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Original Article

Prostate Volume Changes during Extreme and Moderately Hypofractionated Magnetic Resonance Image-guided Radiotherapy

S.E. Alexander *†, H.A. McNair *†, U. Oelfke ‡, R. Huddart *†, J. Murray *†, A. Pathmanathan *†, P. Patel *†, K. Sritharan *†, N. van As *†, A.C. Tree *†

* The Royal Marsden NHS Foundation Trust, Sutton, UK
† The Institute of Cancer Research, London, UK
‡ The Joint Department of Physics, The Royal Marsden Hospital and the Institute of Cancer Research, London, UK

Abstract

Aims: Prostate morphological changes during external beam radiotherapy are poorly understood. Excellent soft-tissue visualisation offered by magnetic resonance image-guided radiotherapy (MRIgRT) provides an opportunity to better understand such changes. The aim of this study was to quantify prostate volume and dimension changes occurring during extreme and moderately hypofractionated schedules.

Materials and methods: Forty prostate cancer patients treated on the Unity 1.5 Tesla magnetic resonance linear accelerator (MRL) were retrospectively reviewed. The cohort comprised patients treated with 36.25 Gy in five fractions ($n = 20$) and 60 Gy in 20 fractions ($n = 20$). The volume of the delineated prostates on reference planning computed tomography (fused with MRI) and daily T2-weighted 2-min session images acquired on Unity were charted. Forty planning computed tomography and 500 MRL prostate volumes were evaluated. The mean absolute and relative change in prostate volume during radiotherapy was compared using a paired *t*-test (P value <0.01 considered significant to control for multiple comparisons). The maximum dimension of the delineated prostate was measured in three isocentric planes.

Results: Significant prostate volume changes, relative to MRL imaging fraction 1 (MRL#1), were seen at all time points for the five-fraction group. The peak mean relative volume increase was 21% ($P < 0.001$), occurring at MRL#3 and MRL#4 after 14.5 and 21.75 Gy, respectively. Prostate expansion was greatest in the superior–inferior direction; the peak mean maximal extension was 5.9 mm. The maximal extension in the left–right and anterior–posterior directions measured 1.1 and 2.2 mm, respectively. For the 20-fraction group, prostate volume increased relative to MRL#1, for all treatment time points. The mean relative volume increase was 11% ($P < 0.001$) at MRL#5 after 12 Gy, it then fluctuated between 8 and 13%. From MRL#5 to MRL#20, the volume increase was significant ($P < 0.01$) for 12 of 16 time points calculated. The peak mean maximal extension in the superior–inferior direction was 3.1 mm. The maximal extension in the left–right and anterior–posterior directions measured 1.7 and 3.7 mm, respectively.

Conclusion: Significant prostate volume and dimension changes occur during extreme and moderately hypofractionated radiotherapy. The extent of change was greater during extreme hypofractionation. MRIgRT offers the opportunity to reveal, quantify and correct for this deformation.

Key words: Hypofractionated radiotherapy; MRI; MRIgRT; prostate cancer; swelling; volume change

Introduction

Prostate cancer accounted for 22.2% of all male cancers in Europe in 2020 [1]; a large number of these men will have received external beam radiotherapy (EBRT) to treat localised cancer. Advances in EBRT delivery over the past 20 years have resulted in safer, more effective treatments [2,3]. These advances include image-guided radiotherapy, associated with improved biochemical control and lower rates of toxicity [4–7]. More recently, international interest and experience of magnetic resonance image-guided radiotherapy (MRIgRT) in prostate cancer has grown. MRI gives superior soft-tissue visualisation compared with computed tomography, as a result reducing inter-observer contouring variability [8] and producing more precise volumes [9].

Author for correspondence: S.E. Alexander, Radiotherapy Research Superintendent Radiographer, Radiotherapy Department, The Royal Marsden NHS Foundation Trust, Downs Road, Sutton SM2 5PT, UK. Tel: +44 208 642 6011.
E-mail address: sophie.alexander@rmh.nhs.uk (S.E. Alexander).

