

Hospital + National Physics Laboratory: Symbiosis for Diagnosis...

Richard Fernandez

Principal Physicist, Dept. of Nuclear Medicine, Guy's & St Thomas' NHS Foundation Trust
Senior Clinical Lecturer, King's College London



Guy's and St Thomas'
NHS Foundation Trust



Nuclear Medicine – Overview (1)

- GSTT – busy London teaching hospital
- Nuclear Medicine dept. – cross site (**G**: London Bridge, **S**: Waterloo)
- **Radiopharmacy**
 - Supply to GSTT & satellite hospitals
- Associated departments
 - Medical Physics (GSTT)
 - PET (Cancer Centre) – King's College London
 - Imaging Sciences – King's College London



Nuclear Medicine – Overview (2)

- Diagnostic – 6 gamma cameras (3 SPECT/CT)
- Dedicated paediatric gamma camera for Evelina Children's Hospital
- In-vitro – Same day Tc-99m GFR service
- Therapeutic – dedicated inpatient therapy facilities



Nuclear Medicine – Overview (2)

■ MRT procedures at GSTT...

<u>Radio-nuclide/pharmaceutical</u>	<u>Indication</u>
I-131 NaI	Thyroid cancer
I-131 NaI	Graves' disease/MNG
I-131 MIBG	NET
In-111 octreotide / Y-90 dotatoc / Lu-177 dotatate	PRRT
Ra-223	Skeletal metastases
Lu-177 PSMA	Prostate cancer
Y-90/Re-186 colloid	Synovectomy
Y-90 'Zevalin'	NHL
P-32 'Biosilicon' spheres	Pancreatic cancer
Sr-89 Cl / Sm-153 EDTMP	Skeletal metastases
P-32	Polycythaemia



Nuclear Medicine – Overview (2)

- Diagnostic – 6 gamma cameras (3 SPECT/CT)
- Dedicated paediatric gamma camera for Evelina Children's Hospital
- In-vitro – Same day Tc-99m GFR service
- Therapeutic – dedicated inpatient therapy facilities
- Challenges in service delivery:
 - Range of **radionuclides**:
 - Tc-99m, In-111, I-123, etc...
 - I-131, Lu-177, Ra-223, Y-90, P-32, Re-186, etc...
 - Range of **activities**: 30GBq - <1MBq



WHY work together?



CONFIDENCE?

Improve patient care

‘Put patients first’



HOW...

Logistical complications...



Shiny, new stuff...



Improved understanding...



Shared knowledge...



Radionuclide calibrator QC

- NPL Good Practice Guide 93

'Protocol for establishing and maintaining the calibration of medical radionuclide calibrators and their quality control'

- Accuracy
- Linearity
- Repeatability (/Precision)
- Reference Source checks
- *Daily QC (HV, Background, Zero Adjust etc.)*
- *Ancillary checks...*



Radionuclide calibrator QC

- NPL Good Practice Guide 93

'Protocol for establishing and maintaining the calibration of medical radionuclide calibrators and their quality control'

- Accuracy
- Linearity
- Repeatability (/Precision)
- Reference Source checks
- *Daily QC (HV, Background, Zero Adjust etc.)*
- *Ancillary checks...*



Logistical complications...



Shiny, new stuff...



Improved understanding...



Shared knowledge...



[1] Logistical complications...



■ Equipment *overload!*

■ Guy's 8

■ STH 3

■ Medical Physics 1

■ PET 2

■ Imaging Sciences 3

■ Satellite 2

■ TOTAL 19!



[1] Logistical complications...

Capintec CRC-25R



Capintec CRC-15R



Amersham ARC-120



Fidelis? Capintec CRC-55R?



[1] Logistical complications...



- Performed **annually** at GSTT (GPG93 recommend annually) - £££
 - Year 1: **Tc-99m** and I-131
 - Year 2: Tl-201 and Ga-67
 - Year 3: I-123 and Sr-89
 - Year 4: **Tc-99m** and In-111
 - Year 5: I-131 and Y-90...
- x2 sources sent to NPL annually
 - **Tc-99m** and one *other* radionuclide
- Performed over 2 days
 - **Logistical challenge!** 19 calibrators, >4 hospital sites *and* reach NPL for 1pm!
 - **Watch your fingers!** Tc-99m **2GBq** dispensed → 100MBq @ NPL on next day

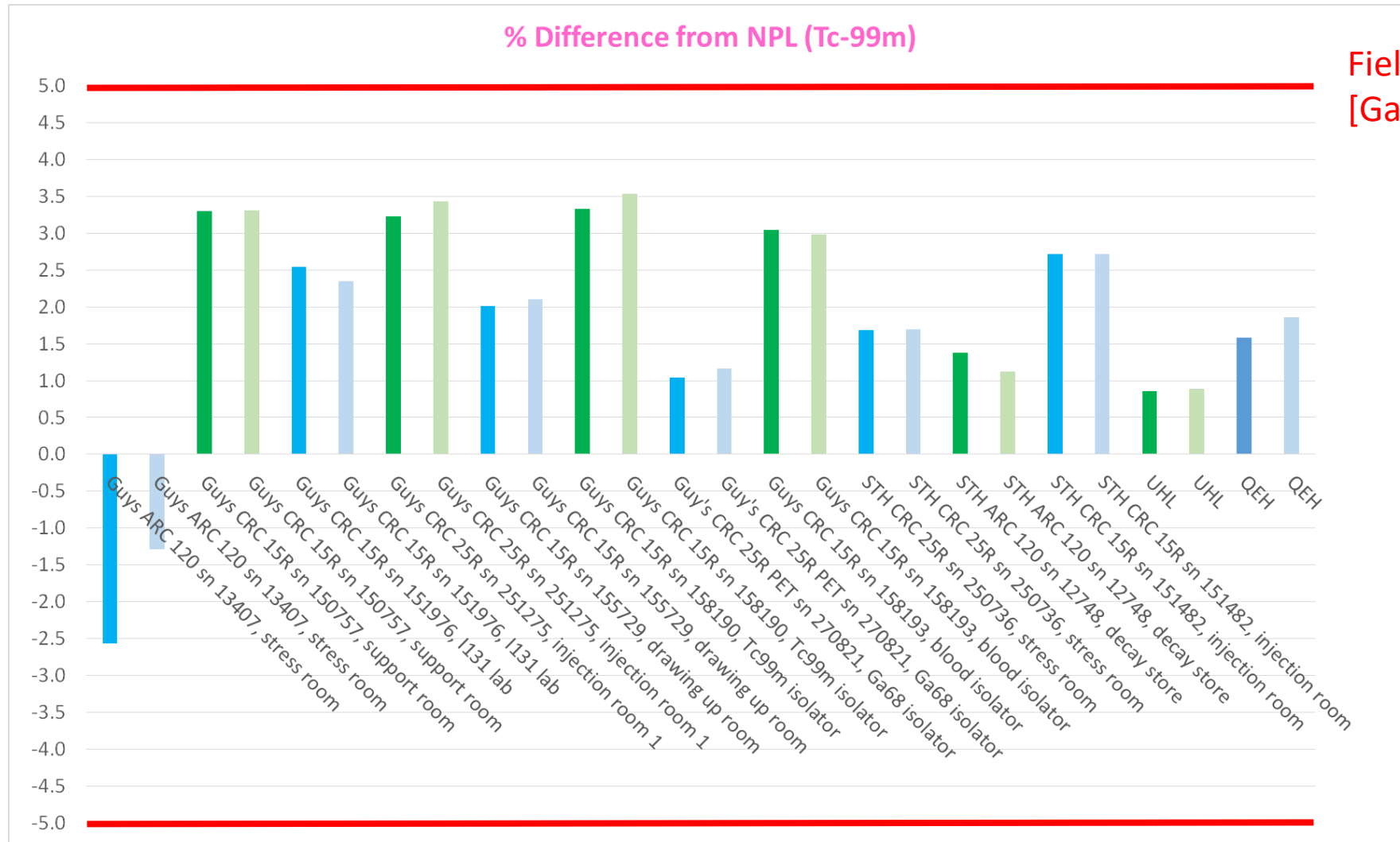


[1] Logistical complications...



