The susceptibility of IMRT dose distributions to intrafraction organ motion: An investigation into smoothing filters derived from four dimensional computed tomography data

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This study investigated the sensitivity of static planning of intensity-modulated beams (IMBs) to intrafraction deformable organ motion and assessed whether smoothing of the IMBs at the treatment-planning stage can reduce this sensitivity. The study was performed with a 4D computed tomography (CT) data set for an IMRT treatment of a patient with liver cancer. Fluence profiles obtained from inverse-planning calculations on a standard reference CT scan were redelivered on a CT scan from the 4D data set at a different part of the breathing cycle. The use of a nonrigid registration model on the 4D data set additionally enabled detailed analysis of the overall intrafraction motion effects on the IMRT delivery during free breathing. Smoothing filters were then applied to the beam profiles within the optimization process to investigate whether this could reduce the sensitivity of IMBs to intrafraction organ motion. In addition, optimal fluence profiles from calculations on each individual phase of the breathing cycle were averaged to mimic the convolution of a static dose distribution with a motion probability kernel and assess its usefulness. Results from nonrigid registrations of the CT scan data showed a maximum liver motion of 7 mm in superior-inferior direction for this patient. Dose-volume histogram (DVH) comparison indicated a systematic shift when planning treatment on a motion-frozen, standard CT scan but delivering over a full breathing cycle. The ratio of the dose to 50% of the normal liver to 50% of the planning target volume (PTV) changed up to 28% between different phases. Smoothing beam profiles with a median-window filter did not overcome the substantial shift in dose due to a difference in breathing phase between planning and delivery of treatment. Averaging of optimal beam profiles at different phases of the breathing cycle mainly resulted in an increase in dose to the organs at risk (OAR) and did not seem beneficial to compensate for organ motion compared with using a large margin. Additionally, the results emphasized the need for 4D CT scans when aiming to reduce the internal margin (IM). Using only a single planning scan introduces a systematic shift in the dose distribution during delivery. Smoothing beam profiles either based on a single scan or over the different breathing phases was not beneficial for reducing this shift. © 2006 American Association of Physicists in Medicine. [DOI: 10.1118/1.2219329]

Key words: IMRT, organ motion, deformable image registration, treatment uncertainty

I. INTRODUCTION

IMRT shapes a high-dose region to conform to the geometry of the target in three dimensions with rapid falloff in all directions outside the target volume. Since the availability of computed tomography (CT), treatment has mostly been designed on a single CT scan that represents a snapshot of the tumor position. The fact that many organs are not stationary but move according to a complex combination of forces within the patient has been known for a long time.1 The use of a single CT scan 3D data set for treatment planning there-
Whereas much research has been done into an understanding of the nature and magnitude of organ motion, there are still few studies based on acquired clinical data of the impact of motion. Some studies in the literature suggest that smoothing beam profiles would make the treatment less sensitive to organ motion. With the availability of 4D CT data, however, it is possible to assess the impact of motion. Some studies in the literature suggest that there are still few studies based on acquired clinical data of the standing of the nature and magnitude of organ motion, there assumptions were made at the start of this study:

(a) It was decided to separate the setup margin (SM) and internal margin (IM) as defined by ICRU Report 62 and to assume a constant SM of 5 mm throughout all fractions. The IM was set to zero in this study. The PTV was therefore equal to the internal target volume (ITV) in this work, i.e., the CTV + SM. The absence of the IM can be understood from the fact that it is the aim of this study to quantify the exact dose discrepancy to the ITV due to internal target motion. In Sec. II A 2 the effect of adding an IM on the dose to the surrounding normal structures will be discussed.

(b) The IMRT delivery technique was not taken into account in this study, as the temporal nature of the delivery technique is irrelevant provided that enough fractions are delivered to yield enough samples of the motion probability distribution of the target. This can be understood in terms of conditional probabilities of statistically independent effects. Let \( A \) be the distribution in target position and let \( B \) be the distribution of the delivered beam (i.e., what the interpreter produces). The problem of finding the average dose distribution over a large number of samples (i.e., fractions) is the conditional probability of finding a certain \( A \_\text{sample} \) given a particular \( B \_\text{sample} \) or \( P(A \_\text{sample}|B \_\text{sample}) \). As \( A \) and \( B \) are statistically independent \( P(A \_\text{sample}|B \_\text{sample}) = P(A \_\text{sample}) \). Bortfeld et al.\cite{bortfeld1997} show that 30 is a sufficient number of samples for finding the average dose distribution. Treatment is nongated. The issue of starting phase in the treatment delivery is therefore equally negligible for this study, as finding the starting phase of treatment amounts to sampling the distribution \( A \) many times and this just gives the average of \( A \).

