Validation Of Multi-Parametric MRI in the Assessment and Staging of Non-Alcoholic Fatty Liver Disease

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Disclosures

☐ This work is academic led and funded by Innovate-UK

☐ I have no financial interests in Perspectum Diagnostics Ltd
Non-invasive testing seeks to:

- Detect steatosis
- Diagnose NASH
- Be sensitive enough to monitor changes in NASH severity
- Accurately stage fibrosis
- (Predict clinically meaningful outcomes)
Aims

Prospective assessment and validation of multi-parametric MRI as a non-invasive test to assess NAFLD in a population of patients with undergoing liver biopsy
T1 Mapping

Hypothesis that hepatic T1 is proportional to extracellular water content, which is elevated in fibrosis

Hepatic iron content inversely proportional to T1

Hoad C et al, NMR Biomed, 2015
Multi-Parametric MRI

- Proprietary algorithm developed by Perspectum Diagnostics Ltd uses T2* to adjust T1 to compensate for the effects of iron
- Proton density fat fraction (PDFF)
- T1 mapping
- T2* mapping → Iron corrected T1 (cT1)
Methods

- Sequential patients undergoing standard of care liver biopsies for the diagnosis or assessment of NAFLD
  - Queen Elizabeth Hospital Birmingham
  - Royal Infirmary of Edinburgh
- MRI in the 2 weeks prior to biopsy
  - Analysed by operator blinded to the histology and demographics
- Histology assessed by expert pathologist blinded to the MRI findings
Recruitment at two centres

54 patients with NAFLD

50 patients included in this sub-group analysis

1 biopsy inadequate for analysis

3 MRI result not available
## Baseline Demographics

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>54 (18-73)</th>
<th>Median (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>28 (56%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>Caucasian</td>
<td>43 (86%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>BMI (Kg/m²)</td>
<td>33.6 (+/-5.1)</td>
<td>Mean (+/-SD)</td>
</tr>
<tr>
<td>Male Waist:Hip ratio</td>
<td>0.98 (+/-0.07)</td>
<td>Mean (+/-SD)</td>
</tr>
<tr>
<td>Female Waist:Hip ratio</td>
<td>0.90 (+/-0.06)</td>
<td>Mean (+/-SD)</td>
</tr>
<tr>
<td>Post transplant</td>
<td>5 (10%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>Type 2 diabetes</td>
<td>26 (52%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>Consume alcohol</td>
<td>13 (26%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>Alcohol intake (UK units/week)</td>
<td>8 (1-20)</td>
<td>Median (range)</td>
</tr>
</tbody>
</table>
**Histology**

Median (range) length 25 (15—50) mm
Confirmed diagnosis of NASH 38 (76%)

<table>
<thead>
<tr>
<th>Kleiner Fibrosis Stage</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>6</td>
<td>12%</td>
</tr>
<tr>
<td>1</td>
<td>10</td>
<td>20%</td>
</tr>
<tr>
<td>2</td>
<td>9</td>
<td>18%</td>
</tr>
<tr>
<td>3</td>
<td>20</td>
<td>40%</td>
</tr>
<tr>
<td>4</td>
<td>5</td>
<td>10%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Total NAS score</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-2</td>
<td>9</td>
<td>18%</td>
</tr>
<tr>
<td>3-4</td>
<td>16</td>
<td>32%</td>
</tr>
<tr>
<td>5-6</td>
<td>22</td>
<td>44%</td>
</tr>
<tr>
<td>7-8</td>
<td>3</td>
<td>6%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Brunt Steatosis Grade</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>1</td>
<td>23</td>
<td>46%</td>
</tr>
<tr>
<td>2</td>
<td>17</td>
<td>34%</td>
</tr>
<tr>
<td>3</td>
<td>10</td>
<td>20%</td>
</tr>
</tbody>
</table>
Significant association between PDFF and Brunt steatosis grade

\[ p < 0.0001 \]
cT1 is significantly elevated in those diagnosed with NASH
Significant association between cT1 and total NAS score

\[ p = 0.013 \]
No significant association between cT1 and fibrosis

≥ F1
AUROC 0.72 (0.47 – 0.97)

≥ F3
AUROC 0.62 (0.47-0.78)
Fibrosis assessment confounded by presence of inflammation
cT1 is a marker of fibrosis and inflammation

\[ p = 0.043 \]

NS

Total NAS score

< 5

\( \geq 5 \)

Kleiner Stage

0-2

3-4

\( cT1 \) (msec)
Multi-parametric MRI has potential to exclude disease

\[ p = 0.015 \]
Conclusions

- Multi-parametric MRI has potential for identification of steatosis
- Multi-parametric MRI has potential to differentiate NASH from simple steatosis
- Strong correlation with severity of inflammation suggests opportunity to monitor disease progression/regression in both practice, research and drug development
- Utility as a tool to exclude significant disease
Multiparametric magnetic resonance imaging predicts clinical outcomes in patients with chronic liver disease

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