Elevated $T_2$-values in MRI of stroke patients shortly after symptom onset do not predict irreversible tissue infarction

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Distinct from signal alterations in diffusion-weighted images, $T_2$-values are also dependent on tissue water content and known to increase with time from symptom onset in acute ischaemic stroke. The purpose of this study was to evaluate whether there is a detectable increase of $T_2$-values in different regions in acute ischaemic stroke in the acute and subacute situation and to study the effect of recanalization on the evaluation of $T_2$-values in the subacute phase. In addition, we sought to evaluate whether this increase in $T_2$-values is reversible. For this purpose, 22 patients with acute ischaemic stroke in the territory of the middle cerebral artery underwent magnetic resonance imaging including diffusion-weighted imaging, perfusion-weighted imaging, fluid-attenuated inversion recovery to determine final infarct size, time-of-flight-angiography (acute and on day 1 or 2) and a triple echo-$T_2$-sequence (calculation of $T_2$ maps) within 6 h after symptom onset. Images were co-registered and regions of diffusion restriction and prolonged time-to-peak as well as surviving tissue (surviving tissue = time-to-peak – final infarct size) and lesion growth (lesion growth = final infarct size-diffusion restriction) were defined and superimposed onto the quantitative $T_2$ map. In addition, patients were dichotomized according to recanalization information. Mean quantitative $T_2$-values were derived for each patient within each region of interest. Mean $T_2$-values for patients with recanalization ($n = 15$) in surviving tissue region of interest were $115.8 \pm 7.2$ ms (mean $\pm$ SD) and in the lesion growth region of interest $114.6 \pm 7.0$ ms. $T_2$-values for patients without recanalization ($n = 7$) were $117.7 \pm 11.4$ ms in surviving tissue region of interest and $117.3 \pm 12.1$ ms in lesion growth region of interest. There was no significant difference between $T_2$-values measured in lesion growth and surviving tissue region of interest for patients with or without recanalization. Even though it has been shown that $T_2$-values increase with time from symptom onset within the infarct core, increased $T_2$-values in areas of perfusion impairment do not identify irreversible damaged brain tissue and high $T_2$-values are even found in tissue that is not part of the final infarct lesion and can therefore normalize. In conclusion, this study suggests that $T_2$-values are not a valid imaging biomarker in acute stroke to predict tissue outcome.

Keywords: brain imaging; cerebral ischaemia; ischaemia; stroke; magnetic resonance imaging

Abbreviations: TICI = thrombolysis in cerebral infarction
Introduction

The discrimination of irreversible damaged brain tissue from tissue at risk of infarction in acute ischaemic stroke is still an unsolved issue by means of MRI (Astrup et al., 1981; Hakim et al., 1989; Albers et al., 2006; Carrera et al., 2011). Up to now, diffusion-weighted imaging displaying decreased apparent diffusion coefficient values is utilized to estimate the extent of irreversibly damaged brain tissue, although it is known that apparent diffusion coefficient values can normalize and therefore apparent diffusion coefficient values do not reliably indicate irreversible damaged brain tissue in acute ischaemic stroke (Kidwell et al., 2000; Fiehler et al., 2002, 2004). However, therapy decisions are currently still mainly based on this information (Hacke et al., 2005). It is, therefore, important to develop and test MRI techniques that might, in combination with other MRI sequences, not only help identify the tissue at risk of infarction, but in addition also determine the tissue that cannot be saved even with recanalization (Kidwell et al., 2003, 2004).

Experimental occlusion of the middle cerebral artery in rats has shown that the immediate brain tissue net water uptake is associated with a decrease in X-ray attenuation and suggests that the ischaemic oedema in acute stroke can be monitored by CT (Dzialowski et al., 2004). Distinct from signal alterations in diffusion-weighted images, T2-values are also dependent on tissue water content and known to increase with time from symptom onset in acute ischaemic stroke. This may indicate that quantitative T2-values, in contrast with apparent diffusion coefficient values, are more directly related to water uptake in ischaemic tissue similar to the hypodensities seen on CT images (Hoehn-Berlage et al., 1995; Von Kummer et al., 2001). In analogy, a preliminary study by Venkatesan et al. (2000) suggested that non-invasive measurements of brain water content can be obtained with MRI in a rat model. Therefore, in theory, an acute infarct should present high signal intensity reflecting prolonged T2 relaxation due to increased tissue water content on conventional T2-weighted and FLAIR images (Noguchi et al., 1997).

