Safety of online MR-based adaptive ultra-hypofractionated radiotherapy for prostate cancer in China: Preliminary analysis of data from a phase II trial

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Article

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Abstract

Background This study aimed to evaluate the feasibility and safety of online adapt-to-shape (ATS) workflow for prostate cancer patients on 1.5-T MR linac in China.

Methods This prospective phase II study enrolled patients with localized or oligometastatic prostate cancer. Ultra-hypofractionated radiotherapy (UHF-RT) with dose of 36.25-40 Gy in five fractions was delivered every other day. After each fraction, feasibility and tolerability of the treatment were assessed. The primary endpoints were acute grade 2 or above genitourinary (GU) and gastrointestinal (GI) toxicities after up to 12 weeks follow-up.

Results From March 2021 to November 2021, 26 patients were enrolled (23 with localized prostate cancer, 3 with oligometastatic prostate cancer). For all fractions, the online ATS plans met the dose criteria for both the target volume and normal tissues. The median on-couch time was 55 (34–95) minutes and 39 (24–50) minutes with T2WI 6-minute sequence and 2-minute sequence scans, respectively. For 98.4% fractions, treatment was well tolerated. Twenty-four patients completed treatment and were followed-up for at least 2 weeks. Grade 2 or above GU and GI toxicities occurred in 33.3% and 8.3% patients, respectively; two patients had RTOG grade 3 GU toxicity (hourly nocturia). IPSS remained unchanged during UHF-RT, increased from week 2 (mean, 9.1) to week 4 (mean, 12.4), and then gradually decreased at week 6. Patient-reported urinary and bowel scores were consistent with IPSS.

Conclusions UHF-RT with ATS workflow is well tolerated by patients with localized and oligometastatic prostate cancer, with only moderate GU and mild GI toxicities.

Trial Registration: NCT05183074, ChiCTR2000033382

Highlights

- UHF-RT with ATS workflow is well tolerated by Chinese prostate cancer patients
- Genitourinary toxicity is comparable to that with conventional radiotherapy
- Rectal toxicity is minimal and returns to baseline within weeks
- The main limitation of the treatment is the long workflow time
- Methods to accelerate workflow have to be found

Introduction

Prostate cancer is currently the sixth most common male malignancy in China [1, 2], and the incidence is expected to increase with the increase in life expectancy. External-beam radiotherapy has long been the mainstay of local treatment for localized prostate cancer. Several randomized controlled trials (RCTs) have shown non-inferior efficacy and toxicity with moderate-fractionated radiotherapy [3–6]. Evidence from recent trials showed that further shortening of the radiotherapy course to five-to-seven fractions is feasible [7], [8]. However, toxicity profiles differed, which might be due to the radiotherapy techniques used. In HYPO-

RT-PC, the majority (80%) of patients received three-dimensional conformal radiotherapy, which did not allow for position control during the fraction [8]. In PACE-B [9], the margins were smaller, and highly conformal technique such as volumetric modulated arc therapy and intrafractional motion monitoring or repeated static images were used to ensure treatment accuracy. Since inter- and intra-fractional motion of prostate and adjacent normal tissues affects the target dose and the toxic effects [10, 11], accurate delivery of treatment is crucial in UHF-RT.

With integrated 1.5-T MRI functionality, MR-linac incorporates several state-of-the-art radiotherapy concepts [12]. First, the superior soft tissue resolution of integrated MR offers much more accurate registration for prostate cancer, making invasive procedures such as insertion of fiducial markers or magnetic transponders unnecessary. Second, MR-linac offers two options for adaptive online planning—adapt-to-position (ATP) and adapt-to-shape (ATS)—the latter being especially suitable for prostate cancer radiotherapy. Moreover, the cine MR acquired during the “beam-on” phase helps guarantee accurate delivery of radiation. Radiotherapy with different fractionation for prostate cancer on 1.5-T MR-linac has been used since 2019 [13, 14] [15]. However, to our knowledge, the feasibility and acute toxicities of UHF-RT with concomitant boost to 40 Gy in five fractions on 1.5-T MR-linac have not previously been reported.

The 1.5-T MR-linac (Elekta, Sweden) was clinically implemented in our center at the end of 2019, and we initiated a prospective observational study with regular follow-up for prostate cancer patients. The study is ongoing. The aim of this paper is to report the preliminary findings regarding feasibility, tolerability and acute toxicities of stereotactic ablative radiotherapy (SBRT) for prostate cancer on 1.5-T MR-linac (XXXxxxxxxxx, XXXXXXxxxxxxxxxx).

