Tumour delineation and cumulative dose computation in radiotherapy based on deformable registration of respiratory correlated ct images of lung cancer patients

J. Orban de Xivry $^{1,2}$, G. Janssens $^{1,2}$, G. Bosmans $^2$, M. De Craene $^1$, A. Dekker $^2$, J. Buijsen $^2$, A. van Baardwijk $^2$, D. De Ruysscher $^2$, B. Macq $^1$, and P. Lambin $^2$

$^1$ Communications and Remote Sensing Laboratory (TELE), Universite catholique de Louvain, 1348 Louvain-la-Neuve, Belgium.
$^2$ Departement of Radiation Oncology (MAASTRO), GROW, U. H. Maastricht, Maastricht, The Netherlands.

2007
Tumour delineation and cumulative dose computation in radiotherapy based on deformable registration of respiratory correlated CT images of lung cancer patients

J. Orban de Xivry 1,2, G. Janssens 1,2, G. Bosmans 2, M. De Craene 1, A. Dekker 2, J. Buijsen 2, A. van Baardwijk 2, D. De Ruysscher 2, B. Macq 1, and P. Lambin 2

1 Communications and Remote Sensing Laboratory (TELE), Université catholique de Louvain, 1348 Louvain-la-Neuve, Belgium.
2 Departement of Radiation Oncology (MAASTRO), GROW, U. H. Maastricht, Maastricht, The Netherlands.

Abstract

Purpose To improve treatment planning in radiotherapy for non-small cell lung cancer by including Respiratory Correlated - Computed Tomography (RC-CT) information in tumour delineation and dose planning.

Methods and materials Dense displacement fields were computed using a combination of rigid and non-rigid registrations between RC-CT phases. These registrations have been performed independently between each phase of the respiratory cycle and a reference phase for 13 patients. A manual delineation in the reference frame was propagated to every other phase according to the deformation fields recovered from the inter-phase registrations. Resulting delineations were compared to two manual delineations drawn by two physicians at each phase. On the other hand, dose distributions computed for every phase were deformed towards the reference phase. These distributions were then added on the reference phase to estimate the total dose received by each voxel through the whole respiratory cycle.

Results The overlap between the deformed and the manual delineations was not significantly different than the overlap between the delineations made by the two physicians for 11 out of 13 patients thus proving that the method accuracy is comparable to inter-observer variability. Calculation of the effective dose distributions showed that these were conserved after deformation.

Conclusion We developed a method to use RC-CT information into the radiation treatment planning, including semi-automatic segmentation of lung tumours on each phase of the respiratory cycle and a total received dose per voxel estimation.

Keywords: RC-CT, deformation, b-spline registration, delineation, dose distribution.

1 Introduction

Organs in the thorax undergo variations in position and shape because of respiratory motion, which makes internal safety margins a necessity in thoracic radiotherapy. The current standard ([1],[2]) is the use of margins to optimise tumour control probability based on a population. However, as the tumour deformation and movement does not depend on its size and position ([3],[4]), these general margins are rather imprecise and usually inappropriate for an individual patient ([5],[6],[7]). A better knowledge of patient specific tumour variations can lead to an individual Internal Target Volume (ITV) definition, as recommended by the AAPM task group 76 ([8]). Moreover, applying a certain margin does not give any information on the total dose received by each part of the tumour during respiration. Respiration-Correlated CT (RC-CT) ([9]) is a new imaging modality that opens the way to a more individualised approach for radiotherapy in the thoracic region. It shows promise in observing movements and deformations in the lungs ([10],[11]), but its use in daily clinical routines is, for the moment, restricted because of the time it requires in order to be fully analysed by a physician. Recent efforts to track tumour contours ([12],[13]) and delivered dose in deforming anatomies ([14-19]) have showed that non-rigid registration was a promising tool to deal with such issues.

In this paper, we first propose a "b-spline" registration method ([20],[13],[14]) to define a patient-specific ITV and compare it with a manual contour. Then we discuss the accuracy of the use of the deformation fields resulting from the registration when computing a cumulative dose distribution.

2 Methods

Patients

Thirteen patients with histological or cytological proven non-small cell lung cancer (NSCLC) (UICC stage I-III) were included in this study. The Medical Ethics Commit-
Dose deformation

The deformation of images reflects volume changes which are due to the variation of the amount of air in the lungs. On the other hand, we assume that the total mass of the tissues is conserved throughout the entire breathing cycle. This allows us to define the deformed distribution by applying the displacement fields to the dose map, without worrying about the volume changes. The dose is locally defined at each point of the volume and the integral of the dose over the volume must not be conserved, as opposed to the integral of the energy which is conserved whatever the volume changes. If we make the hypothesis that the displacement fields are a reliable representation of the physical deformations of the lung tissues, we can map the dose distribution from each phase to the reference phase and then track the total dose received by each physical voxel of the tumour ([13],[17]). To do this, the inverse of the field resulting from the registration was computed. This operation was found to be acceptable as it added small errors to the deformation field compared to the accuracy of the registration process itself.