Correspondingly, hyperintensities on FLAIR and T2-weighted images are interpreted as reflecting vascular brain oedema. The potential benefit of evaluating hyperintense lesions in FLAIR images for treatment guidance has attracted enormous interest in recent studies (Thomalla et al., 2009; Aoki et al., 2010; Ebinger et al., 2010; Petkova et al., 2010). The pathophysiological background of these changes is predominantly reflected by increase in T2 time. Increase of T2 time in acute stroke lesion core has already been shown to be detectable as a time dependent phenomenon (Siemonsen et al., 2009). The purpose of this study was to evaluate whether there is a detectable increase of T2-values in different regions in acute ischaemic stroke in the acute and subacute situation and to study the effect of recanalization on the evaluation of T2-values in the subacute phase. In addition, we sought to evaluate whether this increase in T2-values is reversible.

Patients and methods

Patients and inclusion criteria

To provide a homogenous population of stroke patients with comparable pathophysiological condition only patients with acute cerebral ischaemia in the territory of the middle cerebral artery, who were treated by intravenous thrombolytic therapy, were identified in a retrospective analysis of our prospective stroke database. Further inclusion criteria were as follows: known time from symptom onset, a complete MRI stroke protocol within 6 h of symptom onset (acute scan), an MRI examination within 1–2 days thereafter (follow-up scan) including T2-weighted imaging and time-of-flight angiography to evaluate recanalization, as well as follow-up imaging (final scan) within 1 week (mean after 7 days, range 5–9 days) including FLAIR sequence to determine final lesion size. Only patients without haemorrhagic transformation or bleeding in acute, follow-up or final scan were included. Based on these criteria, 22 consecutive patients (11 male and 11 female) were enrolled in the study. The study was approved by the local institutional review board and patients or their guardians provided informed consent.

Magnetic resonance imaging

All examinations were conducted on a 1.5-T MRI scanner (Siemens Avanto or Sonata). The MRI protocol included diffusion-weighted imaging for determination of apparent diffusion coefficient, FLAIR, time-of-flight angiography and a multi-echo T2 mapping sequence. Time-of-flight angiography was obtained by a 3D fast low angle shot (FLASH) sequence with venous saturation, magnetization transfer saturation pulse and tilted optimized non-saturation excitation (TONE)-up pulse. For diffusion-weighted imaging, a single-shot, spin-echo, echoplanar-imaging isotropic diffusion-weighted imaging sequence (echo time = 105.2 ms, repetition time = 4800 ms, field of view = 240 mm, matrix 256 × 256, 20 slices, 6 mm slice thickness, 10% gap) was used and images were collected with b = 0 and b = 1000, from which the apparent diffusion coefficient was determined. T2-FLAIR sequence parameters were echo time = 108 ms, repetition time = 8140 ms and inversion time = 2500 ms (field of view = 230 mm, matrix 184 × 184, 24 slices, 5 mm slice thickness and 30% gap). For perfusion-weighted imaging, a gradient echo echoplanar-imaging sequence was employed. Time-to-peak maps were generated by finding the time to the maximum signal drop of S(t) from S0 for each voxel. For T2 determination, a fast spin-echo sequence with 15 echoes per shot was used to acquire images at three different echo times of 12, 84 and 156 ms within a total acquisition time of 74 s (repetition time = 4550 ms, field of view = 240 mm, matrix = 74 × 128, number of slices = 24, slice thickness = 5 mm, no gap, flip angle = 150°).

