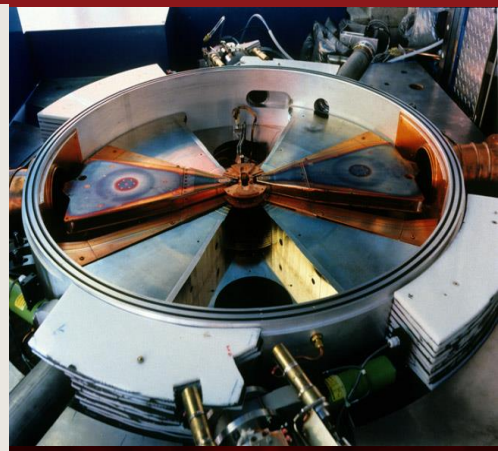
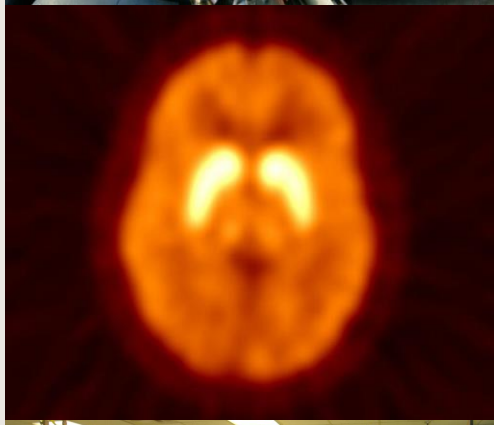
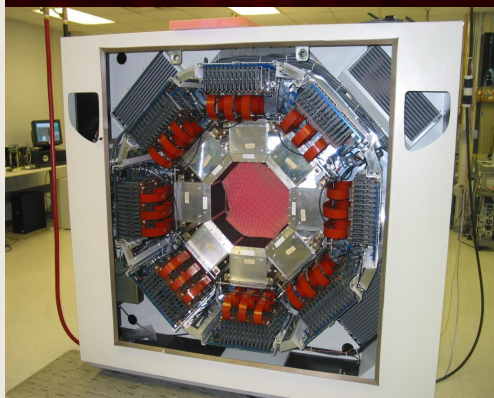
TRIUMF

Canada's National Laboratory for Particle and Nuclear Physics
Laboratoire national canadien pour la recherche en physique nucléaire et en physique des particules

From Vision to Seeing: Tracing Erich's role in bringing positron emission tomography to BC and Canada.





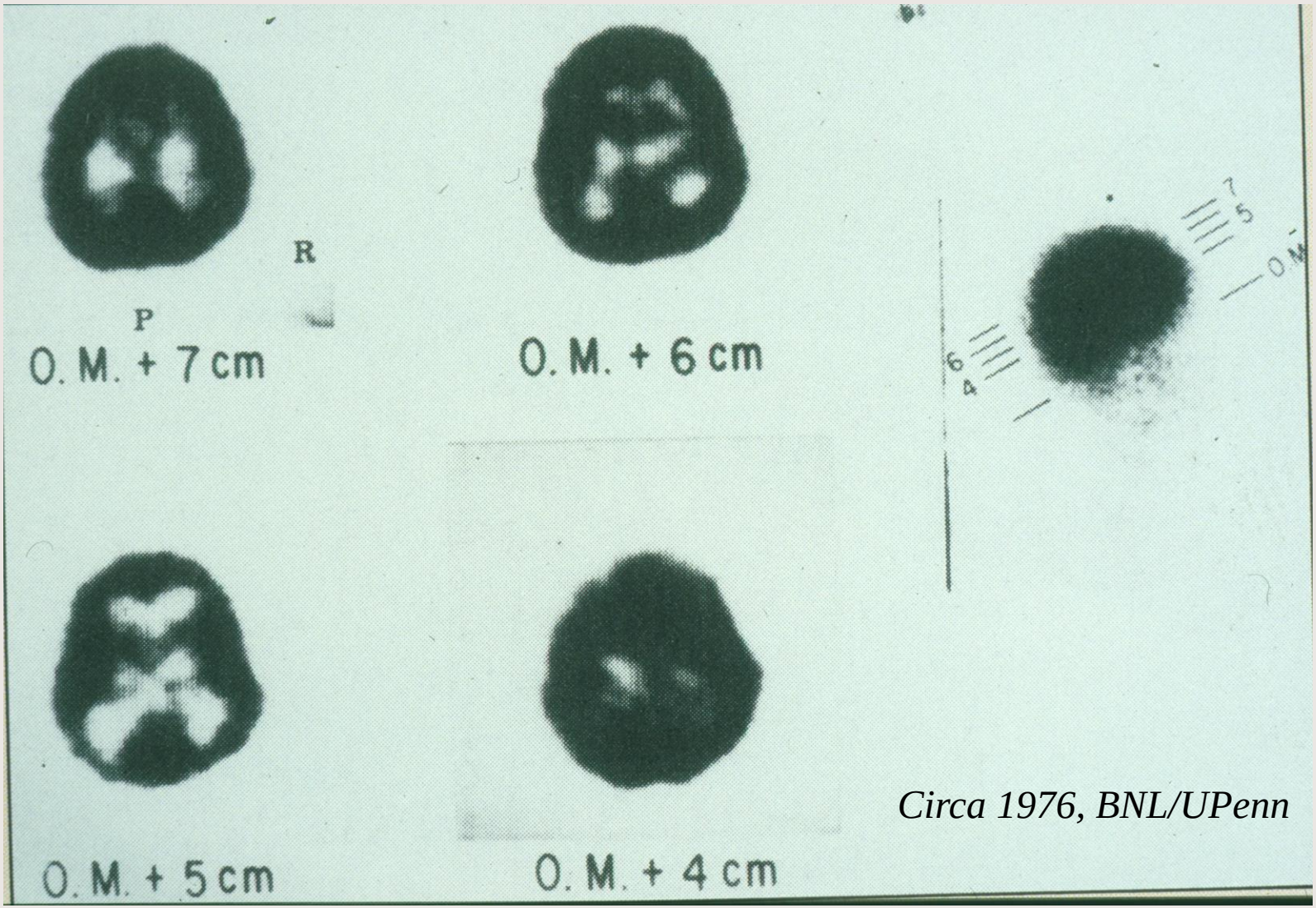


Thomas J. Ruth, PhD
Senior Research Scientist , Emeritus
TRIUMF/BC Cancer Agency

Brief History of PET

- 1950s – Brownell & Sweet at Harvard
- 1950s/60s – Hospital based cyclotorn production of $H_2{}^{15}O$, Ter Pogossian, Wash. U.
- 1960s – ^{11}C-chemistry, Wolf team at BNL
- 1960s – ^{14}C-deoxyglucose, Sokoloff, NIH
- 1960s/70s – Kuhl & Edwards, MkIV camera
- 1970s – Phelps & Hoffmann, PET scanner, Wash. U.
- 1970s – ^{18}F-fluorodeoxyglucose, Wolf, Fowler, Ido
- 1970s – 1st FDG scan, Reivich, Kuhl, PENN
- 1980 – NIH funded 10 sites for NeuroPET

FDG scan on MkIV – Kuhl,et al.



Circa 1976, BNL/UPenn

PET @ UBC/TRIUMF

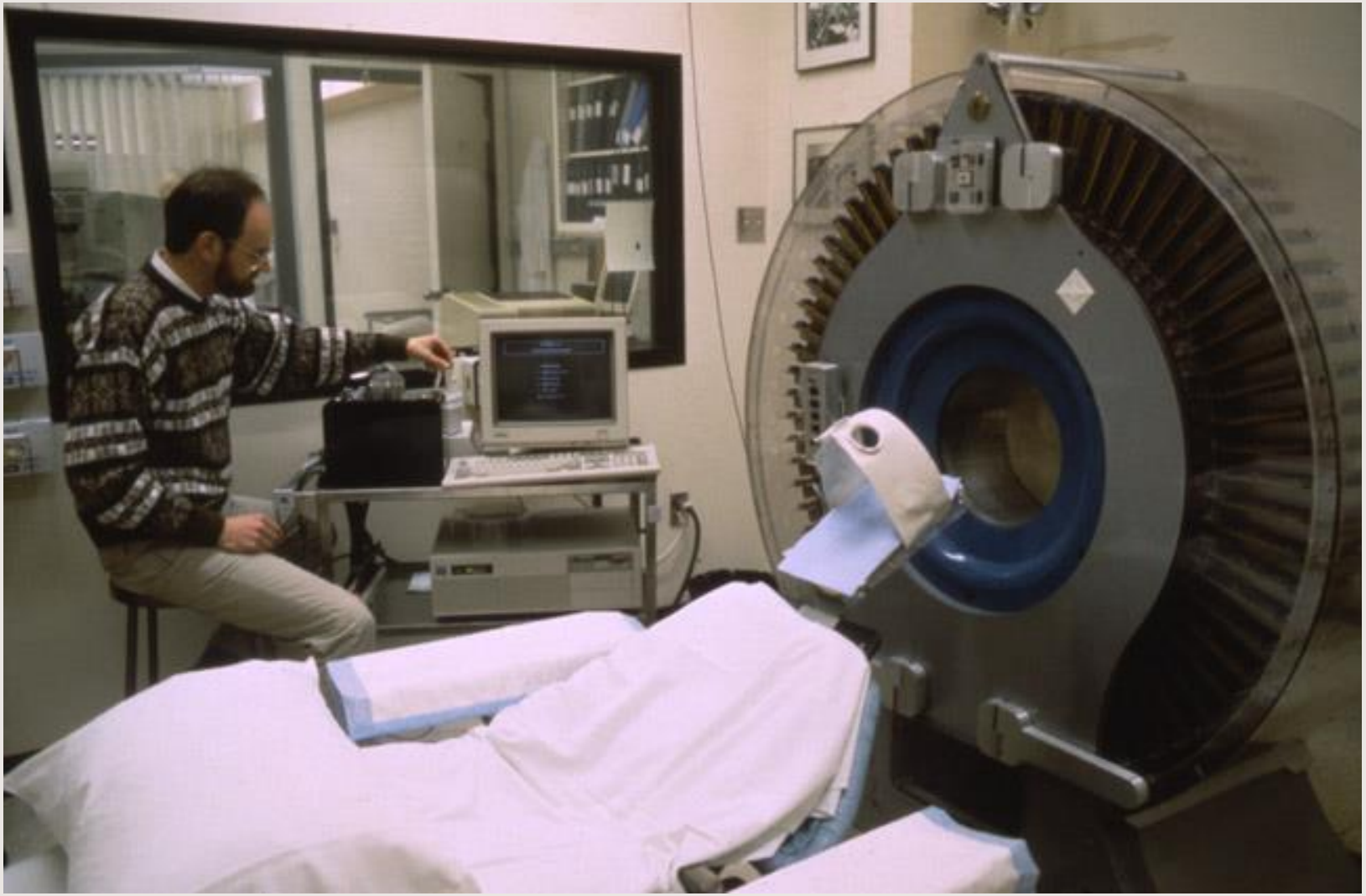
- Pat McGeer, Brian Pate, Bernie Reidel,Laurie Hall
- Building infrastructure:
  - CP-42 Beam Line
  - PETTVI Scanner
  - Pipeline
- Erich Vogt

CP-42 Switching Magnet

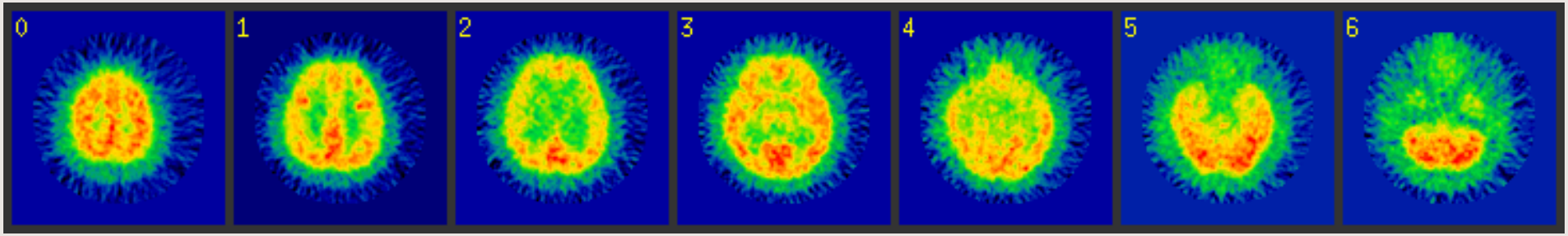
Funded by Vancouver Foundation, circa 1982

PETTVI Dedication 1982

PETTVI Scanner



PETTVI – FDG image



PETTVI:

4 detector rings separated by septa: 7 imaging planes

In plane spatial resolution 9.2 cm

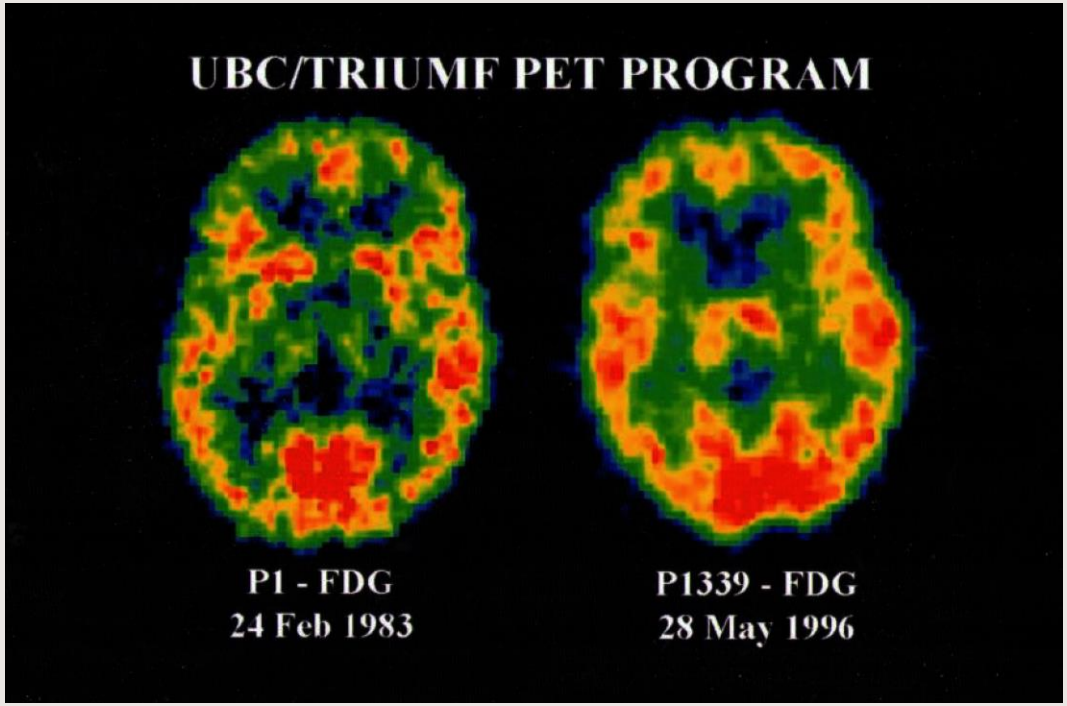
Axial slice width: 11.6 mm

Slice – to –slice distance: 14.4 mm

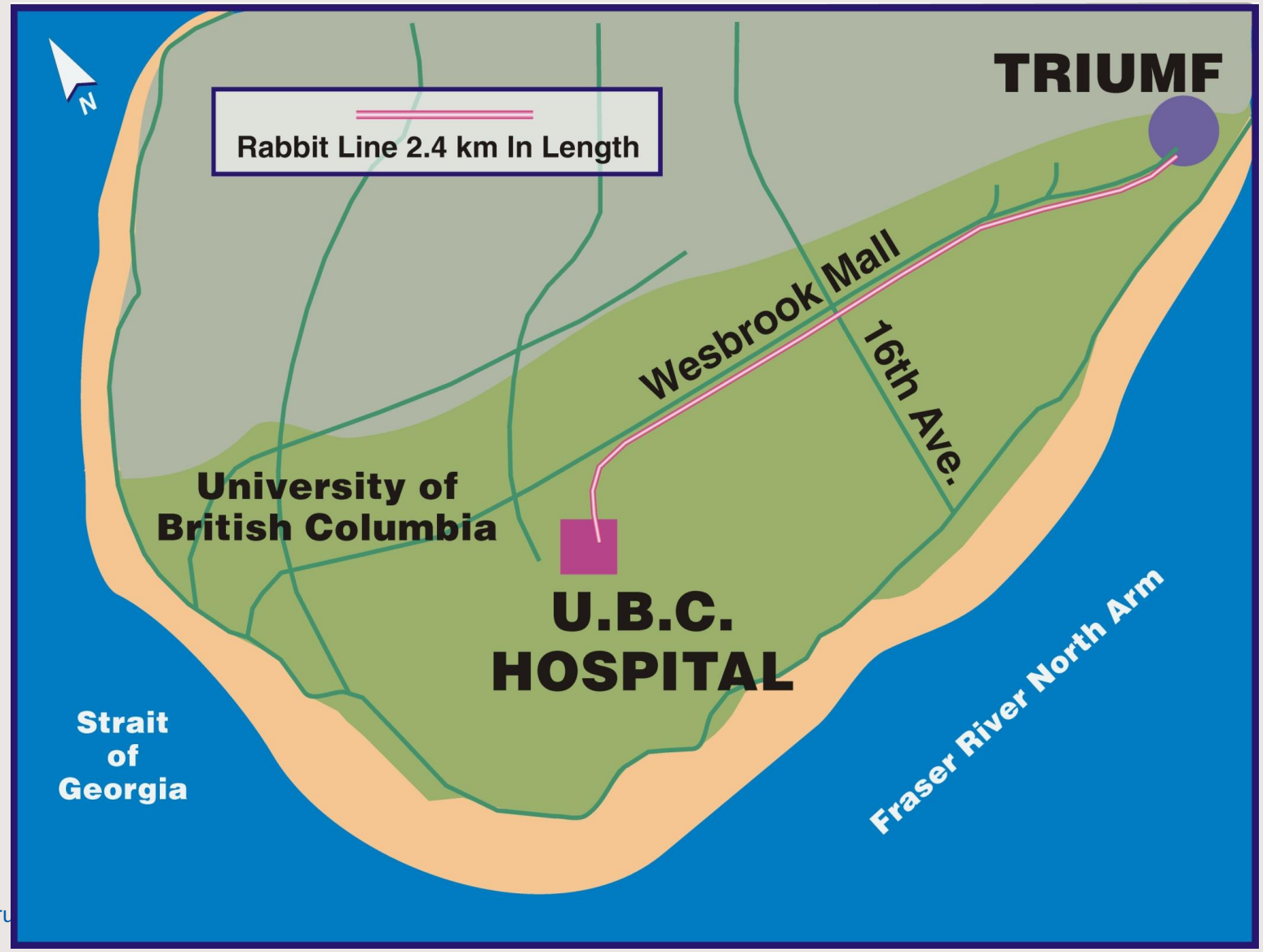
Sensitivity < 0.5%

It wobbled!

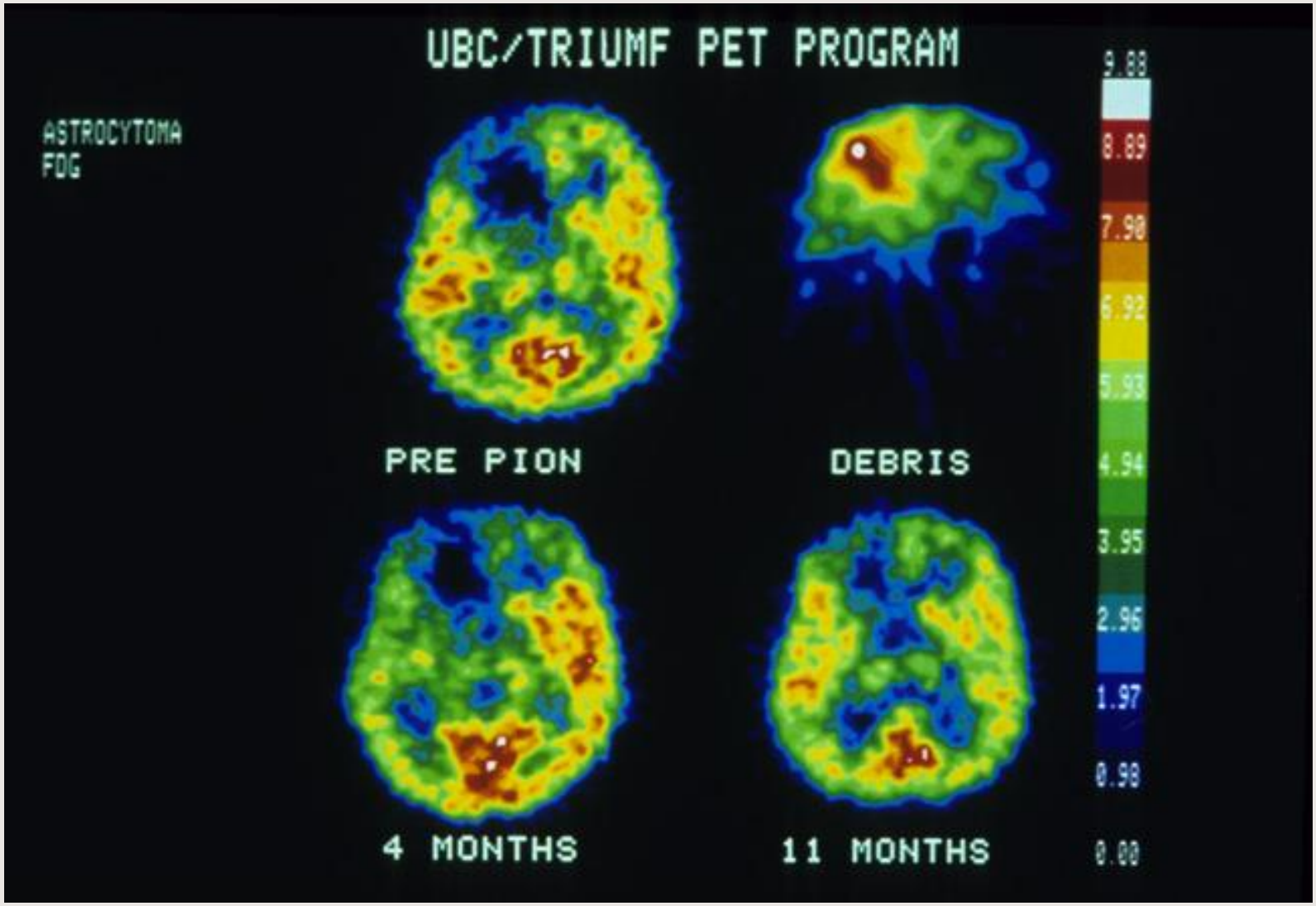
1st and Last Scans on the PETTVI



Pipeline 1983



Pion Therapy @ TRIUMF



Parkinson's Disease

- A common neurodegenerative disorder
- Loss of dopamine neurons and nerve terminal causing loss of motor skills and speech
- Most common form of treatment is with L-dopa which is transformed into dopamine in the body

Donald B Calne
1981

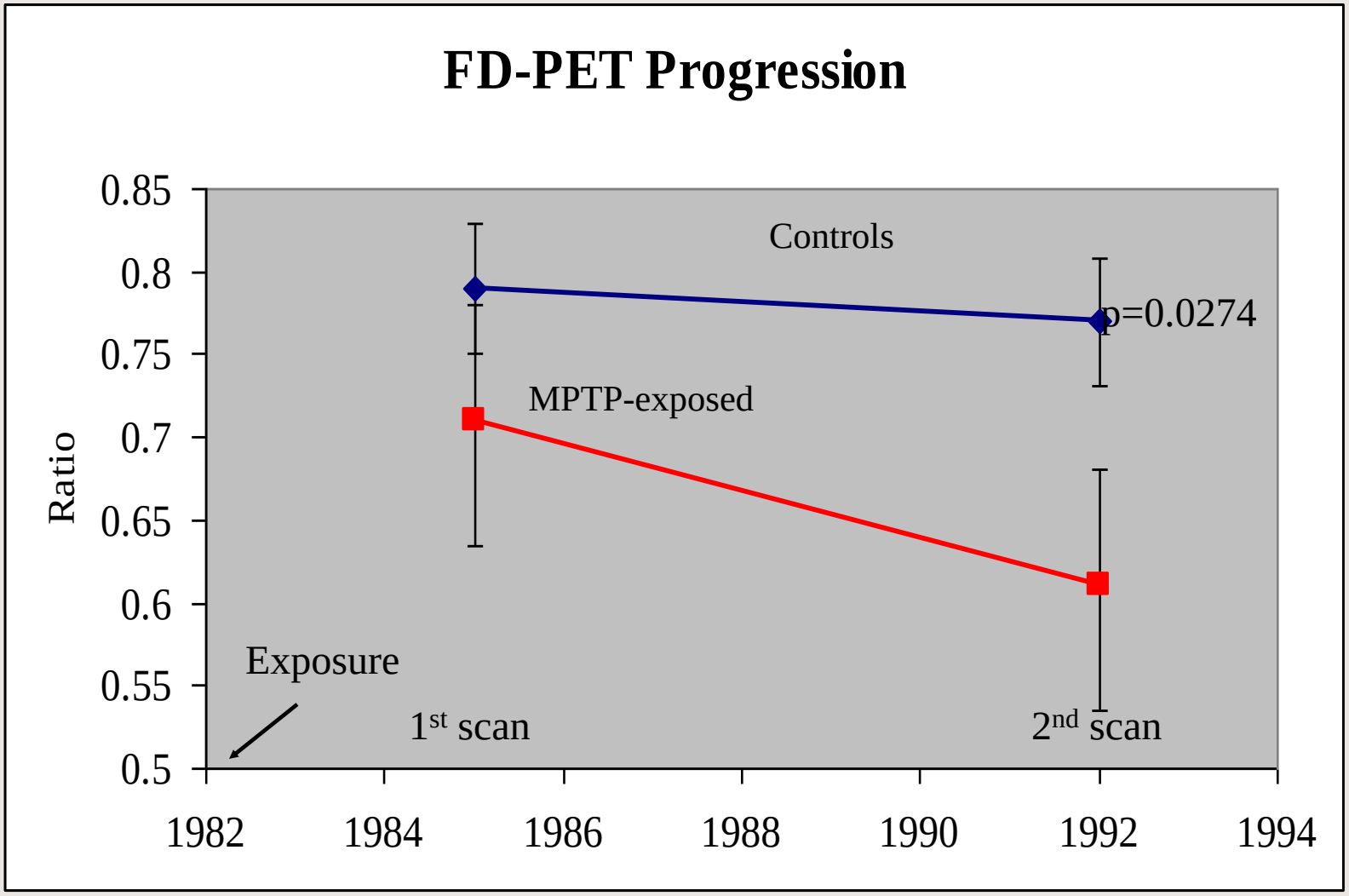
Preclinical Changes in Brain

The first demonstration of subclinical dopaminergic impairment in people exposed to MPTP and in people carrying asymptomatic Parkinson-causing mutations.

MPTP

In the 1980's a designer drug with a small contaminant (MPTP) causing Parkinsonian symptoms was sold to several to drug users.

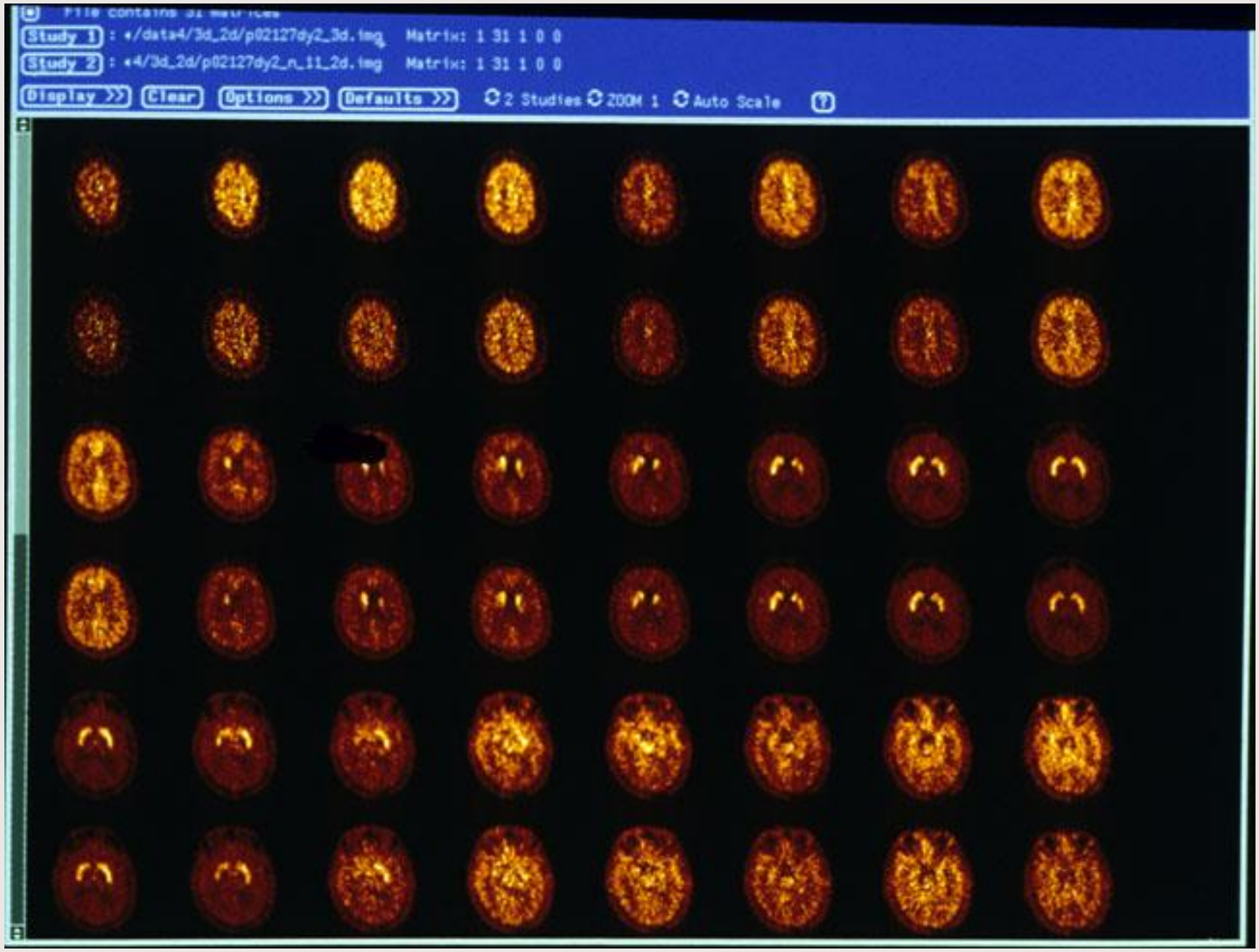
Normal Progression vs MPTP Exposure



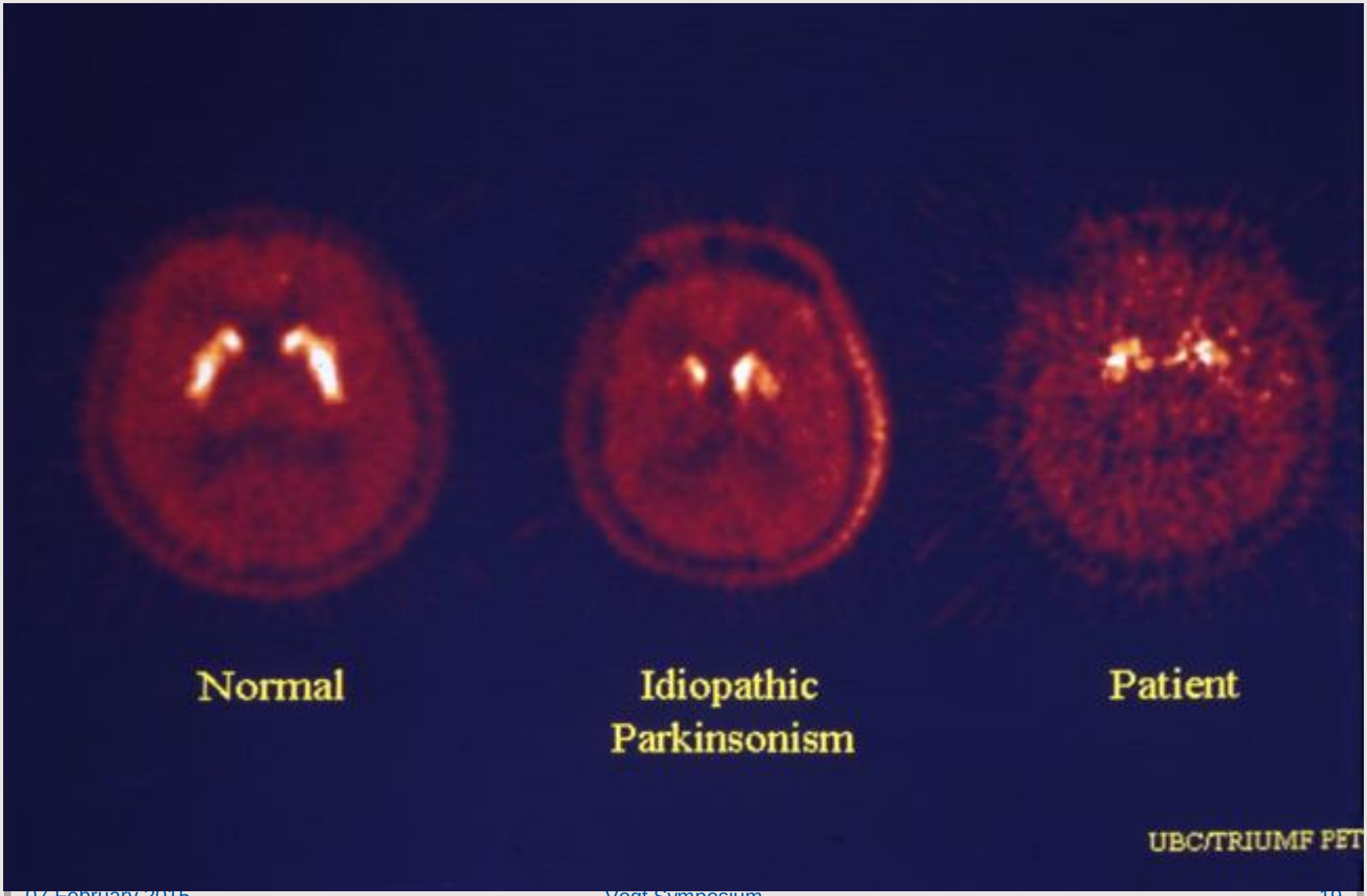
Bob Miller (VPR, UBC) & Erich

ECAT 953B, Ruth, Miller, Gardner

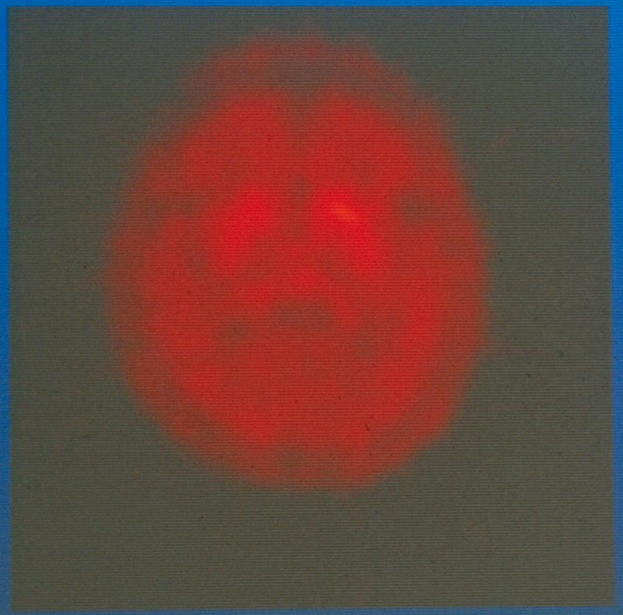
Screenshot from ECAT 953B



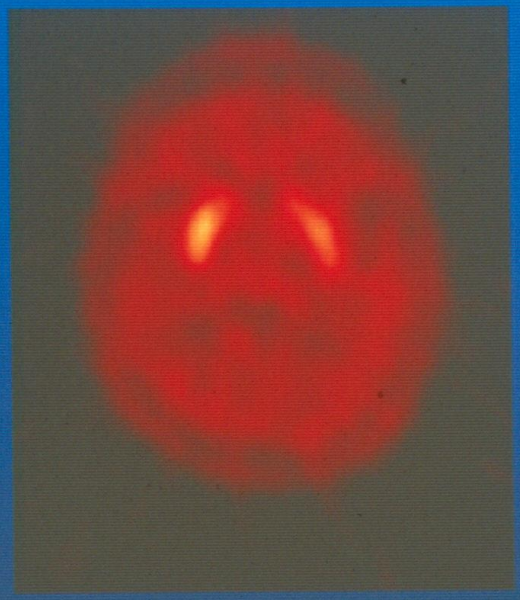
^{18}F-Dopa Scans



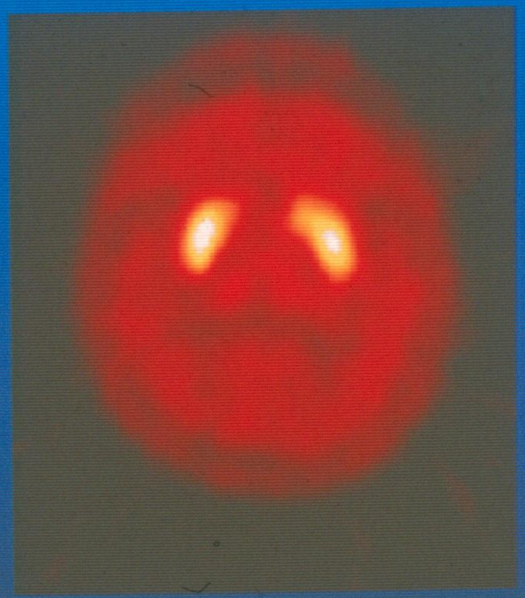
Fetal Cell Transplant



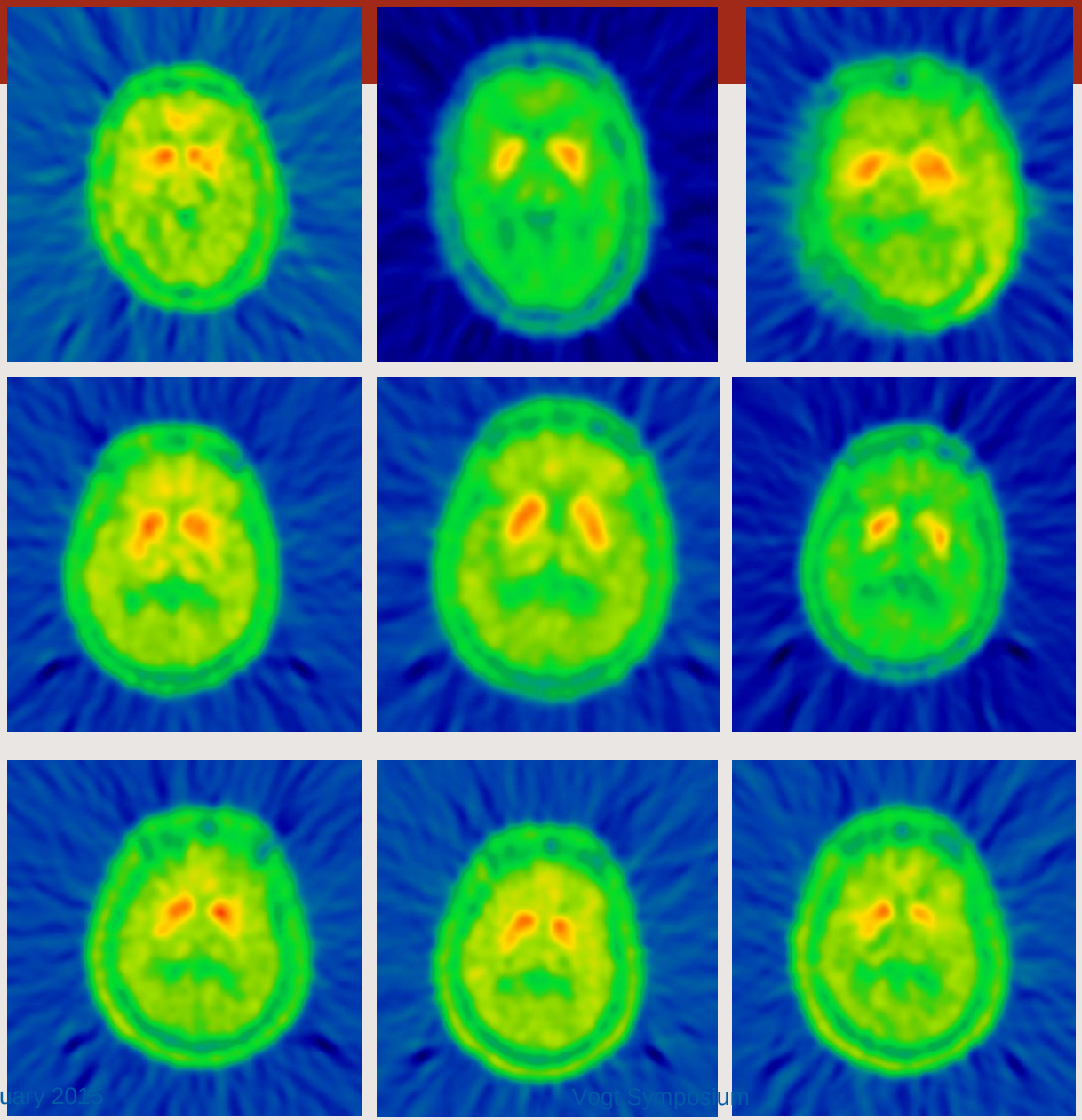
Baseline



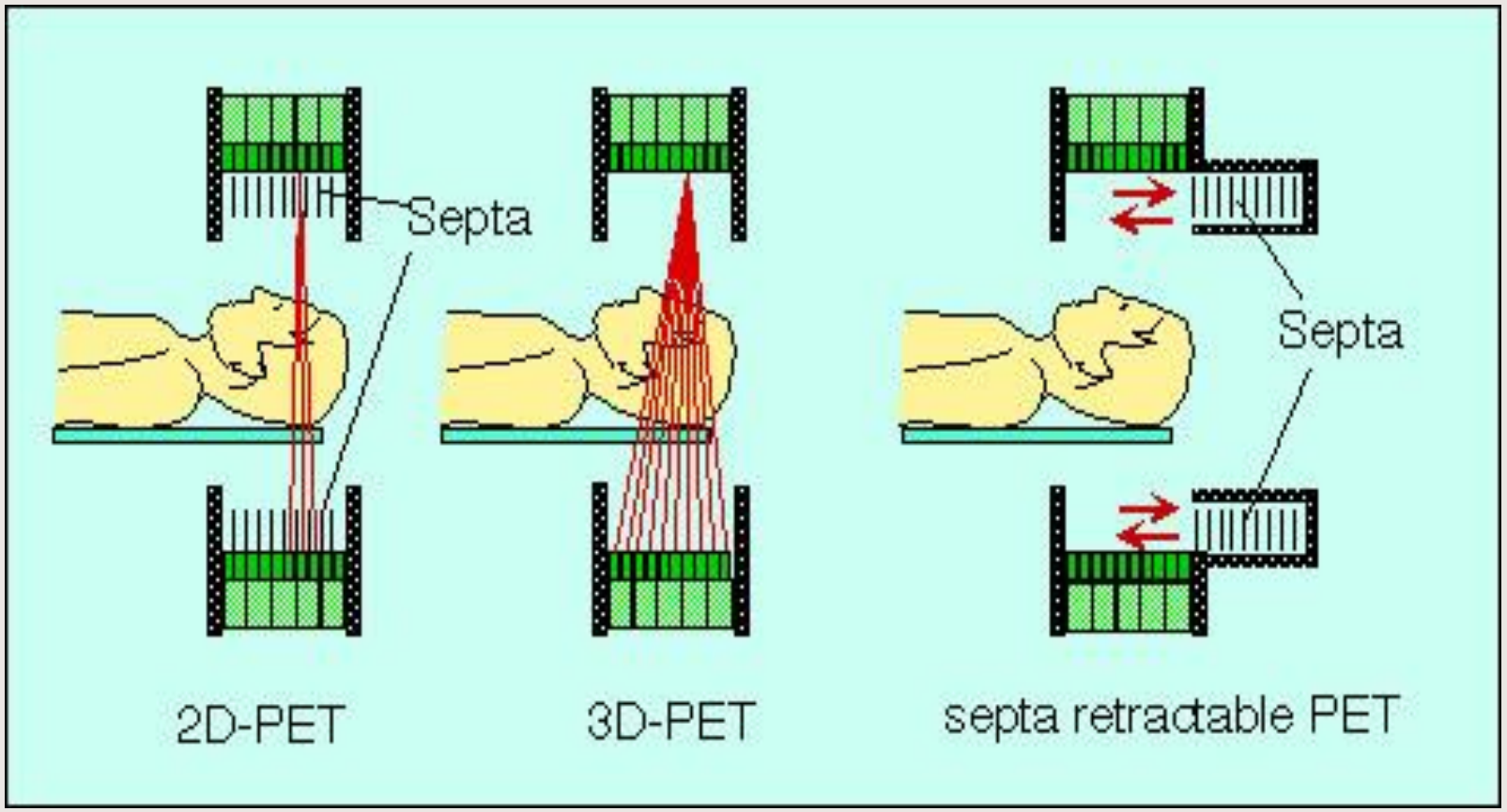
6 Months



12 Months

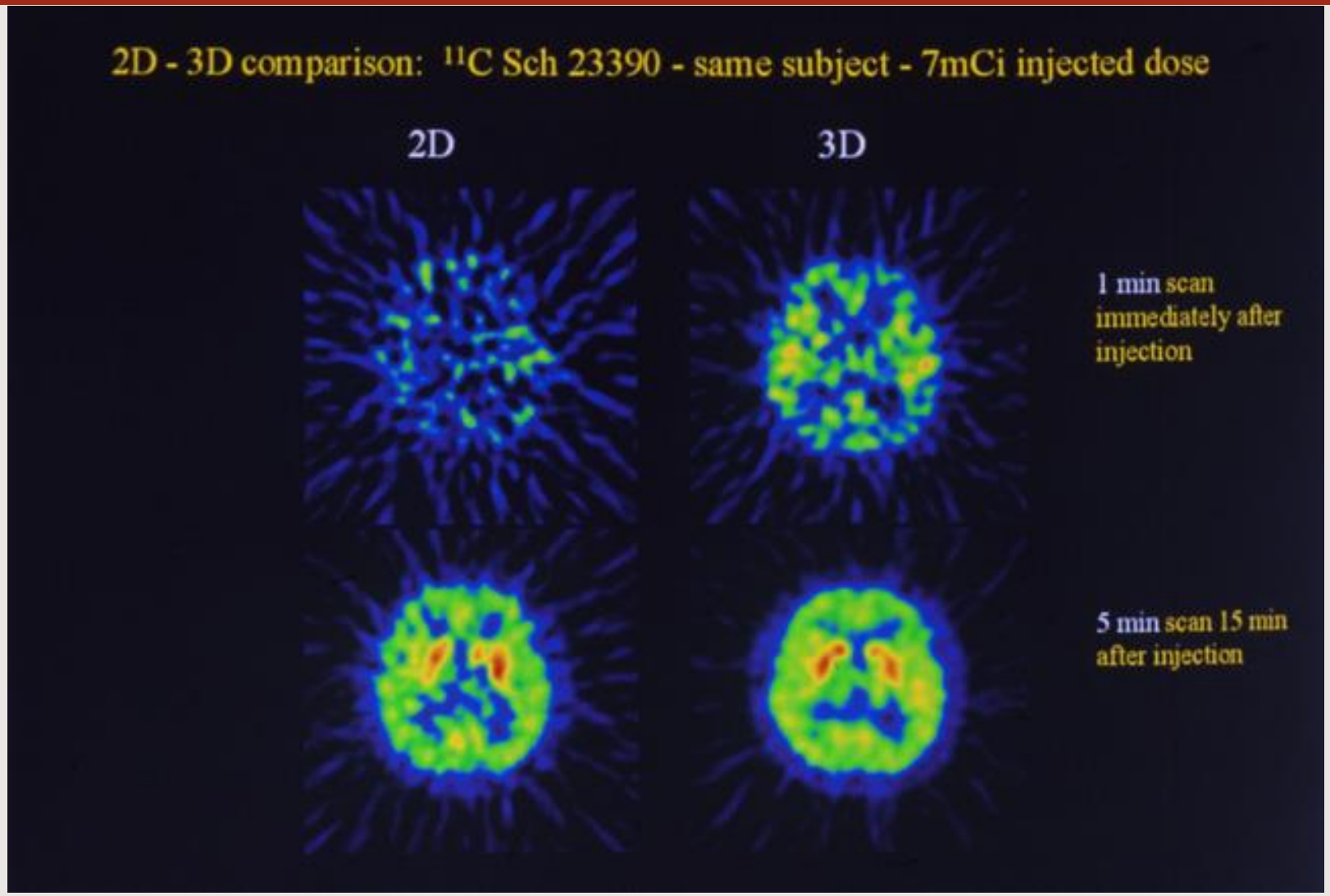

Pre- transplant
1 yr after
2yrs after
4 donor- group
1-donor group
placebo

ECAT 953B Scanner

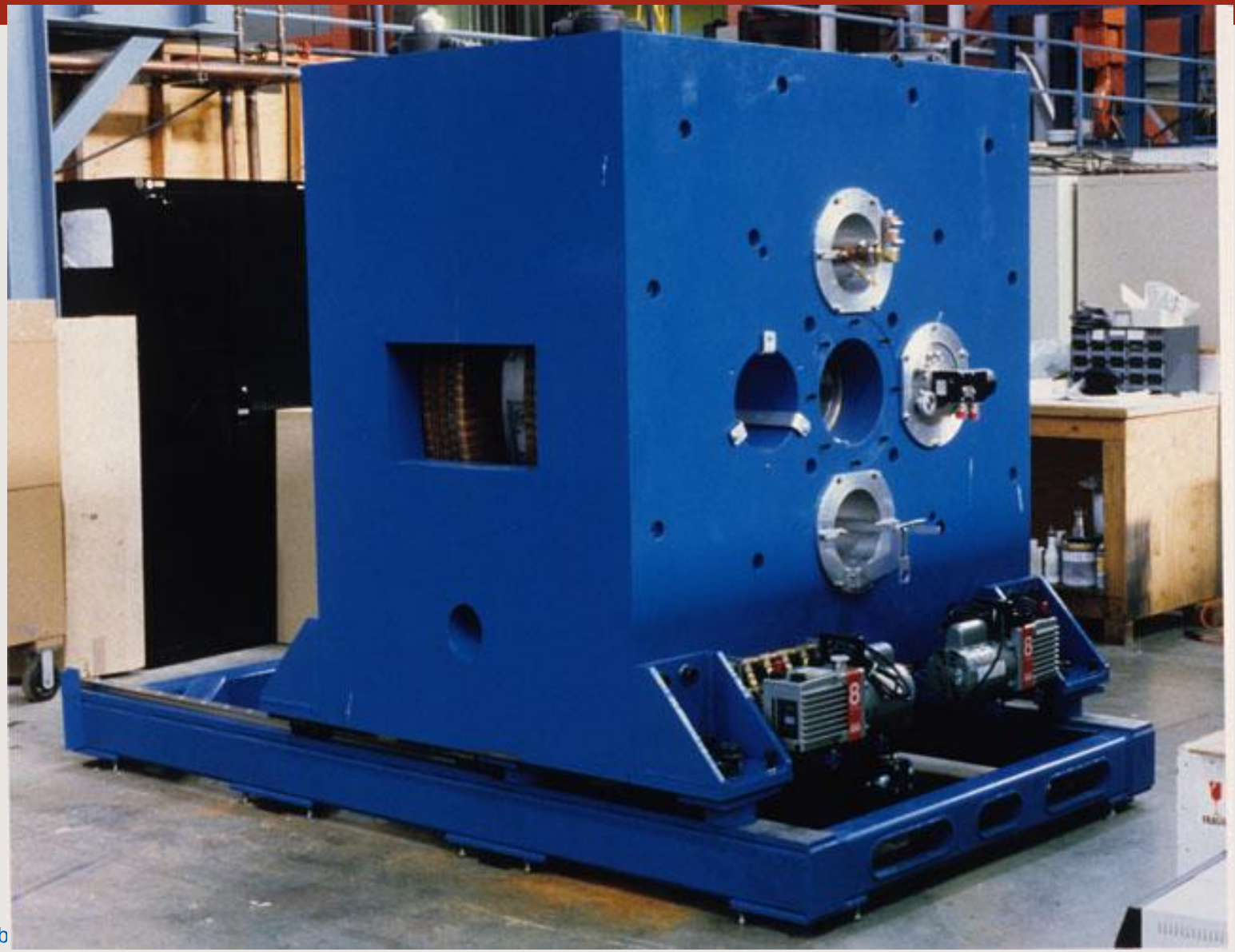


Paul Kinahan, UBC MSc student developed first 3D reconstruction code

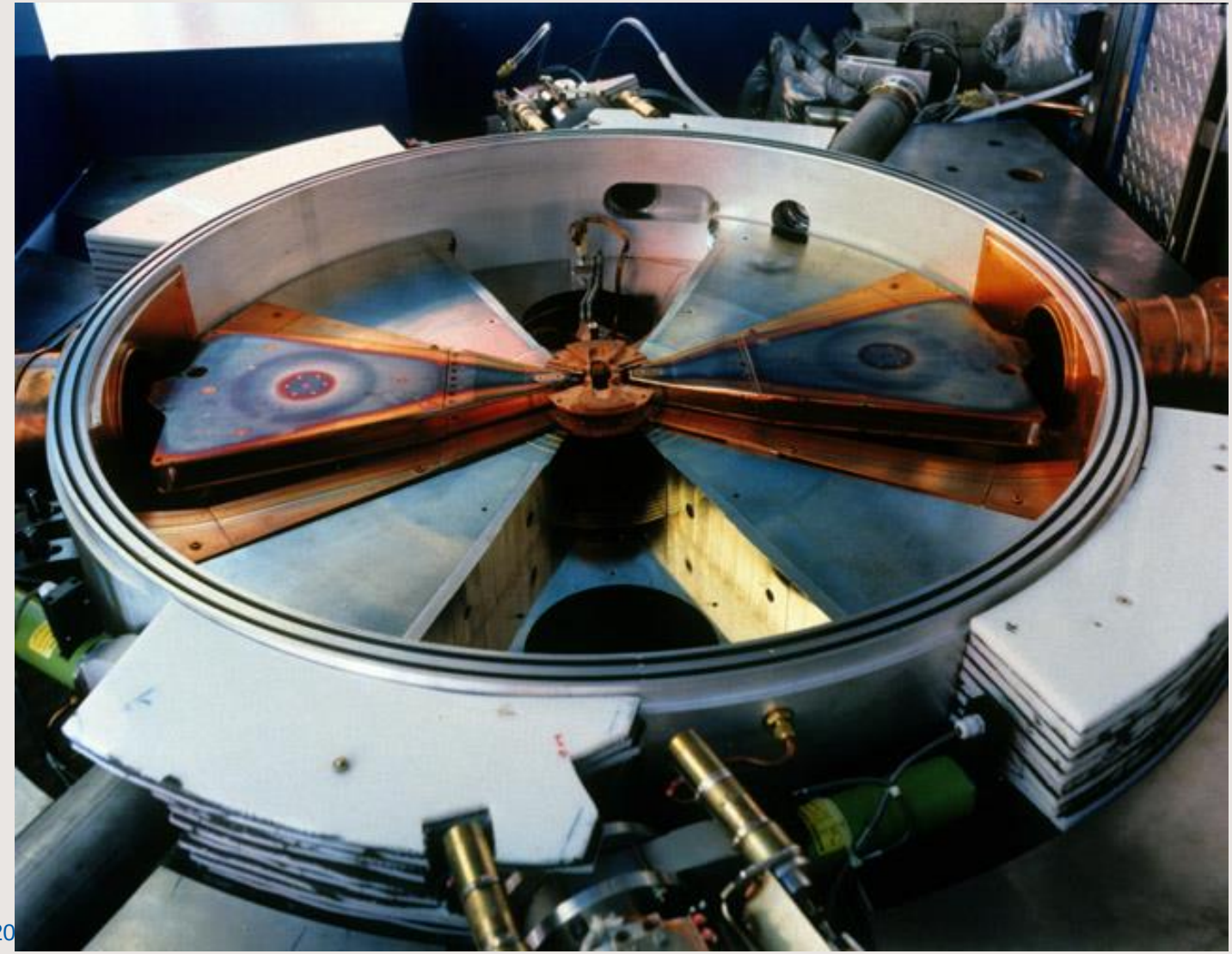
Early 3D Scans – ECAT 953



TR19 (13) Magnet in factory



TR13 Dees



TR13 Cyclotron 1993

Radiopharmaceuticals

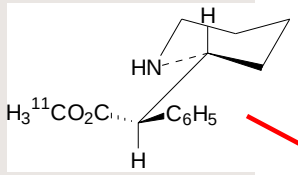
- Dopamine system
  - ^{18}F-FDOPA
  - ^{11}C-Methylphenidate
  - ^{11}C-Dihydrotetrabenazine
  - ^{11}C-Raclopride

Pacific Parkinson's Research Centre

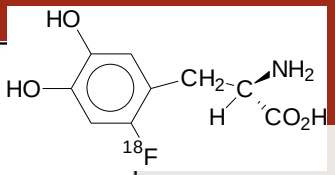
- Goals:
  - Determine the origins of PD
  - Follow natural history of disease (Progression)
  - Develop treatments
  - Control complications of treatment

