Automation of pencil beam scanning proton treatment planning for intracranial tumours

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ABSTRACT
Purpose: To evaluate the feasibility of comprehensive automation of an intra-cranial proton treatment planning.

Methods: Class solution (CS) beam configuration selection allows the user to identify predefined beam configuration based on target localization; automatic CS (aCS) will then explore all the possible CS beam geometries. Ten patients, already used for the evaluation of the automatic selection of the beam configuration, have been also employed to training an algorithm based on the computation of a benchmark dose exploit automatic general planning solution (GPS) optimization with a wish list approach for the planning optimization. An independent cohort of ten patients has been then used for the evaluation step between the clinical and the GPS plan in terms of dosimetric quality of plans and the time needed to generate a plan.

Results: The definition of a beam configuration requires on average 22 min (range 9–29 min). The average time for GPS plan generation is 18 min (range 7–26 min). Median dose differences (GPS-Manual) for each OAR constraints are: brainstem –1.60 Gy, left cochlea –1.22 Gy, right cochlea –1.42 Gy, left eye 0.55 Gy, right eye –2.33 Gy, optic chiasma –1.87 Gy, left optic nerve –4.45 Gy, right optic nerve –2.48 Gy and optic tract –0.31 Gy. Dosimetric CS and aCS plan evaluation shows a slightly worsening of the OARs values except for the optic tract and optic chiasma for both CS and aCS, where better results have been observed.

Conclusion: This study has shown the feasibility and implementation of the automatic planning system for intracranial tumors. The method developed in this work is ready to be implemented in a clinical workflow.

Introduction
Proton therapy has the potential to reduce organ at risk (OAR) dose by taking advantage of the Bragg peak and the finite range of protons in matter. At the moment proton therapy is both an established treatment option for many cancers and an active area of research in other areas [1]. According to the particle therapy co-operative group (PTCOG; available at www.ptcog.ch) [2], the number of particle therapy facilities in operation in Europe is still increasing: 27 particle therapy facilities are in operation, 4 under construction and 8 in a planning stage. The large number of upcoming proton therapy centres implies a substantial increase in the need of expertise in this field. Several skills are required to start clinical operations: while some of them can be translated from conventional radiotherapy, other are proton therapy specific. Among them, treatment planning [3] is one of the most important.

Proton treatment planning differs from photon’s in a number of aspects, mainly related to the presences of range uncertainties, the use of a small number of fields, the need of taking into account distal end effects due to an increased linear energy transfer (LET) [4,5]. In addition, especially before the introduction of robust optimization and evaluation, the minimization of the effect of uncertainties during treatment planning phase has been driven by planner experience, making plan quality often centre dependent [6].

The use of automatic planning system in proton therapy could be a powerful tool for several reasons.
In recent years, automated planning systems have been developed in
order to improve the efficiency and quality of plan optimization. They are now available in several commercial platforms and installed in an increasing number of centres [7]. Automated planning improves plan consistency and it may improve plan quality [8]. In the specific case of proton therapy, it could help newcomers in becoming familiar with this specific planning technique, allow bias-free comparison in the evaluation of new planning techniques, support the generation of high number of plans for plan comparison, including photons vs protons comparisons, provide a reference for quality assurance (QA) of plans, etc.

Currently, there are three major approaches to autoplanning for conventional radiotherapy (RT): Knowledge-based (KB), Template-based and Multi-Criterial optimisation (MCO). KB uses prior knowledge to predict an achievable dose in a new patient belonging to a population of similar cases in terms of anatomy and dose prescription for whom plans had already been generated. The biggest limitations of this approach are that plan quality of the generated plans strongly depends upon the quality of the plans used for training [9–11], the model generation can be time consuming (requiring for example several fine-tuning of the model) and a continuous model updating is often suggested, especially if KB plan and additional planner adjustments significantly improve plans across the cohort [12]. A template-based approach provides a user-defined template, including the necessary clinical objectives for planning approval, to generate a plan that satisfies all such objectives. This process is often supported by the automatic generalization of new objectives and “dummy structures” in a way which mimics an experienced manual planner. Although a general improvement of the overall plan quality was reported for this approach, in specific cases the human planner still performed better [13,14]. The MCO “a posteriori” and “a priori” approaches search for a Pareto optimal solution. The “a priori” approach can be combined with lexicographic optimization, as in the ‘Erasmus-iCycle’ optimizer [15], where the constraints cannot be violated and the objectives, according to a priority set by the user, are progressively turned into constraints without compromising already achieved constraints. Here, the set of constraints and objectives define the so-called ‘wish-list’, which is specific to treatment site and protocol. In the near future, a massive use of deep learning model, as reviewed in [16], may lead to the prediction of the 3D dose distribution including also the beam geometry.

