

Scientific Article

Bowel and Bladder Reproducibility in Image Guided Radiation Therapy for Prostate Cancer: Results of a Patterns of Practice Survey



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Received August 17, 2021; accepted December 16, 2021

Abstract

Purpose: Optimal management of patients with prostate cancer (PCa) to achieve bowel and bladder reproducibility for radiation therapy (RT) and the appropriate planning target volume (PTV) expansions for use with modern image guidance is uncertain. We surveyed American Society of Radiation Oncology radiation oncologists to ascertain practice patterns for definitive PCa RT with respect to patient instructions and set up, daily image guidance, and subsequent PTV expansions.

Methods and Materials: A pattern of practice survey was sent to American Society of Radiation Oncology radiation oncologists who self-identified as specializing in PCa. Respondents identified the fractionation regimens routinely used, and their practices regarding diet, bowel, and bladder instructions for patients with PCa before RT simulation and throughout treatment. Questions regarding PTV margins, daily set up practices, and use of image guidance were included.

Results: Of 190 respondents, 158 reported using conventional fractionation (CFx), 49 moderate hypofractionation (MHF), and 61 stereotactic body radiation therapy (SBRT). Diet modifications during RT were advised by 84% of respondents, treatment with full bladder by 96%, and bowel instructions by 78%. Prescription of bowel medication was higher for respondents using SBRT (95.1%) versus those using CFx/MHFx (55.1%; 34.7%). The most common implantable device reported was fiducial markers, with increased use in SBRT (86.0%; 68.9%) versus CFx/MHFx. Cone beam computed tomography was the most common daily imaging technique across fractionation regimens. SBRT showed correlation between PTV margin expansions, fiducial marker use, and image guidance.

Conclusions: Survey results indicate heterogeneity in treatment modality, dose, patient instructions, and PTV expansions used by radiation oncologists in the treatment of patients with PCa. Further investigation to define appropriate patient instructions on bowel preparation to maximize target reproducibility in PCa is needed, as is continued guidance on evidence-based approaches for image guidance and PTV margin selection.

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Sources of support: This research was funded by the intramural research program at the National Cancer Institute (grant No. ZID BC 010990).

Disclosures: Dr Salerno reports the following: American College of Radiology (TXIT examination committee chair, travel expenses); *International Journal of Radiation Oncology, Biology, and Physics* (associate senior editor); *Journal of Surgical Oncology* (associate editor); Johnson &

Johnson (stock-family member). All other authors have no disclosures to declare.

Data sharing statement: Research data are stored in an institutional repository and will be shared upon request to the corresponding author.

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<https://doi.org/10.1016/j.adro.2022.100902>

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Introduction

Current practice guidelines for the definitive management of localized prostate cancer (PCa) include a variety of radiotherapeutic options, including brachytherapy, conventionally fractionated external beam radiation therapy (CFx), moderately hypofractionated radiation therapy (MHFx), and ultrahypofractionated regimens, such as stereotactic body radiation therapy (SBRT)/stereotactic ablative radiation therapy.¹⁻⁴ Patterns of practice have shifted over the past decade, with increased utilization of hypofractionated and stereotactic regimens based on data suggesting equivalent outcomes relative to CFx with these approaches.^{5,6,7-19} These initial large series of altered fractionation schemas used varying preparative regimens before simulation or treatment, with differing treatment planning margins and image guided radiation therapy (RT) approaches.^{11-14,16}

Few published evidence-based guidelines define the optimal bowel or bladder regimens, localization methods, and planning margins for these various fractionation regimens. Therefore, we conducted a national pattern of practice survey to identify how radiation oncologists interpret and implement the available data and manage their patients with PCa when using CFx, MHFx, and SBRT. Herein, we report the results of this survey and the practice patterns related to bladder and bowel preparation for simulation and treatment, image guidance approaches, and planning target volume (PTV) margin expansions used for different fractionation regimens.

Methods and Materials

Survey development

The proposed research was reviewed and determined exempt by an institutional review board and office of human subjects protection. To create the survey, we conducted a literature review of the current evidence regarding dietary, bowel, and bladder instructions; use of image guidance; and PTV margin expansion recommendations for the simulation and treatment of patients with PCa. We then developed a radiation oncology-specific practice pattern survey based on this evidence, available guidelines, and previously published questionnaires.^{20,21} The survey then underwent an additional review by a selected group of genitourinary radiation oncologists before dissemination.

Survey questions addressed overall practice patterns using definitive external beam RT for the treatment of PCa. On the questionnaire, CFx was defined as 180 to 200 cGy per fraction, MHFx as >200 to 500 cGy per fraction, and SBRT as >500 cGy per fraction. Dose escalated conventional fractionation (CFx-DE) was defined as >7800

cGy. Other questions captured respondent demographics, treatment modalities used, patient instructions on bowel and bladder preparation for simulation and treatment, use of implantable devices, daily image guidance, and size of PTV margin expansions (Supplementary Material).