II. METHOD

The aim of the study was to obtain information on the discrepancy between planned and delivered IMRT dose distribution in the presence of organ motion. For this reason “4D” CT data of a patient with liver cancer was used. Since it is now understood that CT scans taken before and after treatment are not necessarily representative of the possible organ movement and actual tumor position at the time of delivery,\cite{gottlieb2001,bortfeld2001} the 4D data set is currently the most realistic representative of 3D organ motion with time. Certain assumptions were made at the start of this study:

(c) The study only considers intrafraction motion and assumes that this intrafraction motion does not change over the different fractions. The interfraction errors are taken into account by the SM as stated in assumption (a).

A. Susceptibility of IMRT dose distributions to deformable organ motion

A reference IMRT treatment plan was made for the liver patient on CT data at the exhale phase of breathing. This was performed with a gradient-descent technique, using a quadratic dose-based cost function.\cite{bortfeld1998} The exhale phase was chosen as this is shown in the literature to be the most likely phase in which liver patients would normally be scanned due to its stability.\cite{bortfeld1997} Although the breathing distribution for this patient peaked at exhale (see Fig. 1) it did not show the ideal Gaussian form. The aim was to assess, if one did not have 4D CT and scanned the patient, e.g., at inhale, what the accuracy would be in using a nonrepresentative scan to plan the treatment. To assess the effect of respiratory-induced organ motion within a single fraction, this reference treatment plan (which is optimum for the exhale geometry) was re-delivered to all other CT scans in the 4D data set, i.e., at the remaining nine phases of the breathing cycle. To quantify the discrepancy between planning and delivery of dose, the ten different dose distributions were then combined together and displayed at the exhale geometry. To combine the resulting dose distributions correctly at different phases of the breathing cycle, information is required about the liver motion and about the precise relocation of each individual voxel with respect to its position in the other CT scans. This motion model was deduced with the use of a B-splines-based nonrigid image registration algorithm\cite{bortfeld1997,bortfeld1999} as reports on liver motion\cite{bortfeld1999,bortfeld2005} confirm that regions of the liver can deform by more than 2 cm during respiration. The liver on the reference set was manually segmented with the ANALYZE software (Biomedical Imaging Resource, Mayo Foundation, Rochester, MN, USA) to exclude any large discontinuities at the regions where the liver slides over adjacent organs.

B-spline control point spacing was set at 40 mm, which was an acceptable balance between increasing the calculation time and significantly improving the accuracy of registration.
since there is little visible structure in the liver to base the interpolation on. A cross-correlation measure was used with quasi-Newton minimization to guide the registration optimization. The initial control point step size was 10 mm, halving down to 1.25 mm in four steps. The accuracy of registration was tested with the use of three markers that had been implanted in the liver and which were visible on all CT scans. The center of each marker was manually identified in the CT scan at inhale and exhale. The difference in position of these marker points before and after registration was then calculated. In summary, registration of the CT scans, at different phases of the breathing cycle, involved performance of the following steps:

1. Segment the liver outline on the reference scan.
2. Warp the outline onto the other scans.
3. Find initial affine transformation to register scans.
4. Find B-spline transformation parameters to account for local deformations.
5. Visually check alignment of liver outline on registered scans.
6. Calculate difference in position of the markers before and after registration to assess the accuracy of registration.

1. Dose recombination with a target motion model

With this 4D model of organ motion during respiration, it was then possible to trace the movement of each individual voxel and calculate a weighted average of the redelivered dose distributions at different phases of the breathing cycle. The overall dose in one fraction in the presence of motion, “\(D_m\)”, was determined as

\[
D_m = \sum_{\varphi=0}^{9} P_{\varphi} D_{\varphi},
\]

with \(P_{\varphi}\) the probability of finding the tumor in a particular phase of the breathing cycle. Let \((x,y,z)\) be the fixed frame of reference within the patient.

