

From Antimatter to disease prediction: How basic physics impacts our health care.

Thomas J. Ruth, PhD

TRIUMF Saturday Lecture Series

20 January 2007

**How can we probe the human body
without a knife?**

**But first some fundamental ideas that
are needed to understand this topic.**

Size matters!

How big is Avogadro's number – 6.02×10^{23} ?

Each Smartie – 1 cm^3 or 1 mL

1 mole of Smarties = $6 \times 10^{23} \text{ mL}$

Assume a truck with a capacity of 90 m^3 ($10 \times 3 \times 3$)
= $9 \times 10^7 \text{ mL}$

The number of trucks needed – 6×10^{15}

If each truck is 13 m long, that means that lined up they would be $7.8 \times 10^{13} \text{ km}$ in length or 200,000,000 earth to moon distances.

1 grain of salt – 0.12 mg

= 2×10^{-6} moles (or 2 micromoles)

= 3×10^{17} molecules

This issue will come up later in our discussion of tracers.

What are tracers?

- Techniques or devices that allow one to follow a process.
- For example –
 - Tracing a phone call in TV mysteries.
 - Dropping a toy boat in a stream that bifurcates to determine which path it will follow.

Tracer Principle in Science

- Tracer behaves in a similar way to the components of the system to be probed.
- Tracer does not alter the system in any measurable fashion.
- Tracer concentration can be measured.

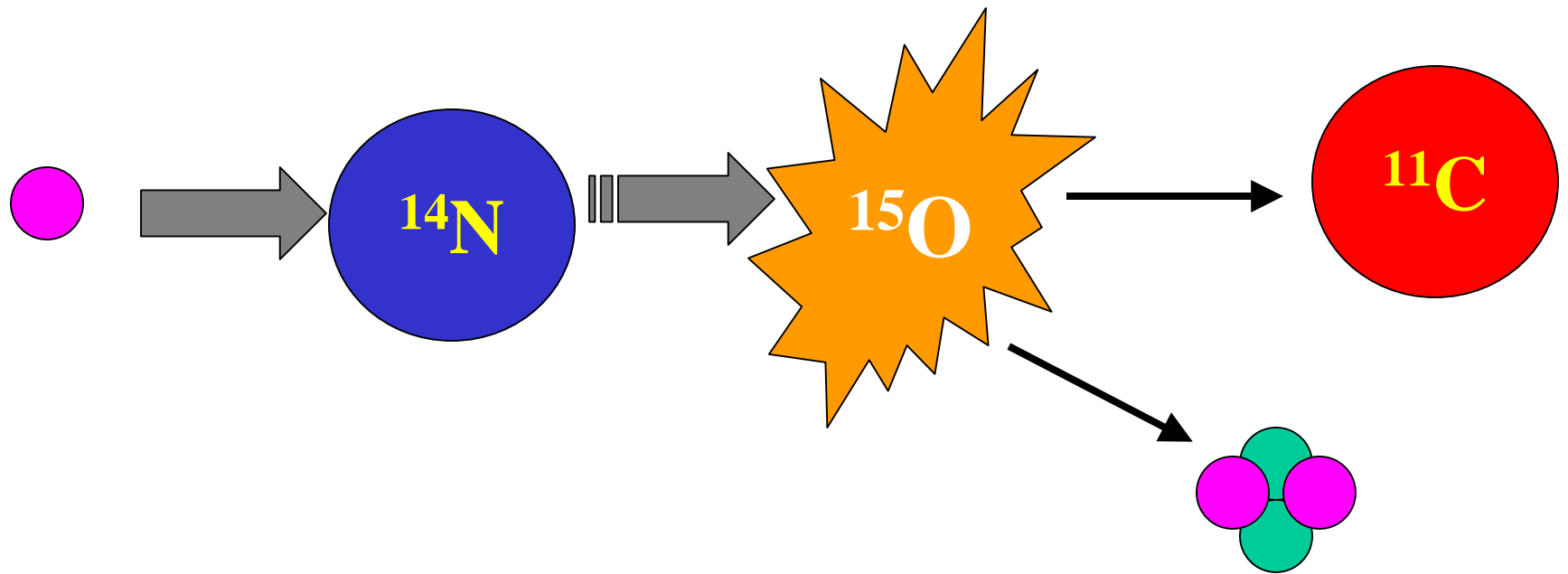
What is a Radiotracer?

- A substance that is radioactive used as a tracer.
- The radioactivity makes it possible to determine where it is and how much is present, an extremely sensitive tool.

Where it all begins!



Production of Radionuclides: True Alchemy



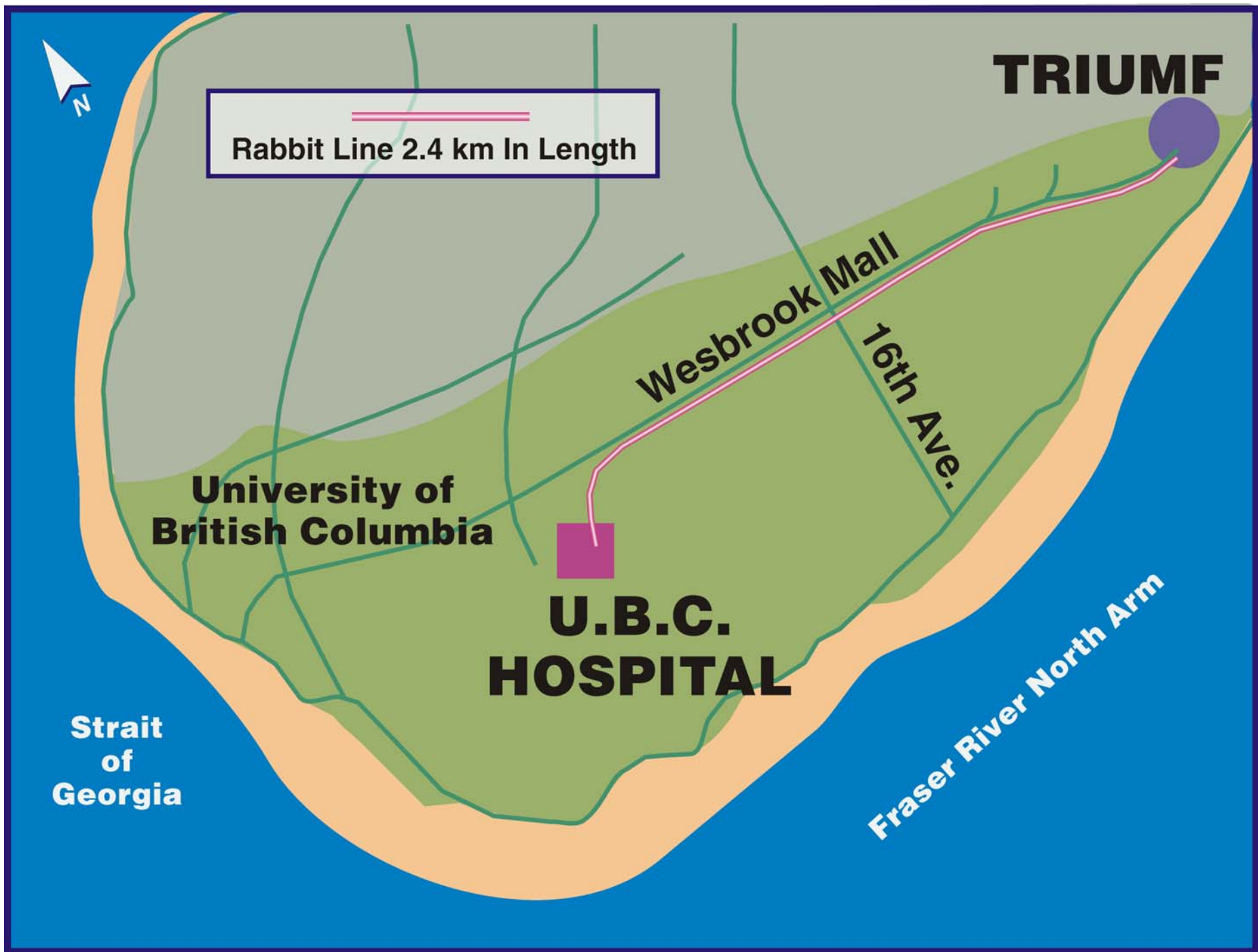
In short:



How do we detect these radiotracers?



[Click here for movie](#)



Diagnostic medicine tries to look into the body
to see what is happening, in life and in death.

