INTRODUCTION: Deep venous thrombosis (DVT) remains a major health problem. Although thrombolytic therapies are effective in recanalising the veins, restoring blood flow and preventing post-thrombotic complications there is still no consensus on the selection criteria for this invasive treatment. Thus, there is a need for a diagnostic technique that identifies patients amenable for venous thrombolysis. The aim of this study was to investigate the merits of a fibrin-specific MRI contrast agent (EP-2104R, EPIX Pharmaceuticals, MA) for the accurate staging of thrombus organization and to identify thrombus suitable for lysis in an experimental animal model of venous thrombosis. METHODS: Venous thrombosis was induced in the inferior cava vein (IVC) of 8-10 weeks old male BALB/C mice using an established technique [1]. MRI was performed at day 2, 4, 7, 10, 14 and 21 following thrombus inductions. Twelve mice were scanned at each time point pre and 2 hours post injection of a fibrin binding MRI contrast agent (5.0 μmol/kg EP-2104R [2]). 6 of 12 mice at each time point were used to correlate fibrin contrast uptake with the histological stage of thrombus. The remaining 6 mice were subjected to intravascular thrombolysis therapy (10 mg/kg of tissue plasminogen activator (Actilyse, Boehringer Ingelheim, Germany)) at each time point. 24 hours after thrombotic treatment mice were scanned again post EP-2104R injection. Two additional mice where scanned with a non-specific Gd-DTPA contrast at each time point for control purposes. All scans were performed on a 3T Philips Achieva Gyroscan scanner (Philips Healthcare, Best, The Netherlands) equipped with a dedicated small animal surface coil. An inversion recovery (IR) 3D segmented gradient echo (TFE) sequence was performed for selective visualisation of the thrombus and the inferior cava vein (IVC). In addition, T1 mapping of thrombus was performed using a Look-Locker based sequence [3]. T1 maps were calculated using custom-made software implemented in Matlab. To evaluate the success of the thrombolytic therapy a phase contrast sequence was performed to measure blood flow in the infrarenal IVC pre and post thrombolysis. Thrombolysis was considered successful if an increase of IVC blood flow of greater than 50% was observed on 24 hours post lysis scans compared to pre lysis scans. Thrombi were harvested after each scan. Sections were stained with hematoxylin and eosin (H&E) for anatomical detail and Martius Scarlet Blue (MSB) trichrome stain for mature fibrin visualization and quantification of thrombus volume on pre contrast IR-LGE images, low T1 relaxation times on T1maps, and the fibrin distribution on MSB stained histological sections (Figure 2). Contrast uptake was positively correlated with the percentage of fibrin in thrombus as measured with histology (R2=0.97, P<0.01). Flow changes in the IVC pre and post thrombolysis were measured with histology (R2=0.97, P<0.01). Flow changes in the IVC were found to have an AUC of 0.993 (CI95%: 0.98–1.00). From Figure 1, a cut-off point of pre contrast T1 relaxation time of 774 ms resulted in a sensitivity of 77% and specificity of 93% to predict successful thrombolysis. There was good spatial correspondence between high signal intensity areas on LGE-IR images, low T1 relaxation times on T1maps, and the fibrin distribution on MSB stained histological sections (Figure 2). Contrast uptake was positively correlated with the percentage of fibrin in thrombus as measured with histology (R2=0.97, P<0.01). Flow changes in the IVC pre and post thrombolysis were measured with histology (R2=0.97, P<0.01). Flow changes in the IVC were found to have an AUC of 0.993 (CI95%: 0.98–1.00). From Figure 1, a cut-off point of pre contrast T1 relaxation time of 774 ms resulted in a sensitivity of 77% and specificity of 93% to predict successful thrombolysis. The difference between the pre and post EP-2104R visualized thrombus enhanced volume before treatment had an AUC of 0.992 (CI95%: 0.98–1.00) to predict successful thrombolysis. The thrombus T1 relaxation time post EP-2104R injection was found to have an AUC of 0.993 (CI95%: 0.98–1.00). For a thrombus T1 relaxation time less than 630 ms on post contrast images, the sensitivity was 94% and specificity 99% to predict successful thrombolysis. CONCLUSIONS: The use of a fibrin specific contrast agent provides information not only on the presence of an intravascular thrombus but also allows assessment of thrombus age and organization. In addition, the presence of fibrin allows identification of thrombus amenable for lysis. Clinical studies are now warranted to validate these findings in humans. REFERENCES: [1] McGuinness CL Thromb Haemost 2001, [2] Overoye-Chan K J Am Chem Soc 2008, [3] Blume U MAGMA 2009, [4] Bradley WG Radiology 1993 [5] Moody J Thromb Haemost 2003