

WITHDRAWN: A study of bladder filling consistency before and during the radiotherapy for pelvic cancer

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Abstract

Background: The purpose of this study was to analyze the consistency of bladder filling before and during radiotherapy for pelvic cancer patients.

Methods: Before radiotherapy, 105 patients followed a strict bladder protocol of consuming 540mL of water immediately after emptying the bladder. Bladderscan device BVI 9400 was used after emptying bladder and measured every 30 minutes until the bladder volume achieve 400mL. When emptying, half an hour and 1 hour after drinking, chief complaint of urgency, the actual bladder volume and corresponding time were described as: $U_0, t_0; U_{0.5}, t_{0.5}; U_1, t_1; U_t, t; U_T, T$. During radiotherapy, 18 patients were randomly selected from 105 patients. They were instructed to keep the same pattern of suppressing urination during the following radiotherapy. The chief complaint of urgency during radiotherapy was observed and recorded. The relative bladder volume was as close as possible to (50%,155%).

Results: Before radiotherapy, patients were no statistically difference between U_1 ($P=0.177$) and U_T ($P=0.052$) in the Immobilization, Simulation CT scan, X-ray Simulation. Bladder volume was concentrated at 298-526mL. There was no statistical difference between U_t and U_T in X-ray Simulation($P=0.198$). Patients emptied bladder volume for 75.2 ± 49.9 min, $U_t=331.2\pm 140.3$ mL. During radiotherapy, 18 (18/105) patients received a total of 450 bladder volume ($18*25$). U_p and U_T were statistical different ($P<0.05$), and the difference was 17.81%. The overall relative bladder volume was negatively correlated with the number of radiotherapy ($r = -0.5726, p = 0.0028$) and the consistency rate was 82.89% (373/450). 15 patients (15/18) passed, and the consistency rate was 96% (360/375). 3 patients (3/18) failed, and the consistency rate was 17.33% (13/75). The consistency rate had no linear correlations with age ($P = 0.2741$).

Conclusions: U_1 was consistent in the Immobilization, Simulation CT scan, X-ray Simulation and during inter-fraction radiotherapy. This indicates that the consistency range is reasonable. Relative bladder volume between (50%,155%) can determine whether the bladder filling of patients with pelvic cancer is consistent with the planned bladder volume before radiotherapy.

Background

Reproducibility of target volume position is a fundamental component of external beam radiotherapy at any site. It is of particular importance where a dose escalated regimen is being employed and where the surrounding organs are both dose and volume sensitive. Thus, consistency in target and organ at risk (OAR) position from planning to treatment is an important basic principle of radiotherapy [1]. The scope of pelvic tumors is relatively large, such as cervical cancer, prostate cancer, rectal cancer, etc.

Preoperative chemoradiation (CRT) is a standard treatment for locally advanced rectal cancer, which increases local control and sphincter preservation rates compared with adjuvant treatments [2–6]. In the pelvic cancer radiotherapy, large variation in bladder volume (BV) could affect the accuracy of treatment

and dose volume histogram of OAR particularly of the small bowel [7]. However, if initial BV is excessively small, dose constraints for the bladder may not be satisfied [8]. As the tumor dose is escalated, the risk of normal tissue toxicity is increased, although dependent on the size of treatment margins [9]. Joost et al reported that bladder filling protected the small intestine better than when it was empty; intensity-modulated radiation therapy (IMRT) reduced the small intestine irradiation volume by 72% and 3D-CRT reduced by 50% when filling [10]. It is important for the bladder to be full, in order that pelvic cancer patients can get the concentrated dose of exposure and decrease the normal tissue of exposure. Hence, there is a need to standardize BV for both planning and treatment to moderate the influence on risk of normal tissue toxicities [11].

However, to date, no recognized standard on whether pelvic cancer patients have been achieving to judge the BV consistency during radiotherapy. Fujioka et al believed that the mean relative bladder volume (RBV) was at least 70%, and based on the results of the mean values of BV receiving more than 70 Gy ($V_{70\text{Gy}}$) and 50 Gy ($V_{50\text{Gy}}$) in each subgroup, the cutoff value (mean + 2standard deviations [SD]) at the upper bounds of the 95% confidence interval was determined [8]. Cramp et al believed that the BV was reasonable when it was 250–350 mL, and the RBV > 50% was considered to be up to standard [11]. Hong In Yoon et al thought that when the bladder volume of patients ranged from 80–120% of that of the simulation CT scan, patients were instructed to keep the same pattern of bladder filling the following day [12].

The aim of this study was to analyze the consistency of bladder filling degree of the three steps before inter-fraction radiotherapy, and to summarize a reference range for judging the consistency during radiotherapy.

Methods

1. Patients

In 2014, 105 pelvic cancer patients from the Sun Yat-sen University Cancer Center (SYSUCC) were included in this study. The clinical profiles of the 105 patients are shown in table 1. The United Nations World Health Organization (WHO) divided age as follows: under the 44 age are youth; 45-59 are middle-age; 60-74 are young elderly people; 75-89 are elderly people. Among them, there were 82 patients in Immobilization (Orfit Industries, Belgian; Nucletron Simulix, Netherlands), 90 patients in Simulation CT scan (Philips Big Bore RT, USA) and 29 patients in X-ray Simulation (Nucletron Simulix, Netherlands). The total number of samples were 518 times, with an average of 4-5 times per person.

18 patients (18/105) with pelvic cancer radiotherapy were randomly selected. The number of treatments per person was 25 times. The prescribed dose of radiotherapy was 240 cGy/fraction, and the total dose was 6000 cGy.

Table.1 Gender and clinical data

Patient Information	Number N=105
Gender	
Male	27
Female	78
Age	
≤44	19
45-59	57
60-74	26
75-89	3
Type of operation	
Pre-operation	69
Post-operation	36
Type of pelvic tumor	
Cervical cancer	68
Rectal cancer	32
Vaginal cancer	3
Prostate cancer	2

2.BV measurement process before radiotherapy

In the Immobilization step, firstly, patients were told to empty their bladder, and the BVI 9400 (VERATHON, Bladderscan BVI 9400, USA) used to measure U_0 . Then patients immediately drank 540mL water, and self-controlled maintenance. Measurement was performed every other 0.5 hour and the time recorded: $U_{0.5}$ $t_{0.5}$; U_1 t_1 ,... When the patient complained of urgency, BV would be measured again and the time would also be recorded. At this moment, measured volume was defined as U_t and the measured time was defined as t ; Each time we told patients the actual BV(U_T) and the importance of bladder filling. Maximum bladder capacity (cystometric) under physiological conditions was 500 to 650mL, so we set 400mL as the target volume. According to relevant reports [8,17], asking about a feeling of bladder fullness, the time of last voiding, and the amount of water drank before irradiation can improve a patient's ability to maintain an appropriate BV. Mullaney et al reported that the 540mL bladder-filling arm resulted in reproducible BVs throughout a course of radiotherapy, without any deterioration in quality of life (QoL) or increase in toxicities for prostate patients [13]. The patient received Immobilization with Or-fit fixture and thermoplastic omentum in prone position when the BV achieved ≥ 400 mL and ≤ 600 mL. At the same time the measured volume and the time were defined as the actual volume and the actual time (U_T, T). If

BV 600mL. We would told patient to urinate appropriately and maintain between 400-600mL. When patient's BV reached the target volume, we would perform Simulation CT scan and X-ray Simulation. Thickness of CT is 5 mm. The method of BV measurement in the Simulation CT scan and X-ray Simulation step was the same as the Immobilization (Fig.1).

