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ENGINEERING FOR HEALTH

A Tool for Radiotherapy Plan Evaluation Analysis: generalise Uniform Ideal Dose (gUIDE)

In radiotherapy, treatment planning is the process in which the appropriate dose distribution is planned for a specific patient. However, there is no consensus on what the 'optimal' plan should be and on how to measure plan quality. The purpose of this study was to develop a tool called a 'generalized Uniform Ideal Dose' (gUIDE) that produces an 'ideal' dose distribution based on single patient anatomy and dose prescription. By comparing the clinical achieved dose distribution with gUIDE a quantitative measure of plan quality can be derived. gUIDE is based on an exponential function of dose fall-off outside the tumor volume. The algorithm does not require any specification of the treatment machine but only patient geometry information. gUIDE fall-off parameter was properly derived in a simple geometry dose profile. Overall, gUIDE showed a lower DVH than the DVH generated using the clinical treatment planning system, as it was expected for a baseline ideal condition. In the clinical validation, although the statistical test showed significant differences between the two groups, overall values were similar for all structures between gUIDE and PlanIQ. A baseline dose gUIDE was implemented, optimised and evaluated. gUIDE could be accurate enough to be used as baseline to help in the plan evaluation process.

INTRODUCTION

There are several steps in the radiotherapy process, where human actions can bring variability in the quality of the delivered treatment. One example lies in contouring variations among radiation oncologists in defining organs at risk (OARs) and tumour areas (target) on the planning CT images of the patient. Concerning medical physicists, we can find the most variation in the plan dose distribution optimisation process. Treatment plan optimisation differences can lead to dosimetrically different plan solutions mainly due to differences between planners in their skills, dedication, ambition, and in time spent on planning. Other steps in the radiotherapy process where human action introduces variation are the different perceptions of plan quality and the consequent different choices of which plan to approve for treatment. There is wide variability in the assessment of treatment plan quality (defined as the ability of the planners and plans to meet the specified goals). Indeed, there is no consensus on what the 'optimal' plan parameters should be for the different treatment sites and on how to measure plan quality quantitatively. In Cagni *et al.* [1], significant variations in plan quality evaluation among radiation oncologists and medical physicists belonging to the same department was found.

Tools have been previously defined based on physical dose distribution, such as dose volume histogram (DVH) or dosimetric endpoints. A dose volume histogram (DVH) shows what portion of the volume of a structure receives a certain amount of dose and is a convenient 2D tool to compare two or more treatment plans for the same patient. In addition, 1D tools, such as specific dosimetric endpoints, such as maximum dose (Dmax) or mean dose (Dmed) received to a specific organ are used.

However, in both 1D and 2D representation, spatial information is lost. The process of plan evaluation also necessarily involves the visual assessment of a 3D dose distribution on patient CT images made by a clinician. Since the ideal plan solution for a certain patient is not *a priori* known, traditional clinical methods of evaluation of treatment plan have been based on the clinical experience.

Ahmed *et al.* [2] use the CT images and DICOM RT structure set of the patient to generate a synthetic dose distribution based on first principle assumptions and series of energy-specific dose-spread calculations. This 3D dose distribution is 'ideal' and is intentionally unachievable. This tool has been implemented in PlanIQ commercial software v2.1 (Sun Nuclear Corp., Melbourne, FL). However, the user can only visualise and export the 2D and 1D information of this ideal dose and not its spatial 3D distribution matrix.

In this study, we developed a tool called a 'generalized Uniform Ideal DosE' (gUIDE). This tool produces an 'ideal' dose distribution based on single patient anatomy and dose prescription. gUIDE can be used as a baseline dose in clinical plan quality assessment. By comparing the clinical dose distribution with our gUIDE dose, we can compute a quantitative measure of plan quality. The novelty of gUIDE is its simple formulation designed to be easily built for every patient and used as baseline to improve the robustness of treatment plan comparison.

MATERIALS AND METHODS

gUIDE tool
This tool was implemented using Matlab version R2020b (Mathworks, Natick,USA). The process of the gUIDE computation is composed of three steps and it is described in Fig. 1.
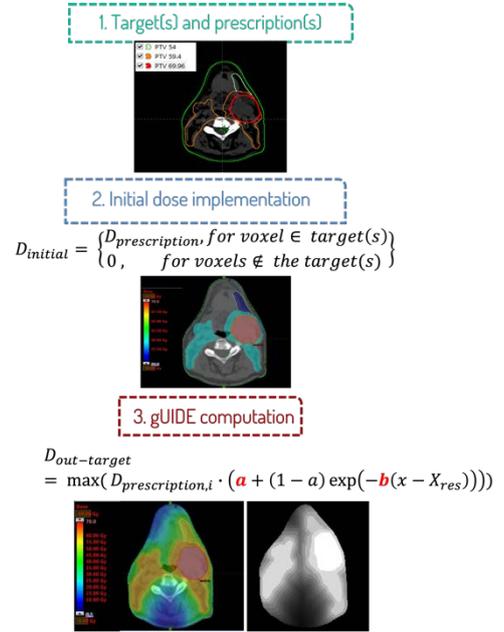
Fig. 1. The process of gUIDE creation.

The algorithm does not require any specification of the treatment machine or beam energy. The inputs needed for the gUIDE tool to generate the dose distribution are the CT simulation scan volume, the structure sets (OARs and tumour volumes), the dose prescription levels and the clinical treatment planning system (TPS) dose grid spatial resolution.

The starting point for gUIDE is the specification of target volume(s) and their prescription(s) together with calculation parameters on patient CT. The initial version of the ideal dose is a basic 3D dose grid (with the user specified resolution parameters) which provides 100% coverage of each of the target volumes with its associated prescribed dose. As the PTV is initially specified in the coordinates and the resolution space of the CT simulation scan, an interpolation of the mask (PTV contours) is carried out to map the mask in the 3D dose grid space. Then the dose grid points [x,y,z] corresponding to the voxels of the dose matrix, are assigned a dose value. In this first step, the dose values are assigned following a simple binary target coverage grid:

$$D_{initial} = \begin{cases} D_p, & for\ voxels \in the\ target(s) \\ 0, & for\ voxels \notin the\ target(s) \end{cases} \quad (1)$$

After this, the algorithm assigns the dose to the non-target voxels. This is achieved by creating successive expansions of the target in an iterative process: the dimension of the expansion margins used in every iteration is equal to the highest dose grid resolution. Then, the voxels inside the expansion are given the prescribed target dose, multiplied by a negative exponential factor depending on the distance of the specific expansion with respect to the target, following this relationship:

$$D_{out} = D_p \cdot \left(a + (1-a) \exp\left(-b(x - X_{res})\right) \right) \quad (2)$$

Where, D_{out} is the dose assigned to every voxel inside the nth expansion, D_p is the target prescription for that sub-dose; a is the plateau parameter describing the minimum percentage of dose showing in the 3D dose map; as our ideal dose needed to be as low as possible, this parameter was set to 0.01; b is the fall-off parameter, determining the steepness of the dose descent; X_{res} is the dose grid resolution, set equal to the maximum resolution of the map (in this work, 3 mm); x is the distance from the target for that specific expansion which is computed by $x=i, X_{res}$, where i is the number of the iteration.

The rationale behind equation (2) formulation was based on the Eclipse Treatment Planning System (Varian Medical Systems, CA), normal tissue objective (NTO) definition, used to decrease the dose outside target region during the optimisation [3]. In the presence of multiple targets, the final gUIDE is composed of the maximum values among all gUIDE sub-doses. The resulting dose derived from the above formula is thus composed of dose steps as it is a collection of isodoses decreasing exponentially with their distance from the target.

Tuning setup and validation strategy
gUIDE dose descent is parametrized with a fall-of variable, which needs to be tuned. We devised a tuning and validation setup using virtual CT scans of a cylindrical phantom with water density. We employed two model geometries, shown in Fig. 2. In both configurations, the centres of the targets were placed at the centre of the phantom with the OAR placed next to the target. We studied two possible configurations: the first one (conf. A) where the PTV (i.e. the target) was comprised of a cylinder with a diameter of 8 cm, with a cylindrical OAR next to it with a diameter of 4 cm. The OAR was placed tangential to the target's surface as we wanted to explore how steep the dose descent would be if the system's priority forced it to a single direction. The second setting (conf. B) had a similar geometry, with a cylindrical PTV with a diameter of 5 cm, with a cylindrical OAR next to it with a diameter of 3 cm. We thought these two configurations were enough to be able to properly model the dimensions of PTVs and OARs typical of a H&N site; for other sites, different configuration setups to tune the dose descend parameters might need to be configured (i.e. a different target site with different OARs for sites like breast).
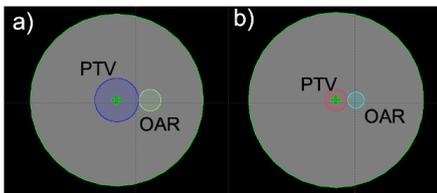
Fig. 2. Configuration A (a) and configuration B (b) used in the model tuning and validation.

Two treatment plans were generated on the two configurations. The dose prescription in these model geometries were 2 Gy to be delivered to the conf. A and conf. B PTVs. The optimization objectives, carried out in the aforementioned TPS, were the same for both configurations. The aim in this plan was to ensure near-perfect conformity of the prescription dose on the target and a dose homogeneity within ±10%. For the OAR, the goal was to make the mean dose as low as possible. After the final dose

calculation was completed, we extracted the dose profiles taken in the perpendicular direction passing in the middle of the OAR (and starting from the target). Then, we fitted the resulting dose profiles using an exponential function having the same form and parameters as the one described in Eq. 2.

