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Original Report

Efficacy of fiducial marker-based image-guided radiation therapy in prostate tomotherapy and potential dose coverage improvement using a patient positioning optimization method

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Abstract

Purpose: To evaluate the dose coverage efficacy of fiducial marker-based prostate tomotherapy and a positioning correction optimization technique for the improvement of suboptimal dose distributions.

Methods: Three gold fiducial markers were implanted in prostate glands for patients who were to receive prostate tomotherapy. TomoTherapy megavoltage computed tomographies (MVCTs; TomoTherapy, Madison, WI) were routinely acquired at treatment and were registered to corresponding planning CTs based on the markers to correct for interfractional positioning deviations using translational table movements. The prostate glands and seminal vesicles were delineated on the MVCTs acquired for 10 patients at different treatment fractions and the treatment dose coverage was computed with the marker-based correction taken into account. The treatment dose coverage was compared with the corresponding plan to evaluate the efficacy of the marker-based image-guided radiation therapy (IGRT) approach. Separately, a hill-climbing optimization algorithm was used to optimize the positioning by maximizing a dose-based objective function. During the optimization, the dose was constantly recomputed with the translational correction until an optimized dose coverage was reached. This optimized dose coverage was compared with the marker-based dose coverage to evaluate dosimetric improvement for treatments in which suboptimal dose distributions were observed after the marker-based corrections.

Results: Suboptimal dose coverage of prostate glands and seminal vesicles were observed in about 8 and 6 of a total 75 fractions, respectively, after the marker-based IGRT positioning corrections. Six of the 10 patients experienced 1 or more factions of suboptimal prostate gland coverage and 2 of the 10 patients experienced 1 or more fractions of suboptimal seminal vesicle dose coverage. Utilization of the proposed positioning correction optimization method led to satisfactory dose coverage of both prostate glands and seminal vesicles for all 10 patients.

Note: An online CME test for this article can be taken at http://astro.org/MOC.

Conflicts of interest: None.

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Conclusions: Given the planning target volume margin size specified in the current study, the fiducial marker-based IGRT approach may not be completely adequate to achieve desired dose coverage of the target volumes at every fraction. Due to relatively poor image quality of MVCTs, additional investigations may be required to confirm the finding. The proposed positioning correction optimization method is shown to effectively improve the observed suboptimal dose coverage of the target volumes.

Introduction

In prostate cancer radiotherapy, often both prostate gland and seminal vesicles need to be irradiated to certain desired dose levels to achieve tumor control. Intensity modulated radiation therapy (IMRT) has been shown to be effective in the management of localized prostate cancers.[1] As an entire course of prostate radiotherapy consists of multiple fractions, target motion and deformation between fractions may cause suboptimal dose coverage of the target volumes and compromise the effectiveness of IMRT.[2-4] To minimize the negative dosimetric impact of this inter-fractional motion, fiducial markers have been utilized in prostate radiation treatment.[5-14] The fiducial markers are implanted inside the prostate gland prior to radiation treatment, and are used to register treatment confirmation images with the corresponding planning images to correct for inter-fractional motion daily. Normally, inter-fractional motion is corrected by translationally adjusting patient treatment table position. Langen et al[15] investigated the precision of prostate patient treatment alignment for image registration methods based on fiducial markers, patient anatomy, and anatomy contours. The benchmark alignment used in the study was the center of mass of the fiducial markers. Langen et al concluded that the fiducial marker-based alignment was advantageous to reduce the inter-user variability of the image registration compared with the other 2 image registration approaches. The underlying assumption of the approach is that the fiducial markers are good surrogates of both prostate gland and seminal vesicles position and that these translational adjustments based on fiducial markers should lead to satisfactory dose coverage of both. However, this may not always be the case as the prostate gland and seminal vesicles (in particular) are non-rigid and their 3-dimensional (3D) geometric relationship relative to the fiducial markers may change from fraction to fraction. While the fiducial markers are implanted in the prostate itself, there is some distance from the markers to the seminal vesicles, which may add some additional error. van der Wielen et al[7] studied the residual geometric uncertainties of prostate glands and seminal vesicles after on-line fiducial marker-based corrections. They found that the fiducial marker-based correction reduced the prostate geometric uncertainty to a fairly low level while the residual uncertainties of the seminal vesicles were still considerable. This result might be expected given the location of the fiducial markers and the greater deformity of seminal vesicles. Gauthier et al[16] investigated the dosimetric impact of fiducial markers on the critical structures in prostate radiotherapy and concluded that use of the fiducial markers in prostate radiotherapy is an effective way to reduce normal tissue toxicities.

