

Displacements in brain cancer imaging

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18th March 2021



Department of Diagnostic Physics



UiO : **Department of Physics**
University of Oslo

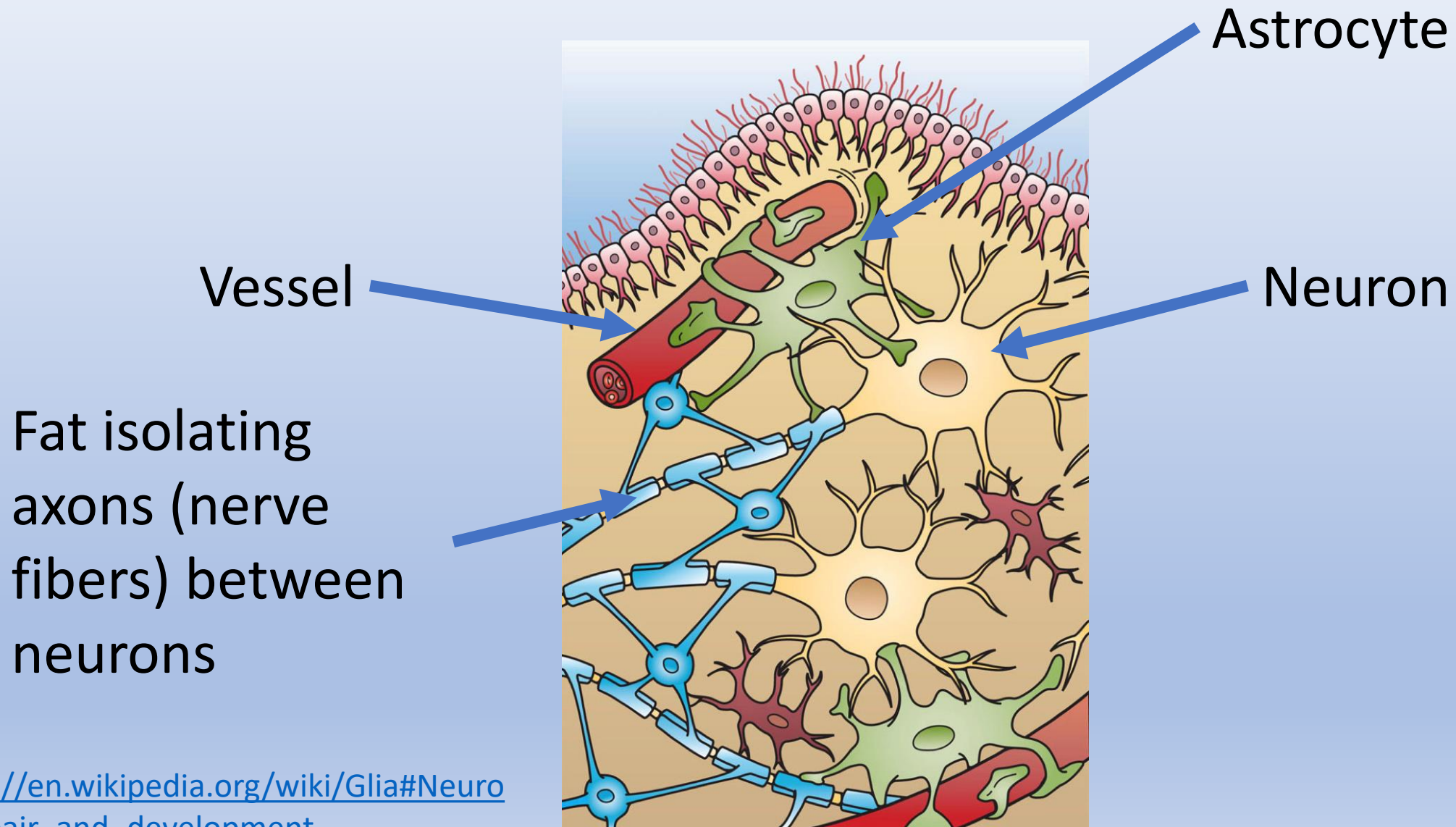
ADF

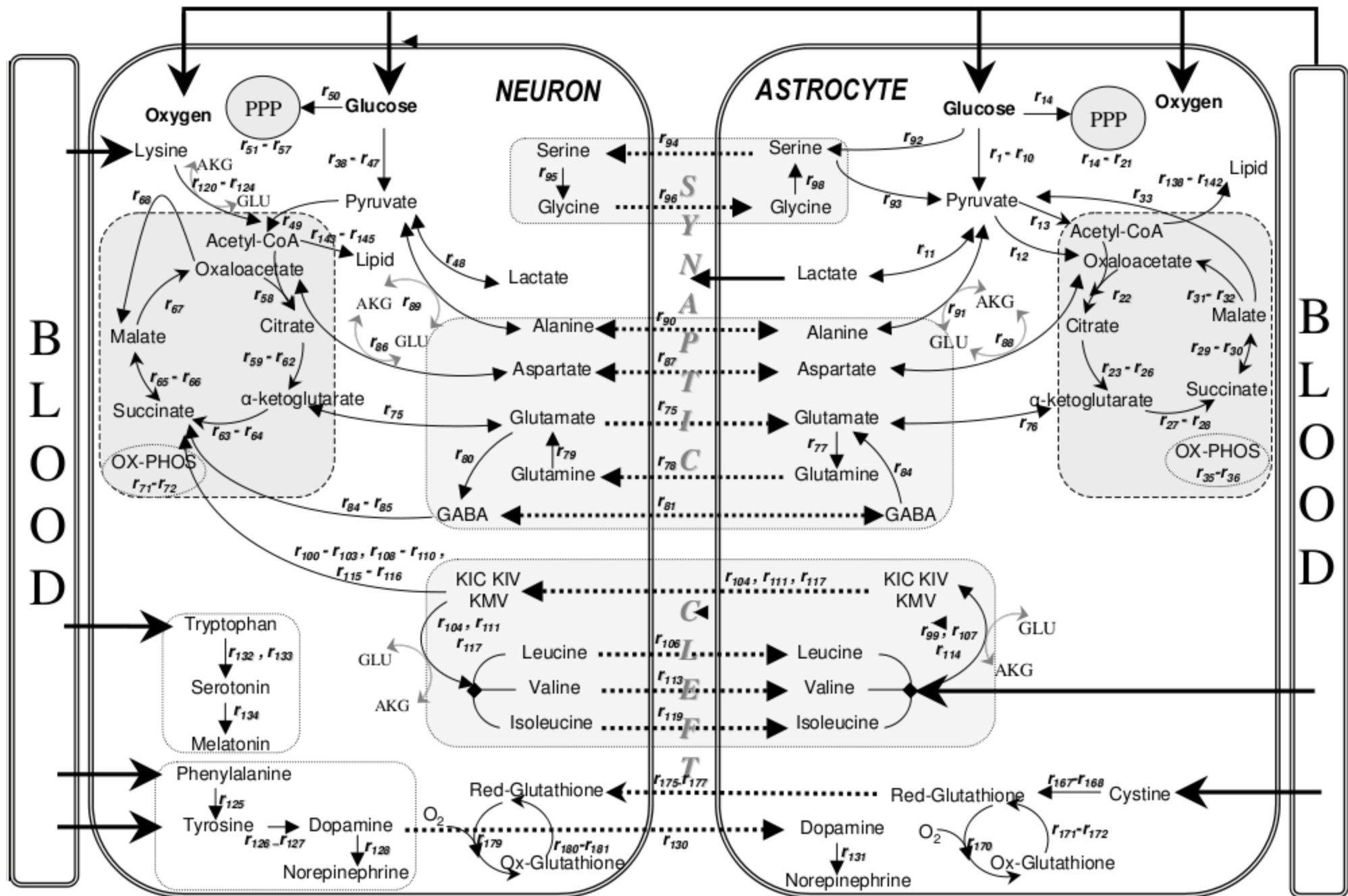


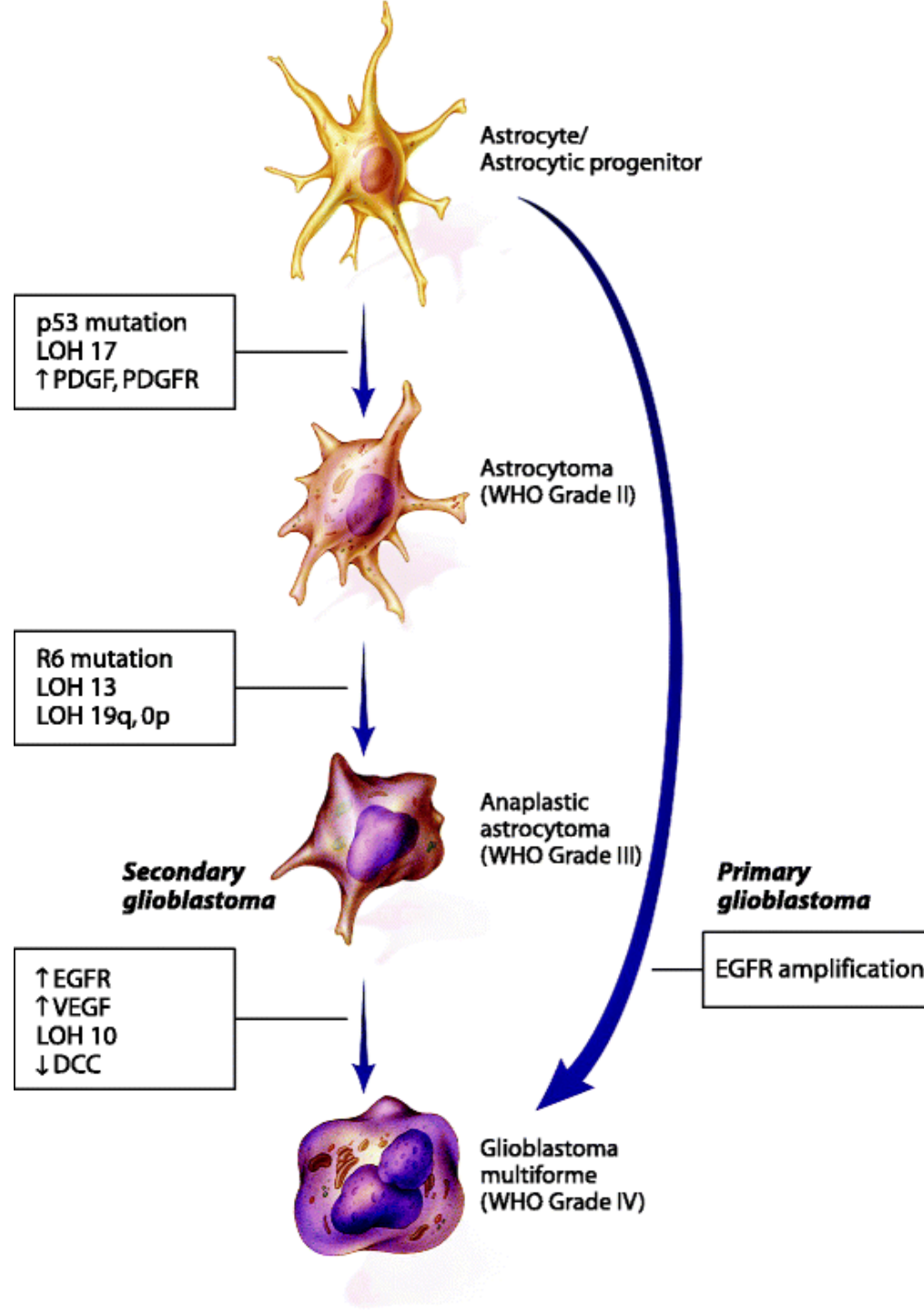
The cancer

- High-Grade Gliomas: WHO grade III and IV central nervous system tumors.
- Grade III: Anaplastic Astrocytoma = Astrocytes evolved to cancer cells.
- Grade IV: Glioblastoma = Multiple cells evolved to cancer cells; astrocytes may be among the originating cell types.
- Areas of necrotic (dead) tissue is a hallmark of grade IV.
- Median survival at 2-5 years (grade III) and 12-15 months (IV) despite extensive surgery and adjuvant and concomitant chemoradiotherapy.

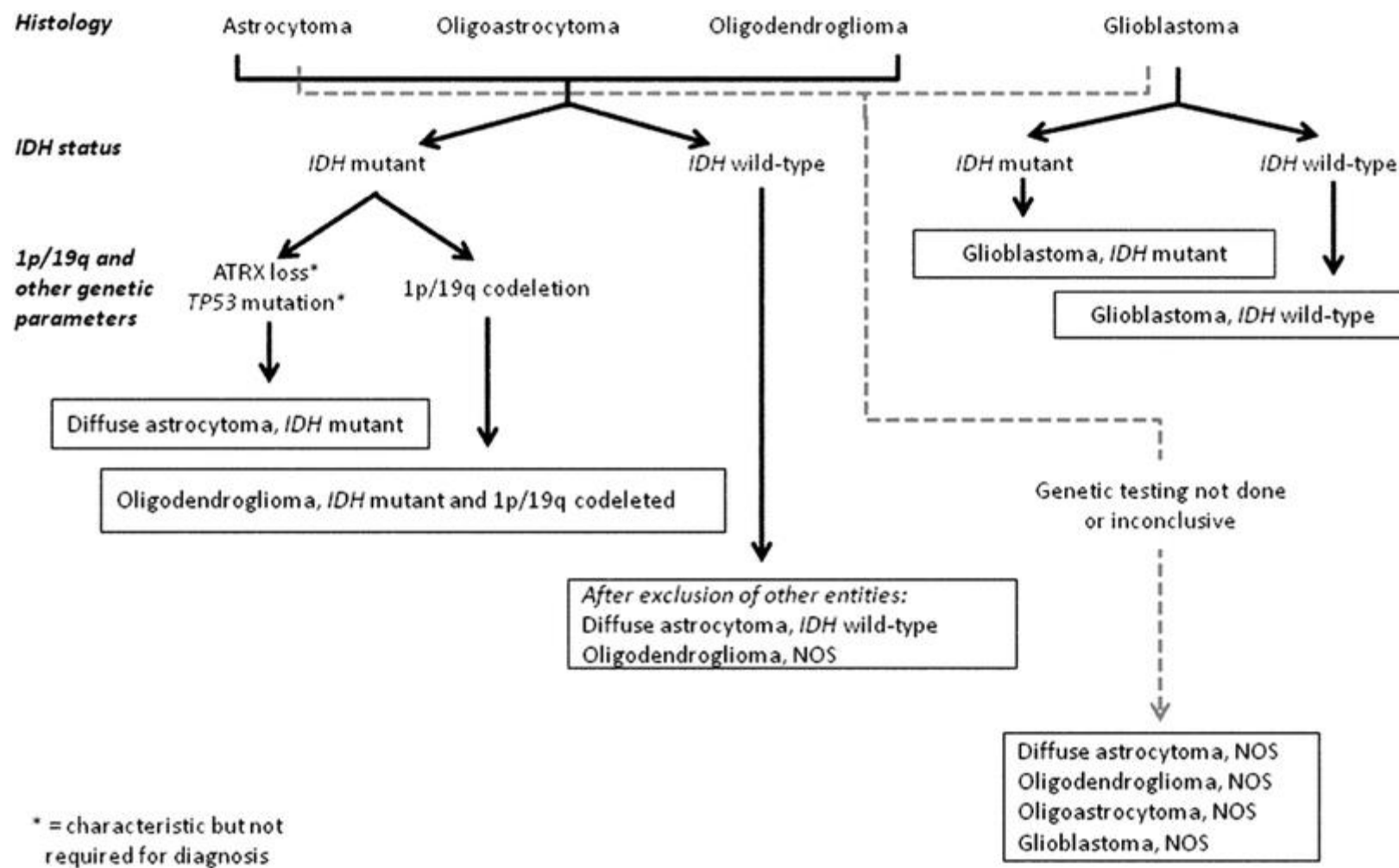
Astrocyte is a type of glial cell







Weingart, Jon D., Matthew J. McGirt, and Henry Brem. "High-Grade astrocytoma/glioblastoma." *Neuro-Oncology of CNS Tumors*. Springer, Berlin, Heidelberg, 2006. 127-138.

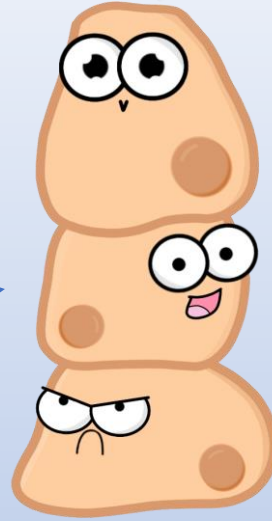
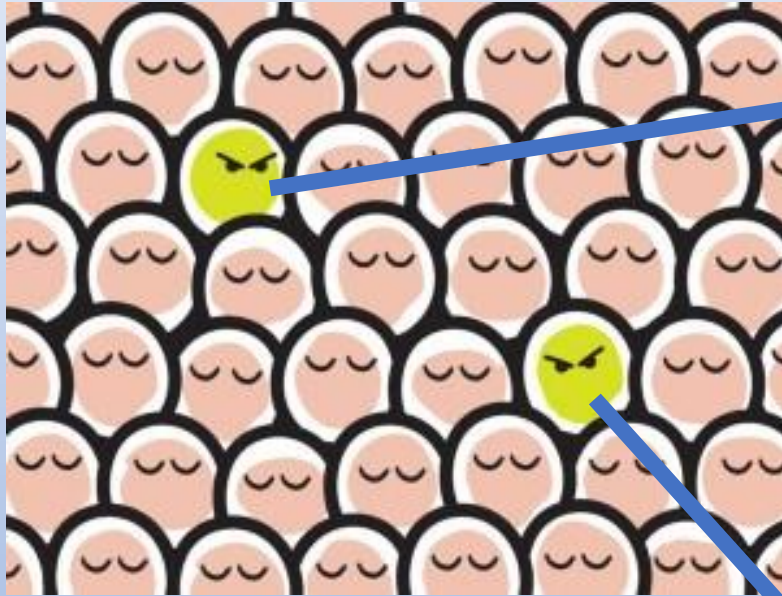


Louis, David N., et al. "The 2016 World Health Organization classification of tumors of the central nervous system: a summary." *Acta neuropathologica* 131.6 (2016): 803-820.