Methods And Materials

Patients

Based on the evidence from STAMPEDE [16] and SABR-COMET [17] of survival benefit from radiotherapy to primary and oligometastases, we enrolled patients with localized and oligometastatic prostate cancer with prostate-in-situ considered suitable for SBRT. This prospective phase trial was approved by the Ethics Committee of National Cancer Center/Cancer Hospital, CAMS & PUMC. All methods were performed in accordance with the Declaration of Helsinki, and informed consent was obtained from all subjects. The eligibility criteria were 1) age ≥ 18 years; 2) pathologically proven prostate cancer; 3) localized low-, intermediate-, or selectively high-risk disease (T3a or minimally T3b, or prostate specific antigen 20–50 ng/mL, or Gleason score 8) or exclusively bone oligometastases (≤ 5 sites, with all sites treated by SBRT safely); 4) prostate volume < 100 mL; 5) International Prostate Symptoms Score (IPSS) ≤ 19; 6) no transurethral prostate resection within the past 6 months; 7) no prior radiotherapy to pelvis; and 8) no contraindications to MR scan (implanted electronic devices or severe claustrophobia). All patients other than those with low-risk disease were encouraged to undergo prostate-specific membrane antigen (PSMA)-PET scan to rule out lymph node or visceral metastases. Neoadjuvant or adjuvant androgen deprivation therapy was allowed as per National Comprehensive Cancer Network (NCCN) guidelines.

Target Delineation and Planning

Patients underwent plain CT scan and enhanced high-resolution MR scan with 3-mm slice thickness, with comfortably full bladder and empty rectum. In view of the long on-couch time of MR-linac, patients were educated to drink 300–400 mL water over 15–20 minutes to ensure slow filling of bladder. As the prediction rate of extraprostatic extension by multiparametric MRI is only around 70%, the combination of clinical characteristics and MRI were used to define targets. As per the ESTRO ACROP consensus guidelines of prostate cancer[16], the clinical target volume (CTV) was defined as whole prostate for low-risk disease (n = 2), and whole prostate plus 3 mm margin (0 mm posteriorly) for patients (n = 19) with potential extraprostatic extension rate of ≥ 20% by Partin table. The proximal 1 cm of seminal vesicles (SV) were included for patients with SV involvement rate ≥ 15% (n = 14), while the whole SV was included for patients with minimal T3b stage (n = 1). The planning target volume (PTV) was defined as the CTV plus a 3-mm margin isotropically. A simultaneous boost of CTV4000 was defined as prostate with contraction of 1 mm for intermediate- to high-risk disease (n = 24). The prescription doses of PTV and CTV4000 were 36.25 Gy and 40 Gy, respectively, in five fractions delivered on alternate days. All organs at risk (OARs), including bladder, bladder wall, rectum, rectum wall, urethra, penile bulb, pelvic bone, and bilateral femoral heads, were delineated. Selective sparing of urethra was not adopted due to fuzziness of urethra on MR without an indwelling catheter.

A reference intensity-modulated radiotherapy plan with 7–10 beams and < 80 segments (< 120 segments was acceptable for complicated plans) was generated on the Monaco (v5.40, Elekta AB, Stockholm, Sweden) planning system. The dose distribution was normalized to ensure that 95% of PTV received 36.25 Gy and 95% of CTV4000 received 40 Gy, with less than 5% receiving 42.8 Gy. Furthermore, we ensured that ≥ 98% of PTV received at least 95% of the prescription dose (34.4 Gy). In case of conflict with OARs protection, 90% of CTV4000 receiving 40 Gy was also accepted. The dose constraints for bladder wall were as follows: V_{37Gy} < 10 cc and $V_{18.1Gy}$ <50%. The dose constraints for rectal wall were as follows: Dmax < 40 Gy, V_{38Gy} < 0.1 cc, V_{36Gy} < 1 cc, V_{29Gy} < 20%, and $V_{18.1Gy}$ <50%. The Dmean of urethra was < 42 Gy. The $V_{14.5Gy}$ of bilateral femoral heads was < 5%.

Online adapt-to-shape procedure

During each treatment session, patients were encouraged to prepare their bladder and rectum as simulation. A pre-MR scan was acquired by T2-weighted three-dimensional sequence with duration of 6 minutes for the first 20 patients, and duration of 2 minutes thereafter. For each patient, the pre-MR was rigidly registered to the simulation CT image for the first fraction and to the previous pre-MR image for the subsequent four fractions. Then, contours were projected to the pre-MR by deformable registration, and manually adapted by the physician. A full online plan re-optimization was started in the Monaco system, starting from the fluence optimization. Shortly before end of the optimization, another position verification MR-scan (PV-MR) was acquired to confirm the position of the target and OARs. If the CTV was still within the PTV, and the anterior rectum wall had not moved ventrally, this ATS plan was accepted, and treatment delivery with real-time cine-MR was started; otherwise, an ATP or new ATS workflow was carried out[14].