Although the use of fiducial markers has been proven to be effective in improving the treatment quality of prostate radiotherapy, there are still some uncertainties, such as residual geometric uncertainty errors and marker migration, associated with their use.[17,18] It has been postulated that these geometric uncertainties may still lead to undesirable dose coverage of target volumes (especially seminal vesicles), despite fiducial marker-based image-guided radiation therapy (IGRT) positioning correction. van Haaren et al investigated the dosimetric impact of marker-based position verification, using daily imaging and an off-line correction protocol, by calculating the delivered dose to the prostate, rectum, and bladder.[19] In that study, the volume and shape changes of the targets and other structures were not taken into account. It is fair to state that the extent of the clinical dosimetric impact introduced by these residual geometric uncertainties and the changes in structural size and shape remain largely unknown for prostate IMRT treatments and are subject to further investigation. Moreover, if there is significant dose distribution deviation after fiducial marker-based positioning correction, it would be desirable to develop a method to target volume dose coverage.

Tomotherapy, as one of the IMRT modalities, has been routinely utilized in our institution to treat prostate cancer, along with IGRT using fiducial markers. This study was designed to evaluate the efficacy of fiducial marker-based prostate tomotherapy in terms of target volume dose coverage, and to explore and evaluate a patient positioning correction optimization technique to improve any suboptimal dose distributions.

Methods and materials

Treatment planning, verification, and delivery

In our institution, 3 gold fiducial markers are routinely implanted inside the prostate gland prior to radiation

therapy. Most of our prostate patients undergo tomotherapy treatments and the plan objective is to deliver, simultaneously, 58 Gy to 95% of the seminal vesicles planning target volume (PTV) and 78 Gy to 95% of the prostate gland PTV in 39 fractions. The planning and treatment strategies are briefly described as follows. The simulation CT images are acquired on a GE LightSpeed 16-slice CT scanner (GE Healthcare, Waukesha, WI). On the planning CT images, the clinical target volumes (CTV) for prostate gland and proximal seminal vesicles are delineated by a radiation oncologist. The PTVs for the prostate and seminal vesicles are constructed by expanding the corresponding CTV by 8 mm relative to the CTV geometric center, except posteriorly where a 6-mm margin is added. The PTV for the seminal vesicles is expanded in such a way that it does not overlap with the prostate PTV. An IMRT plan was then designed with a TomoTherapy Hi-Art treatment planning system (TomoTherapy Inc, Madison, WI), and the treatment is delivered with a TomoTherapy Hi-Art treatment machine. At every fraction, a set of TomoTherapy 3D MVCT images are acquired to verify the target positioning. The verification is performed by registering the MVCT images with the corresponding planning CT images based on the location of the fiducial markers. The detected inter-fractional motion is corrected by translational treatment table adjustments. Radiation is delivered right after the positioning correction.

Evaluation of efficacy of the fiducial marker-based image-guided strategy

The study was conducted retrospectively. The target volumes (prostate gland and seminal vesicles) were delineated by the same experienced radiation oncologist on the TomoTherapy verification MVCT images for 10 patients at various points during their radiation course (number of fractions ranged from 6-8 per patient). These patients and fractions were selected because the MVCT images acquired at the treatments contained the entire prostate gland and seminal vesicles. Because the MVCTs were acquired at treatment to position patients by matching the fiducial markers, in many cases the MVCT images only covered small portions of patient anatomy that contained fiducial markers. Many of the MVCT images did not include the entire prostate gland and seminal vesicles and were not usable for the study. The treatment dose coverage was simulated by computing the dose coverage for the delineated target volumes based on the MVCT verification images after the fiducial marker-based registration, utilizing the original planned beam doses and parameters. The simulated treatment dose coverage was compared with the corresponding plan to evaluate the efficacy of the fiducial marker-based IGRT approach. The efficacy is defined as the effectiveness of using the fiducial marker-based approach to achieve the planned dose coverage. The efficacy is proportional to the success rate of treatment achieving target dose coverage equivalent to or better than the corresponding plan when the method is applied to positioning patients at treatment.