- Aware of other operators in NM – e.g. testing **dial/button** settings
- Different departments – different methods of performing measurement...
 - x3 measurements with [GMT] time recorded for *each* measurement?
 - x3 measurements and [GMT] time recorded for *middle* measurement
 - 1-2 minute error acceptable? **PET** vs **NM**
- Increased **Complexity** e.g. **Source container**
 - *and* multiple sites, operators, calibrators...

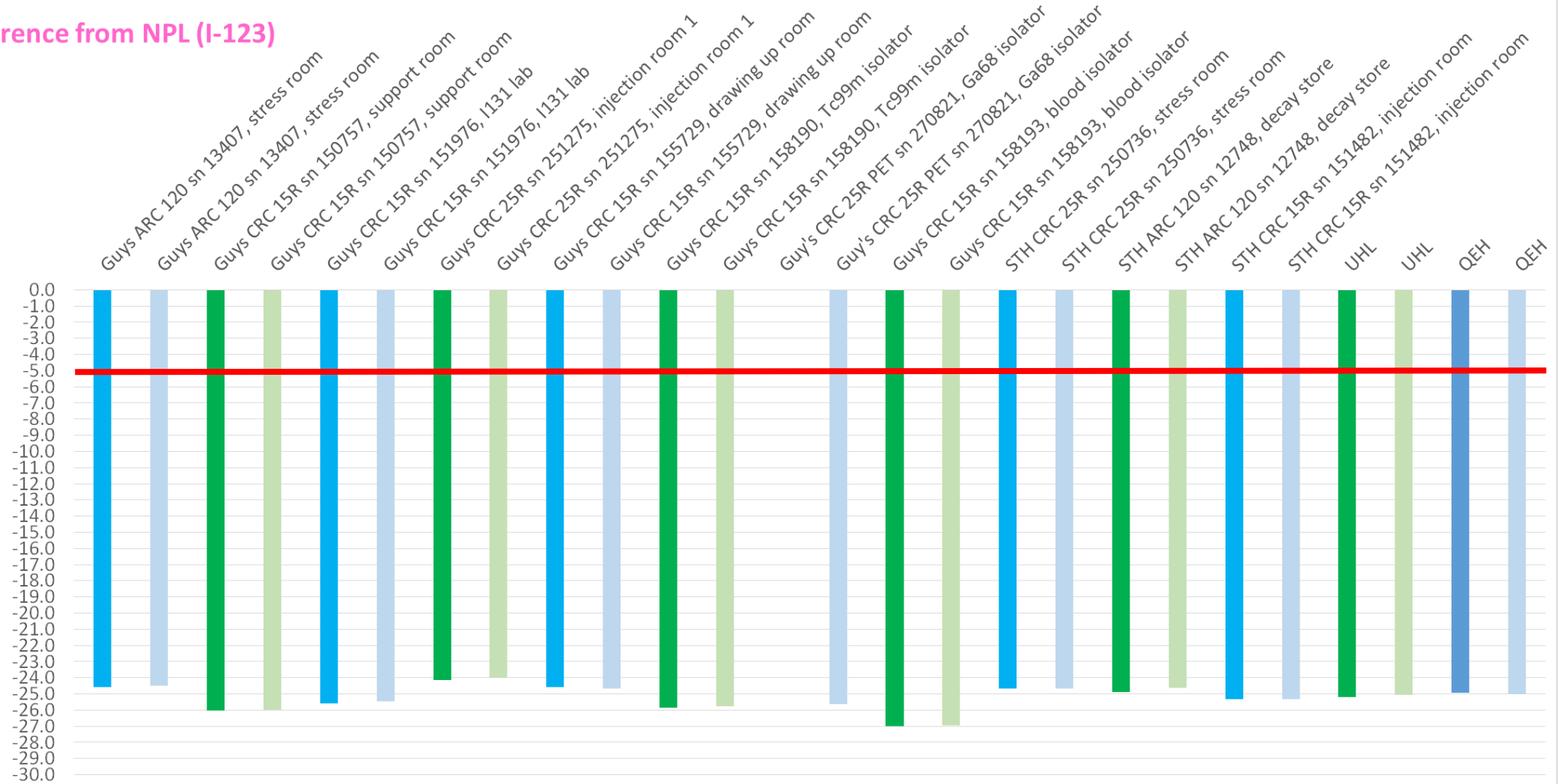




Field instrument
[Gamma, >100keV]



% Difference from NPL (I-123)





Non-standard geometry!



'Subsidiary' calibrations

- GPG93 recommends *"If there is a difference between the container/volume specified by the manufacturer and those routinely used... Subsidiary Calibrations should be applied. In the UK at the time of writing, a volume of 4 ml in a 10R Schott vial is recommended as a reference source"*
- Important to inform NPL of geometry *and pharmaceutical*
 - Different form may have different container adherence – **stickiness!**
 - Omit surfactant step in sub-dispensing process = **2.5%** discrepancy from NPL
- Lu-177 Dotatate
 - Calibration vial (Chloride) £1,000
 - Patient vial (Dotatate) **£11,000** (£15,000?)



Logistical complications...



Shiny, new stuff...



Improved understanding...



Shared knowledge...



[2] Improved understanding of equipment...

- NPL Good Practice Guide 93

'Protocol for establishing and maintaining the calibration of medical radionuclide calibrators and their quality control'

- Accuracy
- **Linearity**
- Repeatability (/Precision)
- Reference Source checks
- *Daily QC (HV, Background, Zero Adjust etc.)*
- *Ancillary checks...*



[2] Improved understanding of equipment...



- **Linearity...** GPG93 *“should be measured over the entire range of activity for which a particular radionuclide calibrator will be used”*
- Usual technique is the “decaying source” method
 - **Field instrument tolerance <5%**
- Two methods...
 - Manual / Automatic





Manual method...challenges

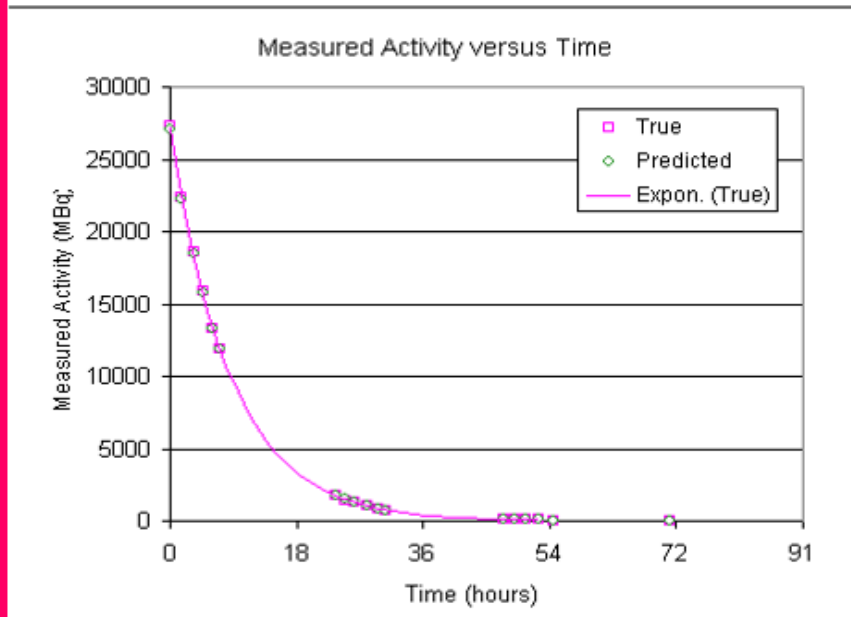
- # of calibrators
- **Logistical** complications
 - e.g. Radiopharmacy isolators, production runs, maintain sterility
- Labour **intensive**
 - prioritise scientific support, communication between teams [C-19]
- Operator **finger dose** – 30GBq!
- Potential for R/A **contamination**
- Source **positioning** error, timing error
- **Clinical** error – incorrect factor selected
- Accuracy – $6 \times 4 = 24$ *adequate* **sampling**?



