Surgical Planning Laboratory
Brigham and Women's Hospital
Boston, Massachusetts USA

a teaching affiliate of
Harvard Medical School

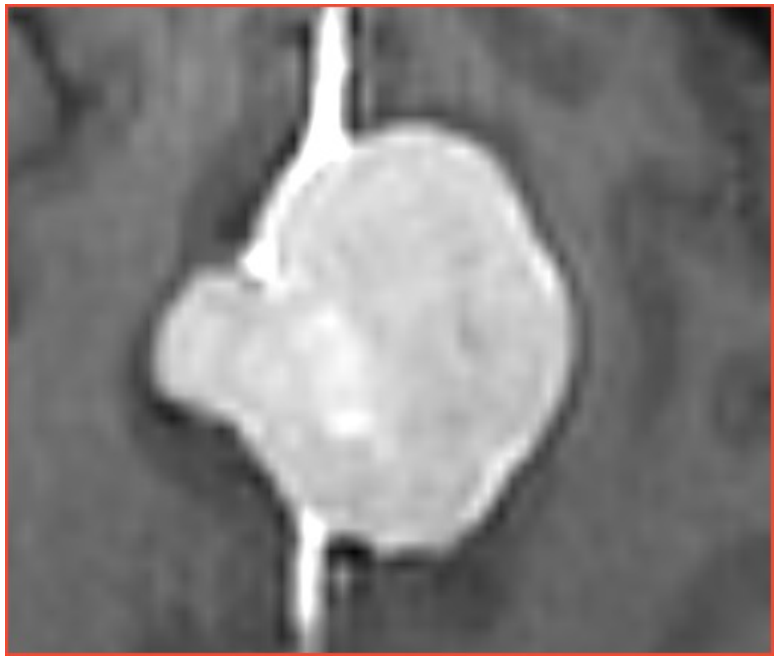
Detection of Volumetric Changes in Asymptomatic Meningiomas from MRI

Andriy Fedorov, Ph.D.

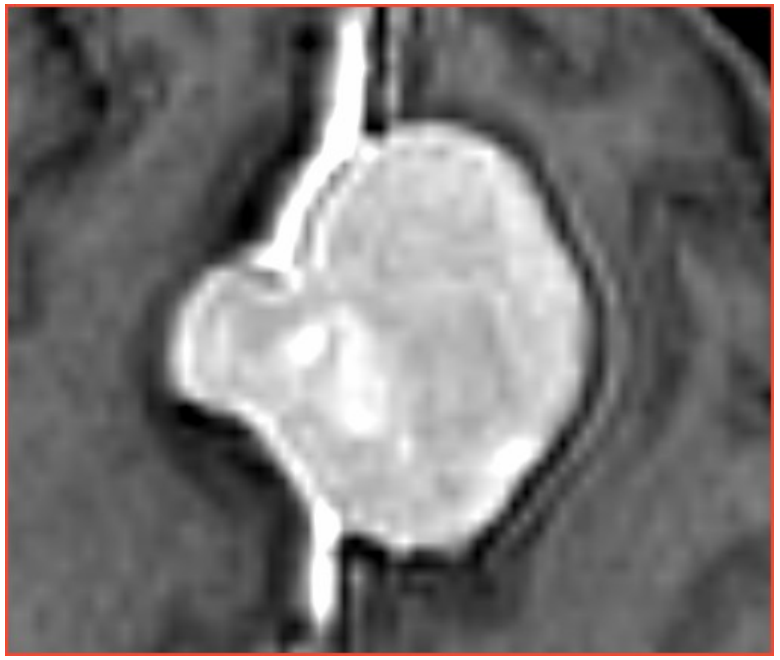
First Monday Seminar

9 November 2009

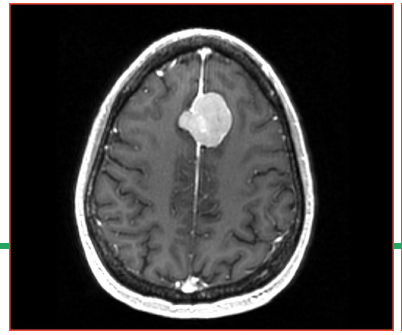
Has the tumor grown?

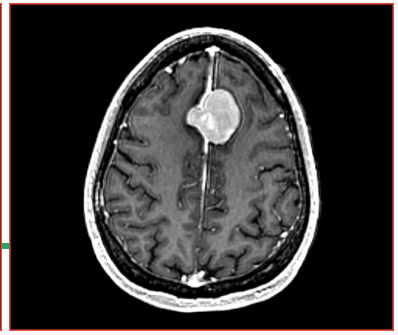


Baseline: June 2006

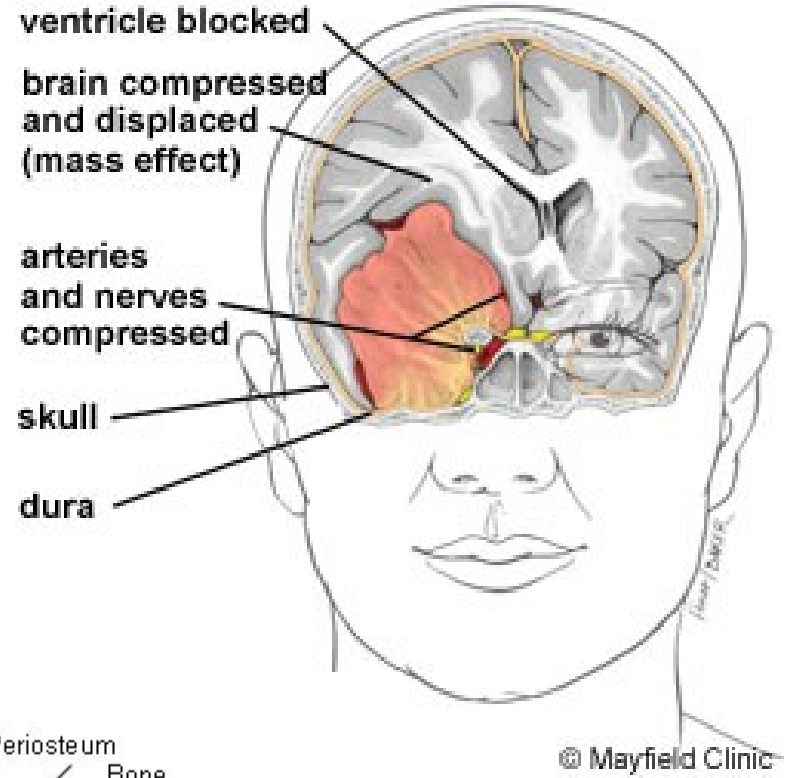


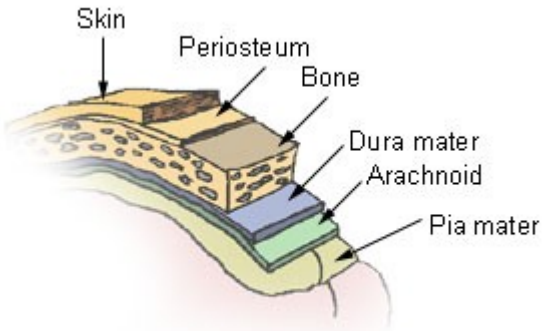
Followup: June 2007





Meningioma





Meninges of the CNS

- Origin: meninges of CNS
- 90% benign
- 2.9-13.0 cases per 100,000
- 4 times more likely in women
- 1/4th of all reported primary brain neoplasms

http://www.mayfieldclinic.com/PE-MENI.htm

Yano *et al.* 2006 study

- Asymptomatic meningioma treatment options
- 213 patients surgery vs 351 patient observation
- Only 6% of conservatively treated patients later developed symptoms

Yano et al., Indications for surgery in patients with asymptomatic meningiomas based on an extensive experience, J.Neurosurg 105, 2006

Incidence of morbidity within 3 months of surgery in 213 patients who initially had no symptoms

Type of Morbid Condition	No. of Patients (%)		
	Age <70 Yrs (159 patients)	Age ≥70 Yrs (54 patients)	Total (213 patients)
medical	6 (3.8)	3 (5.6)	9 (4.2)
surgery related	16 (10.1)	4 (7.4)	20 (9.4)
neurological	27 (17.0)	6 (11.1)	33 (15.5)
persistent	7 (4.4)	5 (9.3)	12 (5.6)

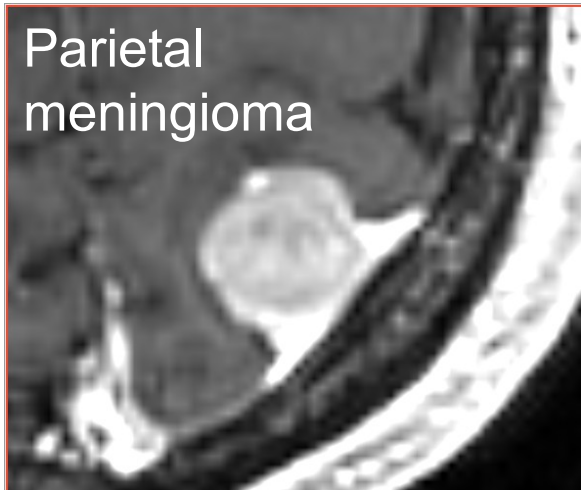
Asymptomatic meningiomas

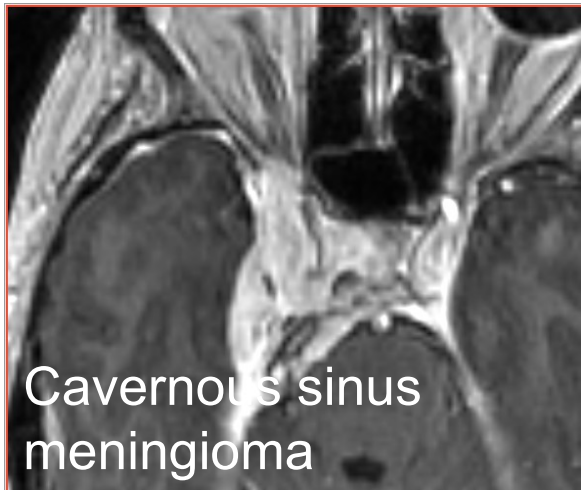
"Some die **from** *meningiomas, other(s) die* **with** *them. A neurosurgeon's role is to recognize these two sets of populations and give the benefit of surgery to those who need it and spare those who do not."*

