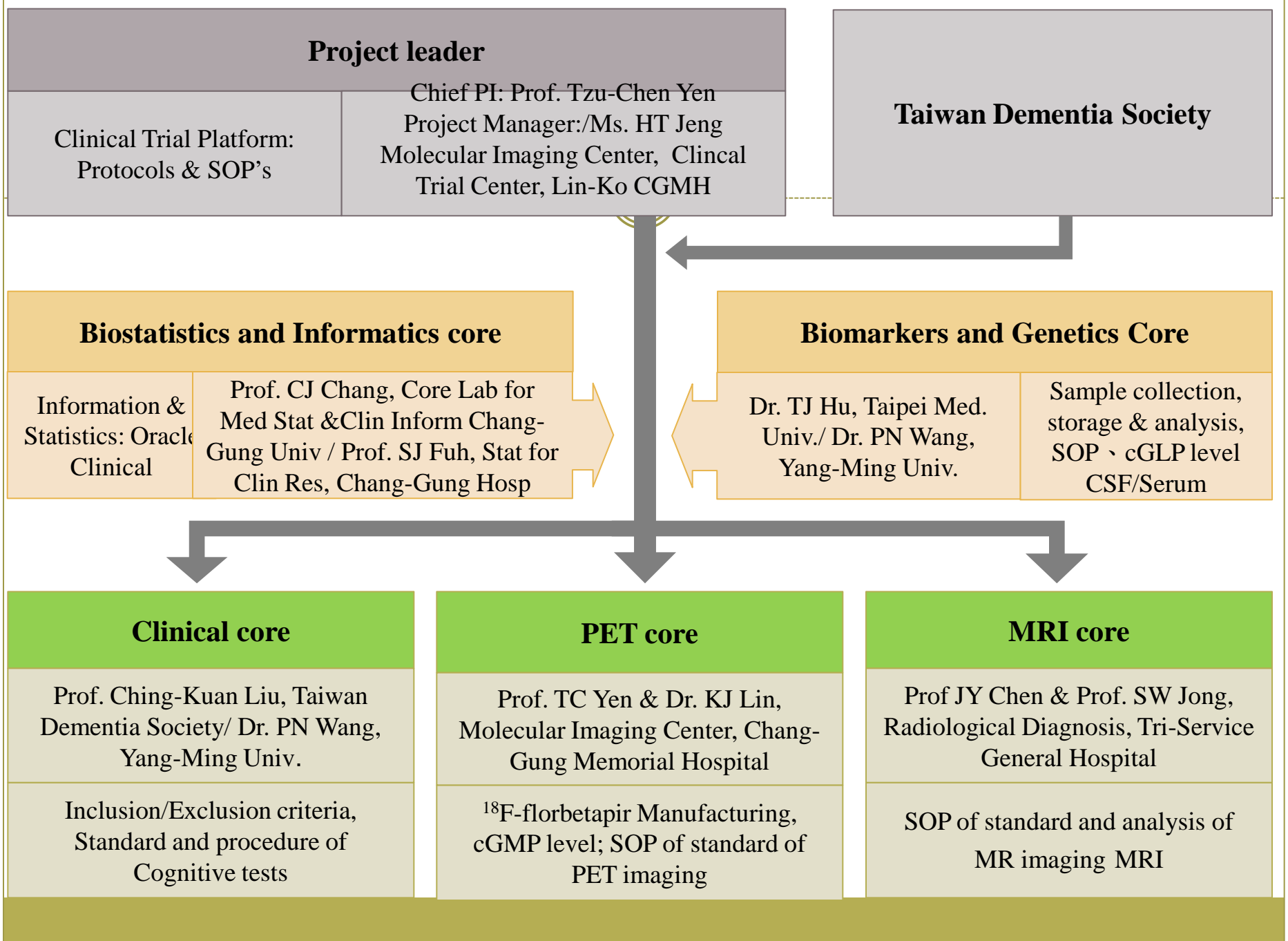


# Taiwan ADNI

## Progress report

**Ching-Kuan Liu, MD,PhD**  
**Kaohsiung Medical University & Hospital**  
**Kaohsiung, Taiwan**



**Project leader**

Clinical Trial Platform:  
Protocols & SOP's

Chief PI: Prof. Tzu-Chen Yen  
Project Manager: /Ms. HT Jeng  
Molecular Imaging Center, Clinical Trial Center, Lin-Ko CGMH

**Taiwan Dementia Society**

**Biostatistics and Informatics core**

Information & Statistics: Oracle Clinical

Prof. CJ Chang, Core Lab for Med Stat & Clin Inform Chang-Gung Univ / Prof. SJ Fuh, Stat for Clin Res, Chang-Gung Hosp

**Biomarkers and Genetics Core**

Dr. TJ Hu, Taipei Med. Univ./ Dr. PN Wang, Yang-Ming Univ.

Sample collection, storage & analysis, SOP, cGLP level CSF/Serum

**Clinical core**

Prof. Ching-Kuan Liu, Taiwan Dementia Society/ Dr. PN Wang, Yang-Ming Univ.

Inclusion/Exclusion criteria, Standard and procedure of Cognitive tests

**PET core**

Prof. TC Yen & Dr. KJ Lin, Molecular Imaging Center, Chang-Gung Memorial Hospital

<sup>18</sup>F-florbetapir Manufacturing, cGMP level; SOP of standard of PET imaging

**MRI core**

Prof JY Chen & Prof. SW Jong, Radiological Diagnosis, Tri-Service General Hospital

SOP of standard and analysis of MR imaging MRI


# Taiwan-ADNI

- Start from north Taiwan
- 6 medical centers
- 200 subjects
- Inclusion and exclusion criteria follow the rules of NA-ADNI

Normal	Early MCI	Late MCI	AD
50	50	50	50



# Diagnosis of NL, MCI and AD



	NL	EMCI	LMCI	AD
Memory complaints	—	+	+	+
MMSE	24-30	24-30	24-30	20-26
CDR	0	M $\geq$ 0.5 Others 0	M $\geq$ 0.5	0.5-1
Logic memory				
edu $\geq$ 16	$\geq$ 9	9-11	$\leq$ 8	$\leq$ 8
edu 6-15	$\geq$ 5	5-9	$\leq$ 4	$\leq$ 4

- **Age between 55-90**
- **Only subjects with  $\geq$ 6 years education will be included**

# T-ADNI

## 3-year longitudinal study



**Recruitment**

**Annual  
evaluation**

**Annual  
evaluation**

**End  
evaluation**

• 2011 Aug

• 2012

• 2013

• 2014

**Neuropsychological Tests**

**Biomarker**

Blood: Apo E polymorphism, amyloid, tau

CSF

**Imaging studies**

MRI

PET: FDG-PET, F18-AV45-PET

Visit name	Screen	Baseline	Month 6	Annual	End
Visit Type	In-Clinic	In-Clinic	In-Clinic	In-Clinic	LP
Explain study	X				
Obtain consent	X				
Demographic data	X				
Medical history	X				
Vital signs	X	X	X	X	
Screening Labs	X				
ApoE genotyping		X			
Collect and process biomarkers		X	X	X	
Concomitant Medications	X	X	X	X	
Neuropsychological tests	X	X	X	X	
Diagnostic Summary	X	X	X	X	
3T MRI Imaging (100%)		X		X	
FDG-PET Imaging (100%)		X		X	
F18-AV45 Amyloid PET Imaging (100%)		X		X	
Lumbar Puncture (LP) (optional)		X			X

# Neuropsychological tests

MMSE	Chinese Version Verbal Learning Test
CDR	Geriatric Depression Scale
WMS III Logical Memory story A recall	Clock drawing Test
Everyday Cognition (ECog)	Neuropsychiatric Inventory Q
Montreal Cognitive Assessment (MoCA)	ADAS-Cog 11 (with Delayed Word Recall)
Category Fluency (Animals)	Activities of Daily Living (FAQ)
Trails A & B	Chinese version Verbal Learning Test
Boston Naming Test (30-item)	

# Qualification Of Neuropsychological Assessment



- Workshop: May and August 2011
- Procedural manual of neuropsychological assessment
- Pre-study training and practice
- Pre-study qualification test



# QC controls of Biofluids markers



- Setting of collection SOP
  - Barcode, collection tube, temperature requirement, sample tracking, shipping, storage
- Regulation of equipment and personnel
- Alarm system-SOP
- Barcode system
- GLP certification
- Test run-July, 2011

# TW-ADNI MRI core - Aims



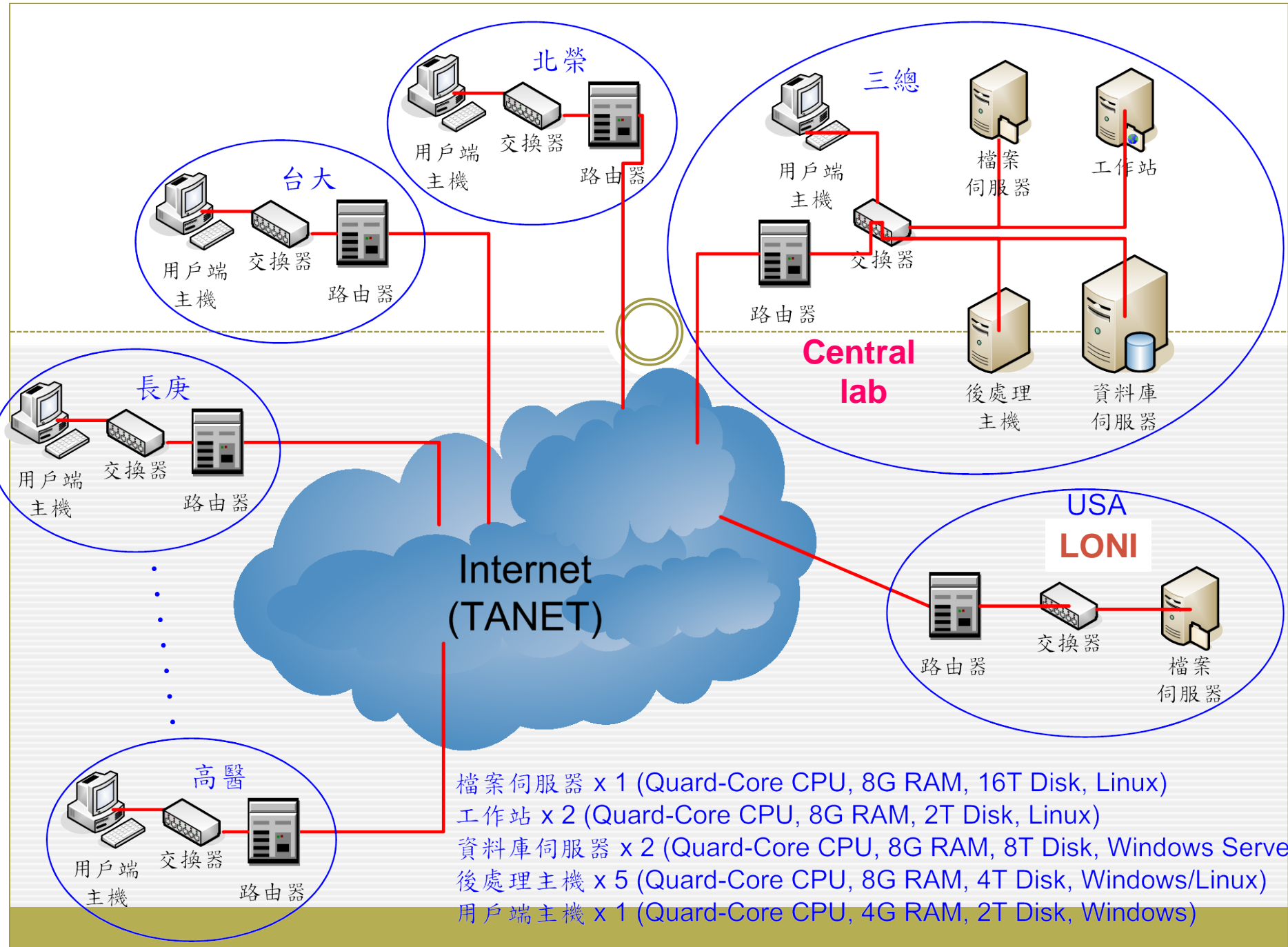
More than a neuroimaging repository for AD

- ◆ Establish *standard protocol* for MRI acquisition
- ◆ Develop and implement *methods for quality control* of MR images
- ◆ Improve the *post-processing methods*
- ◆ Investigate *functional connectivity of brain*

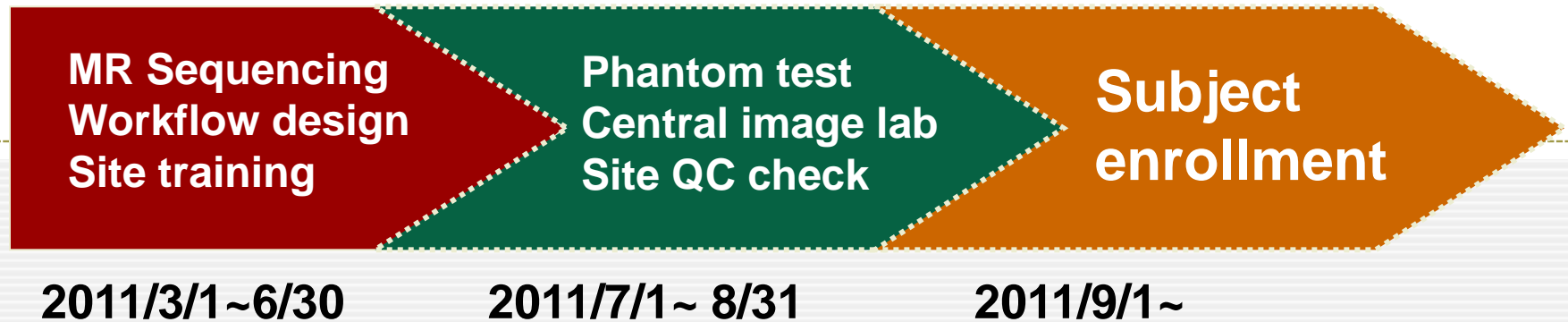
# MRI core sequence and substudies



- 3D T1 volume
  - Cortical surface reconstruction (self-organization map, SOM)
  - Voxel-based morphometry (VBM)
  - Cortical thickness (cortex reconstruction)
- Diffusion tensor imaging (DTI)
  - FA/ADC VBM, Tractography
  - Tract-specific analysis (DTI Studio)
  - Tract-based spatial statistics (TBSS)(FSL)
- Resting state functional connectivity (RSFC)
  - seed-based correlation analysis (SCA)
  - independent component analysis (ICA) (MELODIC)
- Magnetic resonance spectroscopy (MRS)
  - Single-voxel MRS (LCModel)
- Susceptibility Weighted Imaging (SWI)



# MRI Core Timeline



Central lab sign in



ADNI phantom



QC qualification

# PET core protocol -Two scans



- All scans will be acquired in pairs of [18F]FDG and [18F]AV45 scans,
- performed on separate days, between **1 day and 2 weeks apart**, with either scan performed first.

# PET Core Timeline



Site qualification

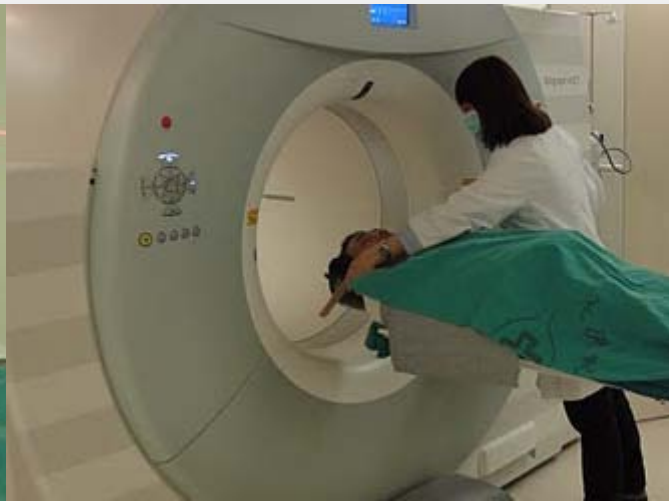
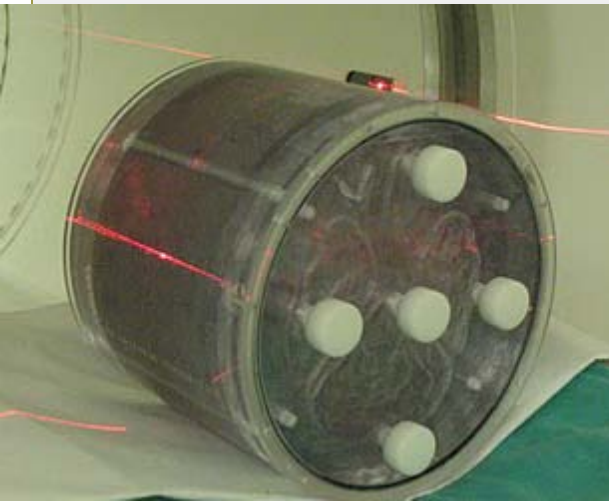
Data acquisition

Data flow and QC

2011/3/1~5/1

2011/6/1~ annual

2011/6/1~





# QC study workflow

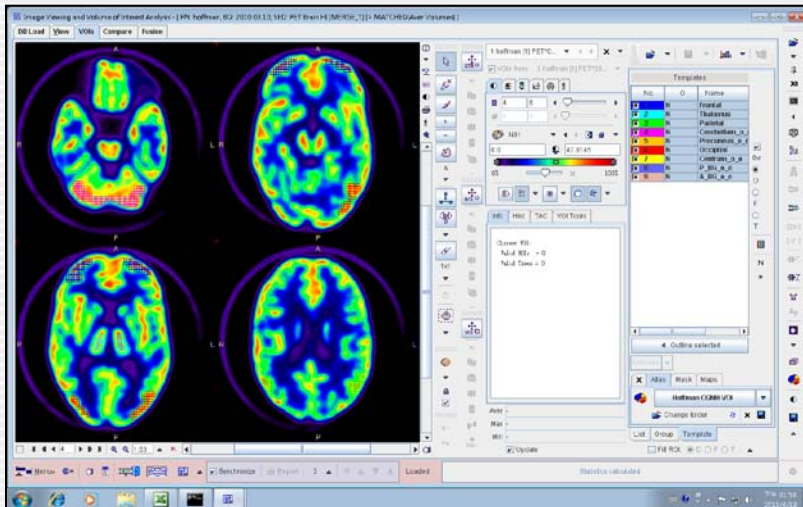


**Study Preparation**



**Phantom Filling**

Dose: 1~2 mCi



**Image analysis**



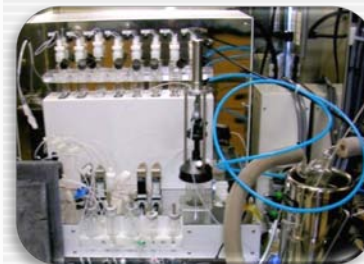
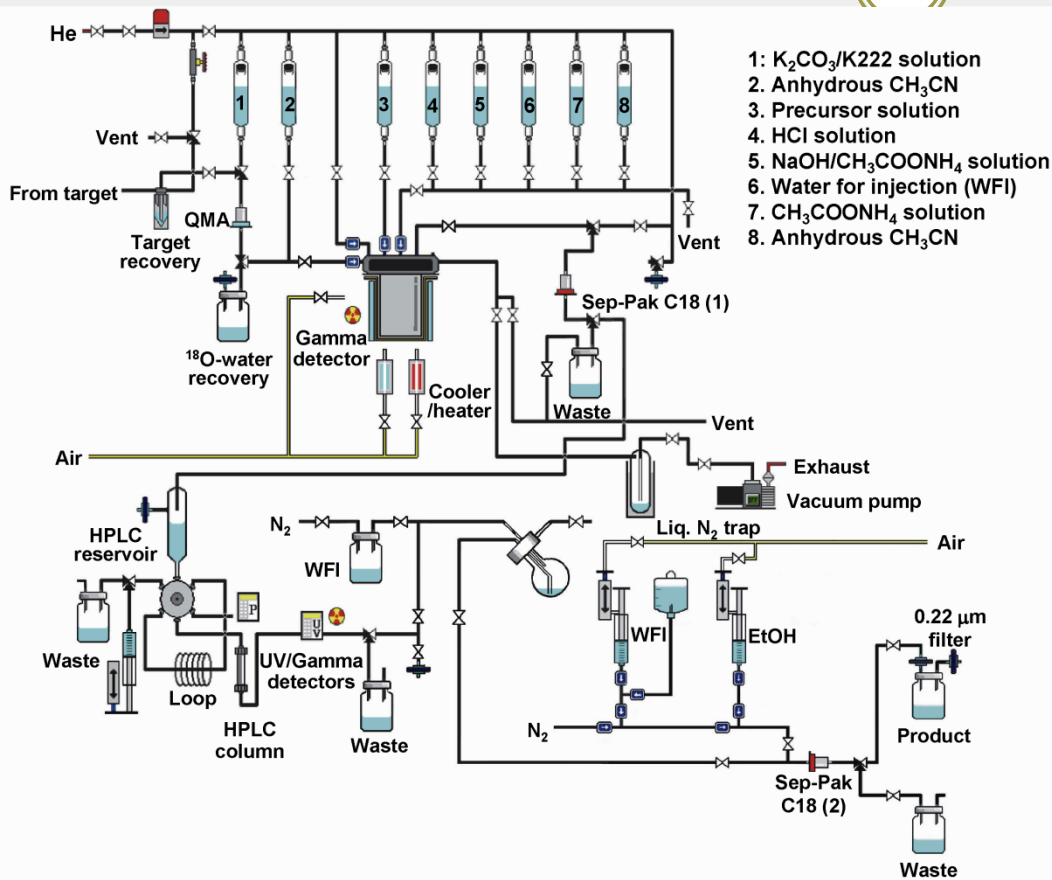
**Imaging**