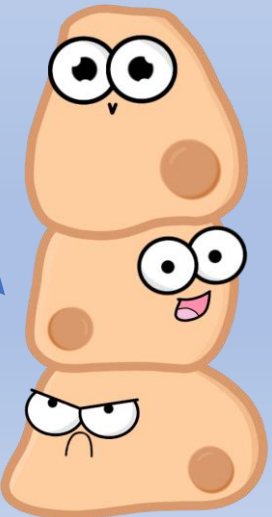
Alterations

Selection

Driver mutation



IDH mutant



IDH wild-type

IDH: isocitrate dehydrogenase

Tumor evolution and cells

- Cells compete by using resources in the environment.
- Genetic and epigenetic alterations lead to cell diversity (in genotype and phenotype) and genetic drift.
- The cells with the best fit mutation to the environment, the driver mutation, survives (selection).
- In tumor evolution, mutation and genetic drift occur continuously while selection occurs periodically.

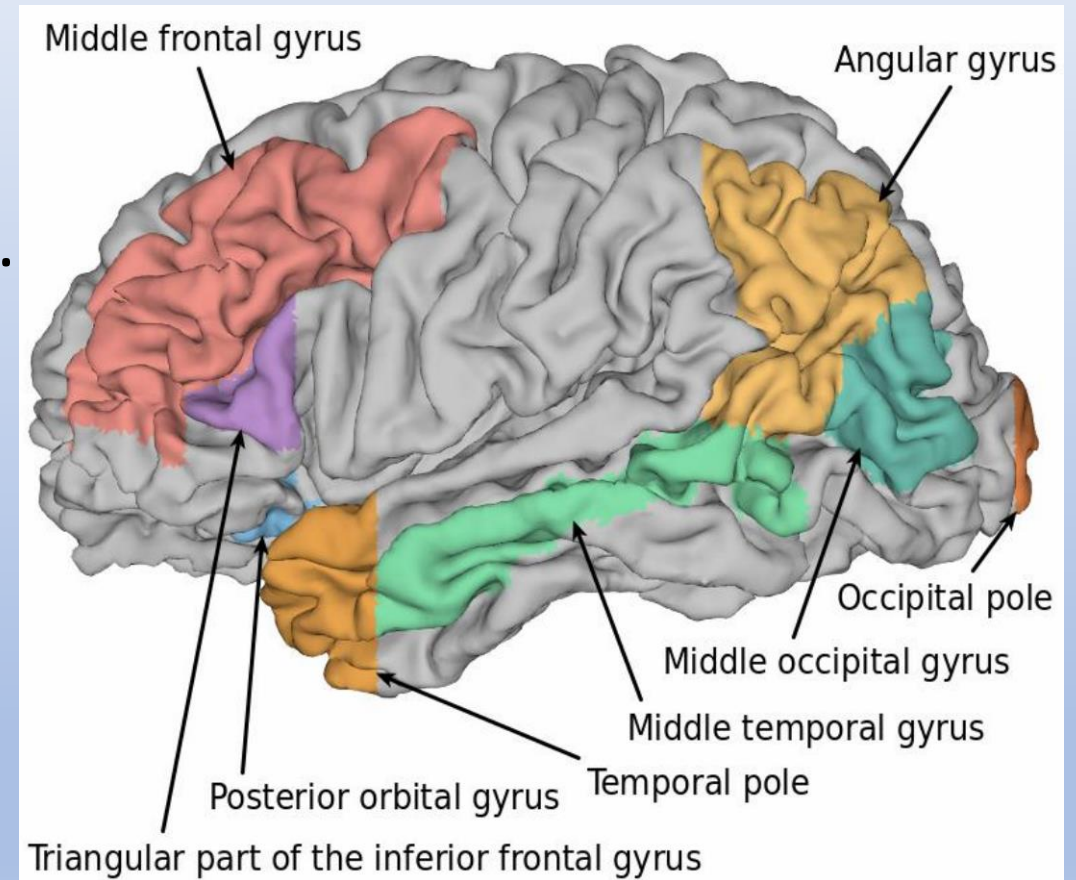
Turajlic, Samra, et al. "Resolving genetic heterogeneity in cancer." *Nature Reviews Genetics* 20.7 (2019): 404-416.

Cancer dynamics make use of

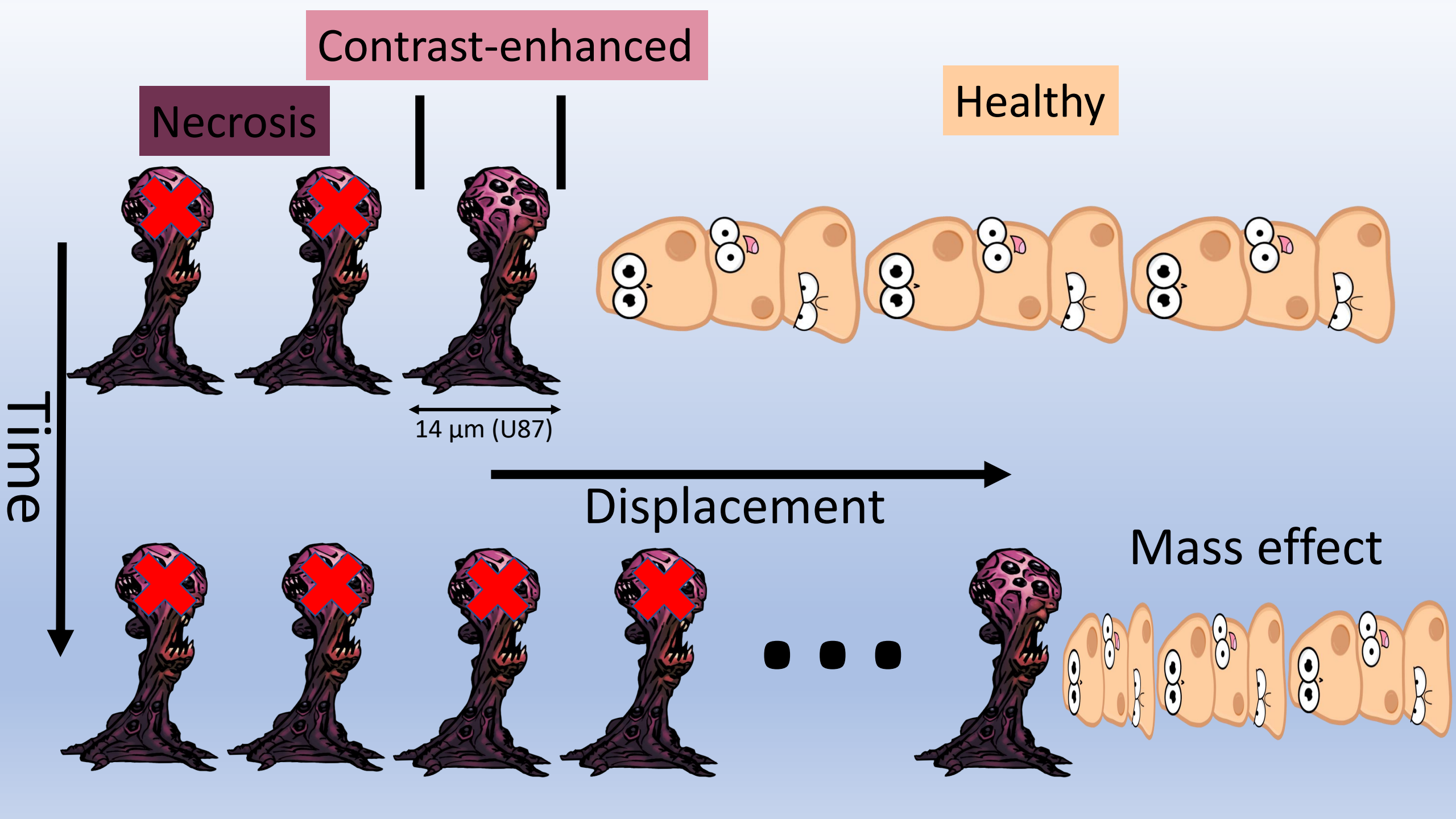
- Proliferation: Multiplication of the number of malignant cells.
- Invasion: Movement of malignant cells into healthy tissue.
- Angiogenesis: Formation of blood vessels to support cancer progression.
- Necrosis: Cells die from lack of supporting environment as a result of cancer progression.
- and more...

Paper 1: Impact of geometric distortion correction on echo-planar imaging CBV estimation

- TOPUP and EPIC distortion correction of magnetic susceptibility induced geometric errors from spin de-phasing.
- Correction led to increase in estimated CBV for both spin- and gradient-echo DSC MRI in multiple cortical and subcortical regions.
- These corrections are important when comparing vascular and structural MRI in glioblastoma.

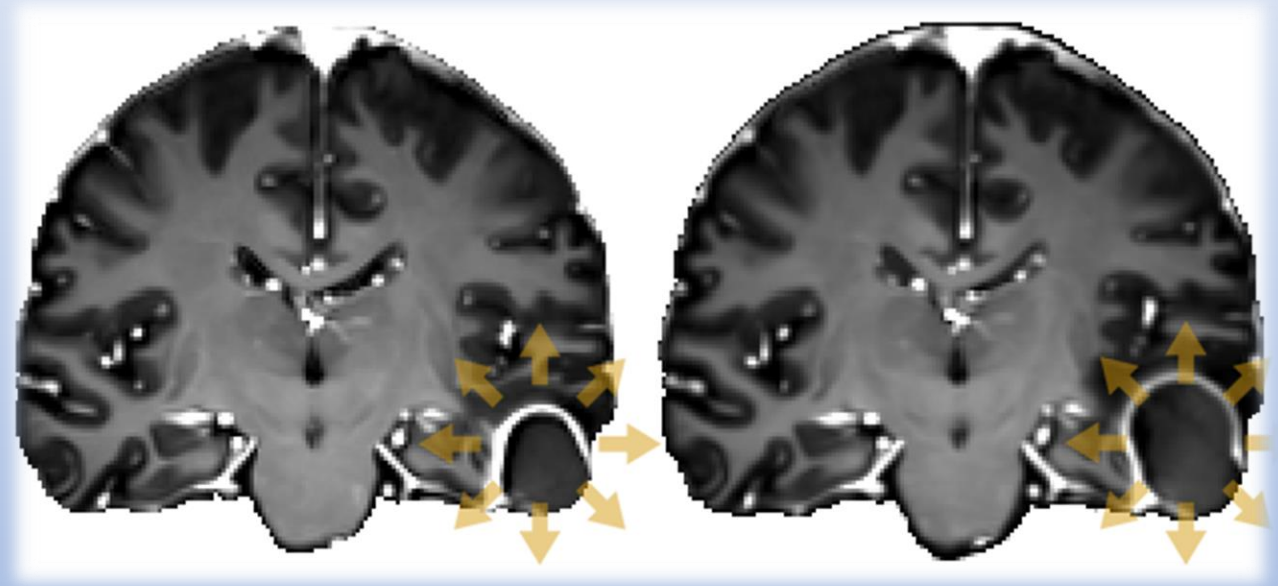


Hovden, Ivar T., et al. "The impact of EPI-based distortion correction of dynamic susceptibility contrast MRI on cerebral blood volume estimation in patients with glioblastoma." *European Journal of Radiology* 132 (2020): 109278.



Paper 2: Displacements to characterize tumor growth from first to second examination

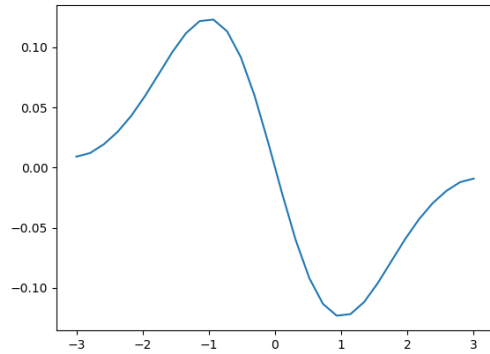
- From non-rigid registration = estimates.
- From model = test cases.
- Error = test case – estimated.
- 27 patients from SAILOR;
23 with glioblastoma and 4 with grade III.
- 5 registration methods.
- Wilcoxon, Kruskal-Wallis and ANOVA to test for significance in error in necrotic, contrast-enhanced and edematous lesions.



Model of displacements from one examination to the next

1D

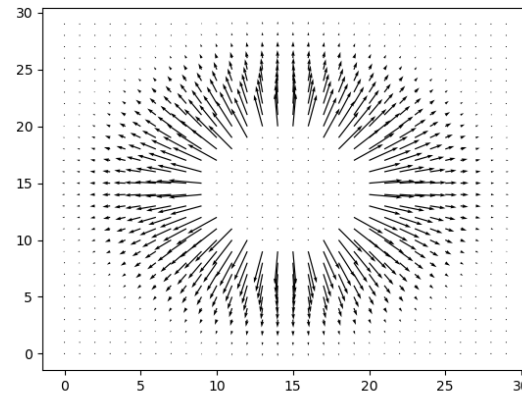
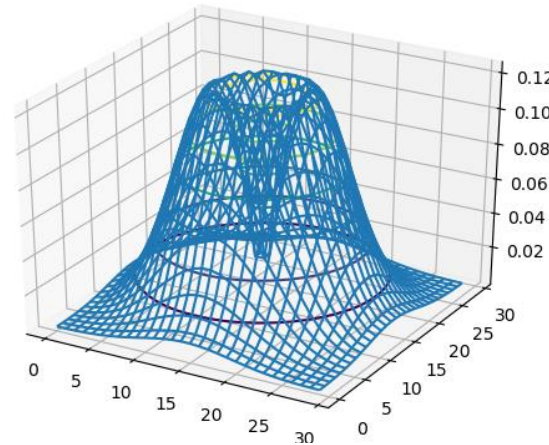
Displacement



