# **Title Page**

**[Article Full Title]**

Automating the Treatment Planning Process for 3D-Conformal Pediatric Craniospinal Irradiation Therapy

**[Author Names]**

Soleil Hernandez, BS\*1,2, Callistus Nguyen, PhD2 , Jeannette Parkes, MBBCh3, Hester Burger4, Dong Joo Rhee, PhD2, Tucker Netherton, PhD1,2, Raymond Mumme, BS2, Jean Gumma-De La Vega, BS2, Jack Duryea, BA2, Alexandrea Leone, MBS2, Arnold C. Paulino, MD5, Carlos Cardenas, PhD6, Rebecca Howell, PhD1,2, David Fuentes, PhD1,7 , Julianne Pollard-Larkin, PhD1,2, Laurence Court, PhD1,2

**[Author Institutions]**

(1) The University of Texas MD Anderson Cancer Center UTHealth Graduate School of Biomedical Sciences, Houston, TX

(2) Department of Radiation Physics, The University of Texas MD Anderson Cancer Center, Houston, TX

(3) Department of Radiation Oncology, Groote Schuur Hospital and University of Cape Town, Cape Town, South Africa

(4) Department Medical Physics, Groote Schuur Hospital and University of Cape Town, Cape Town, South Africa

(5) Department of Radiation Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX

(6) Department of Radiation Oncology, University of Alabama at Birmingham, Birmingham, AL

(7) Department of Imaging Physics, The University of Texas MD Anderson Cancer Center, Houston, TX

**[Corresponding Author Name & Email Address]**

\*Soleil Hernandez

Department of Radiation Physics, The University of Texas MD Anderson Cancer Center

1515 Holcombe Boulevard, Houston, TX 77030, USA

[Shernandez6@mdanderson.org](mailto:Shernandez6@mdanderson.org)

Phone: 913-972-0198

Fax: 713-563-2546

**[Word Count]**

**Abstract: 264**

**Main text: 4170**

**[Number of:]**

**Tables=0**

**Figures=6**

**Supporting Information files=1**

**[Short Running Title]**

Automated Pediatric Craniospinal Irradiation Planning

**[Key words]**

craniospinal irradiation therapy, pediatric medulloblastoma, automated treatment planning, automated contouring, global radiation therapy access

**[Abbreviations Key]**

|  |  |
| --- | --- |
| **CSI** | Craniospinal Irradiation |
| **LMICs** | Low- and middle-income countries |
| **DSC** | Dice similarity coefficient |
| **HD** | Hausdorff distance |
| **AI** | Artificial intelligence |
| **JXN** | Junction |
| **SSD** | Source to surface distance |
| **ROI** | Region of interest |

**[Previously published meeting abstracts]**

Presentation name, meeting name and date, and publication site of the abstract

1. Automating the Contouring and Treatment Planning Process for Single-Field Pediatric 3D Craniospinal Irradiation Therapy. Southwest Association of Physicists in Medicine Young Investigator Symposium (March 2022). Not published online.
2. Automating the Contouring and Treatment Planning for Pediatric 3D-Craniospinal Irradiation Therapy. Pediatric Radiation Oncology Society (PROs) Annual Meeting (June 2022). <https://intpros.org/congress/pros-congress-2022/posters-abstracts-on-site/>
3. Automating the Contouring and Treatment Planning for Pediatric 3D-Craniospinal Irradiation Therapy. American Association for Physicists in Medicine Annual Meeting (July 2022). Medical Physics Volume 49, Issue 6, Pages E336-E337

# **Abstract**

**Purpose:** Pediatric patients with medulloblastoma in low- and middle-income countries (LMICs) are most treated with 3D conformal photon craniospinal irradiation (CSI), a time-consuming, complex treatment to plan, especially in resource-constrained settings. Therefore, we developed and tested a 3D conformal CSI autoplanning tool for varying patient lengths.

**Methods and Materials**: Autocontours were generated with a deep learning model trained:tested (80:20 ratio) on 143 pediatric medulloblastoma CT scans (patient ages, 2-19 years, median=7 years). Using the verified autocontours, the autoplanning tool generated 2 lateral brain fields matched to a single spine field, an extended single spine field, or 2 matched spine fields. Additional spine sub-fields were added to optimize the corresponding dose distribution. Feathering was implemented (yielding 9-12 fields) to give a composite plan. Each planning approach was tested on 6 patients (ages, 3-10 years). A pediatric radiation oncologist assessed clinical acceptability of each autoplan.

**Results:** The autocontoured structures’ average Dice similarity coefficient ranged from 0.65-0.98. The average V95 for the brain/spinal canal for single, extended, and multi-field spine configurations was 99.9±0.06%/99.9±0.10%, 99.9±0.07%/99.4±0.30%, and 99.9±0.06%/99.4±0.40%, respectively. The average maximum dose across all field configurations to the brainstem, eyes (L/R), lenses (L/R) and spinal cord were 23.7±0.08 Gy, 24.1±0.28 Gy, 13.3±5.27 Gy, 25.5±0.34 Gy, respectively (prescription=23.4 Gy/13 fractions). Of the 18 plans tested, all were scored as clinically acceptable as-is or clinically acceptable with minor, time-efficient edits preferred or required. No plans were scored as clinically unacceptable.