Some studies on KB automated planning for Intensity Modulated Proton Therapy (IMPT) have been published in the last years. [17–19]. In addition to automated IMRT and VMAT plan generation, the Erasmus-iCycle optimizer has also an option for fully-automated IMPT planning [20–24]: this feature is still not in clinical use and can therefore not replace manual IMPT planning yet.

The aim of this study is to evaluate the feasibility of a comprehensive automatic proton planning based on a priori MCO approach, but with some novelities such as a benchmark dose distribution and a customizible wish list. The evaluation will be performed in a clinical TPS, from the automatic beam configuration definition to the dose distribution optimization for intra-cranial tumour.

Material and methods

The study has been organized in three steps:

1. Automated generation of the beam configuration based on target location and further identification of a predefined set of beam configuration provided by experienced proton medical physicists, in terms of number of fields, gantry and couch angles. From such predefined beam configuration, an automatic exploration of the selected gantry angles, based on the user selection of gantry range and angle step, identifies the best beam path in terms of HU standard deviation;
2. Training of a dose optimization algorithm based on an automatic generation of a benchmark dose distribution that allows a faster convergence to the optimal patient specific dose distribution. A wish list approach based on three priority levels has also been included in the algorithm to achieve a further patient specific dose optimization;
3. Validation of the automated planning solution considering the accuracy of the target localization, the time required to generate the beam configuration and OARs dosimetric constraints comparison between the manual delivered plans and the automatic plans.

Step 1 - Automated generation of the beam configuration

Ten patients with intracranial lesions treated at Trento Proton Therapy Center (Table 1) were selected to validate the automatic beam configuration generation. Chordomas and chondrosarcomas do not represent the most common (supratentorial) brain tumors; however, because of the target proximity to organs and risk, they are included in the typical clinical scenario for which proton therapy could be beneficial. For this reason, skull base tumors (including chordomas, chondrosarcomas and other type of tumors such as meningiomas listed in Table 1) can be considered representative of the considered clinical scenarios.

Table 1 Characteristics of the patients included in step 1 of the study for the automatic beam configuration (ABC) selection. Clivus chordoma or chondrosarcoma dose prescription refers only to the low-risk volume (up to 54 GyRBE); to avoid bias between the manual and automatic plan comparison, sequential treatments (up to 70–72 GyRBE) have not been considered.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Diagnosis</th>
<th>Dose prescription</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABC 1</td>
<td>Left fronto-insular anaplastic astrocytoma</td>
<td>1.8 Gv × 33 fractions</td>
</tr>
<tr>
<td>ABC 2</td>
<td>Pituitary macroadenoma</td>
<td>2 Gv × 27 fractions</td>
</tr>
<tr>
<td>ABC 3</td>
<td>Benign left sphenoid-oralis meningioma</td>
<td>2 Gv × 27 fractions</td>
</tr>
<tr>
<td>ABC 4</td>
<td>Right fronto-temporo-parietal anaplastic astrocytoma</td>
<td>2 Gv × 25 fractions</td>
</tr>
<tr>
<td>ABC 5</td>
<td>Clivus chordoma</td>
<td>1.8 Gv × 30 fractions</td>
</tr>
<tr>
<td>ABC 6</td>
<td>Left temporal gemistocytic astrocytoma</td>
<td>2 Gv × 30 fractions</td>
</tr>
<tr>
<td>ABC 7</td>
<td>Right insular anaplastic astrocytoma</td>
<td>2 Gv × 30 fractions</td>
</tr>
<tr>
<td>ABC 8</td>
<td>Atypical meningioma of the skull base</td>
<td>2 Gv × 30 fractions</td>
</tr>
<tr>
<td>ABC 9</td>
<td>Right frontal anaplastic oligodendroglioma</td>
<td>1.8 Gv × 33 fractions</td>
</tr>
<tr>
<td>ABC 10</td>
<td>Clivus chondrosarcoma</td>
<td>1.8 Gv × 30 fractions</td>
</tr>
</tbody>
</table>
gantry exploration option and define any Gantry range and Gantry angle step. The values used in this study are 20° and 5°, respectively. The script will explore, based on the gantry range and gantry angle step, all possible beams geometries, considering as a starting point those provided by the CS and resulting in a correspondent number of auto class solutions (aCS). At this stage, couch angle exploration is not available due to the increase in both computation time and treatment time. The first task of the automatic script is the target localization. All these settings are depicted in Fig. 1S in the Supplementary materials.

