Factors Influencing the Detection of Early CT Signs of Cerebral Ischemia
An Internet-Based, International Multiobserver Study

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Background and Purpose—Early CT signs of cerebral ischemia are subtle. Little is known of which factors influence the detection of infarct signs. We compared neuroradiologists’ scan readings with those of other specialists involved in the care of stroke patients.

Methods—We used the Internet to show 63 CT scans, all acquired <6 hours after stroke and representing different patient ages, times to scanning, stroke severity, and early CT signs of ischemia to physicians involved in stroke care. They completed a structured scan interpretation proforma over the Internet. We compared the detection of early ischemic signs stratified by severity and the effect of prior stroke between different specialties.

Results—Among 207 observers, neuroradiologists saw significantly more of “any early ischemic changes” than did stroke physicians, general radiologists, geriatricians, or neurologists (all P<0.0001), predominantly due to neuroradiologists’ greater detection of “mild” hypoattenuation or swelling. Detection of “severe” hypoattenuation or swelling, and hyperattenuated arteries did not differ between specialties. Old infarcts impaired recognition of early ischemic signs. Nonneuroradiologists did not “overcall” signs. Years of scan-reading experience did not account for these differences, but neuroradiologists took, on average, 30 seconds longer to read each scan than did most other specialists (P<0.0001).

Conclusions—Nonneuroradiologists should realize that they are unlikely to overcall signs, that old infarcts may distract them from seeing early ischemic signs, and read stroke CT scans more slowly, as these factors may help them perform more like neuroradiologists. (Stroke. 2007;38:1250-1256.)

Key Words: cerebral infarction ▪ computed tomography scanning ▪ early infarct signs ▪ stroke

CT scanning early after stroke can make a positive diagnosis of ischemic stroke and exclude other causes of acute focal neurology. CT is widely available and can be used in virtually all stroke patients. However, early CT signs of ischemia are subtle, and physicians may lack confidence in their ability to detect or exclude early CT signs of ischemia, especially if thrombolysis is being considered.

Detection of CT signs of early ischemia is not good.1 In a recent systematic review, the interobserver agreement for “any early CT sign” was 0.14 to 0.78 (κ), with sensitivities and specificities for infarct sign detection of 20% to 87% and of 56% to 100%, respectively. Most studies had relatively few observers who were not categorized by experience or training, tested few scans, compared observers with only 1 or 2 experts, and gave little information on how the scans had been selected. Therefore, it was difficult to generalize from those studies to routine acute stroke diagnosis, determine which early ischemic changes were best recognized, or determine which factors (eg, observer experience, knowledge of symptoms, and patient-related factors like previous stroke) might influence scan interpretation. The comparison with only 1 or 2 experts may have made the observers’ recognition of early CT signs appear relatively poorer than it actually was in day-to-day practice. Comparison with a broader group of neuroradiologists (whose day-to-day role is to read CT brain scans but who may not have had the advantage of reading very large numbers of hyperacute stroke CT scans) might provide a more realistic estimate of how well neurologists, stroke physicians, and others involved in stroke patient care might perform on a daily basis.

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We therefore performed a large observer-reliability study to determine which ischemic changes were most reliably detected, whether there were differences in observer performance attributable to their scan-reading experience, and which scan-related factors might impair detection of CT signs of early ischemia.

Methods

We established an Internet-based scan-reading tool (www.neuroimage.co.uk). To achieve as large a group of observers as possible, participants viewed CT scans and recorded their responses over the Internet. We applied STARD principles to the study design and report.2

CT Scans

We selected CT scans by (1) patient characteristics (age, duration of symptoms, and stroke severity) and (2) presence of specific signs. Scans chosen for specific patient characteristics came from 120 sequential patients admitted to a teaching hospital and who underwent CT scanning within 6 hours of acute stroke, from which we randomly chose 22 scans representing time to scanning (half <3 hours and half 3 to 6 hours after stroke); patient age (half <70 years and half >70 years); and stroke severity (National Institutes of Health Stroke Scale score; half ≤12 and half >12), independently of which signs the scans showed. Scans chosen for specific early ischemic changes (n=10) independent of patient characteristics came from previous3 and ongoing (www.IST3.co.uk) trials of thrombolysis in stroke.