**Conclusion:** The autoplanning tool successfully generated pediatric CSI plans for varying patient lengths in 3.50 ± 0.4 minutes on average, indicating potential for an efficient planning aid in resource-constrained settings.

**Key words:** craniospinal irradiation therapy, pediatric medulloblastoma, automated treatment planning, automated contouring, global radiation therapy access

# Introduction

Eighty percent of children with cancer live in low- and middle-income countries (LMICs), where a larger pediatric population (under the age of 15 years) compared to high-income countries, prevails (37% vs. 17% of the total population, respectively, in 2015).1 The 5-year survival rate of patients in LMICs is much lower than in high-income countries (20% compared with 80%).2 Radiation therapy is a key component to a multimodality cancer treatment for more than half of pediatric patients in LMICs.3 In 2012, 4 million adult and pediatric patients in LMICs required radiation therapy, and the Collaboration for Cancer Outcomes, Research and Evaluation projects this number to increase by 78% by 2035.3 Access to high-quality radiation therapy in LMICs is variable, in part due to a lack of properly trained radiation oncologists and medical physicists to prepare and deliver the radiation treatment plans.4–7 Having limited personnel creates demanding workflows, with medical physicists dedicating 50% of their time to generating treatment plans and 50% to completing other necessary clinical tasks.8

To this end, artificial intelligence (AI) has been used to develop radiation therapy treatment planning tools,9 and our group has focused specifically on the clinical needs of LMICs.10 Algorithms have automated contouring, treatment planning, and quality assurance for radiation therapy to various disease sites such as the cervix, chest wall, spine and head and neck (HN).10–15 To date, these algorithms have been trained, validated, and tested exclusively on adult patient cohorts. More widely, while AI has been introduced to pediatric healthcare, it has yet to be integrated into pediatric radiation oncology.16,17

This study aimed to expand the use of AI in radiation therapy by automating the generation of 3D conformal radiotherapy treatment plans for craniospinal irradiation therapy. We selected medulloblastoma as the testing disease site because it is the most common malignant pediatric brain tumor in both high-income countries (20-25%) and LMICs (up to 49%),18 it is a solid tumor, and it requires craniospinal irradiation therapy (CSI) for all patients older than 3 years.18 Planning is a challenging task because it requires multiple treatment fields that must be optimized and shifted during treatment to mitigate potential inhomogeneous dose distributions (“feathering”).19

To our knowledge, this is the first work to develop comprehensive autocontouring and autoplanning tools specifically for pediatric radiation oncology. While medulloblastoma was selected as the disease site for this work, the autocontouring tool and autoplanning tool developed herein are translatable to other pediatric disease sites.

# Methods

We developed a comprehensive automated contouring and planning tool for 3D-conformal craniospinal irradiation therapy and assessed its performance on a cohort of pediatric patients with medulloblastoma. Retrospective patient data used in this work was collected following an institutional review board approved protocol.

## Autocontouring

Normal tissue contours and landmark contours were automatically generated to guide the automation of CSI treatment plans. The structures defined included the brain, brainstem, left and right (L/R) eye, L/R lens, L/R lung, L/R kidney, spinal canal, thyroid, and heart. We also elected to contour landmark structures (i.e., structures that guide field apertures, which physicians may not always contour for manual planning). The landmark structures defined included the cribriform plate, vertebral column, mandible, and shoulders.

### Adult HN Model Testing

An in-house autocontouring tool originally designed to contour 16 adult HN normal tissue volumes14 was tested on a data set of pediatric patients. The structures tested included the brain, brainstem, L/R eye, and L/R lens. The data set consisted of 143 pediatric patients with medulloblastoma CSI CT scans. Of the 143 CT scans, 1, 127, and 36 were performed on Philips, GE, and Siemens machines, respectively. The median (range) number of slices, slice thickness, and tube voltage peak was 347 (133-523), 2.5 (1.25-2.5) mm, and 120 (80-120) kVp, respectively. The patients in the data set had a median age of 7 years (range, 1.5-19 years) and a male to female ratio of 2:1. which is comparable to what is reported in the literature.20

### Pediatric Autocontouring using nn-UNet

The remaining normal tissue and landmark structures needed for treatment planning were the thyroid, L/R kidneys, cribriform plate, vertebral column, mandible, spinal canal, and shoulders. The landmark structures were manually contoured and added to the existing clinical structure set. The spinal canal was contoured to begin at the base of the brainstem and continue through the S2/S3 interspace, as this is where 75% of spinal canal contours end in pediatric patients.21 The cribriform plate was contoured as the thin horizontal plate of ethmoid bone between the two medial orbital walls.22

To automatically generate the pediatric specific models for these structures, we divided the same data set of 143 pediatric patients into training and testing sets (3:1 ratio) for a nn-UNet model.23 This architecture was selected for the experiment because it generates a data signature to optimize the training hyperparameters, making the training process less sensitive to heterogeneities in the data (e.g., patient positioning, image scanning protocols, anatomy variation with age). Using the optimized hyperparameters, a 3D full-resolution nn-UNet model was trained with 5-fold cross validation to further maximize the limited data set.

