

Original Software Publication



SWANe: Standardized workflow for advanced neuroimaging in epilepsy

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ABSTRACT

Standardized Workflow for Advanced Neuroimaging in Epilepsy (SWANe) software provides researchers with a platform to analyze multimodal imaging modalities and to automatically combine the data from each modality into an integrating three-dimensional fashion. The software comes with a GUI and is designed to be user-friendly and for the not-technical public. SWANe is implemented in Python language and falls within the MIT license. The toolbox builds on a combination of existing methods to improve the user's power to perform analyses on different types of structural, functional, and metabolic imaging. SWANe has been developed in principle for the study of focal epilepsies of any age but it might be prospectively applied in different neurological diseases and for pre-surgical planning.

1. Motivation and significance

Drug-resistant epilepsy (DRE), found in approximately 30% of epileptic patients, represents a considerable health problem [1]. In DRE, the Epileptogenic Zone (EZ) identification [2] is the main issue to be solved to propose epilepsy surgery which represents the only curative option for these patients [3]. The neuroradiological approach to identifying the EZ includes imaging modalities beyond the structural Magnetic Resonance Imaging (MRI), like MR perfusion techniques (i.e. Arterial Spin Labelling, ASL), [18F] fluorodeoxyglucose Positron

Emission Tomography (FDG-PET) and functional MRI (fMRI) [4]. Furthermore, to generate an optimized plan for surgical resection/ablation, data from the different diagnostic studies should be interpreted in an integrated fashion [5]. Considering the urgent need to implement a multimodal imaging approach for epilepsy evaluation, platforms of multimodal imaging integrations have been developed, and the yield of certain imaging techniques evaluated [5–9]. Imaging postprocessing is time-consuming, requires high computational power, and relies on advanced technical expertise. To avoid those problems, the most popular neuroimaging toolboxes come with a Graphical User interface (GUI)

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that guides step-by-step users into the processing pipeline. However, so far, available pipelines do not respond to the need to have a single instrument to cover all the analyses of the most important imaging techniques. This can be discouraging, especially for beginners and clinicians who often lack advanced coding skills and have restricted time for research activities.

The main motivation behind the development of SWANe is to consolidate the diverse knowledge mentioned, streamlining the use of multimodal imaging techniques in a clinical research setting. SWANe comes with a GUI and is designed to be user-friendly and for non-technical users. Its functionality is the result of the combined expertise of expert epileptologists, neurosurgeons, engineers, neuroradiologists, and nuclear medicine physicians across many Italian centers, under the auspicious of the Italian League against Epilepsy (LICE). SWANe is organized in two parallel workflows, one optimized for the identification of the EZ, and the other for the integration of different imaging modalities for the creation of three-dimensional models potentially navigable in the surgical theater. SWANe runs within Python and incorporates open, third-party codes mainly from Freesurfer [10], FSL [11], and 3Dslicer [12]. A full list of external dependencies is provided in the next section.

1.1. List of tools and software used

SWANe requires Python3 (≥ 3.7) and the following external Python libraries as mandatory dependencies:

- matplotlib: Copyright 2012–2023, The Matplotlib development team
- network: Copyright 2014–2023, NetworkX developers
- nibabel: Copyright 2009–2019, Matthew Brett
- nipy: Copyright 2009–21, Neuroimaging in Python team
- psutil: Copyright 2009, Jay Loden, Dave Daeschler, Giampaolo Rodola
- pydicom: Copyright 2008–2020, Darcy Mason and pydicom contributors
- pyshortcut: Copyright 2018, Matthew Newville, The University of Chicago
- pyside6: Copyright 2023, The Qt Company Ltd

SWANe requires third-party software for its core functionality:

- Dcm2niix: Copyright 2014–2021, Chris Rorden
- FMRIB Software Library (FSL): Copyright 2018, The University of Oxford

The following third-party software are optional dependencies:

- FreeSurfer: Copyright 2011, The General Hospital Corporation (Boston, MA) "MGH"
- 3DSlicer: Copyright 2022, BWH and 3D-Slicer contributors
- Graphviz: Copyright 2023, The Graphviz Authors

2. Software description

SWANe consists of a library of predefined workflows that can be managed through a user-friendly GUI, which guides the users step by step to all the operations without any text-based command interface. The GUI was carefully crafted with the user in mind, featuring easy installation and updates, an intuitive interface that presents tasks individually, and a straightforward few-click process for starting workflows. These characteristics are in line with the criteria established for a device's "usability" as stated by ISO 9241–11 standard [13] and adopted in different other contexts [14].

SWANe pipeline is structured in different independent modules. This structure permits to be diffusely adopted overcoming the difficulties of collecting advanced imaging (especially metabolic and functional) in

small and/or peripheric epileptic centers. The analyses of different imaging modalities are all performed in the same reference space, the patient 3D-T1 weighted image (named "ref" image).

