Calibration of Pure-Beta-Emitting Brachytherapy Sources by Destructive Radionuclidic Assays

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Overview

- Radioactivity & Its Measurement
- LS Spectrometry
- Intravascular Brachytherapy Sources
  - Importance
  - Need for characterizations
  - Why destructive assays ?
  - Recent work on three kinds of sources

Measure of radioactivity

Number (dN) of <u>spontaneous</u> nuclear transformations per unit time interval (dt)

$$-dN/dt = N\lambda \qquad [\lambda = \ln(2)/T_{1/2}]$$

SI unit

$$s^{-1} = \mathrm{Bq}$$

A counting process (of emitted radiations)

- **"absolute"; primary; fundamental**
- **relative; secondary**

<u>detection efficiency</u> concept in both

Typical measurement model

$$R(t) = C/T$$

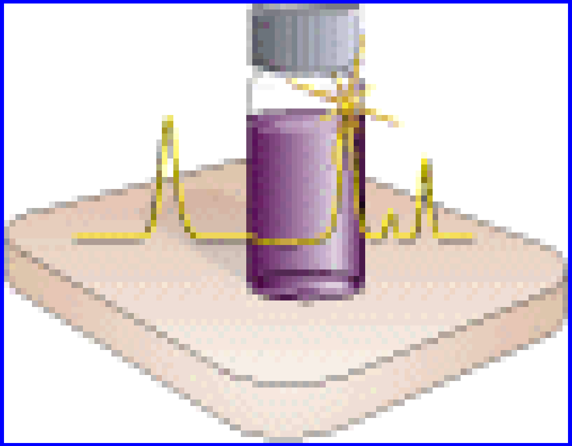
$$= R_B + A_0\,(m/M)\,\varepsilon\,\Gamma\,G(t)\,f_i\,f_j\,\ldots + A_x\,\varepsilon_x\ldots..$$

LS Spectrometry

NIST -- one of premier experimental LS groups in the world

- CIEMAT/NIST method co-originator
- cocktail composition effects

A principal and powerful tool ("workhorse") of the Radioactivity Group



Recent LS activities

- long-term stability carrier-free Po solutions
- verify dilutions $^{36}Cl/Cl$ AMS standards
- compare ^{226}Ra standards issued since 1947 series
- find 2-keV delayed isomeric state in ^{205}Po
- precise determination of ^{222}Rn half-life
- resolve calibration bias for electret radon monitor
- ^{209}Po activity for branching ratios
- ^{63}Ni half-life (by decay) + consistency of standards over 27 years
- long-term (7 year) stability of Rn-in-water standard generator
- intercompare French (LPRI) & NIST ^{3}H-water standards
- EUROMET ^{55}Fe & ^{63}Ni intercomparison
- cocktail composition effect studies (new classification scheme)
- resolve $^{210}Pb/^{226}Ra$ in aged radium
- destructive assays for intravascular brachytherapy sources

Scintillation Counting 1

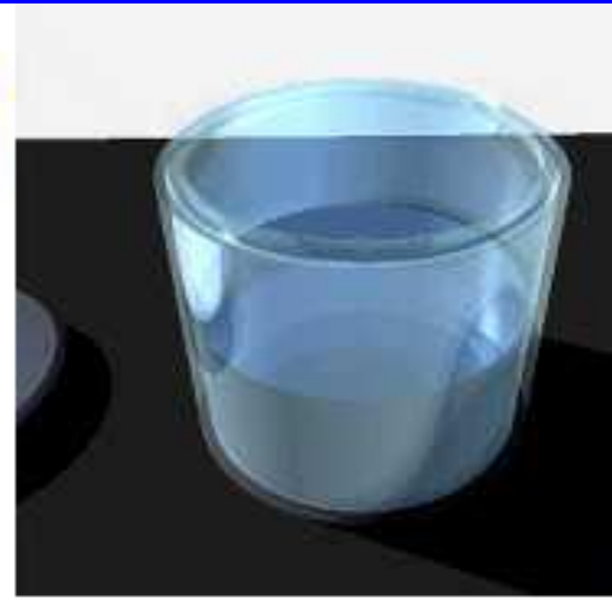
Liquid Scintillation Cocktail

Components:

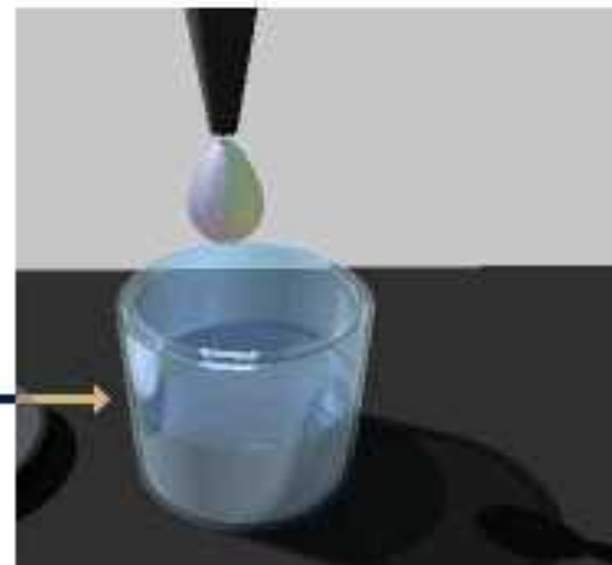
Solvent: Typically toluene, xylene pseudodocumene, or an alkyl benzene type solvent.

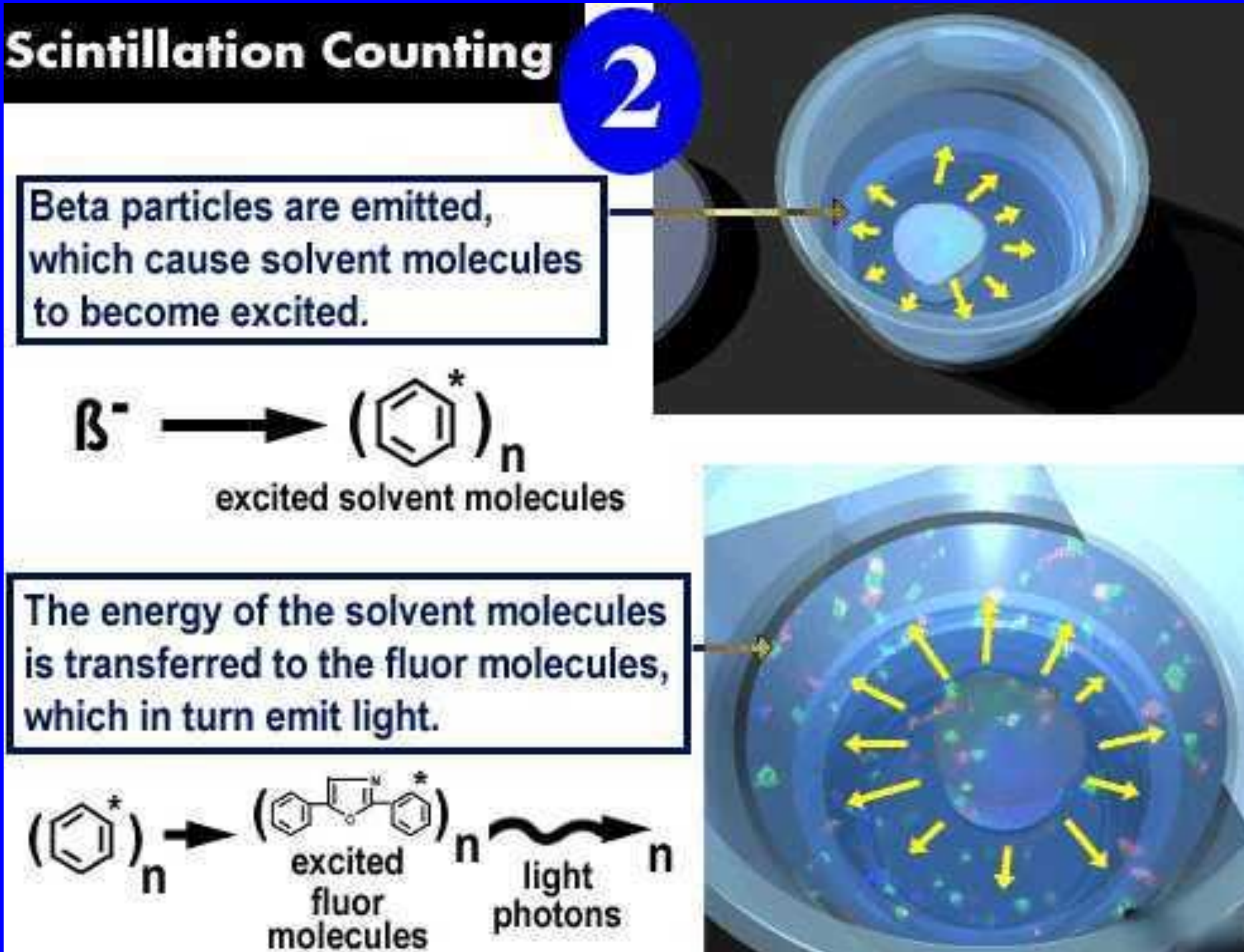
Emulsifier: A detergent type molecule that ensures proper mixing of aqueous samples.

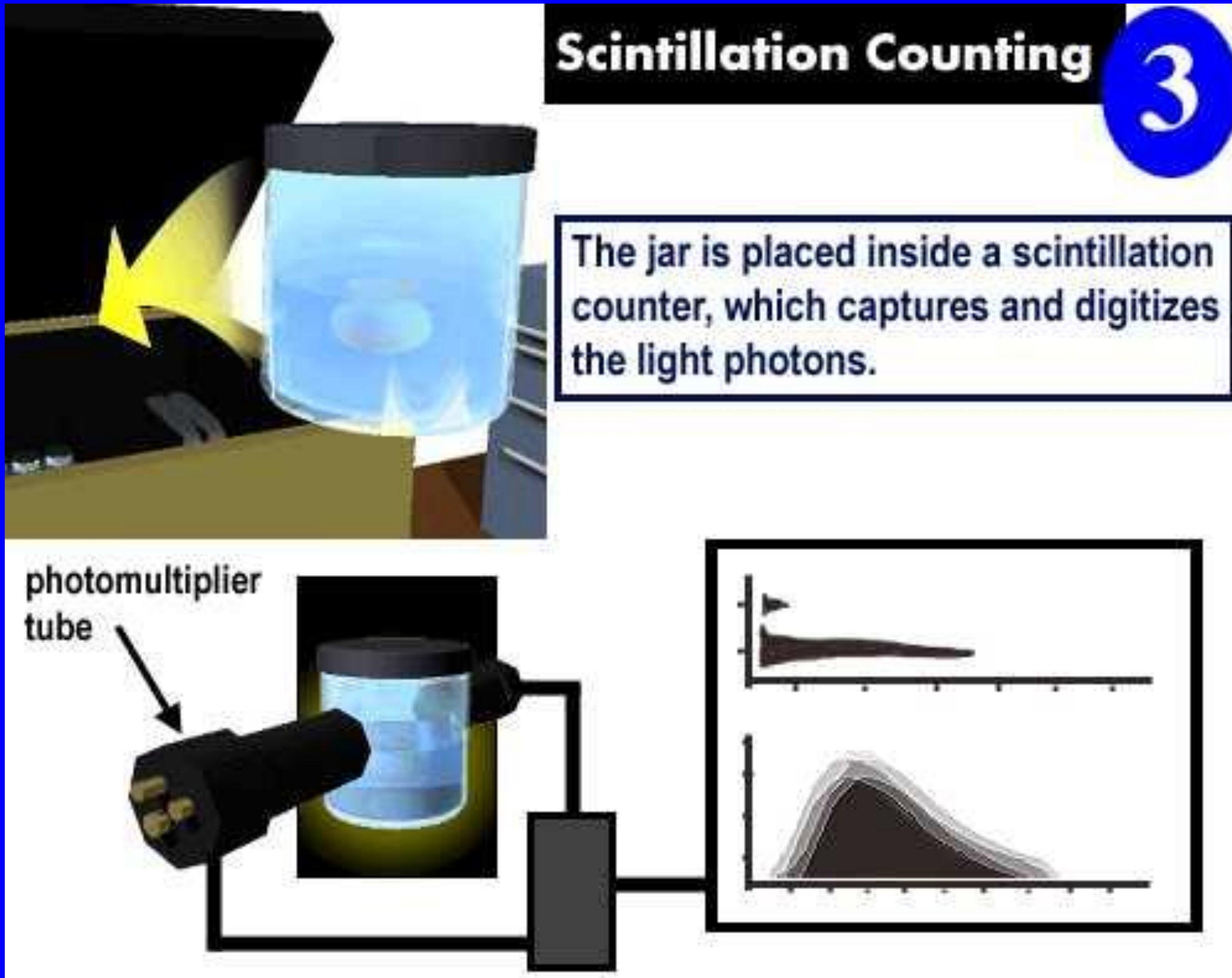
Fluor: A fluorescent solute.



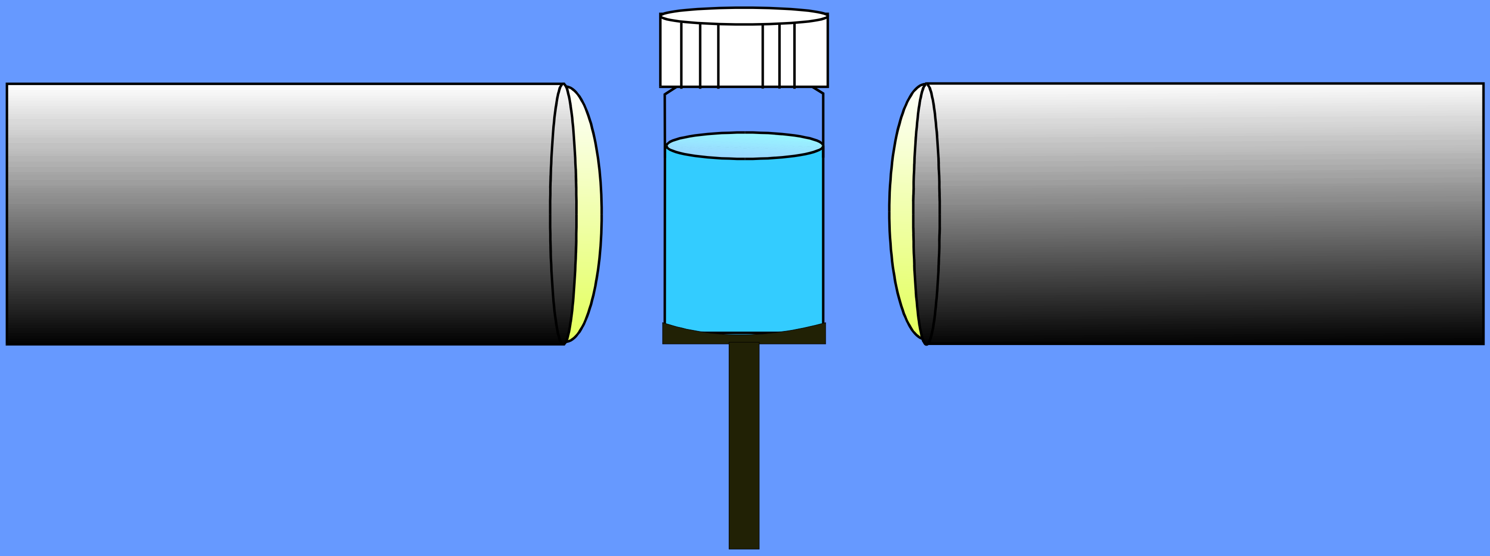
Process: Radioactive Sample is added to scintillation cocktail.




