Volumetric Functional MRI Criteria for Assessing Tumor Response

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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
Tumor Size
WHO/RECIST/RECIST Rev 1

World Health Organization
(WHO Criteria)
Response Evaluation Criteria in Solid Tumors
(RECIST Criteria)
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
Tumor Enhancement

EASL

mRECIST

(for HCC)

European Association for the Study of Liver Disease (EASL Criteria)

Modified RECIST (mRECIST)
Enhancement as a monitor of response

T1 Postgad. Before TACE

T1 Postgad. After TACE
## Modified RECIST (mRECIST) Assessment for Hepatocellular Carcinoma

Riccardo Lencioni, M.D.,¹ and Josep M. Llovet, M.D.²,³

*Semin Liver Dis* (2010), 30:52-60

### Table 2  Assessment of Target Lesion Response: Conventional RECIST and mRECIST Assessment for HCC Following the AASLD-JNCI Guideline

<table>
<thead>
<tr>
<th>RECIST</th>
<th>mRECIST for HCC</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR = Disappearance of all target lesions</td>
<td>CR = Disappearance of any intratumoral arterial enhancement in all target lesions</td>
</tr>
<tr>
<td>PR = At least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum of the diameters of target lesions</td>
<td>PR = At least a 30% decrease in the sum of diameters of viable (enhancement in the arterial phase) target lesions, taking as reference the baseline sum of the diameters of target lesions</td>
</tr>
<tr>
<td>SD = Any cases that do not qualify for either partial response or progressive disease</td>
<td>SD = Any cases that do not qualify for either partial response or progressive disease</td>
</tr>
<tr>
<td>PD = An increase of at least 20% in the sum of the diameters of target lesions, taking as reference the smallest sum of the diameters of target lesions recorded since treatment started</td>
<td>PD = An increase of at least 20% in the sum of the diameters of viable (enhancing) target lesions, taking as reference the smallest sum of the diameters of viable (enhancing) target lesions recorded since treatment started</td>
</tr>
</tbody>
</table>

AASLD, American Association for the Study of Liver Diseases; JNCI, Journal of the National Cancer Institute; HCC, hepatocellular carcinoma; mRECIST, modified Response Evaluation Criteria in Solid Tumors; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease.
RECIST

mRECIST

EASL

mRECIST ??

EASL ??
MR findings after cryoablation

No tumor recurrence

Kuszyk et al, Radiology 2000; 217:477-486
MR findings after cryoablation

Macroscopic tumor recurrence

Kuszyk et al, Radiology 2000; 217:477-486
Value of MR imaging
Multi parametric approach

- Anatomic (WHO, RECIST)  
  - T1, T2

- Physiologic (quantifiable)  
  - Diffusion: cellular integrity (ADC map)  
  - Enh./perfusion: vascular integrity (EASL)  
  - Elastography: tissue elasticity, stiffness

- Metabolic (quantifiable)  
  - Spectroscopy: biochemistry
Value of MR imaging
Multi parametric approach

• Anatomic (WHO, RECIST)
  – T1, T2

• Physiologic (quantifiable)
  – Diffusion: cellular integrity (ADC map)
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  – Elastography: tissue elasticity, stiffness

• Metabolic (quantifiable)
  – Spectroscopy: biochemistry
**DWI: When to image after TACE?**

**Pre**

**24 hrs**

**2 wks**

Kamel et al *Radiology* (2009) 250; 466-473
Why not assess **FUNCTION** in entire tumor **VOLUME**, **EARLY** (3-4 wks) after therapy?
3D Volumetric Functional Changes

- Analyses the entire tumor volume
- Can be multiparametric:
  - Enhancement, ADC, etc....
- Two approaches:
  - Mean 3D Changes
    Requires tumor segmentation
    Calculate values pre and post then compare
  - Threshold 3D Changes
    Requires co-registration and tumor segmentation
    Changes above a predetermined threshold
Steps for image analysis

1. Image registration

2. Tumor segmentation

3. Volumetric functional maps

- Compare histograms
- Changes in relation to threshold
Advanced Image Analysis

Functional Maps

(Registration of pre and post treatment studies)

Poor Registration  Adequate Registration
Lesion Segmentation
Semi-automated

Mark tumor & background liver

Automatic Contour
HCC: PR

Pre

Post

Pre Post

ADC

Change

Pre-ADG Histogram

Post-ADG Histogram

ADC Change Histogram

Decreased, 37.9 %
Unchanged, 18.61 %
Increased, 73.37 %
Hepatocellular Carcinoma: Response to TACE Assessed with Semiautomated Volumetric and Functional Analysis of Diffusion-weighted and Contrast-enhanced MR Imaging Data

Purpose: To determine the association of early changes in posttreatment apparent diffusion coefficient (ADC) and venous enhancement (VE) with tumor size change after transarterial chemoembolization (TACE) by using an investigational semiautomated software.

Susanne Bonekamp, DVM, PhD
Prashant Jolepalem, MD
Mariana Lazo, MD, MPH
Mehmet Akif Gulsun, BSc
Atilla P. Kiraly, PhD
Ihab R. Kamel, MD, PhD

Volumetric Response to LRT by Functional MRI: Hepatocellular ca.

Radiology 260 (3) 752-61, 2011
HCC: Can volumetric MRI (1 mo) predict survival?