Additional post-processing algorithms were applied to improve the consistency of the autocontours and to prevent autocontouring errors from propagating through to treatment planning. For example, the spinal canal and mandible were post-processed within the treatment planning system. The spinal canal post-processing was designed to remove any slice of the contour that had an area <0.10 cm2. Additionally, the algorithm checks for a gap between the auto-contoured spinal canal and brain stem contour. If a gap is present, the algorithm extends the spinal canal superiorly to fill the gap so that the final target volume is a continuous structure. The mandible post-processing algorithm removes any mandible contour that extends below the top of the shoulders. This is to prevent the final mandible structure from containing a volume that may have been misidentified as mandible by the autocontouring algorithm (i.e., high attenuation areas like the humerus, radius, or ulna).

## Autoplanning

The autoplanning approach (Fig. 1) was designed based on recommendations from the International Society of Paediatric Oncology (SIOP) Paediatric Oncology in Developing Countries radiotherapy working group18 and scripted in Raystation 10B (RaySearch Laboratories, Stockholm, Sweden)24. International collaborators supplied patient data to test and refine the script design. In summary, we used a standard supine CSI beam arrangement with 2 lateral head fields and either 1 or 2 matching posterior spinal fields. A collimator rotation was applied to the lateral head fields to match the beam divergence of the spinal field. The junction of the brain and spine fields was shifted twice during treatment to ensure dose homogeneity and limit risk of over or under exposure due to setup inaccuracies during treatment. Finally, a composite treatment plan was created.

Isocenter Placement

The brain isocenter is placed first (Figure 2). The longitudinal distance between the mandible and shoulder landmark contours is calculated. If this distance is less than 2.5 cm, the algorithm warns the user that there is insufficient space between the shoulders and the mandible to safely (automatically) feather the junction. If the distance is greater than or equal to 2.5 cm, the brain isocenter is placed 2.5 cm superior to the shoulders. In all cases, the brain isocenter is centered within the spinal canal for the selected slice.

Next, the length of the spine field required for the patient is determined by calculating the longitudinal distance between the brain isocenter and the most inferior slice of the vertebral column contour. If the distance is less than or equal to 40 cm, a single spine field is used. If the distance is greater than 40 cm, the tool either uses an extended source to surface distance (SSD) to increase the effective field size or uses 2 fields with 2 spine isocenters. The corresponding spine isocenter coordinates are then set (Figure 2). In a single field setup, the spine isocenter is placed 20 cm inferior to the brain isocenter coordinate. In the extended field setup, the AP/PA coordinate of the isocenter is shifted posteriorly to the surface of the treatment couch. In a multiple field setup, the upper isocenter is placed 20 cm below the brain isocenter and the lower is placed at the halfway point of the remaining length of the spine field.

### Target Definition

Target contours are generated for both treatment fields to guide jaw and multi-leaf collimator placement. The brain target volume is defined as a combination of the brain, brainstem, cribriform plate, and upper spinal canal autocontours. The spine target is defined as the vertebral column autocontours. Additionally, prescription volumes are defined. The brain field prescription contour is set to the brain autocontour. The spine field prescription volume is a truncation of the spinal canal autocontour to longitudinally shift the structure away from the field borders by 3 cm superiorly and 1 cm inferiorly. In the multi-field configuration, the spinal canal is separated into two volumes, one for the upper spine field and another for the lower.

### Field Generation

One to two spine fields are generated depending on the required field configuration of the patient, after which two lateral opposed brain fields are generated and matched to the spine field. All fields are blocked to their respective target volumes described in the Target Definition section. All field expansions applied to the brain and spine target may be re-configured to cater to user preferences.

The superior border of the spine field is set to the longitudinal location of the brain isocenter point. The inferior border of the spine field is set to match the z-location of the most inferior slice of the vertebral column contour (S2/S3 interspace). The Y2 (superior) jaw of the spine field(s) is set to 20 cm to allow for more consistent treatment setup. The multi-leaf collimators are set to apply a 0.5-cm lateral expansion of the vertebral column autocontour and automatically conform to the curvature of the vertebral column autocontour. In the multi-field configuration, an additional spine field is generated around the lower spine isocenter to cover the remaining length of the spinal canal.

After the spine field(s) are generated, the brain field is automatically generated to cover a default 1-cm expansion of the brain target volume. The Y1 jaw is set to 0 to create a half-beam block and avoid a couch rotation. A parallel opposed field is then generated. Because the Y2 jaw of the most superior spine field is set to a constant 20 cm in the single and multi-field configurations, the collimator angle is kept constant to allow for simpler and more consistent patient setup. In the extended field configuration, the collimator rotation is calculated using Equation 1, where L1 is defined as the length of the spine field and S is defined as the source to isocenter distance.