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MRIgRT provides an exciting opportunity to examine the effect of radiotherapy on prostate morphology at every fraction. Prostate morphological changes during EBRT are not well understood. Significant prostate swelling during extreme hypofractionated radiotherapy has been reported. However, only one study has examined this during daily MRIgRT [10]; analysis in the others was limited to two time points, in the middle and at the end of treatment [11,12]. For conventionally fractionated schedules, prostate volume is described as increasing transiently before reducing [13–15], although data assessment time points are again limited.

Identifying and correcting for changes in prostate shape and size during radiotherapy is intrinsic to a real-time adaptive MRI-guided workflow. However, at present, limited availability of adaptive technology means that most patients are treated without adaptive strategies. Having a better understanding of prostate deformation, gleaned through MRIgRT, provides an opportunity to assess the resulting impact on EBRT, irrespective of the workflow adopted. This becomes even more crucial for extreme hypofractionated schedules, less forgiving of set-up inaccuracies.

Therefore, the aim of this study was to quantify prostate volume and dimension changes that occur at each fraction of extreme and moderately hypofractionated radiotherapy, with the purpose of presenting better insight into prostate deformation during EBRT. This was possible as the cohort included were treated using MRIgRT.

Materials and Methods

The prostate volumes of 40 patients who underwent prostate radiotherapy on the Unity 1.5 Tesla magnetic resonance linear accelerator (MRL; Elekta, Stockholm, Sweden) [16] at The Royal Marsden NHS Foundation Trust (Sutton, UK) were included. The cohort included 20 patients treated consecutively with 60 Gy in 20 fractions between July 2019 and November 2020 and 20 patients treated consecutively with 36.25 Gy in five fractions (including 40 Gy to prostate clinical target volume [CTV] with no margin, as per PACE trial) [17] between March 2020 and May 2021. As per our standard MRL practice, a 5 mm (3 mm posterior) margin was grown around the prostate and proximal 1–2 cm of the seminal vesicle CTV, depending on clinical risk group; to create planning target volume (PTV)_6000cGy and PTV_3625cGy for the 20 and five-fraction groups, respectively.

Patients gave permission to use their images for research as part of radiotherapy consent. Some patients within this cohort were also recruited to the PRISM (NCT03658525), PERMIT (NCT03727698) or PACE-C (NCT01584258) trials. Prostate contouring methodology was standard across all patients and was carried out by clinical oncologists.

For planning and treatment, all patients were positioned supine with head support, arms across chest and knee and ankle fixation using the Combifix™ baseplate system (Civco Radiotherapy, Orange City, Iowa, USA). For planning and treatment, patients were given bladder and rectal preparation to achieve a comfortably full bladder and empty rectum as per local standard clinical practice. Five-fraction regimens were delivered on alternate days over 2 weeks, excluding weekends, whereas 20-fraction regimens were delivered daily over 4 weeks, excluding weekends.

Pre-treatment prostate volumes were delineated on computed tomography (Siemens Healthineers AG, Erlangen, Germany), with slice thickness $\leq$2 mm, for all patients. T2-weighted dedicated planning 1.5 Tesla MR-images (Siemens Aera) were fused with the planning computed tomography to inform contouring for 39 of the 40 patients. Pre-treatment computed tomography-based prostate delineation, using fused MRI, was carried out in RayStation (RaySearch Laboratories, Stockholm, Sweden). All contours were reviewed, modified (as required) and approved by a consultant clinical oncologist as per standard local practice.

During radiotherapy, the prostate was delineated using Monaco (Elekta) on Elekta T2-weighted 2-min 1 mm slice thickness session images, acquired during each treatment session before radiotherapy delivery and utilised to develop the online daily adapted plan. Six clinical oncologists delineated this patient cohort online on a rota basis. Each was experienced in MRI prostate delineation and had their contouring skills peer reviewed and quality assured by the lead clinician before independently contouring on the MRL. In total, 40 reference planning computed tomography contours and 500 MRL treatment contours were evaluated (Table 1).

Data were analysed by fractionation group; the five-fraction and 20-fraction groups will henceforth be addressed as 5#MRIgRT and 20#MRIgRT, respectively. For each patient, the 'prostate_only' volume (cm^3), delineated as the prostate excluding the seminal vesicles, as calculated by the radiotherapy planning system, was recorded from the planning computed tomography scan and for every MRL radiotherapy fraction. Delineated prostate volume and prostate volume change relative to the baseline MRL volume (MRL#1) was calculated. To test whether the average change in prostate volume at the various time points was significant, a two-tailed paired *t*-test was used and a *P*-value < 0.01 considered significant (to control for multiple comparisons).