Calibrator QC - Linearity

Calibrator: Capintec CRC15R, serial number 151976
Location: I-131 Laboratory, Guy's (Tc99m isolator, Rm 14 until Jan 2007)

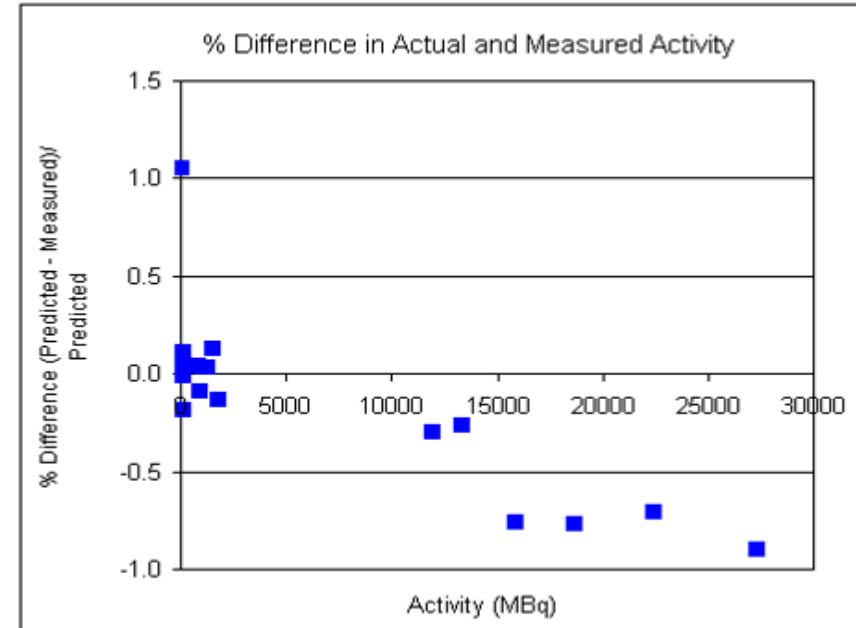
Tests performed by:
Date performed:



The Tc-99m half life calculated over all the data points is 5.99 hours.
The Tc-99m half life calculated over the 60.47 to 1,028.33 MBq range is 5.99 hours.
The actual Tc-99m half life is 6.02 hours.

Results approved by:

Physicist, Head of Section or EQCO

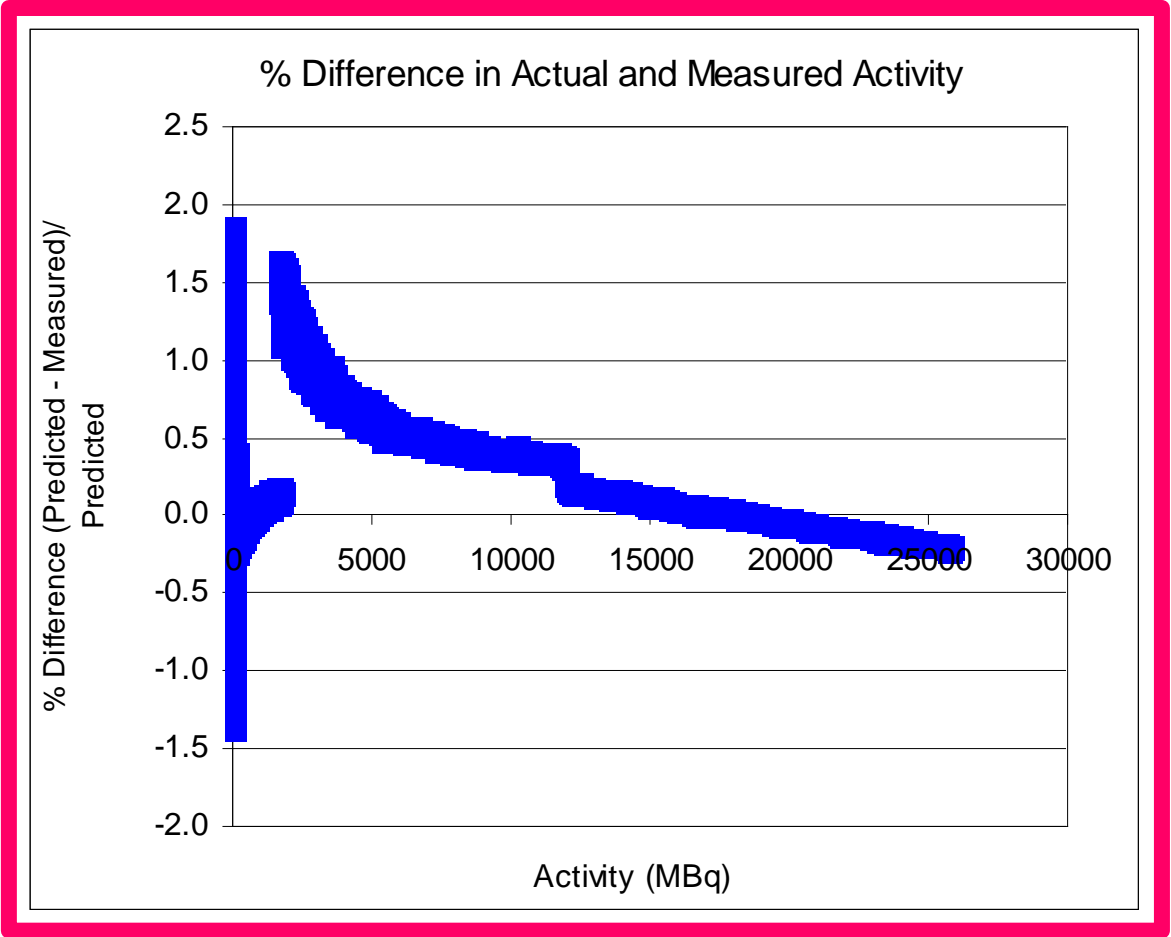
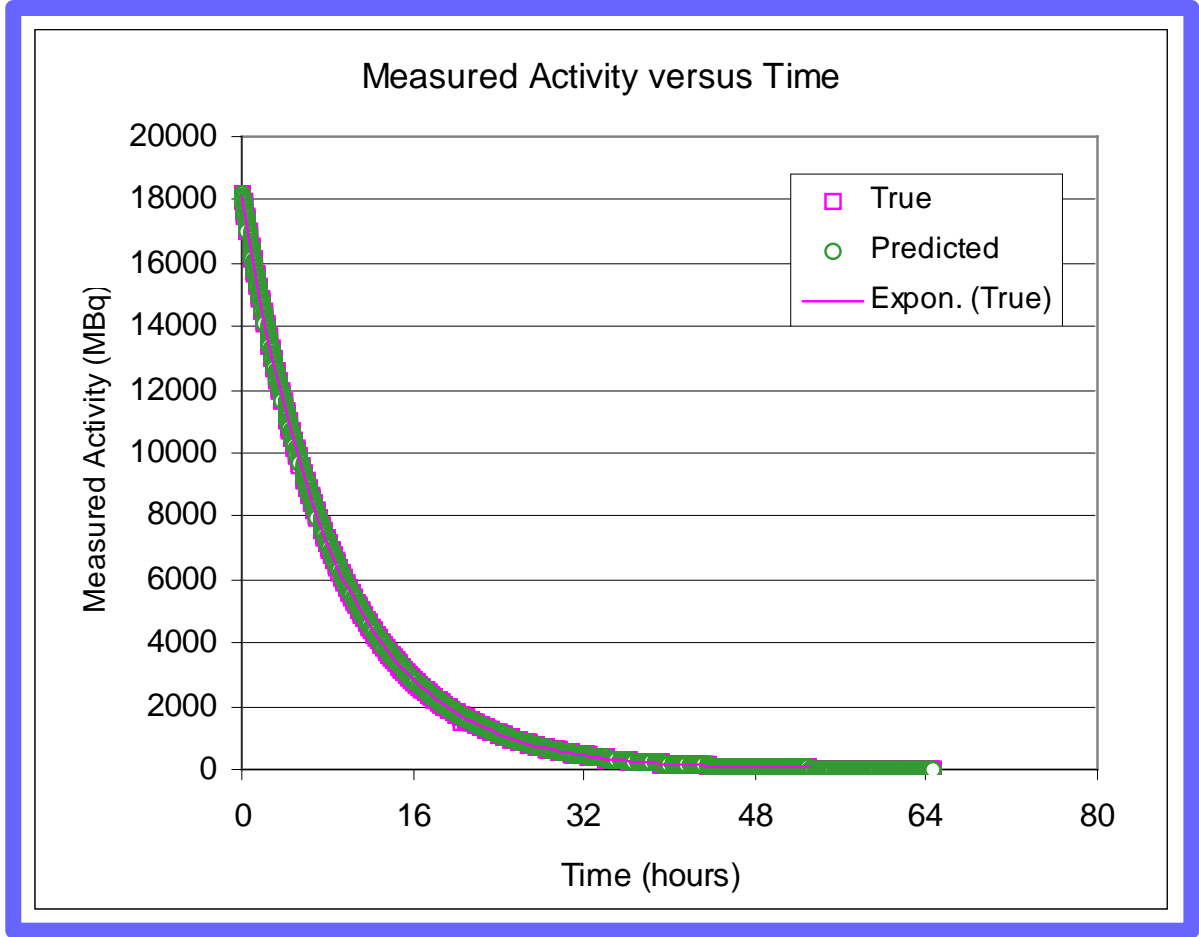


