Liquid Scintillation Counting in Quality Control of PET Radiopharmaceuticals

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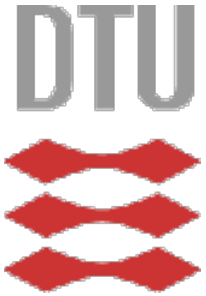
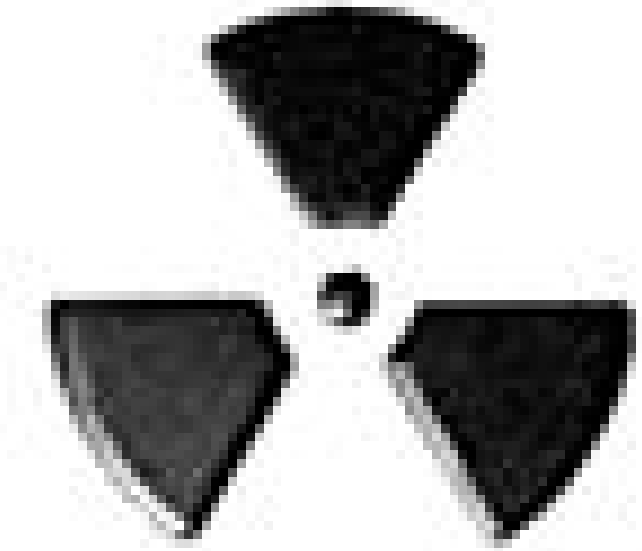
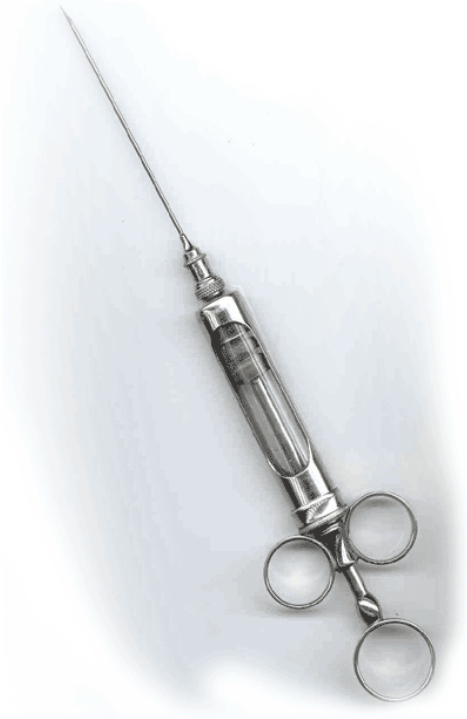
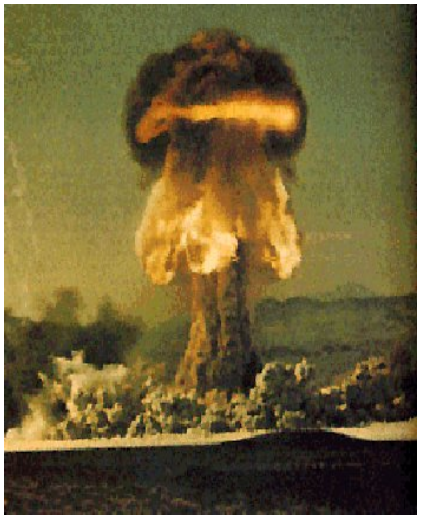


LSC 2017 Copenhagen, May 2017

Why Radioactive Materials for injection into fellow human beings in 2017 ?





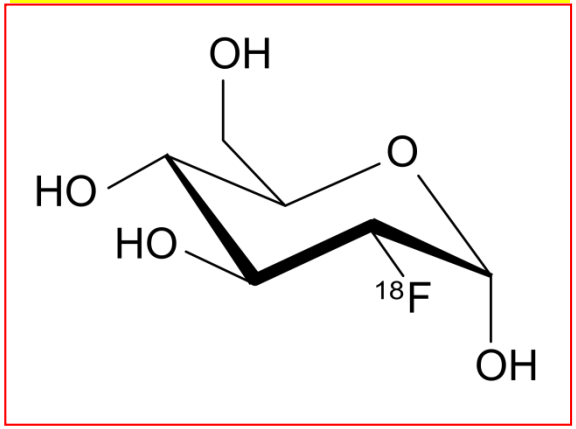


62 years post Hiroshima, 31 years post Chernobyl,
…….Fukushima still in clear memory !