The following modules have been implemented in SWANe:

- 3D-T1w analysis
- 3D-FLAIR analysis
- 2D Cor/Sag/Tra FLAIR analysis
- Post Contrast 3D-T1w analysis
- FlaT1 analysis
- Diffusion Tensor Imaging (DTI) analysis
- FDG-PET/Arterial Spin Labelling (ASL) analyses
- Task fMRI analysis
- Venous MRA (Magnetic Resonance Angiography) analysis

Table 1 and Supplementary Fig. 1 summarize all the modules (including inputs, intermediate and final outputs) that will be reported in the following paragraphs (see paragraph 2.1)

SWANe includes an easy-to-use interface for managing patient records, importing DICOM images, generating and executing workflow, and exporting results. Each of the pre-processing and analysis steps has default values. However, all workflow parameters can be customized using the Workflow Preferences on the Workflow execution subtab through the GUI.

2.1. Software architecture

SWANe is designed with Python for Ubuntu > 20.XX and macOS > 12.5.

SWANe is structured in two parallel workflows:

- The "Morpho-Functional" workflow aims to better characterize and delineate the EZ, by inspecting the results of the analyses on different imaging modalities. These are specifically: (a) surface and voxel-based morphometry analyses on volumetric T1w and FLAIR images. The first approach, obtained by processing the anatomical high-resolution images (3DT1w) with the Freesurfer toolbox [15,16], aims to segment the brain pial surfaces and evaluate cortical thickness [17,18,19,20]. The latter analysis (namely FlaT1) investigates abnormalities of the gray-white matter junction and gray-matter gyration, comparing at voxel-level the patient's 3D-T1 and 3D-FLAIR images with a normative dataset; (b) Linear registration of post-contrast 3D-T1w and 3D (or 2D) FLAIR images to the ref image; (c) FDG-PET and ASL analyses, including coregistration of PET and ASL-CBF map to the ref image; estimation of the asymmetry index (AI) which identifies voxels with significant asymmetry in glucose metabolism and CBF between brain hemispheres [21,22]; estimation of PET and ASL z-score which shows glucose metabolism and CBF divergences of cortical gray matter from the average of basal ganglia; projection of the obtained AI and z-score maps on the pial surface models created by the Freesurfer pipeline.
- The "Structural" workflow aims to build up the multimodal three-dimensional scene of all imaging modalities fused in the patient anatomical space and allows for evaluation of the relationships between EZ/lesion, brain vessels, and white matter tracts, PET and ASL alterations, task-based fMRI results, also on the pial/white matter surfaces. The structural workflow includes the following modules: (a) venous MRA analysis: linear registration of the venous MRA sequence to the ref and generation of 3D models of the veins displayed onto the pial surfaces; (b) DTI analysis and generation of 3D white matter tracts; (c) task-based fMRI analysis including pre-processing of fMRI data based on user-defined parameters and generation of fMRI results. All Structural workflow results are collected into a multimodal scene in 3D-Slicer.

The two workflows are not rigidly independent: each of them might

Table 1

RH: right hemisphere; LH: Left hemisphere. 3D-T1w: 3D-T1 weighted image; DTI: diffusion tensor imaging; ASL: Arterial Spin Labelling; PET: Positron Emission Tomography.

SWANe analysis modules			
Modules	Required data	Description	Outputs
3D-T1w	3D-T1w DICOM	Generation 3D-T1 NIFTI files to use as reference.	3D-T1 Nifti file Skull stripped 3D-T1 Nifti file
3D-FLAIR	3D-FLAIR DICOM	Generation 3D-FLAIR NIFTI files Linear registration to 3D-T1 reference space.	Skull stripped 3D-FLAIR Nifti file
2D-FLAIR	2D Cor/Sag/Tra FLAIR DICOM	Generation 2D-FLAIR NIFTI files Linear registration to 3D-T1 reference space.	Skull stripped 2D-FLAIR Nifti file
Post-contrast 3D-T1w	Post-Contrast 3D-T1w DICOM	Generation post-contrast 3D-T1w NIFTI files Linear registration to 3D-T1 reference space.	Skull stripped post-contrast 3D-T1w Nifti file
FreeSurfer	3D-T1w DICOM	FreeSurfer cortical reconstruction Segmentation of the hippocampal substructures and the nuclei of the amygdala.	RH/LH hemisphere pial/white matter surfaces Aparc/Aseg parcellation in 3D-T1 reference space RH/LH labels from segmentation of the hippocampal and amygdala substructures
FlaT1	3D-T1w DICOM 3D-FLAIR DICOM	Whole brain voxel based morphometry analysis on 3D-FLAIR/3D-T1 resulted image	Extension z-score map in reference space Junction z-score in reference space Binary flair in reference space
Diffusion Tensor Imaging (DTI)	DTI DICOM 3D-T1w DICOM	DTI preprocessing workflow Fractional anisotropy calculation.	Fractional anisotropy map in reference space Total number of generated tracts not rejected by inclusion/exclusion mask criteria for RH/LH side
PET/ASL	PET/ASL DICOM 3D-T1w DICOM	PET/ASL registration to 3D-T1 reference PET/ASL Z-score and asymmetry index maps Projection of PET/ASL analysis (Asymmetry index and z-score) on FreeSurfer pial RH/LH surface.	PET/ASL maps in reference space PET/ASL map projection on RH/LH pial surface PET/ASL Asymmetry index in reference space PET/ASL Asymmetry index projection on RH/LH pial surface PET/ASL z-score statistics compared to Basal Ganglia (BG) PET/ASL z-score map projection on RH/LH pial surface
Task fMRI	Task fMRI DICOM 3D-T1w	fMRI first level analysis for a single or double task with constant task-rest paradigm. Up to three different fMRI runs can be loaded and analyzed with different parameters.	For rArA design: - Cluster of activation (task vs rest) in reference space For rArBrArB design: - Cluster of activation (task A vs task B) in reference space - Cluster of activation (task B vs task A) in reference space
Venous MRA	Venous MRA	Analysis of phase contrasts images (in	Intracranial veins in reference space