Once the target localization has been completed, the script first generates an avoidance volume on the paranasal sinuses to reduce as much as possible range uncertainties [25]. Then it explores all CS gantry angle and couch angle combinations.

For each CS combination, a Hounsfield Unit (HU) analysis finds the best solution for each explored angle in terms of HU standard deviation (HUsd) along the beam path. In aCS, each beam is ranked based on the HUsd values, and the beam with the lowest HUsd is proposed as the first choice. Similarly, the most parallel and orthogonal beams with respect to the target are highlighted. This information could be useful especially if a serially responding OAR (e.g. the brainstem) is located distally to the target and reported in the user interface, as shown in Fig. 1S. Finally, the user may select between 2 and 4 beams, with a minimum separation of 30°, as well as the use of range shifter for each beam. The selected beams are then added automatically to the beams list in the TPS.

Step 2 - Dose optimization algorithm based on benchmark dose and wish list

The automation of dose optimization is based on a general planning solution (GPS, version 4.0) that aims at a personalized treatment plan based on an automatic generation of a benchmark patient specific dose distribution. The benchmark dose distribution essentially consists in perfect target coverage and OAR irradiation at high doses estimated under the assumption of steep dose gradients all around the target [26,27]. This dose is the starting point of the optimization algorithm and allows a faster convergence towards the optimal patient specific dose distribution since OARs sparing can’t be further improved. GPS is an external module implemented in the RayStation TPS written in CPython 3.6, while the benchmark dose computation is an external dynamic link library coded in C++.

The benchmark dose is generated using patient specific information extracted from the planning CT and takes into account both dose prescription and beam configuration (see an example in Fig. 1). The plans were optimized on the PTV used for the clinical plans: an objective function is automatically generated to obtain a homogeneous dose to the PTV and a sparing of the OARs as close as possible to the benchmark dose. For each OAR, a cost function is defined in terms of equivalent uniform dose (EUD) function with a dose level equal to the OAR average dose of the benchmark dose distribution. OARs type is identified by a parameter in the optimization function: for parallel

Fig. 1. Benchmark dose distribution with display of DVH and dose statistics for the target and priority 1 organs.
OARs, mean dose will strive towards the specified dose of the cost function and dose is reduced everywhere in the volume in order to reduce the mean dose to the specified EUD value. With serial OARs, the dose is reduced everywhere but sparing at high doses is emphasized.

To ensure additional dose customization, a dose optimization based on a wish list [28,29] has been included in the algorithm. Depending on the priority of the OAR, the system will automatically change the initial cost function to ensure the achievement of the set goals. To do so, two main operations are performed: 1) change of the EUD value set for the corresponding OAR, based on the dose value established in the clinical goals (1st iteration); 2) change of the plan objective weight.

Then, a series of optimization cycles will follow up to a maximum of 5 iterations (this limit was set based on a series of tests carried out during the training phase of the optimization). For this project, wish-list-based optimization has been set only for priority 1 OAR, with the aim of extending in future work also to lower priority organs.

We optimized the GPS on the same cohort used for the automatic selection of beam configuration.

**Step 3 - Validation of the automated planning solution**

The validation cohort consisted in an additional set of patients treated at Trento Proton Therapy Center, Italy. Such cohort (see Table 2) is a good representation of the clinical scenarios encountered in the proton therapy treatment of intracranial lesions.

Several parameters have been considered for the automated planning solution validation:

- the time to generate CS and aCS has been scored for each patient included in the cohort of step one;
- the automated target localization provided by the script has been compared with the real one;
- GPS has been evaluated comparing the clinical OARs constraints between the manual plans and the GPS plans, employing the same beams geometry as the manual plan.

