

“SENSIBLE ADVICE”

One of the roles of the UK Radiopharmacy Group is to provide “sensible advice” to the nuclear medicine community on issues where many people have raised questions or concerns.

Sestamibi for parathyroid imaging

Many of you will be aware of a paper by M Karam *et al* entitled, “Increasing the radiochemical purity of ^{99m}Tc sestamibi commercial preparations results in improved sensitivity of dual-phase planar parathyroid scintigraphy” which appeared in the December 2005 issue of *Nuclear Medicine Communications* (vol 26, no 12, pp 1093-8). The authors reported a relationship between the % impurities in ^{99m}Tc-sestamibi and the parathyroid washout ratio, implying that the radiochemical purity affected the diagnosis.

This paper has raised a lot of concern in the nuclear medicine community and the UKRG discussed it recently. While the results cannot be discounted, the implication of the paper that a special formulation of sestamibi is required for parathyroid scintigraphy is based on a false premise. The ^{99m}Tc-sestamibi used in the group of patients in which the relationship was observed (Group 1) had abnormally low radiochemical purity with an average of 91.9% bound, range 85.1% to 96.2%. Indeed, in 5 of the 42 patients the RCP was less than 90% yet the material was still injected. This low RCP might have resulted from the addition of 18.5 GBq ^{99m}Tc to the kit; the limit is 5.5 GBq in the USA where this study was performed. In contrast, the modified formulation used in Group 2 had an average RCP of 96.5%, range 92.2% to 98.8%.

However, UKRG members report that they routinely obtain RCP values of 96-97% with the standard formulation prepared in the proper manner. A retrospective review of 249 preparations showed an average RCP of 96.3% (Decristoforo C *et al*, *Nucl Med Commun* 2000;21:349-54). There is one caveat: lower RCP (90-95%) is sometimes seen when using the first eluate of a new generator or a Monday eluate. This is presumably due to the low tin content of the kit being swamped by the build-up of ⁹⁹Tc.

We would therefore offer the following “sensible advice”:

- There is no need for a special formulation of ^{99m}Tc-sestamibi for parathyroid imaging.
- Radiochemical purity of ^{99m}Tc sestamibi should be checked regularly, particularly if the generator has not been eluted for more than 24 hours.
- To add a margin of safety while further investigation is undertaken, it might be a good idea to apply a limit slightly higher than 90% RCP.

UKRG EVENTS

Report on Bournville

The workshop on 13 January 2006 attracted a record 60 participants, including speakers and exhibitors. Not only were the numbers good, but the level of participation and interaction was also high. It is an excellent forum for sharing experiences, problems, and questions.

The morning started off with a survey of the use of Zevalin and the more general issue of radiochemical purity testing presented by Elvir Zahirovic from Lablogic. It was not too startling to learn that the use of Zevalin is limited by its cost. This was followed by two talks on Zevalin from north of the border. Alistair Millar from Edinburgh presented validation of radiochemical purity testing comparing five different methods of measurement. You can't have Edinburgh without Glasgow getting in on the show, so Tom Murray presented some radiochemical purity, radiation safety, and patient dosimetry aspects of Zevalin. Ironically, neither of these centres uses Zevalin currently as the Scottish Medicines Consortium (“Tartan NICE”) has not approved its use.

This was followed by Dr J Bomanji from the University College London Hospitals with a thorough and practical review of thyroid blockade in nuclear medicine studies. There is conflicting guidance from ARSAC and the manufacturers.

In the final talk of the morning, Mr Mysore Chandrashekar, one of the first consultant surgeons

in oncological surgery, described the use of nuclear medicine in breast cancer surgery. The three main applications are sentinel lymph node detection, scintimammography, and labelled white cell imaging for investigation of postsurgical infection. The talk was well illustrated, such that one of the women exclaimed afterward: "I've never in my life seen so many breasts."

The afternoon session consisted of the popular Controversy Corners, the outcomes of which are summarised in an appendix to the Newsletter.

