Chapter 2

Problem and proposed solution

In this chapter the problem to be solved will be formally stated, the existing approaches to it will be overviewed and an own solution proposed.

2.1 Problem statement

In hybrid PET/CT thorax imaging with two separate detectors connected in conjunction and sharing the same bed, the CT can be acquired really quickly with modern machines. The newest CT scanners can acquire images in less than 0.5 seconds. If the whole area of interest is within the equipment's field of view, this would be the total acquisition time. In order to cover a larger region, the couch is shifted and the operation repeated as many times as necessary. The patient is usually asked to stay in breath-hold position, so that the different images are acquired at (approximately) the same lung tidal volume (current air volume in the lungs minus the minimum possible value, which is not zero liters) and can be assembled easily.

Due to the detection geometry and the inherent acquisition nature of PET, images cannot be taken instantly. An average PET study is done over a period of 10-15 minutes [28], during which the patient breathes. This results in a certain diaphragmatic motion and hence image blurring. This involves a loss of both resolution and accuracy in a possible posterior fusion process.

This movement is for example especially critical in conformal radiation therapy, when the goal is to deliver high doses to a volume that conforms with the shape of the target tumor (BTV, biological tumor volume), no matter that it may be close to radiosensitive healthy tissues. Image blurring leads to errors in the standardized uptake value (SUV, which is important in order to determine a lesion's malign or benign character) and thus in tumor size,

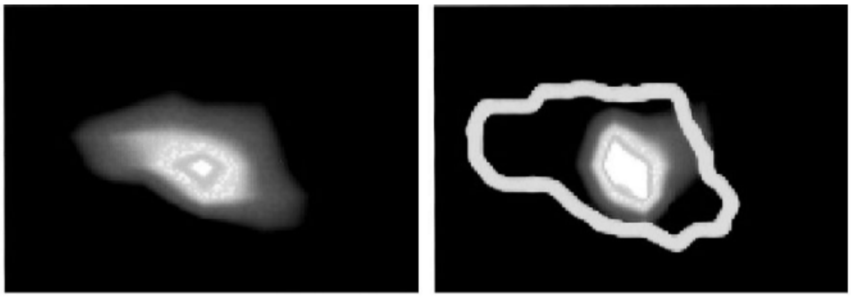

Figure 2.1: PET Simulations from a) a moving tumor and b) the same tumor but still. The area the tumor covered in the first image is marked on the second one.

and it also causes contrast loss.

Not being sure about the exact extension of a tumor forces one to cover a bigger volume than desired if the purpose is to radiate the whole cancer, and hence damaging more healthy tissue than desired. Or maybe it will not be possible to cover the whole tumor because of the impossibility of affording to radiate the healthy tissue around it (figure 2.1).

The purpose of this thesis work is to evaluate a novel method for correcting this unwanted blurring by means of a software correction.

2.2 Existing approaches

One of the possible ways of eliminating the effects of motion on the image is to make the patient stay in breath-hold position, with voluntary or imposed techniques. This is not feasible for a PET study (a typical length is 20 minutes), and even not always possible for CT or radiotherapy treatment because many patients cannot tolerate holding their breath [29].

One suggested method to overcome this limitation has been through respiratory gated PET [30] [31]. The PET is hence gated, using an external device such as spirometer or a passive reflective marker recorded by a camera. The coincidences around just a certain respiratory phase are considered for reconstructing a time frame. The cycle was divided in ten stages in the cited study PET [30], leading to ten different images. The problem with this technique is that, if one wants to keep the PET statistics (number of coincidence events), one has to multiply the scan time by the number of phases (assuming that the patient stays approximately the same time in each phase).

Even with the fastest PET scans, gating results in a too long acquisition time, which may even spoil the statistics for certain isotopes, due to their decay process. A too long time also reduces the patient throughput, which is of course undesirable. It must also be said that these scanning times are becoming smaller and smaller, though. The UCLA Department of medicine [32] has been able to acquire a PET image in 3 minutes, but the study has not been published yet.