Plan comparison has been performed only when the target coverage required by the clinical goal was achieved; therefore, the comparison has been performed only on the OARs constrains. Target dose distribution was in any case compared and evaluated in terms of hot spot (D1), target coverage (D95 and D98) and homogeneity index (HI = D5/D95) [30] for the validation patients’ cohort. Also PTVs volume, monitor unit per fraction and number of spots included were in the analysis as additional parameters for the comparison between the manual and automatic plan. The following OARs constraints have been considered: brainstem D1; cochlea (left and right) mean dose; healthy brain tissue (Brain-CTV) D1; eye (left and tight) D1; optic chiasm D1; optic nerve (left and right) D1 and optic tract D1. Time required to generate a GPS plan on the validation cohort has also been registered.

After GPS validation, a dosimetric evaluation of the CS and aCS beams geometry has been performed comparing the clinical OARs constraints between the manual delivered plans and the plans obtained by the CS and aCS beams geometry. The comparison has been performed only considering the first solution provided by the automatic system for the CS beams geometry and the respective first solution with the lowest HUsd for the aCS beam geometry (see the Supplementary materials for details).

**Results**

**Selection of CS and aCS**

Table 1S (Supplementary materials) shows the result of CS and aCS solutions in terms of gantry angle, couch angle and HUsd compared with the clinical plan. Fig. 2 reports the HUsd for each patient included in the beam configuration evaluation, for the manual (M), the CS and aCS plan, considering the sum of the HUsd for each beam configuration solution.

Manual plans have a slightly lower HUsd than CS and aCS plans in 60 % of the cases, with a mean sHUsd difference of −25.9 HU and 7.7 HU, respectively.

Table 3 lists the time required to generate the CS and aCS beam configuration solutions for the patients in the validation cohort. Target localization performed accurately in 100 % of the cases.

**Dosimetric evaluation of the GPS**

Absolute dose difference of the OARs among the patients is depicted in Fig. 3. The box plots include only the OARs with priority = 1. The GPS plan has been optimized with the same beam configuration of the manual delivered plan.

The mean dose differences for each OAR are: brainstem D1 −1.60 Gy, left cochlea mean dose −1.22 Gy, right cochlea mean dose −1.42 Gy, D1 healthy brain tissue 0.13 Gy, D1 left eye 0.55 Gy, D1 right eye −2.33 Gy, D1 optic chiasm −1.87 Gy, D1 left optic nerve −4.45 Gy, D1 right optic nerve −2.48 Gy and D1 optic tract −0.31 Gy. All OARs constraints were within tolerance for both the GPS and manual plan for three patients (GPS2, GPS3, GPS7, and GPS10). Considering the entire patient cohort, OARs constraints are.

- within tolerance both in the manual and GPS plan in 77 % of the cases
- out of tolerance both in the manual and GPS plan in 6 % of the cases (twice in the brainstem, twice in the healthy brain tissue and once in the optic tract)
- within tolerance in the GPS plan but out of tolerance in the manual plan in 14 % of the cases
- out of tolerance in the GPS plan (once in brainstem and twice in the optic tract) but within tolerance in the manual plan for 3 % of the cases.

Table 2S in the Supplementary materials reports the time needed to generate a plan for each patient in the evaluation cohort of the GPS. The average value for the plan generation is 18 min (range 7–26 min). The time to generate the plan is strongly dependent on the target size and the feasibility to achieve the clinical goals. PTV coverage (D95 and D98), as well as hot spot (D1) and homogeneity index are reported in Table 3S (Supplementary materials). In 80 % of the cases, automatic PTV D95 was comparable or better than manual plans. PTV D1 was almost comparable: the highest variation was 1.93 Gy. HI is higher than 0.9 for both the