Endpoints

Treatment toxicities—graded by Common Terminology Criteria of Adverse Events [CTCAE] version 5.0)—were recorded weekly during radiotherapy, every two weeks post radiotherapy for 8 weeks, and then at 12 weeks post radiotherapy. The primary endpoint was defined as clinician-reported (CROM) acute grade 2 or above GU toxicities (urinary frequency, urgency, obstruction, incontinence, hematuria, radiation cystitis) and GI toxicities (diarrhea, incontinence, proctitis, rectal pain, bleeding) occurring within 12 weeks post SBRT. Acute GU and GI toxicities were also assessed by Radiation Therapy Oncology Group (RTOG) scales at the same time points. Patient-reported outcome (PROMs) of GU, GI, and sexual adverse effects, and general quality of life (QoL) were also recorded, using the International Prostate Symptom Score (IPSS), the 26-item Expanded Prostate Cancer Index Composite index (EPIC-26), the Functional Assessment of Cancer Therapy—Prostate questionnaire (FACT-P), the EORTC quality-of-life questionnaire Core-30 (EORTC-QLQ-C30), and the International Index of Erectile Function (IIEF-5). The secondary endpoints were patient satisfaction and toleration of the ATS procedure, local control, and late GU and GI toxicities (at 2 years).

Results

From March to November 2021, 26 patients were enrolled (23 with localized prostate cancer and 3 with oligometastatic disease; Table 1). Nine patients (60%) with unfavorable intermediate-risk or high-risk disease were staged by PSMA-PET scan and the remaining patients by CT and bone scan. A quarter of the patients were on α-blockers due to lower urinary tract symptoms. Half of the patients had moderate IPSS score.

Table 1
Baseline characteristic of the 26 patients

Variables	Number (%)	Median (Range)
Age		72 (57–88)
WHO performance status		
0	22 (84.6)	
1	4 (15.4)	
NCCN risk score		
Low-risk	2 (7.7)	
Intermediate-risk	13 (50)	
High-risk	8 (30.8)	
Oligometastatic	3 (11.5)	
T stage		
T1	2 (7.7)	
T2	20 (76.9)	
T3a	4 (15.4)	
T3b	1 (3.8)	
Gleason Score[#]		
3 + 3	6 (23.1)	
3 + 4	7 (26.9)	
4 + 3	4 (15.4)	
4 + 4	6 (23.1)	
PSA (ng/mL)[#]		
≤ 10	10 (38.5)	
10–20	5 (19.2)	
20–50	8 (30.8)	
Prostate volume (mL)		
≤ 40	11 (42.3)	
40–80	12 (46.2)	
≥ 80	3 (11.5)	

Variables	Number (%)	Median (Range)
IPSS score		6.5 (0–17)
Mild	14 (53.8)	
Moderate	12 (46.2)	
Severe	-	
Androgen deprivation therapy		
Yes	24 (92.3)	
No	2 (7.7)	
-blockers at enrollment		
Yes	6 (23.1)	
No	20 (76.9)	
5- reductase inhibitors at enrollment		
Yes	1 (3.8)	
No	25 (96.2)	

*NCCN: National Comprehensive Cancer Network; IPSS: International Prostate Symptoms Score

#only includes localized disease

Of the 26 patients, 25 received all five fractions. Among the overall 125 fractions delivered, 114 (91.2%) with ATS workflow were completed as scheduled; for nine fractions, another ATS workflow was started with the rectum into PTV on Position Verification-MR scan, and for another two fractions, another ATP was started because of delivery interruption by the magnetron arc. For three fractions with rectum included in the PTV during beam-on period, the delivery was paused and not resumed until the rectum moved out to its original position after 3–5 minutes.

The median on-couch time was 51 (24–95) minutes for all fractions, 55 (34–95) minutes for 6-minute scan and 39 (24–50) minutes for 2-minute scan. Figure 1 shows the mean time of each ATS step.

After each session, the patients completed a questionnaire on the tolerability of the procedure and their satisfaction. Only two fractions (1.6%) were scored as “intolerable”, the reasons being too long on-couch time (95 minutes) or discomfort due to too full bladder.

By November end, 24 patients had completed follow-up for at least 2 weeks post radiotherapy, with 15 (57.7%) completing more than 12 weeks follow-up. By the end of 12 weeks post radiotherapy, 8 (33.3%) patients had CTCAE grade 2 or above acute GU toxicities, and 2 (8.3%) patients had grade 2 or above acute GI toxicity (Table 2 and Fig. 2A). Among them, 2 patients had hourly nocturia, which was scored as RTOG

grade 3 GU toxicity; both of these patients had obvious baseline lower urinary tract symptoms and shortened radiotherapy course (two sessions delivered on two consecutive days due to the patients' personal reasons). No RTOG grade 2 acute GI toxicity occurred.