Calculation of quantitative T2 images

Quantitative T2 maps were based on a fast spin echo imaging acquisition, with three different echo times (12, 84 and 156 ms for T2) and a voxel-wise fit of the image intensities to an exponential decay function yielding the time constant T2. Quantitative T2 maps were calculated by fitting the single exponential term S(t) = S0 e−T2/t to the signal decay curve of the multi-echo T2 data [SI(t)] for acute (quantitative T2) and follow-up (follow-up quantitative T2) time points.
Image preparation

A complete data set of an individual patient consisted of the apparent diffusion coefficient, time-to-peak of Day 0, quantitative T2 maps and time-of-flight angiography of Day 0 and Day 1, as well as a T2-FLAIR image of Days 5–9 (final FLAIR). All acquired images were coregistered intraindividually to the corresponding T2-weighted image (third echo, echo time 156 ms) to assure an optimal 3D comparability between the modalities. For this purpose, a co-registration of the acute apparent diffusion coefficient map, third echo of T2 follow-up images and acute perfusion scan (first time point scan) as well as final FLAIR to the corresponding T2-weighted image (third echo, echo time 156 ms) of the acute scan using the coregistration procedure of Minc Tools (MNI) was performed. The transformation parameters were consecutively applied to the calculated time-to-peak and follow-up quantitative T2 map.

Fluid attenuated inversion recovery and time-of-flight reading

Regions of interest defining final infarct as observed on final FLAIR were outlined by two experienced neuroradiologists (S.S. and U.L.). Only voxels marked by both raters were included in the analysis as part of the final infarct. Final FLAIR images were rated independently by each observer. In reading, the corresponding acute diffusion-weighted imaging and apparent diffusion coefficient images were available for comparison. We considered this information to be crucial because some patients presented with hyperintense lesions in FLAIR due to microangiopathy not corresponding to the acute stroke lesion detected in apparent diffusion coefficient images. The reading strategy was chosen to resemble the clinical setting where clinical information and other MRI data are available for a summary evaluation. In addition, the acute time-of-flight angiography and time-of-flight angiography of Day 1 were independently rated for recanalization. Recanalization was defined on time-of-flight angiography of Day 1 when there was recanalization with remaining mild stenosis or normal arterial calibre. The existence of tissue swelling with space-occupying oedema was visually assessed in T2-FLAIR at all imaging time points by an experienced reader.

Region of interest definition

Three-dimensional regions of interest were defined and analysed using the MNI Display software (MNI, McConnell Brain Imaging Centre, Montreal Neurological Institute, McGill University). To obtain corresponding normal values for time-to-peak for each patient, a manually defined region of interest was placed in white matter in the unaffected side on third echo of T2-weighted images for each patient and then transferred intraindividually to the time-to-peak map. Regions of decreased apparent diffusion coefficient below a threshold of 550 × 10−9 mm²/s and regions of prolonged time-to-peak (4 s delay in comparison with individual normal values in contralateral hemisphere) were then defined for each patient in the acute scans and superimposed onto the corresponding acute quantitative T2 and follow-up quantitative T2 maps.

The acute apparent diffusion coefficient lesion was used to define the ischaemic core (diffusion restriction region of interest), whereas the final infarct size was defined by final FLAIR regions of interest. The region of interest of the time-to-peak-lesion on Day 0 (acute time-to-peak) revealed an estimate of the initial perfusion impairment. Lesion growth from Day 0 to final infarct volume corresponding to final FLAIR lesion region of interest was derived by subtracting diffusion restriction region of interest from final infarct size region of interest (lesion growth = final infarct size − diffusion restriction), and surviving tissue was calculated by subtracting final infarct size from acute time-to-peak (surviving tissue = time-to-peak − final infarct size).

These regions of interest are schematically visualized in Fig. 1. Subsequently, predefined regions of interest were then transferred to corresponding acute quantitative T2 and follow-up quantitative T2 maps defining the voxels of interest (voxel size 1.8 × 1.8 × 6.5 mm³). Mean quantitative T2-values were derived for each patient within each of the above defined regions of interest. These values were consecutively analysed by statistical testing. In addition, patients were dichotomized according to recanalization information applying the thrombolysis in cerebral infarction (TICI) perfusion categories (i.e. no recanalization group = TICI 0 and TICI 1; recanalization group = TICI 2 and TICI 3) (Higashida et al., 2003).