[2] Improved understanding of equipment...

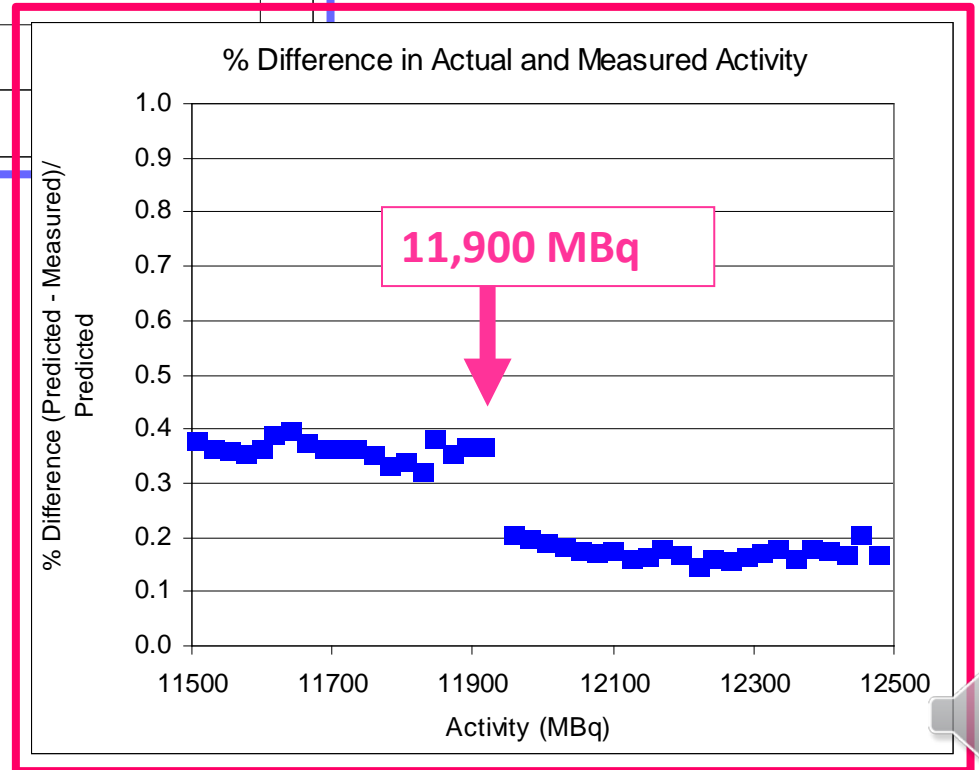
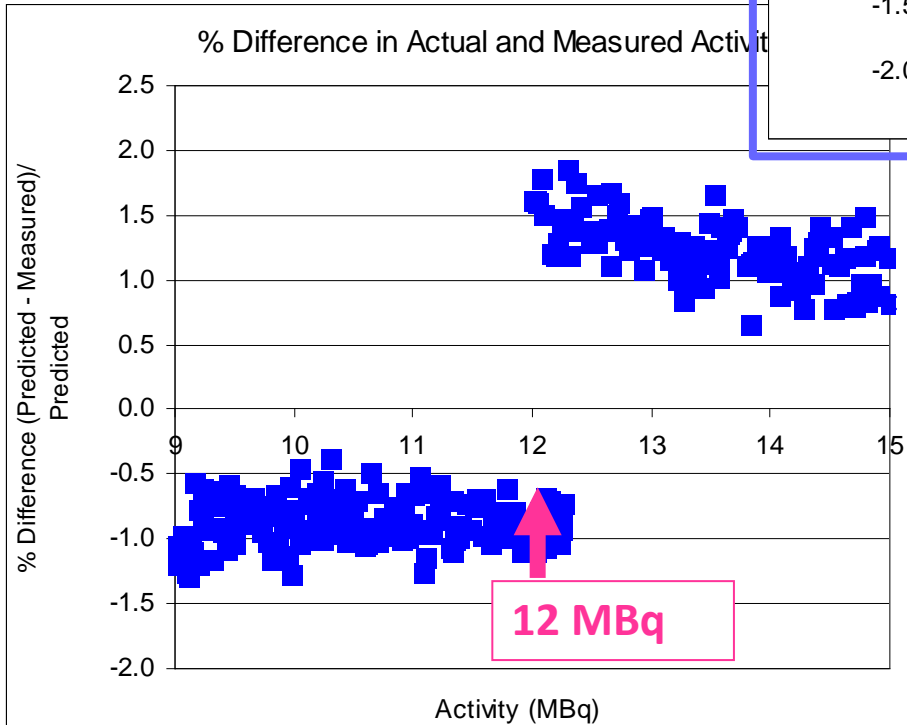
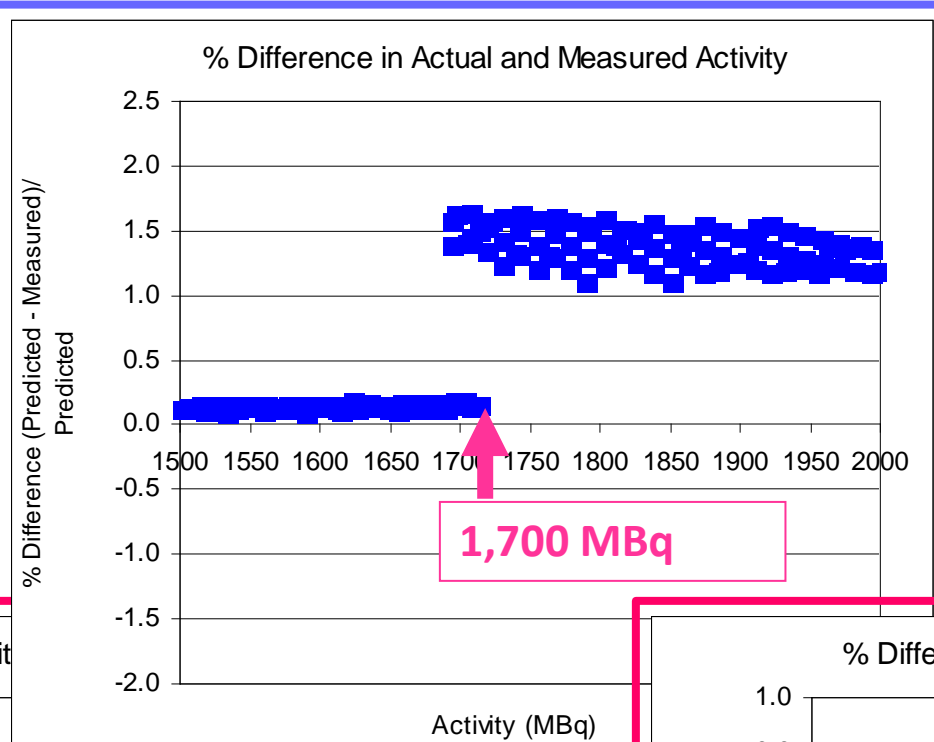


