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ICT and Technology in Medical and Health Research
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Quantitative assessment of biological functional parametric images using PET and SPECT

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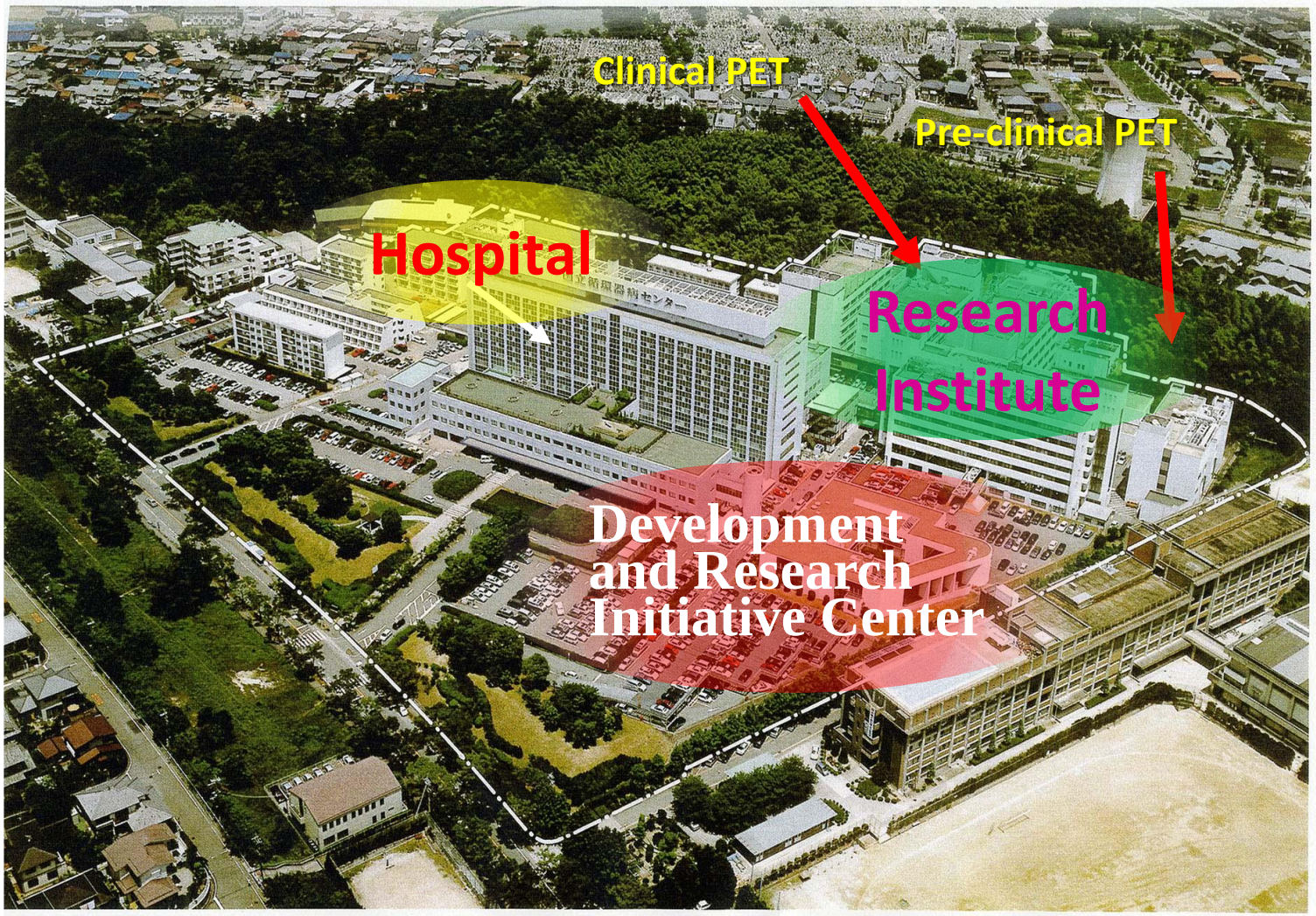
Topics

- ^{15}O-rapid PET for stroke research
- SPECT for multicenter clinical studies
- Future directions

National Cerebral & Cardiovascular Research Center

Ministry of Health, Labor and Welfare (MHLW), Japan

NCVC



国立循環器病センター　〒565-8565　大阪府吹田市藤白台５－７－１　TEL 06-6833-5012　FAX 06-6833-9865

Imaging devices for preclinical research at NCVC

Fuji Fuluoro image analyzer

Cyclotron

GE 3T MRI
Signa3T

Angiography

Siemens micro PET Focus120

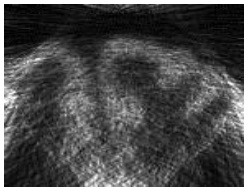
BioScan
NanoSPECT

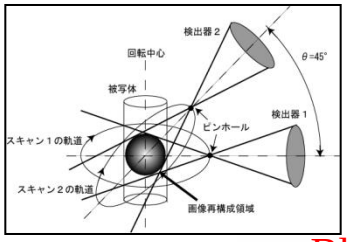
Hot Labo

Siemens PET ECAT
Accel

Toshiba SPECT
GCA7200A

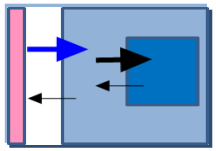
SPECT (inhouse)





Phantom

Blood radioactivity monitor



Our activity includes application of imaging techniques to preclinical research, and also development of equipment and novel software.

国立循環器病研究センター
National Cerebral & Cardiovascular Center

Uniqueness of PET/SPECT

- Functional (biological) imaging
  - ✓ Physiological functions
    - perfusion, metabolism,
    - Receptor BP & occupancy
  - ✓ Tracing therapeutic compound (DDS)
- Quantitative assessment
  - ✓ Kinetic modeling (math, physics)
- High sensitivity

