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# Adaptive prostate IGRT combining online re-optimization and re-positioning: a feasibility study

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**Abstract**

In prostate radiation therapy, inter-fractional organ motion/deformation has posed significant challenges on reliable daily dose delivery. To correct for this issue, off-line re-optimization and online re-positioning have been used clinically. In this paper, we propose an adaptive images guided radiation therapy (AIGRT) scheme that combines these two correction methods in an anatomy-driven fashion. The AIGRT process first tries to find a best plan for the daily target from a plan pool, which consists of the original CT plan and all previous re-optimized plans. If successful, the selected plan is used for daily treatment with translational shifts. Otherwise, the AIGRT invokes the re-optimization process of the CT plan for the anatomy of the day, which is afterward added to the plan pool as a candidate for future fractions. The AIGRT scheme is evaluated by comparisons with daily re-optimization and online re-positioning techniques based on daily target coverage, organs at risk (OAR) sparing and implementation efficiency. Simulated treatment courses for 18 patients with re-optimization alone, re-positioning alone and AIGRT shows that AIGRT offers reliable daily target coverage that is highly comparable to daily re-optimization and significantly improves from re-positioning. AIGRT is also seen to provide improved OAR sparing compared to re-positioning. Apart from dosimetric benefits, AIGRT in addition offers an efficient scheme to integrate re-optimization to current re-positioning-based IGRT workflow.

(Some figures in this article are in colour only in the electronic version)

## 1. Introduction

In prostate radiation therapy, inter-fractional variations of the target volume and position due to the change of fillings in nearby organs, i.e. the bladder and the rectum, make delivering

  

uniform dose to the target challenging on a day-to-day basis. The technical development and clinical implementation of image-guided radiation therapy (IGRT) for prostate cancer has enabled online reviewing of the daily anatomy, and consequently has created increasing demands for more conformal target coverage as well as better organ/tissue sparing of the daily treatment. Many of the current IGRT techniques focus on target coverage, such as daily match of PTV volumes using on-board cone beam CT (Olivera *et al* 2000, Wu *et al* 2006, Court *et al* 2006, Feng *et al* 2006). To further balance the PTV coverage and organs at risk (OAR) sparing, adaptive radiation therapy for prostate cancer treatment was introduced by several groups to re-optimize initial plan based on daily image sets of the first few fractions in an off-line fashion (Yan *et al* 1997, 2000, Wu *et al* 2002, 2004, Birkner *et al* 2003, Rehbinder *et al* 2004, de la Zerda *et al* 2007, Ghilezan *et al* 2010, Yan 2010) due to the time constraints of the re-planning process. Online re-optimization and adaptation approaches, recently proposed by several research groups (Court *et al* 2005, 2006, Mohan *et al* 2005, Feng *et al* 2006, Song *et al* 2007, de la Zerda *et al* 2007, Wu *et al* 2008, Fu *et al* 2009, Mestrovic *et al* 2009, Ahunbay *et al* 2010), provide high-quality daily treatment by implementing fast re-optimization and/or fast MLC aperture modification to adapt treatment plans based on daily CT or CBCT image. However, extra clinical work, such as quality assurance (QA) effort, and plan approval are required for the modified plans, which adds cost of time and machine resources to the clinical implementation. Therefore in current clinical practice, patient re-positioning based on soft-tissue matching is still the most widely used technique to account for inter-fractional patient anatomy variation, due to its high efficiency. Lei and Wu (2010) investigated a hybrid strategy of off-line re-planning and online image guidance using patient geometrical information and analyzed its benefit for margin reduction. However, the dosimetric benefits of such strategy are yet to be investigated, and the efficiency of an online implementation is also of interest as it maximizes the benefits of such a strategy.

The hybrid scheme for adaptive images guided radiation therapy (*AIGRT*), proposed and evaluated in this paper, integrates the high-quality re-optimization and the high-efficiency re-positioning techniques. The aim is to provide highly conformal daily target coverage and minimize OAR sparing with high efficiency for maintaining the clinical patient flow.

## 2. Methods and materials

### *2.1. Original CT plan*

Data from 18 prostate cancer patients treated at Duke University Medical Center, Durham, NC, USA, were retrospectively studied. For each patient, a planning CT image set was acquired using a CT simulator (Lightspeed, GE Healthcare Technologies, Waukesha, WI) with 1 mm in-plane resolution and 3 mm slice thickness. Structures of interest (SOIs) were the clinical target volumes (CTV, including the prostate and the seminal vesicles) and organs at risk (OARs, including the bladder and the rectum). Femoral heads were also assigned as OARs during original planning but not evaluated in this study. A uniform 5 mm margin was used to construct the PTV from the CTV.

The initial IMRT plan, 'original CT', was optimized with the treatment planning system (Eclipse, Varian Medical System, Palo Alto, CA), using seven co-planar 15 MV beams following the clinical conventions for prostate IMRT treatment planning at our institution. The beam angles are 25°, 75°, 130°, 180°, 230°, 285° and 335° for all patients. The primary dose constraints start from the adopted Radiation Therapy Oncology Group (RTOG) protocols based on 76 Gy target prescription dose (Rx) over 38 fractions (Pollack *et al* 2006). For this feasibility study, the same prescription dose was used for the entire CTV, i.e. prostate

and seminal vesicles (SV). These constraints can easily be met using an IMRT planning technique. More stringent secondary dose constraints were set according to institutional template constraints to achieve as much sparing as possible. The dosimetric constraints to the bladder and the rectum were 70, 62 and 39 Gy to <20%, 30% and 50% volumes, and 70, 56 and 39 Gy to <20%, 30% and 50% volumes, respectively. A priority weight for each constraint was also assigned to gain a better control in balancing target coverage and OAR sparing. A trial-and-error scheme was used to manually adjust these constraints and the associated weights during the optimization process. The plans are normalized so that 100% prescription dose covers at least 98% of PTV.

### *2.2. Daily treatment simulation*

In addition to the original CT data, ten daily CBCT images for all 18 patients were acquired using an on-board imaging system (OBI, Varian Medical Systems, Inc., Palo Alto, CA) with the patient in the treatment position, prior to any IGRT corrections. The images were acquired everyday during the first week, and once a week for the rest of the treatment course. These daily images were used to simulate ten treatment fractions for all online IGRT techniques. The CBCT images were reconstructed with a voxel size of 1 mm in-plane and 2.5 mm slice thickness. The daily SOIs were delineated by one attending physician, so the contouring was consistent with original IMRT planning. A previous study (Yan *et al* 2000) has shown that for prostate IMRT, sufficient CTV coverage can be achieved through the entire treatment by setting the target to the bounding volume constructed based on daily CT images during the first 2 weeks of treatment, i.e. ten fractions. This implies that ten daily CTV shape/positions can represent most the treatment scenarios through the course of the treatment. Based on this result, we assume that for subsequent treatment fractions, the CTV coverage is very likely to follow the results of this study based on the simulated ten fraction treatment courses.