3.Consistency judgment method

All individual observations were obtained from the selected reference population, and statistical methods were used to establish percentile limits, in order to obtain the fluctuation range of individual observations, using a 95% reference value range [14]. There are 2 standard errors in the 95% confidence interval [15]. Generally, when calculating the distribution probability, the normal or near-normal distribution data can be used (mean \pm 2SD) to specify the probability range [14]. There have been different understandings and definitions of the consistency of BV, but they have not proved whether it is suitable for most patients with pelvic cancer [8,11]. Judgment consistency cannot blindly expand the reference range, it should be judged according to the actual situation of the patient. Based on this, we set the lower limit of the reference range to 50% and the upper limit of the 95% confidence interval to 155%. (mean=1.001, SD=0.27671) Special concepts in radiotherapy were shown in table 2.

Table 2. Special concept in radiotherapy

Name	Definition
RBV	U_T / U_p
Reference range	50%,155%
Consistency	Up to reference range
Consistency rate	Numbers of consistency / Times (25)
Pass	Consistency rate>50%
Fail	Consistency rate <=50%

4.BV measurement process during radiotherapy

18 patients were randomly selected from 105 patients. Firstly, a full bladder training was offered to patients before radiotherapy. Secondly, the patients emptied bladder and drank water 540mL immediately. Thirdly, BV was measured by the BVI 9400 and patient's complaint of urgency. At the same time, patients were informed the actual BV (U_T) and the importance of reaching the planned BV(U_p) was emphasized. If patients' BV was not up to standard, they should continue to suppress urine. Until they complained of urgency and then BV was measured. Patients were asked to seriously experience the feeling state when the BV reached the standard, so that U_T and U_p would be consistent

5.Statistical analysis

The volume measured in each step was compared by SPSS 20.0 statistical software package, using Kruskal-Wallis test and independent sample t-test. GraphPad Prism 8.0.1, Origin Pro 9.0 was used for linear regression of RBV in radiotherapy. All reported P values were 2-tailed, and significance was defined at $P < 0.05$.

Results

1. Analysis of the consistency of BV before treatment

1.1 Influencing factors of bladder filling in patients with pelvic cancer

In three steps, U_1 was comparative analysis with gender and age ($N=77$). According to the independent sample t-test there was statistical difference between male and female ($P=0.003$). After emptying the bladder, female hold little more than male within 1 hour.

We divided age into two groups as follows: 18-59, 60-89. According to the independent sample t-test, there was a statistical difference between the youth and the middle-age ($p=0.008$). It means that the older, the more difficult to reach the target volume, and more time spent. (Table 3)

Table 3. Analysis of gender and age factors

Gender/Age	Number (N=77)	Standard deviation	P Value
Male	24	269.9±148.9	P=0.003
Female	53	385.2±152.0	
18-59	55	377.9±160.6	P=0.008
60-89	22	277.6±134.3	

1.2. Comparison and analysis of patient's BV in three steps

In three steps, the comparison of patient's BV was shown in table 4. According to the independent samples t-test, compared with the three steps, there was a statistical difference between U_0 ($P=0.000$) and $U_{0.5}$ ($P=0.006$). There was no statistical difference between U_1 ($P=0.177$) and U_T ($P=0.052$). It means that bladder filling had consistency between U_1 and U_T . The volume measured in Simulation CT scan was larger than Immobilization and X-ray Simulation ($U_0=143.0±43.6\text{mL}$, $U_{0.5}=371.4±78.6\text{mL}$, $U_1=430.8±154.3\text{mL}$, $U_T=434.2±115.1\text{mL}$).

BV increased with the chief complaint of urgency time in five patients (P1, P2, P3, P4, P5) as shown in fig.3(a). After self-controlled maintenance for 1 hour, U_{P5} was $> 600\text{mL}$, and it didn't conform to the requirement of bladder filling before radiotherapy. Therefore, P5 was required to urinate properly and

control the BV within the target volume. Fig. 3(b) shows the actual volume of patients. U_T of the three steps was 412.4 ± 114 (Mean \pm SD) mL. According to the box-plot, U_T was concentrated at 298-526mL.

Table.4 Comparison of BV in three steps(Mean \pm SD)

Step	U_0	$U_{0.5}$	U_1	U_T
Immobilization	42.1 \pm 51.3	209.5 \pm 166.2	327.2 \pm 162.5	399.6 \pm 112.3
Simulation CT scan	143.0 \pm 43.6	371.4 \pm 78.6	430.8 \pm 154.3	434.2 \pm 115.1
X-ray Simulation	60.5 \pm 83.1	230.3 \pm 169.2	376.0 \pm 149.2	381.1 \pm 105.9
P Value	P=0.000	P=0.006	P=0.177	P=0.052

1.3. Distributions and analysis of U_t and U_T in three steps

A comparison between U_t and U_T in the patients with pelvic cancer in three steps was shown in table 5. According to the independent sample t-test, there was a statistical difference between U_t and U_T in the Immobilization and Simulation CT scan (P=0.000 P=0.001). In X-ray Simulation step, there was no significant difference between U_t and U_T (P=0.198). It may be easier to obtain the target volume because of the previous two steps of self-control maintenance training and self-feeling. Therefore, U_t was consistent with U_T . In the Immobilization and Simulation CT scan step, patients didn't have training before. Besides, the patient's first contact with the radiotherapy will generate a strain of tension, leading to the inconsistency of U_t and U_T .

After emptying the bladder, the time to chief complaint was 75.2 ± 49.9 min. Fig.4(a) was the time to chief complaint, which showed that the time to chief complaint of urgency was between 40-100 min. There were 6 patients who took too long time because of prostatitis or catheterization, resulting in difficult for them to self-control maintenance. Besides, patients spent more time to suppress urination and the maximum was 320 min. After emptying the bladder, $U_t = 331.2 \pm 140.3$ mL. Fig.4(b) was the volume distribution about the chief complaint of urgency, and the volume measured at the time focused on 100-500mL.

Table5. Three steps of comparison between U_t and U_T (Mean \pm SD)

Step	U_t	U_T	P Value
Immobilization	318.6±142.2 (N=56)	399.6±112.3 (N=82)	P=0.000
Simulation CT scan	500.0±17.5 (N=3)	434.2±115.1 (N=90)	P=0.001
X-ray Simulation	339.0±133.5 (N=26)	381.1±105.9 (N=29)	P=0.198

1.4. Analysis of frequency of and time to chief complaint of urgency in three steps

Frequency of and time to chief complaint of urgency was analyzed in three steps was shown in table 6. In the Immobilization and Simulation CT scan, patients had the first chief complaint of urgency in about 60 minutes and more than half of the patient's BV could reach the target volume. But some patients also had the second or third time to complain of urgency, which may be related to the patient's status differences. The Simulation CT scan step was usually performed on the same day as the X-ray Simulation step. Patient already had self-controlled maintenance at the X-ray Simulation, and the volume might still be in the range of the target volume by the time of Simulation CT scan. Therefore, the time to chief complaint of urgency would be shorter than "X-ray Simulation" and "Immobilization ". If patient had too much urine, he/she needed to urinate properly and then continued to suppress urination.

Table 6. Analysis about frequency of and time to the chief complaint in three steps

Frequency of chief complaint	N	Immobilization		
		Average time(min)	Effective Number	Effective mean time(min)
First	42	66.5±31.6	25	60.7±21.1
Second	9	108.8±66.8	3	78.3±10.4
Third	5	153±94.2	3	105±10
Frequency of chief complaint	N	Simulation CT scan		
		Average time(min)	Effective Number	Effective mean time(min)
First	3	21.7±22.5	2	32.5±17.7
Second	-	-	-	-
Third	-	-	-	-
Frequency of chief complaint	N	X-ray Simulation		
		Average time(min)	Effective Number	Effective mean time(min)
First	18	52.9±27.3	10	53±24.3
Second	6	97.5±52.6	4	75±27.4
Third	2	125±7	1	130

2. Analysis of the consistency of BV during radiotherapy

2.1 Comparison of U_P and U_T

The comparison of U_P and U_T in 18 patients with pelvic cancer was shown in Table 7. The difference between U_P and U_T was statistically significant ($P < 0.05$), and the difference was 17.81%.