Sample selection and survey distribution

Invitations including a link to the survey were sent via e-mail to American Society of Radiation Oncology (ASTRO) members in the United States who self-identified as radiation oncologists specializing in prostate cancer. Surveys were collected between June and October 2018. Responses were included in the analysis if the respondent provided at minimum their radiation fractionation regimen. The SurveyMonkey web-based platform was used to administer the survey and collect deidentified participant data and responses.²² Results were transferred into Excel (Microsoft v.16) for data analysis.

Statistical analysis

Descriptive statistics were used to analyze participant demographics and survey responses. Diet and bladder and bowel preparation recommendations provided for simulation and for daily treatments were compared between CFx/CFx-DE, MHFx, SBRT, and demographics. Differences between diet and bladder or bowel protocol recommendations were calculated using 2-sided proportion test using the R software environment with *P* values of <.05 considered significant.²³ Correlation analysis was used to assess relationships between technique (CFx/CFx-DE, MHFx, SBRT) and use of implantable devices, image guidance, and PTV margin expansion. For this correlation analysis, PTV margin expansions (anterior, posterior, lateral, superior, inferior) were grouped as ≤ 5 mm, >5 mm to <10 mm, 10 mm, or >10 mm. Moderate and strong correlations were considered $r \geq 0.5$, and $r \geq 0.7$, respectively.

Results

Demographic information

An initial 1395 survey requests were sent by e-mail. A total of 190 (13.6%) respondents completed the questionnaire with adequate information for analysis. Respondent demographic information is listed in Table 1. Most respondents had been in practice >10 years, with two-thirds practicing in a hospital system, and one-third practicing in a free-standing clinic or satellite clinic. Over half

Table 1 Radiation oncologist demographic and treatment information

Demographic	n = 190
Years in practice	
Currently in training	1 (0.5%)
0-5 y	53 (28%)
6-10 y	33 (17%)
11-20 y	47 (25%)
≥20 y	56 (29%)
Primary practice location	
Hospital	129 (68%)
Free-standing/satellite clinic	61 (32%)
Primary employer	
Private practice/community-based system	109 (57%)
Academic/university system	65 (34%)
Government/public sector	10 (5%)
Independent contractor/locum tenens	5 (2.5%)
Industry	1 (0.5%)
Number of patients on treatment at a time	
1-10	136 (72%)
11-20	36 (19%)
>20	18 (9%)
Fractionation*	
CFx (180-200 cGy)	158 (83%)
CFx-DE (>7800 cGy)	77 (49%)
MHFx (200-500 cGy per fraction)	49 (25%)
SBRT	61 (32.1%)
Treatment technique for standard or MHFx*	
Photon 3D conformal	3 (1.5%)
IMRT	185 (97%)
VMAT	153 (81%)
Static IMRT	72 (38%)
TomoTherapy	17 (9%)
Proton therapy	12 (6%)
SBRT fractionation n = 61	
≤7.25 Gy per fraction	46 (75%)
>7.25 Gy per fraction	15 (25%)
>7.25 but <8 Gy per fraction	6 (10%)
≥8 Gy per fraction	9 (15%)
Abbreviations: 3D = 3-dimensional; CFx = conventional fractionation; CFx-DE = conventional fractionation-dose escalated; IMRT = intensity modulated radiation therapy; MHFx = moderate hypofractionation; SBRT = stereotactic body radiation therapy; VMAT = volumetric modulated arc therapy.	
* Respondents were allowed multiple responses.	

(57%) of respondents practiced in a private or community system, and a third (34%) practiced in academic-based system.

Radiation fractionation and technique

Of the 190 respondents, 83.1% (158/190) reported treating with CFx, 48.7% (77/158) of whom used dose escalation above 7800 cGy. SBRT use was reported by 33.7% (61/190) of respondents and MHFx by 25.8% (49/190). Intensity modulated RT was the most commonly used modality for radiation delivery (97.4%; 185/190). Less than 10% reported using TomoTherapy (8.9%; 17/190), proton therapy (6.3%; 12/190), or photon 3-dimensional conformal RT (1.6%; 3/190). For SBRT, 75.4% of respondents used doses of >500 to ≤725 cGy per fraction, with few using ≥800 cGy per fraction (14.7%) and a single respondent using 950 cGy per fraction (Table 1).

