# Developing a framework for CBCT-to-CT synthesis in paediatric abdominal radiotherapy

Adam Szmul<sup>1</sup>, Sabrina Taylor<sup>1</sup>, Pei Lim<sup>2</sup>, Jessica Cantwell<sup>2</sup>, Derek D'Souza<sup>2</sup>, Syed Moinuddin<sup>2</sup>, Mark Gaze<sup>2</sup>, Jennifer Gains<sup>2</sup>, and Catarina Veiga<sup>1</sup>

<sup>1</sup> University College London, London, United Kingdom
<sup>2</sup> University College London Hospitals NHS Foundation Trust, London, United Kingdom

**Abstract.** We proposed a CBCT-to-CT synthesis framework tailored for paediatric abdominal patients. Our approach was based on the cycle-consistent generative adversarial network (cycleGAN) modified to preserve structural consistency. To adjust for differences in field-of-view and body size from different patient groups, our training data was spatially co-registered to a common field-of-view and normalised to a fixed size. The proposed framework showed improvements in generating synthetic CTs from CBCTs compared to the original implementation of cycleGAN without field-of-view adjustments and structural consistency constrain.

**Keywords:** Cone-beam computed tomography (CBCT), computer tomography (CT), cycle-consistent generative adversarial networks (cycleGANs), synthetic images, childhood cancer, abdominal neuroblastoma, paediatric radiotherapy

## 1 Introduction

Synthesizing computed tomography (CT) images from cone-beam CT (CBCT) using cycle-consistent generative adversarial networks (cycleGANs)<sup>1</sup> is becoming a popular method to verify and adapt radiotherapy treatments. However, current approaches still cannot guarantee sufficient structural consistency between source and synthetic images<sup>2-4</sup>. Furthermore, application of this methodology to abdominal images of children is particularly challenging<sup>5</sup>. The abdominal region is complex due to the inter-fractional variability in bowel filling. The paediatric cancer population is simultaneously diverse (ranging from infants to adolescents, therefore exhibiting large anatomical variability across development ages) and rare, making it difficult to collect large datasets for data-driven approaches. This work proposes a novel framework for CBCT-to-CT synthesis tailored for paediatric abdominal patients aiming to addresses these challenges.

# 2 Materials and Methods

Fully anonymised scans from 21 patients aged 2 to 22 treated at University College London Hospital were used in this study. Subjects treated for malignancies in the

thoracic-abdominal-pelvic region were combined to increase the dataset size. The inclusion of young adults provides additional variability in patient size. One planning CT and 2 to 6 CBCTs were available per patient. The data were split as 15/6 patients for training and evaluation, respectively.

The synthetic CT (synCT) generation pipeline with the proposed field-of-view adjustment and structural consistency included the following key steps:

(1) Smart slice selection: The CT/CBCT training set was spatially normalized to a reference anatomy using an atlas-based method developed in-house<sup>6</sup>. From the spatial and anatomical distribution of the slices available, a region of interest was defined from fusing the mapped body contours (50% majority voting). This adjusted field-of-view approach reduced the number of slices from 4291 to 3740 for CBCT.

(2) Image pre-processing: To prevent the networks from adding elements such as tubes and internal lines to unseen synthetic images, these external elements and other artifacts were semiautomatically removed from the training images. Then, the images were resized to a fixed size of 256x256 (axial normalization) to account for variation in body size across ages.

(3) Network design: A 2D cycleGAN approach for CT-to-CBCT synthesis was applied, known for its good performance in unpaired data style conversion<sup>1</sup>. To promote preservation of the CBCT anatomy, the original formulation was extended by introducing a structure consistency loss in the form of locally normalized cross correlation (LNCC), between the original images and their synthesized counterparts.

We trained six cycleGAN networks with combinations of including or not axial normalization, consistent field-of-view and structure consistency loss in the pipeline. The networks were trained for 150 epochs.

Evaluating the quality and plausibility of synthetic images is a challenging task due to the lack of a ground-truth (i.e., pairs of simultaneously acquired CT/CBCT scans). To address this, we have generated a virtual CT (vCT) scan matched to the anatomy of the CBCTs. The vCT was generated by deformably registering the planning CT to the CBCT. The vCT was then corrected by replacing gas regions deformed from the original CT as water, and gas regions directly from the CBCT as air. The gastrointestinal gas was semi-automatically delineated in all scans using ITK-Snap<sup>7</sup>. The synCT were globally compared to the vCT by computing three image similarity metrics between the two images: sum of squared differences (SSD), normalised cross-correlation (NCC) and normalised mutual information (NMI). Voxels outside the body contour were excluded from analysis based on semiautomatic binary masks. Intensities in all images were clipped to [-1000, 1000].

