

Displacement in brain cancer

validating registration algorithms by fitting a
synthetic model to real data



Paper #2

A Parametric Evaluation of State-of-the-art Image Registration Methods for Assessing Glioblastoma Growth by Synthetic Modeling.

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Sognsvannsveien 20, 0372 Oslo, Norway***

Email: ivarth@student.matnat.uio.no

Phone: +4790857292

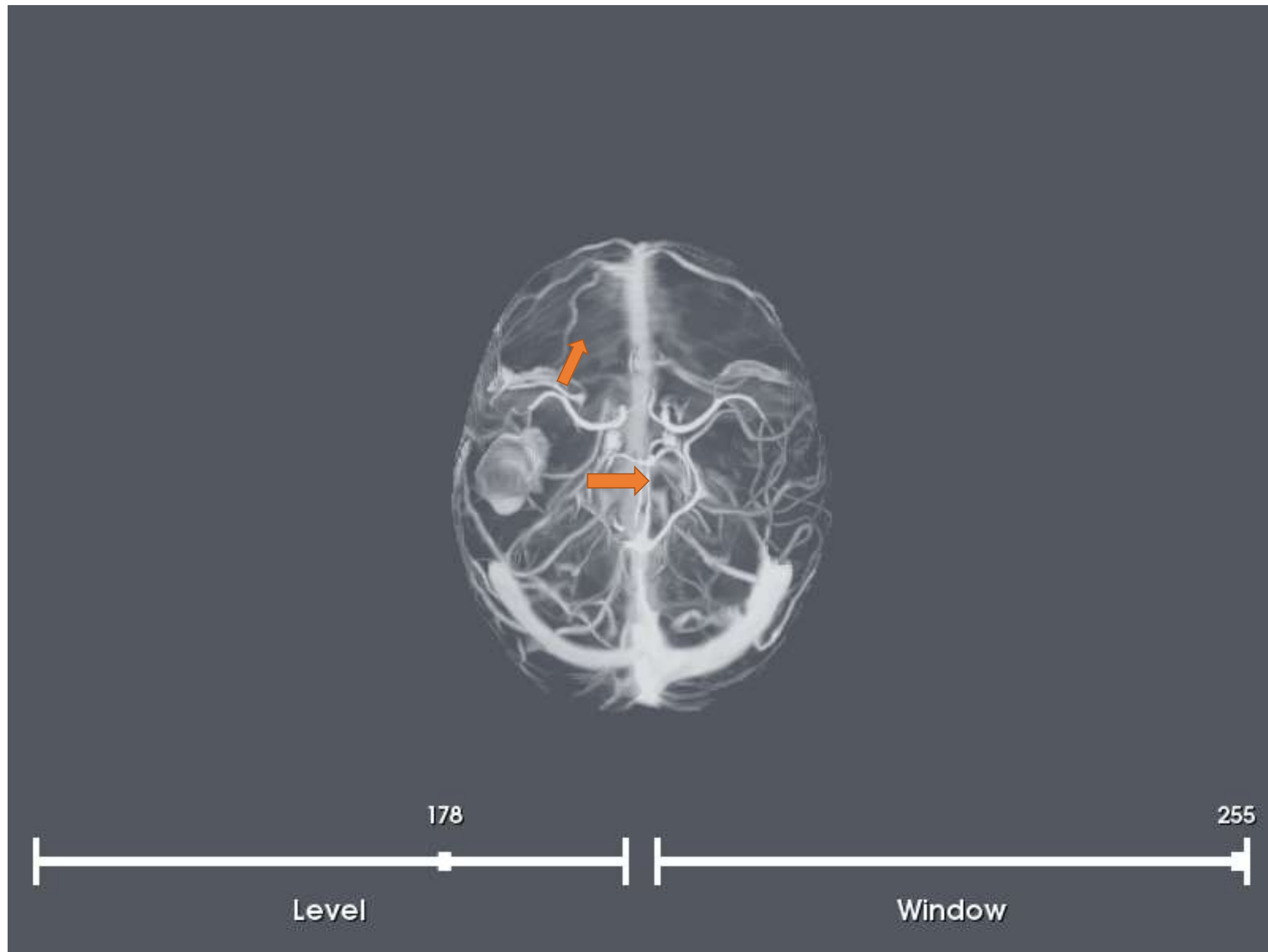
Real
growth
case

T1-weighted
post-
contrast ~3
years
glioblastoma

Maximum
Intensity
Projection
(MIP)

(SAILOR)

animation



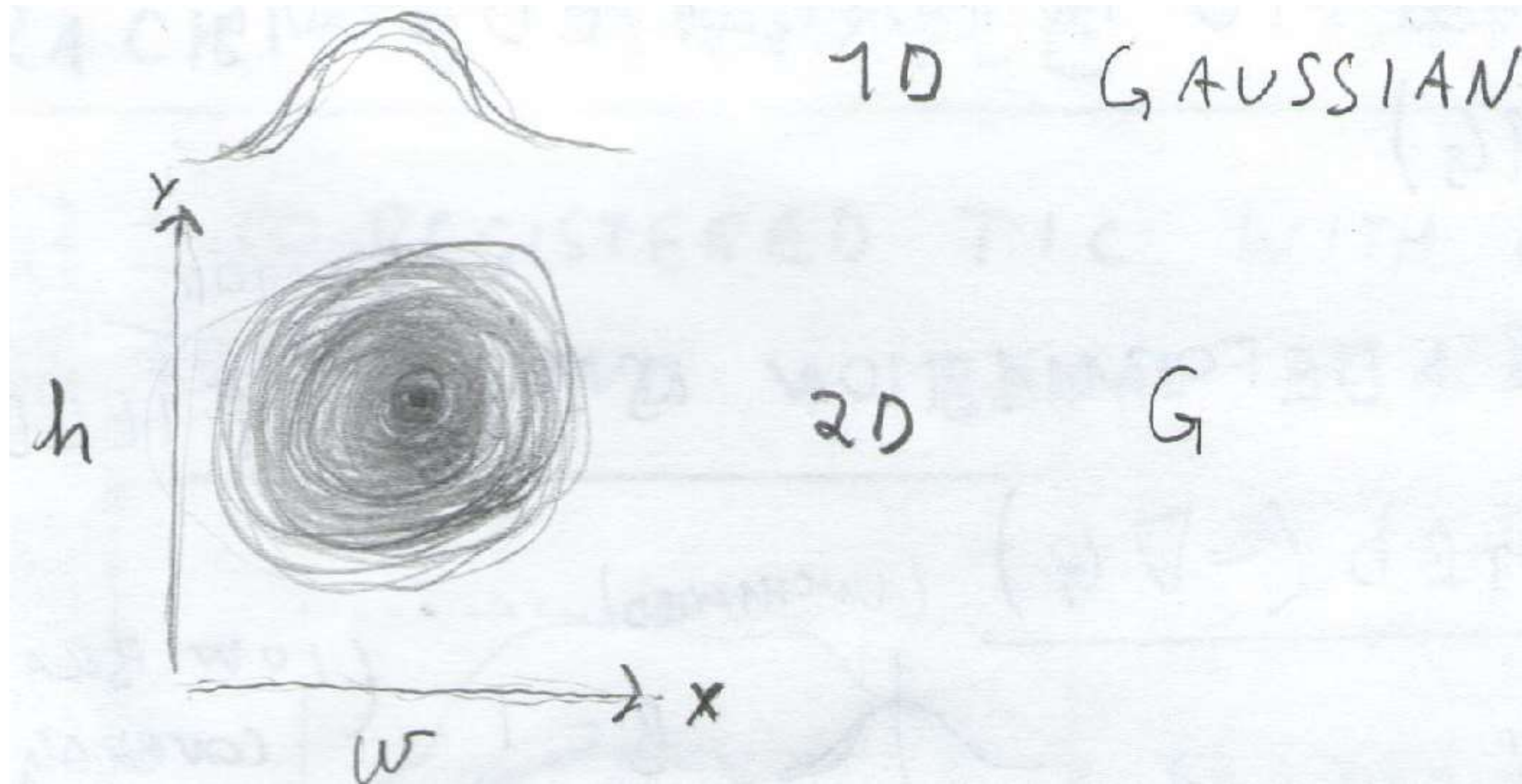
Mass effect and survival

- Progression of cancer within a fixed skull volume (expanding deformation?)
- Human eye: Visible [1,2] and “invisible” [3] displacement caused by mass effect are associated with decreased survival

[1] T. C. Steed *et al.*, “Quantification of glioblastoma mass effect by lateral ventricle displacement,” *Sci Rep*, vol. 8, no. 1, p. 2827, 12 2018, doi: 10.1038/s41598-018-21147-w.

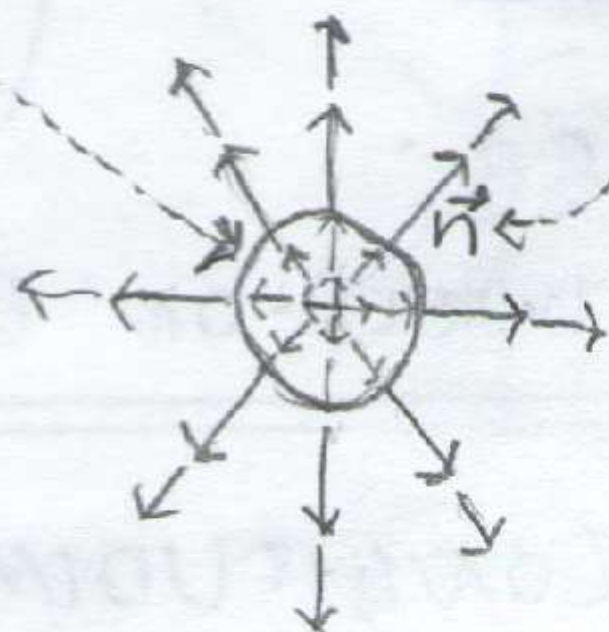
[2] E. S. Gamburg, W. F. Regine, R. A. Patchell, J. M. Strottmann, M. Mohiuddin, and A. B. Young, “The prognostic significance of midline shift at presentation on survival in patients with glioblastoma multiforme,” *Int J Radiat Oncol Biol Phys*, vol. 48, no. 5, pp. 1359–1362, Dec. 2000, doi: 10.1016/s0360-3016(00)01410-3.

[3] P. Prasanna *et al.*, “Mass Effect Deformation Heterogeneity (MEDH) on Gadolinium-contrast T1-weighted MRI is associated with decreased survival in patients with right cerebral hemisphere Glioblastoma: A feasibility study,” *Sci Rep*, vol. 9, no. 1, p. 1145, 04 2019, doi: 10.1038/s41598-018-37615-2.



"INFLECTION RING"

UNIT VECTOR: $|\vec{n}| = 1$



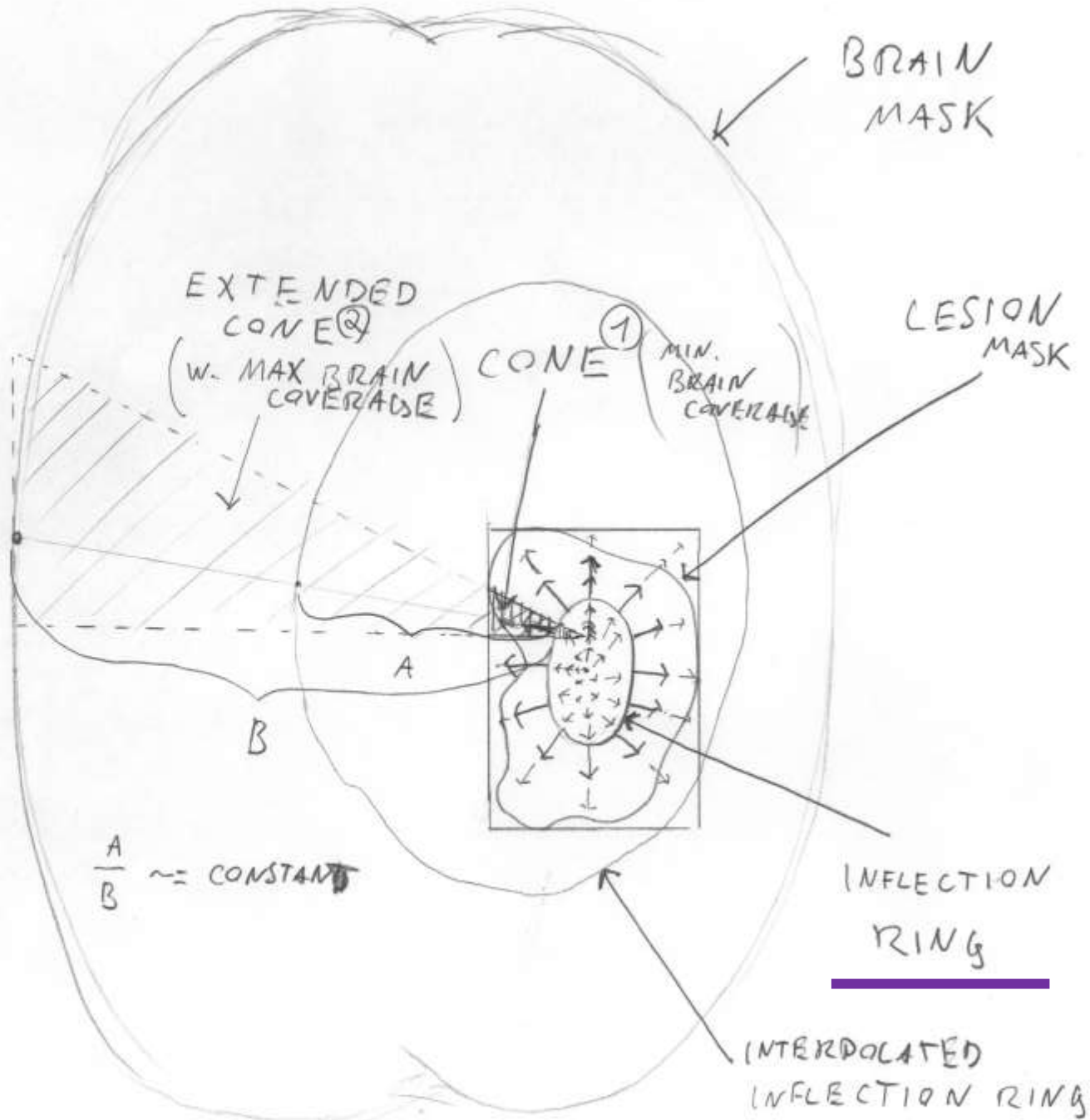
$-\nabla G = \text{EXPAND } (+)$

$$\nabla = \text{GRADIENT} = \begin{bmatrix} \frac{\partial G}{\partial x} \\ \frac{\partial G}{\partial y} \end{bmatrix}$$

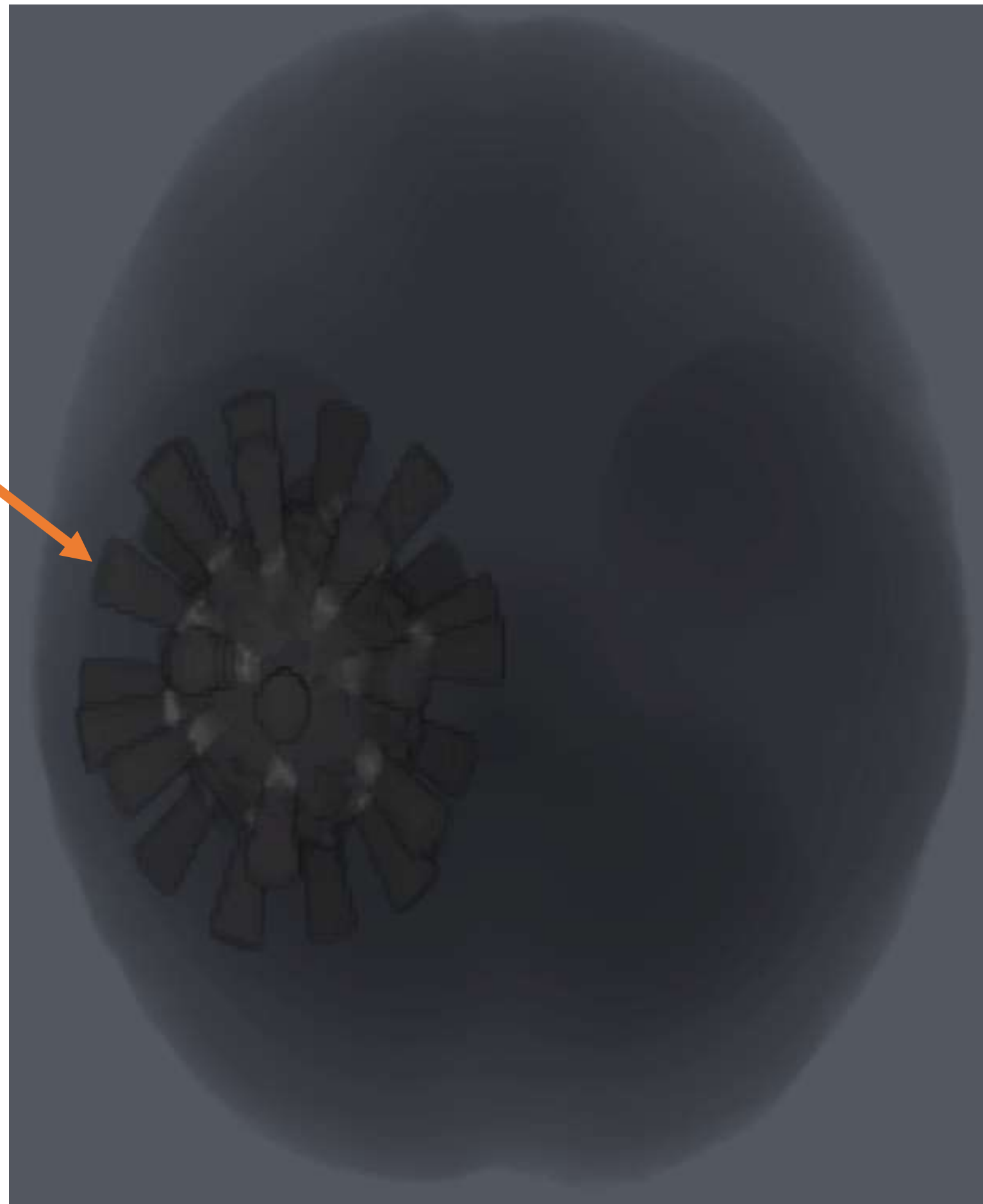
CANCER-SIM v1:

DISPLACEMENT VECTORS
INSIDE CONE⁽¹⁾ ARE
INTERPOLATED (STRETCHED)
TO FILL EXTENDED
CONE⁽²⁾

THE EXAMPLE IS
WITH.
= MAX BRAIN COVERAGE
SETTING



cone (1)



Validating non-rigid registration methods for clinical use

- 1-3; Optical flow: Gunnar-Farneback¹, Iterative Lucas-Kanade² and TV-L1³ versions
- 4-5; ANTs: Symmetric image Normalization (SyN)^{4,5}, cross-correlation⁴ and mutual information versions
- We validate registration methods by measuring the displacement error between cancer-sim synthetic displacement field and estimated displacement field in and around lesion areas: Necrotic, edematous and contrast-enhanced lesions

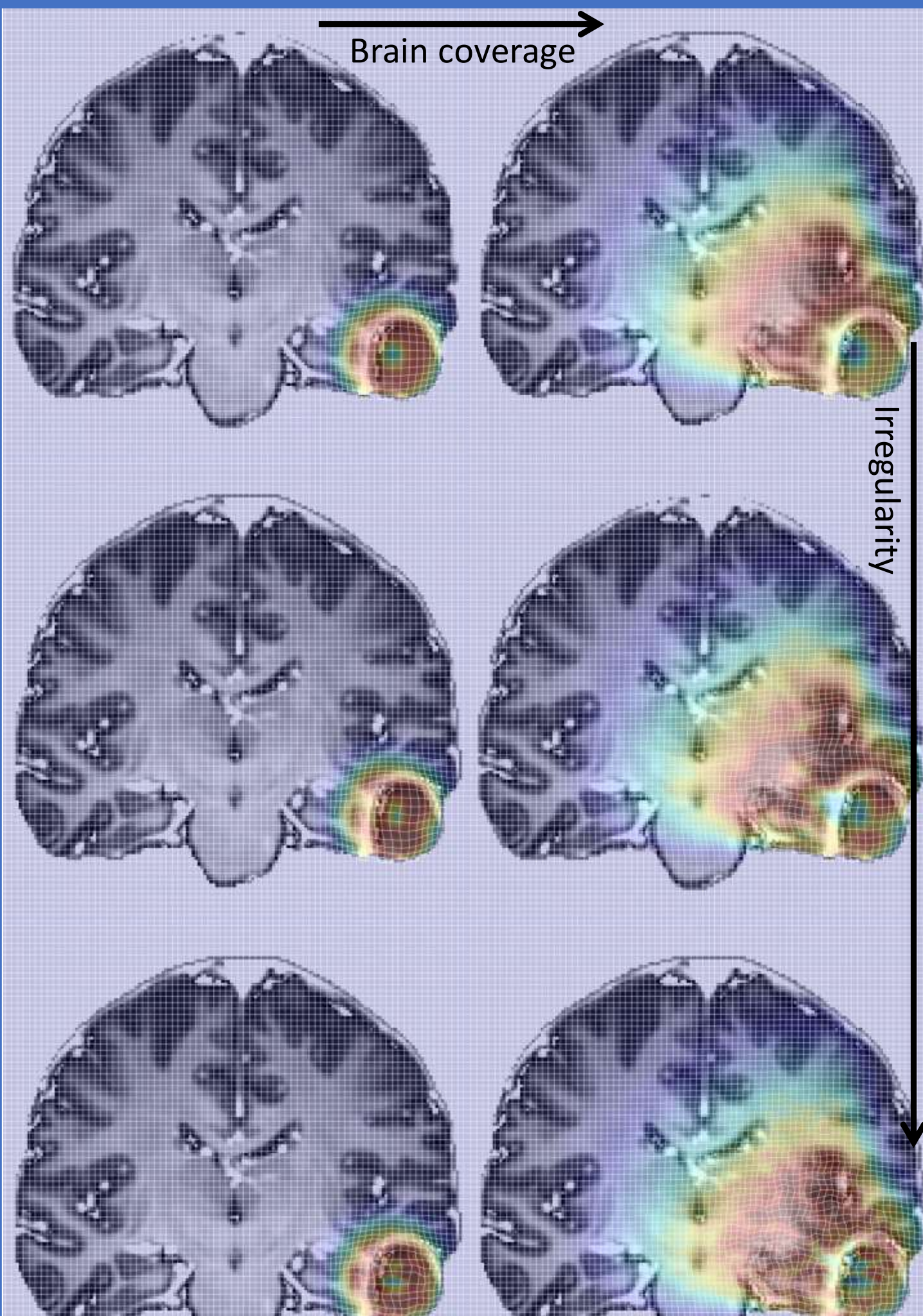
- 1) Farneback, Gunnar. "Two-frame motion estimation based on polynomial expansion." *Scandinavian conference on Image analysis*. Springer, Berlin, Heidelberg, 2003.
- 2) Le Besnerais, Guy, and Frédéric Champagnat. "Dense optical flow by iterative local window registration." *IEEE International Conference on Image Processing 2005*. Vol. 1. IEEE, 2005.
- 3) Zach, Christopher, Thomas Pock, and Horst Bischof. "A duality based approach for realtime tv-l 1 optical flow." *Joint pattern recognition symposium*. Springer, Berlin, Heidelberg, 2007.
- 4) Avants, Brian B., et al. "Symmetric diffeomorphic image registration with cross-correlation: evaluating automated labeling of elderly and neurodegenerative brain." *Medical image analysis* 12.1 (2008): 26-41.
- 5) Avants, Brian, C. L. Epstein, and James C. Gee. "Geodesic image normalization in the space of diffeomorphisms." 2006.

Deformable registration validation

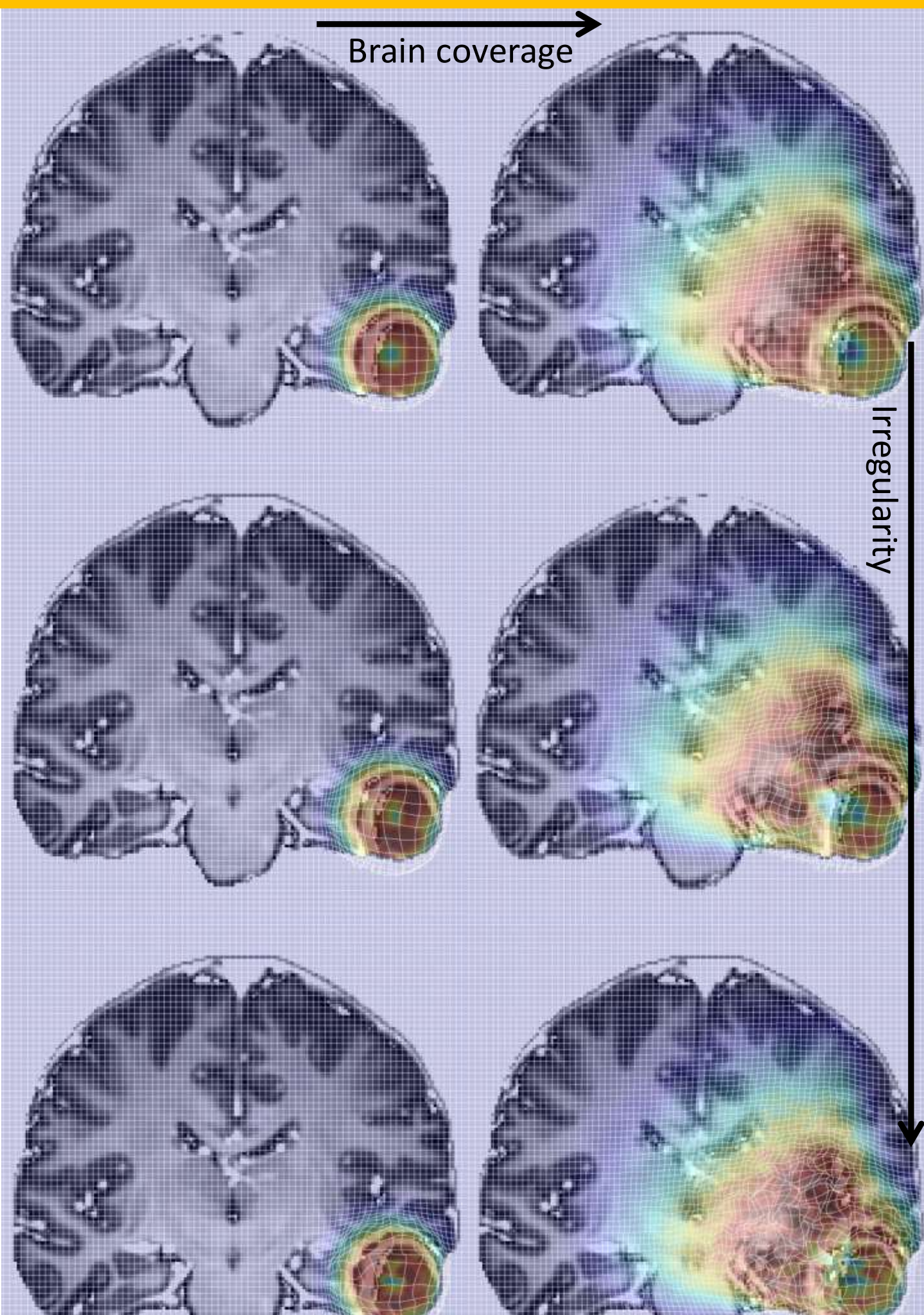
- Created dataset of 27 (patients) * 12 (models) = 324 models

Models patient	Model	Magnitude [<i>mm</i>]	Brain coverage	Irregularity
	1	3	High	No
	2	3	High	High
	3	3	High	Intermediate
	4	3	Low	No
	5	3	Low	High
	6	3	Low	Intermediate
	7	8	High	No
	8	8	High	High
	9	8	High	Intermediate
	10	8	Low	No
	11	8	Low	High
	12	8	Low	Intermediate

3 mm



8 mm



Deformable registration validation

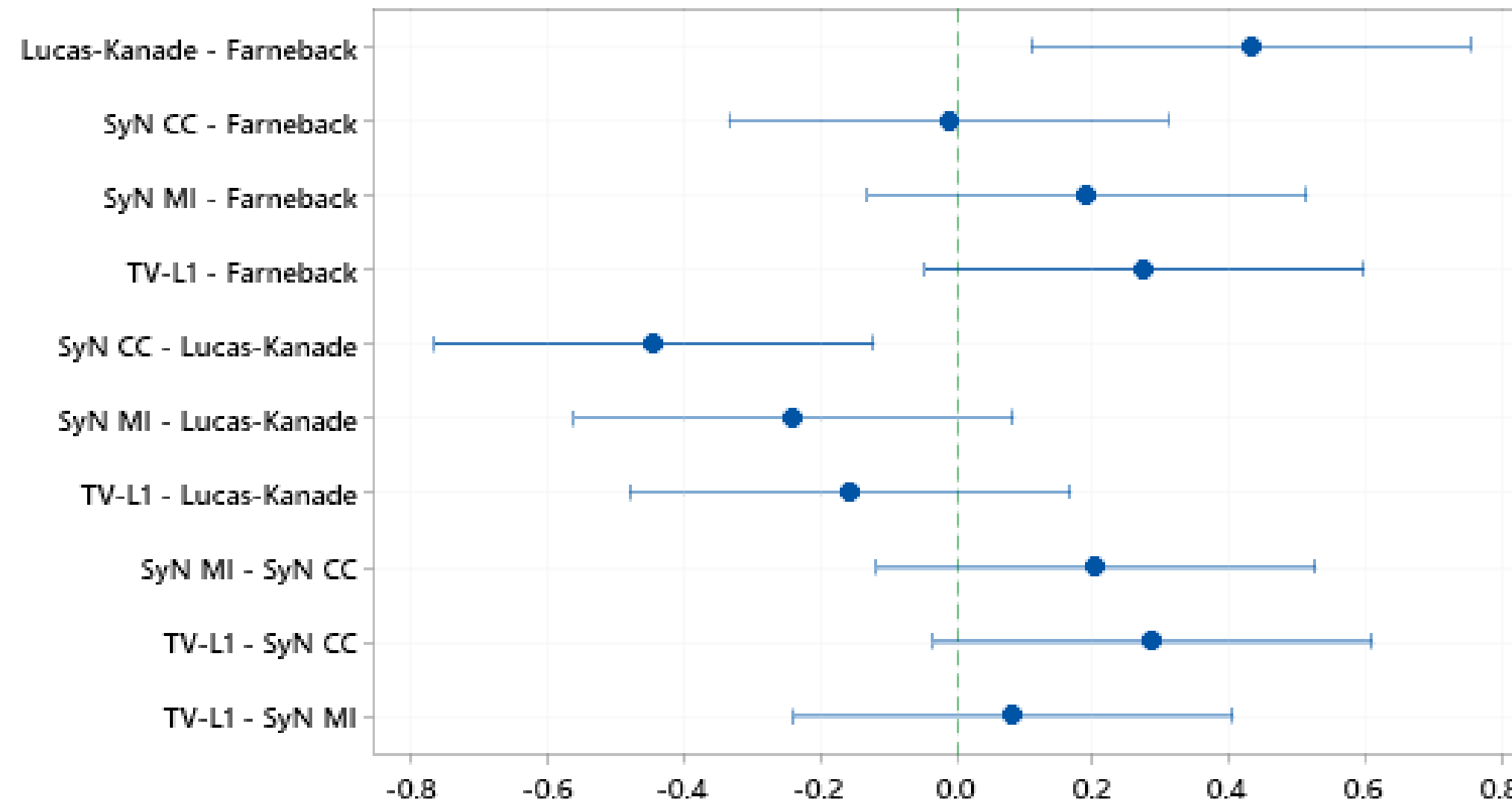
- Created dataset of 27 (patients) * 12 (models) = 324 models
- Ran the five registration methods on 324 real-synthetic pairs to estimated displacement fields
- Computed voxel-wise absolute and relative displacement error in necrotic, edema and enhancing tumor regions
- Wilcoxon signed-rank and Kruskal-Wallis nonparametric tests, and One-way ANOVA analysis on absolute and relative errors (when appropriate) to investigate differences in registration performance as function of model parameters, registration method and lesion tissue type

Results (in progress)

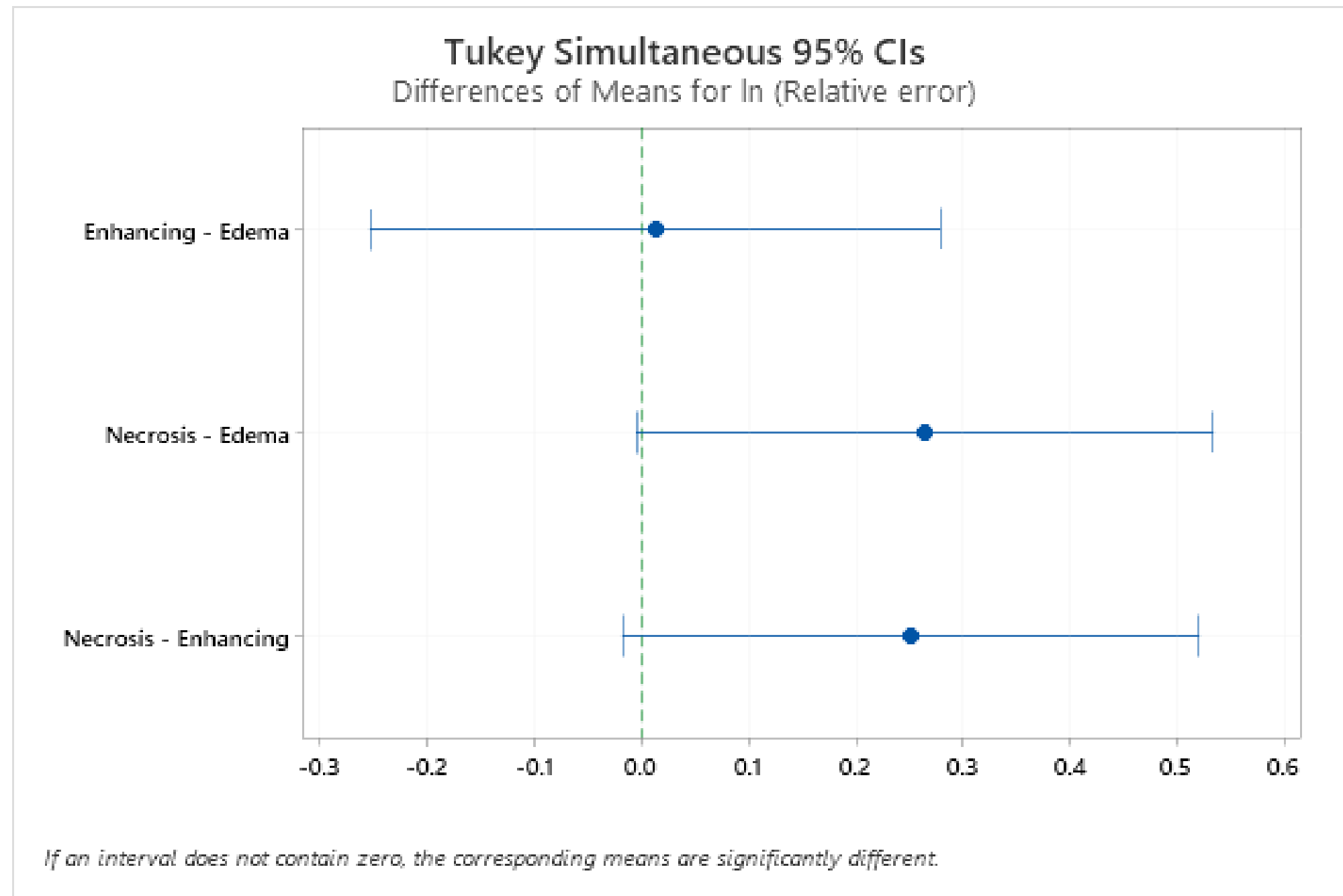
- Difference in method performances (relative errors) for low and high brain coverage (K-W, $p=0.02$). Best performance for high brain coverage.
- SyN CC and Farneback methods had best performances with lowest absolute and relative errors (K-W, ANOVA; $p<0.037$).
- Different performances as a function of tissue type (K-W; $p=0.019$, absolute error, ANOVA; $p\leq 0.035$, relative error). Best performance in enhancing tissue.