### *2.3. Three simulated IGRT techniques*

*2.3.1. Soft-tissue-based IGRT.* For each CBCT, the current clinical IGRT technique based on the soft tissue target alignment was applied and the delivered plan was named as *Soft-Plan* plan. For most treatment couches, the current clinical IGRT protocol only performs translational corrections. The matching was performed via finding the translations that yielded the maximal overlap between the target (PTV) on CT and the corresponding CTV on the CBCT images, in order to maximize the likelihood of daily CTV being covered by the dose distribution optimized to conform the PTV on CT. Delivered dose was calculated on the CBCT images within the Eclipse treatment planning system.

*2.3.2. Re-optimization-based IGRT.* The IMRT re-optimization technique was also applied to all CBCT images, generating another set of delivered plans (*Re-Plan* plans). The *Re-Plan* plans were generated using daily SOIs contoured on the CBCT images by a single physician. The 5 mm PTV margin was also used in the re-optimization process (Thongphiew *et al* 2009). The re-optimization-based IGRT technique represents the most optimal coverage for the daily CBCT anatomy.

*2.3.3. Adaptive IGRT (AIGRT).* The concept of the *AIGRT* explores the advantages of the two IGRT techniques: re-optimization (re-planning) and patient re-positioning, in order to account for the daily anatomical variations at different levels of complexity and utilize IGRT to its optimal efficiency. By applying the re-planning technique through the entire treatment course,

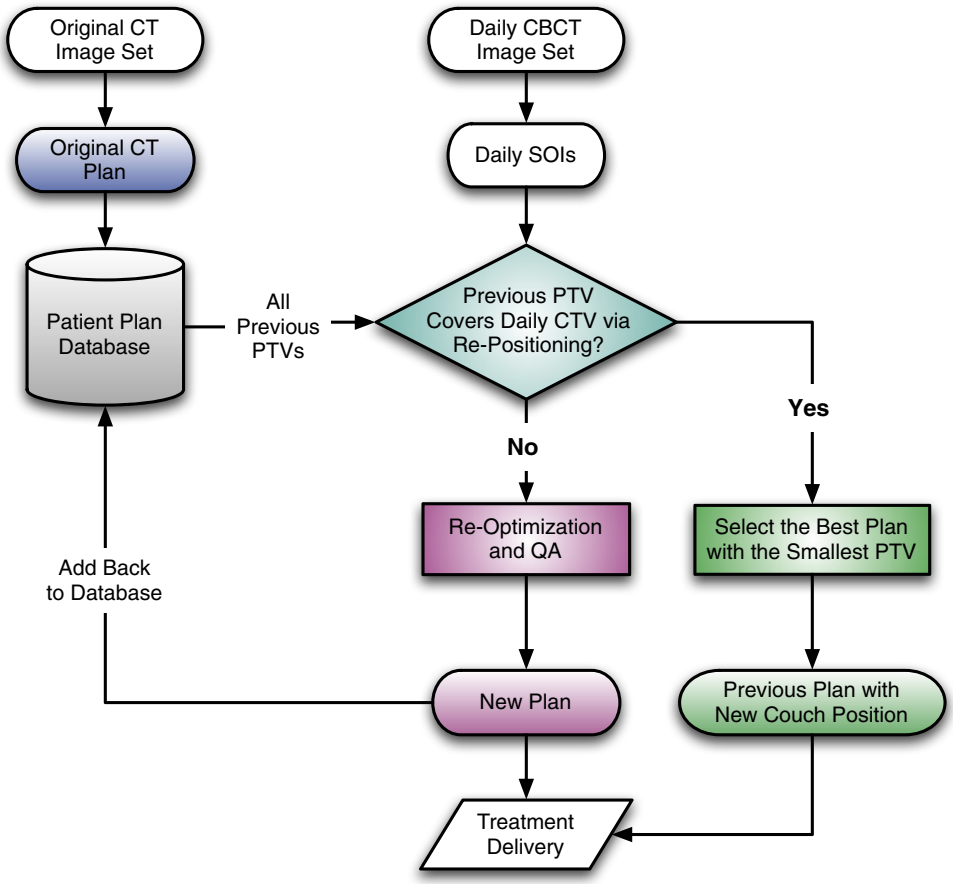


**Figure 1.** The scheme of the *AIGRT* technique.

the best treatment plan quality is expected since the plan is customized to maximally match the daily anatomical structures. On the other hand, the patient re-positioning technique is the existing IGRT technique that is intuitive and effective for simple target variations. Therefore in the *AIGRT* implementation the selection of the re-positioning versus re-optimization for each fraction is anatomy driven.

Figure 1 illustrates the *AIGRT* technique. On the treatment day, the CTV is defined on the CBCT. Instead of using only Original CT plan to treat the patient, the daily CTV will be compared with PTV(s) from the plan(s) in the patient-specific database. The database consists of the Original CT plan and previously re-optimized plans if exist. If the daily motion/deformation of the target volume can be accounted geometrically by any plan(s) in the database, the best-matching plan will be selected using our automatic algorithm as detailed in the next paragraph and the couch shift will be applied to the plan to treat the patient for that fraction. If none of the plans in the database satisfies the coverage criteria, a re-optimized new plan will be created for that treatment fraction and added to the patient plan database as a candidate for future fractions.