Let \((x_{\varphi},y_{\varphi},z_{\varphi})\) represent the patient voxel at phase \(\varphi\). For a particular phase (e.g., here \(\varphi=exhale\)) \(y_{\varphi}\) may be identified with \(y\) (i.e., \(y_{\text{exhale}}=y\)). Let \(D_{\varphi}(x_{\varphi},y_{\varphi},z_{\varphi})\) be the dose obtained by delivering the IMBs of the reference plan, \(I(x,\varphi=\text{exhale})\), on the \(\varphi^{th}\) phase in the 4D CT set. This dose \(D_{\varphi}\) was obtained by applying the phase \(\varphi\) transformations from the deformable model \(T_{\varphi}\) to the dose in the original coordinate system of scan \(\varphi\), \(D(x,y,z)\):

\[
D_{\varphi}(x,y,z) = T_{\varphi}(D(x,y,z)).
\]

The weight or probability for each time point was obtained from the abdominal surface displacement and was calculated as

\[
P_{\varphi} = \frac{\Delta t(\varphi)}{T},
\]

with \(\Delta t(\varphi)\) the fraction of time spent at phase \(\varphi\), and \(T\) the period of one breathing cycle. This time fraction was determined using the Varian R.P.M system.

2. Usefulness of an internal margin

To test the robustness and impact of using a 1 cm isotropic IM to cover the extent of internal target motion an IM was grown on the ITV. This will be referred to as PTV. The size of the IM is slightly larger than the maximum liver motion (7 mm) in the superior-inferior direction and is frequently used clinically to account for breathing motion. An IMRT plan was calculated on the PTV at the exhale phase. This plan was then redelivered to the scan at inhale only to determine if the added IM would indeed cover the range of motion and to establish the consequences for the surrounding sensitive structures.

3. Plan comparisons

Dose distributions from the reference treatment plan and the delivered plan were compared by calculation of dose-difference distributions. These were then displayed superimposed on the patient geometry. In addition, dose-volume histograms (DVHs) of the plans were compared in terms of dose to the PTV, healthy liver, and spinal cord. The kidneys were situated sufficiently out of the field of the treatment beams to justify ignoring them in the analysis. To quantitatively assess the impact of beam mismatch on the dose distribution, the following ratios were calculated:

\[
R_{50,\text{OAR}} = \frac{\text{Dose to } 50\% \text{ of the OAR}}{\text{Dose to } 50\% \text{ of the PTV}},
\]

\[
R_{PTV}^{95} = \frac{\text{Dose to } 95\% \text{ of the PTV redelivery}}{\text{Dose to } 95\% \text{ of the PTV optimal}}.
\]

The 50% level was chosen as it represents the median dose delivered to the PTV. The values for \(R_{50,\text{OAR}}\) are an indicator of the magnitude of separation between the DVH for the OARs (healthy liver, spinal cord) and PTV at the 50% volume level, i.e., coverage-sparing ratio or quality of the plan. Values of \(R_{PTV}^{95}\) show the discrepancy between the 95% coverage level of the optimal and delivered dose distribution. To assess the impact of a change in dose coverage on the clinical outcome of treatment, normal tissue complication probability (NTCP) values were calculated, based on the Lyman model with volume effect parameter \(n=0.40\), steepness \(m =0.26\), and 50% tolerance dose \(TD_{30}=43\) Gy according to Cheng et al. The dose to 30% of the liver volume \((D_{30})\) has been shown to be a good indicator of complication and therefore this parameter was compared, too. Parameters for the calculation of TCP for liver tumors are not readily available through the literature and therefore TCP was not calculated.
B. The effect of smoothing fluence profiles on motion susceptibility

Given that smoother beams contain more low-frequency components than the original unconstrained IMBs, the hypothesis is that they are also less sensitive to movement. Which filter to use must be based on what type of noise needs to be removed. In light of earlier work, however, it is clear that it is very difficult to distinguish between essential structure and noise, i.e., wanted and unwanted modulation, within a beam fluence profile. A filter that removes small-scale local extrema, while preserving major features in the beam profile such as large gradients, would therefore be the best smoothing filter to use. The median window filter (MWF) is such a filter and has also been suggested in the literature as the most useful smoothing filter with respect to more efficient delivery of treatment.23–26

Two methods of smoothing beam fluence profiles were used to investigate a possible reduction in sensitivity to organ motion. The first method (see Sec. II B 1) involved applying the MWF to the fluence profiles calculated on the CT scan at inhale and exhale and then redelivering them to a CT scan at another phase. The second approach (see Sec. II B 2) did not involve a direct filtering of IMBs within a single optimization but averaged the optimal fluence profiles, calculated on their ten respective CT scans. This method mimicked the 3D convolution of a static dose distribution with a realistic motion kernel and allows the investigation of the postulated benefits with this technique.

