Declaration of Financial Interests or Relationships

Speakers Names: Maria Burniston, Pei San Chan, David Hutt

I have no financial interests or relationships to disclose with regard to the subject matter of this presentation.

Technical and practical aspects of DPD imaging
DPD – regulatory aspects and issues in quantitation

Maria Burniston
Barts Health NHS Trust and
National Amyloidosis Centre

Regulations in the use of radioactive materials in medicine

Environment Agency

Permit

The Environmental Permitting (England & Wales) Regulations 2010

Environment

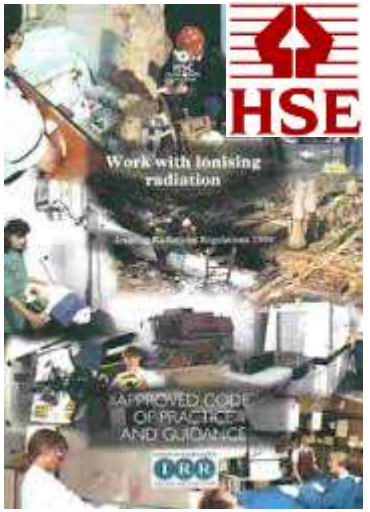
ARSAC

THE IONISING RADIATION (MEDICAL EXPOSURE) REGULATIONS 2000

(together with notes on good practice)

Patient

Care Quality Commission



Staff and public

ARSAC application form

- Who -(a) name, address, qualifications and relevant experience of the applicant and the post or position which the applicant holds or is to hold and the premises in which they propose to administer the radioactive medicinal products specified in the application
- What -(b) particular descriptions or classes of radioactive medicinal products the applicant proposes to administer or to have administered and the purpose for which they are to be administered
- Where? - (c) information as to the equipment, facilities and staff available to the applicant for the proposed administration of radioactive medicinal products
- (d) such other information as the health ministers may reasonably require.

A12	Experience Please specify details of training and experience, with reference to Appendix IV of the Notes for Guidance, relevant to your application if the additional items require vastly different techniques from those already demonstrated for the issue of your current certificate.		
	Scope of Experience	Name of institution	Period of training/Number of Procedures

- Extensive curriculum, including fundamental physics of radiation, principles of radiation detection, instrumentation and equipment, calibration techniques, radiopharmaceuticals, radiation protection
- Specific knowledge of procedure and clinical question with alternative approaches for diagnosis/ treatment
  - Inform risk/benefit analysis
- Aside from ARSAC do not forget IR(ME)R requirements for NM and CT aspects (local DRLs for CT etc)

Applying for DPD serial

B1.3	For investigations using serials **not listed** in Appendix I Parts A and/or B of the ARSAC Notes for Guidance please specify:				
Radionuclide	Chemical Form	Nature of Investigation	Route of Administration	Usual activity per test (MBq)	ED per test*(mSv)
Tc99m	Phosphonates and phosphates	Cardiac imaging to detect cardiac amyloid in patients with known or suspected amyloidosis	I.V.	700	5.6

*Effective Dose, in mSv, estimated as in Appendix II of the Notes for Guidance. Please provide a reference or attach a summary of the calculation.

Quantitation

- Which parameters might you want to measure and when?
  - Planar (typically whole body ANT+POST for geometric mean)
    - H/CL, H/WB, % retention, soft tissue to femur
  - SPECT/ SPECT CT
    - SUV, % injected dose, polar plots
    - Dynamic SPECT, retention indices
    - Gated data, ejection fraction, wall motion
- What implications does this have for acquisition and processing protocols
  - Need for CT(and quality), scatter windows, absolute outputs from polar plots
- Validate all results via phantom work (same reconstruction parameters, consider gating options etc)
- Audit both accuracy AND clinical benefit
  - Just because we CAN measure something, it does not mean we should!

world class expertise local care

Royal Free London NHS
NHS Foundation Trust

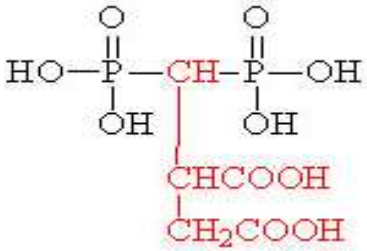
^{99m}Tc-DPD : A radiopharmacy perspective

Pei San Chan
Lead Radiopharmacist,
Nuclear Medicine

DPD

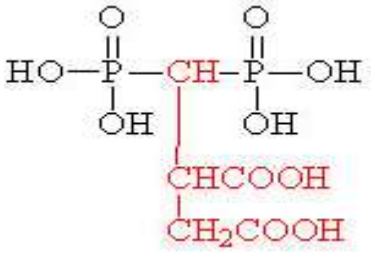
- 3,3-diphosphono-1,2-propanedicarboxylic acid

- Dicarboxypropane diphosphonate (DPD)

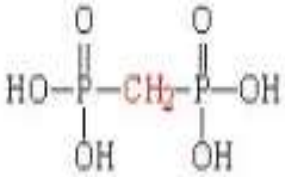


Diphosphonates

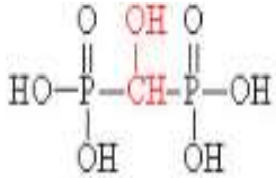
- Dicarboxypropane diphosphonate (DPD)

