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

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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 – $6.02 \times 10^{23}$?

Each Smartie – 1 cm$^3$ or 1 mL
1 mole of Smarties = $6 \times 10^{23}$ mL
Assume a truck with a capacity of 90 m$^3$ (10x3x3) = $9 \times 10^7$ mL
The number of trucks needed – $6 \times 10^{15}$

If each truck is 13 m long, that means that lined up they would be $7.8 \times 10^{13}$ km in length or 200,000,000,000 earth to moon distances.
1 grain of salt – 0.12 mg

= \(2 \times 10^{-6}\) moles (or 2 micromoles)

= \(3 \times 10^{17}\) 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:

\[ ^{14}\text{N}(p,\alpha)^{11}\text{C} \quad t^{\frac{1}{2}} = 20.3 \text{ min.} \]

\[ ^{18}\text{O}(p,n)^{18}\text{F} \quad t^{\frac{1}{2}} = 109.7 \text{ min.} \]

\[ ^{64}\text{Ni}(p,n)^{64}\text{Cu} \quad t^{\frac{1}{2}} = 12.7 \text{ h} \]

\[ ^{16}\text{O}(p,\alpha)^{13}\text{N} \quad t^{\frac{1}{2}} = 9.97 \text{ min.} \]
How do we detect these radiotracers?
Diagnostic medicine tries to look into the body to see what is happening, in life and in death.
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

Blood → Cells

Glucose ↔ Glucose
FDG ↔ FDG

Glucose → Glucose-6P → Glycolysis
FDG → FDG-6P
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
vesicles with the transmitter dopamine

tyrosine

L-dopa

dopamine

DAT

synapse

dopamine receptor

the message is passed on

receiving cell

cell nucleus
FD-PET Progression

Controls

MPTP-exposed

p=0.0274

Exposure

1st scan

2nd scan

What causes Parkinson’s?

*Genetic factors*

- Increased risk in 1º relatives
- Twin studies show low concordance
- Familial nature does not necessarily imply inheritance – shared environment
Four year follow-up

% Normal

Baseline  F/U  Baseline  F/U

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

Tsui et al., Can. J. Public Health, 1999
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

RUQ – right upper quadrant
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?
Background Radiation

Average population exposure – 2.8 mSv/year

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

Adapted from TRIUMF Radiation Safety Manual
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)

Adapted from TRIUMF Radiation Safety Manual
The modern Alchemist!

Photo by Will Brown/courtesy of Chemical Heritage Foundation
The modern Alchemist!
Colleagues from PPRC
Neuroscience Models
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.