Prostate volume changes were also divided into 'small prostate' and 'large prostate' subgroups; patients were grouped relative to their prostate volume being less than or greater than the median prostate volume at MRL#1. For the 5#MRIgRT group only, prostate volume changes were also analysed by patient's androgen deprivation therapy (ADT) status. To test subgroup significance, a two-tailed unpaired *t*-test was used and a *P*-value of <0.01 considered significant.

In addition, the maximum dimension of the delineated prostate in mm was measured in three planes; left–right (Xmax), superior–inferior (Ymax) and anterior–posterior (Zmax), using a greatest extent approach [11]. This was achieved by drawing two rectangular boxes around the longest and widest extent of the 'prostate_only' volume on coronal and sagittal views, utilising Monaco contouring tools. The Xmax, Ymax and Zmax values are therefore the

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sides of the smallest rectangular prism that precisely contains the delineated prostate.

Results

The characteristics for the cohort are presented in Table 2.

Statistically significant differences in prostate volumes relative to MRL#1 were seen at all time points for the 5#MRIgRT group (Figure 1a). Volume differences also occurred in the 20#MRIgRT group (Figure 1b), first reaching significance at MRL#5 but not consistently achieving this for subsequent time points. Supplementary data with standard deviations and significance values are presented in Supplementary Tables S1 and S2.

5#MRIgRT

The mean prostate volume as delineated on planning computed tomography (fused with planning MRI) was 6% larger than the MRI-delineated prostate volume at MRL#1. The relative volume difference was not statistically significant ($P = 0.046$). Significant prostate swelling relative to MRL#1 was seen at every treatment time point. The mean relative volume increase observed was 14% ($P < 0.001$) at MRL#2 after 7.25 Gy, rising to a maximum volume increase of 21% ($P < 0.001$) at MRL#3 and MRL#4 after 14.5 Gy and 21.75 Gy, respectively. The mean relative volume dropped slightly to 16% ($P < 0.001$) at MRL#5 after 29 Gy. The median prostate volume was 39 cm^3; there was no significant difference in mean relative volume change between small and large prostate subgroups (Figure 2).

Fourteen patients (70%) were on ADT at the time of radiotherapy; the median ADT duration prior to radiotherapy start was 4 months. When grouped by ADT status, the peak mean relative volume increase was 22% ($P < 0.001$) at MRL#3 and MRL#4 for the ADT group and 19% ($p < 0.005$) at MRL#3 for the no-ADT group (Figure 2). A trend for the ADT group to swell more is apparent but mean relative volume differences between the ADT and no-ADT groups were not significant.

Prostate expansion was greatest in the superior–inferior (Ymax) direction, with an increase in mean maximum dimension of 4.3–5.9 mm from fraction 2 to fraction 5 (Figure 3). Left–right (Xmax) and anterior–posterior (Zmax) extension was less, with a peak mean maximum change of 1.1 and 2.2 mm, respectively, at MRL#4; both dimensions appeared to reduce at fraction 5 (Figure 3).

20#MRIgRT

The mean prostate volume as delineated on planning computed tomography (fused with planning MRI) was 3% smaller than the MRI-delineated prostate volume at MRL#1. The relative volume difference was not statistically significant ($P = 0.31$). Prostate swelling relative to MRL#1 was found from MRL#2 until the end of radiotherapy, first reaching significance at MRL#5. The mean relative volume increase observed was 11% ($P < 0.001$) at MRL#5 after 12 Gy, and subsequently fluctuated between 8% and 13%. From MRL#5 to MRL#20, swelling was significant ($P < 0.01$) for 12 of 16 time points calculated.

There was no systematic significant difference in mean relative volume change between those smaller than or larger than the median volume. However, significant differences between the groups ($P < 0.01$) were seen for MRL#15 (42 Gy) and MRL#19 (54 Gy), with the small prostate subgroup experiencing greater relative volume gains (Figure 4). All patients were on ADT at the time of radiotherapy; the median ADT duration prior to radiotherapy commencement was 4 months.