Johns Hopkins Criteria

Okuda 1 Responders (n=57)
Median: 31 mo

Others (n=84)
Median: 19 mo

Okuda 1 Responders (n=22)
Median: 37 mo

Others (n=119)
Median: 21 mo

Response by ADC (inc. ≥ 25%)

Response by ADC (inc. ≥ 25%) and Enh (dec. ≥ 50%)

p<0.0001
HCC: Can volumetric MRI (1 mo) predict survival?

*Johns Hopkins Criteria*
Volumetric Response to LRT by Functional MRI: Neuroendocrine mets
Neuroendocrine Response: Johns Hopkins Criteria

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>3-4 wk after TACE</th>
<th>% change</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor *</td>
<td>339.2</td>
<td>270.3</td>
<td>-20.8%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ADC †</td>
<td>1.24</td>
<td>1.55</td>
<td>20.3%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>AE ‡</td>
<td>54.2%</td>
<td>31.5%</td>
<td>-33.2%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>VE †</td>
<td>82.5%</td>
<td>60.4%</td>
<td>-16.7%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>RECIST</td>
<td>7.9 cm</td>
<td>7.4 cm</td>
<td>-8.6%</td>
<td>&lt;0.002</td>
</tr>
<tr>
<td>mRECIST</td>
<td>6.5 cm</td>
<td>5.2 cm</td>
<td>-18.2%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>EASL</td>
<td>42.2 %</td>
<td>25.8 %</td>
<td>-47.9%</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

N = 71
Endpoint: Survival

Do not fulfill response criteria

ADC: +40%
Ven. Enh: - 80%
Neuroendocrine Response: Johns Hopkins Criteria

Responders (n=40)
Median: 40 mo

Non Responders (n=31)
Median: 16 mo

n = 71
p<0.001

Response by ADC (inc. ≥ 15%)

Response by Enh (dec. ≥ 25%)
Volumetric Response to LRT by Functional MRI: Cholangio ca.

Cholangiocarcinoma Response

**RECIST vs. EASL vs. Volumetric MRI**

<table>
<thead>
<tr>
<th>Mean value</th>
<th>Baseline</th>
<th>1 month after TACE</th>
<th>% change</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>RECIST</strong></td>
<td>10.0</td>
<td>9.8</td>
<td>-3.1%</td>
<td>0.224</td>
</tr>
<tr>
<td><strong>Tumor volume</strong></td>
<td>400.4</td>
<td>317.9</td>
<td>-20.2%</td>
<td>0.074</td>
</tr>
<tr>
<td><strong>Volumetric ADC</strong></td>
<td>1.54</td>
<td>1.92</td>
<td>25.1%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>Volumetric AE</strong></td>
<td>40.6</td>
<td>37.5</td>
<td>-5.6%</td>
<td>0.546</td>
</tr>
<tr>
<td><strong>Volumetric VE</strong></td>
<td>79.0</td>
<td>70.0</td>
<td>-9.1%</td>
<td>0.105</td>
</tr>
</tbody>
</table>

N = 29; Endpoint: Survival
RECIST: 0-CR; 2-PR; 25-SD, 2-PD
EASL: 8/29 (28%) could not be assessed
Volumetric ADC: 21-PR; 8-SD/PD
Cholangiocarcinoma Response

Johns Hopkins Criteria

Responders: Increase ADC ≥ 25%
NR: all others

<table>
<thead>
<tr>
<th>Mean %</th>
<th>≥ 10 months</th>
<th>&lt; 10 months</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RECIST</td>
<td>-4.6%</td>
<td>1.7%</td>
<td>0.215</td>
</tr>
<tr>
<td>ADC</td>
<td>31.0%</td>
<td>6.7%</td>
<td>0.002</td>
</tr>
<tr>
<td>AE⁺</td>
<td>3.2%</td>
<td>13.0%</td>
<td>0.766</td>
</tr>
<tr>
<td>VE⁻</td>
<td>-15.8%</td>
<td>12.1%</td>
<td>0.236</td>
</tr>
</tbody>
</table>

Comparison between patients who survived ≥ 10 months (75.9%) vs. patients who survived < 10 months (24.1%). The only difference between the 2 groups was in ADC.

Responders
Median: 19 mo

Non Responders
Median: 9 mo
Partial Response

PR by ADC

Prior Study ADC
ADC: 1313 ± 192.719 [924, 3191] units

Current Study ADC
ADC: 1649 ± 276.013 [881, 3481] units

PR by Enh.

Prior Study Enhancement
Arterial: 45.24 ± 23.14 %, V.E.: 93.95 %, C3A: 75%
Venous: 86.04 ± 20.52 %, V.E.: 99.06 %
AEF: 71.1 ± 17.9 %

Current Study Enhancement
Arterial: 31 ± 54.459 %, V.E.: 75.705 %, C3A: 88%
Venous: 42 ± 59.109 %, V.E.: 93.057 %
AEF: 79.3 ± 51 %
Conclusions

- New era of cancer imaging that will change our practice
- DWI and/or enhancement should be included in oncology trials
- New Johns Hopkins Criteria, need validation
- Different criteria for different tumors and different chemotherapeutic agents
- Multi-parametric MR imaging (possibly multimodality) approach more valuable than single parameter
Thank You