Rangachary and Suskind, "Meningioma in the elderly and asymptomatic meningiomas", 1991

Radiologic appearance

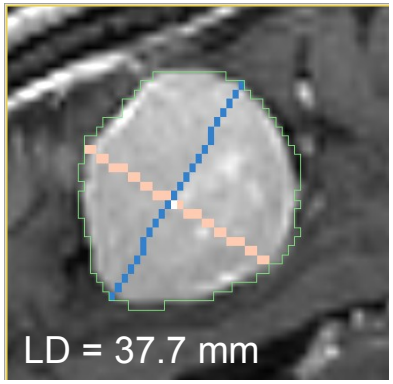
- Iso-intense to mildly hyper-intense in MRI
- Homogeneous enhancement w/ Gadolinium administered
- Most attached to meninges
- Morphology
  - Sessile or peduncular
  - *en plaque* (carpet-like)
  - detached (intra-ventricular)

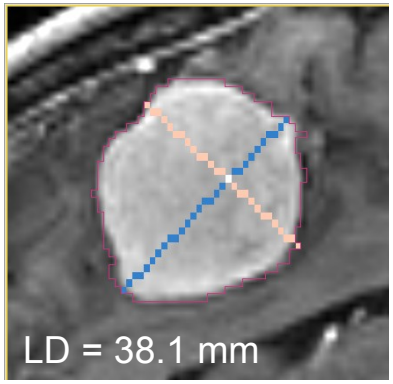


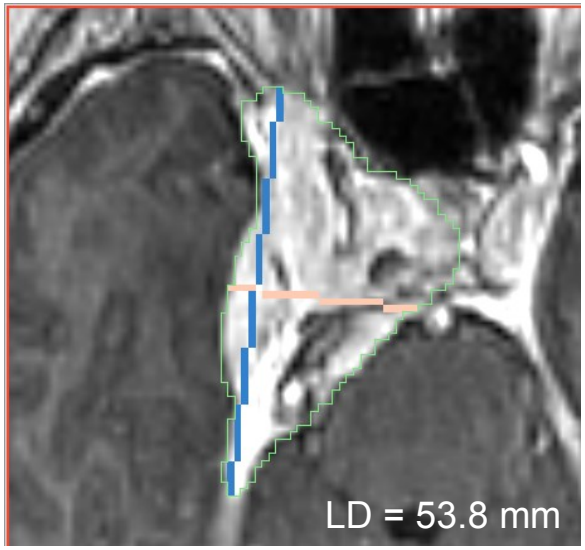


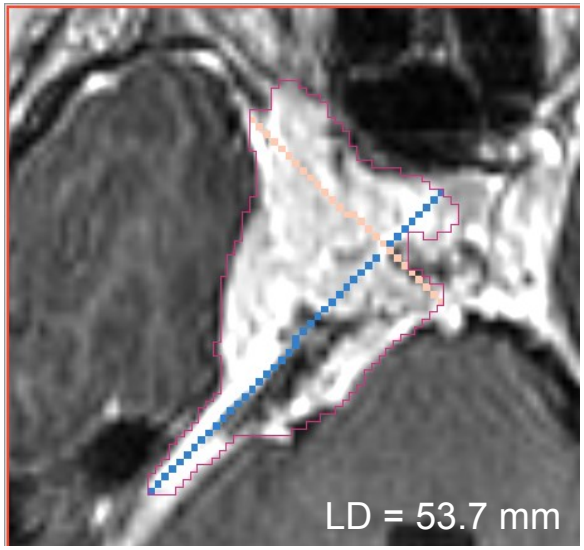
Tumor growth detection in clinic

- WHO: largest diameter and its perpendicular
- RECIST: Largest Diameter (LD) only
- “Progressive disease” at 20% LD increase



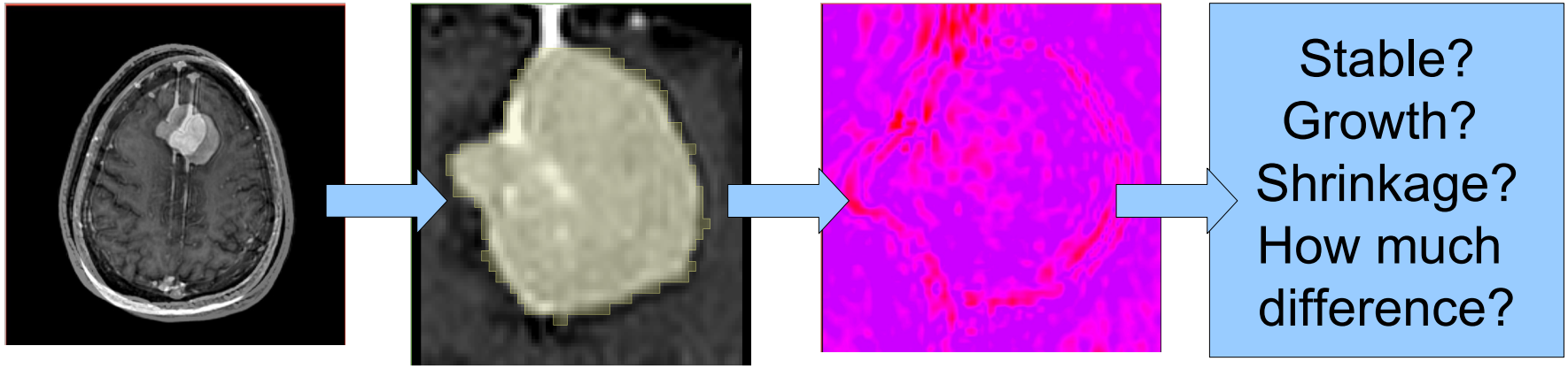






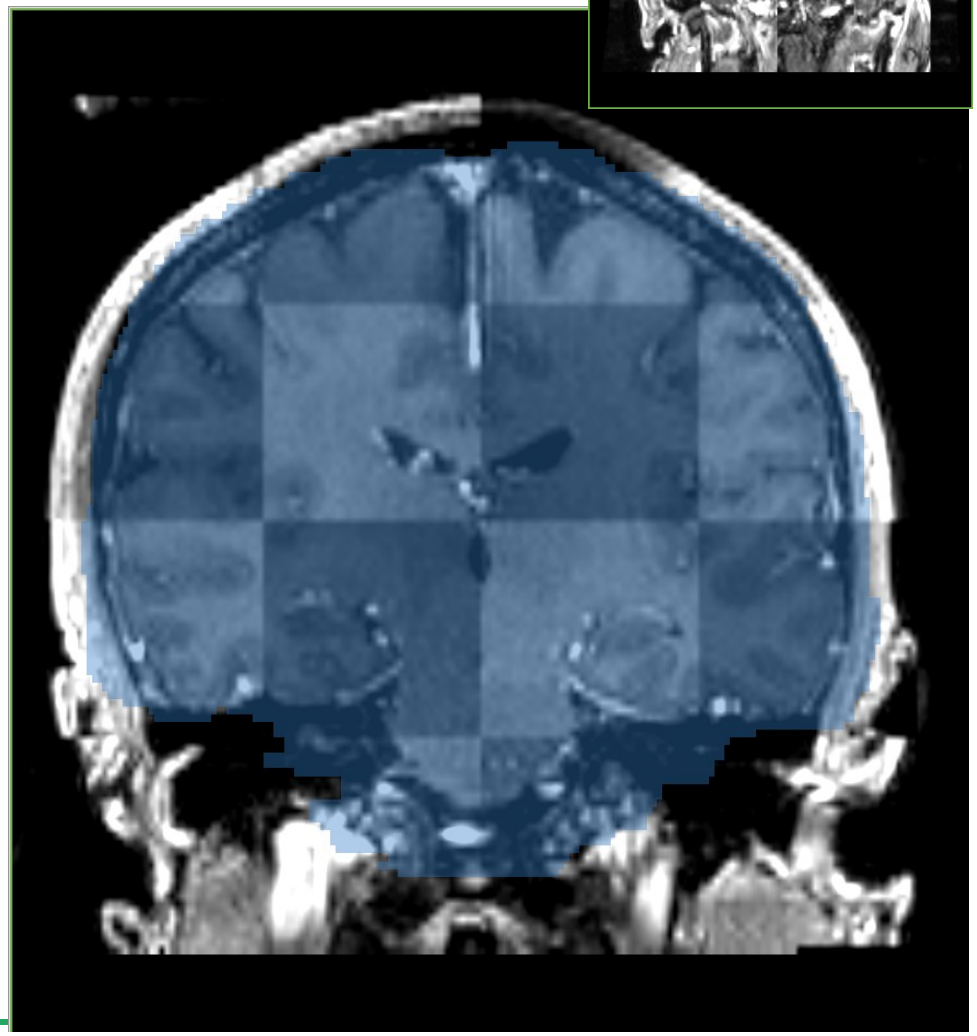
Proposed approach

- Eliminate all sources of difference irrelevant to tumor growth, analyze residual difference
- Global-to-local analysis
- *Automated* clinical research tool



