Medical Image Analysis (2024)



Contents lists available at ScienceDirect

Medical Image Analysis



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Generating Synthetic Computed Tomography for Radiotherapy: SynthRAD2023 Challenge Report - Supplementary Document B

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This document is a supplementary document to Huijben and Terpstra et al. "Generating Synthetic Computed Tomography for Radiotherapy: SynthRAD2023 Challenge Report".

1. Supplementary analyses and results

This document provides additional analyses and results from the SynthRAD2023 challenge, which defined two tasks: 1) magnetic resonance imaging (MRI) to computed tomography (CT) synthesis and 2) cone beam CT (CBCT) to CT synthesis. These additional analyses include comparing the performance differences between all teams for each evaluation metric and investigating their statistical significance. In addition, we analyze the runtime of each team's algorithm and examine the average performance per patient in the test set. Finally, we visually analyze the results for two low-performing patients.

1.1. Teams' performance and significance

To state the significance of a team outperforming another in terms of individual metrics, we employed the Wilcoxon signed-rank test (Wilcoxon, 1945) with Holm's adjustment for multiple testing (Holm, 1979) for each metric separately (Figures 1 and 2). The significance level for this test is set at $\alpha = 0.05$. Based on the image similarity metrics, high-ranking teams robustly outperform lower-ranked teams. Statistical significant improvements were observed when comparing all image metrics between a team and another team ranked at least seven places lower for task 1, or six placed lower for task 2. However, for the dose metrics, this relation is weaker. In task 1, no statistical significant differences were observed between the top fourteen teams regarding the proton dose metrics. In task 2, no statistically significant differences were observed between the top eight teams regarding the photon and proton dose metrics, except for the fifth team (Pengxin Yu), which significantly outperforms the sixth team (KoalAI) regarding the proton DVH metric. Furthermore, Figure 3 shows a detailed overview of the resource utilization per team per subtask.

1.2. Data influence

For task 1, we performed a more detailed analysis of the influence of magnetic field strength on sCT generation performance. However, the absence of variability in magnetic field strengths for centers B and C constrained this analysis to center A (Figure 4). For the brain, the only significant difference was observed for γ_{photon} , which decreased from 98.99 ± 1.43 for 1.5T to 97.33 ± 3.23 for 3T. In contrast, for the pelvis, a significant increase in performance was observed for 3T compared to 1.5T. Specifically, the SSIM increased from 0.83 ± 0.05 to 0.84 ± 0.05, γ_{photon} increased from 97.51 ± 3.45 to 98.75 ± 2.59, and γ_{proton} increased from 93.29 ± 4.05 to 95.64 ± 3.42.

In analyzing the synthetic CT (sCT) generation performance at the patient level for both tasks, we present the mean SSIM and mean photon gamma pass rate per patient in Figure 5. One pelvis patient in center A for task 2 is severely underperforming in terms of photon gamma pass rate, while multiple brain patients from center B are underperforming in task 1. A visual inspection of two of these patients (1BB183 and 2PA039) (Figure 6) reveals that for patient 1BB183 (Figure 6a), the image quality of sCTs is high. However, the table of the CT scanner is still visible in the ground truth CT but not in the MRI. Jetta_Pang was able to synthesize a table, increasing the gamma pass rate ($\gamma = 90.24\%$) while the other teams did not synthesize a table, which led to large dose errors ($\gamma = 75 - 79\%$). This leads to higher dose deposition within the target while omitting the dose deposition in the table, which received more than 10% of the target dose and is therefore included in the gamma pass rate analysis, causing low gamma pass rates for these patients. Further investigation shows this happened for multiple brain patients from center B in task 1. Furthermore, patient 2PA039 (Figure 6b) suffers from a low-quality CBCT with a central artifact combined with a small field-of-view, making image synthesis difficult.

References

Holm, S., 1979. A simple sequentially rejective multiple test procedure. Scandinavian journal of statistics , 65–70. Wilcoxon, F., 1945. Individual comparisons by ranking methods. Biometrics Bulletin 1, 80–83. doi:10.2307/3001968.



Fig. 1: Significance map of task 1. Visualizing pairwise comparisons of team performances for the individual metrics, where teams are sorted based on the performance for the respective metric. Yellow shading in the upper triangle indicates that the team on the x-axis performs significantly better than the y-axis, while blue indicates no significantly better performance. Blue in the lower triangle indicates that the team on the x-axis performs significantly worse than the team on the y-axis.



Fig. 2: Significance map of task 2. Visualizing pairwise comparisons of team performances for the individual metrics, where teams are sorted based on the performance for the respective metric. Yellow shading in the upper triangle indicates that the team on the x-axis performs significantly better than the y-axis, while blue indicates no significantly better performance. Blue in the lower triangle indicates that the team on the x-axis performs significantly worse than the team on the y-axis.



Fig. 3: Resource utilization during inference for tasks 1 (left) and 2 (right), represented by inference time and GPU usage. Values are averaged over 60 patients per subtask for each team, with different teams distinguished by colors. A cross represents brain averages, while a circle represents pelvis averages.



Fig. 4: Boxplots of the teams' performance for task 1 in terms of SSIM and gamma pass rates for photon and proton, grouped by different region, acquisition center and magnetic field strength. The number of test cases per subgroup is indicated by "n=x". Statistical significance (Mann-Whitney U-test, $\alpha = 0.01$) was calculated for center A between different field strengths of the same region and is indicated by an asterisk if significant.

Fig. 5: Mean SSIM versus mean photon gamma pass rate per patient, averaged over all participants. The hue encodes the center. Two patients are clear outliers, while multiple patients of center B are underperforming.

(a) Example sCTs for outlier patient 1BB183. The image quality is high, but the CT still contains the table, which is difficult to synthesize if not present in the input. The image error map has been masked with the provided mask.

(b) Example sCTs for outlier patient 2PA039. The challenging anatomy and artifacts make accurate sCT generation difficult. The image error map has been masked with the provided mask.

Fig. 6: Examples of underperforming patients: patient 1BB183 for task 1 (MRI-to-CT; a) and patient 2PA039 for task 2 (CBCT-to-CT: b). The model input is shown in the upper left, and the ground truth is in the center-left. The sCT of the top five participants for task 1 and task 2 are shown in the top row. The difference from ground truth CT after masking with the provided mask is shown in the middle row. On the bottom left is the planned irradiation based on the CT for a photon (a) and proton (b) plan. The bottom row shows the dose difference when the treatment plan is applied to the sCT (CT dose - sCT dose).