Strengths and Limitations of Brain Tumor Volumetric Assessment when Evaluating Tumor Treatment Response

Elizabeth Bullitt MD
University of North Carolina-CH
http://caslab.med.unc.edu/

New and Exciting Treatments are Emerging for Brain Tumors

- Anti-angiogenic
- Genetic and immune
- Molecular

Is a Tumor Responding to Therapy?

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

Traditional Method: Monitor Tumor Volume on T1-GAD

Follow change in tumor volume over time.
With successful treatment tumor should get smaller or stop growing
Outline

1) 3 methods of estimating tumor volume on T1-GAD images: advantages and disadvantages
   1) 3D
   2) 1D
   3) 2D
2) Two common pitfalls
3) Using T1-Gad images in general: advantages and disadvantages

3D Volumetric Assessment:

Advantages

Tumors are 3D structures! The most accurate way to measure 3D volume is to measure volume in 3D.

Disadvantages

1) Automatic, accurate, fast tumor segmentation has yet to be developed
2) Manual tracing slice by slice is too onerous for clinical use

1D Estimate of Tumor Volume (RECIST)

- Response Evaluation Criteria in Solid Tumors (RECIST) 1994
- Define the longest line inside the tumor using a single slice (1 slice per tumor)
- Most common measure
**Advantages of RECIST**

1) Fast and easy to do (two mouse clicks)
2) Calculation of distance between two points is available on almost all clinical display systems

**Disadvantages of RECIST: Sensitivity to Slice/Point Selection**

It is not always obvious which slice and points to choose and reasonable choices can differ by 10% or more.

**Disadvantages of RECIST: Sensitivity to Slice Angle**

The same hot dog, scanned at two different acquisition slice angles, will have two different “longest lines”

**Disadvantages of RECIST: Misses Asymmetrical Tumor Response**

RECIST and 3D estimates of tumor volume at 2 time points. The dramatic response was totally missed by RECIST.
Disadvantages of RECIST: Insensitivity to Change

- RECIST criteria require change of >= 20% in line length as significant.
- Even if tumors were all spherical (not so), a 20% change in radius is associated with about a 50% change in volume.

2D Estimates of Tumor Volume: WHO Criteria

1) World Health Organization criteria 1979
2) Product of the two longest, bidimensional lines within a tumor (one slice per tumor).

Advantages of WHO Criteria

1) Relatively simple and fast to do (4 mouseclicks, one multiplication)
2) Calculation of distance between two points is available on almost all clinical display systems
3) More sensitive than 1D RECIST to changes in tumor volume

Disadvantages of WHO Criteria:

- Sensitivity to slice, point, and angle between lines selection (1D RECIST was actually proposed later to reduce user selection variability)
- Sensitivity to acquisition slice angle (although less so than RECIST)
- May miss asymmetrical tumor response to therapy

The volume of a sphere is \( \frac{4}{3}\pi r^3 \).
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.

Common Pitfalls 1: Change in Slice Angle (Head Position)

A Change in slice angle changes results

1) Will affect RECIST a great deal, WHO criteria to some extent, and 3D volume calculation little.
2) Solution is to standardize slice angle.

Common Pitfalls 2: Anisotropic Voxels

- Radiologists are accustomed to looking at slices, but the problem is really in 3D.
- Anisotropic voxels affect the accuracy of 1-, 2-, 3D measurements.
- Solution: Isotropic voxels!

Use of T1-GAD to Assess Tumor Activity: Advantages

1) T1-GAD images are likely to be obtained at all institutions.
2) The enhancing margin of a tumor gives something reasonably objective to follow over time.
3) It is a reasonable assumption that an active tumor will grow.
Use of T1-GAD to Assess Tumor Activity: Disadvantages (1/2)

- T1-GAD does not correctly define tumor margins
- Necrosis can mimic tumor growth
- Difficulty in definition of resected, cystic, or small lesions

Use of T1-GAD to Assess Tumor Activity: Disadvantages (2/2)

- Steroid administration decreases enhancement
- Estimates of tumor volume provide only anatomical information and not true functional information

Other Directions

- PET
- Perfusion/Permeability
- MR spectroscopy
- Vessel attributes MRA

Vessel Analysis MRA

1) Resolution of abnormalities with effective therapy
2) Murine study: detects carcinomas > 1mm³
3) Early prediction treatment failure?

http://casilab.med.unc.edu
More research is needed.

When measuring tumor volume from T1-GAD, 3D measurements are most accurate but time-consuming. 1D and 2D measurements are faster but less accurate. There is disagreement in clinical studies as to which method is best.

Summary (1/3): Measurement Method

- When measuring tumor volume from T1-GAD, 3D measurements are most accurate but time-consuming. 1D and 2D measurements are faster but less accurate. There is disagreement in clinical studies as to which method is best.

Summary (2/3): Avoiding Pitfalls

- Standardizing head position can reduce errors related to change in slice angle that affect 1- and 2D volume estimates.
- Using isotropic or close to isotropic voxels should be viewed as mandatory when making any 1-, 2-, or 3D volume assessment.

Summary (3/3):

- Use of T1-GAD images has many drawbacks and is likely to be supplanted by a better method yet to be defined, proven, and globally accepted.
- More research is needed.

Other

- Supported by R01EB000219 NIH-NIBIB, R01CA124608 NIH-NCI

Selected references

- WHO Handbook of Reporting Results of Cancer Treatment. (1979) Geneva (Switzerland): World Health Organization.