Radiotherapy and Oncology 169 (2022) 15–24

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Review Article

Seminal vesicle inter- and intra-fraction motion during radiotherapy for prostate cancer: A review

Victor J. Brand *, Maaike T.W. Milder, Miranda E.M.C. Christianen, Mischa S. Hoogeman [1], Luca Incrocci [1]

Erasmus MC Cancer Institute, University Medical Center Rotterdam, Department of Radiotherapy, Rotterdam, Netherlands

ARTICLE INFO

Article history:
Received 18 June 2021
Received in revised form 26 January 2022
Accepted 2 February 2022
Available online 11 February 2022

Keywords:
Prostatic neoplasms
Seminal vesicles
Motion
Radiation dose hypofractionation

ABSTRACT

A review of studies on seminal vesicle motion was performed to improve the understanding of these treatment uncertainties. This will aid planning target volume margin reduction, which is necessary for hypofractionation of high-risk prostate cancer. Embase, Medline, Web of science Core collection, Cochrane CENTRAL register of trials and Google scholar were searched for publications including 3D information on seminal vesicle motion. In total 646 publications were found of which 22 publications were eligible for inclusion. The mean, systematic and random error of inter- and intra-fraction translations are reported, as well as rotations. The translations of the seminal vesicles is smallest in the left–right direction, whereas the rotation was largest around this axis. Although rectal and bladder filling status were the main cause for seminal vesicle motion, no apparent effect on magnitude of motion was seen when different bladder and rectal preparation protocols were used. Inter- and intra-fraction motion of the seminal vesicles is significant. In the studies, systematic and random errors range between 1–7 mm and 1–5 mm respectively, and are largely uncorrelated to prostate motion. The maximum correlation between seminal vesicle and prostate motion was reported with an R^2 of 0.7, while 3 other studies report lower and/or non-significant correlations. Five studies report a planning target volume margin of approximately 8 mm. This margin is in line with the results of four relevant dosimetric studies. Mitigating the inter- and intra-fraction motion of the seminal vesicles, including prostate tracking, has the potential to reduce planning target volume margins.

One of the common treatment modalities for prostate cancer (PCa) is external-beam radiotherapy [1]. Considering the relatively low alpha/beta ratio for PCa [2,3], hypofractionation could yield higher tumour control rates with acceptable genitourinary and gastrointestinal toxicity rates [4]. Dose-escalation has shown improved treatment outcomes [5] and the use of modern image-guidance techniques, like fiducial markers, have lowered the margin needed around the prostate and thereby lowered side effects [6,7]. Furthermore, multiple randomized trials on low and favourable intermediate risk PCa reported a non-inferiority regarding tumour control and toxicity rates of moderate hypofractionation [8,9] and ultra-hypofractionation [10] compared to conventional fractionation schemes. Here, ultra-hypofractionation is defined as a dose per fraction of 5 Gray (Gy) or more.

A next logical step would be the use of ultra-hypofractionation for high-risk patients, but this is challenging as the entire seminal vesicles (SV) are normally included in the target volume [11]. The SV belong to the male reproduction system and are about 3–5 cm long and 1 cm in diameter [12], however their exact shape and size can differ substantially. The SV are attached bilaterally to the prostate on the cranioposterior side and they lie superior to the rectum, inferior to the fundus of the bladder and posterior to the prostate [12]. The motion of the SV, similarly to the prostate, is caused by changes in bladder and rectal filling status. The SV can show tumour involvement [11], the probability of which can be predicted with the use of nomograms [13,14]. Recently, the addition of MRI imaging to these clinical prediction tools was shown to increase the robustness of these models [15–17].

Due to their inter- and intra-fraction motion, the SV require a relatively large planning target volume (PTV)-margin [18–21], which in combination with a high fraction dose could result in unacceptable dose to the organs at risk and thereby higher toxicity rates. A number of papers have recently been published showing the feasibility of ultra-hypofractionation (5 fractions of 7 Gy or 7.25 Gy) in small groups of patients including the SV in the clinical target volume (CTV) using different treatment modalities [22–24].

To safely introduce ultra-hypofractionation for high-risk PCa patients, strategies to optimize PTV-margins around the SV are required. Understanding the different types of treatment uncer-

* Corresponding author.
E-mail address: v.brand@erasmusmc.nl (V.J. Brand).
[1] Co-senior authorship: Mischa S. Hoogeman and Luca Incrocci both equally contributed.

https://doi.org/10.1016/j.radonc.2022.02.002
0167-8140/

tainties that contribute to a PTV-margin is crucial in this process. The last review on this topic was published in 2001 [25]; since then several articles have been published with methodologies that are more in line with the current technological advancements in PCa treatment. Therefore, this article critically reviews all relevant existing literature since 2001 on the inter- and intra-fraction motion of the SV during external-beam radiation of PCa with the aim of improving the understanding of these treatment uncertainties, which is needed to design adaptive treatment strategies for PTV-margin reduction.

Materials and methods

Search strategy

In collaboration with the Erasmus MC Medical Library, Embase, Medline, Web of science Core collection, Cochrane CENTRAL register of trials and Google scholar were searched for relevant publications. This search was first performed on the 7th of February 2020 and last updated on the 18th of January 2021. There were no restrictions regarding date of publication or language in the initial search. See Appendix A for the detailed search queries.

In- and exclusion process

These searches yielded 646 unduplicated results. All articles before 2001 were excluded as the last review on this subject dates from 2001 [25] and the image guidance for prostate treatments has changed significantly since then. Using Endnote (version X9 build 12062), these results were screened on title/abstract and full text afterwards. This was done by VB with MM as second reviewer.

Publications that were not written in the English language, as well as publications without a specific record of SV motion, deformation, volume changes and/or PTV-margins were excluded. Publications with abstracts referring to quantitative values for motion, deformation, volume changes and/or margins of the prostate and the SV were eligible for full text screening. This yielded 170 publications.

Translations, rotations, deformations, volume changes and/or margins of the entire SV had to be reported for inclusion in the final review. Studies in which the prostate and the SV are combined in a single CTV or PTV and analysed as such were excluded, as well as studies which only incorporated part of the SV. After screening done by VB and MM, one article on volume changes was added outside of this search. In total 22 publications were included in this review [26–47] (see Fig. B.1 in Appendix B).

Data extraction

The general data extracted from the publications, if provided, were the author and year of publication, number of patients, number of scans (planning and repeat scans), average patient age, fractionation scheme and tumour stage. The extracted data regarding the SV motion were image modality, specific inter- or intra-fraction motion, reference point of motion, type of image registration used, rectal and bladder preparation, motion surrogate used (e.g. centre of mass (COM) of the SV), and finally the SV displacement in the form of the mean, the standard deviation (SD) and the systematic and random errors, in mm or degrees, along the 3 principal axes. If present the, anisotropic, PTV margins were also extracted.

Data analysis

The three publications reporting a PTV margin used the "van Herk" margin-recipe [34,40,42].

$$\text{PTV - margin} = 2.5\,\Sigma + 0.7\,\sigma, \tag{1}$$

in which, Σ represents the systematic error and σ the random error (1 SD) based on translations only [48].

Hence, we have used the same formalism to calculate PTV margins, if not reported, from datasets. To compare publications reporting systematic errors to those reporting means of motion, for the latter the standard deviation of the group mean was used as the systematic error. A limitation for the application of this margin recipe to SV is the lack of inclusion of rotations and deformations. The margins stated in this review are based on conventional fractionation schemes and will have to be adjusted when hypofractionation is used. Another limitation is that this recipe is only valid for conventional fractionation schemes, with a need to increase the margin when hypofractionation is used. Therefore, the margins in this review only indicate a lower limit. Table 1 summarizes the error parameters used in this study.

Results

The number of publications regarding inter-fraction motion, volume changes and/or margins exceed those reporting intra-fraction motion, volume changes and/or margins by 19 to 4. One article describes both. The number of patients ranges between 9 and 90 and the number of scans used for data collection ranges between 21 and 771. Multiple image modalities (CBCT, CT or MRI) have been used as well as multiple points of reference (bony anatomy, prostate or first image in series) to which the motion was measured. A range of protocols to control bladder and rectal filling, such as the use of laxatives [28,30,45,47] or instructions to drink a certain amount of water before treatment [28–30,32,34,38,47], have been employed in the studies. Table 2 summarizes the 22 articles included in this review.