1. Smoothing with a median window filter (MWF)

Beam profiles, calculated from the CT scans at inhale and exhale, respectively, were smoothed with a MWF in two ways. The first approach consisted of applying a MWF at every fourth step within the optimization process. This was done for a $3 \times 3$ and $5 \times 5$ filter and is based on previous work which showed that, for nonmoving data, this filter size and smoothing frequency were optimal in terms of delivering efficiency and sparing of OARs.

The second approach involved applying the $3 \times 3$ MWF only once, i.e., after the optimization had finished, which is the (only) option available on the commercial TPS ADAC Pinnacle (v6.2b, Milpitas, USA) used at this Institute. Applying the filter only once after optimization of optimal fluence profiles will not be as successful as the previous method in balancing the coverage of the PTV and sparing of OARs. However, if proven to give comparable results, this smoothing method would be readily clinically available. The $3 \times 3$ and $5 \times 5$ filter are both two-dimensional filters and smoothing was done in the direction of leaf travel and perpendicular to it. This was considered advantageous over a one-dimensional filter in this case since the liver has been shown to deform in all directions. In theory, however, the $3 \times 3$ window size should cover the whole range of motion (7 mm) since one pixel will irradiate a $1 \times 1 \text{ cm}^2$ area at the isocenter level. The $5 \times 5$ MWF was applied to compare any possible differences in outcome with the $3 \times 3$ MWF.

In both approaches, independent of the filtering frequency, the smoothed profiles at exhale and inhale were then redelivered to the CT scan at the (respective) other extreme phase of the breathing cycle at which they were planned, to be able to assess the possible reduction in motion effects. To quantify the efficiency of smoothing over the breathing cycle the smoothed profiles would also have to be redelivered to all other phases and the resulting dose distributions combined using the deformation transformations.

2. Averaging of optimal fluence profiles

In the second smoothing method, optimal fluence profiles were calculated on each of the ten CT scans within the 4D data set, i.e., at ten phases of the breathing cycle. The average of those fluence profiles was then calculated, weighted with the temporal probabilities of each phase. To assess the impact of this type of smoothing, first of all, the mean weighted fluence profiles were delivered to inhale and exhale scans to show the impact on the extreme phases of the breathing cycle. In addition, the averaged fluence profiles were redelivered to all other CT scans such that the impact of delivering averaged beam profiles over the whole breathing cycle could be assessed. This was done, as explained in Sec. II A 1, by applying the registration transformations to these recalculated dose distributions such that they can be linked and summed together.
III. RESULTS

A. Effect of intrafraction motion on IMRT dose distributions

1. Accuracy of deformable image registration

A total of three fiducial markers were present in the liver, i.e., one close to the dome, one in the PTV, and one in the middle of the liver. The presence of these markers made it possible to establish the accuracy of the image registration process, which is given in Table I. The manual marker selection error was 1 mm. Therefore, the actual accuracy of registration (without manual error) was, on average, 2 mm. Given that (1) the average distance in marker position due to liver motion is approximately 7.5 mm and (2) the accepted dose calculation accuracy in the penumbra area for MLC shaped fields is 3 mm,28 this level of registration accuracy was considered acceptable for assessing, in first-order approximation, the susceptibility of IMRT dose distributions to organ motion.

2. Dosimetric effect of intrafraction organ motion

Once the transformations had been established between the CT scans at different phases of the breathing cycle, a realistic estimate could be made of the effect of motion during a single fraction. The probability of finding the tumor in a particular phase is given in Fig. 1 as a percentage of the phase at inhale. As a large part of the breathing cycle is spent at exhale (which corresponds here to 40–60%) the highest probability of occupancy is found there. Conversely, the inhale phase (corresponding to 0/100%) has a lower probability.

