Noninvasive Monitoring of Brain Tumor Therapy

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New and Exciting Treatments are Emerging for Brain Tumors

❖ Anti-angiogenic

❖ Genetic and immune

❖ 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
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-Onkology 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
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.
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

http://mct.aacrjournals.org/content/2/6.cover-expansion
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 (“Wiggliness”)

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

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Multimodal Imaging: How Combine the Information?

http://crmbm.timone.univ-mrs.fr/IMG/jpg/fig3.JPG
A Few References