Table 1 (continued)

SWANe analysis modules			
Modules	Required data	Description	Outputs
	3D-T1w DICOM	single or two series) to obtain in-skull veins in reference space.	

be personalized with additional analyses (of the other workflow). The choice of which workflow and preference settings can be easily accessed via the GUI.

2.2. Software functionalities

All functionalities are fully documented and explained in the software manual (<https://github.com/LICE-dev/swane/wiki>) which contains a complete overview of the workflows and accompanying theoretical basis of more complex methodologies.

SWANe currently implements the following workflows (Table 1, Fig. 1):

2.2.1. Morpho-functional workflow

- **3D-T1w** - Generate T13D NIFTI files to use as reference.
- **3D-Flair** - Generate 3D-Flair Nifti files and perform linear registration to reference space.
- **2D Cor/Sag/Tra Flair** - Generate 2D Flair Nifti files and perform linear registration to reference space.
- **Post-contrast 3D-T1w** - Generate post-contrast 3D-T1w Nifti files and perform linear registration to reference space.
- **FreeSurfer** - Perform FreeSurfer cortical reconstruction and, if enabled, segmentation of the hippocampal and amygdala substructures.
- **FlaT1** - Creation of a junction and extension z-score map based on 3D-T1w, 3D-Flair, and a mean template.
- **PET & Arterial Spin Analysis (ASL)** - Analysis for:
 - Registration to reference;
 - Z-score and asymmetry index map;
 - Projection on FreeSurfer pial surface.

2.2.2. Structural workflow

- **Diffusion Tensor Imaging Preprocessing** - DTI preprocessing workflow and fractional anisotropy calculation.
- **Tractography** - Tractography execution for chosen tracts using FSL extract protocols.
- **Task fMRI** - fMRI first-level analysis for a single or double task with a constant task-rest paradigm.
- **Venous MRA** - Analysis of phase contrasts images (in single or two series) to obtain in-skull veins in reference space.

3. Illustrative examples

To demonstrate the major functions of SWANe, pipelines and outputs of the different modules will be discussed using a representative imaging dataset (see Fig. 1). Input data for SWANe are in DICOM format [23]. DICOM data require conversion into NIFTI format using the dcm2nii software. We anticipate expanding the SWANe configuration to promote the storing and conversion of the original DICOM images according to the recently implemented Brain Imaging Data Structure (BIDS) standard [24].