Fig. 1a shows the mean values for inter-fraction translation, M_{inter}, of the SV. 7 out of 9 articles used a prostate match (matched on fiducials or COM of the prostate) to obtain these values. The means were derived from relative values, i.e. negative and positive directions of translation. As expected from unbiased studies, M_{inter} is below or around 1 mm, with the exception of two articles that reported values up to −3.3 mm [35,40]. Fig. 1b shows the mean intra-fraction translation of the SV, M_{intra}. The reported intra-fraction translation depends strongly on the reference point and shows values of −1.5 up to 7 mm. Only two publications [35,44] reported the intra-fraction translation, both relative to the prostate, with values ranging from −0.4–1.2 mm.

The systematic error for inter-fraction translation, $\sum_{inter}$, is shown in Fig. 1c. These systematic errors vary from 1 to 7 mm with only 2 publications reporting values above 4 mm. Higher values for systematic errors were reported in the anteroposterior (AP) direction, 1.7–7.3 mm, and craniocaudal (CC) direction, 1.3–4.5 mm, compared to the left–right (LR) direction, 1.0–2.0 mm with one outlier of 3.6 mm [27]. The systematic errors obtained from a match on bony anatomy [30,42] appear to be larger, all show values >3 mm, than the systematic errors obtained from a prostate match of which 4 out of 6 publications show values <3 mm. Fig. 1d shows the systematic errors of intra-fraction translation, $\sum_{intra}$. The range shown, 1.6–4.1 mm, is smaller to that of $\sum_{inter}$, 1.4–7.3 mm. However, these datasets use different reference points: $\sum_{inter}$ is reported relative to the prostate and other reference points, whereas $\sum_{intra}$ is only reported relative to other reference points than the prostate.

Fig. 1e shows the random errors of the inter-fraction translation, σ_{inter}. These range from 1 to 5 mm, and are in magnitude comparable to the systematic errors. Similarly to the values of $\sum_{inter}$, σ_{inter} in the LR direction are smaller, ranging from 1.2 to 2.3 mm, than the random errors in the CC and AP direction, ranging

Table 1
Definitions of used error parameters; x = individual measurements; n = number of measurements per patient; N = number of patients in the study; μ_p = mean per patient; SD_p = standard deviation of the patient mean.

Error parameter	Definition
Patient mean (μ)	$\mu = \frac{\sum_i x_i}{n}$
Standard deviation of patient mean (SD)	$SD = \sqrt{\frac{\sum_i (x_i-\mu)^2}{n-1}}$
Group mean (M)	$M = \frac{\sum_p \mu_p}{N}$
Systematic error (Σ)	$\Sigma = \sqrt{\frac{\sum_p (\mu_p - M)^2}{N-1}}$
Random error (σ)	$\sigma = \sqrt{\frac{\sum_p SD_p{}^2}{N}}$

from 1.7–3.3 mm and 1.9–5.0 mm respectively. None of the included publications in this review reports random errors of intra-fraction translation.

Besides translations, rotations also have an impact on treatment uncertainty. Two studies were identified in which SV rotations – relative to the prostate – were analysed. First, van der Burgt et al. [46] reported on inter-fraction rotations of the whole SV, after a prostate match. Three groups of 30 patients, with each 8 CBCTs, were divided by level of SV invasion: none, minimal (<5 mm) and extensive (>5 mm). Means, systematic ($\Sigma_{rotation}$) and random ($\sigma_{rotation}$) rotations were given around the LR, CC and AP axis. The means of the rotations in the LR-axis for the minimal and extensive group, 2.0° and 2.3° respectively, and the CC rotation for the extensive group, 1.0°, were significantly different from 0. The systematic and random errors of the LR rotations were found to be higher, ranging from 5.0°–6.7°, compared to the rotations in the CC and AP-axes, ranging from 1.8°–2.4° and 1.6°–2.7° respectively. Two rotations were significantly lower in the extensive group compared to the no invasion group: $\Sigma_{rotation}$ in AP-axis (1.6° vs 2.3° respectively) and $\sigma_{rotation}$ in LR-axis (5.2° vs 6.3°). Secondly, de Boer et al. [28] analysed inter-fraction rotations around the LR-axis for 20 patients with repeat CBCTs. They found a mean rotation around the LR-axis of −0.4°, a $\Sigma_{rotation}$ of 7.2° and a $\sigma_{rotation}$ of 6.4°. These rotations were significantly correlated ($p < 0.001$) with prostate translations in the CC and AP direction and with prostate rotations around the LR and AP axes.

Apart from translations and rotations, deformations are also considered a source of uncertainty in the treatment of SV. Deformations of the SV were discussed in 5 publications of which one reported intra-fraction deformation and one reported both intra- and inter-fraction deformation. The deformations were measured after a prostate match in all cases. Sheng et al. [44] described intra-fraction deformations of 15 patients with 5 pairs of CBCT (before and after treatment). Mean edge-to-edge distance in millimetres (with 95% data range) for Left, Right, Cranial, Caudal, Anterior and Posterior border were reported to be <1.1 mm. Li et al. [35] reported on both intra- and inter-fraction deformation. Similarly, all intra-fraction deformations were reported to be <1.1 mm. In contrast, the inter-fraction deformations showed values up to 2.8 mm (caudal border) and −2.9 mm (posterior border). Inter-fraction deformations were studied by Hollander et al. [33] in 10 patients with weekly verification scans (66 scans in total). They found mean edge-to-edge displacements < 0.6 mm of all borders, except for the anterior border with a deformation of 2.4 mm (-3.9–8.8 mm). Van der Wielen et al. [47] reported inter-fraction deformations for 21 patients with 3 repeat CT scans. Standard deviations along local surface normals for lateral SV, SV tip, Anterior SV and Posterior SV were 1.7 mm, 2.3 mm, 2.4 mm and 2.6 mm respectively. Lastly, Mayyas et al. [39] studied 10 patients with 20 CBCTs and looked at percentage of CBCTs in which deformation vector fields exceeded 3, 5 or 10 mm. For both 3 and 5 mm poste-

Table 2
Summarized general study information of the included articles. * = Abstract only; n/a = not applicable; Pts = patients; CBCT = Cone-beam Computed Tomography; COM = center of mass; SV = seminal vesicle; ERB = Endorectal balloon; CT = Computed Tomography; MRI = magnetic resonance imaging; prep = preparation; ROI = Region of interest; EPI = electronic portal images; '-' = Not reported in the study.

Author and year	# pts	# scans	Inter/Intra	Reference point	Registration	Image modality	Motion surrogate	Bladder prep	Rectal prep
Bairstow 2020 [26]	10	50	Inter	n/a	n/a	CBCT	n/a	Full	Emtpy
Chin 2019* [27]	10	71	Inter	Prostate	-	CBCT	COM	-	Full/ERB vs empty
De Boer 2013 [28]	20	100	Inter	Prostate	Chamfer matching	CBCT	SV surface	Full	Empty
De Crevoisier 2007 [29]	46	92	Intra	Bony anatomy	Non-Rigid	CT	COM	Full	None
Frank 2008 [30]	15	369	Inter	Bony anatomy	-	CT	COM	Full	Empty
Frank 2010 [31]	15	360	Inter	n/a	n/a	CT	n/a	-	-
Gill 2014 [32]	11	21	Intra	First image in series	-	MRI	COM	Full	Empty
Hollander 2012* [33]	10	66	Inter	Prostate	-	-	COM	-	Full/ERB
Kershaw 2018 [34]	19	209	Inter	Prostate	Rigid (ROI)	CT	COM	Full	Empty
Li 2014 * [35]	10	110	Inter + Intra	Prostate	-	CBCT	COM	-	-
Liang 2009 [36]	24	384	Inter	Prostate	Rigid (ROI)	Helical CT	COM	-	-
Liu 2012 [37]	28	448	Inter	n/a	n/a	Helical CT	n/a	-	-
Mak 2012 [38]	24	771	Inter	Prostate	-	CT	COM	Full	Empty
Mayyas 2014 [39]	10	200	Inter	Prostate	Non-rigid	CBCT	SV surface	Full	Empty
Mercuri 2008 * [40]	10	390	Inter	Prostate	-	EPI	Implanted markers	-	-
Miralbell 2003 [41]	9	63	Inter	n/a	n/a	CT	n/a	Empty	-
Ogino 2008 [42]	76	304	Inter	Bony anatomy	-	CT	COM	Empty	Empty vs digital gas removal
Oksuz 2014 * [43]	10	160	Inter	Prostate	-	CBCT	-	-	-
Sheng 2017 [44]	15	148	Intra	Prostate	-	CBCT	COM	-	-
Smitsmans 2011 [45]	13	296	Inter	Prostate	Grey value	CBCT	-	-	Empty
Van der Burgt 2015 [46]	90	720	Inter	Prostate	Grey value	CBCT	COM	-	None
Van der Wielen 2008 [47]	21	84	Inter	Prostate	Non-rigid	CT	SV surface	Full	Empty