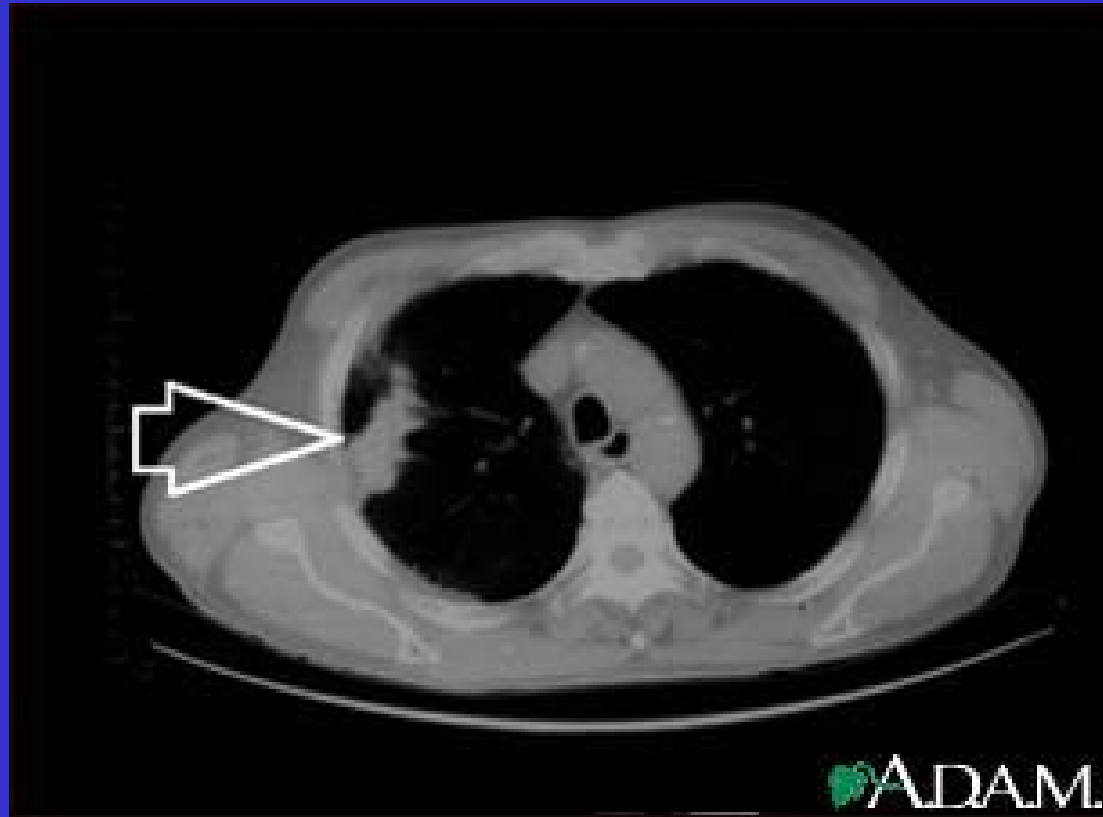


Rembrandt - anatomy lesion

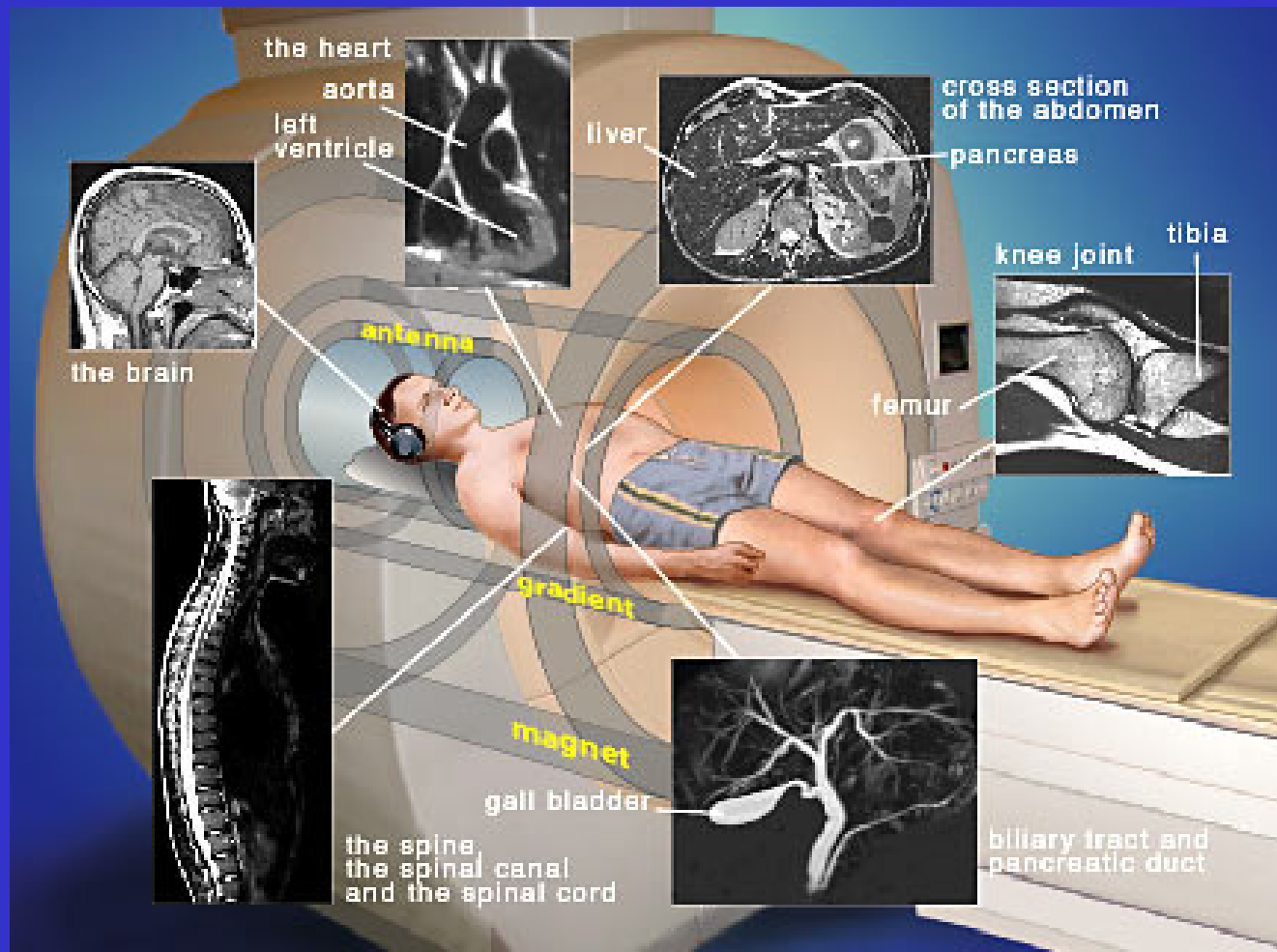
So we come back to our initial question –

***How can we probe the human body
without a knife?***

CT image of lung mass



Magnetic Resonance Imaging (MRI)

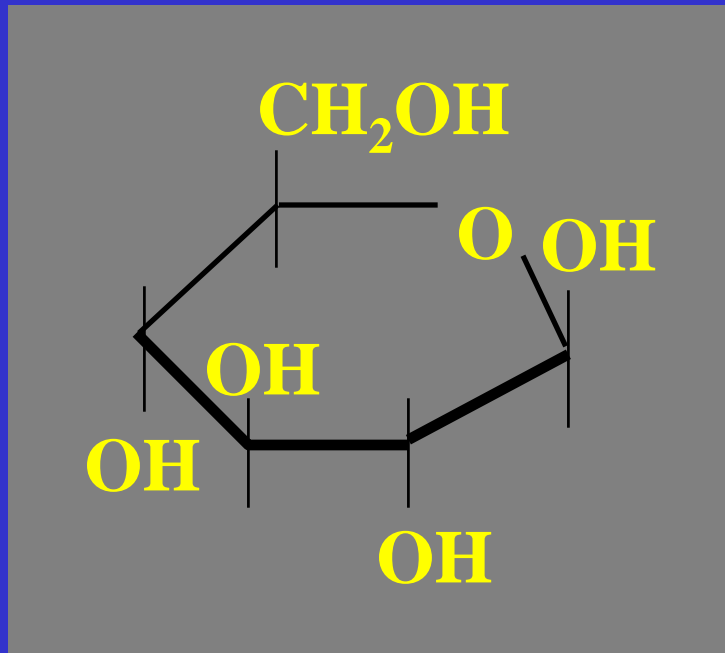


**All of the images shown thus far look at
structure.**

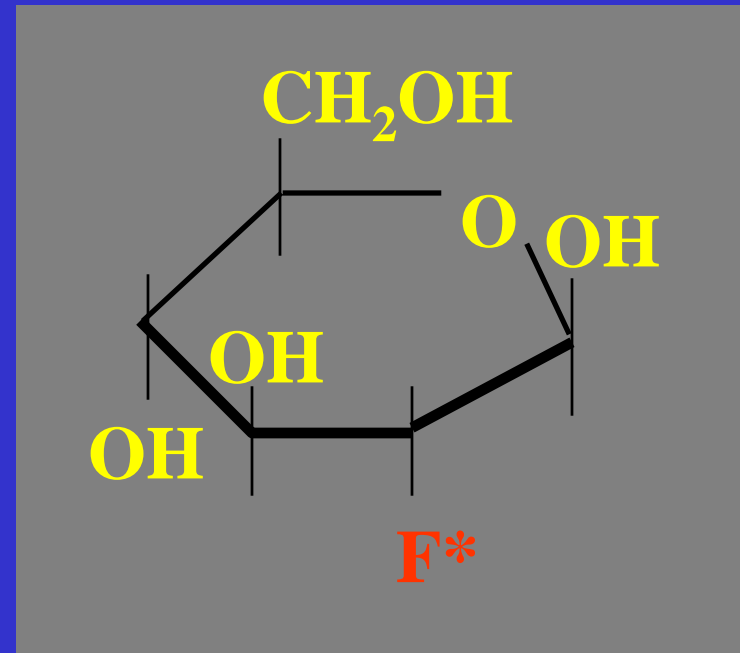
**Many of these images would look the same
in a living person or in a cadaver.**

What about function?