3.1. Multimodal imaging registration

SWANe's modular structure enables users to run the software with

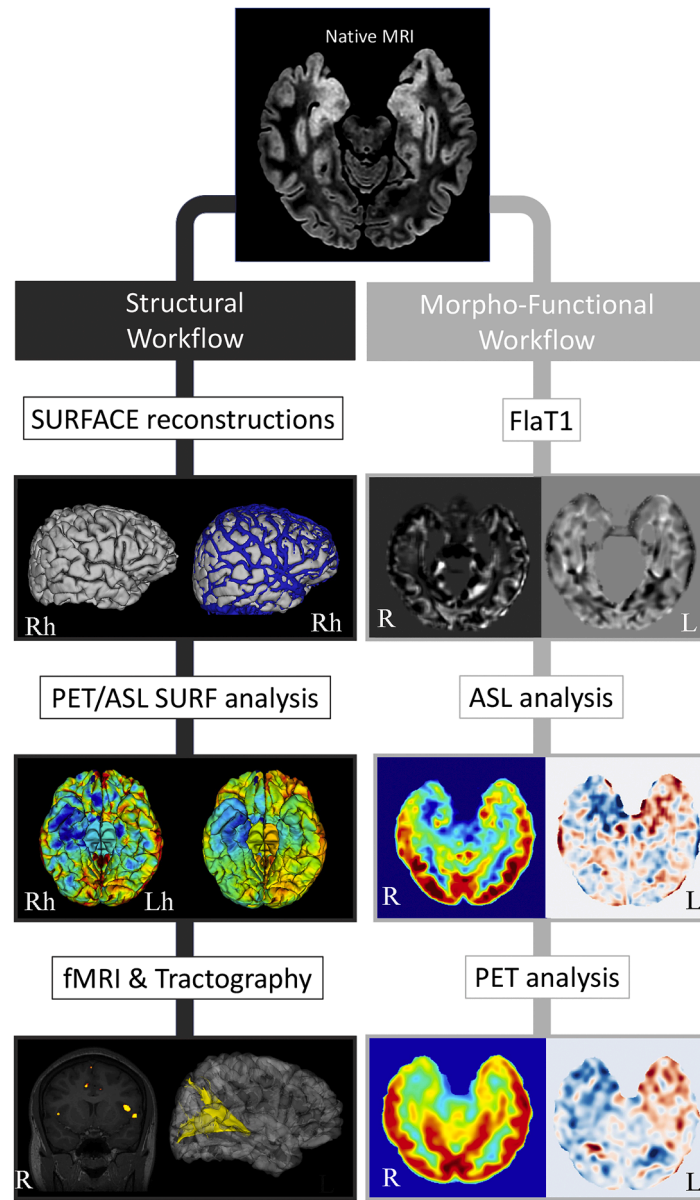


Figure 1

Fig. 1. Illustrative example of SWANe application and graphical representation of workflows in a representative example with right temporal lobe epilepsy. *L*=Left; *R*=Right; *Lh*=Left Hemisphere; *Rh*: Right Hemisphere, SURF: Surface.

any available imaging modalities/sequences, rather than requiring all of them. The 3D-T1w is the sole image needed (“ref”) and serves as the starting point for all subsequent analyses. All other optional imaging modalities are registered to the ref image using FSL’s linear rigid registration (FLIRT) with 6 degrees of freedom, trilinear interpolation, and the correlation ratio cost function [11]. Anatomical images (FLAIR2D/3D, 3D-T1W, post-contrast 3D-T1W, venous MRA) are submitted to skull and scalp removal (Brain Extraction Tool function, FSL) before linear registration.

3.2. T1W analysis

SWANe processes T1W images using Freesurfer recon-all [10] command to perform tissue classification and extract cortical surface models, to estimate subject-level measures of cortical thickness, and to estimate various neuroanatomical measures (i.e. surface of cortical/subcortical structures). These metrics are stored in the FS

(“Freesurfer”) folder which is generated automatically during the process. As an option, volumes of subnuclei of the amygdala and hippocampus extracted by validated pipelines [25] can be estimated automatically by SWANe if the function is selected by users.

3.3. FlaT1 analysis

FlaT1 is a voxel-based morphometric analysis exclusive of SWANe based on functions and codes of FSL. Voxel-based morphometric approaches have been adopted in epilepsy to increment the sensitivity of the human eye to recognize lesions [26,27,28]. FlaT1 analysis expands previous approaches by adopting a different input, the ratio between 3D-FLAIR and 3D-T1W images. This image is characterized by higher contrast resolution between gray and white matter than conventional 3D-T1, thus improving the detection of regions with abnormal gray–white matter junctions. Two images were derived from the analysis of FLAIR/T1 ratio image: a ‘junction image’ which highlights brain regions

with blurred gray–white matter junction [29] and an ‘extension image’ which emphasizes gray matter extending abnormally into the white matter [30].

Calculation of the ‘junction image’ requires 1) normalization of FLAIR/T1 ratio image to the standard brain of the Montreal Neurological Institute (MNI); 2) segmentation and intensity correction of the normalized image into the gray matter, white matter, and cerebrospinal fluid images, and simultaneously corrected for intensity inhomogeneities; 3) calculation of the binary image of junction by applying higher and lower thresholds to the normalized image, considering the lower threshold as mean intensity signal of gray matter + standard deviation (SD) of gray matter and the upper threshold as mean intensity signal of white matter - SD of white matter; 4) filtering of the binary image by performing a 3D-convolution kernel with a matrix of 5mm^3 . To compensate for variability concerning the thickness of the gray–white matter junction in different regions of the brain, the convolved image is compared with the mean image obtained by healthy controls. 3D-FLAIR and 3D-T1 images of 258 healthy subjects (age range 2–65 years; 137 females) were processed in the same way as described for patients and then averaged. The resulting mean image is subtracted voxel-by-voxel from the convolved patient image to obtain the junction image. The SD evaluated in the control group analysis is used to calculate the z-score map of the junction image. Bright regions in this z-score ‘junction’ map correspond to the areas with less definition of gray–white matter junction compared to healthy controls.

Calculation of ‘extension map’ requires: 1) normalization of FLAIR/T1 ratio image to the MNI; 2) segmentation of a gray matter image; 3) smoothing of the segmented gray matter image by a Gaussian filter, and 3) comparison with the normal database by subtracting the mean gray matter image of the normal database from the smoothed gray matter map of the analysed patient. The SD evaluated in the control group analysis is used to calculate the z-score map of the extension image. Bright regions in this z-score ‘extension’ map correspond to the areas with abnormal distribution of gray matter as compared to healthy control.

