Standardization of Imaging in the ADC Program

Steering Committee

Duane Beekly (UW/NACC)
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Emily Rogalski (Northwestern)
Andy Saykin (Indiana)

Nina Silverberg (NIA)
Cerise Elliott (NIA)
John Hsiao (NIA)

FINAL AGENDA

Imaging Meeting

FRIDAY, APRIL 20, 2018 6 – 9PM SANTA BARBARA ROOM C, LOBBY LEVEL

NOTE: Light refreshments will be served.

6:00 pm	**Overview — Bill Jagust, MD** UNIVERSITY OF CALIFORNIA, BERKELEY • Overall goals **Accomplishments to date with NACC data — Charlie DeCarli, MD** DIRECTOR, UNIVERSITY OF CALIFORNIA, SAN DIEGO
6:20	**Resources — Nina Silverberg, PhD** DIRECTOR, ADC PROGRAM, NIA/NIH • Funding • Optional participation
6:50	**Proposal for standardization** • Use of ADNI protocols as imaging standards with review of protocols by Steering Committee • Feedback/challenges to implementation
7:30	**Steering Committee responsibilities: Protocol management, data analysis, QC etc** • Data uploads and curation – Duane Beekly DIRECTOR OF COMPUTING, NACC • List of tasks: divided as necessary/required and optional/desirable
8:15	**Future projects, optimal growth of the program** • Scientific questions • Harmonization of legacy data • Advanced informatics and data analysis
9:00	**Adjourn**

Imaging in the ADC Program: Why Standardize?

ADCs should be a major resource to Alzheimer's Research

Standardization will allow detection of smaller effects in smaller subgroups

Standardization will facilitate collaboration between centers

Standardization will improve imaging capabilities across the ADC network

What is the Role of Imaging in the ADCs?

Imaging has moved from an ancillary measurement to a core participant characteristic

Proposed new research framework stresses biomarker/imaging characterization

Unique opportunity for ADCs to validate research and clinical criteria

Imaging is central to describing the aging and dementia phenotype

Imaging is crucial for modern clinical trials

What Do ADCs Contribute?

ADCs reflect the “state of the art” in clinical evaluation

ADCs recruit a clinically diverse sample of participants

- **Vascular and other comorbidities, non-AD dementias, range of severity**

ADCs have rich affiliated data on participants

- **Postmortem (autopsy) data, cognitive measures, -omics, sleep, novel biomarkers, mobile technologies etc**

Multiple affiliated databases (genetics/UDS)

Current Status
Imaging of ADC Participants

26 Centers (93%) collect MRI

24 Centers (86%) collect amyloid PET

21 Centers (75%) collect tau PET

7 Centers (25%) collect FDG PET

In most cases, funding for these studies is at least partly non-ADC and only part of the clinical cohort is examined

Standardization of acquisitions between and even *within* centers is not the rule

Image Uploads and Analyses are Already Happening

Current NACC data:

6582 Scan Sessions
4616 UDS Subjects
7706 T1 scans
2589 T2 scans
4917 FLAIR scans
4935 DTI scans
1629 DWI scans

Data analyses by Charlie DeCarli

Important Considerations

- **Standardization should not stifle innovation**
  - Centers should pursue their scientific interests, including novel approaches to imaging
- **Centers differ in technical capacity**
  - Standardization needs to include support for training/advice and technical resources
- **Some approaches to standardization are resource intensive, others require relatively little**

The Process So Far

Overall goal: Define what is needed to do the best possible science across all the ADCs using imaging modalities (MRI, amyloid PET, tau PET)

Steering Committee has met in person and via phone conference on multiple occasions

We soon recognized that there were things we could do in the short term to begin the process, and long term goals that will take more time and resources

Short term (necessary)

Survey centers to define how much variability at present (MR/PET)

Examine existing imaging protocols to define a “gold standard” that most, if not all, sites can adhere to

Propose those standards to ADCs and determine what is necessary to implement

Long term (optimal)

Broaden the scope of images acquired

Maximize image QC and analysis

Develop an infrastructure across the ADCs for decision making

MRI Recommendations (29 ADCs)

Sequence	"Combinability" (1 low, 10 high)	Comments	Recommendation
3D T1	9	All sites acquire, most ~1mm^3	Accept 3D ~1mm^3, MPRAGE or IR-SPGR
FLAIR	5	Almost all acquire, about half 2D vs 3D, variable resolution and orientation	Accept all, analyze 2D and 3D separately
GRE/SWI	5	Most acquire, 2/3 2D GRE, variable resolution	Accept all, analyze 2D and 3D separately
DTI	3	Most acquire but highly variable direction #, mix of single and multi shell	Accept but limit analyses to simple measures (no TBSS etc)
3D T2	9	Only 8 sites acquire	Do Not Accept
fMRI	3	Highly variable TR, duration	Do Not Accept
ASL	2	Most 2D, variable spatial resolution	Do Not Accept

All recommendations are for 3T, GE/Siemens/Philips instruments

PET Recommendations (31 ADCs)

Tracer	# of Centers	Comments	Recommendation
PIB	12	Most centers collect similar data	Accept 40-60 or 50-70 min averaged frames
Florbetapir	14	Most centers collect similar data	Accept 50-70 or 50-60 min averaged frames
Florbetaben	5	Most centers collect similar data	Accept 90-100 min averaged frames
Flortaucipir	15	Most centers collect similar data	Accept 80-100 min averaged frames
MK6240	5	No consensus on timing	Do not accept or accept all as development?
Others	2	GTP1/PI2620	Do not accept

Survey did not examine instrument (PET vs PET/CT vs PET/MR), resolution

Q1: Regarding MRI

Can your center acquire and upload scans that meet the proposed standards?

a. We are interested and could do it tomorrow

b. We could initiate this with minimal resources

c. We would need substantial resources

d. We are not likely to be capable or interested

Q2: Regarding PET

Can your center acquire and upload scans that meet the proposed standards?

a. We are interested and could do it tomorrow
b. We could initiate this with minimal resources
c. We would need substantial resources
d. We are not likely to be capable or interested

Steering Committee Responsibilities: Short Term

- Review site protocols for conformation with recommendations
- Advise on acquisition and implementation of standard protocols
- Help sites with uploading data
- Annotation\labeling of the data as part of curation
- Develop new policies, new protocols for sequences tracers

Steering Committee Responsibilities: Long Term

- Establish infrastructure for steering committee decision making and activites
- Prescribe MR sequences/PET acquisition with support from NIH
- Every scan undergoes QC, feedback to sites on per-scan basis – QC function
- Develop new standards for additional new sequences and new tracers DTI, etc
- Standard centralized data analysis to produce fully available quantitative metrics for all (some?) modalities
- Advice to sites in downloading and analyzing data
- Assistance to sites in utilizing analyzed data
- Analytic methods to better harmonize legacy data
- Advanced informatics for database management/queries
- Standard sequences or scans for all participants
- Add imaging metrics to UDS and feedback to centers: amyloid status/hippocampal volume
- Feedback data use to Centers

Q3: Other goals

What other goals or projects do you think the steering committee should adopt over the short or long term?