Table 2
Cumulative acute toxicities in the 24 patients followed up for at least 2-weeks (NCI-CTCAE 5.0 and RTOG scale)

Toxicities	0	Grade I	Grade II	Grade III	Grade IV
CTCAE 5.0					
Fatigue	15	9	0	0	0
Urinary frequency	7	10	7	0	0
Urinary urgency	10	12	2	0	0
Urinary pain	13	11	0	0	0
Urinary Incontinence	21	2	1	0	0
Cystitis	9	8	7	0	0
Hematuria	22	2	0	0	0
Diarrhea/Proctitis/Rectal Pain	9	13	2	0	0
Fecal incontinence/bleeding	23	1*	0	0	0
RTOG scale					
GU	7	9	6	2	0
GI	9	15	0	0	0

*: This patient had baseline irritative enteritis which was again induced with SBRT.

CTCAE: Common Terminology Criteria of Adverse Events; RTOG: Radiation Therapy Oncology Group, GU: genitourinary; GI: gastrointestinal

As Fig. 2 shows, the GU and GI toxicities peaked 4 weeks after treatment initiation and recovered by about 8 weeks.

The 24 patients followed-up for at least 2 weeks completed all QoL questionnaires on schedule, though one patient missed IIEF-5 assessment at week 4. Figure 3 shows the mean changes in IPSS and EPIC-26 subdomain scores over time (Table 3). Clinically significant reductions from baseline to week 4 were observed in all EPIC-26 subdomains (urinary incontinence, urinary irritative/obstructive, bowel, and general subdomains), which was consistent with the transient increase in IPSS at week 4. Since the majority of patients were on androgen deprivation therapy, IIEF-5 was not analyzed.

Table 3
Mean changes in IPSS and QOL scores in the 24 patients with at least 2-weeks follow-up

	Baseline	W1	W2	W4	W6	W8	W10	W14	W24
IPSS	6.4	8.8	9.1	12.4	8.2	6.1	6.6	4.3	3.9
EPIC urinary incontinence	93.5	-	91.2	89.2	92.1	92.6	93.4	91.9	93.6
EPIC urinary irritative/obstructive	84.4	-	80.9	75.5	80.9	83.6	83.7	89.5	83.4*
EPIC bowel	94.7	-	91.8	85.1	93.2	98.0	98.8	97.7	96.9
EPIC sexual	25.3	-	25.2	20.6	25.2	23.4	22.3	23.2	22.9
EPIC general	86.3	-	90.2	83.7	90.3	89.9	89.6	89.6	87.5
FACT-P score	125.3	123.2	125.8	120.4	129.8	-	128.5	130.4	124.5

IPSS: International Prostate Symptoms Score; EPIC: expanded prostate cancer index composite short form; FACT-P: the Functional Assessment of Cancer Therapy—Prostate questionnaire.

Discussion

This prospective clinical study to assess treatment of prostate cancer with 36.25-40 Gy in five fractions delivered on 1.5-T MR-linac demonstrated good patient tolerability of online ATS workflow, with moderate and transient acute GU toxicities and very mild acute GI toxicities.

With online adaptive contouring and planning, SBRT delivered on MR-linac is noninvasive, avoiding need for fiducial marker insertion; however, it is time and cost intensive. The time-consuming steps of ATS workflow include MR scan acquisition, online target contouring, online plan re-optimization, and treatment delivery, with mean times of 6 minutes, 10.5 minutes, 10.5 minutes, and 10.5 minutes, respectively, as per our data. The median on-couch time was 51 (24–95) minutes, which is close to the 53 (34–86) minutes reported by Alongi et al. [15], although the fractionation dose was higher in our study. The 1.5-T MR-linac offers two prespecified online MR scan sequences for prostate cancer: 0.6-mm slice thickness for 6-minute scan and 1-mm slice thickness for 2-minute scan. Since the resolution of the 2-minute scan was good enough for online registration and contour propagation, we switched to the 2-minute scan after the first 20 patients. This decreased the overall median on-couch time from 55 minutes to 39 minutes—a clinically significant reduction welcomed by the patients. Consistent with other series [17], around 9% of sessions needed another ATS or ATP workflow due to technical problems or organ motions. Although it is difficult to complete one fraction within 30 minutes with the current workflow, self-referrals are common with this noninvasive procedure and high-precision MRgRT, as was demonstrated by the high proportion of patients (98.4%) expressing satisfaction with the treatment (only two fractions were scored as “unsatisfactory or intolerable”).