Another possibility is to gate and still use all of the coincidences, but transforming their position according to the estimated motion before they are fed to the reconstruction algorithm. In [33], they correct the heart's motion due to respiration. They reconstruct the gated PET images for every phase. This data is pretty noisy (small acquisition time), but still good enough to estimate the parameters for a simple linear rigid-body transformation. These transformations are then applied to the coincidence pairs (in the projection domain), depending on the phase in which they were recorded. The final image, which considered all of the events, was then reconstructed.

The solution in this thesis will be based on this last algorithm, but with three differences. The first one is that a much more complex transformation will be used, as the effects of respiratory motion around the lungs cannot be modelled with a simple rigid-body transform, which appeared to be sufficient for the heart. The second one is that CT images will be used in order to estimate the transformation parameters between the different phases. As the transforms will be much more complicated, better quality images, with much more information, are required. The last difference is that, as the projection data is not available, the reconstructed volume for each phase will be used, compensating them and superimposing them.

2.3 Proposed solution

The proposed solution is based on the availability of a set of respiratory gated CT images and a set of PET data gated in the same manner. It will be assumed that there are no motion artifacts in the CT images. One can thus assume that it is possible to reconstruct "perfect" volume images for certain tidal volumes. This assumption is of course not true, as the CT acquisition time is not zero but half a second. There are proposed solutions to compensate this [10], but no compensation algorithms will be applied on the images in this thesis, as the respiratory cycle is slow enough (around 4 seconds) not to make the CT images very blurry (check figure 2.2).

Before finding any final solution to the problem, it is important to evaluate and analyze the extent and the behavior of the respiratory motion. In [34], a gold implant is placed in a tumor and tracked in order to study the tumor

Figure 2.2: Sample CT transverse slice from healthy lungs. The image is sharp.

motion in a lung cancer case. An important result from the study is that the trajectory of the tumor is approximately constant during the study (although it may differ in different days).

The extent of the motion was measured to reach almost 3 cm in some cases, being the time-averaged position close to the exhale position, and showed an hysteresis of 1-5 mm in around a 50% of the cases. This suggests that one should avoid stacking images from different couch positions at similar tidal volumes if they are not also in the same respiratory phase (inhale, exhale).

This study also showed that cardiac motion was yet another source of blurring in tumors located close to the aorta artery or the heart. The dynamics of this motion are too fast (a typical rest heart rate is 60Hz) to be studied with CT:s taken every 0.75 seconds. However its effect is a tumor motion with an amplitude of 1-4 mm in only 7 out of 20 patients, which will be regarded as negligible.

The solution's flow diagram is depicted in figure 2.3. The first step to find a solution is to analyze the behavior of the respiratory motion based on the CT/spirometer data set. The characteristics of the respiratory motion for a single case will be quantified, following it during several cycles and calculating a similarity measure between the images, to find out that the acquired CT volume is directly dependant on the tidal volume.

The second step would be to evaluate the possibility of co-registration of images acquired at different respiratory phases, that is, finding out the transformations from one image volume to the other one. Since the PET and

