p=0.01$. The contours comparing the precision of the oncologist show a negligible change in target over-dosing (mean difference 1.3%, SD 2.5), but larger (mean difference 5.2%, SD 6.2) change in target underdosing, which is significant at $p = 0.035$ (Wilcoxon signed rank test, two-tailed). These precision results give us an idea of the typical systematic error expected. The greater target underdosing suggests that larger PTVs may result from using the re-contoured scans in the planning process. Our results agree with others reported in the literature for prostate patients.[4,6] Zhou et al.[4] reported some small but significant increases in extreme contour dimensions (projected areas in AP and lateral plane) with the use of enhanced scans. Although Zhou et al. measured change in size related to dimensional changes, rather than our arguably more accurate volume quantification, the data suggest similar results.

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These results highlight some difficulties inherent in this study and in the marking-up process more generally. When first marking-up for treatment, the oncologist may have additional information, which he/she will not have when re-contouring months later. They may, for example, have seen and examined the patient that day or may perhaps have spoken with the surgeon regarding tumour extent and geographic infiltration. Excluding the effect of these factors is obviously difficult. Clinicians when marking-up will use input from other diagnostic scans which may not have been performed with the patient in the treatment position: pre-surgery scans for example. When contouring, the clinician will therefore have to mentally translate visual information on certain planes into contours in a different 3D plane, which unavoidably leads to increased inaccuracies in the final contour volume. Oncologists tend to be conservative and if the tumour is difficult to visualise, may over-estimate the volume to ensure all the tumour is included in the GTV in accordance with ICRU50.[5] This may explain the results presented here showing the oncologist marking a 19% larger GTV than the radiologist.

In this work, with a small sample size, all cases have been analysed together as a single group, which is perhaps not ideal. In some cases for example, tumours may enhance very strongly, whereas others may not enhance at all. The cases include those with tumour in-situ and some post resection, where again, very different anatomy is being marked up, and very different sizes of GTV are involved (GTV values range from 3.8 – 79.6 cm^3 and PTVs from 149.5 – 790.6 cm^3). With a sufficient sample size at the close of the study, it should be possible to separate cases into tumour types and obtain improved correlation for certain tumours. It is important not to forget that other sources of information are also used during mark-up. Although it may be intuitive that the use of contrast should improve tumour visibility, when marking-up on the unenhanced scan, this is not the only information that the clinician will use to aid in definition of the tumour contour. The clinician may have additional diagnostic images such as MRI scans at his/her disposal when contouring. In this case, a contrast enhanced CT scan may offer no additional information to that already at hand. In cases of these types, the enhanced contours may differ little to the original unenhanced contours.

Considering the contours based on enhanced scans, the smaller differences in PTVs compared with GTVs show the lesser overall impact on the final plan due to the use of contrast. This shows the different impact of contrast for diagnostic or radiotherapy use. In diagnostic imaging, contrast is an essential part of routine imaging and its impact is undeniably important. Our results for cases in the brain and head and neck regions thus far suggest that its impact on the eventual treatment plan is much less crucial, due partly to the large margins often used when defining PTVs. This general statement should be qualified by highlighting multi-phase treatments. In this case, an additional boost dose (of perhaps 10 Gy) may be given conformally to the GTV, such that this becomes the target. For these cases, the impact of contrast may in fact be very important.

Finally, it must also be accepted, that although an expert in interpretation of medical images, the radiologist will not be as expert in the interpretation of for example tumour cavities as an oncologist viewing this anatomy on a daily basis. In certain circumstances, the radiologist may mark a considerably different contour to the oncologist, but from our data it is not possible to ascertain whether it is more or less accurate.

CONCLUSIONS

In the study, all patients were treated using the unenhanced scans marked-up by the oncologist. It is not possible, therefore, to compare the outcome of patients treated on plans generated with and without contrast and therefore it is not possible to say *clinically* whether use of contrast scan or radiologist information resulted in improved treatment i.e. the tumour targeting accuracy was definitively improved. However, it is possible to analyse the significance of any differences in the defined contour volumes in terms of size, geographical location and dose between original contours and those generated which include additional input from the use of IV contrast scans and marking-up by a radiologist. For this interim study, with a small sample size, it is perhaps more appropriate to note some observations rather than draw concrete conclusions:

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Influence of Contrast

The use of contrast seems to lead to a significantly ($p < 0.05$) different size of GTV being marked-up. This is in agreement with others.[3] Only the re-contouring with enhanced data lead to a significant contour volume change from the original unenhanced contour. However, this difference is not significant when the GTV had margins added to generate a PTV. No significant geographical shift was noted, so although the re-contoured GTV/PTV may vary in size and shape, they appear to be marked in the same geographical position. This is also in agreement with other studies.[3] The difference in tolerance doses for target under-dosing between enhanced and unenhanced targets are significantly different ($p = 0.01$) suggesting that the use of enhanced data can result in larger PTVs being generated. The largest impact of contrast will be when planning multi-phase treatments and targetting the GTV conformally.

Influence of the Radiologist

The input of the radiologist certainly leads to large differences in contour mean volume, with again no significant geographical shift in the contour centres. However, at this point with small patient numbers, the SD on the mean volume differences is so large as to make the differences statistically not significant. This data should be studied further when additional cases are available.

Contouring precision of the oncologist

In many of these cases, with poor tumour visibility, without the use of contrast, the contouring precision of the oncologist has a large SD. Importantly, although not analysed here, other authors have reported that the use of enhanced scans significantly improves the precision and reliability of marking-up.[3] When marking-up prostates was performed by seven observers on unenhanced and enhanced scans, the interclass correlation coefficient improved from 0.8 (unanhanced scans) to 0.92 (enhanced scans). For results presented here, no significant geographical shifts were noted. Differences in target tolerance volumes for under-dosing, were found to be significantly different ($p = 0.035$).

Acknowledgements

The authors gratefully acknowledge support from Weston Park Research Fund (MM) and Yorkshire Cancer Research (MHR).

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