MRI guided Thrombolysis of Acute Stroke in a Canine Model

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Purpose The value of intraarterial (IA) rt-PA in the reestablishment of vessel patency for treating acute thromboembolic stroke is documented. We have developed a canine model of embolic stroke by the catheter directed injection of autologous blood clots into the ICA that is reversible via IA rt-PA administration. We have tested the hypothesis that MR imaging can be successfully used to monitor and guide thrombolysis in real-time. Furthermore we have validated a method for measuring quantitative CBF with MRI (qCBF), in a setting of acute stroke by comparing qCBF with gold standard fluorescent microsphere CBF measurements.

Material and Methods

A series of adult dogs were instrumented with 6-F femoral arterial sheaths placed bilaterally. Under X-ray guidance, one 4F catheter was placed in the ICA and one 5F catheter in the left atrium. Autologous emboli prepared by mixing freshly drawn arterial blood and thrombin, were injected into the ICA via the microcatheter. X-ray DSA confirmed middle cerebral artery (MCA) vessel occlusion. Fluorescent microspheres were injected before and after clot injection, and post rt-PA infusion to validate perfusion changes. MR imaging was performed with IA injections of Gd-DTPA, on a whole body 3T MR (Trio, Siemens Medical Solutions, Erlangen, Germany) system. The frontal sinuses of the dogs were filled with a viscous material (surgilube), via bilateral cranial burrholes, to prevent significant field inhomogeniety artifact resulting from difference in magnetic susceptibility between sinuses and brain tissue. Quantitative CBF (qCBF), DWI, and dynamic MRA (3D TRICKS) acquisitions were acquired before, during and after rt-PA administration to document stroke evolution and clot lysis. qCBF measurements were acquired with a novel imaging technique utilizing pre- and post-contrast T1 measurements, with an inversion-recovery segmented True-FISP (IR FISP) pulse sequence, during the distribution phase of the contrast agent [1]. A 2 mg bolus injection of rt-PA preceded a 6 mg slow infusion (45 min). Stroke resolution was confirmed with MRA and MR perfusion images. Fluorescent microsphere measurements served as a reference standard for validation of MRI derived qCBF values. Post mortem staining with Triphenyltetrazolium chloride (TTC) was performed to confirm residual infarct.

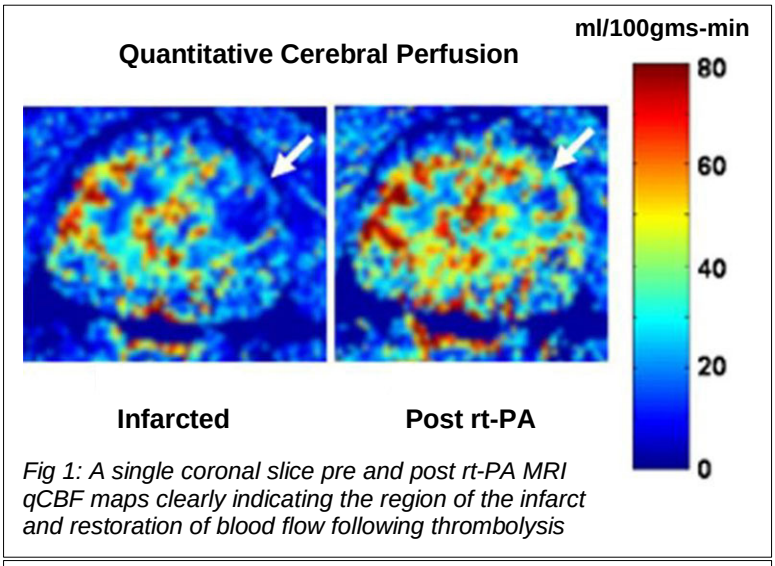

Fig 1: A single coronal slice pre and post rt-PA MRI qCBF maps clearly indicating the region of the infarct and restoration of blood flow following thrombolysis

Results

Strokes were produced in all animals embolized, with DSA confirming MCA occlusion. qCBF measurements, DWI and microspheres confirmed the presence of the stroke. In embolized animals, the MRI qCBF difference between infarcted (36.96+-21.52 ml/100g-min) and contralateral hemispheres (64.08+-16.12 ml/100g-min) was significant ($p<0.05$) and confirmed by microsphere derived CBF (39.94+-23.32 infarcted and 67.59+-19.01 ml/100g-min normal) (Fig 2). The average CBF (grey and white matter) measured with MRI (53.83±25.23 ml/100g-min) was in agreement with microsphere CBF (50.59±23.02 ml/100g-min). IA rt-PA successfully reestablished blood flow (Fig 1) to the affected region. MR angiograms re-confirmed the location of the embolus prior to thrombolysis.

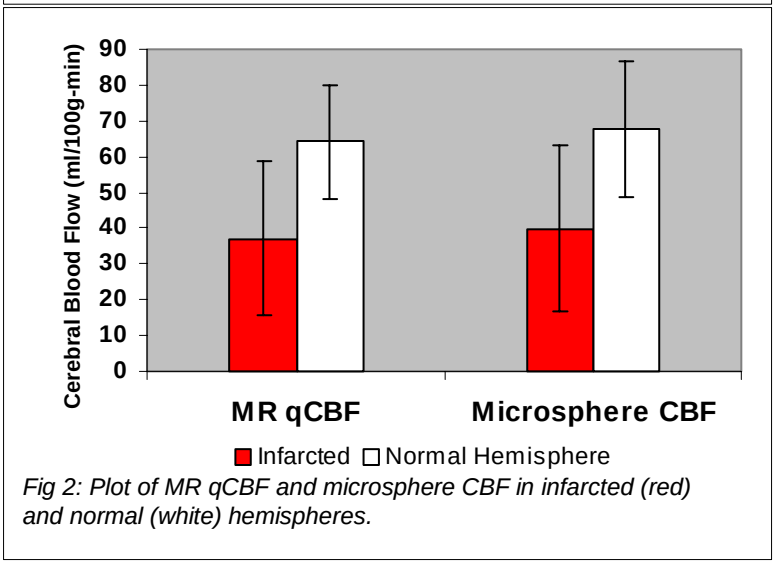

Fig 2: Plot of MR qCBF and microsphere CBF in infarcted (red) and normal (white) hemispheres.

Conclusion

Our initial results indicate we can reliably create and lyse embolic strokes in conjunction with MR imaging. This model of stroke, may provide a more realistic scenario for the eventual clinical implementation of these techniques than synthetically induced strokes using embospheres or balloon occlusion. Average MRI qCBF values correlate well with gold standard microsphere flow values indicating the ability to quantify CBF with MRI in a setting of acute stroke. Futhermore, we conclude that combined DSA X-ray/MRI treatment regiment to be feasible The introduction of combined /MRI imaging units will facilitate the development of this approach in acute stroke treatment.

References

1. Sakaie et al., J Magn. Reson. Imag.; Currently in Press.