Completion rate of CROM and PROM forms was almost 100%. A cumulative 33.3% and 8.3% of patients presented with grade 2 or above GU and GI toxic effects by CTCAE criteria, and 33.3% and 0% by the RTOG scale. Only two patients had RTOG grade 3 acute GU toxicity (urinary frequency, urgency, and hourly nocturia). To date, only small series on the acute toxicities of MRgRT have been published. There are marked differences in previous reports of toxicity rates. Bruynzeel et al. [18] and Ugurluer et al. [19] enrolled, respectively, 101 and 50 patients treated on MRIdian with 0.35-T MR and online daily adaptive planning. Bruynzeel et al. [18] reported 23.8% and 5% patients with grade 2 or worse GU and GI CTCAE toxicity, respectively, compared with 36% and 0% reported by Ugurluer et al. [19]. Alongi et al. used 1.5-T MR-linac and reported grade 2 GU and GI acute toxicities in only 12% and 4% patients, respectively. It is difficult to compare our results directly with other studies investigating acute toxicity of MRgRT for several reasons. First, the prescription dose and normalization definition were different. The optimal SBRT schedule for prostate cancer is still unclear. NCCN guidelines, which are based on the evidence from PACE-B [9] and HYPO-RT-PC [8], recommend 36.25-40 Gy in five fractions or 42.7 Gy in seven fractions. We adopted a regimen of 36.25 Gy to PTV, with concomitant boost of 40 Gy to prostate, which is similar to PACE-B, and encouraged 100% prescription dose normalized to 95% PTV volume, which meant 36.25 Gy to 95% PTV and 40 Gy to 95% CTV4000. The margin was 3 mm in the studies by Bruynzeel et al. [18] and Ugurluer et al. [19], and 5 mm in the study by Alongi et al. [15], all of which assumed that 95% prescription dose received by PTV was acceptable without boost dose within prostate; this means that 34.4 Gy was mandatory for PTV in the study by Bryunzeel et al. [18], whereas only 33.2 Gy was required in the study by Alongi et al. [15]. The higher dose in our study may explain the higher frequency of grade 2 or above GU toxicity in our cohort. Second, we did not use urethra sparing as in the other two studies, because it was hard to distinguish urethra online without an indwelling catheter. Even so, with Dmean of urethra lower than 42 Gy, most urinary symptoms resolved at 4 weeks post radiotherapy. Finally, we gathered data much more frequently: weekly during SBRT, at end of radiotherapy, two-weekly thereafter up to 8 weeks, and then at 12 weeks. In comparison, Alongi et al. [15] only collected toxicity data at baseline and end of treatment, Ugurluer et al. [19] at baseline and at 3 months after SBRT, and Bruynzeel et al. [18] at 6-week follow-up. As our study (Figs. 2 and 3) and PACE-B [20] show, the incidence of acute side effects peak at around 2 weeks after completion of SBRT and then declines slowly to baseline levels at around 4–6 weeks post radiotherapy. This change in toxicities over time was reflected in the patient-reported QoL analysis in our study. More frequent assessments, along with the nearly 100% completion of questionnaires, make our findings more reliable.

With prescription dose and the follow-up schedule similar to PACE-B [20], we found comparable acute grade 2 or above GU side effects (33.3% in our study vs. 30.8% in PACE-B) and less grade 2 or above GI toxicities (8.3% in our study vs. 15.7% in PACE-B). Actually, baseline urinary function was worse in our cohort, with 23% patients on α-blockers, 58% having prostate volume > 40 cc, and 46% presenting with moderate IPSS. Furthermore, we enrolled more intermediate-risk patients and high-risk patients, and 58% of our patients had proximal SV included in the PTV. Despite the less favorable patient profile, no grade 2 or above RTOG acute GI toxicities occurred in our study, as compared to the 10% reported by PACE-B [20]. The interfraction variations in prostate and adjacent organ positions can affect the dose received by the target and OARs. Peng et al. [10] compared 486 CT scans from CT-on-rail of 20 prostate cancer patients (treated with

conventionally fractionated radiotherapy) with their planning CT scans, and found that the actual dose received by rectum was higher than the planned dose, with increase of V45Gy by > 15% in 5.6% of fractions and increase of V70Gy by > 5% in 11.6% fractions. If intrafraction motions are considered, the dose variations of rectum might be larger. Moreover, Gunnlaugsson et al. [21] demonstrated significant prostate swelling during UHF-RT of prostate cancer, which can only be covered by adaptive radiotherapy with tight margin. Degree of reduction of rectal toxicity varies in different MRgRT series: Bruynzeel et al. [18] reported reduction of grade 2 and above GI toxicity by 5%, Alongi et al. [15] reported reduction of 4%, and Ugurluer et al. reported reduction of 0% [19]. With daily online adaptive contouring and plan re-optimization it is possible to correct for any target or OAR deformation and motion, and deliver high-precision SBRT; this is probably the main reason for the lower incidence of rectal side effects.