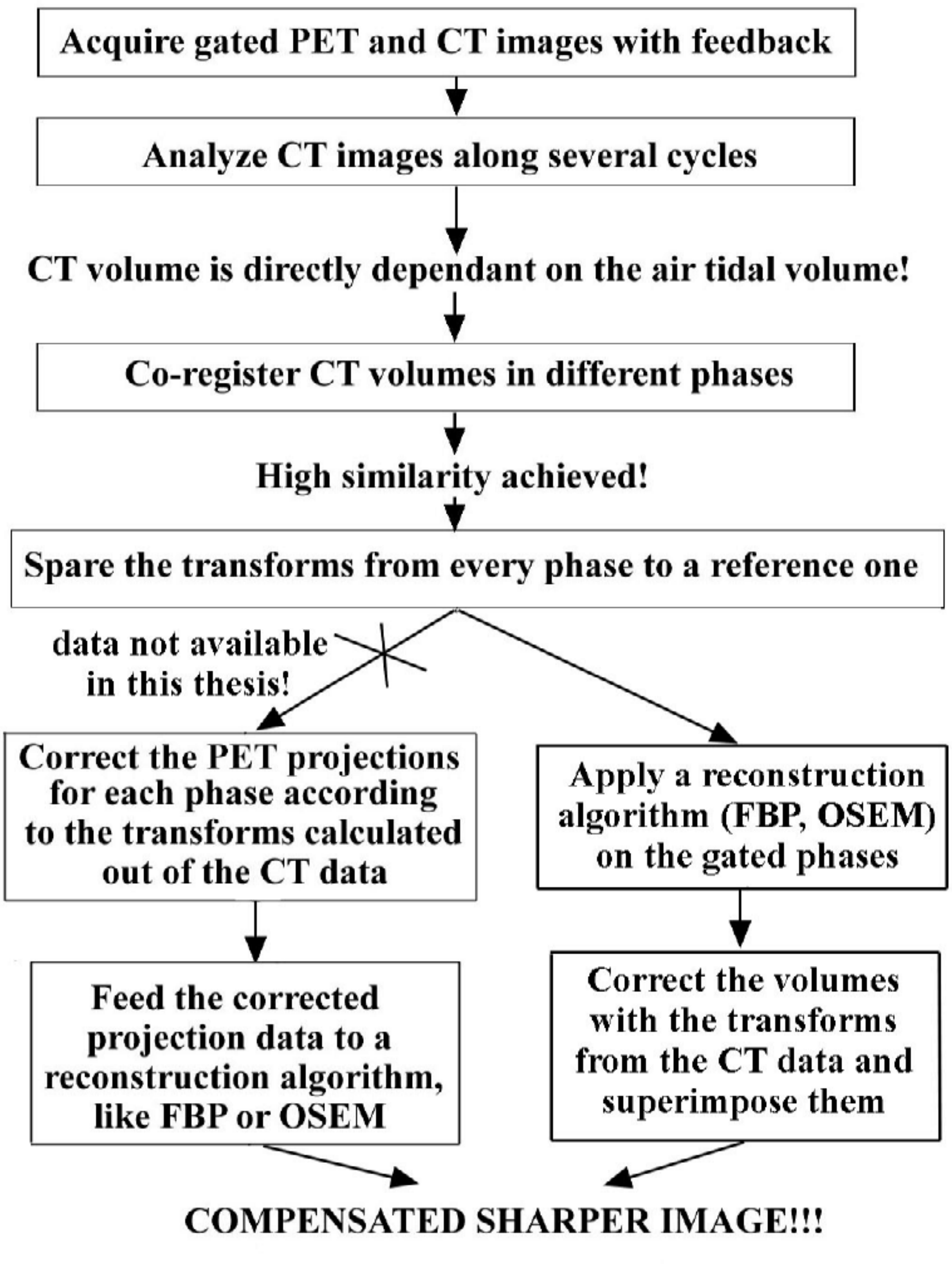

Figure 2.3: Solution flow diagram

CT data are intercorrelated, it should be possible to use the transformations obtained from the CT on the PET images afterwards.

Once it is possible to co-register the images and measure their similarity (mean square, crossed-correlation, or mutual information measures), the process will be repeated in order to be able to transform the image volume from any respiratory phase to a reference one, that could be the one in which the region of interest (ROI) is better appreciated. This possibility is of utter importance, as already mentioned, in radiation therapy planning. In that case there might be an optimal respiratory phase where an optimum benefit with most injury to the tumor and least damage to the healthy tissue might be achieved.

It will be assumed, as said before, a direct dependance between respiratory phase and image volume. In [35] it is shown that the breathing cycle varies a lot from time to time, but it can be kept fairly constant with audio or audiovisual feedback techniques. An even though the patient may breathe with a different frequencies and amplitudes at different times during the study, it is assumed that it is only the air volume in the lungs and not the frequency that determines the image volume. It is shown in [36] that this assumption does not lead to big errors.

