

Title

AI-driven combined deformable registration and image synthesis between radiology and histopathology

Authors

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Purpose or Objective

Although widely used for all steps of cancer treatment, radiologic imaging modalities (CT, MRI, ...) provide insufficient assessment of tissue properties and cancer proliferation. A complete understanding of tumor micro-environment often goes through additional pathologic examination on surgically excised specimens requiring a multimodal registration between 2D histological slide and 3D anatomical volume. Yet, this step is substantially difficult because of the extreme shrinkage and out-of-plane deformations that the tissue undergoes through histological process, the differences in resolution scales and color intensities, often imposing a burdensome time-consuming manual mapping. The aim of our work is to provide an end-to-end deep learning framework to automatically register 2D histopathology with 3D radiology in an unsupervised and deformable setting. The latter could directly be integrated into the treatment plan for better delineation and comprehension of tumor heterogeneity towards dose painting.

Materials and Methods

We have settled a private cohort made of 75 patients (45/10/20 for train/validation/test sets) on whom were acquired both pre-operative H&N CT scan and digitalized whole slide images after total laryngectomy. The number of histopathology slides per patient ranges from 4 to 11 with a theoretical spacing of at least 5mm between them. Our work's novelty is two-fold: first, to solve the multimodal issue, we developed a generative framework based on cycleGANs that predict CT from histology and vice versa. Second, concerning the dimensional constraint, the resulting 2D synthetic CT along with the original 3D CT become the input for a multi-slices-to-volume registration pipeline in a fully unsupervised learning context. End-to-end integration allows a direct mapping CT/histology and provides the radiation oncologist with additional biological insights.

Results

Figure 1 presents the pipeline with one example from the test set. For the GAN-based generative pipeline, we report a Structure Similarity index of 0.78 (1 = perfect reconstruction). The 2D-3D registration model enables direct pixel-wise mapping between histology and CT scan. Visually, the deformed CT looks very close to the original histology, and we computed normalized mutual information of 0.89 on the masked predictions (1 = perfect correlation). Annotations on both modalities (tumor, OARs) are in progress and will soon assess the functional quality of the registration through metrics like Dice score.

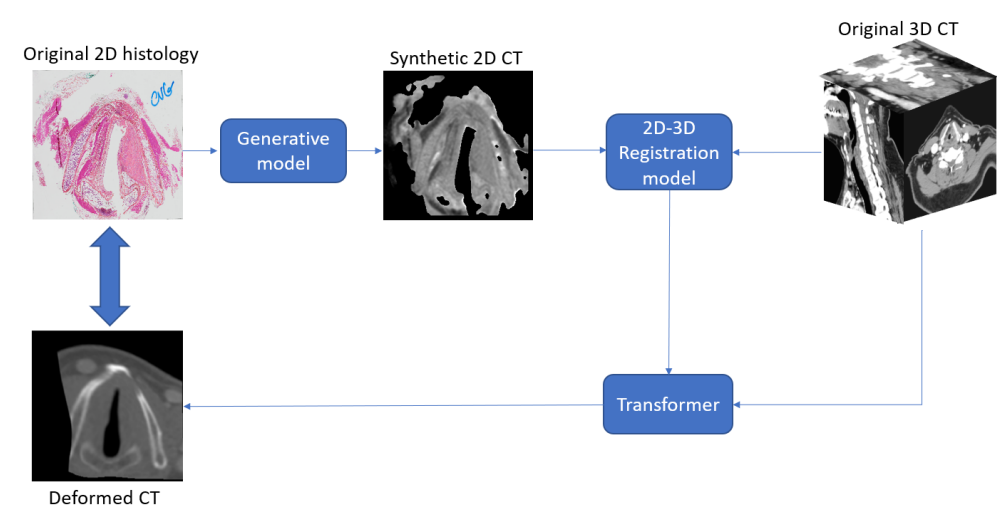


Figure 1: General pipeline from generation of synthetic CT to deformable 2D-3D registration to map histology with CT

Conclusion

To our knowledge, this framework is the first to automatically register radiology and histopathology in a deformable and 2D-3D setting. The same model can be applied to other anatomical imaging like MR and will enable pixel-wise comparison of tumor annotations with gold standard histology. Next, meaningful biological signatures from anatomical modalities will straightforward be extracted. Finally, it is one more step towards in-vivo virtual histology that could be a game-changer in oncology.