) (1)

### Dose Calculation and Optimization

The dose prescription and fractionation scheme are a user configurable parameter. The default prescription is 23.4 Gy in 13 fractions with a 5,5,3 fractionation scheme for each of the feathered fields. The 95% isodose line is prescribed to cover 95% of the brain and 98% of the spine prescription volumes defined in the Target Definition section.

After the initial dose has been calculated, automatic optimization is applied to the spine field (Fig. 3). The objective of the spine field optimization algorithm is to minimize the volume of 95% of the prescription dose that lies 5 mm or more anterior of the spinal canal autocontour (“over-coverage region”). To achieve this, a planning structure is created to include the over-coverage region (volume of 95% isodose more than 5 mm anterior to the canal). A sub-field is then generated to block this over-coverage region and given an initial weight of 1% of the primary field. The algorithm re-calculates the over-coverage volume region using the new 95% isodose line. If the volume is increased from the non-optimized plan, the algorithm deletes the sub-field. If the volume is decreased, the algorithm continues to weigh the beam from 1% to 10% and iteratively recalculates the over-coverage region until the volume is no longer minimized. The maximum sub-field weight is kept to 10%, to avoid unintended excessive dose to the anterior tissue or posterior neck region.

### Feathering

To perform feathering, the borders of the inferior brain and superior spine field are shifted by 1 cm and 2 cm on JXN2 and JXN3 plans, respectively. In the multi-field configuration, both fields are feathered to optimize the dose distribution at both match lines. Finally, a composite plan is generated to assess the summed dose distribution.

## Algorithm Testing

The performance of the autocontouring model was quantitatively assessed using the Dice similarity coefficient (DSC) and Hausdorff distance (HD). The performance metrics of the pediatric autocontours that were generated from the adult model were compared with those achieved on the adult data set using an unpaired *t* test for each structure (*P* < 0.05 as statistically significant). The performance of the landmark autocontouring models (shoulders and mandible) was also quantified with sensitivity.

The end-to-end CSI autoplanning tool was used to generate single, extended, and multi-field spine configuration plans on 6 patients (ages: 3-10 years, median=7), resulting in 18 treatment plans. The autoplanning tool’s ability to cover the necessary targets and limit the dose to organs at risk was quantified using dose coverage metrics and mean and maximum dose, respectively. The optimization component of the autoplanning tool was assessed by calculating the “over-coverage region” in the spine field before and after optimization.

The autoplanning tool’s performance was then qualitatively assessed using physician review. First, the outputs of each step of the autoplanning code were reviewed by an experienced pediatric radiation oncologist and physicist. Second, the plan quality for each patient and field configuration was assessed individually for clinical acceptability by the same experienced radiation oncologist. The pediatric radiation oncologist evaluated the total plan with individual scores allocated for the brain and spine dose distributions. The lower of the two scores was assigned as the overall plan distribution score. All scoring took the dose distributions at the junctions into account. Each plan was scored on a scale of 1-5 where 5=acceptable – use -as-is, 4=acceptable – preferred stylistic minor edits, 3=acceptable – minor clinically necessary edits, 2=Unacceptable – major edits, 1=Unacceptable – unusable. Further details of the planning score rubric can be found in Table 1 of the supplementary documentation.

# Results

## Autocontouring

The autocontouring tool successfully contoured all structures in 20 ± 1.2 minutes. The performance of the autocontouring algorithms is shown in Fig. 4. The average DSC and HD achieved on the structures translated from the adult algorithm (brain, brainstem, L/R eye, and L/R lens) ranged from 0.65 to 0.98 and 0.46 to 0.97 cm, respectively. The difference between the DSC and HD achieved on the pediatric and previously published adult data sets14 was not statistically significant for each structure tested (*P* < 0.05), suggesting that adult contouring algorithms can be used to accurately contour structures in the HN region for pediatric patients.

The mean DSC and HD of the L/R kidney, spinal canal, thyroid, cribriform plate, vertebral column, mandible, heart, L/R lung, and shoulders ranged from 0.73 to 0.95 and 0.90 to 3.10 cm, respectively. Five structures achieved a mean DSC >0.90 and a HD <1 cm. The models were able to identify the superior slice of shoulders and inferior slice of the mandible with 100% sensitivity.

## Autoplanning

The algorithm successfully generated treatment plans for all 3 spine field configurations in 3.50 ± 0.4 minutes. Fig. 5 summarizes the resulting dose distributions across 18 plans. Plans were evaluated for a standard prescription dose of 23.4 Gy in 13 fractions. The average V95 for the brain for single, extended, and multi-field spine configurations was 99.9 ± 0.06%, 99.9 ± 0.07%, and 99.9 ± 0.06%, respectively. The average V95 for the spinal canal for single, extended, and multi-field configurations was 99.9 ± 0.10%, 99.4 ± 0.30%, and 99.4 ± 0.40%, respectively. The average V95 for the cribriform plate was 96.8 ± 2.50% across all 3 spine field configurations. Finally, the average V20 for the kidneys was 5.54 ± 3.07% across all 3 spine field configurations.