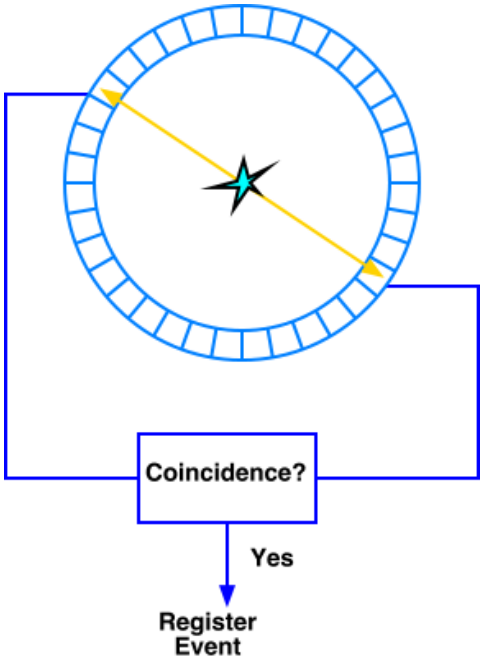
The success of clinical PET-CT

- ^{18}F Pure beta$^+$ decay
- Low beta$^+$ energy
- Reasonable half life
- Usefull chemistry
- FDG is glucose analog
- 109.77 min half-life
- Distributed, local production

[^{18}F]FDG



PET has grown into an important tool in oncology

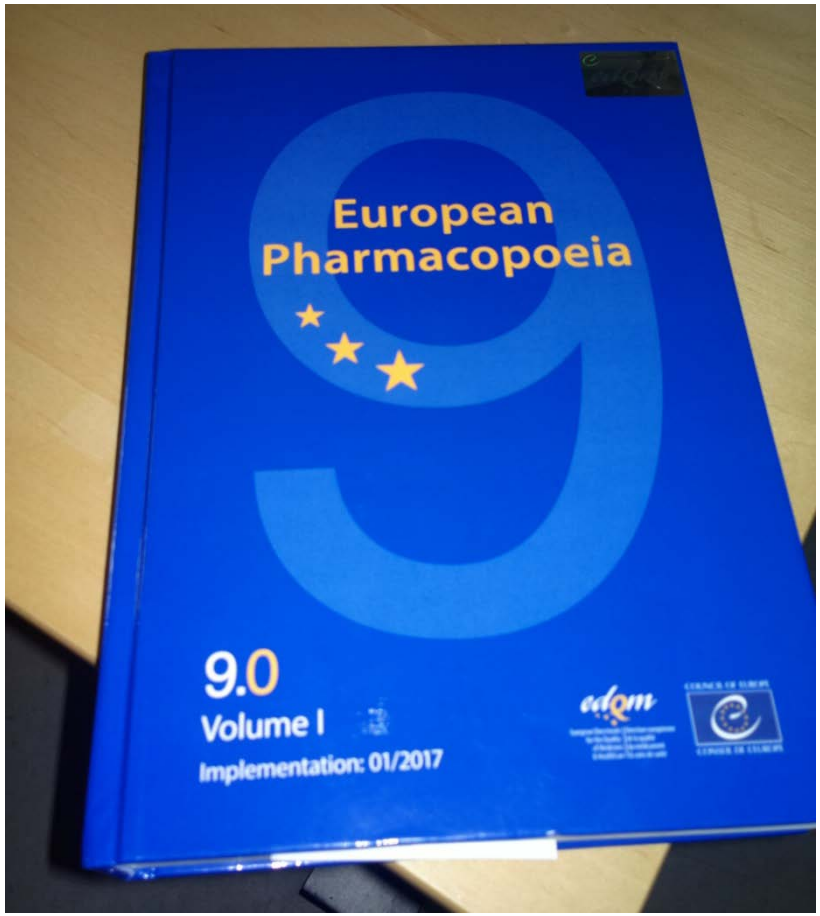


Before Chemotherapy

After Chemotherapy

Molecular imaging of tumor metabolism and apoptosis
U Haberkorn, A Markert, W Mier, V Askoxylakis and A Altmann
Oncogene (2011) **30,** 4141–4151