Scintillation Counting
2
Beta particles are emitted, which cause solvent molecules to become excited.
ß⁻
n
excited solvent molecules
The energy of the solvent molecules is transferred to the fluor molecules, which in turn emit light.
n
n
n
excited fluor molecules
light photons

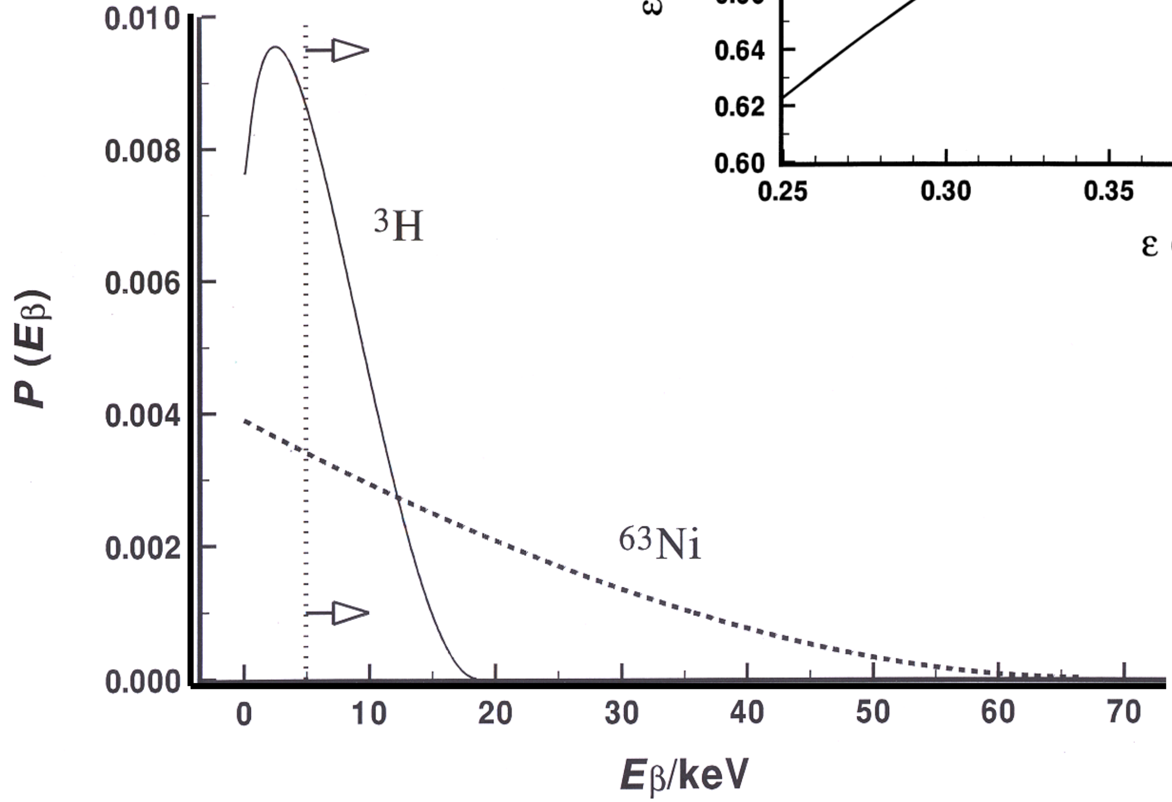

Scintillation Counting
3
The jar is placed inside a scintillation counter, which captures and digitizes the light photons.
photomultiplier tube

Two-Phototube Coincidence Liquid Scintillation Counting with the CIEMAT/NIST Efficiency Tracing Method

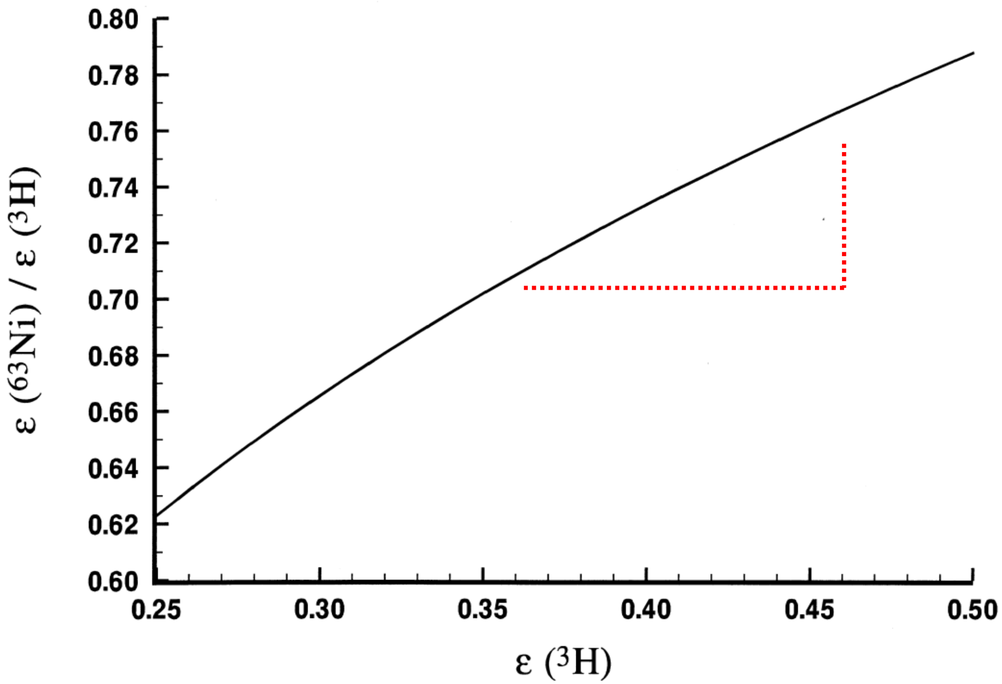


$$\varepsilon = \int_0^{\mathrm{Emax}} \left\{1 - \exp\left[-M^{-1} E \mathrm{Q}(E) \mathrm{W}(E)\right]\right\}^2 \mathrm{P}(Z,E)\,\mathrm{d}E \times \left(\int_0^{\mathrm{Emax}} \mathrm{P}(Z,E)\,\mathrm{d}E \right)^{-1}$$

5 keV

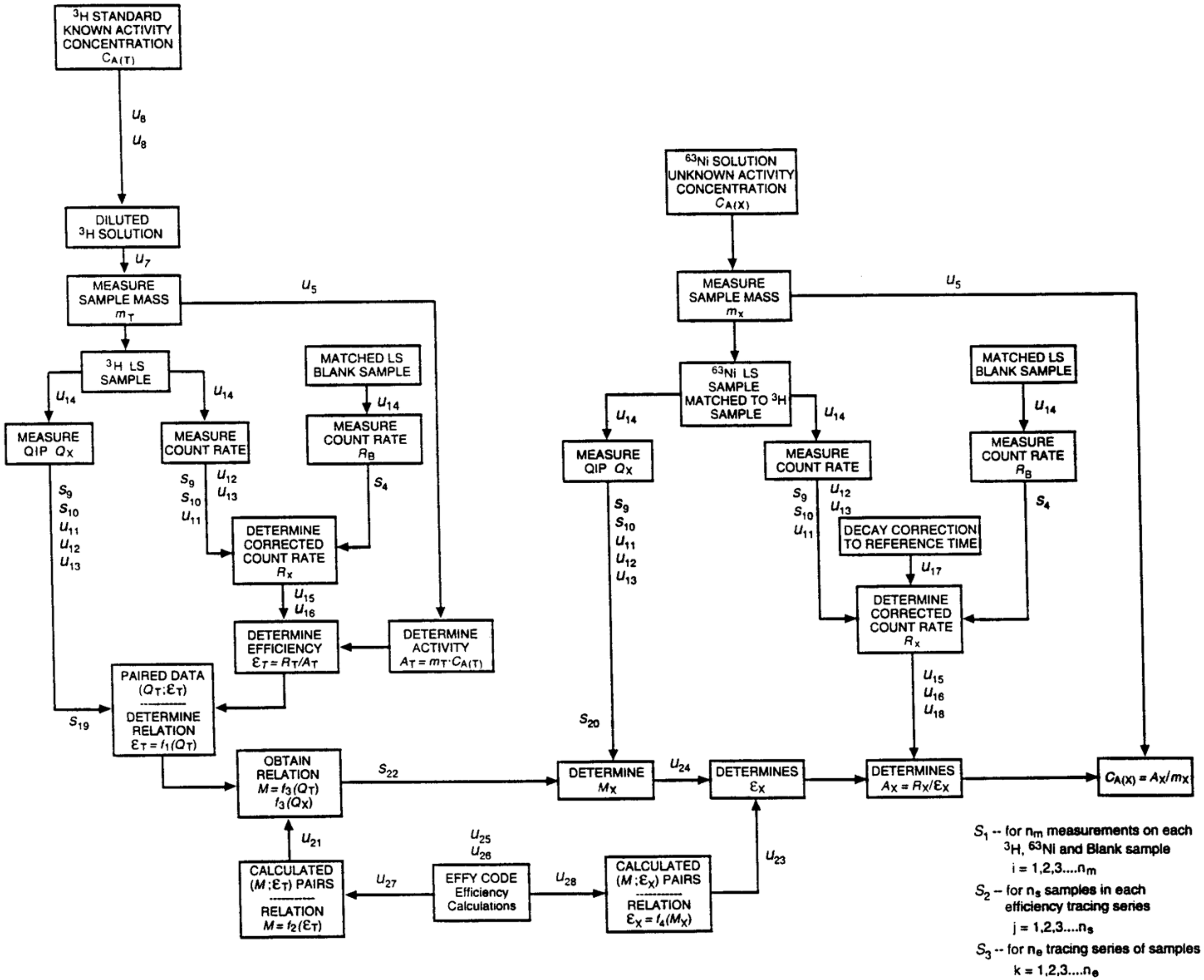


0.010
0.008
0.006
0.004
0.002
0.000
0
10
20
30
40
50
60
70
P (Eβ)
Eβ/keV
3H
63Ni



0.80
0.78
0.76
0.74
0.72
0.70
0.68
0.66
0.64
0.62
0.60
0.25
0.30
0.35
0.40
0.45
0.50
ε (63Ni) / ε (3H)
ε (3H)

CIEMAT/NIST method -- measurement & uncertainty model



characteristics LS Spectrometers

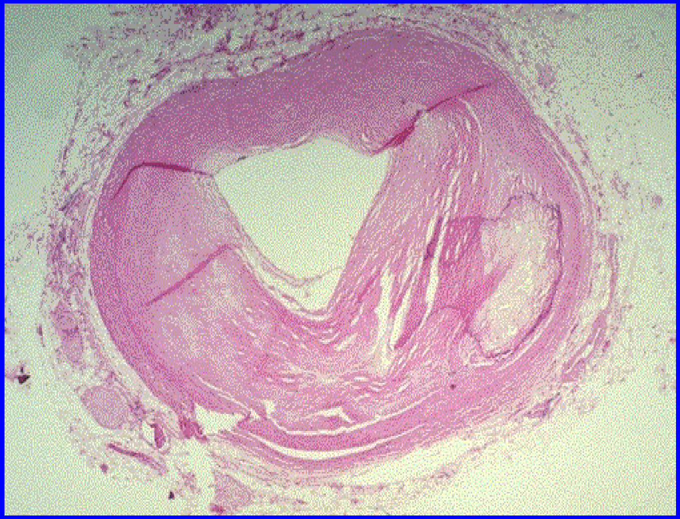
Characteristic	System B	System P
LS spectrometer model	Beckman LS7800	Packard Tri-carb A2500TR
Operating mode	sum-coincidence	sum-coincidence
Photomultiplier tubes	Hamamatsu R331-05	Hamamatsu R331-08
Operating temperature	ambient	ambient
Coincidence resolving time	22 ns	18 ns
Sum-coincident pulse amplification	logarithmic	linear
Pulse resolving time	5 μs to 33 μs (variable with pulse height)	12 μs (fixed)
Spectral analog-to-digital converter (ADC) capacity	1000 channels	2048 channels
Nominal conversion gain (energy per channel)	variable (with logarithmic energy)	≅ 1 keV
Detection threshold (nominal)	≤ 1 keV	≤ 1 keV
Live-time determination method (and standard uncertainty)	gated oscillator (scaled) (± 0.1 %)	gated oscillator (scaled) (± 0.1 %)
Quench indicating parameter (QIP)	Horrocks number (H)	transformed Spectral Index of the External Standard (tSIE) (proprietary)
External γ-ray source for QIP determination (and location)	^{137}Cs (side)	^{133}Ba (bottom)

Importance and Impact

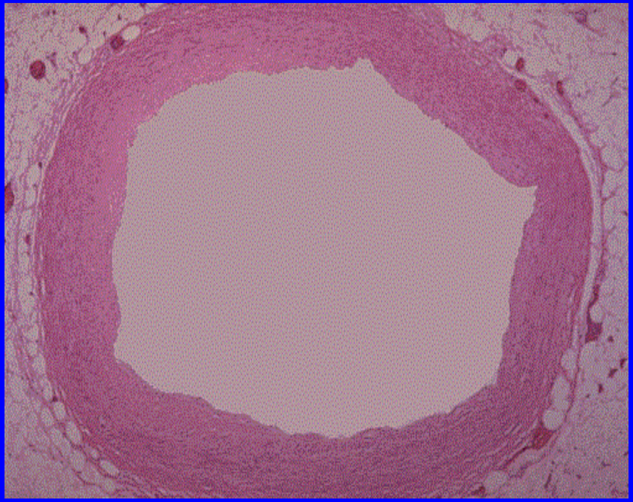
CAD is on of the leading causes of both morbidity and mortality in the US & western world

- ***caused by atherosclerotic narrowing (stenosis) of heart's arteries from formation of fatty tissue plaques***