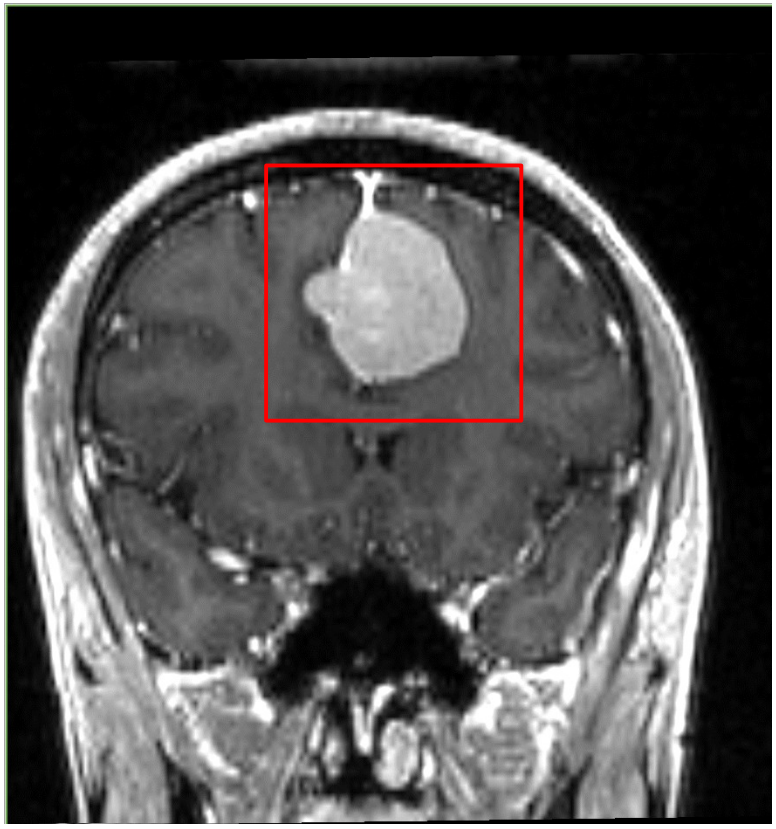
Spatial alignment

- Challenges:
  - Non-tumor-related anatomy changes
  - Scanner mis-calibration
  - Intensity profile differences
- Automatic image registration:
  - Mask brain volume
  - 12 DOF transformation
- User-supervised



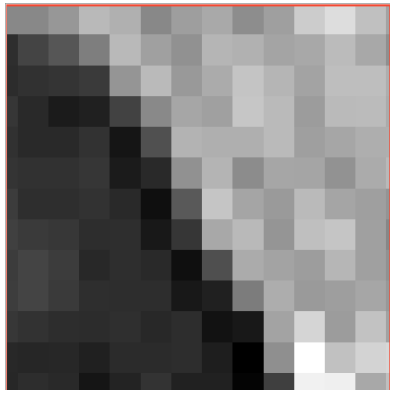
Spatial alignment

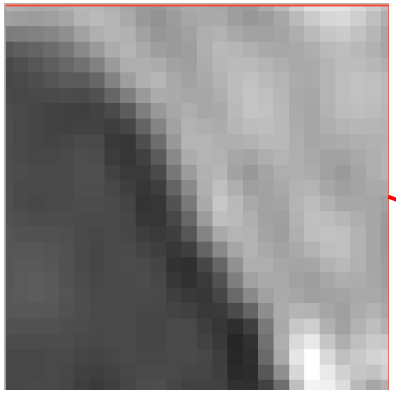
- Improved qualitative assessment
- User-guided subvolume selection
- Quantitative analysis within subvolume

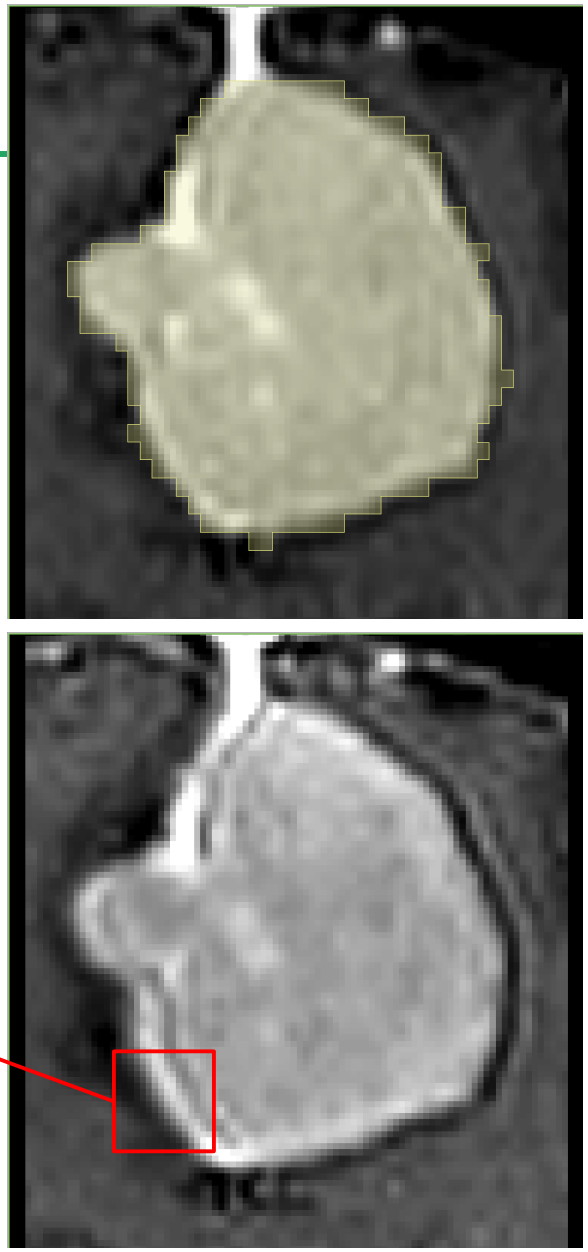


Subvolume analysis

- Focus on the subvolume with the tumor
- User provides segmentation of the tumor in the baseline scan
- Increase image resolution to account for partial volume effect

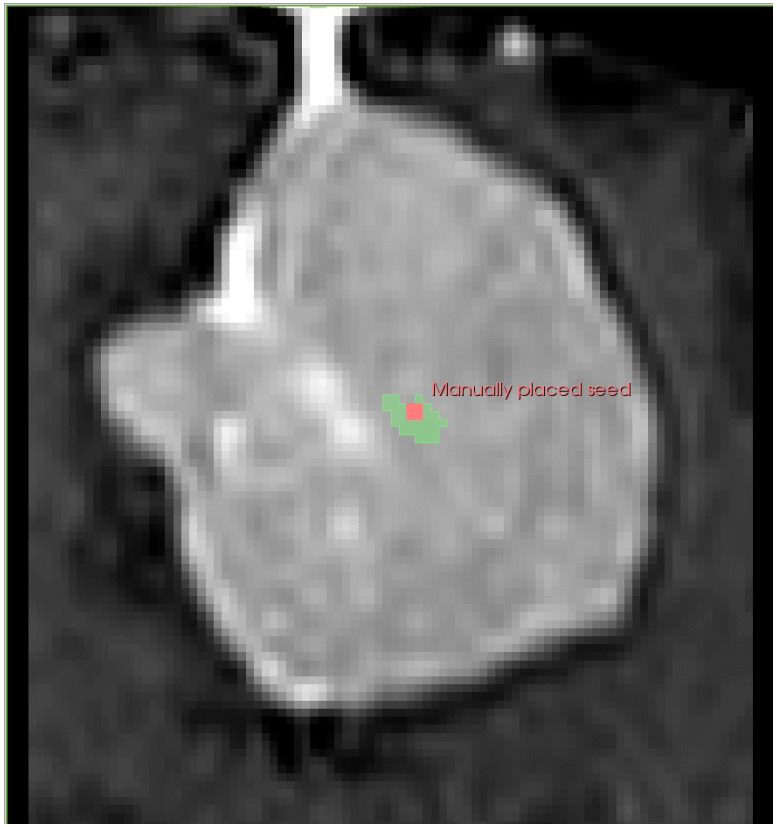






Automated tumor segmentation

- User input is required to place seed(s) within tumor volume
- Segmentation algorithm “learns” intensity distribution from seed(s)
- Interactive control of segmentation boundary expansion

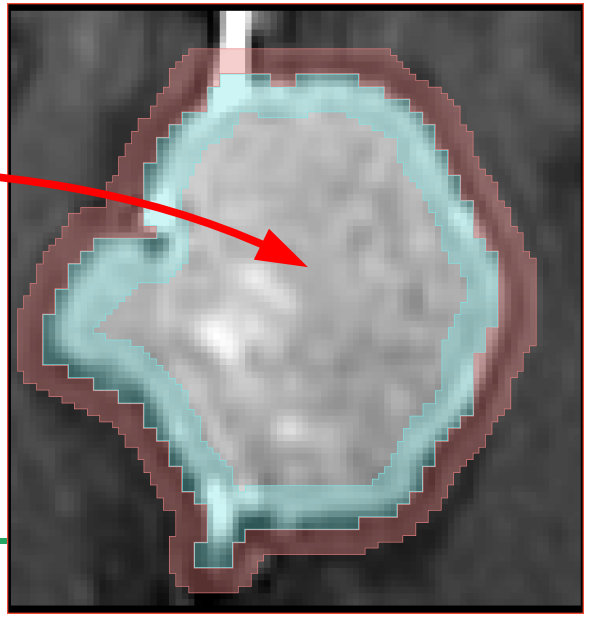


Pichon E, Tannenbaum A, Kikinis R. A statistically based flow for image segmentation. Med Image Anal. 2004 Sep;8(3):267-74

Intensity-based metric

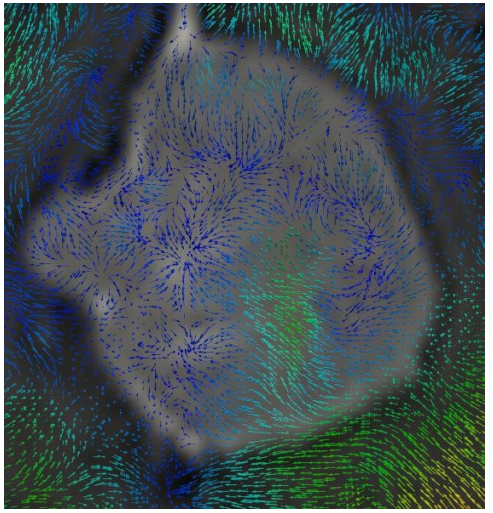
- Find pixel-wise subvolume difference
- Assume change if the intensity difference is *sufficiently* large
- Use baseline tumor segmentation to differentiate growth/shrinkage regions

