MR enterography evaluation of Crohn’s Disease Activity and Mucosal Healing

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Disclosures

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Overview

• MR enterography performance for assessing pediatric CD activity
• MR enterography-based CD activity scoring systems
• MR enterography assessment of treatment response/resistance
Potential radiation risk associated with CT imaging in CD patients provides impetus for MRI as CD imaging modality

- High incidence of diagnosis during childhood and adolescence
- Episodic nature leads to frequent symptomatic recurrence over pt lifetime
- 16% of CD pts in one study exceeded 75 mSv radiation over 15 yrs, 80% from CT
- CD patients diagnosed during childhood receive higher cumulative radiation from imaging

Desmond AN *Gut* 57: 1524 (2008)
MRE offers several advantages over CTE including:

- LACK OF IONIZING RADIATION
- Superior soft tissue contrast for characterizing bowel inflammation
- Ability to assess the biliary tree and anal sphincter complex
MRE pulse sequences are helpful for assessing IBD activity
(Cinematic bSSFP helpful for evaluating underdistended bowel)

Normal

Active inflammation
MRE pulse sequences are helpful for assessing IBD activity
(Multi-phase post contrast, T2-weighted and diffusion-weighted imaging)
Evidence of MRE as a biomarker of pediatric CD activity
Multiple studies validating MRE as biomarker of pediatric CD activity

<table>
<thead>
<tr>
<th>Authors</th>
<th>Journal</th>
<th>Study Size</th>
<th>Reference</th>
<th>Sens (%)</th>
<th>Spec (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>JR Dillman, PJ Strouse et al</td>
<td>Pediatr Radiol</td>
<td>32 pts/149 segments</td>
<td>Histo w/i 2 mos</td>
<td>66%</td>
<td>90%</td>
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<td></td>
<td>(2011)</td>
<td></td>
<td></td>
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<tr>
<td>MS Gee, K Nimkin et al</td>
<td>AJR (2011)</td>
<td>21 pts/53 segments</td>
<td>Histo w/i 45 days</td>
<td>83%</td>
<td>83%</td>
</tr>
<tr>
<td>DB Wallihan, DJ Podberesky et al</td>
<td>Acad Radiol</td>
<td>45 pts/91 segments</td>
<td>Endo or surg w/i 45 days</td>
<td>92% patient</td>
<td>75-100% patient</td>
</tr>
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<td></td>
<td>(2012)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>I Absah, JG Fletcher et al</td>
<td>AJR (2012)</td>
<td>48 pts/144 segments</td>
<td>Endo w/i 2 wks</td>
<td>79-90% segmental</td>
<td>64-85% segmental</td>
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<tr>
<td>F Maccioni, C Catalano et al</td>
<td>AJR (2014)</td>
<td>50 pts/450 segments</td>
<td>US, SBFT, endo</td>
<td>95%</td>
<td>97%</td>
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</table>
Similar performance of CTE and MRE for detecting active CD

- A few studies performed CTE and MRE in the same patients
- Comparison vs endoscopic and histologic reference
- Accuracy and sensitivity ranges 80-90%
- MRE superior to CTE for detecting fibrotic strictures

HA Siddiki et al, AJR (2009)
SS Lee et al, Radiology (2009)
KB Quencer, MS Gee et al, Abdom Imaging (2013)
Numerous Imaging Findings of Bowel Inflammation in CD

- Wall thickening >3 mm, luminal narrowing, bowel obstruction
- Mural hyperenhancement and edema, mural restricted diffusion
- Perienteric stranding, fibrofatty proliferation, vasa recta engorgement
- Penetrating disease: ulcer, sinus tract/fistula, abscess, inflammatory mass

SAR/AGA consensus guidelines for CTE/MRE (2017 submitted)
Wall thickening and mural hyperenhancement are important MRE features of active disease in pediatric CD

- Pts ≤ 18yo
- 59 MRE pts/317 bowel segs with histo w/i 28 d
- WT and MH performed best for activity detection
- Logistic regression model including WT and MH best predicted activity

HI Gale, MS Gee et al, Pediatr Radiol (2017)
Several MRE features correlate well with serum (CRP) and clinical (PCDAI) markers of activity

Magnetic resonance enterography has good inter-rater agreement and diagnostic accuracy for detecting inflammation in pediatric Crohn disease

- MRE from 48 pediatric CD patients
- wCDAI >12.5, CRP>5 considered positive
- Part of ImageKids consortium generating Pediatric Inflammatory Crohn’s MRE Index (PICMI)

MRI Index of Activity (MaRIA)

