

Challenges in the registration of serial CT images from lung radiotherapy patients

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Abstract. Radiation induced lung damage is an unwanted side effect of curative radiotherapy. Radiological findings are often used as indicators of lung damage, which is identifiable as changes in the baseline imaging features (e.g., anatomy shape, intensity and texture). In this work we qualitatively investigate the challenges in registering baseline and follow-up CT images acquired 12 months after radiotherapy.

1 Introduction

The exposure of lung tissue during radiotherapy can lead to physiological changes in the lung, commonly denominated as radiation induced lung damage (RILD). Lung toxicity is a limiting factor in high dose radiotherapy and one of the main causes of loss of quality of life of cancer survivors. According to Defraene *et al.*, using current planning paradigms around 15% of the patients experience some type of lung toxicity [1]; this implies a relevant incidence of treatment related side effects and poor tumour dose optimization for the remaining population.

RILD is commonly divided in two processes with varying timelines, one acute (pneumonitis) and other chronic (fibrosis). The pneumonitic phase occurs approximately 1 to 3 months following radiotherapy; these changes slowly stabilize into definitive fibrotic damage between 1 to 2 years after irradiation [2]. CT imaging is a sensitive indicator of RILD, which is identifiable as changes in anatomy position, shape, volume, density and/or texture.

Recognizing the importance of RILD, there have been several efforts to understand the relationship between lung damage and dose [3], attempting to predict and improve outcome using baseline CT imaging features [1,4]. Deformable image registration (DIR) is used to automatically detect lung damage, by comparing pixel-by-pixel and/or volumetric characteristics between baseline and follow-up. Different open-source and commercial DIR algorithms have been used to map anatomy [5,6,7] and dose between timepoints [8]. However, the accuracy of registration is limited when damage occurs. In this work we qualitatively and critically assess some of the challenges in registering baseline and follow-up CT images acquired 12 months after radiotherapy.

2 Methods and Materials

2.1 Patient data acquisition

A total of 12 lung patients treated with conventional radiotherapy were included in this study. This non-randomized phase I/II trial enrolled stage II and III NSCLC patients, who received tumour RT doses between 63 Gy and 73 Gy in 30 fractions, concurrent with two cycles of cisplatin and vinorelbine [9]. Each patient received a baseline PET-CT or diagnostic CT before treatment, and a diagnostic CT for follow-up after 12 months (median: 432 days, range: 358-498 days). The median image resolution for the baseline scan was $0.77 \times 0.77 \times 2.25$ mm³ (range: 0.64 - 1.37×0.64 - 1.37×0.8 - 5 mm³), while for the follow-up scans was $0.85 \times 0.85 \times 2.5$ mm³ (range: 0.70 - 0.88×0.70 - 0.88×1 - 5 mm³).

2.2 Image registration settings

A virtual CT was created by deforming the baseline onto the follow-up CT. All the registrations were performed using the open-source DIR software NiftyReg (<http://cmic.cs.ucl.ac.uk/home/software/>). Rigid registrations were performed using a Block Matching based affine registration [10], followed by a non-rigid stationary velocity fields implementation of the popular B-Spline algorithm [11].

3 Results

Fig. 1 shows some examples of the challenges in registering serial CT of radiotherapy lung patients, which will be described in further detail in the next paragraphs.

Fig. 1(A) represents the most commonly radiological changes reported in the literature. The gross tumour volume was located anteriorly on the right lung; at follow-up its volume shrank accompanied by an increase of the nearby irradiated lung tissue density. In this particular case the parenchyma was not heavily modified, and DIR was able to globally align the internal lung anatomy even in the presence of lung damage.

There is a lack of standardization of radiological findings for late fibrosis assessment [12]. Chronic lung damage may manifest in different ways than local intensity and/or texture changes in the lung, such as changes in the curvature of the diaphragm (Fig. 1(B)). Other dramatic changes, such as fissure thickening and pleural effusion, can develop on the irradiated lung at 12 months (Fig. 1(C)). DIR attempts to reproduce pleural effusion by unrealistically deforming the vertebrae and surrounding tissue.

Finally, for the patient in Fig. 1(D) the relative volume of different regions of the left lung was modified drastically after radiotherapy: the upper lobe occupies a smaller volume while the lower lobe expanded. DIR was able to capture generally the new shape of the lung, but failed when it came to distinguish relative volume and shape of the lobes.

