

SlicerDMRI: Open Source Diffusion MRI Software for Brain Cancer Research

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Abstract

Diffusion MRI (dMRI) is the only noninvasive method for mapping white matter connections in the brain. We describe SlicerDMRI, a software suite that enables visualization and analysis of dMRI for neuroscientific studies and patient-specific anatomic assessment. SlicerDMRI has been successfully applied in multiple studies of the human brain in health and disease, and here, we especially focus on its cancer research applications. As an extension module of the 3D Slicer medical image computing platform, the SlicerDMRI suite enables dMRI

analysis in a clinically relevant multimodal imaging workflow. Core SlicerDMRI functionality includes diffusion tensor estimation, white matter tractography with single and multi-fiber models, and dMRI quantification. SlicerDMRI supports clinical DICOM and research file formats, is open-source and cross-platform, and can be installed as an extension to 3D Slicer (www.slicer.org). More information, videos, tutorials, and sample data are available at dmri.slicer.org. *Cancer Res*; 77(21); e101-3. ©2017 AACR.

Introduction

Diffusion MRI (dMRI) extends MRI beyond static contrast techniques (e.g., T1- or T2-weighted imaging) to measure the molecular motion (diffusion) of water molecules (1). dMRI is applicable to a number of physical questions requiring understanding of tissue structure and compartmentation. In the brain, the cellular membranes and myelin of axonal bundles in the white matter directionally impede water diffusion with aggregate effects measurable at MRI scale (mm). dMRI is thus the only noninvasive technique that can map the brain's white matter fiber tracts (brain connections). dMRI also enables modeling and quantification of tissue microstructure. In cancer research, dMRI has two main applications: tractography to map white matter fiber tracts and imaging of cellular microstructure. dMRI tractography techniques (Fig. 1A and B) may strongly inform which interventions will maximize safety for an individual patient with an acute disease state, such as epilepsy or brain cancer.

SlicerDMRI is a suite of open-source software tools for dMRI research with a strong focus on the needs of clinical researchers. SlicerDMRI is used for both neuroscience research and cancer imaging research. In this article, we focus on the unique needs of patient-specific oncological neuroimaging research, where each

tumor can have a differing presentation. Standard neuroscience imaging software that relies on common reference atlas spaces is often not well suited for individual patient analysis due to the effects of brain tumors. To meet single-patient clinical research needs, SlicerDMRI is built upon and deeply integrated with 3D Slicer, an NIH-supported open-source platform for medical image computing. 3D Slicer provides critical tools, including automated and semiautomated image segmentation (2) to label tumor tissue, image registration to align images across time points or modalities (3), and data interchange with clinical informatics systems (4). 3D Slicer is downloaded over 75,000 times per year, with active users and contributing developers from around the world. SlicerDMRI builds on this foundation to provide a unique environment for end-to-end dMRI analysis in clinical oncology, including imaging studies and intervention planning research. The integrated functionalities of SlicerDMRI, combined with its user base, enhance its value as a testbed for implementing and testing new methods of dMRI visualization and analysis, for both clinical and preclinical research.

SlicerDMRI is currently in use at multiple international research centers. Recent applications of SlicerDMRI in neurosurgery and oncology include visual deficits in pituitary macroadenoma (5), preoperative facial nerve localization in vestibular schwannoma (6), tractography in edematous corticospinal tracts (7), and microstructure alterations in Chiari malformation type I (8). We maintain a list of publications using 3D Slicer diffusion functionality, such as tensor estimation, fiber tractography, fiber selection, and tractography visualization at dmri.slicer.org/citations.

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Note: Supplementary data for this article are available at Cancer Research Online (<http://cancerres.aacrjournals.org/>).

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Computer Resource: SlicerDMRI Functionality

SlicerDMRI includes clinician-accessible tools for end-to-end diffusion MRI analysis, including computation of tissue

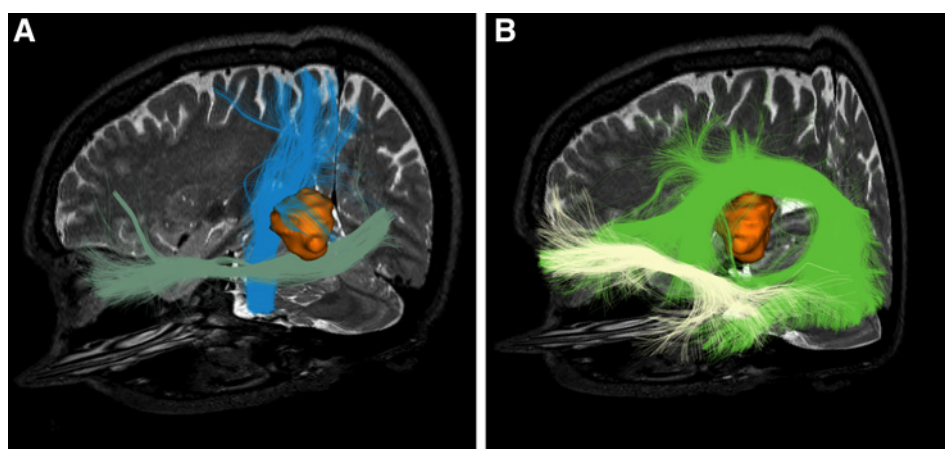


Figure 1.

Example visualization of a neurosurgical case using SlicerDMRI, with tracts from the UKF two-tensor tractography method. The patient presented with a history of right side paresthesia and aphasia, leading to the diagnosis of a left insular glioblastoma. **A**, The corticospinal tract (blue) wraps around the medial and superior aspect of the lesion and the inferior fronto-occipital fasciculus (pastel green) is relatively close to the inferior pole of the tumor. **B**, The arcuate fasciculus (green) fibers spread along the superior surface of the tumor, lateral to the corticospinal tract, and the uncinate fasciculus (white) is distant from the lesion.

microstructure models (e.g., diffusion tensors), tracing of fiber tracts (tractography), and quantitative analysis of diffusion-derived measures. See Supplementary Videos S1 and S2 for a quick tutorial covering the installation and basic usage of SlicerDMRI. Technical computing expertise is not required to use the graphical user interface of SlicerDMRI. For studies in which multiple datasets will be processed in the same way (batch analysis), SlicerDMRI supports scripting of most computations.

Core functionality

Here, we describe the main functionality of SlicerDMRI, along with brief examples of usage in clinical cancer research, as well as relevant software modules in italics.

Support for clinical and research file formats. Support of data interchange is crucial for integration in clinical research workflows. SlicerDMRI is compatible with clinical Digital Imaging and Communications in Medicine (DICOM) diffusion-weighted imaging formats as well as research imaging formats, such as nrrd and NIFTI. SlicerDMRI has recently introduced support for the new DICOM tractography interchange format.

Integrated DTI estimation and visualization. Diffusion tensor imaging (DTI) is the most widely used method for analyzing diffusion MRI data. SlicerDMRI provides a graphical user interface to calculate diffusion tensor images from diffusion-weighted image sequences, with several options for brain masking and tensor fitting. Options for visualization in both 2D and 3D include tractography, diffusion tensors (as ellipsoids), and derived quantitative measures such as fractional anisotropy (FA) and mean diffusivity images. An example application in cancer research is visualization of FA to give insight into the location and condition of the white matter in proximity to a tumor. Slicer 4.6 modules in this workflow include DWIConvert, DiffusionBrainMasking, DiffusionTensorEstimation and Volumes.

Tracing of brain connections via fiber tractography. The process of computationally tracing white matter fiber tracts using dMRI is called tractography. Slicer supports both single-fiber (DTI) tractography and multifiber tractography.

DTI tractography. After tensor estimation, tractography may be seeded (initiated) in two clinically relevant ways: from a region of

interest created with the Slicer editing tools, or from an interactively visualized 3D object that can be manipulated by the user. After seeding, individual tracts may be isolated via region selection tools. All settings and selection objects may be interactively adjusted, in both 2D slice and 3D view windows, with tractography results updated immediately to match. Interactivity allows for rapid isolation of tracts of specific interest. Slicer 4.6 modules in this workflow include TractographySeeding and TractographyDisplay.

