Validation of real-time intensity based 2D/3D registration for image guided radiotherapy

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Abstract. Patient motion during radiotherapy or intra-fractional motion, is one of the major sources of uncertainty in dose application. 2D/3D registration is an intensity based method used successfully to track tumor motion with the potential to reduce uncertainty. Despite promising results, validation remains a problem due to the lack of a gold standard. In this paper, we demonstrate the use of clinical datasets acquired with the VERO LINAC to validate intensity based 2D/3D registration. The patient considered in this study had a gold marker implanted to enable live tumor tracking. We verify our results against the tracked gold marker position. Our results show that it is possible to accurately track the tumor using only intensity based 2D/3D registration. The mean error of our registration is of $1.6 \pm 0.3mm$ and as low as $1.1 \pm 0.5mm$ when looking only at the cranial-caudal direction. The results pave the way for a possible clinical application of the method.

Keywords: 2D/3D registration, motion tracking, radiation therapy, validation

1 Introduction

Tumor motion during radiotherapy treatments is one of the main factors of uncertainty in dose application. To account for this uncertainty the planned target volume (PTV) has to be enlarged in order to cover the tumor with sufficient dose to achieve local control [6] typically leading to increased dose delivery to organs at risk (OAR). In the case of lung tumors, breathing is the main cause of motion, but depending on the tumor location, other factors such as heartbeat can also contribute.

Motion management can be done by tracking the tumor position during treatment in order to reduce the uncertainty. Among the approaches used to track tumor position, intensity based 2D/3D registration [8] particularly using fluoroscopy has shown good results in dealing with periodical and aperiodical motion patterns present in this type of treatment [4][3]. Despite the promising results, the lack of a gold standard to validate registration results has so far limited the applicability of the technique.

Clinical treatments performed with the VERO linear accelerator (LINAC) use a hybrid approach to manage tumor motion [2]. It relies on a breathing motion model constructed with fluoroscopy data, chest marker tracking and periodical model updates again using fluoroscopy. A similar approach is also used with the CyberknifeTM system[1]. In both cases, the patients have gold markers implanted in or near the tumor, providing a very reliable way to detect the tumor position using a pair of orthogonal kV x-ray images.

In this work we aim to validate our intensity based 2D/3D registration framework by using datasets collected from clinical treatments with the VERO. We used the markers present in the images as the gold standard tumor position and compared these with the results of registration. To our knowledge this is the first of this kind of validation. The results are very promising and are the first step towards a clinical implementation of purely intensity based tracking methods.

2 Materials and methods

2.1 2D/3D registration

Intensity based 2D/3D registration methods are a widely used approach in image-guided interventions and also in the particular case of image-guided radiotherapy (IGRT). It is an optimization process which aims to find the spatial transform for a volume dataset of the patient that generates a digitally reconstructed radiograph (DRR) that best matches a real x-ray image acquired during treatment. In our method, the first step consists of generating a pair of DRRs from one of the phases of the planning 4DCT. The initial transform or initial guess for the first generated DRRs is defined manually, by trying to align the CT as best as possible with the patient tretment position. The DRRs are then compared to an x-ray pair acquired during treatment by means of a merit function. An optimizer searches for the rigid spatial transformation T generating the best match between the DRRs and the x-rays. The final translational and rotational parameters $(t_x, t_y, t_z, \omega_x, \omega_y, \omega_z)$ represent the tumor displacement.

DRR generation is the most time consuming step therefore we used raycasting implemented on a general purpose graphics processing unit (GPGPU). We used normalized mutual information [7] as the metric function. The merit value is the combined (added) value of each of the x-ray/DRR pair merit. Finally, for the optimization we used the NEUWOA algorithm proposed by Powell [10].