Diet recommendations

The majority of respondents reported providing some diet recommendations before simulation (77.9%; 148/190) and during treatment (83.7%; 159/190), though specific recommendations varied. Provision of diet recommendations did not differ for fractionation regimens at simulation and during treatment, with specific recommendations presented in Figure 1. Diet recommendations at simulation for CFx and MHFx were, however, more common among respondents in private (83.8%) versus academic practice (63.2%) and among those with >20 patients on treatment at a time (100% vs 69.4%) ($P < .006$).

Bladder and bowel recommendations

Bladder protocols for set up and reproducibility were consistently advised, with 95.8% of respondents (182/190) reporting that they direct patients to have a comfortably full bladder for simulation and treatment. The remaining 8 respondents reported treating with empty bladders. There were no significant differences in the rates of bladder instructions between fractionation regimens.

In contrast, there was more variation among survey respondents regarding frequency and type of bowel protocol recommendations (ie, any bowel instructions or directions) between different fractionation approaches. Most respondents (>76%) provide bowel recommendations to patients at simulation and treatment, without significant difference by fractionation schemes (Fig. 2). Bowel recommendations included instruction to patients to empty bowels before simulation/treatment, directives on bowel regimens, and prescription of medications. When using

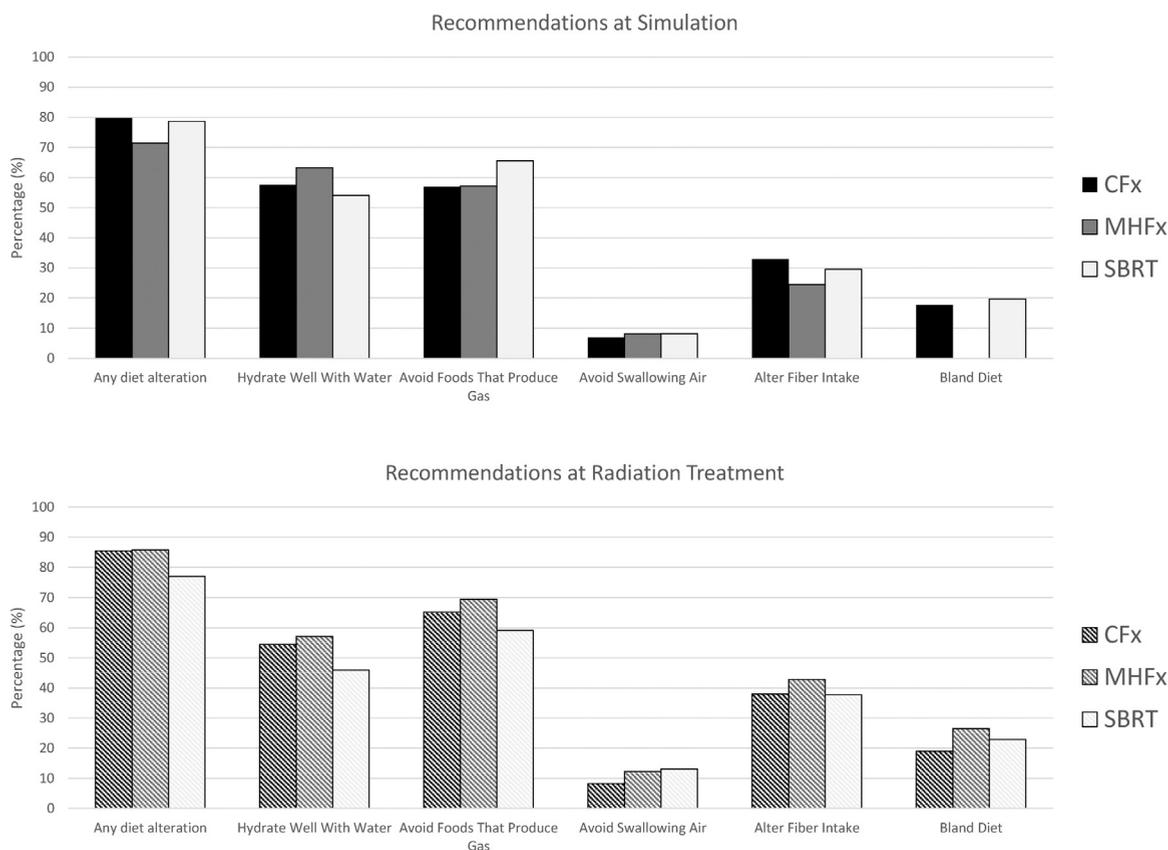


Figure 1 Diet recommendations for patients receiving radiation therapy at simulation (solid columns) and during radiation treatment (hashed columns) by conventional fractionation (CFx), moderately hypofractionated radiation (MHFx), or stereotactic body radiation therapy (SBRT).

