Introduction
Hemorrhagic transformation (HT) is a potentially fatal complication of recombinant tissue plasminogen activator (rt-PA) therapy in acute ischemic stroke (AIS) [1]. Early prediction of HT could substantially improve the safety of thrombolytic therapy, thereby improving patient outcome. Early Gadolinium (Gd) enhancement on post-contrast T1-weighted (T1w) MRI has been used to predict HT in subacute stroke (7 hours from symptom onset) [2]. However, assessment at earlier time points (< 4 hours from symptom onset) did not reliably predict HT [3]. An alternative to visual inspection is texture analysis, which discriminates textural information related to higher-order statistics and spectral properties not obvious to even an expert eye (trained radiologist) [4]. This method can quantify dependencies between neighboring pixels as well as patterns of variation within a region-of-interest (ROI). In this study we performed texture analysis, based on a co-occurrence matrix of post-contrast T1w images, to assess the prediction of HT in AIS patients and to compare it with visual inspection of Gd enhancement.

Materials and Methods
Thirty four acute ischemic stroke patients (aged 38-80 years) were examined < 4 hours of symptom onset. Fifteen out of 34 patients received rt-PA. Post-contrast T1-weighted MRI was performed as part of the acute stroke protocol with the following imaging parameters: FOV 240mm, 256×192 matrix, slice thickness 5mm, 22 slices, TR=750ms, TE=20ms. Prior to post-contrast T1 acquisition, standard anatomical, diffusion-, permeability, perfusion-weighted as well as contrast-enhanced MRA were acquired. All imaging was performed on a 1.5T GE Signa MRI system (GE Healthcare, Milwaukee, USA). Hemorrhagic transformation was determined by follow-up imaging with either CT and/or MRI. Two regions of interests (ROI) were defined on the DWI images, one being placed on the core region of the diffusion abnormality and the second one being placed in the contralateral hemisphere. Both ROIs were then copied to the post-contrast T1w image for texture analysis. Texture analysis was performed using MaZda (version 3.2, Piotr M. Szczypiński, Institute of Electronics, Technical University of Lodz). A co-occurrence matrix was calculated for each region of interest as described by Haralik [5], enabling the following textual features to be extracted: (f1) angular second moment (a measure of homogeneity); (f2) contrast (a measure of local variation); (f3) correlation (a measure of gray-tone linear-dependencies); and (f9) entropy (a measure of the disorder or randomness). Mean values for these 4 parameters were recorded for all patients who were grouped based on whether they received rt-PA, and whether they experienced HT (table 1). A paired t-test compared mean f1, f2, f3 and f9 values between lesions and contralateral areas. The relationship between all parameters was investigated for all patients, and both sides, using linear regression.

Results
Twelve of the 34 patients developed HT; 6 of these received rt-PA. Only two of the assessed texture features, namely f2 and f3, showed statistical differences (see figures 1 and 2). A significant decrease in f2 was observed in the lesion of HT patients (1098 ± 107) compared with non-HT patients (1568 ± 115; p < 0.01). A significant increase in f3 was observed in the lesion of HT patients (0.61 ± 0.04) compared with non-HT patients (0.54 ± 0.03; p < 0.01). Both f2 and f3 are highly correlated (r = 0.98). ROC analysis for f2 indicated a 92% sensitivity and a 63% specificity for a threshold of 1396. ROC analysis for f3 indicated a 75% sensitivity and a 68% specificity for a threshold of 0.61. In contrast, ROC analysis for the visual inspection of Gd enhancement indicated only a 33% sensitivity and a 86% specificity.

Discussion
This study shows that texture analysis of post T1w images is superior to visual inspection for the prediction of HT in early AIS. To our knowledge, this is the first application of texture analysis in AIS. Further studies are needed to validate our results.

References
1. NINDS Group. Stroke 1997;
2. Vo K et al., AJNR 2003;
3. Mikulis D et al. ASNR 2006;
5. Haralick RM et al., IEEE Tran Syst Man Cybern. 1973

Table 1. Patient groups, based on rt-PA treatment and subsequent HT

<table>
<thead>
<tr>
<th>rt-PA</th>
<th>HT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 (N = 13)</td>
<td>-</td>
</tr>
<tr>
<td>Group 2 (N = 9)</td>
<td>✓</td>
</tr>
<tr>
<td>Group 3 (N = 6)</td>
<td>-</td>
</tr>
<tr>
<td>Group 4 (N = 6)</td>
<td>✓</td>
</tr>
</tbody>
</table>

Figure 1. Mean weighted f2 for the four groups, demonstrating decreased f2 in patients who later on hemorrhaged.

Figure 2. Mean weighted f3 for the four groups, demonstrating increased f3 in patients who later on hemorrhaged.