The scans were shown anonymized in batches of ~10, the first 5 batches without any clinical information and the last batch with the side of brain symptoms. The scans were managed electronically with a DICOM reader Digital Jacket (DesAcc, Inc, Chicago Ill) and were optimized for gray/white matter differentiation.

Observers

We sought as many observers as possible through relevant conferences, newsletters, professional organizations, and journal articles.4,5 Participation was encouraged by awarding 5 Continuing Professional Development credits from the UK Royal Colleges for reading all scans and several monetary prizes.

Scan Reading

Observers logged onto the Web site (www.neuroimage.co.uk), registered which specialty (chosen from a list, Table 1) most closely represented their work (Table 1), years of training in that specialty, and country of origin. They optimized monitor settings (contrast/brightness) and ambient light for detecting subtle gray-scale differences with a Society of Motion Picture Television Engineers test on the www.neuroimage.co.uk Web site. They read a test scan to familiarize themselves with the Web scan-viewing tool (the Figure) and the structured questionnaire. Thereafter, study scans were assigned in batches. Each scan could be viewed in “light box” or “stack” mode (Figure). The time taken to complete the questionnaire was recorded.

Structured Questionnaire

The questionnaire was developed and tested on acute stroke CT scans outside the study cohort. The signs of early ischemia on CT are (1) decreased parenchymal x-ray attenuation, (2) tissue swelling (mass effect), and (3) hypodense artery sign (arterial occlusion).6 The final questionnaire recorded scan quality; any change in attenuation or swelling (and whether mild or severe); the arterial territory(s) affected; tested 3 scoring systems (1/3 MCA rule,7 IST3 method,8 and the Alberta Stroke Program Early CT Score [ASPECTS]);9 and whether there was any hypodensified artery or other abnormality (atrophy, tumor, hemorrhage, or old infarct). We defined mild hypodensification as gray matter reduced to that of normal white matter attenuation; severe hypodensification as gray or white matter attenuation less than normal white matter; mild swelling as effacement of the ipsilateral cortical sulci or slight effacement of the lateral ventricle, and severe swelling as complete effacement of the lateral ventricle or midline shift.

Statistical Analysis

We analyzed data from readers who completed all 63 scans. Data were normally distributed. The readings of 1 observer, a neuroradiologist internationally acknowledged to be very experienced in interpretation of CT in acute stroke, were used to independently determine the proportion of scans with each CT sign. This was to characterize the scans, not to compare other readers with this 1 expert, as the latter analysis would not be generalizable to routine practice: 1 expert’s CT scan readings are not a perfect “gold standard,” so sensitivity/specificity analyses would not be appropriate, nor would a k of each individual versus the expert address day-to-day practice. Therefore, for each scan, we calculated the proportion of neuroradiologists who recognized any sign and each individual sign and compared that with the proportion of each other specialty who recognized those signs. We then compared the proportion of neuroradiologists to the proportion of each other specialty (ie, continuous variables) by Bland-Altman analysis, with probability values calculated from 1-sample t tests.10 We also examined whether the presence of old infarcts, atrophy, or periventricular white matter lesions affected the proportion of each specialty’s ability to recognize signs by χ2 tests. Significance was set at the P<0.05 level.

Results

Demographics of Scan Readers

Two hundred seven readers from 36 countries, mostly the UK (40%), Germany (18%), and Italy (14%), completed all 63 scans (Appendix). Nearly half of the 207 participants classified themselves as neurologists (99, 48%), then general radiologists (25, 12%), neuroradiologists (24, 12%), geriatricians (21, 10%), stroke physicians (16, 8%), and “others” (22, 11%; general practitioners, emergency medicine physicians, miscellaneous; Table 1).

Approximately one third (63/207) of readers had been reading CT scans for stroke as part of their routine daily work.

<table>
<thead>
<tr>
<th>Specialty</th>
<th>Years of experience</th>
<th>Neuroradiologists</th>
<th>General Radiologists</th>
<th>Neurologists</th>
<th>Stroke Physicians</th>
<th>Geriatricians</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5</td>
<td></td>
<td>25%</td>
<td>21%</td>
<td>26%</td>
<td>44%</td>
<td>24%</td>
<td>67%</td>
</tr>
<tr>
<td>5–10</td>
<td></td>
<td>38%</td>
<td>36%</td>
<td>36%</td>
<td>44%</td>
<td>57%</td>
<td>19%</td>
</tr>
<tr>
<td>&gt;10</td>
<td></td>
<td>38%</td>
<td>44%</td>
<td>37%</td>
<td>13%</td>
<td>19%</td>
<td>14%</td>
</tr>
<tr>
<td>Total No.</td>
<td></td>
<td>24</td>
<td>25</td>
<td>99</td>
<td>16</td>
<td>21</td>
<td>22</td>
</tr>
</tbody>
</table>