2.2 Image datasets and Image preprocessing

For the evaluation, we used image data from one patient undergoing routine treatment with the VERO LINAC. The data consists of a 4DCT and pairs of

2D x-rays taken during irradiation for six treatment gantry angles. There are two x-rays sources which are respectively at -45 and 45 degrees from the treatment beam. The images are taken as simultaneous pairs at a rate of 0.5 Hz. We had between 12 and 20 image pairs per gantry angle. The patient had one Visicoil gold marker of 0.75mm diameter and 10 mm length implanted in or near the tumor. Markers are clearly visible in all x-rays and provide a gold standard location of the tumor. The marker locations were manually annotated in each of the x-rays. Apart from the gold markers, the patient had also six spheres attached on the chest wall for the purpose of chest motion tracking during therapy. The gold and chest markers seen in the x-rays were masked out by means of a region of interest (ROI) mask in order not to bias the registration procedure. For each of the 2D images the ROI mask consisted of three parts: a) a rectangular region, defined manually, selecting the area of the images where the motion can be considered rigid, b) circular regions, excluding the chest markers, detected using the hough transform for circles and, c) regions around the gold markers, extracted using thresholding and region growing. Figure 1 shows an example of the x-ray pairs, the process of ROI generation and the final images used in registration.

For the DRR generation one of the phases of the 4DCT was used, in particular the phase at 0%, corresponding to maximum inspiration. There was no specific criteria for this choice. The chest and gold markers should also not appear on DRRs and therefore, these markers were removed from the CT used for DRR generation. Figure 2 shows an example for one of the datasets used with a 3D rendering showing the markers on the chest, a CT slice where the gold marker and one of the spheres is visible and the same slice with the markers removed.

2.3 Evaluation methodology

The evaluation assessed the mean registration error of our 2D/3D intensity based method using the gold marker center of mass position as the gold standard position. The registration was performed in 3DOF (t_x, t_y, t_z) for all x-ray pairs and for all gantry angles available. We calculated the RMS registration error in all three directions separately and the 3D RMS error defined as the Euclidean distance between the two points, gold marker and 2D/3D registration position.

3 Results

Table 1 summarizes the results for all gantry angles. The table shows for each angle, the translation error in each axis, the total magnitude of the error defined as the difference between both points (2D/3D and marker position) in 3D space and the registration time. The error when looking at the individual axis is of $0.8 \pm 0.4mm$ for left-right (LR), $1.1 \pm 0.5mm$ for cranial-caudal (CC) and $0.8 \pm 0.3mm$ for anterior-posterior (AP) directions respectively. The total error is of $1.6 \pm 0.3mm$ and the mean registration time is of $0.96 \pm 0.23s$.

Figure 3 shows in the first three columns, plots of individual registration results compared with marker positions for each x-ray in a sequence, for the LR,

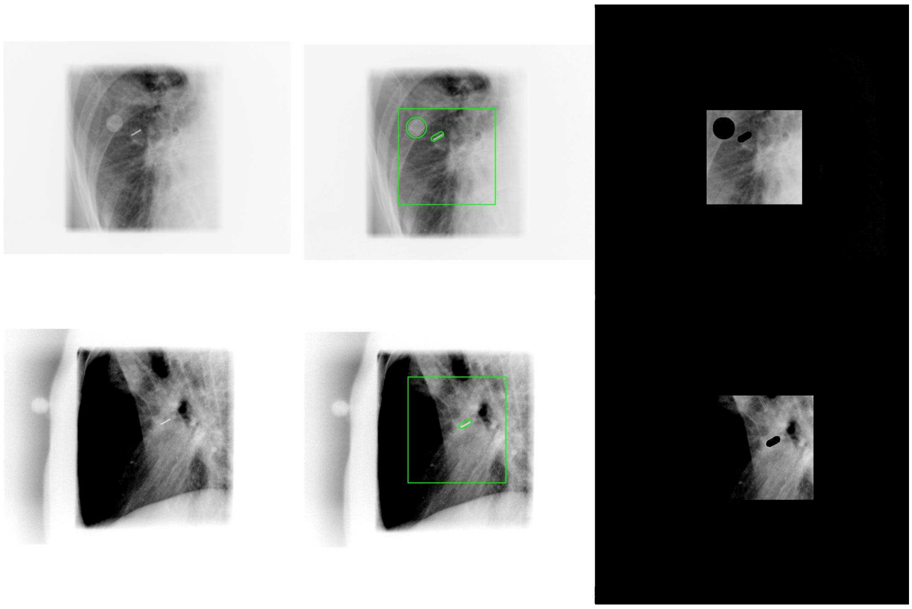

Fig. 1. Example x-ray data acquired during treatment at gantry angle 139. The two rows show x-rays from imager 1 and 2 which are orthogonal. The first column shows the acquired x-rays where the gold and chest markers are well visible. The second column illustrates the process of ROI definition, with a rectangular region defined manually, the chest marker extracted with the hough transform for circles and the marker with thresholding and region growing. The third column shows the final x-ray pair used in registration. The pixels in black will not be used in the merit function calculation.

