Moving Beyond RECIST

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Outline

• Standard measures to assess treatment response (oncologists)
• Limitations of current methods esp. after RF, TACE, cryo.
• Novel imaging approach to monitoring disease response
Why Assess Response?

- To determine *EARLY* if therapy worked.
- To decide if there is a need to re-treat (quantify response; not binary).
- To improve patient survival (dec. morbidity from over-treatment).
- To communicate with *patients* and *physicians*. 
What is a Favorable Response?

• Tumor death; cell “kill”
  – Technical success; index lesions

• Patient survival
  – Ultimate success; all lesions
Assessment of disease status

- “Tumor markers alone cannot be used…”
- “When the primary endpoint of the study is objective response evaluation, ultrasound should not be used…”
- “PET is useful for remote disease, also metabolism”.
- “CT and MR as the best…for response assessment”

Therasse P et al, JNCI 2000; 92: 205-216
Standard Criteria for Response (Based on change in tumor size)

- **WHO:**
  - product of perpendicular diameters
- **RECIST:**
  - replaced WHO
  - single long axis diameter
- **Aim:**
  - *standardize and simplify* methodology rather than increase accuracy

*Therasse P et al, JNCI 2000; 92: 205-216*
Standard description of response (based on change in size)

- Complete response  \textit{CR}
- Partial response  \textit{PR}
- Progression of disease  \textit{PD}
- Stable disease  \textit{SD}

\textbf{Response Evaluation Criteria in Solid Tumors (RECIST Criteria)}
New Guidelines to Evaluate the Response to Treatment in Solid Tumors


- **Major application intended for trials where response is primary endpoint**

- **Identify up to 10 measurable lesions; maximum 5 per organ. Follow sum of longest diameters (SLD)**

- **Response Categories:**
  - **PR = 30% decrease in SLD compared to baseline**
  - **PD = 20% increase in SLD compared to lowest value on study**

- **CT scan preferred imaging modality. No ultrasound.**

*Therasse P et al, JNCI 2000; 92: 205-216*
RECIST Guidelines

- Assumes spherical growth of round / ovoid tumors
- Uni-dimensional measurement technique
  - Less cumbersome, simple math
- Arbitrary number of measurable lesions
  - 5/organ; 10/patient
- Target lesions: >1cm (helical); >2cm (non-helical)
- Measurement on axial images

*Therasse P et al, JNCI 2000; 92: 205-216*
Limitations of RECIST

- **Tumor morphology**
  - Confluent, irregular borders, unusual config.
  - Circumferential (e.g. mesothelioma)
- **Discordant results due to RECIST technique**
  - Uni-dimensional measurement
  - Shape changes may confound results
- **Non-spherical, asymmetric tumor growth**
- **Sub-centimeter tumors**
- **Choosing representative tumor burden**
  - Problematic when tumor burden is substantial
  - Differential tumor response
Limitations of RECIST

- Updated imaging technology not considered
  - Multiplanar capability
  - Automated tumor detection
  - 3-D data acquisition: volumetric tumor measurement

- Criteria for tumors treated by non-cytotoxic drugs? (eg: Radio-frequency ablation)

- Metabolic and physiological changes predate tumor size change
Issues Arising since RECIST Implementation in 2000

1. Can fewer than 10 lesions be assessed?
2. How to account for cavitation?
3. Change tumor size in cc direction.
4. Use of RECIST in randomized trials
5. Use of newer imaging technologies such as PET and MRI.
6. Use of RECIST in trials of non-cytotoxic drugs.
• \(n = 37\) patients with breast ca. metastases

• Uni. vs. bi.: Discordance = 3%

• Uni. vs. volume: Discordance = 32%

• Bi. vs. volume: Discordance = 34%

• *Volumetric measurements* provide better assessment of tumor burden.

*Prasad et al. Radiology 2002; 225:416-419*
RECIST Rev 1

- 5 lesions/2 per organ
- For LNs: Measure SHORT axis ($\geq 15$ mm)
- PD: 20% increase AND min. 5 mm increase over lowest sum.

Eisenhauer et al. EORTC 10/22/08
Enhancement as a monitor of response

EASL recommends CT with contrast at 4 wks post. therapy

Enhancement = viability
Non-enhancement = necrosis

* Bruix et al. J. Hepatology 2001; 35:421-430
EASL Criteria

- **CR:** disappearance of areas of enhancement
- **PR:** decrease >50% of enhanced areas
- **PD:** increase >25% of enhanced areas or the appearance of new lesions
- **SD:** none of the above
Limitations

• May be reactive.
• HAP vs PVP not defined.
• Difference between hypo vs hypervascular tumors not defined.
• Difficult to assess on CT without unenhanced acquisitions.
• Difficult to assess on CT after TACE.
Value of MR imaging
Multi parametric approach

- **Anatomic (WHO, RECIST)**
  - T1, T2

- **Physiologic (quantifiable)**
  - Diffusion: cellular integrity (ADC map)
  - Perfusion: vascular integrity (EASL)
  - Elastography: tissue elasticity, stiffness

- **Metabolic (quantifiable)**
  - Spectroscopy: biochemistry