Selection between re-positioning and re-optimization techniques in the *AIGRT* is achieved by an automatic plan selection algorithm based on the patient's daily structures of interest. Let the plan database contain $N$ previous treatment plans (original CT and re-optimized plans)

$P_i$; $i = 1, 2, \ldots, N$. Each plan dataset contains the beam information (e.g. beam angles and fluence maps) and PTV structure $\mathrm{PTV}_i$ according to plan $P_i$. The daily CTV is aligned with all $\mathrm{PTV}_i$. The plan $P_i$ that provides sufficient coverage is the plan such that all voxels $j$ in the CTV are in the $\mathrm{PTV}_i$ of the plan $P_i$:

$$\mathrm{CTV}_j \subseteq T_i(\mathrm{PTV}_{i,j})$$

where $T_i(\mathrm{PTV}_{i,j})$ represents the transformation (or re-positioning) of the PTV voxel $j$ of the $\mathrm{PTV}_i$. In order to spare the dose to the OARs, the overlapping region of the $\mathrm{PTV}_i$ and the daily OARs needs to be minimized, which can be done by comparing the PTV–OAR overlapped region. Alternatively, this can be done by selecting the plan $P_{i^*}$ with the smallest $\mathrm{PTV}_i$ that provides the complete coverage for the daily CTV:

$$i^* = \arg\min_i \left( \frac{\mathrm{PTV}_i}{\mathrm{CTV}} \right).$$

The delivered plans, from re-positioning or from re-optimization, are named as *AIGRT* plans.

### *2.4. Treatment plan comparison*

In order to assess the efficacy of our *AIGRT* concept, delivered plans are compared based on the IGRT techniques applied: (1) soft-tissue-based re-positioning of all fractions (referred to as the *Soft-Plan* technique); (2) re-optimization of all fractions (referred to as the *Re-Plan* technique); and (3) the *AIGRT* technique. The dose distributions and DVHs of the daily CTV, bladder, and rectum for these techniques were calculated and compared.

The target coverage evaluations are based on directly comparing the minimal dose to the hottest 99% target volume (D99) among the three techniques. Such comparisons are made for CTV (prostate and SV) and for SV alone to assess the performance of these three techniques for different parts of the target. To evaluate dose delivered to the OARs, volumes that receive 100% prescription dose (V100%) and 65% prescription dose (V65%) are calculated for the bladder and the rectum. Deviation from V100%/V65% of the daily re-optimized plan (*Re-Plan* plan) is chosen as the evaluation parameter to represent the performance of a plan in achieving OAR sparing for daily anatomy, against the *Re-Plan* plans which are the most-conformal to daily anatomy. The histogram of such deviations was generated for comparison.

A recently published multi-institution study by Michalski *et al* has shown that the volumes of rectum receiving 70 Gy (V70Gy) reported from multiple centers converge at about 20%, indicating that V70Gy at 20% is the likely threshold for late rectal toxicity (Michalski *et al* 2010). Therefore in this paper, the V70Gy of rectum is specifically compared among the three techniques to evaluate the performance as an index of rectal toxicity. Since our original CT plan was based on a prescription dose of 76 Gy with 2 Gy per fraction, 70 Gy translates into 92% prescription dose, which is used to calculate V70Gy in plan DVHs.

The OARs' V100%/V65%/V70Gy comparison is performed by calculating the difference between the daily V100%/V65%/V70Gy at evaluation, either from *Soft-Plan* or *AIGRT*, and the *gold standard* values from the daily *Re-Plan* for that particular fraction. The differences of the total 180 cases are then binned into histograms, which are compared between *Soft-Plan* and *AIGRT*. By always setting the reference at the optimal V100%/V65%/V70Gy for the particular daily anatomy at evaluation, the influence by the daily variance of OARs' shapes and position is removed.

For a particular fraction of treatment, if our *AIGRT* algorithm does not select re-positioning technique, it suggests that no plan in the patient-specific plan pool is capable of providing satisfactory coverage for the daily target volume, and plan re-optimization is needed. The re-optimization produces the most conformal daily plans; however, it requires additional efforts,

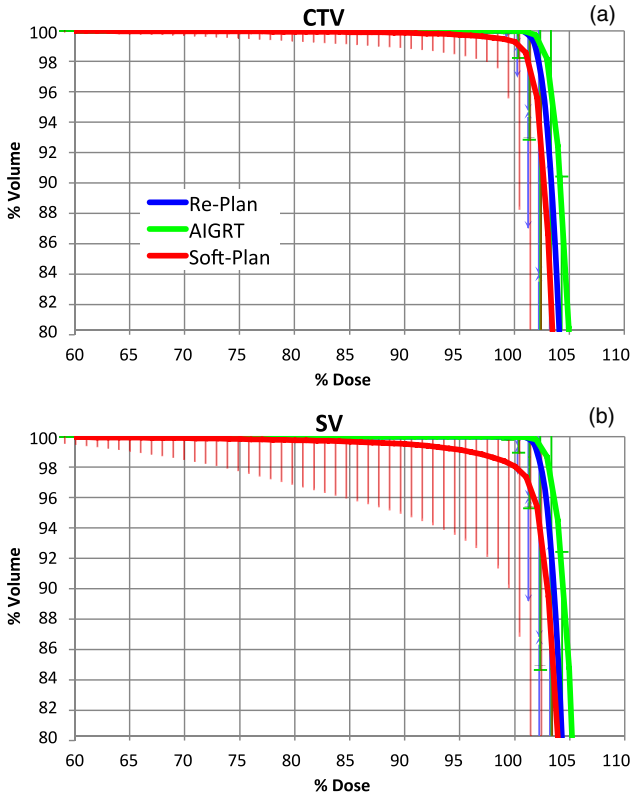


**Figure 2.** Mean DVHs and standard deviation of CTV (a) and SV (b) of all 180 plans. The red bar, blue bar with arrow and green bar with flat cap show the standard deviation of *Soft-Plan*, *Re-Plan* and *AIGRT* DVHs, respectively.

e.g. quality assurance and plan approval, which add costs to the clinical flow. On the other hand, re-using previously delivered plans will have minimal impact on the current clinical flow and is therefore preferred in terms of efficiency. *AIGRT* improves the efficiency of plan adaptation by re-using existing plans and reducing the number of fractions that would otherwise require re-optimization to achieve conformal daily treatment. The effectiveness of *AIGRT* on improving efficiency is evaluated by comparing the number of fractions requiring re-optimization to the total number of fractions requiring adaptation (re-positioning or re-planning). If *AIGRT* is able to reduce the frequency of re-optimization in the total number of adapted fractions, implementing *AIGRT* is beneficial in terms of efficiency.

## 3. Results and discussion

### *3.1. CTV coverage*

Figure 2 shows the comparison between mean target DVHs of all 180 plans with standard deviation for the three techniques. Only *Soft-Plan* is observed to have underdosed the CTV and SV region. Quantitative analyses are presented below.