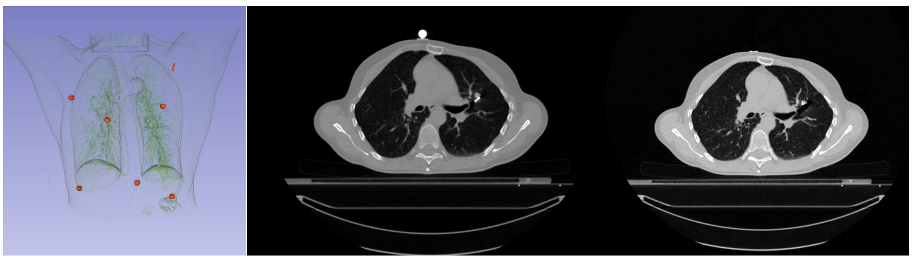

Fig. 2. Example of patient 3D image data. On the left we show a volume rendering of the dataset where the chest markers are very well visible. On the center we show a slice of the CT where both one of the chest markers and the gold marker (on the left lung, right side of the image) are visible. On the right, we show the same slice with the chest and gold markers removed. This last dataset was used for DRR genaration.

CC and AP directions. In almost every case, motion extracted with registration correlates very well with the gold marker motion. Exceptions are when the amplitude of the motion is too small as compared with the typical registration error. Good correlation is particularly visible in the CC direction where the motion amplitude is more significant. This is in accordance with the results shown in the table where the lowest errors are in this direction. The fourth column shows plots the total magnitude of the spacial error for each of the x-rays.

	RMS error (mm)				Registration time (s)
Gantry angle (deg)	t_x	t_y	t_z	Total	
24	1.5	0.4	0.8	1.8	0.8
105	0.6	0.8	0.9	1.3	1.1
139	0.8	1.5	1.2	2.1	1.3
179	0.6	1.5	0.6	1.7	0.7
205	0.5	0.8	0.8	1.2	0.8
329	0.5	1.5	0.4	1.6	1.1

Table 1. Summary of the results: for each gantry angle we show the RMS error in translation for each of the axis, the total RMS error and the registration time.

4 Discussion and Conclusions

Motion management is of high importance in radiotherapy of lung tumors. The use of a method such as 2D/3D registration able to track the tumor is of special importance. Tracking of surrogate structures such as the diaphragm might not yield accurate results as the tumor motion correlates with the diaphragm motion in phase but not in amplitude [5] and can even be in opposite phase [3].

Our results show that 2D/3D intensity based registration is a feasible approach to manage tumor motion. As seen in table 1 the registration error is quite small. This is especially significant for the CC direction which is the direction where motion amplitude is higher than in other directions. Also, looking at the plots of figure 3 we can see that the motion extracted by registration correlates very well with the gold standard marker motion. This finding is clinically relevant, meaning that the low error from markerless tracking is a good tradeoff against possible complications imposed by implanted markers [9].

Another very important finding, is the fact that registration works equally good for every gantry angle. This seems to suggest that for cases where the tumor is not so well visible in one of the panels, the image from the other panel compensates for the missing information helping to achieve a good result.

These results are still preliminary and a much larger study - which is already underway - has to be undertaken to assess their validity. For the future we plan also to perform registration in 6 DOF verifying rotation extraction by annotating the marker end positions and calculating the gold standard rotation in space.