Statistics

Statistical analysis was conducted using R software (R version 2.7.0, The R Foundation for Statistical Computing). Mean absolute values and standard deviations for quantitative T2-values were calculated for each region of interest in acute and follow-up images. Mean quantitative T2-values measured within different regions of interest were compared between acute and follow-up images and between patient groups (recanalization versus no recanalization) and tested for significant differences (i.e. paired and unpaired t-test, two-way ANOVA). Other than for the histograms displayed in Fig. 3, a voxel-wise analysis was not conducted since all tests returned significant results due to the very high number of voxels.

Results

The mean patient age was 64 ± 14 years (mean ± SD), and ages ranged from 37 to 84 years. The right hemisphere was affected in
five patients and the left hemisphere was affected in 17 patients.
The interval between symptom onset and acute MRI was
160 ± 71 min (mean ± SD). In the evaluation of magnetic reson-
ance angiography data, occlusion of the internal carotid artery and
the middle cerebral artery or a carotid T-occlusion was seen in
three (13.6%) patients, occlusion of the middle cerebral artery
trunk was seen in eight (36.4%) patients, occlusion of the
middle cerebral artery trifurcation was seen in three (13.6%) pa-
tients and occlusion of a middle cerebral artery branch in eight
(36.4%) patients. Follow-up magnetic resonance angiography
showed recanalization in 15 (68.2%) patients, no recanalization
in seven (31.8%) patients. Five patients showed no recanalization
(TICI 0), two patients showed minimal recanalization (TICI 1) in
follow-up time-of-flight, while five patients presented with partial
(TICI 2) and 10 patients with full recanalization (TICI 3) in
follow-up scans.

T2-values in different stroke regions/
regions of interest

Acute scans
Mean quantitative T2-values measured in acute scans in the affected
hemisphere in different regions of interest were: 114.94 ± 12.27 ms
in diffusion restriction region of interest; 115.45 ± 13.02 ms in lesion
growth region of interest; and 116.41 ± 8.49 ms in surviving tissue
region of interest. There were no significant differences between
mean quantitative T2-values measured in different region of interest
localizations in the acute scan (Fig. 2 and Table 1).

Follow-up scans
Mean quantitative T2-values measured in follow-up scans within
defined regions of interest in the affected hemisphere were:
147.14 ± 25.18 (mean ± SD) in diffusion restriction region of
interest; 140.0 ± 20.70 ms in lesion growth region of interest;
and 125.95 ± 13.02 in surviving tissue region of interest. In
follow-up scans, mean quantitative T2-values in diffusion restric-
tion region of interest (147.14 ± 25.18 ms) were significantly
higher (P < 0.01) than quantitative T2-values measured in surviv-
ing tissue region of interest, while there were no significant dif-
fferences between quantitative T2-values measured in diffusion
restriction region of interest and quantitative T2-values measured
in lesion growth region of interest (P = 0.07). In addition, quanti-
tative T2-values in lesion growth region of interest were signifi-
cantly higher than quantitative T2-values measured in surviving
tissue region of interest (P < 0.01) (Fig. 2 and Table 1). Tissue
swelling with space-occupying oedema in the follow-up and
final FLAIR scans was observed in four patients. In this patient
group, three patients revealed minimal and one patient revealed
moderate swelling. In all cases, the swelling mainly resulted in a
slight deformation of the adjacent lateral ventricle. No swelling
was observed in the acute scans.

Figure 2 Mean T2-values in different regions of interest in acute and follow-up scans. DR = diffusion restriction; FU = follow-up;
LG = lesion growth; qT2 = quantitative T2; ROI = region of interest; ST = surviving tissue.
When comparing acute and follow-up scans, we found mean quantitative T2-values measured in follow-up images to be significantly higher in comparison with corresponding values measured in acute scans for all regions of interest ($P < 0.01$) (Table 1). An increase of T2-values from acute to follow-up scans was observed in lesion growth (22/22, 100%) and surviving tissue region of interest (19/22, 86%). When excluding the four patients that showed swelling in follow-up scans there was still a significant difference between T2-values measured in acute and follow-up scans for all three region of interest localizations ($P < 0.05$).