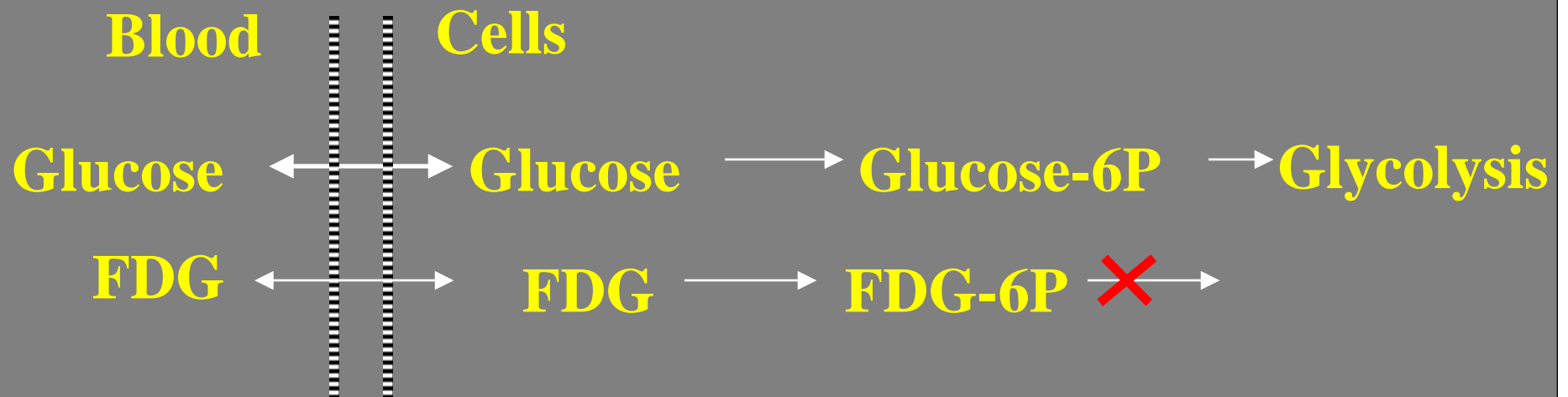
Glucose



Fluorodeoxyglucose (FDG)



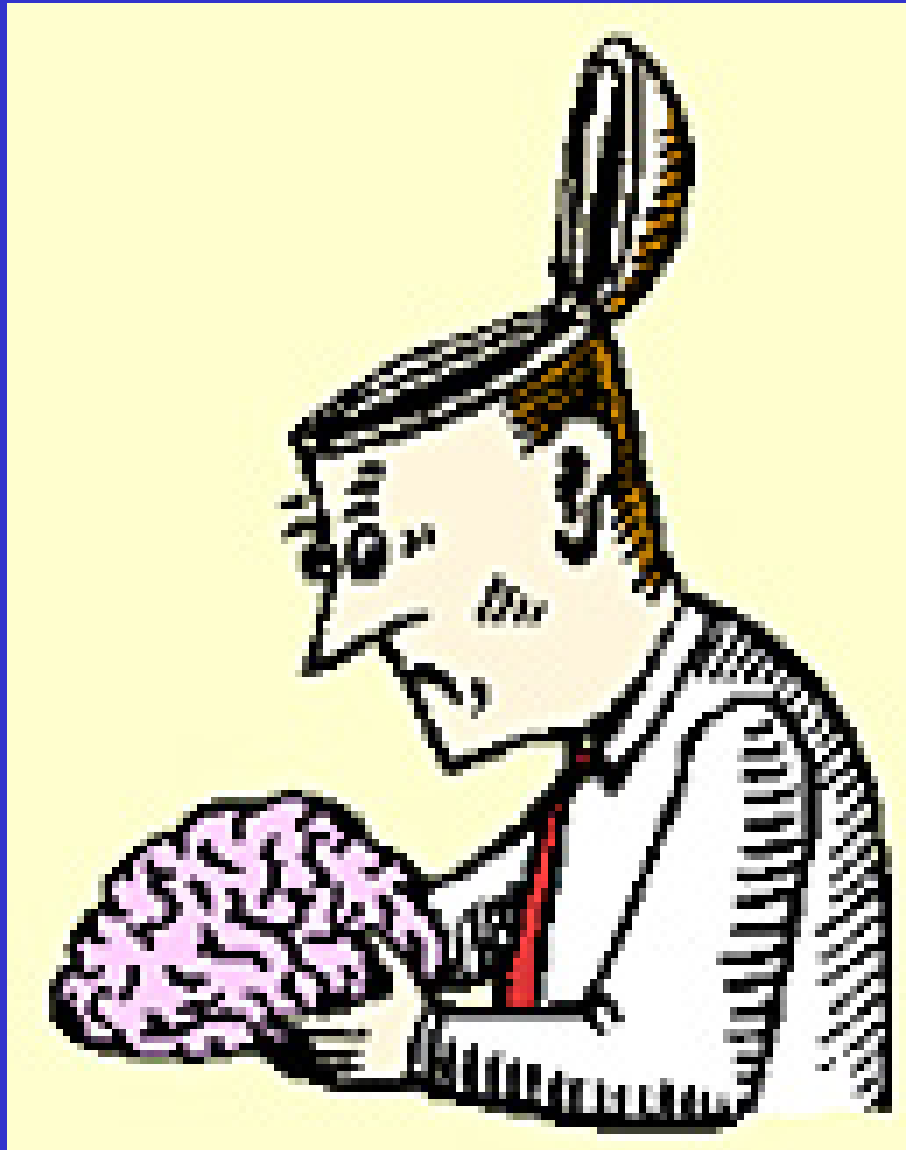
FDG Uptake and Retention





[Click here for movie](#)

Brain Research

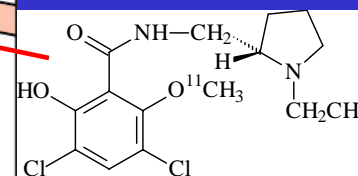
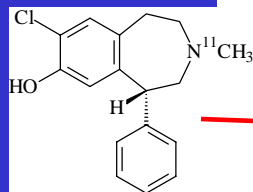
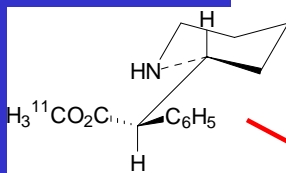
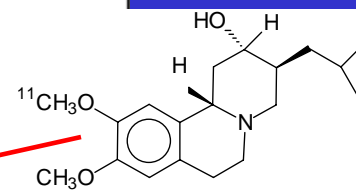
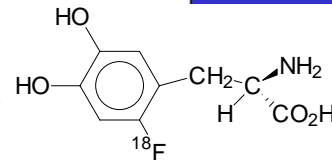
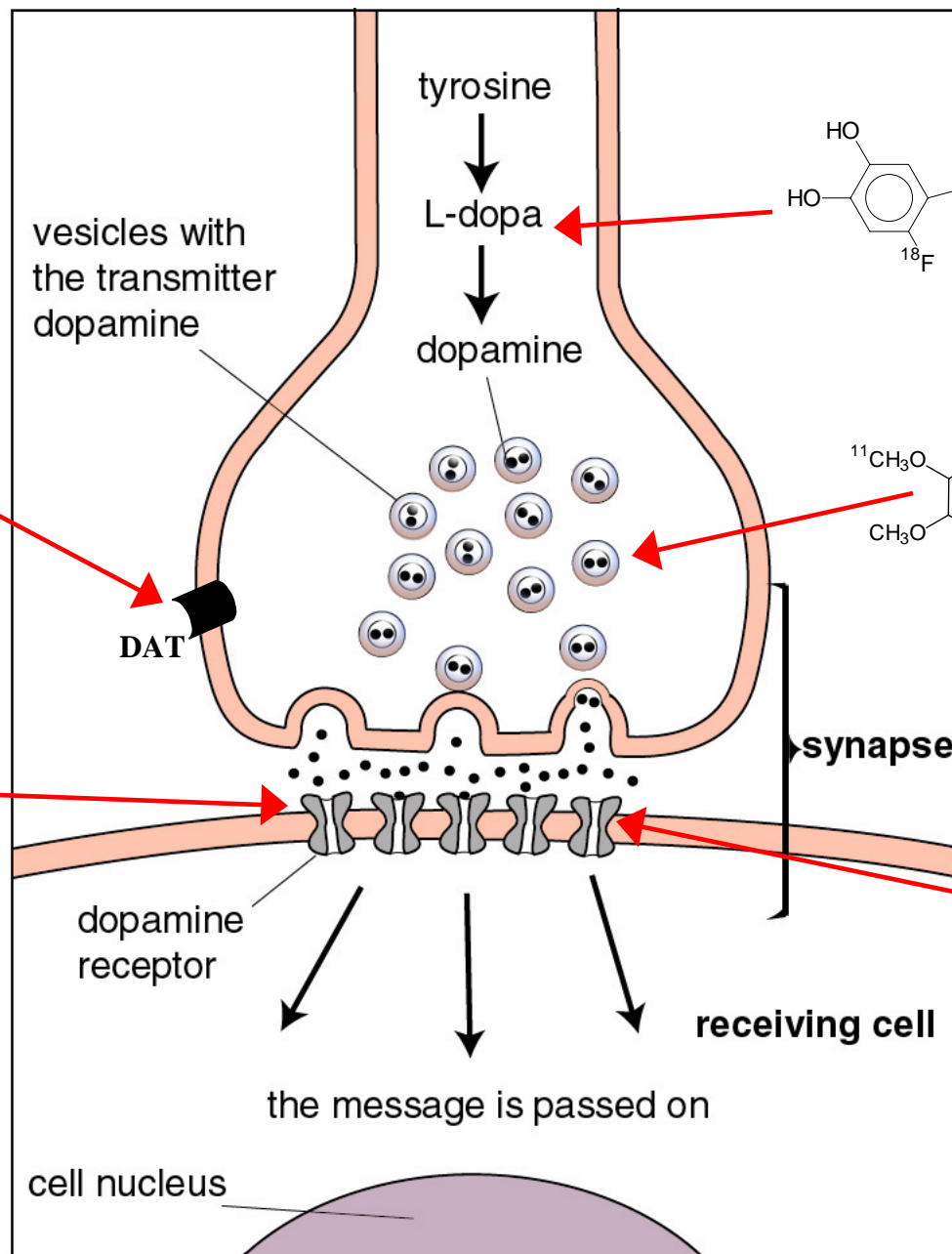