- 'Automatic' method
 - Reduced operator extremity dose, clinical disruption, improved sampling
- 2008 – GSTT develop *in-house* automatic method for CRC-15R calibrators
 - Radionuclide Calibrators User Forum - John Keightly (NPL)
 - Software code for data export from calibrator – VB for Windows **NT**
 - Hardware required (serial port) cable/connector





Range-changing effects...



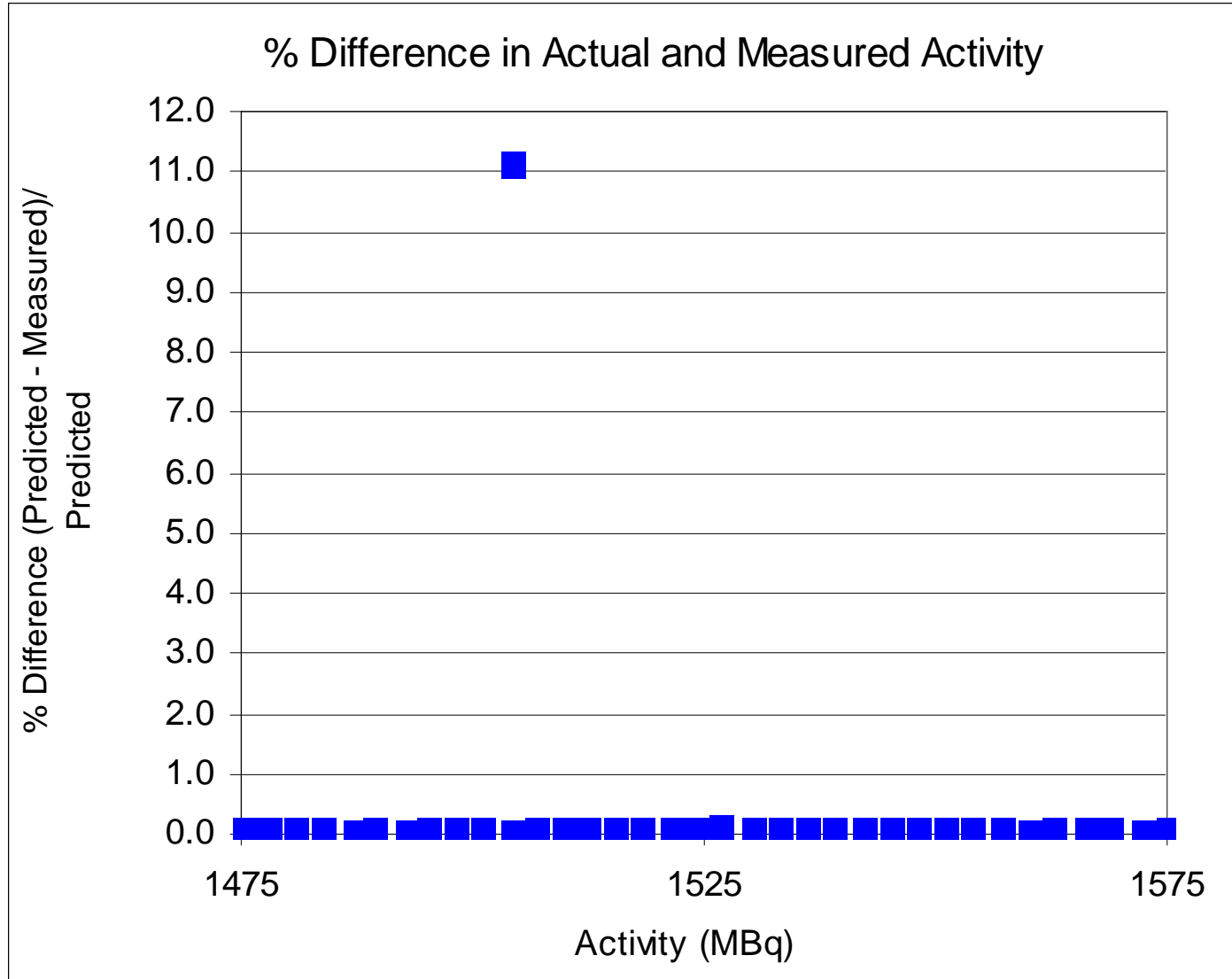
[2] Improved understanding of equipment...



- 'Automatic' method
 - Reduced operator extremity dose, clinical disruption, improved sampling

- Challenges...
 - Technical - e.g. Generator testing, laptop power saving
 - *Human!*
 - Spurious readings...





Microsoft Excel - Guy's initial testing with source - support room RF

File Edit View Insert Format Tools Data Window Help

Type a question for help

100% Arial

Reply with Changes... End Review... Security...

L3823 =IF(A3823>0,EXP(K3823),NA())

Copy worksheet: File -> Move or Copy Sheet

Please only enter data into white cells, and set the linear activity range as appropriate. All calculations are then performed automatically.

Please contact the Qrep or EQCO if this form needs updating. Yellow cells and calculations are locked.