Coronary Artery Disease



Mild Atheriosclerosis

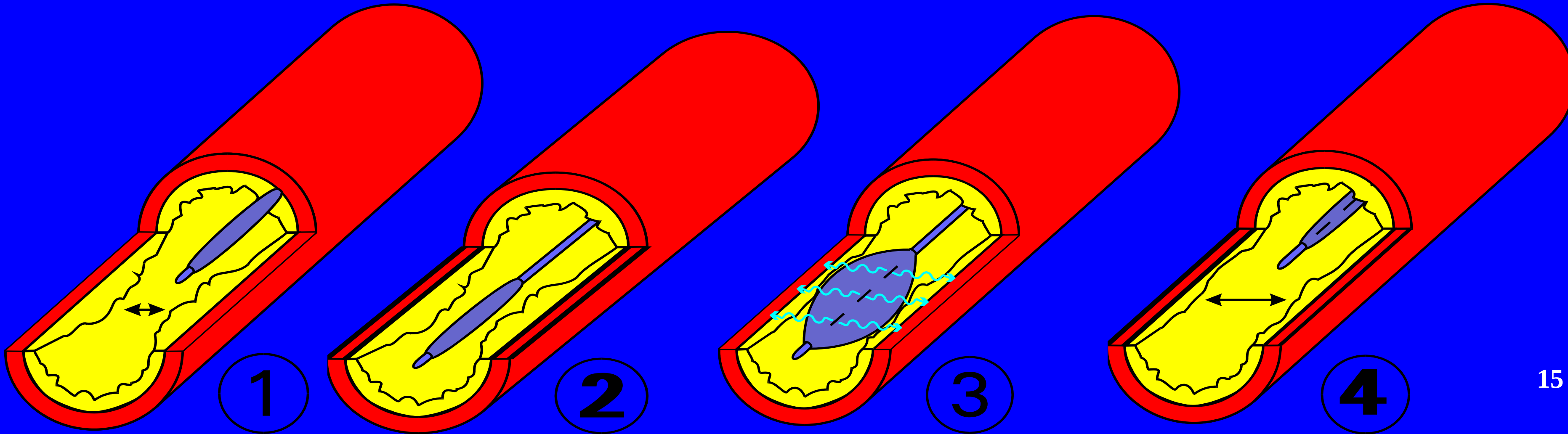


Normal

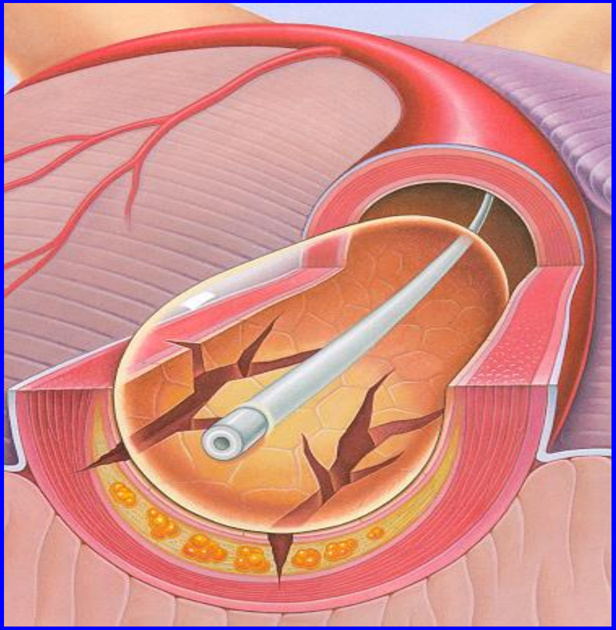
Advanced CAD cases -- prior to bypass surgery -- usually treated by PTCA procedures

PTCA = percutaneous transluminal coronary angioplasty

PTCA - “Balloon Angioplasty”



Nearly 460,000 PTCA procedures in US in 1996



Increasing at rate of about 35,000 additional procedures per year

About 30 % to 50 % of patients experience restonis within 1 year

Radiation treatment (8 to 30 Gy) with intravascular brachytherapy sources is one approach being researched for reducing rate of restenosis

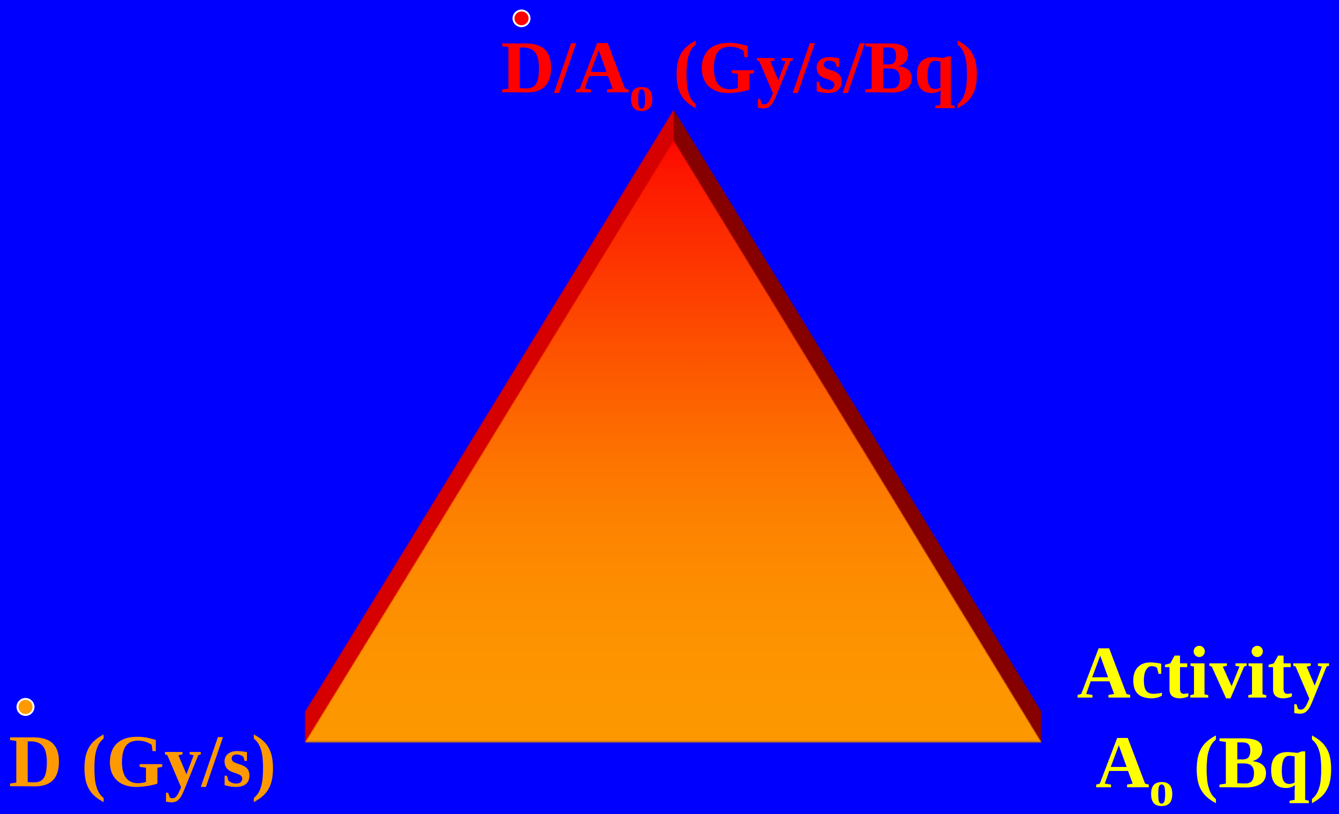
Medical and Economic impacts may be vast

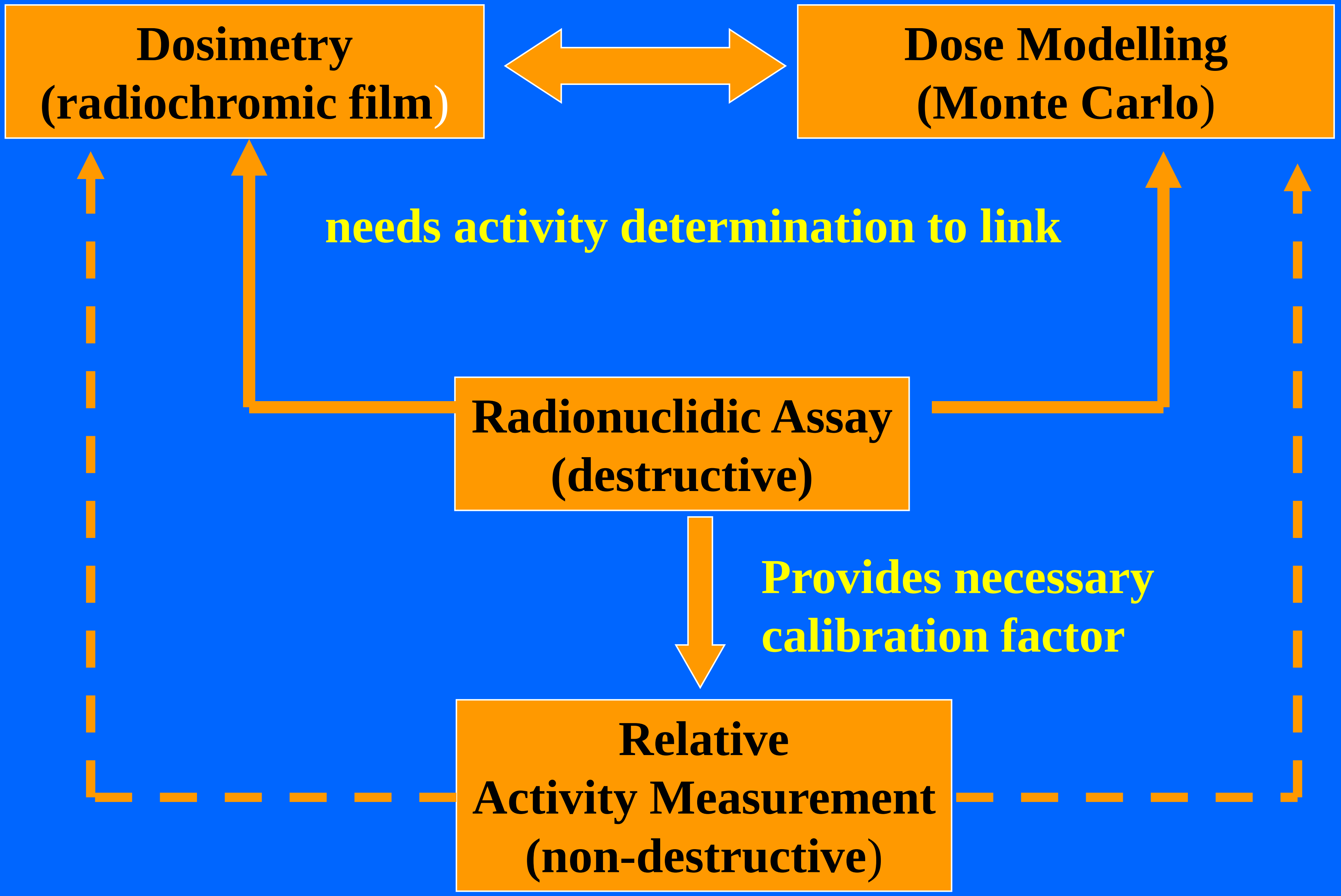
- Few patients receive intravascular radiation treatments now -- about 4000 in 1998
- Potential = 600,000 per year in US alone
- Tremendous commercial interest

Intravascular Brachytherapy Sources

- ***Need for activity characterizations***
- ***Why destructive assays ?***

source characterization




Dosimetry
(radiochromic film)
Dose Modelling
(Monte Carlo)
needs activity determination to link
Radionuclidic Assay
(destructive)
Provides necessary
calibration factor
Relative
Activity Measurement
(non-destructive)

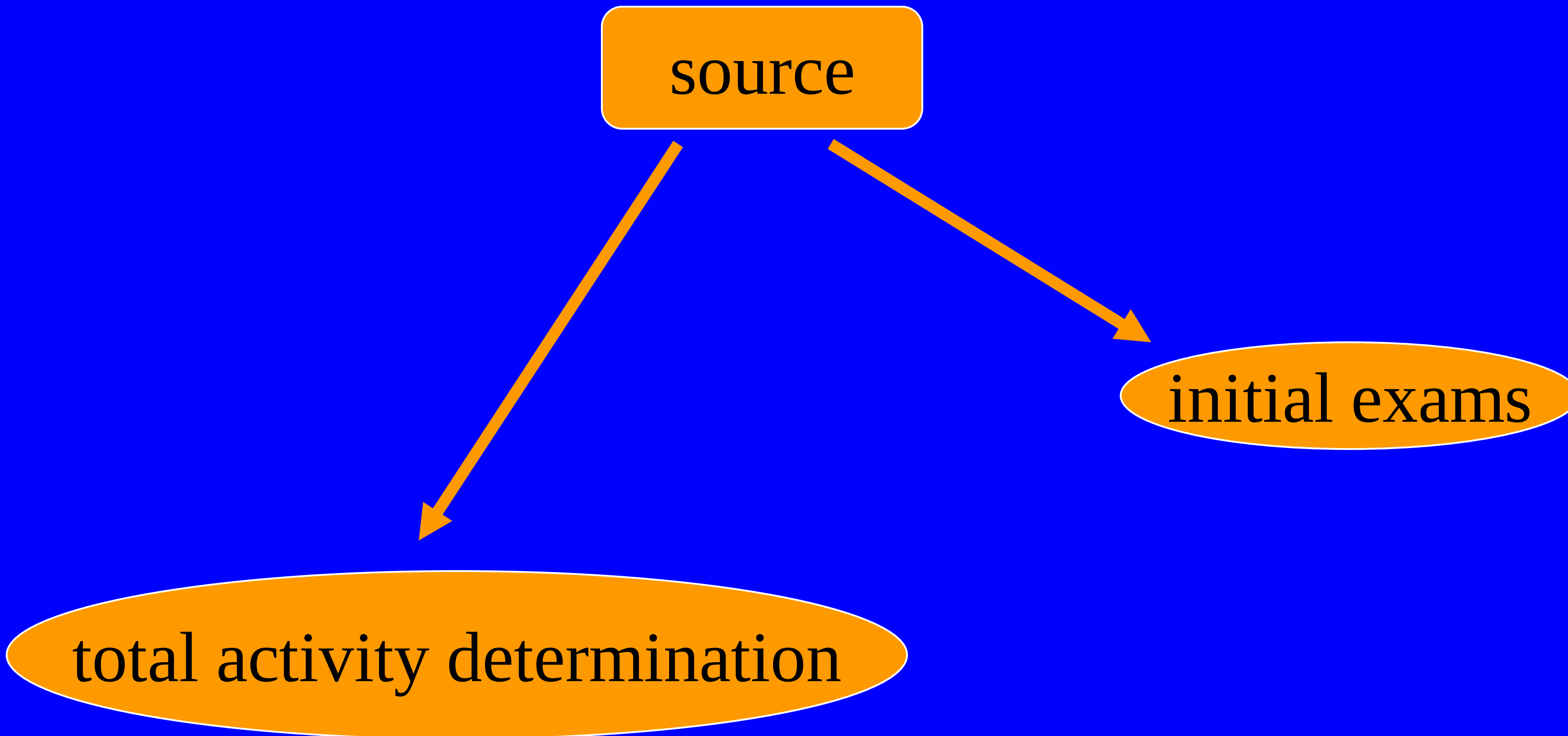
NIST calibrations of intravascular brachytherapy sources

manufacturer	Guidant	Novoste	Isostent	Radiance	Cedar Sinai Med. Center	Washington Hosp. Center	Interventional Technologies
nuclide (half-life)	^{32}P 14 d	^{90}Sr-^{90}Y 29 a (64 h)	^{32}P 14 d	^{32}P 14 d	^{188}Re 17 h	^{133}Xe 5 d	^{99m}Tc 6 h
source configuration	encapsulated seed in long wire	encapsulated seed for catheter train	stent	"hot wall" balloon catheter	liquid-filled balloon	gas-filled balloon	liquid-filled perfusion catheter
external dimensions	27 mm 0.5 mm OD	2.5 mm 0.6 mm	15 & 25 mm 3 mm OD (expanded)	33 mm 3 mm OD (inflated)	25 to 35 mm 3 mm OD (inflated)	25 to 35 mm 3 mm OD (inflated)	30 mm 3 mm OD
source composition (proprietary)	highly inert polymeric material	highly refractory "ceramic" matrix	ion-implanted SS	thin film / inert matrix	^{188}Re-MAG3 in saline solution	^{133}Xe in CO_2 carrier gas	liposome-encapsulated ^{99m}Tc in saline solution
encapsulation	TiNi jacket	SS jacket	none	enveloped in double wall of polyethylene balloon	balloon wall	balloon wall	none

