

Noninvasive Monitoring of Brain Tumor Therapy

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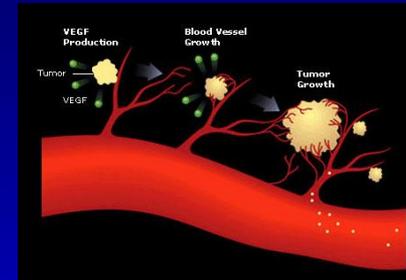
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<http://casilab.med.unc.edu/>

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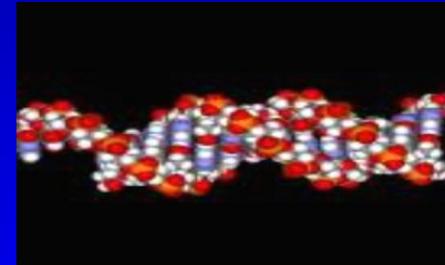
New and Exciting Treatments are Emerging for Brain Tumors

❖ Anti-angiogenic



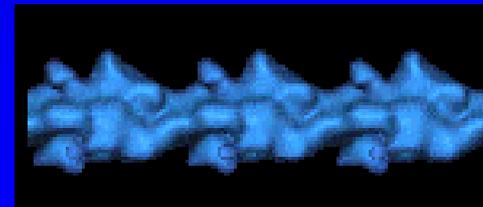
<http://www.gene.com/gene/research/images/angiogenesis.jpg>

❖ Genetic and immune



www.accelrys.com/reference/gallery/ls_dna.html

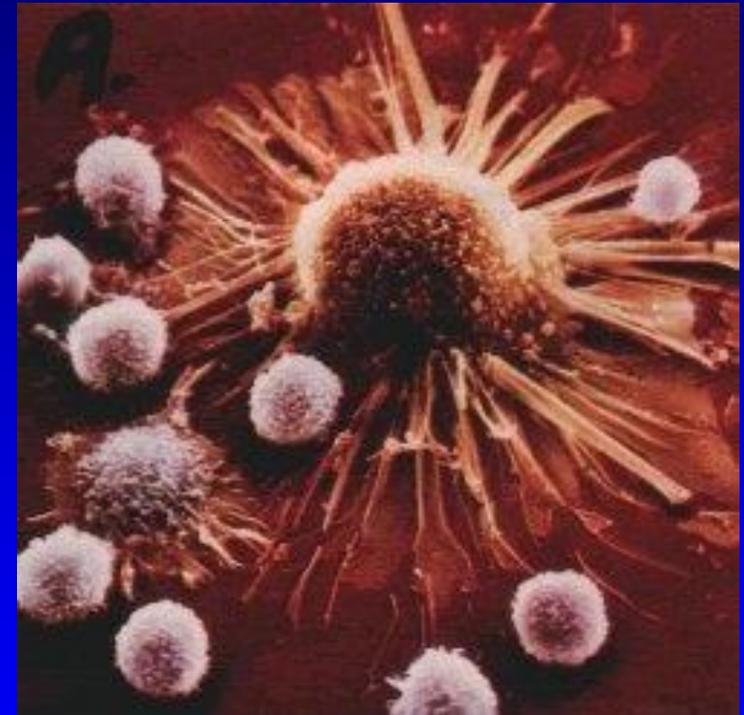
❖ Molecular



http://www.rockefeller.edu/labheads/darst/structures.htm#core_row

Is a Tumor Responding to Therapy?

- ❖ Clinical treatment
- ❖ Drug development and testing
- ❖ Human tumors and animal tumor models