The mean and maximum doses were quantified for selected normal tissue contours of interest. The average maximum dose across all field configurations to the brainstem, L/R eye, L/R lens, and spinal cord were 23.7 ± 0.08 Gy, 24.1 ± 0.28 Gy, 13.3 ± 5.27 Gy, and 25.5 ± 0.34 Gy, respectively. The average mean dose to the heart, lungs, and thyroid across all 3 field configurations was 11.3 ± 1.10 Gy, 2.56 ± 0.15 Gy, and 16.5 ± 2.41 Gy, respectively.

The performance of the spine optimization algorithm is summarized in Fig. 6. The algorithm was able to reduce the spine over-coverage region for all 18 plans tested. The average amount of over-coverage length reduction was 11.5 ± 7 cm, 13.5 ± 6 cm, and 9.50 ± 2.4 cm for single, extended, and multiple field configurations, respectively. The weight of the sub-field ranged from 4% to 5% for single field, 3% to 5% for extended field, and 5% to 6% for multi-field configurations. The number of monitoring units given to the sub-field ranged from 7 to 12 across all spine configurations.

An experienced pediatric radiation oncologist concluded that the algorithm correctly placed isocenters, generated fields, optimized field match lines, and feathered junctions for each of the 18 plans tested. Of the 18 plans tested, all were clinically acceptable with no or minor edits. The individual brain and spine dose distributions of the 18 plans were scored ≥3 across each spine field configuration. For the brain dose distributions across all spine field configurations, 50% were scored as clinically acceptable with minor, stylistic edits preferred (score=4) and 50% were scored as acceptable with minor, clinically necessary edits required (score=3). For single, extended and multiple spine field configuration dose distributions, all were clinically acceptable with majority scored as ‘use-as-is’. Ten, 5, and 3 plans were scored as 5, 4, and 3, respectively. For the overall dose distribution (brain and spine), 9 plans were scored as clinically acceptable with minor, stylistic edits preferred (score=4), and 9 plans were scored as acceptable after incorporating minor clinically necessary edits that are more efficient than creating a new plan (score=3). No plans required major edits or were clinically unacceptable (score <3).

Examples of necessary edits are illustrated in Fig. 5A. For the brain fields, examples of minor edits included adjusting multi-leaf collimator positions to optimize cribriform plate coverage and adding optimization fields to eliminate small hotspots (107%) in the frontal lobe. Under-coverage was attributed to the autocontouring model’s inconsistently identifying the most superior slice of the cribriform plate. The results of the review emphasized that cribriform plate coverage is prioritized at the expense of increased lens dose. For the spine fields, examples of minor edits include adjusting the weighting of the optimization sub-fields. In patients with very small anatomy, the 107% isodose line began to approach the posterior spinal canal. The physician review suggested that the dose distribution in this scenario could be improved by adjusting the sub-field beam weighting or adding an additional sub-field.

# Discussion

In this work, we successfully autocontoured selected normal tissue and landmark structures to guide CSI autoplanning. Nine of the tested structures achieved a DSC score above 0.90 and an HD less than 1 cm. We used the autocontours to successfully script a comprehensive autoplanning workflow that mimicked the manual planning workflow of pediatric radiation oncologists. In summary, the autoplanning tool successfully generated, optimized, and feathered 18 treatment plans across 3 spinal field configurations to cater to spine length variability observed in pediatrics. The dose metrics of the target volumes and the selected normal tissue contours was comparable to what has been recommended by the results of clinical trials in pediatric radiation oncology.25,26 Finally, of the 18 plans tested, all were clinically acceptable and did not require major edits.

To our knowledge, this is the first work to test an adult autocontouring algorithm on pediatric patients. Our results suggest that adult contouring algorithms can be used to accurately contour structures in the HN region, including the brain, brainstem, eyes, and lenses of pediatric patient scans. The DSC and HD achieved on the pediatric autocontours were comparable to published data from adult patient cohorts.14,27 Careful review must be done before using the contours, especially for small patients.

A major benefit of our work is the potential to expedite radiation therapy workflows by decreasing the treatment planning time. Significant delays in radiation therapy have been associated with poor outcomes of pediatric brain tumor patients in resource-constrained centers.28 Recent trials from the SIOP group have emphasized a need for expediting radiation therapy planning because delaying treatment more than 7 weeks increases the risk of relapse.29,30 Our experience indicates that manual CSI contouring and planning takes hours to complete. Therefore, automating each process should save significant time per patient. This is supported by Zieminski et al., who reported that auto-contouring 6 normal tissue structures for CSI treatment planning saved radiation oncologists over 2 hours of labor.31 Our comprehensive auto-contouring tool generated 16 normal tissue structures in 20 ± 1.2 minutes and a full plan in an additional 3.50 ± 0.4 minutes without user involvement. Additional time may be required to apply minor edits to the plans such as adjusting MLCs to increase cribriform plate coverage. Our results yield potential for strong clinical impact, and we suspect that further optimization could further expedite the algorithms. The autocontouring and autoplanning process requires minimal user intervention, which allows the radiation oncology team to dedicate saved planning time to other necessary clinical tasks.