UKRG INITIATIVES

Postgraduate Course in Radiopharmacy

The annual postgraduate course in radiopharmacy, sometimes known as the Easter course, is being offered 13-16 March at King's College London. Information is being circulated with this Newsletter, posted on the UKRG website, or can be obtained from jim.ballinger@kcl.ac.uk.

Radiopharmacy Audit

The UKRG Radiopharmacy Audit, which is available on the website, was devised some 10 years ago. This document has been used as part of the BNMS audit of nuclear medicine departments and also in conjunction with regional pharmacy QA audits of Section 10 units. The group spent a day prior to the Bournville meeting discussing ways of updating and broadening the audit document. We intend to finish this revision at our summer meeting and post the revised document shortly thereafter.

Radiopharmacy Handbook

Revision of the UKRG Radiopharmacy Handbook (available on the website) is also underway. It is hoped that the revised Handbook will appear in the next few months.

Survey of clinical activities

What clinical activities are you involved in? Would you like to become more involved? What are other people doing? We'd like to answer all these questions, but in order to do so we need input from everyone. A survey devised by Sanjay Patel (Guy's) and Jilly Croasdale (City Hospital Birmingham) is being distributed with this Newsletter. If it doesn't come with the Newsletter you can contact Sanjay for a copy (sanjay.patel@gst.nhsl.uk). Please give us your input.

Error reporting

A form for reporting errors or near misses in radiopharmacy has been devised based on a

system developed by the national CIVAS group (www.civas.co.uk). A copy of the radiopharmacy error reporting form should be circulated with this newsletter. If it is not, you can obtain a copy from paul.maltby@ribuht.nhs.uk.

WORKFORCE ISSUES

Training staff for PET/CT

The BNMS is preparing a document on training of the different craft groups required to support the expansion of PET/CT in the UK. The UKRG has input in this process. This document will be a companion to the Intercollegiate Report on PET/CT issued in August 2005, in which provision of an adequate supply of suitably trained staff was identified as a major limitation.

Registration of clinical technologists

The voluntary register of clinical technologists is due to close shortly, after which entry for staff who have been in post less than three years would require a course such as the degree in clinical technology run by People's College in Nottingham. As the degree involves practicals in clinical scanning, its relevance for radiopharmacy techs is questionable. UKRG will approach the organisers with a suggestion of practicals in different specialties.

National Occupational Standards

Pharmacy is now coming under the NOS system and it is recognised that the radiopharmacy standards are a good model. UKRG members have been consulted to assist in shaping the pharmacy standards.

As reported previously, the radiopharmacy NOS standards are posted on the Skills for Health web site (www.skillsforhealth.org.uk). The standards are now linked to KSF levels but at the moment these are for guidance only.

Work related upper limb disorders

Matt Brown from Shrewsbury is conducting a survey of work related upper limb disorders (WRULD) due to repetitive strain of working in isolators and laminar flow hoods. If you have not already received the survey and would like to take part, please contact jim.ballinger@kcl.ac.uk for a copy.

REGULATORY ISSUES

Quality assurance of aseptic services

The 4th edition of "Quality assurance of aseptic services" edited by Alison Beaney is now available from Pharmaceutical Press (www.pharmpress.com) at £29.95, ISBN 0 85369 615 2.

Annex 1

The draft of a revised Annex 1 to the Orange Guide is now being circulated for comments. It is available through regional quality controllers. There is more detail on continuous particle monitoring. If there are reasons that particle monitoring cannot be performed continuously, the MHRA expects the licence holder to have validation that a Grade A environment is maintained throughout the process. However, there are also indications that the MHRA recognises there are differences between hospitals and industry (manual vs automated processes, reliance on liquid disinfection, etc.) and is developing guidance on this topic.

Hand washing facilities

The longstanding dispute between the HSE and MHRA over the location of hand washing facilities adjacent to controlled areas has again reared its ugly head, if that isn't too mixed a metaphor. However, a meeting has been held between inspectors from the two agencies in an attempt to find common ground.