Table 7. Comparison of U_P and U_T in 18 patients with pelvic cancer(mL)

Item	N (Frequency)	Mean	SD	P value
Planned volume	18	342.89	105.206	0.025
Treatment volume	450	281.82	54.221	

2.2 The RBV distribution during inter-fraction radiotherapy in 18 patients

The interquartile range (IQR) indicated that the RBV was not very discrete (Fig.5). The overall RBV was negatively correlated with the number of radiotherapy ($r=-0.5726$, $p=0.0028$). As the inter-fraction radiotherapy continued to increase, the RBV gradually decreased, and the overall decrease was 5.53%. (Fig. 6)

2.3 The consistency rate of BV of 18 patients

18 patients obtained a total of 450 BV (18×25), and the consistency rate was about 82.89% (373/450). 15 patients (15/18) passed, and the consistency rate was 96% (360/375). Indicating that although the reduction in bladder capacity caused by radiotherapy was unavoidable, after suppress urination training, the vast majority of BV can be consistent with the planned BV (U_p). 3 patients (3/18) failed, and the consistency rate was 17.33% (13/75), as shown in Fig.7. The consistency rate was linearly independent of age ($P = 0.2741$).

Discussion

1.The consistency of BV before radiotherapy

Radiotherapy is the main method of postoperative prevention and local recurrence treatment in the pelvic cancer. Day-to-day anatomical variations complicate bladder cancer radiotherapy treatment [16]. Treating with a full bladder leads to unpredictability in bladder filling, and some authors suggest that this becomes more pronounced as treatment progresses, which could be due to poor patient compliance, disease-related anatomical changes that interfere with bladder innervation, or treatment-associated toxicity [24-28].

First of all, there were differences in BV between gender and age. U_1 of patients over 60 years was 277.6 ± 134.3 mL, which was much different from the target volume. Thus, it is suggested that patients above 60 years drank more 180 mL water after self-controlled maintenance for 30 minutes, so that the BV is closer to the target volume. It can be seen that the capacity of bladder to self-controlled maintenance varies from person to person. Chang Jee Suk et al reported that patients were asked to drink unspecified volume of water because we thought there were wide variations of abilities in drinking water and suppressing urination [32]. Besides, retaining urine was anticipated to become more difficult over the course of treatment because of radiation cystitis [33].

Secondly, the comparison of BV in three steps showed that there was no significant difference between U_1 and U_7 . It was indicated that when patients drank 540 mL water after emptying bladder and then waiting for 1 hour, the bladder volume before and during radiotherapy was consistent. We consider that using the BVI 9400 to measure the BV can better ensure that the bladder reached the filling state during radiotherapy. There was significant difference in bladder volume between U_0 and $U_{0.5}$. Thus, Bladder scan was a strategy that has been considered for increasing consistency with bladder volume. Similar to

Cramp et al resulted [11]. Most patients will go to Simulation CT scan on the same day after Immobilization. By this time, patient's BV has reached the target volume, then go to CT room to report. While waiting for the Simulation CT scan, the BV continued to increase, resulting in a larger amount of BV in the Simulation CT scan than the other two steps. Therefore, it was recommended that the radiation therapist can allow patients to empty their bladder before Simulation CT scan, and then drank water to self-controlled maintenance.

Thirdly, there was a statistical difference between U_t and U_T in the "Immobilization" and "Simulation CT scan" steps. However, there was no statistical difference between the U_t and the U_T in the X-ray Simulation. It was previously reported that biofeedback could improve the consistency of BV despite a lack of statistical significance [18]. The method (drinking 540mL water after emptying bladder and then waiting for 1 hour) can improve and obtain the reliable feeling about self-controlled maintenance. Because the patient was subjected to the Simulation CT scan after the Immobilization was completed.

Moreover, most patients can achieve the target volume on the first chief complaint of urgency. Some patients still needed the second or the third complaint of urgency. In addition to the patient's physical factors, it was possible that the patient's chief complaint of urgency was not true. Waiting for (75.2 ± 49.9) min after emptying the bladder, patients complained of urgency. Because patients' waiting for a long time leads to tension, impatience and urgent completion of the treatment, they tell the radiation therapist "urgency". But their volume doesn't reach expected standards. In order that the patient can get the better cooperation with treatment, the radiotherapy can be more accurate and the burden of work can be reduced, the radiation therapist should tell each patient the importance of filling bladder and how long it will take to wait. While patients are waiting, the radiation therapist need to appease the patient's mood.

2.The consistency of BV during radiotherapy

There are many uncertain factors in the treatment of pelvic cancer, and the most concerned is the filling state of the bladder. The BV changes during the course of radiotherapy [17-22]. Bladder and rectal volumes tend to decrease as a function of time during treatment [23]. A research reported that during the first week of radiotherapy treatment, 50% of patients had more than 50% change in BV. And on the fifth week of treatment 64% of patients had more than 50% change in BV compared to the planned BV [2]. Hynds et al found that 76% (828/1090), 53% (579/1090), 36% (393/1090) BV during radiotherapy were >50mL, >100mL, >150mL difference [1]. Compared with the planned volume, all men had at least one BV reduction of more than 50% during treatment. The reduction in BV was probably correlated with incidence and severity of acute diarrhea [2].

In the result of BV measurement process during radiotherapy, first of all, it showed that there were statistically significant differences between U_p and U_T of 18 patients with pelvic cancer ($P < 0.05$), with a difference of 17.81%. The RBV was negatively correlated with the number of radiotherapy ($r = -0.5726$, $p = 0.0028$). With the inter-fraction radiotherapy, the overall RBV of 18 patients gradually decreased and the overall decrease was 5.53%. The larger the standard deviation was, the greater the degree of

dispersion would be. Stam et al believed that SD = 47.2% can be considered that the daily variation of BV was large [18], while the overall SD = 2% of 18 patients was much less than 47.2% during radiotherapy. The change in the RBV between the inter-fractions was small.

Secondly, it showed that 18 patients obtained a total of 450 BV (18*25), and the consistency rate was about 82.89% (373/450). 15 patients (15/18) passed, and the consistency rate was 96% (360/375). The consistency rate has no linear relationship with age ($P = 0.2741$), similar to Mullaney [13]. It showed that although the reduction of bladder capacity caused by radiotherapy was unavoidable, but patients drank 540mL of water before radiotherapy and urination suppressing training; therefore, most patient's BV can be consistent with the planned BV.

Thirdly, it showed that 3 patients (3/18) failed, and the consistency rate was 17.33% (13/75), but their BV remained relatively consistent between inter-fractions. The reason for the failure may be that ultrasound assessment of BV was less satisfactory in real patients than in normal volunteers. It was noted that there was considerable variability in the shapes of different bladders and at varying volumes. These methods were not applicable to all patients, either because the bladder outline was too indistinct or the bladder was too large to demonstrate on a single scan [34]. Although BS provides an effective means of assessing BV prior to treatment, studies showed that improvements in BV consistency are more difficult to attain [1,18,35,36]. Nevertheless, there are some articles which have supported the use of the BS in a radiation therapy setting [17,35,36]. The plausible explanation is that if the BV for the first time of radiotherapy cannot reach the planned BV (U_p) due to the poor condition of the patient or the measurement error of the radiation therapist. But during clinical treatment, the patient's actual BV is used as the treatment BV and the first radiotherapy is used as the reference standard, so the patient's BV fails during the entire radiotherapy process. Therefore, for a small number of special patients, attention should be paid to rational determination of BV before treatment.