As in manual planning, errors in the autoplanning design can introduce risk.32 CSI cases are difficult to plan as they require multiple, matched fields to cover the target volume. If the fields are not matched correctly, serious complications can occur.33 To this end, QA checks have been designed in our autoplanning workflow to check the jaw positions in the composite plan to make sure that the junctions’ shifts are correctly spaced. Moreover, our algorithm uses autocontours to perform additional QA checks such as evaluating and flagging the mandible dose from spine field beam divergence. The algorithm makes use of pre-determined beam geometries, which allows for a more consistent approach to patient setup. Additional QA algorithms may be integrated into the workflow to reduce risk. Examples of such algorithms include automatically identifying and flagging hotspot volumes above a certain tolerance and automatically verifying field shapes.34

Our study has some limitations. While the autocontouring tool was tested on 30 patients, final testing of the autoplanning tool was limited by the number of available CT images compatible with the planning technique. To this end, future, extensive testing will assess robustness of the planning tool on a larger dataset. The autoplanning tool described in this work is limited to a single approach to CSI planning based on recommendations from an experienced pediatric radiation oncologist and SIOP.18 However, the autoplanning tool may easily be re-configured to cater to alternative planning approaches such as different brain field shapes, different brain field gantry angles, and different field margins. Moreover, the autoplanning tool proposed in our work addresses a single radiation therapy planning technique (3D-conformal CSI), although this technique was selected because 84% of resource-constrained clinics have access to and are regularly using it to treat pediatric medulloblastoma.18

The auto-contouring and auto-planning algorithms can be directly integrated into treatment planning systems that support scripting (i.e. Raystation and Eclipse) and treatment machines that support MLCs. After extensive clinical testing, the auto-contouring and auto-planning tools will also be integrated into the Radiation Planning Assistant (RPA) for use in resource-constrained centers.10 To use the RPA, the user submits a patient’s CT scan and the RPA will automatically generate the necessary contours and treatment plan. The user then applies any edits to the contours or plan. As in a manual workflow, the physician is responsible for approving the final contours and plan before treatment.

Regarding barriers of using the tool in resource-constrained settings, McGinnis et al., summarized their experience piloting RPA teaching sessions in Sub-Saharan Africa and Central America. In a post session survey of 30 providers (91% response rate), 87% of users expressed interest in using the RPA in their routine clinical workflow. Potential barriers reported included lack of reliable internet connection (80%), potential subscription fees (60%) and a need for functionality in additional disease sites (48%). The responses provided an initial framework to establish how to address these barriers before RPA deployment.35

In conclusion, we quantitatively assessed the use of an adult autocontouring model in a pediatric cohort of 143 patients with medulloblastoma. We generated pediatric-specific autocontouring models for normal tissue structures and used them to guide an autoplanning tool. The end-to-end autoplanning tool successfully generated composite plans for 18 plans tested across 3 spine field configurations, indicating that the algorithm is robust in its adjustment to spine field-length variations found in pediatric CSI. Automating the contouring and planning workflow for pediatric CSI has the potential to increase the efficiency of workflows in resource-constrained cancer centers and subsequently improve access to high-quality radiation therapy.

# **Conflict of Interest Statement for All Authors**

Hester Burger is currently employed by Varian Medical Affairs, with a sessional lecturing position at the University of Cape Town.

# **Acknowledgements**

SH is supported by a Cancer Prevention and Research Institute of Texas (CPRIT) Training Award (RP210028) and the Dr. John and Mrs. Charlene Kopchick training fellowship. Editorial support was provided by Bryan Tutt, Scientific Editor, of the Research Medical Library at MD Anderson. We acknowledge the support of the High-Performance Computing for research facility at The University of Texas MD Anderson Cancer Center for providing computational resources that have contributed to the research results reported in this article.

# References

1. Parkes, J. *et al.* Recommendations for the treatment of children with radiotherapy in low- and middle-income countries (LMIC): A position paper from the Pediatric Radiation Oncology Society (PROS-LMIC) and Pediatric Oncology in Developing Countries (PODC) working groups of . *Pediatr. Blood Cancer* **64**, e26903 (2017).

2. Childhood cancer funding archives - American childhood cancer organization (ACCO). https://www.acco.org/blog/tag/childhood-cancer-funding/.

3. Yap, M. L. *et al.* The Benefits of Providing External Beam Radiotherapy in Low- and Middle-income Countries. *Clin. Oncol.* **29**, 72–83 (2017).

4. CAMPEP: Commission on Accreditation of Medical Physics Educational Programs, Inc. https://www.campep.org/.

5. Standards for accreditation of residency educational programs in medical physics.

6. American Board of Radiology (ABR). https://www.theabr.org/radiation-oncology/initial-certification/initial-certifications-requirements.