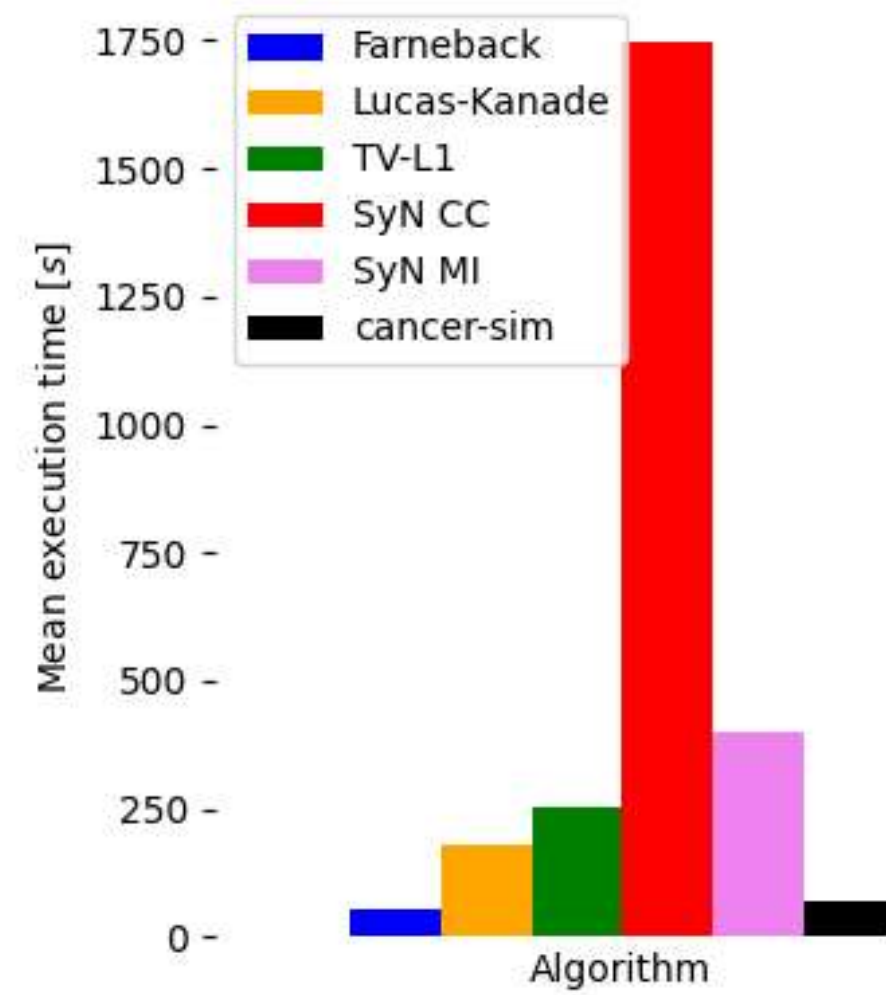
Tukey Simultaneous 95% CIs

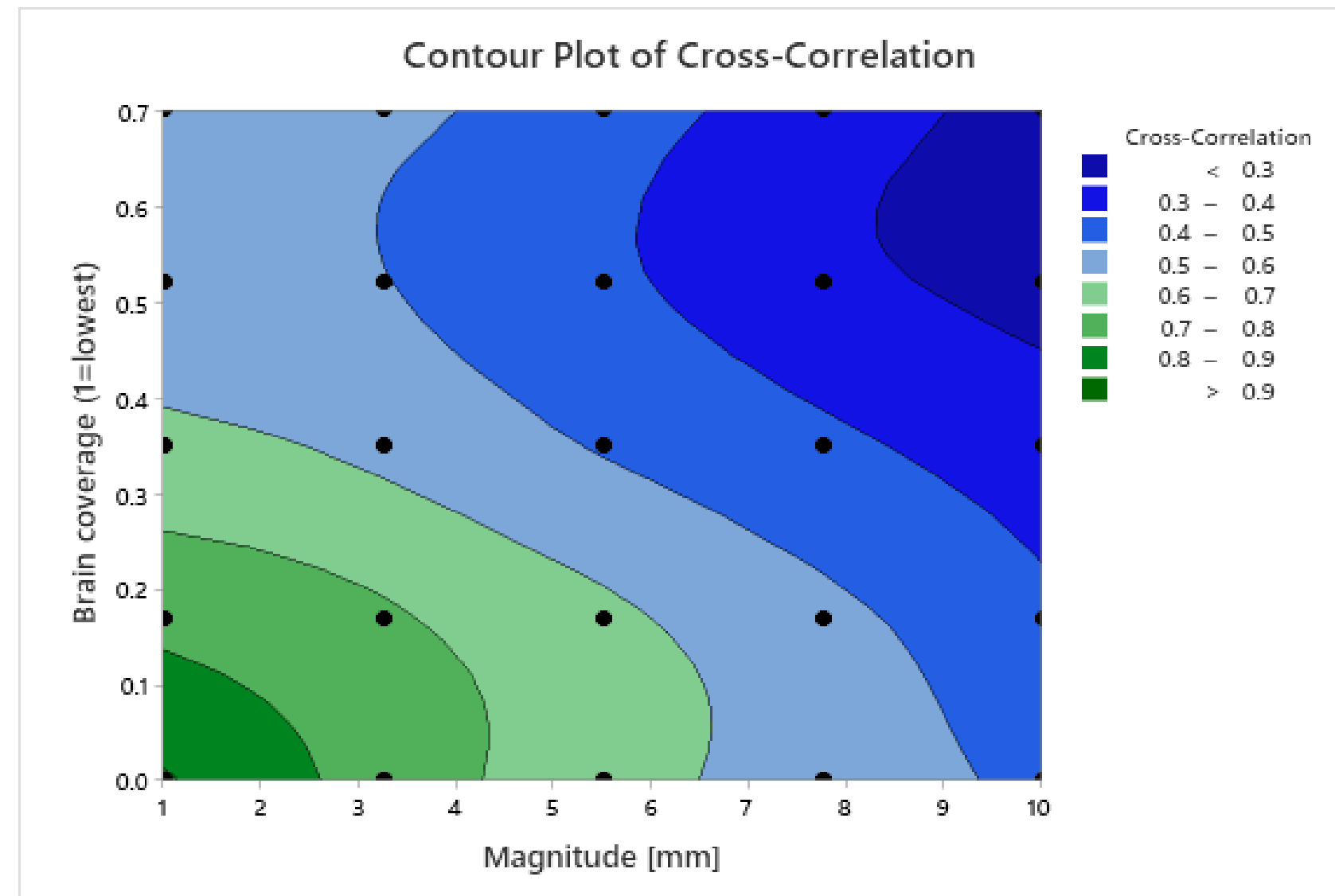
Differences of Means for ln (Relative error)



If an interval does not contain zero, the corresponding means are significantly different.







cancer-sim v1 example: Best fit model on each time interval

from grid search on displacement magnitude and brain coverage

ITK-SNAP Toolbox

Main Toolbar



Cursor Inspector



Cursor position (x,y,z):

49 115 65

Intensity under cursor:

Layer	Intensity
true	19
synth	44.16
normmask	0

Label under cursor:

0 Clear Label

Segmentation Labels

Active label:

Label 1

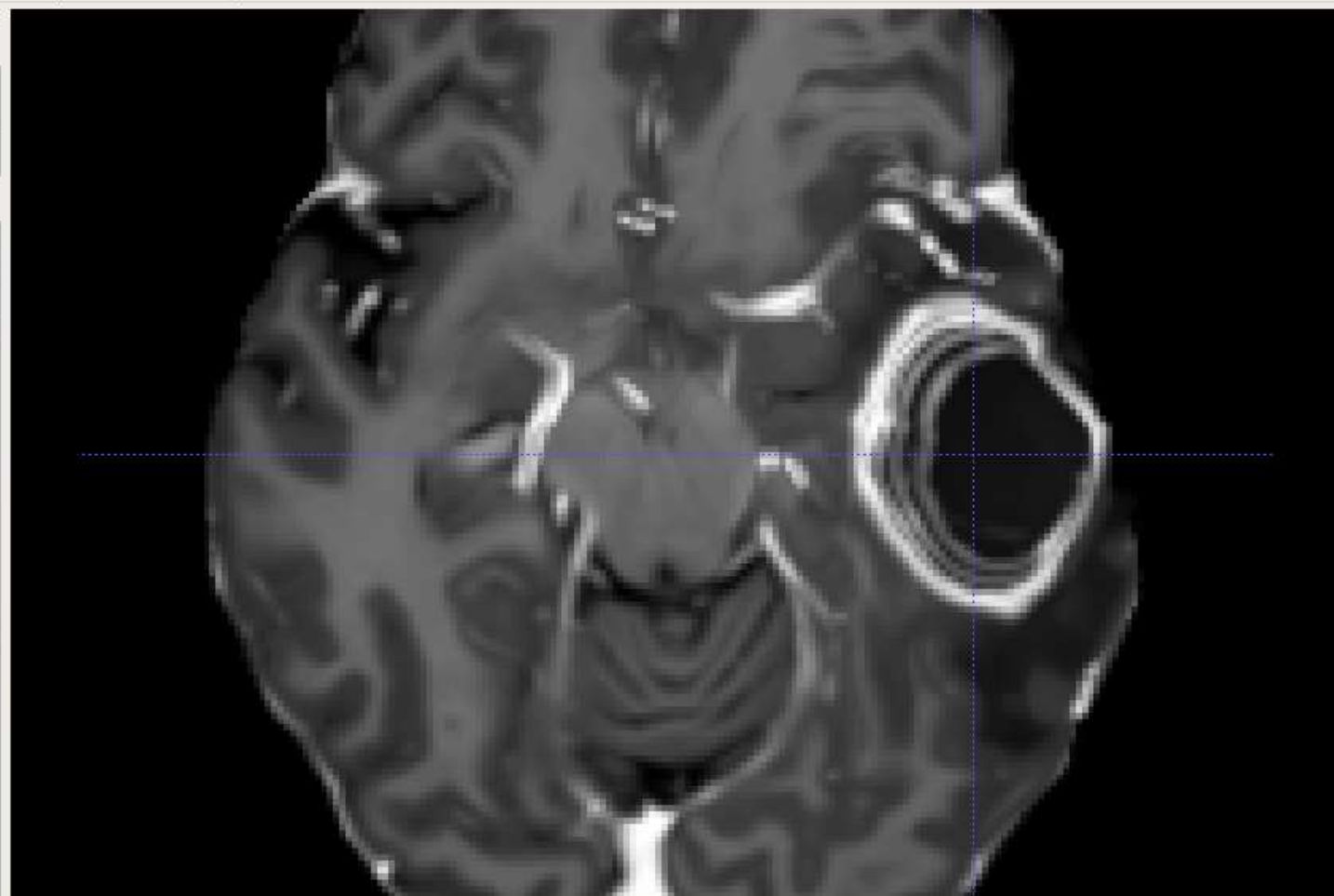
Paint over:

All labels

Overall label opacity:

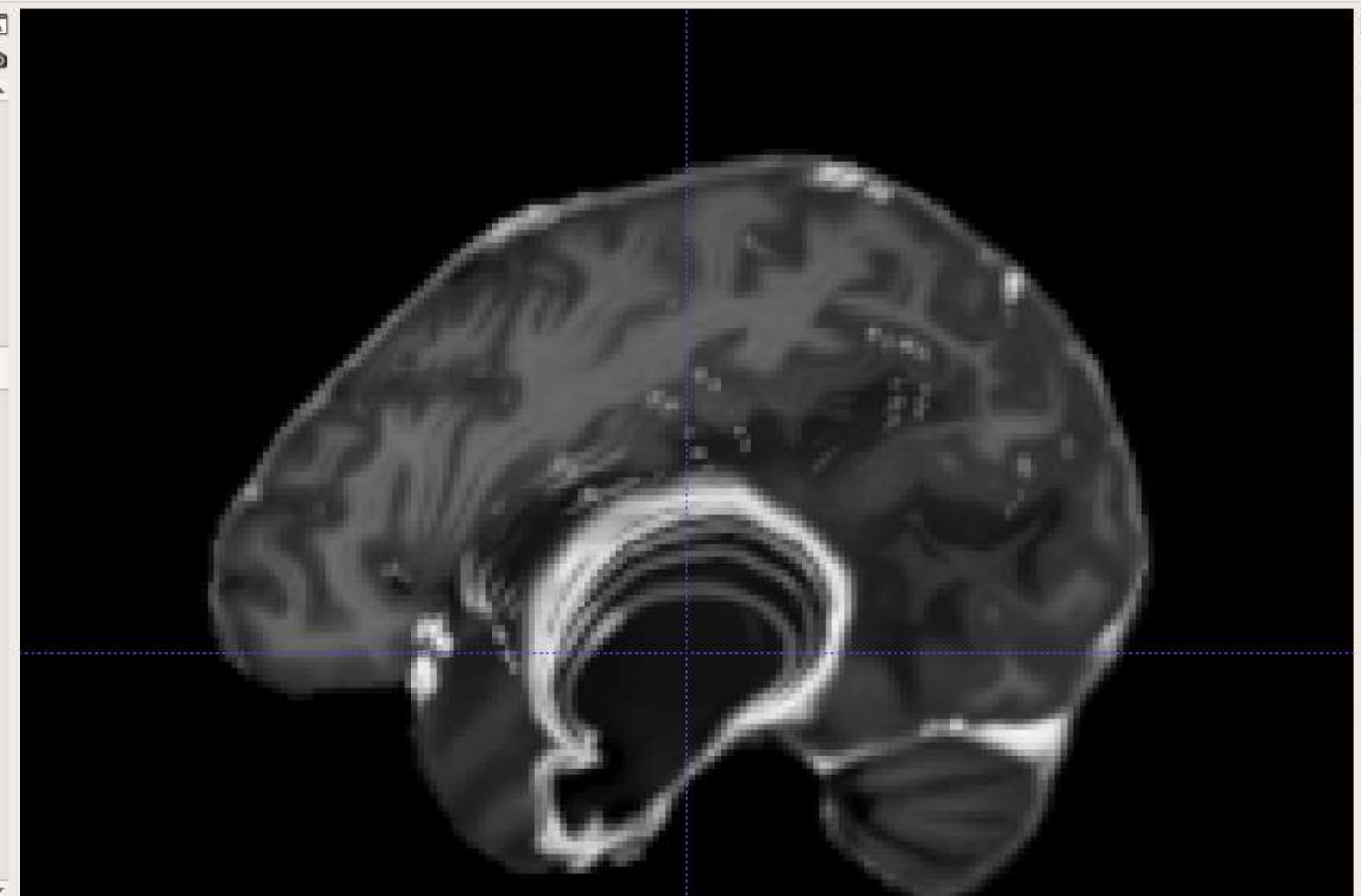
50

3D Toolbar



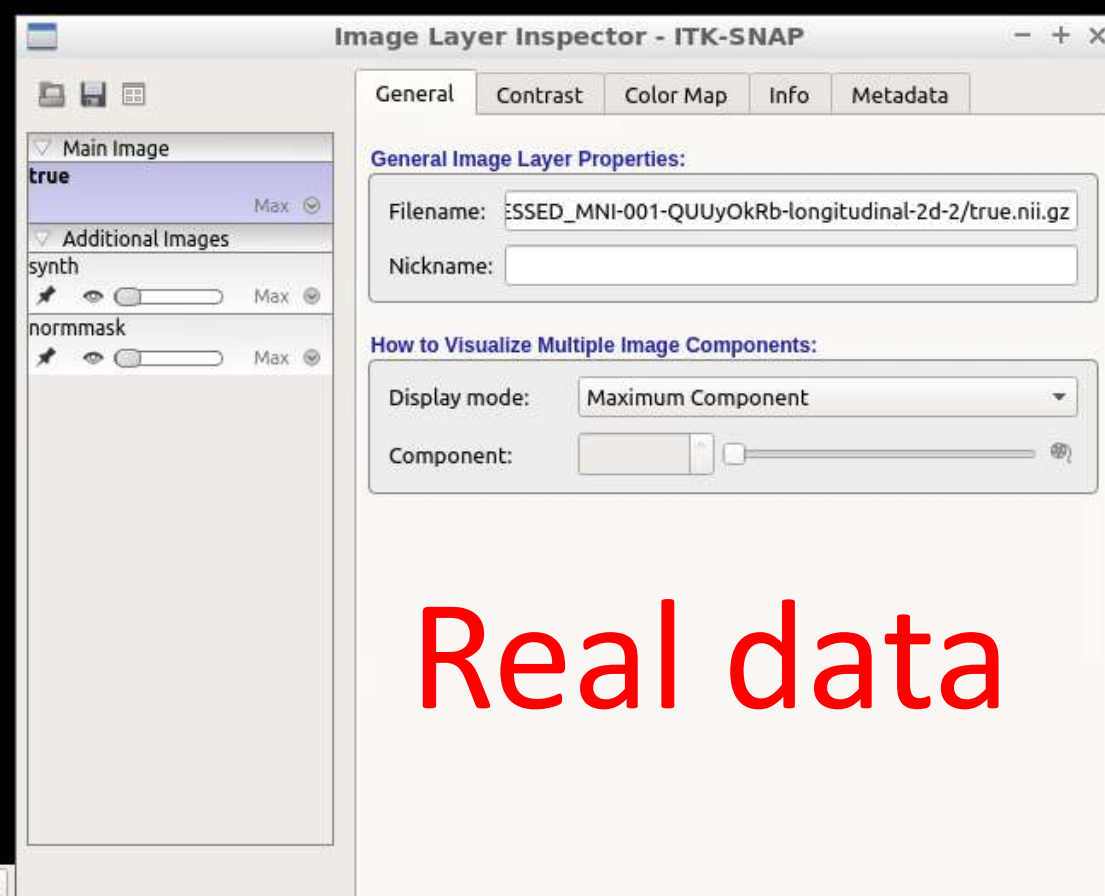
zoom to fit

65 of 193

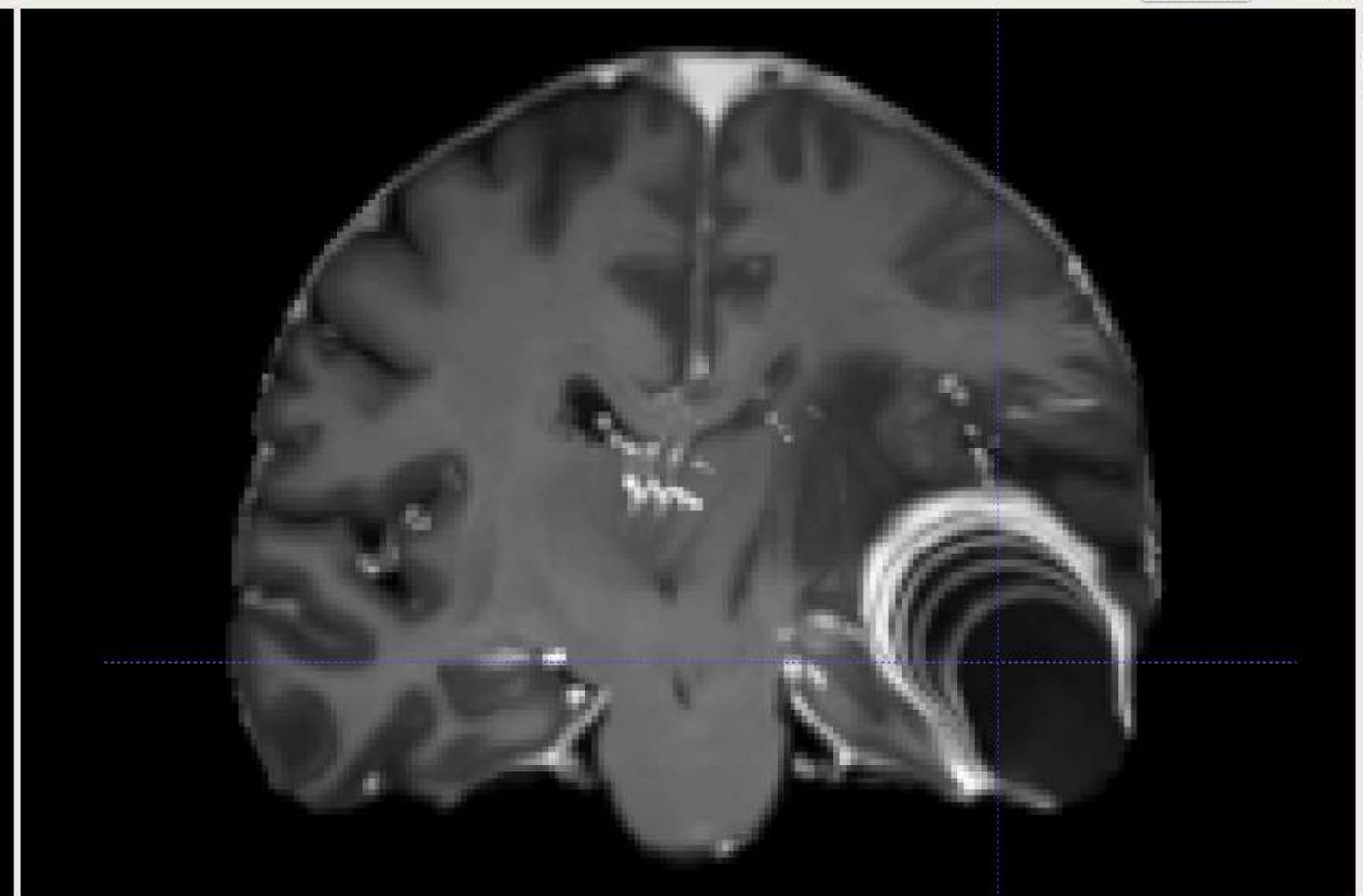


zoom to fit

49 of 193

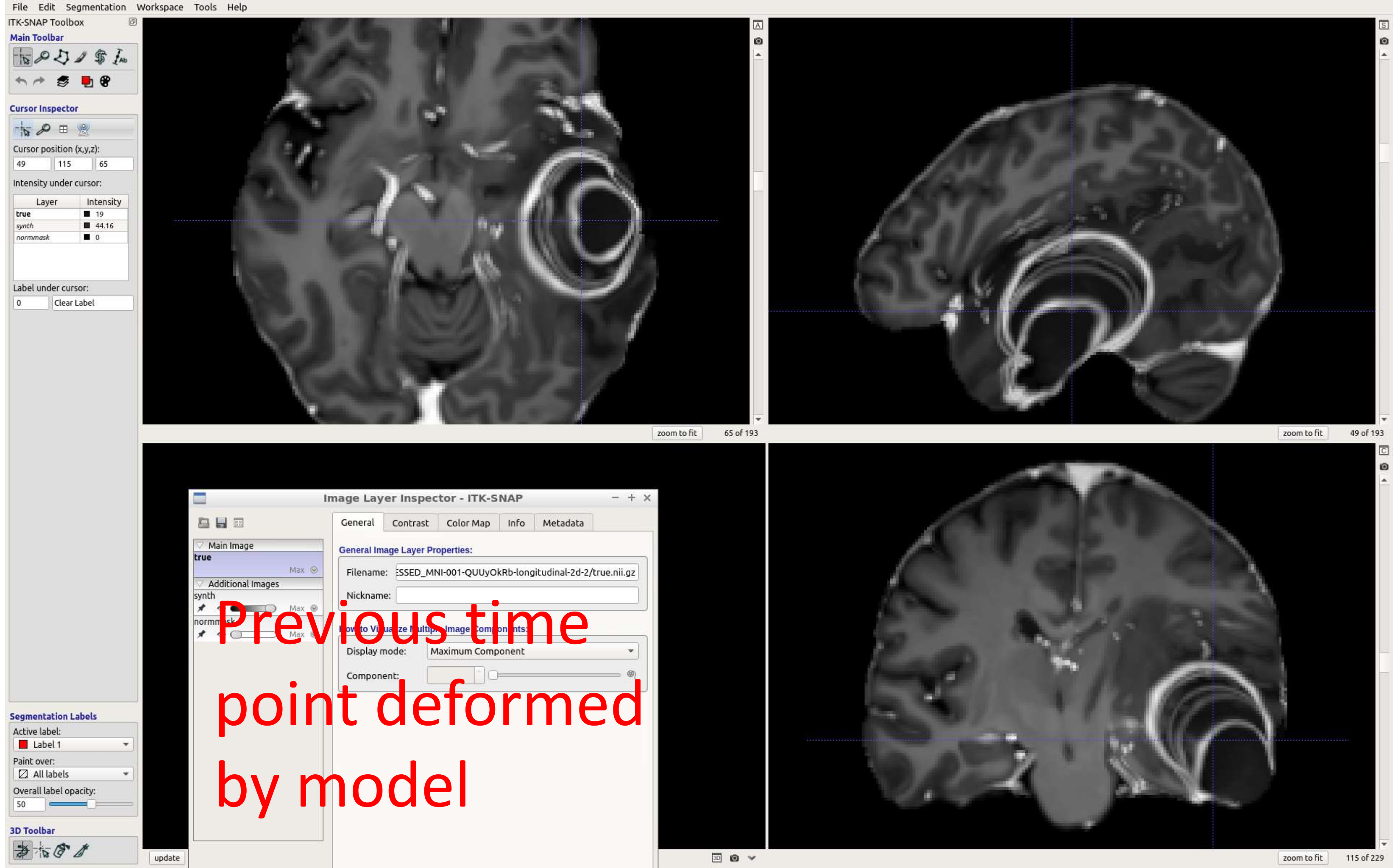


Real data



zoom to fit

115 of 229



ITK-SNAP Toolbox

Main Toolbar



Cursor Inspector



Cursor position (x,y,z):

49 115 65

Intensity under cursor:

Layer	Intensity
true	19
synth	44.16
normmask	0

Label under cursor:

0 Clear Label

Segmentation Labels

Active label:

Label 1

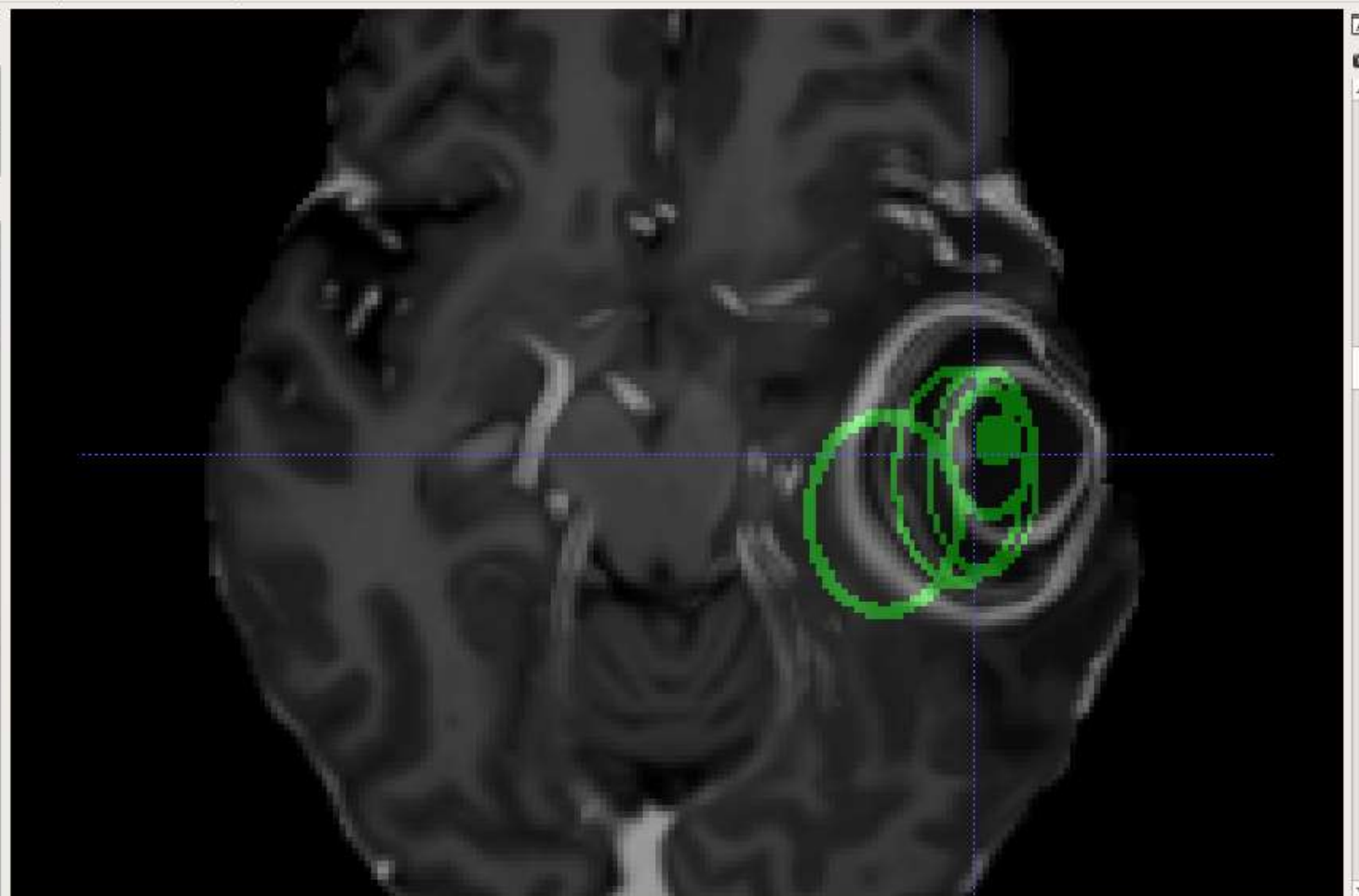
Paint over:

