ADNI Biostatistics Conference Call
1 July 2008

Present on call: Danielle Harvey, Hao Zhang, Fred Immermann, David Shera, Mike Weiner

Danielle updated everyone on the status of analyses of ADNI data. We just finished a set of analyses for Neil Buckholtz focusing on cognitive change and change on some of the imaging measures in the Normals. Mike Donohue and Anthony Gamst also generated a summary report for Neil that included change on the cognitive measures across the diagnostic groups. The focus now is on the analyses for ICAD. We have overlap of 198 subjects across the three PET labs and three of the MRI processing labs. The PET vs 1.5T MRI comparison will be restricted to the measurements generated by these six labs for the 198 subjects. The three PET labs all provided change data on 265 subjects, so we will be able to use more subjects to compare across the PET labs. Danielle is still identifying the maximal overlap for comparing across all of the MRI labs on the 1.5T data. Nick Fox, Norbert Schuff, and Gene Alexander all provided data for the 1.5T vs 3T comparison, although the numbers are still small so results will be very preliminary for this comparison. The numbers are small here because there are only about 200 subjects in the 3T arm and not all of them have completed the m12 visit.

Hao is busy generating reports based on the data submitted by the labs (focusing on the individuals that are shared in common for the comparisons of interest). We will start communicating with the labs directly about the results next week to make sure what we are finding is in line with what they would expect and that there are no errors in the data. Later next week, we anticipate starting the analyses that will do the formal comparisons across the labs. Laurel wrote up a document on our proposed strategy for these comparisons, which has been circulated to the Biostat Core. If anybody has feedback, please let us know. As we get results, we will share them with the labs, Mike Weiner, and the Biostat Core.

Fred mentioned that one thing of particular interest to industry is subgroup analyses. Elan and Wyeth recently released results of a Phase II trial in which the treatment was more effective in e4-non carriers, so industry is very interested in looking at differences in trajectories between carriers and non-carriers as well as other stratification variables. Danielle mentioned that right now, we have not looked too much at that (although we did some for the analyses of the Normals); we have focused more on descriptives of change in the different diagnostic groups, but there are plans to eventually incorporate other information including e4-status.

There was a question about when all of the year 1 data would be available. Mike confirmed that the hope is to have all year 1 data processed by each of the labs by the end of the calendar year. However, he also mentioned that some of the labs have not been processing as many images as others, so he's not certain that we will have full-processing by all of the labs. He said that it might help if industry starts putting some pressure on the labs also, since the labs did agree to analyze the year 1 data. The original plan was to also have money left over for a few labs to process all of the available data, but money is running out, so it is unlikely that the longer follow-up (years 2 and 3) images will be analyzed. Industry should be aware of that, so they don't expect complete processing of all ADNI data.

Mike also mentioned that based on comparisons done within his lab between the more time intensive landmarking of the hippocampus and the freely available software package FreeSurfer, they have decided to switch over to FreeSurfer (unless someone gives them a good reason to continue doing the landmarking approach). This will serve as a replication of the

results generated by the Dale lab down at UCSD as well as providing data on images that the Dale lab is not processing (in particular for the 1.5T vs 3T comparison).

Mike also mentioned analyses being done by Anthony Gamst and Mike Donohue at ADCS on the potential of baseline biomarkers to reduce required sample sizes for clinical trials. Since the primary outcome for most trials is cognitive change (usually using ADAS-Cog), which requires a very large number of subjects to detect change, we might be able to reduce the variance by incorporating a baseline biomarker in the model. Anthony and Mike are running a series of analyses using imaging and fluid biomarker data as potential predictors of cognitive change and seeing how the predictor variable might impact sample size calculations.

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