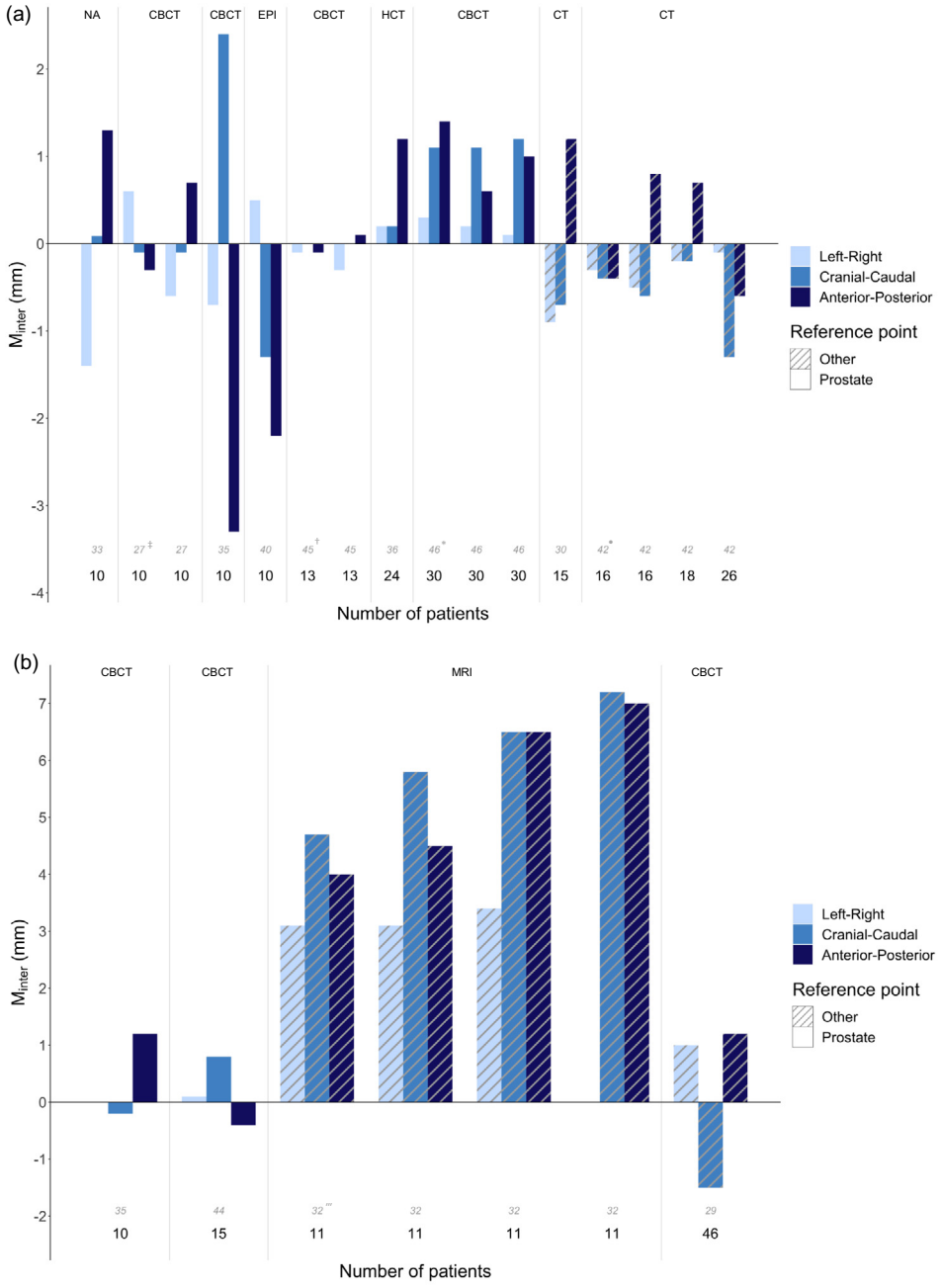

Fig. 1. a–f: Means, systematic errors, random errors and PTV-margins of the seminal vesicles (SV) per number of patients, grouped by reference point. *Row in italics at the bottom: article numbers*; Top row: the image modality used in that article. M_{inter} = interfraction mean; $\sum_{inter}$ = interfraction systematic error; σ_{inter} = interfraction random error; M_{intra} = intrafraction mean; $\sum_{intra}$ = intrafraction systematic error; PTV = Planning target volume; CBCT = Cone-beam Computed Tomography; CT = Computed Tomography; MRI = magnetic resonance imaging; EPI = electronic portal images; HCT = Helical Computed Tomography; [27]‡ = 2 different patient groups reported: with an empty rectum or with an endorectal balloon in place; [32]‴ = Cinematic Magnetic Resonance Imaging sequence with multiple measurements after 3, 5, 10 and 15 min respectively; [34]^{i} = 2 different methods reported: on a treatment couch with 3 degrees of freedom or 6 degrees of freedom; [42]• = 4 different patient groups described: digital gas removal yes or no and treated with whole pelvic radiation or only on prostate and SV; [45]† = 2 different analysis methods reported: with and without correction for rotation; [46]* = 3 different patient groups described: no invasion, minimal invasion or extensive invasion of the tumor in SV.

rior and caudal directions showed the highest deformations (max 50%) whereas left and right showed the lowest (max 14%). No deviation vector field exceeded >10 mm except 1% in caudal direction.

In addition, volume changes of the SV can lead to additional treatment uncertainties and may need to be accounted for during treatment. Bairstow et al. [26] analysed 10 patients with at least 4 CBCTs. Two outliers showed considerable volume changes with a mean variance for patient 1 of 0.29 cc ± 0.45/0.53 cc ± 0.72 depending on the delineator. Patient 2 showed a mean variance of 0.3 cc ± 0.54/1.69 cc ± 1.3, depending on the delineator. Miralbell et al. [41] analysed 9 patients with repeat CT-scans and reported a volume variance of 1.08 (±0.20) in the consecutive scans compared to the simulation scan.

The anisotropic PTV-margins, including both the margins reported in the publications and the margins calculated by us using the van Herk formula, are shown in Fig. 1f. PTV-margins based on systematic and random errors are reported to be around 8 mm, a value widely used in clinical practice for the SV [19,20]. Larger values (>9 mm margins) were found in 2 out of 8 articles with reported PTV–margins up to 10.5 mm [38] and 14.9 mm [42].