A. Jon Stoessl - Director

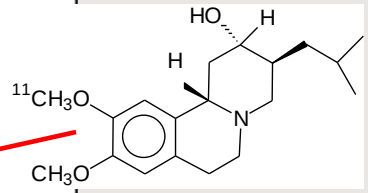
Tracers available with TR13



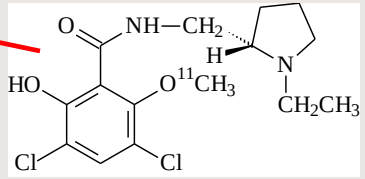
Methylphenidate



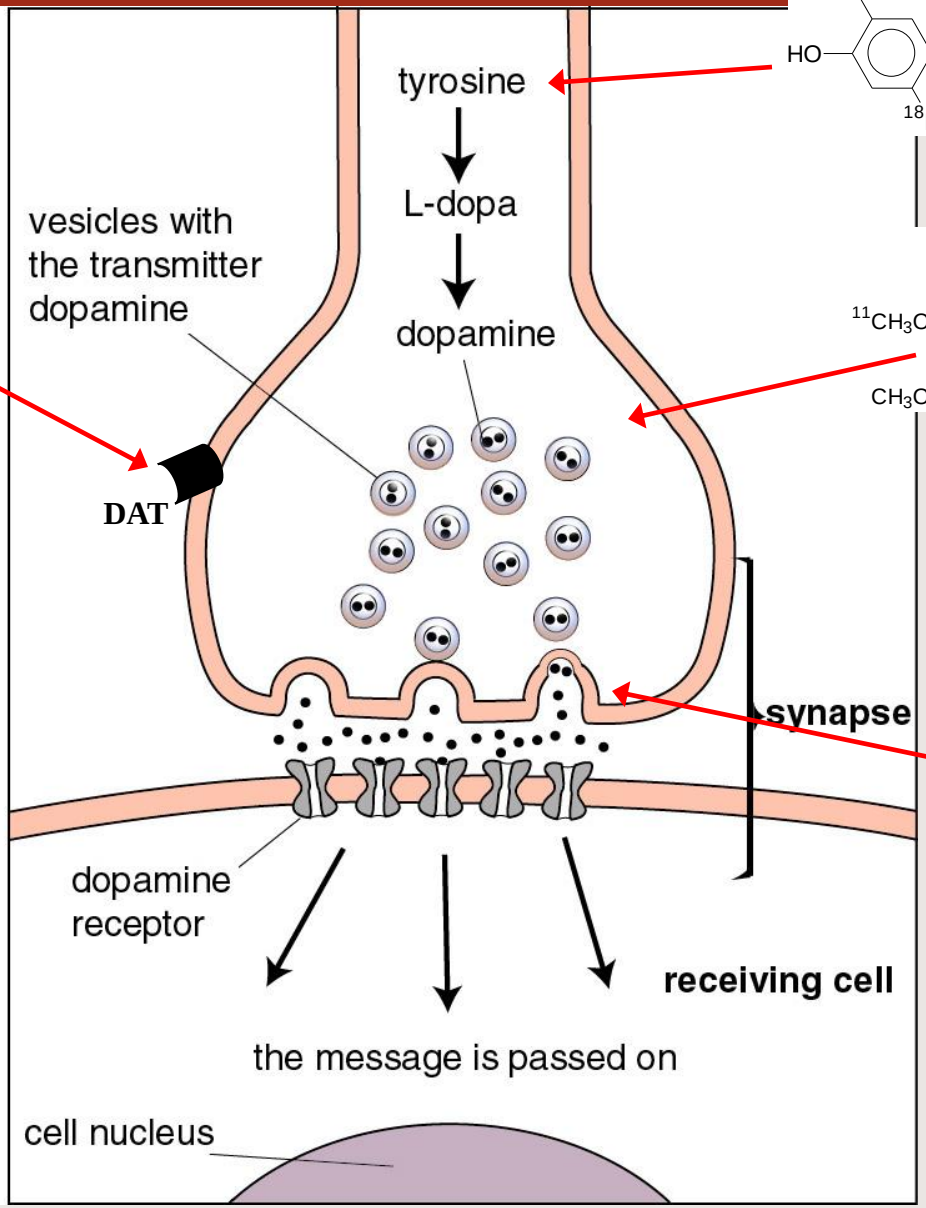
F-Dopa

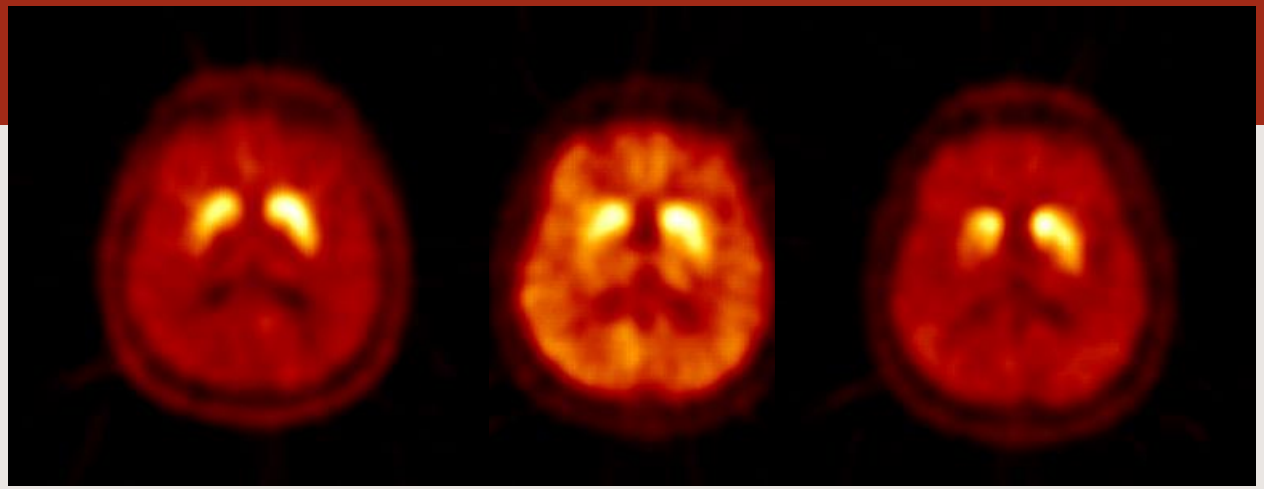


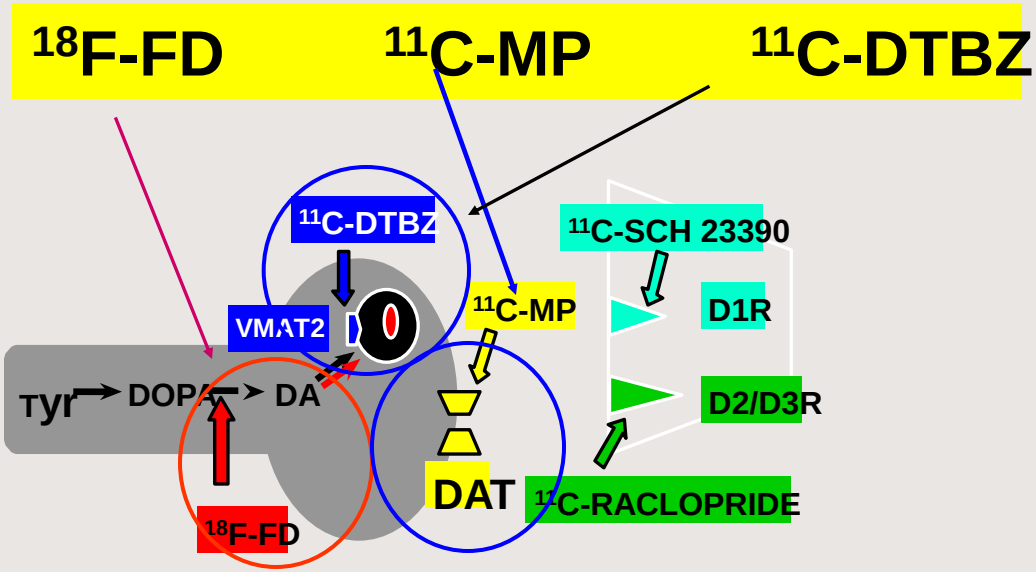
Dihydrotetrabenazine



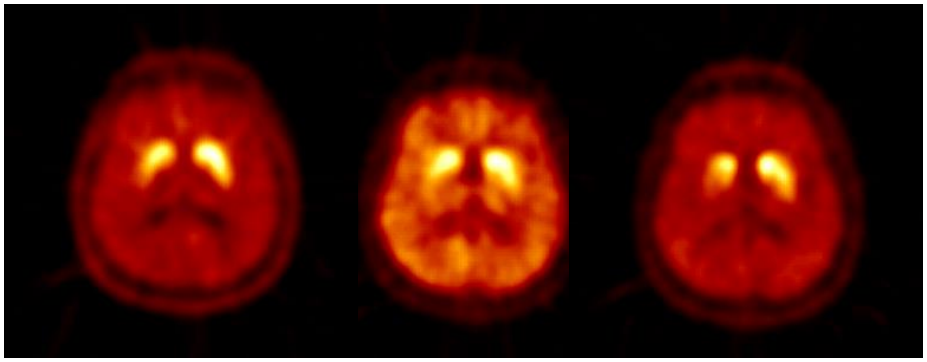
Raclopride



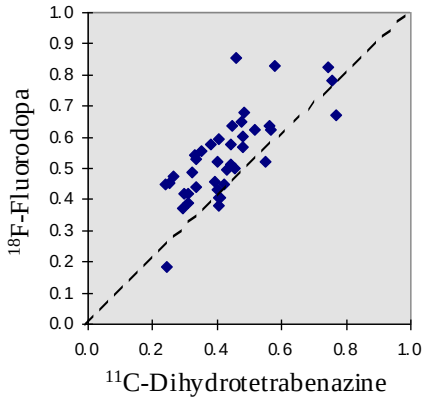


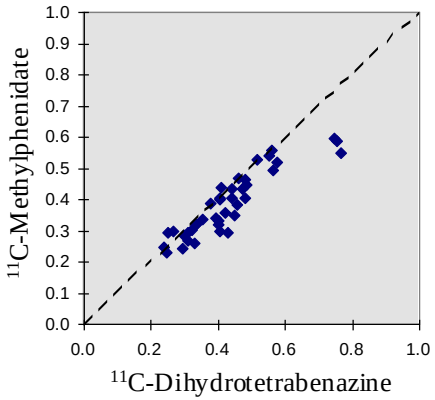

18F-FD
11C-MP
11C-DTBZ
11C-DTBZ
VMAT2
Tyr
DOPA
DA
18F-FD
11C-MP
DAT
11C-SCH 23390
D1R
D2/D3R
11C-RACLOPRIDE

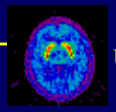
Asymmetric Parkinson's



^{18}F-Fluorodopa ^{11}C-Methylphenidate ^{11}C-Dihydrotetrabenazine

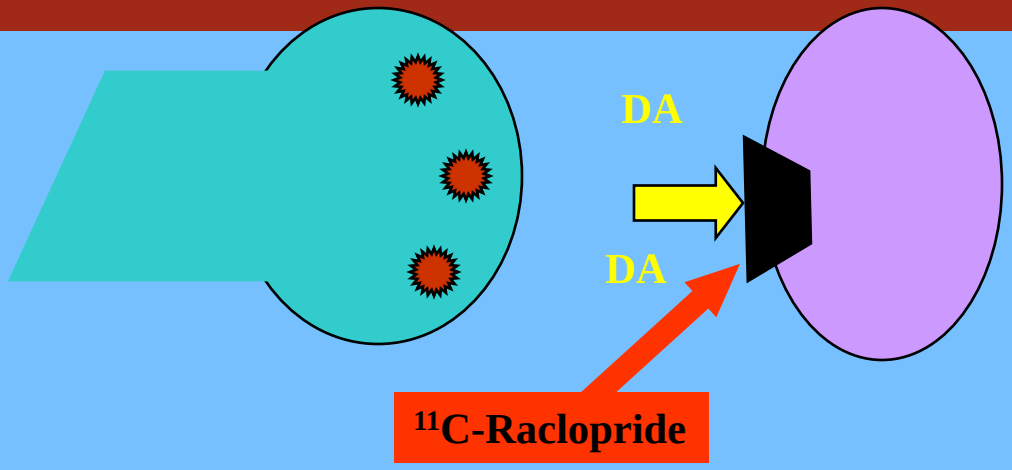


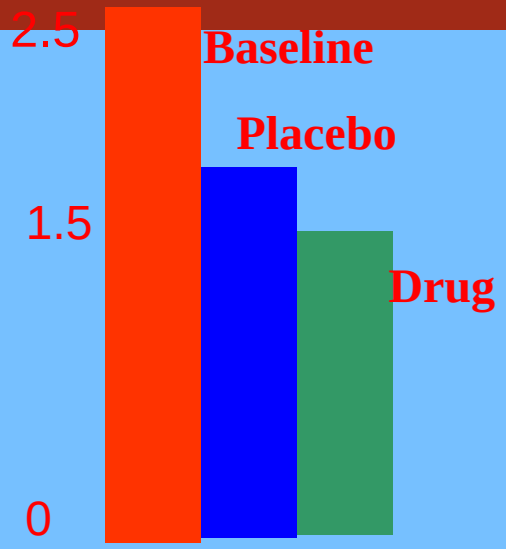




UBC/TRIUMF PET

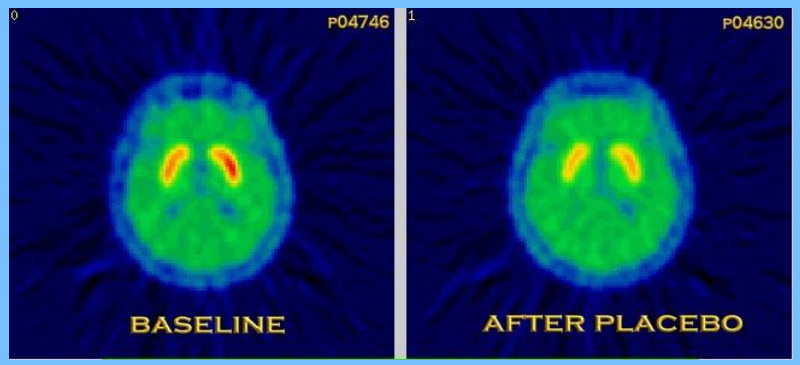
In vivo assessment of endogenous DA concentration