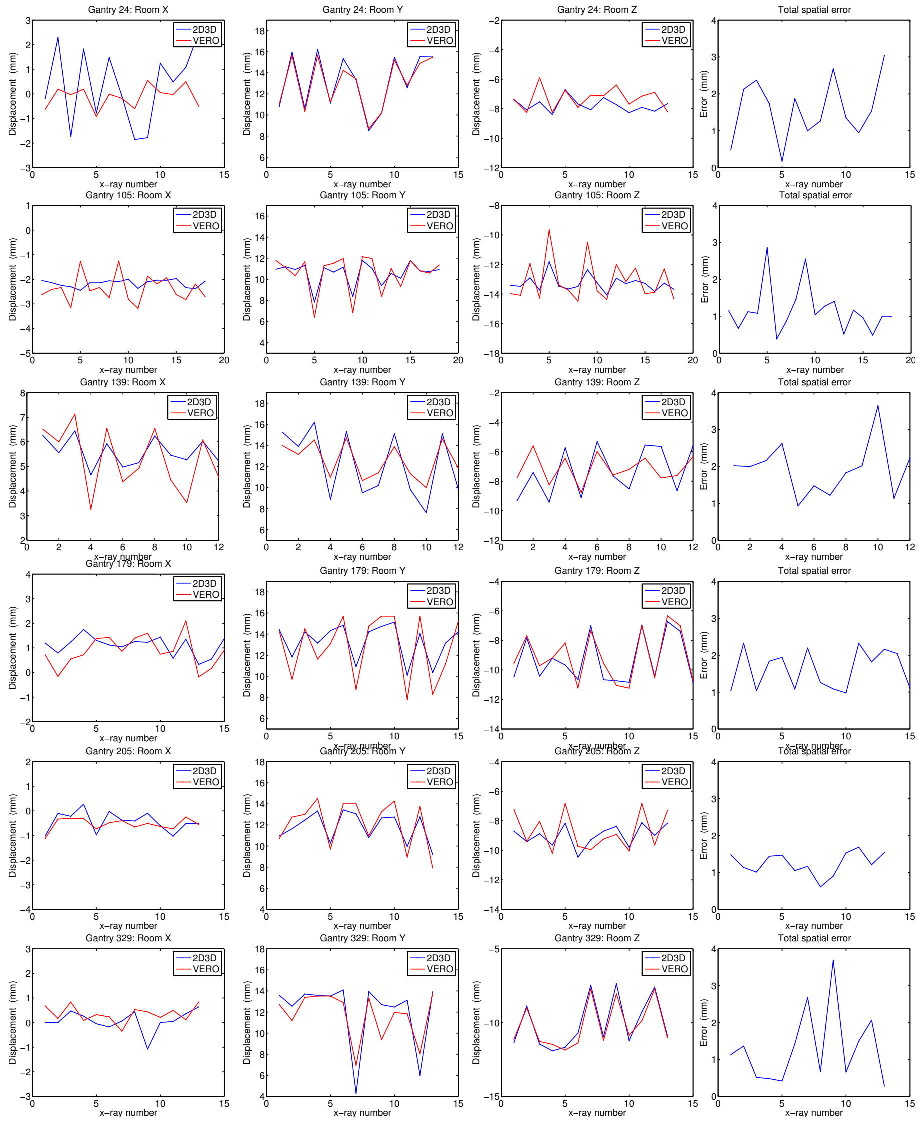

Fig. 3. Plots of the 2D/3D registration extracted tumor motion versus the gold standard motion for each of the gantry angles in the treatment for one patient. The blue lines represent registration results and the red lines the gold standard position along X (first column), Y (second column) and Z (third column) axis in room coordinates. The last column shows a plot of the total error for each x-ray pair in a sequence.

Registration times are proportional to the number of pixels within the ROIs. In this case, since the images are of high spacial resolution and the ROIs quite large, the registration times are consequently relatively high. Nevertheless, they are always lower than the image acquisition rate. Increased use of GPU processing not only for the ray-casting but also for the merit function calculation, is expected to result in a reduction of the processing time.

Despite the preliminary nature of the results, they indicate a clear trend towards the validity of purely intensity 2D/3D registration based tracking for tumor motion management providing a first step for a clinical implementation.

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