Shogo Hatanaka et al reported that the decrease of BV will lead to the increase of bladder dose, for both the small and large bowel, and they found a significant association between the D_{max} values and BV variation (the dose of small and large bowel less than 60Gy and 65Gy) [29]. Yaparpalvi R et al found that the small intestine area with 45 Gy was greater in the bladder emptying condition compared to the bladder filling state (The average was 328.0 ± 174.8 vs 176.0 ± 87.5 cm) [25]. Frizzell B et al made a definitive treatment for prostate cancer, according to the influence of BV on rectal radiotherapy dose. The filling of bladder was compared with emptied bladder, the average exposure dose of rectum decreased by 27.6 Gy, and there was significant difference ($P=0.031$) [30]. Buchali et al found that when the BV increased, the exposure dose decreased. A full bladder led to a mean reduction in organ dose in median from 94-87% calculated for 50% of the BV. For 66% of the BV the dose could be reduced in median from 78-61% and for the whole bladder from 42-39% [31]. Fujioka C et al reported optimal BVs at treatment planning must be investigated to both maintain reproducibility of the BV and dose constraints for the bladder [8].

At present, the standard of "pass" bladder volume before radiotherapy for patients with pelvic cancer is not clear. In actual clinical practice, the radiation therapist usually judges whether the measured BV meets the planned BV (U_p) based on experience. Patients who fail to reach the planned BV need to suppress urination for many times, which virtually increases the patient's mental tension and physical discomfort, and reduces the efficiency of radiotherapy. However, urination suppressing training before radiotherapy and the maintenance intervention during radiotherapy showed that 82.89% (373/450) of the 18 patients in the range of (50%, 155%) were able to keep consistency with U_p and U_T . This indicates that the consistency range is reasonable. (50%,155%) can determine whether the bladder filling of patients with pelvic cancer is consistent with the planned BV before radiotherapy, reducing the patient's mental pressure and physical discomfort, improving the efficiency of radiation therapy. However, urination suppressing training used in the present study was frequently used in clinical practice in the setting of dose escalation to the pelvic cancer patients. Despite these limitations, there are very few data in the literature on the optimal BV at treatment planning and during radiotherapy in pelvic cancer; therefore, we hope that the present results will serve as reference values for other institutions.

Conclusion

Patients emptied the bladder and immediately drank 540 mL of water. After 1 hour of suppressing urination, patients complained of urgency and achieved the target volume (400 mL). At this time, the BV was consistent in the Immobilization, Simulation CT scan, X-ray Simulation and during inter-fraction radiotherapy. This indicates that the consistency range is reasonable. (50%,155%) can determine whether the bladder filling of patients with pelvic cancer is consistent with the planned BV before radiotherapy.

Abbreviations

BV: Bladder volume;

U_0, t_0 : Emptied bladder volume and time;

$U_{0.5}, t_{0.5}$: 0.5 hours after drinking of bladder volume and time;

U_1, t_1 : 1 hour after drinking of bladder volume and time;

U_t, t : Chief complaint of urgency of bladder volume and time;

U_T, T : Actual bladder volume and time;

U_p : Planned bladder volume;

RBV: Relative bladder volume;

CRT: Preoperative chemoradiation;

IMRT: Intensity-modulated radiation therapy;

QoL: Quality of life;

IQR: Interquartile range;

U_{p5}: Patient 5's bladder volume.

Declarations

1. Ethical Approval and Consent to participate

This project was approved by the Ethical Committee of Sun Yat-Sen University Cancer Center and informed consent was obtained from all patients.

2. Consent for publication

All the authors listed have approved the manuscript that is enclosed.

3. Availability of supporting data

The data are fully available without restriction in the Research Data Deposit public platform (RDD Number: RDDA2020001544,

<https://www.researchdata.org.cn>) and are available upon reasonable request.

4. Competing interests

None of the authors have any competing interests (financial and nonfinancial) in the manuscript.

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6. Authors' contributions

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All authors have read and approved the final manuscript.

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References

1. Hynds S, MCGarry C K, Mitchell D M, et al. Assessing the daily consistency of bladder filling using an ultrasonic Bladderscan device in men receiving radical conformal radiotherapy for prostate cancer[J]. *British Journal of Radiology*, 2011, 84(1005):813-818. DOI:1259/bjr/50048151
2. Sauer R, Becker H, Hohenberger W, et al. Preoperative versus Postoperative Chemoradiotherapy for Rectal Cancer[J]. *The New England Journal of Medicine*, 2004, 351(17):1731-1740. DOI:1056/NEJMoa040694
3. Peeters K C M J, Marijnen C A M, Nagtegaal I D, et al. The TME trial after a median follow-up of 6 years - Increased local control but no survival benefit in irradiated patients with resectable rectal carcinoma[J]. *Annals of Surgery*, 2007, 246(5):693-701. DOI: 1097/01.sla.0000257358.56863.ce
4. Sebag-Montefiore D, Stephens R J, Steele R, et al. Preoperative radiotherapy versus selective postoperative chemoradiotherapy in patients with rectal cancer (MRC CR07 and NCIC-CTG C016): a multicentre, randomised trial[J]. *The Lancet*, 2009, 373(9666):811-820. DOI: 10.1016/S0140-6736(09)60484-0
5. Sauer R, Liersch T, Merkel S, et al. Preoperative Versus Postoperative Chemoradiotherapy for Locally Advanced Rectal Cancer: Results of the German CAO/ARO/AIO-94 Randomized Phase III Trial After a Median Follow-Up of 11 Years[J]. *Journal of Clinical Oncology*, 2012, 30(16):1926-1933. DOI:1200/JCO.2011.40.1836
6. Navarro M, Dotor E, Rivera F, et al. A phase II study of preoperative radiotherapy and concomitant weekly irinotecan in combination with protracted venous infusion 5-fluorouracil, for resectable locally advanced rectal cancer[J]. *International Journal of Radiation Oncology Biology Physics*, 2006, 66(1):201-205. DOI: 10.1016/j.ijrobp.2006.04.007
7. Sithamparam S, Ahmad R, et al. Bladder filling variation during conformal radiotherapy for rectal cancer[J]. *Journal of Physics: Conference Series*, 2017, 851(1):12-26. DOI: 10.1088/1742-6596/851/1/012026.
8. Fujioka C, Ishii K, Yamanaga T, et al. Optimal bladder volume at treatment planning for prostate cancer patients receiving volumetric modulated arc therapy[J]. *Practical Radiation Oncology*, 2014, 90(1):688-689. DOI: 1016/j.ijrobp.2014.05.2023
9. Dearnaley D P, Hall E, Lawrence D, et al. Phase III pilot study of dose escalation using conformal radiotherapy in prostate cancer: PSA control and side effects. [J]. *British Journal of Cancer*, 2005, 92(3):488-498. DOI: 10.1038/sj.bjc.6602301