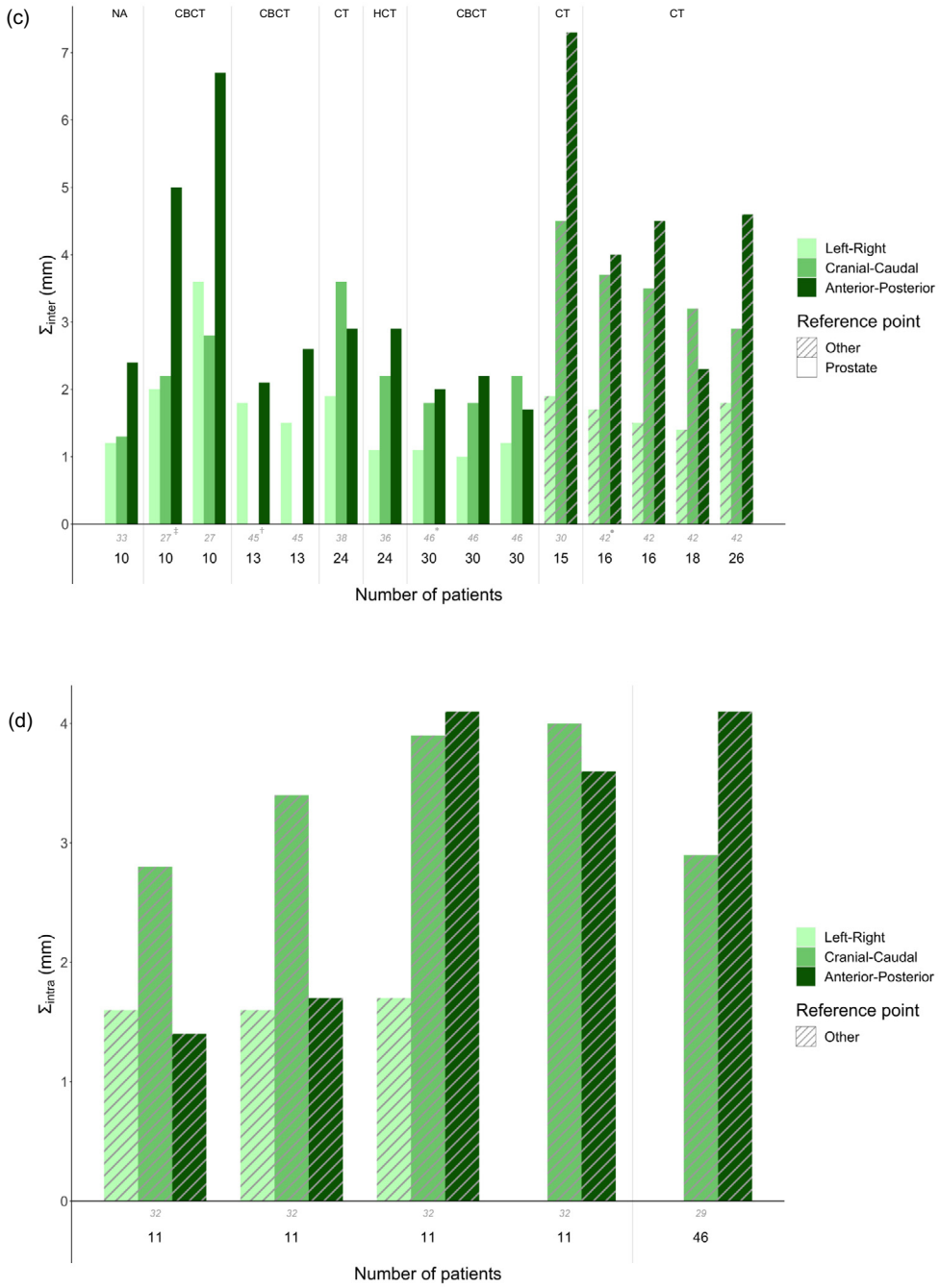

Fig. 1 (*continued*)

When the systematic and random errors are measured relative to the bony anatomy, the PTV-margins are larger than those based on a prostate match. Due to the absence of published random errors, no margins correcting purely for intra-fraction motion can be/are reported. Fig. 2 shows the different proposed PTV margins, maximum stated values isotropically applied, in a typical prostate patient case.

To visualize the effect of preparation protocols on the motion of the SV, in the form of the inter-fraction mean, systematic error, random error and PTV-margin were plotted for rectal and bladder preparation protocol (figs. C.1 and C.2, Appendix C). From these figures, no apparent trend between rectal and bladder preparation and magnitude or direction of motion was observed. Similarly, the effect of rectal and bladder preparation on intra-fraction motion is inconclusive.

Discussion

This review focuses on understanding the inter- and intra-fraction motion of the SV during external-beam radiation therapy of PCa and the PTV-margins needed to correct for this motion. This is required to devise safe PTV volume reduction strategies to enable the ultra-hypofractionated treatment of high risk PCa. The literature reported in this review show an extensive variety in methods used for obtaining and reporting motion, making a secondary analysis or generating average values not possible.

Inter- vs intra-fraction translations

The mean inter-fraction translation, M_{inter}, of 7 out of 9 publications is below 1.5 mm, suggesting a limited group mean error. Two

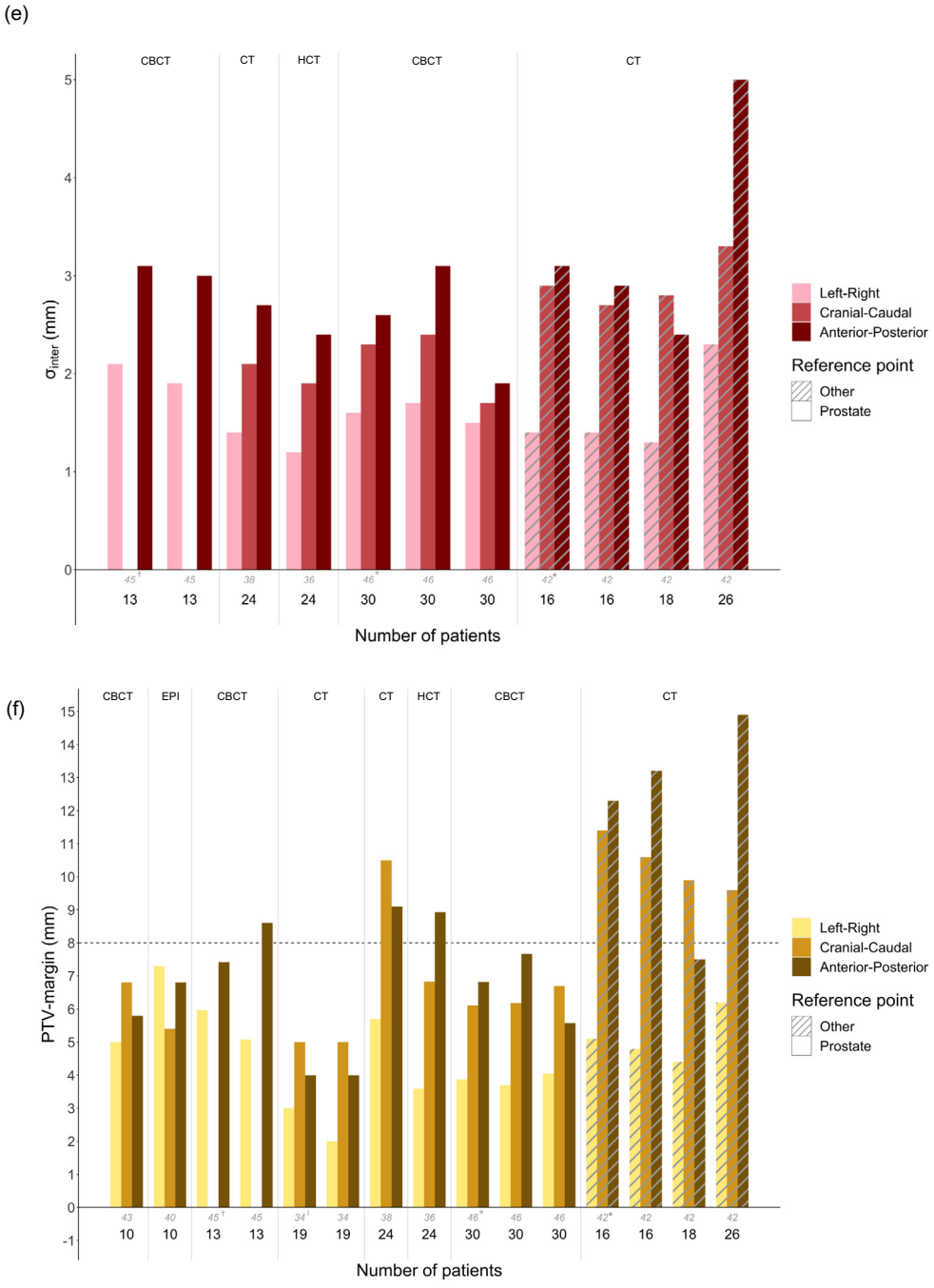

Fig. 1 (*continued*)

publications report means above 2 mm, both of which report on a small set of 10 patients [35,40]. For the intra-fraction translation 2 of the 3 available publications report means, M_{intra}, up to 1.5 mm. Regarding study [32] reporting means of up to 7 mm, it remains unclear whether relative or only absolute values of translation were reported, as well as which reference point was used. Overall, the values of M_{inter} and M_{intra} are comparable and in the order of 1 mm, which would be expected from unbiased data. However, especially on intra-fraction translation, the number of publications are still limited with only four studies.

The systematic inter-fraction error, $\sum_{inter}$, shows values between 1 and 3.5 mm. Note that the $\sum_{inter}$ values reported by Chin et al. [27] and Frank et al. [30] were derived from the SD of the M_{inter} that was given. There are only two reports that discuss the systematic errors of intra-fraction translation, $\sum_{intra}$ [29,32]. Both articles report motion of 1.5–4 mm. These values for $\sum_{intra}$ were derived by us by using the SD of the group mean. Comparing $\sum_{inter}$ and $\sum_{intra}$ proves difficult due to the variety in the data and the limited number of publications reporting on intra-fraction translation of the SV. However, comparing $\sum_{inter}$ based on a prostate match with $\sum_{intra}$, shows similar values of 3–4 mm.