The steepest dose profiles were then recorded and fitted using the gUIDE equation, parametrized with the fall-off parameter (b) and the plateau parameter (a). However, as the plateau parameter takes into consideration the low-gradient effects which we are not interested in modelling, we did not use it in our fit. In fact, only the fall-off parameter of the Eq. 2, used in the dose descent in gUIDE, was used in our tuning strategy. Said parameter was set as the mean among the values found from every analyzed configuration.

gUIDE computation for clinical case
Our gUIDE was used on 15 clinical head and neck cancer patient datasets to extract their ideal dose distribution. To assess the feasibility of our results, gUIDE doses were compared with a "benchmark" ideal dose, generated by a commercial tool, planIQ (Sun Nuclear Corp, Melburne, FL). PlanIQ allows the user to create a feasibility DVH (fDVH), introduced by Ahmed *et al*. [2], able to generate a synthetic feasible ideal DVH for a given patient, using a similar approach of gUIDE. For the purpose of our future applications and based on the considerations reported in the introduction section, 3D dose distribution is mandatory for our study, thus necessitating the implementation of an independent system. Our comparison with the benchmark was performed for spinal cord, brainstem, left and right parotids, oral cavity, mandible, oesophagus and larynx.

RESULTS

gUIDE tuning setup
In Fig. 3, a horizontal dose profile, passing through the middle of the PTV and OAR associated with the 2 configurations described in Fig.2 are reported. The graph can be divided in two parts. The first one (above the black line, shaded in orange) concerns the doses over 0.4 Gy, i.e. 20% of the maximum value (2 Gy in this case) is the part of the graph which was used in the fit and in the validation, as it describes the fall-off parameter. The other part of the graph simply shows that, for lower doses, the gUIDE differs from the experimental data, but it is expected as in the gUIDE modelling, the low gradient effects [2] were not taken into consideration. The fits exhibited a mean R2 >0.98±0.01 and the final fall-off parameter was set as b=1.9.
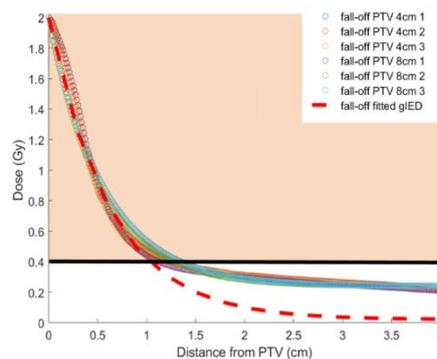
Fig. 3: Results from the fall-off parameter tuning.
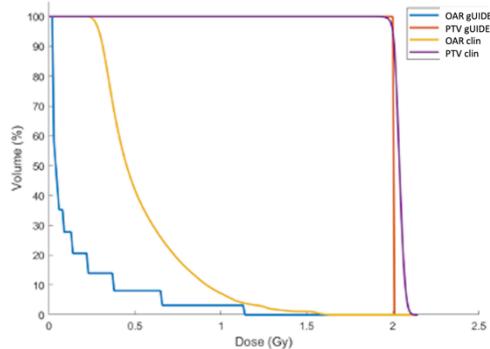
Fig. 4. Dose distributions from two examples of the dose calculation in configuration A and B. The red arrow shows the direction the dose profile was taken for the tuning of the gUIDE fall-off parameter.

Fig. 4 shows for configuration A (PTV=8 cm), the obtained DVHs related to the two involved structures. As expected, the PTV DVH for the gUIDE is a step function where all the prescription dose is delivered to the PTV, while the OAR DVH is composed of steps as a result of the isodoses with descending values implementation. The PTV DVH of configuration A cannot reach the step function given to the gUIDE, by definition. Regarding the OAR DVHs, it is expected that the gUIDE would be lower as the tuning was performed using the steepest one-dimensional dose descent in the OAR while in the real dose distribution the OARs receive the sum of various profile contributions.

