1.a. Full Title:
Quality of Optical Coherence Tomography Angiography in EyeDoc study

b. Abbreviated Title (Length 26 characters):
OCT angiography quality

2. Writing Group:
Writing group members:
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I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. xk_____ [please confirm with your initials electronically or in writing]

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3. Timeline:
First set of analysis Apr 2018. First draft Dec 2018

4. Rationale:
Optical coherence tomography angiography (OCTA ) is a novel non-invasive technique for imaging the microvasculature of the retina and choroid. It has the potential to become an
important screening and diagnostic tool for vascular and choroidal diseases as well as a potential marker for small vessel diseases in the brain. This however requires good image quality in the target population. The EyeDOC study aims to study the associations between ocular vascular parameters with cognitive outcomes in older adults enrolled in ARIC. Using quality control data from EyeDOC, we will assess the quality of OCTA in the older adult participants enrolled in the EyeDoc study, and identify demographic and clinical characteristics of participants associated with capturing good quality images. Understanding the generalizability of inferences and feasibility of using OCTA in a community setting will provide great insights on the value of OCTA as a screening tool for cognitive risk in the future.

5. **Main Hypothesis/Study Questions:**
Using quality control data from EyeDOC, we will 1) assess the quality of OCTA images in the older adult participants enrolled in the EyeDoc study, 2) identify demographic and clinical characteristics of participants associated with obtaining high quality images, and 3) assess the reproducibility of the eye structural parameters measured from OCTA images.

6. **Design and analysis (study design, inclusion/exclusion, outcome and other variables of interest with specific reference to the time of their collection, summary of data analysis, and any anticipated methodologic limitations or challenges if present).**
OCTA images are obtained for EyeDOC participants at time of enrollment. This quality assessment study uses the cross-sectional OCTA data and vision function data from EyeDOC, as well as relevant demographic and clinical assessment data from the ARIC V6 visit. The outcome variable will be high quality of an OCTA image (yes/no), presence of image artifacts (e.g. movement), OCTA microvascular parameters (e.g. vessel density) and exposure variables include age, sex, race, study center, vision function evaluation results, ocular history variables, and OCTA image type. Descriptive analysis (means and proportions) of image quality (overall and by type of artifact) by image type will be conducted. Logistic regression with GEE will be used to regress high image quality on participant characteristics and vision/eye variables to assess predictors of poor image capture. Bland-Altman analysis will be conducted to assess the reproducibility of each quantitative OCTA microvascular parameter and to estimate the level of bias from grading. Components of variability will also be assessed including between image grader variability, between image variability and between eye variability.

7.a. Will the data be used for non-CVD analysis in this manuscript? __X__ Yes  ____ No

b. If Yes, is the author aware that the file ICTDER03 must be used to exclude persons with a value RES_OTH = “CVD Research” for non-DNA analysis, and for DNA analysis RES_DNA = “CVD Research” would be used? __x__ Yes  ____ No
(This file ICTDER has been distributed to ARIC PIs, and contains the responses to consent updates related to stored sample use for research.)

8.a. Will the DNA data be used in this manuscript? ____ Yes  __X__ No

8.b. If yes, is the author aware that either DNA data distributed by the Coordinating Center must be used, or the file ICTDER03 must be used to exclude those with value RES_DNA = “No use/storage DNA”? ____ Yes  ____ No
9. The lead author of this manuscript proposal has reviewed the list of existing ARIC Study manuscript proposals and has found no overlap between this proposal and previously approved manuscript proposals either published or still in active status. ARIC Investigators have access to the publications lists under the Study Members Area of the web site at: http://www.csc.unc.edu/ARIC/search.php

  _X___ Yes   _______ No

10. What are the most related manuscript proposals in ARIC (authors are encouraged to contact lead authors of these proposals for comments on the new proposal or collaboration)?
This is a new area of study for the ARIC. Though there are retinal images from V3 and V5, OCT has not previously been used. The closest proposals would be those using the retinal photographs. Ron Klein and Jennifer Deal are both authors on a number of those projects.

11.a. Is this manuscript proposal associated with any ARIC ancillary studies or use any ancillary study data? _X_ Yes   _____ No

11.b. If yes, is the proposal
  _X_  A. primarily the result of an ancillary study (list number* EyeDOC____)
  ___  B. primarily based on ARIC data with ancillary data playing a minor role (usually control variables; list number(s)* __________ __________ __________)

*ancillary studies are listed by number at http://www.csc.unc.edu/aric/forms/

12a. Manuscript preparation is expected to be completed in one to three years. If a manuscript is not submitted for ARIC review at the end of the 3-years from the date of the approval, the manuscript proposal will expire.

12b. The NIH instituted a Public Access Policy in April, 2008 which ensures that the public has access to the published results of NIH funded research. It is your responsibility to upload manuscripts to PubMed Central whenever the journal does not and be in compliance with this policy. Four files about the public access policy from http://publicaccess.nih.gov/ are posted in http://www.csc.unc.edu/aric/index.php, under Publications, Policies & Forms. http://publicaccess.nih.gov/submit_process_journals.htm shows you which journals automatically upload articles to PubMed central.