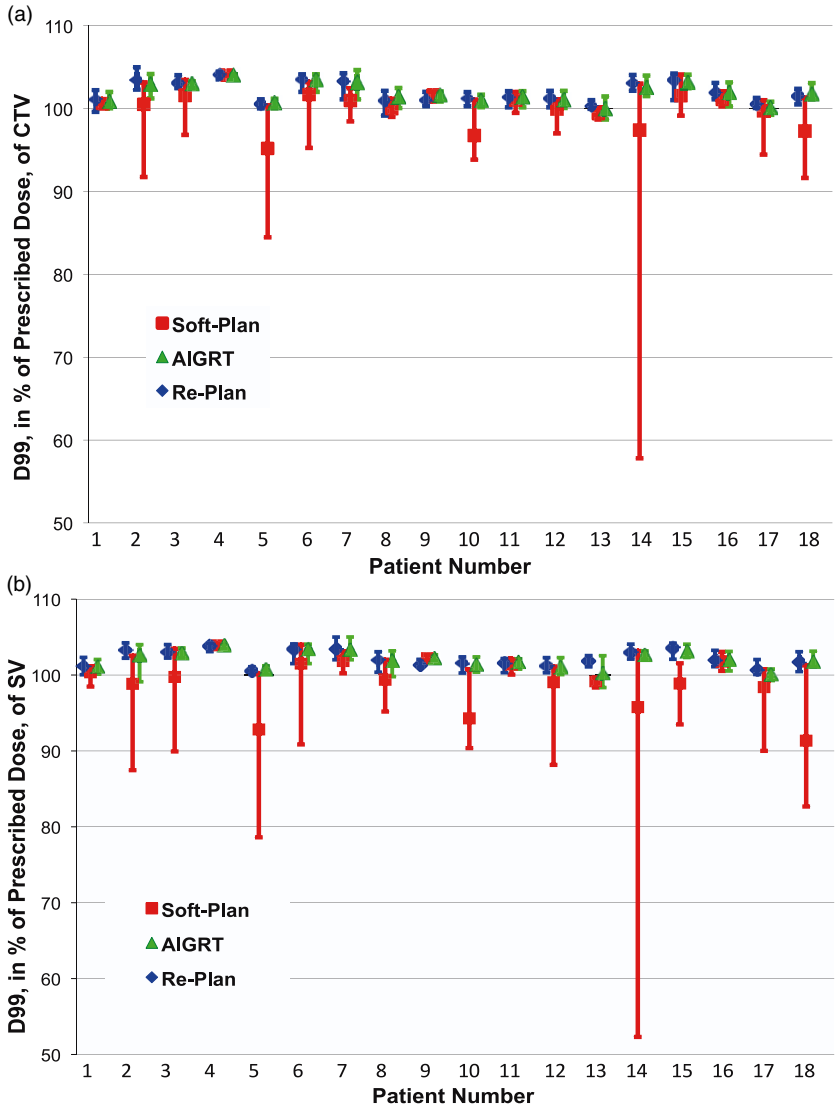


**Figure 3.** D99 of CTV (a) and SV (b) plotted for 18 patients. Markers show the mean value of D99s of all fractions for each patient; bars show the range of D99 for each individual patient.

The mean and range of the daily D99 to the CTV of each patient are plotted in figure 3(a). The ranges of 18 patients' mean D99 are (100.3–104.1%), (95.2–104.1%) and (100.0–104.1%) for the *Re-Plan* plans, the *Soft-Plan* plans and the *AIGRT* plans, respectively. For the total 180 plans, the ranges of daily D99 of all patients/fractions are (99.6–105.1%), (57.8–104.1%) and (98.7–104.7%) for the *Re-Plan* plans, the *Soft-Plan* plans and the *AIGRT* plans, respectively. The smaller ranges of daily D99 of *AIGRT* plans demonstrate highly uniform CTV coverage throughout the treatment fractions for all patients. The consistency of uniform CTV coverage of *AIGRT* plans is comparable to that of the *Re-Plan* technique, i.e. the gold standard. However,

**Table 1.** Number of plans with D99 < 98% prescription dose of CTV and SV.

| Technique | *Soft-Plan* | *Re-Plan* | *AIGRT* |
|---|---|---|---|
| Total number of plans | 180 | 180 | 180 |
| Number of plans with D99 < 98% for CTV | 25 | 0 | 0 |
| Number of plans with D99 < 98% for SV | 44 | 0 | 0 |

in *Soft-Plan* plans, large variations in daily CTV dose, i.e. CTV underdosage, is seen for some patients.

In addition, D99 of SV was calculated separately to assess dosimetric coverage of this particular target region. As shown in figure 3(b), the pattern of D99 variation is similar between CTV and SV for each patient, and the ranges of 18 patients' mean D99s are *Re-Plan* (100.6–103.9%), *Soft-Plan* (91.4–103.9%) and *AIGRT* (100.1–103.9%). For the total 180 plans, the ranges of daily D99 of all patients/fractions are *Re-Plan* (100.0–105.0%), *Soft-Plan* (52.31–104.1%) and *AIGRT* (98.3–105.0%), respectively. Similar to the CTV coverage results, D99 of SV reveals that *AIGRT* and *Re-Plan* are able to delivery uniform dose to the SV throughout the entire treatment, while *Soft-Plan* frequently fails to do so.

Statistics in table 1 on D99 for CTV support the indication that *AIGRT* provides reliable target coverage (D99 $\geqslant$ 98% prescription) for all patients, as does *Re-Plan*. In contrast, *Soft-Plan* plans are prone to target underdosage for both CTV and SV. Table 1 shows the number of plans fails to provide sufficient coverage, i.e. D99 < 98% prescription dose, for the three techniques. *Soft-Plan* has 25 and 44 out of 180 plans with D99 < 98% for CTV and SV respectively, whereas no plan with insufficient coverage to CTV or SV was seen using *Re-Plan* or *AIGRT*.

For the 18 patients in this study, SVs are often under-dosed with current soft-tissue matching technology, due to their displacement caused by bladder and rectum volume changes. As shown in table 1, 44 out of 180 *Soft-Plan* plans have D99 < 98% prescription dose when SV is evaluated separately, compared to 25 out of 180 if the entire CTV (prostate + SV) is evaluated. This result indicates that the SV part of the CTV is prone to more frequent under-dosage in *Soft-Plan* plans. With the *AIGRT* technique, uniform daily coverage to the prostate and the SV are achieved. Figure 4 shows an example of significant CTV shape change due to displaced SV. *Soft-Plan* fails to provide coverage for the upper part of daily CTV, i.e. SV region, whereas *AIGRT* selects a previous delivered plan that sufficiently covers the daily CTV, although its rectum sparing is slightly inferior compared to *Re-Plan*.