TABLE 1. Total Number of Participants and Years of Experience of Reading CT Scans for Acute Stroke, by Specialty.
for <5 years, 77 of 207 (37%) for between 5 and 10 years, and 66 of 207 (32%) for 10 or more years (Table 1). Excluding others, general radiologists had the largest proportion of experienced readers (44% with >10 years’ experience), and stroke physicians had the largest proportion of least-experienced readers (44%). Neuroradiologists, neurologists, and geriatricians had similar experience to each other (Table 1, P=NS).

The average time taken to read a scan and complete the questionnaire was 3.4 minutes (2SD=10 minutes; range, 6 seconds to 10 minutes). The mean time to read a scan was 222 seconds/scan for neuroradiologists versus general radiologists 193 seconds, neurologists 193 seconds, and geriatricians 189 seconds; ie, neuroradiologists took 29 seconds longer on average than both general radiologists and neurologists and 32 seconds longer than geriatricians (all P=0.0001); stroke physicians’ times were not significantly different from those of neuroradiologists (P=0.8).

Detection of Early CT Signs of Ischemia
There were early CT signs of ischemia in 43 of 63 (68%) scans according to the reference expert. The proportion of readers who identified any acute ischemic change per scan was highest among neuroradiologists. More than 50% of neuroradiologists identified signs of acute ischemia in 43 of 63 scans. Compared with neuroradiologists, other specialties combined identified any early signs of ischemia less often, on average by 12.3±1.4% (P<0.0001, Table 2). Compared with neuroradiologists (and excluding others), neurologists recognized the least of any acute ischemic change (14.6±1.3% less often than neuroradiologists), followed by geriatricians (13±1.8% less often), general radiologists (6.8±2.2% less often), and stroke physicians (6.4±1.7% less often), all P<0.005.

A pattern similar to that for any early signs of ischemia was seen for neuroradiologists versus the other specialties in recognizing mild hypoattenuation or mild swelling. On average, neuroradiologists saw mild hypoattenuation (13.5±1.7%) and mild swelling (13.4±1.4%) more often (P<0.0001) than other specialties (Table 2). There was no difference between specialties in recognition of severe hypoattenuation or swelling (Table 2). There was no difference between neuroradiologists and most other specialists’ recognition of the hyperattenuated artery sign. Only general radiologists saw hyperattenuated arteries significantly less often (8.7±1.8%, P=0.0001) than neuroradiologists (Table 2).
There was little “overcalling” of any signs by any specialty compared with neuroradiologists (minus numbers in Table 2) and none that reached statistical significance. Because the minus numbers that do occur for parenchymal signs are in the detection of severe hypoattenuation or swelling (not mild), this may simply reflect use of terminology in calling a finding severe rather than mild, rather than in seeing a sign that was not there.

**Effect of Old Infarcts**

Neuroradiologists were less likely to be distracted by old infarcts from seeing early ischemic changes than were those in other specialties. Overall, neuroradiologists identified the largest proportion of acute ischemic changes, whether old infarcts were present or not (Table 3). When an old infarct was present (Table 3), neuroradiologists, general radiologists, and stroke physicians were not particularly distracted from

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**TABLE 2. Difference Between Neuroradiologists and Other Specialties in the Proportion of Readers Who Detected Any Ischemia, Mild or Severe Hypoattenuation and Swelling, and Hyperattenuated Arteries**