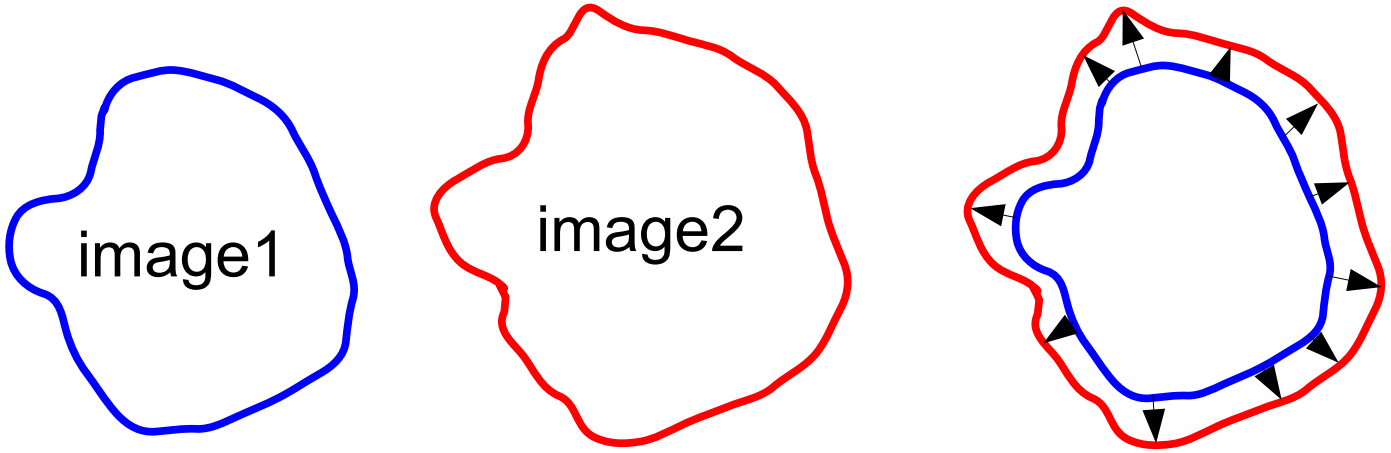
Konukoglu et al. Monitoring Slowly Evolving Tumors. Proc of IEEE ISBE, 2008



Non-rigid registration of subvolumes

- “Demons” deformable registration
- *Deformation field*: correspondence between the pixels in the subvolumes of baseline and followup



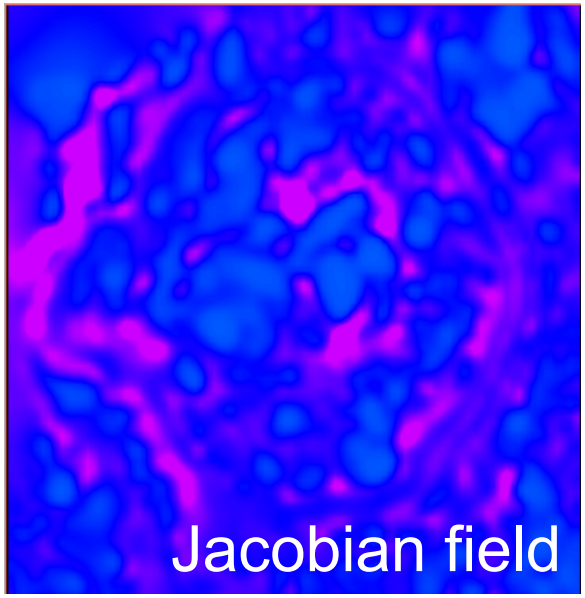


Vercauteren T. et al. Non-parametric Diffeomorphic Image Registration with the Demons Algorithm. Proc. MICCAI'07

Deformation-based change detection

- Deformation Metric #1
  - Use deformation field to project tumor outline in the baseline image onto followup image
  - Find the change as difference between the baseline tumor volume and projected tumor volume

- Deformation Metric #2
  - Calculate “change map” (Jacobian)
  - Integrate local changes over initial tumor volume



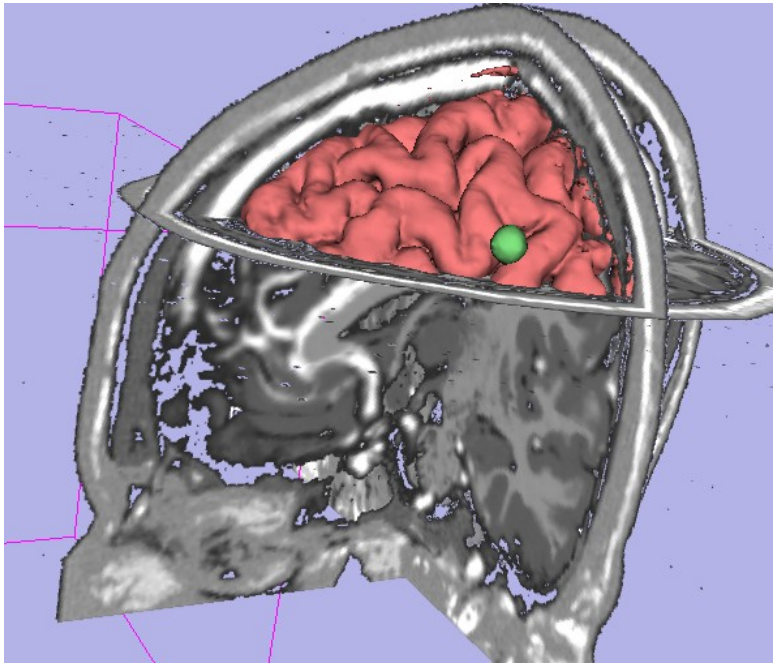
Change detection workflow summary

1. Spatial alignment of scans
2. Identification of subvolume containing the tumor
3. Segmentation of the tumor in the baseline image
   - Manual contouring

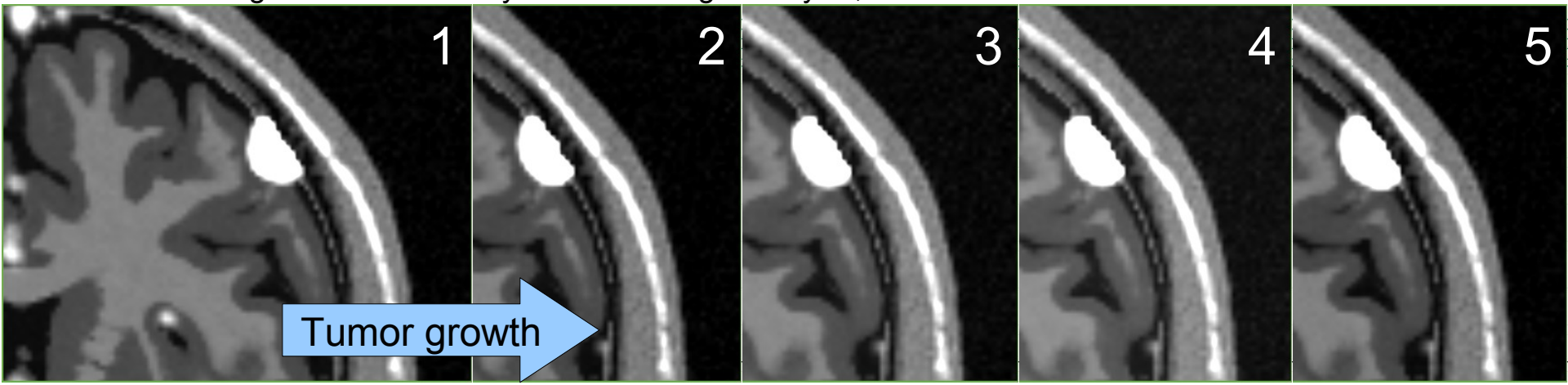
     OR
   - Automated expert-guided segmentation
4. Quantification of the changes
   - Analysis of the subtract image (Intensity Metric)
   - Two metrics based on the “demons” deformation field (Deformation Metrics 1 and 2)

Evaluation: Simulated tumor growth

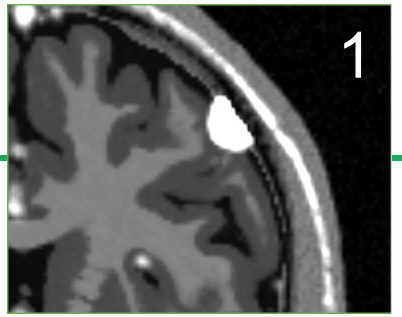
- Bio-mechanical simulation of tumor growth and associated brain and skull interaction
- Gadolinium enhancement modeled
- 5 “snapshots” of simulated tumor evolution over time

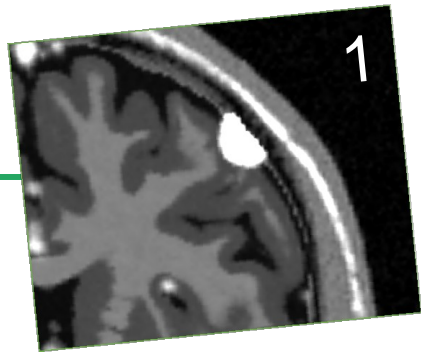


M.Prastawa et al. Simulation of Brain Tumors in MR Images for Evaluation of Segmentation Efficacy. Medical Image Analysis, 2009