7. Human Health Campus - Accreditation and Certification. https://humanhealth.iaea.org/HHW/MedicalPhysics/TheMedicalPhysicist/EducationandTrainingRequirements/Accreditation\_and\_Certification/index.html.

8. Datta, N. R., Samiei, M. & Bodis, S. Radiation Therapy Infrastructure and Human Resources in Low- and Middle-Income Countries: Present Status and Projections for 2020. *Int. J. Radiat. Oncol.* **89**, 448–457 (2014).

9. Wang, M., Zhang, Q., Lam, S., Cai, J. & Yang, R. A Review on Application of Deep Learning Algorithms in External Beam Radiotherapy Automated Treatment Planning. *Front. Oncol.* **10**, (2020).

10. Court, L. E. *et al.* Radiation planning assistant - A streamlined, fully automated radiotherapy treatment planning system. *J. Vis. Exp.* (2018) doi:10.3791/57411.

11. Kisling, K. *et al.* Fully Automatic Treatment Planning for External-Beam Radiation Therapy of Locally Advanced Cervical Cancer: A Tool for Low-Resource Clinics. *J. Glob. Oncol.* (2019) doi:10.1200/jgo.18.00107.

12. Kisling, K. *et al.* Automated treatment planning of postmastectomy radiotherapy. *Med. Phys.* (2019) doi:10.1002/mp.13586.

13. McCarroll, R. E. *et al.* Retrospective Validation and Clinical Implementation of Automated Contouring of Organs at Risk in the Head and Neck: A Step Toward Automated Radiation Treatment Planning for Low- and Middle-Income Countries. *J. Glob. Oncol.* (2018) doi:10.1200/jgo.18.00055.

14. Rhee, D. J. *et al.* Automatic detection of contouring errors using convolutional neural networks. *Med. Phys.* (2019) doi:10.1002/mp.13814.

15. Netherton, T. An automated treatment planning framework for spinal radiotherapy and vertebral level second check. *Int. J. Radiat. Oncol. • Biol. • Phys.* (2022).

16. Shu, L.-Q., Sun, Y.-K., Tan, L.-H., Shu, Q. & Chang, A. C. Application of artificial intelligence in pediatrics: past, present and future. *World journal of pediatrics : WJP* vol. 15 105–108 Preprint at https://doi.org/10.1007/s12519-019-00255-1 (2019).

17. V, G. & P, G. Technology, big data, and the future of paediatric neuroscience: let us go then, you and AI. *Dev. Med. Child Neurol.* **62**, 884 (2020).

18. Parkes, J. *et al.* SIOP PODC adapted treatment recommendations for standard-risk medulloblastoma in low and middle income settings. *Pediatr. Blood Cancer* **62**, 553–564 (2015).

19. Kiltie, A. E., Povall, J. M. & Taylor, R. E. The need for the moving junction in craniospinal irradiation. *Br. J. Radiol.* **73**, 650–654 (2000).

20. Pediatric Radiation Oncology - Louis S. Constine, Nancy J. Tarbell, Edward C. Halperin - Google Books. https://books.google.com/books?hl=en&lr=&id=j9ufDAAAQBAJ&oi=fnd&pg=PT24&ots=N5silhjyEl&sig=ZBUfI0bmT-CVHF0khXxAvoIVJwM#v=onepage&q&f=false.

21. Giebeler, A. *et al.* Standardized treatment planning methodology for passively scattered proton craniospinal irradiation. *Radiat. Oncol. Lond. Engl.* **8**, 32 (2013).

22. Ajithkumar, T. *et al.* SIOPE – Brain tumor group consensus guideline on craniospinal target volume delineation for high-precision radiotherapy. *Radiother. Oncol.* **128**, 192–197 (2018).

23. Isensee, F., Jaeger, P. F., Kohl, S. A. A., Petersen, J. & Maier-Hein, K. H. nnU-Net: a self-configuring method for deep learning-based biomedical image segmentation. *Nat. Methods* **18**, 203–211 (2021).

24. D, B. RayStation: External beam treatment planning system. *Med. Dosim. Off. J. Am. Assoc. Med. Dosim.* **43**, 168–176 (2018).

25. AREN0532: Treatment for Very Low and Standard Risk Favorable Histology Wilms Tumor. https://childrensoncologygroup.org/aren0532.

26. Leavey, P. J. *et al.* Phase III Trial Adding Vincristine-Topotecan-Cyclophosphamide to the Initial Treatment of Patients with Nonmetastatic Ewing Sarcoma: A Children’s Oncology Group Report. *J. Clin. Oncol.* **39**, 4029–4038 (2021).

27. Cardenas, C. E., Yang, J., Anderson, B. M., Court, L. E. & Brock, K. B. Advances in Auto-Segmentation. *Semin. Radiat. Oncol.* **29**, 185–197 (2019).