3.4. PET&ASL analysis

Electrical changes occurring in the EZ are associated with alteration of perfusion and metabolism around the EZ [22,31,32,33]. These changes can be captured using ASL and FDG-PET respectively. SWANe incorporates the registration of ASL/PET data to anatomical images (flirt fsl), thus allowing a visual qualitative analysis and two voxel-based quantitative approaches, both exploring differences of perfusion and metabolism at voxel level without the need of normative data. The first is the estimation of the Asymmetry Index (AI) using the following formula: $AI = (\text{Right}-\text{Left})/(\text{Right}+\text{Left})$. The output image illustrates asymmetries in perfusion/metabolism between each voxel of one hemisphere and its contralateral. The second approach estimates the mean and standard deviation of ASL and PET values of the basal ganglia (BG) and generate z-score maps as $ASL/PET\text{-}zscore = \frac{ASL/PET\text{ value} - \text{mean } ASL/PET(BG)}{\text{standard deviation } ASL/PET(BG)}$. SWANe generates three scalar maps obtained by the projection of pet/asl_AI, pet/asl zscore and pet/asl on pial/white surfaces using the function `mri_vol2surf` as implemented in `freesurfer` [10].

3.5. DTI and tracts generation

SWANe analyses DTI images using FSL Diffusion Toolbox (FDT) tools and XTRACT protocols [11,34,35]. DTI preprocessing includes scalp removal, correction of motion and eddy current artifacts, linear registration to reference space and non-linear registration to MNI atlas. DTI metrics (i.e. mean diffusivity, fractional anisotropy, eigenvectors and eigenvalues) are calculated with `dtifit`. Diffusion parameters and crossing fibers modeling are estimated with `BEDPOSTX`.

For each white matter tracts chosen by user in the workflow preferences, probabilistic tractography is performed using XTRACT and PROBTRACKX for both left and right brain hemispheres. XTRACT provides tract-specific protocols including seed, target, way order, stop and exclusion Region of Interests (ROI), optimal number of samples (i.e. the streamlines drawn in each seed voxel) and a flag to enable an inverse-tractography run. To reduce computation time, each tractography is parallelized over multiple threads taking advantage of the random seed function of PROBTRACKX and each process outputs are finally summed together. To obtain more comparable results, tracts image values are normalized by division by the way total output of PROBTRACKX.

3.6. Multimodal scene generation

The visualization of SWANe output requires 3DSlicer software [12]. SWANe output includes the creation of a folder named “scene” which includes all the images analyzed registered to ref as “r_volume”.nii.gz, specifically: FLAIR, PET, ASL, PET-AI, ASL-AI, PET-zscore, ASL-zscore, junction z-map, extension z-map, venous MRA, fractional anisotropy map, fMRI map, `aparc_aseg` Freesurfer segmentation, hippocampus/amygdala Freesurfer segmentation. In addition, the scene folder contains the scalars of PET/ASL/thickness created automatically and the DTI tracts. SWANe reconstructs automatically a 3D model of lh/rh pial and white surface, veins, and tracts. The .mrb file inside the scene folder once uploaded into 3DSlicer displays automatically all the 2D and 3D outputs.

4. Impact

The main research question in epilepsy surgery is the definition and delineation of EZ in potential surgical candidates [36]. This need includes the planning of the surgical procedure to optimize the resection/disconnection of all the epileptogenic areas while preserving vital and eloquent structures [37]. SWANe combines both needs in one platform that does not require computational and coding expertise. The use of integrated imaging modalities in epilepsy surgery is well-established [5,38,39] and single software platforms for multimodal imaging integration have been developed [40] and implemented in the clinical practice [41,42]. SWANe represents a departure from already available software because, by using a unique solution, (i) it combines the multimodal imaging integration with advanced analysis of structural, metabolic, and perfusional imaging modalities, (ii) it comes with a user-friendly GUI and (iii) it is free available for download. As far as the multiple imaging analyses integrated in SWANe, the automatic estimation of AI and z-score maps for FDG-PET and ASL is innovative and has not been implemented in previous pipelines. FlaT1 analysis, while providing a similar outcome to already available pipelines [28,29,43], adopts a different strategy by using as input the ratio between FLAIR and T1 weighted images.

Validation test of SWANe is currently underway in 10 Italian hospitals covering both pediatric and adult epilepsy patients. SWANe’s ultimate goal is to create a versatile tool that can be utilized by epilepsy centers at all levels, resulting in a substantial increase in productivity and publications within the field. Originally designed for treating epilepsy, SWANe has the potential to be utilized in other areas of research, including neurooncology for the surgical approach of supratentorial tumors and in the future to the analysis of PET imaging involving new PET tracers for neurodegenerative diseases.

