A comparison of the ADC and $T_2$ mapping in an assessment of blood-clot lysability

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The structural characteristics of blood clots are associated with their susceptibility to thrombolysis. As their morphology can be characterized by MRI, several attempts have been made to link the lysability of blood clots with their MRI properties; however, so far no study has associated a clot’s lysability with the diffusion properties of the water in the clot. The apparent diffusion coefficient (ADC) is highly sensitive to changes in serum mobility and may be used to distinguish between the non-retracted and the fully retracted regions of the blood clot. Therefore, the ADC may be a suitable, or even a better, marker for an assessment of the clot’s retraction and consequently for its lysability than the relaxation time $T_2$. The purpose of this study was to evaluate whether it is possible to predict the outcome of clot thrombolysis by ADC mapping prior to treatment. After two hours of thrombolysis using a recombinant tissue plasminogen activator in plasma, whole-blood clots were efficiently dissolved in regions with ADC $\geq 0.8 \times 10^{-9}$ m$^2$/s or $T_2 \leq 130$ ms, whereas dissolution was poor and prolonged in regions with ADC $< 0.8 \times 10^{-9}$ m$^2$/s or $T_2 > 130$ ms. An analysis based on a comparison between the initial and final ADC and $T_2$ maps after two hours of thrombolysis showed that the ADC can more accurately detect the different grades of clot retraction than $T_2$ and predict the regions of a clot that are resistant to thrombolysis. Therefore, the ADC could be used as an efficient prognostic marker for the outcome of thrombolysis. However, in vivo studies are needed to test this idea. Copyright © 2009 John Wiley & Sons, Ltd.

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INTRODUCTION

Blood clots represent an important problem in Western society since they are associated with cardiovascular dysfunction, ischaemic cerebrovascular strokes and massive pulmonary embolisms. Restoring vessel patency by dissolving blood clots is the goal of thrombolysis, which has gained worldwide recognition for its role in treating myocardial infarction (1–4). As a result, thrombolysis is now moving into the realm of treating acute ischaemic strokes (1–3). Thrombolysis is also of value in treating haemodynamically significant pulmonary embolisms (1,2), as well as in selective cases of acute or sub-acute arterial thrombosis (3,4). Since a thrombolytic treatment always carries the risk of serious bleeding, it would be very valuable to know in advance whether the offending thrombus is susceptible or inherently resistant to any thrombolytic treatment.

Diffusion-weighted imaging (DWI) is well recognized for its diagnostic role in strokes. Recently, the reduced apparent diffusion coefficient (ADC) has been of value in organized haematomas, compared to normal white matter (5–7). This suggested that similar patterns might also occur in blood clots. Several studies have attempted to link the final outcome of thrombolysis with the properties of the thrombolytic agent, the characteristics of the molecular transport into the clot and the impact of blood flow regimens on clot dissolution (8–10). $T_1$- and $T_2$-weighted MRIs were used to assess the lysability of arterial thrombi in vivo (11) and to characterize ex vivo the pulmonary emboli (12). One study employed ADC mapping for the discrimination of tissue oedema (13), but no MRI study imaged the clot structure based on its diffusion properties and linked them to the outcome of the thrombolysis. Our study is based on the fact that in vivo intravascular thrombi, as well as in vitro model clots, change over time due to the retraction and reorganization of the platelets (14). This process of retraction is caused by the active movement of the platelets inside the clot, with the formation of new platelet–fibrin bonds that result in compaction of the fibrin network and the expulsion of serum from the clot (15,16). It is known that clot retraction is associated with a shortening of the relaxation time $T_2$; therefore, a $T_2$-weighted MRI is considered as an appropriate technique for displaying blood-clot retraction (17,18). Due to the nature of the retraction we expected that the diffusion would be faster in non-retracted (serum-rich) areas of the blood clots, characterized as hypointense regions in the DWI, and slower in retracted (serum-poor) areas of the blood clots, characterized as hyperintense regions in the DWI.

In this study, we tested the possible prognostic potential of ADC mapping in comparison to $T_2$ mapping for an assessment of blood-clot lysability prior to initiating the thrombolytic treatment.

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Abbreviations used: ADC, apparent diffusion coefficient; DWI, diffusion-weighted imaging; Ht, haematocrit; NR, non-retracted; ROI, region of interest; rt-PA, recombinant tissue plasminogen activator.
with a fibrin-specific recombinant tissue plasminogen activator (rt-PA) (19).