<http://www.cancer-info.com/cancerdeath.htm>

Cancer cell attacked by
killer T-cells

Outline: Advantages and Disadvantages of Various Modalities

- ❖ T1-Gd
 - ❖ T2 and FLAIR
- **Commonly used clinically**

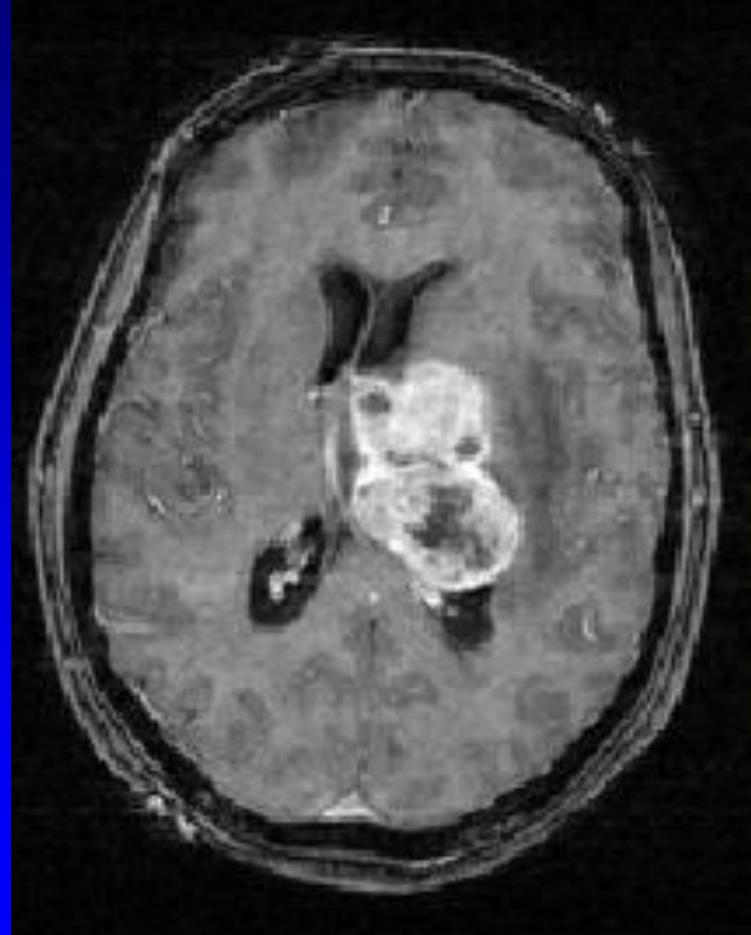
*******More Experimental*******

- ❖ PET, MR-spectroscopy, diffusion
- ❖ Perfusion and permeability
- ❖ Vessel shape from MRA

T1-GAD: Traditional Method

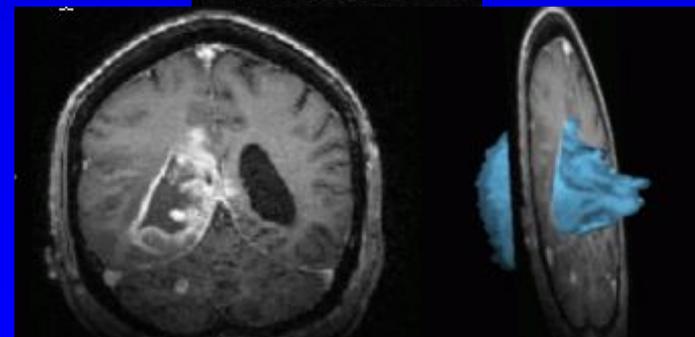
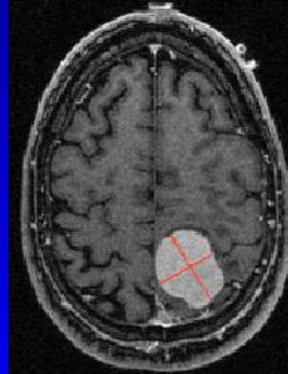
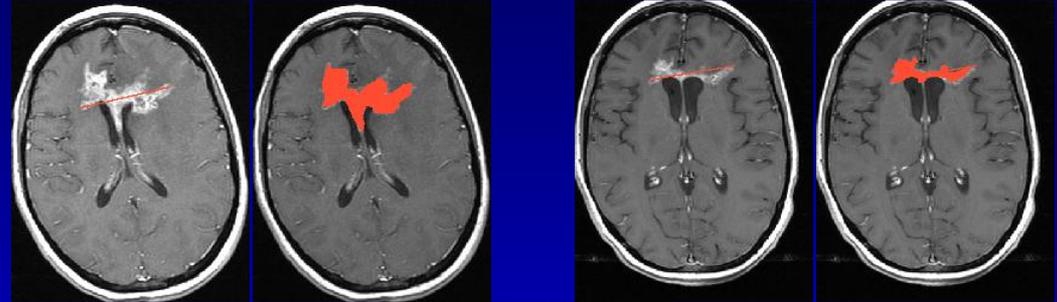
Follow change in
tumor volume
over time.

