

## TOF-MRA Measurements of Cranial Arteries in Cholesterol-fed Rabbits

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### INTRODUCTION

To study the effect of Alzheimer's Disease (AD)-like changes in the vessels of an animal model, we have used cholesterol-fed rabbits with trace amounts of copper added to the drinking water. Cholesterol-fed rabbits have at least 12 pathological markers seen in AD, suggesting that the cholesterol-fed rabbit is a good animal model for studying AD (1). Despite the critical role played by cholesterol and copper in nutrition and normal brain function, both may play roles in the etiology of AD by inducing beta-amyloid accumulation. Trace amounts of copper in drinking water may influence clearance of beta-amyloid from the brain at the level of the interface between the blood and cerebrovasculature and combined with high cholesterol may be a key component to the accumulation of beta-amyloid in the brain, having a significant impact on learning and memory. The goal of this study was to establish if the cholesterol plus copper fed rabbits exhibit changes in the cranial vessels measurable by time-of-flight magnetic resonance angiography (TOF-MRA).

### METHODS

Animals were anesthetized by ketamine (2.5cc) / xylazine (0.5cc) at 0.6cc/kg injected sc. Scanning was performed on a GEMS 3T long-bore Excite clinical scanner using a Nova Medical 12cm quadrature transmit/receive coil. The rabbits underwent 4 MRI scans: a 3-plane localizer, axial T1-weighted 3D IR-SPGR, axial T2-wtd FSE, axial TOF-MRA. All image sets covered below the most caudal end of the cerebellum to a slice past the rostral end of the olfactory bulbs. TOF and 3D-SPGR images were 1.6mm slices reconstructed every 0.8mm (Zip2) with inplane resolution of 0.156mm x 0.156mm. Maximum intensity projection (MIP) images were calculated by rotating about the long axis of the animal in steps of 10 degrees. The vessel diameters were measured following the full width half maximum signal method. The axial reconstructed 512 x 512 TOF images were loaded into the image processing software package MRVISION (MRVISION inc.) The common carotids, external and internal carotids just above the bifurcation, mid-basilar, vertebral arteries at cervical vertebrae C1, intradural vertebrals, posterior cerebral communicating, and rostral (cavernous) internal carotid arteries were identified. Then projections from the images were extracted by using the line drawing tool to obtain a plot of the signal intensity values across each vessel. The vessel diameter was measured as the full width half maximum of the TOF-MRA signal obtained using graphing software (Kaleidagraph). Beta-Amyloid accumulations were measured in the hippocampus (HIPP) and temporal cortex (TC) as described in reference 2.

### RESULTS

Beta-amyloid accumulations in the hippocampus and temporal cortex increased by +81.92% and 139.72% respectively. The arteries that demonstrated statistically significant changes were the basilar artery and the posterior communicating arteries on the left and right side. Those arteries narrowed by -26.32%, 30.43% and 45.83% respectively. These changes in arterial diameter were correlated with the beta-amyloid accumulations (see figure).

### CONCLUSIONS

At 3T using TOF-MRA, rabbit vessel diameters could be measured without using gadolinium-based contrast that could have contaminated beta-amyloid accumulation counts. The cholesterol-fed rabbit AD-model showed arterial narrowing in vessels that feed the same brain regions that demonstrated significant beta-amyloid accumulations.

### REFERENCES

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