MATERIALS AND METHODS

Preparation of model clots

The blood was drawn from the cubital vein of human subjects, the authors of the study, who showed no evidence of coagulation disorders or acute illness. The model blood clots were prepared from whole blood collected in vials (Vacutainer, Becton-Dickinson, Germany) containing 1 volume part of 0.129-M Na-citrate per 9 volume parts of blood. The haematocrit of the anti-coagulated blood was determined after centrifugation at 3000 rpm for 30 min. The clotting was induced in vitro in Teflon vials with a diameter of 5 mm and a height of 30 mm by adding 20 μL of 2-M CaCl₂ and 100 μL/mL of a thrombin solution (Thrombin, Sigma-Aldrich, Germany) to a final concentration of 1.25 NIH unit/mL. The model clots were either allowed to spontaneously retract, or retraction was pharmacologically inhibited by adding the phosphodiesterase inhibitor UDCG (1.25 NIH unit/mL of sample). The initial clot mass (m₁) was measured with an electronic balance (Mettler Toledo, Switzerland). Five minutes after the addition of the thrombin, the clots were gently detached from the inner surface of the test vials with a needle and allowed to retract spontaneously for 90 min at room temperature (20–24°C). The separation of the fluid expressed from the retracted clot was performed at 30-min intervals. After the separation of the expressed fluid, the mass of the retracted clots (m₂) was measured and the mass of the expressed serum (m₃) was calculated as the difference between m₁ and m₂. All the masses were converted to volumes by assuming a specific density of 1 g/cm³. The erythrocyte fall-out during the retraction was quantified by measuring the haematocrit of the expressed serum. The extent of the retraction was evaluated by calculating the “cellular” part of the retracted clot, i.e. its haematocrit (Ht₀) as

\[ Ht₀ = \frac{(V₁ \times Ht - V₂ \times Htₚ)}{V₀} \]  

Here, V₁ stands for the volume of the non-retracted whole-blood clot, V₂ for the volume of the expelled serum and V₀ for the volume of the retracted clot. Ht is the haematocrit of the citrated blood, corrected for the additional dilution with the calcium and thrombin solutions, and Htₚ is the haematocrit of the serum expelled from the retracted clots.

The haemoglobin concentration of the volunteers’ blood was 125–145 g/L; the haematocrit (Ht) concentration was 35–42%; and the plasma fibrinogen concentration was 1.2–1.8 g/L. The blood gas analysis of the venous blood upon sampling revealed an oxyhaemoglobin saturation of 0.45, corresponding to 45% of the diamagnetic oxyhaemoglobin and 55% of the paramagnetic deoxyhaemoglobin.

Pure fibrin clots were prepared from lyophilized human fibrinogen powder (KabiVitrum, Sweden), grade L, which was completely dissolved and divided into small aliquots of 10 and 20 mg of fibrinogen in 1 mL of physiological solution. The clotting was initiated by the addition of calcium (2-M CaCl₂, 30 μL/mL of fibrinogen sample) and thrombin (Thrombin, Sigma-Aldrich, Germany) to a final concentration of 1.25 NIH unit/mL of sample.

All the vials containing model whole-blood or fibrin clots were only filled up to 50% of the total vial volume and then closed after the gelation time had elapsed (90 ± 35 s), allowing the retraction to occur without any mechanical compression of the clots’ original volume.

Conditions of thrombolysis

The thrombolysis of the model blood clots was performed in an artificial perfusion system using a remodelled transfusion set (Emitelk, Italy). The model clots were incubated in the latticed chamber of the transfusion set, which was connected by a flexible hose to a pump that generated a pulsatile plasma flow with a pulse pressure of 30 mmHg. The hose connecting the pump to the clot was 1.7 m long (3.4 m to the clot and back) and had a 3 mm inner diameter. During each experiment, the artificial perfusion system was filled with approximately 250 mL of single-donor blood plasma of a matching ABO blood group. The clots were perfused in eight 15-min runs of the perfusion system, interspersed with 25-min periods for MR scanning. Eight non-retracted and 14 retracted whole-blood model clots were incubated in a plasma milieu with fibrin-specific thrombolytic rt-PA (Actilyse, Boehringer Ingelheim, Germany) to a final concentration of 2 mg/mL, while five clots served as controls and were incubated in a plasma milieu without the thrombolytic agent. The plasma was thermoregulated at 36°C body temperature.