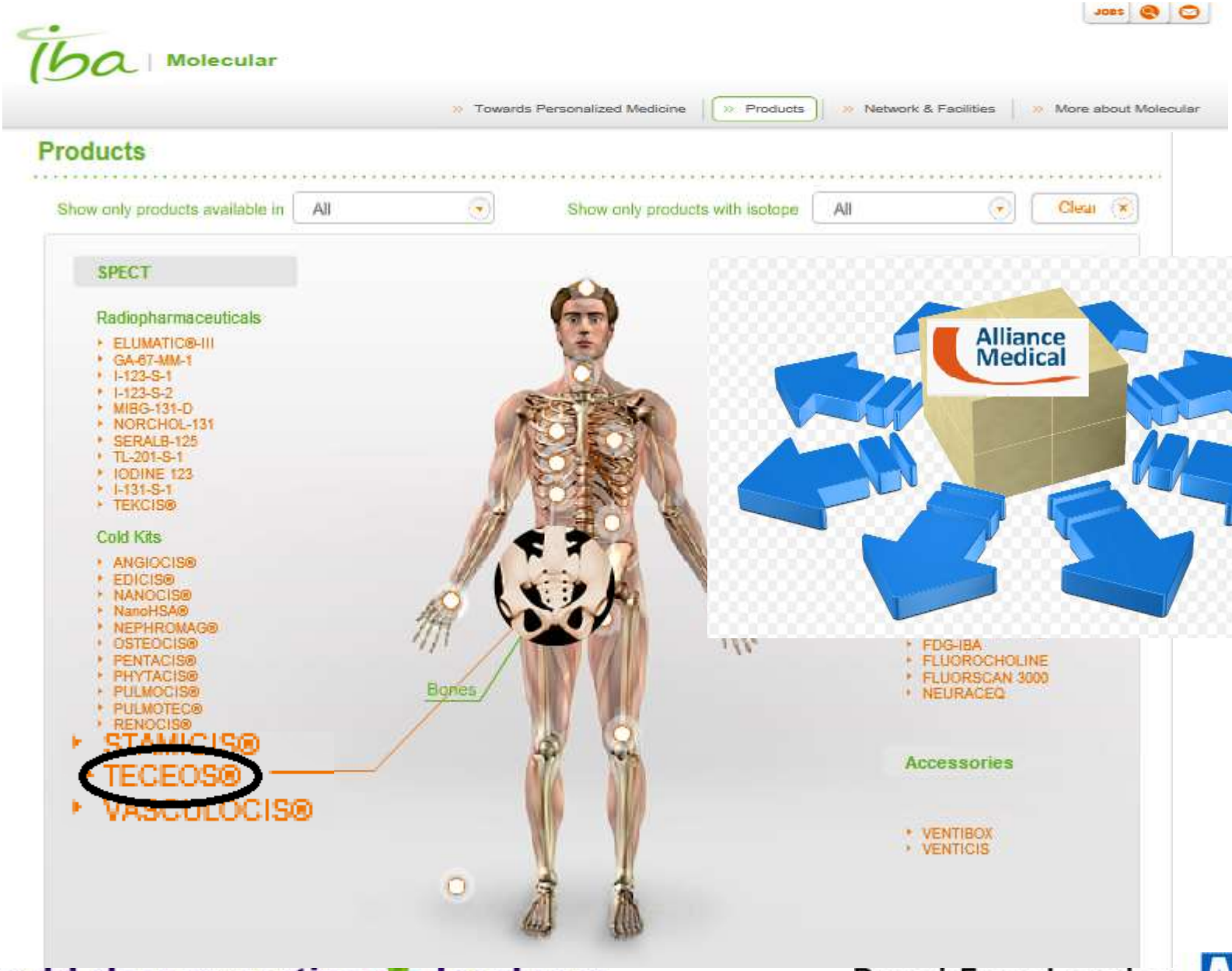


- Medronate
- Methylene diphosphonate (MDP)



- Oxidronate
- Hydroxymethylene diphosphonate (HDP / HMDP)