Prostate expansion fluctuated more for the 20#MRIgRT group than for the 5#MRIgRT group (Figure 5). As per the 5#MRIgRT group, the greatest change in dimension during radiotherapy (excluding planning computed tomography) was in the superior–inferior (Ymax) direction, with the increase in mean maximum dimension ranging from 0.3 to 3.1 mm (Figure 5) during radiotherapy, with a median change in maximum dimension of 2.3 mm. The expansion range was greater in the anterior–posterior (Zmax) direction (0–3.7 mm) but the median change in maximum direction was less, 1.2 mm. Left–right (Xmax) changes were modest, with a range of −0.3 to 1.7 mm and a median change in maximum direction of 0.2 mm.

Discussion

This study revealed statistically significant prostate swelling during both extreme and moderately hypofractionated radiotherapy schedules. A significant increase

Table 1
Number of prostate contours reviewed

	Number of patients	Number of CT volumes included	Number of T2-weighted 2-min MRI volumes included
Patients who received 36.25 Gy in 5 fractions on the MRL	20	20	100
Patients who received 60 Gy in 20 fractions on the MRL	20	20	400
Total	40	40	500
Total prostate volumes included	540		

CT, computed tomography; MRI, magnetic resonance imaging; MRL, magnetic resonance linear accelerator.

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Table 2
Patients' baseline characteristics

5-Fraction MRIgRT group ($n = 20$)		20-Fraction MRIgRT group ($n = 20$)	
Age (years)		Age (years)	
Median (range)	71 (58–82)	Median (range)	72 (57–81)
Tumour stage		Tumour stage	
T2	18	T2	14
T3	2	T3	6
Gleason grade		Gleason grade	
3 + 3	1	3 + 3	0
3 + 4	16	3 + 4	11
4 + 3	3	4 + 3	6
4 + 4	0	4 + 4	1
4 + 5	0	4 + 5	2
Presenting PSA (ng/ml)		Presenting PSA (ng/ml)	
Mean (SD)	8.1 (4.9)	Mean (SD)	9.3 (3.1)
Prostate volume at diagnosis (MRI) cm^3		Prostate volume at diagnosis (MRI) cm^3	
Mean (SD)	48.50 (25.81)	Mean (SD)	38.55 (17.22)
ADT		ADT	
Yes	14	Yes	20
No	6	No	0
ADT duration prior to EBRT commencement ($n = 14$)		ADT duration prior to EBRT commencement ($n = 20$)	
Median months	4	Median months	4
Radiotherapy planning MRI		Radiotherapy planning MRI	
Yes	20	Yes	19
No	0	No	1
Duration from planning CT to MRL#1		Duration from planning CT to MRL#1	
Median days	21	Median days	17

ADT, androgen deprivation therapy; CT, computed tomography; EBRT, external beam radiotherapy; MRIgRT, magnetic resonance imaging-guided radiotherapy; MRL#1, magnetic resonance linear accelerator fraction 1; PSA, prostate-specific antigen; SD, standard deviation.

in prostate volume when using extreme hypofractionation has previously been reported [10,11]. Patients in the report by Gunnlaugsson *et al.* [11] were prescribed 42.7 Gy in seven fractions (6.1 Gy/fraction); a prostate cancer α/β ratio of 3 Gy was assumed. They reported a mean relative volume increase of 14% on MRI, acquired mid-schedule (EQD2 = 33 Gy) and 9% at the end of radiotherapy (EQD2 = 67 Gy). The degree of prostate swelling was greater in our study for patients prescribed 36.25 Gy in five fractions (7.25 Gy/fraction, with 8 Gy per fraction to the CTV) compared with those receiving treatment in 20 fractions. A maximum mean relative volume increase of 21% was seen at MRL#3, assuming an α/β of 3 Gy; EQD2 at this time point was 30 Gy, very similar to the dose causing maximum swelling in the earlier study [11]. Also akin to previous findings, prostate swelling in our extreme hypofractionation group seemed to decline towards the end of the course [11].

