A plethora of studies have shown that some Gadolinium based Contrast Agents used in MR imaging can deposit gadolinium in the body. This study found that multiple administrations of the macrocyclic, ionic agent, gadoteric acid (Dotarem®), does not lead to significant increases in signal intensity ratios within the dentate nucleus of the brain.

**Introduction**

- Recent studies have associated the repeat administration of some Gadolinium-based Contrast Agents (GdCAs) used in MR imaging to brain hyper-signal intensities, which indicate Gadolinium retention.
- These high signal areas have been reported:
  - On unenhanced T1 weighted images, predominately in the dentate nucleus (DN).
  - After multiple injections of the linearly structured GdCAs.
  - In patients with normal renal function.
  - Many years after the last GdCA injection.
- The aim of this study was to investigate whether the repeated administrations of the macrocyclic GdCA, gadoteric acid (Dotarem®) led to significant increases in signal intensity ratios (SIR) compared to a control group of patients having undergone multiple non-contrast MRI.

**Analyses**

- Ratio differences were calculated between the first scan and then following an average of 6.2 scans for the gadoteric acid group and 5.2 scans for the non-contrast group.
- Paired T-tests (α = 0.05) were performed using SPSS to compare the ratio differences between the gadoteric acid and non-contrast groups.
- Full demographic and scanning information is given in the table below.

**Demography**

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Gadoteric acid n=51</th>
<th>Non-contrast n=17</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>50.0 ± 13.8</td>
<td>35.8 ± 19.9</td>
<td>0.012</td>
<td></td>
</tr>
<tr>
<td>Male/Female</td>
<td>20/31</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of Scans (range)</td>
<td>6.2 ± 1.6 [5 – 12]</td>
<td>5.2 ± 1.9 [2 – 10]</td>
<td>0.032</td>
</tr>
<tr>
<td>Cumulative Dose (ml)</td>
<td>51.7 ± 16.1</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>Time Interval (days)</td>
<td>Between each scan</td>
<td>Between last injection and analysed image</td>
<td></td>
</tr>
<tr>
<td>139.6 ± 148.7</td>
<td>152.0 ± 152.4</td>
<td>420.9 ± 355.4</td>
<td>0.001</td>
</tr>
<tr>
<td>421.9 ± 348.6</td>
<td>&lt;0.081</td>
<td></td>
<td></td>
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</tbody>
</table>

- Age differences are likely due to contrast scans being used to diagnose more pathologies that affect older populations.
- Contrast scans are likely repeated as part of annual surveillance while contrast-enhanced scans are performed on a more frequent basis.

**Method**

- Images from patients who have undergone multiple brain MRI were split into 2 groups; solely gadoteric acid (administered at 0.1 mmol/kg) enhanced vs those who have never had contrast.
- SIRs were calculated for the dentate nucleus (DN) to pons, DN to middle cerebellar peduncle (MCP) and DN to cerebrospinal fluid (CSF). Images below show example ROI placement.

**Results**

- No significant difference in the difference between final and baseline DN/Pons, DN/MCP or DN/CSF SIR was seen between images acquired after multiple administrations of gadoteric acid vs multiple non-contrast scans.
- SIR measurements for gadoteric acid enhanced scans are comparable with previously published results by Radbruch et al. and Weberling et al.

**Images**

- In some cases only sagittal unenhanced T1 images were available.
- SIR values from baseline axial and sagittal images were compared.
- There was no significant difference (p<0.001) in SIR calculated using either slice orientation.

**Discussion & Conclusion**

- There was no significant change in the SIR measurements DN/Pons, DN/MCP and DN/CSF, following an average of 6 gadoteric acid enhanced MRI compared to multiple non-contrast MRI.
- Signal intensity ratios measured on axial and sagittal images can be used interchangeably. These results add to the continually growing evidence base that the macrocyclic GdCA, gadoteric acid (Dotarem®), does not cause brain hyper-signal intensities.

**References**