10. Nuyttens J J, Robertson J M, Yan D, et al. The influence of small bowel motion on intensity modulated radiation therapy (IMRT) for rectal cancer[J]. *International Journal of Radiation Oncology Biology Physics*, 2000, 48(3):168. DOI: 10.1016/S0360-3016(00)80130-3
11. Cramp L, Connors V, Wood M, et al. Use of a prospective cohort study in the development of a bladder scanning protocol to assist in bladder filling consistency for prostate cancer patients receiving radiation therapy[J]. *Journal of Medical Radiation Sciences*, 2016, 63(3):179-185. DOI:1002/jmrs.162
12. Yoon H I , Chung Y , Chang J S , et al. Evaluating Variations of Bladder Volume Using an Ultrasound Scanner in Rectal Cancer Patients during Chemoradiation: Is Protocol-Based Full Bladder Maintenance Using a Bladder Scanner Useful to Maintain the Bladder Volume?[J]. *Plos One*, 2015, 10(6). DOI:10.1371/journal.pone.0128791
13. Mullaney L M, O'shea E, Dunne M T, et al. A randomized trial comparing bladder volume consistency during fractionated prostate radiation therapy[J]. *Practical radiation oncology*, 2014, 4(5):203-212. DOI:1016/j.ppro.2013.11.006
14. Li K, He J. *Medical Statistics [M]*. People's Medical Publishing House, 2013.22
15. Kirkwood B R, Sterne J A C. *Medical Statistics[M]*. 2003.
16. Webster G J, Stratford J, Rodgers J, et al. Comparison of adaptive radiotherapy techniques for the treatment of bladder cancer[J]. *British Journal of Radiology*, 2013, 86(1021):20120433. DOI 1259/bjr.20120433
17. O'Doherty U M, Mcnair H A, Norman A R, et al. Variability of bladder filling in patients receiving radical radiotherapy to the prostate[J]. *Radiotherapy and Oncology*, 2006, 79(3):335-340. DOI: 10.1016/j.radonc.2006.05.007
18. Stam M R, Lin E N J T V, Vight L P V D, et al. Bladder filling variation during radiation treatment of prostate cancer: can the use of a bladder ultrasound scanner and biofeedback optimize bladder filling? [J]. *International Journal of Radiation Oncology Biology Physics*, 2006, 65(2):371-377. DOI: 10.1016/j.ijrobp.2005.12.039
19. Pinkawa M, Asadpour B, Gagel B, et al. Prostate position variability and dose-volume histograms in radiotherapy for prostate cancer with full and empty bladder[J]. *International Journal of Radiation Oncology Biology Physics*, 2006, 64(3):856-861. DOI: 10.1016/j.ijrobp.2005.08.016
20. Nakamura N, Shikama N, Takahashi O, et al. Variability in Bladder Volumes of Full Bladders in Definitive Radiotherapy for Cases of Localized Prostate Cancer[J]. *Strahlentherapie Und Onkologie*, 2010, 186(11):637-642. DOI 1007/s00066-010-2105-6
21. Cambria R, Jereczek-fossa B A, Zerini D, et al. Physical and clinical implications of radiotherapy treatment of prostate cancer using a full bladder protocol[J]. *Strahlentherapie Und Onkologie*, 2011, 187(12):799-805. DOI 1007/s00066-011-2259-x
22. Mak D, Gill S, Paul R, et al. Seminal vesicle interfraction displacement and margins in image guided radiotherapy for prostate cancer[J]. *Radiation Oncology*, 2012, 7(1):1-9. DOI 1186/1748-717X-7-139

23. Antolak J A, Rosen I I, Childress C H, et al. Prostate target volume variations during a course of radiotherapy[J]. *International Journal of Radiation Oncology Biology Physics*, 1998, 42(3):661-672. DOI 1016/S0360-3016(98)00248-X
24. Chen V E, Gillespie E F, Manger R P, et al. The impact of daily bladder filling on small bowel dose for intensity modulated radiation therapy for cervical cancer[J]. *Medical Dosimetry*, 2018, 44(2):102-106. DOI 1016/j.meddos.2018.02.010
25. Yaparpalvi R, Mehta K J, Bernstein M B, et al. Contouring and Constraining Bowel on a Full-Bladder Computed Tomography Scan May Not Reflect Treatment Bowel Position and Dose Certainty in Gynecologic External Beam Radiation Therapy[J]. *International Journal of Radiation Oncology Biology Physics*, 2014, 90(4):802-808. DOI 1016/j.ijrobp.2014.07.016
26. Ahmad R, Hoogeman M S, Quint S, et al. Inter-fraction bladder filling variations and time trends for cervical cancer patients assessed with a portable 3-dimensional ultrasound bladder scanner[J]. *Radiotherapy and Oncology*, 2008, 89(2):172-179. DOI 1016/j.radonc.2008.07.005
27. Turner S L, Swindell R, Bowl N, et al. Bladder movement during radiation therapy for bladder cancer: implications for treatment planning[J]. *International Journal of Radiation Oncology Biology Physics*, 1997, 39(2):355-360. DOI 1016/S0360-3016(97)00070-9
28. Jhingran A, Salehpour M, Sam M, et al. Vaginal motion and bladder and rectal volumes during pelvic intensity-modulated radiation therapy after hysterectomy[J]. *International Journal of Radiation Oncology Biology Physics*, 2012, 82(1):256-262. DOI 1016/j.ijrobp.2010.08.024
29. Hatanaka S, Kawada Y, et al. The Impact of Variation in Bladder Volume on the Doses of Target and Organ-at-Risk in Intensity-Modulated Radiation Therapy for Localized Prostate Cancer[J]. *Journal of Cancer Therapy*, 2016, 7(10):741-751. DOI:10.4236/jct.2016.710075.
30. Frizzell B, Lovato J, Foster J, et al. Impact of bladder volume on radiation dose to the rectum in the definitive treatment of prostate cancer[J]. *The Journal of community and supportive oncology*, 2015, 13(8):288-291. DOI 12788/jcso.0156
31. Buchali A, Koswig S, Dinges S, et al. Impact of the filling status of the bladder and rectum on their integral dose distribution and the movement of the uterus in the treatment planning of gynaecological cancer[J]. *Radiotherapy and Oncology*, 1999, 52(1):29-34. DOI:1016/S0167-8140(99)00068-7
32. Chang J S, Yoon H I, Cha H J, et al. Bladder filling variations during concurrent chemotherapy and pelvic radiotherapy in rectal cancer patients: early experience of bladder volume assessment using ultrasound scanner[J]. *Radiation oncology journal*, 2013, 31(1):41-47. DOI 3857/roj.2013.31.1.41
33. Moiseenko V, Liu M, Kristensen S, et al. Effect of bladder filling on doses to prostate and organs at risk: a treatment planning study[J]. *Journal of Applied Clinical Medical Physics*, 2007, 8(1):55-68. DOI 1120/jacmp.v8i1.2286
34. Hartnell G G, Kiely E A, Williams G, et al. Real-time ultrasound measurement of bladder volume: a comparative study of three methods[J]. *British Journal of Radiology*, 1987, 60(719):1063-1065. DOI 1259/0007-1285-60-719-1063

35. Gawthrop J, Oates R. Measured bladder volume for radiotherapy of the prostate using the hand-held BladderScan BVI 3000[J]. Radiographer, 2012, 59(1):8-12. DOI 1002/j.2051-3909.2012.tb00167.x
36. O'Shea E, Armstrong J, O' Hara T, et al. Validation of an external ultrasound device for bladder volume measurements in prostate conformal radiotherapy[J]. Radiography, 2008, 14(3):178-183. DOI 1016/j.radi.2007.06.001

Figures

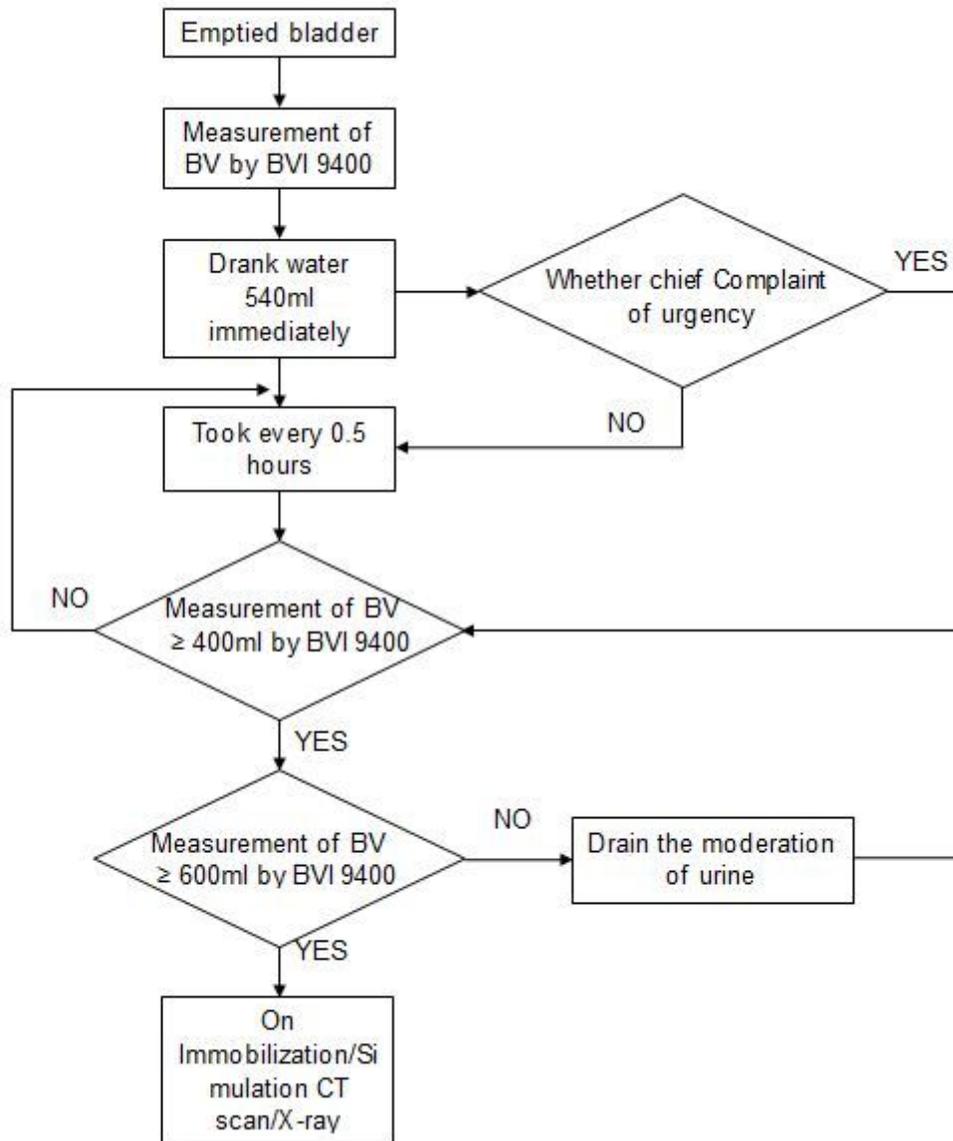


Figure 1

Flow chart of measuring BV in three steps before radiotherapy.

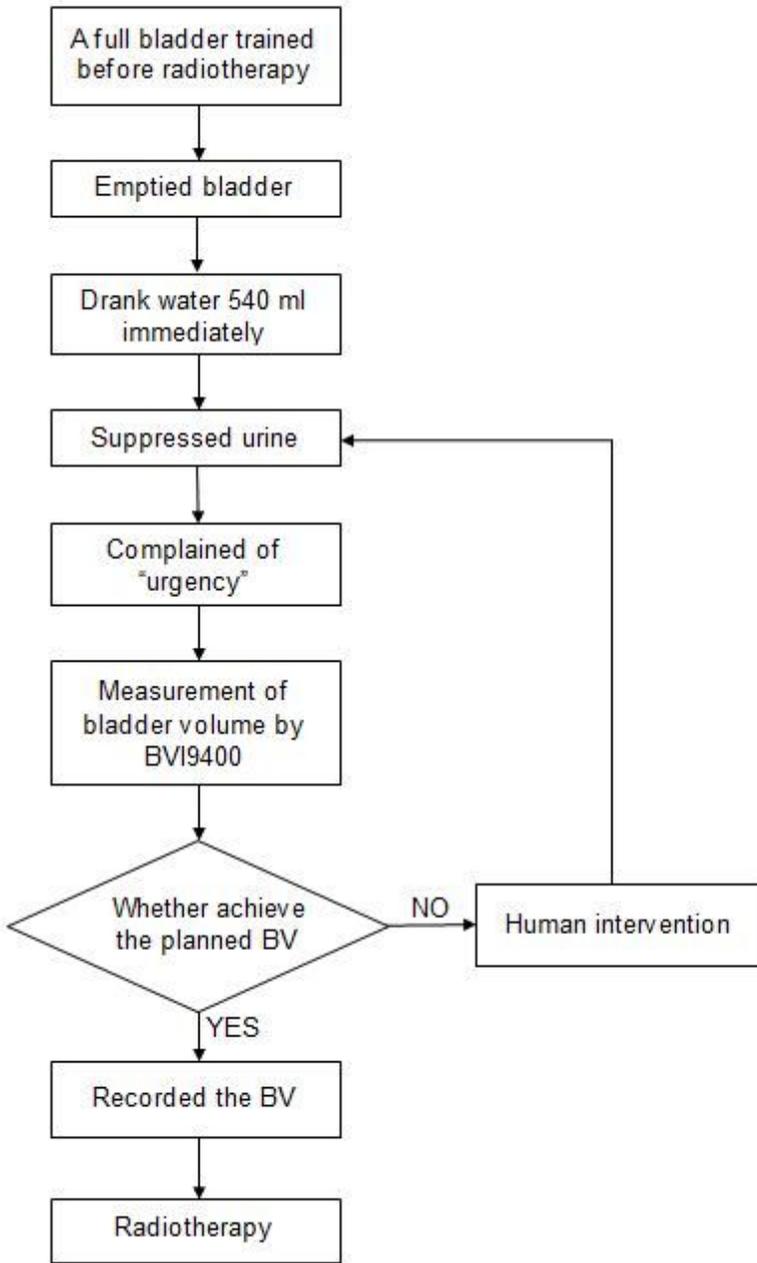


Figure 2

BV monitoring process during radiotherapy

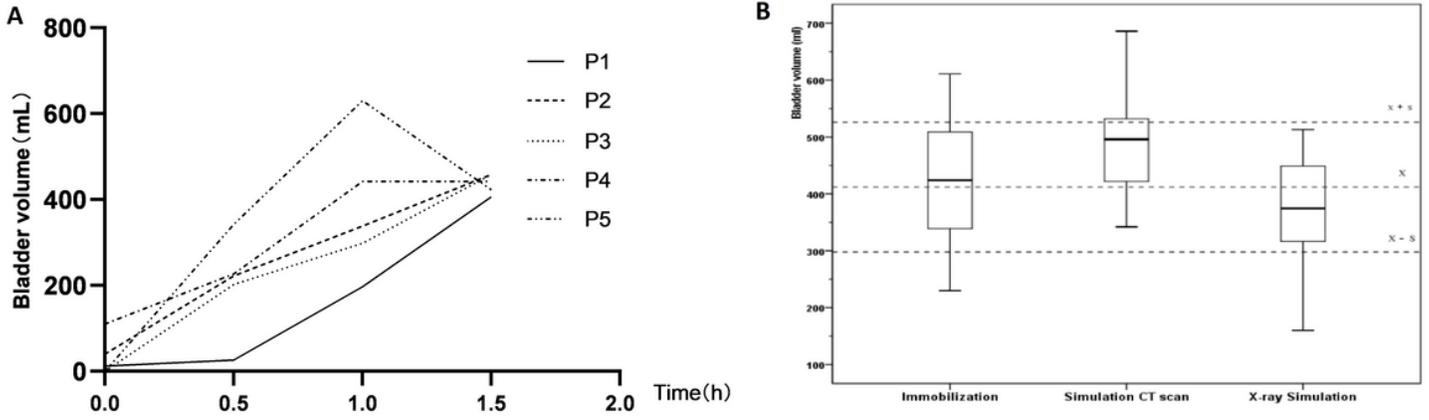


Figure 3

a). Trend of the chief complaint of urgency in 5 typical patients. b). Box-plot of actual volume (UT) distribution in 105 patients.