3 mm seed

^{32}P ion-implanted SS stents

Generic procedure



Generic procedure

initial exams

test for removable surface activity

high resolution photonic-emission spectrometry to look for impurities

ion chamber measurements to establish non-destructive calibration factor

total activity determination

understand composition / design chemistry

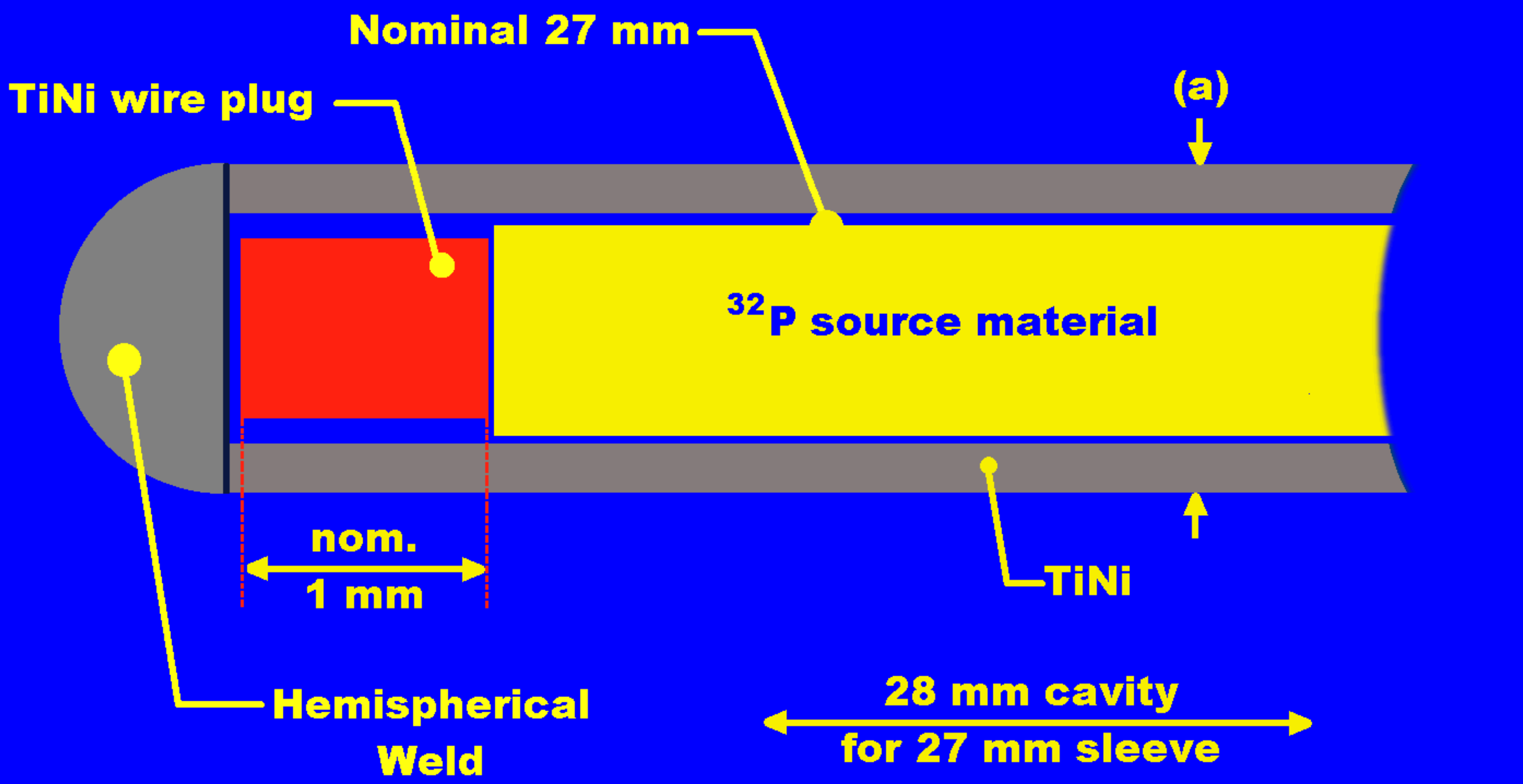
digest source

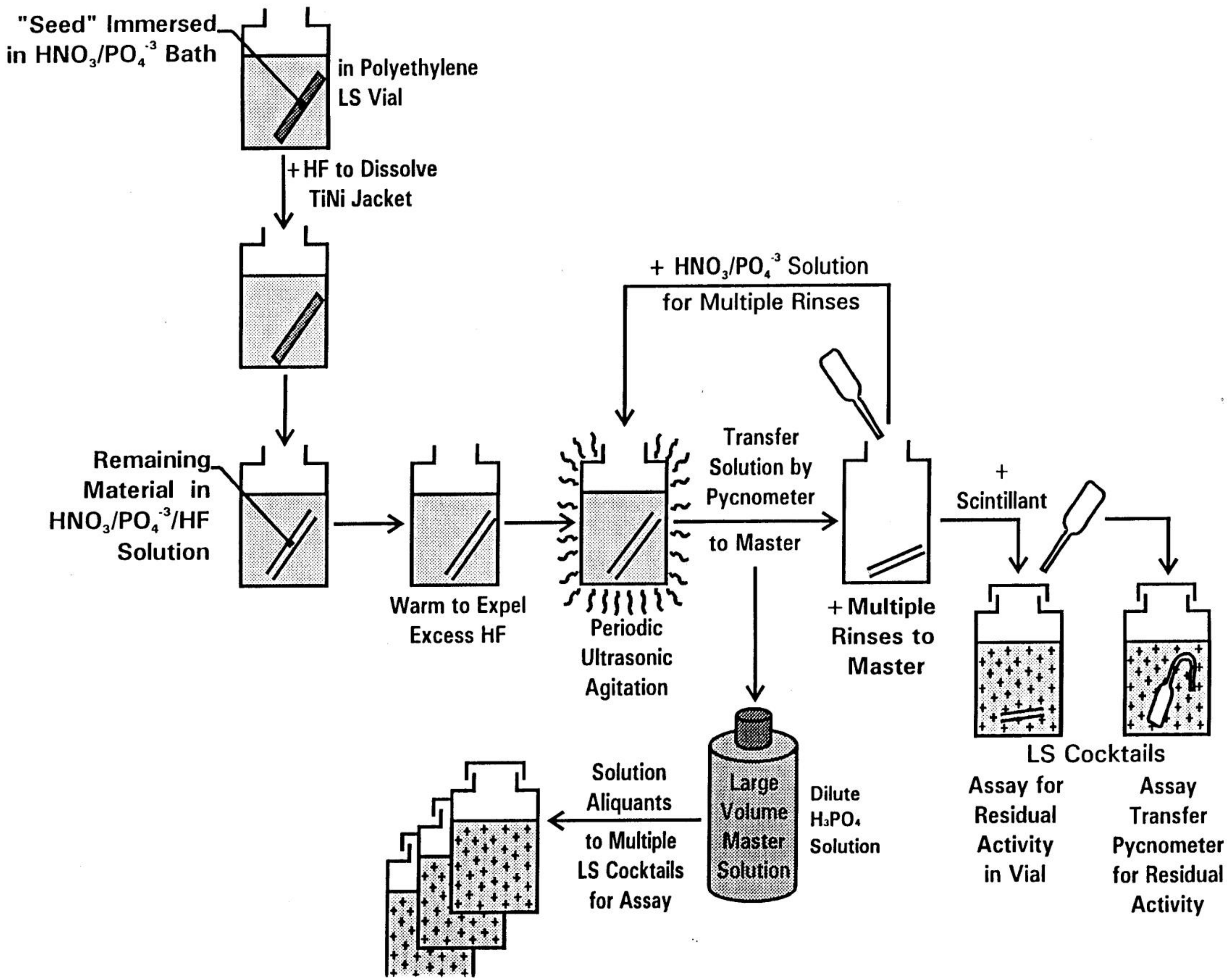
collect & dilute solution

measure any residual activity

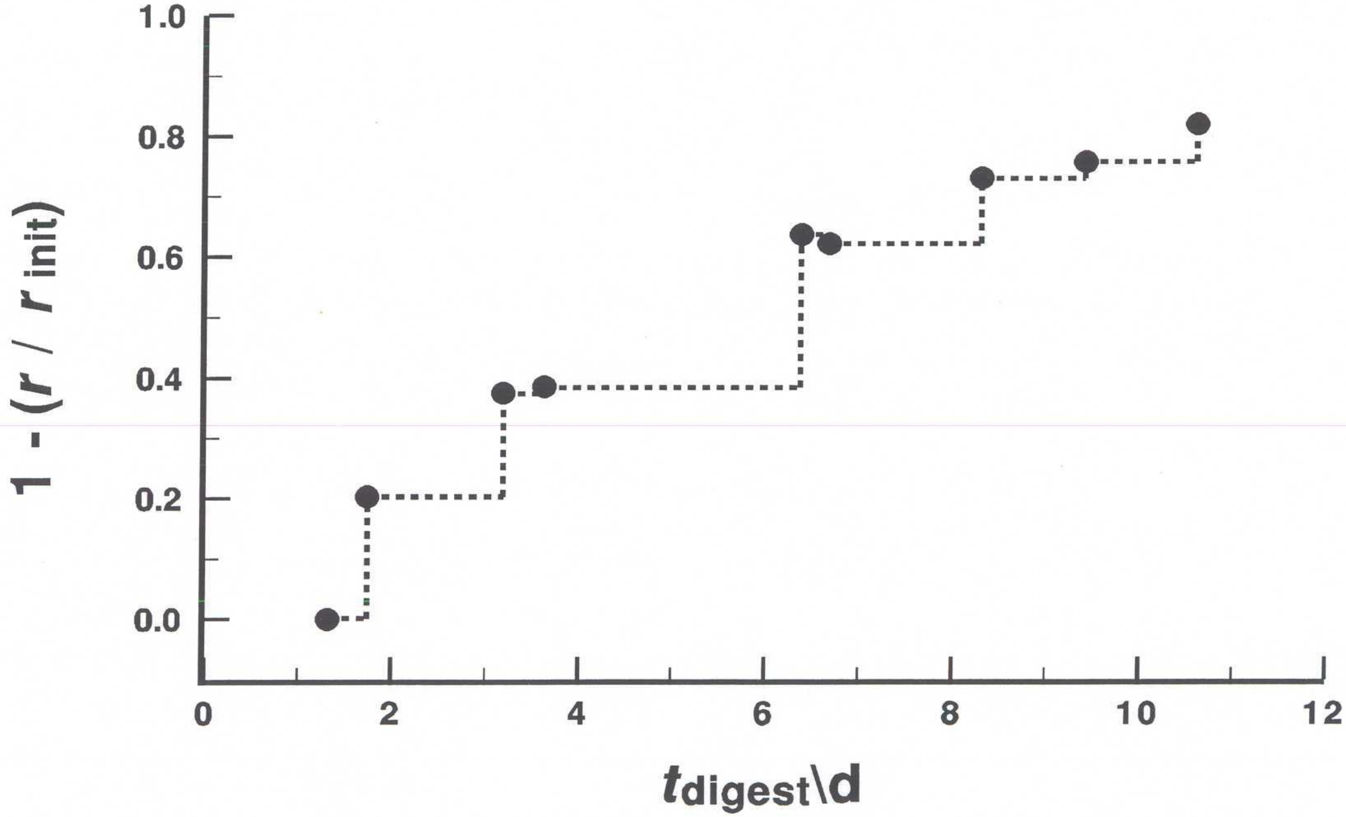
Assay aliquants by LS

Measure any activity on apparatus

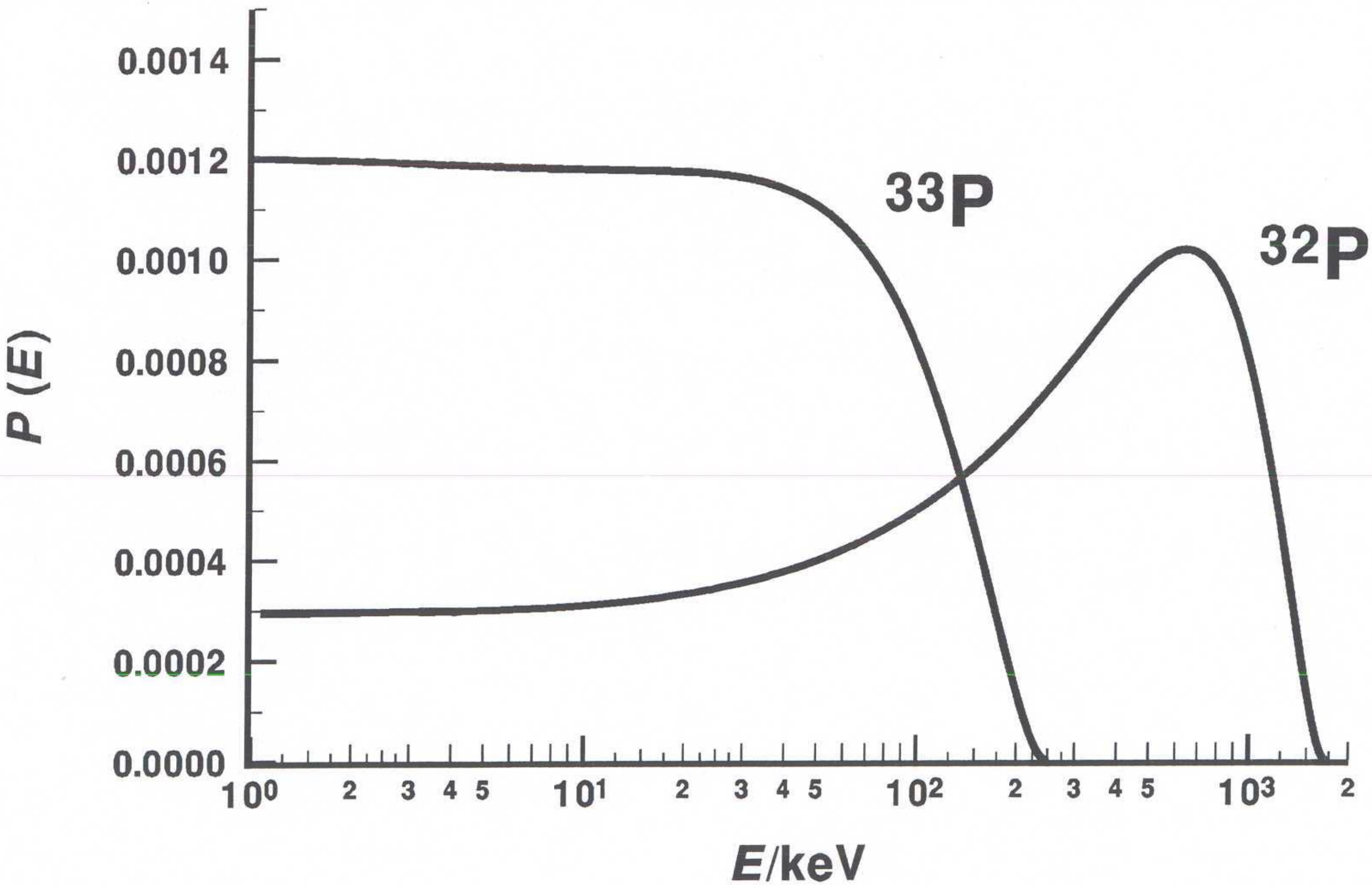

Nominal 27 mm
TiNi wire plug
(a)
^{32}P source material
nom.
1 mm
TiNi
Hemispherical
Weld
28 mm cavity
for 27 mm sleeve
(a) 0.457 mm


"Seed" Immersed in HNO_3/PO_4^{-3} Bath
in Polyethylene LS Vial
+HF to Dissolve TiNi Jacket
Remaining Material in $HNO_3/PO_4^{-3}/HF$ Solution
Warm to Expel Excess HF
Periodic Ultrasonic Agitation
+ HNO_3/PO_4^{-3} Solution for Multiple Rinses
Transfer Solution by Pycnometer to Master
+Multiple Rinses to Master
+ Scintillant
LS Cocktails
Assay for Residual Activity in Vial
Assay Transfer Pycnometer for Residual Activity
Large Volume Master Solution
Dilute H_3PO_4 Solution
Solution Aliquants to Multiple LS Cocktails for Assay

