# Ultrahigh-resolution MRI Imaging of Intracranial atherosclerosis at 17.6 Tesla: an ex vivo Study with Histological Comparison

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**TARGET AUDIENCE:** Scientists and clinicians who are interested in vessel wall imaging.

**PURPOSE:** Intracranial atherosclerotic disease is a major cause of stroke worldwide and is responsible for 8-10% of strokes in the US. 3D Black blood MRI (BBMRI) has emerged as an effective method to identify pathological features of extracranial vessels [1]. Recently, the 3D BBMRI has been extended to evaluate intracranial vessels, specifically to detect atherosclerosis [2]. However, the characterization of atherosclerotic plaque components in intracranial arteries remains a technical challenge given the small size of these vessels as well as the lack of a standard reference for intracranial vessels. Here we sought to identify and characterize intracranial atherosclerotic plaque components using ultrahigh-resolution MRI *ex vivo* and correlate with histology.

**METHODS:** Human intracranial arterial specimens were obtained from 13 cadavers (7 male; mean age 72.6±13 years) with atherosclerotic plaques reported during the brain autopsy. The specimens included the major intracranial arteries of the circle of wills and were immersion fixed in 10% neutral buffered formalin. Specimens were then transferred to phosphate-buffered saline for 48h before MRI imaging. MR imaging was first performed on a horizontal 11.7 T MR scanner (Bruker Biospin, Billerica, MA, USA) for a fast scan to determine the plaque location using 3D T1W fast low-angle shot (FLASH) and 3D T2W Turbo rapid acquisition with refocused echoes (TurboRARE) sequences. Following imaging of the circle of willies vessel tree, each vessel segment with identified plaque was extracted, inspected and placed in a smaller diameter polyethylene tube for a higher resolution imaging on a vertical 17.6T MR scanner (Bruker Biospin, Billerica, MA, USA) which is equipped with a 15 mm transmit-receive birdcage coil. The temperature was calibrated and controlled at 37°C using a variable temperature system. Forty-nine intracranial arterial plaques (ACA, 4; ICA, 5; MCA, 8; basilar, 16; PCA, 5; and vertebral, 11) from 13 cadavers were imaged. Ultrahigh resolution multi-contrast MRI images were obtained. T1W 2D RARE images were acquired with TR/TE, 160ms/8.1ms; RARE factor, 8; NSA, 8; scan time, 5.28 min. T2W 2D RARE images were acquired with TR/TE, 5000ms/20.6ms; RARE factor,8 ; NSA, 2; scan time, 5.20 min. T1W 2D Fast-FLASH images were acquired using TR/TE, 79ms/3.4ms; NSA, 16; scan time, 5.23min. All images were obtained with the same resolution (in-plane resolution, 47 $\mu m^2$; slice thickness, 1mm) and volume coverage (16 slices, FOV=12x12mm). T1 relaxation times were determined using a variable TR method with TR ranging from 165 to 4000 ms. T2 relaxation times were determined using a CPMG sequence with Tα of 10 ms. Plaque components were characterized based on previous established criteria for carotid MRI [3]. All matched MRI images were correlated to blinded histological analysis (H&E and Movat's Pentachrome). Agreement between MRI and histology was estimated by Cohen's Kappa statistics.

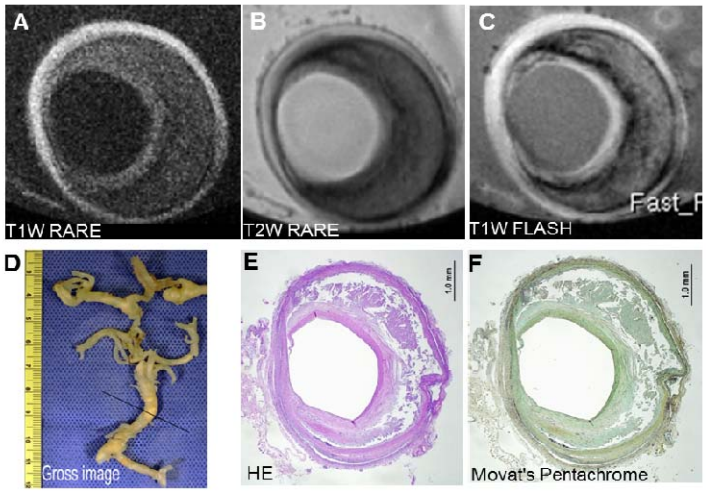


**Figure 1**: A Basilar Artery Plaque with a Lipid-rich Necrotic Core with Calcification. A: T1W RARE; B: T2W RARE; C: T1W FLASH; D: Gross image, the line indicates the plaque location; E: H&E stain; F: Movat's pentochrome stain.

**RESULTS AND DISCUSSION:** 132 histological cross sections were coregistered with MRI images (T1W RARE, T2W RARE and T1W FLASH) and used for the analysis. Representative images are shown in Figure 1. T1W RARE image (A) reveals a large plaque with hyperintense rims along the lumen and the ourterwall. These rims are also hyperintense on T2W RARE (B) and T1W FLASH (C) images, consistent with fibrous cap and media on histology (E and F). The profound hypointense areas interior of the plaque on all MRI images (A, B and C) correspond to the lipid-rich necrotic core on histology (E and F). A dark band underneath the fibrous cap is signified on FLASH image (C), corresponding to the calcification identified by histology. Lipid core and calcification were identified in 62 and 72 sections and no intraplaque hemorrhage was noted by both MRI and histology. The ultrahigh resolution MRI imaging correctly identified 84% of lipid-rich regions with sensitivity and specificity of 95% and 74%, respectively. The overall agreement between MRI and histology in plaque classification was 78% (κ=0.68). The T1 and T2 measurements revealed the variation in relaxation times among plaque components (e.g., lipid core versus fibrous tissue, T1: 1980±394ms versus 1619±250ms, respectively). T1 values determined at 17.6T were anticipated higher than those reported at lower field [4].

**Table 1**. T1 and T2 Relaxation Times of Plaque Components in Intracranial Artery Specimens at 17.6 T

| | **Lipid core** | **Fibrous tissue** | **Media** | **Calcification** |
|---|---|---|---|---|
| T1 (ms) | 1980±394 | 1619±250 | 1348±232 | 1275±100 |
| T2 (ms) | 28.8±8.0 | 29.9±6.3 | 32.6±6.4 | 5.98±3.2 |

**CONCLUSIONS:** Ultrahigh-resolution MRI imaging can accurately characterize intracranial plaque components *ex vivo*, owing to their inherent variation in relaxation times.

**REFERENCES:** [1] Fan Z, et al., JMRI 2010; 31:645-654. [2] Qiao Y, et al., JMRI 2011; 72:627-634**.** [3] Cai JM et.al. Circulation 2002:106:1368-73. [4] Toussaint JF et al., Circulation 1996:94:932-938.
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