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Prognostic factors associated with the accuracy of deformable image registration in lung cancer patients treated with stereotactic body radiotherapy

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A B S T R A C T

We evaluated the accuracy of an in-house program in lung stereotactic body radiation therapy (SBRT) cancer patients, and explored the prognostic factors associated with the accuracy of deformable image registrations (DIRs). The accuracy of the 3 programs which implement the free-form deformation and the B-spline algorithm was compared regarding the structures on 4-dimensional computed tomography (4DCT) image datasets between the peak-inhale and peak-exhale phases. The dice similarity coefficient (DSC) and normalized DSC (NDSC) were measured for the gross tumor volumes from 19 lung SBRT patients. We evaluated the accuracy of DIR using gross tumor volume, magnitude of displacement from 0% phase to 50% phase, whole lung volume in the 50% phase image, and status of tumor pleural attachment. The median NDSC values using the NiftyReg, MIM Maestro and Velocity AI programs were 1.027, 1.005, and 0.946, respectively, indicating that NiftyReg and MIM Maestro programs had similar accuracy with an uncertainty of < 1 mm. Larger uncertainty of 1 to 2 mm was observed using the Velocity AI program. The NiftyReg and the MIM programs provided higher NDSC values than the median values when the gross tumor volume was attached to the pleura ($p < 0.05$). However, it showed a different trend in using the Velocity AI program. All software programs provided unexpected results, and there is a possibility that such results would reduce the accuracy of 4D treatment planning and adaptive radiotherapy. The unexpected results may be because the tumors are surrounded by other tissues, and there are differences regarding the region of interest for rigid and nonrigid registration. Furthermore, our results indicated that the pleural attachment status might be an important predictor of DIR accuracy for thoracic images, indicating that there is a potentially large dose distribution discrepancy concerning 4D treatment planning and adaptive radiotherapy.

Introduction

In recent years, deformable image registration (DIR) has become commercially available for use in radiotherapy. DIR

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is an exciting and interesting technology for multimodality image fusion, anatomic image segmentation, 4-dimensional (4D) planning, and lung functional imaging. Furthermore, DIR is now playing an important role in modern radiotherapy, including image-guided radiotherapy and adaptive radiotherapy. A considerable number of studies have already investigated these modalities.[1-7] For thoracic cancer, previous studies have demonstrated the benefit of 4D dose calculation.[2,8] Valdes *et al.* have reported that 4D dose calculations are not necessary for most patients treated with stereotactic body radiation therapy (SBRT), but they might be valuable for irregularly shaped target volumes.[8] In addition, McCann *et al.* have shown that the 4D dose calculations based on DIR can be used to evaluate a robust-inspired planning strategy for lung radiotherapy.[2] However, several studies have reported that the accuracy of 4D dose calculation depends on DIR accuracy.[9,10] Cunliffe *et al.* reported that a 1-mm increase in DIR error would result in a 0.42 Gy increase in the dose-mapping error.[10]

Many software programs can perform DIR; however, different DIR software programs may show different results regarding image and dose because of the different optimization algorithms and models used. Validations concerning different types of DIR software have been reported in a number of studies; they found that it is important that the investigator who uses DIR software understands the characteristics of the software.[3,11-13] Wu *et al.* found that the B-spline algorithm tended to exhibit reduced accuracy near the pleura.[14] Boundary matching, which imposes a heavy penalty for mismatching, was introduced. This author reported that this method led to better accuracy near the pleura in the lung and on the rib.[14] In addition, Samavati *et al.*[15] reported a hybrid biomechanical intensity-based deformable image registration system for lung 4-dimensional computed tomography (4DCT). They stated that this approach showed efficacy regarding registration, and was accurate and consistent in using evaluation metrics such as target registration error, the dice similarity coefficient (DSC), and so on. These developed algorithms have been effective in the boundary, where the lungs can slide against the chest wall to create discontinuities. However, factors which are relevant to DIR accuracy regarding lung tumors have not been reported. Additionally, the tendency of the fast free-form deformation (FFD) algorithm to reduce accuracy has not been described in the case of lung images.

The objective of the present study was to evaluate the accuracy of an in-house program involving a free-downloadable DIR software library package (NiftyReg) and 2 commercial DIR software programs (MIM Maestro and Velocity AI) in lung cancer patients treated with SBRT. The FFD was implemented in the NiftyReg and the MIM Maestro programs. The Velocity AI program was based on the B-spline algorithm. Furthermore, we explored the prognostic factors associated with the accuracy of the DIRs and explained the case which lead to unexpected results in thoracic images.

Materials and Methods

DIR software

We evaluated 3 DIR algorithms, including 2 commercial software programs: MIM Maestro (Software Inc., Cleveland, OH, USA) and Velocity AI (Varian Medical Systems, Atlanta, GA, USA). The deformation processes in the commercial DIR programs were performed using the manufacturers' settings. The region of interest (ROI) for deformation was set so that it was similar in the 3 DIR programs for deformation in the whole body. Using the NiftyReg program, a rigid registration for the whole body and a nonrigid registration for the lung and body were performed using our established optimal DIR parameters. In the case of the MIM program, a rigid registration for the whole body and a nonrigid registration for the lung, as well as selection of local volumes in the body by the software, were performed. Using the Velocity AI program, nonrigid registration for the whole body was performed when the application range was set to encompass the whole body.

In the case of the in-house program using the NiftyReg software,[16-21] it was configured using 3 rigid and nonrigid registration processes. The first step involved an affine registration using a block-matching algorithm for the whole body of the patient.[16] The second and third steps entailed the deformation inside the lung and body, respectively, using the FFD algorithm. Finally, the whole body was focused on because deformation occurs not only in the tumor and lung but also in the surrounding organs. The FFD algorithm comprises 3 components: deformation of the image using a deformation model; an objective function; and an optimization. The deformation model is computed from the local control point positions using a cubic B-spline interpolation. The objective function is composed of normalized mutual information and the bending energy. The normalized mutual information is an intensity-based similarity measure based on entropy. The bending energy as a penalty term is calculated from the deformation model. The objective function is a balance between the similarity metric and the deformation penalty.

The MIM maestro software[11,22,23] initially used a rigid registration to make a choice automatically or manually. In the present study, the rigid registration was defined automatically. The nonrigid registration was defined using an intensity-based FFD algorithm, which was performed to minimize a global penalty function consisting of an image similarity measure and a deformation smoothness term. This algorithm was developed with limitless degrees of freedom depending on the required accuracy and execution speed.