Histograms of quantitative T2-values measured voxel-wise in lesion growth, surviving tissue and diffusion restriction regions of interest for acute and follow-up scans are shown in Fig. 3. These plots show not only that mean absolute values are increasing from acute to follow-up scans in all region of interest localizations but also that ranges of mean quantitative T2-values are wider in follow-up scans for all regions of interest, i.e. the variation increases. When conducting a two-way

<table>
<thead>
<tr>
<th>Region of interest localizations</th>
<th>Mean quantitative T2-value (ms) versus mean quantitative T2-value (ms)</th>
<th>$P$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute DR versus follow-up DR</td>
<td>114.94 147.14</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>Acute LG versus follow-up LG</td>
<td>115.45 140.09</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>Acute ST versus follow-up ST</td>
<td>116.41 125.95</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>Acute DR versus acute LG</td>
<td>114.94 115.45</td>
<td>0.762</td>
</tr>
<tr>
<td>Acute DR versus acute ST</td>
<td>114.94 116.41</td>
<td>0.464</td>
</tr>
<tr>
<td>Acute LG versus acute ST</td>
<td>115.45 116.41</td>
<td>0.338</td>
</tr>
<tr>
<td>Follow-up DR versus follow-up LG</td>
<td>147.14 140.09</td>
<td>0.074</td>
</tr>
<tr>
<td>Follow-up DR versus follow-up ST</td>
<td>147.14 125.95</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>Follow-up LG versus follow-up ST</td>
<td>140.09 125.95</td>
<td>0.002</td>
</tr>
</tbody>
</table>

DR = diffusion restriction; LG = lesion growth; ST = surviving tissue. Bold numbers indicate significance of $<.05$.

Figure 3 Histograms of T2-values measured from scans in different region of interest localizations in acute diffusion restriction region of interest (A); acute lesion growth region of interest (B); acute surviving tissue region of interest (C); follow-up diffusion restriction region of interest (D); follow-up lesion growth region of interest (E); and (F) follow-up surviving tissue region of interest. DR = diffusion restriction; FU = follow up; LG = lesion growth; ROI = region of interest; ST = surviving tissue.

Table 1 Mean quantitative T2-values and $P$-values for comparison of quantitative T2-values measured in different region of interest localizations and acute versus follow-up images

Acute versus follow-up scans

Acute T2 increase does not predict later infarction

ANOVA (Factor A = acute/follow-up, Factor B = region of interest localization: diffusion restriction, lesion growth, surviving tissue) on these data, we found a significant effect of Factor A ($P < 0.01$) and a significant effect of Factor B ($P = 0.015$). Also, there was a significant interaction between both factors with $P < 0.01$.

**Differences between quantitative T2-values**

In addition, T2 increases were analysed by calculating and comparing differences between quantitative T2-values measured in follow-up scans and quantitative T2-values detected in acute scans for each defined region of interest (i.e. differences in diffusion restriction, lesion growth and surviving tissue). Quantitative T2-values measured in diffusion restriction regions of interest showed a significantly higher increase of quantitative T2-values from acute to follow-up scan than quantitative T2-values measured in surviving tissue region of interest ($P < 0.001$) while there was no significant difference between T2 increase in diffusion restriction and T2 increase in lesion growth region of interest ($P = 0.077$). Accordingly, we found a significantly higher increase of quantitative T2-values from acute to follow-up scans in lesion growth region of interest than in surviving tissue region of interest ($P < 0.002$).

**Recanalization group**

Within the recanalization group quantitative T2-values measured in follow-up images were significantly higher than those measured in acute images for diffusion restriction region of interest, lesion growth region of interest and surviving tissue region of interest ($P < 0.01$). When comparing quantitative T2-values determined in different regions of interest in acute images within this patient subgroup there were no significant differences found. In contrast, quantitative T2-values in diffusion restriction region of interest and lesion growth region of interest in follow-up images were significantly higher than those measured in surviving tissue region of interest ($P < 0.02$) while there was no significant difference between quantitative T2-values detected in follow-up diffusion restriction and follow-up lesion growth regions of interest ($P = 0.57$) (Fig. 4).

**No recanalization group**

In patients with no recanalization in follow-up imaging, quantitative T2-values in diffusion restriction, lesion growth and surviving tissue region of interest were significantly higher in follow-up than in acute images ($P < 0.02$). In this group, there were no significant differences between acute quantitative T2-values in any regions of interest. In follow-up images, we found significantly increased quantitative T2-values in diffusion restriction region of interest in comparison with quantitative T2-values detected in lesion growth ($P < 0.01$) and surviving tissue regions of interest ($P < 0.02$) (Fig. 4).

