A method to estimate accumulated dose uncertainties induced by deformable image registration discrepancies for adaptive proton therapy

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INTRODUCTION

Deformable image registration (DIR) is widely used in radiotherapy. For the evaluation of adaptive proton therapy outcomes, DIR is used to accumulate the dose on a reference geometry.

DIR as an ill-posed problem can lead to **geometric discrepancies** in the resulting deformation vector fields (DVF) applying different algorithms [1-3]. This induces **dosimetric uncertainties** for the dose accumulation in adaptive therapy [3].

The AAPM TG132 report highly suggests **to quantify and evaluate geometric and dosimetric DIR uncertainties** before application in radiotherapy [4]. Therefore, this study **proposes a clinical feasible method to estimate these uncertainties** in the context of adaptive proton therapy of non-small-cell lung cancer patients. However, the proposed framework could be useful for further DIR related applications.

AIM

- Propose a **clinical feasible** method to estimate **dosimetric uncertainties** as a consequence of **geometric discrepancies** caused by **DIR** for inter-fractional dose accumulation in adaptive proton therapy.
- Validate the approach for seven non-small-cell lung cancer patients.

METHOD

Patient data and DIR application:

- 7 NSCLC patients (1 reference CT, 9 repeated CTs)
- Each repeated CT was deformably registered to the reference CT with five DIR algorithms (Plastimatch Bspline & Demon, Velocity, Mirada and Raystation Anaconda).

Proposed method: The proposed framework, together with its validation branches, is shown in Figure 1. The method includes three main components

I. **DVF uncertainty;** the geometric DVF uncertainty is calculated in a first fraction by taking the maximum-minimum vector magnitude of all five DVFs at each voxel. By correlating this magnitude difference with one reference DVF a patient-specific model for the geometric uncertainties is built. For the following fractions the DVF uncertainty is estimated with the model from the first fraction.

II. **Dose gradient;** the gradient of the daily fraction dose is used to convert the geometric DVF uncertainties to the dose difference estimation. This is achieved by multiplying for each voxel the DVF uncertainty with the dose gradient.

III. **Direction factor;** the estimation from above holds only if the dose gradient and the DVF direction coincide. Therefore, an additional direction weighting factor is incorporated. The voxel-wise direction factor is calculated as the absolute value of the cosine similarity between the dose gradient and the reference DVF direction.

Validation and evaluation:

- The **gray branch** in Figure 1 shows the estimation of the dosimetric uncertainties using the method described in a previous study and serves for our work as 'ground-truth' (GT) dosimetric uncertainty. For each repeated CT the daily fraction dose is warped with each of the five DVFs and the voxel-wise maximum-minimum dose value serves as dose uncertainty estimation.
- The **green branch** represents our proposed method and is compared with the GT by taking the difference of the estimated dose uncertainty map (GMU) and the GT (GMU-DD).
- The **blue branch** is used to validate the method in absence of the modelling part. For this reason, the DVF uncertainty is for all fractions calculated as max-min magnitude difference of all five DVFs instead of modelling the geometric uncertainty. For the comparison again the difference to the GT is calculated (GU-DD).
- Additionally, it is validated if an upscaled gradient alone could give a reasonable estimation of the dosimetric uncertainty (G-DD).