<table>
<thead>
<tr>
<th></th>
<th>GR</th>
<th>NG</th>
<th>SP</th>
<th>GT</th>
<th>OT</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identifying any ischemia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>6.8%</td>
<td>14.6%</td>
<td>6.4%</td>
<td>13.0%</td>
<td>22.8%</td>
<td>12.3%</td>
</tr>
<tr>
<td>SD</td>
<td>17.4%</td>
<td>10.7%</td>
<td>13.5%</td>
<td>14.4%</td>
<td>22.2%</td>
<td>11.4%</td>
</tr>
<tr>
<td>P value</td>
<td>0.0028</td>
<td>0.0001</td>
<td>0.0004</td>
<td>0.0001</td>
<td>0.0001</td>
<td>0.0001</td>
</tr>
<tr>
<td>Identifying mild hypoattenuation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>10.0%</td>
<td>14.3%</td>
<td>8.4%</td>
<td>15.2%</td>
<td>16.1%</td>
<td>13.5%</td>
</tr>
<tr>
<td>SD</td>
<td>17.6%</td>
<td>13.4%</td>
<td>13.5%</td>
<td>17.0%</td>
<td>19.1%</td>
<td>13.3%</td>
</tr>
<tr>
<td>P value</td>
<td>0.0001</td>
<td>0.0001</td>
<td>0.0001</td>
<td>0.0001</td>
<td>0.0001</td>
<td>0.0001</td>
</tr>
<tr>
<td>Identifying severe hypoattenuation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>2.6%</td>
<td>1.2%</td>
<td>−0.8%</td>
<td>0.4%</td>
<td>−4.0%</td>
<td>−0.2%</td>
</tr>
<tr>
<td>SD</td>
<td>11.3%</td>
<td>9.5%</td>
<td>10.7%</td>
<td>12.8%</td>
<td>16.2%</td>
<td>9.7%</td>
</tr>
<tr>
<td>P value</td>
<td>0.0744</td>
<td>0.2988</td>
<td>0.5541</td>
<td>0.8194</td>
<td>0.0533</td>
<td>0.8937</td>
</tr>
<tr>
<td>Identifying mild swelling</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>11.9%</td>
<td>14.2%</td>
<td>9.9%</td>
<td>15.0%</td>
<td>23.1%</td>
<td>13.4%</td>
</tr>
<tr>
<td>SD</td>
<td>15.0%</td>
<td>11.5%</td>
<td>14.0%</td>
<td>14.7%</td>
<td>23.1%</td>
<td>11.3%</td>
</tr>
<tr>
<td>P value</td>
<td>0.0001</td>
<td>0.0001</td>
<td>0.0001</td>
<td>0.0001</td>
<td>0.0001</td>
<td>0.0001</td>
</tr>
<tr>
<td>Identifying severe swelling</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>0.2%</td>
<td>−0.1%</td>
<td>−1.4%</td>
<td>−1.2%</td>
<td>−0.5%</td>
<td>−0.9%</td>
</tr>
<tr>
<td>SD</td>
<td>1.7%</td>
<td>2.0%</td>
<td>4.3%</td>
<td>3.4%</td>
<td>2.4%</td>
<td>3.0%</td>
</tr>
<tr>
<td>P value</td>
<td>0.3104</td>
<td>0.6908</td>
<td>0.0146</td>
<td>0.0092</td>
<td>0.0027</td>
<td>0.0565</td>
</tr>
<tr>
<td>Identifying hyperattenuated artery</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>8.7%</td>
<td>−2.3%</td>
<td>−2.5%</td>
<td>1.2%</td>
<td>−0.9%</td>
<td>−0.4%</td>
</tr>
<tr>
<td>SD</td>
<td>14.3%</td>
<td>13.1%</td>
<td>19.4%</td>
<td>16.7%</td>
<td>15.6%</td>
<td>12.9%</td>
</tr>
<tr>
<td>P value</td>
<td>0.0001</td>
<td>0.1784</td>
<td>0.3011</td>
<td>0.5682</td>
<td>0.6534</td>
<td>0.8212</td>
</tr>
</tbody>
</table>

GR indicates general radiologists; NG, neurologists; SP, stroke physicians; GT, geriatricians; OT, other specialties (emergency physicians, general practitioners); and All, all nonneuroradiology specialties combined. A positive No. indicates that neuroradiologists saw the feature more often; minus indicates that neuroradiologists saw the feature less often than the given specialty.