All labels

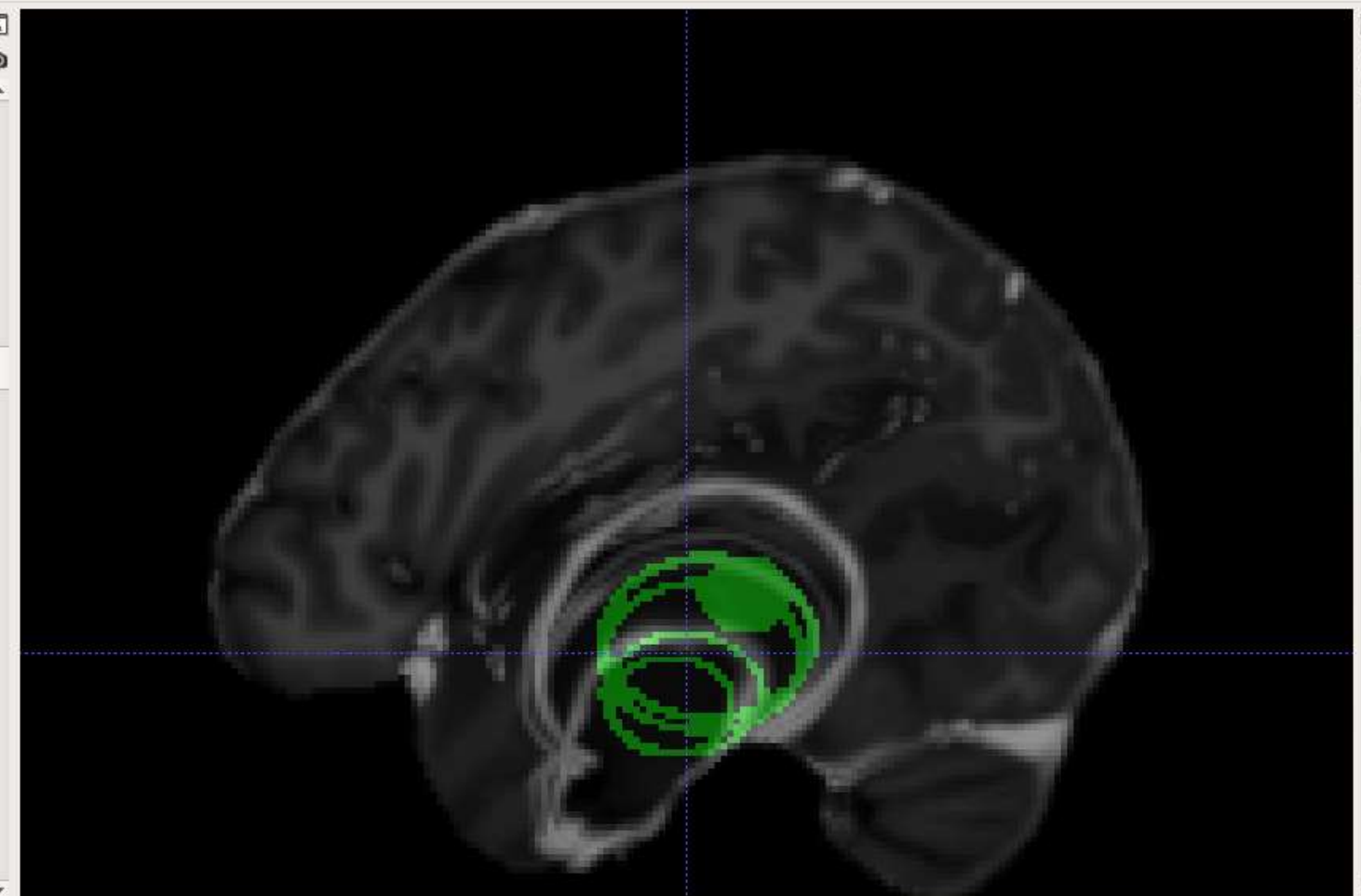
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50

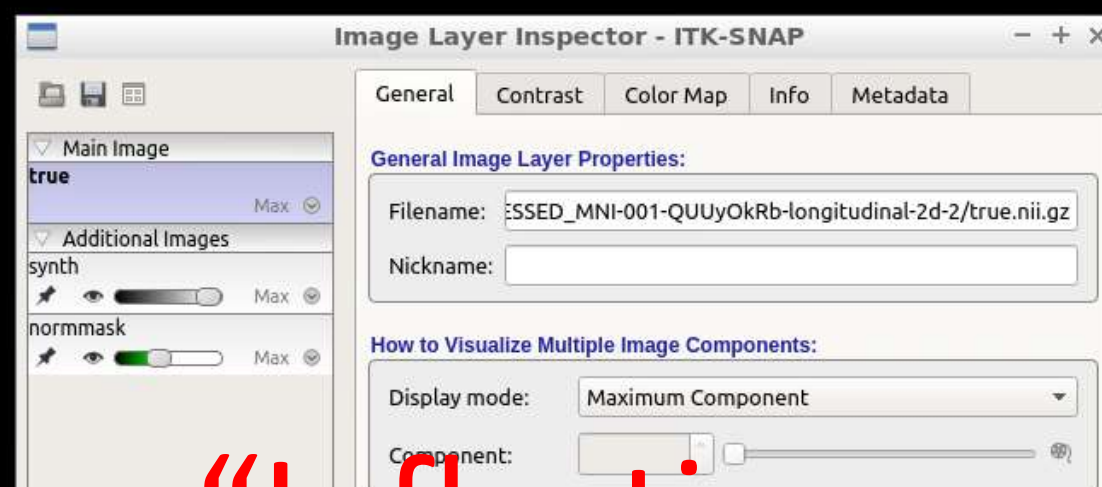
3D Toolbar



zoom to fit 65 of 193



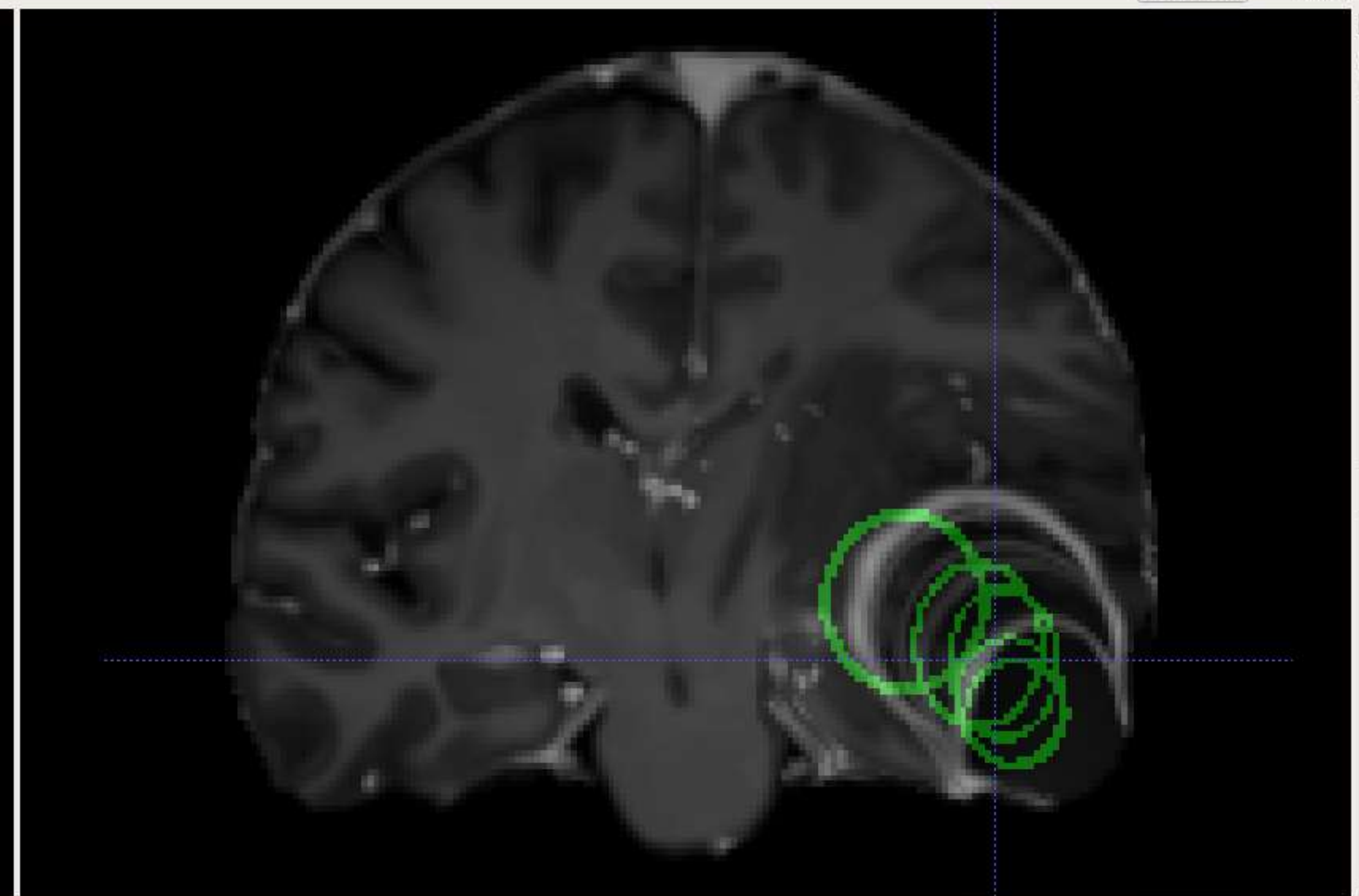
zoom to fit 49 of 193



“Inflection
ellipsoids”

update

zoom to fit 115 of 229



zoom to fit 115 of 229

Displacement maps in glioblastoma

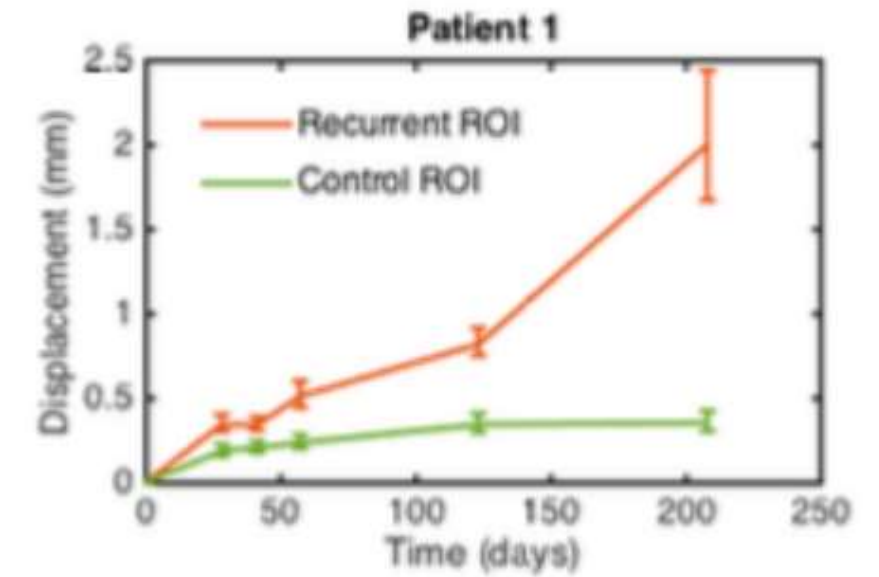
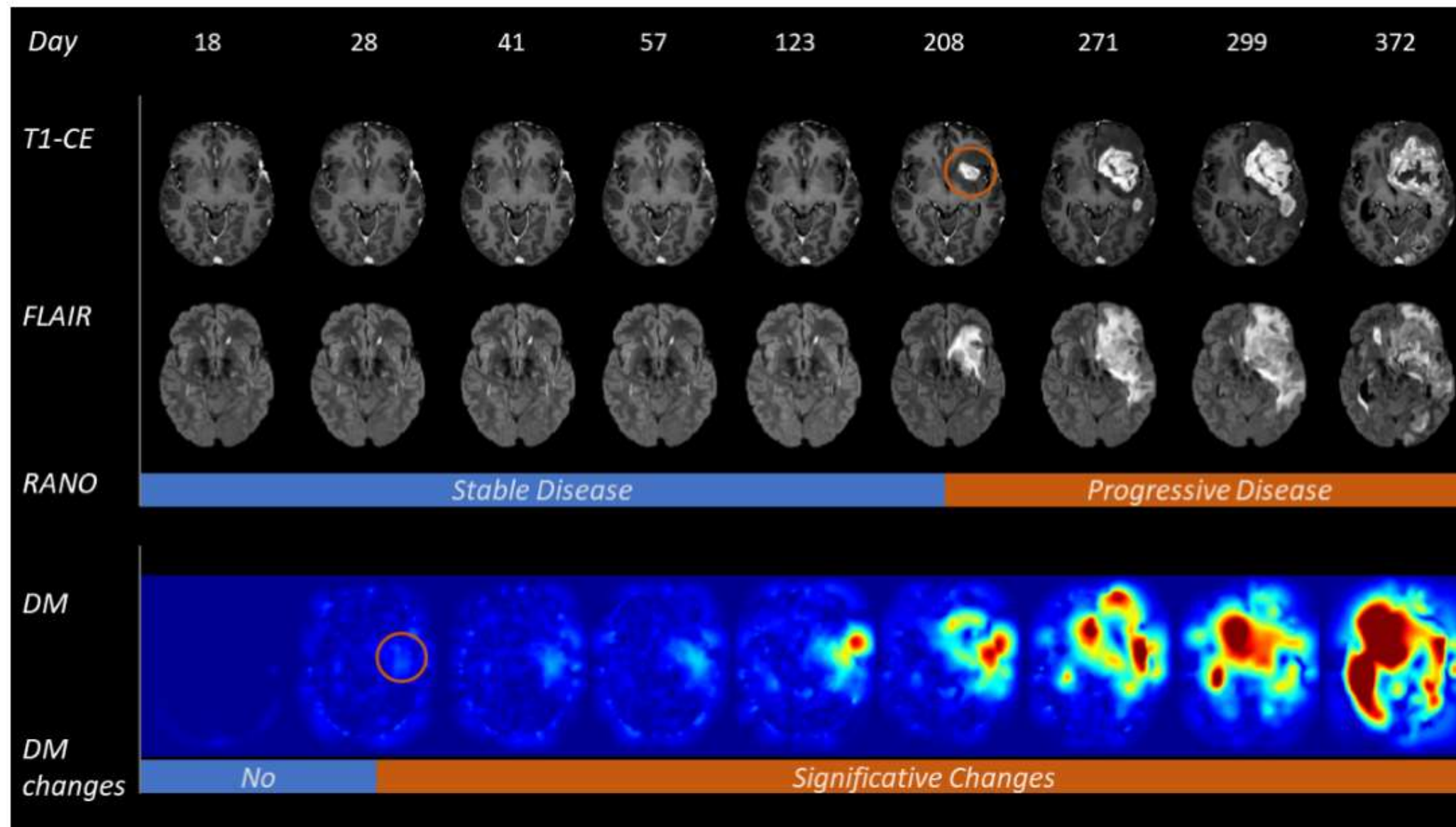
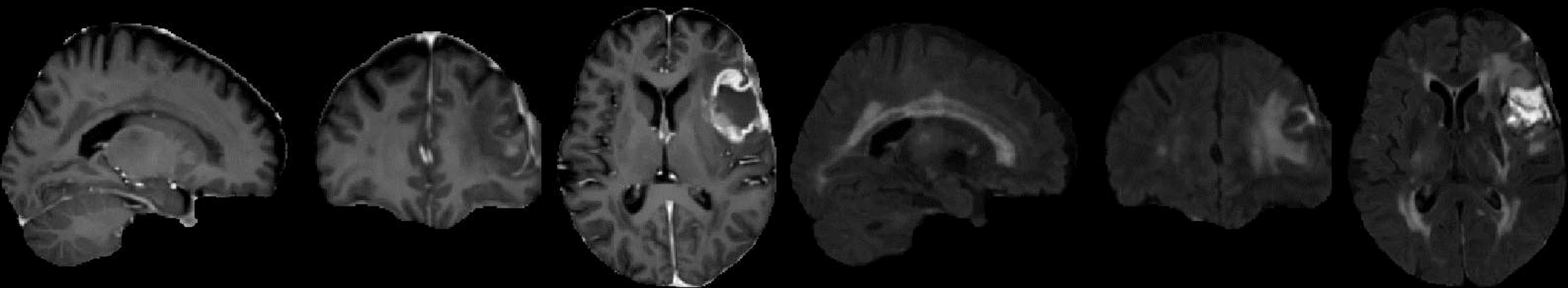
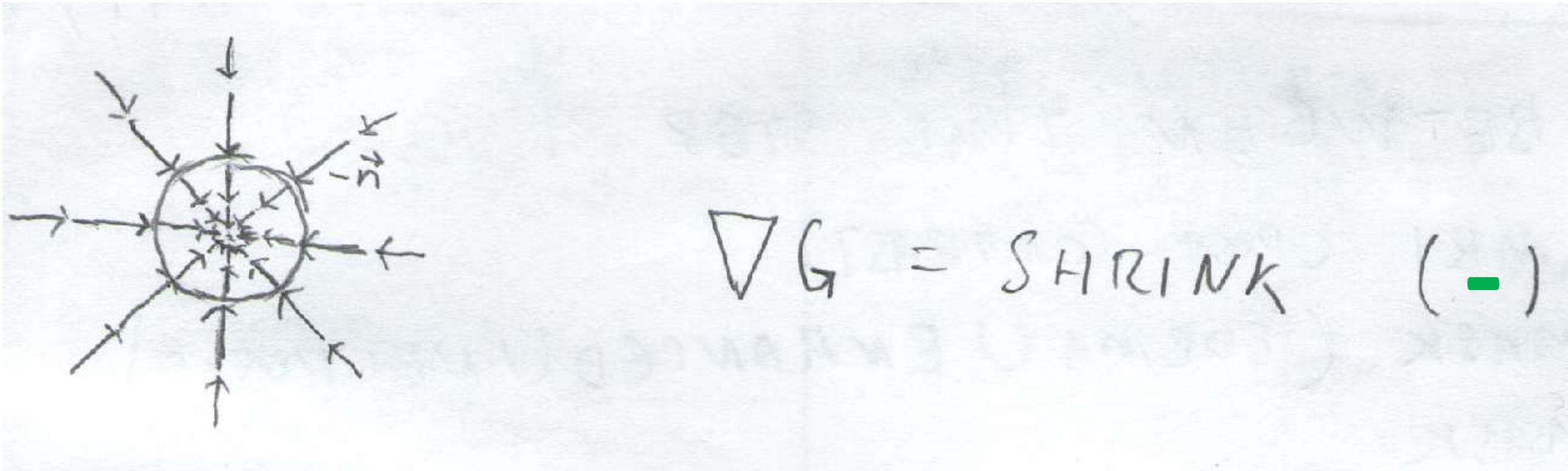


Fig. 2. Longitudinal evolution of Patient 1 from day 18 after starting radiochemotherapy treatment to day 372. According to RANO criteria tumor progression started on day 208, however displacement maps (DM) show significant deformations already at day 28.

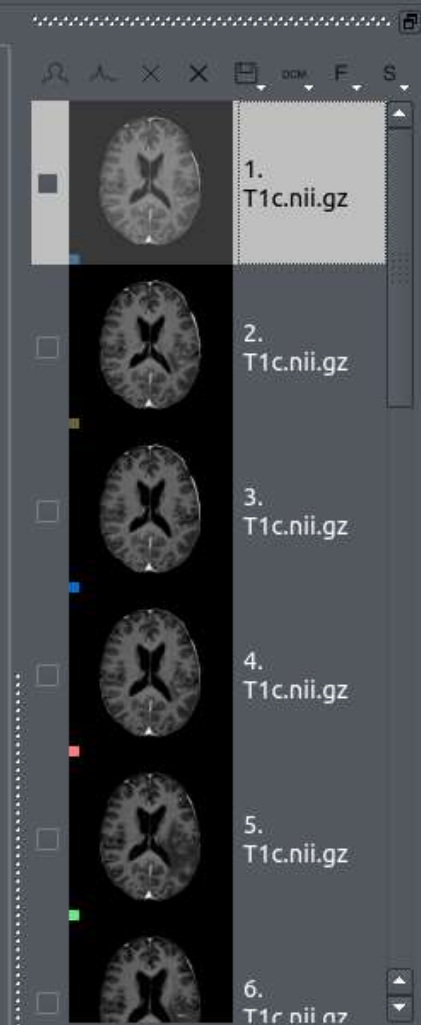
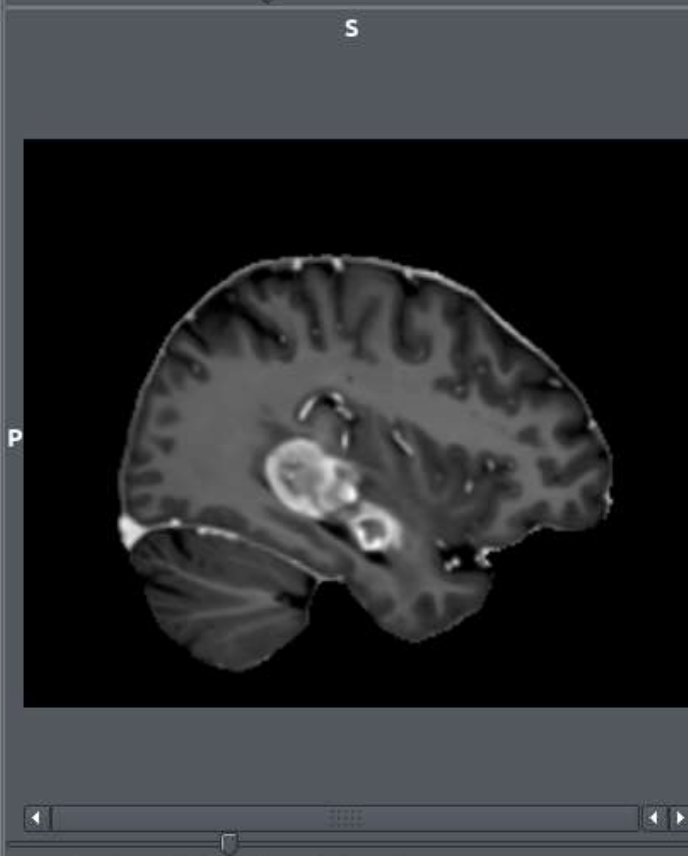
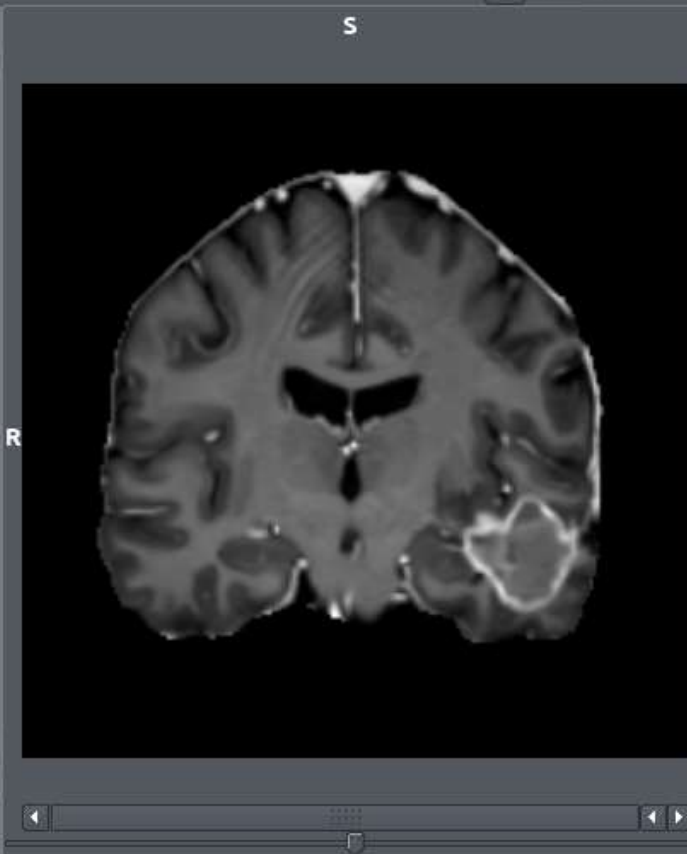
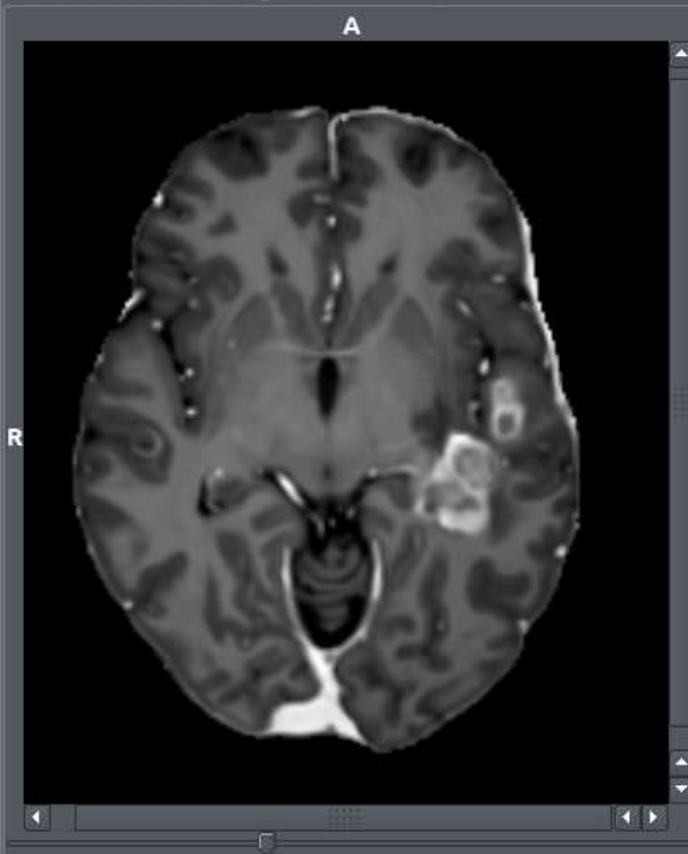
Elies Fuster-Garcia 2019/2020





Z, MPR Y, MPR X, Histogram

Maximum intensity projection, CPU



T1c.nii.gz

193 x 229 x 193

unsigned char

[0, 255]

LPI

X left to right

Y posterior to anterior

Z inferior to superior

3D OpenGL views:

GL_R8 193x229x193 (no filtering)

3D+t

120 ms Acq.