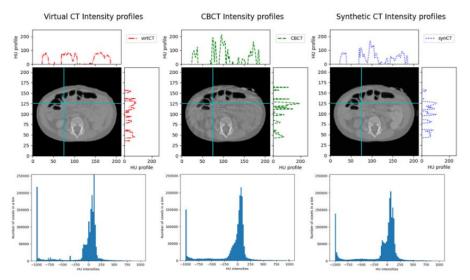
#### **3** Results and Discussion

We summarized the obtained numerical results in Table 1, where we compared the raw CBCTs versus vCTs, as well as different approaches for synCTs generation. Considering the cycleGAN with default data selection approach as baseline, improvements were observed when the proposed improved data presentation was applied. For each data representation, the structure consistency constrain term contributed to further improvements in the network performance. In fact, the biggest improvement was observed between the original cycleGAN method with and without structure constrains.

Method	Dataset	SSD	NCC	NMI
Original CBCT	N/A	66±9	0.956±0.008	$0.585 \pm 0.011$
cycleGANs	No data selection	146±17	0.710±0.095	$0.925 \pm 0.008$
cycleGANs+LNCC		62±8	0.956±0.009	0.930±0.008
cycleGANs	Axial normalisation	72±10	0.934±0.015	0.933±0.008
cycleGANs+LNCC		61±7	0.958±0.008	0.931±0.008
cycleGANs	Axial normalisation &	69±7	0.943±0.010	0.931±0.009
cycleGANs+LNCC	consistent field-of-view	63±6	0.955±0.007	0.933±0.008

Table 1. Quantitative evaluation between vCT, CBCT and synCT with different methods.

Examples of vCT, CBCT and synCT slices are shown in Fig. 1. The synCTs generated with our improved network represented well the anatomy of the CBCTs and reduced imaging artifacts. The original cycleGANs algorithm had poorer performance in terms of anatomical realism and consistency across adjacent slices. Upon visual inspection, the images generated with LNCC structure constrain were more accurate anatomically. Typical patterns of failure were also visually identified, and included the algorithm removing/adding vertebrae to the synCTs as well as adding inexistent bowel contrast.



**Fig. 1.** Example 2D slices of vCT, CBCT and synCT (generated with consistent field-of-view and structure consistency), along with cross-sectional intensity profiles and 3D histograms.

### 4 Conclusions

The proposed framework showed improved quality of synCTs generated from CBCTs when employing strategies to preserve structural consistency and to account for variable field-of-view in the training dataset. Our study demonstrated the advantages of a thought-through data pre-processing and presentation to the AI method to improve its performance on challenging real-world applications, with scarce and diverse data. Further evaluation using metrics of anatomical plausibility and realism, as well as impact on dose calculations, is need to provide insights into clinical utility.

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#### References

- 1. Zhu, J.-Y. et al, "Unpaired Image-to-Image Translation using Cycle-Consistent Adversarial Networks," IEEE International Conference on Computer Vision (ICCV) (2017)
- Liang, X. et al, "Generating synthesized computed tomography (CT) from cone-beam computed tomography (CBCT) using CycleGAN for adaptive radiation therapy," Phys Med Biol. 64(12):125002 (2019)
- 3. Kurz, C. et al, "CBCT correction using a cycle-consistent generative adversarial network and unpaired training to enable photon and proton dose calculation," Phys. Med. Biol. 64(2):225004 (2019)
- 4. Liu, Y. et al, "CBCT-based synthetic CT generation using deep-attention cycleGAN for pancreatic adaptive radiotherapy," Med. Phys 47(6):2472-83 (2020)
- Uh, J., et al, "Training a deep neural network coping with diversities in abdominal and pelvic images of children and young adults for CBCT-based adaptive proton therapy," Radiother. Oncol. (in press, 2021)
- 6. Veiga, C. et al: Atlas construction and spatial normalisation to facilitate radiation-induced late effects research in childhood cancer," Phys. Med. Biol. 66(10):105005 (2021)
- Yushkevich, P. et al: "User-guided 3D active contour segmentation of anatomical structures: Significantly improved efficiency and reliability," Neuroimage 31(3):1116-28 (2006)