**TABLE 3. Detection of Early Ischemic Changes and Old Infarcts, by Specialty**

<table>
<thead>
<tr>
<th>Infarct Type Present?</th>
<th>Old</th>
<th>Early</th>
<th>Neuroradiologists</th>
<th>General Radiologists</th>
<th>Neurologists</th>
<th>Stroke Physicians</th>
<th>Geriatricians</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>24</td>
<td>22</td>
<td>16</td>
<td>22</td>
<td>18</td>
<td>17</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>5</td>
<td>7</td>
<td>13</td>
<td>7</td>
<td>11</td>
<td>12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>25</td>
<td>15</td>
<td>17</td>
<td>22</td>
<td>16</td>
<td>15</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>9</td>
<td>19</td>
<td>17</td>
<td>12</td>
<td>18</td>
<td>19</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Numbers are No. of scans (of the total of 63) identified by 50% or more of the specialists in each group as having acute or old ischemic change, neither or both.
identifying early signs of ischemia, but neurologists, geriatricians, and others classified more scans as having only an old infarct and missed the presence of acute ischemic changes significantly more often than did neuroradiologists ($\chi^2 P<0.05$).

**Discussion**

This large study of reader reliability of early ischemic stroke signs on CT has demonstrated that neuroradiologists identified early ischemic signs more often than did other specialists, but most of this difference was due to the neuroradiologists’ greater detection of mild hypoattenuation and tissue swelling. Other specialists saw hyperattenuated arteries and severe parenchymal changes as often as neuroradiologists. Parenchymal hypoattenuation and tissue swelling were recognized equally. There was little if any overcalling of early ischemic changes by other specialists compared with neuroradiologists. The chances of missing early ischemic changes were increased by the presence of an old infarct.

These differences between specialties were not simply due to years of observer experience, as stroke physicians (who performed most like neuroradiologists) included more observers with fewer than 5 years’ experience of scan reading than most other groups; neurologists (who saw fewer mild signs) had very similar years of experience in acute stroke CT reading to neuroradiologists.

It may be that improved detection of early ischemic changes was related to the time taken to read a scan, as neuroradiologists took significantly longer, even though by only half a minute, to read scans than did all other groups except stroke physicians. Perhaps the advice from this study is “slow down, and don’t be put off by old infarcts—keep looking.” Whether or not the neuroradiologists and stroke physicians also approached the scan reading in some more organized way that improved detection of CT early ischemic changes or not we are unable to say, but the structured questionnaire used in the study encouraged all observers to examine the scan in the same structured way.

How does the present study compare with previous work? We tested more scan-observer interactions (13 041), the scans from the present study remain available for training in acute stroke to new readers (www.neuroimage.co.uk), with feedback from the reference standard, a panel of experts, all readers and readers grouped by specialty, and the 24-hour follow-up scan showing where the infarct developed.

What are the implications? Differences in the detection of subtle early signs of ischemia might lead to differences in estimation of prognosis or in treatment decisions about whether to use thrombolysis, depending on whether a neuroradiologist was available or not, especially if a strict cutoff were used on a scoring system like ASPECTS. However, the available evidence suggests that the relation between ASPECTS scores and prognosis is not sufficiently precise for strict cutoffs to be valid. Physicians should not just rely on radiological findings when making treatment decisions.

The scans from the present study remain available for training in acute stroke to new readers (www.neuroimage.co.uk), with feedback from the reference standard, a panel of experts, all readers and readers grouped by specialty, and the 24-hour follow-up scan showing where the infarct developed.

**Appendix**

**Participants Who Read All 63 Study CT Scans**

- **Argentina:** Dr Claudia Gandolfo, Churrusa Hospital, Buenos Aires; Dr Guillermo Povedano.
- **Australia:** Prof Lesley Cala, Australian Research Centre for Medical Engineering, Perth; Dr Sandy Patel.
- **Austria:** Dr Birgit Glawar; Dr Erich Gatterbauer, Vienna; Dr Klaus Hohensinner.
- **Belgium:** Dr Andre Peeters, UCL St Luc, Brussels; Dr Philippe Demaerel, University Hospital, Leuven; Dr Vincent Thijs.
- **Brazil:** Dr Luciano Farage, Hospital de Clinicas de Uberlandia UFU, Brasilia DF.
- **Canada:** Dr Jessica Simon; Dr Michael Hill; Dr Nicole Isaac, Lakeridge Health Oshawa, Toronto; Dr Steve Phillips, Queen Elizabeth II Health Sciences Centre, Halifax.
- **China:** Dr Henry Ka Fung Mak; Dr Ming Hua Wu, Stroke Center of Jiangsu TCM Hospital, Nanjing; Dr Xianrong Zeng, Chinese Medical Science Institution of Sichuan, Chengdu.
- **Denmark:** Dr John Bath Larsen.
- **Finland:** Dr Anna Saukkonen, North Karelian Central Hospital, Joensuu.
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References


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