European Society of Cardiology – Paris, France 2011
Session: Myocardial oedema - a new diagnostic target?

Cardiovascular magnetic resonance in acute myocardial infarction

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DECLARATION OF CONFLICT OF INTEREST

US Government Cooperative Research and Development Award (CRADA) - Siemens
The goal of this talk...

- To discuss cardiac MRI of acute myocardial infarction...
- …without overlapping too much with the other speakers...
  - Cardiovascular T2 and T2 mapping – Dr. Aletras
  - Area at Risk and Myocardial Salvage – Dr. Eitel
  - Microvascular Obstruction – Dr. Bogaert
- I decided to focus on late gadolinium enhancement of acute MI and what we have learned about LGE from imaging myocardial edema.
A comment from Ray Kim has haunted me ever since we started doing T2-weighted images of AAR

• “If T2 abnormalities in acute MI represent edema, why don’t we see gadolinium enhancement of the area at risk?”

• How can gadolinium depict the MI if it also corresponds to area at risk?
LGE is well validated for imaging acute MI

Correlation between MRI Infarct Size and TTC Staining

Detection of MI by MRI: First Multicenter Study

Distribution of Contrast in Tissue Defines Viability/Fibrosis

Normal intact cell membrane

Acute MI ruptured cell membrane

Chronic MI collagen matrix

Arai AE. Journal of Nuclear Cardiology (in press)
Peri-Infarct Zone on Early Contrast-Enhanced CMR Imaging in Patients With Acute Myocardial Infarction

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- Early Gadolinium Enhancement (EGE) depicts salvaged myocardium and infarcted myocardium.
- Late Gadolinium Enhancement (LGE) highlights infarcted myocardium.
- The combination of EGE and LGE can delineate AAR, salvage, and MI size from a single dose of contrast.
Early Gadolinium Enhancement corresponds to AAR

Matsumoto H et al. JACC Cardiovasc Imaging 2011; 4: 610
Gadolinium Can Depict Area at Risk and MI: A Double-Edged Sword?

“Rather than concluding that gadolinium overestimates acute infarct size, the more appropriate and challenging conclusion is that understanding the kinetics of gadolinium contrast enhancement and washout will help determine why gadolinium can show both the penumbra of the area at risk and the core of late gadolinium enhancement that represents the infarct.”

Arai AE. J A C C : Cardiovascular Imaging 2011; 4: 619
Imaging Time After Gd-DTPA Injection Is Critical in Using Delayed Enhancement to Determine Infarct Size Accurately With Magnetic Resonance Imaging

John N. Oshinski, Zequan Yang, Jeffrey R. Jones, Jaime F. Mata and Brent A. French

Circulation 2001;104:2838-2842
Early Gadolinium Enhancement of the “rim” around an Acute MI in rabbits

Thus, multiple papers over the years have suggested LGE should be \( \sim 20 \) minutes post-contrast.
How should we interpret acute infarct size when calculating myocardial salvage?

Dall’Armellina E et al. Circ Cardiovasc Imaging 2011; 4; 228
Extent of “LGE at 12-48 hrs” was a poor predictor of functional recovery post-MI

“LGE” was performed ... 5 to 10 minutes after the administration of 0.1 mmol/kg contrast agent (Gadodiamide, Omniscan)...

Dall’Armellina E et al. Circ Cardiovasc Imaging 2011; 4; 228
Kramer also concluded that transmural hyperenhancement overestimated irreversible injury in Acute MI

- Twenty-three patients with a reperfused first MI were studied. On day 3 +/- 1 after MI,
  - Tagged MRI at baseline and during infusion low dose dobutamine
  - Contrast-enhanced MRI (first pass and delayed imaging) after a bolus infusion of gadolinium DTPA.

- Transmural regions with hyperenhancement on delayed contrast-enhanced images were defined as:
  - COMB (first pass hypoenhancement) or
  - HYPER (normal first pass signal enhancement).

Kramer et al. JACC 2000; 36: 1835
Kramer also concluded that transmural hyperenhancement overestimated irreversible injury in Acute MI

- HYPER regions demonstrate both contractile reserve in response to dobutamine acutely and late functional recovery.
- COMB regions demonstrate first pass contrast hypoenhancement and are associated with greater myocardial damage.

At least 1 set of 10 delayed images in each of the same three planes was acquired 5 to 7 min after the first pass imaging...
We found a better relationship between LGE and ultimate recovery of function post-MI.