<table>
<thead>
<tr>
<th>Patient</th>
<th>Diagnosis</th>
<th>Dose prescription</th>
<th>Dose prescription</th>
</tr>
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<tbody>
<tr>
<td>GPS 1</td>
<td>Grade II ependymoma of the posterior cranial fossa.</td>
<td>1.8 Gy × 30 fractions</td>
<td>1.8 Gy × 30 fractions</td>
</tr>
<tr>
<td>GPS 2</td>
<td>Left frontal atypical meningioma.</td>
<td>2.0 Gy × 30 fractions</td>
<td>2.0 Gy × 30 fractions</td>
</tr>
<tr>
<td>GPS 3</td>
<td>Left vestibular schwannoma progressing after surgery.</td>
<td>1.8 Gy × 28 fractions</td>
<td>1.8 Gy × 28 fractions</td>
</tr>
<tr>
<td>GPS 4</td>
<td>Craniospinalcygroma progressing after surgical resection</td>
<td>1.8 Gy × 30 fractions</td>
<td>1.8 Gy × 30 fractions</td>
</tr>
<tr>
<td>GPS 5</td>
<td>Benign meningioma of the left sphenoïd wing</td>
<td>2.0 Gy × 25 fractions</td>
<td>2.0 Gy × 25 fractions</td>
</tr>
<tr>
<td>GPS 6</td>
<td>Right fronto-insular grade II astrocytoma</td>
<td>2.0 Gy × 27 fractions</td>
<td>2.0 Gy × 27 fractions</td>
</tr>
<tr>
<td>GPS 7</td>
<td>Benign meningioma of the left cavernous sinus</td>
<td>2.0 Gy × 25 fractions</td>
<td>2.0 Gy × 25 fractions</td>
</tr>
<tr>
<td>GPS 8</td>
<td>Benign meningioma of the right cavernous progressing after surgery and RT</td>
<td>1.8 Gy × 30 fractions</td>
<td>1.8 Gy × 30 fractions</td>
</tr>
<tr>
<td>GPS 9</td>
<td>Left temporal high-grade glioma</td>
<td>2.0 Gy × 30 fractions</td>
<td>2.0 Gy × 30 fractions</td>
</tr>
<tr>
<td>GPS 10</td>
<td>Partially resected craniopharyngioma</td>
<td>1.8 Gy × 30 fractions</td>
<td>1.8 Gy × 30 fractions</td>
</tr>
</tbody>
</table>
manual and the autoplan (maximum variation within 0.05) in all but one case, where OARs sparing (brainstem) lead to a lower HI value in both plans and a HI difference of 0.17, in favour of the automatic plan. PTV volumes, MU and number of spots are reported for manual and automatic plan in Table 3S.

**Dosimetric evaluation of the entire autoplanning solution (GPS + automated beam selection)**

Dosimetric differences between the GPS plan and the clinical plan have been computed considering the first solutions proposed by CS and aCS with the lowest. An example is shown in Fig. 4 (patient ABC1).

Figs. 5 and 6 summarize the differences in OAR dose between the clinical plan and the CS and aCS solutions, respectively. The results for the OARs with priority 2 and 3 are summarized in Fig. 3S and 4S in the Supplementary materials.

**Table 3**

<table>
<thead>
<tr>
<th>Patients</th>
<th>Time to generate automatic beam geometry (number of solutions CS + aCS)</th>
<th>Auto-identified target position (√/×)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABC 1</td>
<td>17 min (1)</td>
<td>anterior cranial left √</td>
</tr>
<tr>
<td>ABC 2</td>
<td>25 min (3)</td>
<td>central √</td>
</tr>
<tr>
<td>ABC 3</td>
<td>9 min (1)</td>
<td>anterior cranial left √</td>
</tr>
<tr>
<td>ABC 4</td>
<td>27 min (2)</td>
<td>right √</td>
</tr>
<tr>
<td>ABC 5</td>
<td>24 min (3)</td>
<td>central √</td>
</tr>
<tr>
<td>ABC 6</td>
<td>25 min (2)</td>
<td>left √</td>
</tr>
<tr>
<td>ABC 7</td>
<td>29 min (2)</td>
<td>left √</td>
</tr>
<tr>
<td>ABC 8</td>
<td>17 min (2)</td>
<td>posterior caudal √</td>
</tr>
<tr>
<td>ABC 9</td>
<td>25 min (1)</td>
<td>anterior cranial right √</td>
</tr>
<tr>
<td>ABC 10</td>
<td>23 min (2)</td>
<td>posterior caudal √</td>
</tr>
</tbody>
</table>
Fig. 4. Dose distribution of the clinical plan (left) compared with the dose distribution obtained by the aCS (center), considering the suggested first solution with the lowest sdHU value. The image on the right shows the percentage difference between the clinical plan and the aCS dose distribution.