Research now supports that the α/β ratio of prostate cancer is around 2 Gy [18]. Recalculating with a α/β of 2 Gy results in the maximum swelling being seen after a EQD2 of 33.53 Gy in our study and 37.06 Gy by Gunnlaugsson and colleagues [11]. The availability of MRI at every fraction, as opposed to one mid-treatment time point, allowed us to identify a previously unnoticed trend for prostate volume increase to plateau from MRL#3 to MRL#4 before a decline in volume. This plateau was not apparent in a recent study also examining prostate volume changes during extreme hypofractionated MRIgRT [10]. Patients in this cohort ($n = 20$) received 40 Gy in five fractions over 2 weeks. Akin to our findings, they report consistent prostate swelling with peak volume expansion seen at fraction 4 after 24 Gy. However, the extent of change was less with a median volume increase of 15.1% relative to baseline MRI [10].

Variations in radiotherapy prescription, imaging parameters and time points, radiotherapy planning software, radiotherapy delivery and study contouring methodology exist between our study and the two previously reported [10,11], probably accounting for some disparity between findings. Despite these confounding factors, all three independently reported significant prostate swelling during extreme hypofractionated radiotherapy, supporting the generalisability of this phenomenon.

The 21% increase in relative prostate volume observed in our 5#MRIgRT group is consistent with prostate brachytherapy studies comparing pre- and post-implant volumes [19–21]. Interestingly, brachytherapy studies predominantly discuss swelling in relation to trauma caused at implantation rather than as an effect of radiation dose [19–22]. Contrary to brachytherapy research findings, there was no trend in our 5#MRIgRT group for smaller volume prostates to experience the greatest relative increase in volume [20,21]. In the 20#MRIgRT group, significantly greater relative prostate volume increases were seen in the small prostate group across two time points.

One, single patient case study was found to assess prostate volume changes during a moderately hypofractionated

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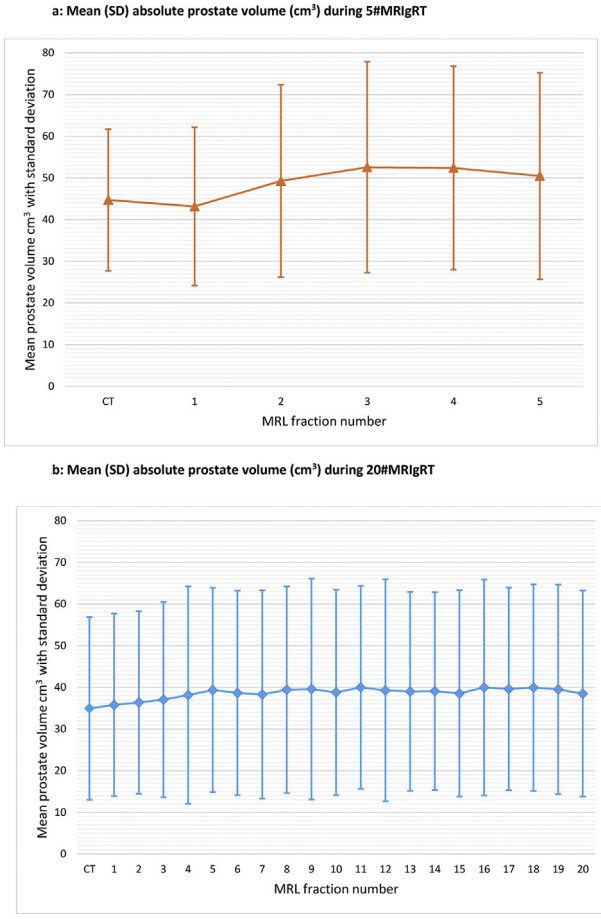

Fig 1. Mean (standard deviation) absolute prostate volume (cm^3) during (a) five-fraction magnetic resonance image-guided radiotherapy and (b) 20-fraction magnetic resonance image-guided radiotherapy. MRL, magnetic resonance linear accelerator.