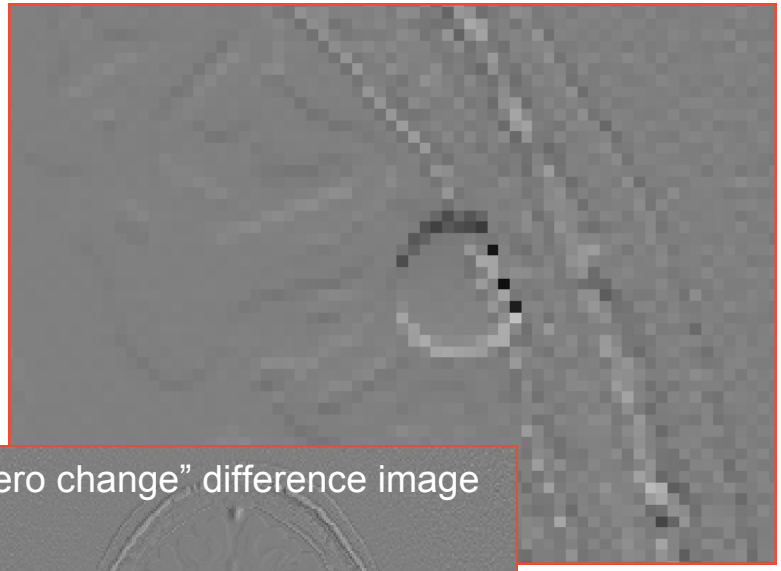
“Zero change” test





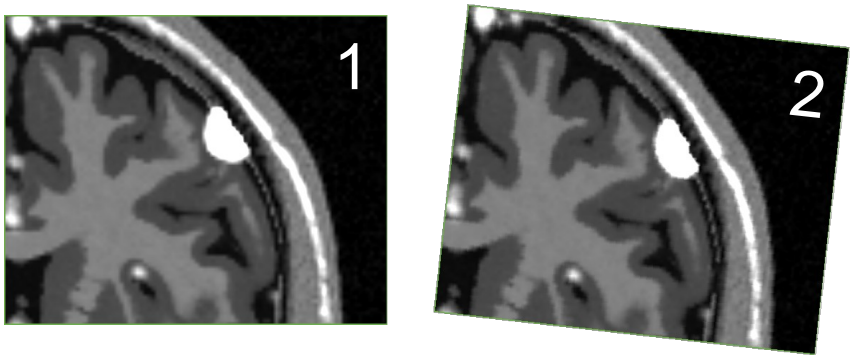
- “Baseline” and “Followup” are identical
- Imitate global registration error

- Intensity metric falsely detects growth due to near-uniform pixel-wise difference
- Deformation-based metrics stable under misalignment

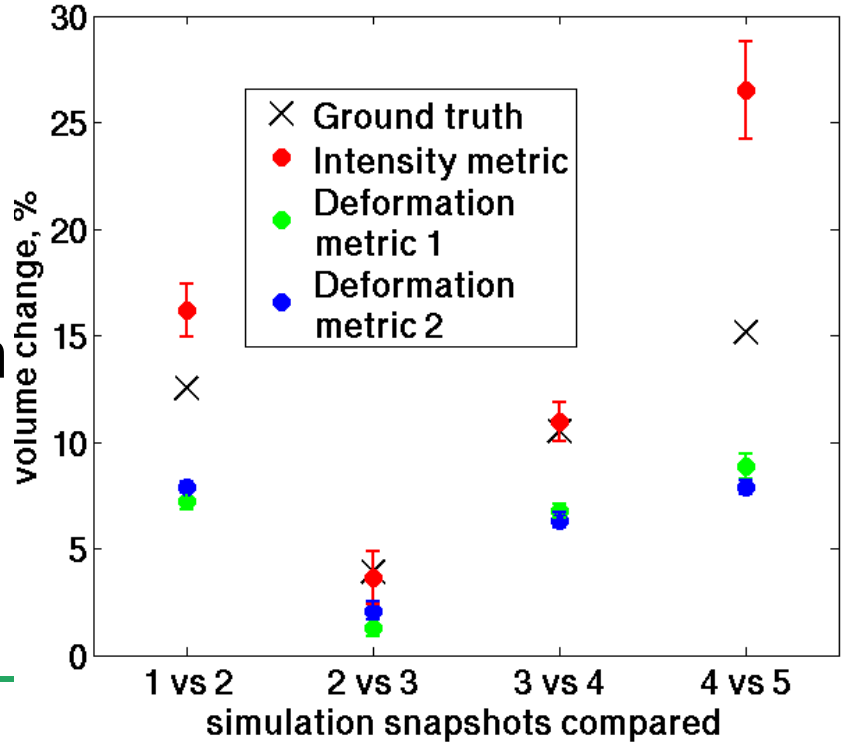


"Known change" test: Sensitivity to mis-alignment

- Ground truth tumor volume difference is known
- Ground truth segmentation of baseline tumor

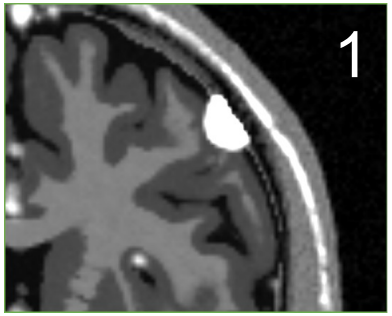


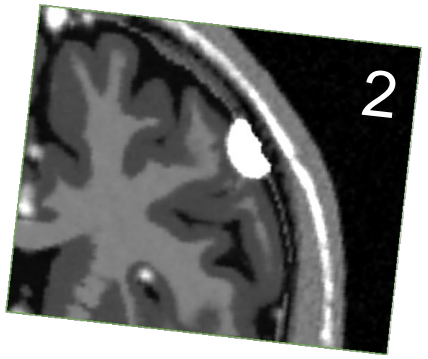
- All metrics correctly detect growth
- Deformation metrics stable under slight mis-registration



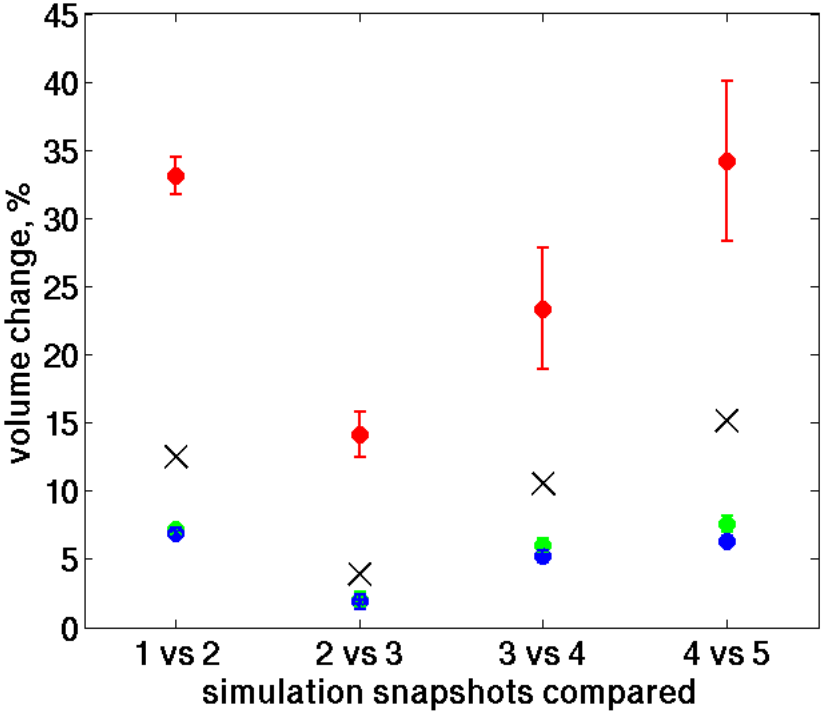
"Known change" test: Sensitivity to baseline segmentation

- Ground truth tumor volume difference is known
- *Automated segmentation of baseline tumor*





- All metrics correctly detect growth
- Deformation metrics are less sensitive to baseline segmentation differences

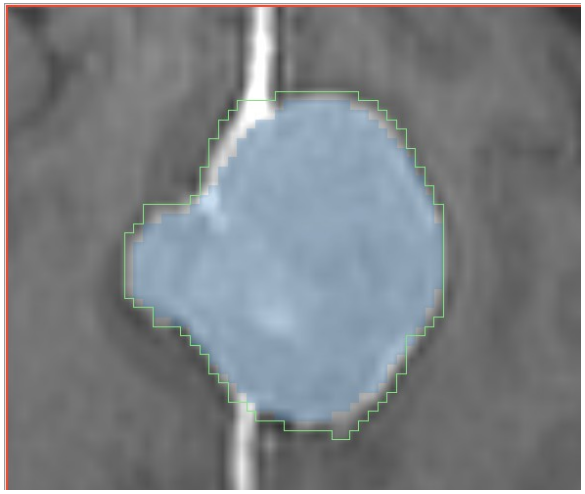


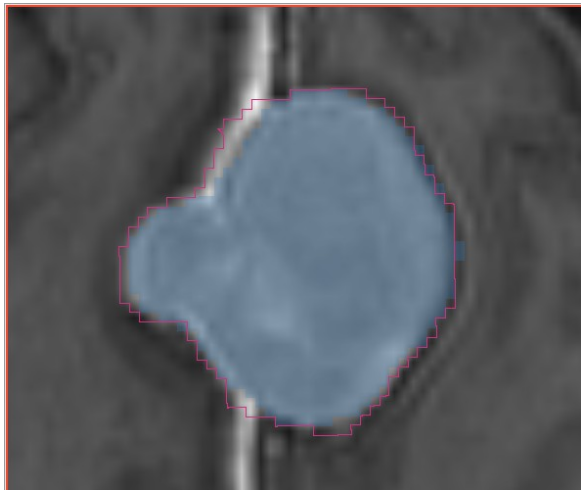
Clinical data

- 9 clinical cases of asymptomatic meningioma
- Post-Gad 3D axial SPGR T1 MRI (clinical sequence)
- Voxel 0.9x0.9x1.2, scan time 8 min
- Mean follow-up period 13.2 months
- Clinical impression: stable tumor size (7 out of 9) or minimum increase in size (2 out of 9)

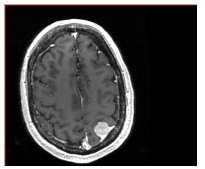
Point of reference

- Raters: two experienced neuroradiologists
- Enhancing mass outlined in each image slice-by-slice
- No pre-processing prior to manual outlining