**The brain, my second most
favorite organ.**

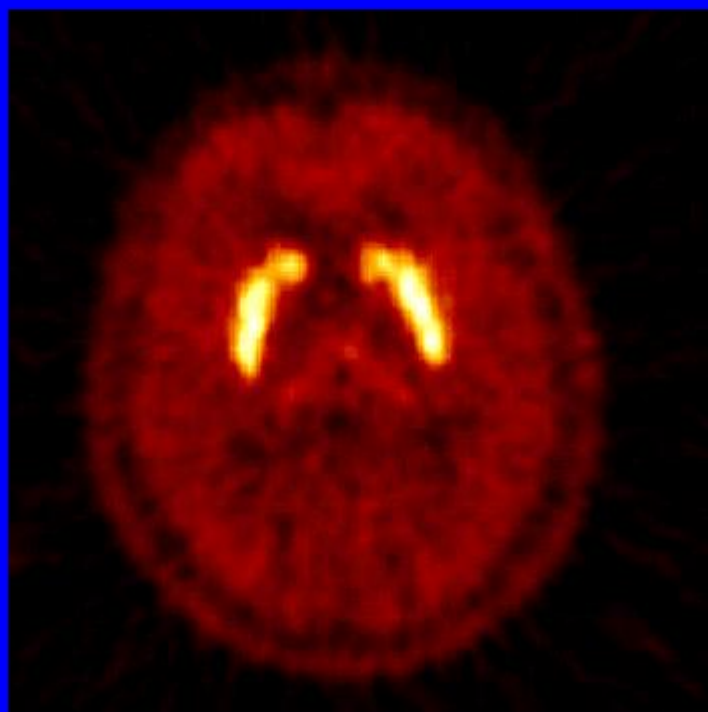
Woody Allen

Pacific Parkinson's Research Centre

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



^{18}F -Fluorodopa PET Scan



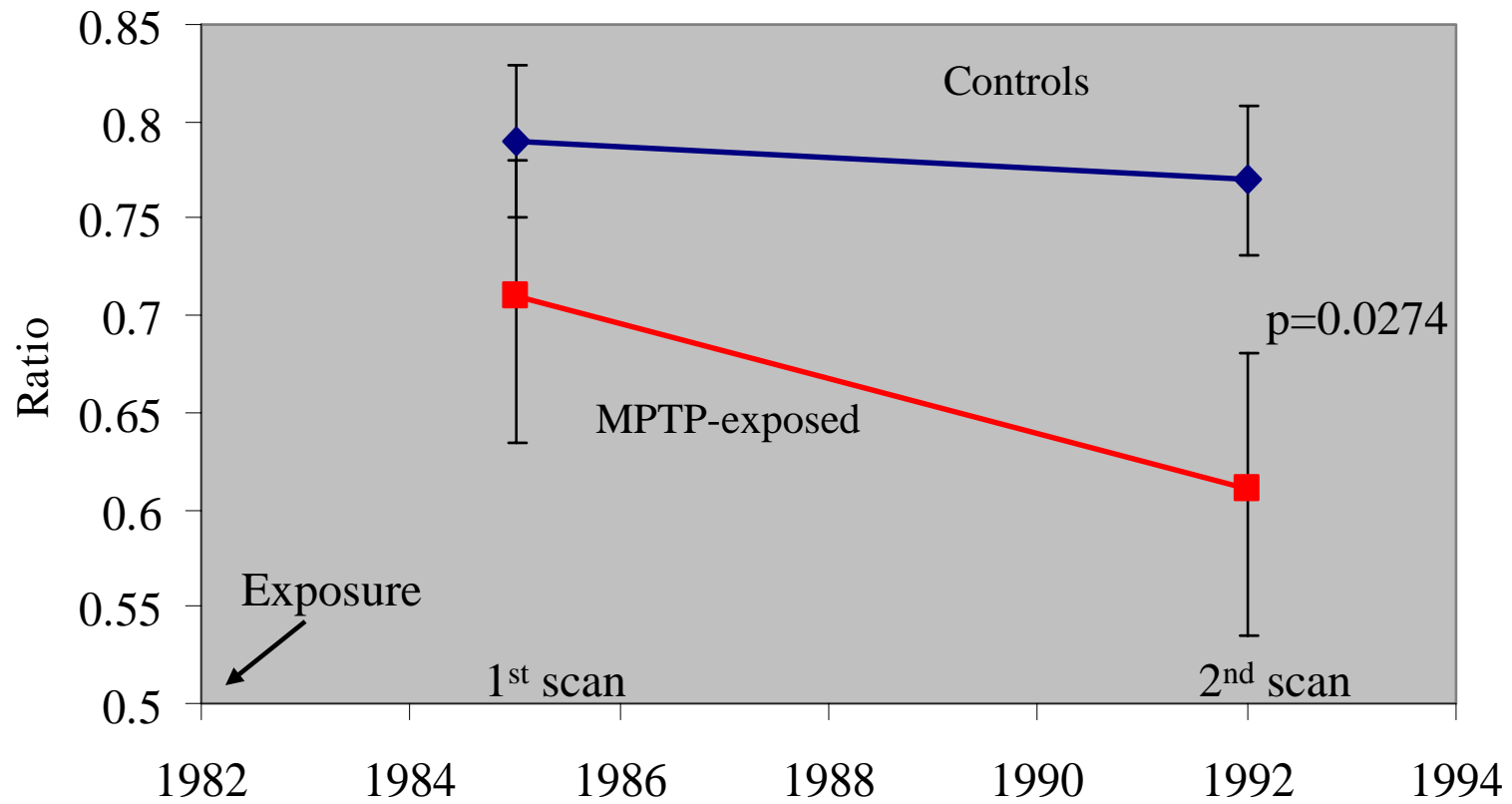
Normal



Parkinson's Disease

UBC/TRIUMF PET Program

FD-PET Progression



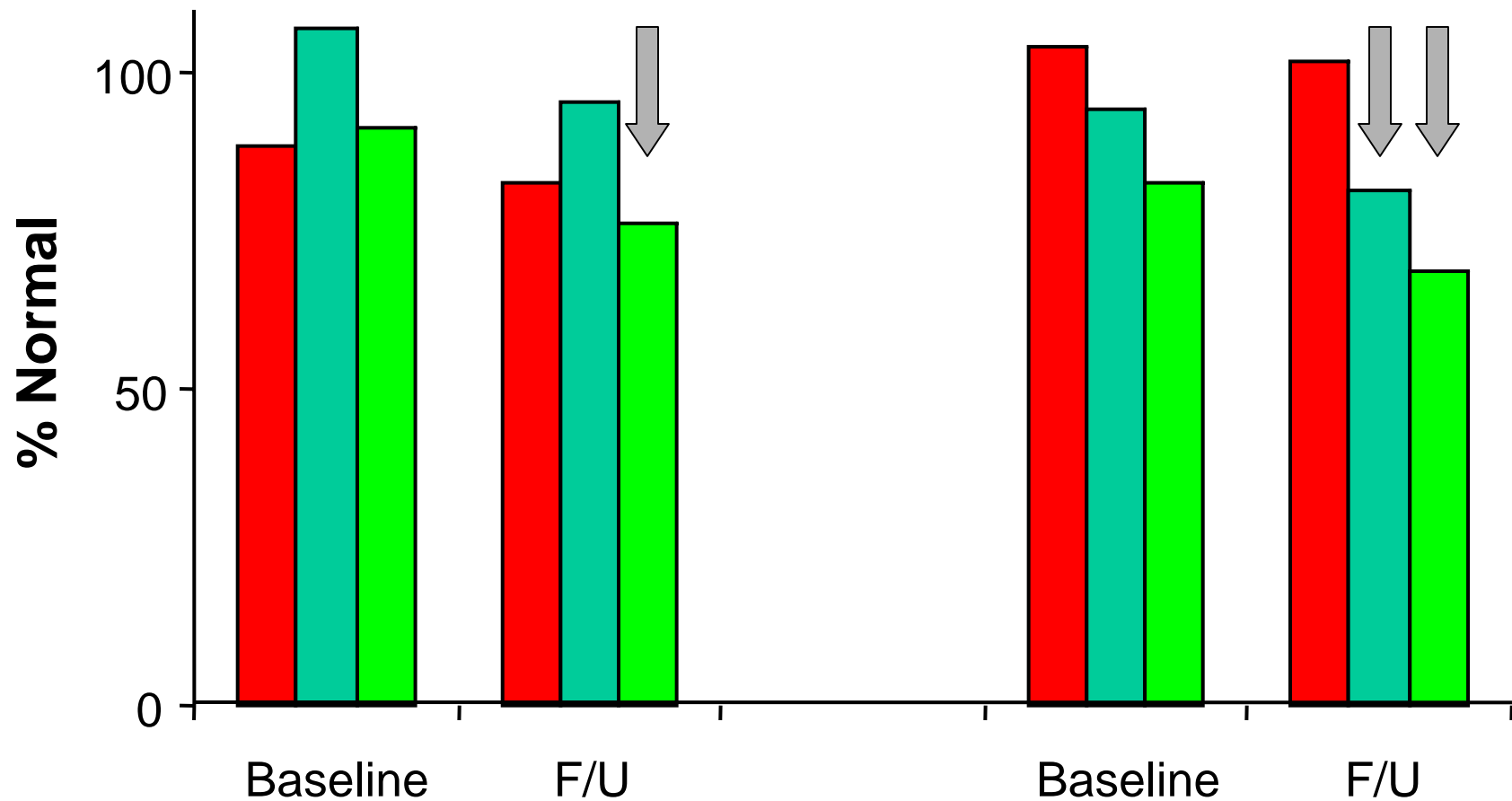
What causes Parkinson's?