Magnetic resonance imaging

The experiments were performed on an MRI scanner consisting of a 2.35-T (100-MHz proton frequency) horizontal bore Oxford superconducting magnet (Oxford Instruments, Oxon, UK), equipped with a Bruker micro-imaging gradient system (Bruker, Ettlingen, Germany) using a TecMag NMR spectrometer and computer software (TecMag, Houston, TX, USA). Maps of the T₂ relaxation times of the whole-blood model clots were measured by the multi-spin-echo imaging method based on a Carr–Purcell–Meiboom–Gill (CPMG) multi-echo train (21). Eight echo images from consecutive echo signals with an inter-echo time of 18 ms were acquired at a field of view of 25 mm from the same single slice oriented axially through the clot. The slice thickness was 4 mm, the imaging matrix was 128 squared and the repetition time was 4150 ms. Each clot was also imaged in an identical slice orientation and in the same field of view and imaging matrix by the DWI method, based on the pulsed-field gradients spin-echo (PGSE) technique (22), with two 10-ms gradient pulses positioned symmetrically with respect to the refocusing RF pulse (Δ = 10 ms, ∆ = 18 ms). The repetition time and the echo time in the DWI method were 2040 and 36 ms, respectively. Four DW images, acquired at different b values of 0 s/mm², 132 s/mm², 317 s/mm² and 635 s/mm², were used to calculate the corresponding ADC images. In each experiment, which took 320 min, a clot was imaged dynamically in eight 40-min imaging blocks. Each imaging block consisted of the DWI method, with a 17-min experiment time, followed by the multi-spin-echo imaging method, with an 8-min experiment time, and 15 min of plasma perfusion. During the MRI scanning, the perfusion system was stopped. The T₂ relaxation time and the ADC maps were calculated using the MRI Analysis Calculator plug-in of the ImageJ (NIH, USA) image-processing software.

In addition to experiments where the ADC and T₂ were imaged dynamically during clot dissolution, a set of imaging experiments was performed on a separate set of blood clots (five non-retracted and eight retracted whole-blood clots and four fibrin clots) in which, instead of clot dissolution, the effect of clot...
retraction on the change of the ADC and $T_2$ was studied. To prevent any spontaneous retraction prior to imaging, the non-retracted clots were prepared by adding a retraction inhibitor (phosphodiesterase inhibitor UDCG 212), while for the retracted clots no addition of the retraction inhibitor was needed. The clot retraction was, as described earlier, followed by a change of the haematocrit level $H_{tR}$ obtained by sample weighing, while the average ADC and $T_2$ values were obtained using the same two imaging methods (DWI and multi-spin-echo) as the mean signal intensities of the ADC and $T_2$ maps in the clot region. In between the imaging experiments the clots were removed from the magnet to measure their mass after the removal of the expelled serum and to estimate the extent of their retraction ($H_{tR}$). The clots (without the surrounding plasma) were then reinserted into the magnet. The measured values of the ADC, $T_2$ and $H_{tR}$ were analysed using a linear-regression analysis.

**Image analysis**

The ADC as well as the $T_2$ relaxation-time dependence on $H_{tR}$ in the clots undergoing retraction was analysed using a linear-regression fit.

Changes in the distribution of the ADC and $T_2$ during thrombolysis were obtained from histograms of the ADC and $T_2$ maps. In the maps, pixels with values in intervals increasing in steps of $\Delta \text{ADC} = 0.1 \times 10^{-9} \text{ m}^2/\text{s}$ or $\Delta T_2 = 10 \text{ ms}$ were counted. The distributions thus obtained were then normalized using the average ADC or $T_2$ of a typical, non-retracted whole-blood clot, using the values $\text{ADC}_{\text{NR}} = 1.2 \times 10^{-9} \text{ m}^2/\text{s}$ or $T_{2\text{NR}} = 210 \text{ ms}$.

The ADC and $T_2$ maps before and after the thrombolysis were quantitatively analysed for the relation between the ADC or $T_2$ value and the proportion of the clot’s lysable area. Specifically, a histogram of the ADC or the $T_2$ map of a clot before thrombolysis was made to obtain the count of pixels having ADC or $T_2$ values within a specific range. Then, the same analysis was applied to the final ADC or $T_2$ map after two hours of thrombolysis. The ratio between the final and the initial pixel count, having the ADC or $T_2$ within a specific range, was used as an estimate of the non-lysable proportion of the clot, and one minus this result was used as an estimate for the lysable proportion of the clot.