Multifiber UKF tractography. In comparison with the single-tensor DTI model, which cannot model anatomic crossing of fibers, modern multifiber tracking approaches are better able to trace important tracts, such as the corticospinal tract and arcuate fasciculus. SlicerDMRI includes the UKFTractography module (9), providing an expanded range of multifiber models, including multitensor and multicompartiment models, along with a tractography tracing technique based on the unscented Kalman filter that uses information from prior steps to stabilize fiber tracking. See Supplementary Video S2 for visualization of UKF multifiber diffusion MRI tractography in a neurosurgical case.

Quantification of dMRI in cancer research. SlicerDMRI provides tools to measure diffusion-derived values, both in regions of interest (DiffusionScalarMaps and LabelStatistics) and in fiber tracts (TractographyMeasurements). An example application in cancer research is measurement of FA to study tissue microstructure.

White matter tract identification in patients. Interactive selection of tractography data can be difficult for a busy clinician. One approach to simplification of tractography is to cluster (group) tracts using measures of shape similarity. The SlicerDMRI WhiteMatterAnalysis package includes tools to create data-driven tractography cluster atlases, and we have recently demonstrated automatic identification of fiber tracts in patients with brain tumors (10).

Integration into the operating room. Building on 3D Slicer's capabilities for integration with surgical navigation devices (11, 12), SlicerDMRI has been used in the operating room under research committee oversight to develop new surgical visualization methods (13, 14). The advantage of this hybrid platform approach is

that clinicians may rely on reliable commercial systems for core navigation guidance, while also gaining access to, and providing feedback for, the development of novel visualization and selection techniques in the operative environment.

Software access

SlicerDMRI installation and user support. The SlicerDMRI extension is available from the 3D Slicer Extension Manager, an "app store" that enables developers to independently implement and distribute software extensions. SlicerDMRI installation instructions, tutorials, sample data, and introductory and clinical application videos can be found at dmri.slicer.org. SlicerDMRI is cross-platform and can be used on Windows, Mac, and Linux. Community support for SlicerDMRI users is available through the 3D Slicer forums (more information at www.slicer.org). The SlicerDMRI developers actively monitor and respond to diffusion-related topics, and participation in the larger Slicer community provides access to experts with a breadth of knowledge on many imaging topics.

SlicerDMRI software information. Originally developed starting in 2001 at the MIT AI Lab in collaboration with researchers at the Surgical Planning Laboratory at Harvard Medical School (Boston, MA; ref. 15), the SlicerDMRI source code is now freely available with a BSD-like license that permits unrestricted use, with all code downloadable at www.github.com/SlicerDMRI. Interested developers may freely include or extend SlicerDMRI functionality in their own extensions for public distribution through Slicer or for private use. Information about Slicer extension development is available in the Slicer developer manual on slicer.org. We welcome potential code contributions to SlicerDMRI via the GitHub pull request system. Although end users do not need any programming experience to install or use the software, interested developers and collaborators are welcome to request or submit features on the GitHub issue tracker at <https://github.com/SlicerDMRI/SlicerDMRI/issues>. Software issues may also be reported on the issue tracker.

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Conclusion

SlicerDMRI provides a platform for diffusion imaging research in a clinical oncology setting with tools for end-to-end diffusion image analysis as well as interoperation with clinical imaging systems.

Disclosure of Potential Conflicts of Interest

A. Yarmarkovich is a software architect at Dentsply Sirona, Inc. No potential conflicts of interest were disclosed by the other authors.

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Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis): D. Wassermann, Y. Rathi, S. Pieper, R. Kikinis, L.J. O'Donnell

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Administrative, technical, or material support (i.e., reporting or organizing data, constructing databases): F. Zhang, A.J. Golby, R. Kikinis, H.J. Johnson

Study supervision: R. Kikinis, L.J. O'Donnell

Other (software development and debugging): I. Norton, G. Kindlmann, R.S.J. Estepar, S. Pieper, L.J. O'Donnell

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