CFx and MHFx, two-thirds or more of respondents asked patients to empty their bowels before simulation and treatment; however, this was less common with SBRT (Fig. 2). In lieu of having patients simply attempt to empty their bowels before treatment, significantly more SBRT respondents reported prescribing enemas (42.6% vs 6.3% vs 4.1%; $P < .00001$) (Table 2). Additionally, respondent in academic (87.1%) practices were significantly more likely to provide bowel recommendations at SBRT simulation than those in private practice (80%), as were those in practice 6 to 10 years (92.9%) versus >20 years (66.7%) ($P < .05$). The reported prescription of stool softeners, rectal suppositories, and laxatives were similar between fractionation regimens (Table 2). Regarding the subclasses of laxatives prescribed, reported use of stimulant, lubricant, and osmotic laxatives were similar between fractionation regimens, with lubricant laxatives rarely or never prescribed.

In addition to bladder and bowel preparative instructions, many respondents used consistent daily patient appointment times to improve set-up and filling reproducibility (62.6%; 119/190). Placement of hydrogel spacers varied between fractionation regimens, with 31.0% of respondents reporting use for CFx/CFx-DE (49/158), 36.7% (18/49) for MHFx, and 60.7% for SBRT (37/

61), being significantly higher for SBRT ($P = .0001$) (Fig. 3).

Implantable devices, image guidance, and reproducibility

The respondents' use of fiducial markers varied by treatment regimen. Overall, fiducial markers were used by the majority of respondents, but the use was highest for SBRT (CFx/CFx-DE 59.5%, 94/158; MHFx 57.1%, 28/49; and SBRT 80.3%, 49/61, $P = .006$) (Fig. 3). Use of radio-frequency transponders was less common overall, but similar between fractionation schemes (Fig. 3). Image guidance was used for set-up verification by the vast majority of respondents (94.7%, 180/190), with daily cone beam computed tomography (CBCT) being the predominant modality reported (97.2%), followed by daily 2-dimensional imaging (22.2%) (Fig. 3). Use of CyberKnife, TrueBeam Auto Beam Hold, or optical surface monitoring was reported by 30.0%.

Respondents were asked their management strategies when an organ position was out of tolerance during image guidance or set-up was not consistently reproducible. Most (75.3%) would ask patients to leave the couch and