Tumor cross section

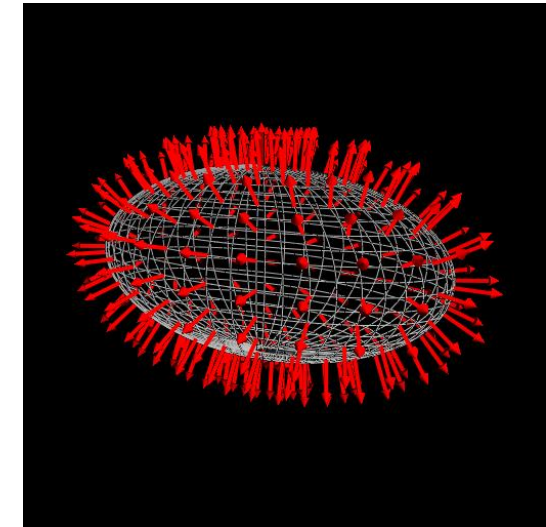
2D

Displacement

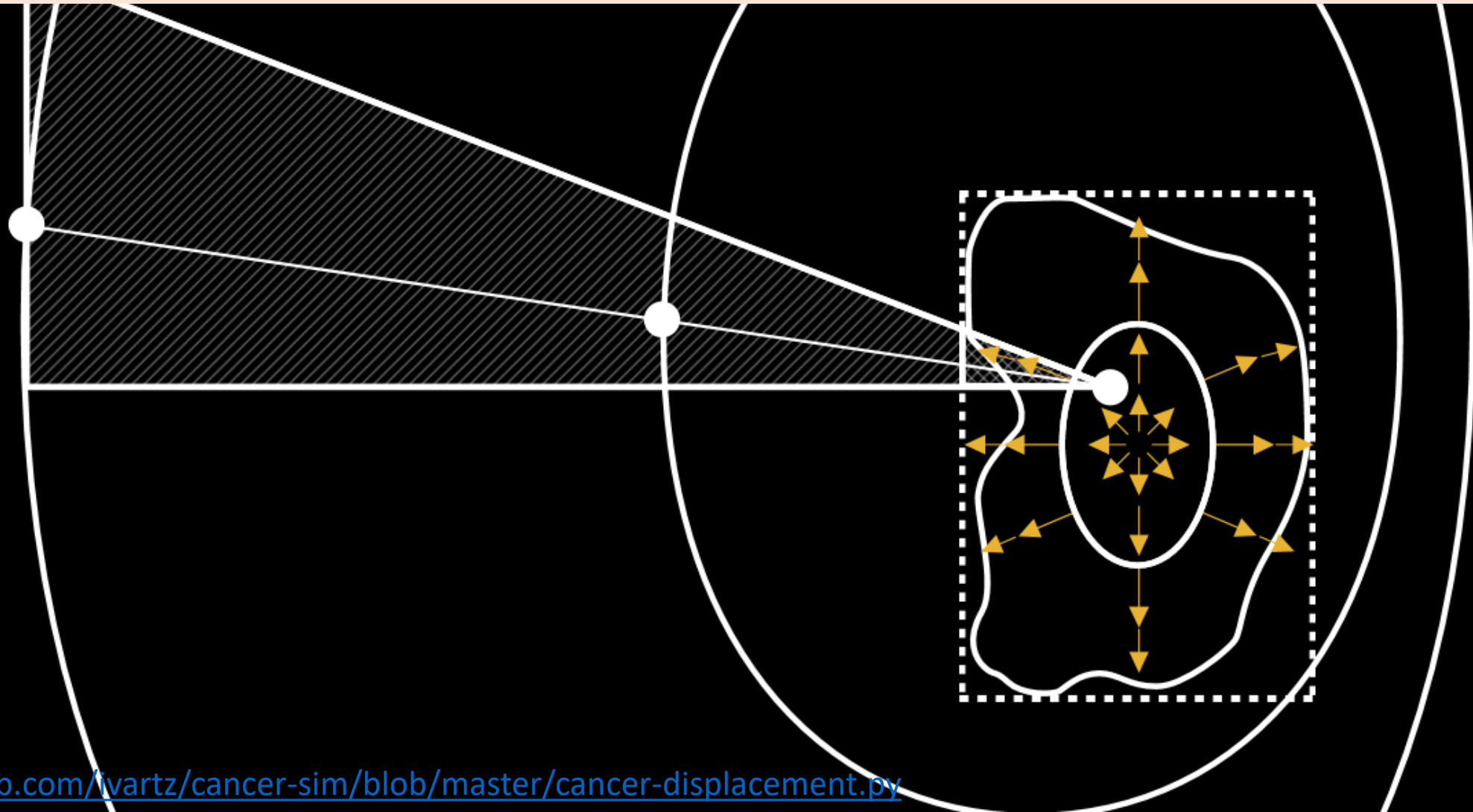


Tumor cross section

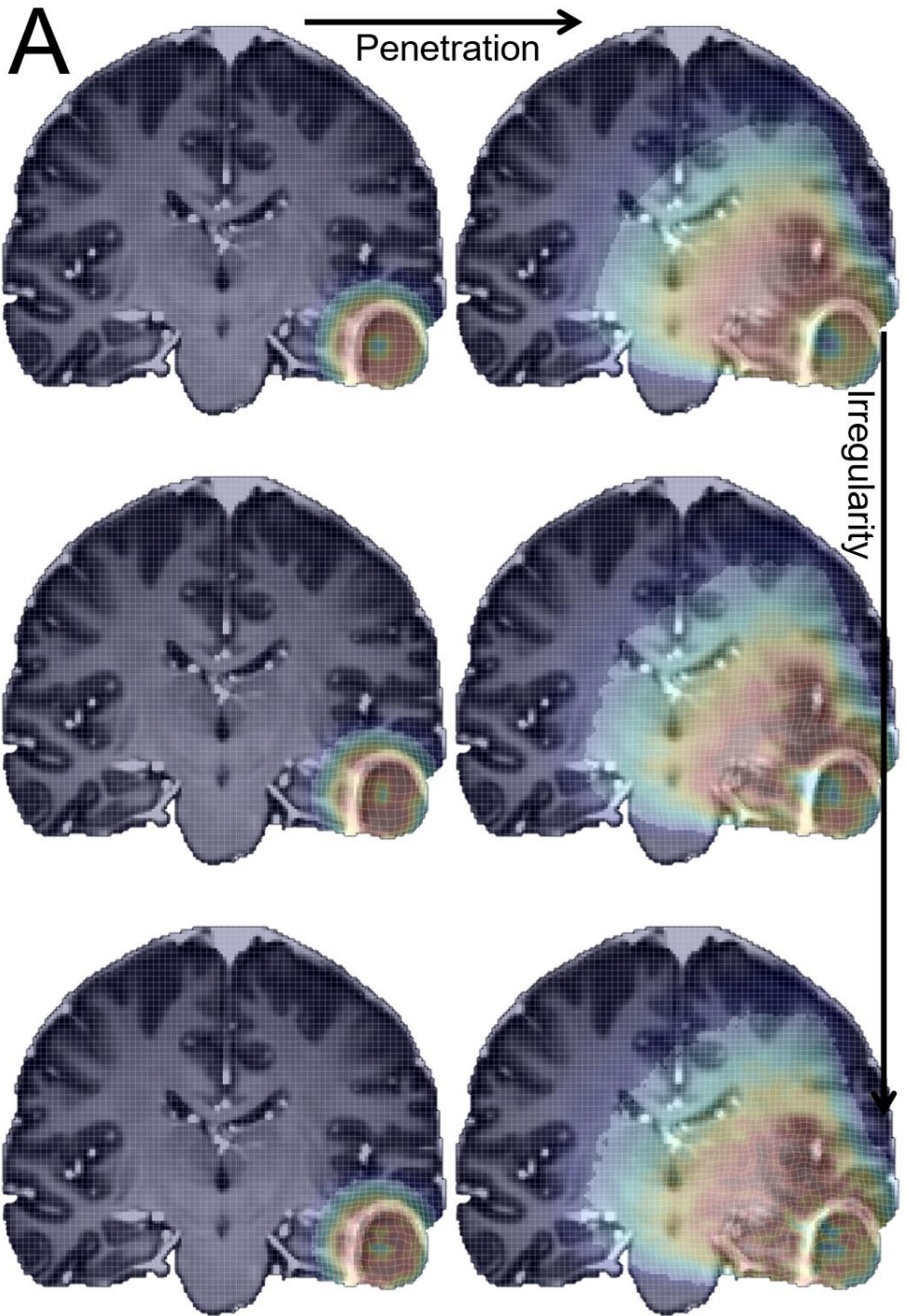
3D



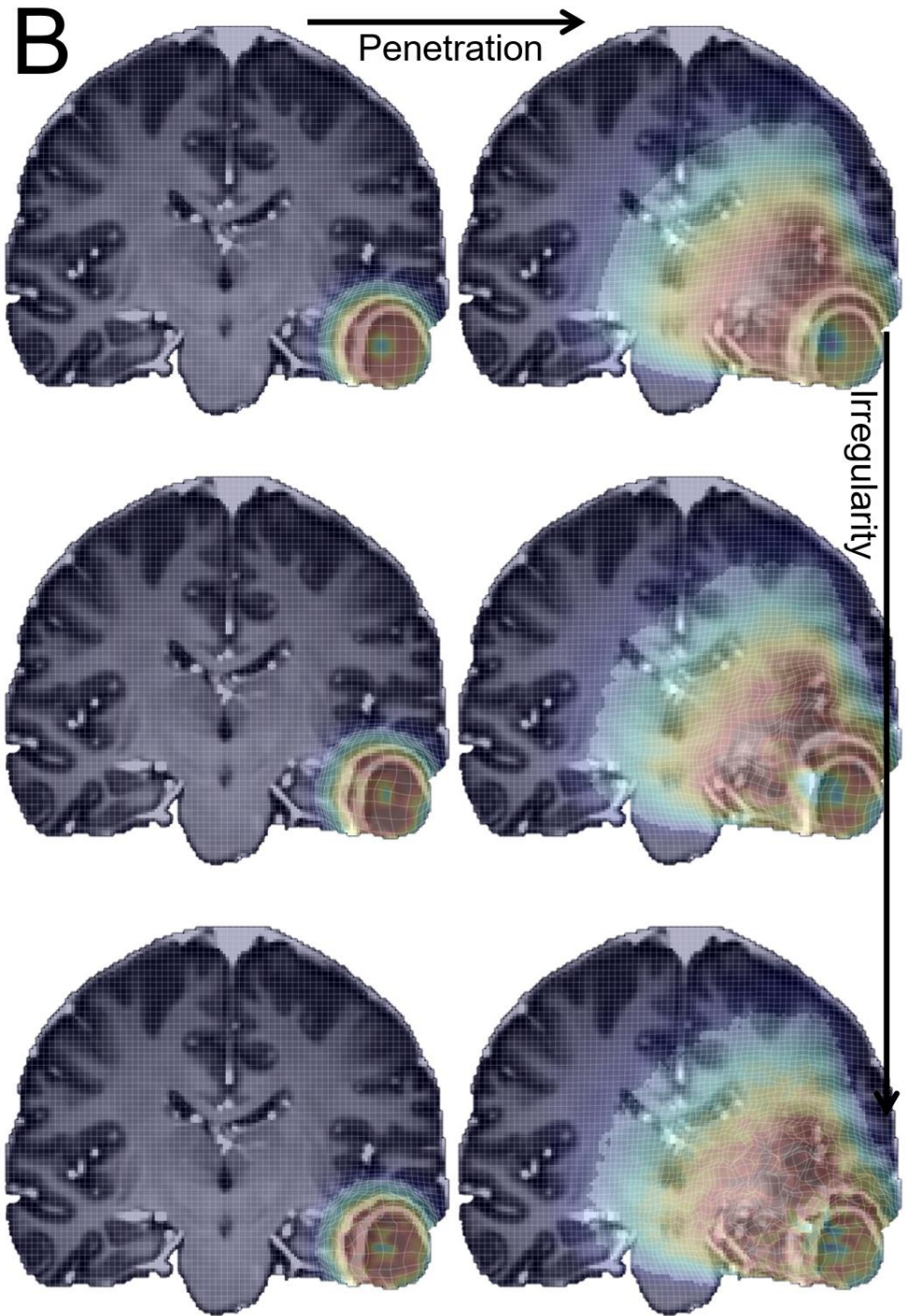
Model of displacements from one examination to the next



3 mm displacement



8 mm displacement



ITK-SNAP Toolbox

Main Toolbar



Cursor Inspector



Cursor position (x,y,z):

41 118 58

Intensity under cursor:

Layer	Intensity
T1c	23
Segmentation	1
warped	22.92
interp-neg-field-3	1.815
transform0Inver...	2.238
transform0Inver...	1.758

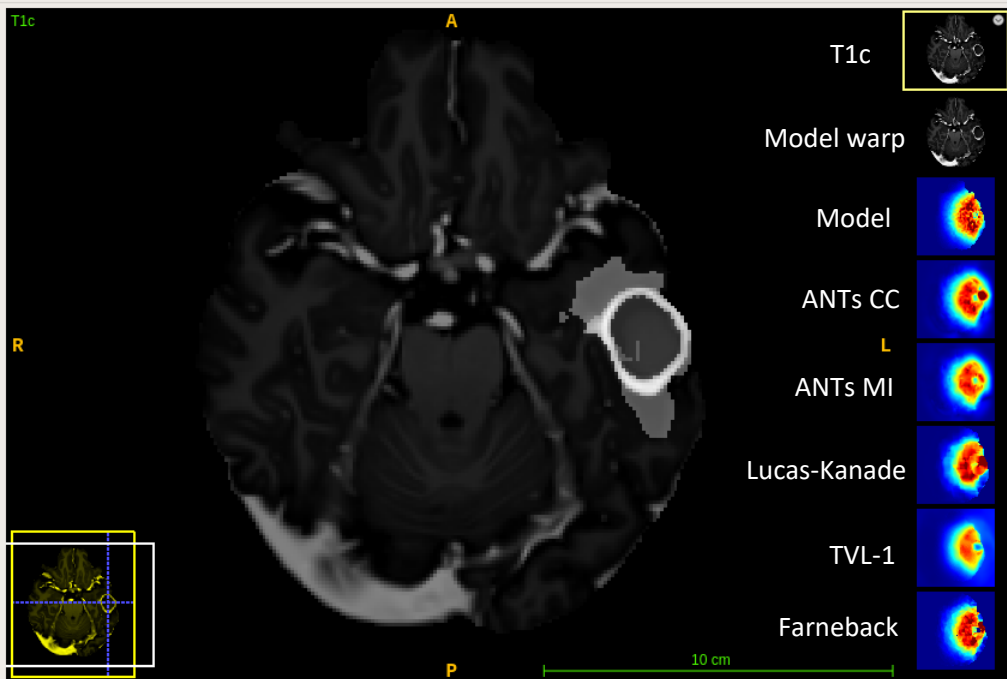
Label under cursor:

0 Clear Label

Segmentation Labels

Active label:
Label 1Paint over:
All labelsOverall label opacity:
50

3D Toolbar



T1c

Model warp

Model

ANTs CC

ANTs MI

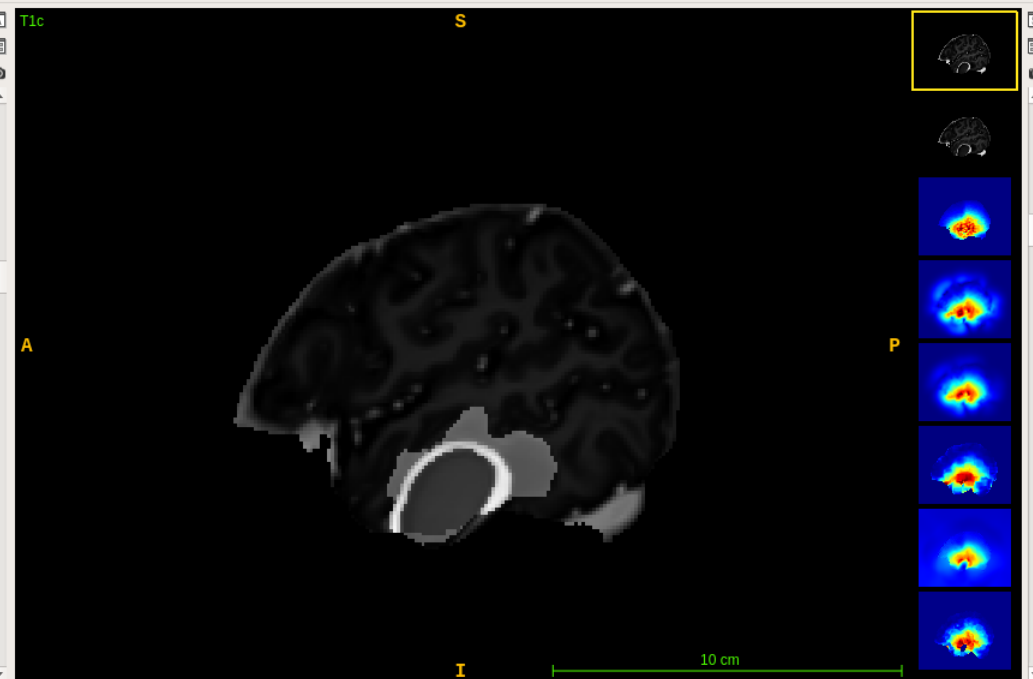
Lucas-Kanade

TVL-1

Farneback

zoom to fit

58 of 193



zoom to fit

41 of 193

Image Layer Inspector - ITK-SNAP

General Contrast Color Map Info Metadata

Linear Contrast Adjustment:

Minimum: 0,00 Level: 127,50 Reset

Maximum: 255,00 Window: 255,00 Auto

Curve-Based Contrast Adjustment:

Index into Color Map

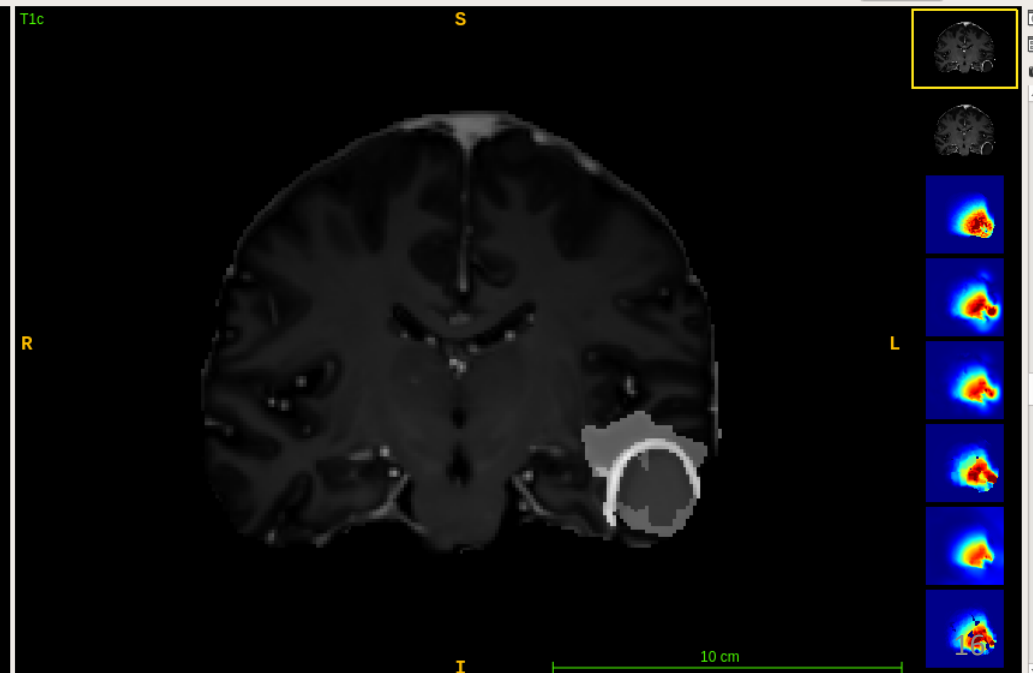
Selected control point:

Id: 1 x: 0,00 y: 0,000 + -

Histogram Display Options:

Bin size: 10 Cutoff: 6,0 % Log scale

Close



zoom to fit

118 of 229

ITK-SNAP Toolbox

Main Toolbar



Cursor Inspector



Cursor position (x,y,z):

41 118 58

Intensity under cursor:

Layer	Intensity
T1c	23
Segmentation	1
warped	22.92
interp-neg-field-3	1.815
transform0InverseWarp-vec	2.238
transform0InverseWarp-vec	1.758

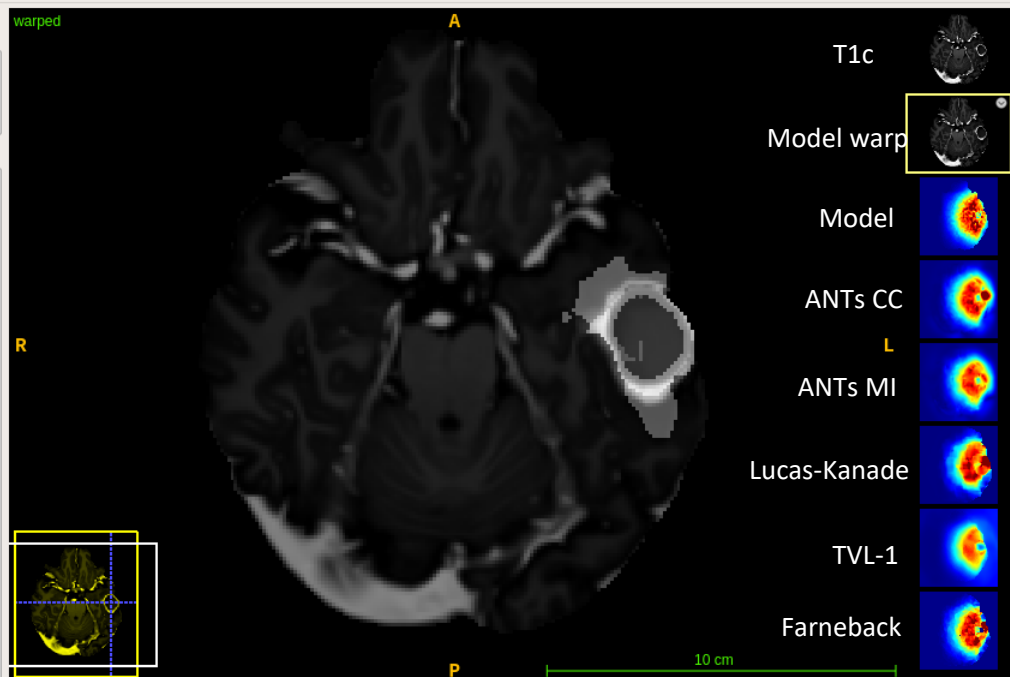
Label under cursor:

0 Clear Label

Segmentation Labels

Active label:
Label 1Paint over:
All labelsOverall label opacity:
50

3D Toolbar



T1c

Model warp

Model

ANTs CC

ANTs MI

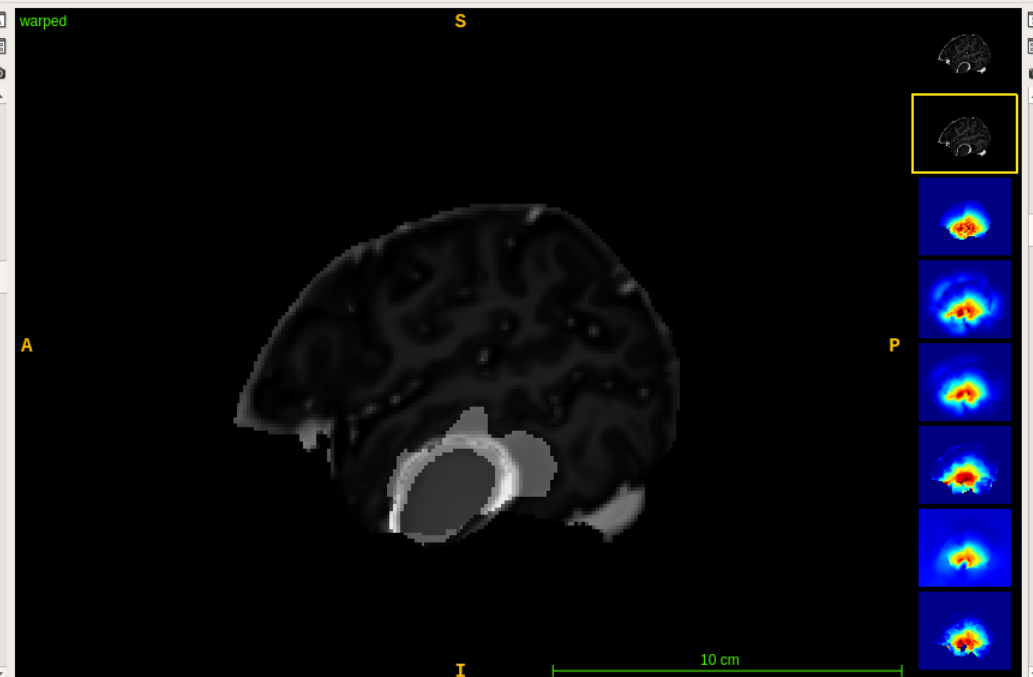
Lucas-Kanade

TVL-1

Farneback

zoom to fit

58 of 193



zoom to fit

41 of 193

Image Layer Inspector - ITK-SNAP

General Contrast Color Map Info Metadata

Linear Contrast Adjustment:

Minimum: 0,00 Level: 127,50 Reset

Maximum: 255,00 Window: 255,00 Auto

Curve-Based Contrast Adjustment:

Index into Color Map

Image Intensity

Selected control point:

Id: 1 x: 0,00 y: 0,000 + -

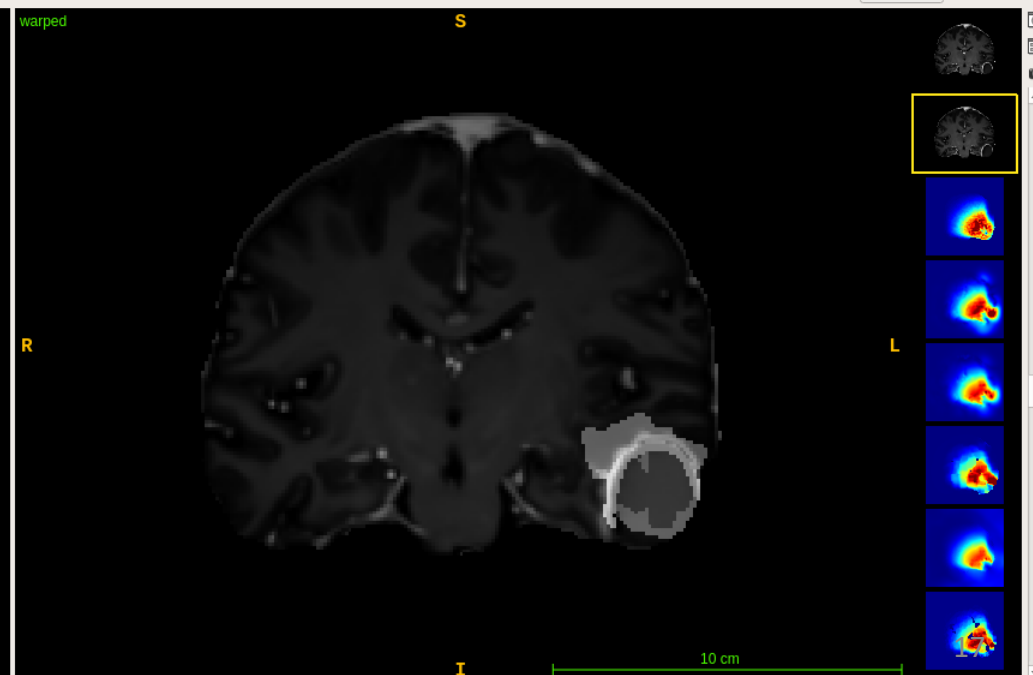
Histogram Display Options:

Bin size: 10 Cutoff: 6,0 % Log scale

Close

update

zoom to fit



zoom to fit

118 of 229

ITK-SNAP Toolbox

Main Toolbar



Cursor Inspector



Cursor position (x,y,z):

41 118 58

Intensity under cursor:

Layer	Intensity
T1c	23
Segmentation	1
warped	22.92
interp-neg-fiel...	1.815
transform0Inver...	2.238
transform0Inver...	1.758

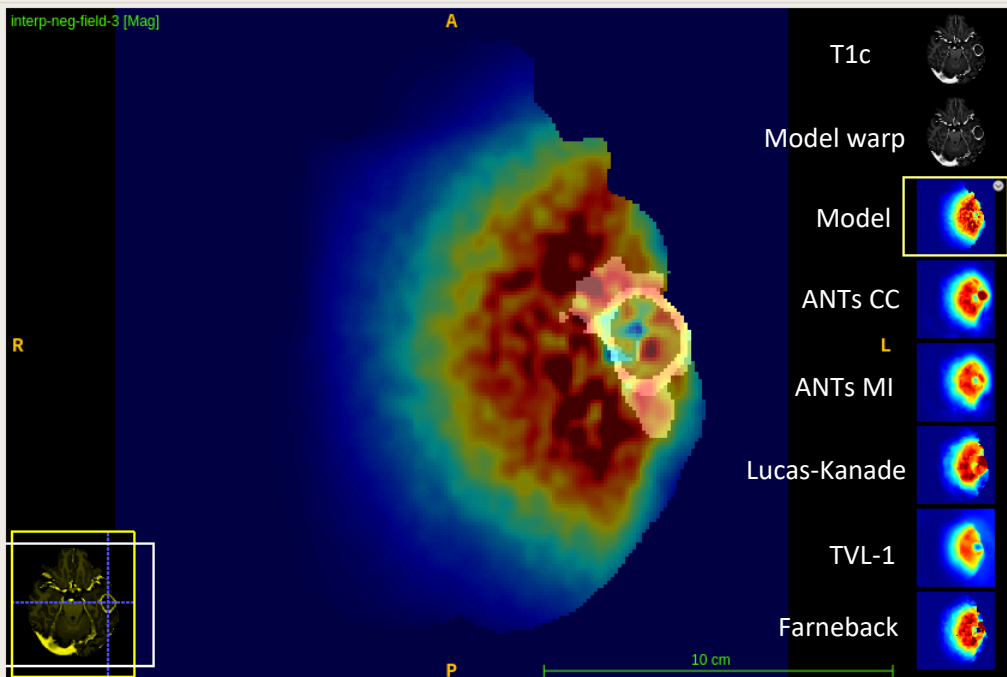
Label under cursor:

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Segmentation Labels

Active label:
Label 1Paint over:
All labelsOverall label opacity:
50

3D Toolbar



T1c

Model warp

Model

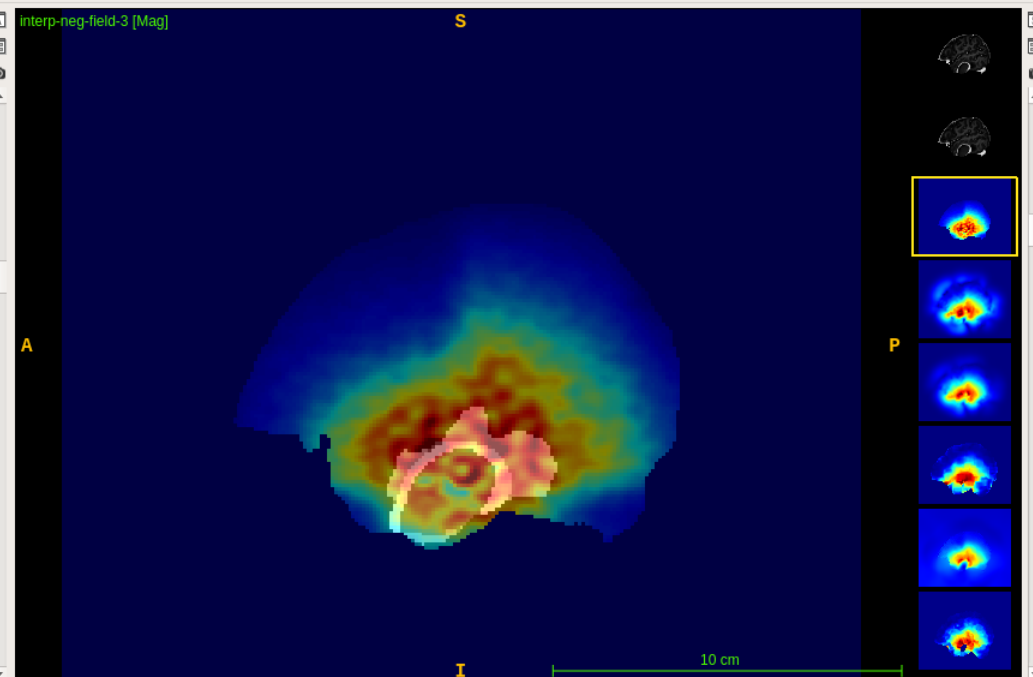
ANTs CC

ANTs MI

Lucas-Kanade

TVL-1

Farneback



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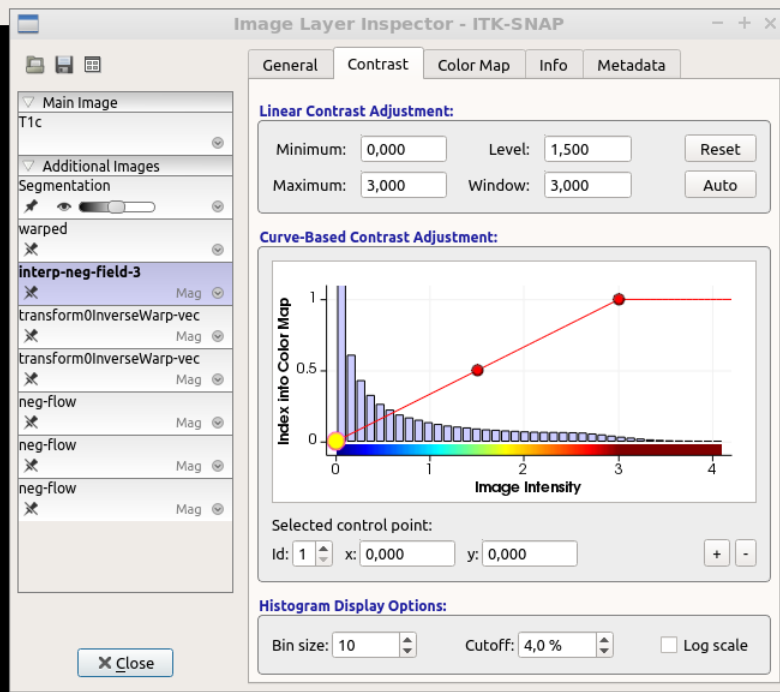


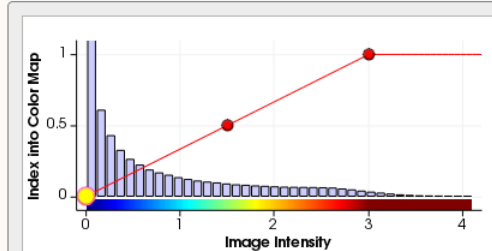
Image Layer Inspector - ITK-SNAP

General Contrast Color Map Info Metadata

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Maximum: 3,000 Window: 3,000 Auto

Curve-Based Contrast Adjustment:



Selected control point:

Id: 1 x: 0,000 y: 0,000 + -

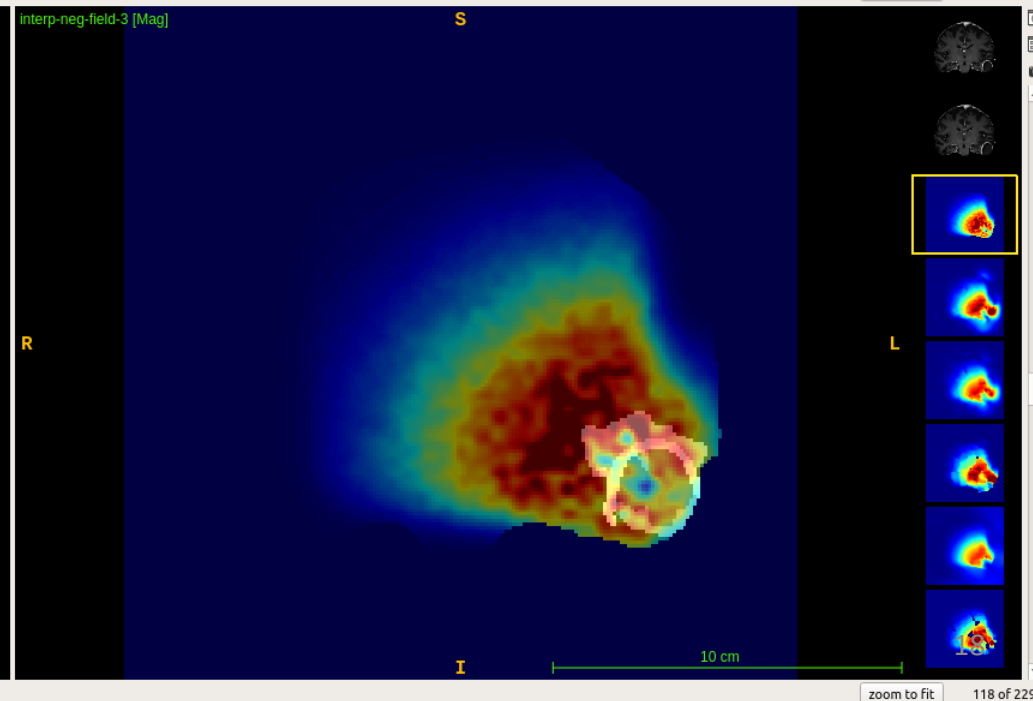
Histogram Display Options:

Bin size: 10 Cutoff: 4,0 % Log scale

update

zoom to fit

58 of 193



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L

zoom to fit

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ITK-SNAP Toolbox

Main Toolbar



Cursor Inspector



Cursor position (x,y,z):

42 120 54

Intensity under cursor:

Layer	Intensity
normdiff-relative	1.713
normdiff-relative	1.705
normnegdiff-re...	1.894
normnegdiff-re...	1.113
Segmentation	1

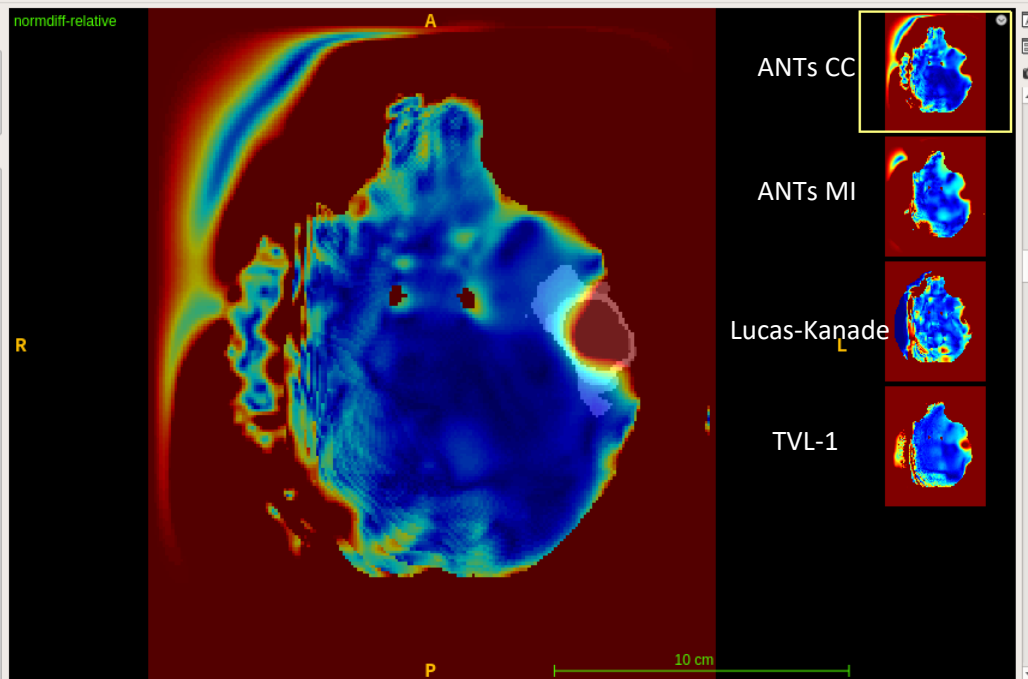
Label under cursor:

0 Clear Label

Segmentation Labels

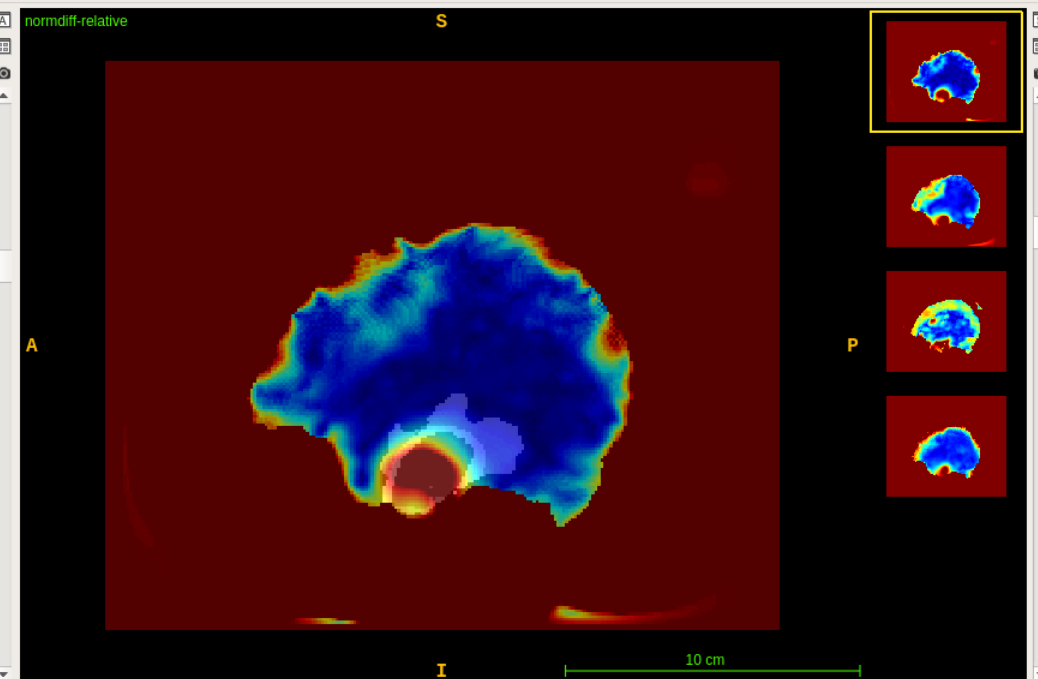
Active label:
Label 1Paint over:
All labelsOverall label opacity:
50

3D Toolbar



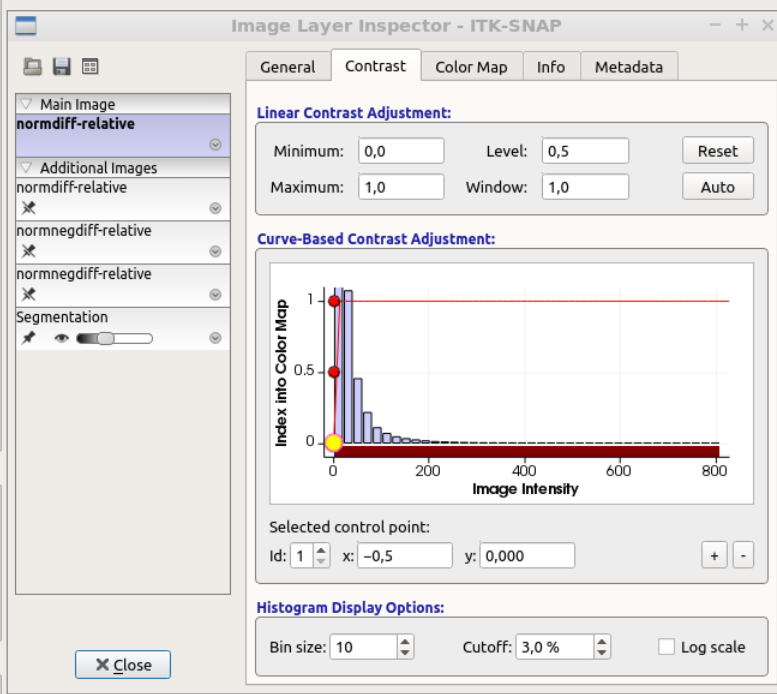
zoom to fit

54 of 193



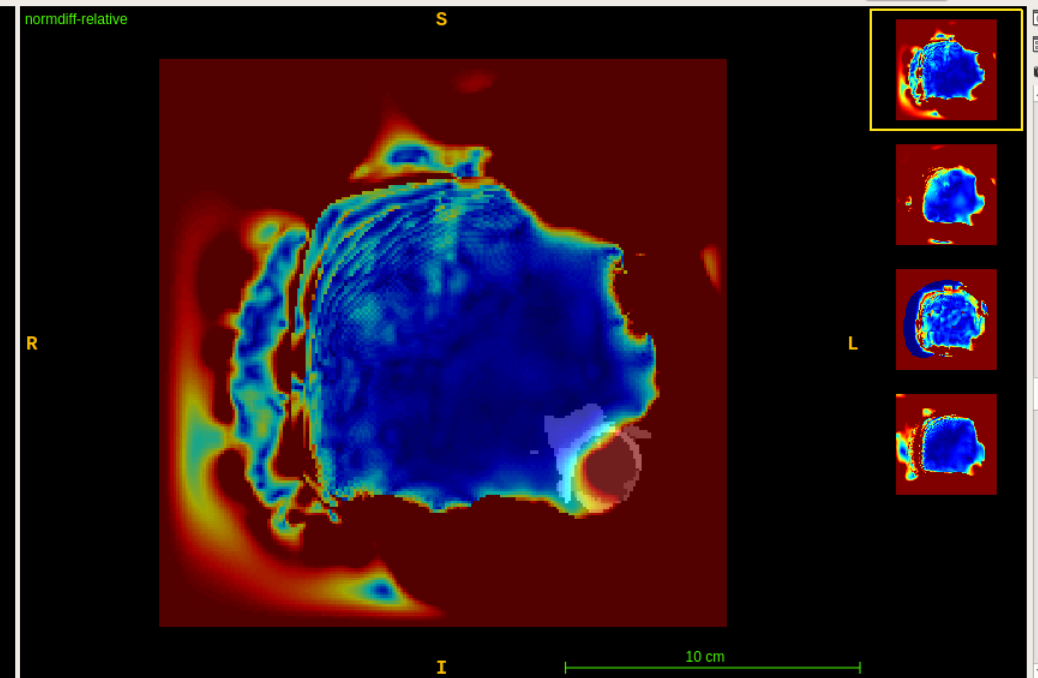
zoom to fit

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update

zoom to fit



zoom to fit

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A

Penetration →

Irregularity ↓

... in edema and contrast-enhanced lesions ($P < 0.03$)

... with ANTs SyN CC and Farneback performing highest ($P < 0.002$)

Non-rigid registration
had highest
performance on:

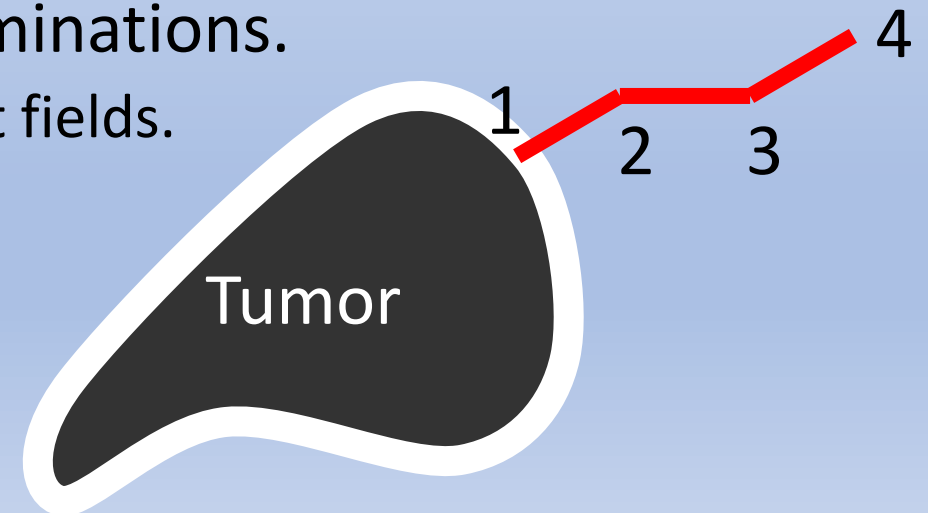
3 mm displacement
(max) ($P < 0.001$)

... high
penetration
($P < 0.001$)

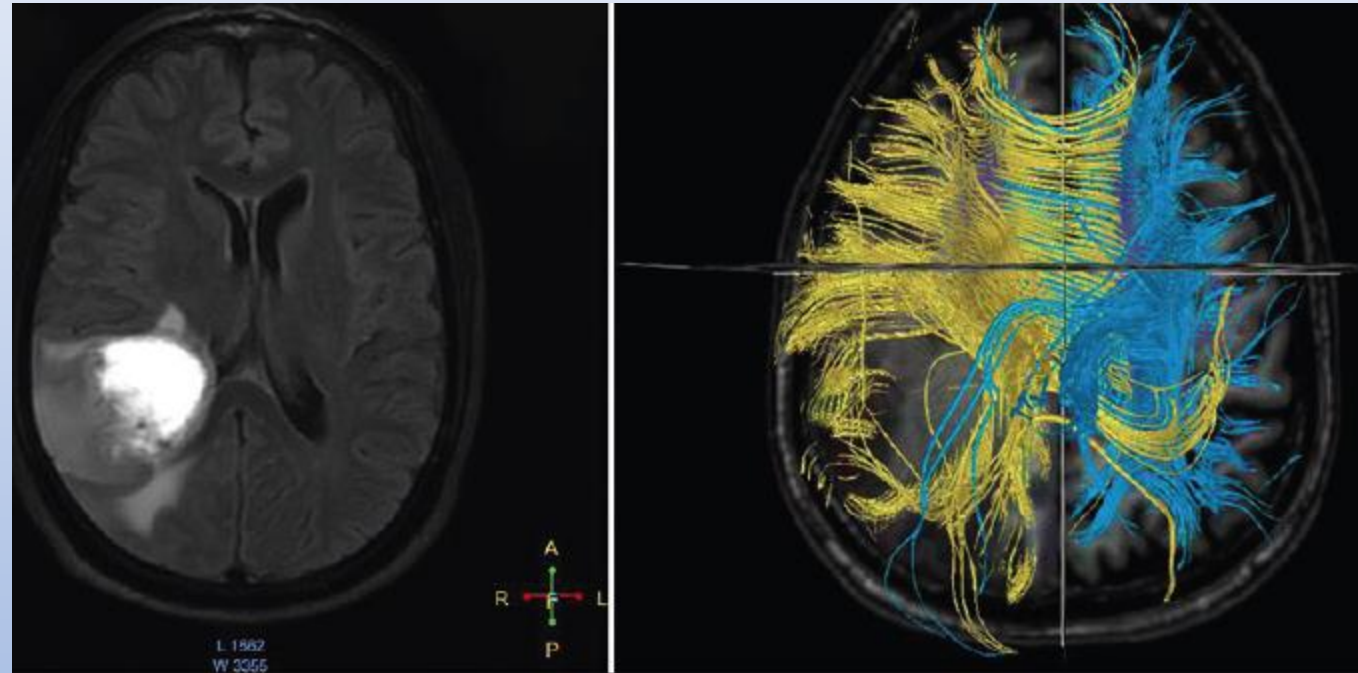
Irregularity ↓

Paper 3?: Displacements to characterize longitudinal tumor behavior

- Paper 2 concludes that non-rigid registration methods such as ANTs SyN CC
 1. can be used to describe small displacement of tissue in cancer progression (3 *mm* opposed to 8 *mm*).
 2. perform well in contrast-enhanced and edema lesions (-"- necrosis).
- We follow all the voxels in the first time-point contrast-enhanced lesion over the time span of all MRI examinations.
 - **Path lines** from a sequence of displacement fields.



In contrast: Fibers from diffusion tractography (diffusion tensor imaging) are stream lines



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

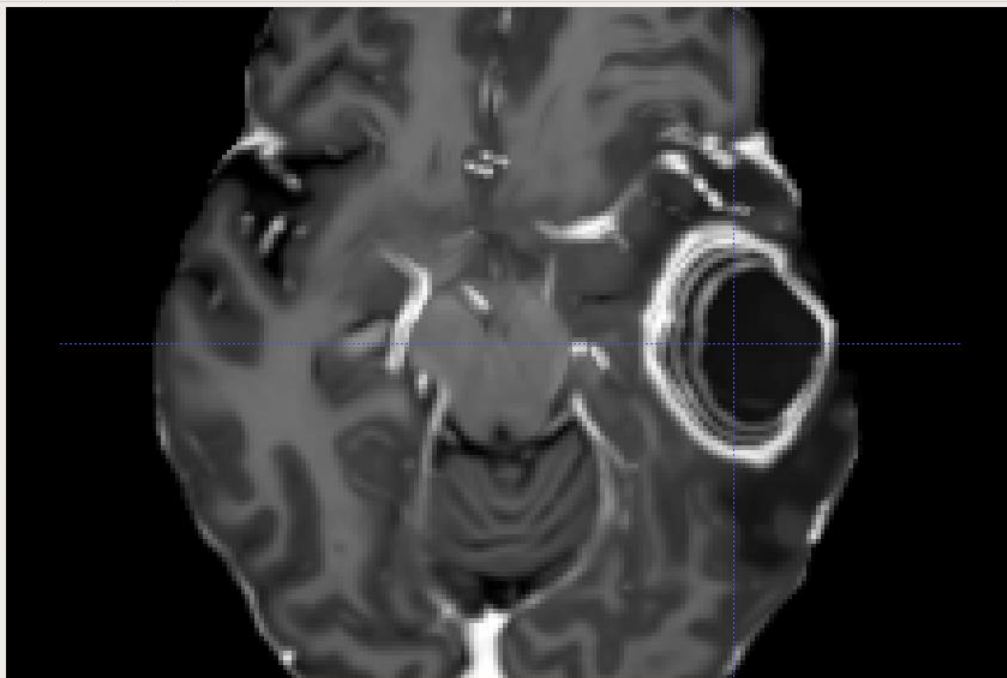
Paint over:

All labels

Overall label opacity:

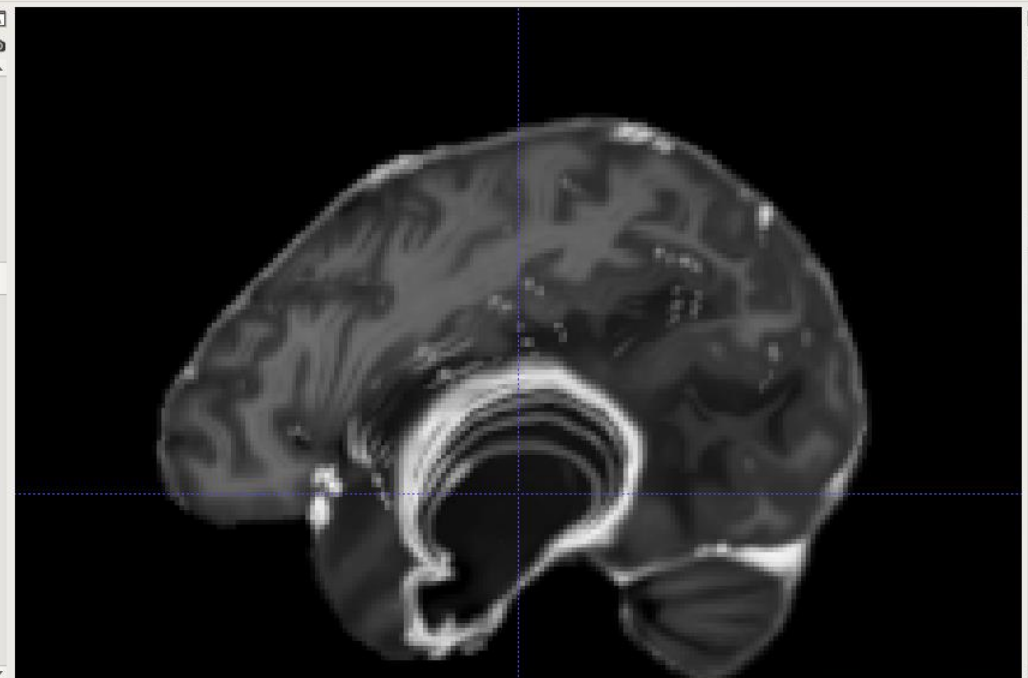
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3D Toolbar



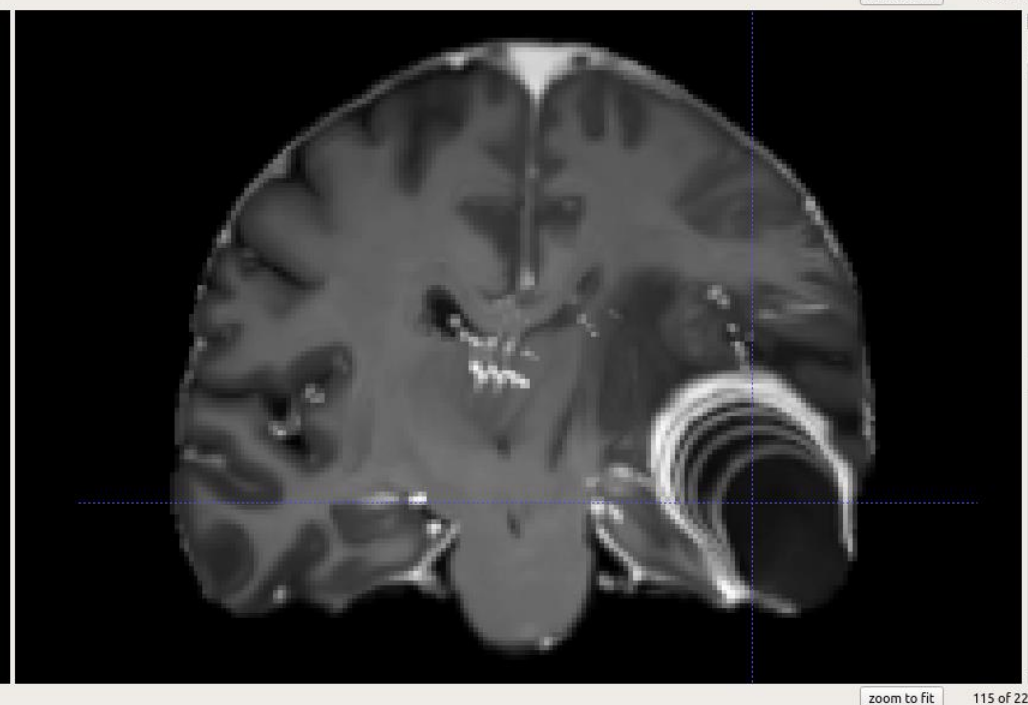
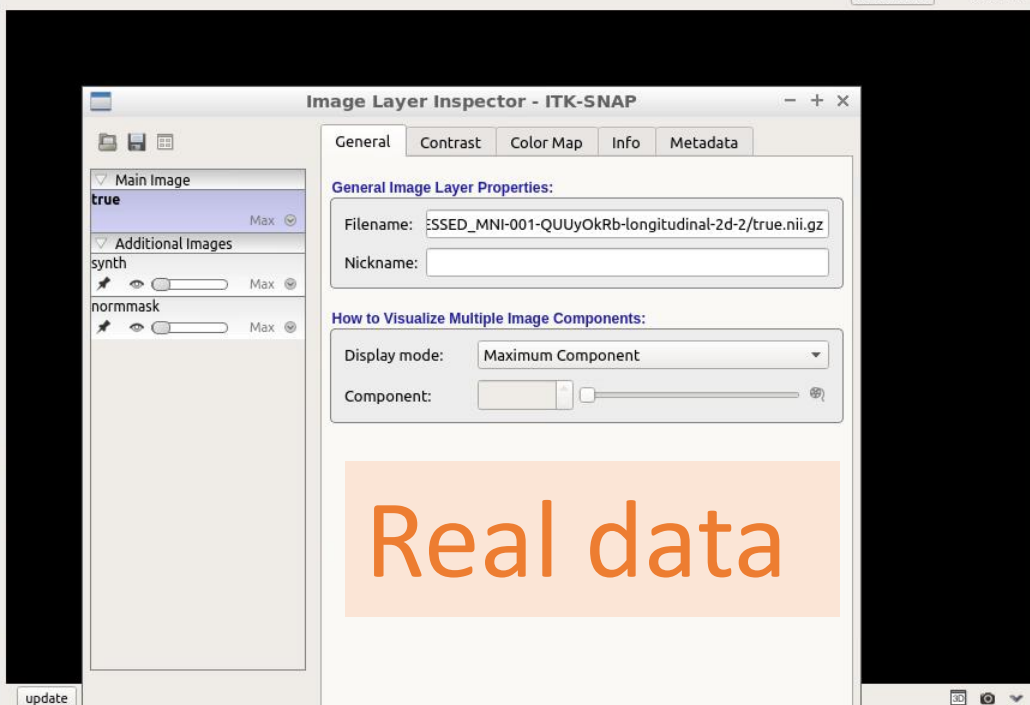
zoom to fit

