Introduction and Purpose:
The disease atherosclerosis causes arterial wall thickening, which can lead to strokes, heart attacks and cardiovascular disease (CVD). Three-fourths of the deaths caused from cardiovascular disease are due to atherosclerosis. The primary source of death and disability to postmenopausal women in the US is owed to cardiovascular disease. Once women reach menopausal ages, CVD dramatically increases throughout life and with age. While some symptoms of menopause have been relieved through hormone replacement therapy (HRT), including improved lipid profiling, there is debate on whether such therapy benefits CVD. In fact, recent studies on HRT have revealed that there may be increases in CVD, breast cancer, thromboembolism, endometrial cancer, systemic lupus erythematosus and ovarian cancer.

The purpose of this larger study is to evaluate the potential of a function food group, flaxseed, as an alternative to HRT. Flaxseed is an edible grain that has shown health beneficial properties, mainly because it is very rich in fiber mucilage, lignans and linolenic acid. In an in vivo study conducted by Sara Campbell, et al., ovariectomized (ovx) female hamsters were fed varying diets including flaxseed and assessed with various imaging and biochemical assays. In this project, the excited heads of the hamsters were imaged at high resolution using a 11.75 T magnet to visualize the cerebral vasculature in hopes of identifying the impact of flaxseed treatment on atherosclerotic plaque regression.

Sample Population:
72 sixth-month-old Golden Syrian hamsters were either sham or ovx, and then divided into six different groups:
1) sham, 2) ovx (control), 3) ovx + 17β-estradiol, 4) ovx+7.5% flaxseed, 5) ovx+15% flaxseed, & 6) ovx+22.5% flaxseed.

The purpose for these groups is to determine whether or not flaxseed will decrease the cause of atherosclerosis lesions, which can be induced with menopause. This project would like to prove that this new diet will be more positive than hormone replacement therapy (HRT).

Why the Hamster?
Although rats are frequently used for experimentation, they seem to be very resistant to atherosclerosis, mainly because they have a high HDL to LDL ratio and due to the fact that they have no gallbladders. In addition, cholesterol synthesis varies notably when compared to humans. The rabbit is a very commonly used animal when studying atherosclerosis, however their lipid profiles do vary greatly compared to humans. Hamsters were chosen not only for their small size, but also because their enzymatic and lipid profiles bear a strong resemblance to humans, making it an appropriate model for studying atherosclerosis. Generally, lipoproteins and metabolic responses to dietary cholesterol changes in hamsters are equivalent in humans, much more so than rodents.

General Procedure:
- Shave the hamster head sample in order to fit it into a 25-mm tube
- Wash sample with phosphate-buffered saline (1xPBS) for at least one day
- Wash sample in a non-protonated fluorinated solution (Fluorinert FC-43, 3M Corp)
- After at least 1-hr wash, the sample is placed into 25-mm tube with the FC-43 solution
- Tube is placed into a 25-mm bircage probe, positioned so that the center of the brain is aligned with the coil center
- The probe is placed within the center of a 11.75-T widebore magnet, tuned and impedance matched to 50 Ω at 500 MHz and shimmed to improve field homogeneity
- After localizer scans are acquired, a 3D gradient recalled echo image was acquired at 50-µm isotropic resolution with an ~11-hr scan. TE = 7.5 ms; TR = 100 ms
- Datasets are transferred to the 3D visualization program AMIRA (Mercury, Inc.) running on an offline computer workstation
- Blood vessels around and within the brain were segmented using AMIRA to visualize the vasculature and quantify diameter changes related to atherosclerotic lesions and potential lesion regression due to treatments (including flaxseed).

Segmentation:
After retrieving MR images from the magnet, AMIRA was used to segment or highlight vascular structures around and within the hamster brain. Using a coronal view, vessels were individually segmented on a slice by slice bases to produce a 3D view of the vasculature. Each vessel segmentation is highlighted with a different color. Below are images in coronal, sagittal and axial views that demonstrate the 3D segmentation achieved for the major vessels.

Conclusion and Future Work:
- The echo time (TE) and repetition time (TR) were chosen to provide a balance between signal-to-noise (SNR) and contrast in the vasculature.
- A 50-µm isotropic resolution was achieved. Higher resolution would be desirable but resulted in excessively large acquisition matrices, low SNR and data storage difficulties.
- In the described fashion, 6 of the hamster samples were scanned at 11.75 T.
- Segments are underway, though at present only one of the datasets (shown above) has been segmented.
- The current segmentation efforts can be quantified to provide volumetric and cross-sectional area measurements of the cerebral vasculature to determine the impact of flaxseed and HRT treatments on lesion regression.
- Further, excised cardiac samples and aorta from the same cohort of ovx hamsters will be available to identify systemic and cardiovascular impacts.

Reference: