

## Magnetic Resonance T1 Mapping Predicts Successful Venous Thrombolysis

P. Saha<sup>1</sup>, M. E. Andia<sup>2</sup>, U. Blume<sup>2</sup>, A. J. Wiethoff<sup>2,3</sup>, T. Schaeffter<sup>2</sup>, C. Evans<sup>1</sup>, A. Ahmad<sup>1</sup>, A. Patel<sup>1</sup>, B. Modarai<sup>1</sup>, R. M. Botnar<sup>2</sup>, A. Smith<sup>1</sup>, and M. Waltham<sup>1</sup>

<sup>1</sup>Academic Department of Surgery, Cardiovascular Division, Kings College London, London, United Kingdom, <sup>2</sup>Division of Imaging Sciences and Biomedical Engineering, Kings College London, London, United Kingdom, <sup>3</sup>Philips Healthcare, Guildford, United Kingdom

**INTRODUCTION:** Novel thrombolytic delivery systems are changing the treatment paradigm for deep vein thrombosis (DVT), but older, well-organised thrombi remain unsuitable for intervention. A technique that identifies thrombi that are amenable to lysis is needed [1].

**METHODS:** Venous thrombosis was induced in the inferior vena cava (IVC) of 8-10 wk (25-30 g) male BALB/C mice using an established technique that involved flow disruption and mechanical endothelial damage [2]. A MRI 3D T1-mapping protocol was developed for imaging venous thrombi induced in mice. T1-relaxation times were quantified between 4 and 28 days after induction (n=33). The thrombus was sectioned along its entire length. Collagen content was measured histologically as a marker of organization and compared with T1-relaxation times in corresponding MR slices. Results were validated by three blinded observers. Tissue plasminogen activator (Actilyse) was injected (10 mg/kg) between 4 and 16 days after thrombus induction (n=16). T1-mapping was performed before and 24hrs after Actilyse administration. Successful thrombolysis (vein recanalisation) was measured as an increase in the velocity of flow across the IVC greater than 0.3cm/s using MR Phase Contrast measurement and confirmed by histology. T1 mapping of the thrombus and vessel wall was performed using a Look-Locker based sequence [3]. T1 maps of 20 slices were calculated using custom-made software implemented in Matlab (Mathworks, Natick, MA, USA). Imaging parameters included spatial resolution 100x100µm, slice thickness of 500µm, TR/TE=9.0/4.6 ms, flip angle=10°. All scans were performed on a 3T Philips Achieva Gyroscan scanner (Philips Healthcare, Best, The Netherlands) equipped with a dedicated small animal surface coil.

**RESULTS:** T1-relaxation time increases with thrombus age (Figure 1) and organisation (Figure 2) (763±22ms, 4d; 617±36ms, 7d; 673±51ms, 10d; 728±58ms, 14d; 945±66ms, 21d; 1194±59ms, 28d). Collagen content is proportional to T1-relaxation time during thrombus resolution (R<sup>2</sup>=0.80, P<0.0001, n=15). T1-relaxation times were significantly shorter in the group successfully treated with thrombolysis (P=0.002, n=16) (Figure 3). ROC curve analysis shows an optimal cut-off point of ~700ms (Figure 4). The sensitivity and specificity for predicting successful thrombolysis was 100% and 88%.

**CONCLUSIONS:** This is the first study to show that T1-mapping quantifies organisation of experimental venous thrombi and predicts response to thrombolysis. This technique enables the objective selection of thrombi that could be successfully treated with lysis in patients presenting with DVT.

**REFERENCES:** [1] Bates S *N Engl J Med* 2004, [2] McGuinness CL *Thromb Haemost* 2001, [3] Blume U *MAGMA* 2009

Figure 1- T1 relaxation time of thrombus at different time point

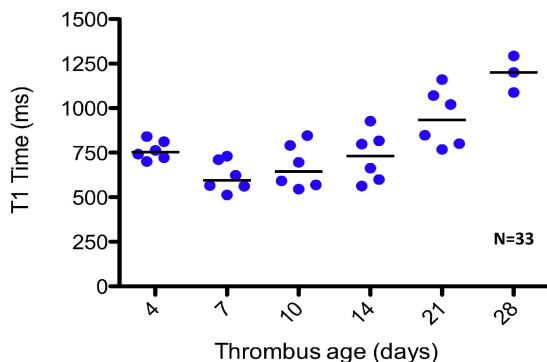


Figure 2- Relation between thrombus T1 relaxation time and thrombus organisation score measured as collagen content

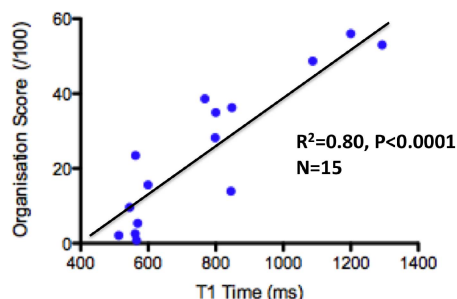


Figure 3- (a) Change in venous flow pre and post thrombolysis versus T1 relaxation time [ms] pre-treatment. (b) Average T1 value of venous thrombus in the successful and unsuccessful thrombolysis group.

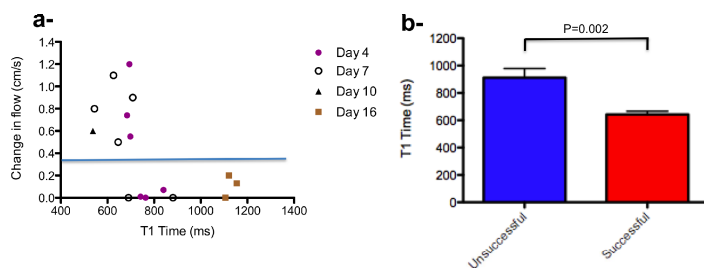
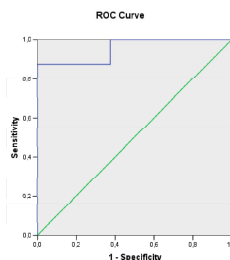


Figure 4- Receiver operating characteristic (ROC) curve for Thrombus T1 Value [ms] as a predictor of successful thrombolysis.



AUC: 0.953 [CI 95%: 0.85-1]

**Optimal Cut-off point: T1 = 709 ms**

Sensitivity = 100% [CI95%: 100-100]

Specificity = 87.5% [CI95%: 47.4 – 97.9]