65 of 193



zoom to fit

49 of 193



zoom to fit

115 of 229



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

Active label:

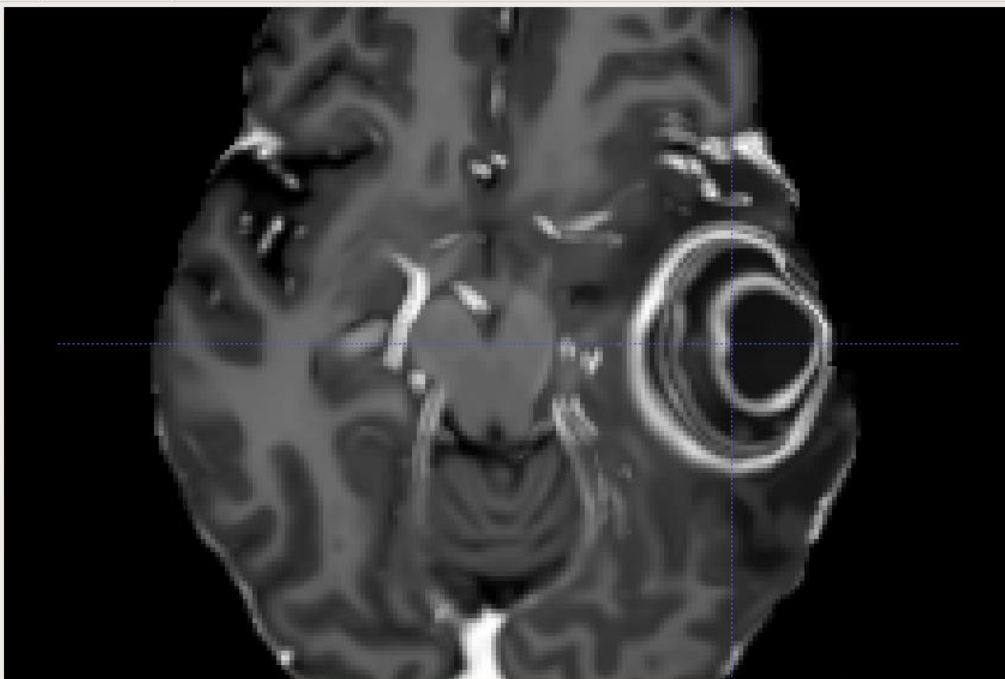
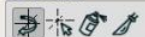
Label 1

Paint over:

All labels

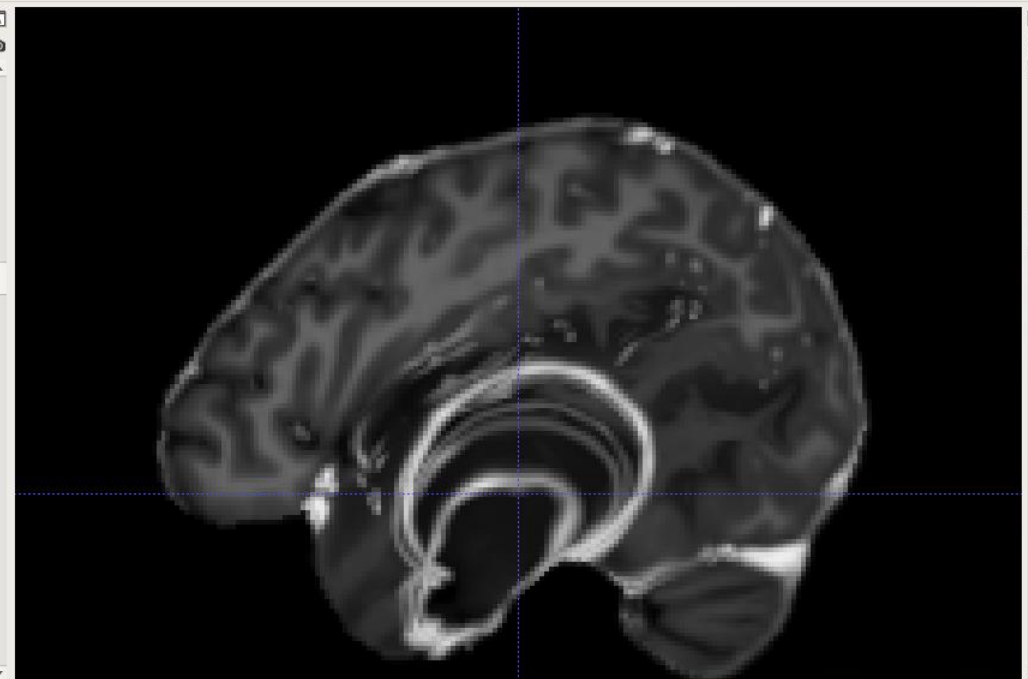
Overall label opacity:

50



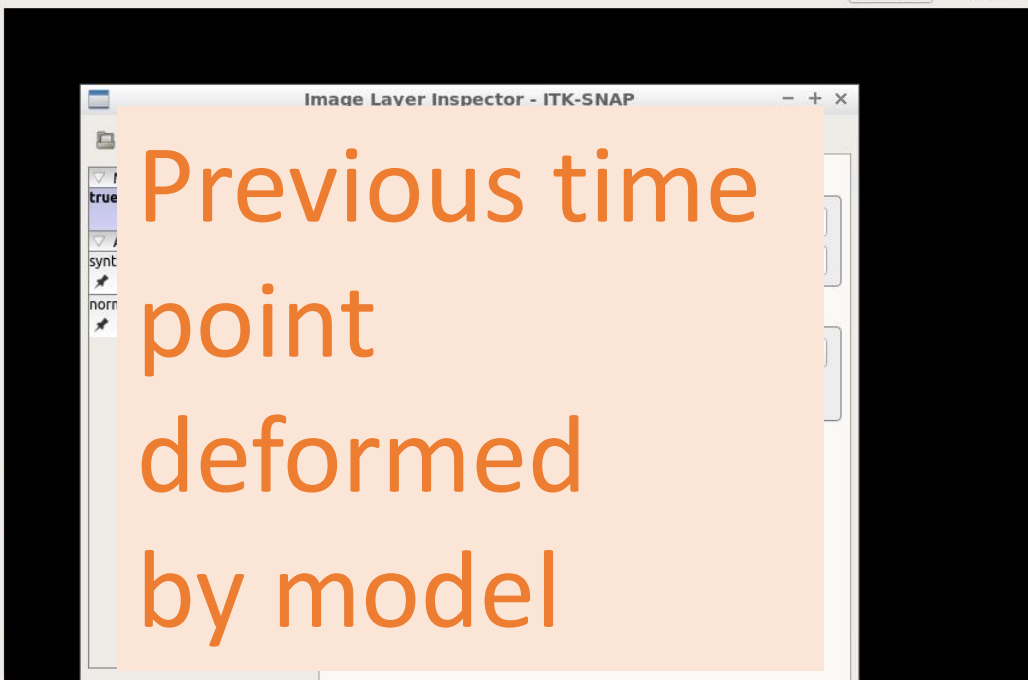
zoom to fit

65 of 193

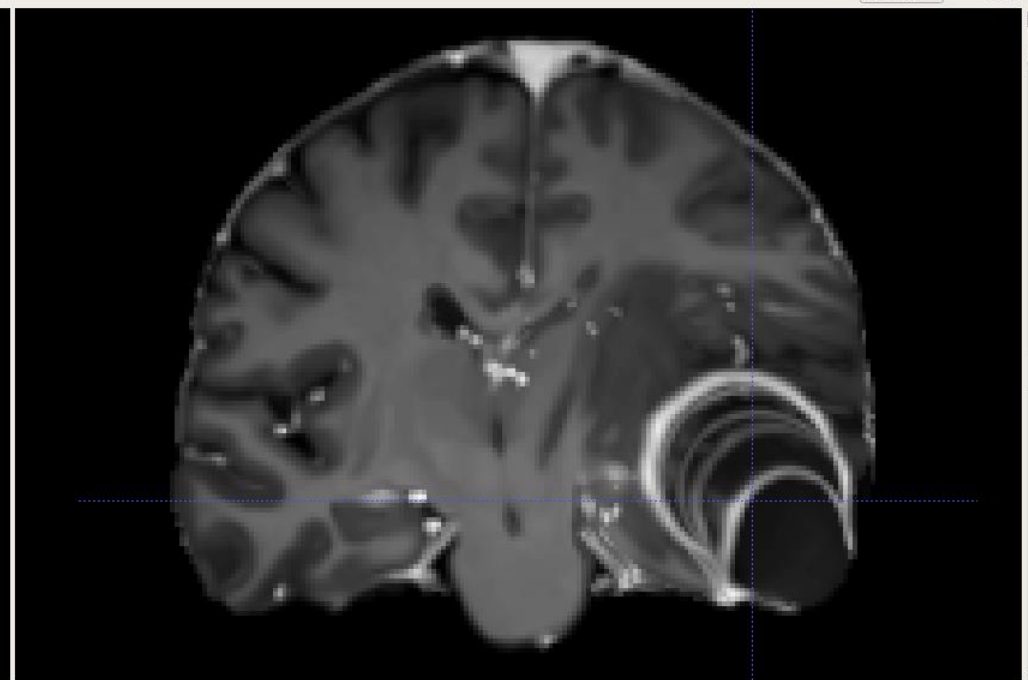


zoom to fit

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update



zoom to fit

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ITK-SNAP Toolbox

Main Toolbar



Cursor Inspector



Cursor position (x,y,z):

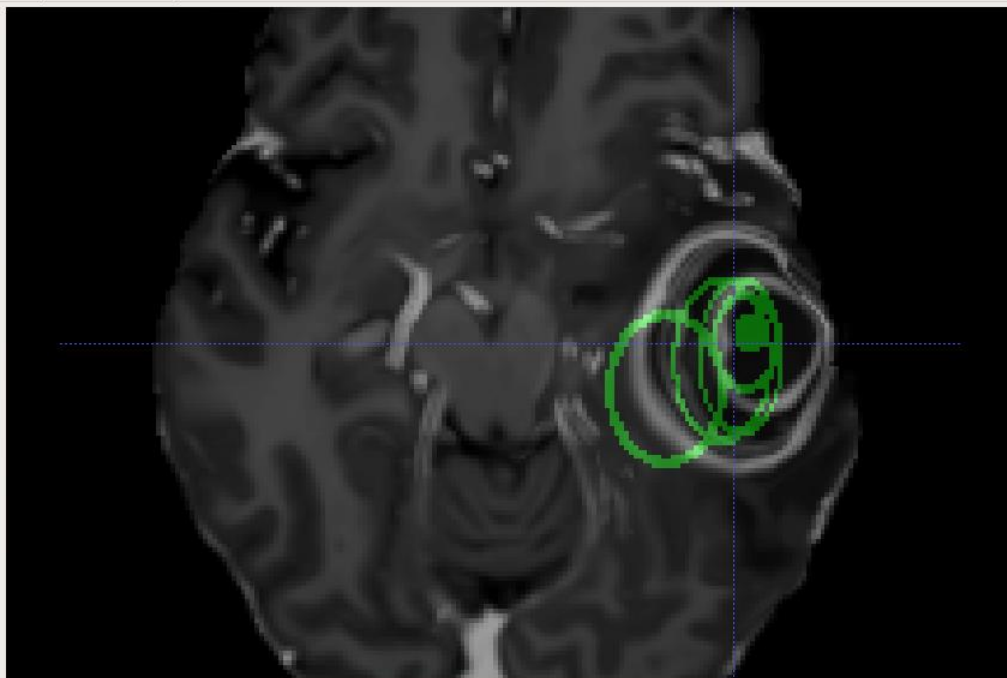
49 115 65

Intensity under cursor:

Layer	Intensity
true	19
synth	44.16
normmask	0

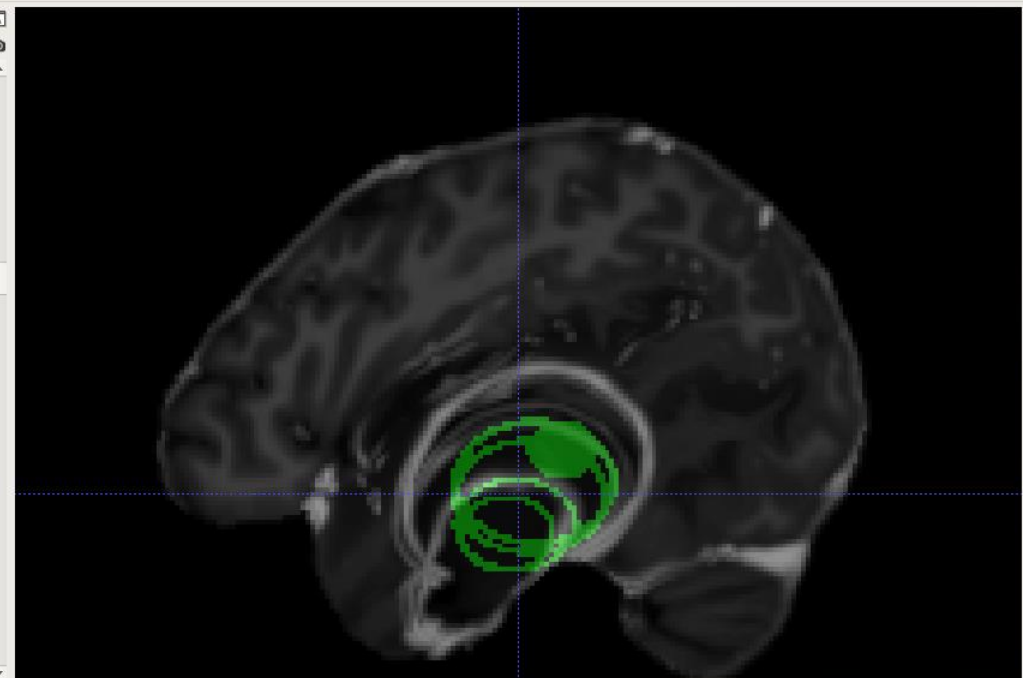
Label under cursor:

0 Clear Label



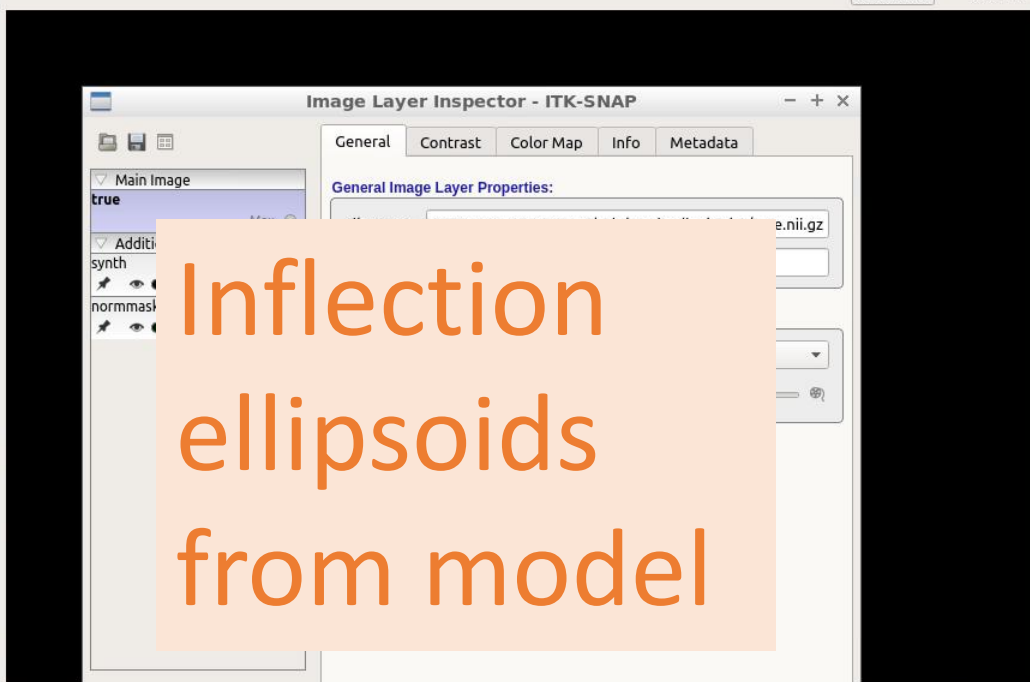
zoom to fit

65 of 193



zoom to fit

49 of 193



update

Segmentation Labels

Active label:

Label 1

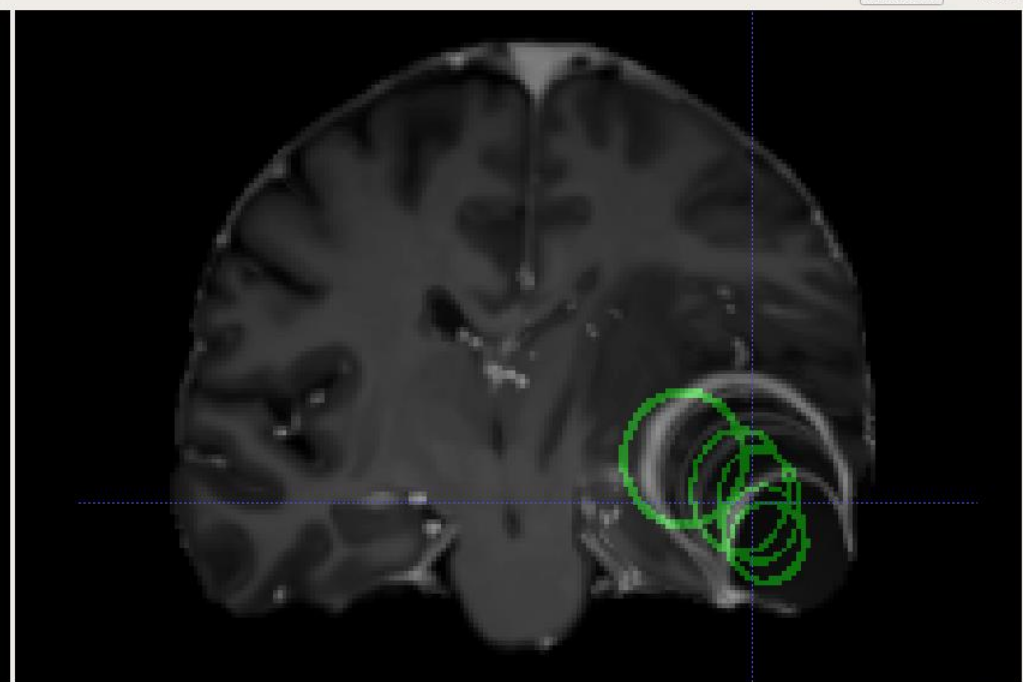
Paint over:

All labels

Overall label opacity:

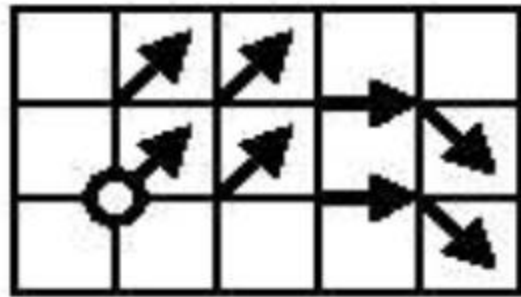
50

3D Toolbar

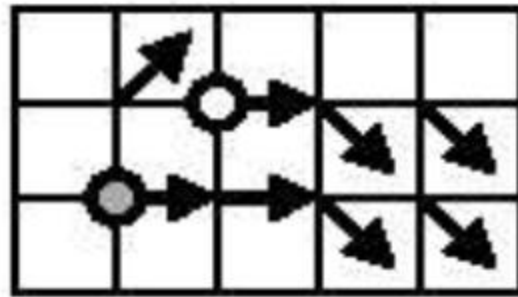


zoom to fit

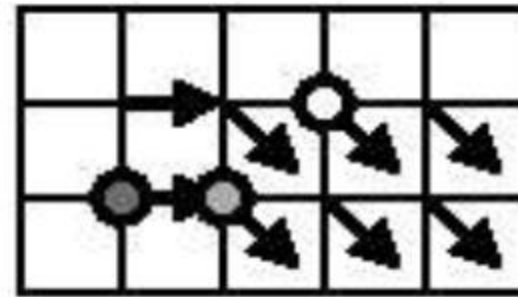
115 of 229



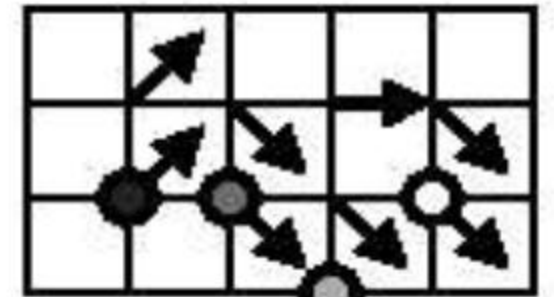
t_0



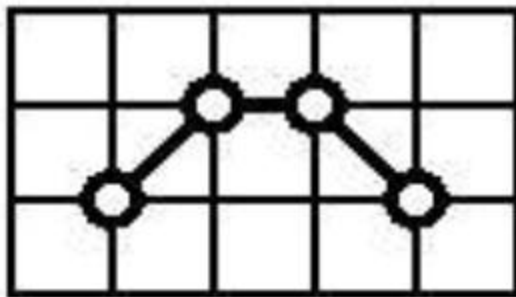
t_1



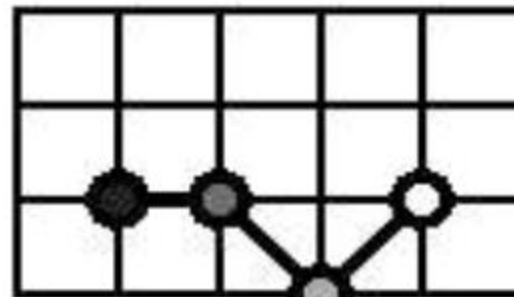
t_2



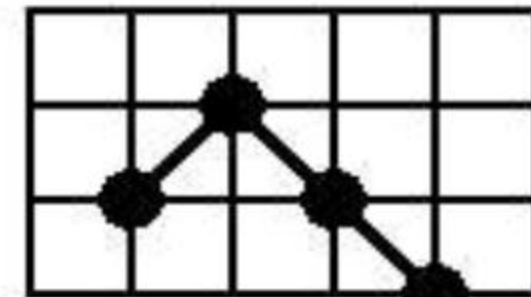
t_3



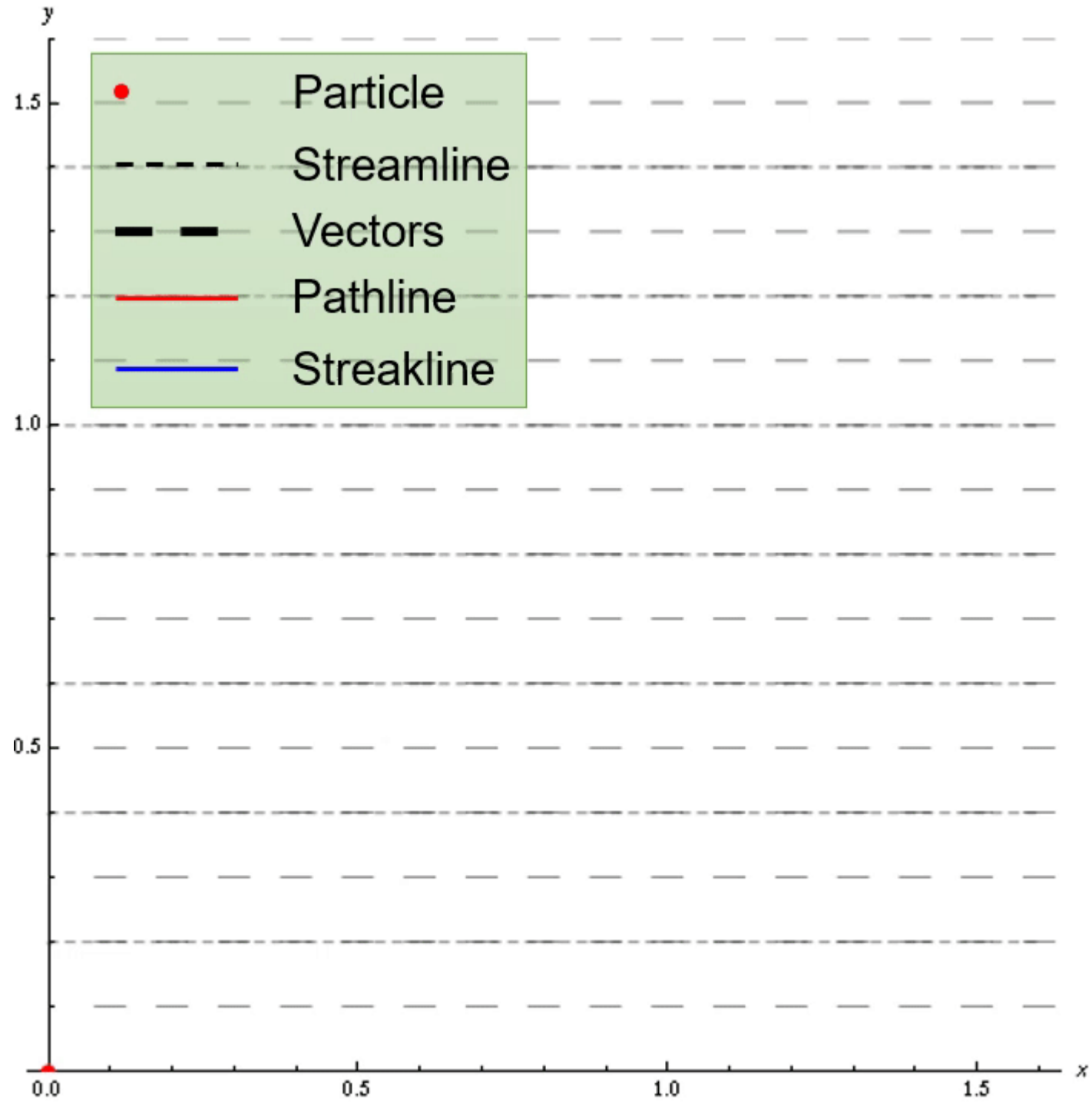
path line



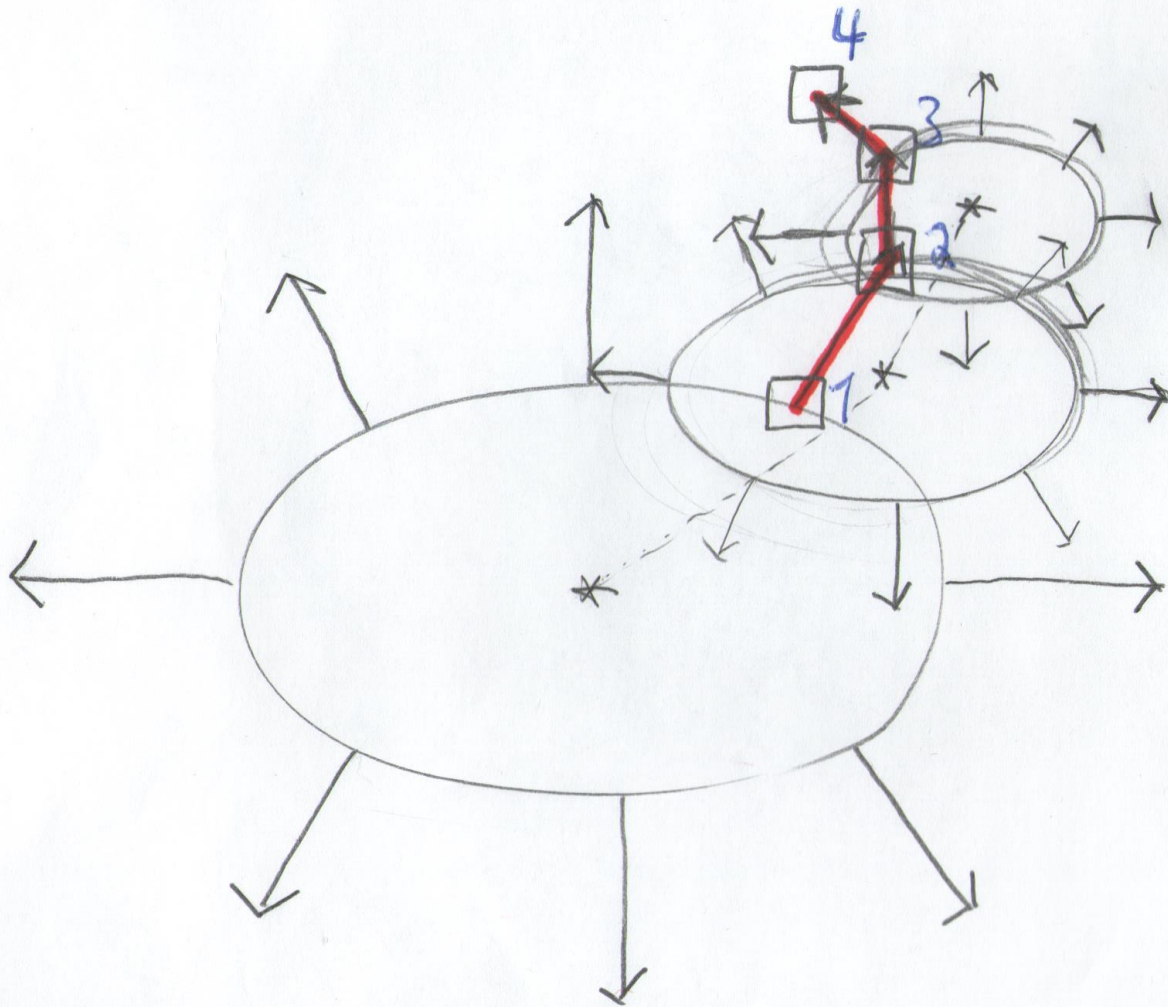
streak line



stream line for t_3



Computing a path line from the model



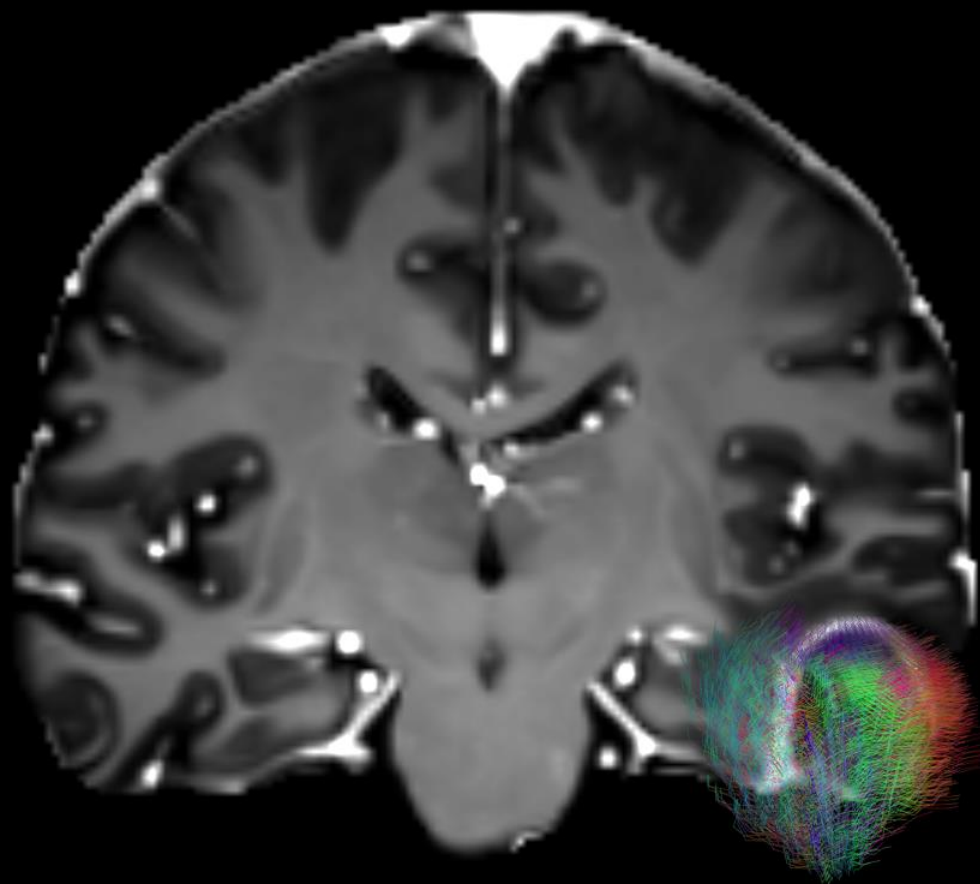
- PATH LINE FOR VOXEL
- VOXEL
- 1-4 TIME POINTS
- PATH OF MODEL
(= CENTER OF TUMOR)

resetCamera

animated

▸ Growth fibers

▸ Tumor volume



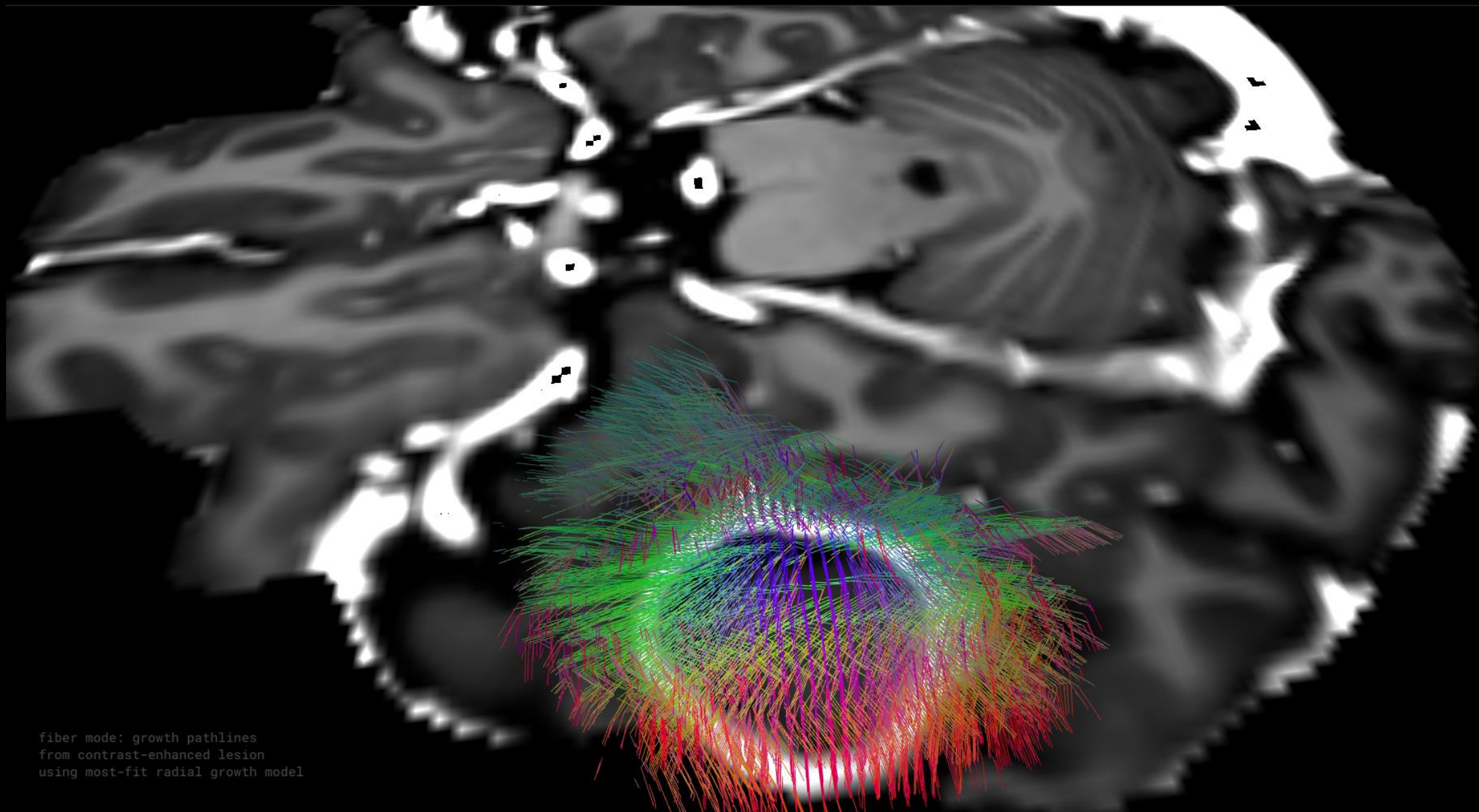
fiber mode: growth pathlines
from contrast-enhanced lesion
using most-fit radial growth model

resetCamera

animated

▸ Growth fibers

▸ Tumor volume



fiber mode: growth pathlines
from contrast-enhanced lesion
using most-fit radial growth model