Genetic factors

- Increased risk in 1° relatives
- Twin studies show low concordance
- Familial nature does not necessarily imply inheritance – shared environment

Four year follow-up

■ [18]F-Dopa ■ [11C]-DTBZ ■ Adj [11C]-MP



Occupational Risk

- *Increased risk for PD:*
 - Other primary: forestry, logging, mining
 - Teaching, social science, law, library
 - Medicine, health
- *Decreased risk for PD:*
 - Construction
 - Management, administration
 - Clerical

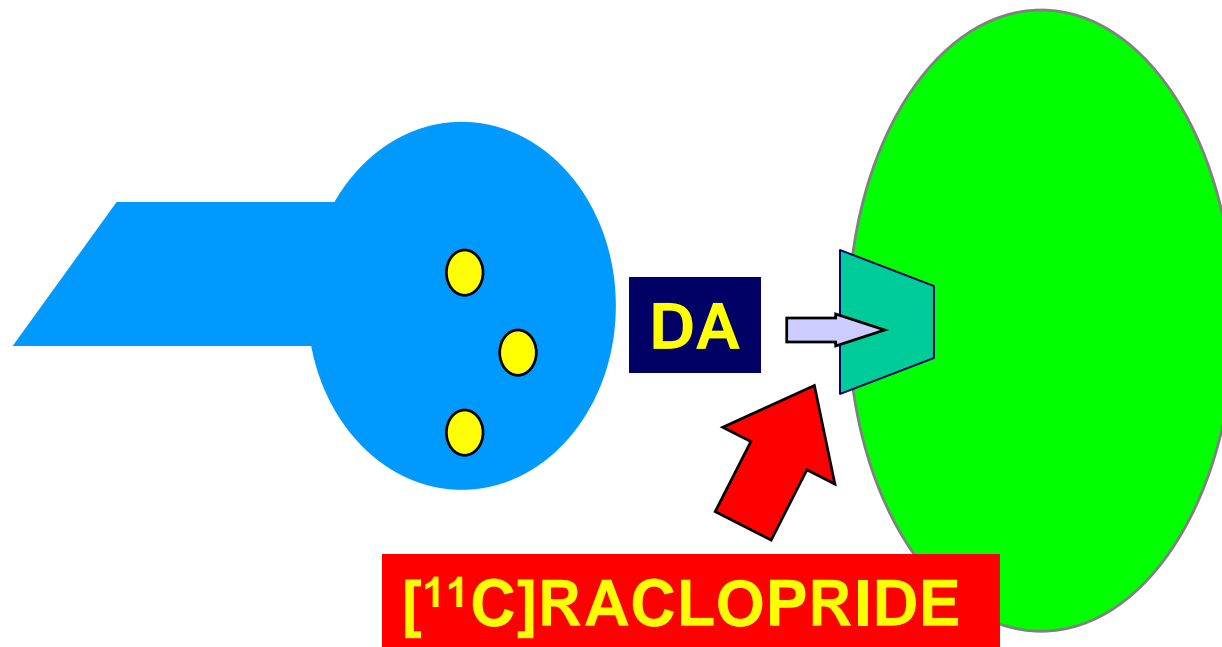
Clusters

- CBC, Vancouver – 4/120
- Community college, eastern BC – 4/32
- Garment factory, Montreal – 3/8

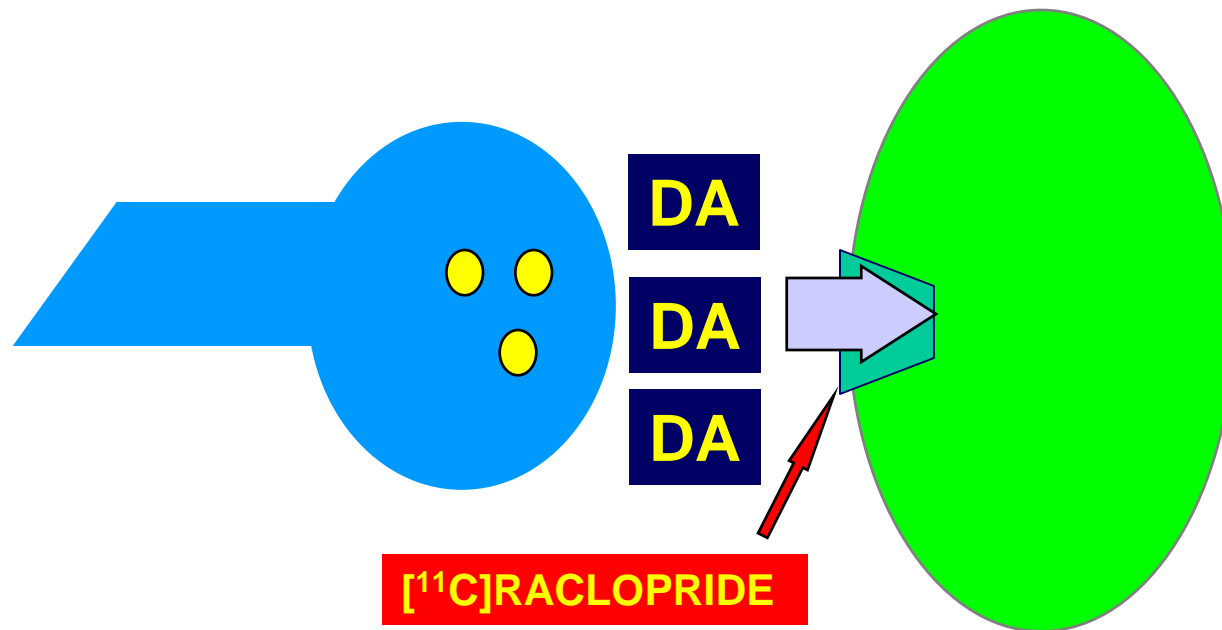
200-300 per 100,000 population.

~ 1% in population aged over 60 years.

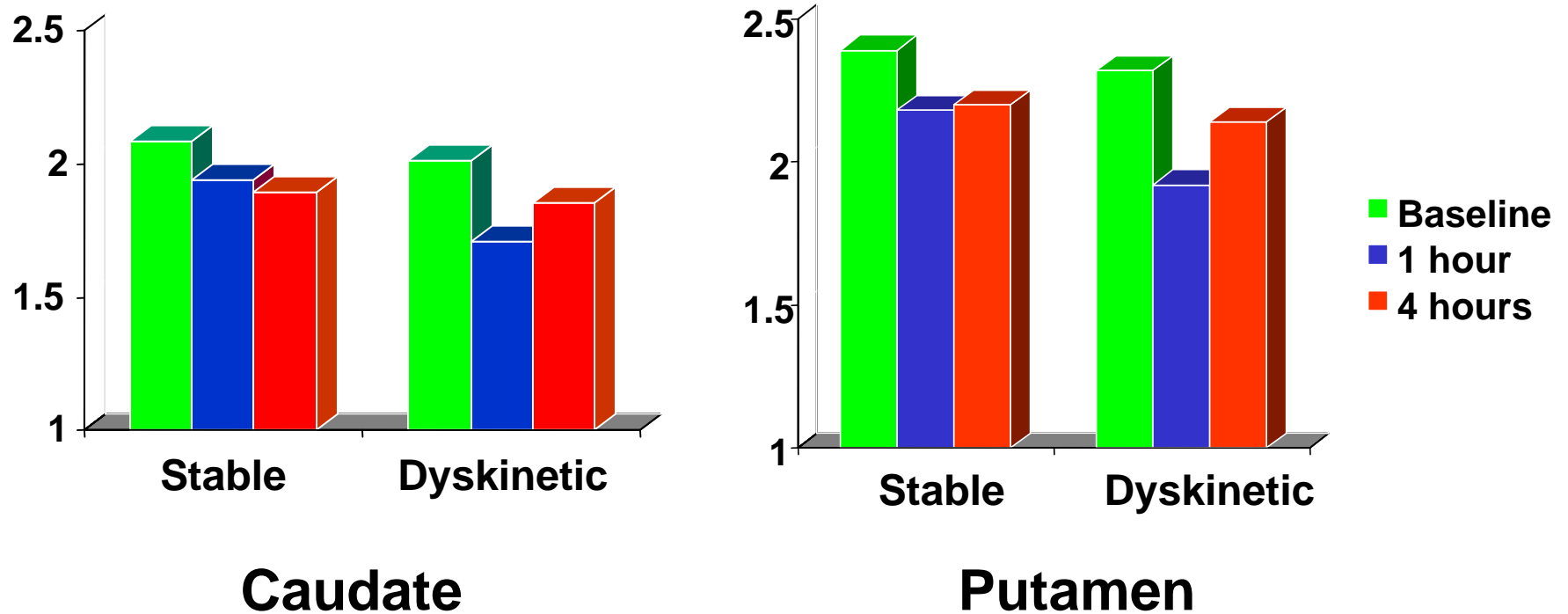
In vivo assessment of endogenous DA concentration



