ADNI Biostatistics conference call, 6 May 2008

Present on call: Laurel Beckett, Danielle Harvey, Hao Zhang, David Shera, Bill Billings, John Kornak.

Laurel reported on the Alzheimer's Association roundtable focused on improved measures that met last week in DC. One theme was the need for improved measures especially in the earlier stages of MCI and transition from normal to MCI. This is particularly important for planning ADNI II. The second concern was whether we could make better use of what we have in ADNI by more subtle examination of the tests and their behavior. For example, Jeremy Hobart presented results of some Rasch models showing which items are most sensitive to differences at the good-performance end of the scale. These issues are important to our work and whether we can get a better way to detect correlation between imaging or biomarker summaries of change, and clinical/ functional/ cognitive/ behavioral change. We are looking at two ideas: better global measures along the lines of Jeremy's work and Z scores, and latent variable analysis. The mixed models/ latent variable approaches are not working well yet as sample sizes are probably too small and too much variation, but the Z score based on ADAS-COG, CDR sum of boxes, and MMSE (using baseline normal mean and SD) did have improved performance compared to individual tests.

Danielle sat in on executive call last week. One theme was follow-up from the meeting in Chicago, and each core spoke on what needed to be done. Industry would like to see more information on 1.5T vs 3T data. We didn't have enough 3T data to present last time so we asked people to try to complete more of that for the July presentation at ICAD. Danielle has provided the labs with a list of participants with both 1.5 and 3T images processed and online at LONI. The other big issue was that they wanted to be able to make a more accurate comparison across labs within modality (e.g. MRI, PET) and across modalities. Danielle has also provided a list of participants with summaries; priority is on MRI and AD with both baseline and month 12. Our goal is to get, as much as possible, all labs to provide summary data on identical subset of people. Danielle also included the cross validation assignments in case the labs doing voxel based want to get started on that. Recall there are two ways to do it: 40% training, 60% test; and leave-10%-out.

There is no MRI call this week because of a meeting that most of them will attend, but there is a PET call tomorrow. Danielle will talk to them and answer questions; John will try to get on as well. The labs have expressed interest in cross validation and they feel more comfortable with the test/ training set approach, but Laurel pointed out that the 10-fold approach will allow more powerful use of the small amount of data so far. However, that may be too computationally intensive for the short time period. Danielle and John will bring this topic up and find out what the labs are thinking and give some advice and help.

David suggested keeping a list of what analyses people are doing so we could avoid duplication. He has put together a group at Merck and they would like to do some analyses. They also need to focus on what the company is most interested in. Danielle and Laurel know a fair amount of what's going on and we could put a list together. We could update it quarterly. The ADCS folks at UC San Diego are also working on some projects, including looking at how regression models might help to reduce variance and

increase power. David is looking at neurocog scores on internal data from their studies and would like to match those analyses in ADNI data.

We have circulated questions about preferred modality and times for a second training session to the people who expressed interest last time, and Pat Cole is circulating to others in Industry group. So far the preference is for another telephone or internet training, and it would be in August or September (after ICAD and JSM). We will keep people posted on this.

John Kornak shares the concern about data-driven analyses followed by inferences that are biased, and would like to see the cross validation used. So far Eric Reiman is the only one who has a data-driven set of results; the others have used a priori regions.

Next call is 20 May, same time!