Case 1: Manual outline analysis



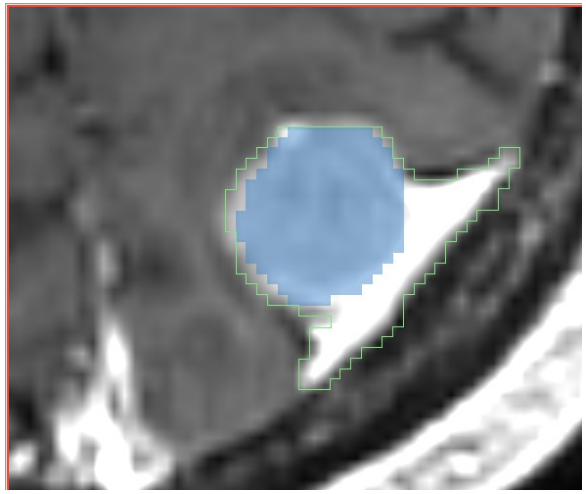
Parietal meningioma

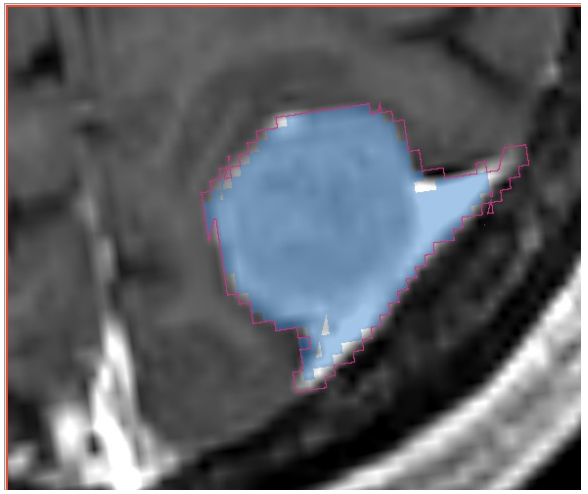
Volume

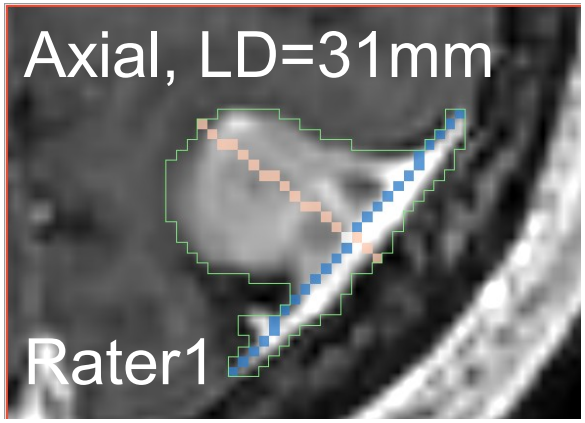
- Rater1: +21%
- Rater2: +39%

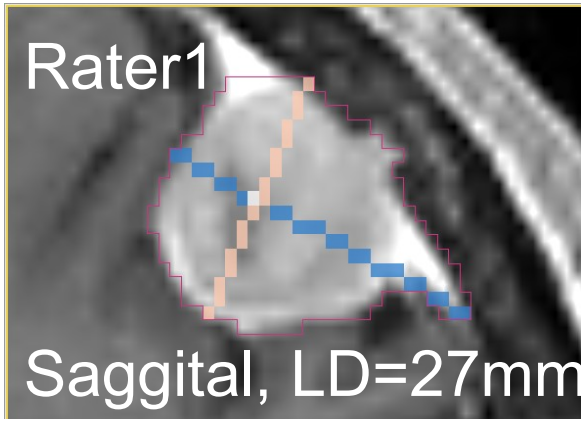
Largest diameter (derived from manual outline)

- Rater1: -11%
- Rater2: +15%

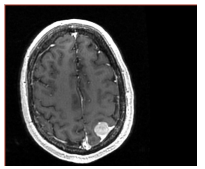




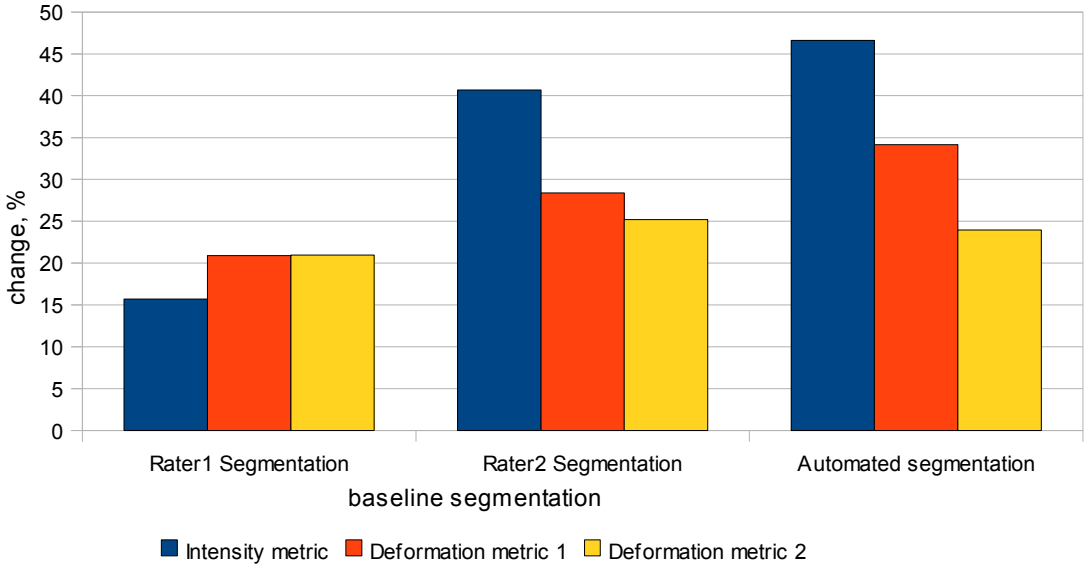




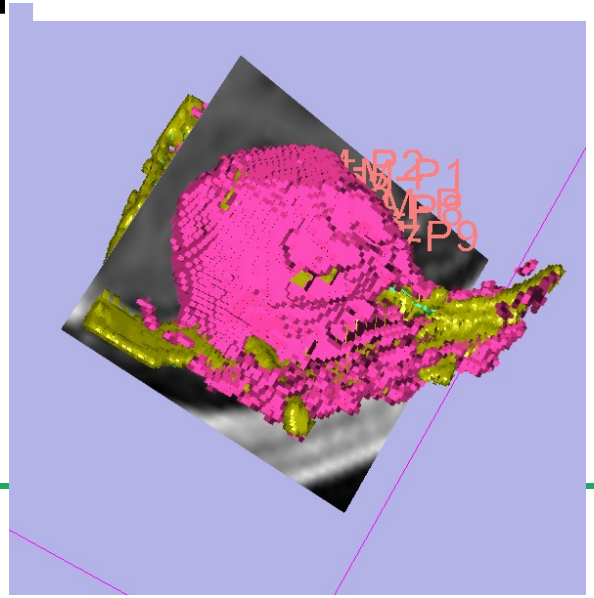
Case 1: Automated analysis

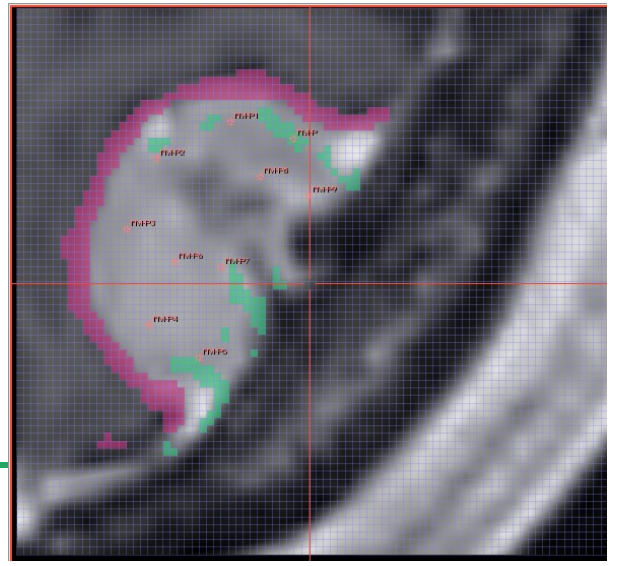


- Automated analysis initialized with different baseline segmentations
- Tumor growth detected by all three metrics
- Deformation metric 2 is least sensitive to baseline segmentation