In vivo assessment of endogenous DA concentration



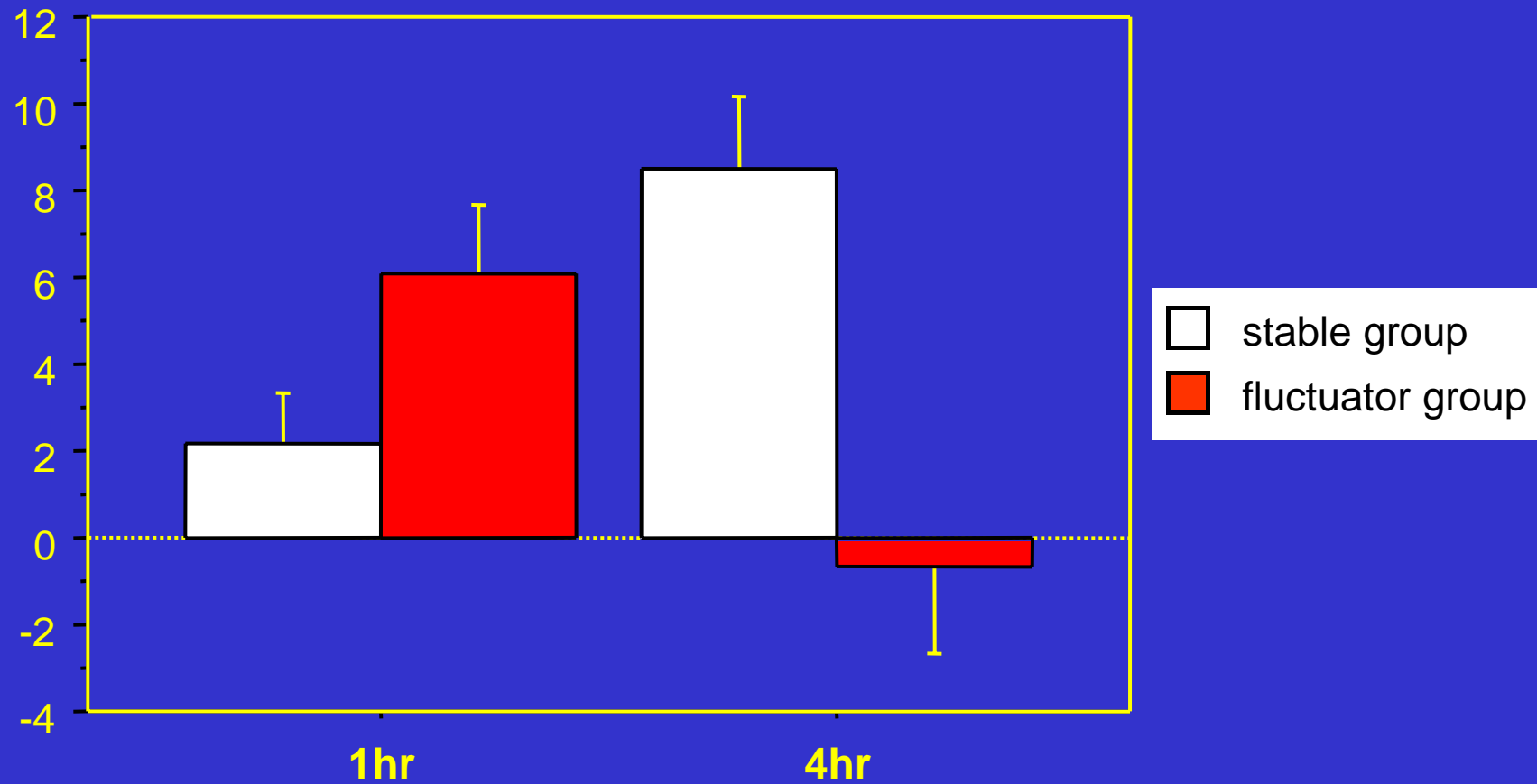
LD-derived DA release is Increased in Dyskinetic Subjects

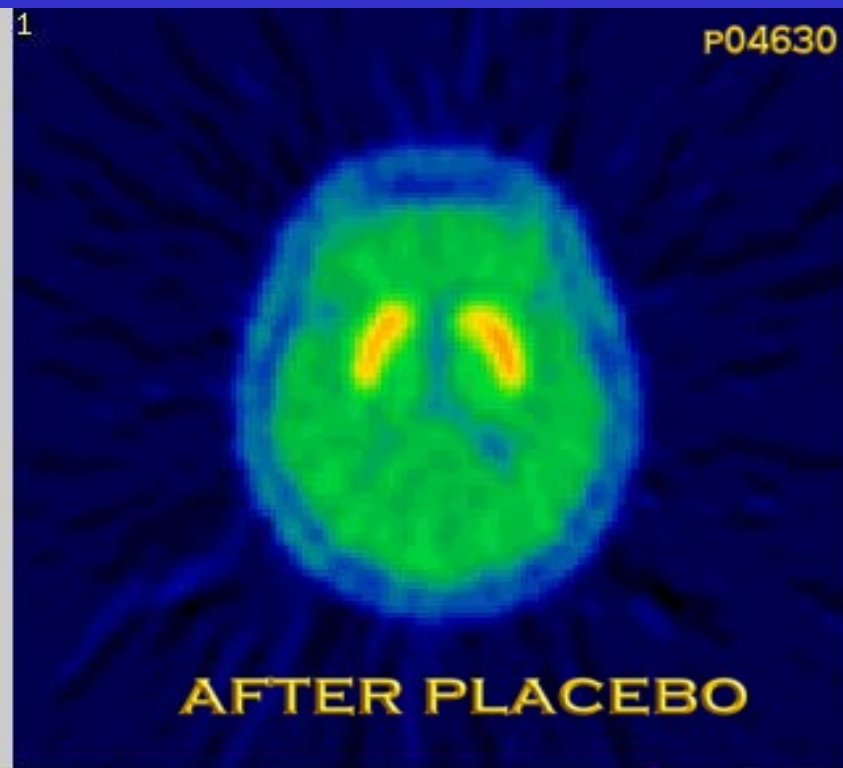
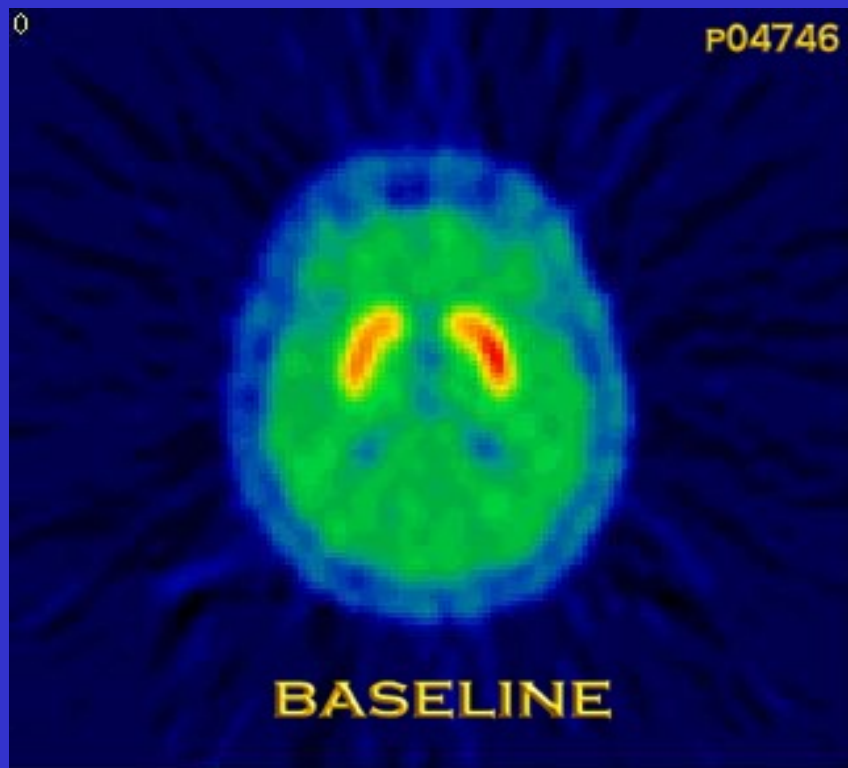


De la Fuente-Fernandez et al., Brain 2004

ESTIMATED LEVODOPA-INDUCED CHANGES IN SYNAPTIC DOPAMINE LEVELS

Error Bars: ± 1 Standard Error(s)







ONE OR TWO PILLS?