world class expertise local care

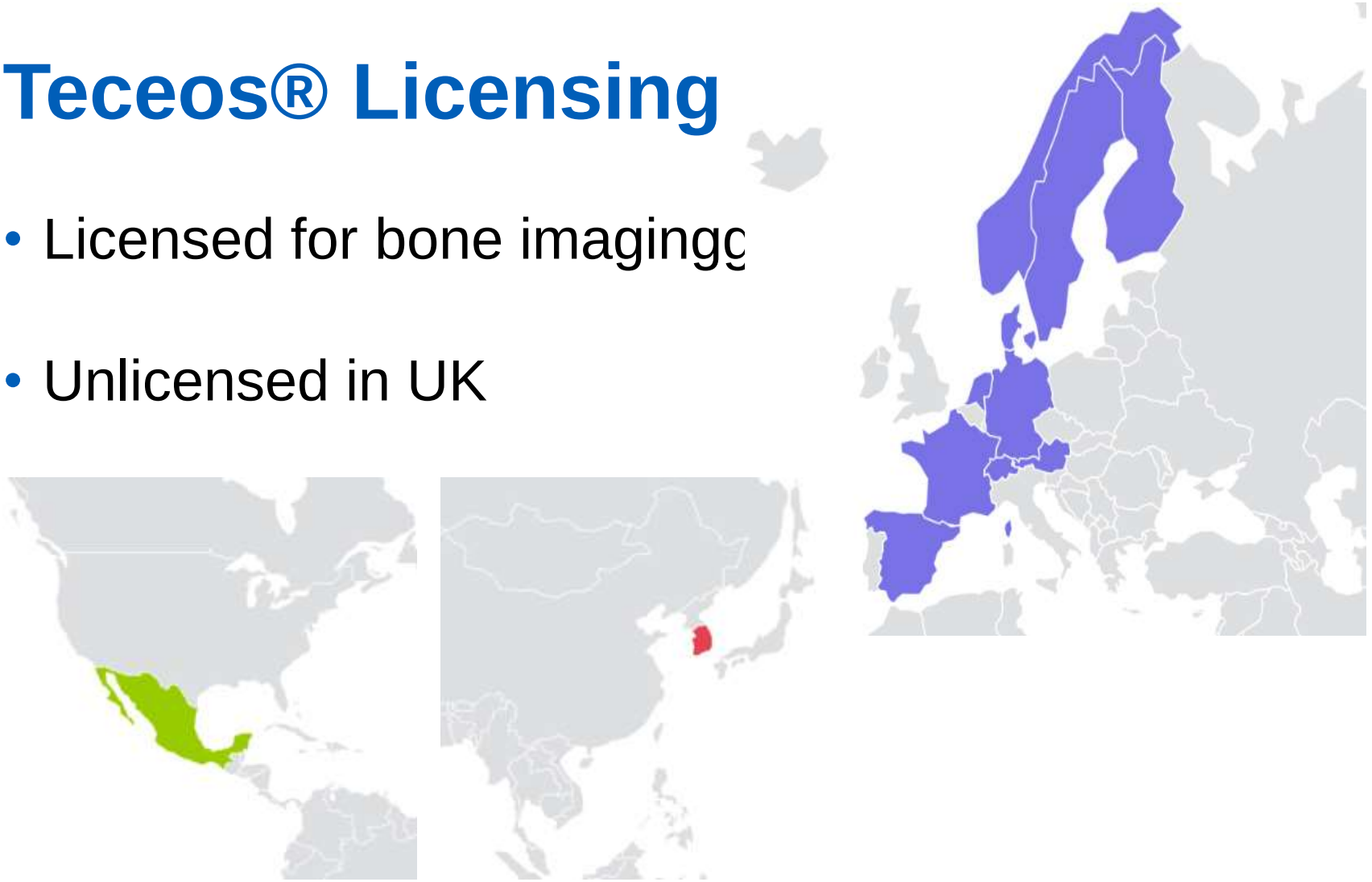
Royal Free London NHS
NHS Foundation Trust

DPD


TECEOS
Kit for the preparation of Technetium (99mTc)
3,3-diphosphono-1,2-propanedicarboxylic acid (DPD) injection
Powder for injection.
TECEOS

Teceos® Licensing

- Licensed for bone imaging
- Unlicensed in UK



world class expertise local care

Royal Free London NHS
NHS Foundation Trust

Teceos® Licensing

- Licensed for bone imaging
- Unlicensed in UK
- Unlicensed for cardiac amyloidosis
- Plans for EMA submission for licence variation

world class expertise local care

Royal Free London NHS
NHS Foundation Trust

Using unlicensed products

- Drugs & Therapeutics Committee (DTC) application

Royal Free London NHS Foundation Trust - Drugs and Therapeutics Committee

Application for INCLUSION of a New Medicine or Significant Change of indication in Use of Medicine in the Royal Free Hospital's Formulary

- *Decisions on applications for inclusion of a new medicine or significant change in indication in use of a medicine in the Royal Free London NHS Foundation Trust's Formulary by the Drugs and Therapeutics Committee are driven by an evidence based approach.*
- *Please complete ALL relevant sections legibly and comprehensively. Any missing or illegible information will delay the application.*
- *If the medicine affects or is intended to be used across a number of specialities then application forms should be completed for all areas.*
- *Return application form, supporting evidence and guidelines to Iris Samuel, Principal Pharmacist, Medicine Management & Formulary, Pharmacy Department, Royal Free London NHS Foundation Trust.*

Name of medicine being applied for:	Manufacturer:

1. Applicant's details:

1.1 Consultant name (block capitals):	
1.2 Email address:	
1.3 Department: Nuclear Medicine	1.4 Division: Urgent Care
Consultant's signature	Clinical Director's signature
Divisional Director Approval (signature)	Divisional Director of Operations Approval (signature)

Proposed Source of Funding (Please tick as appropriate)

Cost Neutral	Divisional Budget	PCT	Other
☐	☐	☐	☐

Checklist

☐ Application Form [A] ☐ Supporting Evidence ☐ Guidelines for Use ☐ Shared Care Protocol

Using unlicensed products

- Disclaimer from ARSAC certificate holder

Nuclear Medicine — Royal Free Hampstead NHS

Declaration for the use of unlicensed radiopharmaceutical products

Name of Radiopharmaceutical product: Tc EOS (e)

Product details: DPD (1,3-diphosphono-1,2-propanedicarboxylic acid) Kit for Tc-99m labelling, 12 mg strength. Supplier: Cis Bio. Imported via Rados.