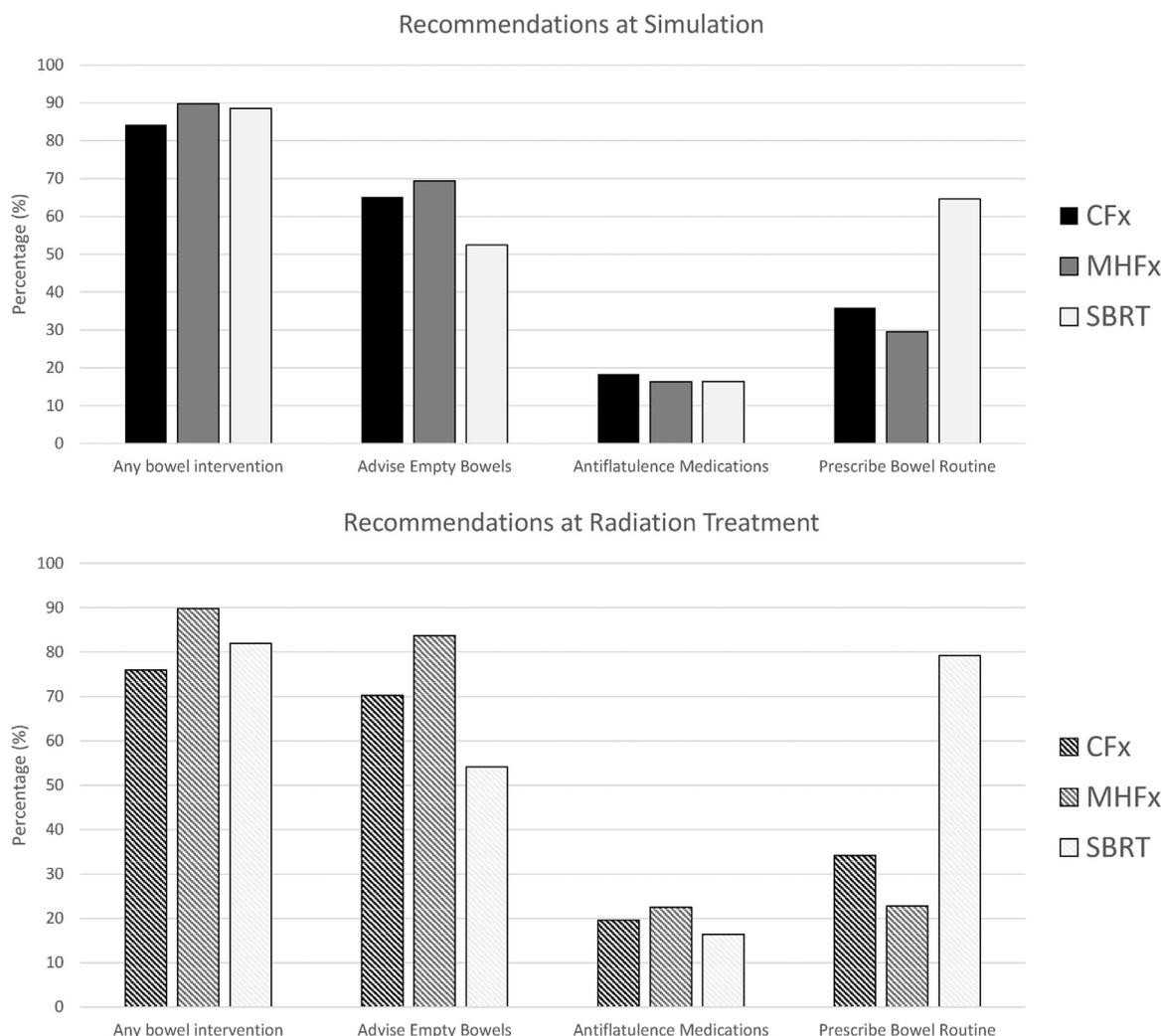


Figure 2 Bowel recommendations for patients receiving radiation therapy at simulation (solid columns) and during radiation treatment (hashed columns) by conventional fractionation (CFx), moderately hypofractionated radiation (MHFx), or stereotactic body radiation therapy (SBRT).

defecate when rectal filling with excess stool was noted on CBCT. For consistent misalignment of organs, 66% of respondents reported they would resimulate the patient and replan. Reported criteria prompting resimulation included: organs outside of tolerance for ≥ 2 fractions, target consistently outside PTV, fiducial misalignment or migration, or when recalculated dose to organs at risk (OAR) on CBCT exceeded $>3\%$ from planned.

PTV margins

The PTV margin expansions for CFx, CFx-DE, and MHFx regimens were similar, with median PTV expansions of 6 mm (range, 3-10 mm) in the anterior, lateral, superior, and inferior directions, and less posteriorly with a median margin of 5 mm (range, 0-8 mm). The range of PTV expansions used for SBRT were broad, at 5 mm (range, 2-10 mm) for anterior, lateral, superior, and

inferior margins, and the median margin posteriorly was 3 mm (range, 0-6 mm). Posterior PTV margin expansions for each fractionation scheme are presented in Figure 4.

Associations between PTV margin expansions, choice of image guidance, and implantable device use were evaluated. CFx, CFx-DE, and MHFx showed no correlation with PTV for use of implantable device or type of image guidance. However, for SBRT PTV margin expansion, moderate correlation was seen with smaller PTV expansions and hydrogel spacer use ($r = 0.66-0.70$; $P < .00001$), and strong correlation was seen with fiducial marker use ($r = 0.80-0.81$) and daily CBCTs ($r = 0.76-0.78$) ($P < .00001$).

Discussion

Set-up reproducibility is critical for delivery of definitive RT for patients with localized PCa. Management

Table 2 Bowel routine prescriptions by fractionation regimen

Bowel routine prescriptions	CFx/CFx-DE (n = 158)	MHFx (n = 49)	SBRT (n = 61)
No medication	44.9%	65.3%	4.9%*
Stool softeners	13.3%	12.2%	14.7%
Rectal suppositories	1.9%	2.0%	1.6%
Enemas	6.3%	4.1%	42.6%*
Laxatives	33.5%	16.3%	36.0%
Laxative class	n = 53	n = 8	n = 22
Stimulant	28.3%	25.0%	31.8%
Bulk-forming	45.3%	37.5%	27.2%
Osmotic	24.5%	37.5%	40.9%
Lubricant	1.9%	0%	0%
<i>Abbreviations:</i> CFx = conventional fractionation; CFx-DE = conventional fractionation-dose escalated; MHF = moderate hypofractionation; SBRT = stereotactic body radiation therapy.			
* $P < .05$.			

strategies to optimize, and account for, set-up reproducibility include patient preparative instructions, diet instructions, hydration, use of medications aimed to alter bowel function, use of fiducial markers, choice of image guidance modality and frequency, and subsequent PTV margin selection. Although some guidelines exist on use of daily image guidance, particularly for conventional fractionation, best practices and evidence-based guidelines are limited for other fractionation regimens.¹⁻⁴ Additionally, evidence to support a benefit from dietary and prescription interventions and patient instructions regarding bowel and bladder preparation is limited and inconsistent, making it challenging to synthesize the data into uniform recommendations.²⁴⁻²⁹ Evidence supporting specific PTV margin expansions for various treatment modalities is available; however, individual radiation oncologists may tailor PTV margins in practice.^{30,31} This survey was created to provide additional data on individual patterns of practice for different fractionation regimens to supplement the existing literature.