With successful
treatment
tumor should
get smaller or
stop growing



T1-Gd: Measure in 1D, 2D, 3D?

- 1) 1D: simplest but least accurate
- 2) 2D: intermediate
- 3) 3D: most accurate but most onerous



Which Measurement Method Best Predicts Clinical Response?

- 1) Shah (neuro-oncology 2006) 1D better predictor than 3D.
- 2) Dempsey (AJNR 2005) Only 3D measurements were predictive.
- 3) Warren (JNCI 2001) No significant difference between methods.
- 4) Galanis (Neuro-Oncology 2006) None of the 3 methods correlate with survival

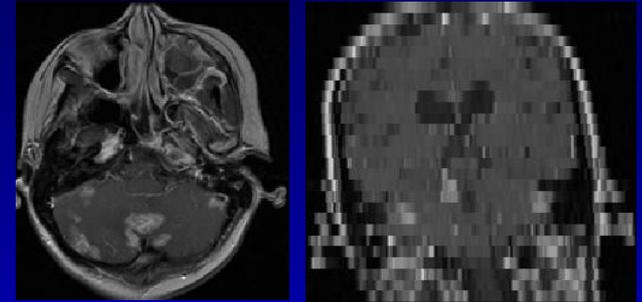
Advantages T1-Gd

- 1) Images always available
- 2) Simple measurements
- 3) Concept of measuring tumor size over time is readily understandable and seems reasonable

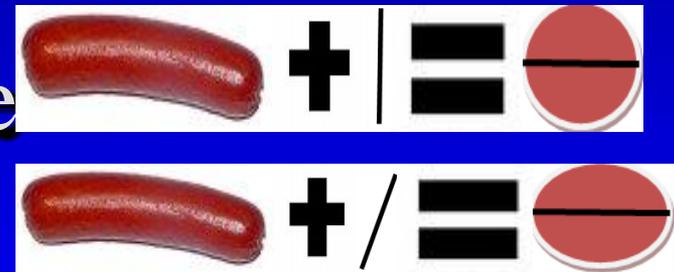
BUT...

Disadvantages T1-Gd (1/2)

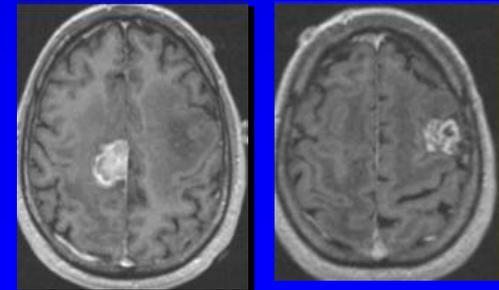
- ❖ Common use of large interslice spacing



- ❖ 1D and 2D measures are subject to slice angle

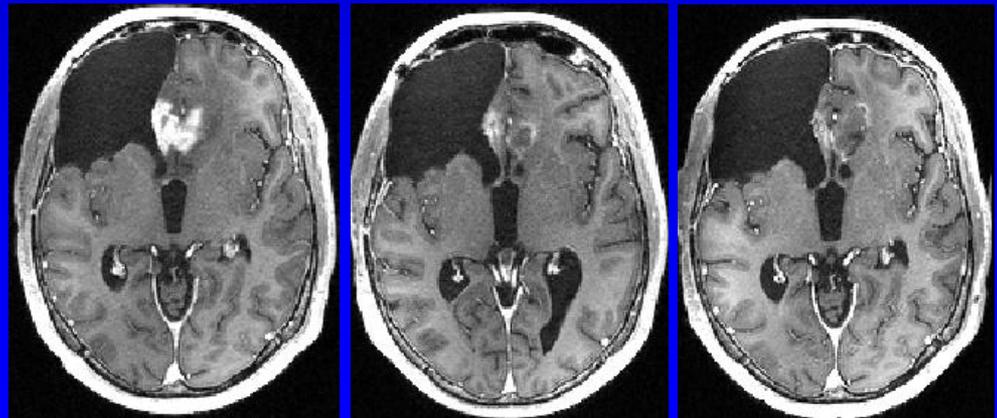


- ❖ Confusion necrosis v tumor growth



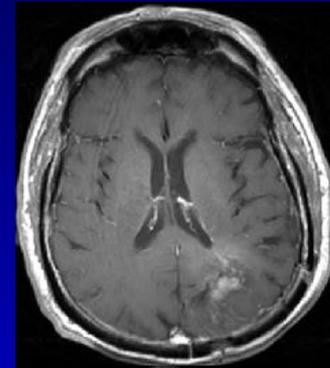
Disadvantages T1-Gd (2/2)