Clinical Indication for use: Imaging cardiac amyloidosis

Alternative licensed radiopharmaceutical available: (Yes) / No — OTHER BONE agents licensed in UK ie. MDP & HDP.

Reason for not using alternative licensed radiopharmaceutical: Other bone seeking radiopharmaceuticals have not been shown to have uptake in the myocardium in patients with amyloid

Declaration:

- I am aware that this product does not hold a product license in the UK (unlicensed).
- I am aware that any supplies of this radiopharmaceutical are made on a named-patient basis.
- I am aware that I hold clinical responsibility and any associated liability for the use of this radiopharmaceutical.
- I am aware that I am responsible for reporting to report any adverse drug events associated with this radiopharmaceutical.
- I confirm that an ARSAC approval is held for the use of this radiopharmaceutical.
- I confirm that records are held of patients administered with this radiopharmaceutical.

Signature: Ann-Marie Quigley Position: Consultant

Name: Dr Ann-Marie Quigley Date: 25/6/10

Using unlicensed products

- Disclaimer letter to distributor

Royal Free London NHS
NHS Foundation Trust

Royal Free Hospital
Pond Street
London
NW3 2QG

Tel: 020 3758 2000

Radiopharmacy Unit/Nuclear Medicine
Direct line: 020 7830 2474

12th May 2016

Alliance Medical Ltd
Unti 19 Quadrum Park
Old Portsmouth Road
Peasmarsh
Guildford
Surrey
GU31 1LU

Re: Teceos

We are aware that the above product, supplied by your company, does not at present have a UK market authorisation.

We are aware of the responsibilities regarding the supply and administration of this material to patients covered by the exemptions in the Medicines Act.

We will ensure that this material is prescribed for and supplied to named patients and that a full record of its use will be maintained.

Yours sincerely

Pei San Chan
Lead Radiopharmacist

world class expertise local care

www.royalfree.nhs.uk

Dominic Dodd, chairman David Sloman, chief executive

Introducing new drug product

- New drug product form
- GMP risk assessment

- Sufficient ^{99m}Tc supply
- New worksheet & labels

- Storage space: at <25˚C
- Inform distributor of intended volume use if significant

Manufacture: ^{99m}Tc radiolabelling

Ref: GE Healthcare

370 - 11,100 MBq

TcO_4^-

in 2 - 10 ml

Cold Kit

DPD

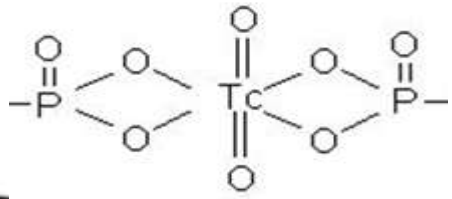
Reconstituted Kit.

