Precision Tracking of Low-Grade Diffuse Glioma Progression Using a Novel DIR Approach

DukeHealth

Edward R Criscuolo[1], Evan Calabrese[2], Deshan Yang[1]

1. Duke University Radiation Oncology, 2. Duke University Radiology

Introduction

- Diffuse glioma is the most common primary brain tumor type in adults
  - Low-grade (LGG) account for 15% of cases
  - LGG is currently incurable and frequently progresses to high-grade disease
- LGG is monitored by serial MRI acquisition to detect radiological changes
  - Changes can be difficult to appreciate in slow-growing tumors
  - Median volume change for clinical detection: ~170%[1]

Sensitive methods to aid physicians in detecting small tumor changes will allow for rapid intervention

- Tumor segmentation lacks longitudinal consistency
  - HD95 errors can be >17mm for enhancing tumor via automated methods[2]

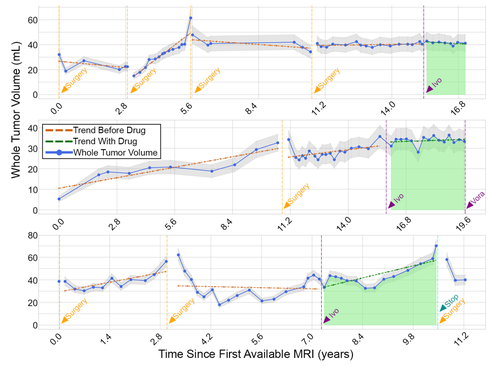

Figure 1: Variation in longitudinal tumor segmentations in a clinical trial. This volumetric uncertainty makes it difficult to identify progression

Deformable image registration (DIR) can be used to detect minor pathological changes by analyzing deformation between scans[3]

Methods

- Our DIR method focuses on the use of anatomical landmarks (blood vessel bifurcations): verifiable and reproducible
  - Blood vessels show up with high contrast on standard T1 contrast-enhanced MRIs
- Vessel segmentation is difficult using traditional methods
  - nnUNet model was trained using simulated data (below)

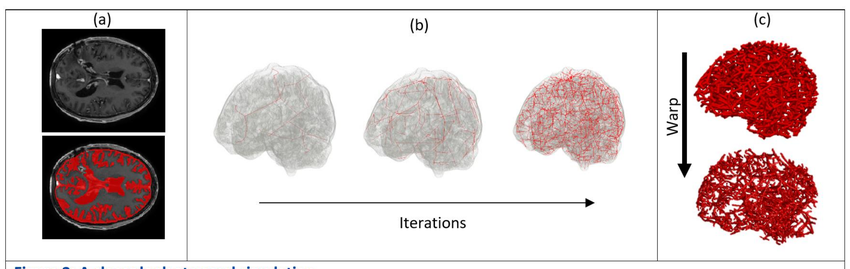

Figure 2: A closer look at vessel simulation.
(a) Vessels are simulated in the space between gyri (red, bottom) where they occur in real patient images (top)
(b) Adaptive constrained constructive optimization approach is used to grow vessels iteratively from a seed point
(c) Vessels are grown in straight lines and are then warped to mimic the curvature found in cerebral vasculature

- After blood vessel segmentation on multiple imaging time points, vessel bifurcations are detected and filtered
- Vessel masks from each scan are co-registered with PTVReg[4], a flexible parametrized DIR algorithm
  - These approximate registrations are used to match bifurcation landmarks in each scan

Methods

- Precise landmarks positions are then refined using a pseudo-twin deep learning model

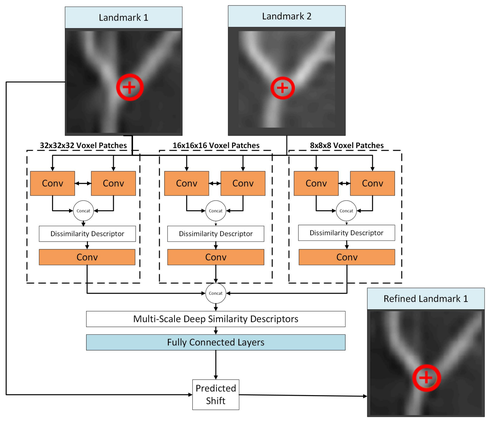

Figure 3: Pseudo-twin model to refine landmark positions

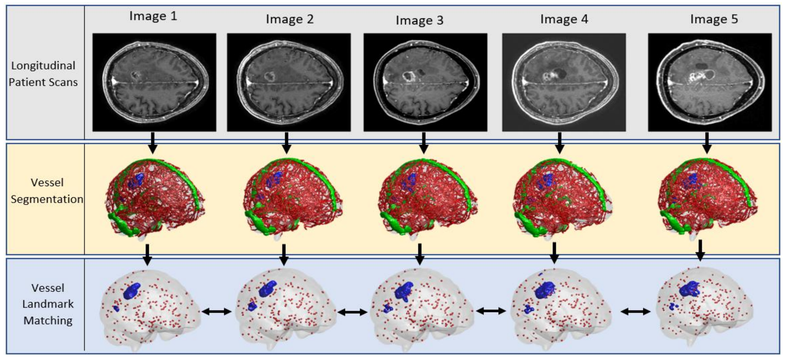

Figure 4: Overview of blood vessel bifurcation matching

- Phantom studies were run to estimate landmark error
  - Artificial deformations were applied to real data
  - Landmark matching was run and compared to ground truth deformation field