- ❖ Difficulty in definition of resected, cystic, or small lesions
- ❖ Actual tumor margins are not defined
- ❖ Problem with Avastin

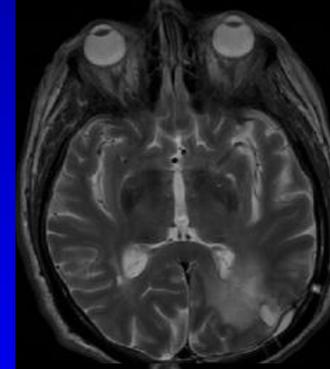


T2 and FLAIR Images

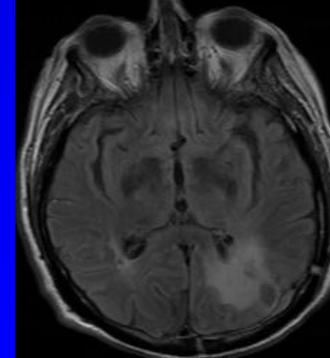
- 1) Many malignant and some benign tumors produce edema (water accumulation) around enhancing tumor margins; in cancer this may also be tumor.
- 2) An increase in “edema” can be ominous



T1-Gd



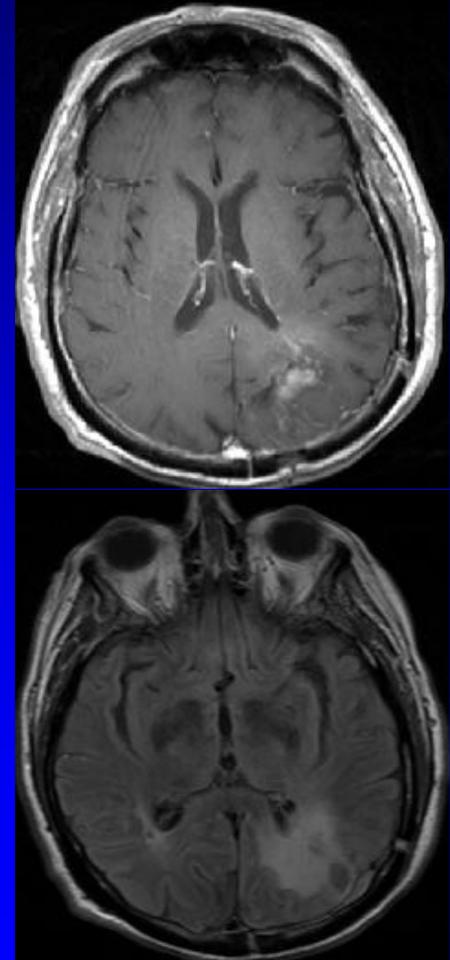
T2



FLAIR

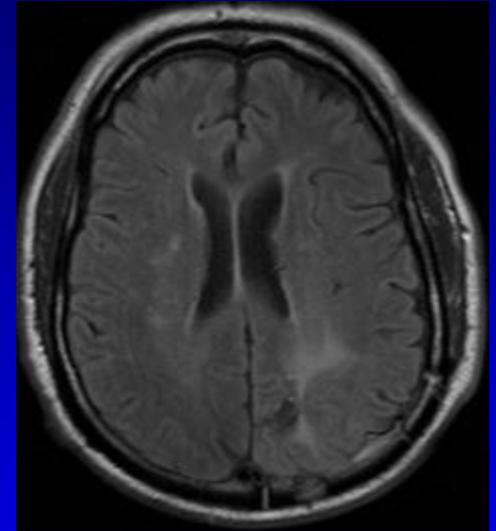
Advantages of FLAIR and T2 Imaging

- 1) More sensitive than T1-Gd in showing extent of tumor influence
- 2) Often used to provide a qualitative assessment when T1-Gd is equivocal and clinician is unsure.



Disadvantages of FLAIR and T2 Imaging

- 1) Changes are non-specific and can increase with age and with tumor treatment.
- 2) Successful treatment can produce necrosis and an increase in edema.
- 3) No easy quantitative analysis of margins—how quantitate?