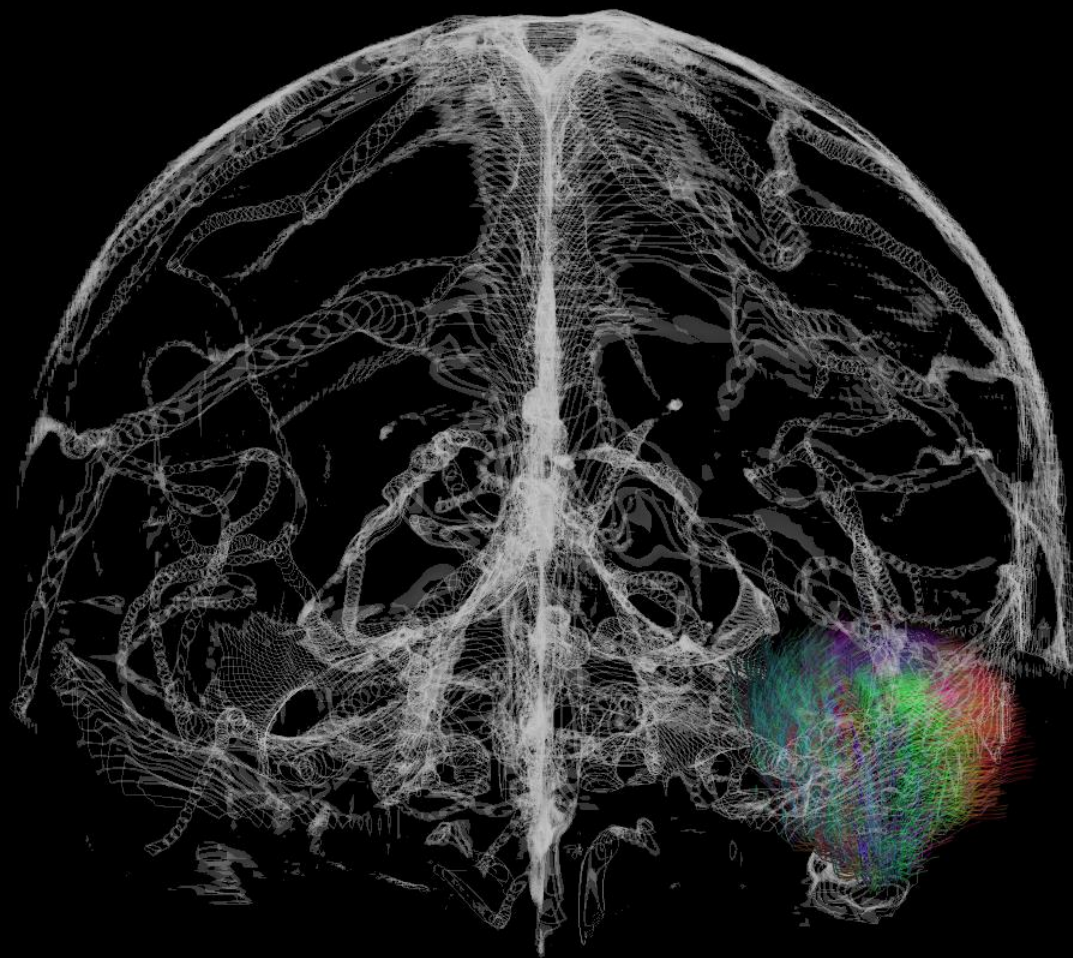
[about](#)

resetCamera

animated

▸ Growth fibers

▸ Tumor volume



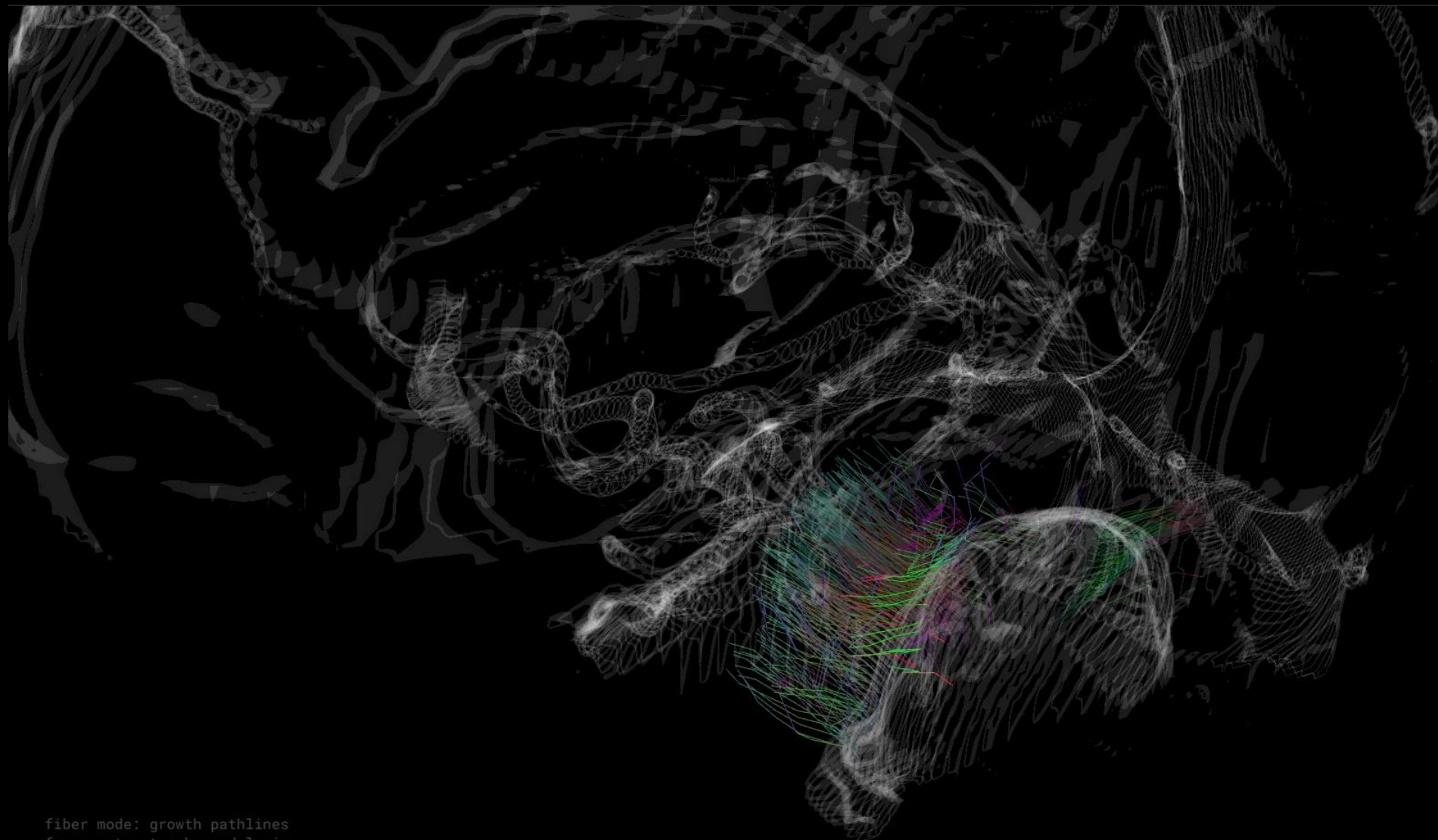
fiber mode: growth pathlines
from contrast-enhanced lesion
using most-fit radial growth model

resetCamera

animated

▸ Growth fibers

▸ Tumor volume



fiber mode: growth pathlines
from contrast-enhanced lesion
using most-fit radial growth model

Skalere retninger for ulike vekstrater

time.perf_time()

Plotte forskjellige baner:

cancer-sim/PhD todo list

- Geometrisk bounding box senter fra cancer-sim
 - * Bruke Elies masker: necrosis, edema & enhancing, union or not
 - * Bruke manuelle segmenterte masker
- Massesenter fra masker
 - * Bruke Elies masker: necrosis, edema & enhancing, union or not
 - * Bruke manuelle segmenterte masker

Variable vekstrater -> re-implementering i Pytorch med bruk av gradient-basert optimalisering.

Freesurfer cube marching av sim.nii.gz, så ikkelineær registrering av objekter

Fikse feil i longitudinal-fit.sh hvor den prøver å simulere med beste parametre for alle tidspunktene

Spatial Transformer to find bounding boxes

pathlines from longitudinal non-rigid registration

voxelmorph as a faster alternative to ANTs SyN

correction: It is not linear radial

original displaced voxel intensity and real intensity difference comparison during pathlines

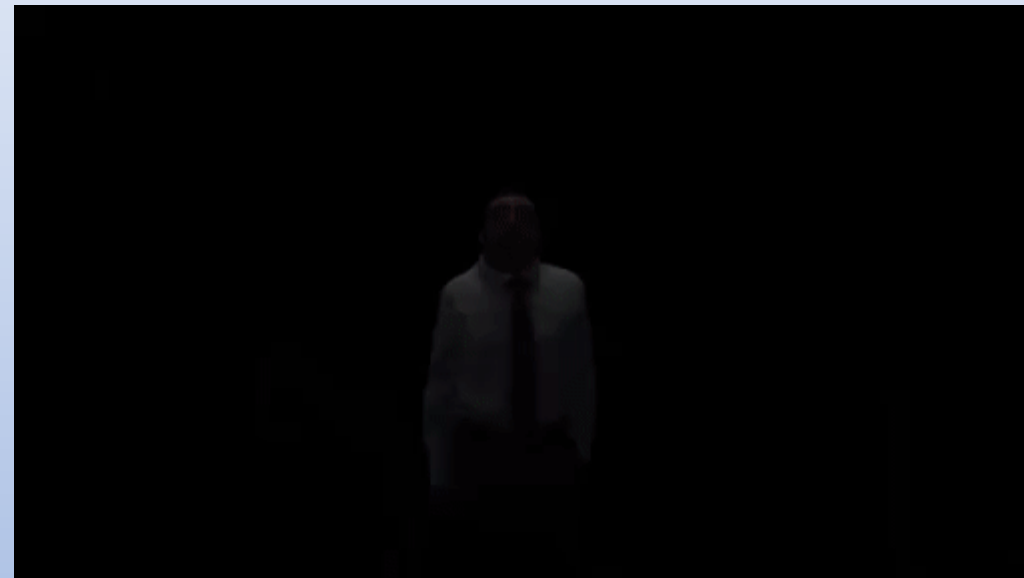
New limitation: interpolation errors in deformation

Fibre i cancer-sim er sentrert - lag nye fibre med fibre som starter i enden av vokal.

Visualisere lengden på fibre der de starter

Encode color as velocity on pathlines

USE cancer sim search to guide forward or backward in time registration



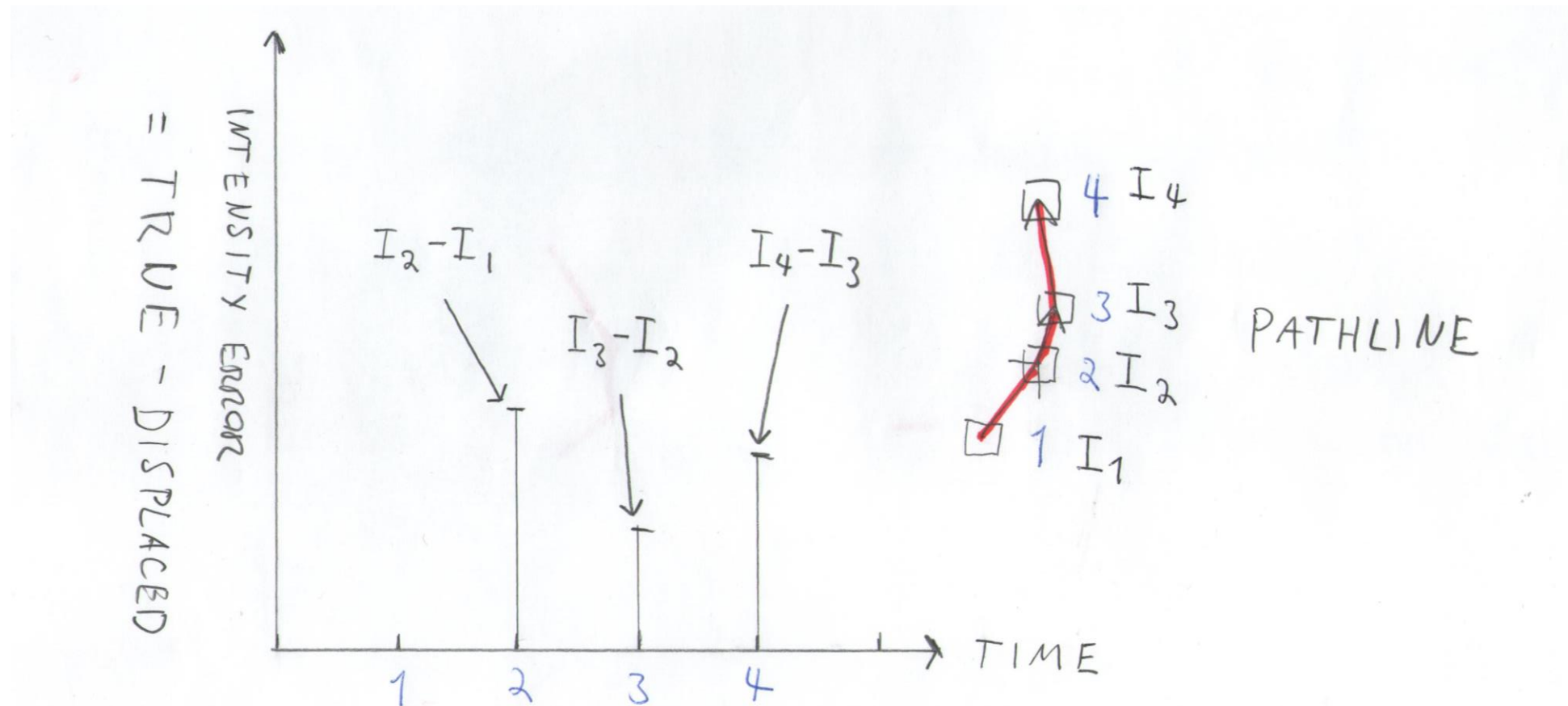
Focus on writing

Prepare tracking demo



Not only displacements

- Quantifying intensity change during displacement



Real
growth
case

T1-weighted
post-contrast
~3 years
glioblastoma

Maximum
Intensity
Projection
(MIP)

(SAILOR)

animation



Contrast-enhanced

Necrosis

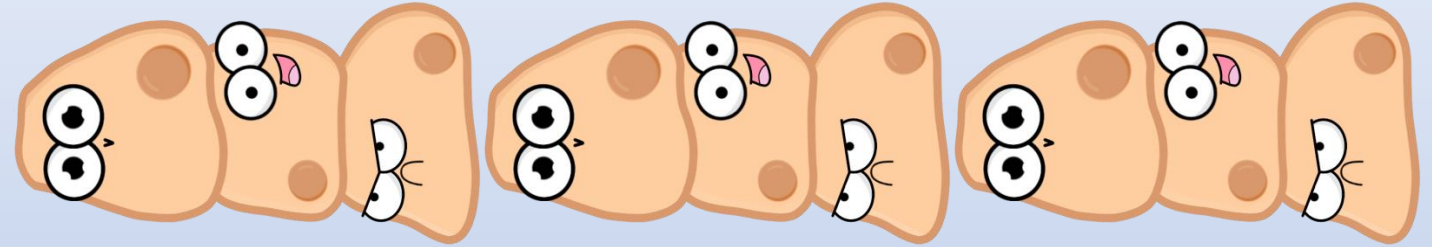
(U87 cell line)

Healthy

Time



14 μm



3 mm ?

Displacement

$$\frac{3 * 10^{-3}}{14 * 10^{-6}} \approx +214 \text{ U87 cells}$$



...