Images were obtained approximately 20 min after intravenous injection of 0.2 mmol/kg gadolinium (Magnevist, Berlex).

Ingkanisorn WPI et al. JACC 2004; 43: 2253
However, Ibrahim et al found overestimation of MI size on day 1 post-MI compared with day 7 or later.

Images were obtained approximately 20 min after intravenous injection of 0.2 mmol/kg gadolinium (Magnevist, Berlex). Window width was manually adjusted.

Ibrahim T et al. Radiology 2010; 254: 88
Quantification of Partition Coefficient ($\lambda$) in does not reach steady state in acute MI with MVO

Klein C et al. JCMR 2007; 9: 653
What other factors can lead to overestimation of acute MI size by gadolinium?
Threshold and optimal TI affect accuracy of gadolinium-determined MI size
Quality of data used to assess FACT algorithm for quantifying MI size

Hsu L et al.
JMRI 2006; 23: 298
Visual impression overestimates MI size

Hsu L et al. JMRI 2006; 23: 298
Human traces, 2 SD threshold, and FWHM all overestimate MI size

<table>
<thead>
<tr>
<th></th>
<th>Error in % of LV</th>
<th>Error in % of MI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ex vivo</td>
<td>In vivo</td>
</tr>
<tr>
<td>FACT</td>
<td>0.5%</td>
<td>1.2%</td>
</tr>
<tr>
<td>Human</td>
<td>3.2%</td>
<td>5.4%</td>
</tr>
<tr>
<td>FWHM</td>
<td>3.1%</td>
<td>6.7%</td>
</tr>
<tr>
<td>2SD</td>
<td>10.4%</td>
<td>9.1%</td>
</tr>
</tbody>
</table>

Errors are expressed as % of LV and % of MI for the difference between MR and TTC measurements.

FACT = Feature analysis and combined thresholding, Human = human manual contouring, FWHM = full width at half maximum intensity thresholding, 2SD = two–standard deviation intensity thresholding.

Hsu L et al. JMRI 2006; 23: 298
Displayed Image Contrast is Dependent on the User Setting of Window Width and Window Level

- At first glance it appears that the contrast between the bright circle and the background is better in panel B than panel A.
- This is actually the same image displayed on too dark a gray scale in panel A.
- Panel B is aggressively windowed to show the background as dark with the noise visible while the bright pixels in the circle approach the top of the gray scale.

Can You Detect 1 Standard Deviation Brighter than the background?

<table>
<thead>
<tr>
<th>Region</th>
<th>Mean +/- SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Square</td>
<td>26 +/- 23</td>
</tr>
<tr>
<td>Ellipse</td>
<td>46 +/- 23</td>
</tr>
<tr>
<td>Text</td>
<td>78 +/- 23</td>
</tr>
</tbody>
</table>
Theoretical arguments against 2 SD threshold

- SNR will change with field strength
- SNR is not uniform in the heart when using parallel imaging
  - Thus it is difficult to define the spatially correct SD
Partial Volume Error can cause overestimation of MI size

Conclusions

- Early gadolinium enhancement depicts area at risk associated with recent acute MI.
- Late gadolinium enhancement depicts infarct size.
- The exact timing of what constitutes early gadolinium enhancement and late gadolinium enhancement is poorly defined.
Conclusions (con’t)

• That presents the double-edged sword in the story:

• …although it is convenient to be able to measure area at risk and infarct size with a single gadolinium injection…

• …we will need to be careful with our timing to avoid hybrid data between the two distinctly different physiological processes…

• …acute MI vs salvaged myocardium
Conclusions (con’t)

• There are a variety of other factors that may lead to apparent gadolinium overestimation of MI size:
  • SNR or CNR (3T, 7T, vs 1.5T)
  • Contrast dose and probably contrast agent
  • Visual impression & subjective window / levels
  • Low thresholds (2 SD in particular)
  • Possibly computer algorithms
  • Partial volume artifact
Recommendations

• Standardization is needed for:
  • Contrast dose
  • Timing of EGE and LGE
  • Quantification of MI size should use methods like FACT primarily based on partial volume arguments and published results.
  • Quantification of atypical LGE or the peri-infarct borderzone will need a lower threshold such as 2 SD recognizing that 5% of normal hearts would get labeled abnormal.