2Dt 3Dt

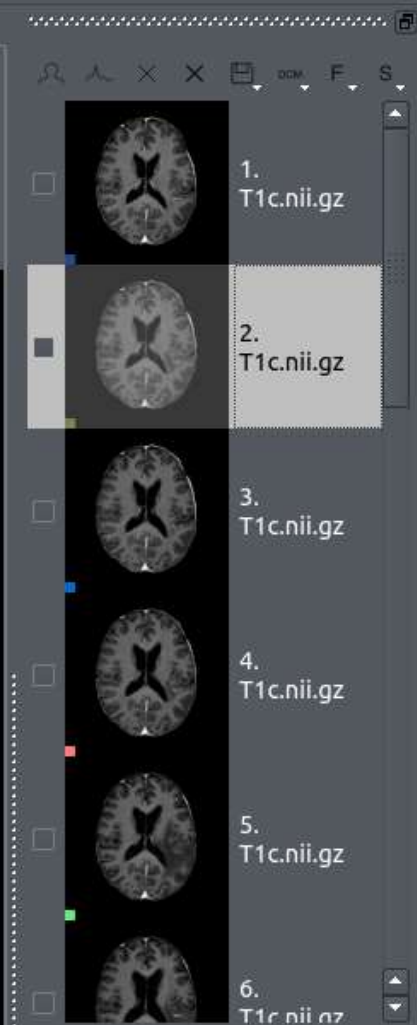
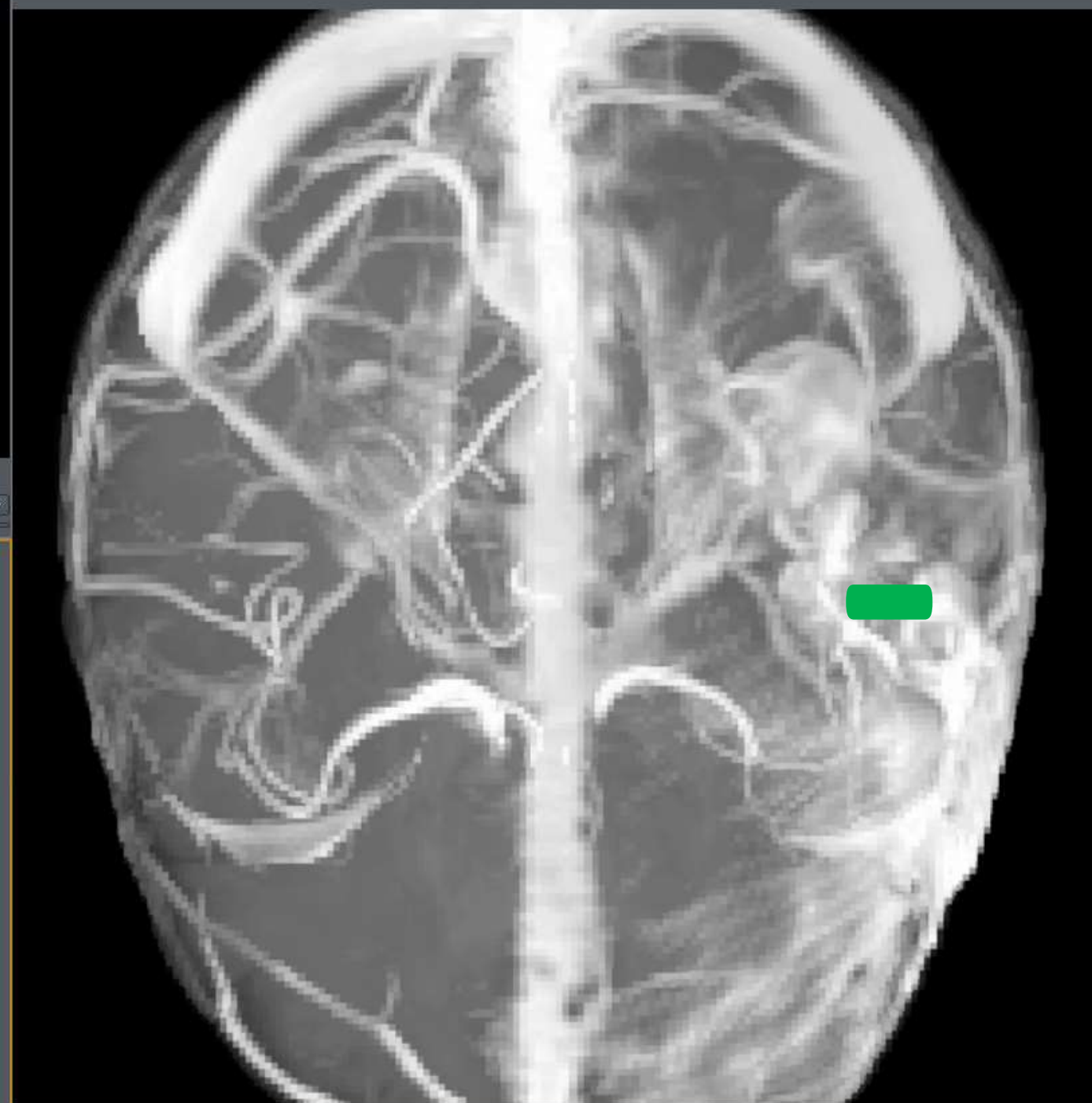
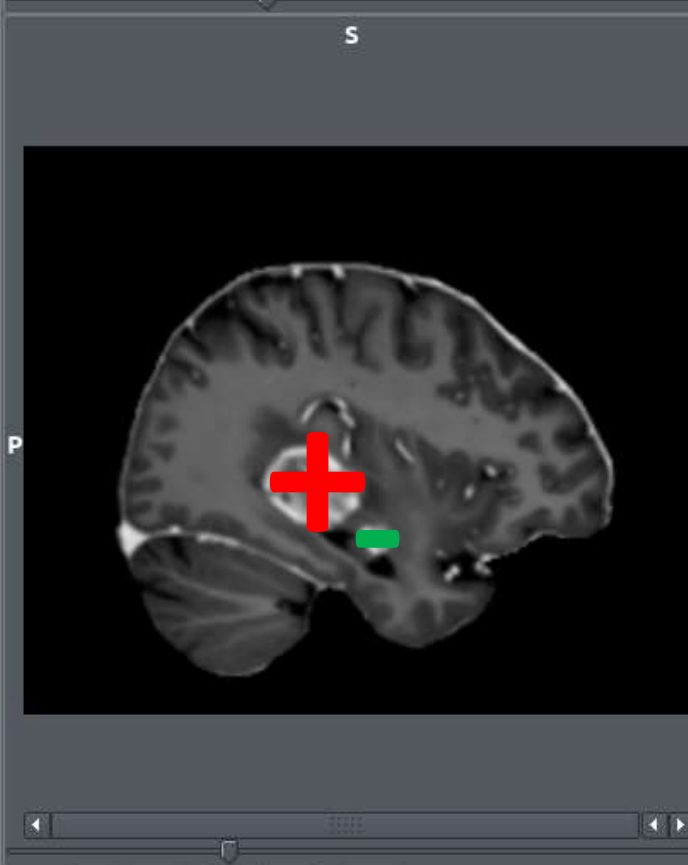
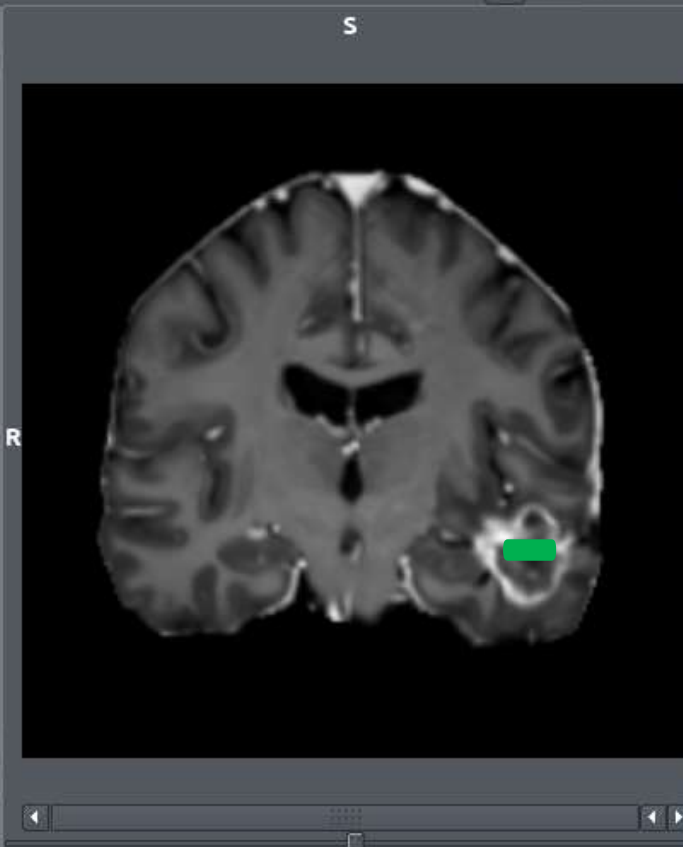
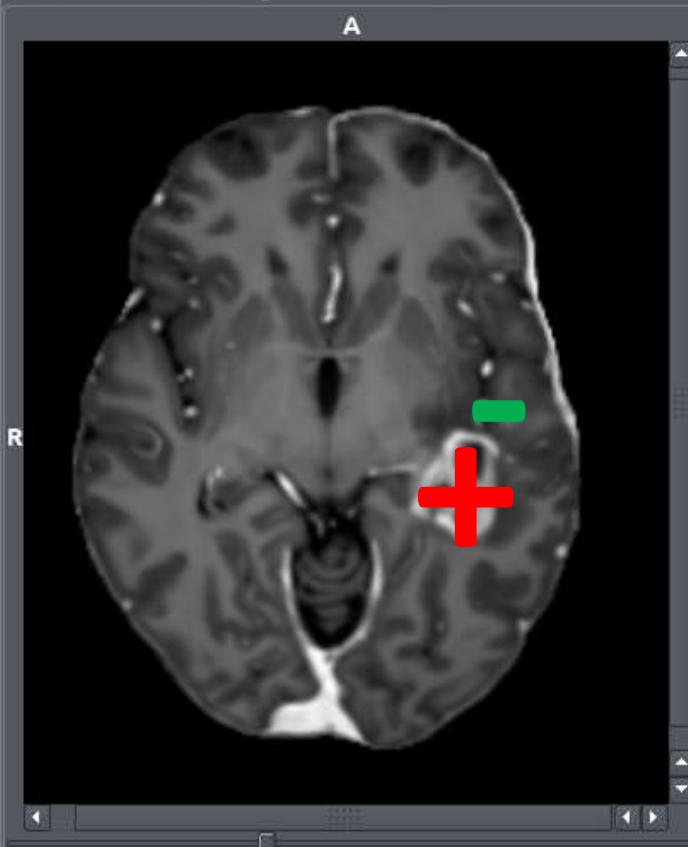
Level 128,000000

Window 255,000000

Linear

Z, MPR Y, MPR X, Histogram

Maximum intensity projection, CPU



T1c.nii.gz

193 x 229 x 193
double

[0, 255]

LPI

X left to right

Y posterior to anterior

Z inferior to superior

3D OpenGL views:

GL_R16F 193x229x193 (no filtering)

3D+t

120 ms Acq.

2Dt 3Dt

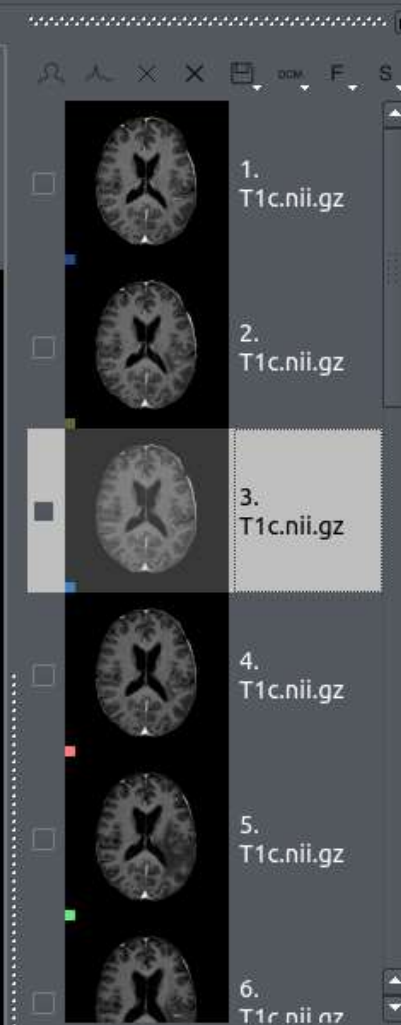
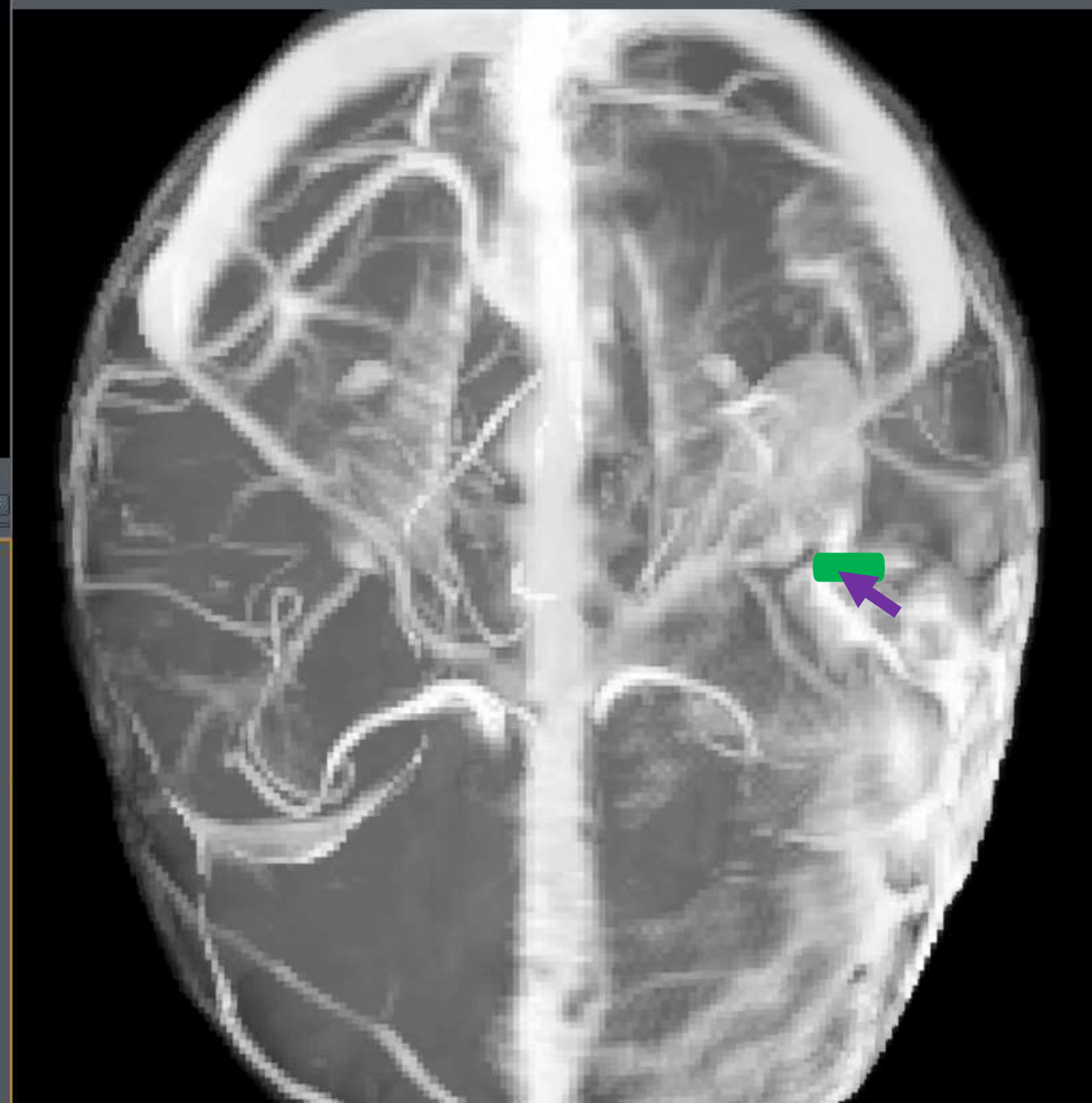
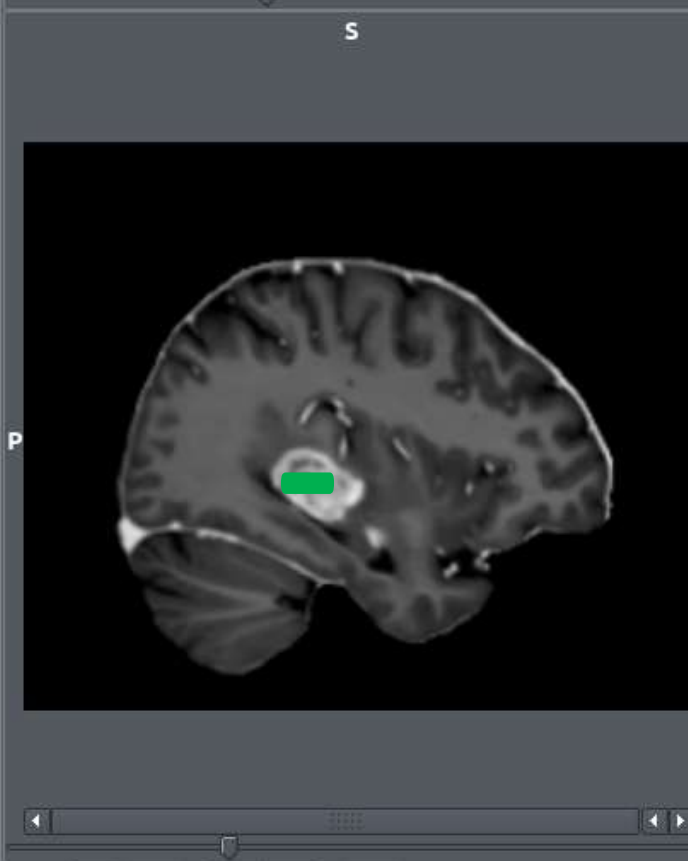
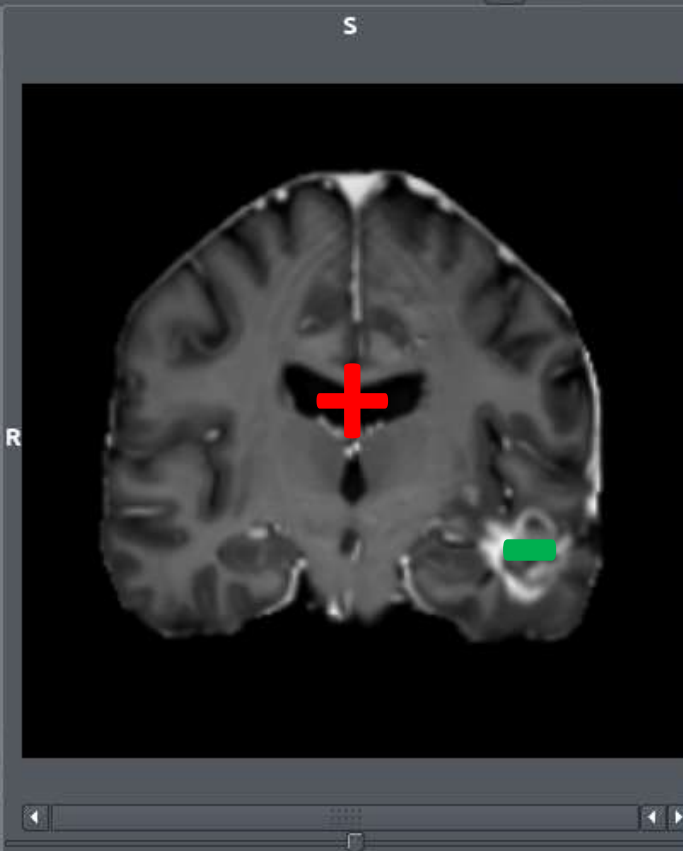
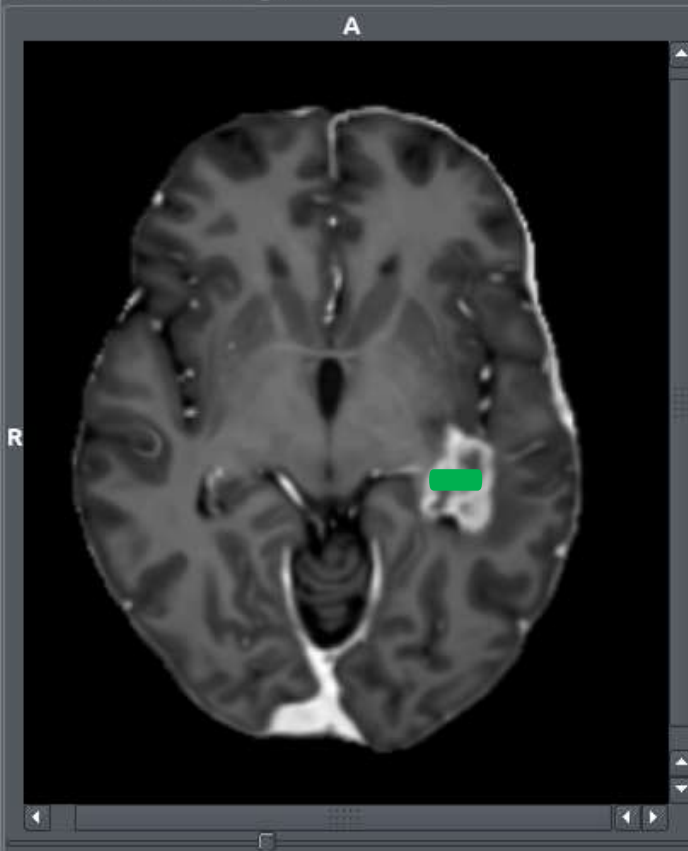
Level 127,000000

Window 255,000000

Linear

Z, MPR Y, MPR X, Histogram

Maximum intensity projection, CPU



T1c.nii.gz
193 x 229 x 193
double
[0, 255]
LPI
X left to right
Y posterior to anterior
Z inferior to superior
3D OpenGL views:
GL_R16F 193x229x193 (no filtering)

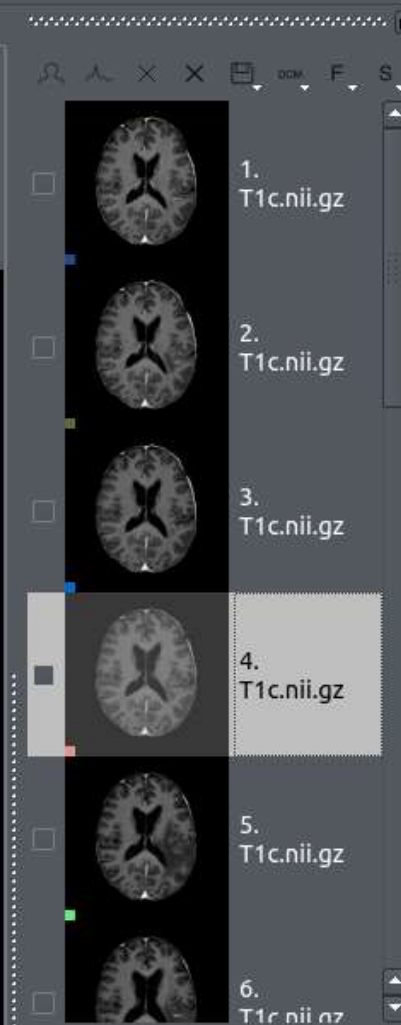
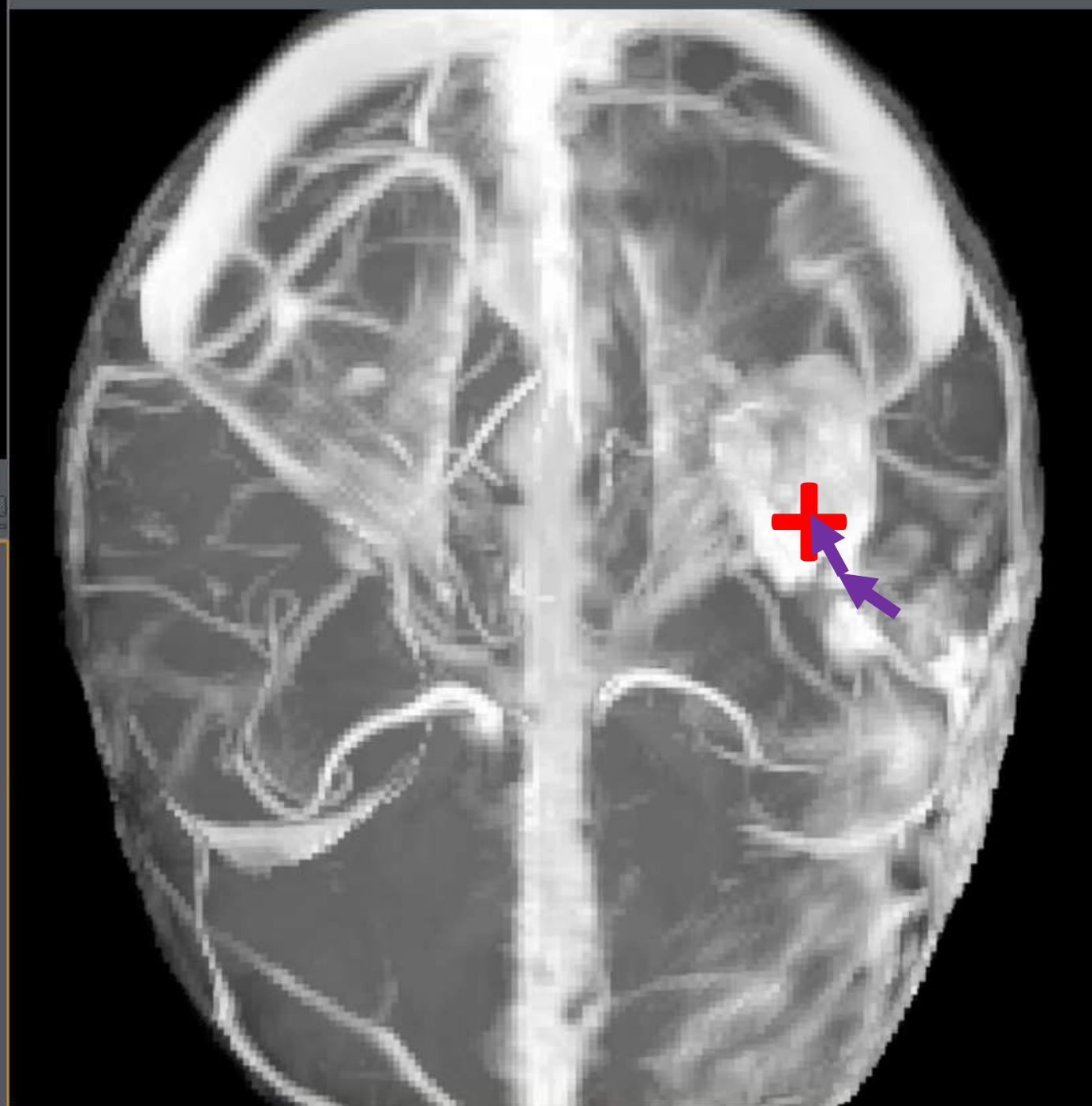
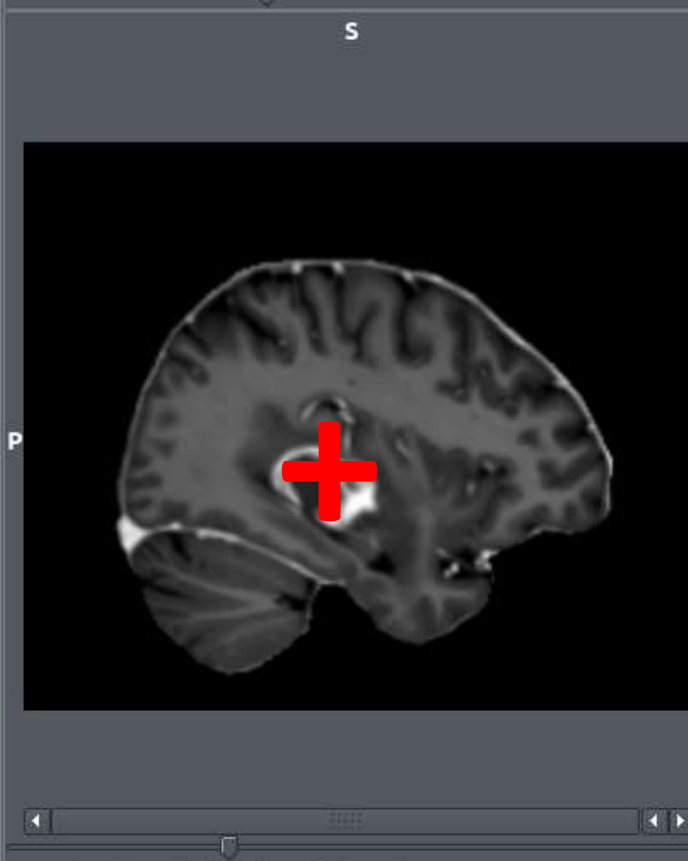
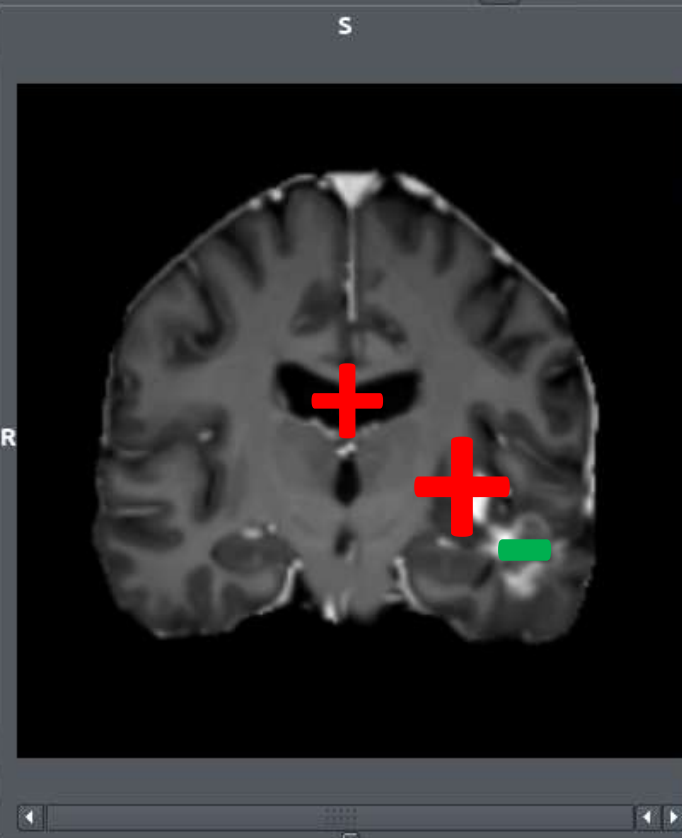
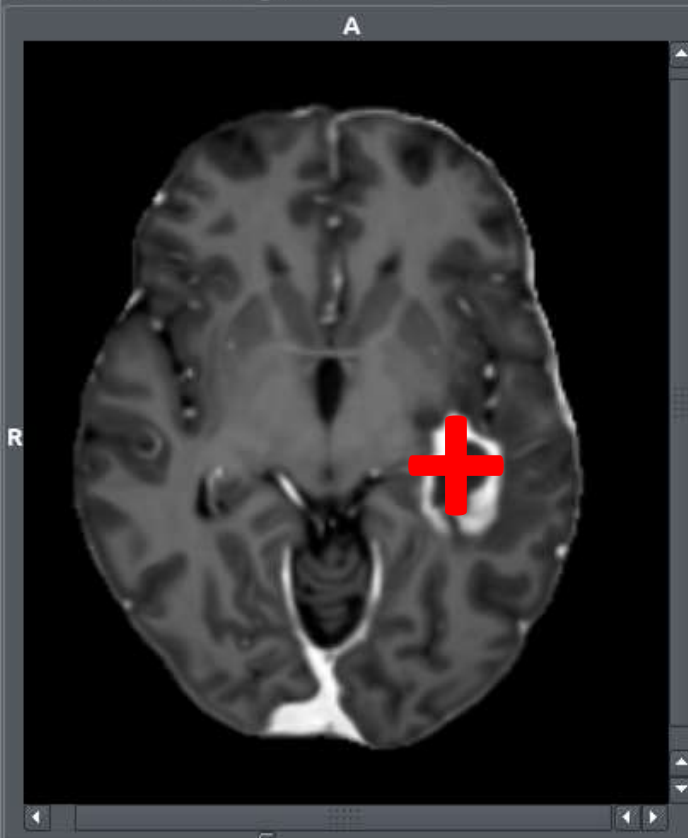
Level 127,000000

Window 255,000000

Linear

Z, MPR Y, MPR X, Histogram

Maximum intensity projection, CPU



T1c.nii.gz
193 x 229 x 193
double
[0, 255]
LPI
X left to right
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3D OpenGL views:
GL_R16F 193x229x193 (no filtering)