5. Conclusions

We introduced and described the SWANe toolbox, which represents a user-friendly instrument to perform the most common analyses on different imaging modalities acquired in epilepsy surgery settings (MRI, PET, ASL, fMRI) and to build up automatically the multimodal scene with all the images registered into the same space (patient’s space) and

with three-dimensional navigable models of white matter tracts, veins, lesion and pial/white surfaces. The toolbox aims to facilitate the work of researchers who are beginning in this field and thus expand the neuroimaging knowledge and its utility across different epilepsy centers with different levels of patients' complexity and mission. In addition, SWANe is a solid platform for more experienced users to expand the actual code with advanced connectome analysis on DTI and fMRI data. SWANe is free, open code, and is available for download, along with its manual at <https://github.com/LICE-dev/swane/wiki>.

Metadata

Nr	Code metadata description	Please fill in this column
C1	Current code version	0.0.6
C2	Permanent link to code/repository used for this code version	https://github.com/LICE-dev/swane
C3	Permanent link to reproducible capsule	-
C4	Legal code license	<p>Copyright (c) 2023 LICE - Commissione Neuroimmagini 2021–2024</p> <p>Permission is hereby granted, free of charge, to any person obtaining a copy of this software and associated documentation files (the "Software"), to deal in the Software without restriction, including without limitation the rights to use, copy, modify, merge, publish, distribute, sublicense, and/or sell copies of the Software, and to permit persons to whom the Software is furnished to do so, subject to the following conditions:</p> <p>The above copyright notice and this permission notice shall be included in all copies or substantial portions of the Software.</p> <p>THE SOFTWARE IS PROVIDED "AS IS", WITHOUT WARRANTY OF ANY KIND, EXPRESS OR IMPLIED, INCLUDING BUT NOT LIMITED TO THE WARRANTIES OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE AND NONINFRINGEMENT. IN NO EVENT SHALL THE AUTHORS OR COPYRIGHT HOLDERS BE LIABLE FOR ANY CLAIM, DAMAGES OR OTHER LIABILITY, WHETHER IN AN ACTION OF CONTRACT, TORT OR OTHERWISE, ARISING FROM, OUT OF OR IN CONNECTION WITH THE SOFTWARE OR THE USE OR OTHER DEALINGS IN THE SOFTWARE.</p>
C5	Code versioning system used	git
C6	Software code languages, tools and services used	python
C7	Compilation requirements, operating environments and dependencies	<p>Ubuntu > 20.XXMacOS > 12.5.</p> <p>XXMandatory Dependencies:</p> <ul style="list-style-type: none"> • Python 3.7 • Dcm2nix 1.0.2021111006 • Fsl 6.0.0 <p>Optional Dependencies:</p> <ul style="list-style-type: none"> • FreeSurfer 7.0.0 • 3D Slicer 5.0.0 • Graphviz 0.2.0
C8	If available, link to developer documentation/manual	https://github.com/LICE-dev/swane/wiki
C9	Support email for questions	dev@lice.it

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CRedit authorship contribution statement

Maurilio Genovese: Writing – original draft, Visualization, Validation, Supervision, Software, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Agostino Arcasensa:** Visualization, Validation, Software, Resources, Methodology, Formal analysis, Conceptualization. **Silvia Morbelli:** Writing – review & editing, Resources, Methodology, Investigation, Formal analysis, Conceptualization. **Matteo Lenge:** Writing – review & editing, Methodology, Conceptualization. **Carmen Barba:** Supervision, Funding acquisition, Conceptualization. **Laura Mirandola:** Writing – review & editing, Investigation, Conceptualization. **Maria Eugenia Caligiuri:** Writing – review & editing, Methodology, Conceptualization. **Massimo Caulo:** Writing – review & editing, Conceptualization. **Ferruccio Panzica:** Writing – review & editing, Conceptualization. **Francesco Cardinale:** Writing – review & editing, Methodology, Data curation, Conceptualization. **Camilla Rossi-Espagnet:** Writing – review & editing, Data curation, Conceptualization. **Domenico Tortora:** Writing – review & editing, Writing – original draft, Visualization, Supervision, Software, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Anna Elisabetta Vaudano:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: ANNA ELISABETTA VAUDANO reports financial support and article publishing charges were provided by Italian League against Epilepsy. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.softx.2024.101703](https://doi.org/10.1016/j.softx.2024.101703).