Reproducibility of set-up and organ positioning is a critical component of fractionated external beam RT. Many behavioral interventions have been suggested to improve daily treatment reproducibility of the bladder and bowel filling. The vast majority of respondents instruct their patients to have a comfortably full bladder for simulation and treatment. On a recent survey of United Kingdom (UK) radiation oncology departments addressing practices for managing patients with PCa receiving RT, 92.5% of departments reported treating with a comfortably full bladder.²⁰ Interestingly, and similar on both surveys, there were occasional recommendations to treat with an empty bladder (<10%).²⁰ As maintaining a reproducible bladder volume over the

course of treatment can be difficult, some oncologists may opt to treat with an empty bladder to improve consistency.³²⁻³⁵ Data support consistent bladder filling as key to achieving planned dose to OARs, with larger bladders at simulation demonstrating the most variation during treatment.^{36,37} Therefore, moderately full bladders, with small variations addressed via daily image guidance, may be the optimal approach for organ management in the modern era.

Bowel toxicity accounts for a significant amount of PCa quality of life concerns after RT.³⁸ Differences in rectal and bowel position over the course of RT may significantly alter the dose received by these organs. Determining management strategies to increase reproducibility of bowel filling is an ongoing area of research.^{35,39} Dietary and behavioral modifications have been studied, including use of antifatulence medications, diets (high fiber, low fermentable oligosaccharides, disaccharides, monosaccharides, and polyols, personalized), and probiotic use.^{26,29,40-42} Unfortunately, although some dietary interventions have shown promise, many have not, and the optimal diet approach to maintain reproducibility during RT remains uncertain.

Despite these uncertainties, most of respondents in the current study, and those in the UK study, provide patients with some type of diet recommendation before and during treatment.²⁰ Both groups commonly recommend avoiding foods, drinks, and behaviors that produce gas, as supported by the available literature.^{41,42} Altering fiber intake was more commonly reported in this survey (24%-43%) compared with the UK departments (8.6%).²⁰ The rationale for these differences is unclear; however, they may result from inconstant data regarding whether fiber alteration is of benefit, and if so, which option is superior.