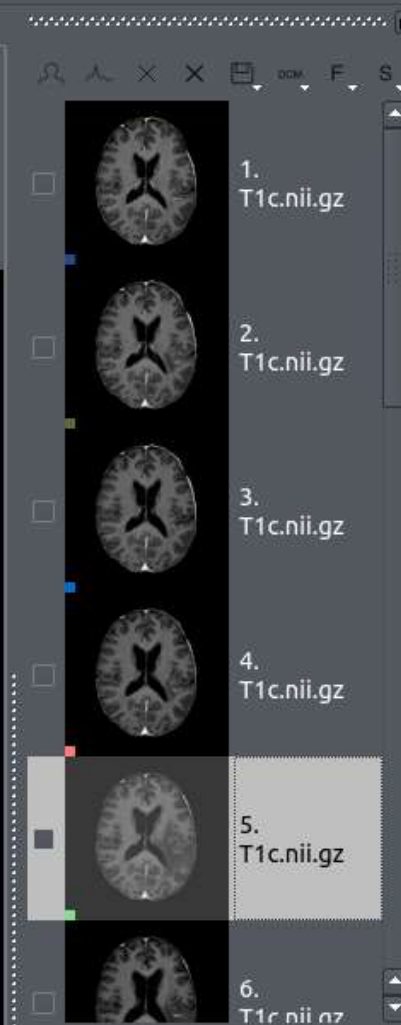
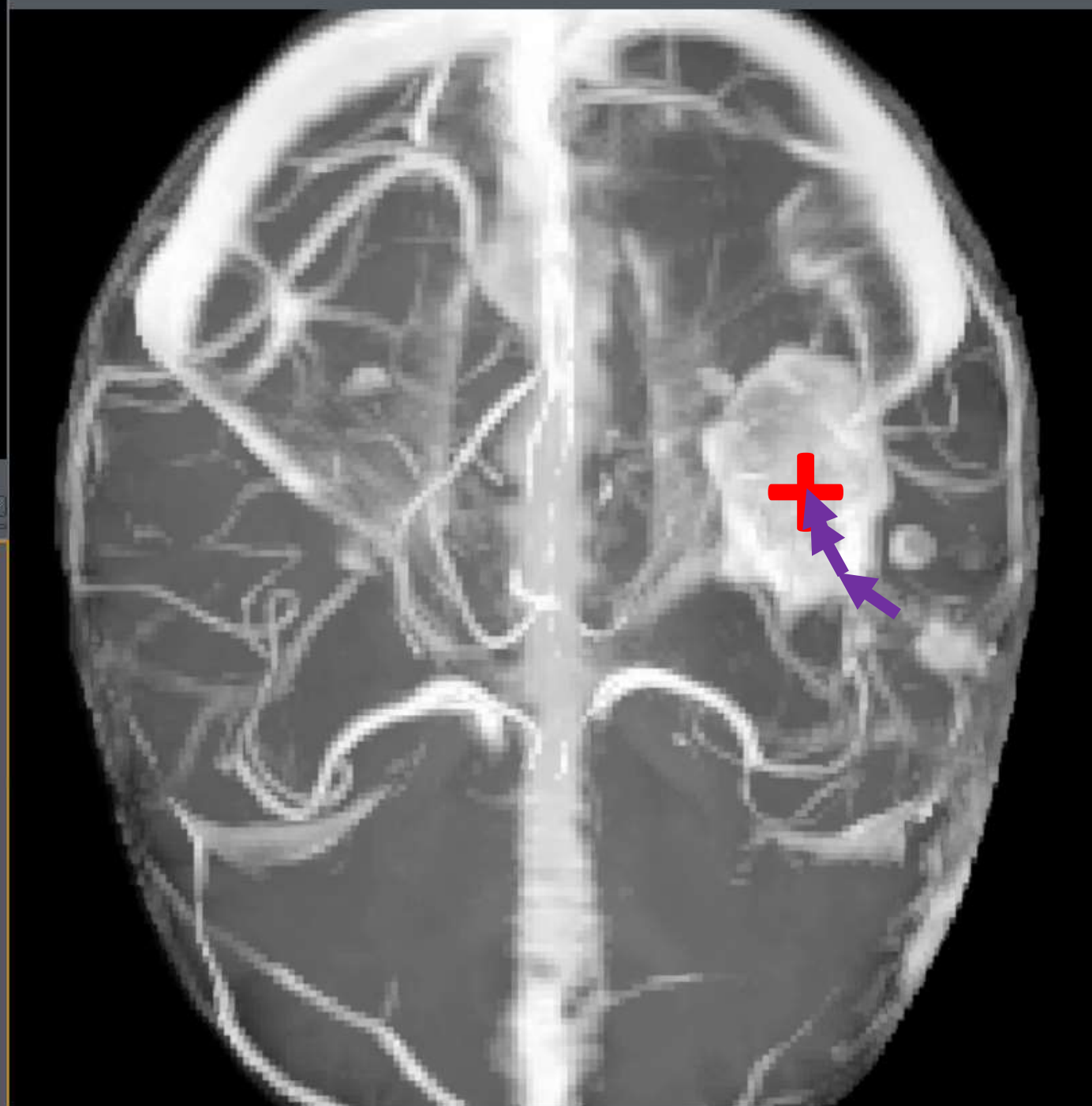
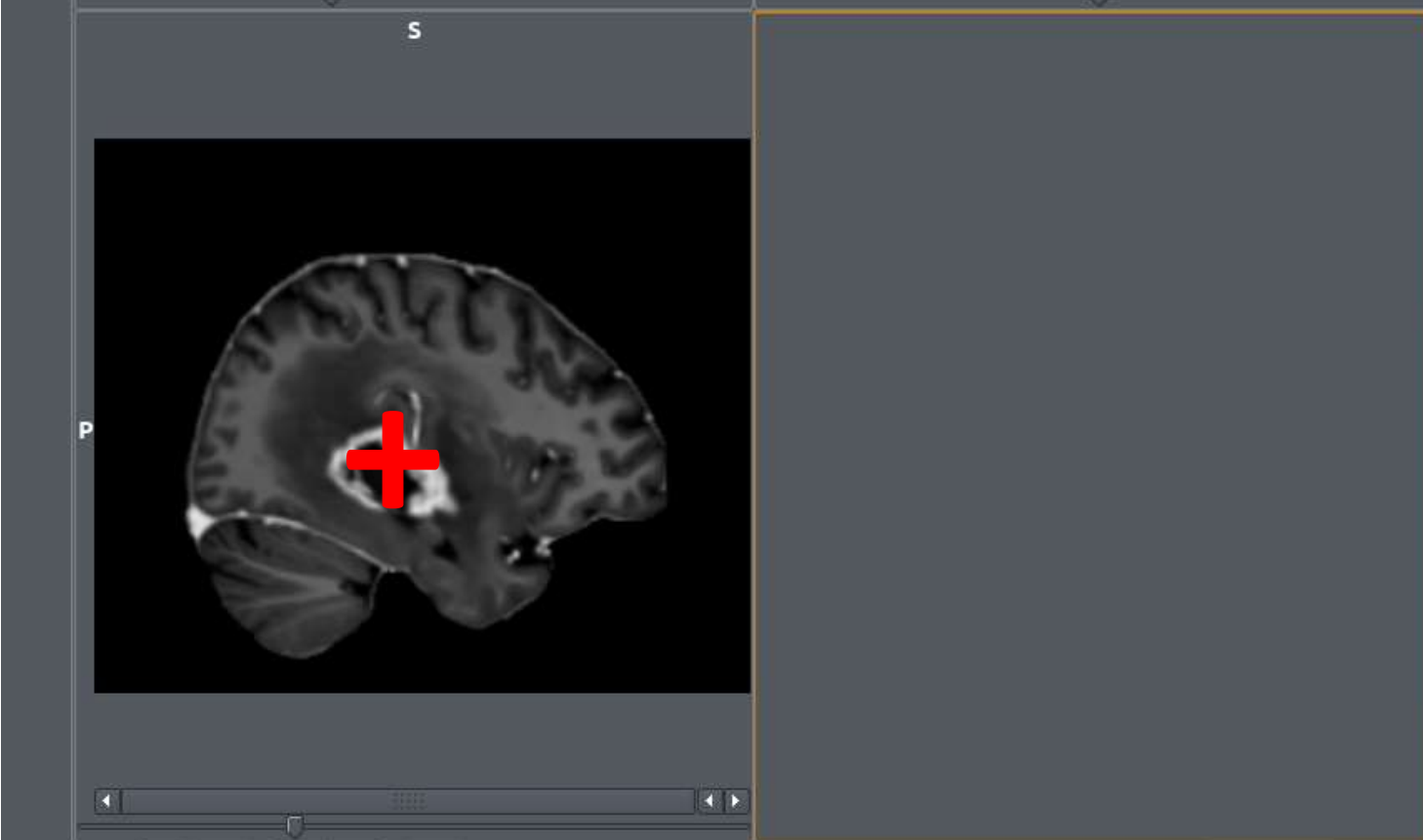
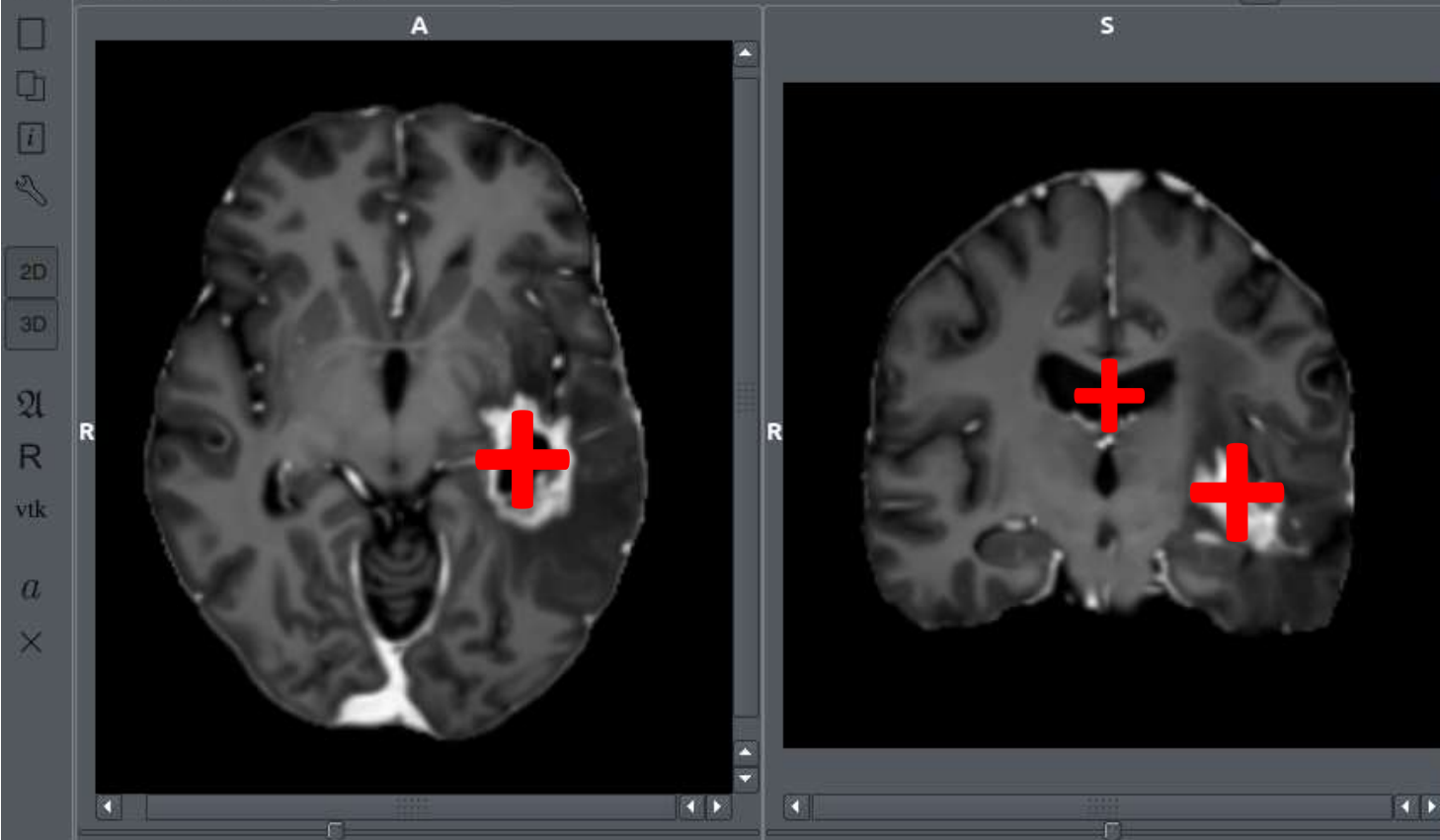
Level 127,000000

Window 255,000000

Linear

Z, MPR Y, MPR X, Histogram

Maximum intensity projection, CPU



T1c.nii.gz
193 x 229 x 193
double
[0, 255]
LPI
X left to right
Y posterior to anterior
Z inferior to superior
3D OpenGL views:
GL_R16F 193x229x193 (no filtering)

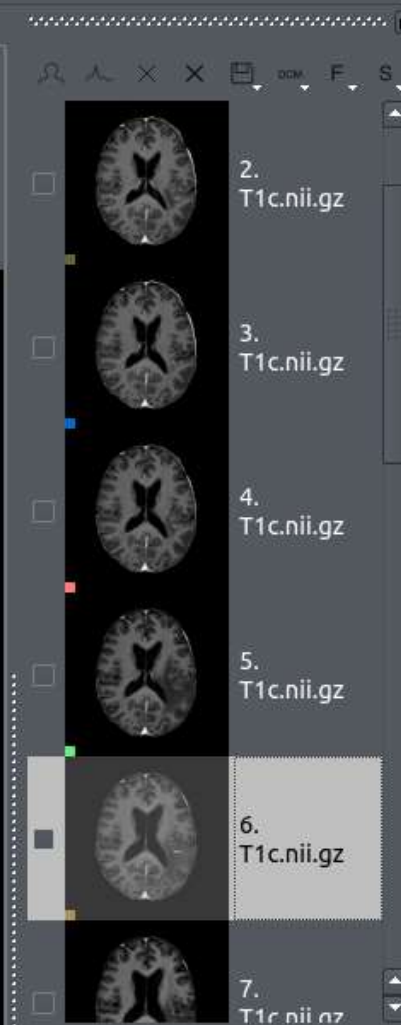
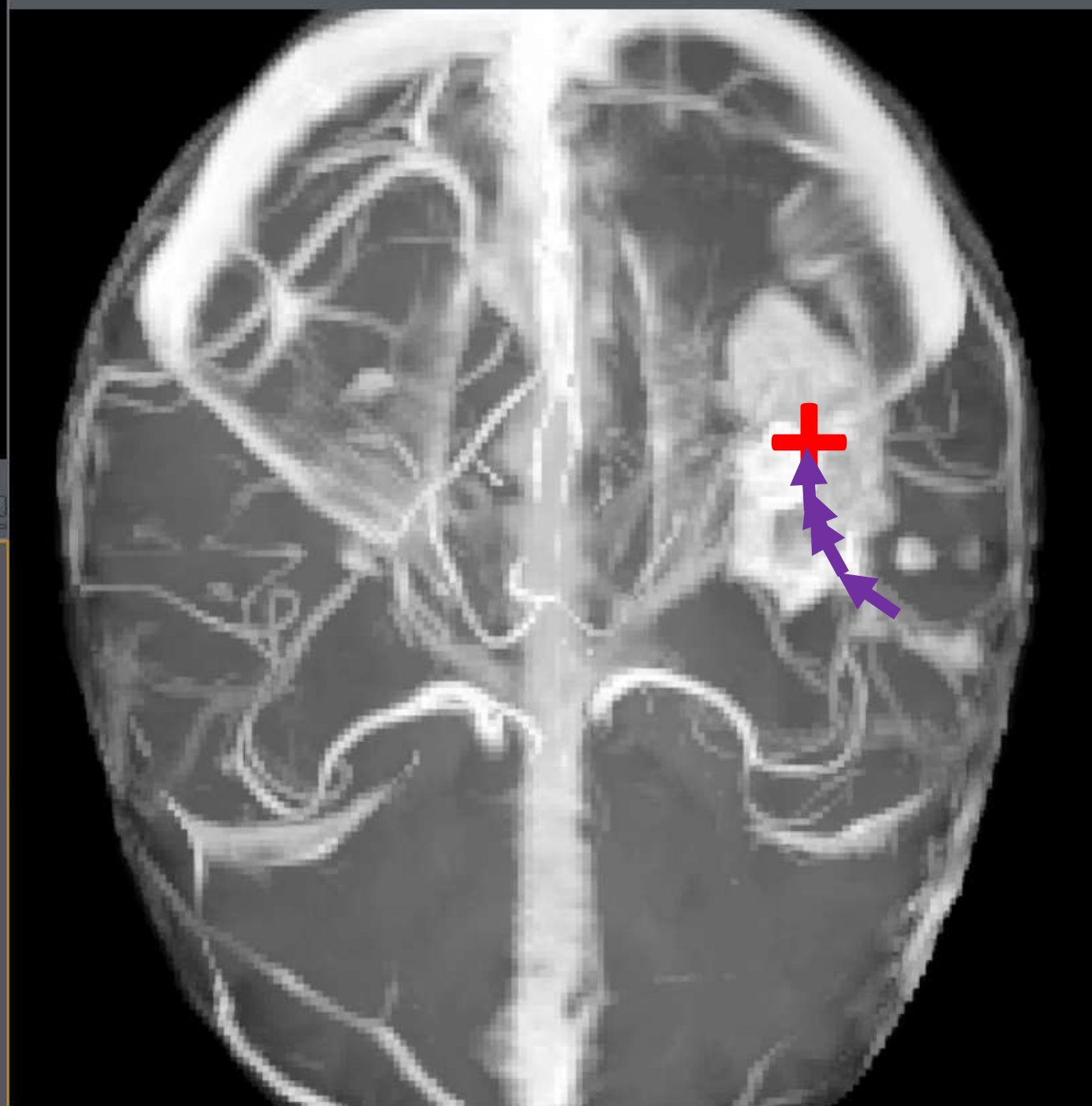
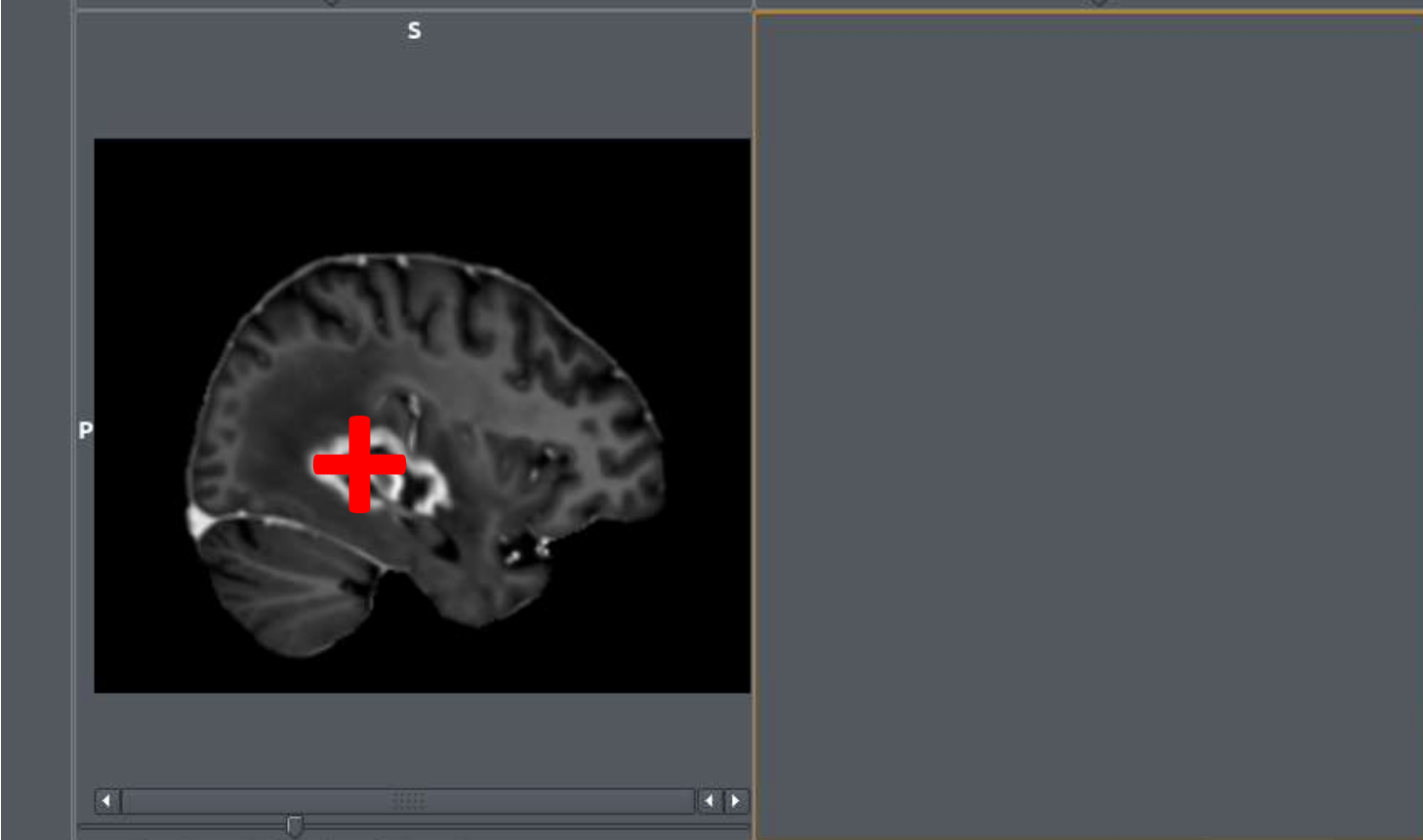
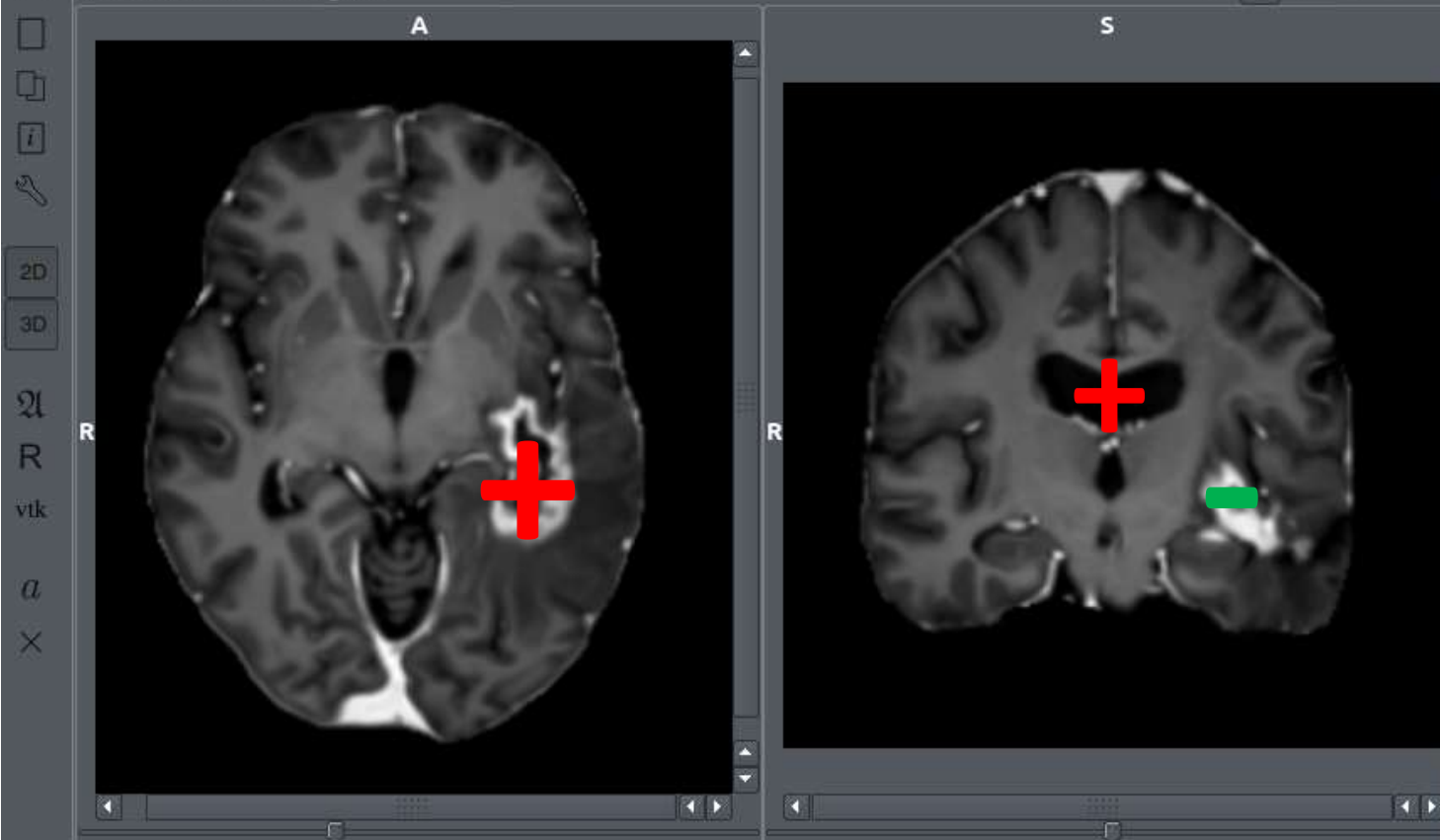
Level 127,000000

Window 255,000000

Linear

Z, MPR Y, MPR X, Histogram

Maximum intensity projection, CPU



T1c.nii.gz

193 x 229 x 193
double

[0, 255]

LPI

X left to right

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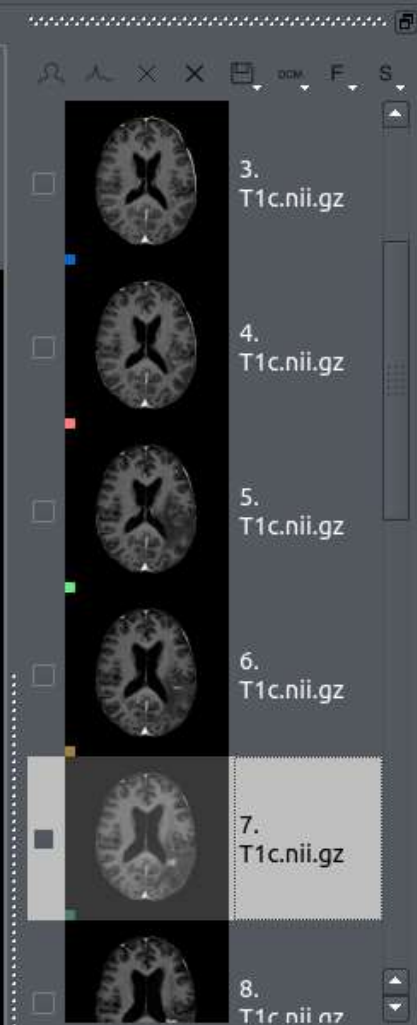
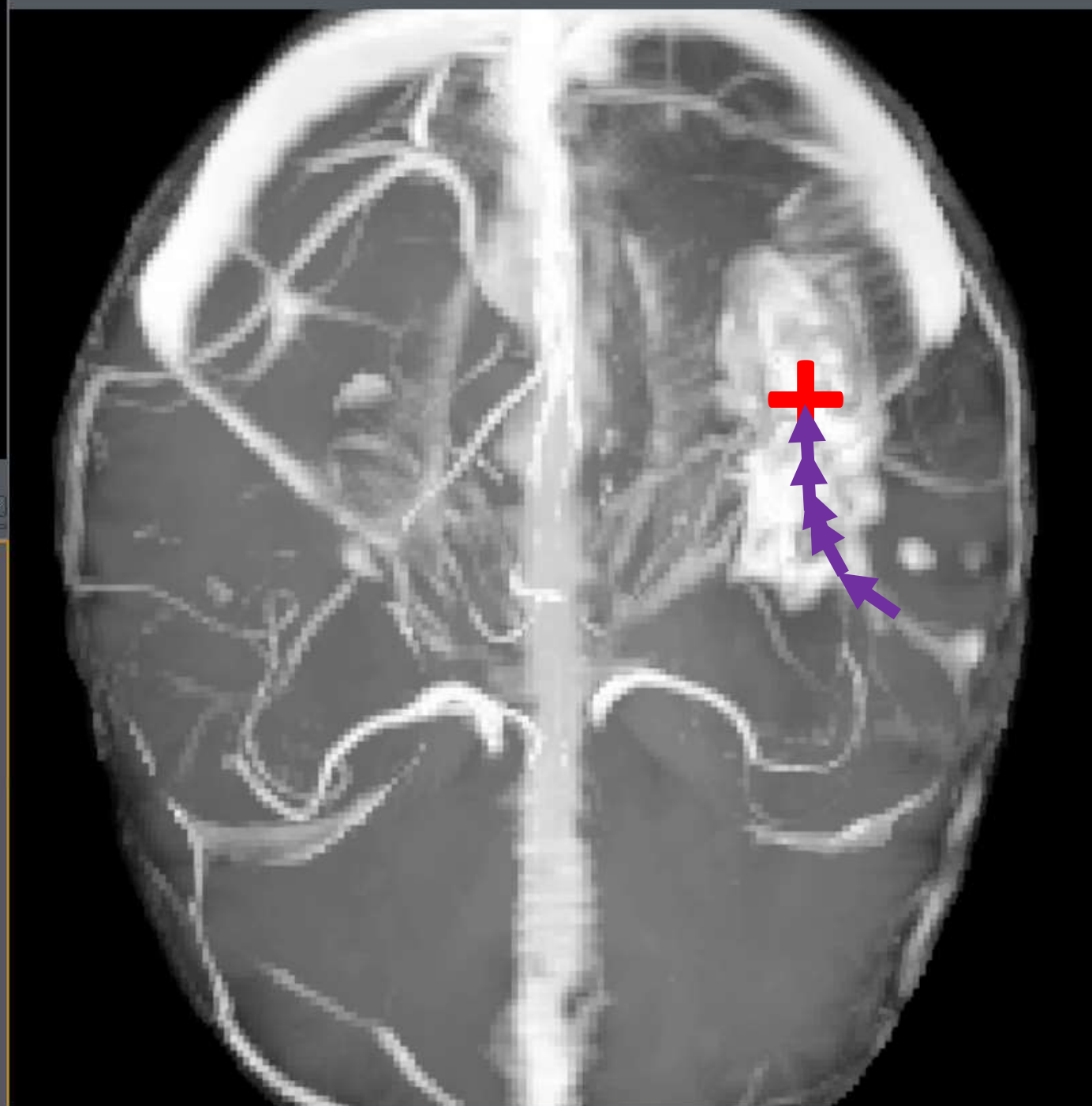
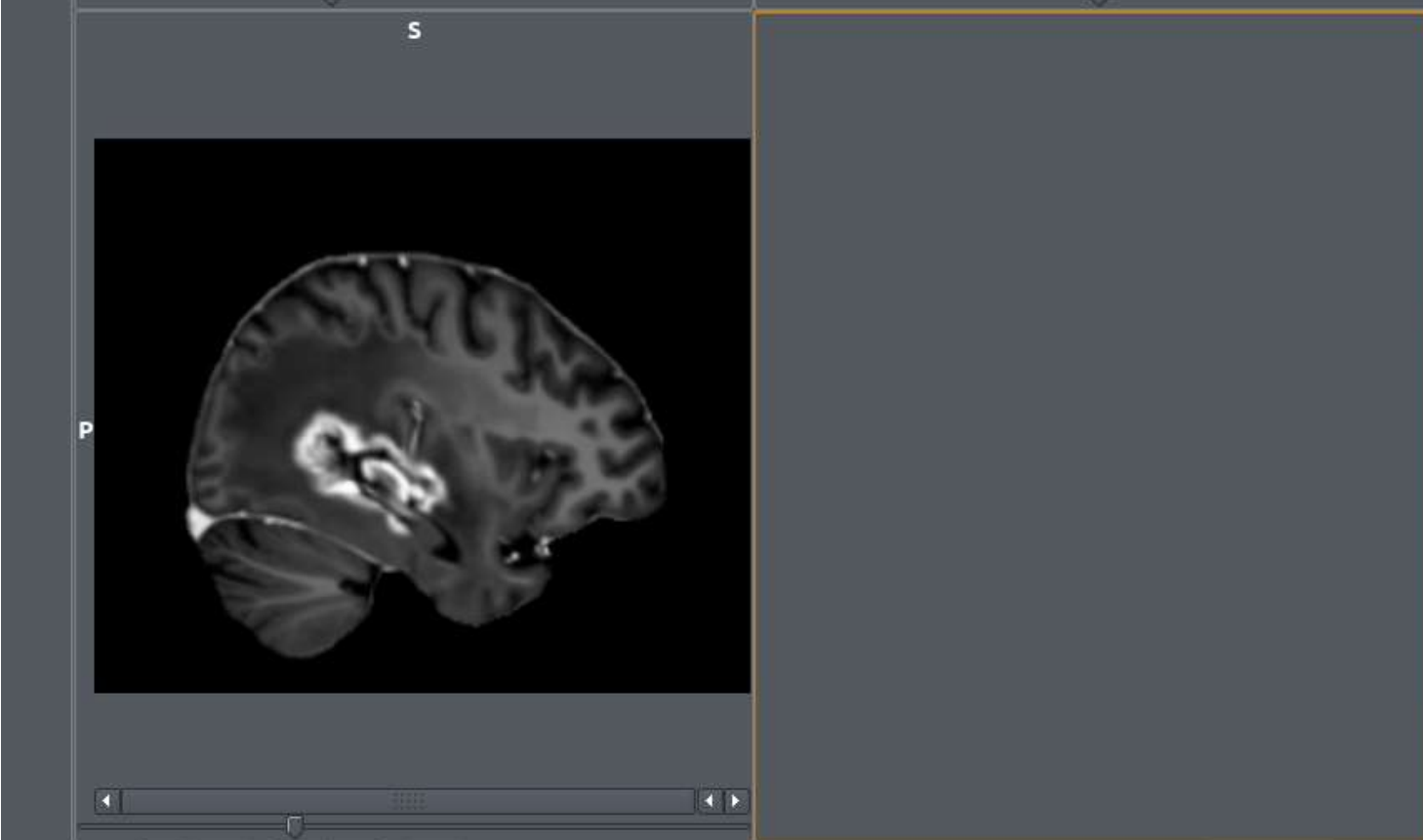
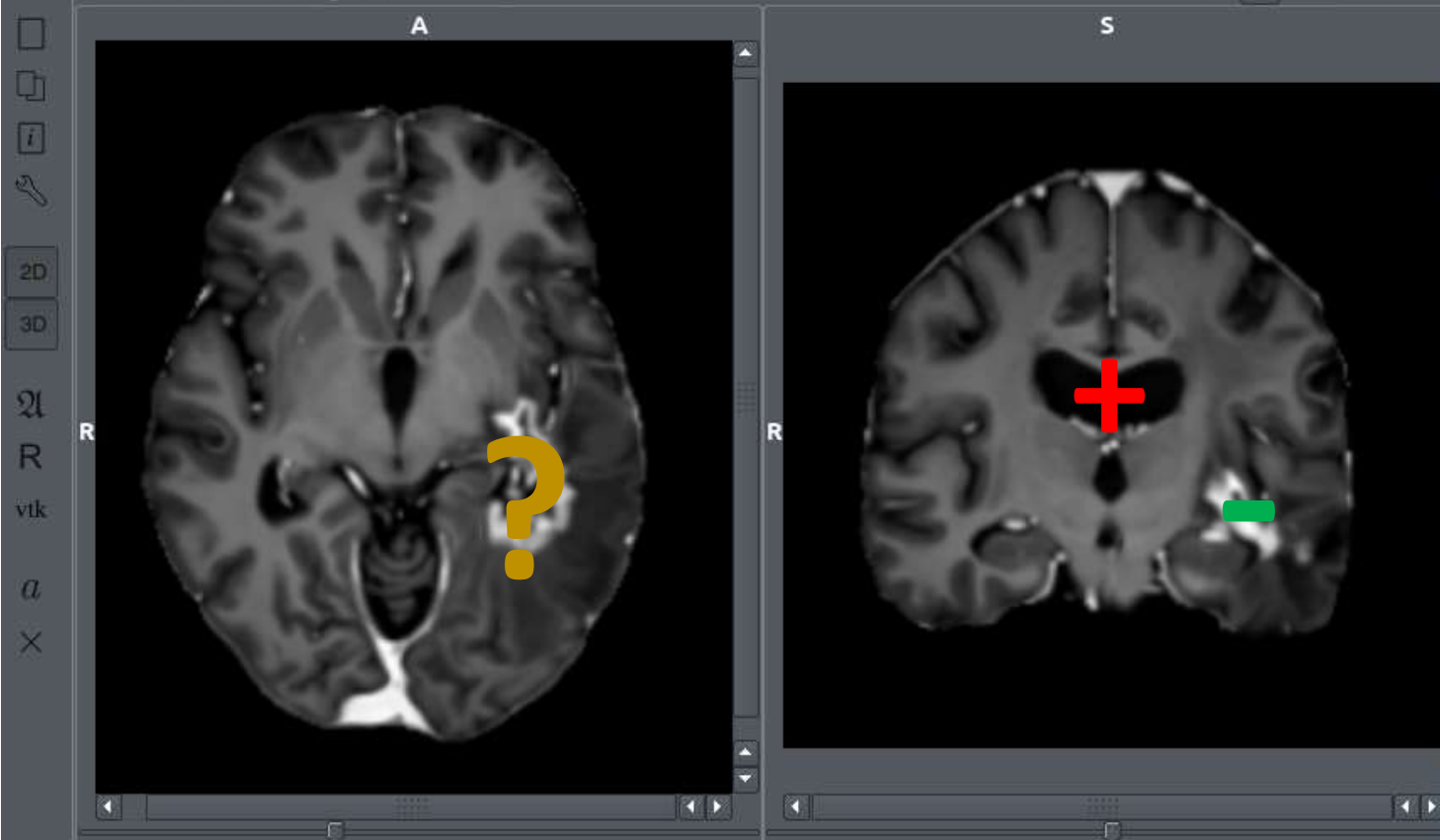
3D OpenGL views:

GL_R16F 193x229x193 (no filtering)

Level 127,000000

Window 255,000000

Linear



T1c.nii.gz

193 x 229 x 193
double

[0, 255]

LPI

X left to right

Y posterior to anterior

Z inferior to superior

3D OpenGL views:

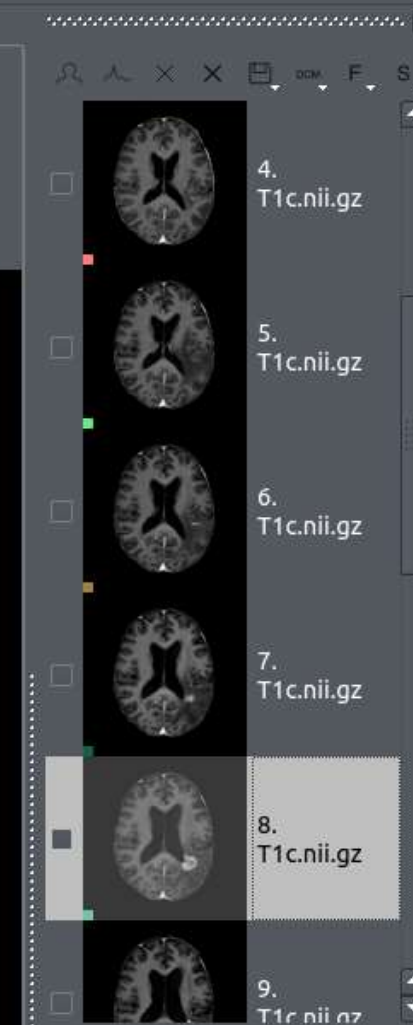
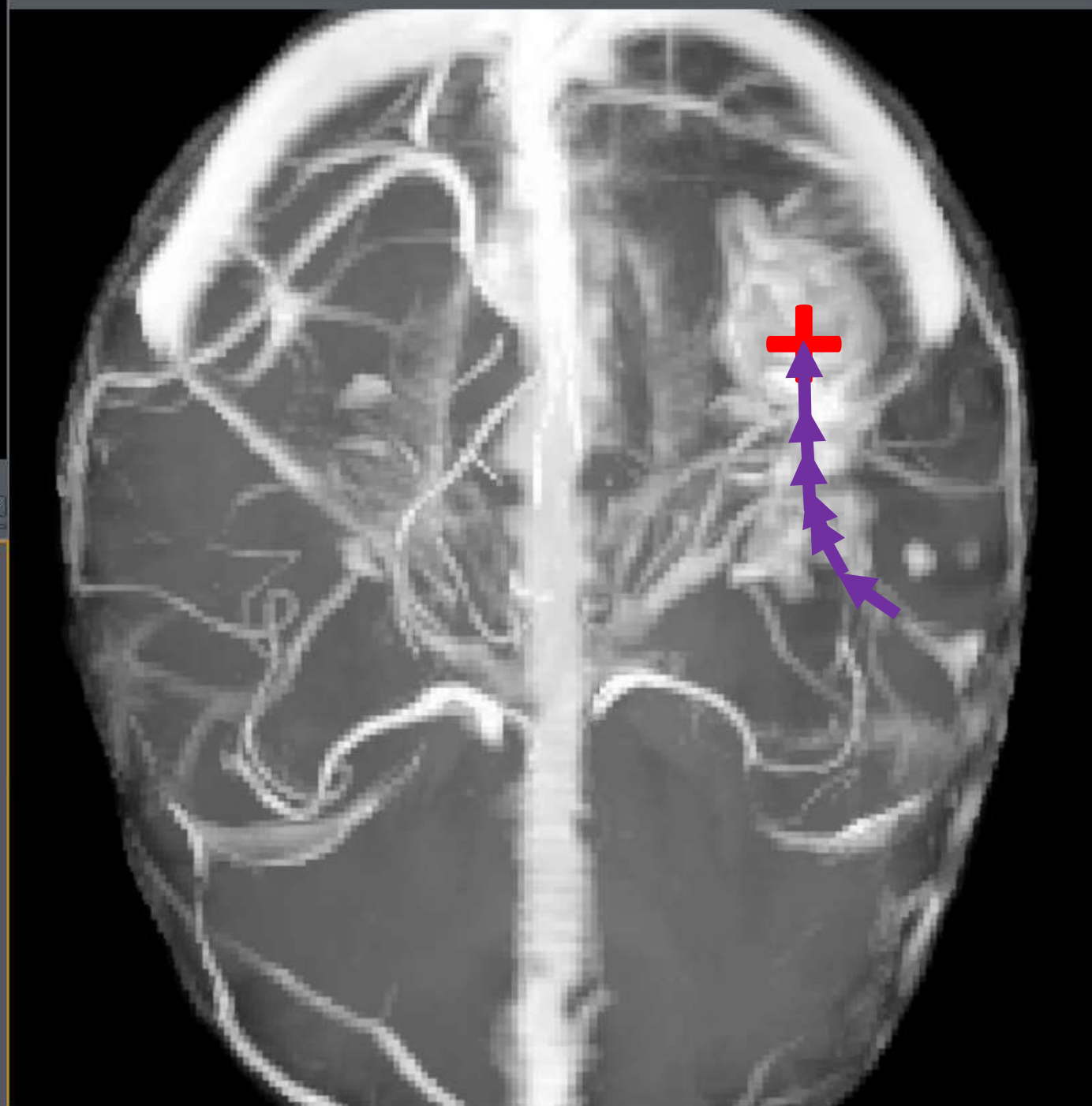
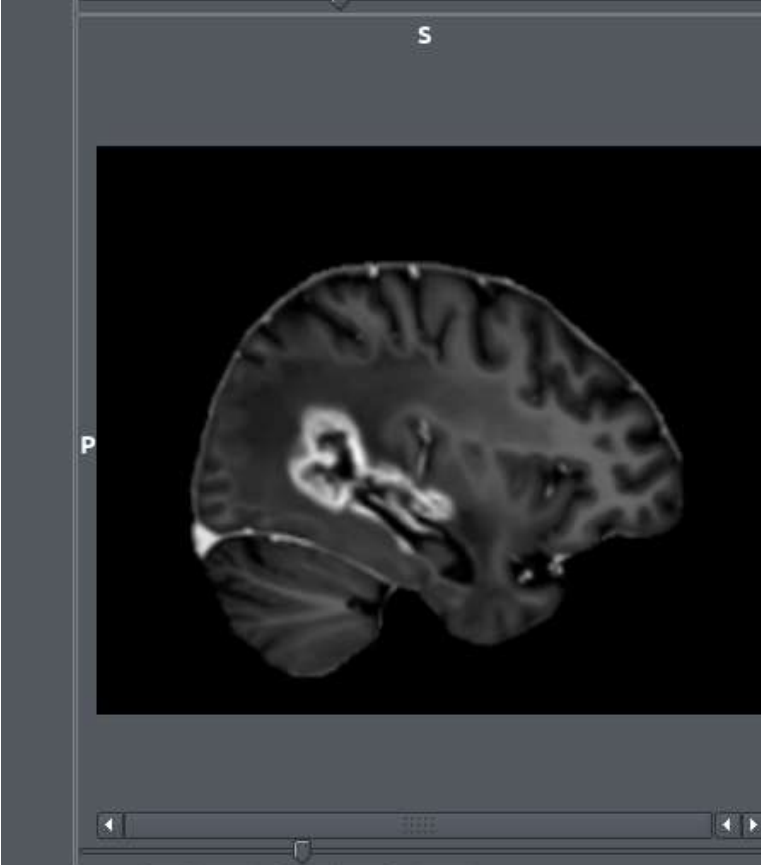
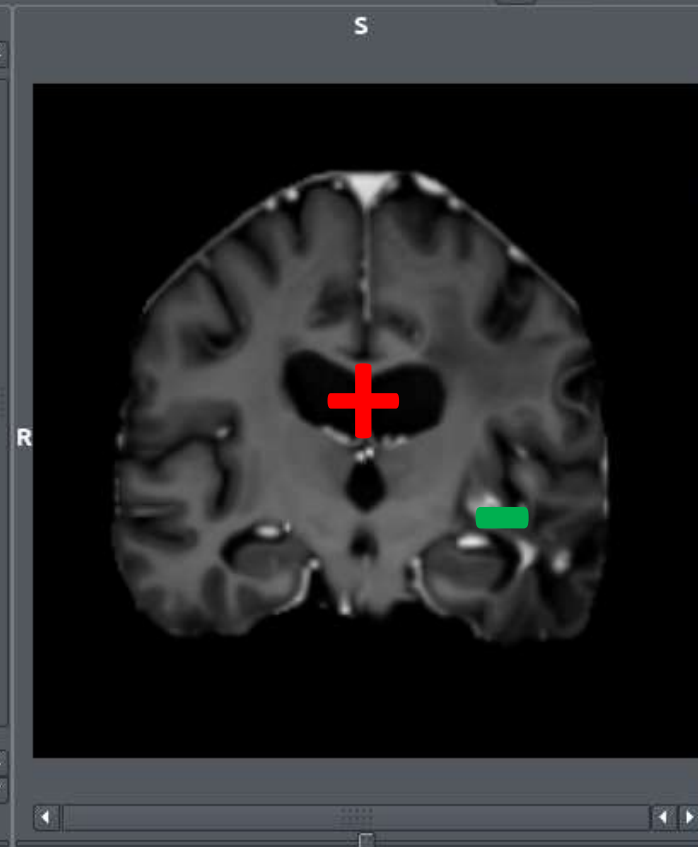
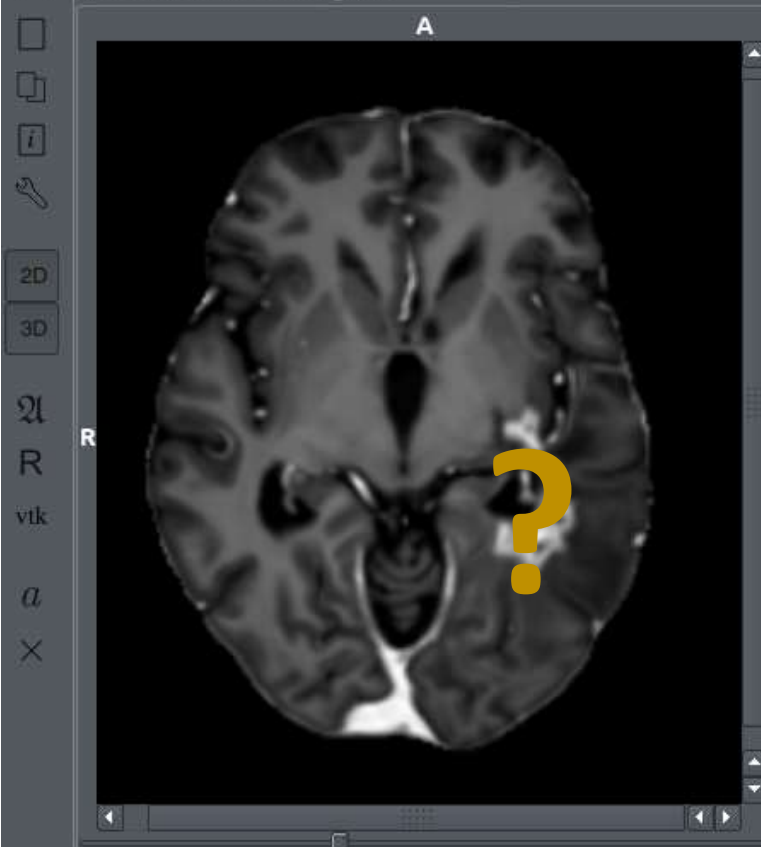
GL_R16F 193x229x193 (no filtering)

Level 127,000000

Window 255,000000

Linear

Z, MPR Y, MPR X, Histogram



T1c.nii.gz

193 x 229 x 193

double

[0, 255]

LPI

X left to right

Y posterior to anterior

Z inferior to superior

3D OpenGL views:

GL_R16F 193x229x193 (no filtering)

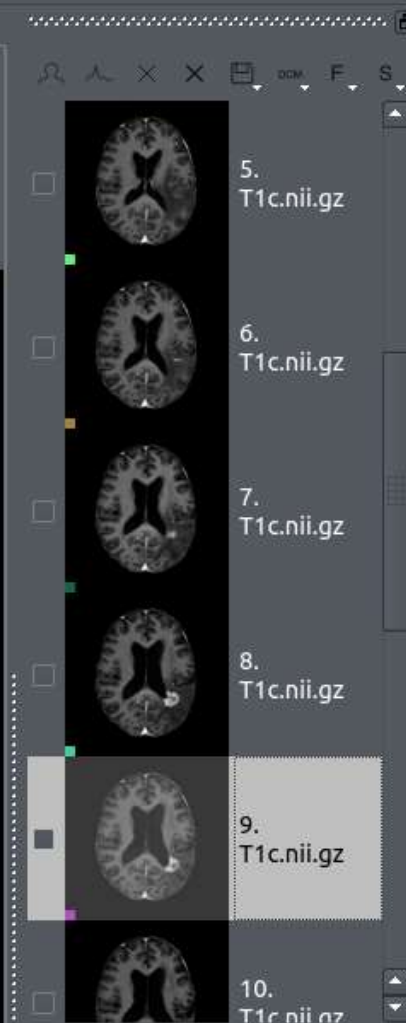
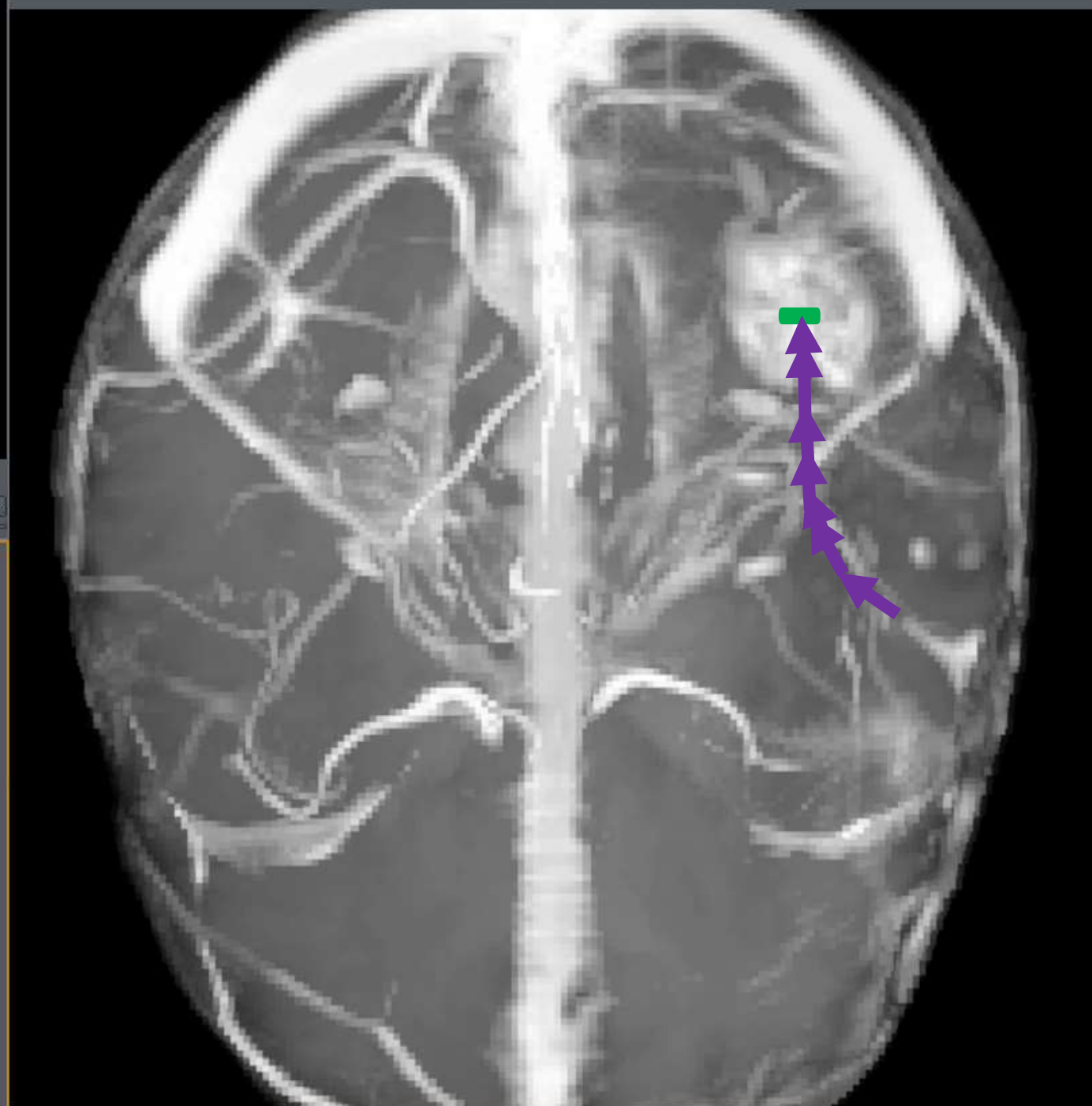
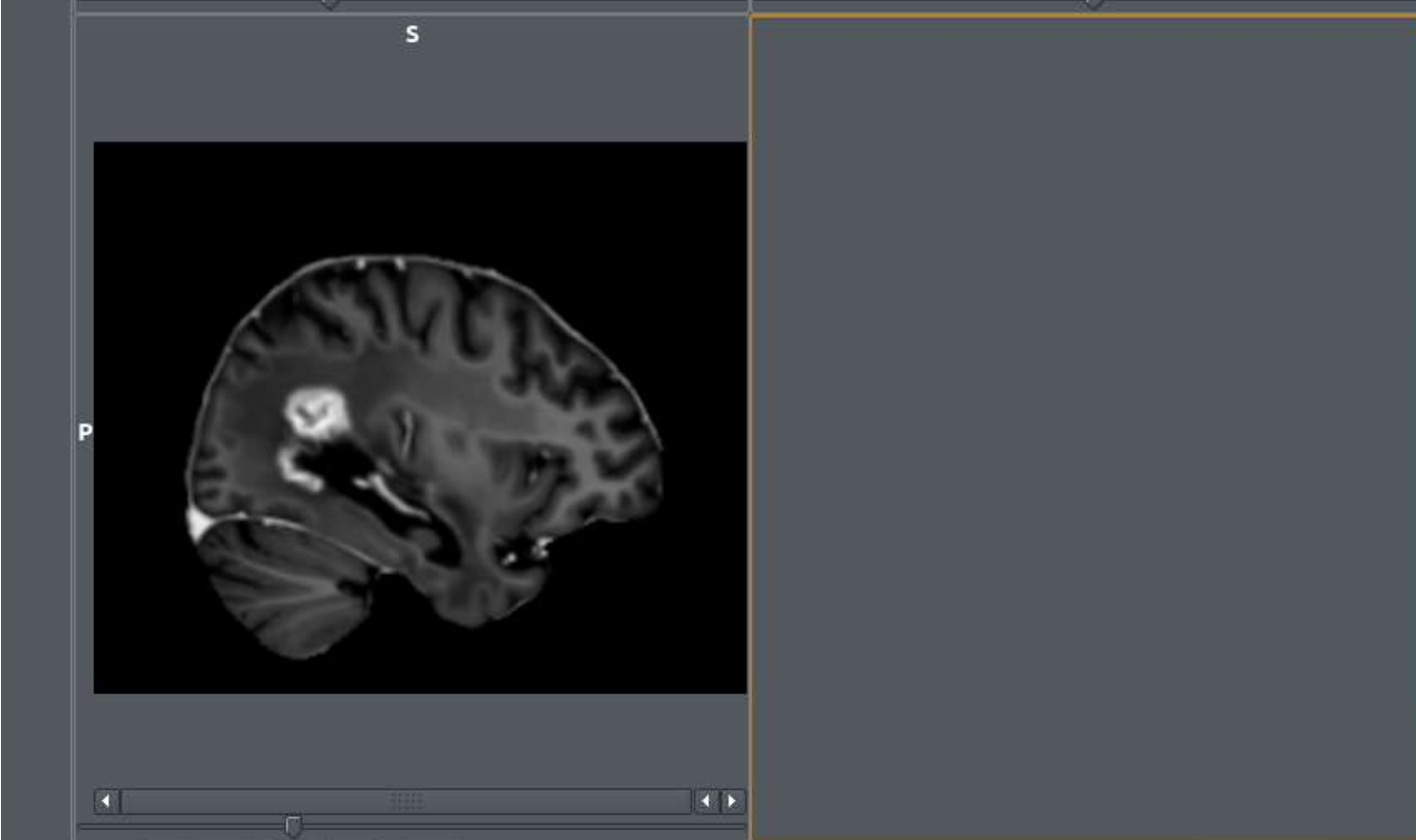
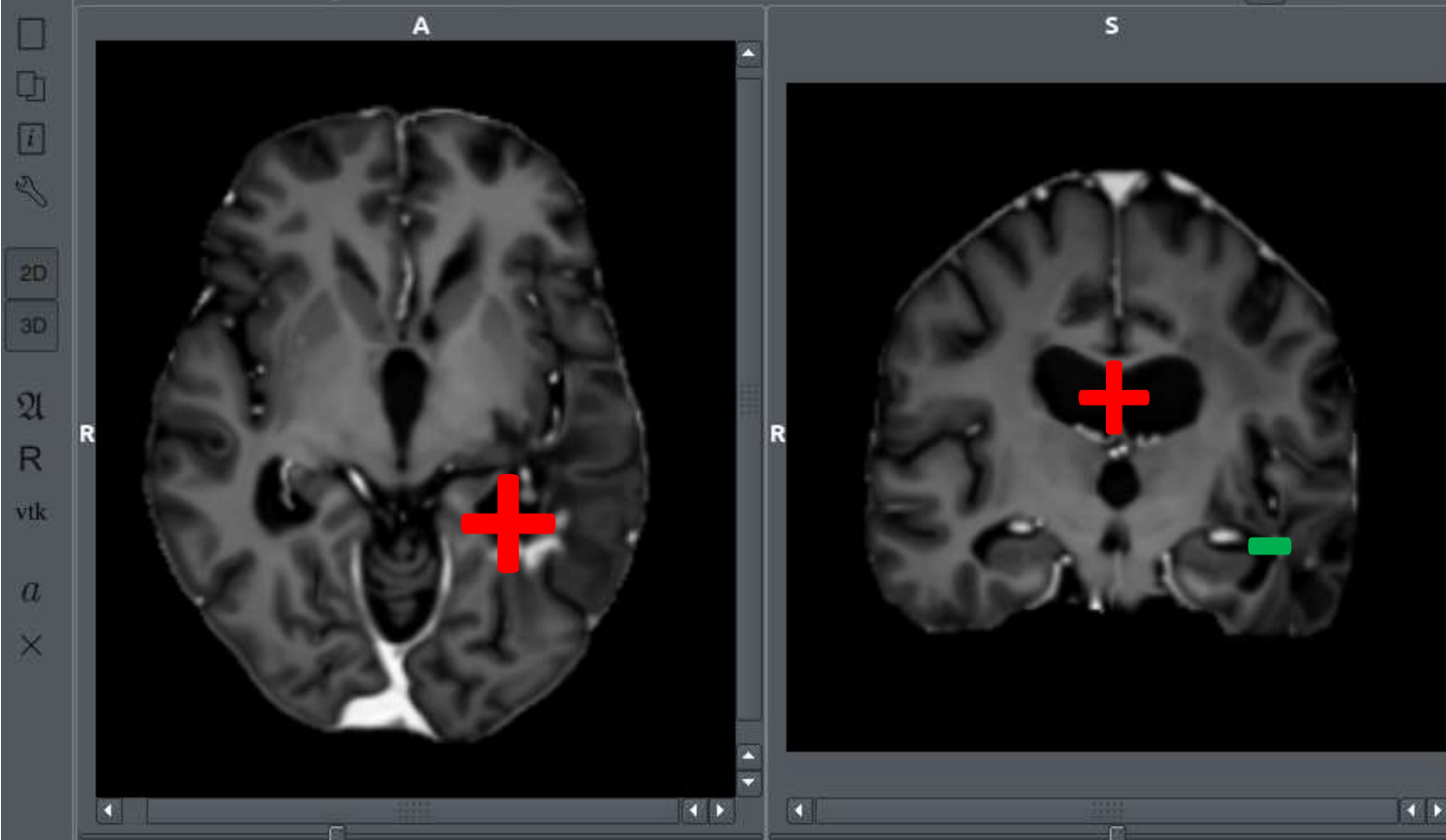
3D+t 120 ms Acq.

