Motion compensation for 4D PET/CT

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Chapter 5

CT-based motion compensation of rapidly acquired 4D PET of the liver - a feasibility study

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Abstract

Purpose: PET imaging has become a vital modality for staging of tumour spread and RT planning of liver tumours. The image quality of PET imaging however is restricted by respiratory motion. Respiration induced artefacts can be reduced by the use of 4D imaging. However, since every bin of a 4D dataset is constructed with a subset of the counts, image quality of 4D PET data is limited compared to 3D. The purpose of this study was to test the feasibility of motion compensation 4D PET data, which was acquired in the time-span of a normal 3D PET scan, using a 4D-CT derived motion model.

Materials and Methods: From 12 patients, PET/CT data was acquired in 2 minutes per bed position, whilst a respiratory signal was recorded. From the raw data both 4D PET/CT and 3D PET/CT reconstructions were created. From the 4D CT, a Mid-Position (MidP) motion model was created, which was used to register the 4D PET data. After registration, the PET data was summed, resulting in a 3D MidP PET dataset. This dataset was compared to the original 3D PET data, in terms of image characteristics, $SUV_{max}$ and apparent tumour volume.

Results: We measured an average top-top amplitude of 12.5 mm. On average, the motion compensated MidP PET scans showed an $SUV_{max}$ increase of 3.6% and an average decrease of apparent tumour volume of 10.4%. Furthermore contrast between organs was improved and an improvement of the attenuation correction characteristics was observed, due to phase-by-phase attenuation correction in the 4D PET.

Conclusions: Motion compensation in 4D PET/CT typically leads to sharper data and improved attenuation correction. The size of the lesions on the motion-compensated PET images decreases compared to the conventional, non-compensated 3D PET scan. These results justify testing the technique on a larger patient population.
5.1 Introduction

The liver is a common site for metastases, especially for colorectal cancer. More than 70% of patients with colorectal cancer will develop a metastasis in the liver during the course of their disease [97]. When liver metastases are discovered, surgical resection is the primary choice of treatment. However, liver metastases are only considered resectable when these are limited in size and number, and when the patient is in relative good health and without extrahepatic metastases. Unfortunately, the vast majority of the patients (80% - 90%) are considered inoperable at the moment of diagnosis [98].

When resection of a liver metastasis is not an option, stereotactic body radiation therapy (SBRT) is an established palliative modality with limited side effects and improved quality of life due to high local control [99]. In the process towards the procedure, whole body FDG PET imaging has taken an integral function in staging and delineation of the tumour, due to its high sensitivity and specificity [98].

The liver exhibits considerable respiratory motion, due to its position directly under the diaphragm. On average it has a top-top amplitude of between 13 and 17 mm, but amplitudes up to 50 mm may occur [41, 82]. This motion causes artefacts, due to incorrect attenuation correction [20] and blurring of the tumour activity over the motion trajectory [61]. These artefacts can change the apparent volume of tumours and can even obscure small lesions [100].

A commonly used method to counteract respiratory blurring is 4D PET imaging [61]. By binning the counts according to an external respiratory signal and creating separate reconstructions for each bin, respiration induced artefacts can be minimized. However, since the bins are constructed with a subset of the total dataset, the signal-to-noise ratio (SNR) drops with every bin. Therefore, 4D PET data generally takes considerably more acquisition time to receive good image quality. An alternative to time resolved imaging is to compensate for motion in the data, and create a motion compensated 3D dataset. A variety of motion compensation techniques have been developed, in particular for lung data. These techniques can be divided in a group of list-mode based techniques [71] and techniques that use 4D PET data as input [64].

In this article we describe and test a retrospective CT-based motion compensation technique for rapidly acquired 4D PET data, and evaluate its potential to improve quantitative imaging of tumour lesions in the liver.
5.2 Materials and Methods

5.2.1 Patient data

Between 2011 and 2014, 12 cancer patients (9 colorectal, 2 breast and 1 unknown) who received PET CT as part of their routine treatment were included in this study. All of these patients had strong suspicion of liver metastasis.

An hour before acquisition, the patients were injected with 170-240 MBq of \[^{18}\text{F} \text{ fluoro}\text{deoxyglucose (FDG).}
\]

First a standard 3D whole body low dose CT (40 mAs, 120 kVp, slice spacing and thickness 3 mm, pitch 0.81) was acquired during free breathing. Subsequently, a whole body PET dataset was acquired in two minutes per bed position, during which the respiration was monitored using a bellows belt (Interactive Breath-hold Control System; Mayo Clinic/Medspira, Minneapolis, MN, USA). From this data a normal 3D PET scan was reconstructed, which was attenuation corrected using the 3D CT scan. Finally, a low-dose 4D CT dataset was acquired around the liver region (10 bins, 30 mAs, 90 kVp, slice spacing and thickness 3 mm, pitch 0.085).

In addition, according to the respiratory signal, the PET data was retrospectively sorted into 10 phase bins and reconstructed into a 4D PET dataset. The 4D CT dataset was used to correct for phase-by-phase attenuation in the 4D PET dataset.

