

Dear Bee Foundation,

I wanted to report on the progress of your incredibly generous grant supporting our research. We have made progress on several fronts.

Original aims:

1. Determine the best way to quantify aneurysm wall enhancement in HR-VWI.
2. Validate 7T vessel wall imaging with 3T.
3. Quantify aneurysm wall enhancement in unruptured intracranial aneurysms with HR-VWI.
4. Determine characteristics of aneurysm instability.

We have determined the best way to measure signal intensity as a surrogate marker of aneurysm inflammation. Prior to our publication in the Journal of Neurosurgery: "Roq JA, Zanaty M, Osorno-Cruz C, et al. *Objective quantification of contrast enhancement of unruptured intracranial aneurysms: a high-resolution vessel wall imaging validation study.* J Neurosurg. 2020;1-8"; no study has compared objectively the best way to quantify signal intensity. Approximately 1000 cases of aneurysms enhancing after the administration of contrast have been published using different methodology to quantify contrast enhancement or signal intensity (SI). These manuscripts reported subjective definition of aneurysm enhancement and objective measurements with regions of interest sampling different areas of the aneurysmal wall. We compared all the reported measurements and methodologies and determined that the ratio of SI normalized to the pituitary stalk is the most accurate quantification of SI (FIG 1 & 2). *In this way we have addressed Aim 1.* Nevertheless, all these approaches to quantify SI are manual and time consuming. We are still working on developing a semiautomatic approach to determine SI.

FIG 1. Postcontrast T1-weighted sagittal projection of a basilar tip aneurysm showing the ROI of the aneurysm wall (yellow), sampling of the genu of the corpus callosum (red), and sampling of the pituitary stalk (black) for normalization. In this case, the maximal CRstalk would be calculated as follows: $446/700 = 0.63$. AR = area; AV = average.

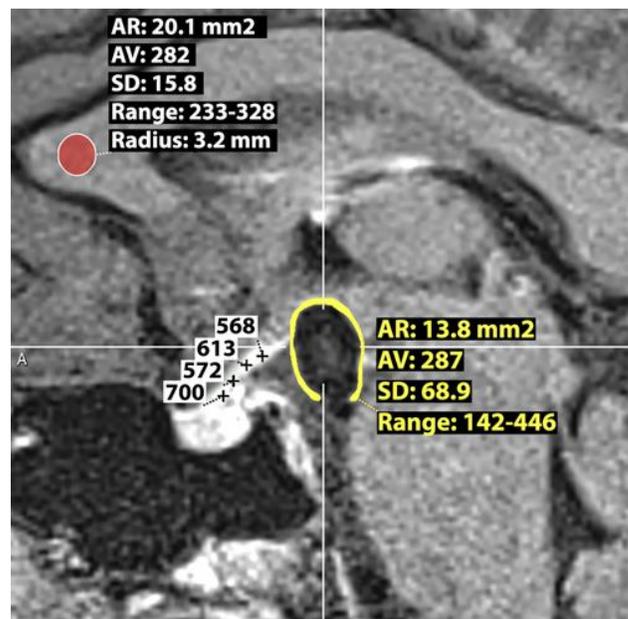


FIG 2. ROC curves for AER, CRstalk, and AEI using maximal (Max) SI values (A) and mean SI values (B).

Normalization with the pituitary stalk was developed in 7T imaging and now has been applied in multiple subjects with 3T imaging. *Aim 2.*

We have adopted a standard method or normalization and quantification of SI. As a result of this experience we were able to analyze 96 unruptured intracranial aneurysms and determine that the use of aspirin is related to decreased SI: Roa JA, Zanaty M, Ishii D, et al. Decreased contrast enhancement on high-resolution vessel wall imaging of unruptured intracranial aneurysms in patients taking aspirin. J Neurosurg. 2020;1 - 7. *Aim 3.*

As part of our work using 7T High-resolution imaging, we have determined that the parent vessel of unruptured intracranial aneurysms also exhibits increased enhancement. This is an important step in understanding aneurysm biology, as increased SI suggests localized inflammatory/vasculopathic processes in the wall of the parent artery that may lead to aneurysm formation and growth. This work has been published this week: Samaniego EA, Roa JA, Zhang H, et al. Increased contrast enhancement of the parent vessel of unruptured intracranial aneurysms in 7T MR imaging. Journal of NeuroInterventional Surgery Published Online First: 18 May 2020. doi: 10.1136/neurintsurg-2020-015915.