**RESULTS**

The analysis of the DW images of the different $b$-values and the analysis of the $T_2$-weighted images at different echo times of the same model clots imaged in the same slice orientation and position yielded the following average ADC and $T_2$ relaxation-time values: $(2.0 \pm 0.1) \times 10^{-9} \text{ m}^2/\text{s}$ and $340 \pm 20 \text{ ms}$ for a fibrin clot, $(1.20 \pm 0.06) \times 10^{-9} \text{ m}^2/\text{s}$ and $210 \pm 20 \text{ ms}$ for a non-retracted whole-blood clot and $(0.50 \pm 0.04) \times 10^{-9} \text{ m}^2/\text{s}$ and $90 \pm 10 \text{ ms}$ for retracted regions of a whole-blood clot, 90 min after the initiation of the clotting. The values were obtained as the average values from the ADC and $T_2$ maps (shown in Fig. 1) in the clot region. The DW and $T_2$-weighted MRI of identical representative model clots showed that the ADC can discriminate between a fibrin clot and a non-retracted whole-blood clot, and can clearly depict the multi-layered morphology of retracted whole-blood clots. In comparison, the maps of the relaxation time $T_2$ showed no significant difference between a fibrin clot and a non-retracted model clot, but could clearly depict only regions with a high level of retraction.

The effect of retraction in model clots resulting from decreased serum mobility was characterized by the ADC and $T_2$ values, which decreased with an increase in $H_{tR}$ during the retraction (Table 1). Ten minutes after clotting the $T_2$ variability was, on average, twice as large as the ADC variability in a non-retracted clot ($H_{tR} = 0.41$; 10% vs. 5% relative error). When the retraction progressed further, the difference between the ADC and $T_2$ variability diminished ($H_{tR} = 0.84$; 10% vs. 8% relative error). The linear-regression fit showed a better negative correlation between the ADC and $H_{tR}$ ($r_{\text{ADC}} = -0.92$) than between $T_2$ and $H_{tR}$ ($r_{T_2} = -0.86$). The linear-regression fit between the ADC and $T_2$ yielded a positive correlation of $r_{\text{ADC},T_2} = 0.96$.

**Figure 1.** Appearance of water, pure fibrin gel, a non-retracted whole-blood clot and a retracted whole-blood clot by (a) apparent-diffusion-coefficient (ADC) mapping and (b) $T_2$ relaxation-time mapping. In contrast to the $T_2$ mapping, which gradually distinguishes the pure fibrin gel and a non-retracted from a retracted whole-blood clot, the ADC can also continually discriminate between the pure fibrin clot, the non-retracted clot and the retracted whole-blood clot.
Table 1. Relation between clot retraction, ADC and $T_2$ values, as obtained from the analysis of the ADC and $T_2$ maps. The clot retraction, expressed by $H_{tr}$, was determined by weighing the clot prior to imaging.

<table>
<thead>
<tr>
<th>$H_{tr}$ (%)</th>
<th>ADC ($\times 10^{-9}$ m$^2$/s)</th>
<th>$T_2$ (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td>41 ± 3</td>
<td>1.18 ± 0.06</td>
<td>210 ± 20</td>
</tr>
<tr>
<td>51 ± 3</td>
<td>0.76 ± 0.04</td>
<td>110 ± 10</td>
</tr>
<tr>
<td>68 ± 4</td>
<td>0.63 ± 0.05</td>
<td>101 ± 8</td>
</tr>
<tr>
<td>84 ± 5</td>
<td>0.47 ± 0.04</td>
<td>69 ± 7</td>
</tr>
</tbody>
</table>

Figure 2 shows the time course of the thrombolysis of a typical non-retracted whole-blood clot (upper row) and a typical retracted whole-blood clot (lower row) in a plasma milieu using a time series of the ADC (a) and $T_2$ (b) maps. Both imaging modalities show a significant decrease in the non-retracted clot size after 120 min of thrombolysis and poor thrombolysis progress in the retracted clot. The ADC maps and $T_2$ maps show the differences in clot retraction equally well; they clearly show the superficial accumulation of serum in the retracted clot and a uniform signal from the interior serum-poor regions of the clot.