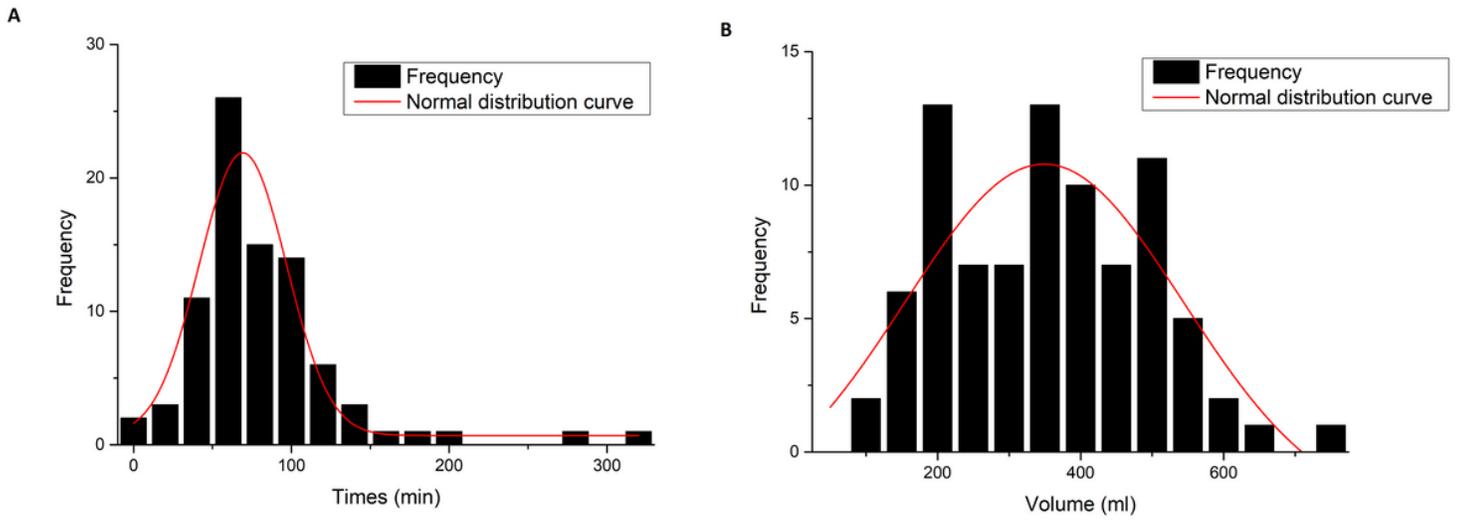


Figure 4

a). Time distribution about the chief complaint of urgency. b). Volume distribution of the chief complaint of urgency.

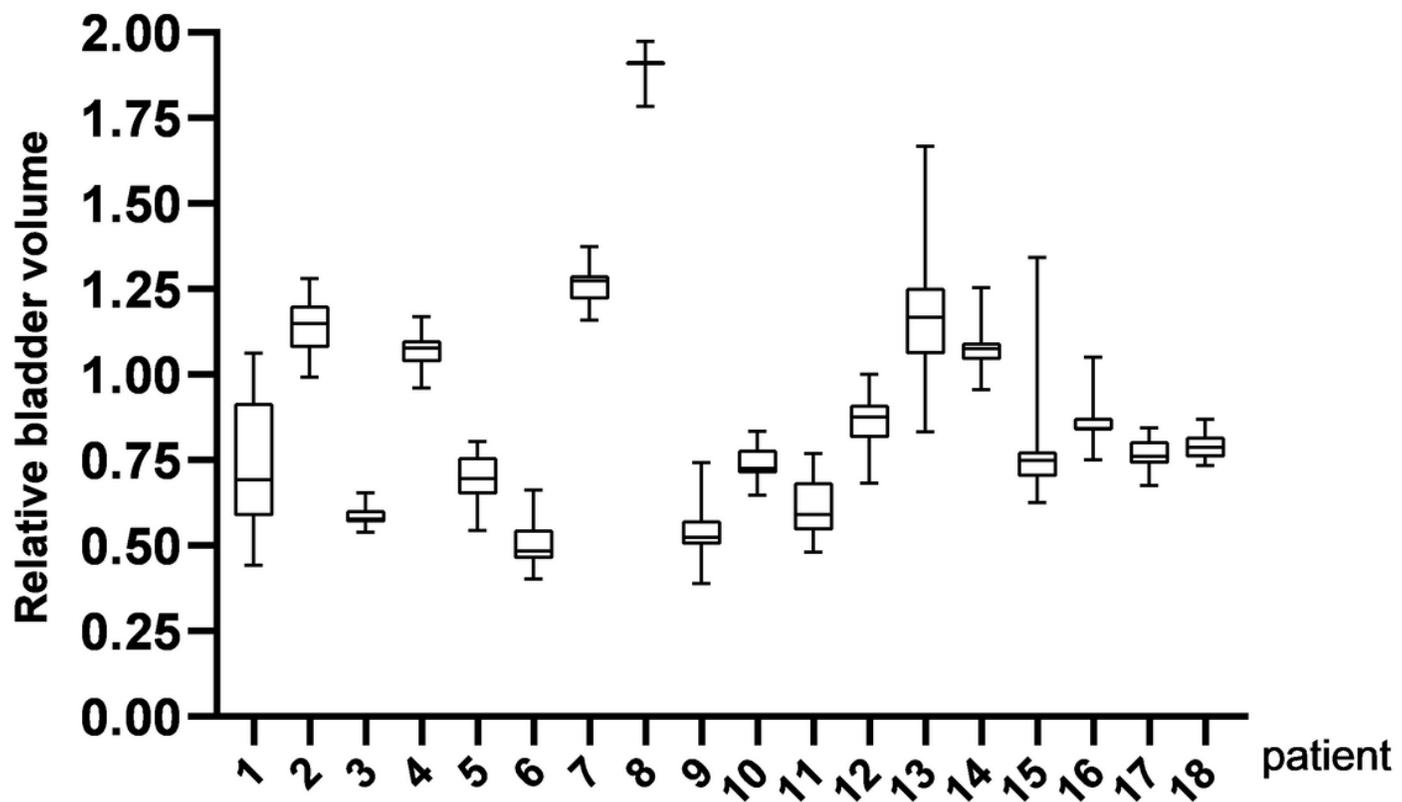


Figure 5

The RBV of 25 inter-fraction radiotherapy in 18 patients.