Out of hours deliveries

One of our members was audited recently by the Department of Transport. Security against terrorism was a major concern. The audit was broad based and extended well beyond transport itself. The quality assurance expectation of the system included training of drivers and documentation thereof, production, packaging, emergency procedures, and delivery arrangements. The Department intends to inspect all 840 sites despatching radioactive material.

Radiopharmacy computer programmes

The Veenstra software is being beta tested at the Mallinckrodt central radiopharmacy located at the new UCL Hospital.

PRODUCT NEWS

Manufactured specials

With the winding down of the NHS pharmacy manufacturing modernisation agenda, a new

national advisory board is being set up. The UKRG is now included in this process and we should have greater input in assuring the continuing availability of specials required for radiopharmacy.

Leukoscan

Leukoscan is still not back on the market, however individual vials are available on a named patient basis.

Product withdrawals

In recent months we have seen withdrawal (or imminent withdrawal) of DTPA and DMSA kits from GE Healthcare and HSA kits from Tyco. Immunomedics has discontinued CEA-Scan. Distribution of depreotide (NeoSpect) will be transferred from GE Healthcare to Schering but the product will be off the market for a number of months during the handover period.

Gavin Bashar from GE Healthcare attended the UKRG meeting to take questions from members. He assured us that no further product withdrawals are envisaged.

Contraindication

It was noted that the product information supplied with ¹²⁵I-radioiodinated human serum albumin now states that it is contraindicated in children under 3 years of age due to the presence of benzyl alcohol in the formulation.

UPCOMING MEETINGS

British Nuclear Medicine Society 26-29 Mar, Manchester. www.bnms.org

European Symposium on Radiopharmacy and Radiopharmaceuticals 30 Mar-2 Apr, Lucca. <http://esrr06.eanm.org>.

Society of Nuclear Medicine 3-7 June, San Diego. www.snm.org

British Nuclear Medicine Society 4-5 Sep, Cambridge. www.bnms.org

7th International Symposium on Technetium in Chemistry and Nuclear Medicine 6-9 Sep, Bressanone. <http://tecnum.dsfarm.unipd.it>

European Association of Nuclear Medicine 30 Sep-4 Oct, Athens. www.eanm.org

9th World Congress of Nuclear Medicine and Biology 22-27 Oct, Soeul. www.wfnmb.org

UPCOMING COURSES

PET: Technology and Application

Imperial College, London. 5-7 Apr 2006. Focuses on research uses of PET rather than clinical.

www.imperial.ac.uk/cpd/pet

DiMI (Diagnostic Molecular Imaging)

A series of short courses on research techniques in molecular imaging are being held at various locations in Europe as part of the European Molecular Imaging Laboratories (EMIL) network of excellence funded by the 6th framework of the European Commission. www.mpifnf.de/dimix/

PEOPLE

We welcome **Len Rogers** as the new representative for Wales. He is at the Heath Hospital, University Hospital of Wales in Cardiff.

Congratulations to **Professor Phil Blower** who has left the University of Kent and Canterbury to join the Division of Imaging Sciences at King's College London as Professor of Imaging Chemistry. Phil is the driving force behind the new MSc in Radiopharmaceutics and PET Radiochemistry programme at KCL. He can be reached at philip.blower@kcl.ac.uk.

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This and previous issues of the Newsletter are available from the UKRG web site and are posted in the library section at www.VirRad.org

APPENDIX: CONTROVERSY CORNERS 2006

How do we achieve BNMS guidelines for particles of MAA in patient doses for lung scans in practice? *Moderator: Paul Maltby*

- We are in the sticky situation that there is only one licenced product on the market – LyoMAA
- The working day is 8 or more hours, yet the expiry of LyoMAA is 6 hours after preparation
 - There is a letter relating to the original licencing of the product which demonstrates stability over 8 hours; however, this letter has no legal standing and shelf-life extension must be validated locally
- If there are paediatric or pregnant patients needing lung scans late in the day, most centres would prepare a fresh MAA kit
- Not everyone was aware of the BNMS guidelines
- Sticking of MAA in syringes is an issue and it not brand dependent
 - It is more related to inadequate resuspension immediately prior to injection
 - There is also the problem of sticking in subdispensed vials