Sequential extractions and solution transfers

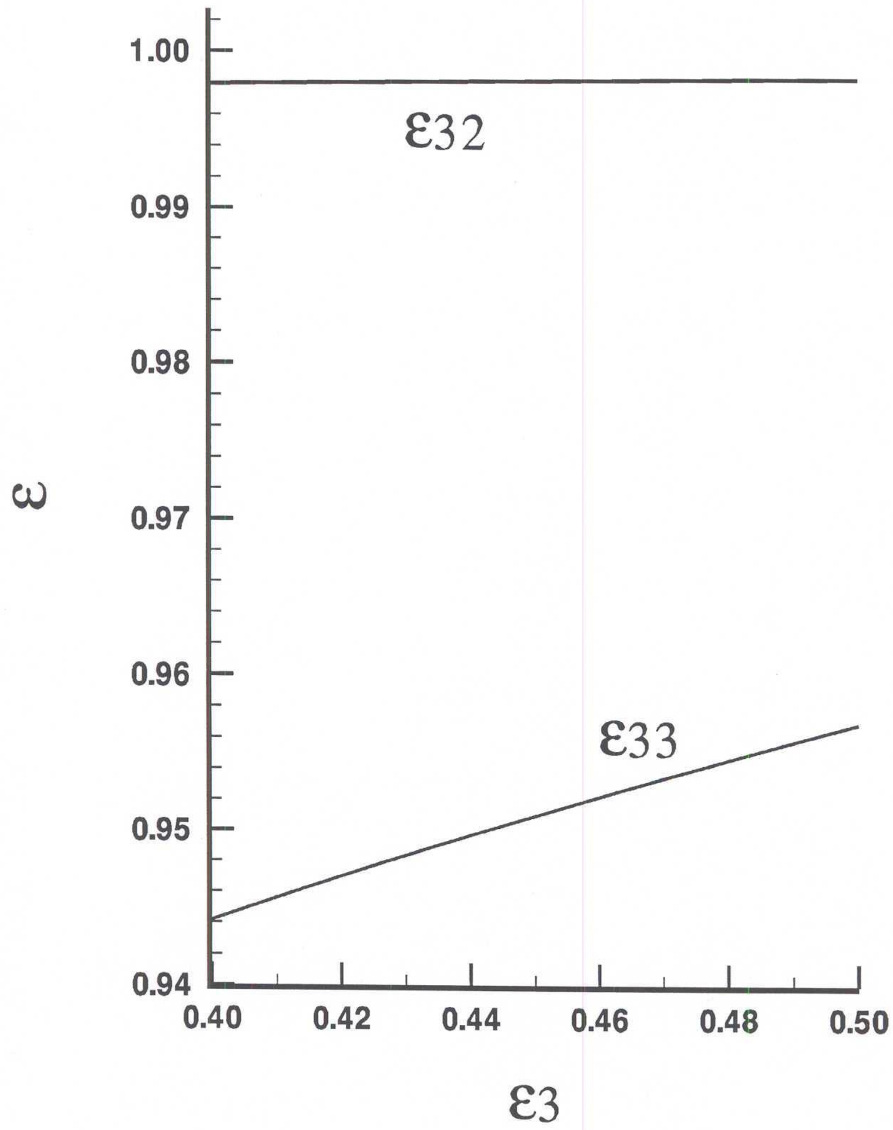


theoretical ^{32}P and ^{33}P beta spectra



LS efficiencies for ^{32}P and ^{33}P

from EFFY code



$$R = A_{32(0)}\varepsilon_{32}\exp(-\lambda_{32}t)$$

$$+ A_{33(0)}\varepsilon_{33}\exp(-\lambda_{33}t)$$

Linear transformation

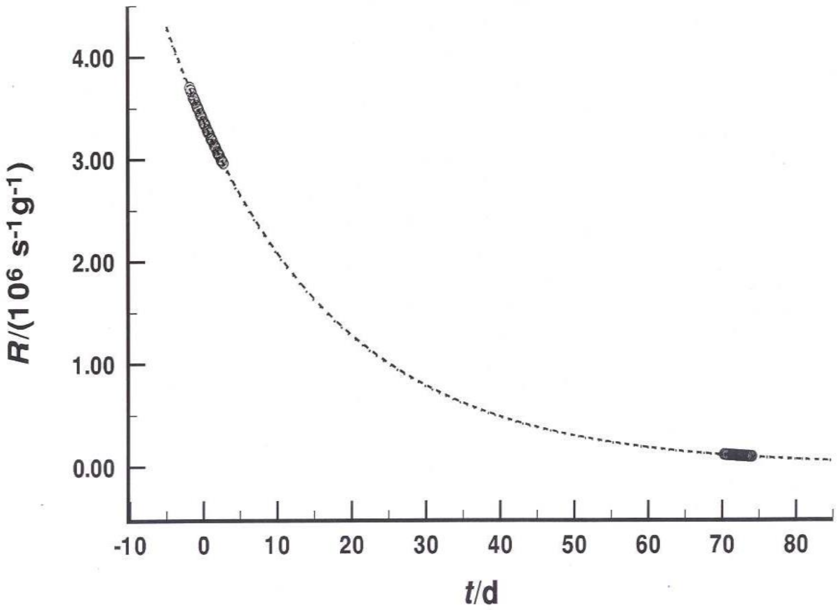
$$Y = A_{32(0)} \quad + A_{33(0)}X$$

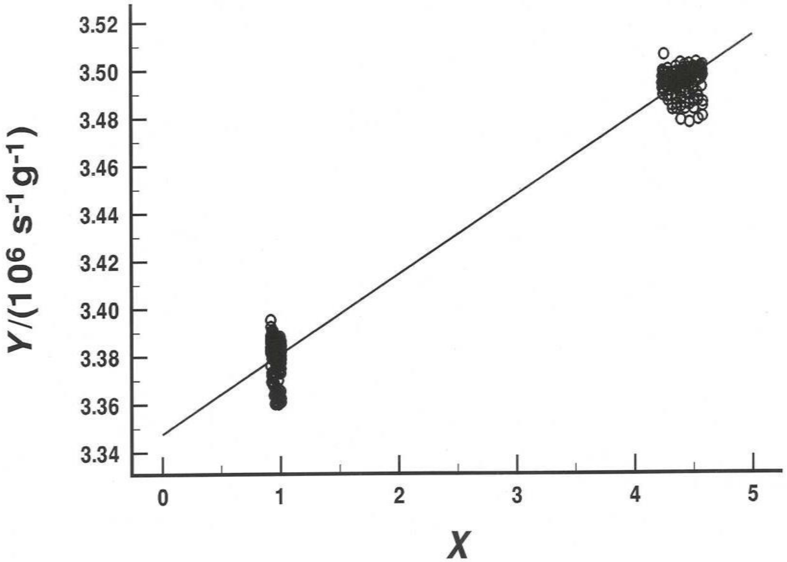
with

$$Y = R/\varepsilon_{32}\exp(-\lambda_{32}t)$$

$$X = \varepsilon_{32}\exp(-\lambda_{32}t)/\varepsilon_{33}\exp(-\lambda_{33}t)$$

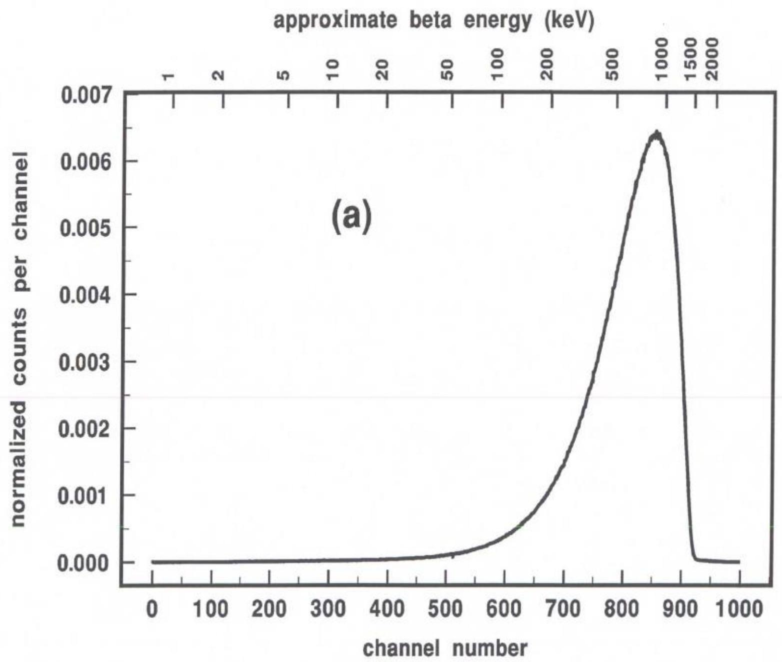
^{33}P and ^{32}P resolution data over 70 d





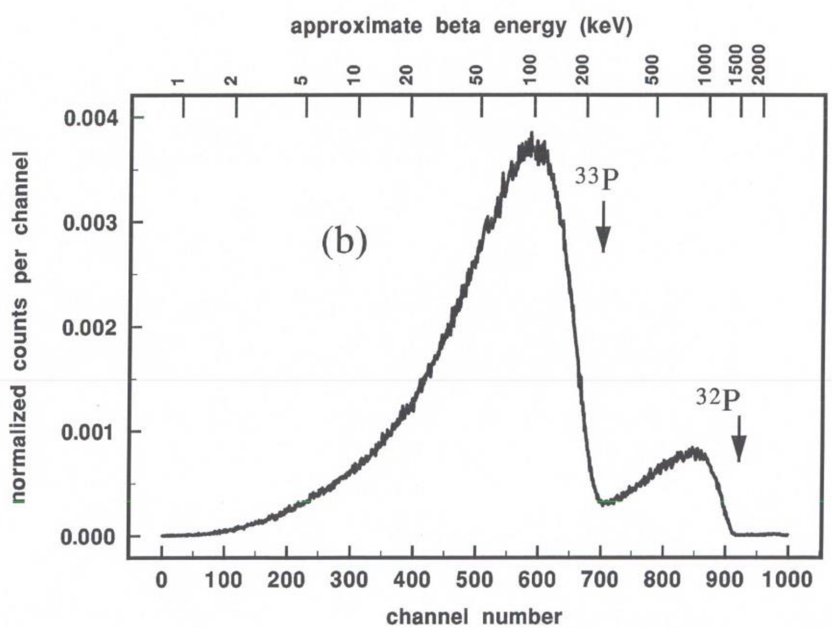
for 0.8 % impurity ratio

LS spectra



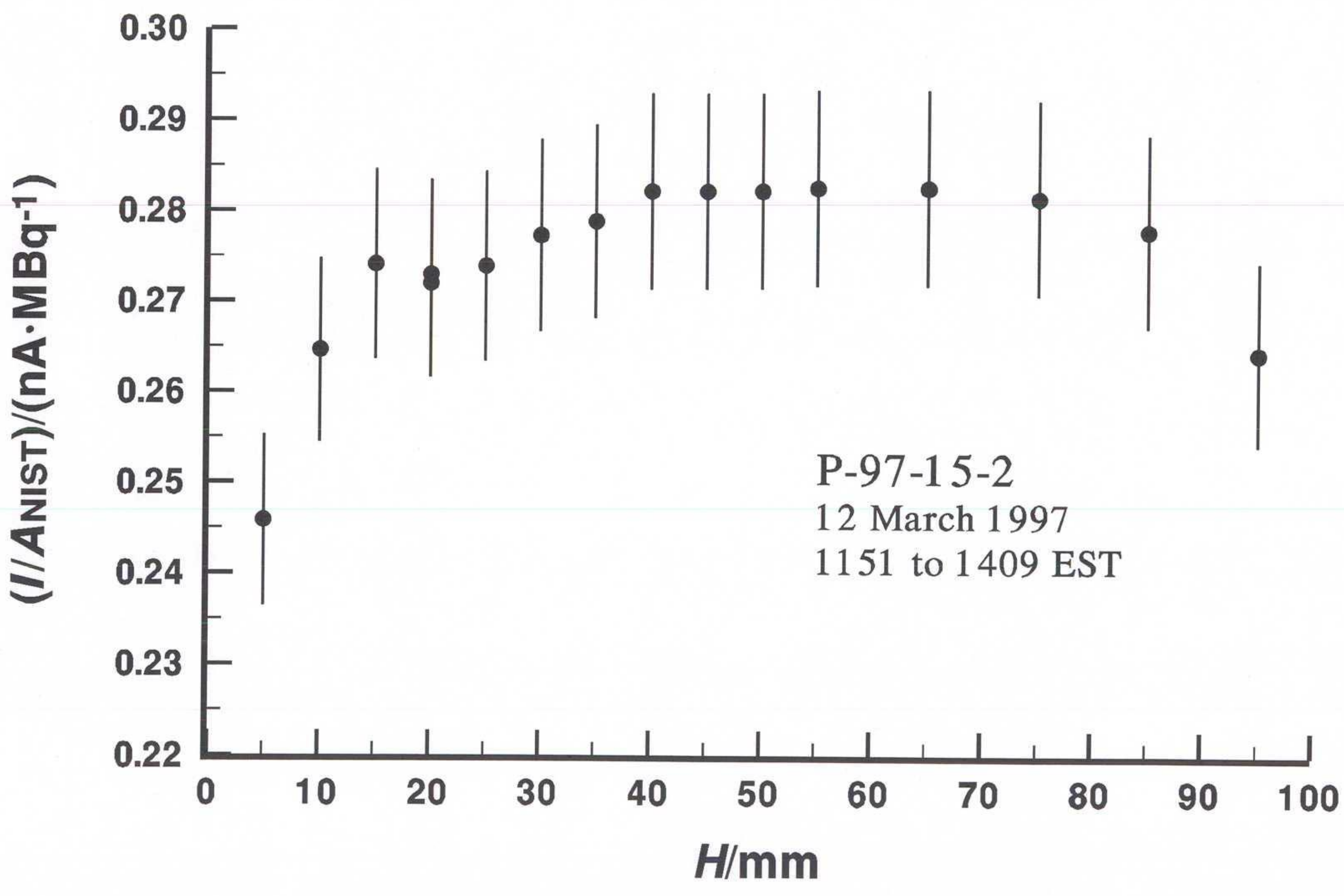
Resultant solution

Aged seed (direct)