2Dt 3Dt

Level 127,000000 Window 255,000000 Linear

Z, MPR Y, MPR X, Histogram

Maximum intensity projection, CPU



T1c.nii.gz
193 x 229 x 193
double
[0, 255]
LPI
X left to right
Y posterior to anterior
Z inferior to superior
3D OpenGL views:
GL_R16F 193x229x193 (no filtering)

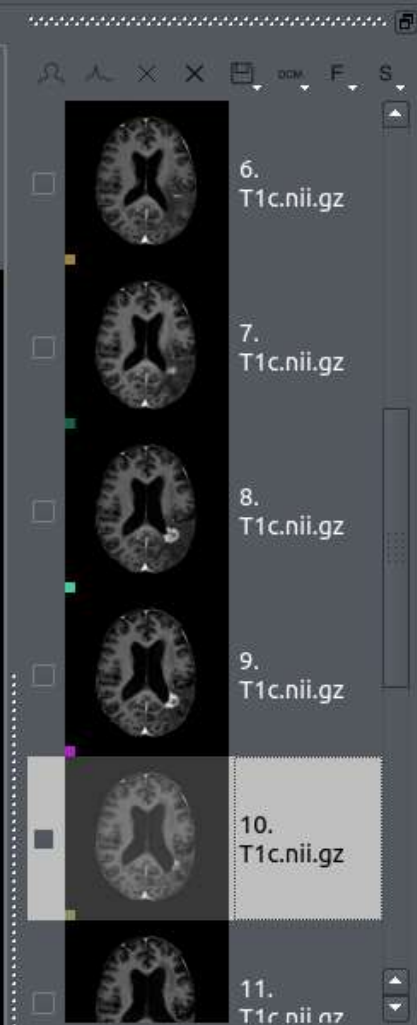
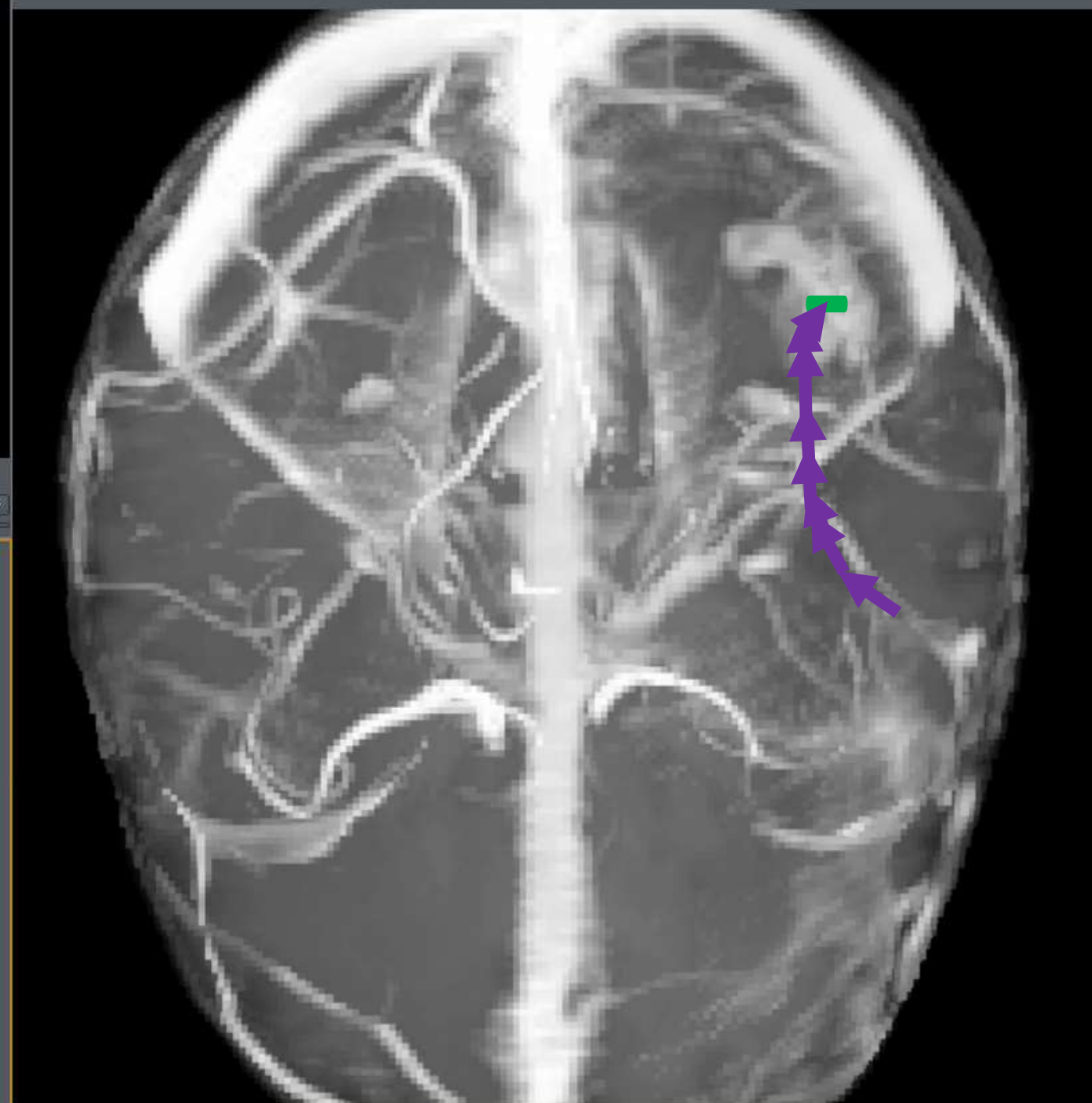
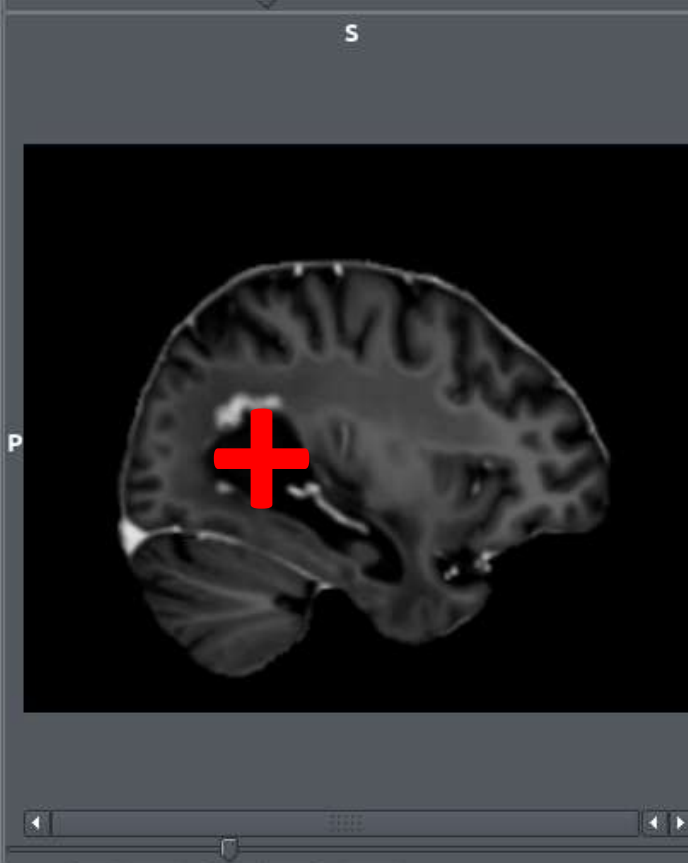
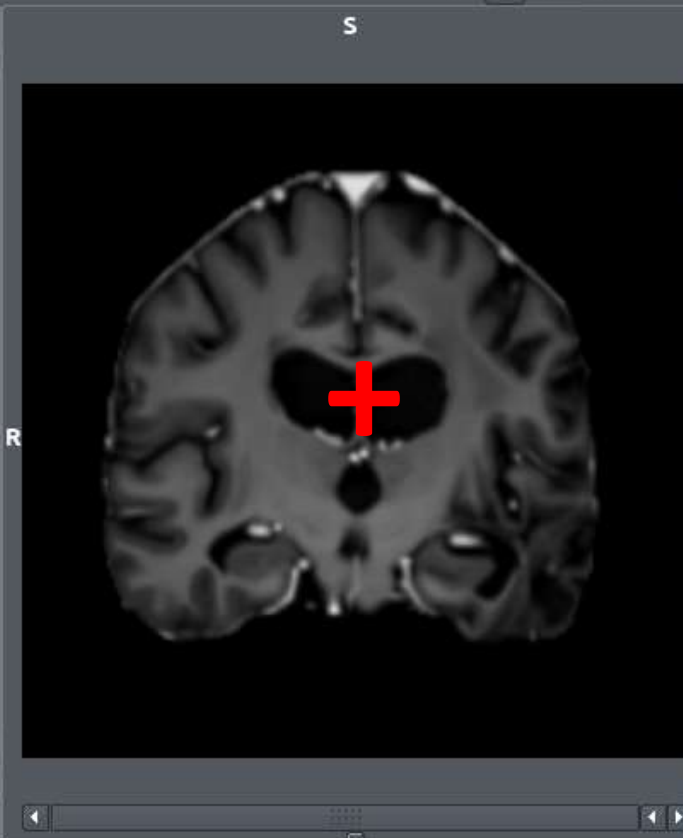
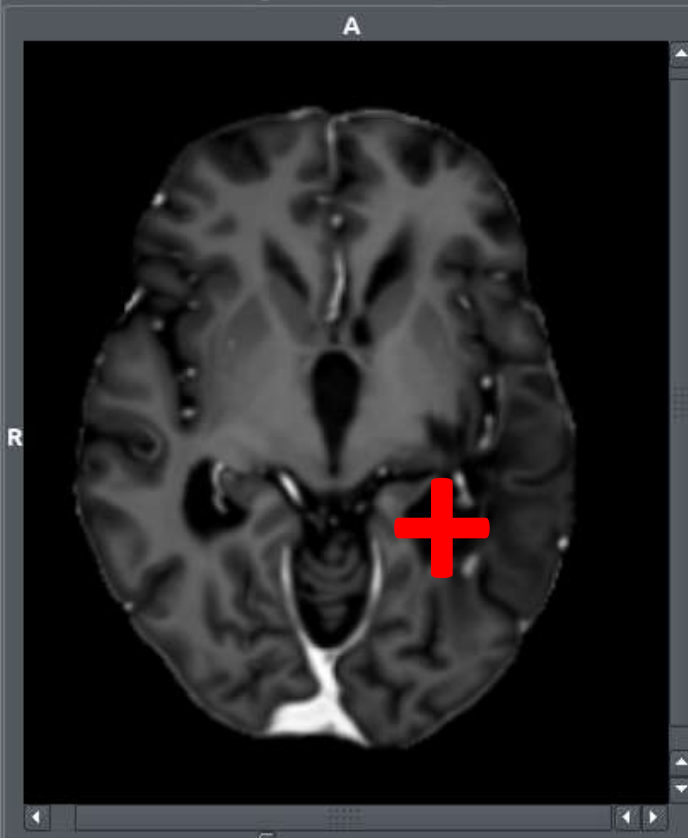
Level 127,000000

Window 255,000000

Linear

Z, MPR Y, MPR X, Histogram

Maximum intensity projection, CPU



T1c.nii.gz

193 x 229 x 193
double

[0, 255]

LPI

X left to right

Y posterior to anterior

Z inferior to superior

3D OpenGL views:

GL_R16F 193x229x193 (no filtering)

3D+t

120 ms Acq.

2Dt 3Dt

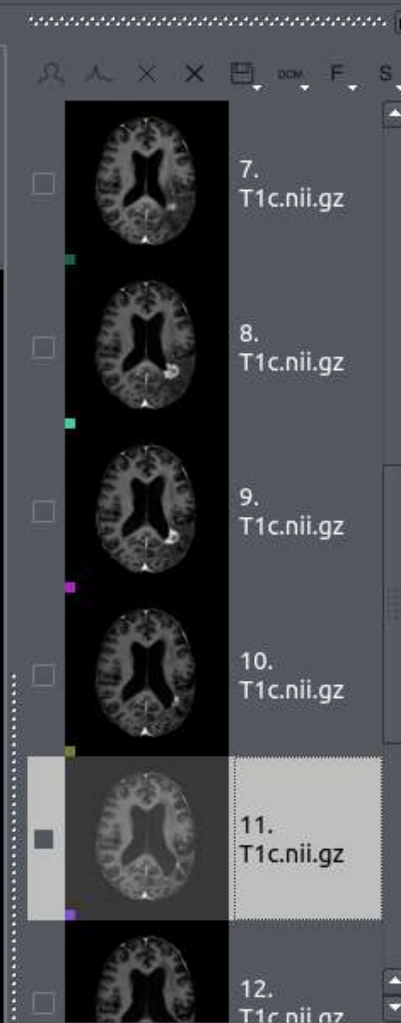
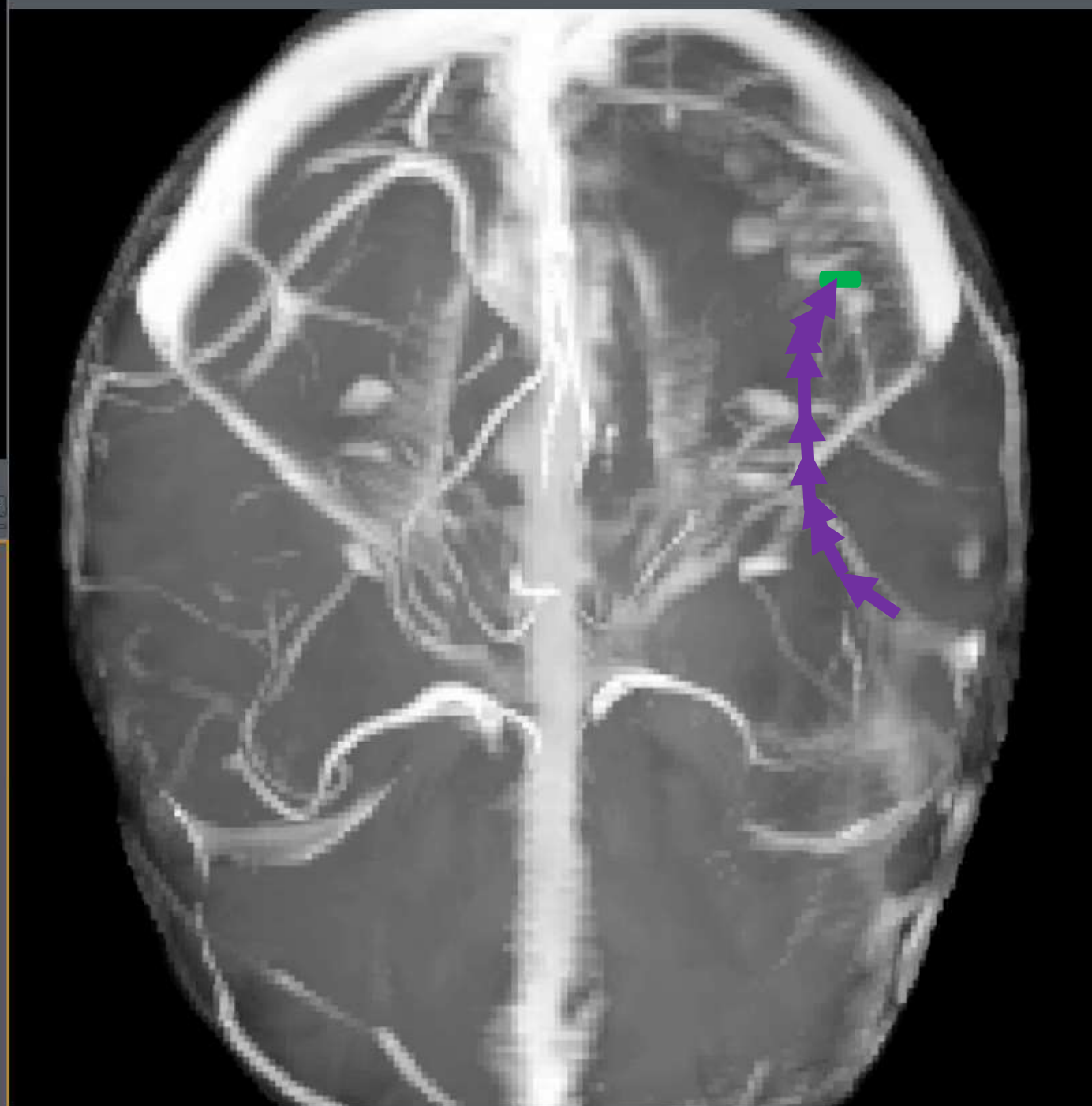
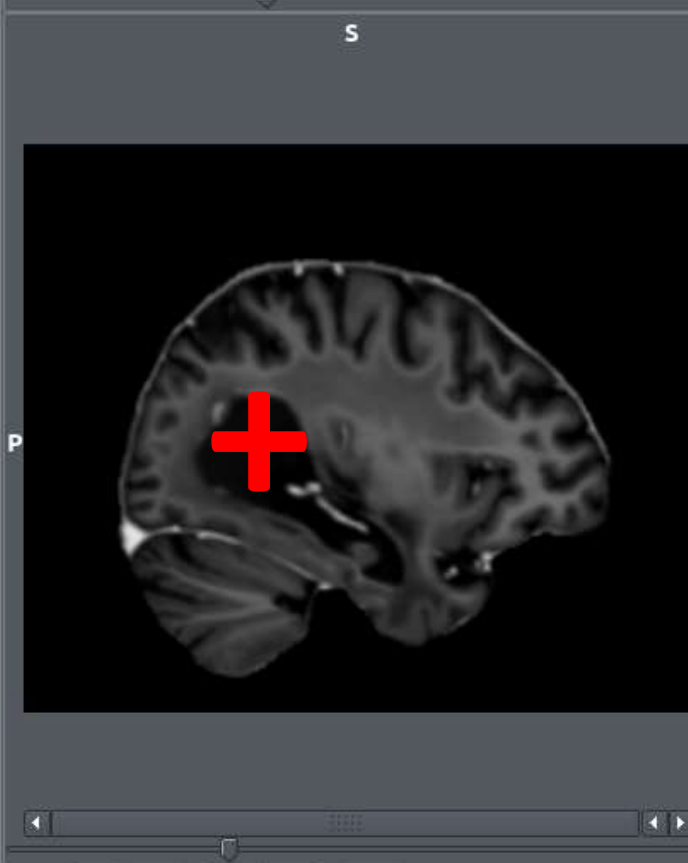
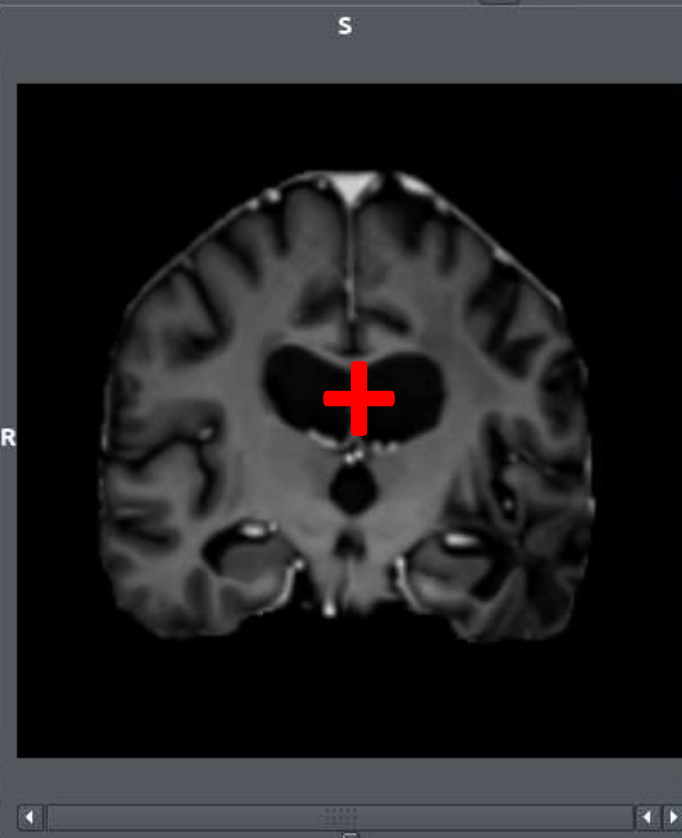
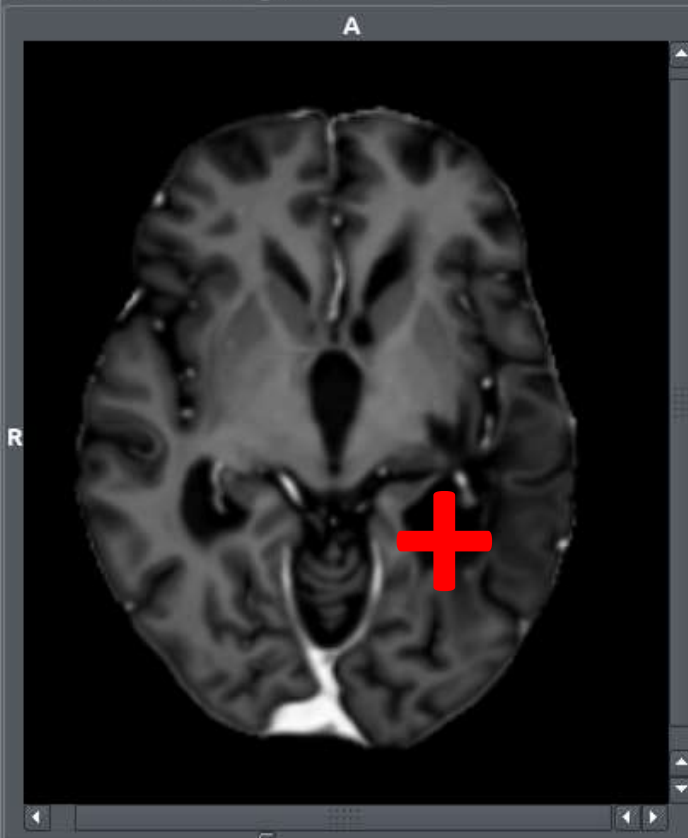
Level 127,000000

Window 255,000000

Linear

Z, MPR Y, MPR X, Histogram

Maximum intensity projection, CPU



T1c.nii.gz

193 x 229 x 193

double

[0, 255]

LPI

X left to right

Y posterior to anterior

Z inferior to superior

3D OpenGL views:

GL_R16F 193x229x193 (no filtering)

3D+t

120 ms Acq.

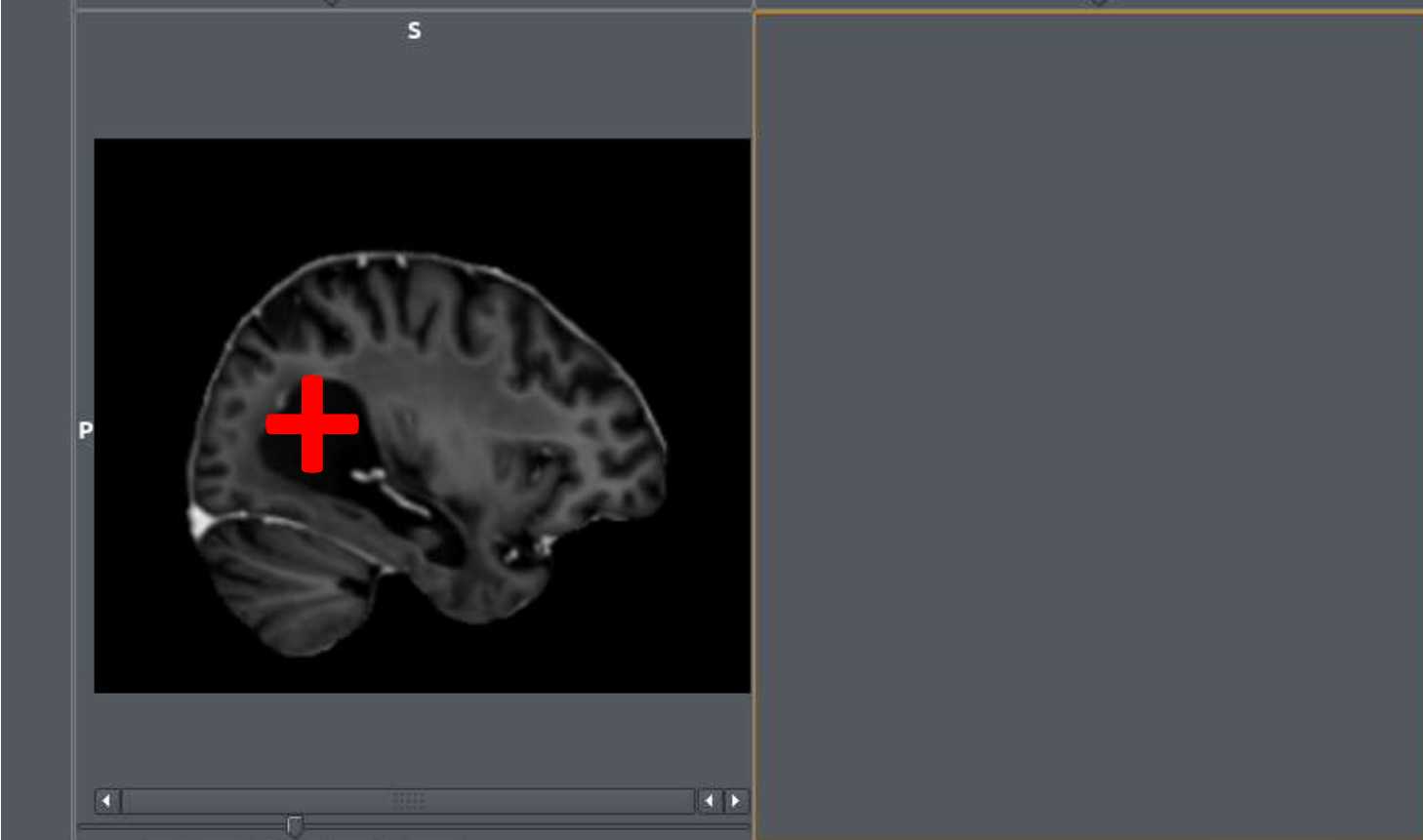
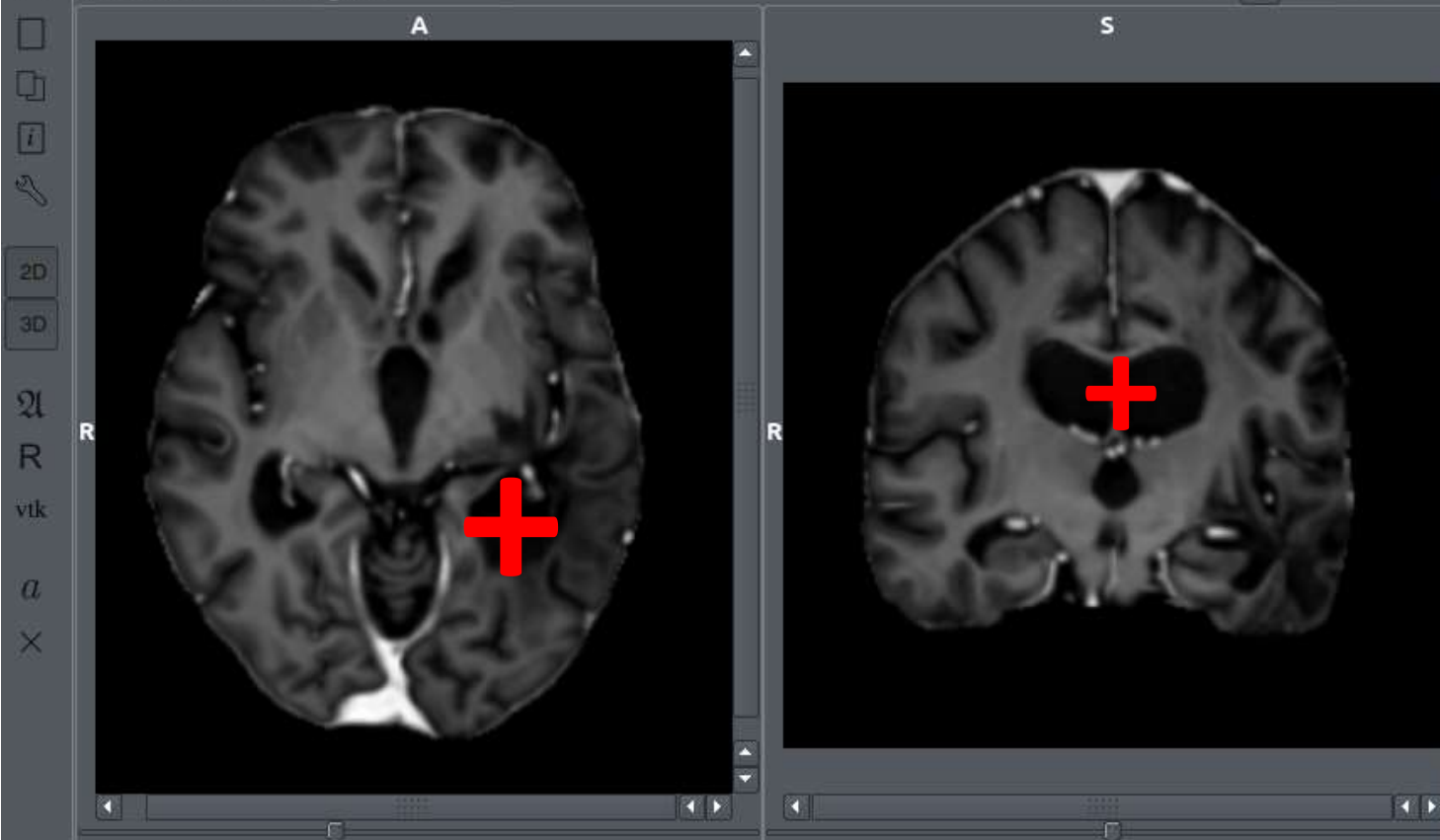
2Dt 3Dt

Level 127,000000

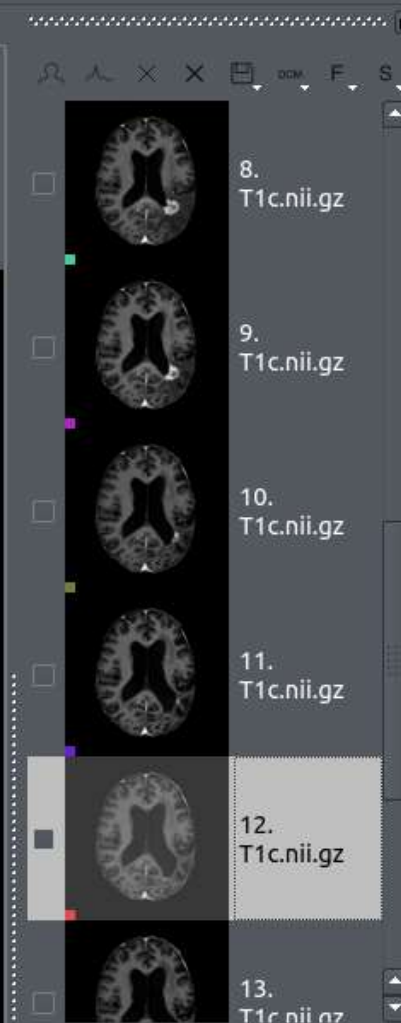
Window 255,000000

Linear

Z, MPR Y, MPR X, Histogram



Maximum intensity projection, CPU



T1c.nii.gz

193 x 229 x 193
double

[0, 255]

LPI

X left to right

Y posterior to anterior

Z inferior to superior

3D OpenGL views:

GL_R16F 193x229x193 (no filtering)