Calibrator QC - Linearity

Medical Physics Quality System
version 1.0, 20 Dec 2006

Calibrator: Capintec CRC15R, serial number 150757

Location: Support Room, New Radiopharmacy, Guy's (Hot Lab bench, room 15, until Jan 2007)

Tests performed by

Date performed 08/02/2008

Isotope Tc-99m

highest activity in linear range 1000

Half life (hours) 6.02

lowest activity in linear range 50

	Date	Time on watch	Time diff. (hours in decimal)	Calibrator Readings (MBq)			Av. Isotope Activity (MBq)	Av Isotope - Backgd (MBq)	ln (Av. Isotope - Bkgd)	ln (Predicted calibrator)	Predicted calibrator readings	Predicted - Measured readings	% Difference	
				1st	2nd	3rd								
1244	09/02/2008	11:06:29	20.42	1707.32	1707.32	1707.32	0.00	1707.32	1707.32	7.44	7.45	1719.01	11.69	0.68
1245	09/02/2008	11:07:29	20.44	1704.93	1704.93	1704.93	0.00	1704.93	1704.93	7.44	7.45	1715.71	10.77	0.63
1246	09/02/2008	11:08:29	20.45	1695.38	1695.38	1695.38	0.00	1695.38	1695.38	7.44	7.45	1712.41	17.02	0.99
1247	09/02/2008	11:09:29	20.47	1695.38	1695.38	1695.38	0.00	1695.38	1695.38	7.44	7.44	1709.11	13.73	0.80
1248	09/02/2008	11:10:29	20.49	1695.38	1695.38	1695.38	0.00	1695.38	1695.38	7.44	7.44	1705.83	10.44	0.61
1249	09/02/2008	11:11:29	20.50	1687.02	1687.02	1687.02	0.00	1687.02	1687.02	7.43	7.44	1702.54	15.52	0.91
1250	09/02/2008	11:12:29	20.52	1683.44	1683.44	1683.44	0.00	1683.44	1683.44	7.43	7.44	1699.27	15.83	0.93
1251	09/02/2008	11:13:29	20.54	1683.44	1683.44	1683.44	0.00	1683.44	1683.44	7.43	7.44	1696.00	12.56	0.74
1252	09/02/2008	11:14:29	20.55	1504.17	1504.17	1504.17	0.00	1504.17	1504.17	7.32	7.43	1692.74	188.57	11.14
1253	09/02/2008	11:15:29	20.57	1687.96	1687.96	1687.96	0.00	1687.96	1687.96	7.43	7.43	1689.48	1.53	0.09
1254	09/02/2008	11:16:29	20.59	1685.09	1685.09	1685.09	0.00	1685.09	1685.09	7.43	7.43	1686.23	1.14	0.07
1255	09/02/2008	11:17:29	20.60	1681.94	1681.94	1681.94	0.00	1681.94	1681.94	7.43	7.43	1682.99	1.05	0.06
1256	09/02/2008	11:18:29	20.62	1678.18	1678.18	1678.18	0.00	1678.18	1678.18	7.43	7.43	1679.75	1.58	0.09
1257	09/02/2008	11:19:29	20.64	1674.97	1674.97	1674.97	0.00	1674.97	1674.97	7.42	7.42	1676.52	1.56	0.09
1258	09/02/2008	11:20:29	20.65	1671.34	1671.34	1671.34	0.00	1671.34	1671.34	7.42	7.42	1673.30	1.96	0.12

Feb 2008 - new software Nov 2007 Nov 2006 - repeat Oct 2006 Oct 2005 Nov 2004 Nov

Draw AutoShapes

Ready

NUM

Start RCUF 2008 Microsoft Excel - Guy'...

12:16



Logistical complications...



Shiny, new stuff...



Improved understanding...



Shared knowledge...

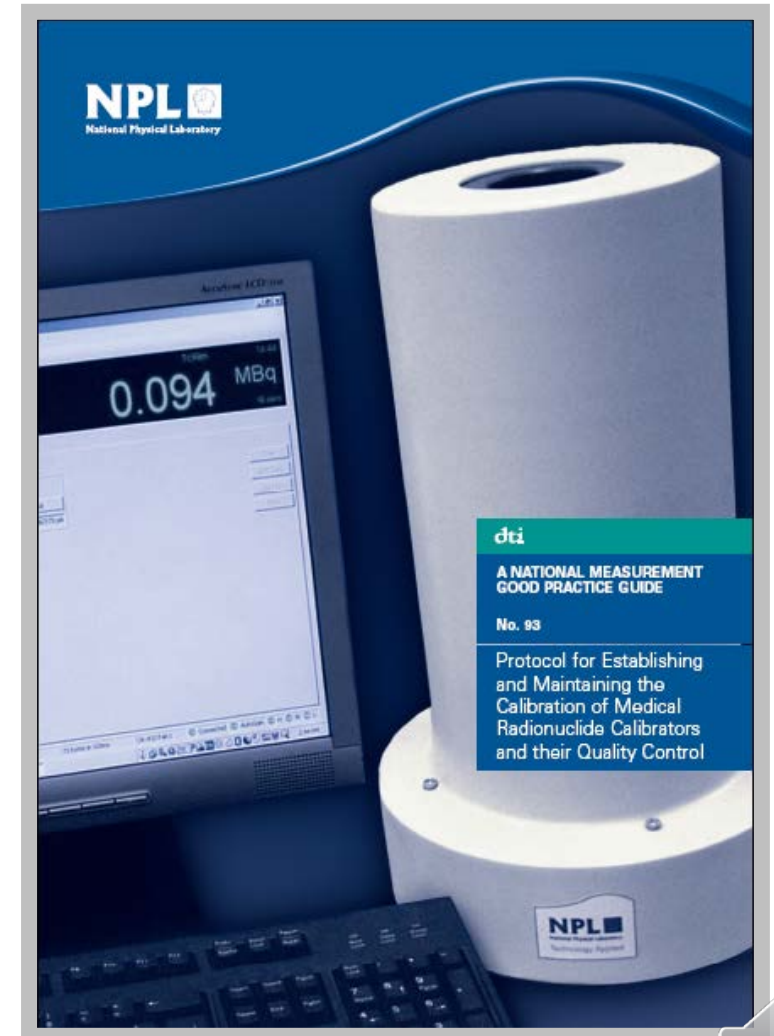


[2] Improved understanding of equipment...

- NPL Good Practice Guide 93

'Protocol for establishing and maintaining the calibration of medical radionuclide calibrators and their quality control'

- Accuracy
- Linearity
- Repeatability (/Precision)
- **Reference Source checks**
- *Daily QC (HV, Background, Zero Adjust etc.)*
- *Ancillary checks...*



Reference source checks

- Long lived test source – Cs-137
- Performed during acceptance testing
- Additional annual check performed at GSTT
- Daily calibrator QC – 2% tolerance limit (for all clinically used radionuclide button settings)



Reference source checks – Leakage!



- Long lived test source – Cs-137
- Performed during acceptance testing
- Additional annual check performed at GSTT
- Daily calibrator QC – 2% tolerance limit (for all clinically used radionuclide button settings)



Reference source checks – Leakage!