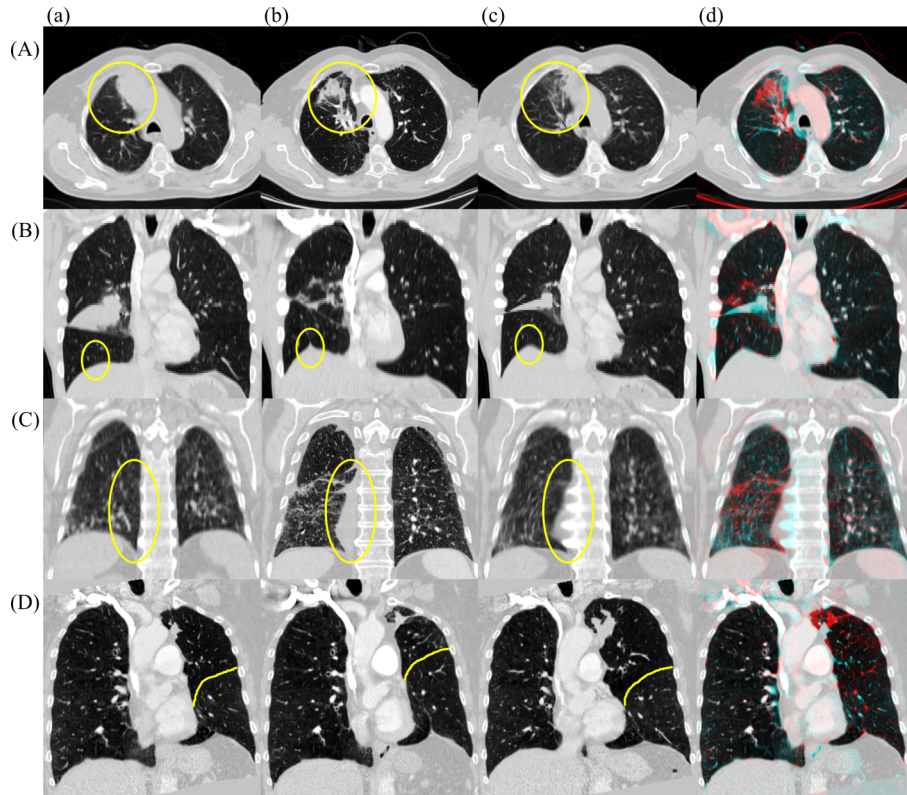


Fig. 1. (a) baseline CT, (b) follow-up CT, (c) virtual CT, and (d) color overlay between follow-up CT (red) and virtual CT (cyan). Examples of lung damage: (A) changes in density/texture, (B) changes in diaphragm curvature, (C) pleural effusion, and (D) changes in lung architecture.

In general, in cases where the internal anatomy was heavily modified after radiotherapy, the accuracy of DIR was hard to assess due to the lack of clear landmarks. DIR failed to deal with sliding motion of the lungs against the pleura for all the patients, distorting the lung architecture near the chest wall even when the remaining of the lung structure was correctly mapped. Registration of the tumour and its surroundings was challenging of both performing and evaluating, as general-purpose DIR miss mechanisms to deal with missing tissue.

4 Discussion

General purpose DIR algorithms map intensities between images, which for many clinical applications is a good surrogate for anatomical mapping. The problem of co-registering serial CT of radiotherapy lung patients in the pres-

ence of chronic lung damage is of increased complexity because there is no real anatomical one-to-one mapping.

Several changes in the lung can occur after radiotherapy: regions of the lung can collapse or re-inflate; the patient may develop abscesses; pleural effusion can accumulate between the lung and the chest wall; local texture and intensity change as inflammation and/or scarring occurs; the shape of the mediastinum, airways and diaphragm modifies as response to changes in lung volume and function; loss of lung function leads to changes in breathing pattern; and the tumour may regress or recur. Patterns of lung damage may result in toxicities and loss of quality of life, hence all these types of changes are important to detect and characterize. However, many of these changes are not reproducible by transformations based on local changes in volume; hence general-purpose DIR algorithms will struggle to accurately map correspondent anatomical points and will result in gross errors. Additionally, differences in image acquisition parameters and setup between timepoints bring additional challenges to accurate anatomical mapping. When the baseline image was PET-CT, the contrast of the lung structure was lower and the registrations more likely to be poorly behaved.

In the literature the issue of registering pre and pos-radiotherapy scans is not yet thoroughly addressed; while acknowledged that the existence of lung damage leads to higher inaccuracies in the registration of serial CT scans [6,7], there is still no method proposed to robustly deal approaches to with this automatically. A recent study by Cazoulat *et al.* combines a biomechanical DIR algorithms with correspondence between vessel trees to improve the anatomical mapping [14]. There is therefore scope to develop approaches that combine both intensity features, to globally define the deformations, with prior knowledge of anatomical landmarks and/or other penalties, to regularize the transformations.

In this short paper we described some of the challenging radiological changes that occur 12 months after lung radiotherapy. We expect this to lay foundation toward developing approaches to standardize and automatically score chronic lung damage.

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