For random inter-fraction error, σ_{inter}, values of 1–3 mm are reported. The larger values of $\sum_{inter}$, σ_{inter} and the PTV-margin in Fig. 1c, e and f correspond to publications in which a match based on bony anatomy was used [30,42]. The effect of these different matches on PTV-margin is shown by Kershaw et al. [34] who found

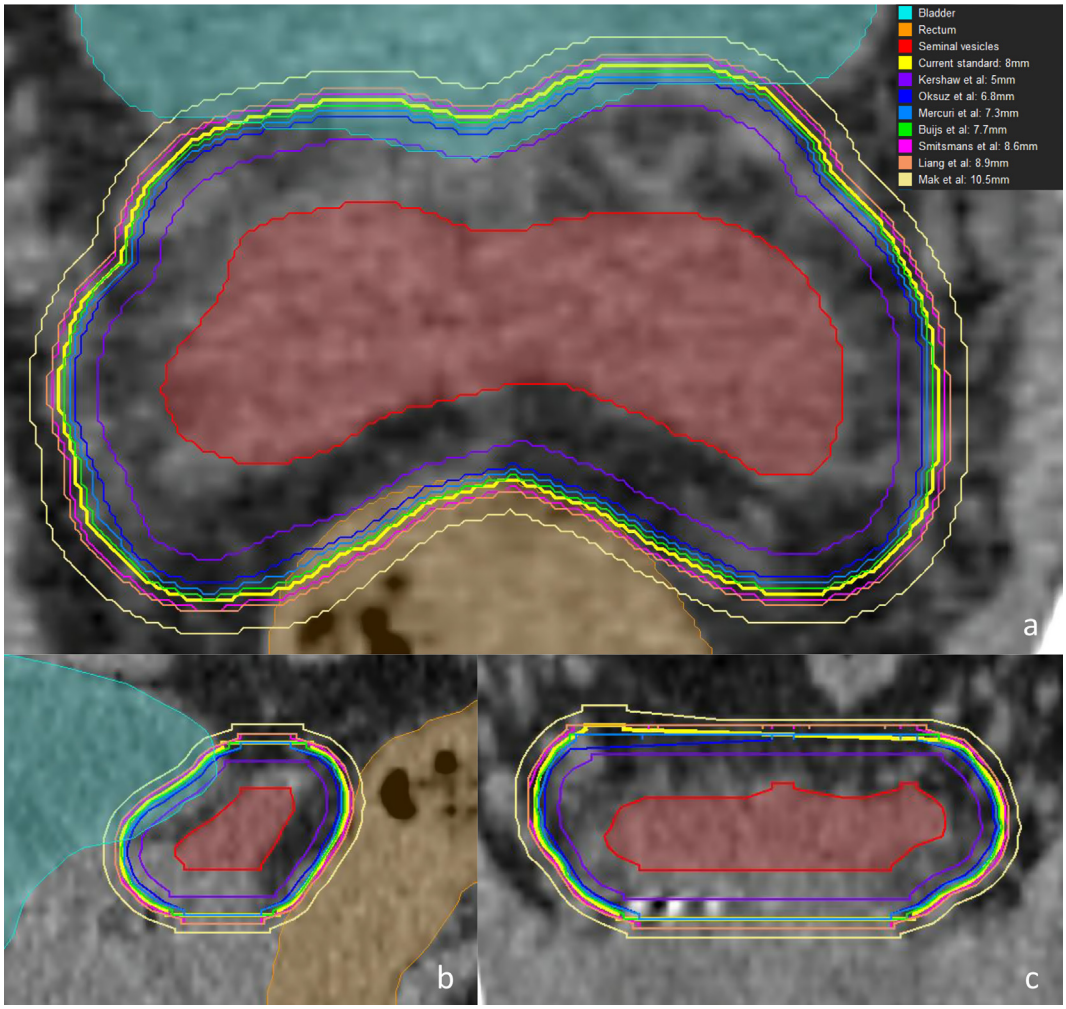

Fig. 2. Variance in reported PTV-margins grouped around the current clinical standard of 8 mm, each article represented by a different line; a: axial view; b: coronal view; c: sagittal view.

anisotropic PTV-margins of 2–5 mm and 4–10 mm after a prostate vs a bone match respectively. Similarly, Meijer et al. [18] reported an isotropic margin of 13 mm when matched on bony anatomy compared to 8 mm when matched on the prostate. This indicates that there is at least some level of correlation between the inter-fraction motion of the prostate and of the SV. Similar to the prostate, the motion of the SV is caused by changes in rectal and bladder distention. However, the reported levels of correlation between prostate and SV motion vary. All publications note that the SV can move semi-independently from the prostate and the amplitude of motion is larger. Smitsmans et al. [45] reported that as much as 42% of the AP SV inter-fraction translation was correlated to the LR prostate gland rotation. Similarly, Liang et al. [36], showed that inter-fraction translation of the prostate and the SV in the AP direction was correlated (R^2 of 0.7), both driven by rectum and bladder changes. No correlations were found for the other directions. De Boer et al. [28] show an inverse correlation between the LR rotations of the SV and the prostate LR rotation. A large interpatient variety in correlation of intra-fraction SV and prostate translation was shown by Gill et al. [32]. The reported Pearson correlation coefficients, R, ranged from −0.23 to 0.82, with the 7 out of 10 patients showing no linear correlation trend. Consequently, imaged-guided strategies that only focus on the prostatic gland will not fully compensate for SV motion.

Gill et al. [32] showed that there appears to be a plateau in SV displacement that was reached 10 min after starting radiation delivery. No significant increase in displacement was seen after this time. It is unclear how this corresponds exactly to on-table time. De Muinck Keizer et al. [49] report that the extent of intra-fraction motion of the prostate is reached after 30 min on-table time.

Rotations, deformations and volume changes

Means of inter-fraction rotations were discussed by two publications [28,46], most of which <1°, as expected in unbiased data, with only three rotations in one publication [46] significantly different than 0. $\Sigma_{rotation}$ and $\sigma_{rotation}$ around the LR-axis were also reported in both articles and range between 5.0° and 7.2°. Van der Burgt et al. [46] reported that these rotations around the LR-axis were larger than the rotations around the CC and AP-axes with max rotations of 2.4° and 2.7° respectively. This is in line with Hoogeman et al. [50] who described that prostate+SV rotations were largest in the LR-axis with $\Sigma_{rotation}$ and $\sigma_{rotation}$ of 3.6° and 5.1° respectively. These rotations were significantly correlated to differences in rectal volume ($p < 0.0001$) [50].

Mean deformations after prostate match were mentioned by five publications [33,35,39,44,47]. All five reported the highest

deformations in the anterior, caudal and posterior borders. This is somewhat in line with the largest translations being in AP and CC axis and the largest rotations being around the LR-axis and can be explained by rectal and bladder volume changes as well [47]. Mean intra-fraction deformations, <1.1 mm [44], appeared to be smaller than the mean inter-fraction deformation, <3 mm [33,47]. This was also described by Li et al. who reported both [35]. Mayyas et al. appear to report higher deformations than the previously mentioned articles (1% >10 mm) [39]. However, this can be explained by the fact that only Mayyas et al. [39] did not use means to report their deformations. Important to note here is that all deformations mentioned are measured after prostate matching. No residual deformations after correction for SV translation were described.

The publications reporting on the magnitude of volume changes show different results, which can be, partially, explained by the different experimental methods. Where Miralbell et al. [41] used the planning scan as reference, Bairstow et al. [26] used the mean SV volume as a reference. The latter also only reported on two extreme cases from their population, where Miralbell et al. [41] reported on all 9 patients. Liu et al. [37] reported a study in which 28 patients with at least 15 follow-up CT-scans were analysed. The volume, compared to the planning scan, decreased significantly in 3 cases and increased significantly in one case. In contrast, Frank et al. [31] found no significant volume changes in 15 patients with repeated CT-on-rails images. As these varying results suggest, no consensus regarding the extent of these volume changes has been reached and further research is needed to clarify the geometrical and clinical effect of these volume changes [26].

PTV-margins to account for SV motion

The three studies reporting PTV-margins [34,40,42] all used the van Herk margin recipe (Eq. 1) [48] except for one article which used an alternate version for a 2D dose distribution: 2.15 Σ + 0.7 σ [45]. This review compares these reported PTV-margins, with margins we calculated from reported systematic (Σ) and random errors (σ) using the same van Herk margin recipe [48]. One publication reports both systematic and random errors and a PTV-margin. The margins recalculated by us are very similar to those reported [42] (i.e. 4.4 vs 4.4 in LR, 10.0 vs 9.9 in CC and 7.4 vs 7.5 in AP respectively).