### *3.2. OAR sparing*

Figure 5 shows the mean OAR DVHs of all 180 plans for three three techniques. *AIGRT* has shown to have lower mean DVH and smaller standard deviation compared to *Soft-Plan,* for both organs. Quantitative analyses are presented below.

Table 2 shows the averages and ranges of V100%/V65% of the bladder and the rectum, as well as the relative/absolute V70Gy volumes for the rectum. On average, *AIGRT* plans feature smaller high dose volume (V100%) and median dose volume (V65%) to the bladder and the rectum, in comparison with soft-tissue matching, as most of the highest values highlighted in red are found with *Soft-Plan* plans. Similar to V100%/V65%, the average rectum V70Gy are lower for *AIGRT* plans than for *Soft-Plan* plans, by 2.8% or 3.1 cc. The relative V70Gy for *Re-Plan* plans and *AIGRT* plans are 15.3% and 19.1%, respectively, whereas for *Soft-Plan* plans, the average is 21.9%, indicating that *Soft-Plan* has slightly higher V70Gy compared to

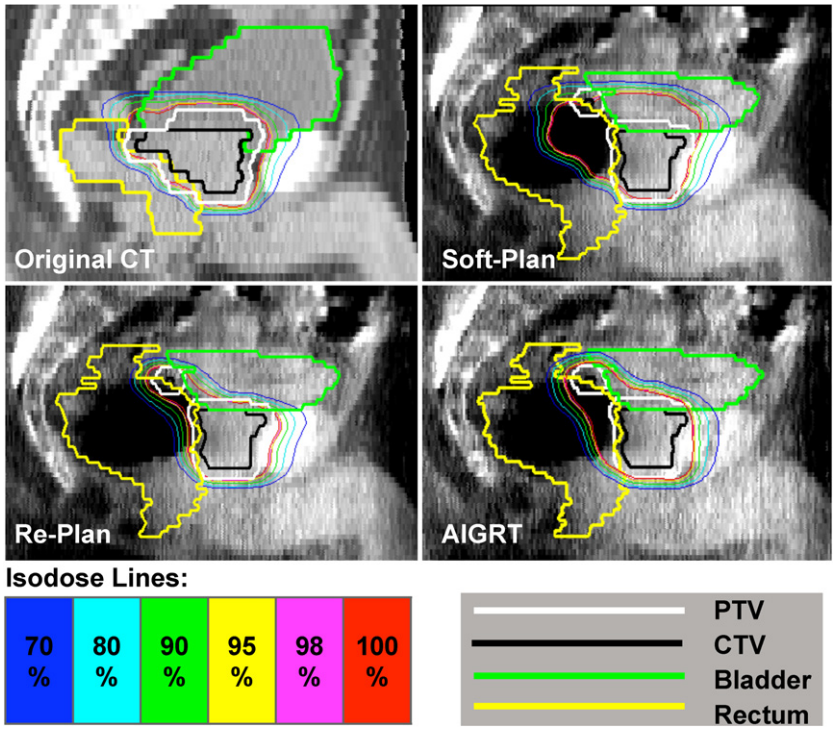


**Figure 4.** Plan comparison between *Soft-Plan*, *AIGRT* and *Re-Plan* for OAR sparing in an example case where daily CTV is significantly deformed compared to that in the original CT plan. The *Soft-Plan* plan is generated by shifting the original CT plan to match soft tissues in the daily CBCT image. The *AIGRT* plan is selected by our algorithm from previous plan library. The *Re-Plan* plan is generated by complete re-optimization based on the CBCT image. Isodose lines on *Soft-Plan*, *Re-Plan* and *AIGRT* are calculated for each plan using the same CBCT image set.

*AIGRT*, although the difference might not be clinically significant. In addition to the averaged values, *Soft-Plan* plans exhibit larger standard deviations and ranges compared to the *Re-Plan* and the *AIGRT* plans, indicating larger variance of daily dose to OARs for some patients.

Figure 6 evaluates the *AIGRT* technique over soft-tissue matching for OAR sparing. In this comparison, re-optimized (*Re-Plan*) plans based on daily anatomy are used as reference since they are the most conformal plans for the daily structures. If a plan, either *Soft-Plan* or *AIGRT*, provides the same level of OAR sparing, i.e. the same V100%/V65%/V70Gy, as *Re-Plan*, the deviation would be centered at zero. The deviations in V100%/V65%/V70Gy may be due to daily variations of OARs' position, volume, shape, or the combination of these factors. Negative variations imply lower OAR volumes receiving V100%/V65%/V70Gy compared to the most-conformal daily *Re-Plan*, i.e. better OAR sparing, whereas positive variations imply increased OAR volumes receiving high V100%/V65%/V70Gy, i.e. worse OAR sparing, relative to daily *Re-Plan*. As seen in figures 6(a)–(f), the histograms for *Soft-Plan* are more skewed toward the positive side and have larger spread compared to those for *AIGRT*, indicating higher dose to OARs in average and larger variations from reference plans. In the meantime, less positive variations of daily V100%/V65%/V70Gy are seen for *AIGRT*, compared with data from *Soft-Plan*, suggesting that the *AIGRT* technique reduces the frequency and severity of over-dosing OARs. Overall, our results on OAR dose–volume