Ominous FLAIR image in a post-treatment patient without Gd enhancement and subsequently did well for > year. Note difficulty in defining margins.

So... What is the Problem and How Solve?

- 1) The current standard of practice is to use T1-Gd images with input from additional images providing subjective assessment of edema.
- 2) Both provide anatomical information that may be difficult to interpret. A more direct method of measuring tumor activity would be desirable.

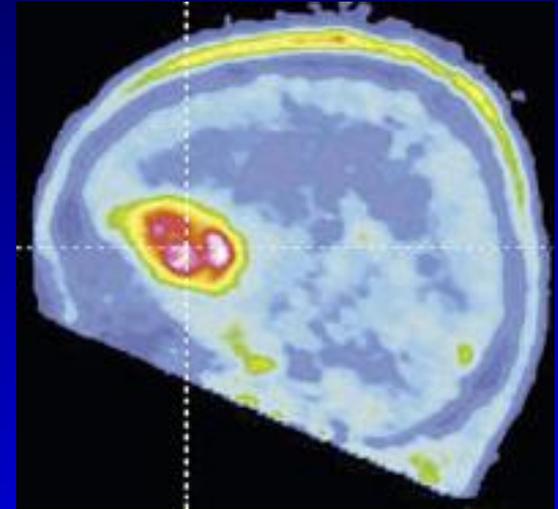
Methods Under Development by Various Groups

- ❖ PET, MR-spectroscopy, diffusion
- ❖ Perfusion and permeability
- ❖ Vessel shape from MRA

All have strong proponents. None is yet widely clinically accepted as providing “The Answer”

PET

- 1) PET: FDG-glucose metabolic activity since 1980s for brain tumors.
- 2) +: Sometimes helps.
- 3) -: Low resolution, high background grey matter
- 4) Research on new agents



<http://www.technologyreview.com/Biotech/18810>

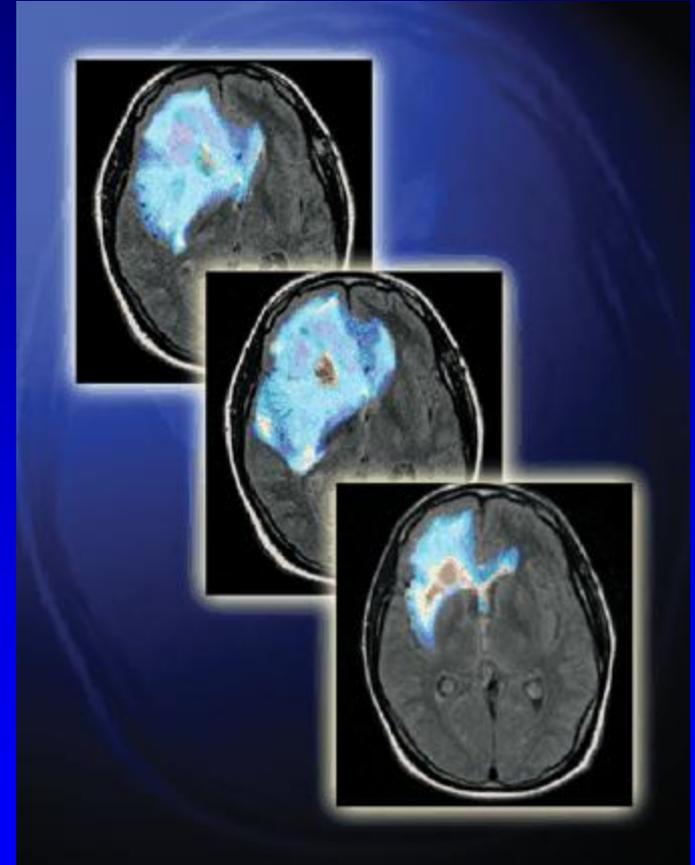
MR-Spectroscopy

- 1) MR-Spectroscopy: Chemical information
- 2) May be useful distinguishing tumor from necrosis (sometimes)