It would also be important to study in how many discrete phases the respiratory cycle has to be divided in order to get good results. It would be desirable to accurately represent the movements with as few CT images as possible, as every CT image radiates the patient as much as around 100 conventional X-ray ones [37].

Once the relationship between the CT images is determined, an attempt of translating it to the PET data will be performed. The idea is to apply to the PET data the same transforms that were found out for the CT data. This is possible because, as it is shown in [38], respiratory motion is consistent between the PET and the CT sessions. The patient's collaboration is very important to achieve this consistency, anyway. In the same study, audio prompting was used to regularized breathing.

There are two ways of applying the transformations on the PET data. The first one is to reconstruct different gated projections and then superimposing the images in the spatial domain. This will be tested with the data from [28]. The second way would be to modify the transforms and apply them directly on the projection domain. As no gated projection data was available, this option was not investigated in this thesis.

The goal of the two approaches described above is to keep the 100% of the PET statistics. Thus, one expects to get a sharp PET image. Registering and fusing the gated PET images directly involves working with already low quality (statistically speaking) images.

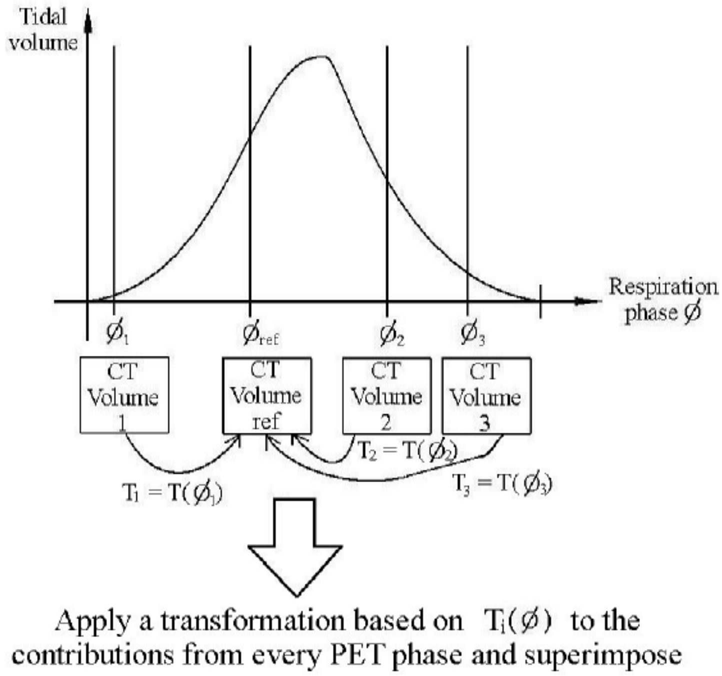

Figure 2.4: Solution scheme

If the transformations were applied on the projections, the way of transforming the data would depend on the reconstruction algorithm that is employed. If for example FBP was used, it would be possible to deform the lines of response (LOR) with the estimated transforms in order to recalculate compensated values for the counts in every detector. The usual FBP algorithm could then be applied.

The solution is summed up in the scheme in figure 2.4.

2.4 Materials and methods

2.4.1 Materials

This work will be based in the data from [36], available at the Medical Radiation Physics (MRF) department at Karolinka Institutet (KI). In that study, a four-slice CT scanner was used to scan three lung cancer patients while their lung tidal volumes were measured with a spirometer. The images were acquired every 0.75 seconds, with an acquisition time of 0.5 seconds. Almost 20 couch positions were used in order to cover the whole thorax, and 15 scans were performed in each position.

In [36] it is shown that stacking images from the different couch positions closest to the tidal volume of interest (as there were not CT images available for all the possible volumes) is an accurate representation of the volume with this specific acquired set of images. It would be even better to gate the CT to have images from exactly the desired phases (or almost), as it is done in [39] and [28].

