Assessment of the generalizability to pediatric protontherapy of a 3D network generating pseudo-CT

Emilie Alvarez Andres[1,2,3], Maélie Caussé[1,3], Lucas Fidon[2,4], Louis Ermeneux[3,5], Stéphanie Bolle[3], Valentine Martin[3], Nikos Paragios[2], Eric Deutsch[1,3], Ludovic De Marzi[6], Charlotte Robert[1,3]

[1]Molecular radiotherapy and innovative therapeutics, INSERM UMR1030, Gustave Roussy Cancer Campus, Université Paris Saclay, Villejuif, France; [2]TheraPanacea, Paris, France; [3]Department of radiation oncology, Gustave Roussy Cancer Campus, Villejuif, France; [4]MICS Laboratory, CentraleSupélec, Paris-Saclay University, 91190, Gif-sur-Yvette, France; [5]Centre for Research in Epidemiology and Population Health (CESP), U1018, Radiation Epidemiology Group, Villejuif, France; [6]Normal and Pathological Signaling: from the embryo to the innovative therapy of cancers, Institut Curie - Inserm – CNRS UMR 3347 – PSL Research University - Paris-Saclay University, Orsay, France.

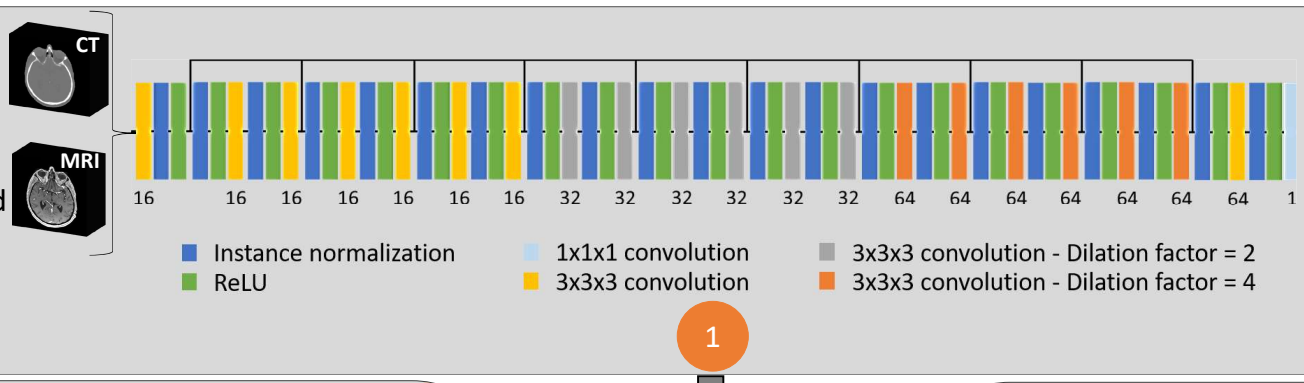
Introduction

Brain tumor radiotherapy treatments require the acquisition of a Computed Tomography (CT) and a T1 weighted Magnetic Resonance Imaging (T1) or contrast-enhanced T1 weighted MRI (T1-Gd). A registration is applied to place all the images in the same spatial frame, which has been reported to produce errors up to 2mm (1) leading to increased margins. As a result, generating pseudo Computed Tomography (pCT) appears to be a relevant approach to boost the patient safety. In this study, a 3D convolutional network, previously trained and validated on adult patients treated with Intensity Modulated Radiation Therapy (IMRT), was tested on an unseen cohort composed of pediatric protontherapy patients to evaluate its generalizability.

Material and Methods

Input data description:

- Brain tumor adult patients treated with IMRT
- 162 CT/T1, 161 CT/T1-Gd
- Training set size= 242 cases
- Validation set size=81 cases



Modified 3D HighResNet (2) architecture advantages:
The residual connections and dilated convolution filters ensure an absence of vanishing/exploding gradients and a high receptive field respectively

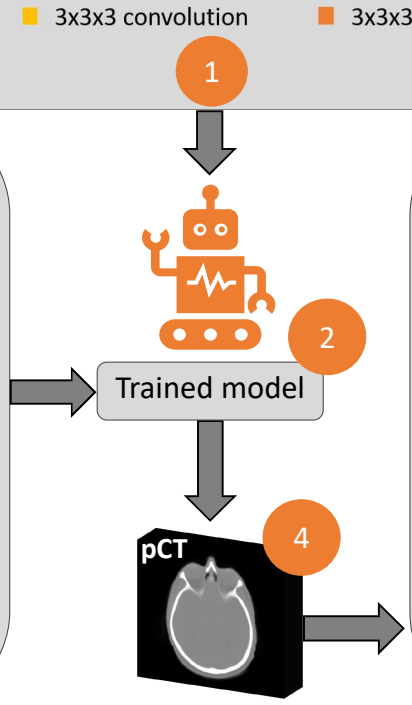
Testing cohort description (18 patients): (3)

- Mean age +/- standard deviation = 12.5 years +/- 3.6 years [minimum = 6.0 years, maximum = 17.4 years]
- Craniopharyngioma
- Double scattering protontherapy
- Dosimetry was performed on a sub-cohort composed of 16 cases treated with 3 beams (2 patients), 4 beams (3 patients), 5 beams (7 patients) and 6 beams (4 patients).