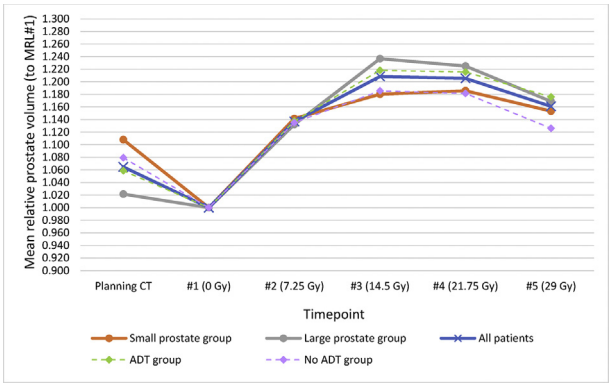

Fig 2. Mean relative prostate volume (relative to magnetic resonance linear accelerator fraction 1 [MRL#1]) for five-fraction magnetic resonance image-guided radiotherapy.

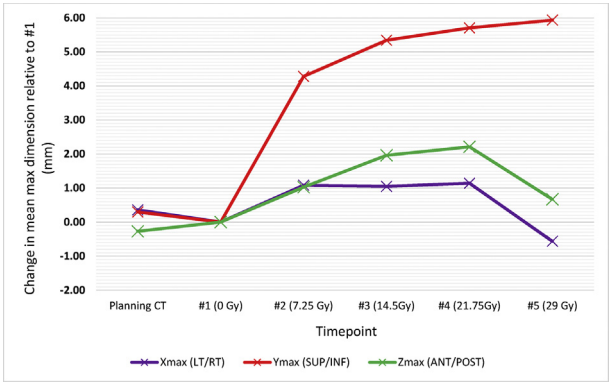

Fig 3. Change in mean Xmax, Ymax and Zmax dimension over five-fraction magnetic resonance image-guided radiotherapy, relative to mean prostate Xmax, Ymax and Zmax at magnetic resonance linear accelerator fraction 1.

regimen as per our 20#MRIgRT group [23]. A maximum prostate volume increase of 27% relative to planning MRI was noted at fraction 9 (24 Gy); by fraction 20 this had reduced to 3% [23]. Although such a marked volume increase was not shown in our 20#MRIgRT cohort, fluctuation in prostate volume and a final prostate volume greater than baseline occurred in both studies.

Further data is available considering prostate volume changes during conventionally fractionated radiotherapy [13–15]. An increase in prostate volume during treatment was found; however, unlike our 20#MRIgRT cohort, prostate swelling occurred transiently before shrinking below the baseline volume [13–15]. Previous studies delivered 1.8–2.0 Gy daily over 38–45 fractions; the overall treatment duration was approximately double our 20#MRIgRT group. Comparing their findings alongside our 20#MRIgRT and 5#MRIgRT results may further support the view that radiotherapy fraction size and course duration impact swelling extent. Comparing against these studies is, however, limited by their reliance on fiducial markers [13], computed tomography imaging [14] and non-daily assessment [14,15] to deduce prostate volume changes.

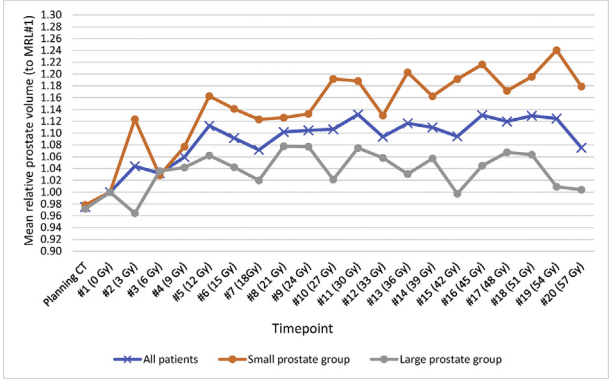

Fig 4. Mean relative prostate volume (relative to magnetic resonance linear accelerator fraction 1 [MRL#1]) for 20-fraction magnetic resonance image-guided radiotherapy.