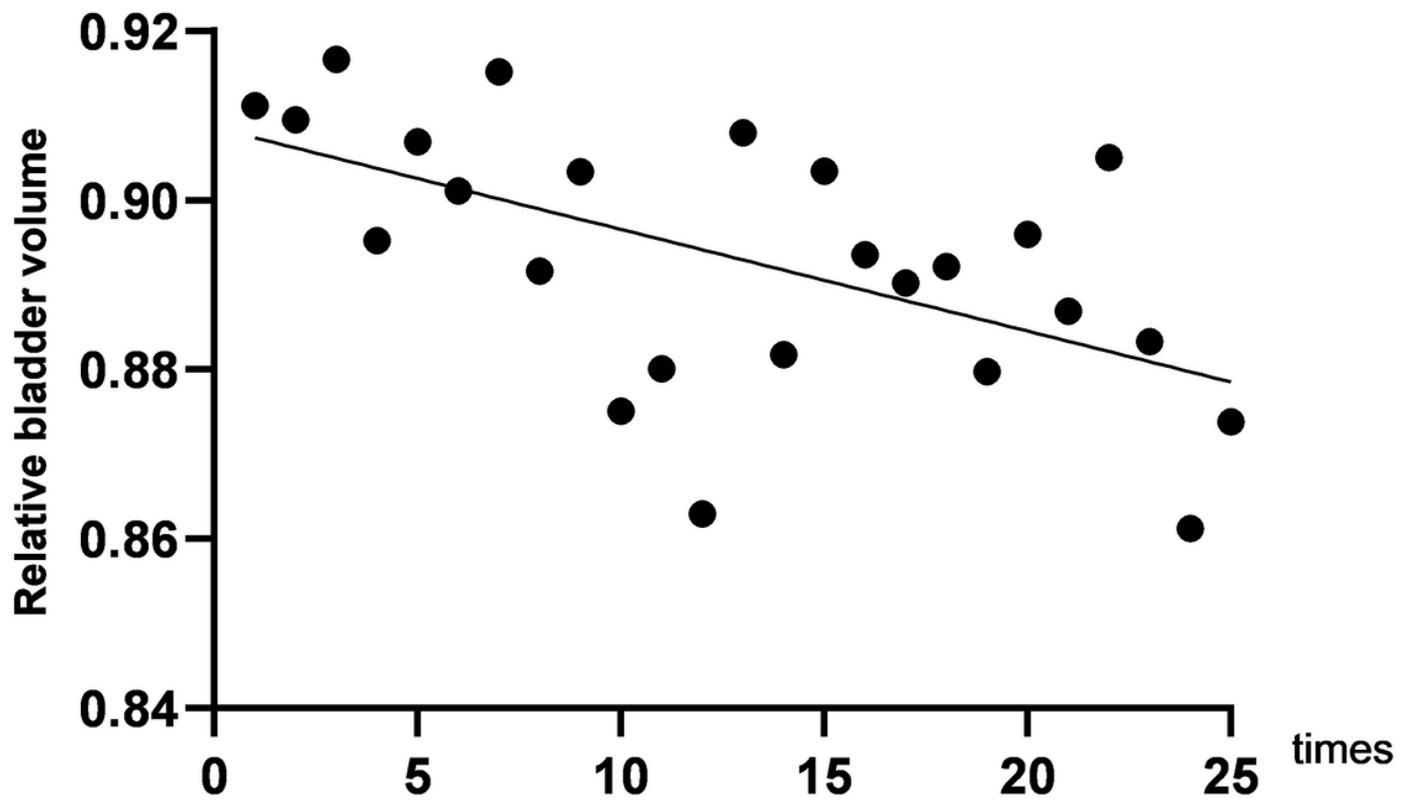


Figure 6

The RBV in 18 patients during inter-fraction radiotherapy. ($p=0.0028$, $r= -0.5726$; $Y=-0.001201 \cdot X+0.9086$)

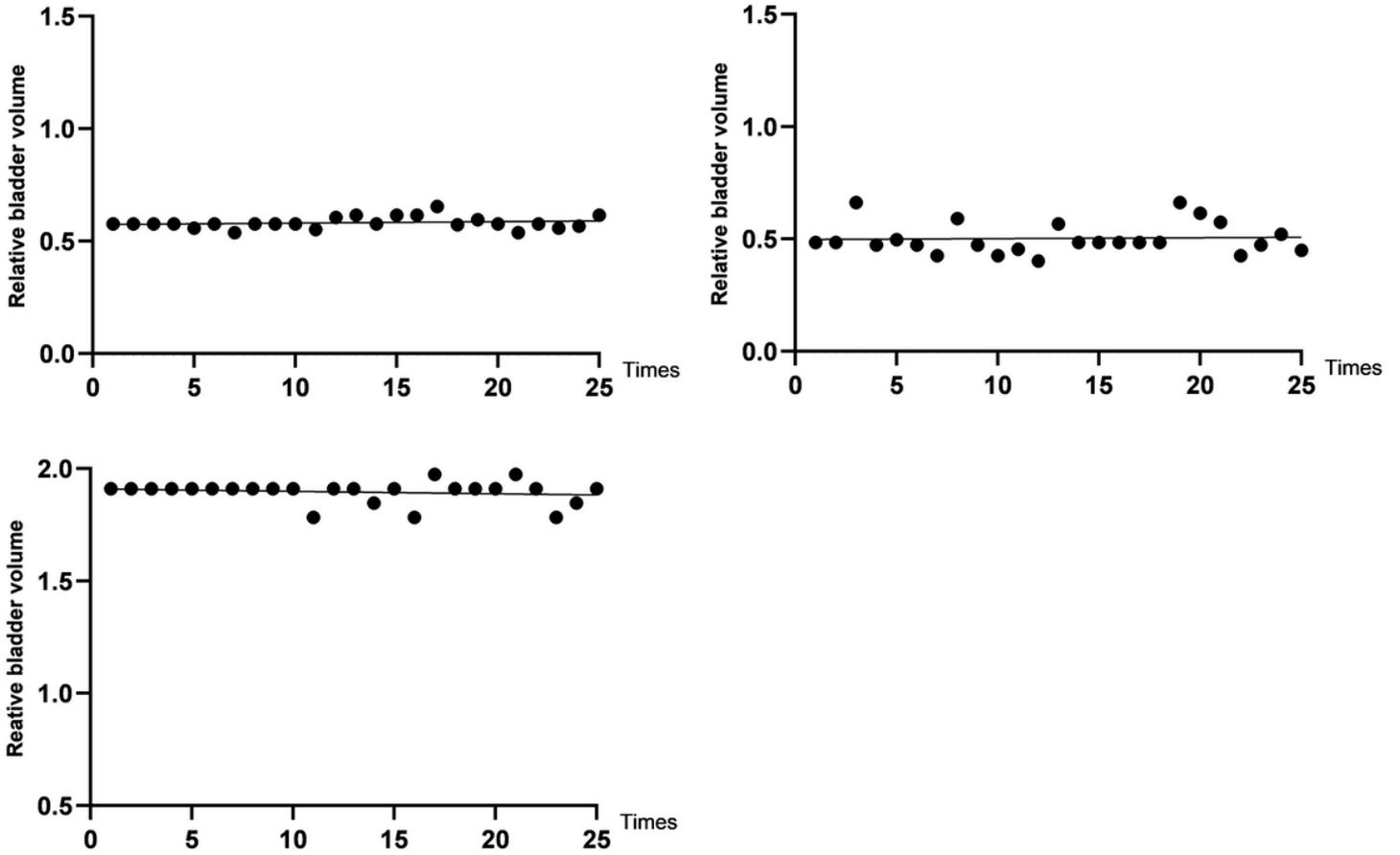


Figure 7

Three patients' BV failed

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