

Standardization of Imaging in the ADC Program

Steering Committee

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Imaging in the ADC Program: Why Standardize?

ADCs should be a major resource to Alzheimer's Research and imaging is a crucial component

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

Extensive (mostly MR) data are available on the NACC website and have been analyzed by multiple laboratories

Important Considerations

Standardization should not stifle innovation

Centers should pursue their scientific interests, including novel approaches to imaging

Many Centers have legacy data collected under R01 or other non-ADC funding

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 Goals

Review current protocols for images acquired by ADCs and propose standards for all uploaded data that will also guide ADCs as they develop their imaging programs

Work with interested centers to assist in protocol review, implementation of acquisition, and assistance with uploads

Improve annotation/labeling of NACC imaging data as image uploads become more complex

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

Long Term Goals

Establish an infrastructure for decision making

Define scientific objectives to guide the allocation of new (but limited) resources

Implement more “hands on” QC of images

Develop more ambitious goals for data standardization – new sequences, new PET tracers

Explore centralized analyses of all images with standard readouts and feedback of results to ADCs

Provide advice to ADCs on use of images and reduced data

Develop approaches to harmonize legacy data

Advanced informatics for database queries