All data were acquired on a combined PET/CT scanner (Gemini TF; Philips Medical Systems, Cleveland, Ohio, USA). The PET scans were reconstructed with a voxel size of \(4 \times 4 \times 4 \text{ mm}^3\) and for the CT a voxel size of \(1 \times 1 \times 3 \text{ mm}^3\) was used.

5.2.2 CT-based PET motion compensation

The 4D PET data was not suitable for motion detection, as it has low spatial resolution and provides little anatomical information. Furthermore, since the 4D PET data was acquired in the same time as a normal clinical 3D PET scan, the individual 4D frames suffered from a high noise level.

Since the expected intrafractional difference in respiratory motion is small (less than 2 mm in all directions \[41\]), we used the 4D CT data to derive a motion model. From the 4D CT, the exhale frame was chosen as a reference, to which all other frames were registered using a multi-scale phase-based optical flow method \[63\]. The local deformations were stored in a Deformation Vector Field (DVF). The choice of the reference frame, introduces a systematic positional error. To correct for this, we repositioned the DVF to the average position, the Mid-Position (MidP). According to this MidP DVF, the 4D PET frames were transformed and subsequently averaged over the 10 frames. This resulted in a 3D MidP PET scan, compensated for motion \[77\].

In order to assess the effects of motion compensation without differences in attenuation correction and reconstruction protocol, we also calculated the average of the
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4D PET data, without motion compensation (4D$_{avg}$). To accompany the MidP PET, we also constructed a MidP CT dataset. For this purpose, we transformed the 4D CT data to the Mid-position and calculated the median per voxel [63].

5.2.3 Image Analysis

Tumours were identified visually on PET. We measured the maximum SUV (SUV$_{max}$) within each individual lesion, for the normal 3D, the 4D$_{avg}$ and the MidP PET.

Since lesions in the liver are surrounded by considerable background activity, we are also interested in the contrast between the lesion and its background. For this, we manually selected a large part of the centre of the liver that did not contain any tumour. Here we measured the average liver uptake (SUV$_{liver}$) and the standard deviation in this region. The difference between SUV$_{liver}$ and SUV$_{max}$ was used to define the SUVcontrast of each individual tumour with its background for both the normal PET and the MidP PET. To automatically segment the lesions, we used the average of SUV$_{max}$ and SUV$_{liver}$ as a threshold. We used the resulting volume to give an indication of the apparent size of the lesions. Within this delineation we measured the average respiration motion in the DVF.

Besides these qualitative analyses, we visually assessed the quality of the motion compensated scans in comparison to the normal 3D data. We assessed the shape of the lesion. We also looked at the sharpness of the lung interface of the liver dome and the homogeneity of the uptake in the upper region of the liver. Furthermore we assessed the contrast between the individual organs.

5.2.4 Results

The reconstruction of the 4D PET data failed for 4 patients due to technical issues during image acquisition or reconstruction. In one patient tumour had spread throughout the entire liver. It was therefore not possible to identify individual lesions and perform analyses.

We performed analyses on the remaining 8 patients. One patient presented 3 individual lesions. In 4 patients, 2 lesions were visible and 3 patients had 1 lesion. This resulted in a total of 14 evaluable lesions. Table 1 gives an overview of the results. The detected lesions moved on average with an top-top amplitude of 12.5 mm. SUV$_{max}$ was on average 3.6% higher in the MidP PET, compared to the 4D$_{avg}$. The difference in contrast between these two was 6.2%. No clear SUV differences were found in comparison to the 3D PET. The size of the tumours was 5.6cc on average. The volume measured on the MidP PET was on average 5.6% smaller than measured on the 4D$_{avg}$ PET and 10.4% smaller than on the 3D PET.
Table 5.1: An overview of the average amplitudes and the average offset and the absolute distance of the Mid-Position. Between brackets the standard deviation is provided. These measurements were performed for the tumour and the diaphragm of the ipsilateral lung. The offset between the A-MidP-CT and P-MidP-4D-CT are reported in millimetres and in percentages of the amplitude.

<table>
<thead>
<tr>
<th>Pat.</th>
<th>Indication</th>
<th>Amp. (mm)</th>
<th>SUV&lt;sub&gt;max&lt;/sub&gt;</th>
<th>SUV&lt;sub&gt;liver&lt;/sub&gt;</th>
<th>Volume (cc)</th>
<th>ΔSUV&lt;sub&gt;max&lt;/sub&gt; (%)</th>
<th>ΔSUV_contr (%)</th>
<th>ΔVolume (%)</th>
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<td>#1</td>
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<td>7.7</td>
<td>2.4</td>
<td>1.2</td>
<td>4.0</td>
<td>7.8</td>
<td>11.4</td>
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<td>#2</td>
<td>mamma</td>
<td>22.1</td>
<td>6.7</td>
<td>*</td>
<td>1.7</td>
<td>6.3</td>
<td>6.3</td>
<td>-11.3</td>
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<tr>
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<td>11.3</td>
<td>11.6</td>
<td>2.4</td>
<td>2.1</td>
<td>14.1</td>
<td>4.5</td>
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<td>13.0</td>
<td>*</td>
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<td>11.1</td>
<td>11.5</td>
<td>-15.5</td>
</tr>
<tr>
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<td>4.7</td>
<td>2.2</td>
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<td>8.0</td>
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<td>3.6</td>
<td>0.8</td>
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We found small differences between the $\text{SUV}_{\text{liver}}$ intensities in the MidP PET and the 3D PET. The average absolute difference was 2.4%. We did not see major differences between the SUV$liver$ of the MidP PET and the 4Davg PET. We also did not see any significant differences in liver background standard deviations between the 3 datasets.