Dosimetric values were estimated for each voxel of the CT image. Previous studies have shown that such a resolution (less than 1 mm pixel spacing in coronal and sagittal directions and 3 mm slice thickness in axial direction) was good enough for a simple trilinear interpolation to be acceptable when deforming the dose distribution.
Figure 1: Registration results (coronal view). Top-left: CT image of a box around the tumour at the reference phase (image to be deformed). Top-center: CT image at reference phase after deformation (result of the registration process). Top-right: CT image at end-inhale phase (image to match). Bottom-left: Difference between CT images at reference and end-inhale phase before registration. Bottom-center: Difference after registration. Bottom-right: CT image at end-inhale phase. Green: Manual delineation at the reference phase. Yellow: Manual delineation at end-inhale phase. Red: Semi-automatic delineation at end inhale phase (after deformation of the green contour).

\[
STD_b = \sqrt{\frac{1}{9} \sum_{i=1}^{10} (g_b(i) - \bar{g}_b)^2}
\]

where \(g_b(i)\) is the gEUD before deformation at phase i, and \(\bar{g}_b\) is the mean gEUD on the automatic CTV delineation before deformation over the 10 phases.

We then compared this to the STD of the difference between the gEUD before and after deformation.

\[
STD_d = \sqrt{\frac{1}{9} \sum_{i=1}^{10} (g_d(i) - \bar{g}_d)^2}
\]

where \(g_d(i) = g_a(i) - g_b(i)\) is the difference between the gEUD after and before deformation at phase i. Finally, for all patients, the mean value of the delivered dose was computed for every voxel of the CTV on the reference phase.

3 Results

Registration and Delineation
In order to visualise the accuracy of the registration, the deformation fields resulting from the registration were first applied to the CT images and then to the manual delineation on the reference phase (see figure 1). Box-plots illustrating at each phase and for each patient the concordance indices between the manual and semi-automatic delineations (method - physician 1 CI) and between the two manual delineations (physician 1 - physician 2 CI) can be seen in figure 2.

The Wilcoxon signed-rank test showed that the method - physician 1 CI was significantly higher \((p<0.01)\) than the physician 1 - physician 2 CI for patient 4, but was significantly lower \((p<0.01)\) for patients 5 and 6. For all other patients there was no significant difference in inter-observer agreement and the method-physician 1 agreement. A view of the resulting ITV for one patient can be seen in figure 3.

Dose deformation
In figure 4, one can see the original dose distribution with corresponding semi-automatic CTV delineation at end-inhale phase (top images) and the deformed dose distributions with the manual CTV delineation on the reference phase (bottom images). Considering the inconsistent CI obtained for datasets of patients 5 and 9, they were not included in this part of the study. The comparison between the inter-phase gEUD variations (as defined in equ.1) and the deformation-induced changes in gEUD (as defined in equ.2) is shown in table 1. Except for two patients with small movement and small inter-phase variation (patients 3 and 4), the changes in dose distribution induced by the deformation were considerably lower than the inter-phase variations. One can see in figure 5 that the dose received throughout the breathing cycle on the CTV does not undergo important variations. Small cold spots can however be seen on the side of the tumour for some patients (see figure 5).
Table 1: Comparison between inter-phase variations in dose distribution and variations between dose distributions before and after deformation. $\bar{g}a$ is the mean gEUD on the 10 phases. $STD_b$ is the standard deviation between gEUD at different phases before deformation. $STD_d$ is the standard deviation (along the 10 phases) of the difference between the gEUD after and before deformation. The last column shows the maximum amplitude of the motion of the tumour center of mass.

<table>
<thead>
<tr>
<th>patient</th>
<th>$\bar{g}a$</th>
<th>$STD_b$</th>
<th>$STD_d$</th>
<th>Maximum movement</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>70.96</td>
<td>0.522</td>
<td>0.079</td>
<td>27.2</td>
</tr>
<tr>
<td>2</td>
<td>70.16</td>
<td>0.260</td>
<td>0.040</td>
<td>20.6</td>
</tr>
<tr>
<td>3</td>
<td>69.26</td>
<td>0.033</td>
<td>0.041</td>
<td>6.0</td>
</tr>
<tr>
<td>4</td>
<td>69.86</td>
<td>0.062</td>
<td>0.074</td>
<td>2.2</td>
</tr>
<tr>
<td>6</td>
<td>69.32</td>
<td>0.319</td>
<td>0.057</td>
<td>7.9</td>
</tr>
<tr>
<td>7</td>
<td>69.86</td>
<td>0.049</td>
<td>0.014</td>
<td>10.3</td>
</tr>
<tr>
<td>8</td>
<td>58.53</td>
<td>0.230</td>
<td>0.064</td>
<td>11.1</td>
</tr>
<tr>
<td>10</td>
<td>70.60</td>
<td>0.134</td>
<td>0.012</td>
<td>6.5</td>
</tr>
<tr>
<td>11</td>
<td>69.52</td>
<td>0.830</td>
<td>0.171</td>
<td>9.0</td>
</tr>
<tr>
<td>12</td>
<td>68.90</td>
<td>0.193</td>
<td>0.053</td>
<td>1.9</td>
</tr>
<tr>
<td>13</td>
<td>69.47</td>
<td>0.230</td>
<td>0.062</td>
<td>4.0</td>
</tr>
</tbody>
</table>