gUIDE validation for clinical cases
In the comparison between gUIDE and planIQ clinical cases, the median DVHs for both cases, together with their 10-90 percentiles are shown in Fig. 5. Overall, the results are quite similar, even if for some OARs the differences between the two methods are more evident, such as larynx. However, the paired two-sided Wilcoxon signed rank test on the mean doses of all 8 OARs considered in the comparison (area under the DVH curve) showed different median values for the two DVH sets, with a p-value << 0.05.
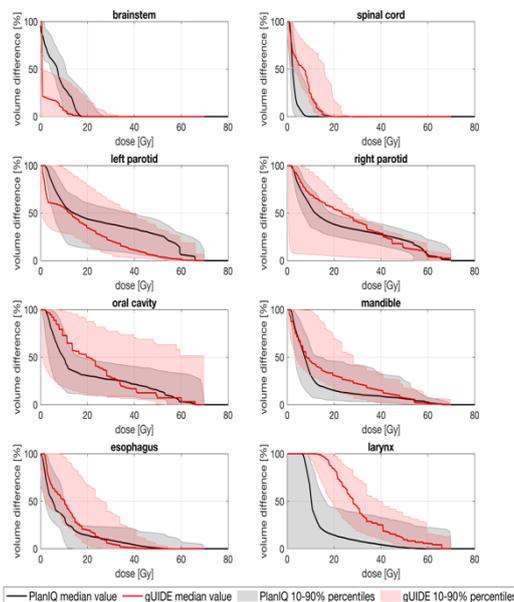
Fig. 5. PlanIQ and gUIDE DVHs difference for principal OARs structure in term median DVHs for the 15 patients with 10-90% percentiles.

Fig. 6 shows this comparison in terms of boxplots commercial PlanIQ (upper panel) and gUIDE (lower panel) mean dose values. Although the statistical test showed significant difference between the two groups, overall values are quite similar for all OARs in the two approaches.
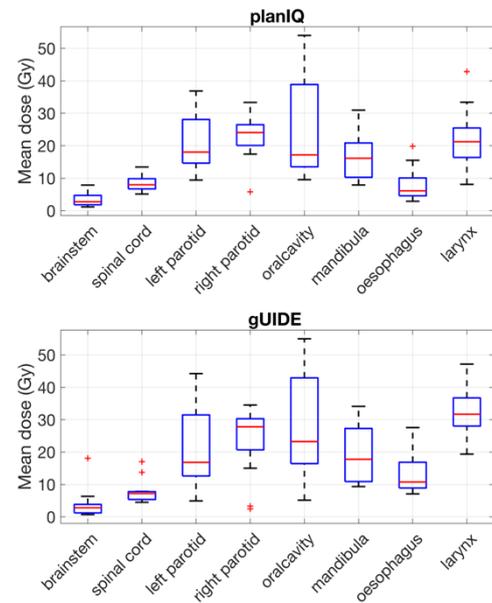
Fig. 6. Boxplots of planIQ and gUIDE DVH area under the curve distribution sorted by OAR. For each box, the central mark represents the median value, while the bottom and top edges of the box are the 25th and 75th percentiles over 15 patients, respectively.

DISCUSSION

In this study an ideal dose, called gUIDE was developed. gUIDE was optimised in a simple geometrical situation and tested on data from a cohort of 15 head and neck cancer patients, through a comparison with a commercial software system.

As the process of evaluation also necessarily involves the visual assessment of a 3D dose distribution, it was thought that the computation of a 'baseline dose', which is not attainable but represents the closest option to the ideal (but physically impossible) situation, could help improve the modelling of the evaluation process. The best achievable dose to specific anatomic regions was not known a -priori by the automatic planning system or the evaluation. gUIDE considers the unique patient anatomy and how that plays a significant role in the best achievable doses. The comparison of these theoretical and synthetic (but patient-specific limits) could give more insight into the evaluation process and could help in highlighting the different personal preferences that observers could employ when evaluating a plan. One key aspect of this study was the very simple formulation of gUIDE, that make it easy to implement and use in a clinical practice. gUIDE formulation presents some limitations because the low-gradient effect, which affects the lower dose is not considered. Nevertheless, gUIDE does not represent a physically achievable dose, but it is intended to be used as a baseline for actual dose distributions comparison.

By using this ideal dose, based on the anatomy of a single patient, together with the dosimetric features (1D endpoints

and 2D DVH metrics) belonging to the different plans (which are strongly influenced by each patient's unique anatomy), the behavioural patterns of the evaluators during the scoring process can be investigated using machine learning (ML) techniques. gUIDE could provide partial but fundamental information about the quality of obtained dose distributions in different patient anatomies and geometries.

In an on-going study, due to the limited number of samples (treatment plans) to model for the clinical set of patients considered in the application, gUIDE has been applied to improve the information of the dataset without adding features for ML classification. Preliminary results of this on-going study showed that the ML approach using gUIDE gives more complete information in comparison to the use of the ML tool without any patient's anatomy and dose distribution information. Results of this application are currently under further study.

CONCLUSIONS

In this study, a baseline dose gUIDE was implemented, optimised and evaluated. From our results, gUIDE could be accurate enough to be used as baseline to help in the plan evaluation process.

Further applications of gUIDE include using it in the ML tool to investigate the process of plan quality assesment among several evaluators in a limited dataset of plans. This could be the basis of useful information for a departmental-wide discussion to improve the consistency of plan quality assessment.

Conflicts of interest
The authors declare no conflict of interest.

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