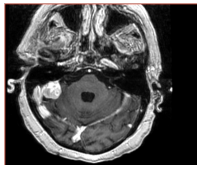
Rater1: +21% Rater2: +39%





BRAINSCIENCE FOUNDATION

Case 2: Manual outline analysis



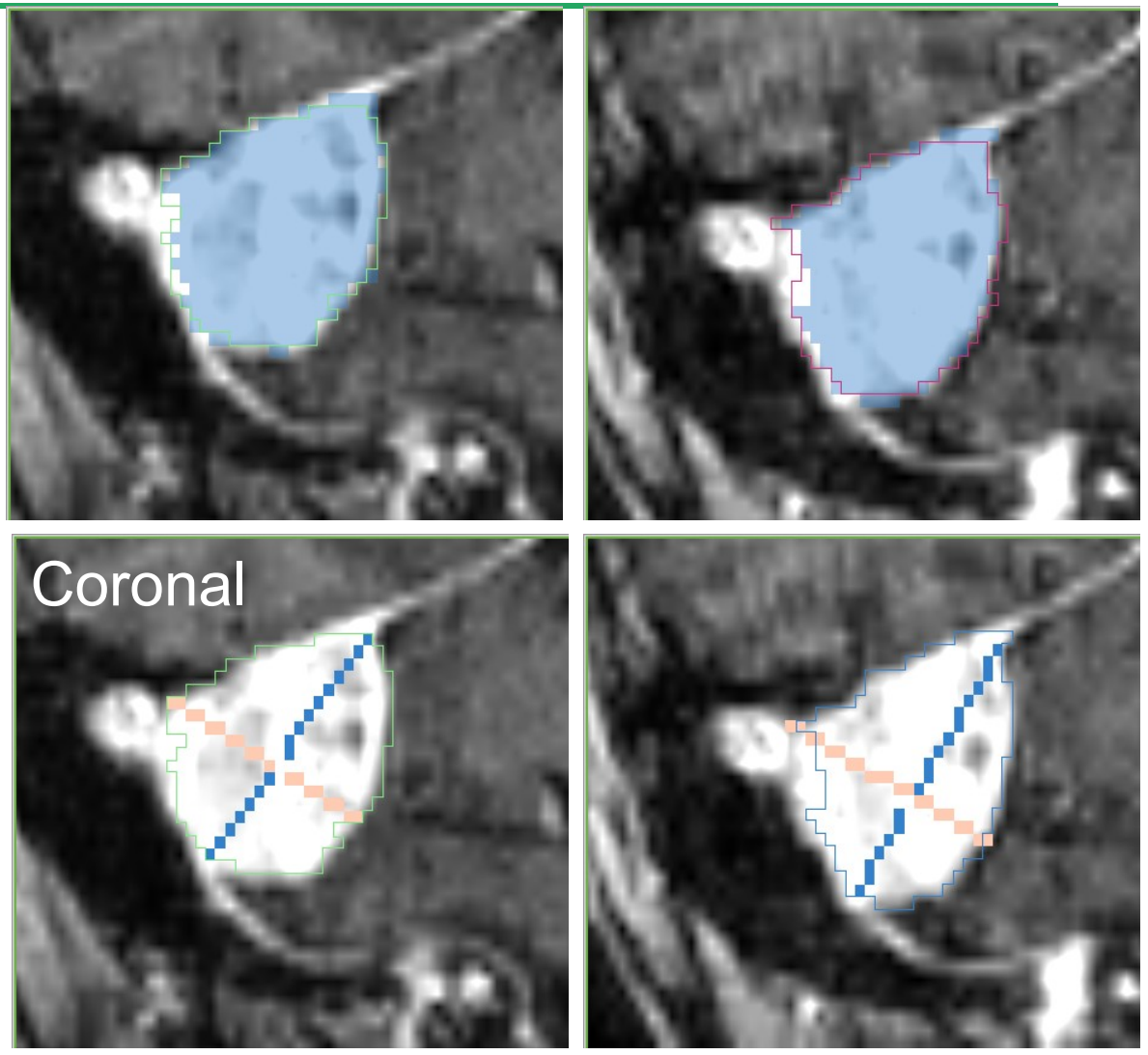
Posterior fossa meningioma

Volume

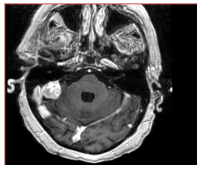
- Rater1: -5%
- Rater2: -6%

Largest diameter (derived from manual outline)

- Rater1: +4%
- Rater2: +3%



Case 2: Automated analysis



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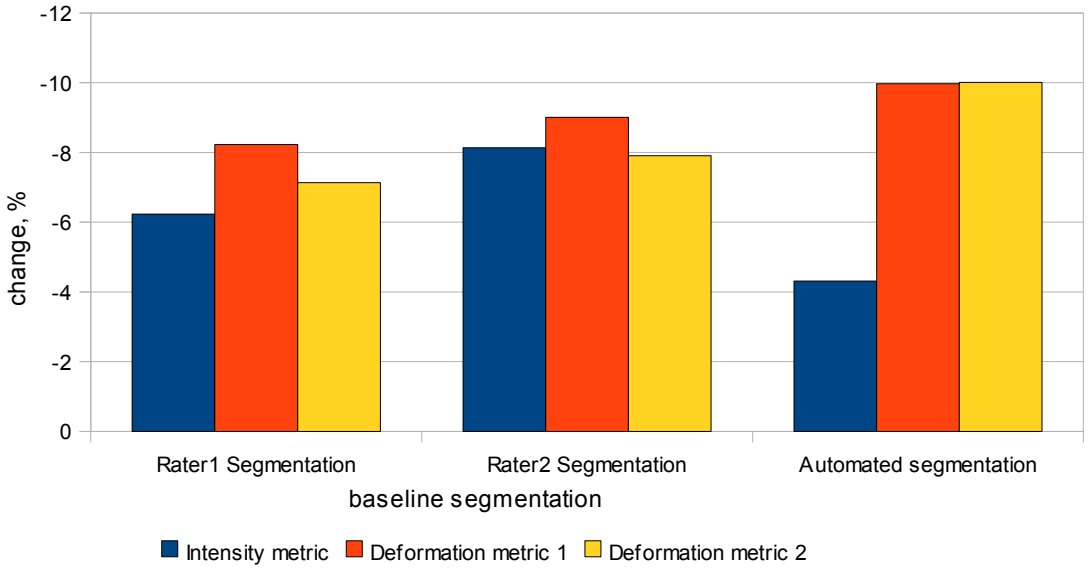
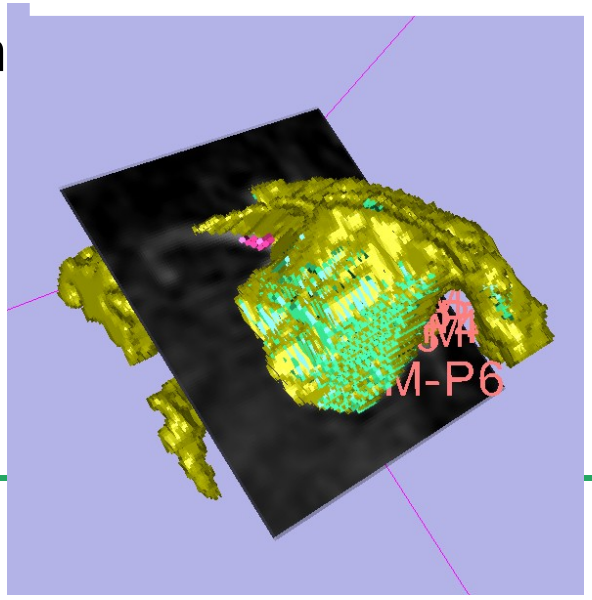
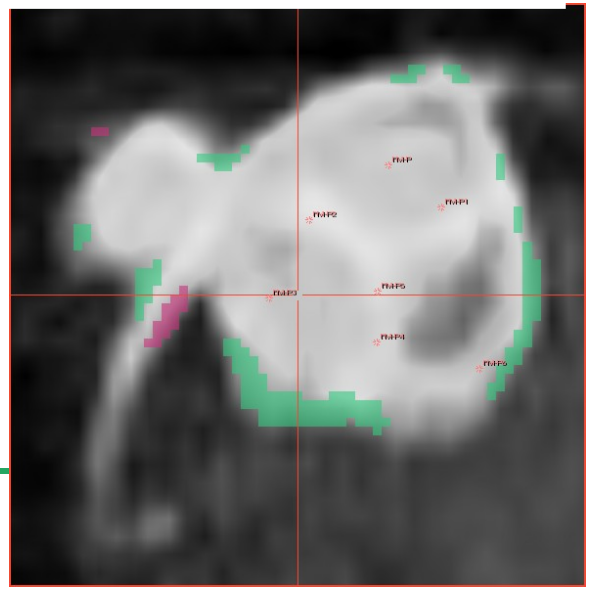
- Tumor shrinkage detected by all three metrics
- Deformation metric 2 is least sensitive to baseline segmentation

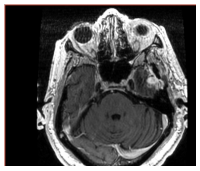


Rater1: -5% Rater2: -6%





Case 3: Manual outline analysis



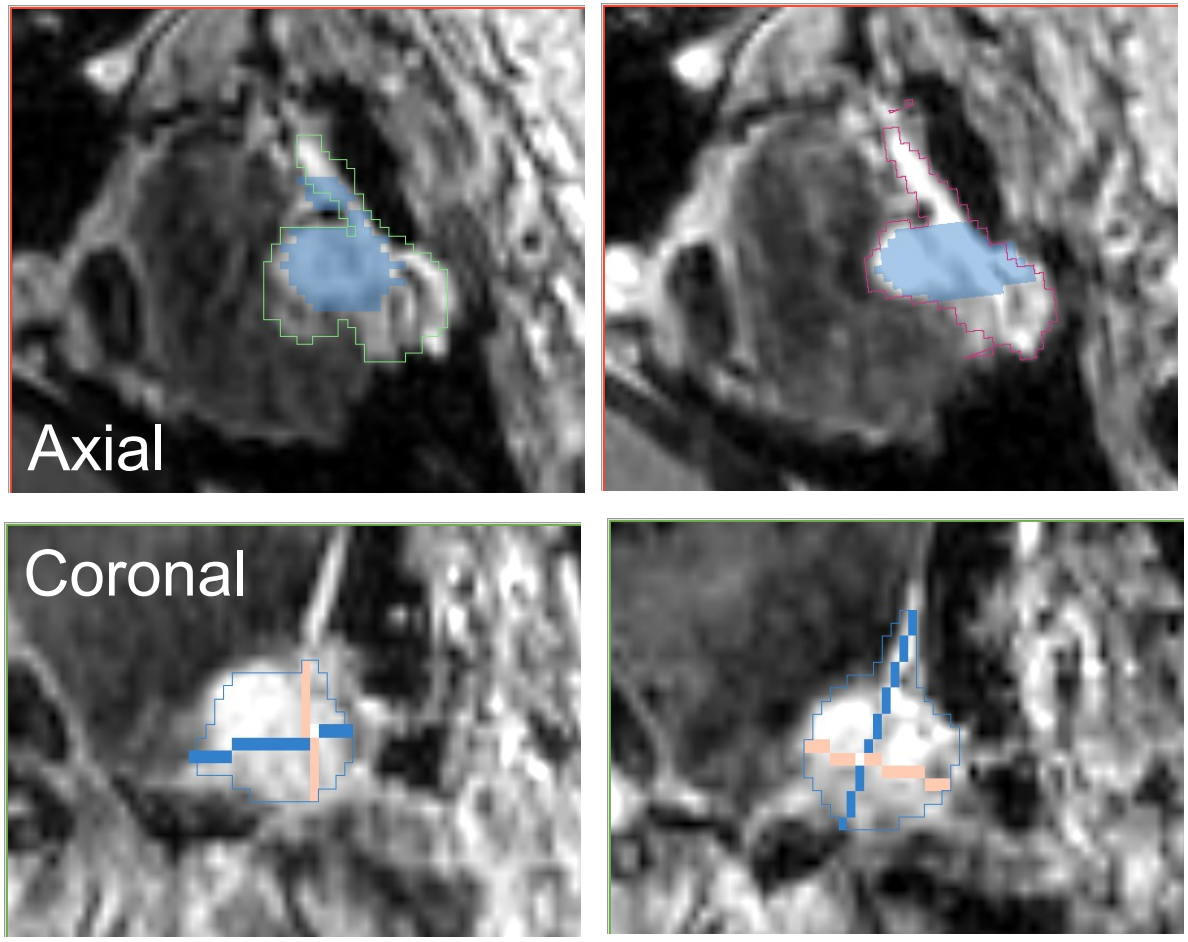
Nodular based enhancement

Volume

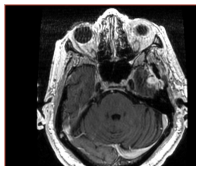
- Rater1: +3%
- Rater2: -4%

Largest diameter (derived from manual outline)