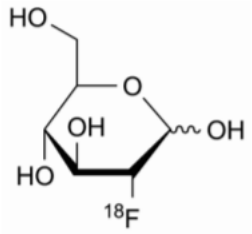
FDG is a RADIOPHARMACEUTICAL



It has a monograph in the European Pharmacopoeia

FLUDEOXYGLUCOSE (^{18}F) INJECT

Fludeoxyglucosi (^{18}F) solutio iniectab



$C_6H_{11}{}^{18}FO_5$ *M*

.....

Sterility. It complies with the test for sterility prescribed in the monograph *Radiopharmaceutical preparations (0125)*. The preparation may be released for use before completion of the test.

Bacterial endotoxins (*2.6.14*): less than 175/*V* IU/mL, *V* being the maximum recommended dose in millilitres. The preparation may be released for use before completion of the test.

RADIONUCLIDIC PURITY

The preparation may be released for use before completion of test B.

Fluorine-18: minimum 99.9 per cent of the total radioactivity.

A. Gamma-ray spectrometry.

Limit: peaks in the gamma spectrum corresponding to photons with an energy different from 0.511 MeV or 1.022 MeV represent not more than 0.1 per cent of the total radioactivity.

B. Gamma-ray spectrometry.

Determine the amount of fluorine-18 and radionuclidic impurities with a half-life longer than 2 h. For the detection and quantification of impurities, retain the preparation to be examined for at least 24 h to allow the fluorine-18 to decay to a level that permits the detection of impurities.

Results: the total radioactivity due to radionuclidic impurities is not more than 0.1 per cent.

.....

RNP – Radionuclidic Purity

RADIONUCLIDIC PURITY

The preparation may be released for use before completion of test B.

Fluorine-18 minimum 99.9 per cent of the total radioactivity.

A. Gamma-ray spectrometry

Limit: peaks in the gamma spectrum corresponding to photons with an energy different from 0.511 MeV or 1.022 MeV represent not more than 0.1 per cent of the total radioactivity.

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Results: the total radioactivity due to radionuclidic impurities is not more than 0.1 per cent

0.1% Impurities ?

But this limit applies throughout the shelf-life of the product!

Normally, shelf-life is set to 10 hours.

Half-life of ^{18}F = 109.77 minutes.

For longer-living impurities 99.9% RNP end-of-shelf-life corresponds to 99.998% RNP at time of release.

We must reliably detect ANY activity at the 20 ppm level.

Detect ANY activity at 20 ppm level ?

- Gamma spectroscopy will miss the "pure" BETA emitters.
- Gamma spectroscopy will have great difficulties finding weak gamma peaks in the Compton region below 511 keV.
- Can you wait until ^{18}F is decayed ?

? ? ?

What isotopes ?

- H-3 from O-18(p,t)O-16

- Co-55,56,57,58,58m
- Nb-93m

And many more coming from the target.

But also:
- Cu-64
- Tc-99m
- Mo-99
- Lu-177
- I-131
- Ra-223
- … and any thing else that you work with

LSC is the universal solution

…if we measure the half life ….

Use full open energy window .

Use as much activity as the dead time will allow

Typically 10-50 kBq.

Repeat measurements every 300-600 seconds.

Three important parameters

$\frac{\varepsilon\ impurity}{\varepsilon\ F^{18}}$ 0.2-1.0 enters the calculation, but constant

Background Keep it low and constant (cave neutrons)

Dead time &
countrate linearity Can be checked with gravimetric methods

What we need from our LSC instrument

Repeated measurements of one sample in same position

Precise reporting (h:m:s.ss) of count period start

Tested, proven, published

Applied Radiation and Isotopes 70 (2012) 430–437

Contents lists available at SciVerse ScienceDirect

Applied Radiation and Isotopes

journal homepage: www.elsevier.com/locate/apradiso

Improved methods to determine radionuclidic purity of F-18 compounds

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Applied Radiation and Isotopes 108 (2016) 108–115

Contents lists available at ScienceDirect

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journal homepage: www.elsevier.com/locate/apradiso