5 minutes

RT

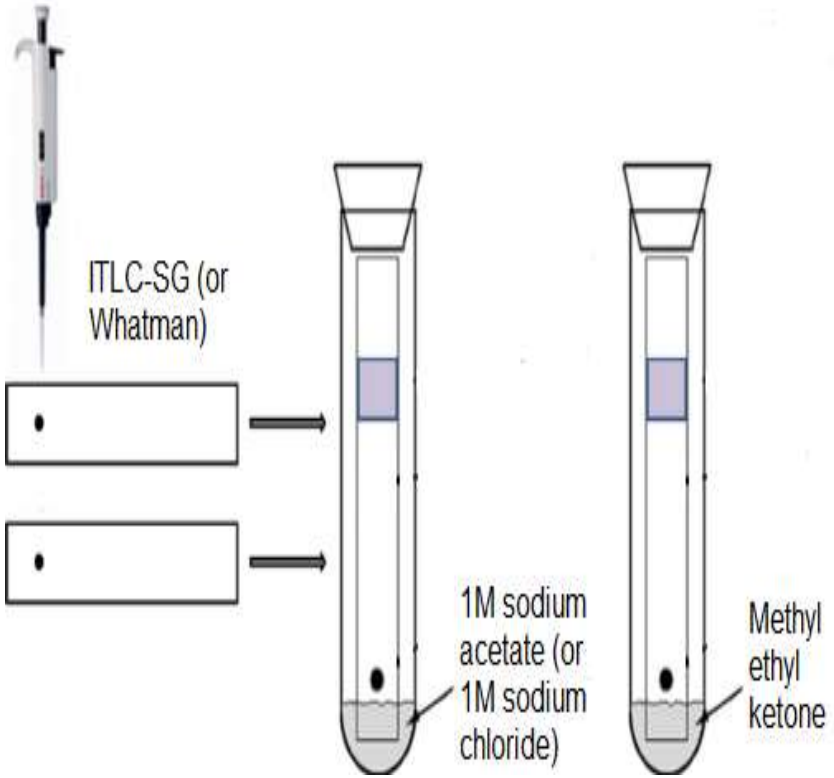
Final Product

^{99m}Tc-DPD

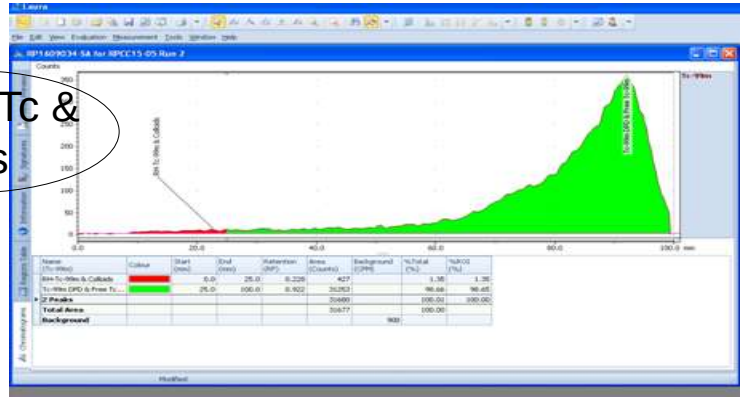


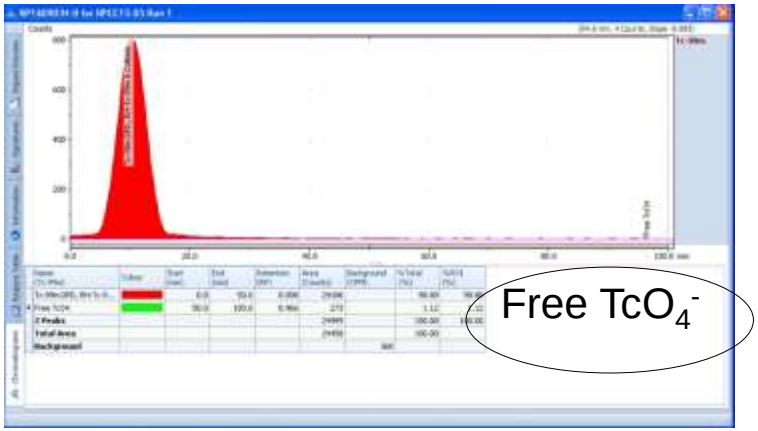
Shelf-life:
8 hours

Quality Control: Radiochemical purity



TLC Chromatograms





RCP PASS = ≥95%

(>2% Free & >2% RH)

world class expertise local care

Royal Free London NHS Foundation Trust

^{99m}Tc-DPD Scintigraphy- Practical aspects for administration and scanning

Administration

1. Patient preparation pre-injection – None

2. Dose – 700 MBq

3. Route – single intravenous injection
   – butterfly needle to reduce risk of extravasation

4. Contraindications – Pregnancy, breastfeeding

5. Patient instructions post-injection
   – drink 0.5 to 1 litre of fluids where possible (fluid restrictions)
   – void bladder frequently

NAC Gamma Cameras

GE Discovery 670 16 slice SPECT-CT

GE Infinia Hawkeye 4 slice SPECT-CT

Scanning Protocol

1. Anterior dynamic injection
2. Whole body sweep – 5 minutes post injection
3. Whole body sweep – 3 hours post injection
4. Cardiac SPECT-CT → non-gated
   → gated

Scanning Protocol

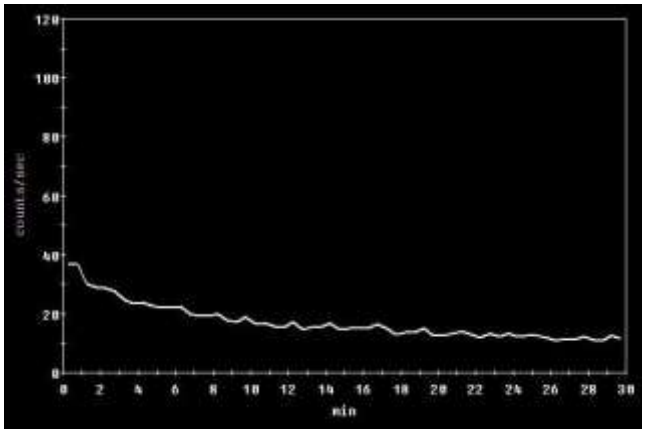
1. Anterior dynamic injection
2. Whole body sweep – 5 minutes post injection
3. Whole body sweep – 3 hours post injection
4. Cardiac SPECT-CT → non-gated
   → gated