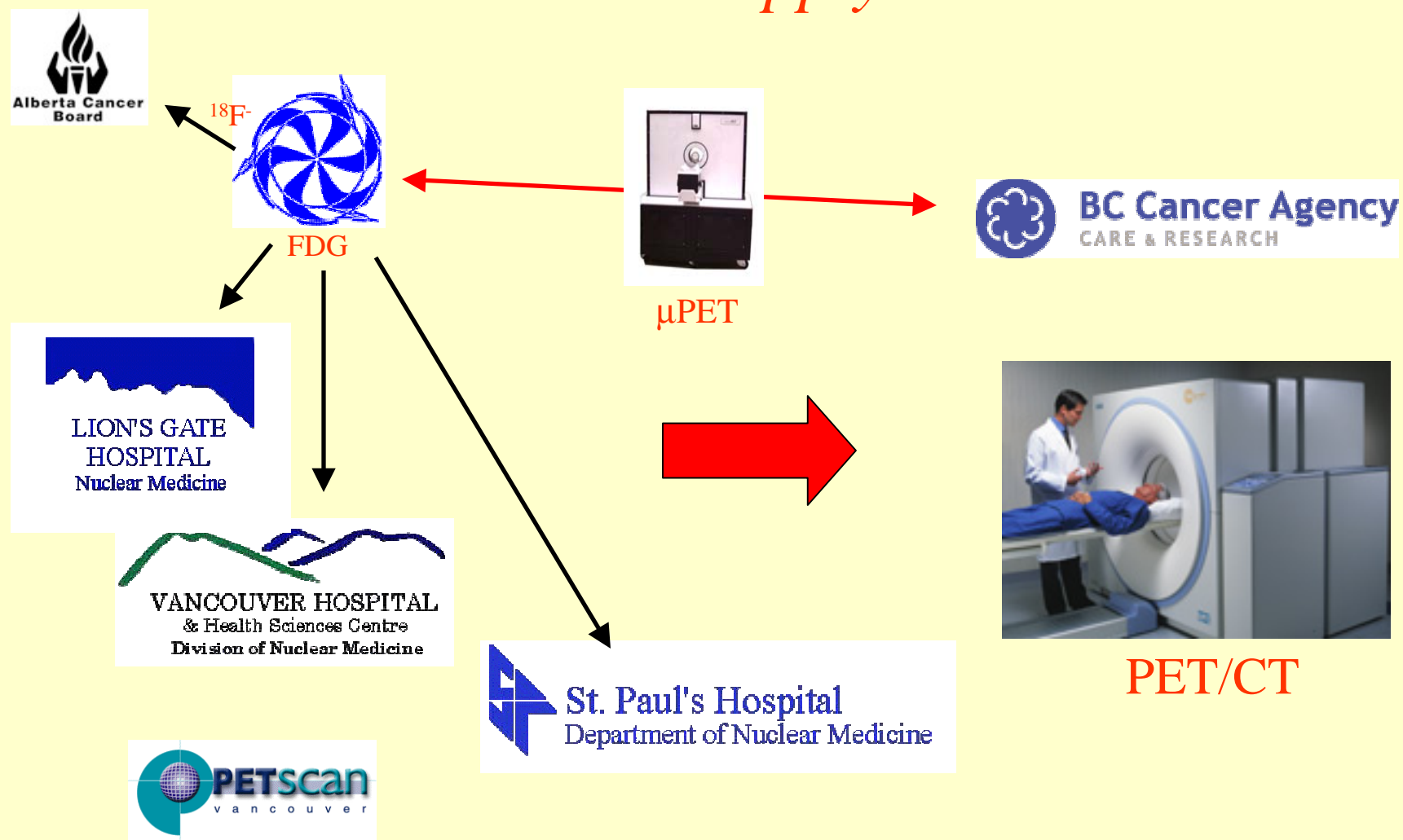
What have we learned about Parkinson's Disease thus far?

- 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.

Psychiatric Research

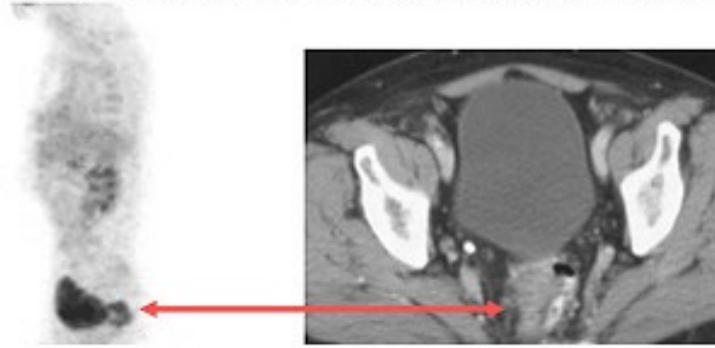
- Treatments currently available for bipolar disorder and major depression are effective in relieving symptoms in only about 70 per cent of the patients.
- Patients have difficulty tolerating the side effects of these medications.
- Using PET to understand the interplay of the chemicals in the brain.

Collaborations Beyond UBC/TRIUMF PET: *FDG Supply*

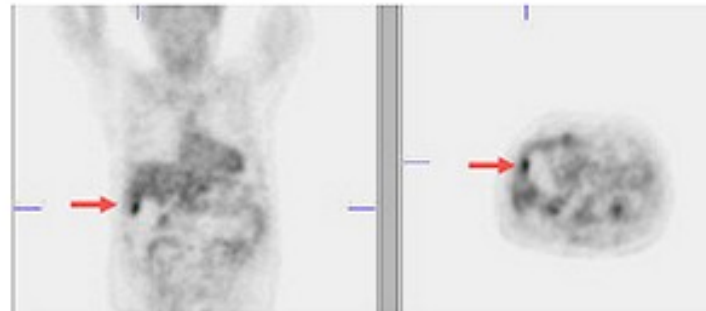


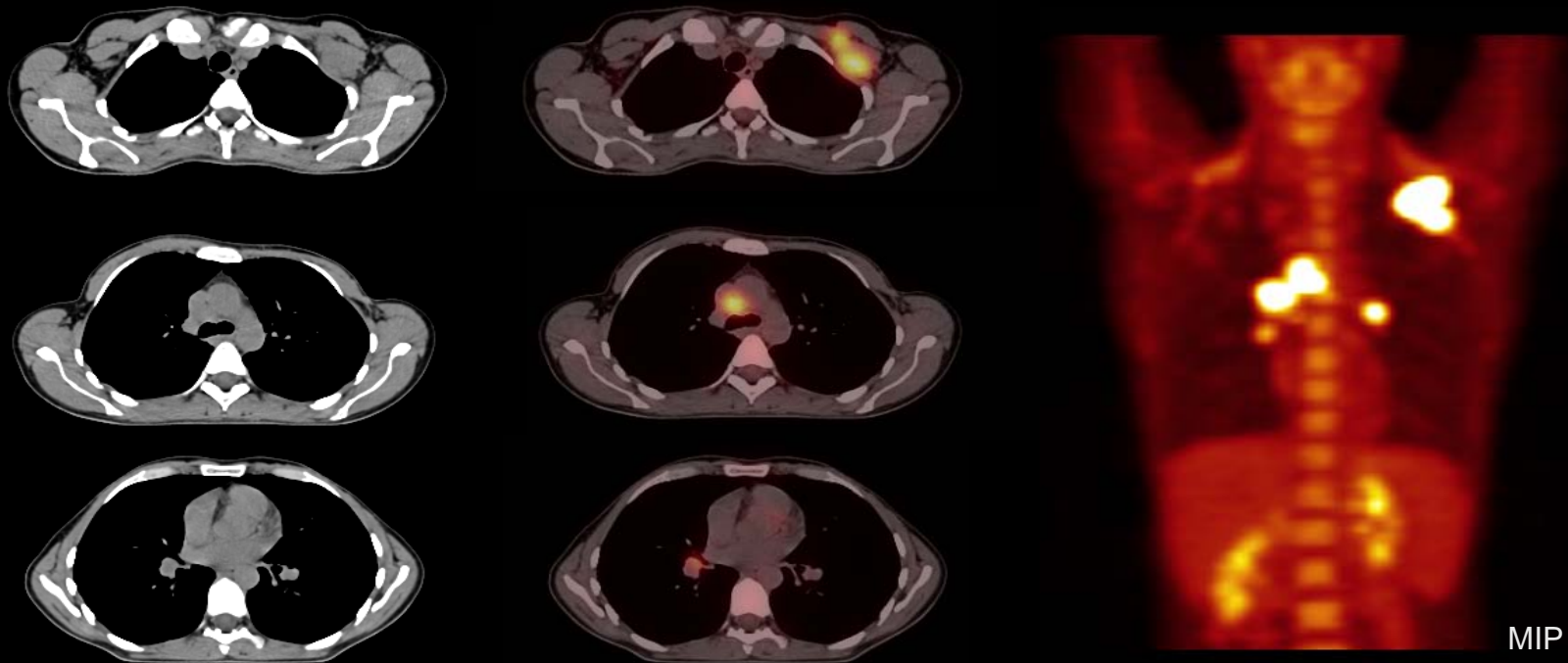
PET in cancer diagnosis.

PET = hypermetabolic focus
at site of rectal cancer.



Additional unexpected RUQ focus





Breast Cancer

37 year old female (53 kg) with history of metastatic breast cancer, for restaging.

biograph Sensation 16 demonstrates multiple areas of increased uptake consistent with metastatic disease, in the mediastinum, bilateral pulmonary hila, left upper lateral chest wall.

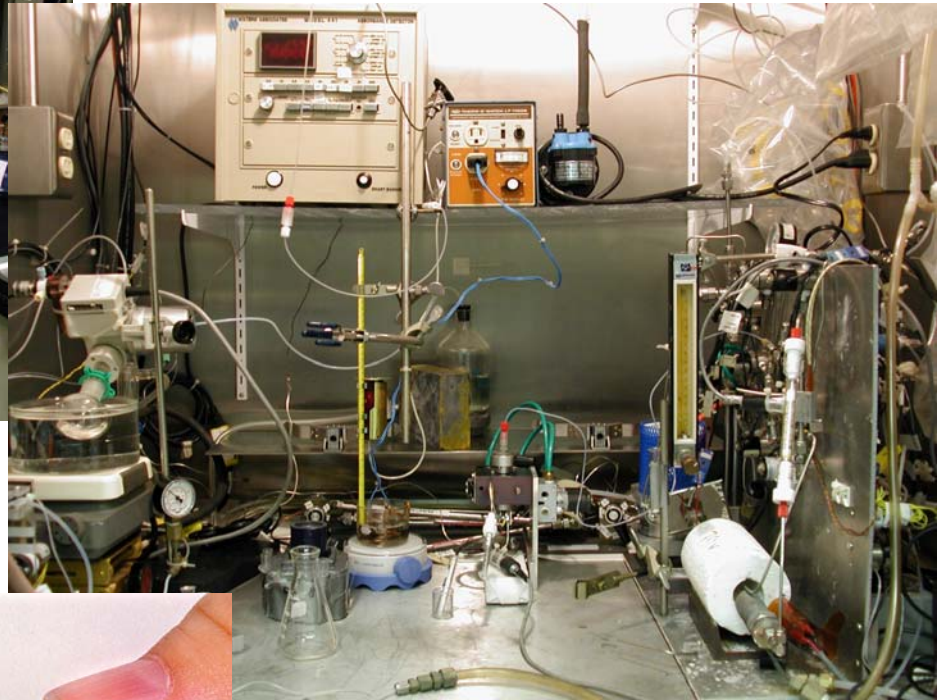
Scan protocol: CT 140 mAs, 120 kV, 5 mm slices