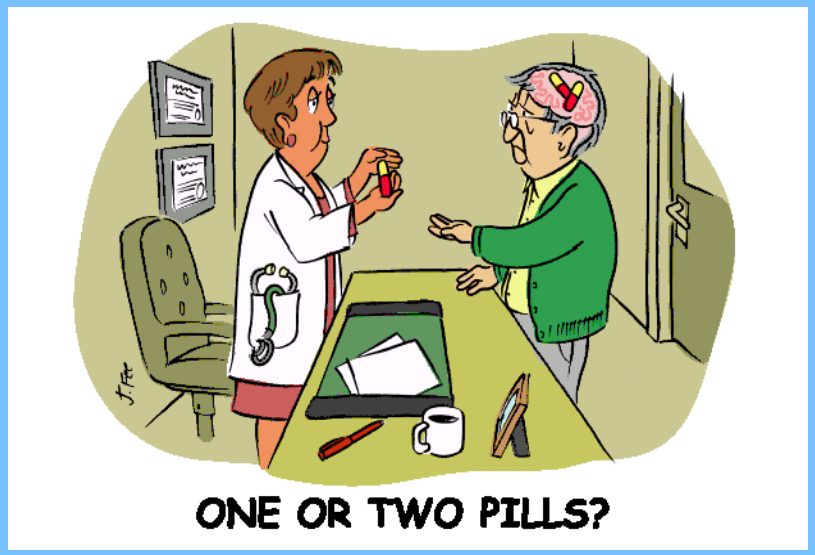


Endogenous DA competes with raclopride for the D2 receptor

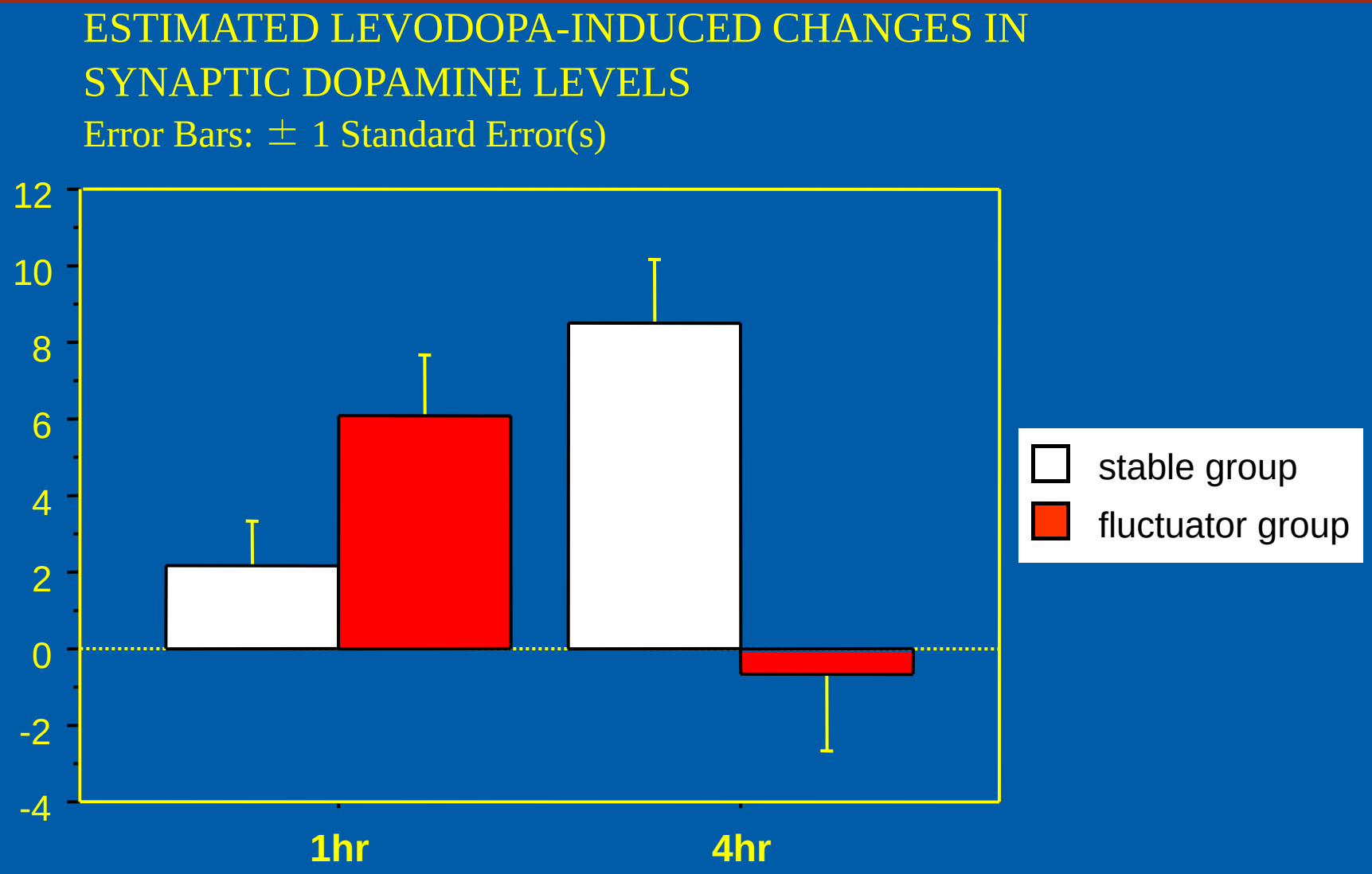
Apomorphine-induced changes in raclopride binding



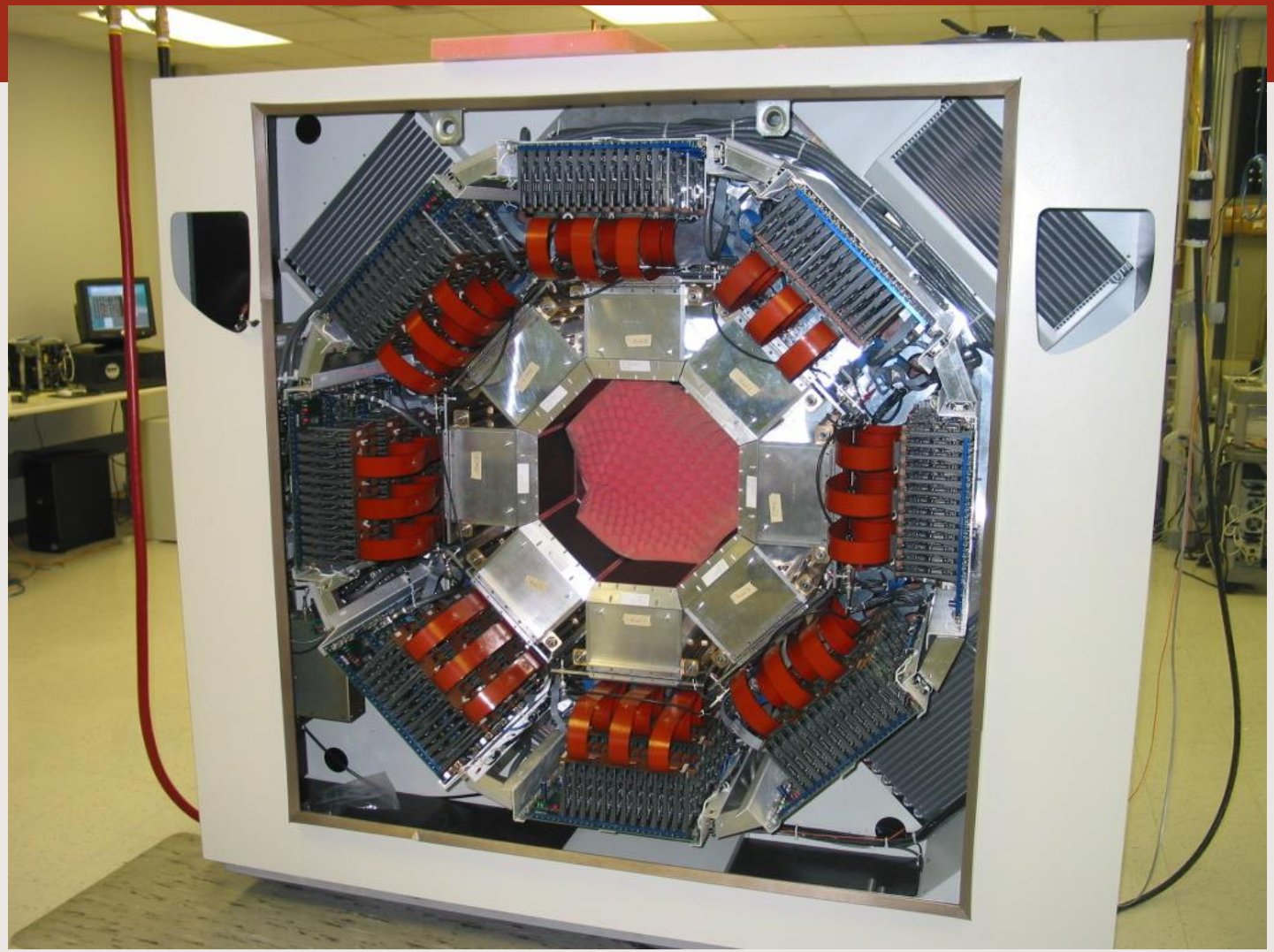
Lower raclopride binding indicates higher dopamine concentration



Relationship between abnormal dopamine release and turnover and the subsequent development of complications of therapy



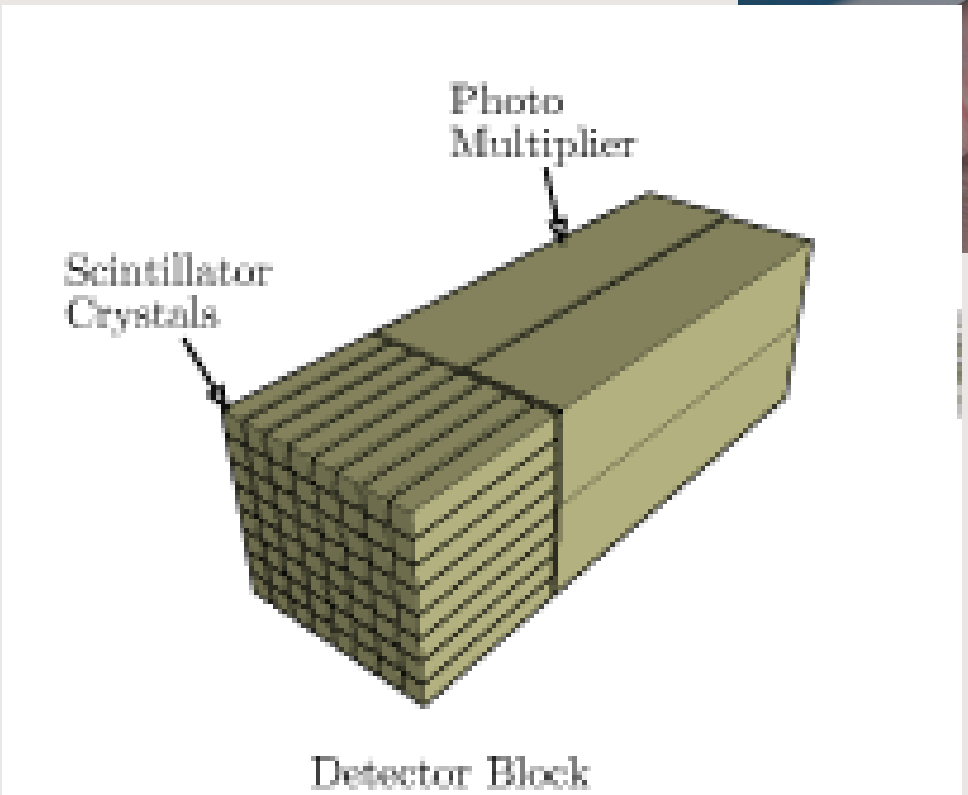
UBC/TRIUMF HRRT

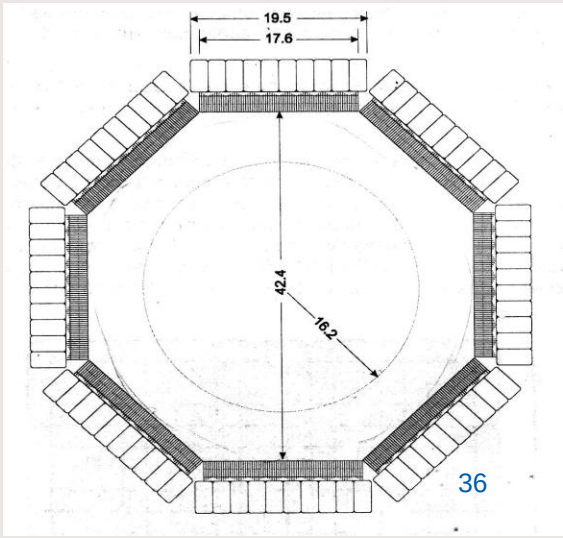


High Resolution Research Tomograph

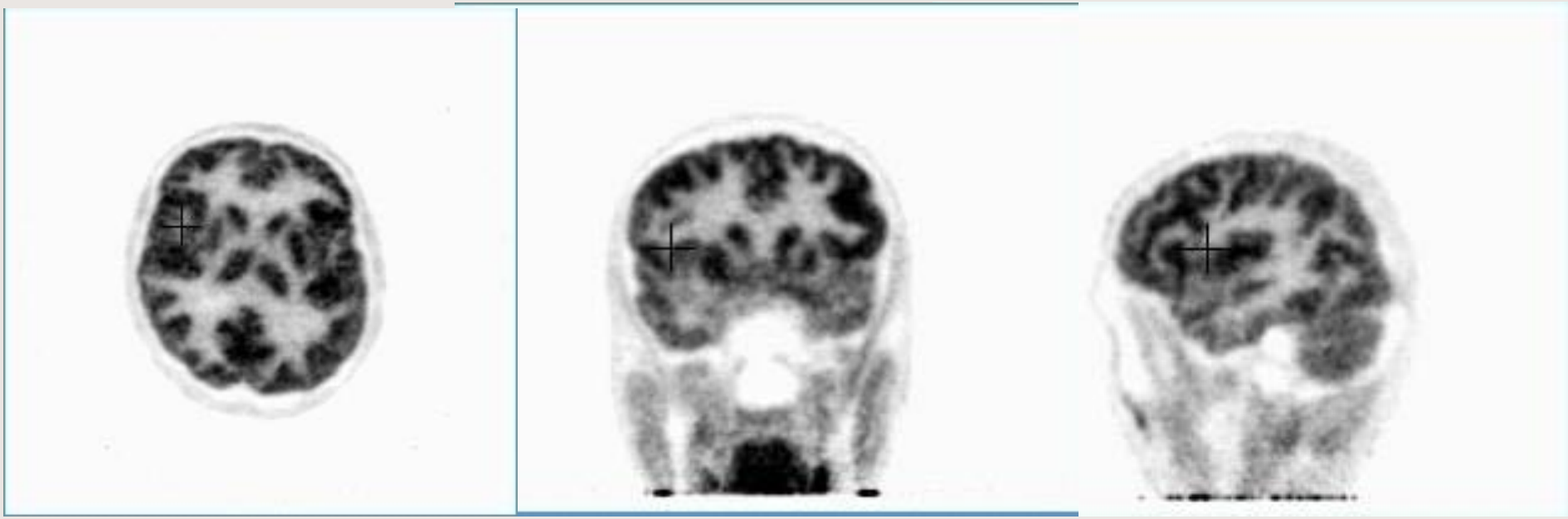
- 119,000 detector elements
- 4,000,000,000 lines of response
- > 1Gbyte of data per image frame