^{15}O-PET for stroke diagnosis

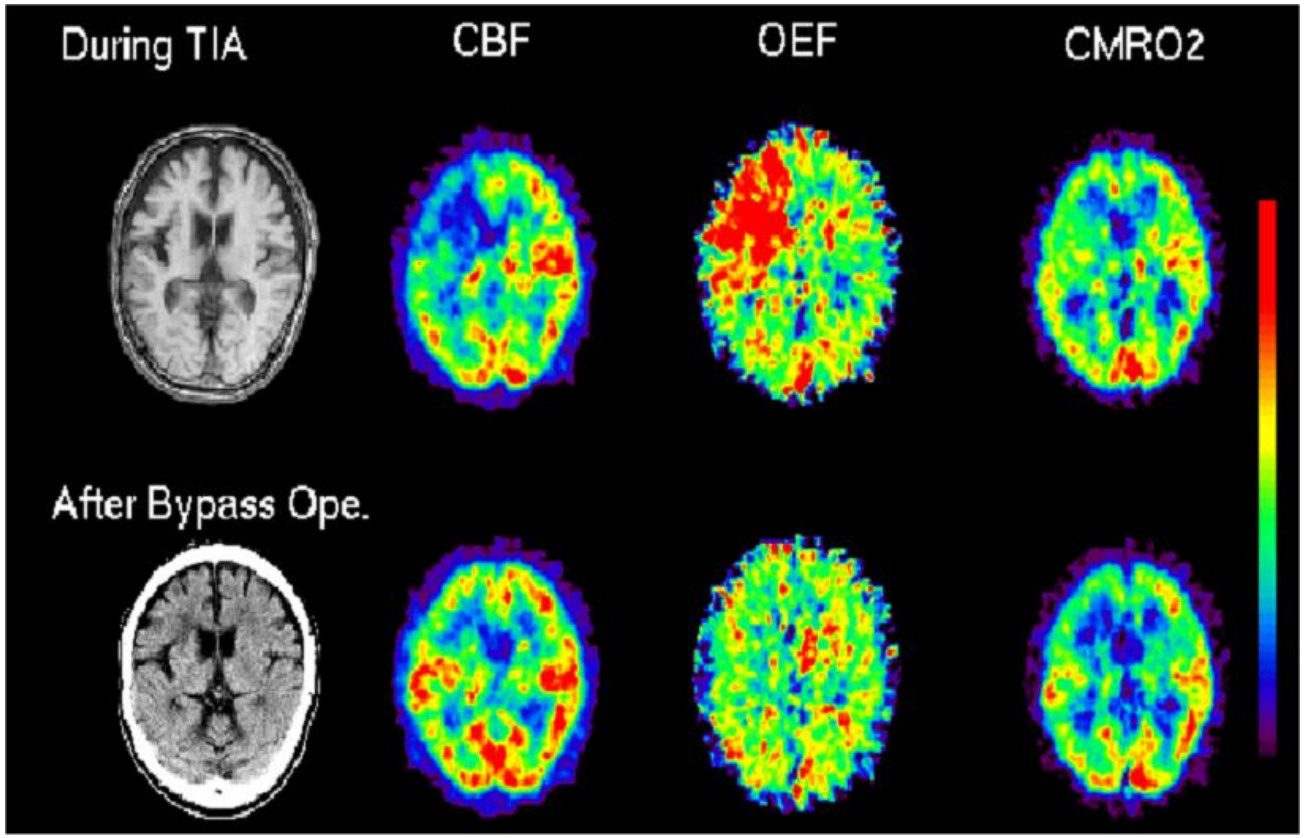
^{15}O-PET provides useful information in relation to ischemic status and neuron survival, but has been limited in clinical environment.

Attributed to:

- The present technique is based on the 3-step approach, requiring $^{15}O_2$, $C^{15}O$, and $C^{15}O_2$ ($H_2{}^{15}O$) administration with TCT, thus long (>1 hr) examination.
- Short half life of 2min, requiring on-site cyclotron, on-site radio-tracer synthesis, and QC for each administration
- Arterial blood sampling needed for determination of arterial input function, which is labor intensive

^{15}O-PET for clinical diagnosis of stroke

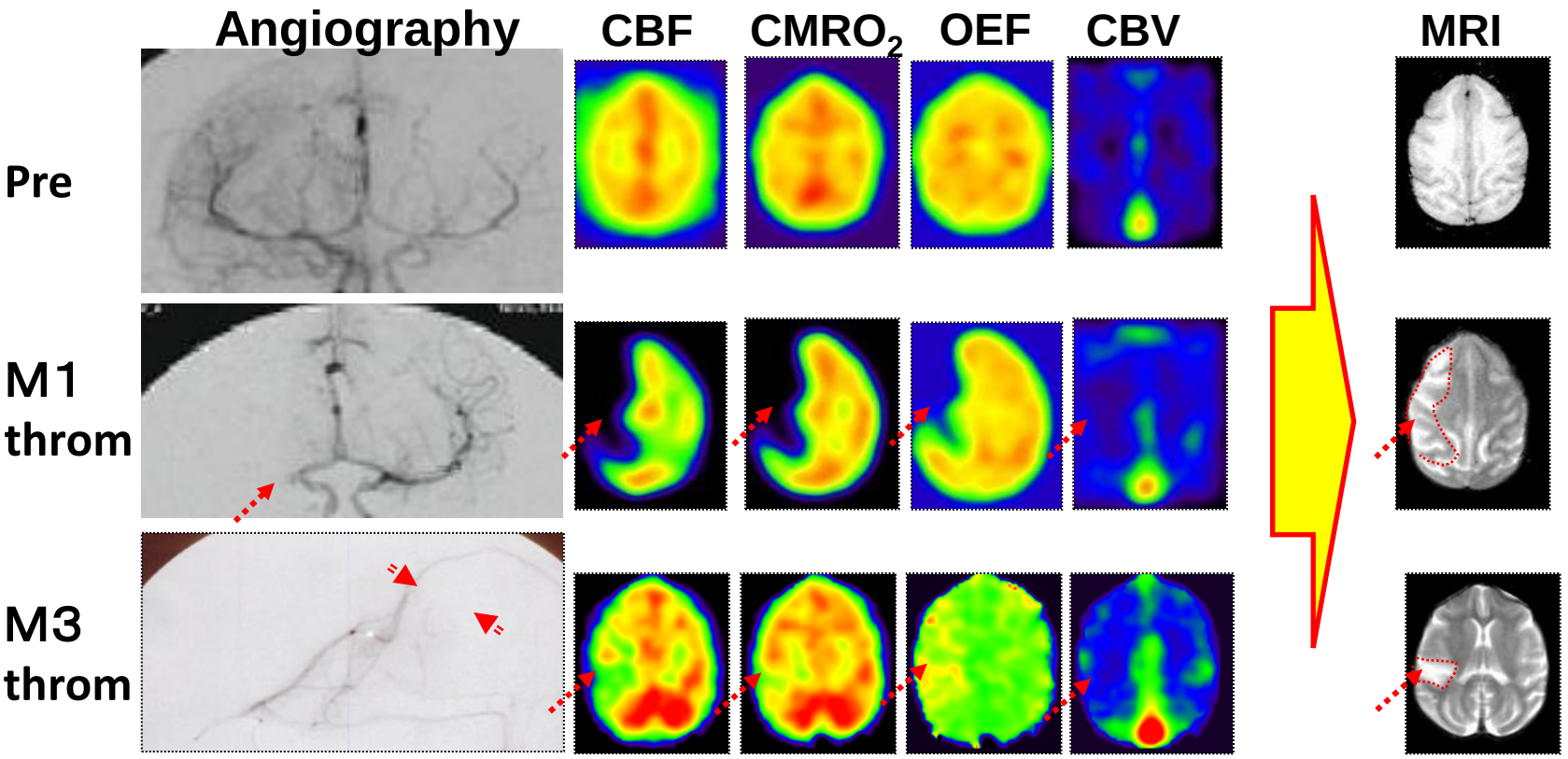
Before and after MCA bypass operation



- Cerebral blood flow (**CBF**) for ischemic status
- Cerebral metabolic rate of Oxygen (**$CMRO_2$**) for neuron survival
- Study consists of CO_2 ($H_2{}^{15}O$), $^{15}O_2$ and $C^{15}O$ inhalation PET scannings
- **Short half life of ^{15}O (approx. 2 min)** requires highly advanced logistics