We found a borderline significant relation ($p=0.08$) between the SUV$_{\text{max}}$ differences between the MidP PET and 4D$_{\text{avg}}$ PET and the tumour top-top amplitudes, as can be seen in fig. 5.1. We could not find such a relationship between MidP PET and 3D PET.

![Figure 5.1: A borderline significant ($p=0.08$) relation was found between the amplitude and the SUV$_{\text{max}}$ difference in the 4Davg-PET and MidP-PET.](image)

In fig. 5.2 some examples of the differences between MidP PET and 3D PET are provided, as well as an example of a MidP CT and a 4D CT frame (fig. 5.3). The motion compensation counteracted the effects of motion blurring, resulting in more focussed uptake and smaller lesion volumes. The reduction in blur also provided better contrast between the liver and surrounding structures, such as the kidneys. The 4D attenuation correction resulted in a better definition of the interface between liver and lung at the diaphragm. This boundary was sharper due to a decrease of blur.
Furthermore, we saw a more homogeneous distribution of uptake in the top of the liver due to the improved phase-by-phase attenuation correction.

Figure 5.2: Three patient examples of differences between 3D-PET (top) and MidP-PET (bottom). In Patient #1 (a) (d) is clearly visible that apparent tumour activity is more focussed after motion compensation. In Patient #4 (b) (e) we see a decrease in tumour activity after motion compensation (bottom). However, paradoxically, the separation of the liver with the nearby kidney became better defined. In Patient #5 (c) (f), similar effects were visible, but also the attenuation correction characteristics were improved at the liver-lung interface in the MidP data (bottom), resulting in a more homogeneous uptake distribution in the top of the liver.

5.3 Discussion

In this article we have demonstrated the feasibility of respiratory motion compensation of hepatic 4D PET data, which was acquired in the time-span of a normal 3D PET scan, by means of a motion model that is derived from the corresponding 4D CT. This yields on average an increase in both SUV_{max} and contrast, and a decrease in tumour volume.

Motion compensation for hepatic PET data is relatively novel. Until now, this has only been described for MR/PET [101]. The main advantage of tagged MR based
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Figure 5.3: A coronal example (Patient #1) of frame from a 4D CT scan, registered to the mid-position (a) and a 3D MidP scan (b). It is visible that the SNR is higher in the MidP scan.

motion compensation is that location specific tagging of the MR signal provides artificial contrast, resulting in more reliable motion models. However, combined MR/PET scanners are still in development and limited in number. Therefore, CT-based options are very valuable.

4D motion compensation for PET/CT is not new. A range of methods have been developed. However, most methods have only been tested on pulmonary data [71, 77, 100]. Image based motion detection on hepatic CT data is considered more difficult, due to lack of contrast, but not impossible [82, 95].

Since respiratory liver motion is larger than lung motion [42, 99], the benefits of motion compensation are likely to be larger for the liver. This is confirmed by research on MR-based motion compensation of PET data [101]. In our dataset, we found an average tumour top-top amplitude of 12.5 mm, which was somewhat smaller than the average motion described in literature [41]. Compensation of this motion led to an increase in image quality in most of our data. It led in general to sharper data, improved attenuation correction and better definition of organs, as illustrated in fig. 5.2.

The differences between the 4D_{avg} PET and the MidP PET were, as expected, dependent on the local respiratory amplitude. With amplitudes smaller than 1 mm, motion compensation sometimes led to negative effects SUV and tumour volume effects. This can be explained by the registration uncertainty. In an earlier study, we found uncertainties of about 2 mm [82]. For this study, we have minimised the CT
dose level. This resulted in considerably more artefacts (fig. 5.2), which may have compromised the registration accuracy.

Analyses of the non affected regions of the liver did not show large SUV differences between the 3D PET and the MidP PET. The tumour SUV$_{\text{max}}$ differences between 3D PET and the MidP PET were however not very predictable. An important reason for this could be the different attenuation correction strategies of both methods.

Our study was limited since only 12 patients were included, of which 4 needed to be excluded and one was not suitable for analyses. Nonetheless, our data show that motion compensation leads to sharper PET data. Furthermore, we found improved contrast between organs and improved attenuation characteristics at the lung interface. These potential benefits of CT-based motion compensation on hepatic data justify further research in this direction.

### 5.4 Conclusion

Motion compensation for PET/CT imaging of liver lesions typically leads to better signal-to-background contrast and sharper images. The phase-by-phase attenuation correction of PET data improves appearance of the liver dome. These results imply a potential for better quantitative measurements and justify development of the technique and evaluation in further studies.