Results

- Vessel segmentation network trained on synthetic data outperformed traditional approaches
  - Sensitivity of 0.9 vs 0.53 via vesselness thresholding, specificity of 0.98 vs 0.93
- Across 5 patients with 5 scans each, an average of 190 vessel bifurcation landmarks were matched between the image phases
  - This leaves a large number to both guide the registration approach and estimate its accuracy on a subset
  - Patient-specific error estimation is a major hurdle for clinical adoption of DIR
- Phantom studies indicate landmark error <1mm
  - Landmark error increases near tumor site by ~0.5mm

Results

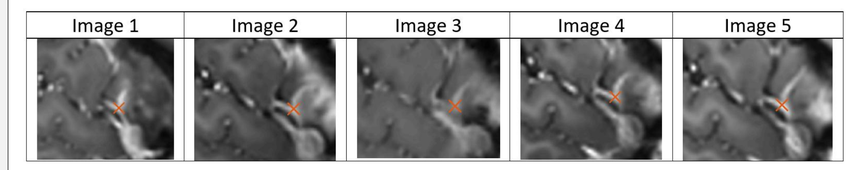

Figure 5: Example of a blood vessel bifurcation landmark matched between 5 longitudinal scans of the same patient. This landmark is 1.3cm from tumor surface, and therefore is sensitive to small changes in local morphology

Conclusions and Future Work

- We developed a fully automated, robust method for matching vessel bifurcation landmarks in longitudinal low-grade imaging data
- The landmark points can be used to guide and verify an end-to-end DIR approach, still in development
  - Jacobian determinant of deformation field can be used to detect progression
- Such an approach avoids the inconsistency of volumetric segmentation and can enhance progression detection

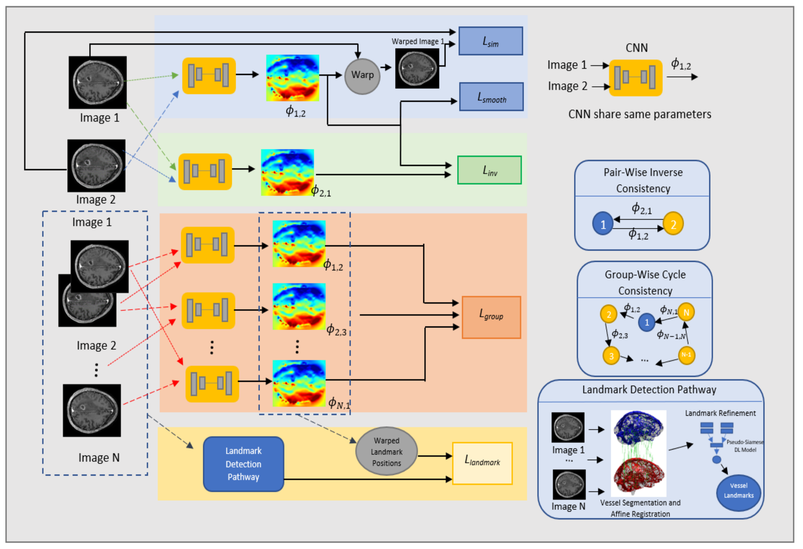

Figure 6: Proposed full registration approach utilizing matched landmarks

References

1. Fathallah-Shaykh Hm, et al. Diagnosing growth in low-grade gliomas with and without longitudinal volume measurements: A retrospective observational study. PLoS Med. 2019 May 28;16(5)
2. Ferreira, André, et al. 'How We Won BraTS 2023 Adult Glioma Challenge? Just Faking It! Enhanced Synthetic Data Augmentation and Model Ensemble for Brain Tumour Segmentation'. arXiv [Eess.IV], 2024
3. Im, J.E, *et al.* A Systematic Review on the Use of Registration-Based Change Tracking Methods in Longitudinal Radiological Images. *J Digit Imaging. Inform. med.* **38**, 2549–2562 (2025).
4. V. Vishnevskiy, etal, "Isotropic Total Variation Regularization of Displacements in Parametric Image Registration," in IEEE Transactions on Medical Imaging, vol. 36, no. 2, pp. 385-395, Feb. 2017