**Recanalization versus no recanalization group**

When comparing quantitative T2-values measured in different regions of interest in the recanalization and no recanalization groups for acute and follow-up images there were no significant differences found. However, in the recanalization group, quantitative T2-values in diffusion restriction region of interest in follow-up images were significantly higher than those measured in follow-up diffusion restriction and follow-up lesion growth regions of interest ($P < 0.02$) (Fig. 4).

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**Figure 4**

Mean T2-values measured in regions of interest in acute and follow-up scans in the recanalization and no recanalization groups. **(A)** Acute regions of interest; **(B)** follow-up regions of interest. DR = diffusion restriction; FU = follow up; LG = lesion growth; qT2 = quantitative T2; ROI = region of interest; ST = surviving tissue.
Acute T₂ increase does not predict later infarction


Discussion

In this study, we found no significant differences between quantitative T2-values measured in diffusion restriction, lesion growth and surviving tissue regions of interest in the acute scans. This finding might be due to the relatively early scanning time of most of the patients, i.e. 14 of 22 receiving an MRI examination within the first 3 h of symptom onset when there might only be a slight increase in quantitative T₂-values as shown in an earlier study (Siemonsen et al., 2009). Accordingly, increased signal intensities in T₂-weighted MRI are reported to appear ~2–4 h after cerebral ischaemia and are thought to reflect irreversible tissue damage (Shimosegawa et al., 1993; Noguchi et al., 1997).

In follow-up imaging, we found a significant increase in quantitative T₂-values in all regions of interest in comparison with acute images. These findings are in line with previous studies, which indicate that in the acute phase of brain ischaemia, diffusion-weighted imaging is theoretically the best examination to demonstrate restricted water motion related to the cytotoxic oedema (Moseley et al., 1990; Benveniste et al., 1992), whereas conventional MRI including FLAIR and T₂-weighted sequences are mainly sensitive to vasogenic oedema observed in the subacute phase of stroke (Alexander et al., 1996).

The increase in quantitative T₂-values from acute to follow-up scans was found to be significantly higher in the diffusion restriction region of interest and in lesion growth than in surviving tissue region of interest, indicating a higher water uptake especially in the subacute phase within the infarct core and later infracting tissue, while there is less T₂ increase in tissue that will survive. Accordingly, quantitative T₂-values in diffusion restriction and lesion growth region of interest were significantly higher than in surviving tissue region of interest in follow-up scans.

These findings indicate that quantitative T₂-values in different stroke regions show further increase beyond the acute imaging time point and that there is less T₂ increase from infarct core to periphery. In line with these observations, Hoehn-Berlage et al. (1995) observed an increase of quantitative T₂-values in the ischaemic territory after middle cerebral artery occlusion in rats, but shortly after vessel occlusion, the area of reduced apparent diffusion coefficient was larger than that of elevated relaxation times while towards the end of the experiment, the area of increased relaxation times approached that of decreased apparent diffusion coefficient. Also, Tourdias et al. (2011) reported that stroke damage may be assessed by subacute stroke volume in FLAIR images, but only if obtained in early subacute stage between Days 3 and 6. However, the mean time to first scan was <3 h in our study so the timing of the T₂ increase cannot be placed beyond 6 h with any certainty.

Nevertheless, in the acute phase quantitative T₂-values obtained in this study did not help to further discriminate between surviving tissue and brain tissue that is already irreversibly damaged being either part of the infarct core or surrounding penumbra. In the acute phase, quantitative T₂-values in surviving tissue region of interest only showed a slight tendency to be lower than in other region of interest localizations. However, when comparing histograms of quantitative T₂-values in the acute phase in different region of interest localizations we observed that quantitative T₂-values in surviving tissue region of interest were scattered less widely between subjects and showed lower standard deviations than quantitative T₂-values measured in diffusion restriction and lesion growth regions of interest. Therefore, ranges of quantitative T₂-values in surviving tissue region of interest, even in the acute phase, seem to be less variable between subjects than for other stroke regions. This might be due to less severe affection of brain tissue that is later part of the surviving penumbra from the beginning due to sufficient collateralization. In analogy with these findings, previous studies found that perfusion parameters such as time-to-peak and mean transit time also show a gradient of severity from infarct core to periphery (Ritzenthaler et al., 2010).