Another issue with adaptive MRgRT is the intrafraction motion and the long on-couch time. Keizer et al. [14] showed that a margin of 5 mm is sufficient and might be further decreased. Our real-time dose analysis (unpublished data) also demonstrated relatively good target coverage during delivery with CTV-PTV margin of 3 mm, with mean of 98.5% ± 1.8% CTV receiving 36.25 Gy and 92.1% ± 0.6% CTV4000 receiving 40 Gy. With intrafraction plan adaptation by cine-MR tracking, it may be possible to safely decrease the margin even further [18, 22].

The main limitations of this study are the small sample size and the relatively short follow-up.

Conclusions

This prospective phase II study demonstrated acceptable online workflow of MRgRT for prostate cancer, with GU toxic effects comparable to those with conventional radiotherapy and decreased rectal toxic effects.

Abbreviations

ATP, adapt-to-position

ATS, adapt-to-shape

CROM, clinician-reported outcome measure

CTCAE, Common Terminology Criteria of Adverse Events

CTV, clinical target volume

EORTC-QLQ-C30, European Organisation for Research and Treatment of Cancer (EORTC) quality-of-life questionnaire Core-30

EPIC-26, Expanded Prostate Cancer Index Composite index-26

FACT-P, Functional Assessment of Cancer Therapy—Prostate questionnaire

GI, gastrointestinal

GU, genitourinary

IIEF-5, International Index of Erectile Function-5

IPSS, International Prostate Symptom Score

IPSS, International Prostate Symptoms Score

MRgRT, magnetic resonance–guided radiotherapy

NCCN, National Comprehensive Cancer Network

OAR, organs at risk

PROM, patient-reported outcome measure

PSMA, prostate-specific membrane antigen

PTV, planning target volume

RCT, randomized controlled trial

RTOG, Radiation Therapy Oncology Group

SBRT, stereotactic ablative radiotherapy

SV, seminal vesicles

UHF, ultra-hypofractionated

UHF-RT, ultra-hypofractionated radiotherapy

Declarations

Ethics approval and consent to participate

This research is approved by the Ethics Committee of National Cancer Center/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College (Approval No.: 20/121-2317)

Consent for publication

Consent to be enrolled in this trial and data for publication had been collected for all patients.

Availability of data and materials

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

Competing interests

The authors declare that they have no competing interests.

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The funder of this study had no role in study design, data collection, data analysis, data interpretation or writing of this manuscript. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Authors' contributions

N.-N.L., S.-J.H., N.-Z.X., and Y.-X.L. designed the study, analyzed the data and wrote the manuscript, N.-N.L., N.-Z.X., and Y.-X.L. contributed to the study concept, N.-N.L., S.-J.H., N.-Z.X., and Y.-X.L. contributed to the study coordination, N.-N.L., S.-J.H., and Y.-X.L. performed the statistical analysis, and all authors contributed to patient enrollment, data collection and interpretation, and finally approved the manuscript.