The changes to the ADC or $T_2$ distributions in a typical retracted and a typical non-retracted whole-blood clot during two hours of thrombolysis are shown in Fig. 3. Both imaging modalities, the ADC mapping and the $T_2$ mapping, show the heterogeneous structure of the retracted clot (Fig. 3a, b). In the initial maps of the retracted clot, the ADC values range from 0.3 to 1.2 of the $ADC_{NR}$ with a broad peak at 0.5 $ADC_{NR}$ while the $T_2$ values range from 0.5 to 1.3 of $T_2_{NR}$ with a peak at 0.6 $T_2_{NR}$. The clot dissolved equally well for all the ADC or $T_2$ values, which can be seen in the almost uniform decrease of the area under the distribution profiles (about 20% after two hours) over the whole range of values. However, there is a small but noticeable shift in the distribution profiles to higher values in the ADC as well as in the $T_2$ profiles. In contrast to the retracted clot, the non-retracted clot has a homogeneous structure and therefore a narrow distribution profile (Fig. 3c, d), which in the ADC as well as in the $T_2$ ranges from 0.9 to 1.1, with a peak at 1.0 (in the normalized ADC or $T_2$ values). After two hours of thrombolysis, the area under the ADC and $T_2$ distribution profiles of the non-retracted clot decreased by about 80%, with no shift to higher values.

Figure 4 shows the proportion of the clot’s lysable area as a function of the normalized ADC (squares) or normalized $T_2$ (circles) values. From the graph, it is clear that the regions with higher ADC or $T_2$ values are more susceptible to thrombolysis.
than the regions with lower ADC or $T_2$ values. The data in the graph in Fig. 4 indicate that a 50% success rate for the two-hour thrombolysis with rt-PA is expected at an ADC value $\leq 0.7 \times 10^{-6} \text{ m}^2/\text{s}$ or $T_2 = 0.6 \times T_{2NR} = 130 \text{ ms}$. The normalized ADC values change over a larger interval with the clot retraction than the normalized $T_2$ values (0.3–1.5 compared to 0.4–0.9), which means the ADC can more accurately detect different grades of clot retraction than $T_2$. In addition, the relation between the ADC and the clot’s lysability is practically linear over the whole range, whereas the relation between $T_2$ and the clot’s

**Figure 3.** Distribution of the ADC (a, c) and $T_2$ (b, d) in a typical retracted whole-blood clot (a, b) and a typical non-retracted whole-blood clot (c, d) during two-hour thrombolysis with fibrin-specific rt-PA. The distribution curves of the ADC and $T_2$ clearly depict the heterogeneous structure of the retracted clot; the normalized ADC value ($\text{ADC}_{NR} = 1.2 \times 10^{-6} \text{ m}^2/\text{s}$) ranges from 0.3 to 1.2, while the normalized $T_2$ ($T_{2NR} = 210 \text{ ms}$) ranges from 0.5 to 1.3. The slight distribution shift to higher normalized values indicates a decrease in the degree of retraction in the course of thrombolysis. In the non-retracted clot, the distributions of the ADC and $T_2$ are much narrower (the relative ADC and $T_2$ range from 0.9 to 1.1) due to the homogeneous structure of the clot. The successful thrombolysis of the non-retracted clot is shown by the significant reduction in the area under the distribution peak.
associated with these effects, i.e. meshwork (23,24), while the changes in T2 molecules between the blood cells entrapped in the fibrin thrombolysis is expected at ADC = SD (n = 6) are shown. The data indicate that a 50% success rate for thrombolysis is expected at ADC = 0.7 × ADCNR = 0.8 × 10^-9 m²/s or T2 = 0.6 × T2NR = 130 ms.

lysability exhibits a steep slope at low values and saturation at high values.

DISCUSSION

The main question examined in this work was whether the outcome of thrombolysis can be predicted on the basis of the MR images of blood clots obtained prior to rt-PA treatment. Two potentially interesting methods that provide a quantitative assessment of the clot’s properties were evaluated in this respect: ADC mapping and T2 relaxation-time mapping. Our study showed that the ADC and T2 mapping are comparable methods for the detection of clot retraction and predicting lysability, but the ADC is associated with lysability in an almost linear fashion, while T2 mapping shows a steep response at short T2 values and reaches a plateau at intermediate and large T2 values. This is because the ADC directly measures the mobility of water molecules between the blood cells entrapped in the fibrin meshwork (23,24), while the changes in T2 are indirectly associated with these effects, i.e. T2 can primarily detect protein concentration (25), which is indirectly associated with a decreased mobility of water. Interestingly, T2-weighted imaging has, until now, been practically the only method reported for clot-retraction assessment (12,18,26).