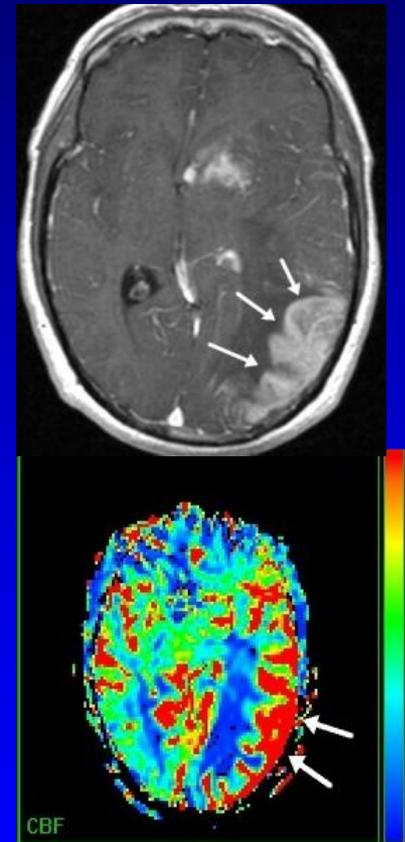
Diffusion Imaging

- 1) Densely packed tissue allows less water diffusion.
- 2) +Some groups find it useful in telling therapeutic response
- 3) -Others have not; problem of tumor variability

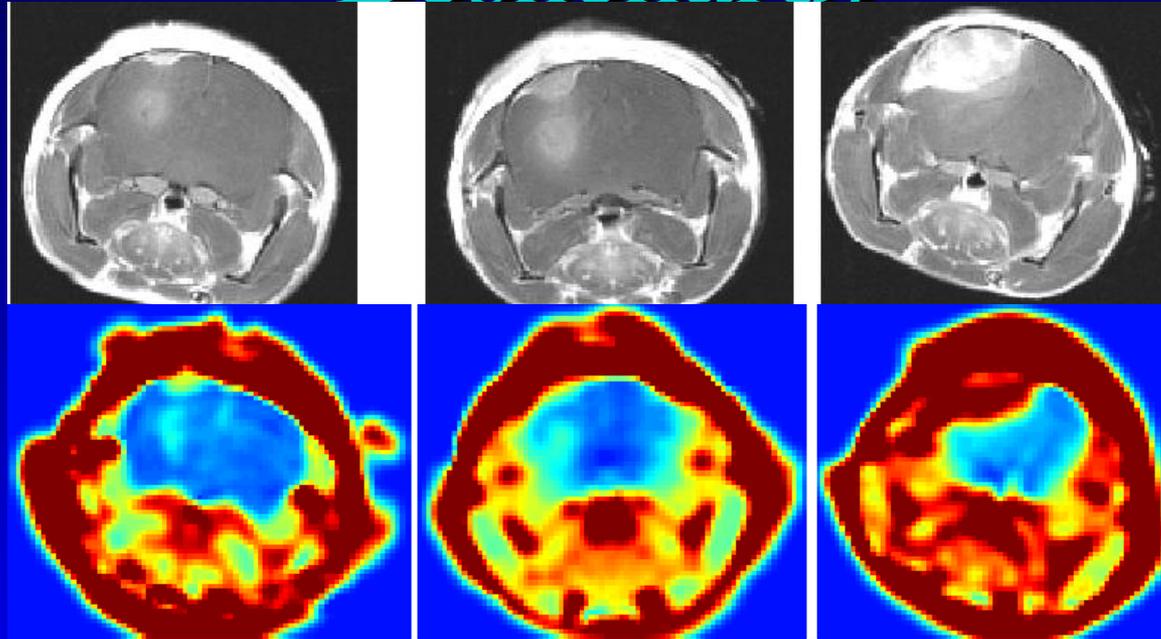


Perfusion Imaging

- 1) Theory: more actively growing tumors will have higher blood flow/volume
- 2) +: Widely available, easy
- 3) -: Noisy, tumors are often heterogeneous, contradictory reports with anti-VEGF treatment.