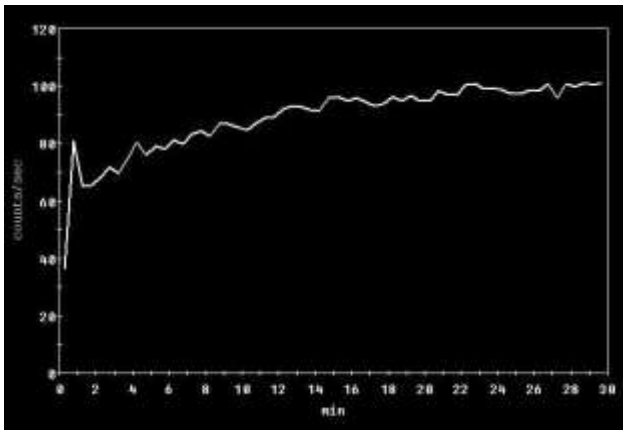
Scanning Protocol

1. Anterior dynamic (30 mins)
   - 60 frames @ 30 sec/frame
   - LEHR collimators
   - 128 x 128 matrix

No Amyloid

Cardiac Amyloid





Scanning Protocol

2. Whole body sweep 5 mins post injection
   - Scan speed 20cm/min
   - No voiding prior to scan (WB retention)

3. Whole body sweep 3 hrs post injection
   - Scan speed 10cm/min
   - Void prior to scan

No Amyloid

Hereditary ATTR

Scanning Protocol

2. Whole body sweep 5 mins post injection
   - Scan speed 20cm/min
   - No voiding prior to scan (WB retention)

3. Whole body sweep 3 hrs post injection
   - Scan speed 10cm/min
   - Void prior to scan

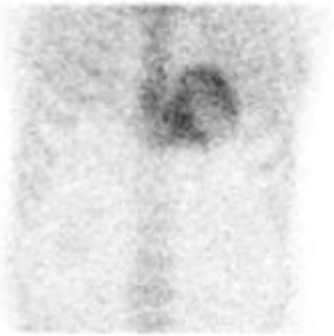
No Amyloid

Hereditary ATTR

Scanning Protocol

4. Cardiac SPECT-CT
   - performed immediately after 3Hr WB scan
   - arms above head where possible
   - all external metallic objects removed including bras

a. <u>SPECT (Non-gated)</u>
   - 360^{o} angular range (H-mode)
   - Step & shoot mode
   - 3^{o} view angle and 17 sec/step
   - 60 views/head (120 total)
   - 128 x 128 matrix
   - No zoom applied
   - Acquire scatter window (120 kev $^{+}$/- 5%)

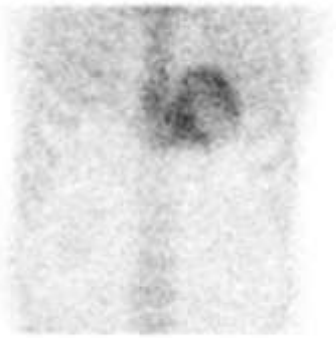


b. <u>SPECT (Gated)</u>
   - 8 frames/cycle (time mode)

Scanning Protocol

4. Cardiac SPECT-CT
   - performed immediately after 3Hr WB scan
   - arms above head where possible
   - all metallic objects removed including bras

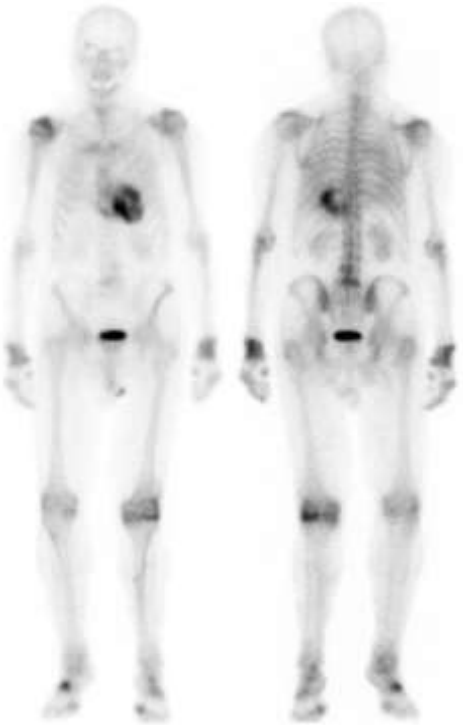
a. SPECT (Non-gated)
   - 360° angular range (H-mode)
   - Step & shoot mode
   - 3° view angle and 17 sec/step
   - 60 views/head (120 total)
   - 128 x 128 matrix
   - No zoom applied
   - Acquire scatter window (120 kev +/- 5%)



b. SPECT (Gated)
   - 8 frames/cycle (time mode)

Image Display/Analysis (NAC)

1. Delayed (3 HR) Whole body image



2. Fused SPECT/CT Image

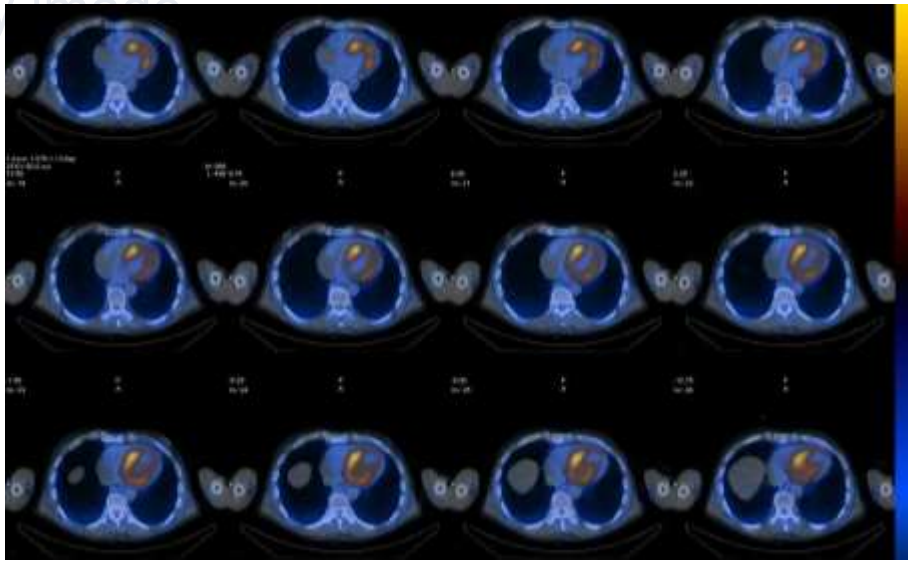
3. Cardiac reconstruction
   (GE Myovation)