Manufacturers' recommendations for activity and volume in kits. Is it possible to deviate? How is it justified? *Moderator: Jim Ballinger*

- It was recognised that the justification of deviations from manufacturers' instructions can be divided into two classes: for technical/efficiency reasons and for purely financial reasons
- Technical/efficiency:
 - Wet labelling for reduction of radiation dose to operator
 - Extended shelf-life for efficiency of use, reduction of radiation dose, and to avoid effect on next day's generator yield
 - Some centres do not have radiopharmacy staff available late in the day
 - Dilution volumes outside manufacturer's instructions, e.g. for paediatric doses
 - Sestamibi prepared at 11 GBq in 3 mL produces an activity concentration too high for easy drawing of doses
 - Storage temperatures for kits before and after reconstitution
 - Most comply with instructions for cold kits in stock, but many have validated alternative conditions for labelled kits
 - Refrigeration of labelled kits is primarily for maintenance of sterility in multidose vials (this is mentioned in several of the package inserts); refrigeration for stability is rarely required for kits containing antioxidants
 - Some centres send products such as MAG3 and sestamibi to be boiled by the end user to save time and radiation exposure at the central radiopharmacy; others felt this practice to be unwise
- Financial reasons:
 - Kit splitting, especially HMPAO, is fairly common
 - Addition of amounts of activity in excess of the manufacturer's limit is common in some centres but not others
- Requirements for validation of deviations:
 - Must be validated in house
 - Must have resources (personnel, equipment) to do this
 - Do not have recourse to manufacturer if product fails
 - ARSAC holder should be informed

Syringe shield policies in radiopharmacy *Moderator: Bev Ellis*

- Preparation of radiopharmaceuticals
 - ^{99m}Tc eluate produces a very high exposure rate
 - Shield must be removed for syringe to be measured in dose calibrator
 - Small volumes/activities can be measured more quickly and accurately without shield
 - Beta shields have their own difficulties
 - Breakage, damage
- Patient doses
 - Usage is variable between centres
 - Depends on factors such as:
 - How busy is the department, how many injections per day, how many staff sharing radiation dose
 - Technique and experience of operator

- Type of vial shield
 - Depends on amount of activity to be injected
 - Depends on radionuclide
- Cleaning and disinfection of syringe shields
 - Radiopharmacy
 - Alcohol based
 - Blood labelling
 - Chlorine based
 - Injection room
 - Some have no disinfection policy
 - Clean only if contaminated
 - Daily clean vs cleaning after each patient
 - Cleaning agents can be corrosive and damage syringe shields
- General issues
 - Individual preference for syringe shield use
 - New staff should use syringe shields
 - Best design for ease of use and durability
 - Lead vs tungsten
 - Size of viewing window

^{99m}Tc generators and manual handling *Moderator: Jilly Croasdale*

- Generator has to be moved to several different levels – delivered on floor, lifted into hatch, from hatch to isolator/laminar flow hood
 - May need to be lifted over shielding to final position
- Weight of generator
 - Move at awkward angles in restricted space
 - At a distance from body to minimise exposure
- Handle of generator can be painful
 - Extend handle so it can be held by two people
- May need to be taken through two stages of change/disinfection, across step-over barriers
- Solutions:
 - Hoist
 - Cost
 - Slow speed
 - Requires storage space
 - Awkward access
 - Sanitisation – chain, motor, etc.
 - Trolley
 - Low vs high – which is more useful?
 - Sanitisation
 - Slide
 - Between different levels of benching, etc.
 - Minimises lifting but pushing can be equally awkward, risk of tipping
 - Ramp
 - Between different levels of flooring
 - Education and training
 - More than standard trust course
 - Recognition of radiation risk and need for speed
- Risk assessments for radiation and manual handling
- Cost of equipment
- Delivery onto trolley reduces number of transfers by radiopharmacy staff