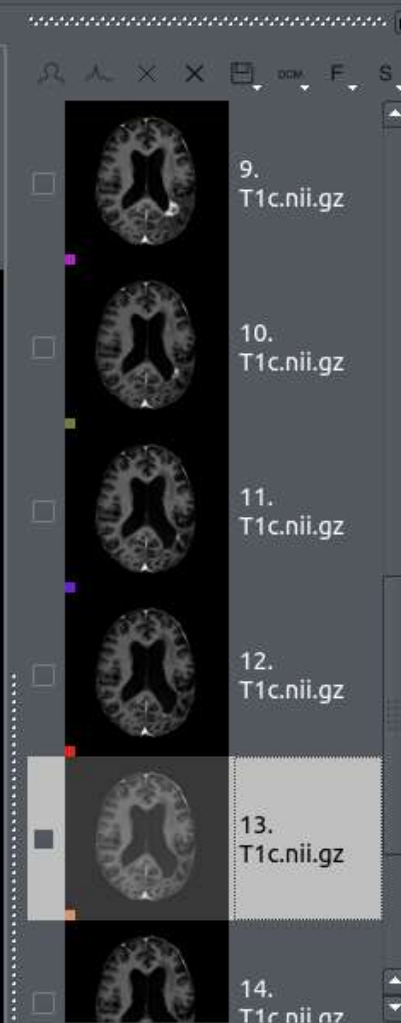
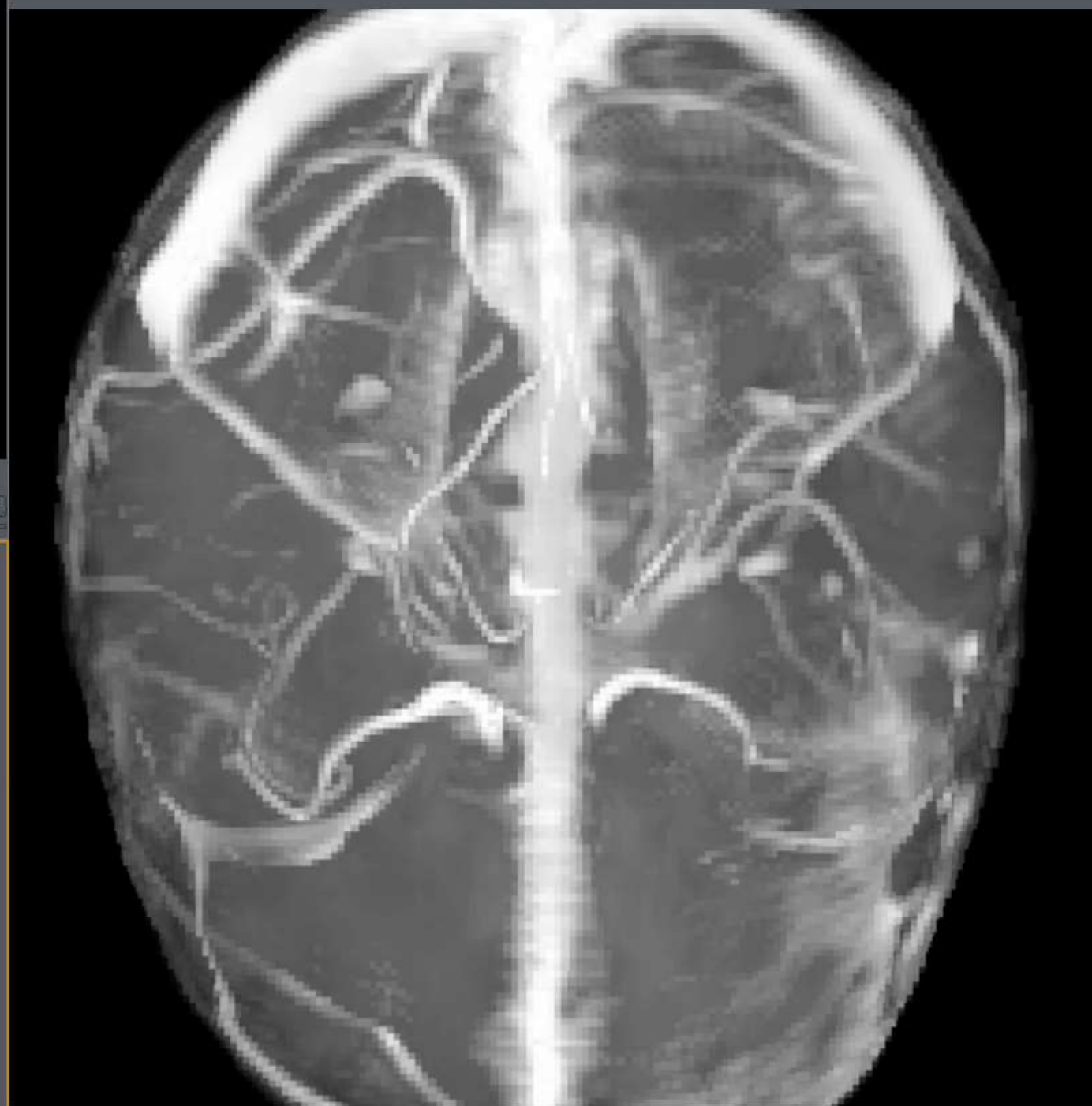
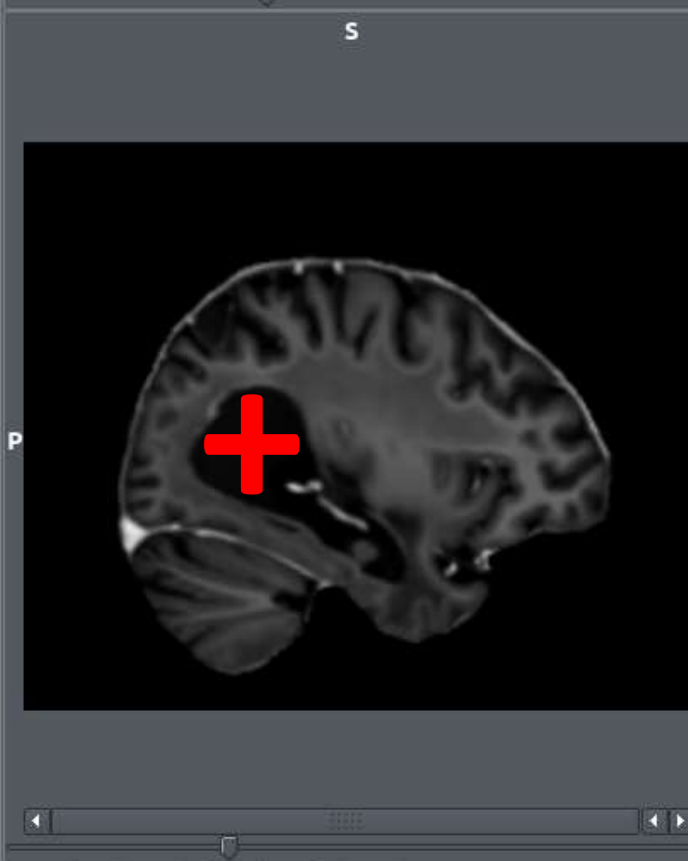
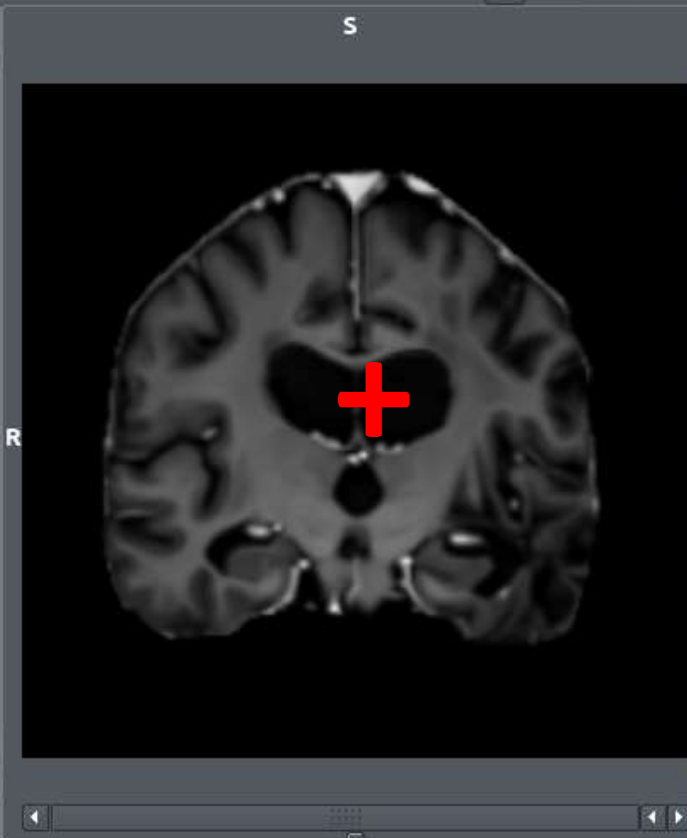
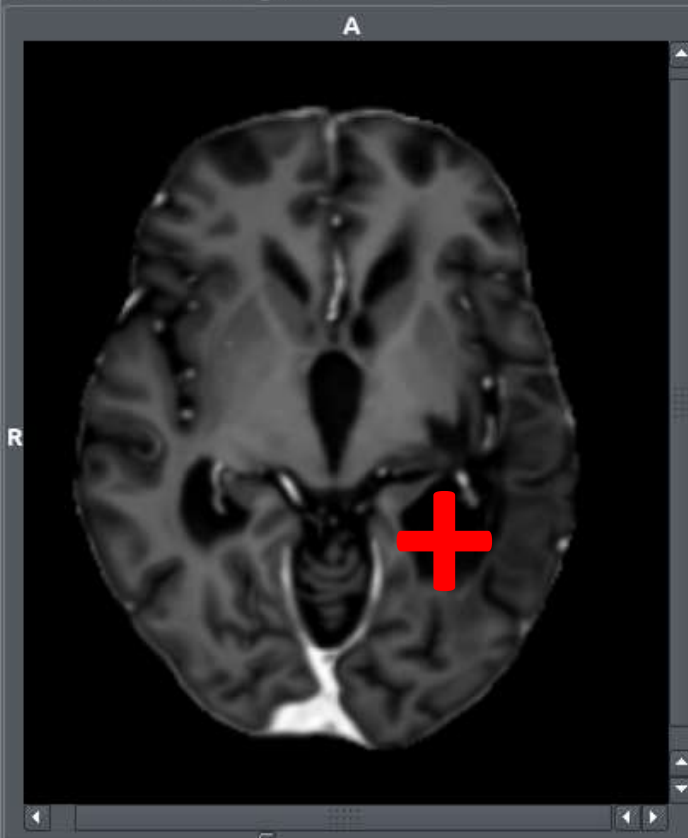
Level 127,000000

Window 255,000000

Linear

Z, MPR Y, MPR X, Histogram

Maximum intensity projection, CPU



T1c.nii.gz
193 x 229 x 193
double
[0, 255]
LPI
X left to right
Y posterior to anterior
Z inferior to superior
3D OpenGL views:
GL_R16F 193x229x193 (no filtering)

3D+t

120 ms Acq.

2Dt 3Dt

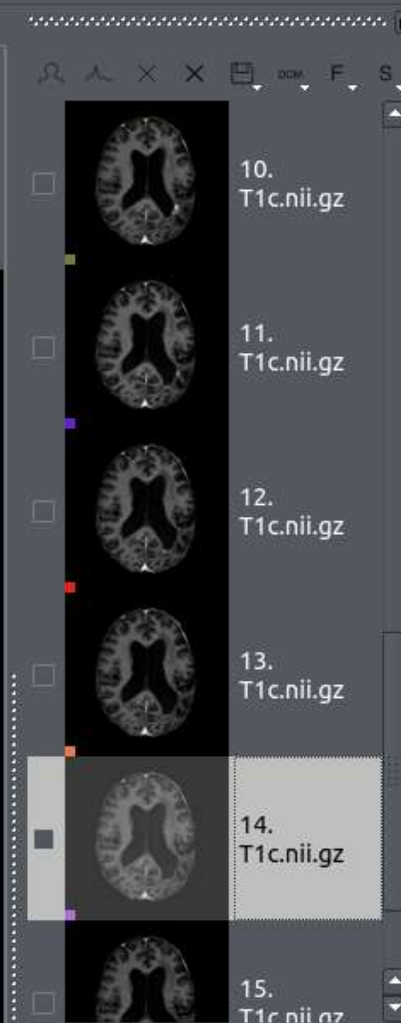
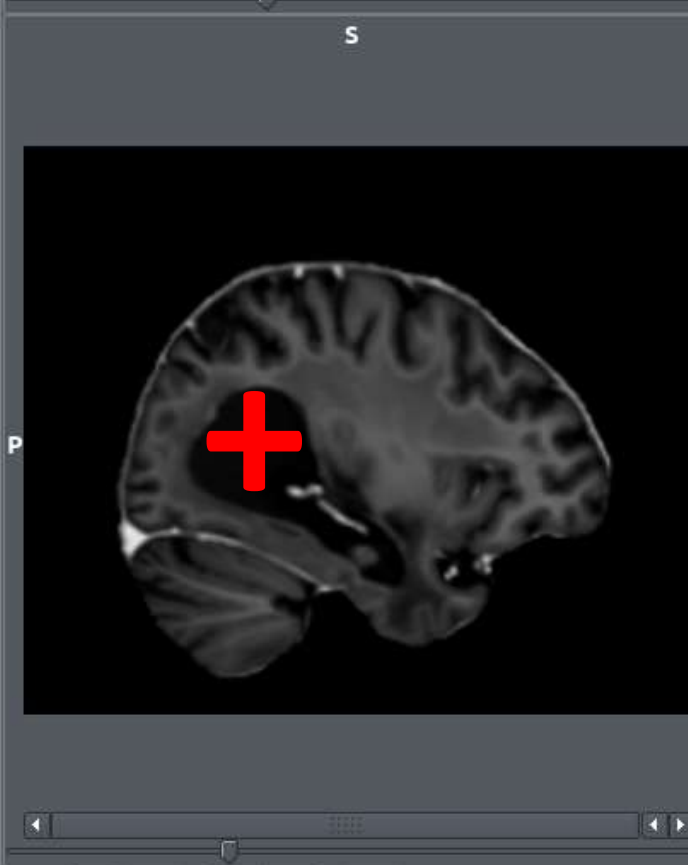
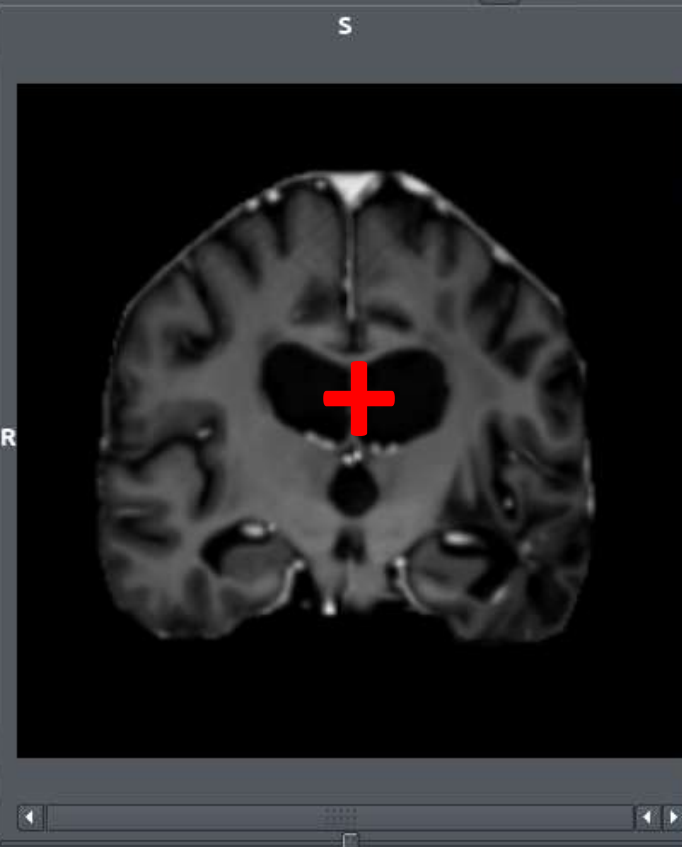
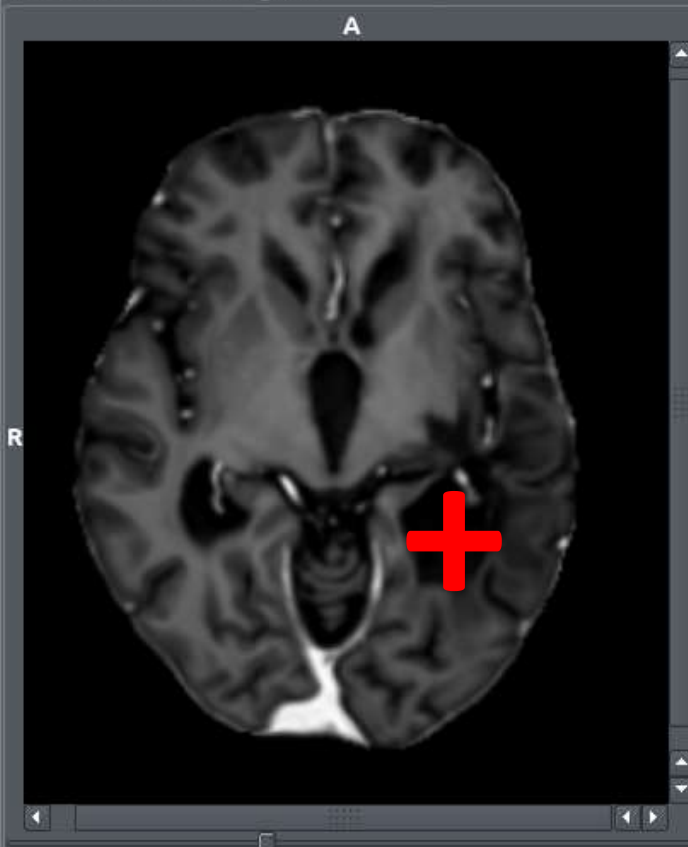
Level 127,000000

Window 255,000000

Linear

Z, MPR Y, MPR X, Histogram

Maximum intensity projection, CPU



T1c.nii.gz
193 x 229 x 193
double
[0, 255]
LPI
X left to right
Y posterior to anterior
Z inferior to superior
3D OpenGL views:
GL_R16F 193x229x193 (no filtering)

3D+t

120 ms Acq.

2Dt 3Dt

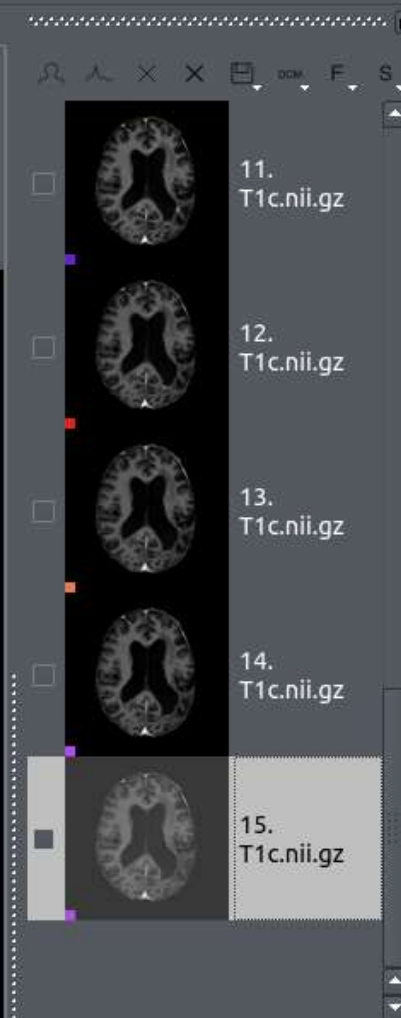
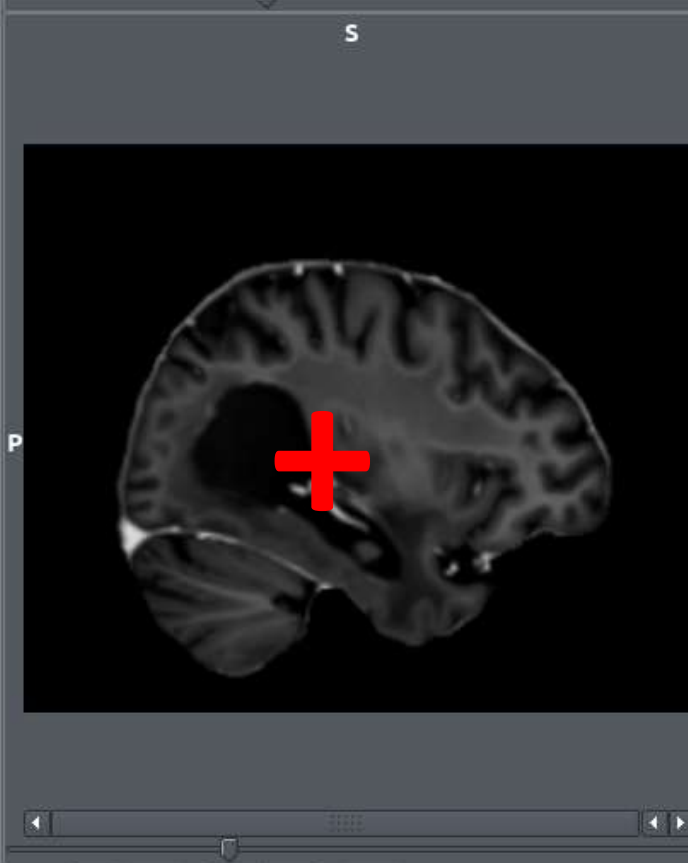
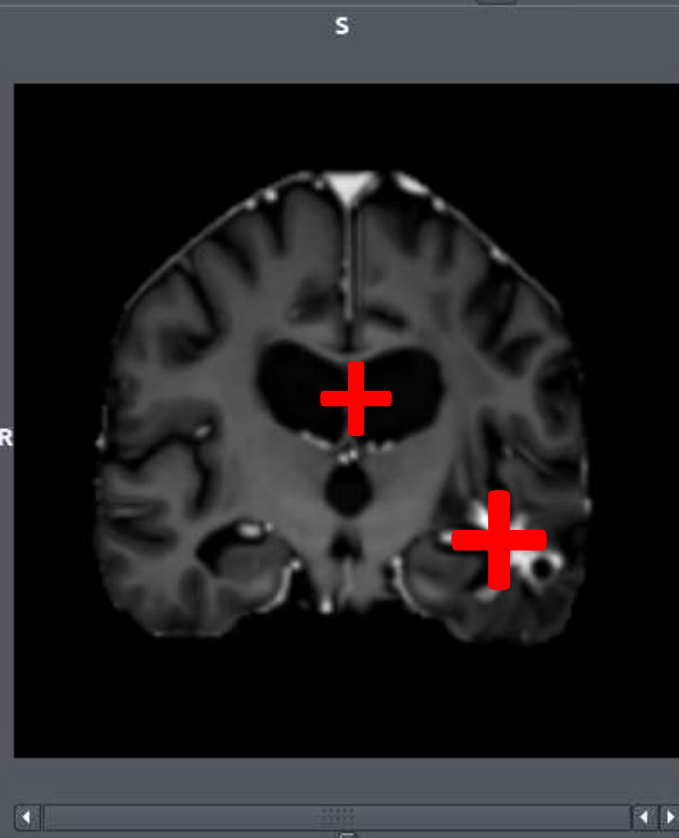
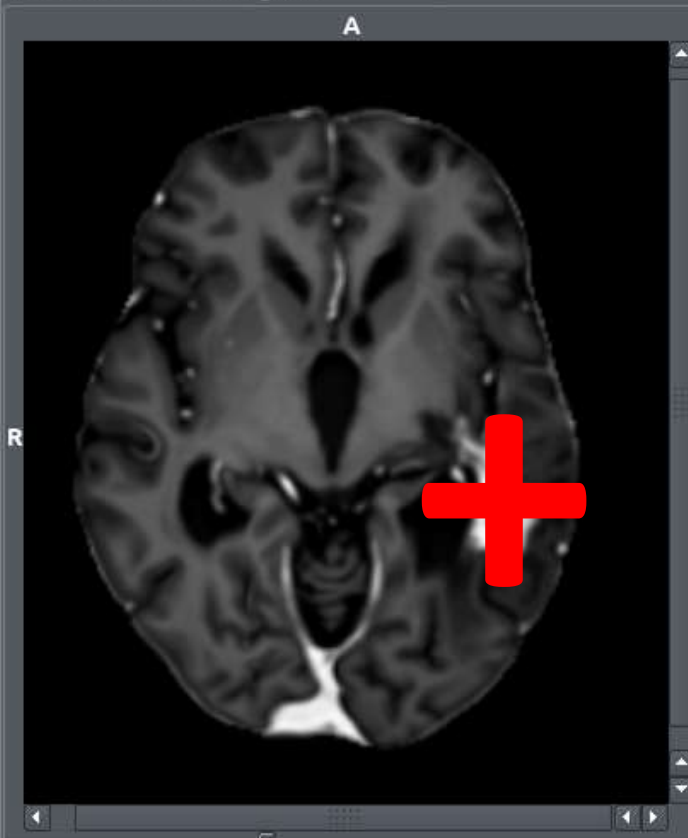
Level 127,000000

Window 255,000000

Linear

Z, MPR Y, MPR X, Histogram

Maximum intensity projection, CPU



T1c.nii.gz

193 x 229 x 193
double
[0, 255]
LPI

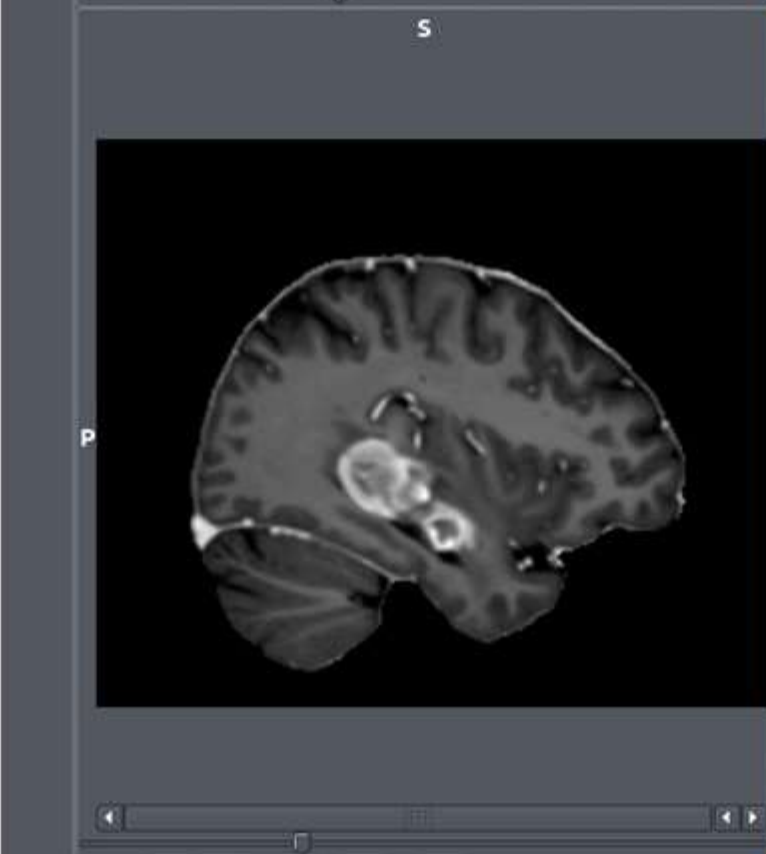
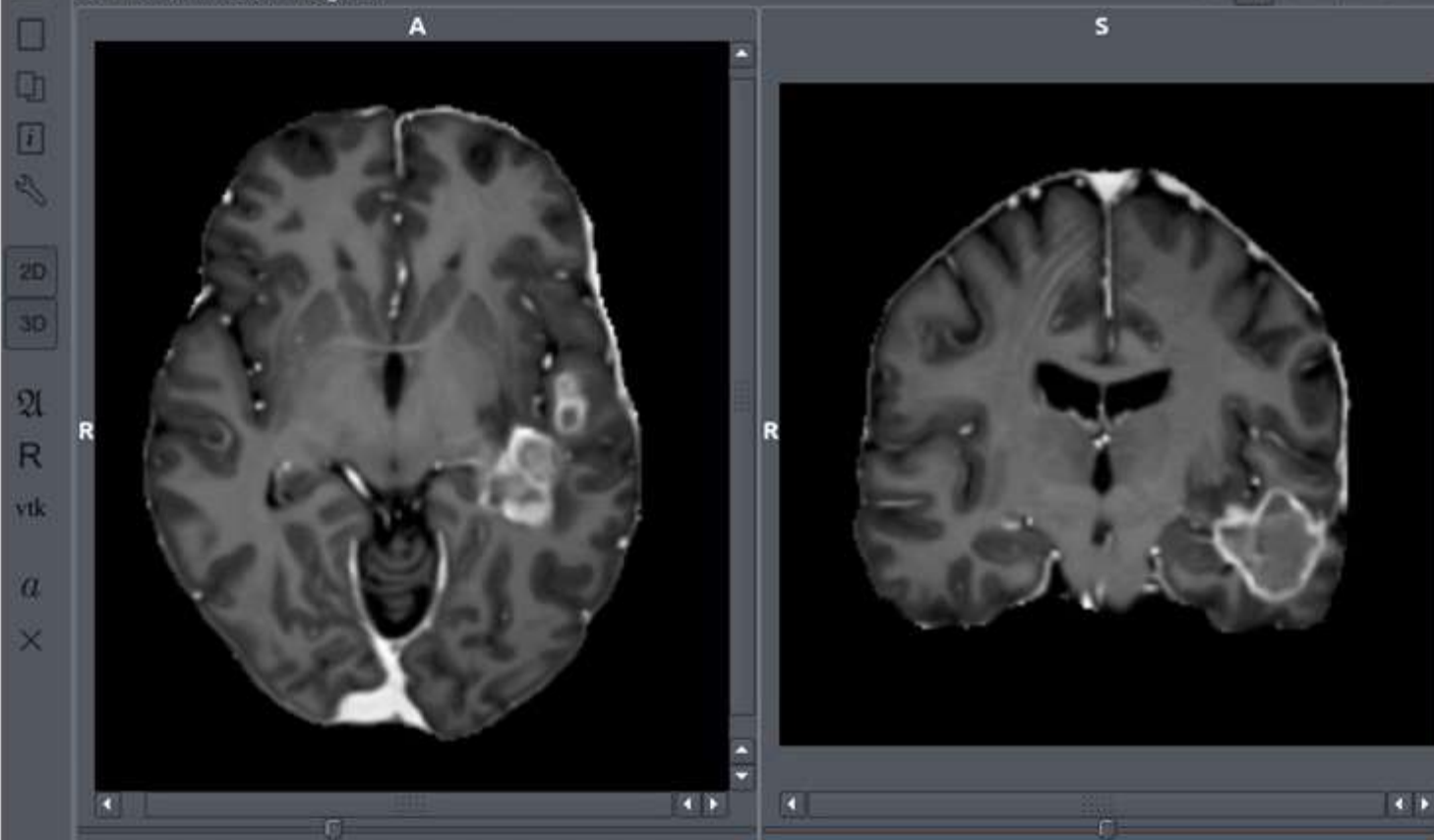
X left to right
Y posterior to anterior
Z inferior to superior

3D OpenGL views:
GL_R16F 193x229x193 (no filtering)

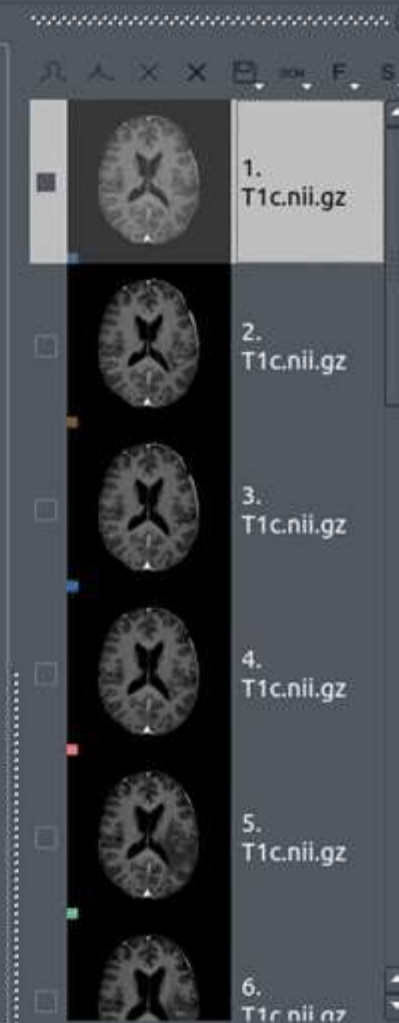
3D+t 120 ms Acq.

2Dt 3Dt

Level 127,000000 Window 255,000000 Linear



(animation)



T1c.nii.gz

193 x 229 x 193
unsigned char
[0, 255]

LPI

X left to right

Y posterior to anterior

Z inferior to superior

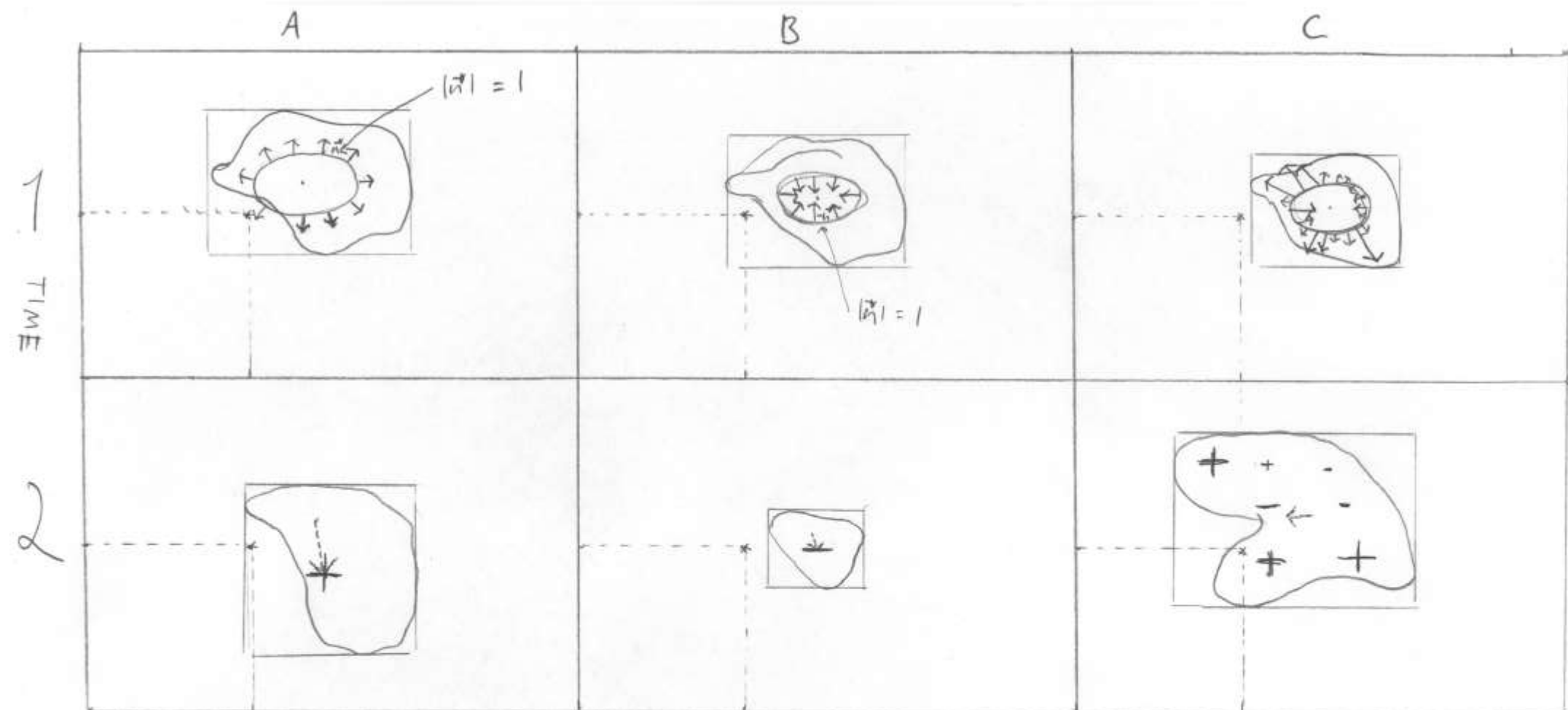
3D OpenGL views:

GL_R8 193x229x193 (no filtering)

Level 128,000000

Window 255,000000

Linear



CANCER-SIM V1 (PAPER #2)

• EXPAND DEFORMATION

CANCER-SIM V2

• EXPAND & SHRINK DEFORMATION

CANCER-SIM V3

• EXPAND & SHRINK DEFORMATION (INITIALIZATION) & REGULARIZATOR
 • GRADIENT-BASED OPTIMIZATION OF "INFLECTION RING" $\Rightarrow$ VARIABLE GROWTH RATE

Thank you!