Scan protocol: 30 min → 6x5 min



# Synthesis of [<sup>18</sup>F]AV-45

17



Sumitomo heavy Industry, Inc.

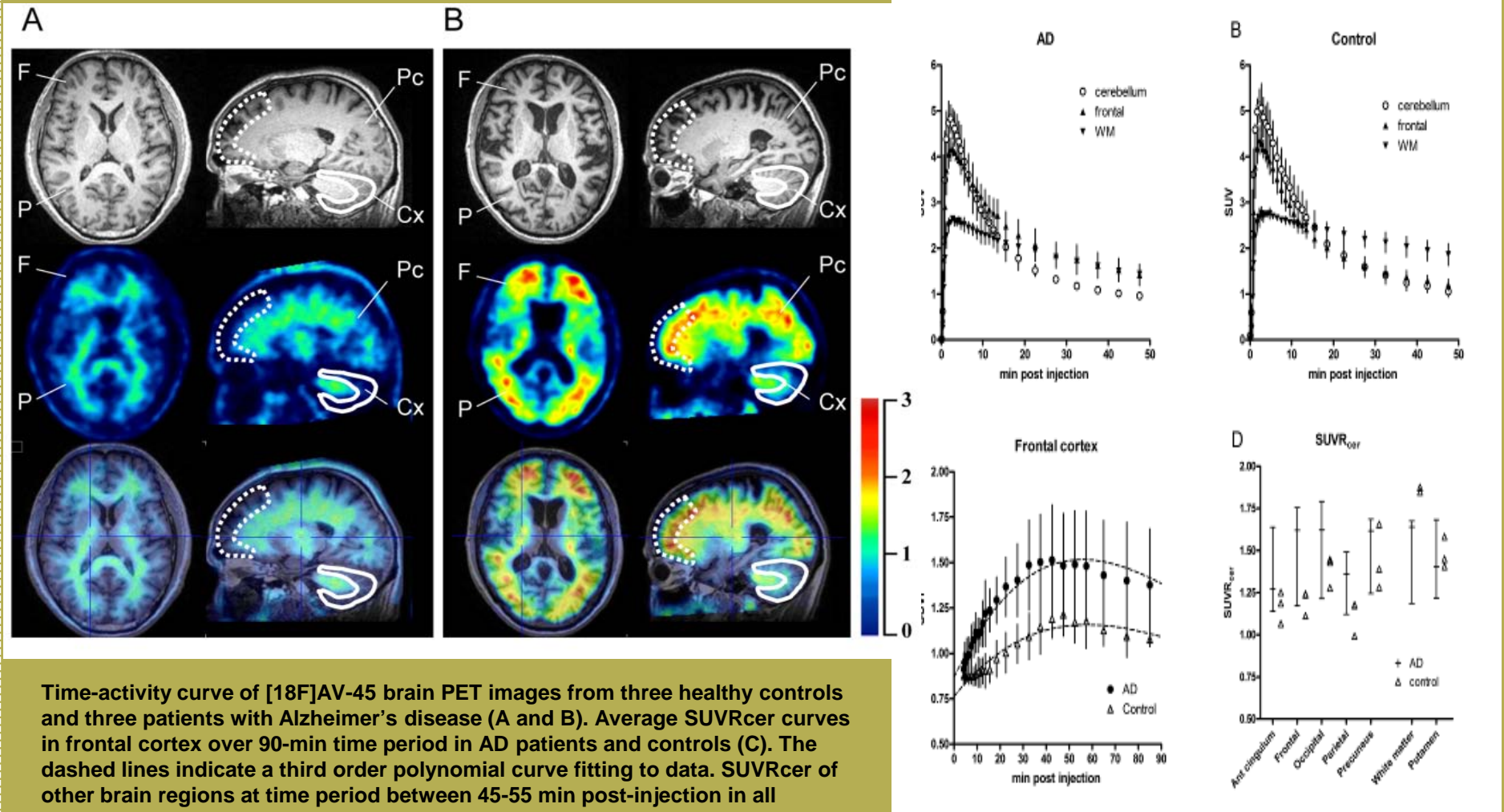
Radiochemical purity:

**95.3 ± 2.2%**

Specific activity:

**12,702 ± 3,649 Ci/mmol**  
(decay corrected)

# 18F-AV-45 Brain Imaging (Phase I)



# Radiotracer deliver




- Phase I:
  - radiotracer will be delivered from Linko CGMH to all participate sites.
  - AV-45 tracer will send to all sites by 貝克西弗 and arrived before 13:00
- Phase II:
  - Two other hospitals will join the tracer deliver (estimated by the end of 2011).
  - Linko CGMH still responsible for AV-45 deliver for other sites.

# T-ADNI PI and training meeting (1)

Date	TADNI	Clinical Core	MRI Core	PET Core	Event
2010-04-17	V				PI meeting
2010-04-21	V				TADNI introduction @ Taiwan
2010-04-23	V				TADNI introduction @ Nation Science Council-Taiwan
2010-05-04				V	E-DA hospital visit for possible AV-45 deliver
2010-05-22	V				PI meeting
2010-06-03	V				PI meeting
2010-08-18				V	Preliminary result report
2010-09-05				V	PI meeting (introducing AV-45 PET imaging)
2010-10-17		V			Neurologic tests work shop
2010-11-23		V			Inclusion criteria discussion

# T-ADNI PI and training meeting (2)



Date	TADNI	Clinical Core	MRI Core	PET Core	Event
2011-01-27	V				PI meeting
2011-02-16		V			eCRF review
2011-03-21			V		PI meeting (MRI technical meeting)
2011-04-11				V	PET phantom validation (4 sites)
2011-04-28	V				PI meeting (Joint IRB review)
2011-04-29			V		PI meeting (MRI core workshop)
2011-05-02			V		MRI phantom validation (4 sites)
2011-05-14		V			Neuropsychological Assessment Workshop
2011-06-08	V				JIRB protocol review discussion
2011-06-09				V	PI meeting (ADNI phantom QC meeting)

# Taiwan ADNI Project



## First stage

1. 台北榮總, [Veterans General Hospital-Taipei](#)
2. 新光醫院, [Shin Kong Wu Ho-Su Memorial Hospital](#)
3. 台北醫學大學, 行政院衛生署雙和醫院, [Shuang Ho Hospital](#)
4. 三軍總醫院, [Tri-service General Hospital](#)
5. 新店耕莘醫院, [Cardinal Tien hospital](#)
6. 林口長庚, [Chang Gung Memorial University Hospital-Linkou](#)

Hospital list updated on 2011-04-21

**Under IRB review**

## Second stage

1. 臺大醫院, [National Taiwan University Hospital](#)
2. 台中榮總醫院, [Veterans General Hospital-Taichung](#)
3. 中國附醫, [China Medical University Hospital](#)
4. 彰化基督教醫院, [Changhua Christian Hospital](#)
5. 成功大學附醫, [National Cheng Kung University Hospital](#)
6. 高雄長庚醫院, [Chang Gung Medical Foundation, Kaohsiung Branch](#)
7. 高醫中和附醫, [Kaohsiung Medical University, Chung-Ho Memorial Hospital](#)
8. 高雄榮總醫院, [Veterans General Hospital-Kaohsiung](#)
9. 花蓮慈濟醫院, [Buddhist Tzu-Chi General Hospital](#)

**ADNI: Alzheimer's Disease Neuroimaging Initiative**