Figure 3: The top images represent sagittal, coronal and axial views of the tumour at reference phase. The red contour represents the union of the GTV at all phases and yellow is after an 20 expansion of 5mm to create an ITV. The bottom images represent the union of all GTV (in red) on the maximum intensity value CT image.

Figure 4: Top: Sagittal, coronal and axial views of the percentage of the prescribed dose in a box around the tumour at phase number 7. In red: CTV of the tumour at that phase. In black: 95% of the prescribed dose. Bottom: Same views of the tumour after deformation towards the reference phase. In red: CTV of the tumour at the reference phase. In black: 95% of the prescribed dose.

Figure 5: Top: Sagittal, coronal and axial views of the mean percentage of the prescribed dose (computed through the breathing cycle by deforming the dose to the reference phase) inside the delineated CTV. A small cold spot can be seen on the right side of the axial view. Bottom: Same views of the standard deviation (through the breathing cycle) of the percentage of the prescribed dose inside the delineated CTV.

Semi-automatic delineations
The first purpose of the method was to perform a semi-automatic definition of an individual ITV based on RC-CT data. We showed that the proposed method was able to estimate tumour motion due to breathing for 11 out of 13 patients. Indeed, the comparison between the method - Physician 1 CI and the Physician 1 - Physician 2 CI showed that the accuracy of the semi-automatic delineations was comparable to inter-observer variability. The assumption that such a method is convenient for daily clinical routines was therefore confirmed for a larger number of patients than previous studies ([12]).

4 Discussion
However, high variability was observed for patients 9 and 12 who had very small tumour only visible on respectively 2 and 4 axial CT slices. Furthermore, the semi-automatic delineations on patient 5 who had a tumour close to the mediastinum led to significantly worse results than the inter-observer variability. This shows that the registration method requires some improvements in such difficult cases.

Since the resulting delineations are dependent on the manual delineation on the reference phase, this delineation is a determining factor for the accuracy of all computed delineations. We can clearly see the advantage of this
method compared to a maximum intensity value segmentation as proposed in [13] in figure 3. Indeed, in the case of a tumour located close to moving tissues of the same intensity in CT images, the lack of contrast between the tumour and surrounding tissues makes segmentation impossible.

Dose tracking

Good results of the semi-automatic delineations and of the dose distribution conservation after deformation showed that the registration was able to correctly represent the deformation. Furthermore, we showed that the movements of tumours in the lungs are smooth enough to be represented by b-spline models, confirming other studies on this issue ([13],[20],[24]). Therefore the computed delivered dose per voxel of the tumour throughout the whole breathing cycle can be assumed to be a good estimation of the actual dose the tumour should receive if there was no setup error. However, to validate the estimation of the delivered dose per voxel, a true voxel tracking should be made using a model incorporating an appropriate physical behaviour ([27]).

Other studies showed that the method did not provide information when considering a PTV- based planning ([17],[18]). In the same way, since the planned dose is in our case uniformly distributed over the ITV, the resulting mean dose distribution did not provide any new information. However if one has the possibility to include setup errors in the computation of such a total received dose (as in dose guided radiotherapy) or if an intensity modulated radiotherapy was to be planned, this method could input much more information into the treatment, such as dose given per voxel, allowing possible adjustments from treatment session to treatment session.

5 Conclusion

We have developed a method to profit from full 4D information for radiation treatment planning. The deformation study first led to the semi-automatic definition of non-uniform margins for an ITV taking into account all phases of the respiratory cycle. This then allowed the estimation of the total dose delivered to each voxel of the tumour throughout the breathing cycle. A possible future application of this dose deformation method in the context of adaptive radiotherapy, would be the adjustment the dose planning according to the deformation between a pre-treatment CT-scan and a CT-scan taken during treatment.

Acknowledgment

We thank Siemens Oncology Care Systems for their financial and technical support. G.Janssens and J.Orban thank the F.R.I.A. for its financial support.

References