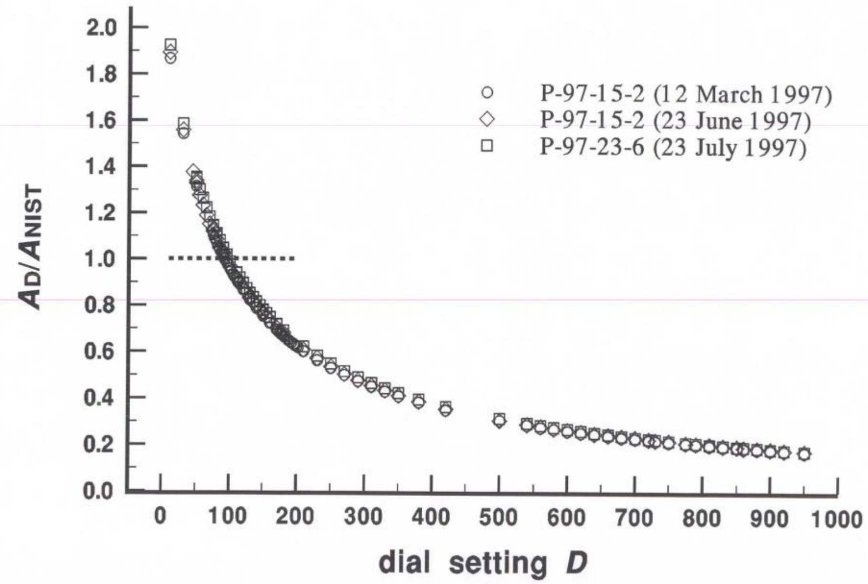


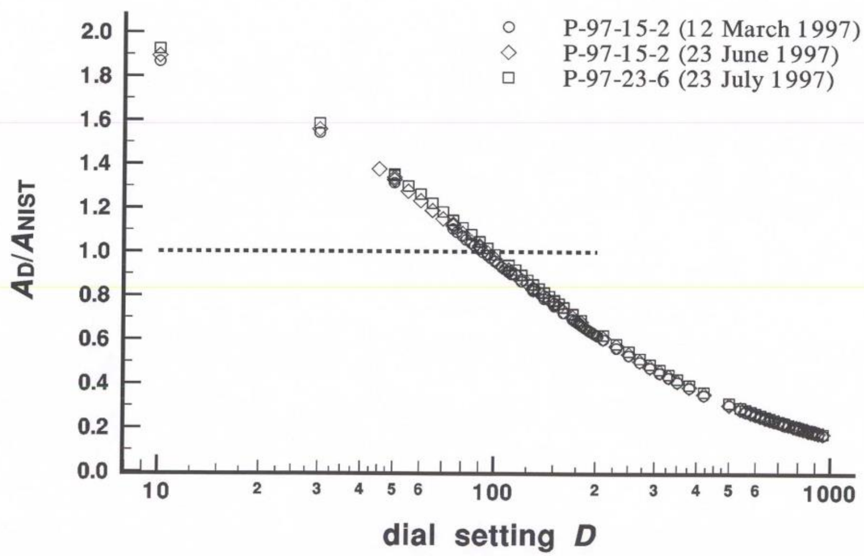
“dose calibrator” (ion chamber) calibrated for subsequent non-destructive assays

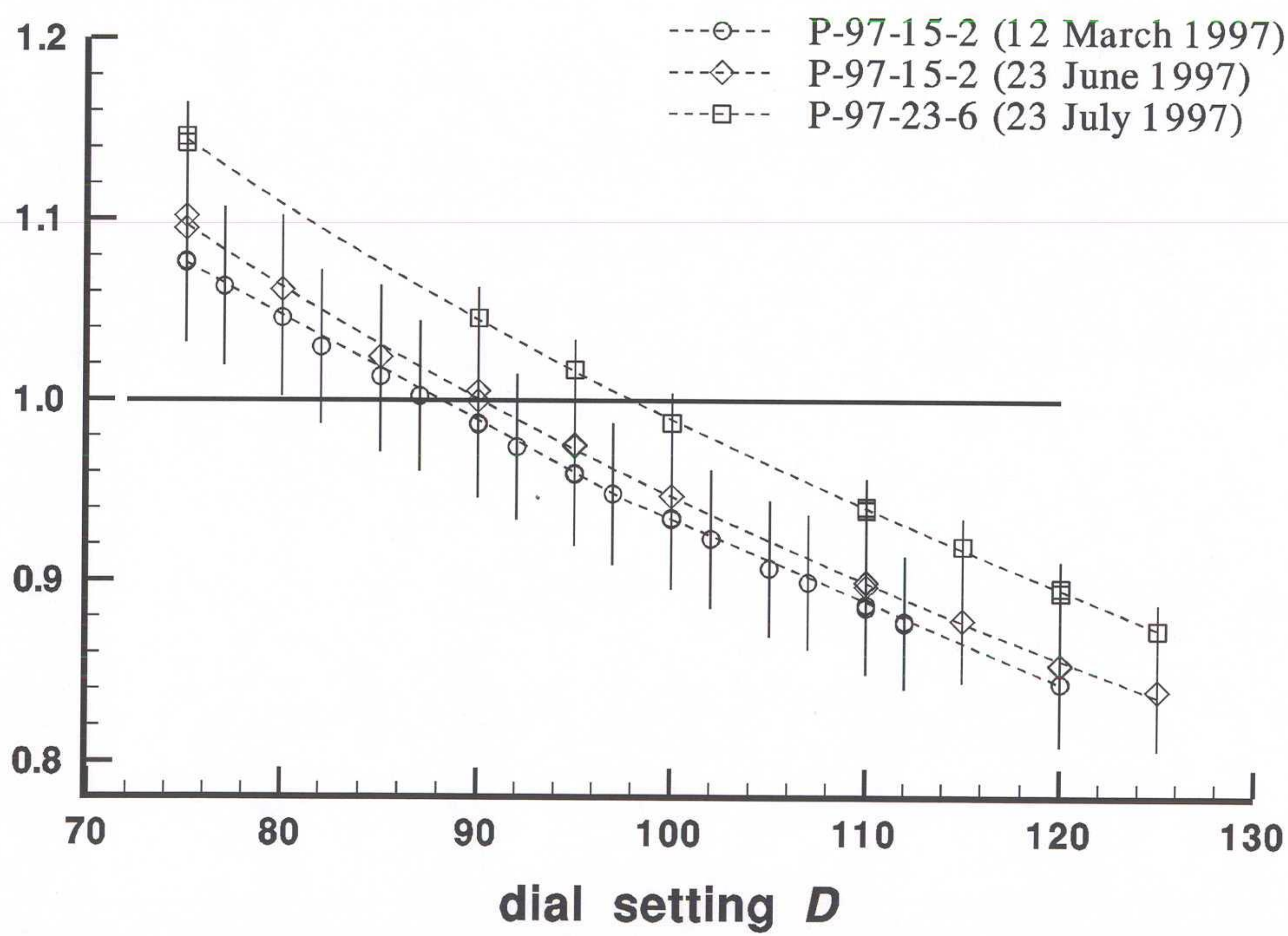
Source positioning



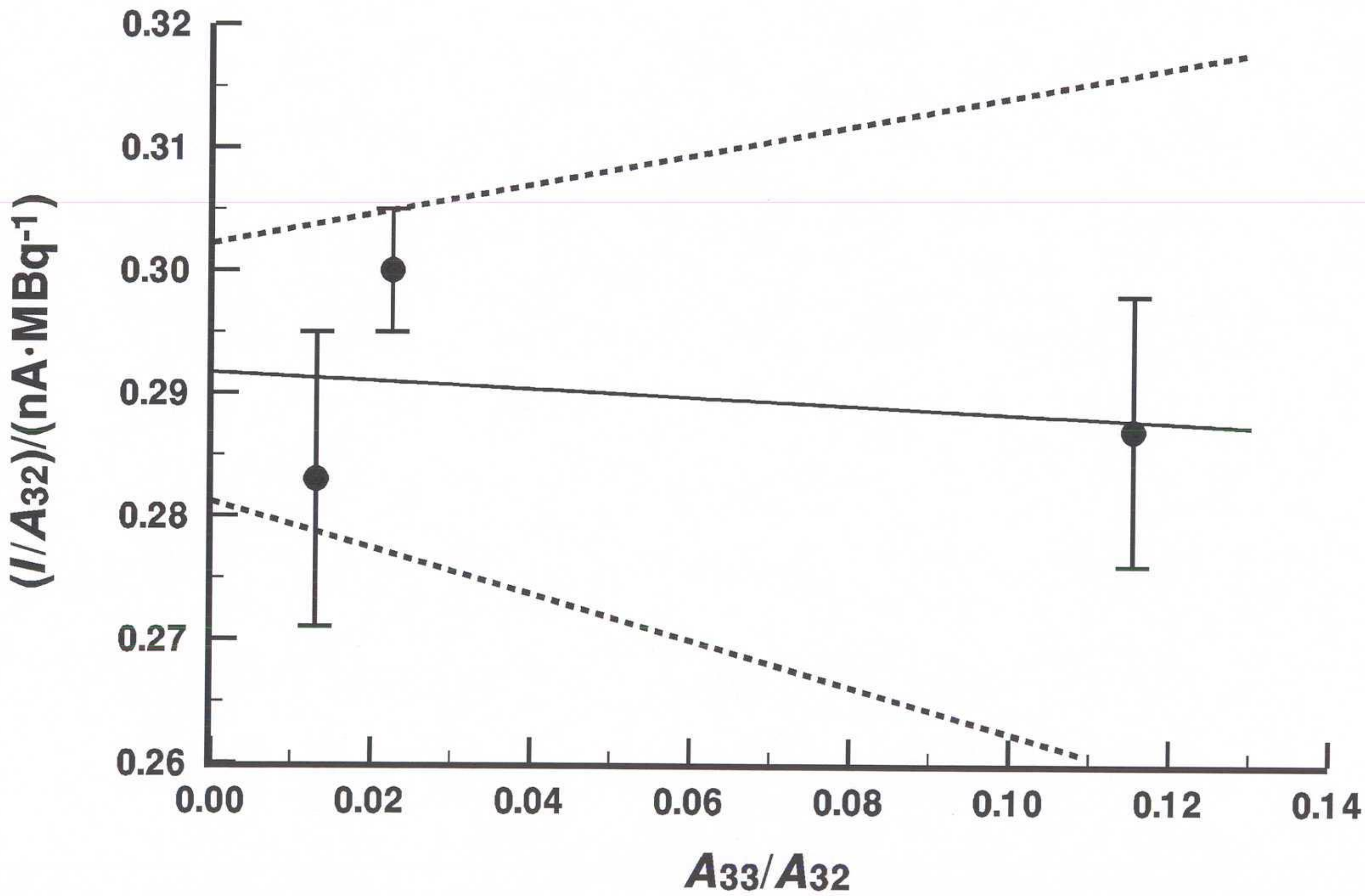
Capintec calibration data



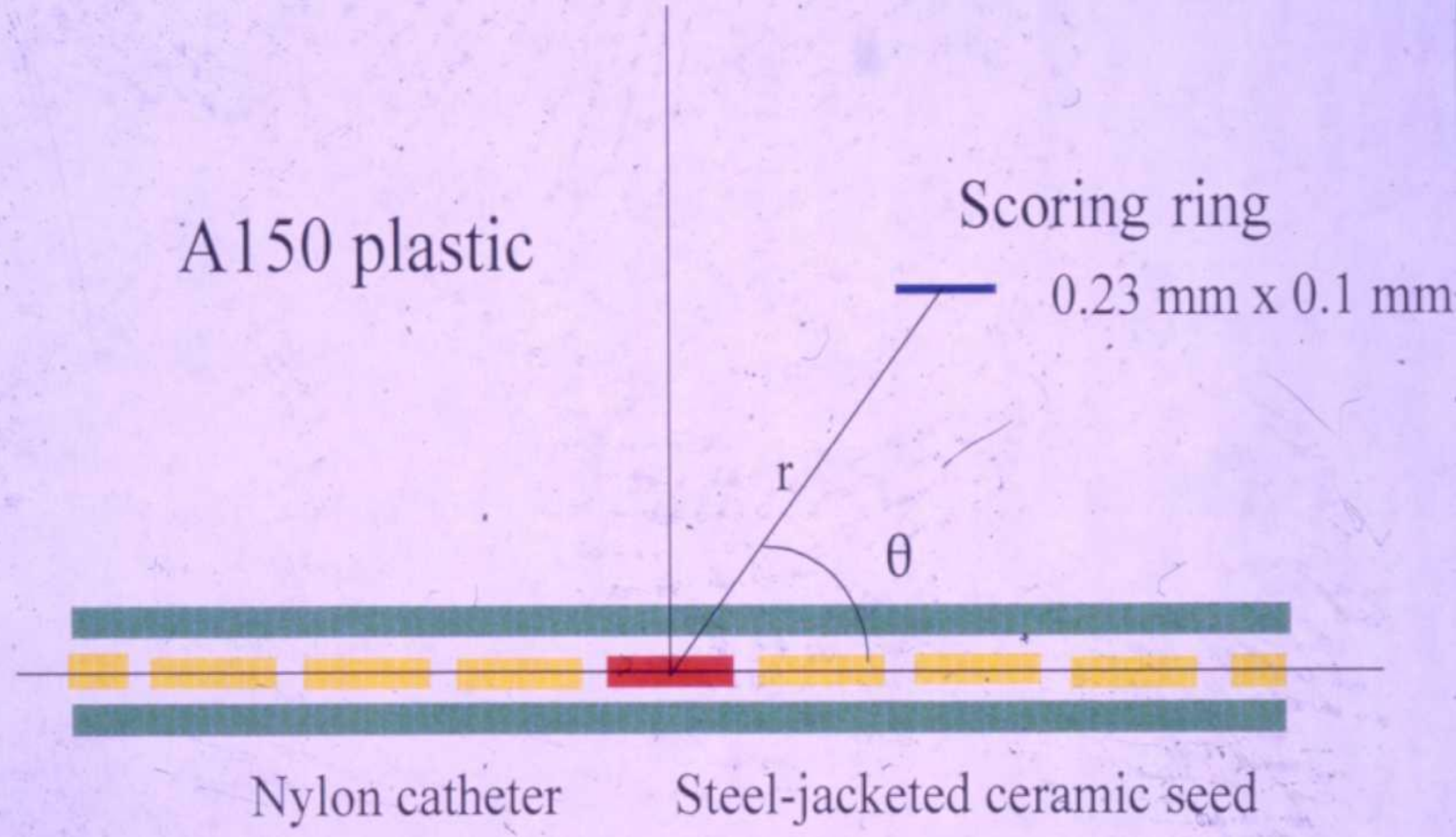



P-97-15-2 (12 March 1997)
P-97-15-2 (23 June 1997)
P-97-23-6 (23 July 1997)
1.2
1.1
1.0
0.9
0.8
AD/ANIST
70
80
90
100
110
120
130
dial setting D