The dose distribution, resulting after redelivery of the exhale plan to all other respiratory phases [Eq. (2)], is shown in Fig. 2 together with the reference plan at exhale. It is clear that there is a systematic shift between the DVH from the planned and delivered treatment plan. The impact of intrafractional organ motion was quantified with the calculation of NTCP and $D_{30}$ values, as well as $R$ values for the liver and spinal cord, which are given in Table II. The dose to 95% of the PTV differs by almost 30%, leading to a serious underdosage of the target volume. In addition, the DVH for the redelivered plan is shallower than the reference DVH, indicating that the dose to the PTV became more inhomogeneous. Due to the several crossover points between both liver DVHs, the difference in $R_{50}$ and $D_{30}$ values for the liver appears not to be very large. This change in DVH also results in a significantly lower liver NTCP. In addition, the spinal cord seems to benefit from the overall misalignment between beam and target as the motion shifts the high-dose region away from the spinal cord, which itself stays static throughout the breathing cycle. The maximum dose to the spinal cord in the delivered plan is approximately 25% lower than in the reference plan from 21.3 to 16 Gy. However, if the plans were renormalized to deliver the same tumor dose, the OARs would be seen to receive a higher dose than in the optimal static situation. Furthermore, the motion could be such that the OARs move into the PTV region, rather than away from it as for this patient, resulting in a detrimental dose increase for these healthy structures. This could occur, for example, in the case of using the inhale phase to produce a reference plan and is illustrated in Fig. 3(b), which shows the differences in DVH from planning on a CT at one ex-
treme of the breathing cycle (inhale) and delivering treatment on the other extreme of breathing (exhale). The detrimental effect on OARs is reflected in the NTCP and $D_{30}$ values, which suggests a higher risk of complication. The volume of liver receiving 30 Gy also increases from 20.2% to 30.4% for this case. More details can be found in Ref. 8.

The discrepancy in the IMRT dose distributions between planning and delivery of a treatment at a different phase is also shown in Fig. 4 in terms of dose differences. The difference in dose between the planned (optimum) plan and the plan redelivered to a different phase is given in units of Gy, with the positive differences and negative differences on two separate images. In other words, for negative differences there is less dose given in the delivered plan than in the planned one.

3. Impact of a standard estimated IM on normal tissue

The DVH comparison between the plan with an isotropic IM at exhale and the static plan at inhale is shown in Fig. 5 indicating that the IM indeed largely overcomes the shift in the dose although the target DVH is slightly shallower at the top of the DVH curve. But, more importantly, the volume of liver receiving 30 Gy increases by 25% when adding an IM. The distance between the DVH of the PTV and spinal cord decreases by approximately a factor of 10, but no change is visible in the maximum dose to the spinal cord in the two situations. The volume of the liver receiving high and low doses shifts upwards but only a small change is visible around 30 Gy, which leads to a change in $D_{30}$ from 24.4 to 27.7 Gy. The overall NTCP of the liver is 13.3%, which is a 10% increase from the situation without an IM.

B. Effect of smoothing on motion susceptibility

1. Medium-window filter

The DVHs resulting from smoothing IMBs with a $3 \times 3$ MWF, at every fourth iteration of the optimization process are shown in Figs. 6 and 7, together with the unsmoothed redeliveries and optimal DVH at exhale and inhale, respectively. In both phases only a very small improvement is vis-

![Fig. 4. Dose difference between the total redelivered dose in one fraction and the optimal exhale plan. The differences are in absolute dose and (a) positive and (b) negative differences are displayed separately up to the maximum value.](image-url)
Smoothing IMRT dose distributions for intrafraction organ motion

A similarly small change is visible in the DVHs of the liver and spinal cord that does not affect the NTCP and $R$ parameters in Table II significantly. No benefit was seen in smoothing fluence profiles only once with a $3 \times 3$ MWF, i.e., after the optimization had finished, as the median dose to the PTV is 3.4% lower than the case where the profiles from the exhale plan were not smoothed when redelivered to the inhale scan.

Smoothing the exhale fluence profiles with a $5 \times 5$ MWF during optimization resulted in DVHs that showed only slight differences with the $3 \times 3$ MWF result. No improvement could therefore be established over the unsmoothed DVHs. Similar results were found for the inhale situation. Considering the small effect of smoothing on the two extreme phases of the breathing cycle, it was not considered relevant to investigate the effect over the whole breathing cycle.

Table II. $R$ values [see Eq. (4)] for the liver and spinal cord for the “optimal” plan at exhale (i.e., planning phase=delivery phase) and the total combined dose after redelivery of the exhale plan to all other respiratory phases.