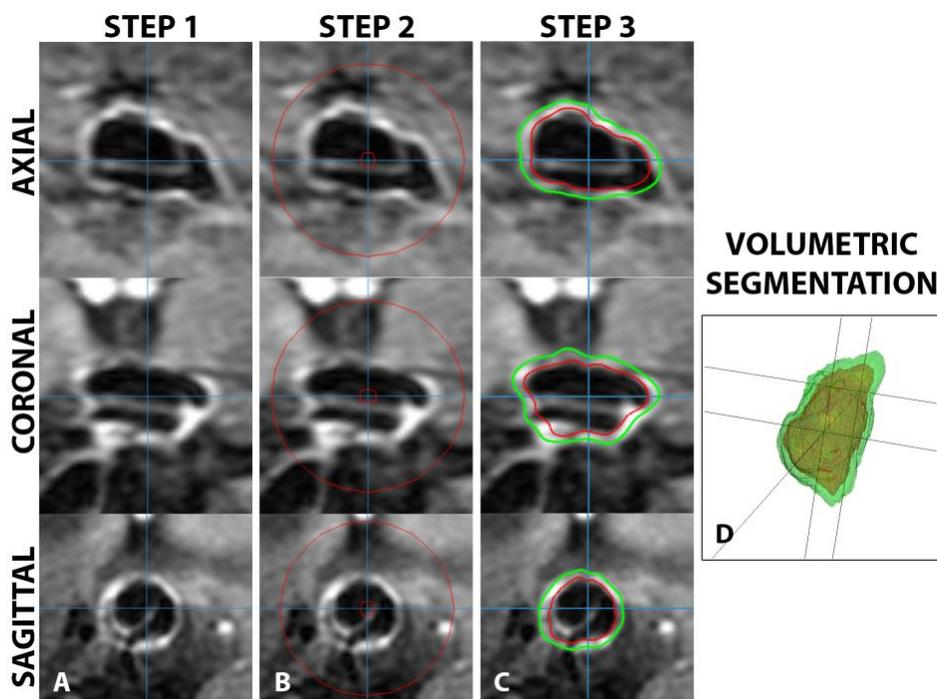
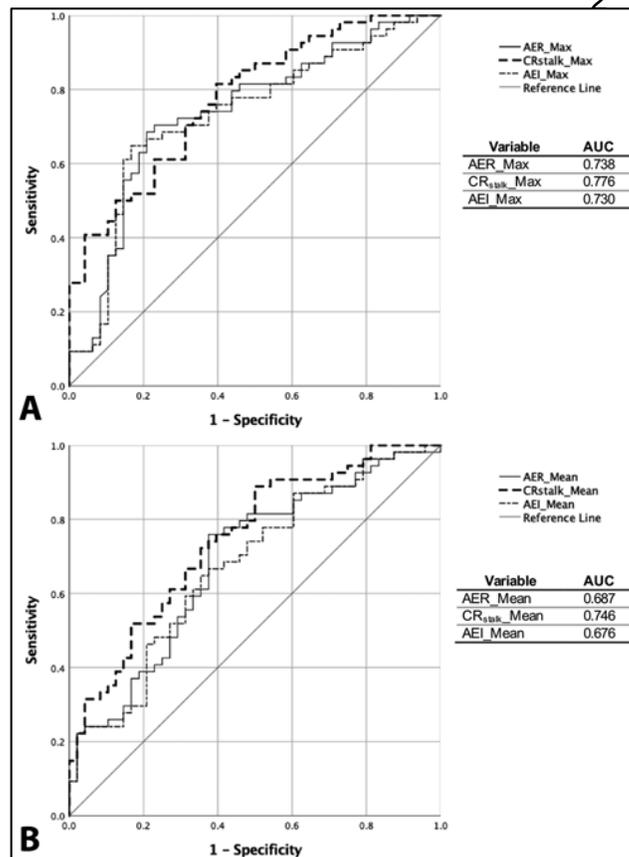


FIG 3.. Manual segmentation technique using PACS Carestream Vue of an ACOM aneurysm. The aneurysm is identified in all the TOF sequences, and T1 pre- and post-contrast images are co-registered. ROIs of the aneurysm’s wall and parent vessel are then drawn on axial (A), coronal (B) and sagittal (C) views of pre- and post-contrast T1-weighted images. Note the 2 different ROIs (3-mm in red stripes, 5-mm in white) drawn over the parent vessel.

Current projects:

We are refining the methodology and coding of a software that will allow semi-automated quantification of SI. This is a pivotal step in using SI as a surrogate biomarker of aneurysm instability and risk of rupture. Furthermore, I am awaiting the score of an R01 grant submitted last cycle. This grant is aimed towards establishing a mechanistic relationship between aneurysm enhancement and inflammation.

I am glad to mention that although the COVID-19 pandemic has limited the number of subjects that we can recruit for imaging with our high-resolution 7T and 3T MRIs, our work has not been completely disrupted. We have been able to analyze previously acquired data and work on coding algorithms for morphological aneurysm analysis.

We thank you for your support and look forward to working with you in the future.

Sincerely,

A handwritten signature in blue ink, appearing to read "Edgar A Samaniego". The signature is fluid and cursive, with a long, sweeping underline that extends to the left.

Edgar A Samaniego MD, MS, FSVIN

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