^{15}O-PET on cynomolgus monkeys

Assessment of irreversible area in acute embolic stroke



JCBFM; 25: 1209–24, 2005

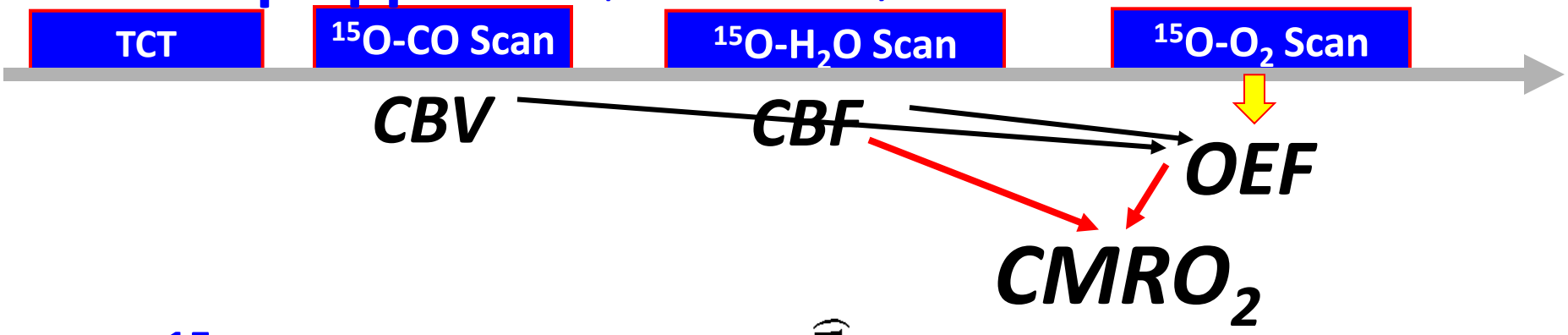
Goal of NCVC ^{15}O–PET project

"On-demand" PET

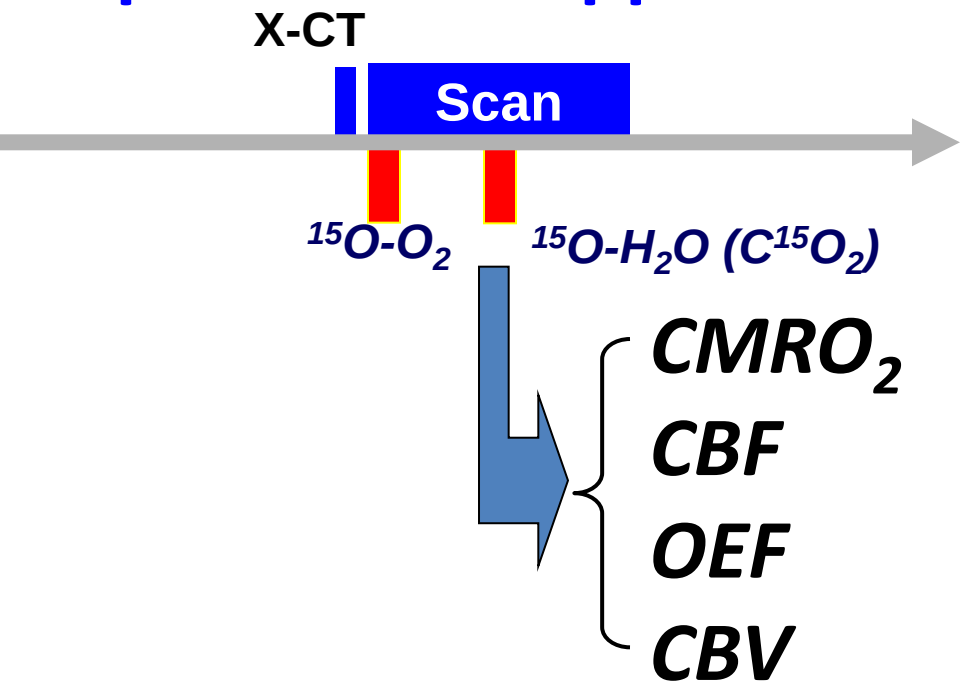
- **Single, short PET scan <10 min, for simultaneous quantitation of $CMRO_2$, CBF, CBV, OEF**
- **Dedicated cyclotron**
- **Fully automated, united system for rapid production, radio-synthesis, and QC for $^{15}O_2$, $C^{15}O$, $C^{15}O_2$ ($H_2{}^{15}O$)**
- **Improved quantitative accuracy in high-sensitive 3D PET**
- **Quantitation without the arterial blood sampling**

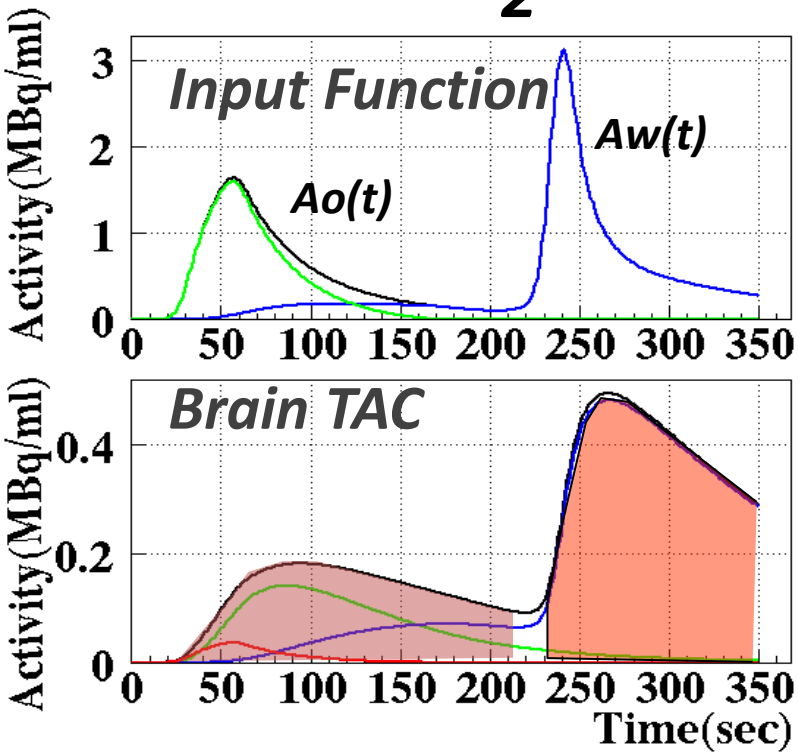
PET Protocols for $^{15}O_2$-based $CMRO_2$/CBF

