## Preserving Tumor Volumes for Unsupervised Medical Image Registration

## **Supplemental Material**

Paper ID 4379

This supplementary material includes additional visualizations of brain dataset examples that were not included in the main paper due to space limitations. Furthermore, we visualize landmark locations in warped images between our method and previous approaches on all datasets, as well as an ablation study demonstrating the efficacy and robustness of our proposed method in estimating tumor masks. These additions provide further insight into the effectiveness, robustness and generalization of our volume-preserving methods.

## 1. More finaltive Comparisons on Similarity-Based Registration and Volume-Preserving Registration

In addition to the results presented in Figure 4. of the main paper, we provide further qualitative results on brain scans using three different networks (VTN, VXM and TransMorph), as shown in Figure 1. These additional results provide further evidence of the effectiveness of our volume-preserving approach in preserving tumor volumes.

Furthermore, we visualize landmark locations in the warped images for the regular similarity-based method and our proposed method, as depicted in Figure 2. These visualizations demonstrate the ability of our approach to align the anatomy in the images comparably to previous methods on different networks.

## 2. Ablation Study on Calculation of Soft Tumor Mask

Table 1 presents the results of various calculation methods used to estimate tumor masks on the LiTs17 dataset with VTN. The study demonstrates the adaptive methods that generate soft masks for tumor estimation (1st and 2nd row) produce similar results, while the use of hard threshold functions that generates binary masks (3rd, 4th, and 5th row) fails to balance the preservation of the tumor size ratio (STSR) with the alignment of image anatomy (Dice and Landmark Distance (Lm. Dist)). Moreover, the study shows that the adaptive volume-preserving loss is robust for different transformation functions. Two different transformation functions in adaptive methods , sigmoid (1st row) and sin (2nd row), achieve comparable performance on all three metrics.

In practice, the complete transformation function for "Sigm" is expressed as  $STM(x) = sigmoid(5 \cdot (D(x) - 1.5))$ , while for "Sin" it is given by  $STM(x) = \frac{1}{2}sin(\pi \cdot (D(x) - 1.5)) + 0.5$ , where D denotes the size ratio change of the voxel at location x. The exact forms have been chosen to ensure that  $STM(x) \approx 1$  when  $D(x) \ge 2$  and  $STM(x) \approx 0$  when D(x) = 1. This is because we observed when the change of size ratio exceeds 2, it is highly probable that tumors are present. Conversely, if the ratio does not deviate significantly (changes close to 1), it is more likely that the observed tissue is normal.

These results provide valuable insights into the optimization of tumor estimation methods and suggest the use of adaptive methods in volume-preserving loss to enhance performance.



Figure 1. Qualitative comparison between similarity-based (regular) and volume-preserving (ours) methods trained on the Brain Tumor Segmentation (BraTS20) dataset. Specifically, the VTN, VXM, and TransMorph (Trans.) networks were tested, both with their regular similarity-based registration versions and our proposed volume-preserving version. The left side of the figure shows two sets of images: Fixed and Ground Truth (GT), and Moving and GT. The first row of the figure displays the warped moving image, while the second row illustrates the organ outlines in green and red for the moving and fixed images, respectively. The yellow overlay highlights the tumors. Our proposed volume-preserving (VP) method ensures the preservation of tumor volume while aligning the images, as demonstrated by reduced number of visible changes in tumor size. In the third row, the Jacobian matrix of the deformation field is visualized. The green and red lines represent the organ and tumor outlines, respectively. The white areas indicate a large Jacobian, which corresponds to a more significant change in volume. The method without volume-preserving loss demonstrates a larger white area in the tumor, indicating a greater volume change of tumor volume. The last row of the figure displays the deformation field.

Trans.	Thres.	Dice ↑	Lm. Dist↓	$STSR \downarrow$
Sigm †		0.908	10.89	1.26
Sin		0.906	10.77	1.29
Hard	1	0.840	12.23	1.27
Hard	1.5	0.877	13.67	1.46
Hard	2	0.904	12.68	1.86

Table 1. Comparison between different calculations of tumor mask on VTN network using LiTS17 dataset. The term "Trans." refers to the transformation function that computes the estimated tumor masks based on the change of size ratio in each voxel. It encompasses various functions, such as sigmoid ("Sigm"), sin ("Sin"), which predict soft tumor masks, and threshold functions ("Hard"), that generate binary masks based on a fixed threshold. "Thres." refers to the threshold for binary tumor mask estimation. The "†" indicates the adoption of this transformation function used in previous experiments.



Figure 2. Comparison of similarity-based (regular) and volume-preserving (ours) methods using landmark visualization trained on the Liver Tumor Segmentation (LiTS17) dataset (1st and 2nd row) and the Brain Tumor Segmentation (BraTS20) dataset (3rd and 4th row). Specifically, the VTN, VXM, and TransMorph (Trans.) networks were tested, both with their regular similarity-based registration versions and our proposed volume-preserving version. The left side of the figure comprises two sets of images, namely, Fixed and its corresponding landmark locations represented by a yellow cross and Moving and its landmark location represented by a red cross. The right side of the figure shows the warped image using different methods, along with the warped landmarks from the moving image represented by a red cross and the corresponding landmarks from the fixed image projected on the plane represented by a yellow cross. The landmark visualization results indicate that our proposed method yields landmark distances that are comparable to those obtained using similarity-based methods while simultaneously preserving tumor volume. This aspect is highly beneficial in tracking tumor growth.