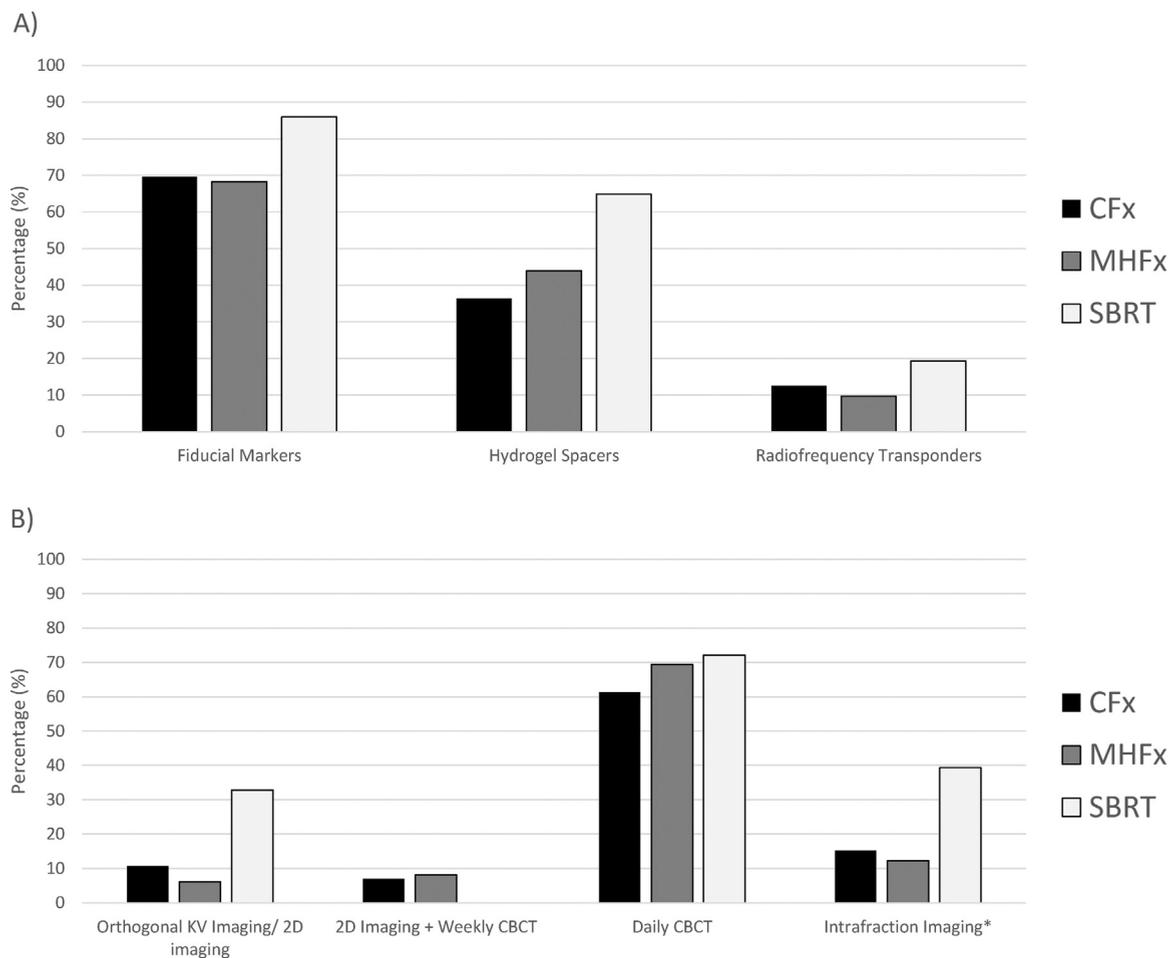


Figure 3 Reported use of implantable devices and image guidance by radiation fractionation regimen. **(A)** Use of implantable devices (n = 190 respondents). **(B)** Modalities of daily image guidance (n = 180 for those who provided responses). *Abbreviations:* 2D = two-dimensional; CBCT = cone beam computed tomography; CFx = conventional fractionation including dose escalated; KV = kilo voltage; MHFx = moderate hypofractionation; SBRT = stereotactic body radiation therapy. *Includes radiofrequency transponders, CyberKnife, TrueBeam Auto Beam Hold, optical monitoring.

For instance, the UK survey was split 50/50 as to whether they recommend high or low fiber diet pretreatment. Some physicians may develop a diet paradigm that works in their particular practices, as respondents with >20 patients on treatment at a time, in the current survey,

were more likely to give diet instructions before treatment. Ultimately, there may not be a single intervention that demonstrates benefit for all patients, but future research may focus on modifications tailored to individual patient situations.

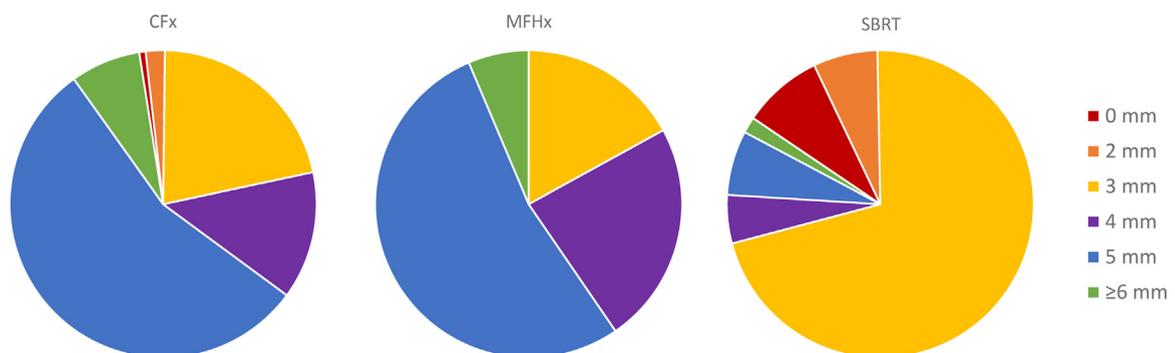


Figure 4 Reported posterior planning target volume expansions by radiation fractionation regimen. *Abbreviations:* CFx = conventional fractionation including dose escalated; MHFx = moderate hypofractionation; SBRT = stereotactic body radiation therapy.

Bowel instructions are employed by most respondents in this survey, which most often included emptying the bowel before simulation and treatment (73.2% and 87.2% respectively). This instruction is similar to the UK survey, in which 77.7% suggested emptying bowel before planning and radiation.²⁰ This advice is supported by the literature, which suggests that emptying bowels increases reproducibility and improves rectal dose-volume histogram throughout treatment.^{37,43}

Prescription medications are also commonly used for prostate RT to minimize variation in bowel and rectal filling. As with diet modifications, some medications have shown promise while many others have not had a significant effect.²⁹ Milk of Magnesia and magnesium oxide are some of the more extensively studied medications, often used with various diet interventions; however, reported efficacy has been mixed.^{27,40,42,44,45} One intervention that has shown benefit in reducing rectal size and improving OAR dosimetry in multiple clinical trials is the use of enemas. However, use of enemas before daily treatment, especially with longer RT courses, is likely to be limited due to the invasive nature of their use.^{25,45,46} The prescription of bowel routines in the current survey was reported by approximately 35% to 95% of respondents, varying over a broad range depending on fractionation regimen. In this study, respondents reported more frequent use of bowel instructions and preparations for delivery of SBRT relative to CFX and MHFX. This difference was most notable regarding use of enemas. Although the UK survey did not address different fractionation regimens, bowel medications were used by 63% of departments, consisting of enemas (41%), laxatives (13%), or both (13%).