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Figures

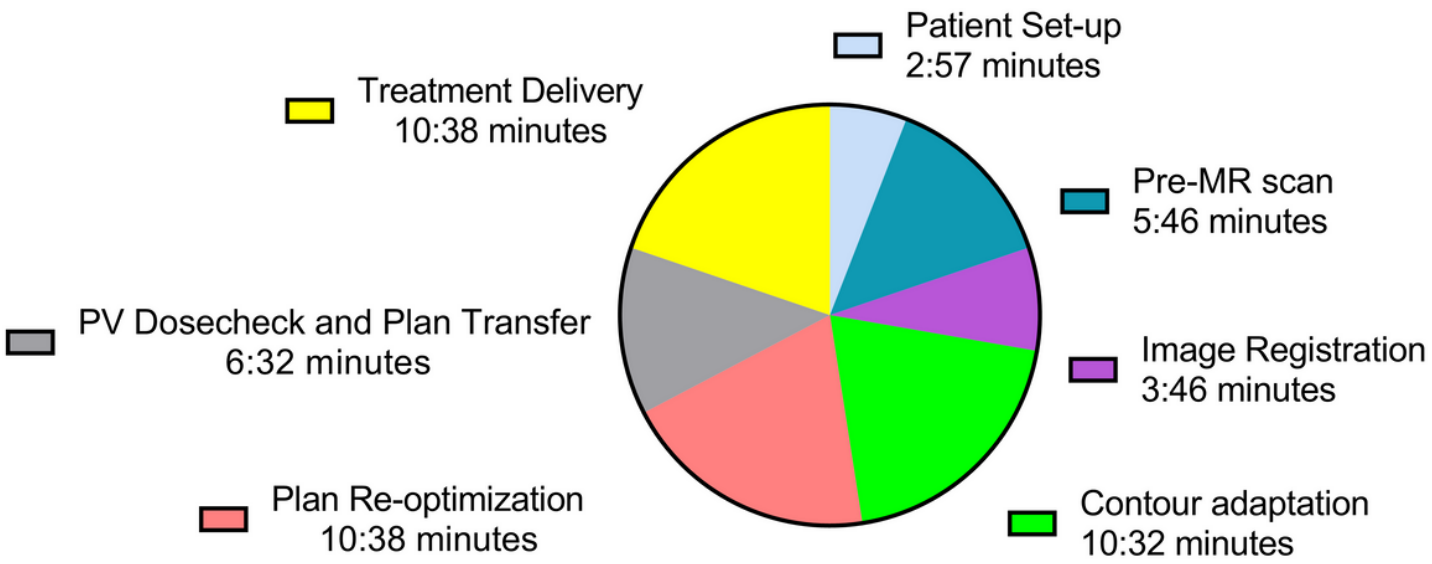

Figure 1

Pie Chart of average time of each ATS step

PV: Position Verification, PV scan is included in “Plan Re-optimization” phase or “PV Dosecheck and Plan Transfer” phase.

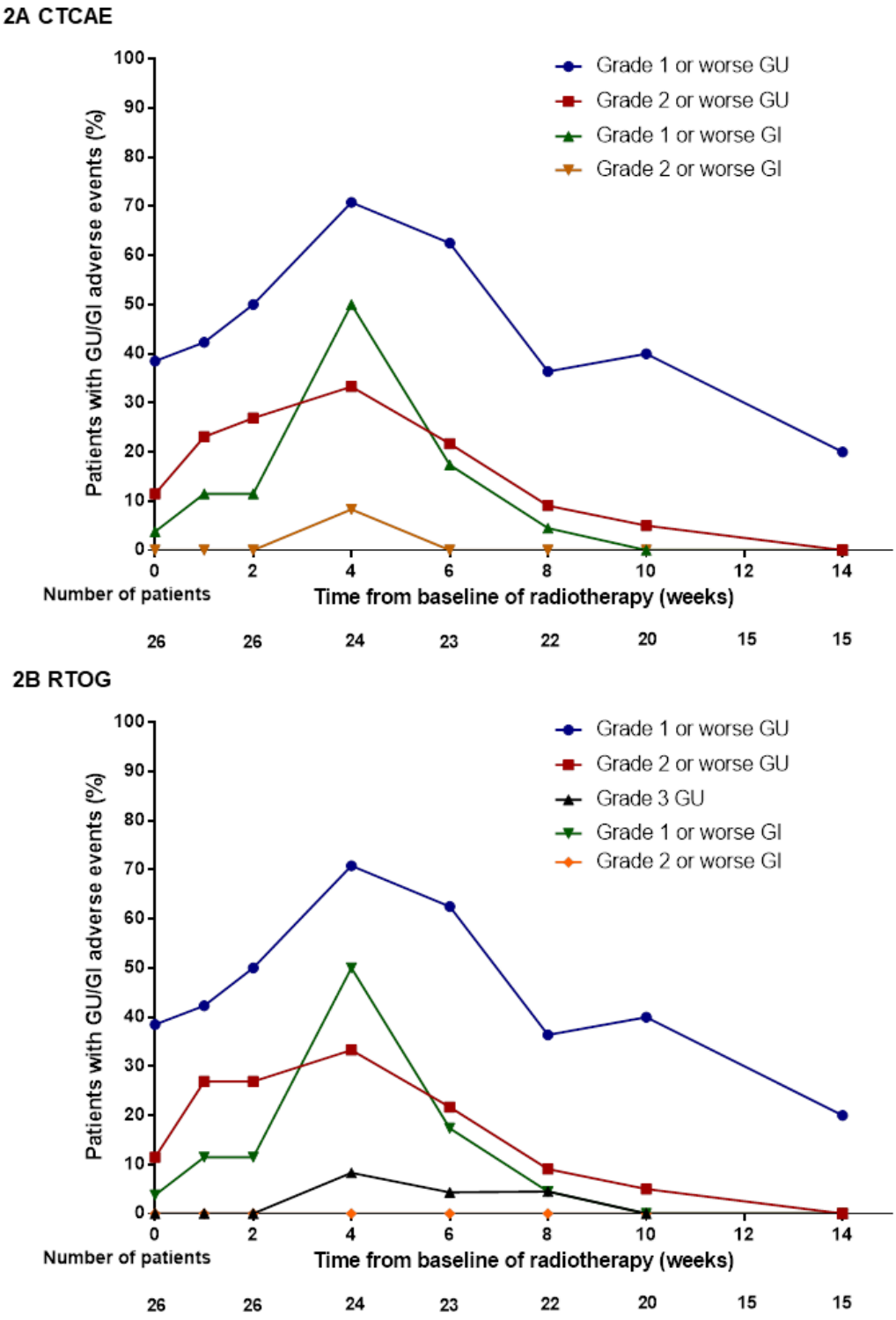

Figure 2

Acute toxicities for genitourinary (GU) and gastrointestinal (GI) symptoms for 24 patients with at least 2-weeks follow-up as per CTCAE (2A) and RTOG (2B) criteria