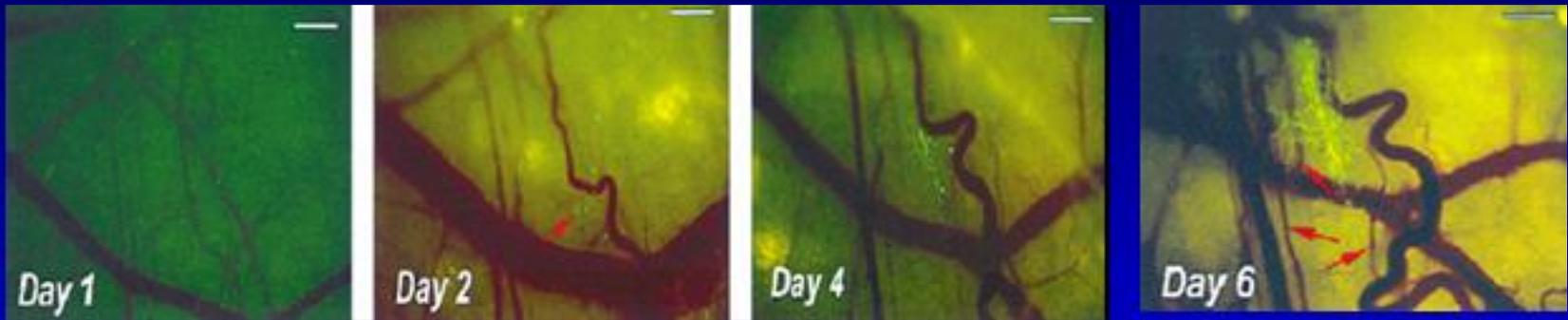


Permeability Imaging (Thomas Besnehard)

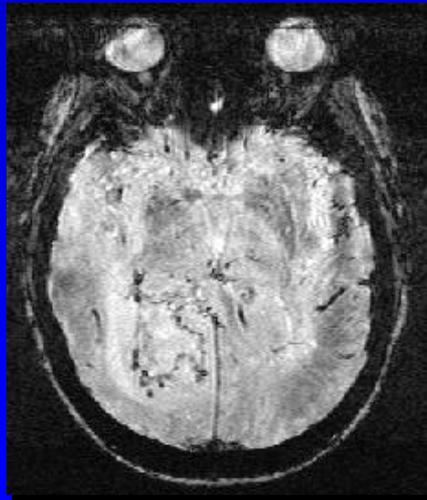


- 1) Evaluates vessel leakiness
- 2) + More effective than perfusion at determining tumor grade
- 3) -Low resolution, noisy, anti-VEGF treatment reduces enhancement

Vessel Analysis MRA: Vessel Tortuosity (“Wiggleness”)

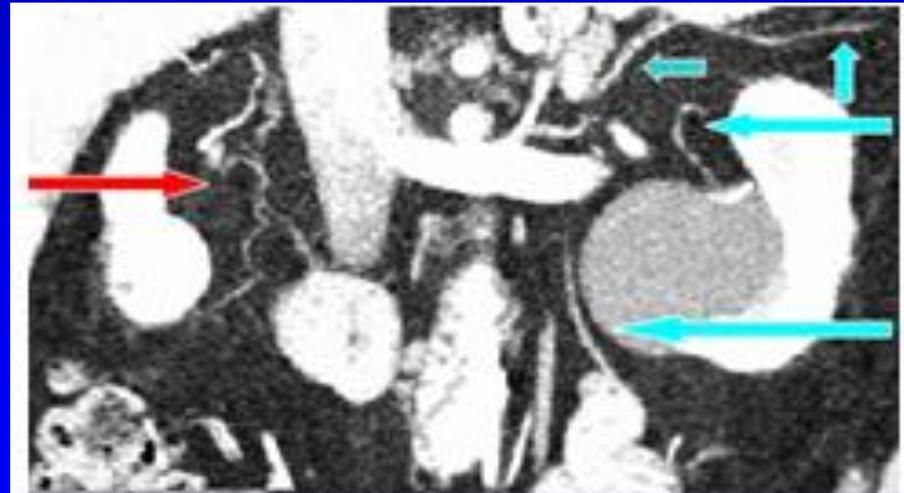
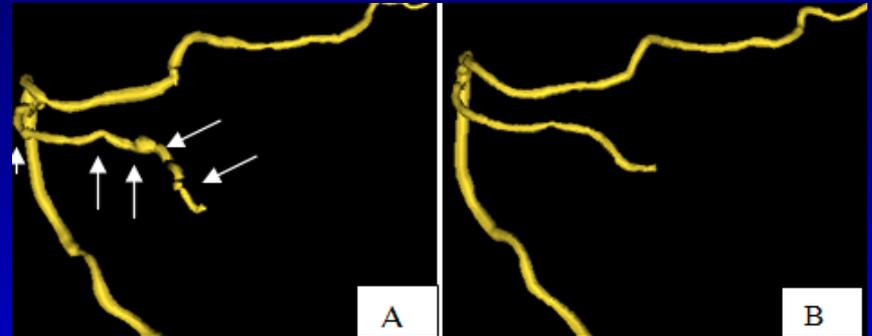


