1. Title: Correlation between atrophy, white matter disease and infarcts in MRI of the Elderly: The ARIC Study

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4. Rationale:

   The ARIC study defines multiple age related brain MRI findings related to the aging brain and categorizes them according to type, region and size criteria. These findings include those related to anatomy, atrophy, white matter disease, and infarcts. While these findings are in and of themselves well known entities, the question often comes up in the daily reading of routine brain MRI in the elderly is how these findings are related in how do they contribute to the "elderly" brain. The age range of the population (50-70) studied is suitable since the findings of those of a more advanced age may be too "end stage" to separate out potential contributing factors.

   We shall investigate relationships between these MRI findings and their grades. The basic question is as follows: what contributes to the picture of the aged brain and how are these factors related? The basic entities are atrophy, white matter disease, and infarction. Limited epidemiological factors will be incorporated into the study. A correlation between atrophy and white matter disease has been shown with only small population studies (1). Other references postulate progressive atrophy in the aging brain to be both an independent process and a process confounded by other variables, namely white matter disease (2). Finding relationships between atrophy, perivascular spaces, white matter disease, and infarcts would lend to and possibly insight into multifactorial processes that age the brain.

5. Study Questions:

(1) Is there a relationship between degree of atrophy and white matter disease? Does atrophy correlate more with central vs. subcortical white matter disease?

(2) Is there a relationship between atrophy and infarcts? Does atrophy correlate more with central (white matter) vs. cortical infarcts?

   Note that for questions (1) and (2) a distinction could be made on the type of atrophy (ventricular, sulcal, frontal horn/inner table measurement): Does one type of atrophy correlate with white matter disease more than the other? Is atrophy from small vessel disease distinct from infarct related atrophy?
(3) Is there a relationship between white matter disease and infarcts?
(4) How do the epidemiological factors of age, sex, hypertension, diabetes, and race relate to atrophy, white matter disease, and infarcts?
(5) Do the measures of atrophy (ventricular grading, sulcal grading, frontal horn/inner table measurements) correlate with each other? What is the "best" measure of atrophy? (This is largely a question for radiologists who daily assess atrophy in a very subjective way).
(6) Is there a relationship between atrophy, white matter disease, or infarcts and the degree of perivascular spaces? (Hypothesis: prominent perivascular spaces is part of the spectrum of white matter disease).
(7) Is there a posterior circulation white matter disease and infarction and the same involving the anterior circulation? (Hypothesis: they have the same risk factors and therefore should be related).
(8) Is there a relationship between small vessel (< or = 3 mm) and large vessel infarction? (Hypothesis: these are distinct entities).
(9) Is there a relationship between the sidedness (right vs. left) of white matter disease and incidence of infarction on the same side? (Hypothesis: white matter disease is a precursor of small vessel infarction)
(10) Is there a relationship between the incidence of white matter disease and the existence of a hemorrhagic infarction? (Hypothesis: vessels with white matter disease are friable and more likely to result in hemorrhage)

6. Data:

The following variables are needed for this analysis: ventricular size grade, sulcal size grade, white matter disease grade, bifrontal horn/inner table measurement, central sulcus width, white matter disease assessment, perivascular spaces assessment, infarct size and distribution. Epidemiological factors are age, sex, hypertension, diabetes, race, and imaging center.

7. Proposed Timeline:

- Review by publications committee: 5/95
- Analysis of Data: Spring/Summer 1995
- Submittal of manuscript: Winter 1995

Possible Journals: *American Journal of Neuroradiology, Radiology*