The fibrin meshwork represents less than 1% of a non-retracted clot’s volume (27), but it has a substantial effect on the serum mobility. During clot retraction, moving platelets form new platelet–fibrin bonds, which compact the fibrin meshwork and change the proportions between the fibrin meshwork, the entrapped blood cells and the serum in favour of the first two. Clot retraction contributes significantly to the reduction of the serum mobility in the clot and therefore impedes the progression of the thrombolytic agent into the clot (28). In addition, retraction expels unbound plasminogen from the clot, which unfavourably affects the biochemical conditions for fibrinolysis (29). Dynamic DWI and T2-weighted MRI were performed during two hours of thrombolysis in order to examine the association between the ADC and T2 and the clot’s lysability, and to find which of the two parameters was more accurate in predicting the outcome of the thrombolysis. The two-hour period was chosen to mimic the time course of thrombolysis in treating a massive pulmonary embolism (30,31). The ADC and T2 maps acquired during the thrombolysis enabled the selection of limiting ADC and T2 values, by which the regions of the clot could be divided into two parts: the efficiently lysable part and the poorly lysable part. The values of ADCNR = 1.2 × 10^-9 m²/s and T2NR = 210 ms were chosen as the average ADC and T2 values of seven non-retracted whole-blood model clots. These limiting values were chosen because the non-retracted (serum-rich) clots are the most susceptible to thrombolysis in a plasma milieu with a fibrin-specific thrombolytic and pulsating flow (32,33).

The comparison between the ADC and T2 mapping, as methods for the prognosis of the outcome of clot thrombolysis, showed that an equal change in clot retraction corresponded to about twice as much difference in the relative ADC values than in the relative T2 values (Fig. 4). This also explains the wider peak in the ADC distribution in the retracted whole-blood clot in Fig. 3a compared to the T2 value for the same clot in Fig. 3b. In addition, the ADC mapping also enables a more accurate detection of the highly retracted clot regions that, to a large extent, do not lyse. For example, in the regions with the lowest ADC measured in the retracted clot (ADC = 0.3 × 10^-9 m²/s) the fraction of successfully lysed clots is not more than 5%, while in regions of the same clot with the shortest T2 (T2 = 85 ms) the fraction is 25%.

The ADC and T2 mapping methods were only tested on venous blood, which had a ratio of paramagnetic deoxyhaemoglobin to diamagnetic oxyhaemoglobin of 55/45. If arterial blood were used instead, slightly increased T2 values would be obtained, compared to those in our experiment. However, the ratios for T2 between the retracted and non-retracted clot would not change. The ADC, on the other hand, is not sensitive to blood oxygenation.

The slice thickness of 4 mm that was used in the MR experiments was not optimal for the imaging of the relatively small model clots, so the partial-volume effect, in which the pixel signal could arise from the clot as well as from the surrounding plasma, was likely. However, the experiments were performed in a relatively low magnetic field of 2.35 T and the selected slice thickness at the given resolution was the best compromise between the partial-volume effect and the signal-to-noise ratio. To reduce the risk of the partial-volume effect, the imaging slice was positioned centrally through the clot, i.e. through the region that is the most resistant to thrombolysis. In addition, the model clots were carefully prepared using the retraction inhibitor UDCG 212, which preserved the relatively high initial homogeneity of the clots during the entire thrombolysis process.

The correlation between the ADC, T2 and HtR was studied on a separate set of clots that was allowed to retract spontaneously. The process of retraction was measured by periodic clot weighing to obtain HtR and by clot imaging to obtain the average ADC and T2 values from the selected ROI of the corresponding ADC and T2 maps. Periodic imaging was associated with the problem of the exact repositioning of the clots in the magnet. This, as it turned out, was not needed, as the clots were very homogeneous. In addition, partial-volume effects did not influence the calculated ADC and T2 values because the clots were imaged outside the plasma and the possible signal voids in the selected ROI within
the imaging slice could only influence the signal's intensity, but not the rate of signal decay, from which the ADC and $T_2$ values were calculated.

The technical parameters for the DWI and $T_2$-weighted MRI were chosen as the best compromise between the ADC and $T_2$ mapping times and accuracy, limited by the two-hour period of thrombolysis, which is clinically relevant. The clot's lysability was studied in vitro as a necessary first step before more relevant in vivo studies can be undertaken.

CONCLUSION
Both $T_2$-weighted MRI and DWI detect clot retraction and predict the lysability of whole-blood clots by rt-PA in vitro. DWI with ADC mapping is the more accurate method of the two, but its clinical utility needs to be tested in vivo.

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