- Long lived test source – Cs-137 (Repeated ‘dropping’ into R/N Calibrator)
- Performed during acceptance testing
- Additional annual check performed at GSTT
- Daily calibrator QC – 2% tolerance limit (for all clinically used radionuclide button settings)





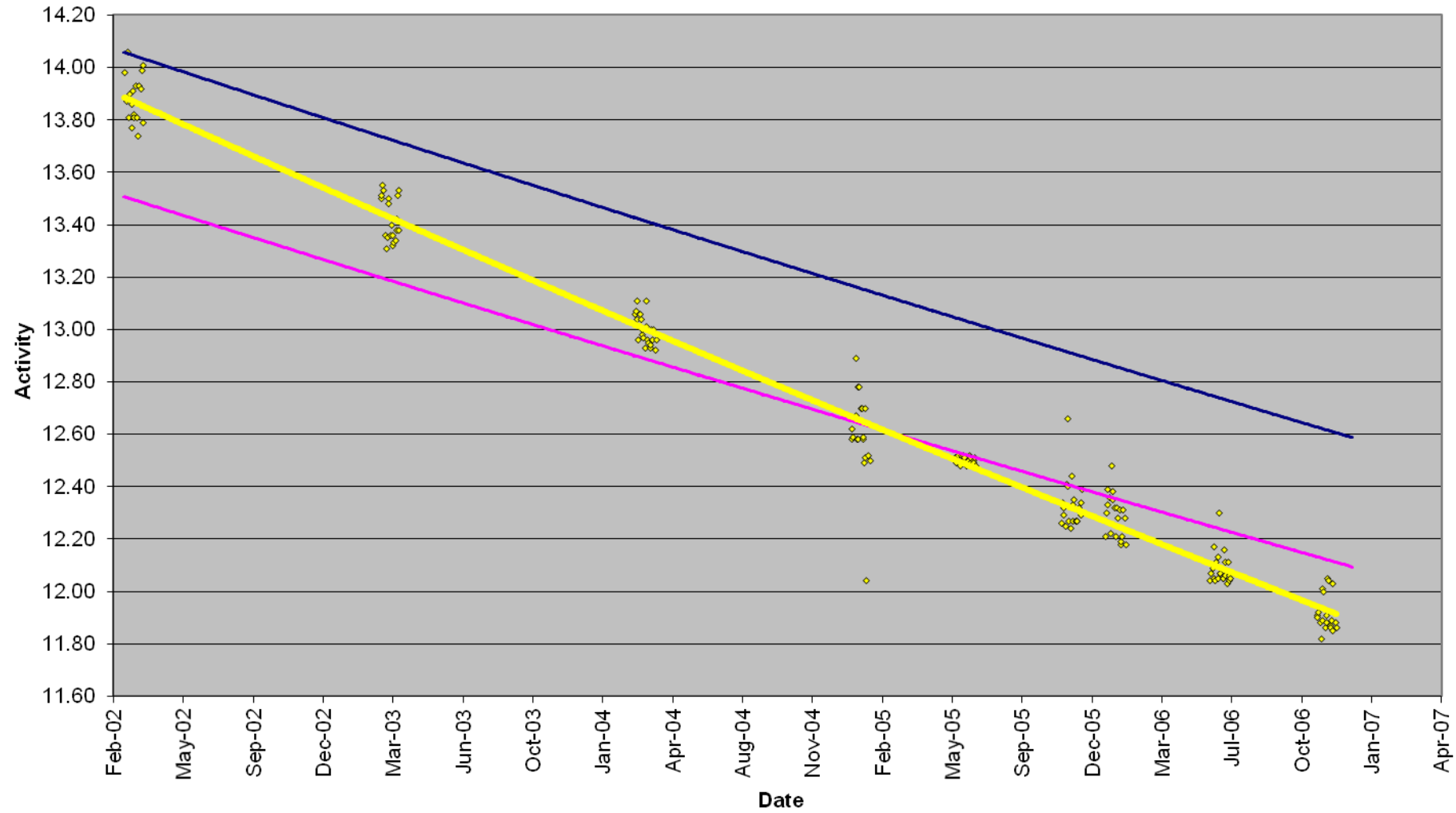
Reference source checks – Leakage!



- Long lived test source – Cs-137 (Repeated ‘dropping’ into R/N Calibrator)
- Performed during acceptance testing
- Additional annual check performed at GSTT
- Daily calibrator QC – 2% tolerance limit (for all clinically used radionuclide button settings)
- Slow drift (decrease) indicative of gas leakage...



Cs-137 Measurements c.f. 2% Tolerance Limits (Tc-99m setting)



Reference source checks – Leakage!



- Long lived test source – Cs-137 (Repeated ‘dropping’ into R/N Calibrator)
- Performed during acceptance testing
- Additional annual check performed at GSTT
- Daily calibrator QC – 2% tolerance limit (for all clinically used radionuclide button settings)
- Slow drift (decrease) indicative of gas leakage...
- 📞 NPL for advice on correct operation of Electrometer



Logistical complications...



Shiny, new stuff...



Improved understanding...



Shared knowledge...



[3] Novel applications



- Clinical trials for MRT...expanding field
 - new radionuclides
 - new vectors
- Sponsor may supply 'Calibration' vial to check equipment...



Trust your feelings...



Trust your **Feelings** Measurements




KING'S
HEALTH
PARTNERS

An Academic Health Sciences Centre for London

Pioneering better health for all

Uncertainties in measurement of ^{90}Y and ^{177}Lu in an ionisation chamber

James Ballinger, Richard Fernandez, Sarah Allen,



KING'S COLLEGE LONDON

Gay's and St Thomas' **AMS**

King's College Hospital **AMS**

South London and Maudsley **AMS**

EANM'13




Lyon, France

Annual Congress of the
European Association of Nuclear Medicine

October 19–23, 2013
Lyon, France

We cordially
invite you to Lyon!

www.eanm.org



Methods: Suppliers of radionuclides

Radionuclide	Activity range	Supplier
^{90}Y	2.5 – 7.4 GBq	Polatom
		Eckert & Ziegler (E&Z)
^{177}Lu	3.3 – 8.4 GBq	ITG Munich
		Advanced Accelerator Applications (AAA)

Methods (1): Traceable calibration

- Site 1 (Guy's & St Thomas's Hospital) performed measurements of **standardised** ^{90}Y and ^{177}Lu sources (volume, container)
- Sent to the National Physical Laboratory (NPL), Teddington, the UK national metrology institute, for calibration against a traceable standard

Methods (2): Comparison with supplier

- Upon receipt, all sources were measured in the same ionisation chamber
- The measured value was compared to the supplier's labelled claim, with correction for decay
- In 2013, a ^{177}Lu standard supplied by AAA was measured in multiple ionisation chambers at four different sites in the UK, then sent to NPL for calibration

Results (1): Single centre calibration against NPL

Radionuclide	Calibrator	Measured/NPL (%)
^{90}Y	1	93.86
	2	92.95
^{177}Lu	1	100.57
	2	101.01