Based on logistic regression of MRE/colonography features associated with active disease on endoscopy

\[(1.5 \times \text{WT}) + (0.02 \times \text{RCE}) + (5 \times \text{edema}) + (10 \times \text{ulceration})\]

Edema and ulceration assessment are binary; RCE and WT are calculated

Segment score ≥ 7 demonstrates 87% sens/spec for endoscopic active disease

J Rimola, Inflamm Bowel Dis (2011)
Role of MRE in Lemann Index of bowel damage

- Way to track cumulative CD progression
- Includes stricturing and penetrating lesions and bowel resections
- Involves both imaging and endoscopy to assess

Pros and cons of MRE activity scoring systems

Pros:
• Reproducible
• Established correlation with CD activity
• Based on traditional MRE parameters
• **Noninvasive assessment of treatment response via serial imaging**

Cons:
• **Time-intensive**
• Sum of segmental scores difficult to incorporate into routine clinical practice
Role of MRE in tracking changes in pediatric CD activity
Change in bowel enhancement on serial MRE during CD therapy associated with improvement in health-related Quality of Life

- 26 newly-diagnosed CD pts with MRE and HRQOL assessment performed pre- and 6 mos post-infliximab Tx
- Significant negative correlation btw MRE bowel enhancement and VAS HRQOL score during treatment

JR Dillman et al, Radiology (2016)
Mucosal Healing as primary goal of pediatric IBD therapy

• Rationale: Marker of therapeutic reversal of mucosal inflammation

• Deep remission: MH + normalization of inflammatory markers

• Recent clinical studies have linked mucosal healing with long-term clinical remission

• Limitations:
  – Endoscopic vs histologic assessment
  – Established mucosal healing criteria in CD (SES-CD/CDEIS score 0 vs <3)
  – Timing of endoscopic re-evaluation

F Nuti, J Crohns Colitis (2016)
JT Osterman, J Clin Gastroenterol (2013)
RM Ruemmele, Gut (2015)
• 2014 study of 48 adult CD pts undergoing MRE and endoscopy at 0 and 12 wks of Tx (steroids or TNFα inhibitor)

• MaRIA <11 showed 90% accuracy for endoscopic ulcer healing, MaRIA<7 showed 83% accuracy for MH (CDEIS < 3.5)
### MR Enterographic Findings as Biomarkers of Mucosal Healing in Young Patients With Crohn Disease

<table>
<thead>
<tr>
<th>MRE feature</th>
<th>Accuracy</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>MaRIA &lt; 8</td>
<td>74</td>
<td>84</td>
<td>62</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Lack of Mural Hyperenhancement</td>
<td>72</td>
<td>98</td>
<td>41</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Lack of Mesenteric Hypervascularity</td>
<td>72</td>
<td>98</td>
<td>41</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Lack of Bowel Wall Edema</td>
<td>72</td>
<td>93</td>
<td>46</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Wall Thickness &lt; 4 mm</td>
<td>72</td>
<td>84</td>
<td>57</td>
<td>0.0002</td>
</tr>
</tbody>
</table>

- Analysis of 30 pediatric CD patients with serial endoscopy to evaluate for mucosal healing and MRE correlation
- Resolution of several individual MRE imaging features had comparable performance to MaRIA for detecting mucosal healing

MP Moy, MS Gee et al, AJR (2016)
Potential role for MRE surveillance in predicting recurrence in asymptomatic pediatric CD patients

<table>
<thead>
<tr>
<th>MRE Feature</th>
<th>Odds Ratio (95%CI)</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mural T2 hyperintensity</td>
<td>6.67 (1.34-33.12)</td>
<td>0.015</td>
</tr>
<tr>
<td>Wall thickness &gt;3mm</td>
<td>8.44 (1.48-48.14)</td>
<td>0.008</td>
</tr>
<tr>
<td>Overall activity assessment</td>
<td>8.94 (1.73-57.72)</td>
<td>0.010</td>
</tr>
<tr>
<td>Mural hyperenhancement</td>
<td>12.00 (2.04-70.44)</td>
<td>0.002</td>
</tr>
<tr>
<td>DWI restriction</td>
<td>14.00 (2.51-77.99)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

* Regression P-values based on Wald Z-statistic

K Chu, MS Gee et al, SPR (2017)
Summary

• Lack of ionizing radiation makes MRE the preferred imaging modality in pediatric CD pts who are likely to need serial imaging over their lifetime.

• MRE has been validated for assessing pediatric CD activity and mucosal healing.

• It is likely that MRE will see increased use as a primary endpoint of CD clinical trials and in surveillance of asymptomatic CD pts on treatment.
Thank you!