Neoadjuvant ADT may be a confounding factor when comparing prostate volume changes across studies, as prostate shrinkage in the range of 20–50% of the initial volume is reported after 3 months of ADT [14]. Across our cohort, 85% (34/40) of patients had neoadjuvant ADT; the

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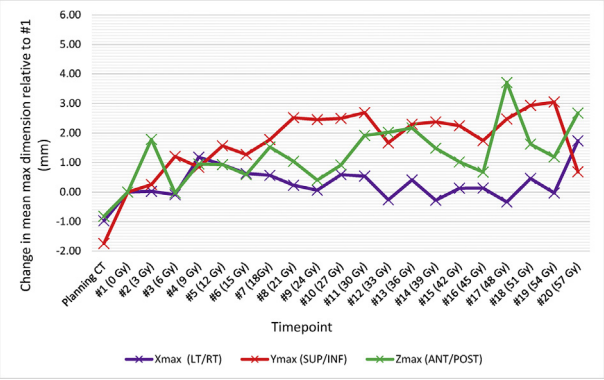

Fig 5. Change in mean Xmax, Ymax and Zmax dimension over 20-fraction magnetic resonance image-guided radiotherapy, relative to mean prostate Xmax, Ymax and Zmax at magnetic resonance linear accelerator fraction 1.

median ADT duration pre-MRL#1 was 4 months. The degree of prostate shrinkage from diagnostic MRI (pre-ADT) to MRL# 1 was modest; 9% and 7% for the 5#MRIgRT and 20#MRIgRT groups, respectively. This value may be distorted by variations in the prostate measuring technique used (ellipsoid volume calculation versus organ delineation) and variable diagnostic MRI slice thickness.

Significant increases in prostate volume have been seen in patients receiving hypofractionated radiotherapy without ADT [11] and here also shown with ADT. Prostate volume changes in the 5#MRIgRT group were not significantly influenced by the patient's ADT status. However, the results do suggest that those on ADT ($n = 14$) experience at least as much swelling as those not on ADT ($n = 6$). This is contradictory to the findings of Ma and colleagues [10] who reported that patients on ADT ($n = 6$) had significantly reduced prostate swelling than those not on ADT ($n = 14$). We consider the number of ADT naïve patients in our cohort too small to establish the true impact of ADT on prostate volume during radiotherapy, but our results reveal that swelling deformation is a risk for all patients irrespective of ADT status.

Incongruent to early published literature that reports computed tomography-delineated prostate volumes 35–40% greater than MRI-delineated volumes [24–26], only modest differences of +6% and −3% between computed tomography- and MRI-delineated volumes presented for our 5#MRIgRT and 20#MRIgRT cohorts, respectively. Poor soft-tissue contrast on computed tomography compared with MRI contributes to delineation uncertainties [21]; fusing computed tomography images with MRI reduces uncertainty and CTV compared with computed tomography alone [27]. Ninety-eight per cent of patients in this study had a dedicated planning MRI fused with computed tomography to aid initial prostate delineation [28]. Alongside this, those contouring were experienced in prostate MRI anatomy and how it relates to computed tomography anatomy; this has been shown to reduce volume variations between modalities [8].

Prostate dimension changes were greatest in the superior–inferior direction for both cohorts. A potential reason is that the prostate–bladder interface provides less resistance against prostate swelling [13] than the obturator internus muscles, rectum and pelvic floor muscles. The pelvic floor sits inferior to the prostate apex. Therefore, this theory would suggest that superior–inferior swelling is predominantly superior at the prostate–bladder interface. A limitation of the methodology used is that this concept cannot be confirmed as true or false; only the change in plane dimension was determined, not the direction. As a result, we cannot be sure if the deformation seen in the superior–inferior direction is superiorly, inferiorly or evenly spread. In addition, the potential effect of prostate rotation on the extension measurement cannot be quantified nor accounted for with this methodology.

It could be argued that the significant change seen in the superior–inferior direction was as a result of prostate contouring uncertainty being greatest at the apex and base [29]. The decision to use clinical contours rather than re-contouring offline by one expert, as carried out in previous studies [10,11], could also be seen as a limitation, acknowledging inter-observer variability in prostate contouring. In response we suggest that as the clinical online contours were created by six different observers over a course of treatment, any systematic under- or over-contouring by one observer would be mitigated.

Variations in bladder and rectal volume between fractions was not quantified. However, these are commonplace during prostate radiotherapy [30,31] and may be a confounding factor. Pressure exerted on the prostate by the bladder and rectum increases with filling and may influence prostate dimension, particularly in the superior–inferior and anterior–posterior planes. Future work will adapt the maximum dimension calculation methodology to examine the prostate centroid direction of change during radiotherapy. This combined with assessment of bladder and rectal filling will allow a greater understanding of swelling direction.