28. Baskin, J. L. *et al.* Management of children with brain tumors in Paraguay. *Neuro-Oncol.* **15**, 235–241 (2013).

29. Lannering, B. *et al.* Hyperfractionated versus conventional radiotherapy followed by chemotherapy in standard-risk medulloblastoma: results from the randomized multicenter HIT-SIOP PNET 4 trial. *J. Clin. Oncol. Off. J. Am. Soc. Clin. Oncol.* **30**, 3187–3193 (2012).

30. Taylor, R. E. *et al.* Impact of radiotherapy parameters on outcome in the International Society of Paediatric Oncology/United Kingdom Children’s Cancer Study Group PNET-3 study of preradiotherapy chemotherapy for M0-M1 medulloblastoma. *Int. J. Radiat. Oncol. Biol. Phys.* **58**, 1184–1193 (2004).

31. Zieminski, S., MacDonald, S., Looney, P. & Wang, Y. Development and Evaluation of the First Pediatric Deep-Learning Auto-Contouring Models for Cranio-Spinal Irradiation (CSI). *Int. J. Radiat. Oncol.* **111**, e176–e177 (2021).

32. Nealon, K. A. *et al.* Using Failure Mode and Effects Analysis to Evaluate Risk in the Clinical Adoption of Automated Contouring and Treatment Planning Tools. *Pract. Radiat. Oncol.* (2022) doi:10.1016/J.PRRO.2022.01.003.

33. Jane Dobbs, H., Parker, R. P., Hodson, N. J., Hobday, P. & Husband, J. E. The use of CT in radiotherapy treatment planning. *Radiother. Oncol.* **1**, 133–141 (1983).

34. Kisling, K. *et al.* A risk assessment of automated treatment planning and recommendations for clinical deployment. *Med. Phys.* (2019) doi:10.1002/mp.13552.

35. McGinnis, G. J. *et al.* Barriers and Facilitators of Implementing Automated Radiotherapy Planning: A Multisite Survey of Low- and Middle-Income Country Radiation Oncology Providers. *JCO Glob. Oncol.* e2100431 (2022) doi:10.1200/GO.21.00431.

# Legends

**Figure 1.** **Outline of craniospinal irradiation auto-planning workflow**. Normal structures and landmark structures are automatically contoured using deep learning methods. The autocontours then guide an autoplanning algorithm scripted in the treatment planning system. Auto-contours are used to automatically set isocenters and define target and prescription volumes. Fields are automatically generated and conformed to the specified targets. The dose is prescribed, and the dose to the spine field is optimized. The original plan is feathered with 2 junction shifts. Finally, a composite plan is generated.

**Figure 2. Outline of isocenter placement.** Brain isocenter is set 2.5 cm above the most superior slice of the shoulder contour (green) and centered within the spinal canal. There are 3 possible spine field configurations designed to adjust to variations in pediatric spine length with age. The algorithm automatically calculates the required length of the spine field and assigns the proper configuration. If the distance is less than or equal to 40 cm, a single spine field is used; if the distance is greater than 40 cm but less than the maximum field size achieved by a specified extended source to surface distance (SSD), an extended spine field is used. Finally, if the spine length is greater than the maximum field size achieved using an extended SSD, multiple fields are used.

**Figure 3. Outline of spine optimization algorithm.** The spine optimization algorithm begins by quantifying how much of the 95% isodose line is greater than or equal to 5 mm anterior to the spinal canal. A sub-field is generated to block this volume. The sub-field is iteratively weighted 1% to 10% of the primary beam weight until the over-coverage region is no longer minimized or the maximum beam weighting has been reached. The resulting dose distribution after optimization is shown here. ROI, region of interest.

**Figure 4. Summary of autocontouring model performance. (A)** Dice similarity coefficient (DSC) and Hausdorff distance (HD) achieved on autocontoured structures**.** Boxplots demonstrating the performance of the adult autocontouring algorithms (blue) and the pediatric-specific algorithms (orange). The adult autocontouring model was tested on 143 pediatric full body CSI CT scans, and the pediatric auto-contouring model was tested on 30 patients (20% of the full data set; 80% was used for training). Among 17 structures, an average DSC above 0.80 was achieved in 14, and an HD below 1 cm was achieved in 13. **(B)** Visual example of auto-contours in the coronal and sagittal plane.

**Figure 5: Summary of autoplanning dose distributions. (A)** Sagittal dose distributions for plans requiring no edits, minor, preferred edits and minor, necessary edits, respectively. **(B)** Dose-volume histogram (DVH) summarizing dose delivered to the targets (brain and spinal canal) and normal tissues (eyes and lenses) averaged across the 18 treatment plans tested. The solid lines represent the mean DVH values, and the shaded portions represent 1 standard deviation in values across the various spine field configurations.

**Figure 6. Summary of spine optimization algorithm performance.** (Left) Boxplot summarizing the distribution of the over-coverage region lengths across 3 spine field configurations before (blue) and after (orange) spine field optimization. (Right) Sagittal CT showcasing the reduction in over-coverage volume before (blue) and after (orange) spine field optimization for a single-field patient.