Experimental implementation and proof of principle for a radionuclidic purity test solely based on half-life measurement

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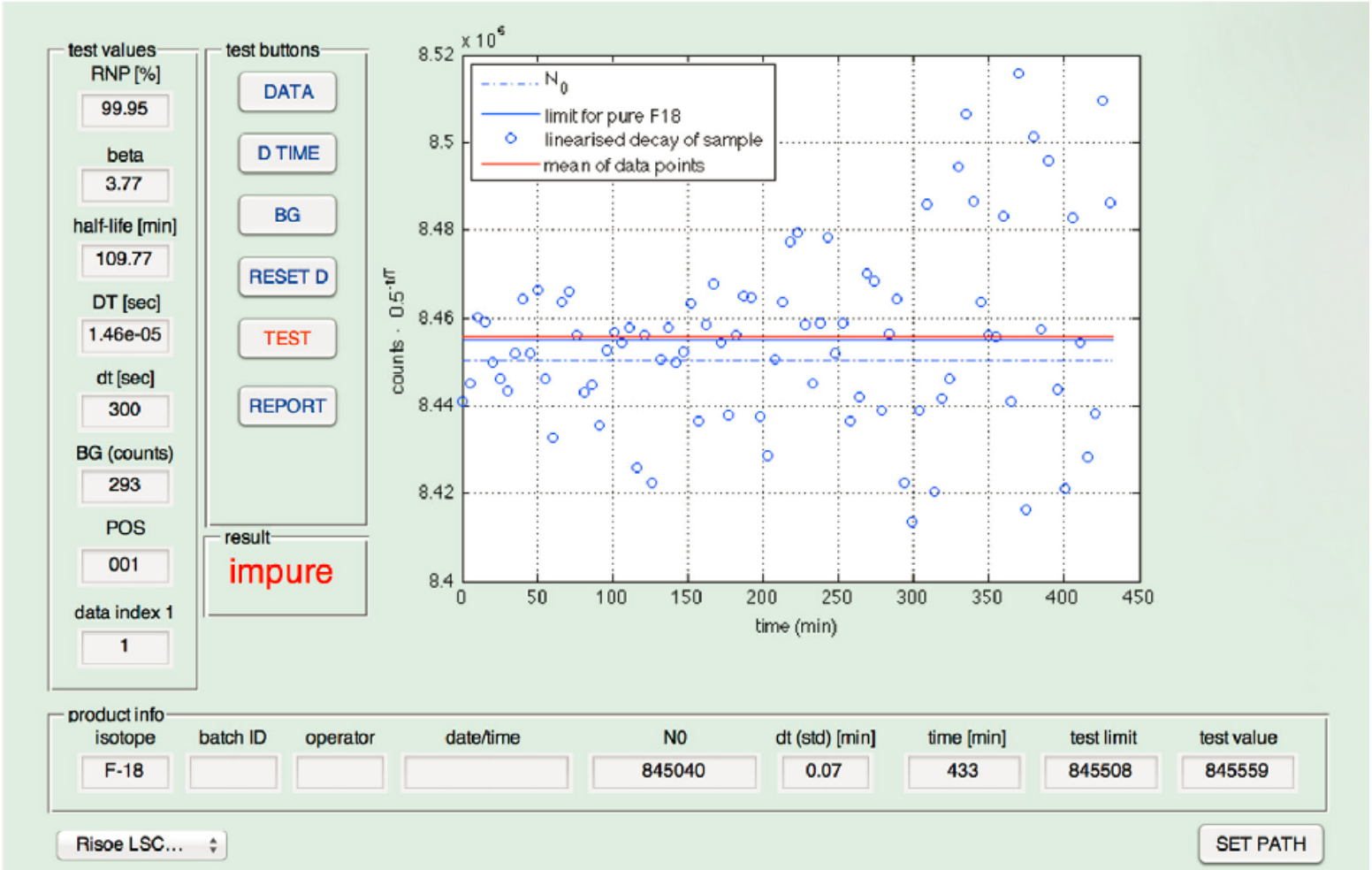
Can detect 0.05 % Cu-64 (12.7 h) in less than 2 hours



Software build in Matlab – does detect and correct for deadtime


Thank you for your attention,
..... Questions ?