An optimization method to improve potentially suboptimal dose coverage at treatment

In addition to the target volume dose coverage calculations and evaluations based on the fiducial marker positioning, a Hill-Climbing optimization algorithm[20] was used to optimize the translational correction by maximizing a dose-based objective function. The optimization method is briefly described as follows.

The objective function is constructed as $f(\vec{r}_{Table}) = \sum_{i=1}^{n}\sum_{j=1}^{m} P_{i,j} V_{Di,j}(\vec{r}_{Table})$, where $V_{Di,j}(\vec{r}_{Table})$ is percent of the ith target volume that receives at least a dose value of Dj with a translational correction of $\vec{r}_{Table}$, n is number of the target volumes under consideration, m is number of constraints, and $P_{i,j}$ is the penalty factor of jth constraint for the ith target volume. The optimization is to search a value of $\vec{r}_{Table}$ so that $f(\vec{r}_{Table})$ reaches its maximum. During the optimization process, the dose coverage is constantly recomputed as the translation correction is adjusted until a maximal value of the objective function is reached. At that point, any change of the patient position would lead to a lower value of the objective function. This objective function was designed to achieve desired target volume dose coverage without taking normal organ sparing into consideration. In the current study, the objective function was constructed with the prostate gland and seminal vesicles delineated from the MVCT verification images, and lower dose limits of 58 and 78 Gy were applied to Dj for the seminal vesicles and prostate gland, respectively. The values of the penalty factors ranged from 1 to 10 and were selected based on the computed dose coverage after the fiducial marker-based correction; ie, a higher value of penalty factor would be used for a target volume if a worse coverage was observed.

The dose coverage derived upon completion of the optimized treatment translational correction was compared with that achieved using the fiducial marker-based table correction alone. In cases where the fiducial marker-based correction was suboptimal (ie, the corresponding target volume dose coverage was inferior to the corresponding plan), the effectiveness of the optimization was evaluated. The optimization method was considered effective if it improved the dose coverage over the marker-based method. For the cases where the dose coverage based on the maker positioning was equivalent or better to the plan, the optimization was considered unnecessary or not applicable (NA).

Table 1 Patient data information

Patients	No. of fractions in the study	Prostate			Seminal vesicles		
		Volume (plan, cc)	Mean volume on the MVCTs (relative to plan)	Volume $\sigma_{prostate}$ (relative to plan)	Volume (plan, cc)	Mean volume on the MVCTs (relative to plan)	Volume σ_{sv} (relative to plan)
RWJ 1	7	63	99.5%	6.3%	11.3	106.7%	10.9%
RWJ 2	5	59	87.7%	3.3%	18.4	91.3%	6.7%
RWJ 3	5	107	90.7%	3.4%	10.1	84.9%	1.9%
RWJ 4	7	32	93.9%	3.9%	5.5	104.8%	4.0%
RWJ 5	9	24	115.3%	9.9%	10.1	84.6%	5.2%
RWJ 6	9	59	98.0%	5.2%	8.5	99.4%	3.8%
RWJ 7	8	53	89.7%	3.4%	7.5	77.7%	14.8%
RWJ 8	7	81	91.5%	1.8%	8.9	95.4%	6.1%
RWJ 9	9	43	97.2%	4.8%	6.8	90.3%	15.5%
RWJ 10	9	29	96.0%	16.5%	3.1	128.4%	27.6%

MVCT, megavoltage computed tomography; RWJ, Robert Wood Johnson; σ, standard deviation.

Results

Patients

Seventy-five treatment fractions were investigated in the current study for 10 patients (Table 1). Number of treatment fractions per patient ranged from 5 to 9. The mean volumes of prostate gland and seminal vesicles delineated on the planning CT images were 55 cc (ranging from 24 to 107 cc) and 9 cc (ranging from 3 to 18 cc), respectively. Compared with the volumes on the planning CT images, the volumes of prostate gland and seminal vesicles delineated from the MV confirmation CT images were smaller for most of the patients and fractions; their mean values and standard deviations (over the available fractions and relative to the corresponding plans) were tabulated in Table 1 for each of the 10 patients. It is notable that the volumes of the delineated prostate glands were more consistent (smaller standard deviations) than for the seminal vesicles.

Efficacy of fiducial marker-based IGRT

Table 2 presents 3 important parameters of the dose coverage distributions of prostate gland and seminal vesicles over the investigated treatment fractions for the 10 patients. The 3 parameters are minimum, mean, and standard deviation values of D_{95} of the target volumes over the investigated fractions. The D_{95} was the least dose that 95% of the target volume received. The dose coverage

Table 2 Efficacy of fiducial marker-based treatments

Patients	Prostate				Seminal vesicles			
	Min D_{95} (Gy)	Mean D_{95} (Gy)	σ_{D95} (Gy)	Percent of the suboptimal fractions	Min D_{95} (Gy)	Mean D_{95} (Gy)	σ_{D95} (Gy)	Percent of the suboptimal fractions
RWJ 1	66	79	5.4	14%	28	55	11.9	14%
RWJ 2	82	82	0.2	0%	61	62	1.5	0%
RWJ 3	80	81	0.4	0%	60	62	2.4	0%
RWJ 4	68	78	5.3	29%	58	60	0.9	0%
RWJ 5	79	81	1.5	0%	61	62	2.2	0%
RWJ 6	48	71	11.9	22%	49	69	12.1	56%
RWJ 7	74	79	3.0	13%	59	66	5.1	0%
RWJ 8	58	78	8.9	14%	63	66	3.4	0%
RWJ 9	78	79	0.4	0%	59	64	6.0	0%
RWJ 10	74	79	2.0	11%	57	65	7.1	0%
Overall	48	78	6.1	11%	28	64	7.4	8%

D_{95}, least dose that 95% of the target volume received; Min, minimum; RWJ, Robert Wood Johnson; σ, standard deviation.

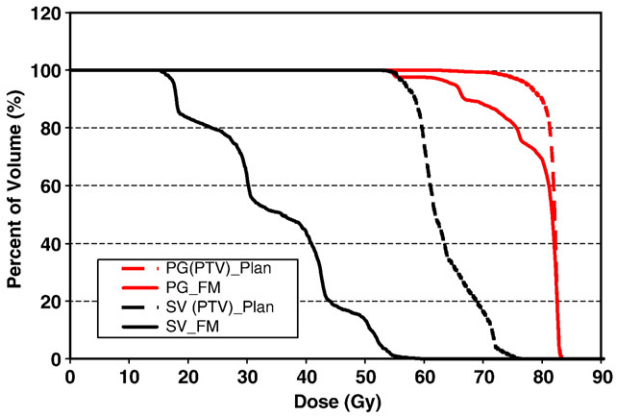

Figure 1 Comparison of plan dose coverage of prostate gland (PG) and seminal vesicles (SV) with that of the fiducial marker-based positioning (FM) at a fraction for patient Robert Wood Johnson 1 (RWJ1). The presented plan dose coverage is for the planning target volumes (PTVs) of the PG and SV.

was computed with the fiducial marker-based positioning correction taken into account. Of the 75 treatment fractions, 11% and 8% of the treatments delivered suboptimal dose coverage to prostate gland and seminal vesicles, respectively. Suboptimal dose coverage was defined as D_{95} (minimum dose to 95% of the volume) of a target volume less than 95% of the corresponding prescription dose in treatment; ie, D_{95} less than 74.1 Gy for the prostate gland and D_{95} less than 55.1 Gy for seminal vesicles in the current study. The minimum and mean D_{95} in this series were found to be 48 and 78 Gy for the prostate gland, and 28 and 64 Gy for seminal vesicles, respectively. Four patients did not have any suboptimal treatments of the prostate gland and another 4 patients had only 1 fraction of suboptimal treatment. Two other patients received suboptimal treatments of the prostate gland in approximately 25% of the fractions. On the other hand, 8 patients received desired treatment of seminal vesicles in all the fractions, 1 patient received 1 fraction of suboptimal treatment, and 1 patient received suboptimal treatment of seminal vesicles in more than 50% of the fractions.