Fig. 5. Difference between the GPS plan and the clinical plan for OARs with priority 1. The geometry for the GPS plan was obtained with CS.

Fig. 6. Difference between the GPS plan and the clinical plan for OARs with priority 1. The geometry for the GPS plan was obtained with aCS.
Discussion

An automatic proton planning approach has been developed for intracranial tumour, from the beam geometry generation to the dose distribution optimization. A set of scripts has been developed in the clinical RayStation TPS to automate the following process:

- intracranial target localization
- automatic beams geometry selection (CS and aCS)
- HU and beam orientation analysis
- Plan creation
- Input dose prescription
- Benchmark dose computation
- Dose optimization and customization based on wish-list approach

Correct target localization has been achieved for 100 % of the targets included in the cohort (Table 3). The time to perform the beam geometry selection (CS + aCS) is dependent on the number of CSs. An average of 22 min is required for these patients’ cohort, with a minimum of 9 min, when the number of CS was only one, up to 29 min for 2 CSs. Most of this time is spent in the computation of the single beam geometry HUsd and the selection of the most parallel and orthogonal beams with respect to the target. The HUsd values describe the heterogeneity of the medium traversed by the beam, and it is well known that higher homogeneity is associated with better plan robustness [31]. Therefore, especially in a learning phase, the user could benefit significantly from this information to define the beam geometry, or as a starting point to further optimize the beam configuration based on other patient specific information. As shown in Fig. 4 and in Table 1S, HUsd and the most parallel and orthogonal beams can provide meaningful information in selecting the beam geometry. While CS is already a quite robust starting point for the selection of beams geometry (based on planner experiences), aCS provides an additional refinement: both CS and aCS provide a robust support to define the most appropriate beam geometry. This is also supported by the fact that the HUsd is quite comparable between CS, aCS and the clinical plan, even though aCS performs slightly better than CS and in some cases is better than the manual plan.

A second option for the beam configuration generation is the automatic HU statistics (Fig. 1S, top left). This solution has been implemented in the script but not further evaluated for the clinical validation due to its computational demands. However, in a context where a fast computation time is not a priority, e.g. in a training phase, it may be useful explore couch exploration too, and to have info on the HUsd for each beam geometry. Even though we obtained plans that are competitive with the clinical solutions, the decision of not including the couch exploration is a limitation of our study. Further investigation should be performed to see the benefits of including couch angle optimization in the workflow.

GPS has been trained on a patient cohort of ten patients, and our results are a further indication that this automatic planning approach does not require validation on a large number of patients. Other approaches (e.g. knowledge-based) may instead require a larger training dataset to create planning models intended for large scale distribution [32]. Employing the benchmark dose as a starting point of plan optimization ensures the best dose conformity that, in addition to a patient specific wish list, makes the GPS a suitable approach, as shown by the results. For the patients included in this study, GPS could maintain the required target coverage while reducing by up to 10 Gy the dose to all priority 1 OARs but healthy brain tissue, left eye and optic tract. Also, GPS shows improvements in OARs sparing even with the same beam geometry as the manual plan. In this study, only priority 1 OARs have been included in the optimization cost function. An additional development of our automatic planning system may include also OARs priority 2 and 3, that are usually not optimized in the manual plan. The average time to generate a GPS plan is 18 min. This result is strongly plan dependent, as the fastest and slowest plan required 7 and 26 min, respectively. Considering the worst-case scenario and the steps of both automated beams geometry definition and plan optimization, a ready to use deliverable plan is generated in about 55 min.

As shown in Table 3S, target coverage was comparable to the clinical plan or better in the 80 % of the cases. In one case (GPS8), a different OARs sparing approach was performed (because of a clinical decision), leading to a better target coverage for the automatic plan. In the remaining two cases (GPS3 and GPS10), the target coverage in the automatic plan is slightly lower but within the clinical goal: this could be due to the small volume of PTVs or to OARs sparing that is improved with respect to the manual plan. The target coverage for small volumes and additional OARs sparing are good examples of what can be achieved with manual fine tuning, after the autoplanning approach reach an initial solution that satisfy all goals in the cost function.