<table>
<thead>
<tr>
<th></th>
<th>Combined dose</th>
<th>Optimal exhale</th>
</tr>
</thead>
<tbody>
<tr>
<td>$R_{30\text{Gy},\text{liver}}$</td>
<td>0.4176</td>
<td>0.3960</td>
</tr>
<tr>
<td>$R_{30\text{Gy},\text{sp cord}}$</td>
<td>0.0353</td>
<td>0.0436</td>
</tr>
<tr>
<td>$R_{50%PTV}$</td>
<td>0.7174</td>
<td>...</td>
</tr>
<tr>
<td>NTCP (%)</td>
<td>4.5</td>
<td>11.2</td>
</tr>
<tr>
<td>$D_{30\text{Gy},\text{liver}}$ (Gy)</td>
<td>24.5</td>
<td>26.5</td>
</tr>
</tbody>
</table>
2. Effect of averaging optimal fluence on motion susceptibility

The combined effect of redelivering the average fluence over the breathing cycle is shown in Fig. 8. For comparison purposes, the combined (unsmoothed) effect over the breathing cycle is also plotted as well as the optimal exhale result for the PTV dose. The results show a degradation of PTV coverage and improved sparing of the OARs because the beams move advantageously for this particular case, i.e., away from the liver and spinal cord. A quantitative comparison between the smoothed and unsmoothed effect is given in Table III. As noted before, it must be stressed that the apparent improvement of liver NTCP is not real since the PTV is severely underdosed. Even though the 95% coverage level is approximately the same for smoothed and unsmoothed redelivery to all phases, the mean PTV dose when averaging beam profiles is 14% lower than the unsmoothed situation, which is already 17.6% lower than the ideal plan.

To illustrate that the dose to the liver would indeed increase if the PTV coverage were comparable to the optimal situation, the DVHs of the smoothed redelivery plan were renormalized to the 50% volume level of the PTV coverage, i.e., 50 Gy (see Fig. 8). After renormalization, $D_{30,liver}$ is 28 Gy, compared to 26.5 Gy in the optimal (exhale-exhale) redelivery (see Table I). This would therefore result in a higher risk of complication.

### IV. DISCUSSION

The use of 4D CT data was an essential part in the development of this study and, although registration algorithms are susceptible to inaccuracies, the combined dose distribution obtained with the nonrigid registration model represents the most accurate representation of reality currently possible of the effect of intrafraction organ motion. As CT scans taken before and after treatment are not necessarily representative of the possible organ movement and actual tumor position at the time of delivery, the 4D data set is currently the most realistic representative of 3D organ motion with time.

There is some loss in accuracy associated with registering images when the image (CT scan region) only just covers the organ of interest (i.e., the liver tumor in this case). The latter arose from the fact that the 4D CT procedure could only encompass ten sets of CT data within the breathing cycle. Since the transformations were generated over the whole liver image this inaccuracy did not have a significant impact on the application of the transformations in this study. However, future developments on 4D CT scanning should aim to remove this restriction such that the entire organ is scanned and not only the region around the tumor.

Results from adding a “standard” IM without patient-specific information of how much the tumor is moving can be quite detrimental to the OARs, especially if a conventional 3D CT scan is used for planning. It would be advised to use a combined CTV from 4D CT information in order to avoid a systematic dosimetric error.

With regard to the use of the exhale phase as the reference phase of the treatment planning scan it must be noted that this was done to mimic the current clinical practice. However, the scan at the middle phase of the breathing cycle is, if available for planning, most likely to represent the average tumor position.

With respect to a reduced beam complexity, neither method of fluence smoothing was able to reduce the susceptibility to organ motion. Small improvements are seen in the DVHs from the MWF-smoothing approach, but the significant reduction in ITV dose due to organ motion could not be overcome even though the smoothing window was adequate.

### Table III. $R$ values (Eq. (1)) for the liver and spinal cord for the optimal plan at exhale and the total combined dose after redelivery of the exhale and average plan to all other respiratory phases.