Three-step approach *(Mintun et al 1984)*



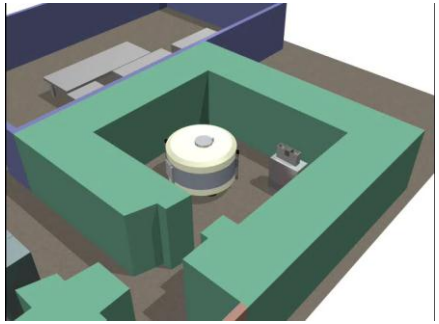
Rapid ^{15}O-PET approach

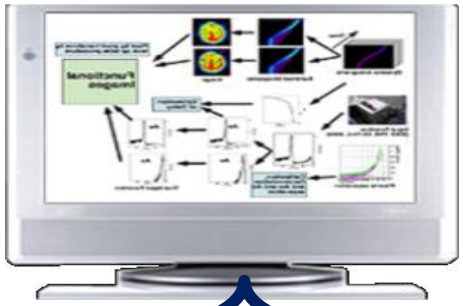




Kudomi et al. JCBFM 2005

Ultra-Rapid ^{15}O-Gas PET System for acute stroke





Fully automated united system

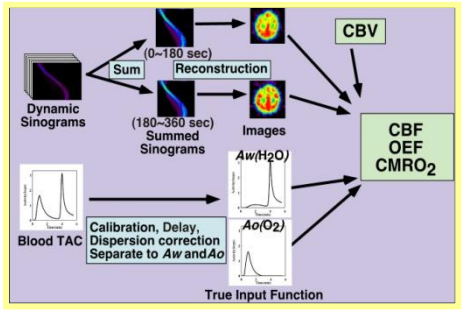
cyclotron

Automated radiosynthesis/QC

Automated rapid system
$^{15}O_2$, $H_2{}^{15}O$, $C^{15}O_2$, $C^{15}O$
(2 min half life)

PET/CT

- Well system
- Continuous input func.
- Gas anal. etc



Data analysis

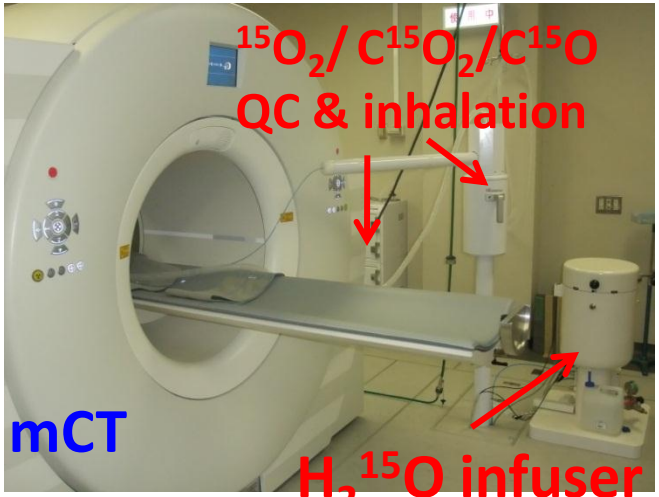
- **Reconstruction scatter corr. atten corr. random comp.**
- **Eqipments**

Towards *"on-demand"* PET

Production, synthesis, & QC for ^{15}O-PET

^{15}O-dedicated cyclotron

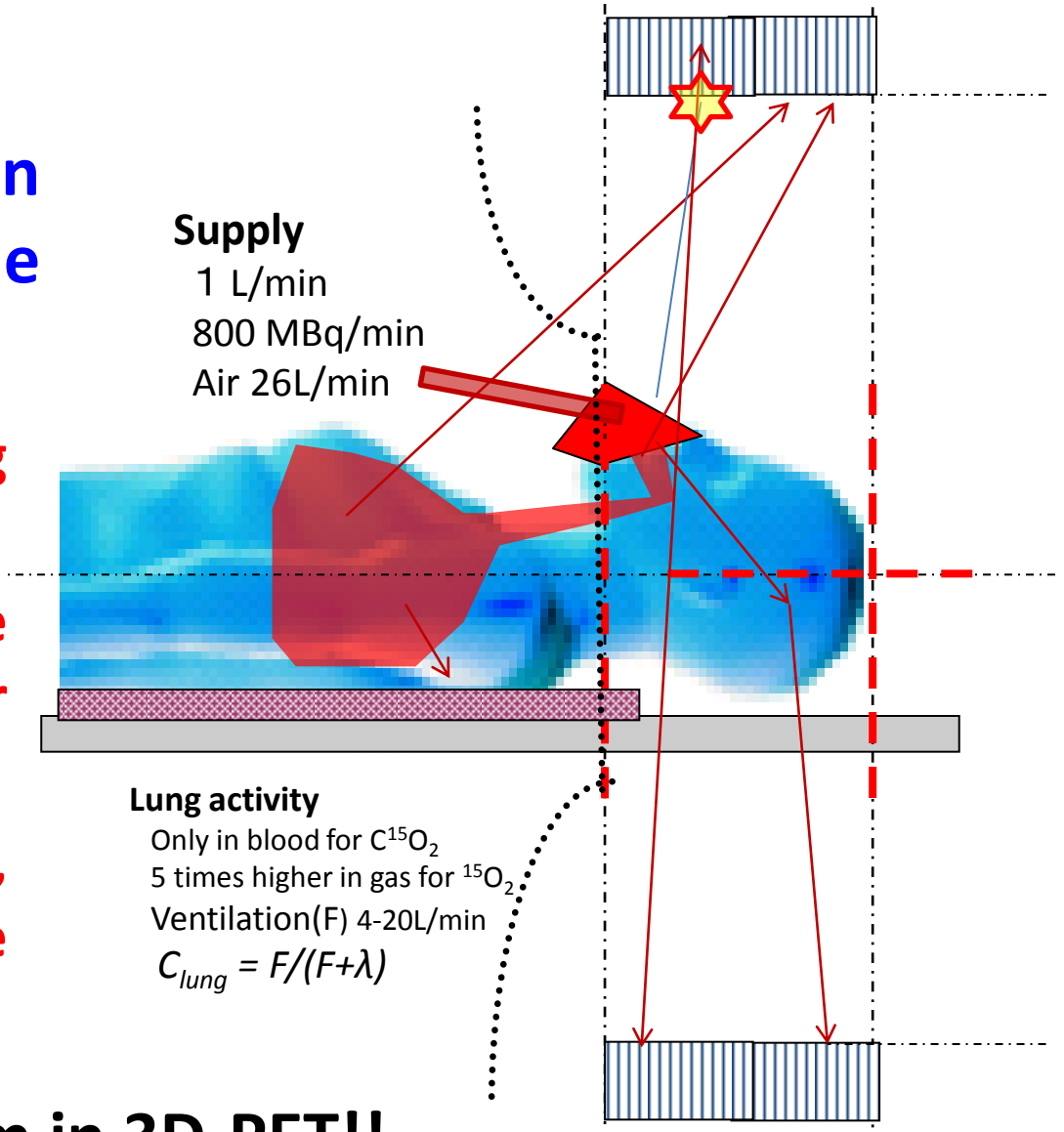
Deuteron at 3.5 MeV



Challenges in $^{15}O_2$ inhalation PET

Strong radioactivity in the gas supply and in the lung causes

- **High single rate, resulting in a large dead-time loss**
- **High random coincidence rate, resulting in poor image quality**
- **High scatter events, resulting in inaccurate quantitation**