Plans deliverability and variation in treatment time were not considered specifically in such study. Nevertheless, Table 3S shows the MU per fraction and number of spots for both the automated and the manual plans. Based on this information, that can be considered a surrogate of plan deliverability and treatment time, automatic plans are not significantly different from manual plans.

The beam configuration generated by CS and aCS was associated with a slight worsening of the OARs values except for the left eye for the aCS and the optic tract for both CS and aCS. Optimization on the optic chiasm performed similarly for CS, aCS, and manual. aCS shows lower dosimetric differences than CS as shown in in Figs. 5 and 6, where the 25th and 75th percentile of all the OARs’ boxplot are within – 2 Gy and 3.7 Gy for the CS, and within –1.9 Gy and 1.6 Gy for aCS. These results suggest that the aCS perform better than CS, so optimizing the CS based on the HUsd slightly improves OARs sparing. Generally, both CS and aCS provide dose distributions that may be considered a good starting point for additional tuning in case dosimetric improvements are required. Fig. 3S and 4S suggest that beams geometry selection can also play a meaningful role for OARs with second and third priority. Even though such OARs have not been optimized in the GPS, some dose differences between the manual plan and the CS or aCS plan can be observed. Higher dose differences appear in the pituitary gland, right and left hippocampus and right lens for both CS and aCS when compared with the manual plan beam geometry. Further study should investigate how the inclusion of OARs with second and third priority in the wish list optimization could improve these results.

Even though autoplanning has been investigated much less than in photon therapy, there are several studies on proton autoplanning, mainly using the knowledge-based approach. Delaney et al. [17] demonstrated that a knowledge-based IMPT planning solution using a single centre model could efficiently generate plans of comparable quality to manual head and neck cancer plans obtained in other centres with differing planning approach. The authors also stated that beam angle optimization and manual review was sometime required to improve OAR doses. Similar knowledge-based mono-institutional experiences have been also performed by other authors [33–36]. KB planning solution has been also employed to support patient selection between proton and photon [19]. Another approach to automatic planning system in proton therapy is the use of the hierarchical optimization. Taasti et al. firstly demonstrated the use of constrained hierarchical optimization to generate automated treatment plans for proton therapy including robustness and dose-volume constraints [37] and then integrated this approach with a Bayesian beam selection to achieve a fully automated treatment planning framework including beam angle selection [38], even though with a low number of patients (five head and neck patients selected from a public database).

Another interesting approach is based on the use of a 3D dose prediction generated by deep learning instead of the benchmark dose used in this study [39,40]. Such an approach has already been tested for proton dose distribution [41]. As reviewed in Wang et al [42], artificial neural network (ANN) [43], convolutional neural network (CNN) [44–46] and, most recently, generative adversarial network (GAN) [47]
have been utilized for 3D dose distribution prediction. GANs seem to be very promising given its capability of generating independent data and produce optimal treatment plan, but further investigations are required. Our study has some limitations.

1) The choice of intracranial lesions is appropriate for developing and validating an autoplanning solution in its first iterations, but there certainly are more challenging planning problems that should be addressed before an autoplanning method can be considered mature.

2) The plans were optimized based on the PTV used for the clinical plans, so we did not perform robustness optimization. We do not expect that including robustness optimization in the process would be a major hurdle, the only likely difference being a somewhat increased optimization time. The same can be said for the planning technique: our solution is based on single field optimization to make it consistent with the clinical plans, but multiple field optimization could be applied too.

Another consideration regarding the intracranial region is that the degrees of freedom (couch and gantry angles) available to define the beams geometry are typically more than in other anatomical sites. This implies a stronger influence of the planner in selecting the optimal beam configuration, and a bigger role of automatic tools to either propose or support the increasing number of proton therapy centres, and it will be an important tool for the future.

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Conclusion

This preliminary study has shown the feasibility of a proton automatic planning procedure for intracranial tumours. Automatic planning system will play a key role in the future, since it will be highly demanded to support the increasing number of proton therapy centres, and it will support the standardization of treatment planning. The method developed in this work is ready to be implemented in a clinical workflow.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found at https://doi.org/10.1016/j.ejmp.2022.11.007.

References


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