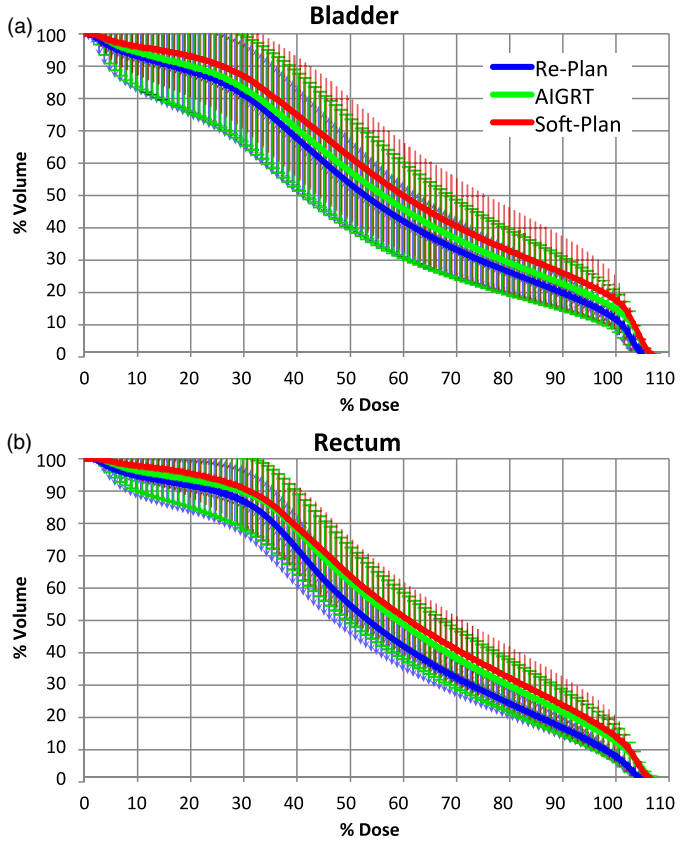


**Figure 5.** Mean DVHs and standard deviation of the bladder (a) and the rectum (b) of all 180 plans. The red bar, blue bar with arrow and green bar with flat cap show the standard deviation of *Soft-Plan*, *Re-Plan* and *AIGRT* DVHs, respectively.

analysis indicate that *AIGRT* generally provides better daily OAR sparing throughout treatment courses.

Results shown in table 2 and figure 6 indicate that the advantage of *AIGRT* over *Soft-Plan* is not confined in CTV coverage. *AIGRT* plans achieve better OAR sparing in comparison to *Soft-Plan* plans. For the example shown in figure 4, in the *Soft-Plan* plan, due to the changes of the bladder (green contour) and rectum (yellow contour), large volumes of these two OARs are included in 100% isodose lines. In the *Re-Plan* plan, such a shift and deformation are fully compensated for by complete re-optimization, and OARs are best spared. In the *AIGRT* plan, although no new plan was generated, OAR sparing is significantly improved compared to that in the *Soft-Plan* plan.

In figure 6, *AIGRT* and *Soft-Plan* are compared against most-conformal *Re-Plans*. Ideally *Re-Plans* should represent the best CTV coverage and OAR sparing. However, frequencies shown on the negative part of the horizontal axis indicate that for some fractions, *Soft-Plan* achieves lower V100%/V65%/V70Gy, i.e. better OAR sparing, than the reference *Re-Plan* technique. Analysis shows that small fraction ($\sim$13%) of *Soft-Plan* plans achieve lower V100%/V65%/V70Gy than the *Re-Plan* and *AIGRT* technique. It needs to be cautioned that such cases are often associated with target (CTV) being underdosed, i.e. the *false* sparing

**Table 2.** OAR sparing. Mean values and ranges are shown for daily V100%, V65% of bladder and rectum and relative/absolute V70Gy for rectum, for all 180 plans generated by three techniques: *Re-Plan*, *Soft-Plan* and *AIGRT*. Highest values in average and upper range among the three techniques are highlighted in bold.

| | | Re-Plan | Soft-Plan | AIGRT |
|---|---|---|---|---|
| Bladder | V100% | 11.7 ± 4.2%<br>(3.1–22.4%) | **17.3** ± 8.9%<br>(2.7–**48.8**%) | 13.6 ± 6.1%<br>(2.5–32.6%) |
| | V65% | 37.5 ± 11.4%<br>(12.4–63.7%) | **44.7** ± 16.3%<br>(13.0–**84.8**%) | 39.9 ± 13.5%<br>(12.5–71.7%) |
| Rectum | V100% | 8.0 ± 2.9%<br>(1.7–19.3%) | **13.7** ± 7.6%<br>(1.1–**34.6**%) | 11.2 ± 5.5%<br>(1.1–31.8%) |
| | V65% | 37.1 ± 7.3%<br>(16.1–54.1%) | **45.6** ± 11.0%<br>(15.6–**66.7**%) | 42.3 ± 9.7%<br>(18.6–**66.7**%) |
| | V70Gy<br>(Percentage Volume) | 15.3 ± 4.2%<br>(5.3–29.6%) | **21.9** ± 8.9%<br>(3.5–**42.8**%) | 19.1 ± 6.8%<br>(4.2–40.9%) |
| | V70Gy<br>(Absolute Volume) | 12.7 ± 6.5 cc<br>(2.8–31.9 cc) | **18.7** ± 13.0 cc<br>(2.4–**71.0** cc) | 15.6 ± 8.6 cc<br>(3.0–50.0 cc) |

of OAR at the cost of compromised CTV coverage, as the example shown in figure 7(a). The majority of *AIGRT* plans feature better CTV coverage, compared to *Soft-Plan* plans (as illustrated in figure 3), as well as lower high/median dose to bladder and/or rectum, as the example shown in figure 7(b).

### *3.3. Efficiency of AIGRT*

Figure 8 illustrates the efficiency of *AIGRT* implementation on reducing the frequency of re-optimization. The total length of the red and blue bars shows the percentage of fractions requiring plan adaptation for each patient, either through re-positioning of the previous daily plan or through daily re-optimization. For patients 4 and 9, the original CT plan is capable of providing satisfactory coverage over all fractions, so no plan adaptation is needed. The blue bar corresponds to the actual frequency of re-optimization (re-planning) and the red bar corresponds to the opportunity of re-using the previous daily plans via re-positioning in the *AIGRT* technique. Therefore, the red bars also indicate that the *AIGRT* technique significantly lowered the re-planning frequency by (43 ± 23)% across all patients, which gives *AIGRT* the advantage in efficiency, as it tries to remove the redundancy of re-optimization for a similar geometry change or deformation by re-using the plans in the patient-specific plan pool.

Additionally, the efficiency of implementing *AIGRT* can be assessed by the percentage of patients requiring re-optimization for a given fraction. Figure 9 illustrates the reduction of need to re-plan a patient as fraction number increases. At the end of ten fractions, only ∼10% patients need re-optimization to ensure complete CTV coverage; the rest can be treated with existing plans selected by the *AIGRT* algorithm. Similarly, Yan *et al* found that using bounding volume of CTVs over the first ten fractions as planning volume is sufficient to provide reliable CTV coverage in subsequent fractions (Yan *et al* 2000). Therefore, we believe the similar efficiency benefit could also be expected when implementing *AIGRT* in a conventional 38 fraction IMRT.