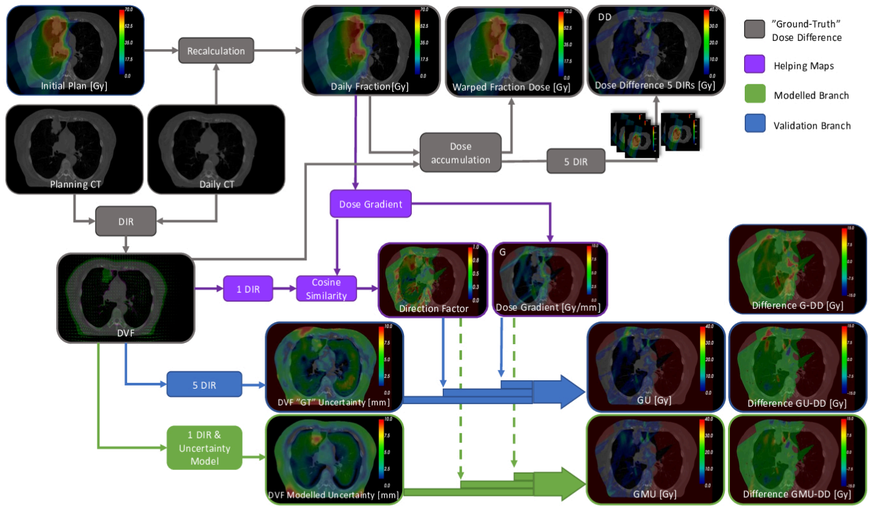


Figure 1: Scheme of the proposed method. The top branch in gray shows the method described in a previous study [3]. The green branch is the newly proposed method including the estimated DVF uncertainty from the patient-specific model, the dose gradient and the direction factor. The blue branch represents the validation branch for which the DVF uncertainty is calculated for each fraction from all five DVFs.

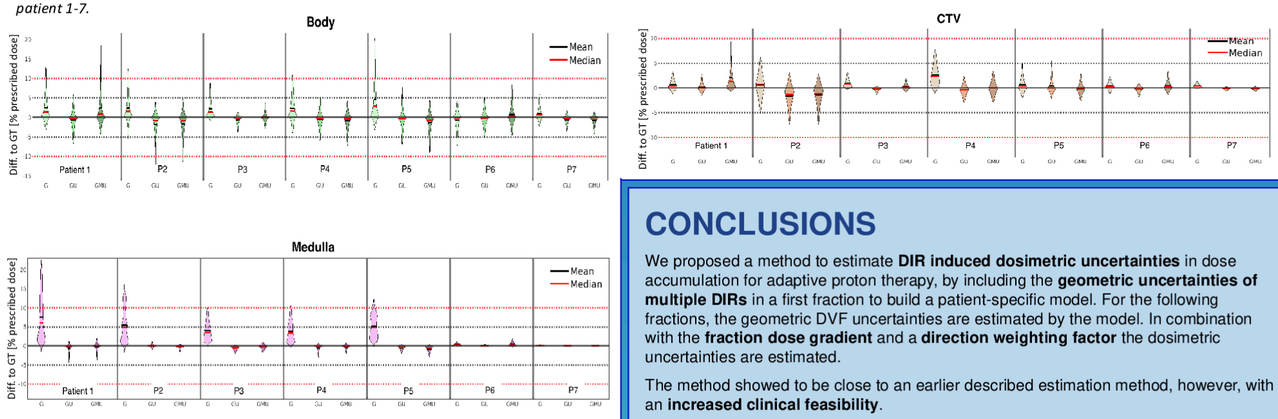
RESULTS

In Figure 2, the difference to the GT distribution of all non-zero dose voxel inside selected structures is shown in violin plots, for each patient and each branch (G) gradient-only, (GU) validation branch and (GMU) modelled branch . Included in each violin are 80% (10th-90th percentile) of the voxels of the respective distribution.

- For the body structure, including all non-zero dose voxels inside the body, most voxels for all branches have a difference to the GT of ±5% of the prescribed dose or less.
- 80% of the body voxels are inside ±10% for nearly all patients in the case of our proposed method and the validation branch.
- Taking the gradient-only method for the medulla could lead to much bigger differences to the GT than taking the newly proposed method.
- The dosimetric uncertainty estimations for the CTV from our method come very close to the earlier described GT dose difference.

Even though, the validation branch is expected to be the closest to the GT for some cases the modelled uncertainty is closer to the GT, this could be because of the simple linear model used for the DVF uncertainty estimation, which could lead to smaller differences than the validation branch.

Figure 2: Difference to GT distribution of the non-zero dose voxels inside the body, medulla and CTV structure for (G) gradient-only, (GU) validation and (GMU) modelled branch. Plotted for patient 1-7.



CONCLUSIONS

We proposed a method to estimate **DIR induced dosimetric uncertainties** in dose accumulation for adaptive proton therapy, by including the **geometric uncertainties of multiple DIRs** in a first fraction to build a patient-specific model. For the following fractions, the geometric DVF uncertainties are estimated by the model. In combination with the **fraction dose gradient** and a **direction weighting factor** the dosimetric uncertainties are estimated.

The method showed to be close to an earlier described estimation method, however, with an **increased clinical feasibility**.

The framework is in general not limited to adaptive proton therapy and could be **extended to other DIR related applications**.

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