An additional evidence-based method for reducing dose to the rectum is use of hydrogel spacers, which has been shown to improve rectal dosimetry, bowel quality of life, and reduce toxicity.⁴⁷ In the current survey, use of hydrogel spacer was more common with increasing dose per fraction. Overall, recommendations and interventions were more common at higher dose per fraction (SBRT), likely reflecting concern for rectal exposure and the increasing magnitude of effect of small variances in patient set-up on dose delivered.

The adoption of image guidance techniques has improved set-up reproducibility and allowed for dose escalation and improved clinical outcomes with modern prostate directed RT.⁴⁸ Daily CBCT was the most common method of image guidance reported in the current survey, with an increased use of CBCT as daily dose per fraction increased. A 2014 survey of ASTRO members regarding their use of image guided RT (IGRT) for a variety of tumor sites similarly found that CBCT or megavoltage CT was the most commonly used image guidance modality in conventionally fractionated prostate treatment at that time.²¹ In the current survey, the use of fiducial markers was significantly higher with increasing hypofractionation, likely demonstrating reduced tolerance

of variation by the treating radiation oncologist as dose per fraction increases.

Appreciable intrafraction motion has been demonstrated during prostate RT,⁴⁹ leading to the development of technologies to monitor and address this motion. The rate of electromagnetic transponder use was similar for CFX between the 2014 and current surveys (8.3% and 10.8%); however, a significant and expected increase was seen with SBRT in the current survey (18.0%). Additional studies into the long-term outcomes of patients treated with or without intrafraction monitoring would be of benefit to determine whether this improved target accuracy is of benefit and worth additional investment in cost and training and additional duration of treatment.

Image guidance is recommended for prostate RT, and literature would suggest that PTV margin expansions can be reduced with enhanced image guidance.^{1,2,4} In the 2014 ASTRO IGRT survey, median posterior PTV expansions were 5 mm (interquartile range, 3.25-5 mm) for intact prostate treated with conventional fractionation, similar to the current survey.²¹ The 2014 IGRT ASTRO survey demonstrated no association between the size of PTV expansions and IGRT modality, paralleling the lack of correlation seen in the current survey for those respondents using conventional fractionation. Though not addressed in the 2014 survey, associations between PTV margin expansion and image guidance were solely seen with the use of SBRT in the current data.

Similar to all survey-based research, this pattern of practice study has inherent limitations. Though the response rate in the current study mirrored those of other similar surveys,²¹ findings may be affected by limited response rates and associated selection bias. Further, the survey specifically targeted ASTRO members who self-identified as specializing in PCa. It is likely that other physicians who do not self-report in this fashion also deliver treatment to patients with PCa, especially in community practices. Additionally, the survey asked questions regarding the daily practices of prostate-focused radiation, and responses cannot be linked to outcome data and clinical efficacy of these patterns of practice.

Although these data suggest some implementation of the existing literature and guidelines, there are areas of inconsistency. As an example, correlations are not always apparent between the use of image guidance and PTV margin selection, similar to prior ASTRO surveys. Therefore, expanded guidelines on best practices for diet and bowel recommendations, image guidance, and associated PTVs would likely still be beneficial to help guide physicians in a standardized and evidence-based manner.

Conclusion

This pattern of practice survey of prostate-focused radiation oncologists describes current management

strategies employed for reproducible PCa radiation treatments, including patient instructions, choice of image guidance modality, and PTV margin expansions. Results indicate that there is heterogeneity in treatment modality, dose, patient instructions, and PTV expansions used for treatment. This survey highlights the need for further research to define best practices for patient behavioral modifications and continued guidance on evidence-based approaches for PTV margin selection, with the aim to improve overall patient outcomes and quality of life.

Acknowledgments

This project has been funded in whole or in part with federal funds from the National Cancer Institute, National Institutes of Health, under contract No. HHSN261200800001E. The content of this publication does not necessarily reflect the views or policies of the Department of Health and Human Services, nor does mention of trade names, commercial products, or organizations imply endorsement by the government of the United States.

Supplementary materials

Supplementary material associated with this article can be found in the online version at [doi:10.1016/j.adro.2022.100902](https://doi.org/10.1016/j.adro.2022.100902).

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