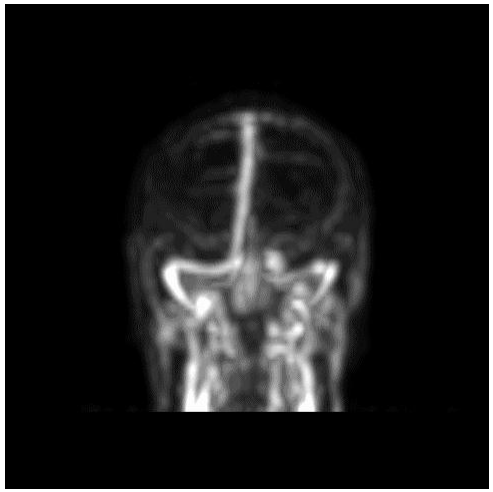


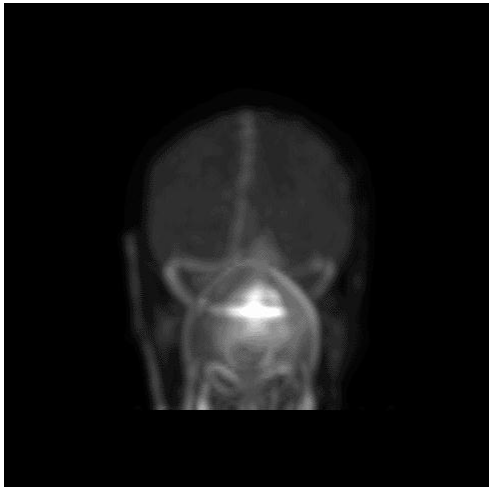
Essential problem in 3D-PET!!

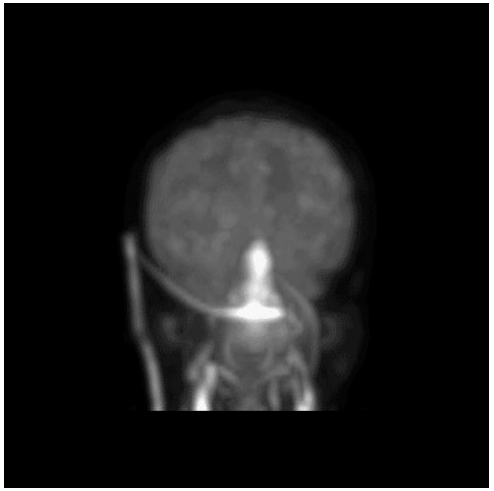
Quantitative assessment in Rapid ^{15}O-PET

3D-PET (Biograph-mCT, Siemens)

$C^{15}O$ → DARG ($^{15}O_2$ + $C^{15}O_2$)

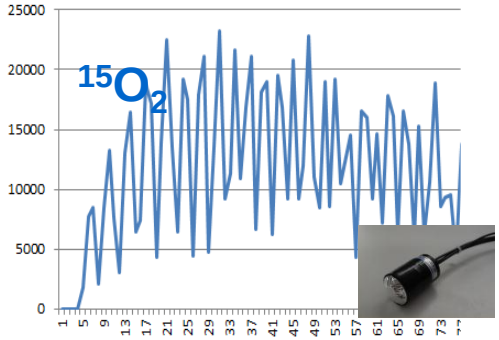




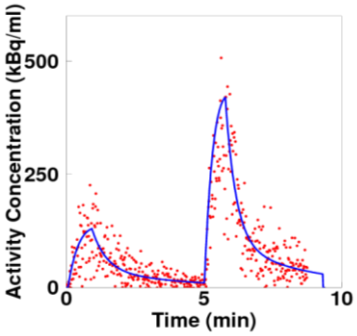


Vasculature radioactivity information for non-invasive arterial input function

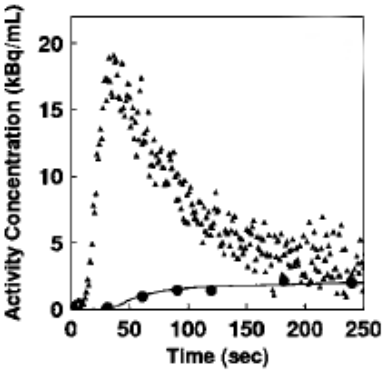
External detector



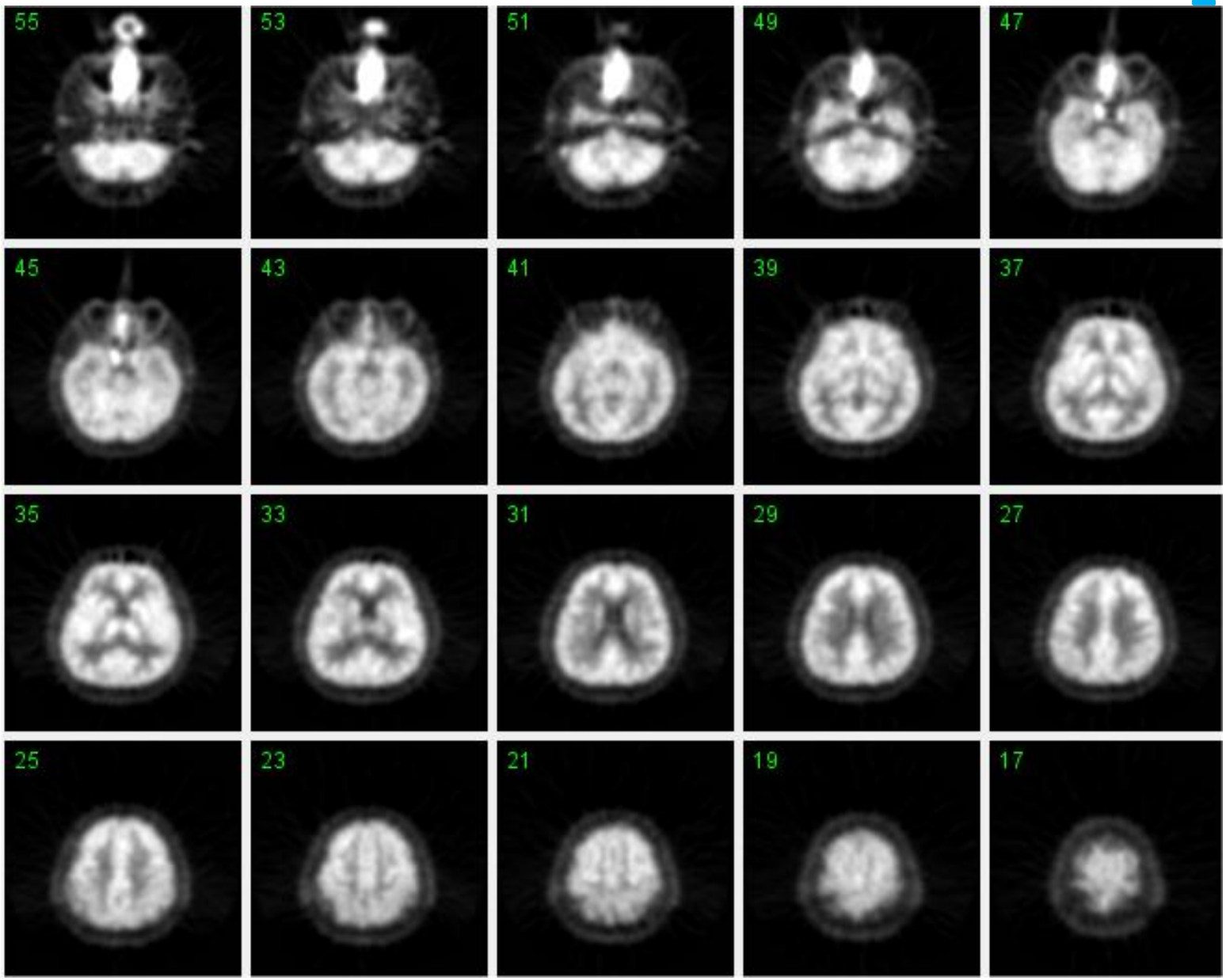
Reconstruction from images



Physiological model for metabolite



Medical Physicist's Brain - $CMRO_2$



study date : 20110208

Clinical trials for patients with acute stroke using rt-PA with additional devices