4. Quantitation

Image Display/Analysis (NAC)

1. Delayed (3 HR) Whole body image

2. Fused SPECT/CT Image

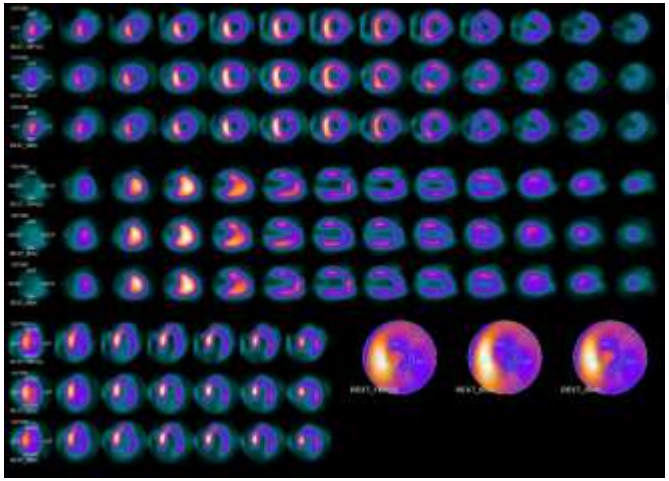


3. Cardiac reconstruction
   (GE Myovation)

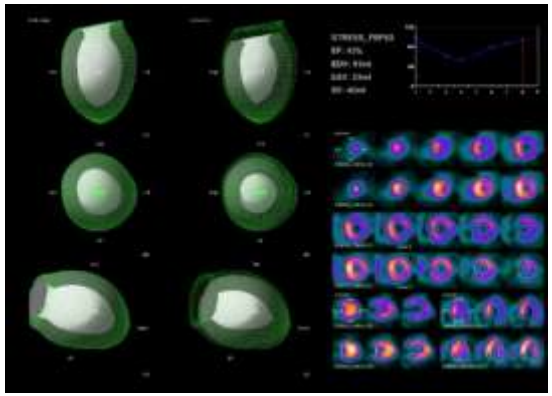
4. Quantitation

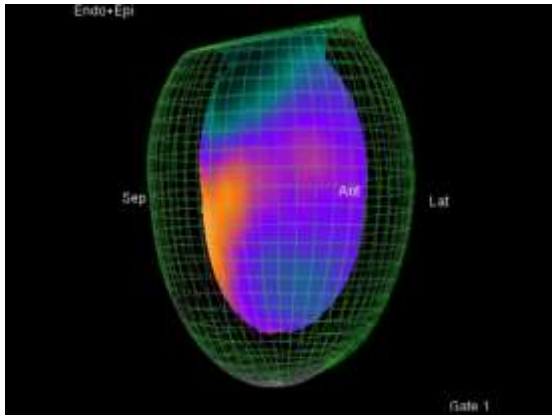
Image Display/Analysis (NAC)

1. dy image



2.





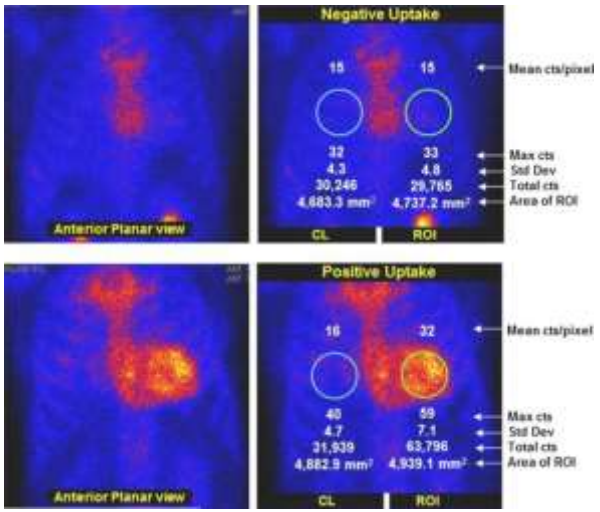
3. Cardiac reconstruction (GE Myovation)