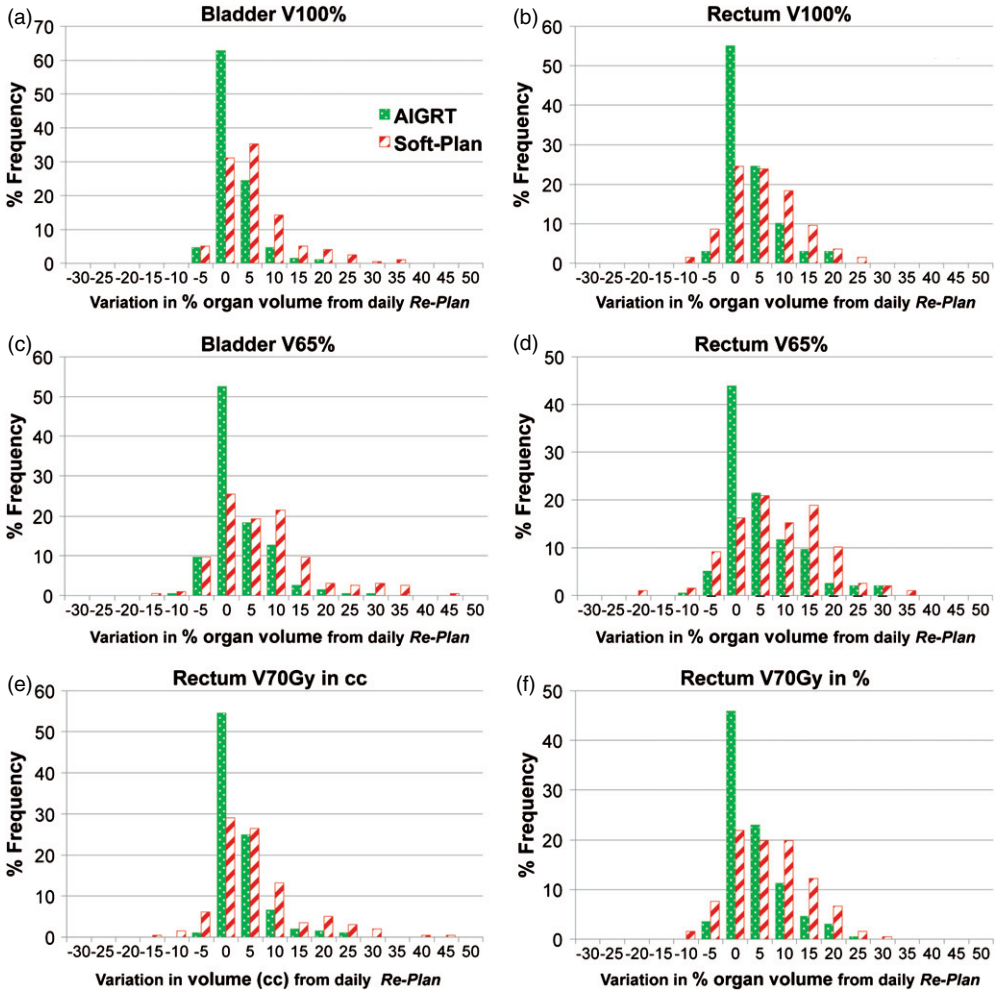


**Figure 6.** Histograms of the variations from the most-conformal *Re-Plan* for (a) bladder V100%, (b) rectum V100%, (c) bladder V65%, (d) rectum 65%, (e) rectum V70Gy in absolute volume cc, and (f) rectum V70Gy in% volume. Green dotted bar: *AIGRT*; red shaded bar: *Soft-Plan*. For each labeled value on the horizontal axis, the corresponding bin extends to ±2.5% or ±2.5 cc from that value.

### *3.4. Further discussion*

The results of this study suggest that the *AIGRT* technique provides higher quality for target coverage and better OAR sparing compared with the soft-tissue-based re-positioning technique. Daily target dose D99 of *AIGRT* plans is very unlikely to fall below clinical dosimetric requirement, making it highly comparable to complete re-planning and substantially better than the current soft-tissue matching technique. In addition, the *AIGRT* technique significantly reduces the frequency of re-optimization required to provide complete daily target coverage, and therefore improves the overall efficiency of plan adaptation. In this study, uniform 5 mm CTV to PTV margin is used for both original CT plans and *Re-Plan* plans. If a different margin is used, the frequency of necessary re-optimization would change, e.g.

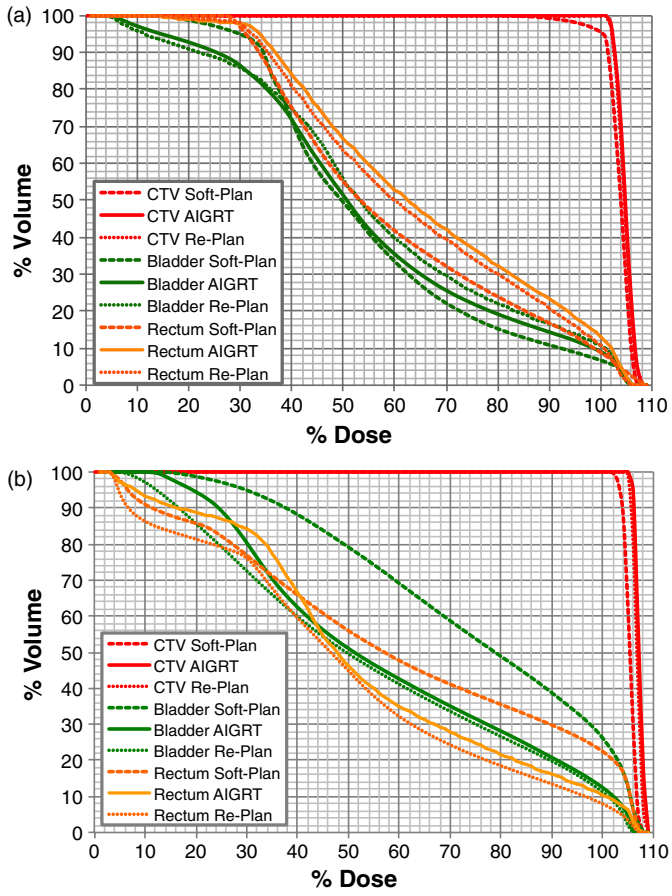


**Figure 7.** (a) One example case showing false OAR sparing associated with CTV underdose (D99 = 92% Rx) in *Soft-Plan*. *AIGRT* and *Re-Plan* DVHs are close to each other for both CTV and OARs. (b) The representative of majority plans: *AIGRT* provides CTV coverage very close to *Re-Plan*, yet still spares bladder and rectum more than *Soft-Plan*.

larger margin would allow more daily CTV to be encapsulated by previous PTVs at the cost of possibly less OAR sparing, and vice versa. Future studies would include investigations on possible margin reduction or non-uniform margin design that may be better suited for this implementation scheme.