Images : CT and T1-Gd

Preprocessing:

- Rigid registration
- Linear resampling to a 1mmx1mmx1mm voxel size
- Zero mean/unit variance standardization
- Hounsfield Units (HU) and MRI intensities clip



(5)

- **Mean Absolute Error** (MAE) defined as:

$$\frac{1}{N} \times \sum_{i=1}^{N} |Intensity\ CT(i) - Intensity\ pCT(i)|$$

With N the total number of voxels. MAE was computed in the whole head, air, bone and water areas

- Dosimetry: Re-calculation of the initial plan on the pCT with the pencil beam algorithm of the treatment planning system DOSIsoft (Isogray). Calculation of **differences in Dose Volume Histograms** (DVH) of the planning target volume and global **gamma indexes** (1%/1mm, 2%/2mm, 3%/3mm) without dose threshold

Results and Discussion

- The computation time for the pCT generation was **83s** on a single GPU GeForce GTX 1080Ti.
- MRI, CT, pCT and gamma maps for two given patients are presented in Figure 1. Reconstruction errors appear to be mostly located in the air and bone regions.
- Mean MAE and standard deviations of **111HU+/-12HU**, 364HU+/-56HU, 279HU+/-27HU and 60HU+/-10HU were obtained for the whole head, air, bone and water areas respectively.
- Regarding the dosimetry results, the 1%/1mm, 2%/2mm and 3%/3mm gamma indexes were equal to **96.44%+/-2.22%, 97.92%+/-1.54%** and **99.59%+/-0.59%** respectively.
- All 2%, 50%, 95% and 98% mean DVH differences were below **0.3%**.
- A previous study (3) tested the network on a cohort of 79 adult patients treated with IMRT. Head MAE of **83HU+/-22HU**, and gamma indexes of **97.90%+/-1.10%, 99.61%+/-0.30%** and **99.83%+/-0.19%** for the 1%/1mm, 2%/2mm and 3%/3mm criteria were respectively obtained.

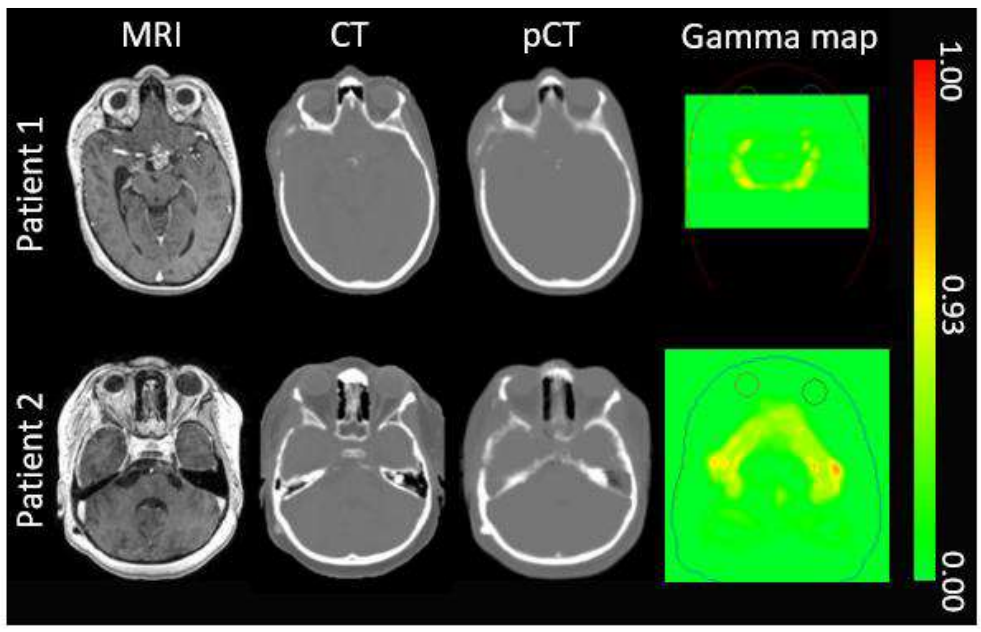


Figure 1: T1-Gd MRI, CT, pCT and gamma maps for the 3%/3mm criterion presented for Patient 1 (17 years old, 6 beams-based treatment, pass rate = 99.69%) and Patient 2 (6 years old, 6 beams-based treatment, pass rate = 99.82%). To improve visibility, external and eye contours are displayed on the gamma maps.

Conclusion

The goal of the study was to evaluate the generalizability of a model trained and validated on an adult cohort, on pediatric cases treated with protontherapy. To our knowledge, it is the first study testing a 3D network with an unseen patient category. Small differences were observed with the study based on the 79 adult patients, suggesting the robustness and the high generalizability of the developed model, and its clinical implementation feasibility.

Acknowledgment and References

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No. 880314.

1. Ulin K, Urie MM, Cherlow JM. Results of a multi-institutional benchmark test for cranial CT/MR image registration. Int J Radiat Oncol Biol Phys. 1 août 2010;77(5):1584-9.
2. Li W, Wang G, Fidon L, Ourselin S, Cardoso MJ, Vercauteren T. On the Compactness, Efficiency, and Representation of 3D Convolutional Networks: Brain Parcellation as a Pretext Task. In: Niethammer M, Styner M, Aylward S, Zhu H, Oguz I, Yap P-T, et al., éditeurs. Information Processing in Medical Imaging. Springer International Publishing; 2017. p. 348-60. (Lecture Notes in Computer Science).
3. Alvarez Andres E, Fidon L, Vakalopoulou M, Lerousseau M, Carré A, Sun R, et al. Dosimetry-Driven Quality Measure of Brain Pseudo Computed Tomography Generated From Deep Learning for MRI-Only Radiation Therapy Treatment Planning. Int J Radiat Oncol Biol Phys. 14 mai 2020;