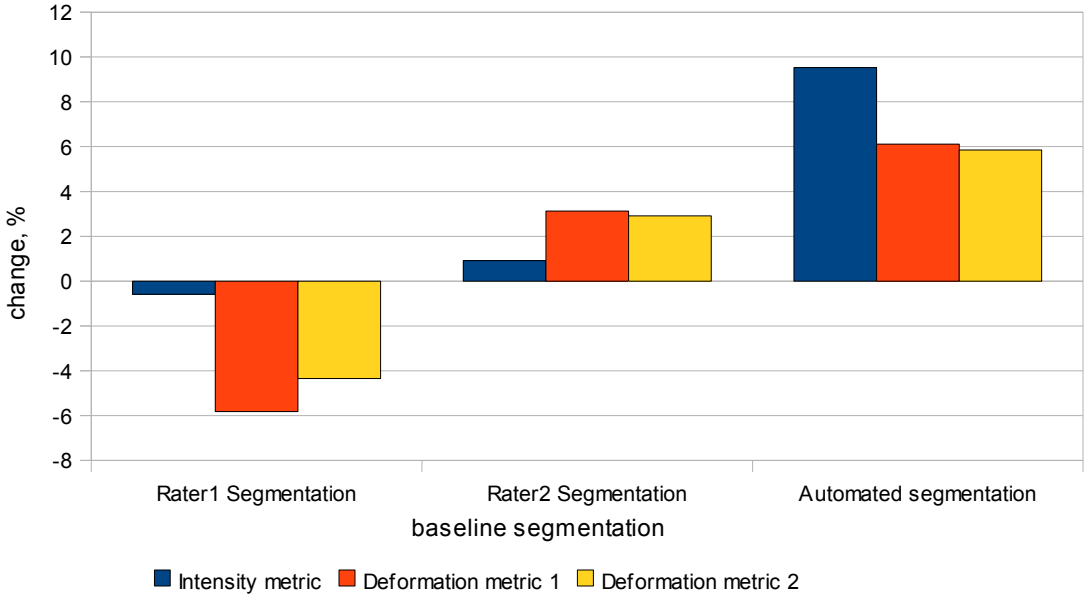
- Rater1: +1%
- Rater2: +38%



Case 3: Automated analysis

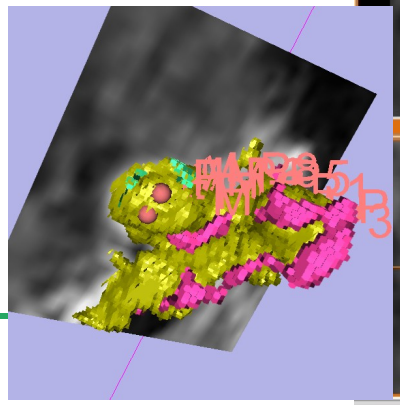


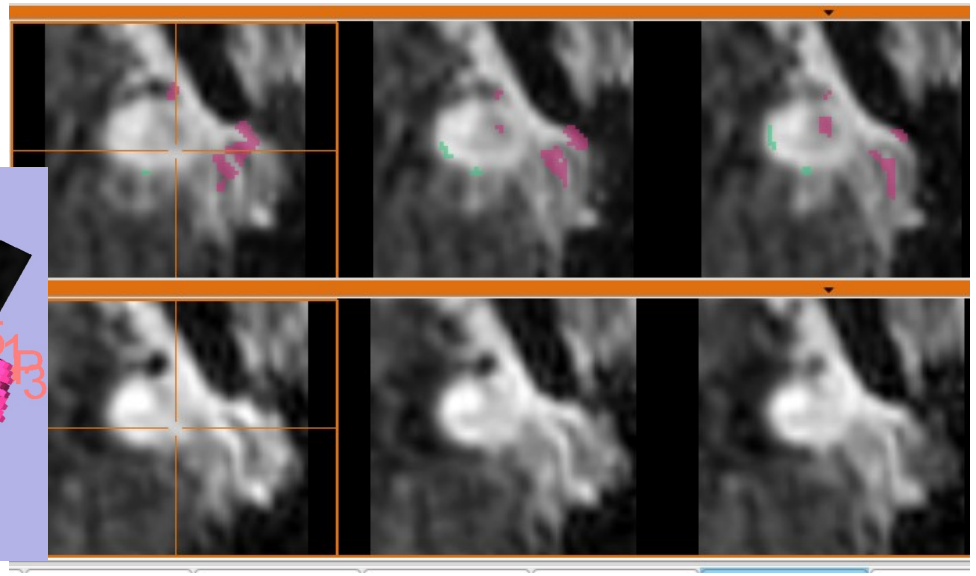
- Agreement among metrics given baseline segmentation
- Sensitivity to baseline segmentation



- Rater1: +3%
- Rater2: -4%

- LD Rater1: +1%
- LD Rater2: +38%





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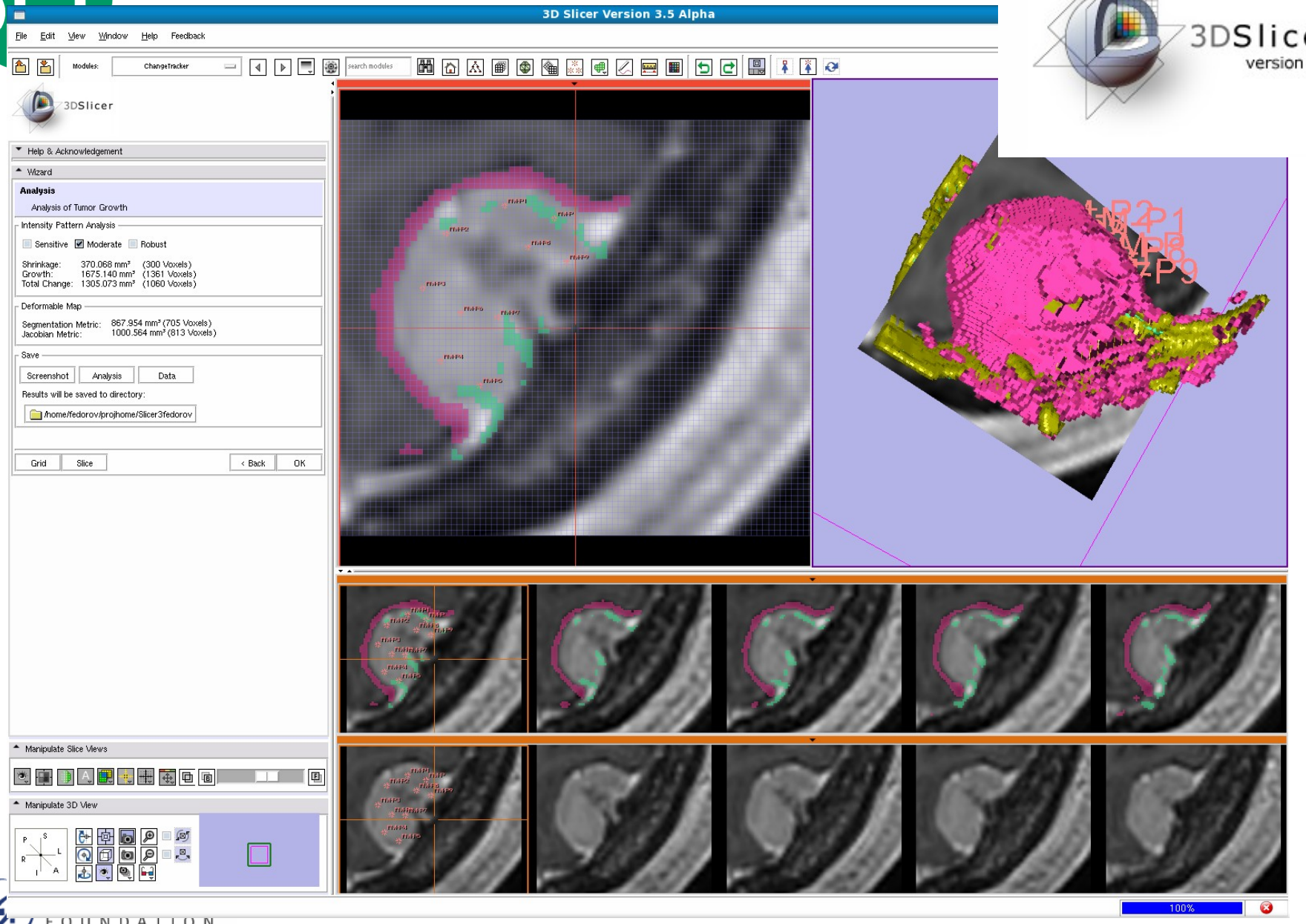
Conclusions

Based on the analyzed 9 clinical cases and available reference segmentations of tumor:

- Reliability of automated change detection is comparable with that of a human rater
- Volumetric analysis is more reliable than diameter-based estimations
- Automated change detection is reproducible and feasible in under 10 minutes of computation with minimum user interaction

Implemented in 3D Slicer *ChangeTracker* module

Google “changetracker slicer”



3DSlicer version 3.4

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- BWH Radiology: Amir Zamani, Donna Oka, Tuan Luu
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- Tumor segmentation: Eric Pichon
- Tumor growth simulation: Marcel Prastawa

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