- **0.6 mg/kg of Alteplase extending to 4.5 hrs**
- **Desmoplase (<9 hrs)** *DIAS III,* ***DIAS-Japan***
- **Stroke MRI（PDM, MRA）…** ***J-ACT II***
- **Neuroprotectives…***NXY-059,* ***Edaravone***
- **US-Thrombolysis…***CLOTBUST, tPA/US/MB,* ***TCT-LoFUT***
- **Devices（Fructure, removal）**
- **Local rt-PA（alone, combined）…** *MELT*
- **Others**

Role of PET in stroke

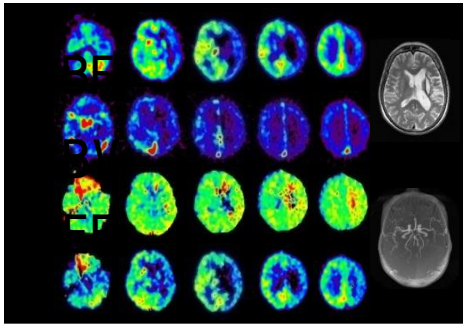
- Pre-operative evaluation of ischemic status &neuron survival
  at >3hrs of onset (**Rapid ^{15}O-PET** required)
- Identification of effective care
  Neuron-, glial cell-, microglia-, ion channel-specific pathophysiology
- Pre-operative prediction of hemorhage

On-going research

Ultra-rapid, automated, on-demand PET for acute stroke

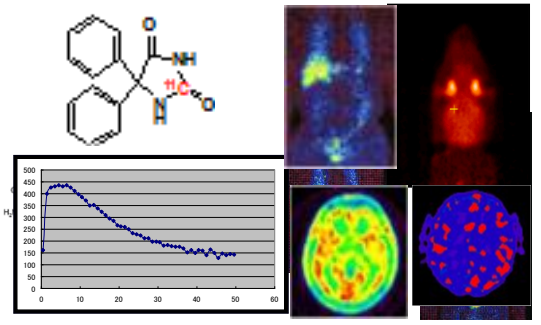
United system (cyclotron, radiosynthesis, acquisition, data processing, data analysis)

New indecies



Hayashi T, et al. JCBFM 2002
Effective oxygen diffusivity

Molecular imaging



Understanding pathophysiol and treatment outcome

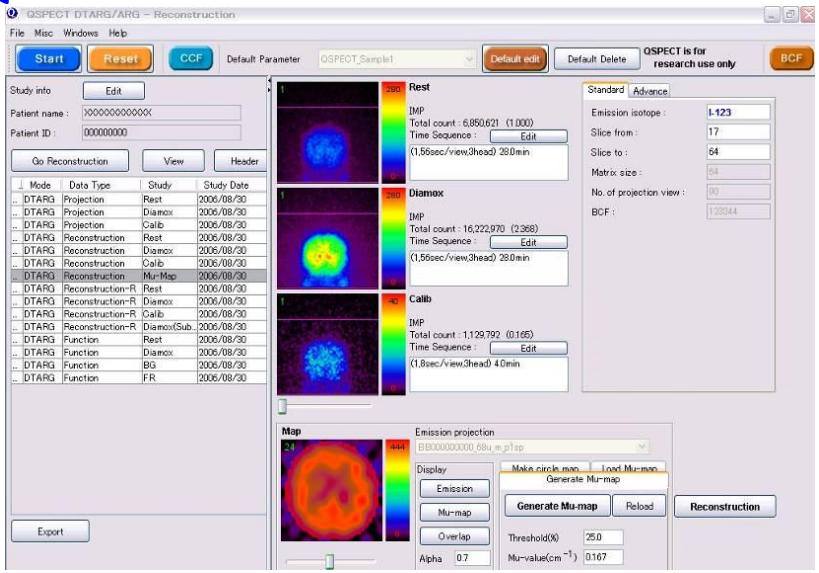
Use of SPECT in clinical research

- **Large scale availability in clinical institutions**
- **Variety of radio-tracers available**
- **Inter-institutional & inter-equipment reproducibility well verified**
- **But quantitative accuracy not well supported**

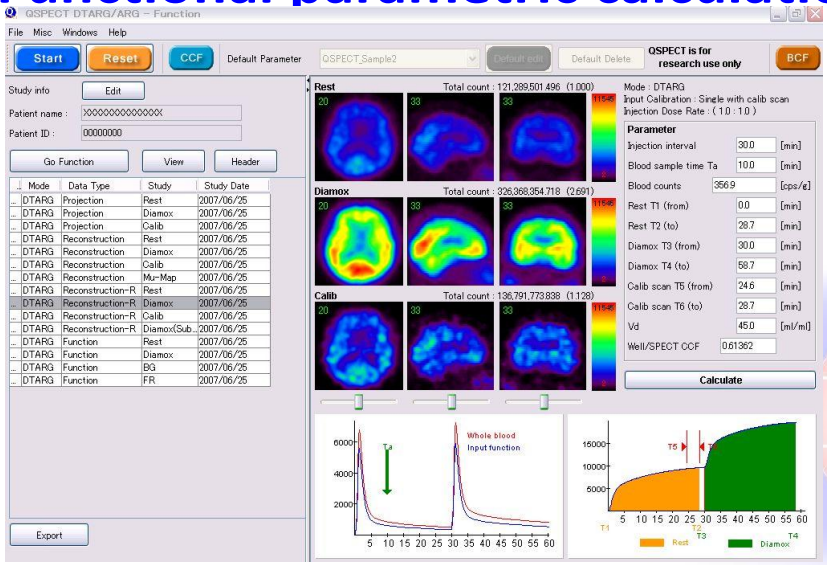
A novel software (QSPECT) developed at NCVC enables quantitative SPECT reconstruction for most of existing SPECT cameras. This software is considered to make SPECT suitable for multicenter clinical studies.