CTCAE: Common Terminology Criteria of Adverse Events, RTOG: Radiation Therapy Oncology Group

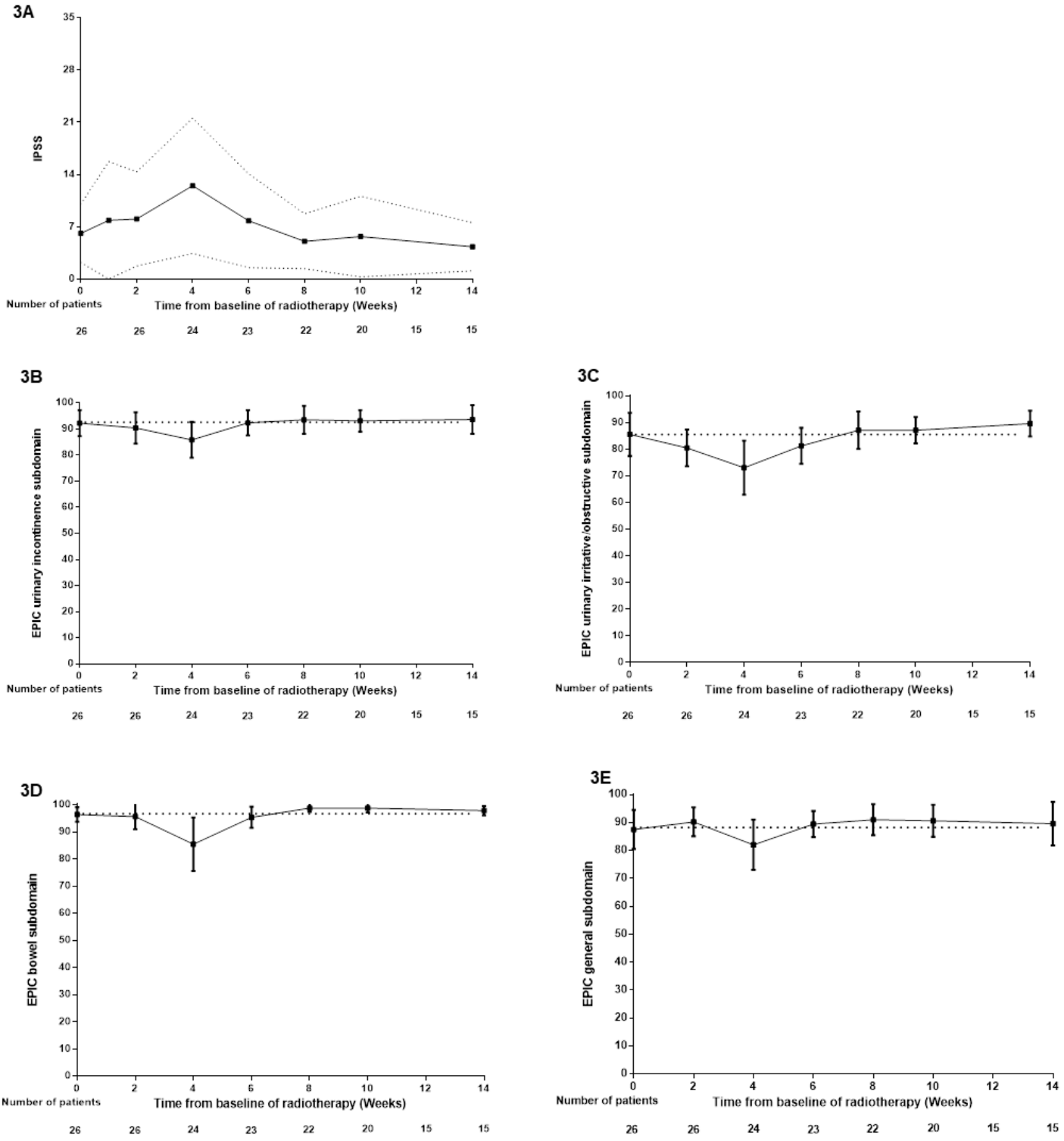

Figure 3

Changes from baseline up to 12 weeks post-RT of IPSS (3A)and EPIC subdomains (3B to 3E) for 24 patients with at least 2-weeks follow-up IPSS: International Prostate Symptoms Score, EPIC: expanded prostate cancer index composite short form