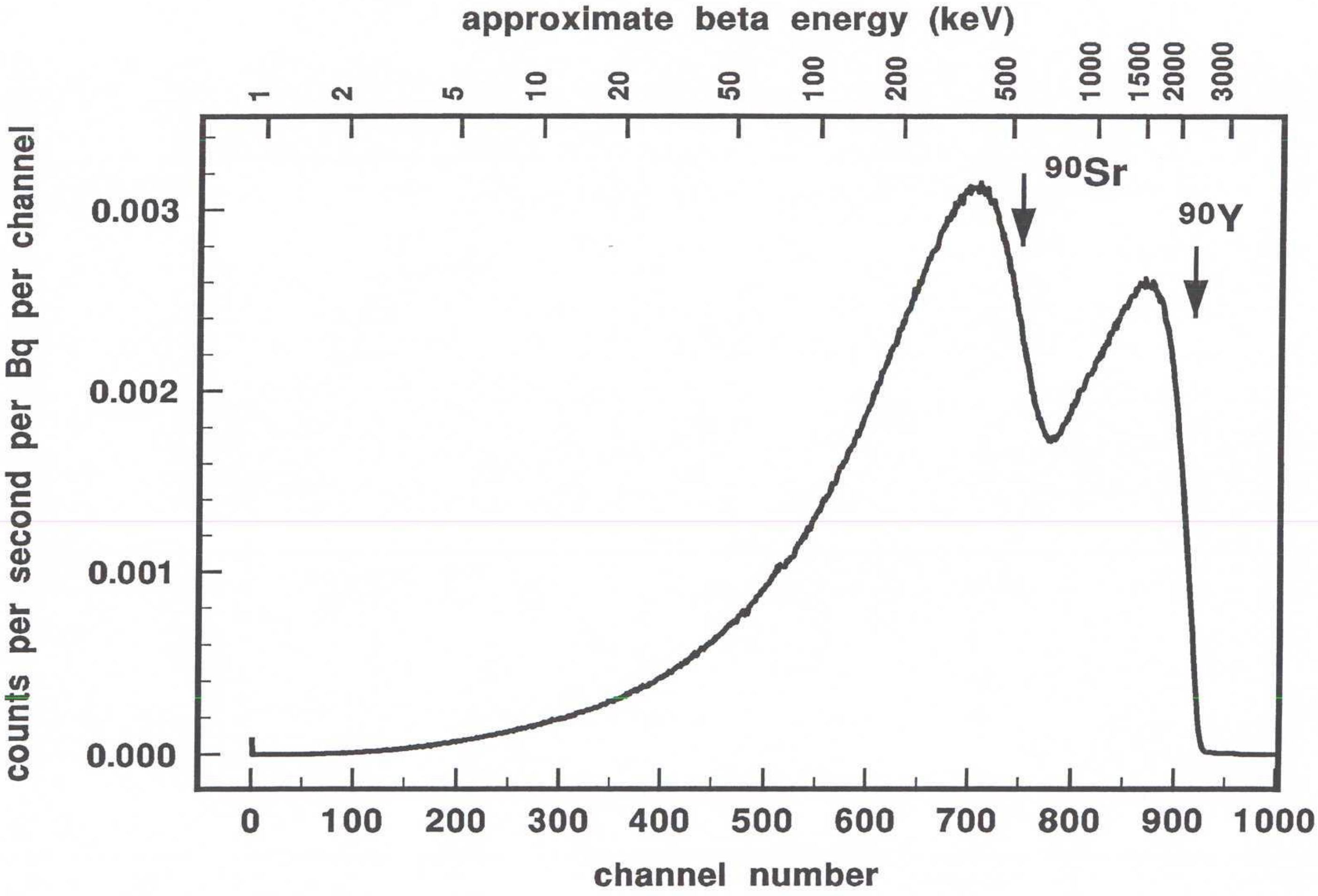
Effect of ^{33}P impurity on calibration factor



$^{90}Sr/Y$ Seed Train Geometry

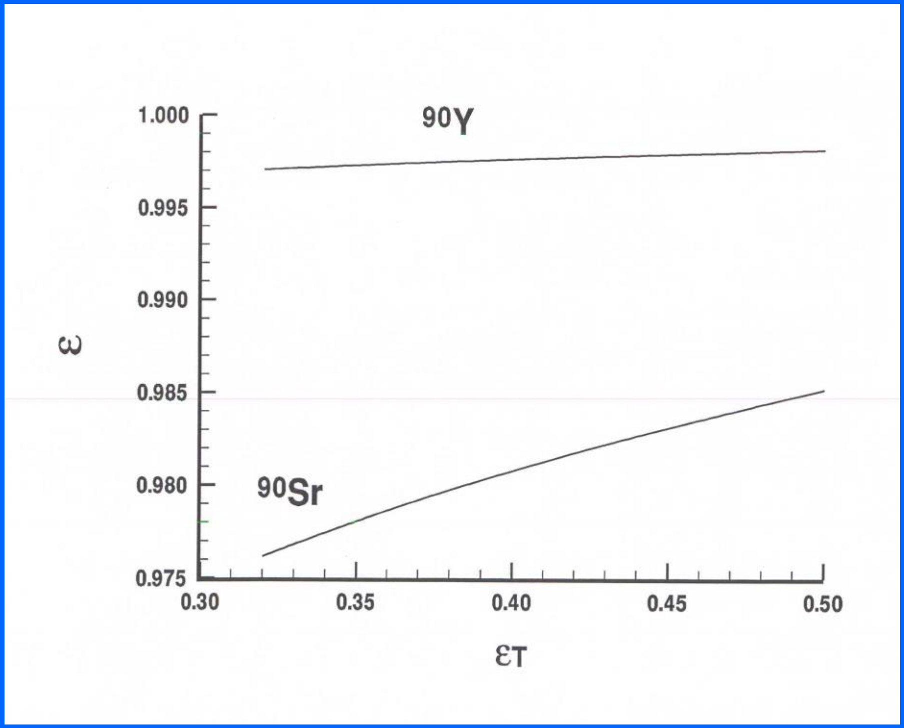


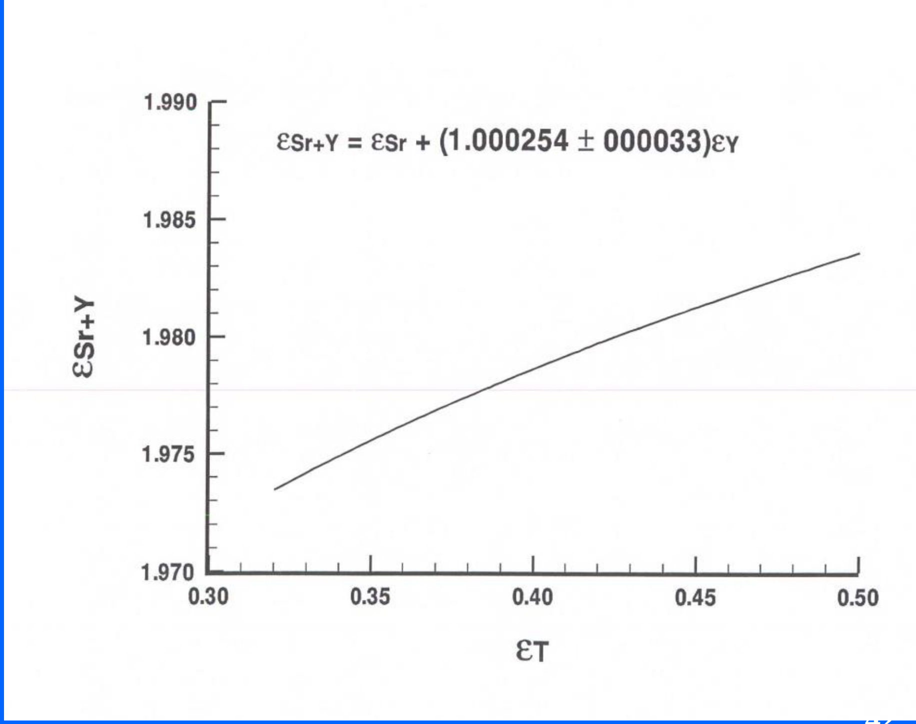
LS spectrum of ^{90}Sr-^{90}Y

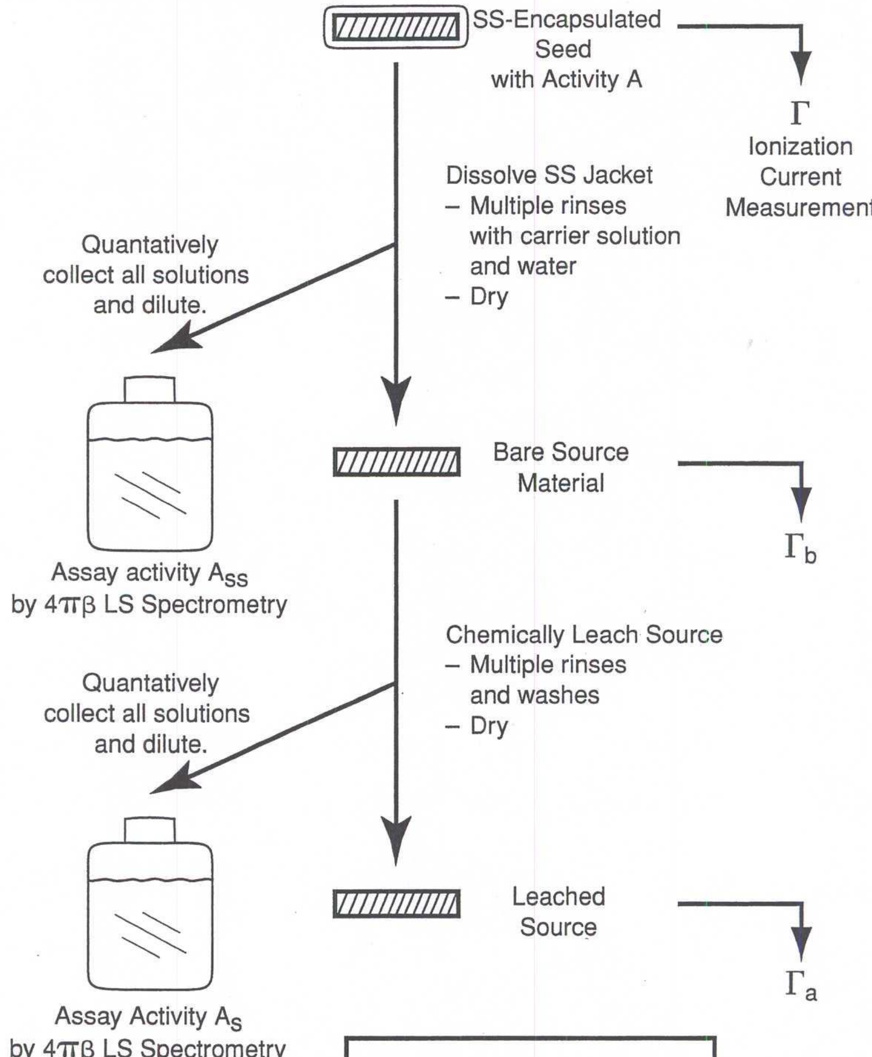


^{90}Sr and ^{90}Y LS efficiencies vs. that for ^{3}H

from EFFY code

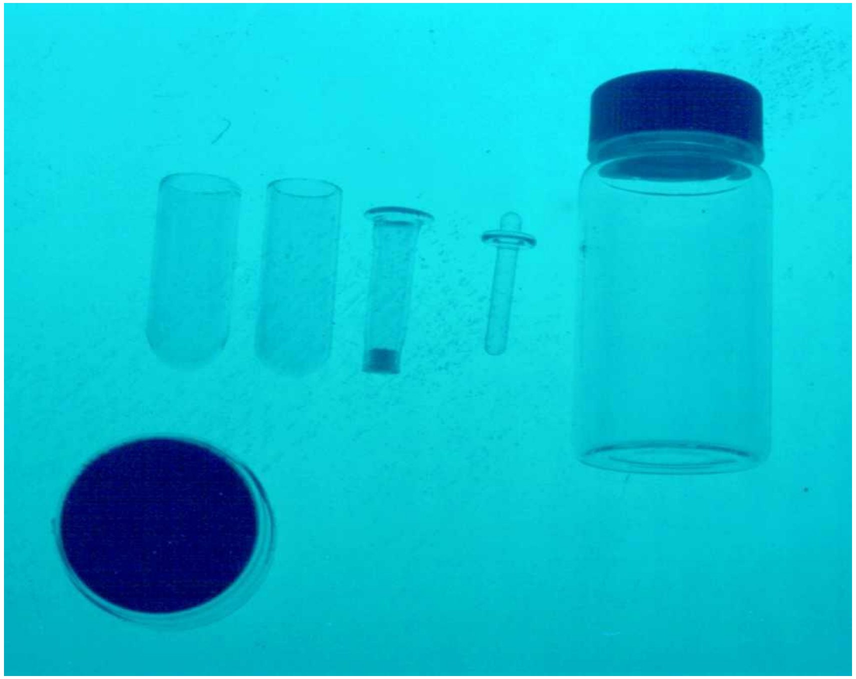


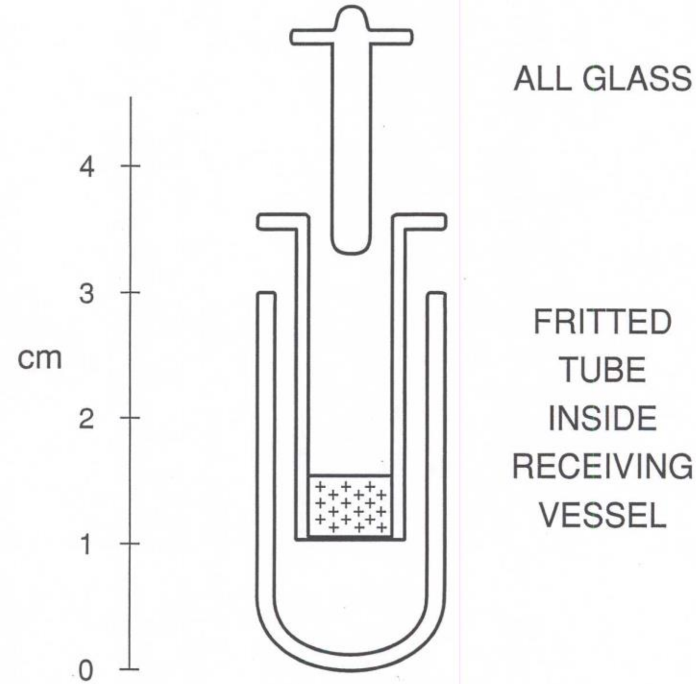




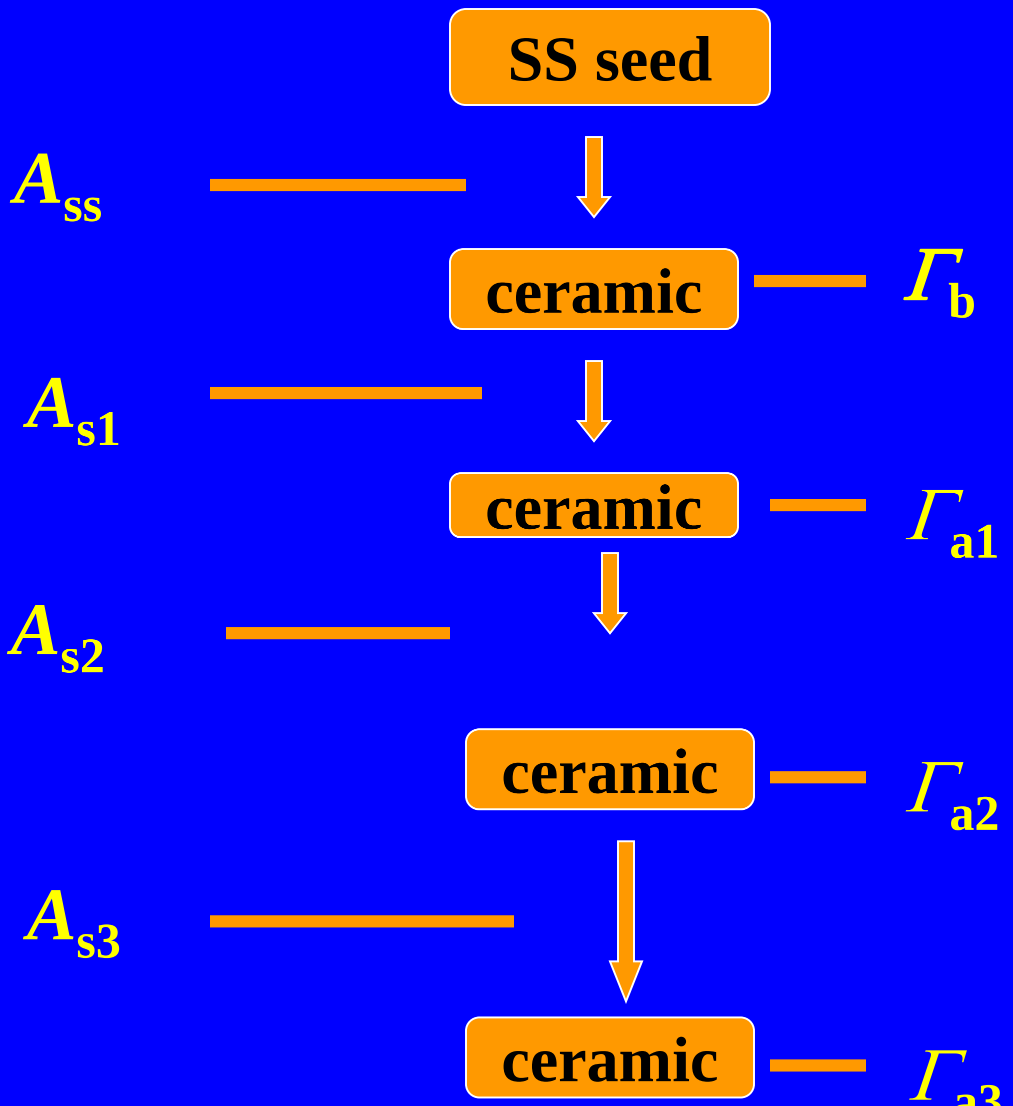
$$A = A_{ss} + \frac{A_s}{\left(1 - \frac{\Gamma_a}{\Gamma_b}\right)}$$

$$K = \frac{\Gamma}{A}$$





Assembly used to hold seed/source for ionization current measurements, and to perform chemical dissolution/extraction.