Figure 1 displays the dose volume histograms of prostate gland and seminal vesicles computed for patient Robert Wood Johnson 1 (RWJ1) in the plan (dashed lines) and at a treatment fraction with the fiducial marker-based table correction taken into account. The plan dose-volume histograms in the figure were those of the PTVs of the prostate gland and seminal vesicles, respectively. It is evident that the fiducial marker-based IGRT strategy failed to provide adequate dose coverage to the target volumes and it was much worse than the desired (plan) for this fraction of treatment.

Apparently, given the margin sizes used in the plans, the fiducial marker-based IGRT approach did not fully account and correct for the inter-fractional motion at every single fraction of patient treatment.

Effectiveness of the proposed optimization method

Table 3 presents the implementation results of the proposed positioning correction optimization method on the treatment fractions in which the fiducial marker-based IGRT approach did not result in satisfactory dose coverage of the target volumes. In the table the effectiveness was defined as the percent of the suboptimal treatment fractions that were improved by the optimization method in terms of target volume dose coverage. In the cases where no suboptimal fractions were observed, the optimization was considered unnecessary and "NA" (not applicable) was entered. The implementation of the optimization method improved the dose coverage of the target volume, and led to the desired dose coverage

Table 3 Effectiveness of the proposed dose coverage improvement method

Patients	Prostate		Seminal vesicles	
	No. of suboptimal fractions after the optimization	Effectiveness	No. of suboptimal fractions after the optimization	Effectiveness
RWJ 1	0	100%	0	100%
RWJ 2	0	NA	0	NA
RWJ 3	0	NA	0	NA
RWJ 4	0	100%	0	NA
RWJ 5	0	NA	0	NA
RWJ 6	0	100%	0	100%
RWJ 7	0	100%	0	NA
RWJ 8	0	100%	0	NA
RWJ 9	0	NA	0	NA
RWJ 10	0	100%	0	NA

NA, not applicable; RWJ, Robert Wood Johnson.

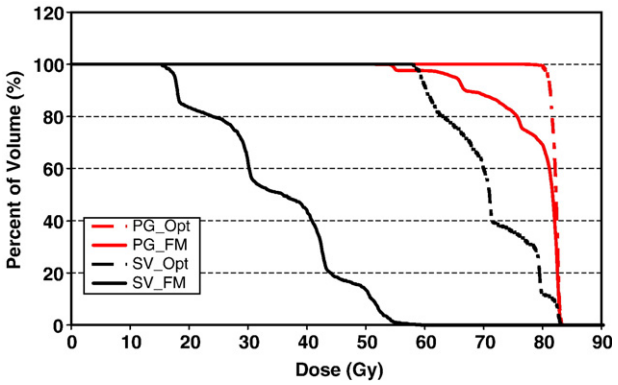

Figure 2 Comparison of dose coverage of prostate gland (PG) and seminal vesicles (SV) after the optimized table correction (Opt) with the fiducial marker-based positioning (FM) at the same fraction as presented in Fig 1 for patient Robert Wood Johnson 1 (RWJ1).

for all the presumed suboptimal treatment fractions, demonstrating that the proposed patient table positioning optimization method was effective and could be clinically useful.

Figure 2 displays the dose volume histograms of the target volumes derived from the implementation of the optimization method (dashed lines) and those based only on the marker-based correction for the same fraction of treatment as in Fig 1. It is clear that the utilization of the optimization method significantly improved the dose coverage for both prostate gland and seminal vesicles and the improvement was dramatic in this particular case.

Discussion

In conventional radiotherapy, the prescription dose is planned to cover the PTV, which is normally a volumetric expansion of the CTV. The expansion size (margin size) is estimated with the consideration of a few factors, including dosimetric accuracy, dose delivery machine accuracy, immobilization accuracy, imaging device accuracy, etc. The idea is to ensure (with a certain level of confidence) the prescription dose coverage of the CTV at treatments given the inevitable treatment uncertainties. To evaluate the quality of a treatment relative to its corresponding plan, dose coverage of the CTV during treatment should be computed and then compared with the dose coverage of the PTV in the plan (eg, Fig 1). Here, the dose coverage of the CTV during treatment (Table 2) was derived from the confirmation MVCT images acquired daily during radiation treatment.