Quantitative SPECT (QSPECT) Reconstruction

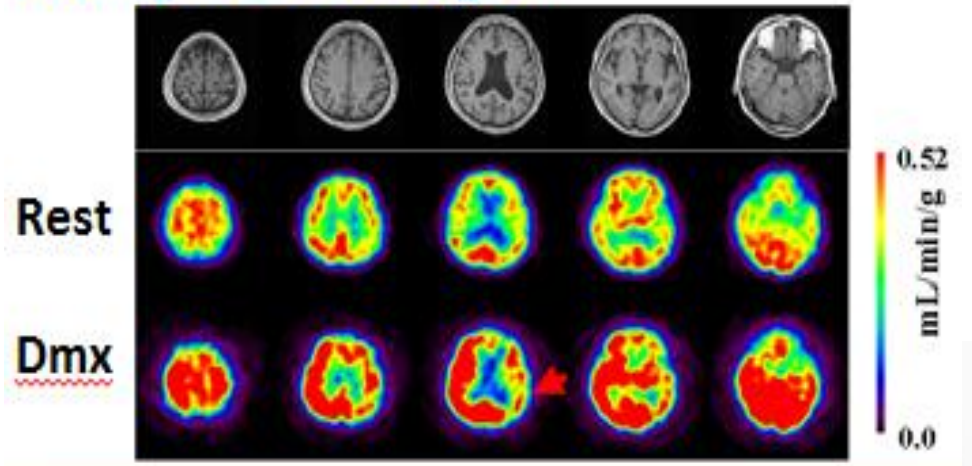
Quantitative reconstruction



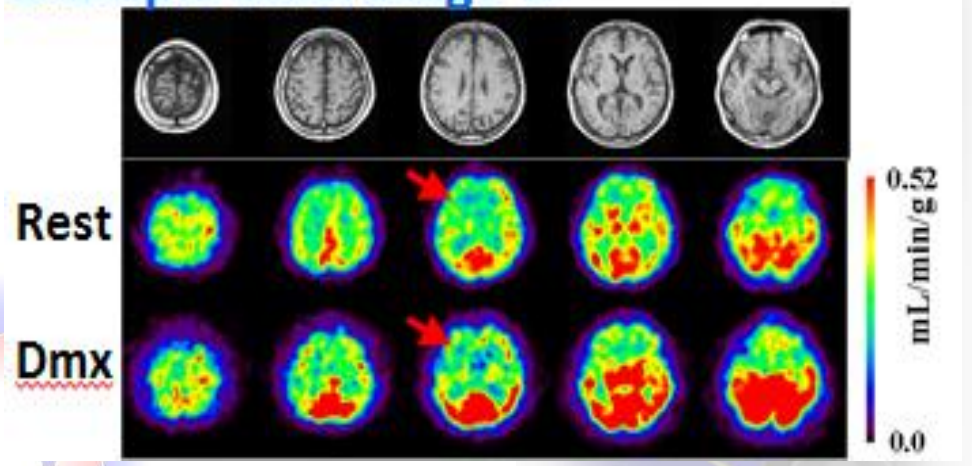
Functional parametric calculation



Example case: Stage-I



Example case: Stage-II

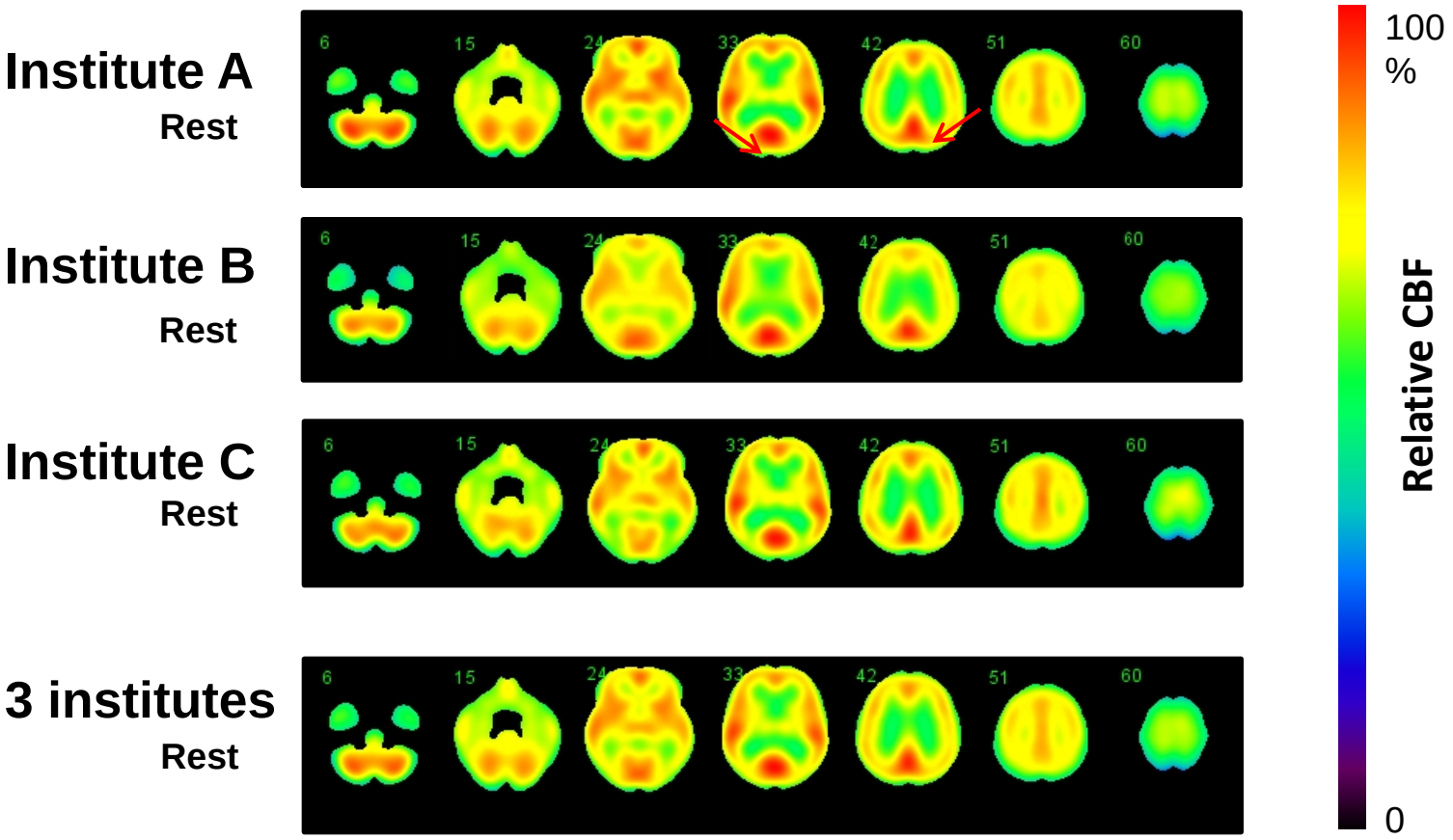


>12k clinical scans/year at 170 institutions

Inter-institutional consistency of SPECT-CBF

Averaged at each institution

Each institute with different SPECT systems



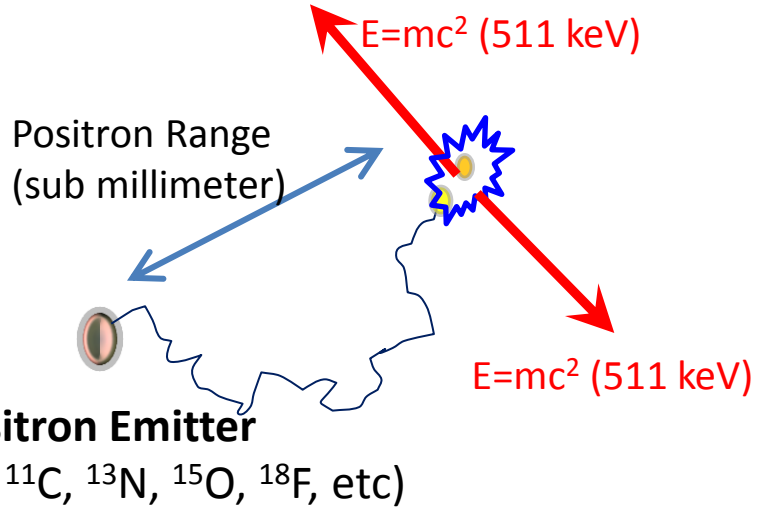
Application of QSPECT

On going multicenter clinical research

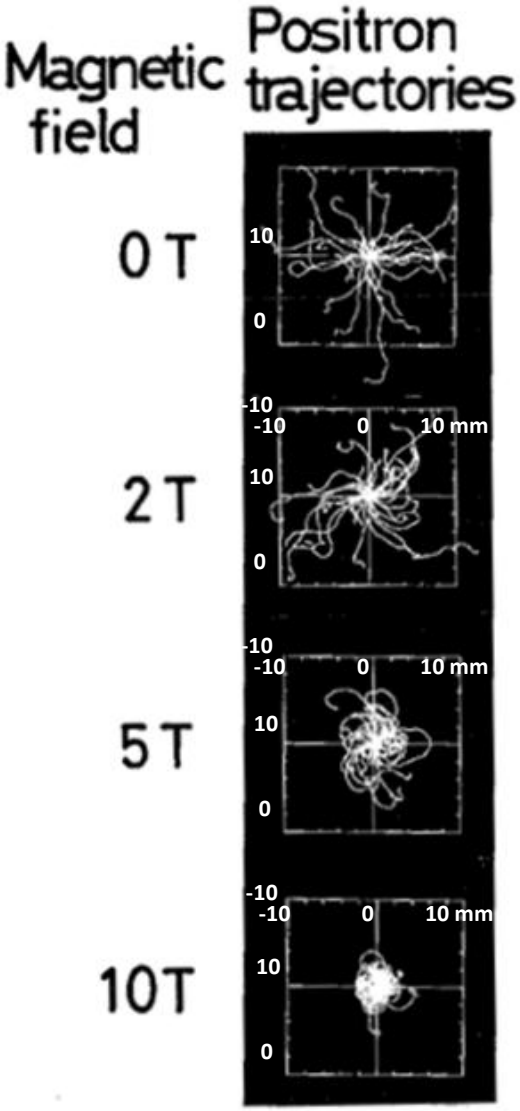
- Outcome evaluation of EC-IC bypass surgery in MCA occlusion (Japan)
- Drug evaluation (cerebral flow reactivity) (Japan)
- Traumatic brain injury (Japan)
- Pre-synaptic dopamine reuptake – normal data base (EU)
- Evaluation of carotid artery stent graft
- others