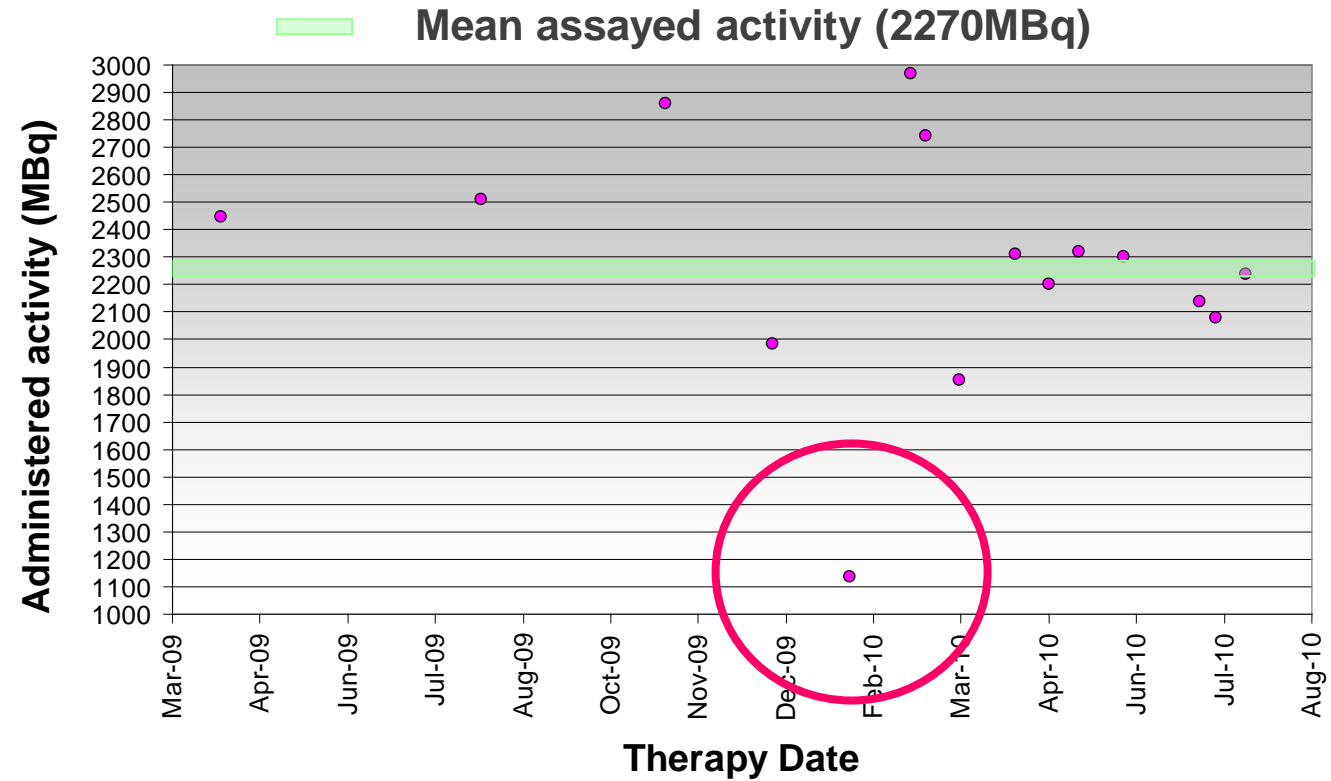
Results (2): Comparison with supplier

Radionuclide	Supplier	Measured / Calc (%)	N
^{90}Y	Polatom	88 ± 23	N = 7
^{90}Y	E&Z	103 ± 5	N = 56
^{177}Lu	ITG	94 ± 2	N = 93
^{177}Lu	AAA	108 ± 3	N = 80

Results (2): Comparison with supplier - ^{90}Y

- The large variation in measurements on Polatom ^{90}Y was due to one shipment at 36%

Measured Y-90 therapeutic activity at GSTT

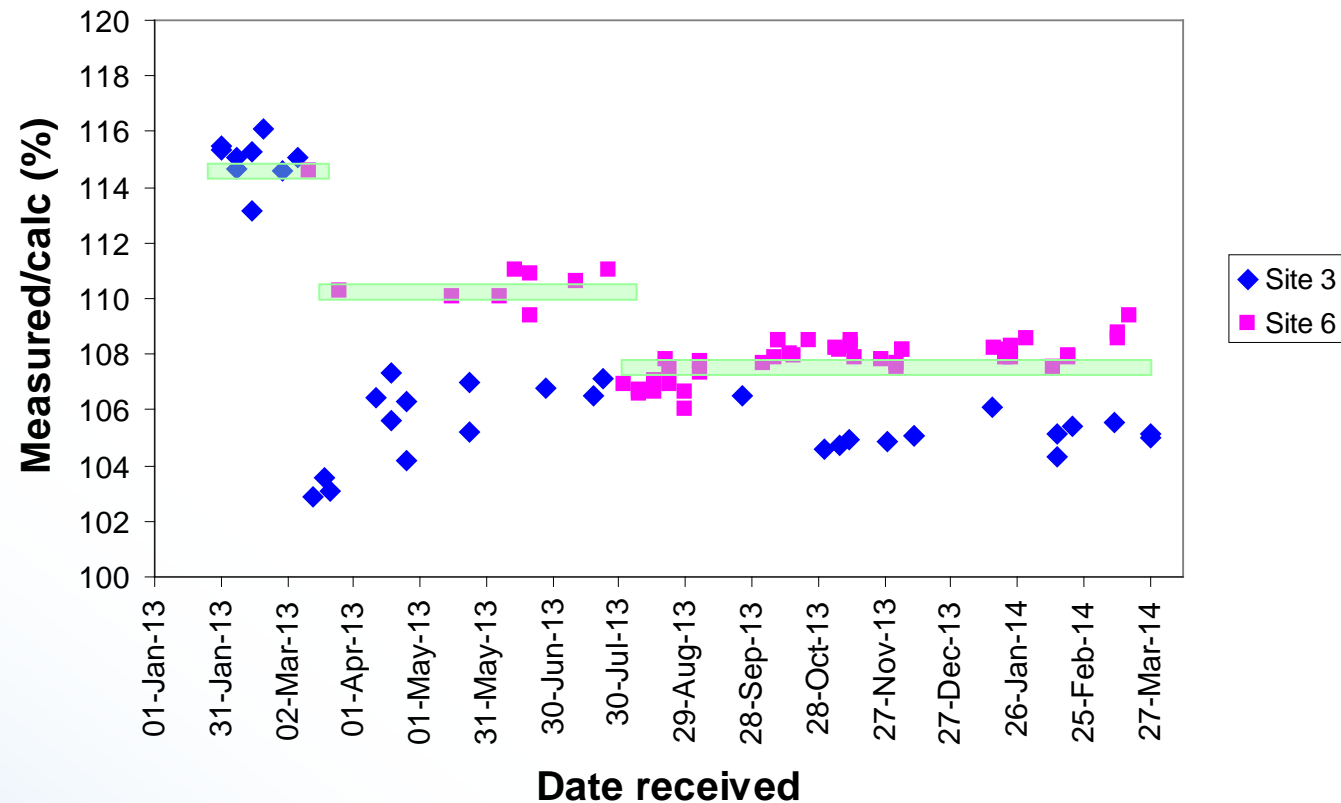


Results (2): Comparison with supplier

Radionuclide	Supplier	Measured / Calc (%)	N
^{90}Y	Polatom	88 ± 23	N = 7
^{90}Y	E&Z	103 ± 5	N = 56
^{177}Lu	ITG	94 ± 2	N = 93
^{177}Lu	AAA	108 ± 3	N = 80

Results (2): Comparison with supplier - ^{177}Lu

- Trend analysis → *step* changes in the AAA ^{177}Lu values over time which differed between the two production sites







2020 Lu-177 clinical trial

- 10% discrepancy between GSTT and Supplier for Lu-177
- Approximately 700MBq difference?
- Wipe test demonstrated ~ 1500cps
- Equivalent to 10MBq Lu-177
- Assume 10% take off fraction?
- Significant activity on *outside* of the vial...
- NOT suitable for *Calibration*



Logistical complications...



Shiny, new stuff...



Improved understanding...



Shared knowledge...



[4] Shared learning...



- STP Trainee **attend NPL** to observe calibration procedure
- NPL staff **attend hospital** site to observe MRT delivery
 - novel PRRT delivery: Lu-177 dotatate
- Conferences, Meetings, Webinars...
- **Ra-223 exhalation**: Decay chain (Radon-219) characterisation
 - Michael Draper [King's College London] → **Steven Bell (NPL)**
 - **BNMS Glasgow 2022**



Logistical complications...



Shiny, new stuff...



Improved understanding...



Shared knowledge...



Hospital + National Physics Laboratory: Symbiosis for Diagnosis...

THANK YOU FOR YOUR ATTENTION