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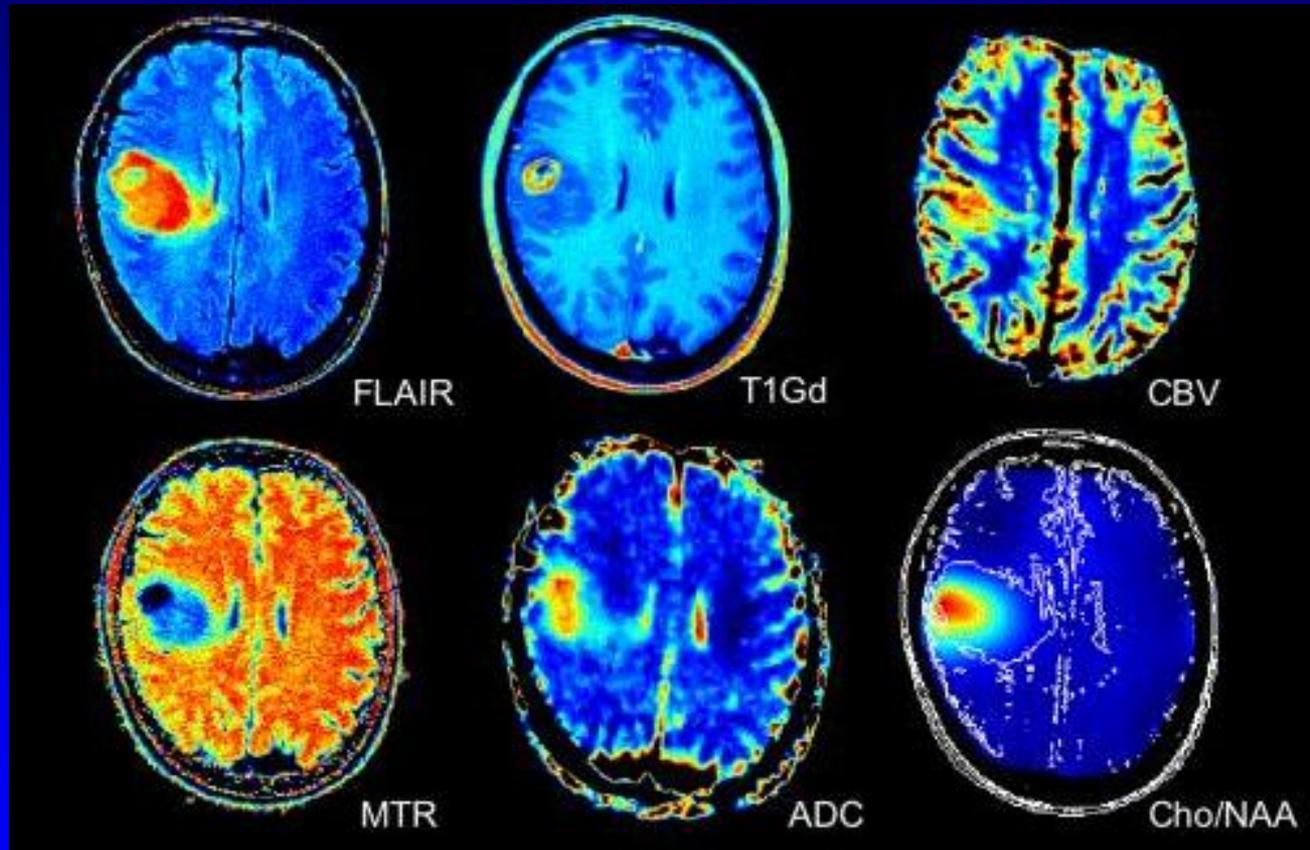


Vessel Analysis MRA

- 1) +Resolution of abnormalities with effective therapy, applies to tiny cancers as well as large, early indicator, works with anti-VEGF therapy
- 2) -Time-intensive



Multimodal Imaging: How Combine the Information?



<http://crmbm.timone.univ-mrs.fr/IMG/jpg/fig3.JPG>

A Few References

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