The impact of superior–inferior prostate dimension extension on image registration methodology should also be considered. Where prostate soft-tissue registration is used, superior–inferior alignment guided by the prostate–bladder interface is usual, as this boundary is easier to distinguish than the prostate apex. If the prostate dimension has increased, aligning to one extreme of the volume, as per this method, would result in swollen prostate tissue being positioned inferiorly. This would increase the risk of under-dosing prostate tissue at the inferior extent of the volume if daily adaption was not used. Fiducial marker matching may offer a solution to distribute increased prostate volume more evenly during registration, resulting in better tissue coverage. However, this is only true if prostate swelling is distributed evenly.

We have shown statistically significant changes in this patient cohort; the question is how clinically significant

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these prostate volume changes are? Deformation is implicitly accounted for by an online adaptive strategy; therefore, no residual deformation error needs to contribute to the CTV−PTV margin [32]. Most prostate cancer patients, however, do not have online daily adapted radiotherapy; for these patients, prostate volume deformation error should be considered in the CTV−PTV margin. Our results indicate that the CTV−PTV margin contribution due to deformation is anisotropic and needs to be greater for extreme hypofractionation prostate schedules, with up to 3 mm indicated for the 5#MRIgRT group. A similar margin extension of 1.5−3 mm, to compensate for prostate swelling, was previously suggested [11].

However, swelling of the prostate during treatment has not been explicitly accounted for in the past, and biochemical control rates after five- and seven-fraction regimens remain excellent [33,34]. It is conceivable that the PTV margin has functioned as a 'prostate swelling margin' ensuring reasonable CTV coverage. In addition, we know that local recurrence is rare, and almost exclusively occurs in the dominant lesion within the prostate [35,36]. Hence, margins should not be expanded to account for this swelling in risk groups that already have high rates of cure. The data does suggest that for higher risk patients, with lower cure rates, prostate margins should not be further reduced and/or adaptive radiotherapy should be used to ensure good target coverage.

Radiotherapy acutely increases obstructive voiding urinary symptoms [8,37]. The aetiology of these symptoms is not fully understood, but prostate swelling, as described here, may be a causative factor. A limitation of the dataset presented is that it does not include patient toxicity data. Correlation between prostate swelling and obstructive voiding symptoms will be examined in future work. Corticosteroids have had variable success reducing the risk of acute urinary retention following prostate brachytherapy [38,39], but are not routinely prescribed during EBRT. If future work finds a relationship between prostate swelling and obstructive voiding symptoms, action to reduce swelling, such as prescribing corticosteroids, could be considered.

Excellent soft-tissue contrast generated by MRIgRT systems enables online contouring and plan adaption, which can account for prostate volume and dimension changes as presented by this study. Further work could be carried out to establish if volume and dimension changes can be visualised and quantified reliably on novel cone beam computed tomography-guided real-time adaptive systems. In the absence of technology facilitating real-time adaption, a scheduled adaptive approach [40] could be used, with a replan scheduled after fraction 2 and fraction 4 for five- and 20-fraction treatments, respectively, to account for peak swelling seen in subsequent fractions.

Conclusion

This study indicates statistically significant prostate volume and dimension changes during both extreme and moderately hypofractionated EBRT. The extent of change measured was greater during 5#MRIgRT, with a peak in mean relative volume of 21%. This is only the second study, known to us, to report volume changes on MRI over each fraction, revealing previously unappreciated deformation trends.

Prostate dimension changes were greatest in the superior−inferior direction, perhaps due to less pelvic floor resistance. Real-time adaptive radiotherapy workflows are ideal for managing volume and dimension changes as presented by this study. However, where not available; scheduled adaptive strategies, CTV−PTV margin considerations and fiducial marker registration may offer some advantage.

Ethics Statement

The patient cohort were consented to ethics approved trials, which specifically ask for consent to use anonymised data for research (PERMIT, PACE and PRISM). Patients also gave consent for their medical images to be used for 'research and audit, for example evaluating new planning methods and technologies' as part of their standard radiotherapy consent. With these measures in place, ethics review specific to this piece of work was deemed not required by our multidisciplinary team having consulted the Health Research Authority decision tool.

Conflicts of Interest

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.clon.2022.03.022

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