References

- [1] Kwan P, et al. Definition of drug resistant epilepsy: consensus proposal by the ad hoc Task Force of the ILAE Commission on Therapeutic Strategies. *Epilepsia* 2010; 51(6):1069–77. <https://doi.org/10.1111/j.1528-1167.2009.02397.x>.
- [2] Rosenow F, Lüders H. Presurgical evaluation of epilepsy. *Brain* 2001;124: 1683–700. <https://doi.org/10.1093/brain/124.9.1683>. Pt 9.
- [3] Ryvlin P, Cross JH, Rheims S. Epilepsy surgery in children and adults. *The lancet neurology*, 13. Lancet Publishing Group; 2014. p. 1114–26. [https://doi.org/10.1016/S1474-4422\(14\)70156-5](https://doi.org/10.1016/S1474-4422(14)70156-5). Nov. 01..
- [4] Sebastiano DR, et al. Identifying the epileptogenic zone by four non-invasive imaging techniques versus stereo-EEG in MRI-negative pre-surgery epilepsy patients. *Clin Neurophysiol* 2020;131(8):1815–23. <https://doi.org/10.1016/j.clinph.2020.05.015>.
- [5] Jin L, et al. Multimodal image integration for epilepsy presurgical evaluation: a clinical workflow. *Front Neurol* 2021;12. <https://doi.org/10.3389/fneur.2021.709400>. Aug.
- [6] Cruces RR, et al. Micapipe: a pipeline for multimodal neuroimaging and connectome analysis. *Neuroimage* 2022;263. <https://doi.org/10.1016/j.neuroimage.2022.119612>. Nov.