Most publications included in this review report anisotropic PTV-margins for the SV of approximately 8 mm (see Fig. 2). This value is also used in multiple studies looking at the effect of margins on target coverage. Meijer et al. [18] showed that an isotropic PTV-margin of 3 mm for the prostate and 8 mm for the SV ensures 95% CTV-coverage for 90% of the patients using a prostate fiducial match. Mutanga et al. [19] reported that an isotropic 8 mm expansion for the SV resulted in a clinically acceptable coverage. Thörnqvist et al. [21] found that an isotropic PTV-margin of 7 mm resulted in 95% coverage of the target volume for 18/19 patients. Stenmark et al. [20] looked at the coverage for the proximal 1 cm as well as the entire SV. For 95% geometrical coverage of the CTV for 90% of the patients 5 mm and 8 mm isotropic margins were required when treating the partial SV and the full SV respectively.

Two publications reported SV margins > 9 mm, one of which used a bony anatomy match to register the SV motion [42]. Using a prostate match, Mak et al. [38] reported larger margins, i.e. 10 mm in the CC-direction, possibly limited by the 5 mm CT slice thickness in this direction.

Sheng et al. [44] reported a 5 mm isotropic margin around the SV to ensure a 95% coverage in 90% of the fractions. However, this margin assumes intra-fraction motion tracking of the prostate. The literature on intra-fraction motion of the SV is still too limited to extract a PTV-margin based on intra-fraction motion alone.

Translation consistently appears to be the smallest in the LR direction (Fig. 1a–f). This offers opportunities of anisotropic PTV-margins. Smitsmans et al. [45] reported margins for the SV of 4.6 mm and 7.6 mm for the LR- and AP-direction respectively, not taking into account deformation and rotation. In addition, the rotations of the SV are largest around the LR axis, which will mostly contribute to motion in CC and AP direction. Most dosimetric studies report isotropic PTV-margins in the order of 8 mm [18–21]. Margin reduction in the LR-direction might have a limited clinical impact, considering most toxicity comes from the bladder and rectum that lie inferior and superior to the SV.

Influencing factors

Bladder and especially rectal volume changes are known to play a significant role in prostate inter- and intra-fraction motion [25]. For the SV similar patterns of correlations between rectal and bladder filling and SV motion have been observed [27,29,30,38,51]. However, fig. C.1, in Appendix C, shows that different efforts to control the rectal filling status do not have a clear effect on the amplitude of inter-and intra-fraction motion. Similarly to rectal filling status, no apparent trend is visible in the amplitude of SV motion, with respect to bladder preparation (Fig. C.2, in Appendix C). The absence of a correlation between rectal and bladder filling protocols and the amplitude of systematic and random errors in our study can be, at least partially, explained by their mixed success rate to effectively control the filling status, as shown by a review on this topic [52].

Only one study reported on the effect of tumour invasion on SV motion. Van der Burgt et al. [53] compared the differences in inter-fraction motion between patient groups with different levels of tumour invasion in the SV. The random displacements in the group with extensive invasion were statistically significantly lower than those of the minimal and the no invasion group. However, this reduction was small and the SV motion remained considerable.

Limitations

There are several limitations in the van Herk margin recipe as in equation 1 that are relevant in applying the margin formula to SV. First of all, only translations are taken into account. Rotations, deformations, and volume changes all contributing to errors in the treatment of SV, are ignored. Studies that do include rotations show that rotational errors can cause a loss in tumour control probability [54], especially for non-spherical targets [28]. An example can be found in de Boer et al. [28] who state a margin of 11.6 mm including rotational errors of the SV and 8.2 mm when correcting for them. Including rotations will lead to anisotropic and location specific margins as the margin will be dependent on the distance to the rotation axes, generally assumed to lie near the apex of the prostate [55,56]. As the correlation between the prostate and SV rotations is limited, there is a residual deformation of the SV in the order of 2–3 mm SD that needs to be taken into account [30]. Hence, deformations, rotations, and volume changes that are not fully corrected for before the start of treatment lead to an increased PTV margin to ensure CTV coverage and the van Herk recipe will only give a lower limit of the margin required. Another limitation is that the van Herk margin is valid for conventional fractionation. To translate the results from the referenced publications to a hypofractionated treatment scheme, the margin will have to be increased. In a treatment consisting of only a few fractions, the average random error might deviate from zero, resulting in an additional systematic error [55,57,58]. As an indication, the PTV margin will have to be increased from 8 mm to 8.5 and 9.2 mm respectively for a 5 and 2 fraction treatment, based on a calculation using equal systematic and random errors.

Possibilities for margin reduction

With conventional image guided radiotherapy (IGRT) [59] PTV-margin reduction for the SV has been achieved, but remains with 8 mm substantial [18–20]. Further margin reduction with IGRT might be difficult to achieve and therefore ultra-hypofractionation for patients with a target volume including the SV remains challenging.

Correcting for inter-fraction motion

Inter-fraction motion can be corrected off- and online by adaptive radiation therapy (ART). ART for prostate has been extensively studied and reported [60–66]. However, only a limited amount of publications on ART for the SV exist. Xia et al. reported on a library-of-plans approach [67] whereas De Boer et al. [28] used a hybrid registration technique, prostate markers followed by a soft-tissue registration of the SV. Both showed promise in possible margin reduction around the SV. However, most recent research regarding prostate ART and margin reduction still focusses on prostate only and is fuelled by the developments of MR-guided radiation treatment systems [68,69]

Correcting for intra-fraction motion

In contrast to inter-fraction motion, intra-fraction motion is more complex to take into account. A straightforward solution is to minimize fraction duration as the displacement increases with time [29,32,35]. Intra-fraction motion correction of the prostate has been demonstrated using Calypso 4D tracking [70], real-time tracking using the CyberKnife [71], a library of plans [72], and soft tissue gating using the MRidian [69]. However, the challenge remains how to apply intra-fraction motion management for adjacent targets, in this case the prostate and the SV, that move semi-correlated. Beam-per-beam online replanning with all its challenges could pose a solution [68,73].

Conclusion

This extensive literature review shows that the inter- and intra-fraction motion of the SV is substantial and largely uncorrelated with prostate motion. Main factors influencing the prostate and SV motion are differences in rectal and bladder filling. Strategies to control rectum and bladder filling status, and thereby reduce treatment uncertainties, appear to lack effectiveness. When calculating PTV-margins for the SV, translations, rotations and deformations need to be taken into account as they can be substantial, even after an initial match on the prostate. To reduce PTV margins around the SV, their inter- and intra-fraction motion needs to be adequately accounted for. Further research is required to quantify the safety and feasibility of PTV-margin reduction for the SV, in particular in context of ultra-hypofractionation for high risk prostate cancers, which will be subject of further studies in our institute.

Support

This work was in part funded by a research grant of Accuray Inc., Sunnyvale, USA.

Conflicts of interest

This work was in part funded by a research grant of Accuray Inc., Sunnyvale, USA. Erasmus MC Cancer Institute also has a research collaboration with Elekta AB, Stockholm, Sweden and Varian Medical Systems, Inc., Palo Alto, USA.

Acknowledgements

The authors wish to thank Wichor Bramer and Sabrina Meertens-Gunput from the Erasmus MC Medical Library for developing and updating the search strategies.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.radonc.2022.02.002.