PET 400 MBq FDG, 167 min p.i, 5 min/bed, 4+2 beds, 30 min scan time

Future Directions

- Miniaturization
- Specificity

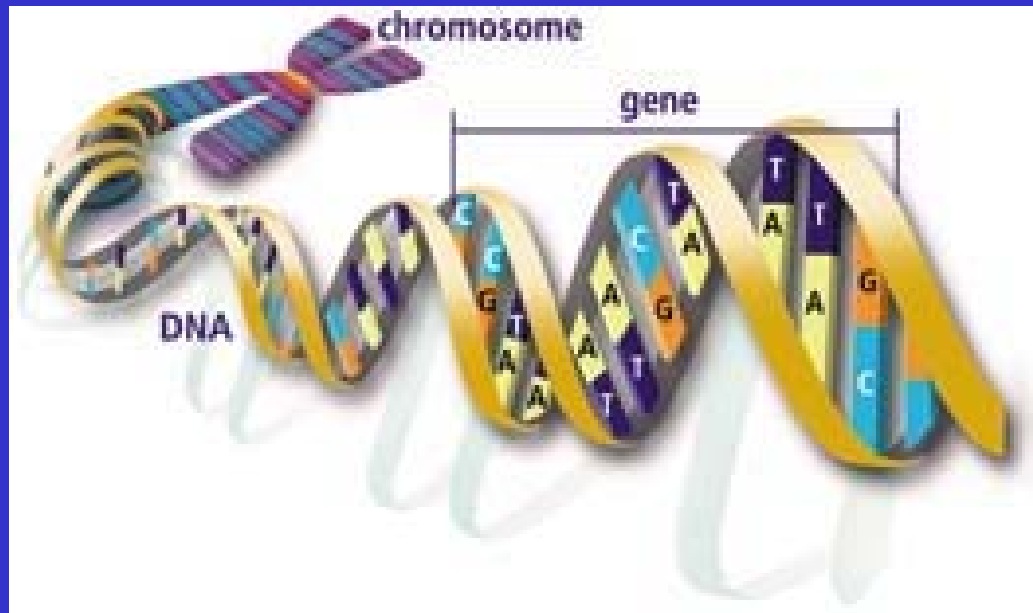
Miniaturization



Even with accurate PET measures with today's tracers we are still looking at the consequence of disease.

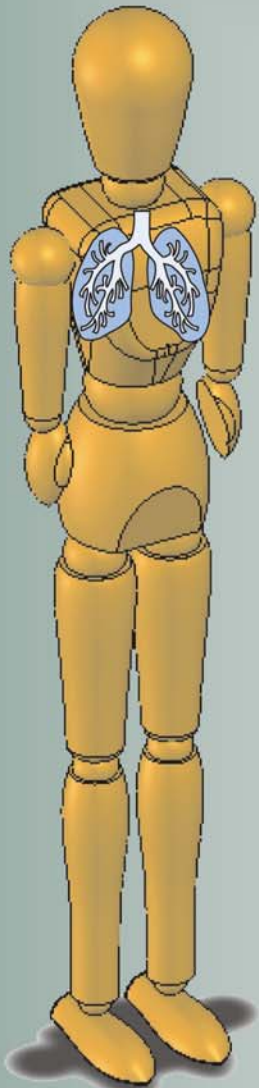
We need access to the disease process itself.

New tracers needed!



New compounds based on oligonucleotides -
Fragments of DNA.

Personalized Medicine?



Lungs



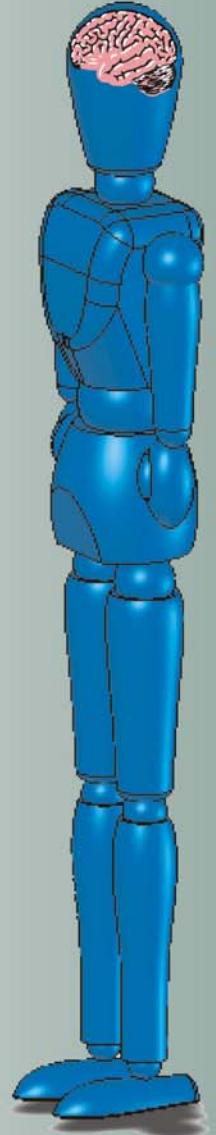
Lymph System



Heart



Nervous System

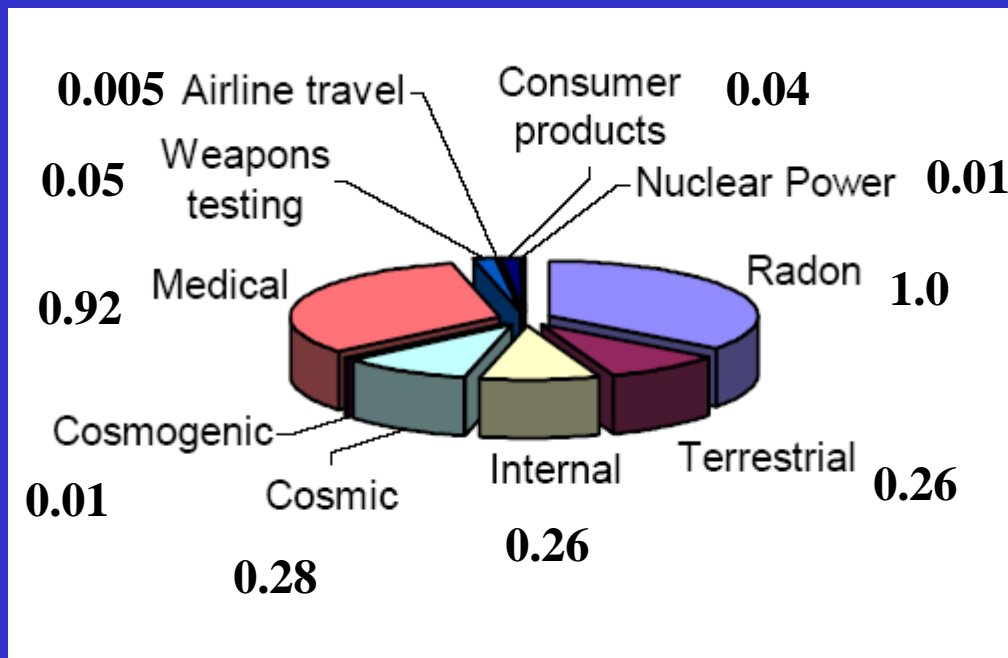


Brain



Background Radiation

Average population exposure – 2.8 mSv/year



This can vary significantly depending upon life style and living location.

Loss of Life Expectancy Due to Various Risk - Days

- Being unmarried male - 3500
- Smoking – 2250
- Heart diseases – 2100
- Being unmarried female – 1600
- Coal Miner - 1100
- Cancer – 980
- Being poor - 700
- Stroke – 520
- All accidents - 435
- Motor vehicle accidents - 207
- Home accidents - 95
- Safest jobs – 30
- Bicycle – 5
- All catastrophes combined- 3.5
- **PET scan – 1 hour**
- Smoking 1 cigarette – 10 min.
- Pap test – (- 4 days)
- Air bags – (- 50 days)

The modern Alchemist!



Photo by Will Brown/courtesy of
Chemical Heritage Foundation

The modern Alchemist!



Bill Brown/courtesy of
Heritage Foundation

Colleagues from PPRC



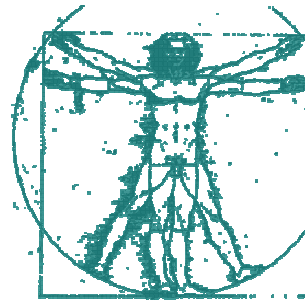
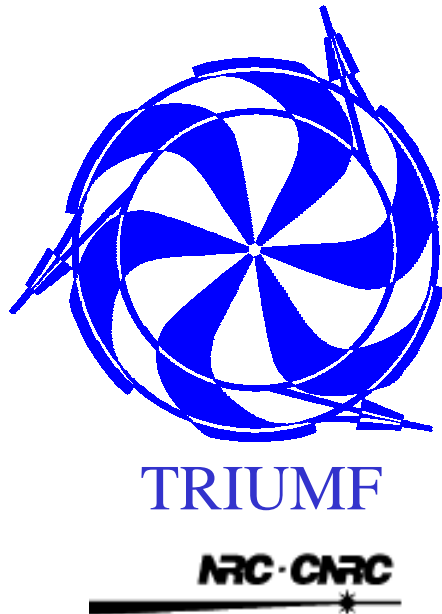
Neuroscience Models



BC Cancer Agency



Support



Pacific Parkinson's
Research Institute



TRIUMF represents the most powerful radioisotope production facility in the world.

I have shown you only a fraction of the potential for exploiting this capability.

I hope I have conveyed to you the sense that Science is a continuum from the most basic studies to applications which in turn are basic studies in a different discipline.

Also I hope you can see that Science is a very human endeavor.