- [7] Y. Kim et al., "BrainSuite BIDS app: containerized workflows for MRI analysis", [10.1101/2023.03.14.532686](https://doi.org/10.1101/2023.03.14.532686).
- [8] Glasser MF, et al. The Human Connectome Project's neuroimaging approach. *Nature neuroscience*, 19. Nature Publishing Group; 2016. p. 1175–87. <https://doi.org/10.1038/nn.4361>. Sep. 01,.
- [9] Říha P, et al. Multimodal combination of neuroimaging methods for localizing the epileptogenic zone in MR-negative epilepsy. *Sci Rep* 2022;12(1):15158. <https://doi.org/10.1038/s41598-022-19121-8>.
- [10] Fischl B. FreeSurfer. *Neuroimage* 2012;62(2):774–81. <https://doi.org/10.1016/j.neuroimage.2012.01.021>. Aug. 15,.
- [11] Jenkinson M, Beckmann CF, Behrens TEJ, Woolrich MW, Smith SM. FSL. *Neuroimage* 2012;62(2):782–90. <https://doi.org/10.1016/j.neuroimage.2011.09.015>. Aug.
- [12] Fedorov A, et al. 3D Slicer as an image computing platform for the Quantitative Imaging Network. *Magn Reson Imaging* 2012;30(9):1323–41. <https://doi.org/10.1016/j.mri.2012.05.001>. Nov.
- [13] ISO. *Ergonomics of human-system interaction - Part 11: usability: definitions and concepts*. Iso/Np 9241-11. 2018.
- [14] Soto-Rey I, et al. User satisfaction evaluation of the EHR4CR query builder: a multisite patient cohort system. *Biomed Res Int* 2015;2015. <https://doi.org/10.1155/2015/801436>.
- [15] Fischl B, Dale AM. Measuring the thickness of the human cerebral cortex from magnetic resonance images. *Proc Natl Acad Sci U S A* 2000;97(20):11050–5.
- [16] Fischl B, Sereno MI, Dale A. Cortical surface-based analysis: II: inflation, flattening, and a surface-based coordinate system. *Neuroimage* 1999;9(2):195–207.
- [17] Macdonald-Laurs E, et al. Intrinsic and secondary epileptogenicity in focal cortical dysplasia type II. *Epilepsia* 2023;64(2):348–63. <https://doi.org/10.1111/epi.17495>. Feb.
- [18] S.-T. Wu et al., "Toward a multimodal diagnostic exploratory visualization of focal cortical dysplasia." [Online]. Available: www.computer.org/cga.
- [19] Azzony S, Moria K, Alghamdi J. Detecting cortical thickness changes in epileptogenic lesions using machine learning. *Brain Sci* 2023;13(3). <https://doi.org/10.3390/brainsci13030487>. Mar.
- [20] Whelan CD, et al. Structural brain abnormalities in the common epilepsies assessed in a worldwide ENIGMA study. *Brain* 2018;141(2). <https://doi.org/10.1093/brain/awx341>.
- [21] Galazzo IB, et al. Cerebral metabolism and perfusion in MR-negative individuals with refractory focal epilepsy assessed by simultaneous acquisition of 18F-FDG PET and arterial spin labeling. *Neuroimage Clin* 2016;11:648–57. <https://doi.org/10.1016/j.nicl.2016.04.005>.
- [22] Tortora D, et al. Comparison of qualitative and quantitative analyses of MR-Arterial Spin Labeling perfusion data for the assessment of pediatric patients with focal epilepsies. *Diagnostics* 2022;12(4). <https://doi.org/10.3390/diagnostics12040811>. Apr.
- [23] Larobina M. Thirty years of the DICOM standard. *Tomography*, 9. Multidisciplinary Digital Publishing Institute (MDPI); 2023. p. 1829–38. <https://doi.org/10.3390/tomography9050145>. Oct. 01,.
- [24] Gorgolewski KJ, et al. The brain imaging data structure, a format for organizing and describing outputs of neuroimaging experiments. *Sci Data* 2016;3. <https://doi.org/10.1038/sdata.2016.44>. Jun.
- [25] Iglesias JE, et al. A computational atlas of the hippocampal formation using ex vivo, ultra-high resolution MRI: application to adaptive segmentation of in vivo MRI. *Neuroimage* 2015;115:117–37. <https://doi.org/10.1016/j.neuroimage.2015.04.042>. Jul.
- [26] Huppertz H-J, Wagner J, Weber B, House P, Urbach H. Automated quantitative FLAIR analysis in hippocampal sclerosis. *Epilepsy Res* 2011;97(1–2):146–56. <https://doi.org/10.1016/j.eplepsyres.2011.08.001>.
- [27] Wagner J, Weber B, Urbach H, Elger CE, Huppertz H-J. Morphometric MRI analysis improves detection of focal cortical dysplasia type II. *Brain* 2011;134(10):2844–54. <https://doi.org/10.1093/brain/awr204>.
- [28] David B, et al. External validation of automated focal cortical dysplasia detection using morphometric analysis. *Epilepsia* 2021;62(4):1005–21. <https://doi.org/10.1111/epi.16853>. Apr.
- [29] Huppertz HJ, et al. Enhanced visualization of blurred gray-white matter junctions in focal cortical dysplasia by voxel-based 3D MRI analysis. *Epilepsy Res* 2005;67(1–2):35–50. <https://doi.org/10.1016/j.eplepsyres.2005.07.009>. Oct.
- [30] Huppertz HJ, Wellmer J, Staack AM, Altenmüller DM, Urbach H, Kröll J. Voxel-based 3D MRI analysis helps to detect subtle forms of subcortical band heterotopia. *Epilepsia* 2008;49(5):772–85. <https://doi.org/10.1111/j.1528-1167.2007.01436.x>. May.
- [31] Wang YH, et al. Comparison between simultaneously acquired arterial spin labeling and 18F-FDG PET in mesial temporal lobe epilepsy assisted by a PET/MR system and SEEG. *Neuroimage Clin* 2018;19:824–30. <https://doi.org/10.1016/j.nicl.2018.06.008>. Jan.
- [32] Salamon N, et al. FDG-PET/MRI coregistration improves detection of cortical dysplasia in patients with epilepsy. *Neurology* 2008;71(20):1594–601. <https://doi.org/10.1212/01.wnl.0000334752.41807.2f>.
- [33] Kojan M, Gajdoš M, Říha P, Doležalová I, Řehák Z, Rektor I. Arterial Spin Labeling is a Useful MRI Method for Presurgical Evaluation in MRI-Negative Focal Epilepsy. *Brain Topogr* 2021;34(4):504–10. <https://doi.org/10.1007/s10548-021-00833-5>. Jul.
- [34] Warrington S, et al. Concurrent mapping of brain ontogeny and phylogeny within a common space: standardized tractography and applications. 2022.
- [35] Behrens TEJ, Berg HJ, Jbabdi S, Rushworth MFS, Woolrich MW. Probabilistic diffusion tractography with multiple fibre orientations: what can we gain? *Neuroimage* 2007;34(1):144–55. <https://doi.org/10.1016/j.neuroimage.2006.09.018>. Jan.
- [36] Bernasconi A, Bernasconi N. Unveiling epileptogenic lesions: the contribution of image processing. *Epilepsia* 2011;52(SUPPL. 4):20–4. <https://doi.org/10.1111/j.1528-1167.2011.03146.x>. Jul.
- [37] Narizzano M, et al. SEEG assistant: a 3DSlicer extension to support epilepsy surgery. *BMC Bioinform* 2017;18(1):124. <https://doi.org/10.1186/s12859-017-1545-8>.
- [38] Murphy MA, Obrien TJ, Morris K, Cook MJ. Multimodality image-guided surgery for the treatment of medically refractory epilepsy. 2004.
- [39] Nowell M, et al. Utility of 3D multimodality imaging in the implantation of intracranial electrodes in epilepsy. *Epilepsia* 2015;56(3):403–13. <https://doi.org/10.1111/epi.12924>.
- [40] Nowell M, et al. A pipeline for 3D multimodality image integration and computer-assisted planning in epilepsy surgery. *J Visual Exper* 2016;2016(111). <https://doi.org/10.3791/53450>. May.
- [41] Vakharia VN, Duncan JS, Witt J-A, Elger CE, Staba R, Engel J. Getting the best outcomes from epilepsy surgery: epilepsy Surgery Outcomes. *Ann Neurol* 2018;83(4):676–90. <https://doi.org/10.1002/ana.25205>.
- [42] Rodionov R, et al. Feasibility of multimodal 3D neuroimaging to guide implantation of intracranial EEG electrodes. *Epilepsy Res* 2013;107(1–2):91–100. <https://doi.org/10.1016/j.eplepsyres.2013.08.002>.
- [43] Czarnetzki C, et al. Yield of non-invasive imaging in MRI-negative focal epilepsy. *J Neurol* Feb. 2023. <https://doi.org/10.1007/s00415-023-11987-6>.