References

[1] Mottet N, Bellmunt J, Bolla M, Briers E, Cumberbatch MG, De Santis M, et al. EAU-ESTRO-SIOG guidelines on prostate cancer. Part 1: Screening, diagnosis, and local treatment with curative intent. Eur Urol 2017;71:618–29.
[2] Brenner DJ, Hall EJ. Fractionation and protraction for radiotherapy of prostate carcinoma. Int J Radiat Oncol Biol Phys 1999;43:1095–101.
[3] Fowler JF. The radiobiology of prostate cancer including new aspects of fractionated radiotherapy. Acta Oncol 2005;44:265–76.
[4] Mangoni M, Desideri I, Detti B, Bonomo P, Greto D, Paiar F, et al. Hypofractionation in prostate cancer: radiobiological basis and clinical appliance. Biomed Res Int 2014;2014.
[5] Kalbasi A, Li J, Berman A, Swisher-McClure S, Smaldone M, Uzzo RG, et al. Dose-escalated irradiation and overall survival in men with nonmetastatic prostate cancer. JAMA Oncol 2015;1:897–906.
[6] Murray J, Griffin C, Gulliford S, Syndikus I, Staffurth J, Panades M, et al. A randomised assessment of image guided radiotherapy within a phase 3 trial of conventional or hypofractionated high dose intensity modulated radiotherapy for prostate cancer. Radiother Oncol 2020;142:62–71.
[7] Chen J, Lee RJ, Handrahan D, Sause WT. Intensity-modulated radiotherapy using implanted fiducial markers with daily portal imaging: assessment of prostate organ motion. Int J Radiat Oncol Biol Phys 2007;68:912–9.
[8] Incrocci L, Wortel RC, Alemayehu WG, Aluwini S, Schimmel E, Krol S, et al. Hypofractionated versus conventionally fractionated radiotherapy for patients with localised prostate cancer (HYPRO): final efficacy results from a randomised, multicentre, open-label, phase 3 trial. Lancet Oncol 2016;17:1061–9.
[9] Dearnaley D, Syndikus I, Mossop H, Khoo V, Birtle A, Bloomfield D, et al. Conventional versus hypofractionated high-dose intensity-modulated radiotherapy for prostate cancer: 5-year outcomes of the randomised, non-inferiority, phase 3 CHHiP trial. Lancet Oncol 2016;17:1047–60.
[10] Widmark A, Gunnlaugsson A, Beckman L, Thellenberg-Karlsson C, Hoyer M, Lagerlund M, et al. Ultra-hypofractionated versus conventionally fractionated radiotherapy for prostate cancer: 5-year outcomes of the HYPO-RT-PC randomised, non-inferiority, phase 3 trial. Lancet 2019;394:385–95.
[11] Bayman NA, Wylie JP. When should the seminal vesicles be included in the target volume in prostate radiotherapy? Clin Oncol (R Coll Radiol) 2007;19:302–7.
[12] McKay AC, Odeluga N, Jiang J, Sharma S. Anatomy, abdomen and pelvis, seminal vesicle. StatPearls [Internet] 2020.
[13] Makarov DV, Trock BJ, Humphreys EB, Mangold LA, Walsh PC, Epstein JI, et al. Updated nomogram to predict pathologic stage of prostate cancer given prostate-specific antigen level, clinical stage, and biopsy Gleason Score (Partin Tables) based on cases from 2000 to 2005. Urology 2007;69:1095–101.
[14] Koh H, Kattan MW, Scardino PT, Suyama K, Maru N, Slawin K, et al. A nomogram to predict seminal vesicle invasion by the extent and location of cancer in systematic biopsy results. J Urol 2003;170:1203–8.
[15] Grivas N, Hinnen K, de Jong J, Heemsbergen W, Moonen L, Witteveen T, et al. Seminal vesicle invasion on multi-parametric magnetic resonance imaging: correlation with histopathology. Eur J Radiol 2018;98:107–12.
[16] Feng TS, Sharif-Afshar AR, Wu J, Li Q, Luthringer D, Saouaf R, et al. Multiparametric MRI improves accuracy of clinical nomograms for predicting extracapsular extension of prostate cancer. Urology 2015;86:332–7.
[17] Morlacco A, Sharma V, Viers BR, Rangel LJ, Carlson RE, Froemming AT, et al. The incremental role of magnetic resonance imaging for prostate cancer staging before radical prostatectomy. Eur Urol 2017;71:701–4.
[18] Meijer GJ, de Klerk J, Bzdusek K, van den Berg HA, Janssen R, Kaus MR, et al. What CTV-to-PTV margins should be applied for prostate irradiation? Four-dimensional quantitative assessment using model-based deformable image registration techniques. Int J Radiat Oncol Biol Phys 2008;72:1416–25.
[19] Mutanga TF, Boer HCJd, Wielen GJvd. Margin evaluation in the presence of deformation, rotation, and translation in prostate and entire seminal vesicle irradiation with daily marker-based setup . . .: Elsevier; 2011.
[20] Stenmark MH, Vineberg K, Ten Haken RK, Hamstra DA, Feng M. Dosimetric implications of residual seminal vesicle motion in fiducial-guided intensity-modulated radiotherapy for prostate cancer. Med Dosim 2012;37:240–4.
[21] Thörnqvist S, Hysing LB, Zolnay AG, Söhn M, Hoogeman MS, Muren LP, et al. Treatment simulations with a statistical deformable motion model to evaluate margins for multiple targets in radiotherapy for high-risk prostate cancer. Radiother Oncol 2013;109:344–9.