4. Quantitation

Image Display/Analysis

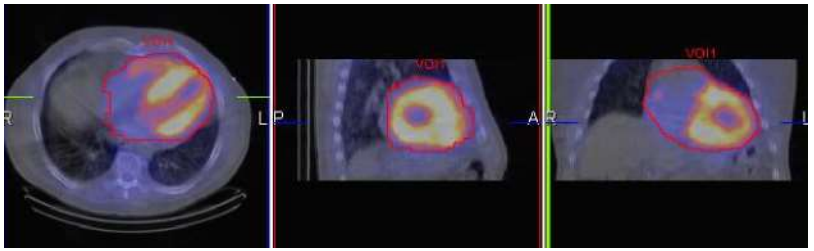
-Heart retention
-WB retention
-H/WB retention ratio

H/CL Ratio



Bokhari et al Circ Cardiovasc Imaging 2013;**6**:195–201

3. Cardiac reconstruction (GE Myovation)



4. Quantitation - Planar
   - SPECT/CT

Thorax CT Protocol

	Infinia Hawkeye (4 slice)	Discovery 670 (16 slice)
Scout	Not available	120 kV, 10 mA
Scan type	Helical	Helical
CT range	Partial	Partial
Voltage (kV)	140	120
Current (mA)	2.5	Smart mA (min 20, max 150)
Pitch	1.9 (fixed)	1.375
Rotation	2.6 RPM	0.8 sec/rotation
Noise Index	N/A	35
Slice Thickness (mm)	5.00	3.75
Exposure Duration	~100-120 seconds	~5-7 seconds

Thorax CT Protocol

	Infinia Hawkeye (4 slice)	Discovery 670 (16 slice)
Scout	Not available	120 kV, 10 mA
Scan type	Helical	Helical
CT range	Partial	Partial
Voltage (kV)	140	120
Current (mA)	2.5	Smart mA (min 20, max 150)
Pitch	1.9 (fixed)	1.375
Rotation	2.6 RPM	0.8 sec/rotation
Noise Index	N/A	35
Slice Thickness (mm)	5.00	3.75
Exposure Duration	~100-120 seconds	~5-7 seconds

Thorax CT Protocol

	Infinia Hawkeye (4 slice)	Discovery 670 (16 slice)
Scout	Not available	120 kV, 10 mA
Scan type	Helical	Helical
CT range	Partial	Partial
Voltage (kV)	140	120
Current (mA)		n 20, max 150)
Pitch		375
Rotation		/rotation
Noise Index		35
Slice Thickness (mm)		75
Exposure Duration	~10	econds

Thorax CT Protocol

	Infinia Hawkeye (4 slice)	Discovery 670 (16 slice)
Scout	Not available	120 kV, 10 mA
Scan type	Helical	Helical
CT range	Partial	Partial
Voltage (kV)	140	120
Current (mA)	2.5	Smart mA (min 20, max 150)
Pitch	1.9 (fixed)	1.375
Rotation	2.6 RPM	0.8 sec/rotation
Noise Index	N/A	35
Slice Thickness (mm)	5.00	3.75
Exposure Duration	~100-120 seconds	~5-7 seconds

Thorax CT Protocol

	Infinia Hawkeye (4 slice)	Discovery 670 (16 slice)
Scout	Not available	120 kV, 10 mA
Scan type	Helical	Helical
CT range	Partial	Partial
Voltage (kV)	140	120
Current (mA)	2.5	Smart mA (min 20, max 150)
Pitch	1.9 (fixed)	1.375
Rotation	2.6 RPM	0.8 sec/rotation
Noise Index	N/A	35
Slice Thickness (mm)	5.00	3.75
Exposure Duration	~100-120 seconds	~5-7 seconds

Thorax CT Protocol

	Infinia Hawkeye (4 slice)	Discovery 670 (16 slice)
Scout	Not available	120 kV, 10 mA
Scan type	Helical	Helical
CT range	Partial	Partial
Voltage (kV)	140	120
Current (mA)	2.5	Smart mA (min 20, max 150)
Pitch	1.9 (fixed)	1.375
Rotation	2.6 RPM	0.8 sec/rotation
Noise Index	N/A	35
Slice Thickness (mm)	5.00	3.75
Exposure Duration	~100-120 seconds	~5-7 seconds

Thorax CT Protocol

	Infinia Hawkeye (4 slice)	Discovery 670 (16 slice)
Scout	Not available	120 kV, 10 mA
Scan type	Helical	Helical
CT range	Partial	Partial
Voltage (kV)	140	120
Current (mA)	2.5	Smart mA (min 20, max 150)
Pitch	1.9 (fixed)	1.375
Rotation	2.6 RPM	0.8 sec/rotation
Noise Index	N/A	35
Slice Thickness (mm)	5.00	3.75
Exposure Duration	~100-120 seconds	~5-7 seconds

Thorax CT Protocol

	Infinia Hawkeye (4 slice)	Discovery 670 (16 slice)
Scout	N/A	120 kV, 10 mA
Scan type	Helical	Helical
CT range	Partial	Partial
Voltage (kV)	140	120
Current (mA)	2.5	Smart mA (min 20, max 150)
Pitch	1.9 (fixed)	1.375
Rotation	2.6 RPM	0.8 sec/rotation
Noise Index	N/A	35
Slice Thickness (mm)	5.00	3.75
Exposure Duration	~100-120 seconds	~5-7 seconds

Acknowledgements

- Clinical team at the National Amyloidosis Centre

- Clinical team in the Royal Free Nuclear Medicine Dept