$$A_1 = A_{ss} + A_{s1}/(1 - \Gamma_{a1}/\Gamma_b)$$

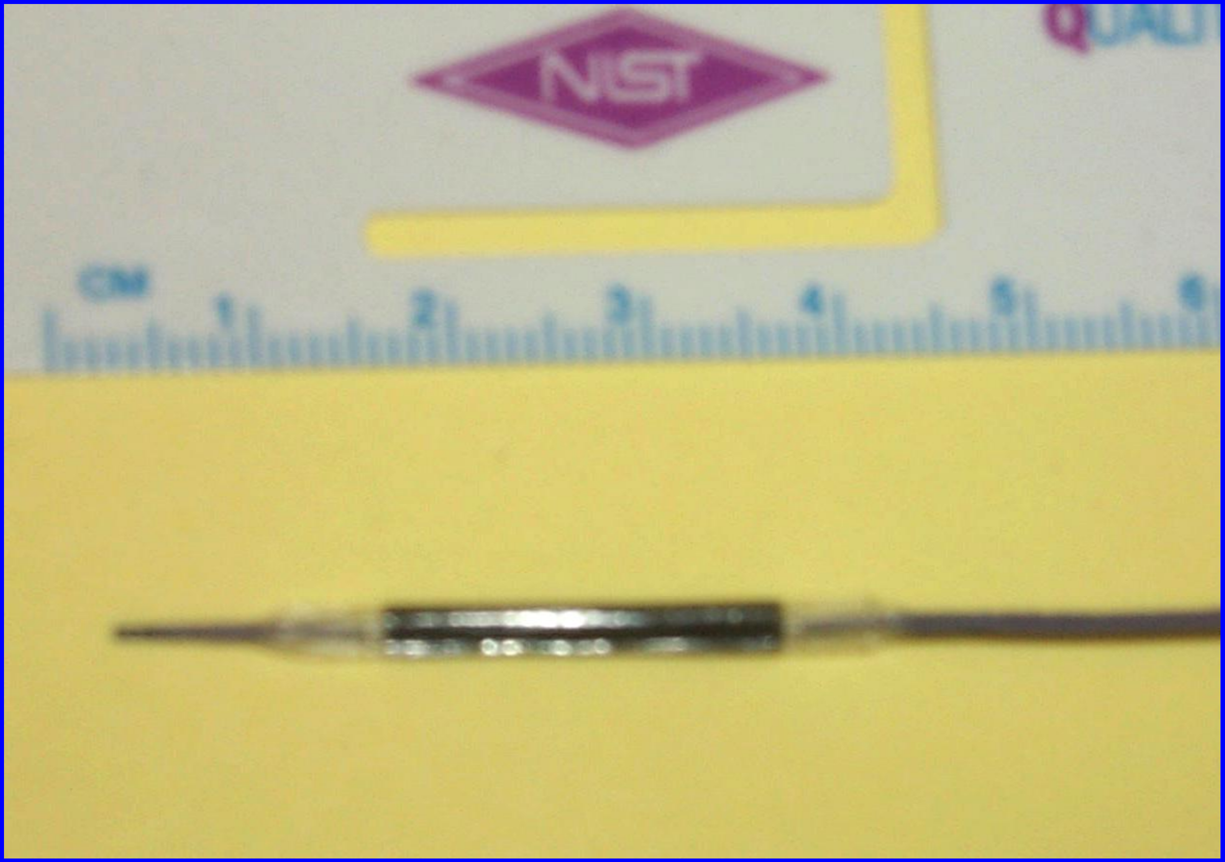
$$A_2 = A_{ss} + A_{s1} + A_{s2}/(1 - \Gamma_{a1}/\Gamma_{a2})$$

$$A_3 = A_{ss} + A_{s1} + A_{s2} + A_{s3}/(1 - \Gamma_{a3}/\Gamma_{a2})$$

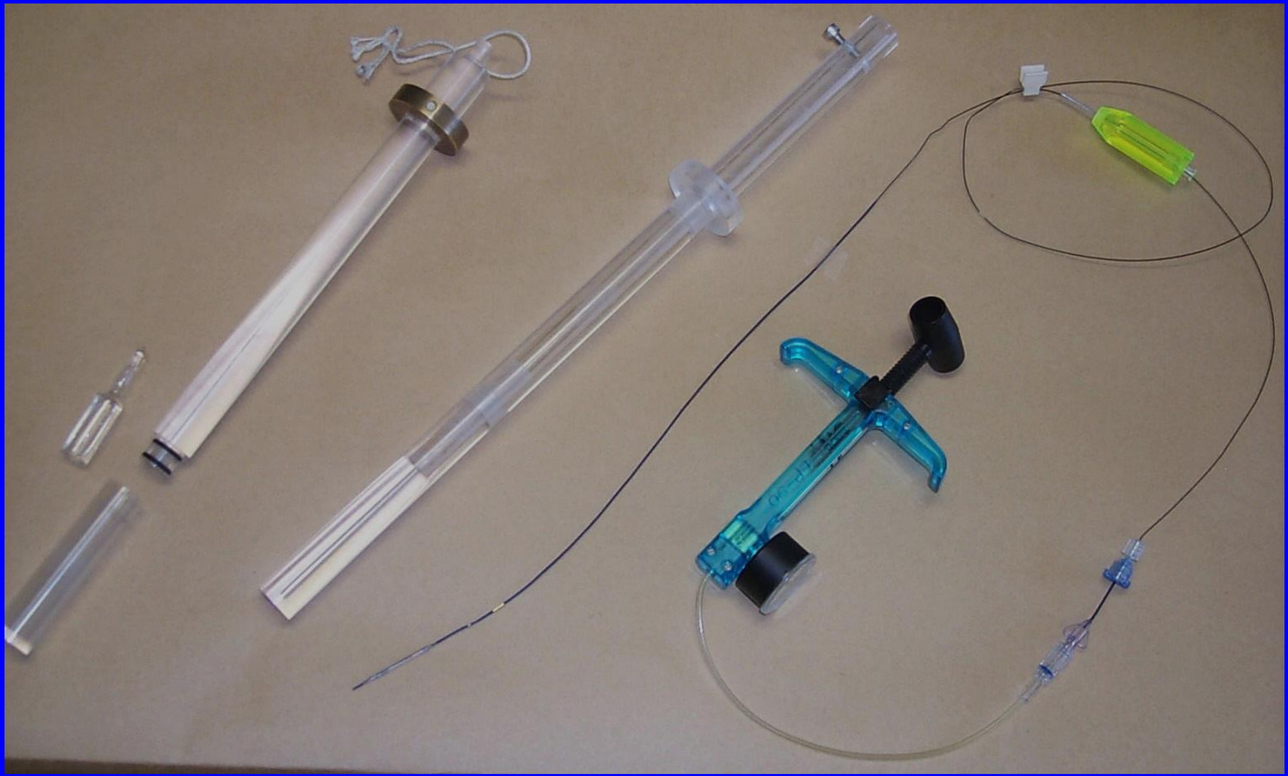
Sequential extraction results

	fraction of activity extracted	Derived total activity in source	Derived $K = \Gamma/A$ for bare seed
after SS removal	0.005	--	0.01154 MBq^{-1}
after 1st extraction	0.48	(128.8 $\pm$ 1.9) MBq	0.01147 MBq^{-1}
after 2nd extraction	0.81	(129.7 $\pm$ 1.1) MBq	0.01149 MBq^{-1}
after 3rd extraction	0.96	(129.7 $\pm$ 0.9) Mbq	0.0117 MBq^{-1}

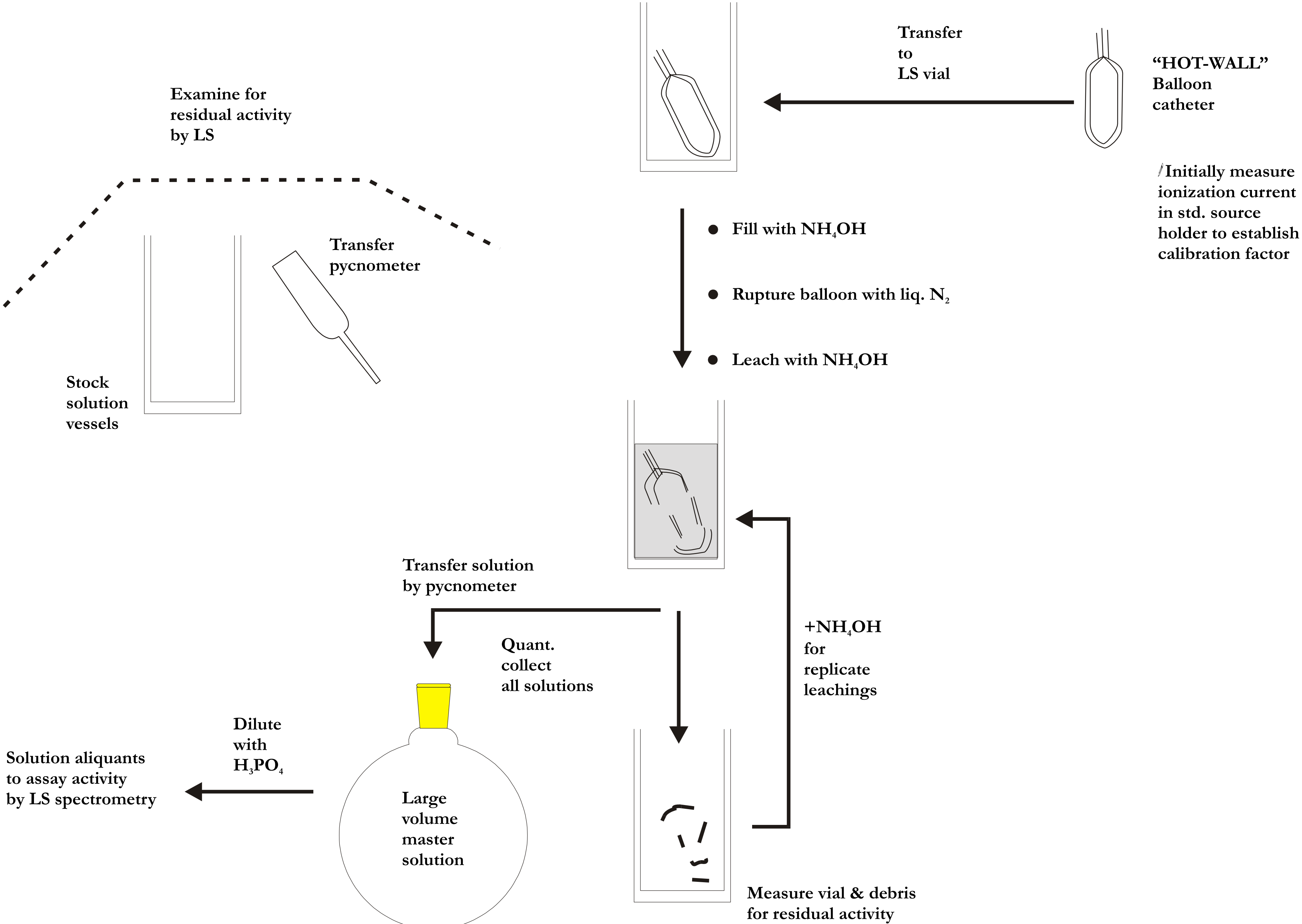
Radiance ^{32}P "hot-wall" balloon catheter



^{32}P “hot-wall” balloon catheter source



… and new catheter source holder for NIST ionization chamber “A”


Transfer
to
LS vial
"HOT-WALL"
Balloon
catheter
Initially measure
ionization current
in std. source
holder to establish
calibration factor
Examine for
residual activity
by LS
Transfer
pycnometer
Stock
solution
vessels
Fill with NH_4OH
Rupture balloon with liq. N_2
Leach with NH_4OH
Transfer solution
by pycnometer
Quant.
collect
all solutions
+NH_4OH
for
replicate
leachings
Dilute
with
H_3PO_4
Solution aliquants
to assay activity
by LS spectrometry
Large
volume
master
solution
Measure vial & debris
for residual activity
by LS

Radiance "hot wall" balloons

Results for the calibration factor determinations

source	NIST "chamber A" $K = \Gamma/A$	Capintec CRC-12 $C = \Gamma/A$
# 200-050C	(3.635 ± 0.026) GBq	(0.1268 ± 0.0011) pA●MBq
#200-050A	(3.645 ± 0.022) GBq	(0.1273 ± 0.0012) pA●MBq
mean	(3.640 ± 0.017) GBq	(0.1271 ± 0.0008) pA●MBq

residual activity results

activity fraction

residual-activity sample	# 200-050C	200-050A
adjacent 3-cm section of catheter	$(5.5 \pm 1.2)10^{-8}$	$(2.7 \pm 0.4)10^{-7}$
digestion vial + balloon debris	$(1.45 \pm 0.58)10^{-2}$	$(2.65 \pm 0.10)10^{-4}$
transfer tools (pycnometers, vials, etc.)	(1.12 ± 0.08)10-3	$(1.54 \pm 0.24)10^{-4}$

Radiance ^{32}P "hot-wall" balloon catheter

Uncertainty assessment for the ^{32}P activity at the certified reference time.

Uncertainty component	Relative standard uncertainty (in percent)	
	#200-050C	#200-050A
LS measurement precision and regression to resolve the ^{32}P and ^{33}P components	0.12	0.061
^{32}P decay corrections and effect of ^{32}P half-life on regression result	0.16	0.14
^{33}P decay corrections and effect of ^{33}P half-life on regression result	0.032	0.089
Losses for the chemical digestion and solution transfers (not accounted for by correction)	< 0.2	< 0.2
Master solution gravimetric dilution	0.15	0.2
Correction for residual activity in digested source debris and digestion vial	0.29	0.0005
Correction for residual activity on tools	0.004	0.0012
Gravimetric preparation of LS counting sources	0.05	0.1
LS cocktail stability, composition and mismatch effects	< 0.1	< 0.03
Counting livetime determinations	0.1	0.07
Effect of timing interval determinations on regression results	0.063	0.053
Effect of ^{32}P and ^{33}P detection efficiencies on regression result	0.38	0.34
Combined standard uncertainty	0.60	0.50
Expanded uncertainty (k = 2)	1.2	1.0

What's next ?

- New source configurations / radionuclides

- Investigate calorimetry of pure β sources
  - non-destructive method
  - independent evaluation of destructive assay

- Continue studies of LS cocktail composition effects


CAUTION
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