Crystal material: LSO/LYSO
Crystal size 2.1 x 2.1 x 10 mm^3





FDG Images from the HRRT



Axial

Coronal

Sagittal

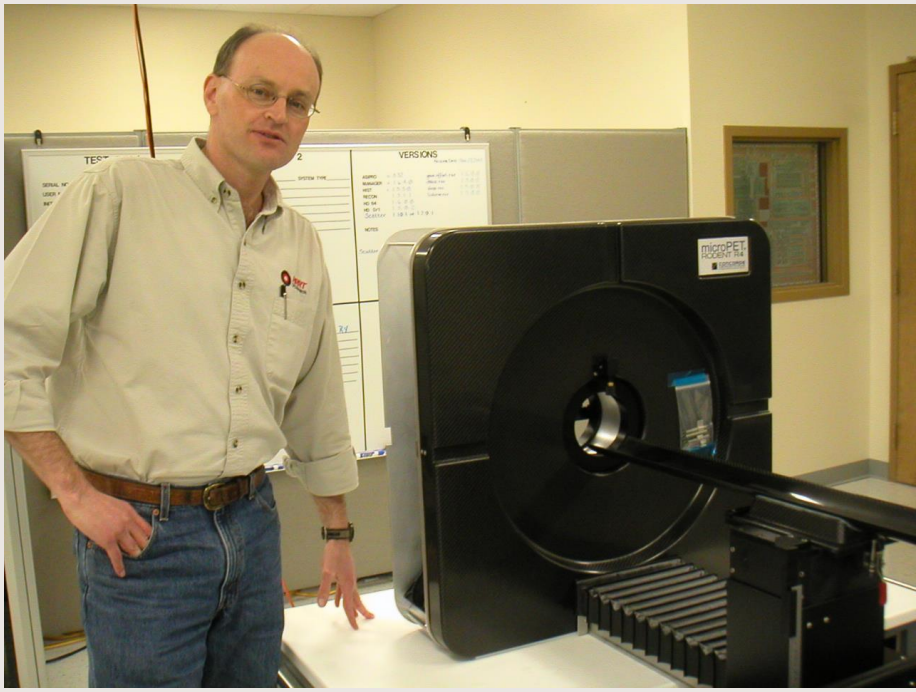
Additional Questions for PET:

- New drugs for diabetes
- Spinal cord research
- Enzymology
- The mouse genome and knock in/out models
- Learning
- Dyskinesia
- Cancer research

microPET

10 April 2003

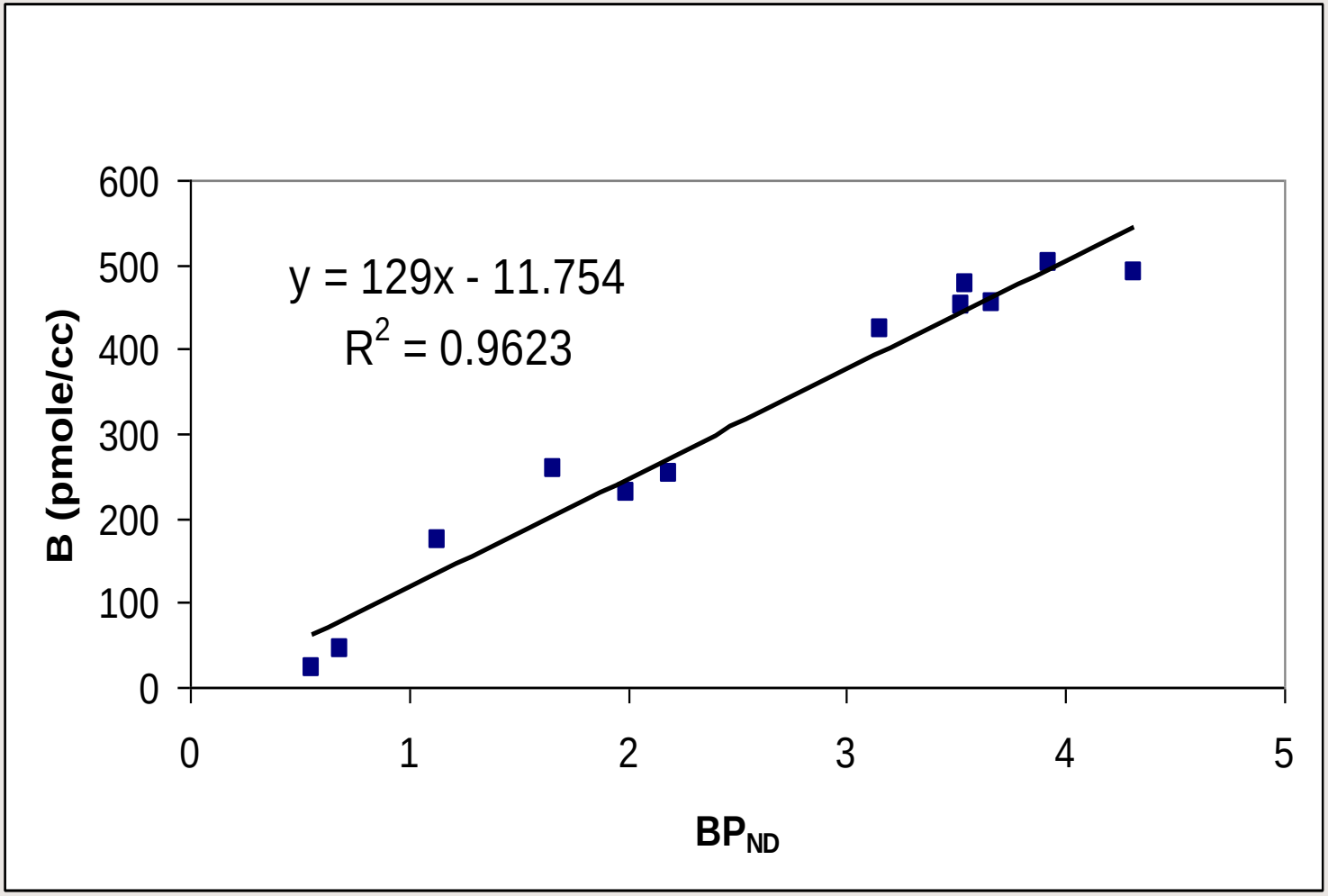
- 32 detector modules (8x8)
- 1920 individual LSO elements
- ring diameter 17.2 cm
- 10 cm transaxial FOV
- 1.8 cm axial FOV
- volume resolution ~ 8 mL
- sensitivity: 200 cps/µCi
- cost ~ $ 450K USD



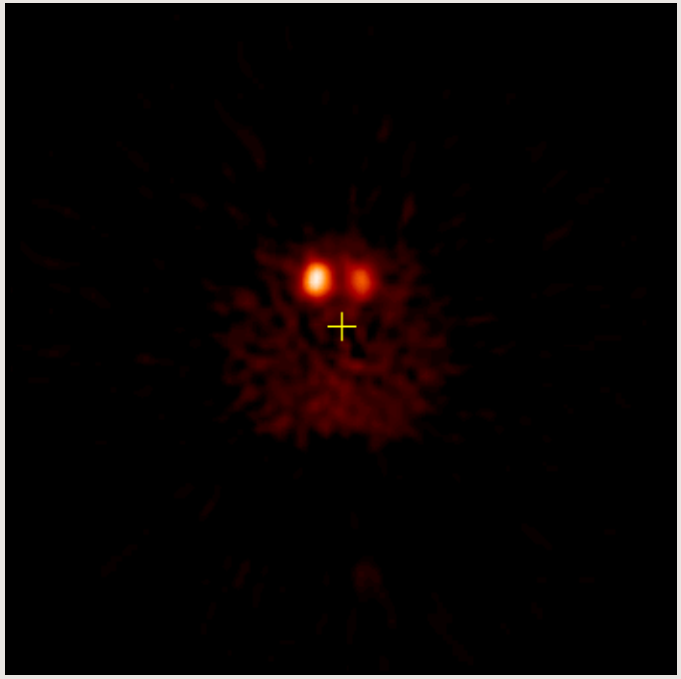
Validation of Tracers

- From the very beginning we validated the tracers we used
- We calibrated the scanners so that the regions of interest could be viewed as Bq/cm^3
- With modelling the results could be interpreted with quantitative biological metrics

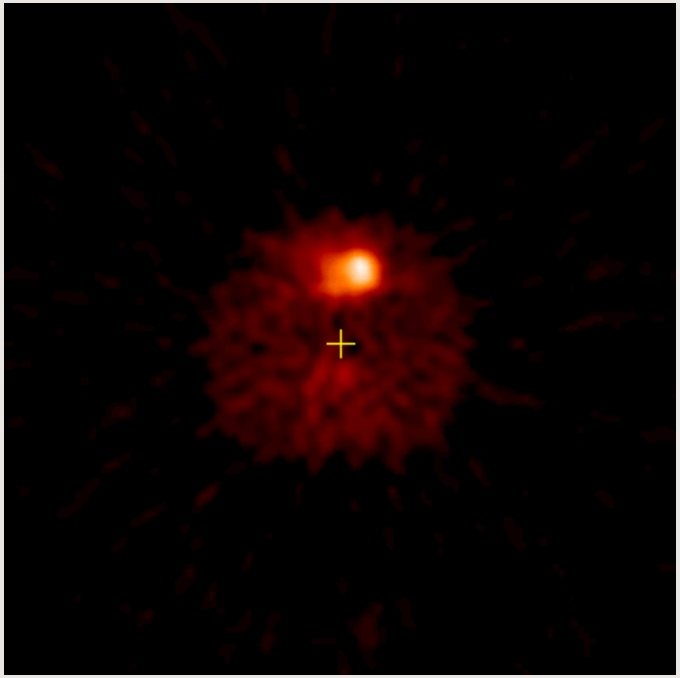
VMAT in lesioned rat (comparing postmortem to Binding Potential (PET))



^{11}C-DTBZ (rat)



^{11}C-raclopride in same rat.

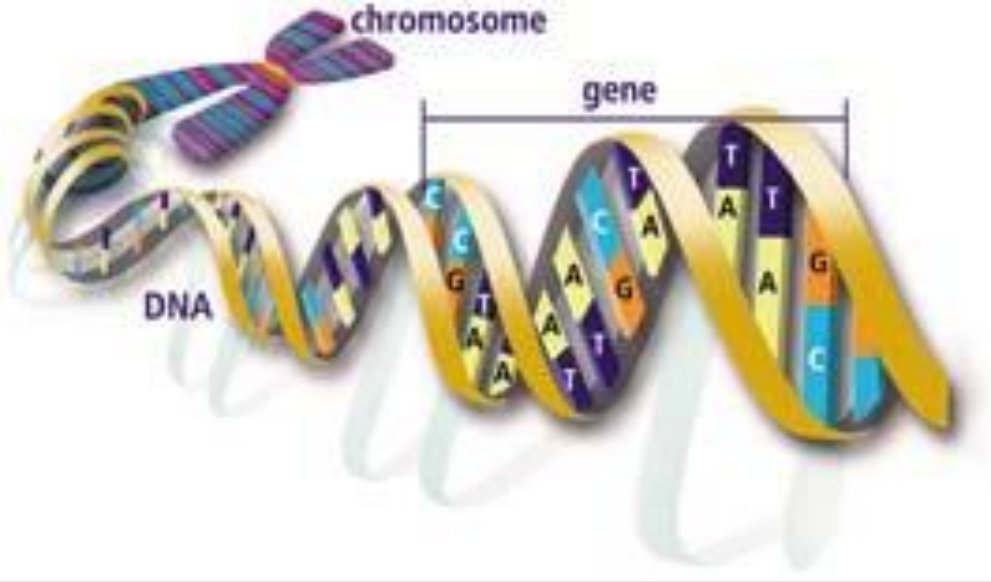


What have we learned about Parkinson's Disease thus far?

- Preclinical changes in PET indices.
- Asymptomatic patients progress to disease.
- Early signs of compensation.
- Singular events can cause parkinsonism.
- Evidence of our *Event* hypothesis including progression.

Future of Research PET

- The tracers we presently use *look* at the system response to disease.
- What we need are tracers that *look* at the disease process itself.
- We need to get closer to the *action*!
- This will provide the basis for personalized medicine.



Collaborations Beyond UBC/TRIUMF PET: *^{18}F & FDG Supply*

Alberta Cancer Board

^{18}F-

FDG

μPET

BC Cancer Agency
CARE & RESEARCH

LION'S GATE HOSPITAL
Nuclear Medicine

VANCOUVER HOSPITAL
& Health Sciences Centre
Division of Nuclear Medicine

St. Paul's Hospital
Department of Nuclear Medicine

PETscan
vancouver

PET/CT

Acknowledgements

- Brian Pate
- Mike Adam
- Salma Jivan
- Ken Buckley
- Donald Calne
- Jon Stoessl
- Doris Doudet
- Many, many, many individuals required to enable a complex collaborative effort to be successful.

No matter how lost I was, Eric could be counted upon to set me straight!

Thank you!
Merci!

TRIUMF: Alberta | British Columbia | Calgary | Carleton | Guelph | Manitoba | McMaster | McGill | Montréal | Northern British Columbia | Queen's | Regina | Saint Mary's |
Simon Fraser | Toronto | Victoria | Winnipeg | York