Even if such data sets are currently difficult to find, it was possible to borrow some real gated PET/CT data from [28]. In that study, the PET data is gated and 10 different PET images corresponding to different respiratory phase intervals reconstructed.

The last images used for testing the different algorithms were generated with the NCAT 4D phantom [40]: a model of the human anatomy that lets the user generate different volumes of a fictitious patient in different respiratory phases.

2.4.2 Methods

Regarding the registration framework component choice, introduced in the first chapter, the following elements were selected:

1. Feature space: as the compared images belong to the same modality, are acquired by the same machine in the same conditions and in close time instants, using the raw voxel data seems the best option for the used data set application. It may lead to a complex registration process, but as the main goal is the matching quality (within a reasonable processing time, of course), the space that contains more information should be used.

2. Search space: choosing the right space is one of the main goals of this master's thesis. The simplest possibilities will be tested first and then the algorithm complexity will be increased until a satisfactory result is obtained, always keeping an eye on the processing times. Anyway, as it is stated in [41], any registration algorithm to be applied for motion correction of thoracic images must take into account that the tissues and organs deform in a nonrigid fashion. It could a priori be thought that global transformations will not work properly (maybe high order polynomials), and that a locally applied algorithm or elastic registration (demons algorithm) will be required. As it has already be mentioned, frequency domain techniques have been discarded from the beginning because they do not offer any kind of local possibilities.

3. Search strategy: the choice of the optimization strategy will depend on the search space. The recommendations at the ITK guide will always be followed.

4. Similarity metric: as previously mentioned, the volumes to register are acquired in very similar conditions, and the corresponding voxels in different images should have very similar values. That is the reason why the squared sum of intensity differences (SSD) or the normalized cross-correlation (NCC) criterion will be utilized: their performance will be good without compromising the computational expense.

2.4.3 Software

The different pieces of software used in this master's thesis, all of them running under Windows Server 2003 Standard Edition, were:

1. Matlab 7, for general computations and some easy image processing.

2. The C compiler gcc 2.95.3, running under CygWin.

3. The MinGW 4.2 C++ compiler.

4. Insight Toolkit 2.0.1, package for C++, very powerful for programming registration algorithms. One can freely combine different cost functions, transforms, interpolation and optimization methods in order to create many different registration methods.

5. The AIR programs, from the UCLA University , that cover ITK's lacks when it comes to polynomials.

6. The NCAT phantom 1.13, that lets the user generate different time frames of a virtual breathing patient.

7. The Qt 4.0.1 package for C++, for programming an own image viewer.

8. UGviewer, an own medical image viewer programmed in C++ / Qt.

9. MRICro 1.39, another medical image viewer.

10. Paraview 2.2, still one more viewer, very suitable for visualizing 3D deformation fields.

11. Texmaker 1.2.1, Latex language editor, for writing this report.

12. MikTex 2.4, Latex language implementation.

2.5 PET/CT prototype based on the proposed solution

In the case of the proposed solution being good enough, a PET/CT scanner incorporating it would perform the following steps:

1. Acquire some CT images from the patient at the same time as spirometer tidal volume measures, or another breathing indicator, as in [39](an analysis of the performance of different indicators is currently being performed at [42]). Feedback can be used in order to keep the respiration process approximately stationary.

2. Calculate the parameters that transform any respiratory phase to the reference one, that might be chosen by the doctor or just be the breath-hold one (as the tidal volume is maximum and the organs are in average more separated from each other).

3. Shift the bed from the CT to the PET scanner.

4. Acquire the respiratory gated PET projection data, based in the same indicator and phases as in the CT.

5. Reconstruct the gated PET data for every phase. Each volume can then be referred to the reference phase by applying the transforms calculated from the CTs. The final image can finally be built by superimposing these corrected gated PET volumes.

Alternatively to the last step, it could be possible to correct the PET projection data towards the reference phase (adapting the transforms from the spatial to the projection domain), and then feed the corrected projections to a reconstruction algorithm. This possibility is not evaluated in this thesis due to the lack of projection data.