Also, when comparing the recanalization group to the no recanalization group, only quantitative T₂-values in diffusion restriction region of interest seemed to show a tendency to be higher in the no recanalization than in the recanalization group, but this difference was not significant. There was no significant difference between the quantitative T₂-values measured in lesion growth and surviving tissue region of interest between the recanalization and no recanalization group. These findings indicate that there is no certain T₂ threshold indicating irreversible tissue damage in the acute phase, even independent of recanalization. Quantitative T₂-values in surviving tissue in the recanalization and no recanalization group were acutely not significantly lower than in the lesion growth region of interest, indicating that even high quantitative T₂-values in the subacute phase can later normalize or become part of final infarct lesion. In comparison, quantitative T₂-values in the recanalization group showed significantly higher T₂-values in lesion growth and diffusion restriction region of interest in comparison with surviving tissue region of interest on follow-up images. These findings might be due to early recanalization and therefore less increase of oedema from acute to follow-up scan, especially within the penumbra. Nevertheless, we only measured quantitative T₂-values in the acute phase and on Day 1. It is still possible that there is a certain T₂ peak that might be reached indicating irreversibly damaged brain tissue, but this peak might be later in the process of timely stroke evolution, maybe corresponding to one of the later phases of ischaemic stroke known from CT, like fogging and haemorrhagic transformation. Another reason for our findings might be that quantitative T₂-values are mainly increased due to vasogenic oedema, which in comparison with cytotoxic oedema, might more likely be reversible, not leaving irreversibly damaged brain tissue. To our knowledge, this is the first study to evaluate quantitative T₂-values in different regions of acute ischaemic stroke patients and their timely evolution.

One limitation of this study is that all acute T₂ measurements are taken at different time points after symptom onset within the first 6 h after symptom onset and therefore low quantitative T₂-values might also be due to an earlier scanning point (Siemonsen et al., 2009).

Determining infarct volume after ~1 week where infarct swelling occurs might lead to overestimation of the final infarct region and thus overestimation of quantitative T₂-values in surviving tissue region of interest only.
tissue and lesion growth regions of interest. However, 22/22 of our patients showed an increase of T2-values from acute to subacute scans in lesion growth and 19/22 in surviving tissue region of interest. Also, when excluding the four patients with noticeable swelling in subacute scans there was still a significant difference between T2-values measured in acute and follow-up scans for all three region of interest localizations. Therefore, the significant increase of T2-values as detected both in surviving tissue and lesion growth regions of interest cannot only be explained by a possible effect of infarct swelling.

In addition, limitations of the quantitative T2-values are that in theory, the more echoes, and thus more points for the calculation of the signal intensity decay curve, would be beneficial for the derivation of T2 than from the triple-echo sequences used for this study. In clinical routine, though, multi-echo magnetic resonance images with more echoes also require a longer repetition time. This leads to a longer magnetic resonance acquisition time and higher sensitivity to artefacts from patient movement, which is most relevant in patients with acute stroke.

In addition, statistical testing was conducted using mean quantitative T2-values measured in the affected hemisphere, therefore regions of interest might comprise white and grey matter leading to slightly decreased quantitative T2-values depending on the amount of grey matter that is comprised within one region of interest.

Conclusion

These findings indicate that high quantitative T2-values in ischaemic stroke in acute and early subacute phase reflecting vascular oedema do not reach a certain threshold indicating irreversible damaged brain tissue and T2 increase is still reversible. Therefore, quantitative T2-values in the acute situation do not identify irreversibly damaged brain tissue. Also, recanalization status did not alter this observation. In conclusion, this study suggests that T2-values are not a valid imaging biomarker to predict tissue outcome in the acute phase of ischaemic stroke. Nevertheless, there might be a certain T2 threshold identifying later infarct, but this threshold might be reached in later course of stroke evolution.

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References