[22] Ugurluer G, Atalar B, Zoto Mustafayev T, Gungor G, Aydin G, Sengoz M, et al. Magnetic resonance image-guided adaptive stereotactic body radiotherapy for prostate cancer: preliminary results of outcome and toxicity. Br J Radiol 2021;94:20200696.
[23] Alongi F, Rigo M, Figlia V, Cuccia F, Giaj-Levra N, Nicosia L, et al. 1.5 T MR-guided and daily adapted SBRT for prostate cancer: feasibility, preliminary clinical tolerability, quality of life and patient-reported outcomes during treatment. Radiat Oncol 2020;15:69.
[24] Telkhade T, Murthy V, Kanala TS, Mathew JM, Phurailatpam R, Mokal S, et al. Safety and efficacy of ultra-hypofractionation in node-positive prostate cancer. Clin Oncol (R Coll Radiol) 2021;33:172–80.
[25] Langen KM, Jones DTL. Organ motion and its management. Elsevier; 2001.
[26] Bairstow R, Cain M, Reynolds P, Bridge P. Evaluation of seminal vesicle volume variability in patients receiving radiotherapy to the prostate. J Radiother Pract 2020;19:20–4.
[27] Chin S, McWilliam A, Brand D, Barton S, Song YP, Van Herk M, et al. Does the use of an endorectal balloon improve seminal vesicle stability for prostate radiotherapy? Radiother Oncol 2019;133:S1107.
[28] De Boer J, Van Herk M, Pos FJ, Sonke JJ. Hybrid registration of prostate and seminal vesicles for image guided radiation therapy. Int J Radiat Oncol Biol Phys 2013;86:177–82.
[29] De Crevoisier R, Melancon AD, Kuban DA, Lee AK, Cheung RM, Tucker SL, et al. Changes in the pelvic anatomy after an IMRT treatment fraction of prostate cancer. Int J Radiat Oncol Biol Phys 2007;68:1529–36.
[30] Frank SJ, Dong L, Kudchadker RJ, De Crevoisier R, Lee AK, Cheung R, et al. Quantification of prostate and seminal vesicle interfraction variation during IMRT. Int J Radiat Oncol Biol Phys 2008;71:813–20.
[31] Frank SJ, Kudchadker RJ, Kuban DA, De Crevoisier R, Lee AK, Cheung RM, et al. A volumetric trend analysis of the prostate and seminal vesicles during a course of intensity-modulated radiation therapy. Am J Clin Oncol 2010;33:173–5.
[32] Gill S, Dang K, Fox C, Bressel M, Kron T, Bergen N, et al. Seminal vesicle intrafraction motion analysed with cinematic magnetic resonance imaging. Radiat Oncol 2014;9:1–8.
[33] Hollander A, Both S, Vapiwala N, Kirk M, Christodouleas J, Bekelman J, et al. Interfraction motion of the full seminal vesicles in prostate radiation therapy using a daily endorectal balloon. Int J Radiat Oncol Biol Phys 2012;84:S388.
[34] Kershaw L, van Zadelhoff L, Heemsbergen W, Pos F, van Herk M. Image guided radiation therapy strategies for pelvic lymph node irradiation in high-risk prostate cancer: motion and margins. Int J Radiat Oncol Biol Phys 2018;100:68–77.
[35] Li T, Sheng Y, Lee W, Wu Q. Sbrt for prostate + seminal vesicles: Fixed margin or online adaptation. Int J Radiat Oncol Biol Phys 2014;90:S18.
[36] Liang J, Wu Q, Yan D. The role of seminal vesicle motion in target margin assessment for online image-guided radiotherapy for prostate cancer. Int J Radiat Oncol Biol Phys 2009;73:935–43.
[37] Liu H, Wu Q. A "rolling average" multiple adaptive planning method to compensate for target volume changes in image-guided radiotherapy of prostate cancer. J Appl Clin Med Phys 2012;13:3697.
[38] Mak D, Gill S, Paul R, Stillie A, Haworth A, Kron T, et al. Seminal vesicle interfraction displacement and margins in image guided radiotherapy for prostate cancer. Radiat Oncol 2012;7.
[39] Mayyas E, Kim J, Kumar S, Liu C, Wen N, Movsas B, et al. A novel approach for evaluation of prostate deformation and associated dosimetric implications in IGRT of the prostate. Med Phys 2014;41.
[40] Mercuri AL, Joon DL, Khoo V, Rolfo A, Daly K, McNamara J, et al. The impact of prostate and seminal vesicle motion during prostate cancer radiotherapy on planning margins. Int J Radiat Oncol Biol Phys 2008;72. S312-S.
[41] Miralbell R, Özsoy O, Pugliesi A, Carballo N, Arnalte R, Escudé L, et al. Dosimetric implications of changes in patient repositioning and organ motion in conformal radiotherapy for prostate cancer. Radiother Oncol 2003;66:197–202.
[42] Ogino I, Uemura H, Inoue T, Kubota Y, Nomura K, Okamoto N. Reduction of prostate motion by removal of gas in rectum during radiotherapy. Int J Radiat Oncol Biol Phys 2008;72:456–66.
[43] Oksuz DC, Dincbas FO, Ergen SA, Iktueren B, Bakir A, Koca S. Seminal vesicle interfraction displacement and dose variations throughout the CBCT-guided radiation therapy for prostate cancer. Int J Radiat Oncol Biol Phys 2014;90: S429–30.
[44] Sheng Y, Li T, Lee WR, Yin FF, Wu QJ. Exploring the margin recipe for online adaptive radiation therapy for intermediate-risk prostate cancer: an intrafractional seminal vesicles motion analysis. Int J Radiat Oncol Biol Phys 2017;98:473–80.
[45] Smitsmans MHP, De Bois J, Sonke JJ, Catton CN, Jaffray DA, Lebesque JV, et al. Residual seminal vesicle displacement in marker-based image-guided radiotherapy for prostate cancer and the impact on margin design. Int J Radiat Oncol Biol Phys 2011;80:590–6.
[46] Van Der Burgt M, Bergsma L, De Vries J, Pos FJ, Kalisvaart R, Heemsbergen W, et al. Impact of tumour invasion on seminal vesicles mobility in radiotherapy of prostate cancer. Radiother Oncol 2015;117:283–7.
[47] G.J. Van der Wielen T.F. Mutanga L. Incrocci W.J. Kirkels E.M. Vasquez Osorio M.S. Hoogeman et al. Deformation of prostate and seminal vesicles relative to intraprostatic fiducial markers Int J Radiat Oncol Biol Phys. 72 2008 1604 11.e3
[48] Van Herk M. Errors and margins in radiotherapy. Sem Radiat Oncol 2004;14:52–64.
[49] De Muinck Keizer DM, Kerkmeijer LGW, Willigenburg T, van Lier A, Hartogh MDD, van der Voort van Zyp JRN, et al. Prostate intrafraction motion during the preparation and delivery of MR-guided radiotherapy sessions on a 1.5T MR-Linac. Radiother Oncol. 2020;151:88-94.
[50] Hoogeman MS, Van Herk M, De Bois J, Lebesque JV. Strategies to reduce the systematic error due to tumor and rectum motion in radiotherapy of prostate cancer. Radiother Oncol 2005;74:177–85.
[51] Nejad-Davarani SP, Sevak P, Moncion M, Garbarino K, Weiss S, Kim J, et al. Geometric and dosimetric impact of anatomical changes for MR-only radiation therapy for the prostate. J Appl Clin Med Phys 2019;20:10–7.
[52] McNair HA, Wedlake L, Lips IM, Andreyev J, Van Vulpen M, Dearnaley D. A systematic review: effectiveness of rectal emptying preparation in prostate cancer patients. Pract Radiat Oncol 2014;4:437–47.
[53] Buijs M, Bergsma L, De Vries J, Kalisvaart R, Pos F, Heemsbergen W, et al. Impact of tumor invasion on seminal vesicles mobility in radiotherapy of T3b prostate cancer. Radiother Oncol 2015;115:S39–40.
[54] van Herk M, Remeijer P, Lebesque JV. Inclusion of geometric uncertainties in treatment plan evaluation. Int J Radiat Oncol Biol Phys 2002;52:1407–22.
[55] Van Herk M, Remeijer P, Rasch C, Lebesque JV. The probability of correct target dosage: dose-population histograms for deriving treatment margins in radiotherapy. Int J Radiat Oncol Biol Phys 2000;47:1121–35.
[56] Stroom JC, De Boer HCJ, Huizenga H, Visser AG. Inclusion of geometrical uncertainties in radiotherapy treatment planning by means of coverage probability. Int J Radiat Oncol Biol Phys 1999;43:905–19.
[57] Gordon JJ, Siebers JV. Convolution method and CTV-to-PTV margins for finite fractions and small systematic errors. Phys Med Biol 2007;52:1967.
[58] de Boer HC, Heijmen BJ. A protocol for the reduction of systematic patient setup errors with minimal portal imaging workload. Int J Radiat Oncol Biol Phys 2001;50:1350–65.
[59] Ghadjar P, Fiorino C, Munck Af Rosenschold P, Pinkawa M, Zilli T, van der Heide UA. ESTRO ACROP consensus guideline on the use of image guided radiation therapy for localized prostate cancer. Radiother Oncol 2019;141:5–13.
[60] Ghilezan M, Yan D, Martinez A. Adaptive radiation therapy for prostate cancer. Elsevier; 2010.
[61] Lei Y, Wu Q. A hybrid strategy of offline adaptive planning and online image guidance for prostate cancer radiotherapy. Phys Med Biol 2010;55:2221–34.
[62] Wu QJ, Thongphiew D, Wang Z, Mathayomchan B, Chankong V, Yoo S, et al. On-line re-optimization of prostate IMRT plans for adaptive radiation therapy. Phys Med Biol 2008;53:673–91.
[63] Li T, Thongphiew D, Zhu X, Lee WR, Vujaskovic Z, Yin F-F, et al. Adaptive prostate IGRT combining online re-optimization and re-positioning: a feasibility study. Phys Med Biol 2011;56:1243.
[64] Qin A, Sun Y, Liang J, Yan D. Evaluation of online/offline image guidance/adaptation approaches for prostate cancer radiation therapy. Int J Radiat Oncol Biol Phys 2015;91:1026–33.
[65] Stanley K, Eade T, Kneebone A, Booth JT. Investigation of an adaptive treatment regime for prostate radiation therapy. Pract Radiat Oncol 2015;5:e23–9.
[66] Li X, Quan EM, Li Y, Pan X, Zhou Y, Wang X, et al. A fully automated method for CT-on-rails-guided online adaptive planning for prostate cancer intensity modulated radiation therapy. Int J Radiat Oncol Biol Phys 2013;86:835–41.
[67] Xia P, Qi P, Hwang A, Kinsey E, Pouliot J, Roach IM. Comparison of three strategies in management of independent movement of the prostate and pelvic lymph nodes. Med Phys 2010;37:5006–13.
[68] Kontaxis C, Bol GH, Kerkmeijer LGW, Lagendijk JJW, Raaymakers BW. Fast online replanning for interfraction rotation correction in prostate radiotherapy. Med Phys 2017;44:5034–42.
[69] Tetar SU, Bruynzeel AME, Lagerwaard FJ, Slotman BJ, Bohoudi O, Palacios MA. Clinical implementation of magnetic resonance imaging guided adaptive radiotherapy for localized prostate cancer. Phys Imag Radiat Oncol 2019;9:69–76.
[70] Tong X, Chen X, Li J, Xu Q, Lin MH, Chen L, et al. Intrafractional prostate motion during external beam radiotherapy monitored by a real-time target localization system. J Appl Clin Med Phys 2015;16:5013.
[71] King CR, Lehmann J, Adler JR, Hai J. CyberKnife radiotherapy for localized prostate cancer: rationale and technical feasibility. Technol Cancer Res Treat 2003;2:25–9.
[72] Antico M, Prinsen P, Cellini F, Fracassi A, Isola AA, Cobben D, et al. Real-time adaptive planning method for radiotherapy treatment delivery for prostate cancer patients, based on a library of plans accounting for possible anatomy configuration changes. PLoS ONE 2019;14.
[73] De Muinck Keizer DM, Kontaxis C, Kerkmeijer LGW, van der Voort van Zyp JRN, van den Berg CAT, Raaymakers BW, et al. Dosimetric impact of soft-tissue based intrafraction motion from 3D cine-MR in prostate SBRT. Phys Med Biol. 2020;65:025012.