Displacements in brain cancer imaging

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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

Fat isolating axons (nerve fibers) between neurons


https://en.wikipedia.org/wiki/Astrocyte
Alterations: IDH: isocitrate dehydrogenase

Selection: IDH mutant

Driver mutation: IDH wild-type
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.

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 multipl. cortical and subcortical regions.
- These corrections are important when comparing vascular and structural MRI in glioblastoma.

Contrast-enhanced

Necrosis

Healthy

14 µm (U87)

Displacement

Mass effect
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

2D

Displacement

3D

Tumor cross section

Tumor cross section
Model of displacements from one examination to the next

Comparison of brain penetration with different displacements:

(A) 3 mm displacement
(B) 8 mm displacement
ANTs MI
Farneback
TVL-1
Lucas-Kanade
ANTS CC
Model warp
Model
ANTS MI
Lucas-Kanade
TVL-1
Farneback

Linear Contrast Adjustment:
Minimum: 0.000
Maximum: 5.000
Level: 1.500
Reset

Curve-Based Contrast Adjustment:
Selected control point:
Histogram Display Options:
Bin size: 10
Cuts/Fl: 4.0 %
Log scale
Non-rigid registration had highest performance on:

- 3 mm displacement (max) (P<0.001)
- ... high penetration (P<0.001)

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

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

Real data
Previous time point deformed by model
Inflection ellipsoids from model
Path line

Streak line

Stream line for $t_3$
https://en.wikipedia.org/wiki/Streamlines,_streaklines,_and_pathlines
Computing a path line from the model

- PATH LINE FOR VOXEL
- VOXEL
- 1-4 TIME POINTS
- --- PATH OF MODEL
  (= CENTER OF TUMOR)
fiber mode: growth brackets from contrast-enhanced lesion using most-fit radial growth model
Skalere retninger for ulike vekstrater
time.perf_time()
Plotte forskjellige baner:

- 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

Fibrene i cancer-sim er sentrert - lag nye fibre med fibre som starter i enden av vokel.
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

3 mm ?

Time

Displacement

\[
\frac{3 \times 10^{-3}}{14 \times 10^{-6}} \approx +214 \text{ U87 cells}
\]

https://bionumbers.hms.harvard.edu/bionumber.aspx?s=n&v=0&id=108941