The dose calculations for daily plans are based on the corresponding CBCT images that shares the same calibration curve with the planning CT. Due to the difference in the CT numbers between CBCT and CT images (Yoo and Yin 2006), dose calculation uncertainty may rise, especially from the inhomogeneity correction process (Papanikolaou *et al* 2004). In general, such uncertainty is small, according to a previous study at our institution (Yoo and Yin 2006): the MU/cGy differences for most phantom cases were less than 1%; the isodose lines from calculations on two modalities agree well, and up to 3% dosimetric error was observed in the plans for the inhomogeneous phantom. Yang *et al* also reported that the dose calculated on CBCT agrees with the planning CT to within 1% in phantom cases, and concluded that CBCT can be directly used in dose calculation (Yang *et al* 2007). Therefore in

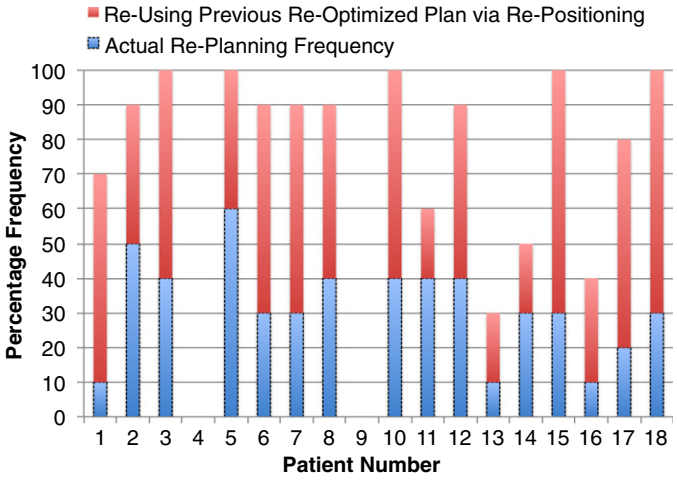


**Figure 8.** Frequency reduction on re-planning with *AIGRT*. The total length of red and blue bars shows the frequency of plan adaptation for each patient. The blue bars show the actual frequency of re-planning in a treatment course, and red bars show the reduction on re-planning frequency due to the re-use of previous daily plans in the *AIGRT* technique. For patients 4 and 9, the original CT plan is capable to provide satisfactory coverage over all fractions, so no plan adaptation is needed.

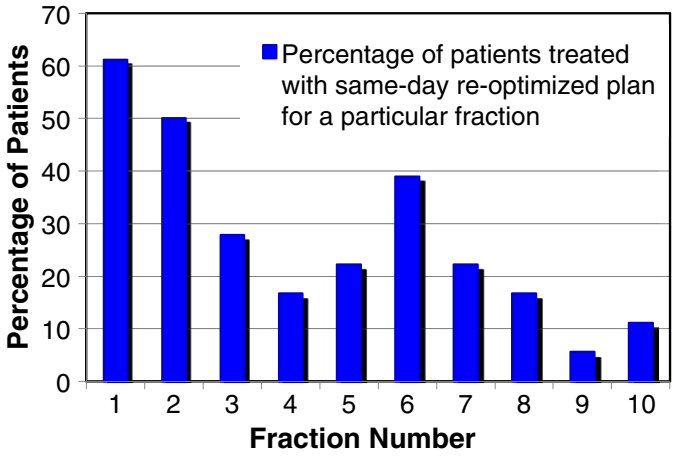


**Figure 9.** Percentage of patients treated with the same-day re-optimized plan for a particular fraction number from 1 to 10.

this study, the uncertainty associated with calculating dose on the CBCT image set is assumed to be small. For dosimetrical evaluation, the dose distributions for the three techniques are calculated on the same image set of each fraction; therefore, the uncertainty is consistent for all techniques. Changes in the rectal gas fillings could further affect the dose distribution due to the heterogeneity of electron densities, which currently is only considered in the daily dose calculation process, not the plan selection process. In future work attention should be given to dramatic bladder/rectum filling variations during the plan selection process.

In this feasibility study, the QA process for re-optimized plans in the *AIGRT* scheme in figure 1 is only included for the completeness of the proposed clinical flow and not thoroughly

investigated. In practice, the re-optimized plan needs to undergo IMRT QA before it can be used to treat the patient. To suit the clinical implementation of *AIGRT*, the desired QA technique would be efficient in time and automatic in process, allowing to be performed with patient on the table.

This study focuses on the overall design of the unified implementation scheme that takes advantage of combining re-positioning and re-optimization techniques to fulfill different clinical needs on daily basis, and shows that the *AIGRT* scheme can be beneficial for both the dosimetry and efficiency. Currently, the time management for each component in *AIGRT*, i.e. contouring, plan selection, re-optimization, and QA, is not considered at this proof-of-concept stage; however, the full clinical implementation of *AIGRT* indeed requires each component in *AIGRT* to be accomplished in a timely manner. Recently, various research groups have developed fast plan optimization algorithms using linear programming (Wu *et al* 2008, Thongphiew *et al* 2009), GPU acceleration (Men *et al* 2009, 2010a, 2010b) and 'SAM+SWO' algorithm (Ahunbay *et al* 2010), high efficiency deformable registration with GPU (Gu *et al* 2010) for propagating contours from planning CT to daily images, and novel QA technique using MLC dynalog files and Monte Carlo simulation (Teke *et al* 2010). These new developments, in conjunction with the proposed *AIGRT* scheme, can be valuable in leading to the clinical implementation of adaptive radiation therapy. Further, the *AIGRT* scheme should be implemented into the commercial treatment planning and record-and-verify systems in order for it to be an integral part of the clinical workflow.

## 4. Conclusion

The *AIGRT* technique was compared against the current soft-tissue matching technique and re-optimization technique for 18 patients. Results demonstrated that it is beneficial to implement such a technique clinically. For target coverage, *AIGRT* achieves highly uniform CTV coverage comparable to *Re-Plan* throughout the simulated treatment course, but requires significantly fewer re-optimization processes. In the meantime, OAR sparing is improved over *Soft-Plan*, although not identical to *Re-Plan*. As a proof of concept, this technique improves the overall efficiency of plan adaptation and has the potential of being integrated into clinical flow. Thus, *AIGRT* can be a valuable and efficient technique for image-guided prostate radiotherapy with precise daily dose delivery.

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