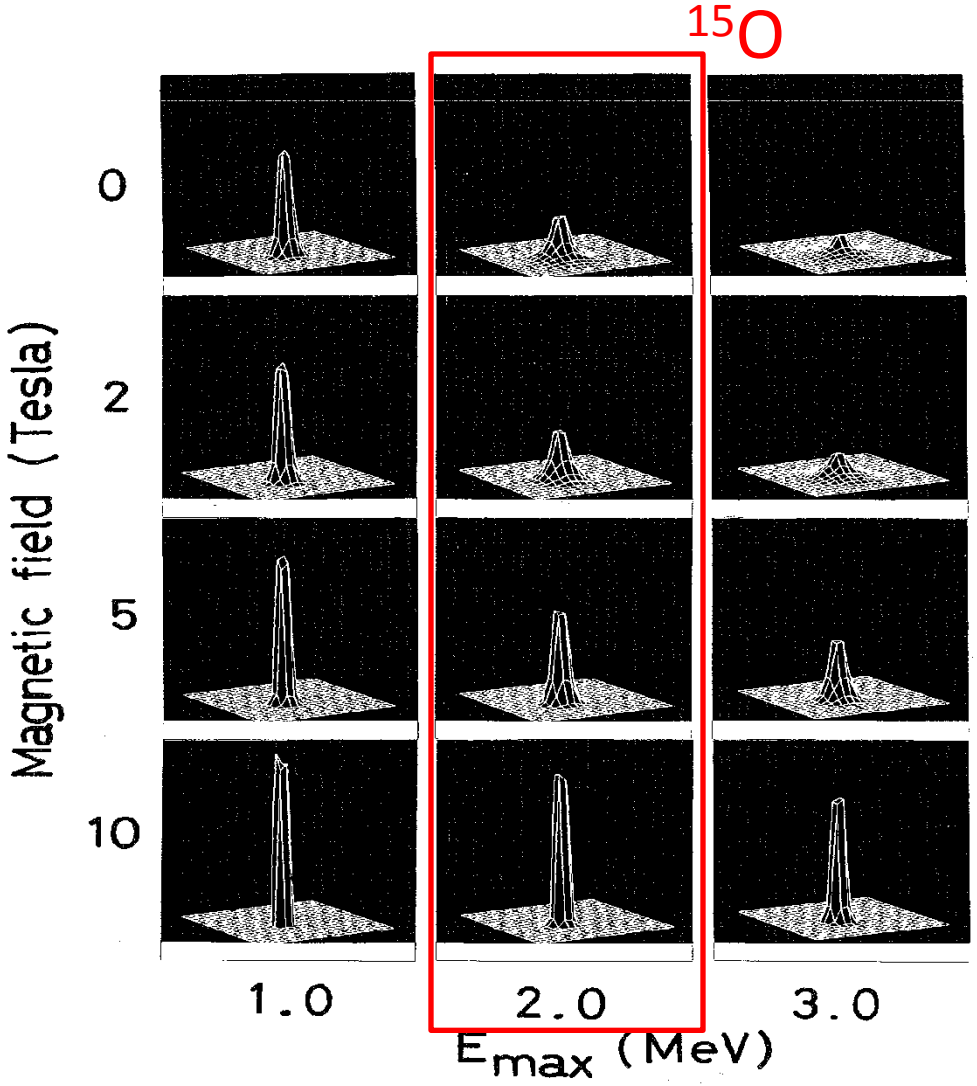
Hybrid PET/MRI System

- **Multiple functional and anatomical images**
- **Shortening the positron range for improved spatial resolution**



Reduction of positron range in high-field MRI





Iida et al., IEEE TNS, 1986

3D-Brain Phantom in Magnetic Field

^{120}I (Maximum energy : ~ 4 MeV)

0 T

3 T

7 T

9.4 T

Jeulich Institute, Germany

Future directions in PET/SPECT

Multi-modality imaging

- Software fusion
- CT/PET, CT/SPECT
- MRI/PET, MRI/SPECT

Shortening scan duration & time resolution

- Multiple functional imaging
- Transient change detection

Standardization among institutions/equipment setup

Summary

- Rapid ^{15}O-PET is being setup for stroke research, but still requires further works.
- SPECT is of use in multicenter clinical study
- Multi-modality, multi-functional imaging is future direction.