<table>
<thead>
<tr>
<th></th>
<th>Exhale-all phases</th>
<th>Exhale-exhale</th>
</tr>
</thead>
<tbody>
<tr>
<td>$R_{50,liver}$</td>
<td>0.4178</td>
<td>0.4176</td>
</tr>
<tr>
<td>$R_{50,sp cord}$</td>
<td>0.0411</td>
<td>0.0353</td>
</tr>
<tr>
<td>$R_{PTV}$</td>
<td>0.6793</td>
<td>0.7174</td>
</tr>
<tr>
<td>$D_{mean,PTV}$ (Gy)</td>
<td>35.3±2.5</td>
<td>41.2±4.2</td>
</tr>
<tr>
<td>NTCP (%)</td>
<td>2.0</td>
<td>4.5</td>
</tr>
<tr>
<td>$D_{30,liver}$ (Gy)</td>
<td>20.5</td>
<td>24.5</td>
</tr>
</tbody>
</table>

![Fig. 8. DVHs for the unsmoothed exhale, average fluence redelivery, and renormalized average redelivery over the breathing cycle of the PTV (a) and the liver and spinal cord (b). In (a) the optimal exhale DVH is also given. Renormalization was done such that 50% of the volume received the mean optimal dose of 50 Gy.](image-url)
in covering the extent of organ motion (one pixel at the height of the MLC projects to a 1 x 1 cm² area at isocenter level within the patient).

For the averaging technique, i.e., convolving the dose distribution with a motion kernel, it must be noted that this method moves away from a static way of treatment planning altogether. Although averaging is a valid smoothing concept, when applied with the goal of motion compensation it did not result in improved tumor coverage in the presence of motion. By averaging the optimal fluence profiles, the motion kernel is effectively applied twice: once during treatment planning and once during dose delivery. A large number of the published studies aim to compensate for organ motion by convolving the dose distribution or fluence profiles with either a Gaussian kernel or a one-dimensional, simplified motion probability function. Although they were important investigations, the approach has two major drawbacks. First of all, the probabilities of finding the tumor in a certain position of the breathing cycle do not follow a Gaussian distribution and, given the irregularity of breathing motion, the statistical distribution of breathing phases should be determined. This was done in this study by determining the probability of finding the tumor in a particular breathing phase, based on abdominal surface trajectory measurements with the Varian RPM system. It was assumed in this study that the level of breathing remains constant throughout the treatment. To achieve this in practice, the patient will most likely have to receive breathing coaching and breathing motion should still be monitored during treatment, as changes in breathing level will introduce discrepancies with the treatment plan. These errors were not considered in this study.

The second drawback concerns the concept of performing a convolution. Whereas a dose or fluence convolution might benefit the coverage of the tumor volume, it is certainly detrimental for the surrounding tissues, as it will increase the margin size. The results in Fig. 8 indicate indeed that using a kernel convolution method is not a correct approach to compensate for organ motion. Whereas smoothing of beam profiles within a single-phase optimization might also increase the dose to OARs, this approach does not artificially enlarge the PTV margin and the extra dose will be an indirect effect of treatment and not due to a direct expansion of the irradiation field. This is important since the main aim of compensating for motion is to allow a margin reduction for sparing of OARs and better tumor dose conformality.

The liver motion in this patient is quite typical (even on the smaller side) and although extremer deformations have been noted, the finding that the movement is sufficiently large that one ends up with a much larger margin or a geometric miss will surely not be helped by filtering if even larger deformations are present. The conclusions would therefore not differ from the ones presented here. The resulting R factors would differ for different patients but this will be not only the result of a difference in motion amplitude but also due to a difference in general patient anatomy and planning parameters (e.g., beam orientations).

V. CONCLUSION

Reducing possible intrafraction dose hot/cold spots is important as they can lead to errors with biological consequences. The aim of the presented study was to obtain the most realistic representation of the effect of intrafraction respiratory organ motion on IMRT dose distributions and to test whether smoothing of the fluence profiles could reduce this sensitivity. The thesis that smoothing IMBs could reduce the sensitivity of IMRT to organ motion could not be proven. Two filtering methods were tested, i.e., applying a MWF in/outside fluence optimization and averaging of optimal IMBs, but neither approach could overcome the large systematic underdosage of the PTV (=CTV+SM) due to liver motion.

Results show that the use of a single planning CT scan could introduce a significant systematic error in the final dose distribution due to the difference in phase of breathing between planning and delivery. For the presented liver results, the effect of intrafraction organ movement has led to an underdosage of the tumor of approximately 30%. The use of a standard IM to account for organ motion was shown to significantly increase the dose to the organs at risk, leading to an associated increase in complication risk of 10%. Therefore, when aiming to reduce the IM size and account for organ motion in a different way, the use of 4D CT information is essential to avoid systematic dosimetric errors.

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