In this study, the suboptimal dose coverage was defined as D_{95} of a target volume in treatment less than 95% of the corresponding prescription dose, although in almost all plans the D_{95} of the corresponding PTVs were no less than the corresponding prescription doses. The rationale behind the definition was the consideration of various uncertainties, especially the uncertainties originated from relatively poor image quality of the MVCT images. The relatively poor image quality made it quite challenging to precisely and accurately localize and delineate the target volumes on the MVCT images. The localization and delineation uncertainties could cause inaccurate evaluation of the dose coverage at treatment. We estimated that their overall dosimetric impact was about 5%. This quantitative value of 5% was estimated and derived by artificially expanding the delineated target volumes for 1-4 mm and comparing the dose coverage of the expanded volume with that of the non-expanded target volumes.

It is known that the MVCT images have inferior image quality to kV CT images in terms of soft tissue differentiation. It is almost certain that the relatively poor image quality of MVCT leads to inconsistent target volume delineation compared with the kV CT images and it may compromise the calculation accuracy of the target dose coverage, which may in turn have some impact on the results and conclusions of the study. Additional studies may need to be carried out to confirm the findings of the current study, especially in the efficacy of the fiducial marker-based IGRT in prostate radiation treatments in target volume dose coverage.

Although the proposed positioning correction optimization method improved the dose coverage of the target volumes in all the investigated cases, the practicality of its clinical use at this time is questionable. This optimization method relies on the delineated target volumes from the treatment verification 3D images. With the technologies currently available in clinic, it is challenging to complete the delineation quickly and reliably enough to make it useful in real time (in this study we had a radiation oncologist contour the volumes on the MVCT images). Furthermore, if the target volumes are not contoured quickly, they may be rendered useless by patient movement after image acquisition. Thus, the clinical utility of this optimization method will rely heavily on a fast and reliable automatic segmentation method.

Ideally, the doses to critical organs, such as the rectum and bladder, should be taken into consideration in the optimization process to avoid unacceptable normal tissue toxicities during radiation treatments. However, as this study was retrospective (most of the MVCT images did not contain adequate anatomic information of both rectum and bladder), it would be inaccurate to incorporate the critical organ doses in the cost function in the study. Additional studies may need to be designed prospectively to improve the optimization process to achieve optimal treatments in terms of not only adequate target volume dose coverage but also reduction of normal tissue toxicities.

Contrary to what otherwise is presumed, the rate of suboptimal dose coverage of seminal vesicles was lower

than that of the prostate gland in the investigated fiducial marker-based IGRT treatments. The reason is that, in the investigated treatment cases, simultaneous boost of the prostate gland was conducted along with the treatment of seminal vesicles. The prescription dose was D_{95} no less than 58 Gy to seminal vesicles and the simultaneous boost prescription dose to the PTV of prostate gland was D_{95} no less than 78 Gy. Because seminal vesicles are adjacent to the prostate gland the higher dose cloud covered portions of the seminal vesicles. Although the fiducial markers are no better surrogates of seminal vesicles than the prostate gland, and seminal vesicles may exhibit greater deformation, the combination of lower prescription dose and their proximity to the higher dose cloud reduced the rate of suboptimal dose coverage of the seminal vesicles.

The results of this study are also highly dependent on the PTV margin sizes used to construct the PTVs from the corresponding CTVs. It is intuitive that fewer fractions of treatment will deliver suboptimal dose coverage if a larger margin size is used in a plan. With the results in the current study, it is still difficult to conclude the magnitude of the additional margin that is required to ensure adequate dose coverage of the target volumes in prostate cancer treatments. Additional carefully designed study is needed to draw definitive conclusions on the subject.

No definite patterns were observed for the suboptimal fractions except for that the suboptimal fractions tended to happen to certain patients, especially for the dose coverage of seminal vesicles. It is postulated that the target volume changes relative to the fiducial markers may be very patient dependent; therefore, patient-specific margin size may need to be applied either in the plan or be determined using an adaptive radiotherapy approach.

Conclusions

Given the PTV margin size specified in the current study, the fiducial marker-based IGRT approach may not be completely adequate to achieve desired dose coverage of the target volumes for every treatment fraction. Due to relatively poor image quality of MVCTs, additional investigations may be required to confirm the finding. The proposed positioning correction optimization method is shown to be effective in improving the observed suboptimal dose coverage of the target volumes.

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