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Feasibility of Using Brain Attenuation Changes on CT to Accurately Predict Time of Ischaemic Stroke Onset

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Background

• Following ischaemic stroke, CT attenuation of affected brain reduces with time
• We piloted whether attenuation of infarct can be used to predict time of stroke onset
• This might enable the safe treatment of ischaemic strokes with intravenous alteplase for patients without a known time of symptom onset

Methods

We selected patients from the Third International Stroke Trial\(^1\) with thin-slice (≤2.5 mm) CT brain imaging available at baseline (<6 hours from stroke onset) and follow-up who had cerebral infarct (but no haemorrhage) visible on their follow-up CT.

A wide range of stroke onset to scan times (time) were selected from among all available baseline and follow-up CT scans.

A neuroradiologist manually applied regions of interest (ROIs) within the infarct and an equivalent contralateral location (normal tissue) at each time point, guided by the infarct location on the follow-up scan (Fig 1).

We derived infarct: normal tissue attenuation ratio.

Cases were assigned to development and testing datasets (75/25%) blind to attenuation ratio.

Attenuation ratio in the development dataset was plotted against time and a best-fit logarithmic function determined (Fig 2) and then used to estimate time in the test dataset.

We assessed accuracy of time estimates and tested the ability of this technique to correctly classify patients as suitable (<4.5 hours from stroke onset) or unsuitable (>4.5 hours) for intravenous thrombolysis based on current European licensing for alteplase.

Results

• We assessed 242 CT scans from 144 patients
• Among all scans, time ranged from 22 minutes to 268 hours
• There were no significant differences between development and test datasets (Table 1)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Development dataset (n=180)</th>
<th>Test dataset (n=62)</th>
<th>P-value for Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>63 (71.16)</td>
<td>61 (70.85)</td>
<td>0.451</td>
</tr>
<tr>
<td>Male Sex</td>
<td>43.7%</td>
<td>40%</td>
<td>0.040</td>
</tr>
<tr>
<td>NIHSS</td>
<td>23.0 (20.0)</td>
<td>18.0 (15.0)</td>
<td>0.036</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>150 (140-210)</td>
<td>140 (130-200)</td>
<td>0.380</td>
</tr>
<tr>
<td>Time from stroke onset to scan (hours)</td>
<td>15 (2.7-34.0)</td>
<td>16.7 (2.8-36.0)</td>
<td>0.805</td>
</tr>
<tr>
<td>Associated to alteplase</td>
<td>40.2%</td>
<td>55%</td>
<td>0.403</td>
</tr>
<tr>
<td>Attenuation ratio</td>
<td>0.70 (0.56-0.86)</td>
<td>0.70 (0.55-0.86)</td>
<td>0.949</td>
</tr>
</tbody>
</table>

Table 1. Comparison of development and test datasets. Results are median (inter-quartile range) or %.

We plan to validate these findings prospectively in a larger dataset and to test reader reliability

Conclusions

• These results suggest it might be possible to predict time after stroke onset using only CT brain attenuation
• We have accurately classified patients as suitable or unsuitable for treatment with IV alteplase using this technique
• We plan to validate these findings prospectively in a larger dataset and to test reader reliability