Molecular radiotherapy: guidance for clinicians

Report from the Intercollegiate Standing Committee on Nuclear Medicine
## Contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foreword</td>
<td>3</td>
</tr>
<tr>
<td>1. Aims</td>
<td>4</td>
</tr>
<tr>
<td>2. Introduction</td>
<td>5</td>
</tr>
<tr>
<td>3. Safe patient care and treatment: clinical, legal and administration responsibilities</td>
<td>6</td>
</tr>
<tr>
<td>Team and individual responsibilities</td>
<td>6</td>
</tr>
<tr>
<td>Management guidelines</td>
<td>6</td>
</tr>
<tr>
<td>Decision to treat</td>
<td>7</td>
</tr>
<tr>
<td>Informed consent</td>
<td>7</td>
</tr>
<tr>
<td>Patient fitness for treatment</td>
<td>7</td>
</tr>
<tr>
<td>Responsibility for molecular radiotherapy administration</td>
<td>7</td>
</tr>
<tr>
<td>Treatment delivery</td>
<td>7</td>
</tr>
<tr>
<td>4. Recommended approaches for specific radionuclide therapies</td>
<td>9</td>
</tr>
<tr>
<td>Benign disease</td>
<td>9</td>
</tr>
<tr>
<td>Malignant disease</td>
<td>9</td>
</tr>
<tr>
<td>Treatment for bone metastases</td>
<td>10</td>
</tr>
<tr>
<td>5. Summary</td>
<td>12</td>
</tr>
<tr>
<td>References</td>
<td>13</td>
</tr>
</tbody>
</table>
Foreword

The third annual report from the Department for Health entitled *Improving Outcomes: a Strategy for Cancer,*¹ published in 2013, emphasised the need to enhance outcomes across the board for those suffering from cancer, including measures to improve inequalities of access to treatment. Access to specialised imaging and therapy using some medical radionuclides presently varies between different centres in the UK.

Furthermore, changes in disease prevalence, improved diagnostic options, developments in therapy, access to electronic patient data, the availability of multiprofessional guidelines and the advent of multidisciplinary working have implications on how medical professionals co-operate for the benefit of the patient. Clinical disciplines that were once distinct are now required to combine their expertise to offer patients optimal treatment. For example, this is true of the disciplines of clinical oncology and nuclear medicine, where training in each of the disciplines will need to be more integrated.

The Intercollegiate Standing Committee on Nuclear Medicine (ICSCNM) is committed to the continuing development of molecular radiotherapy. Close liaison between clinicians from a number of different specialties is essential to ensure high-quality service delivery in radionuclide therapy across a range of clinical indications. This document sets out the roles and responsibilities of those who may be involved. It covers the licensing and organisational aspects of handling radioactive isotopes, as well as issues that relate to clinical practice, delegation and team working. The guidance provides a very welcome and helpful framework for all those who may be involved in radionuclide therapy.

On behalf of the ICSCNM, I would like to thank, most sincerely, the working party of the Intercollegiate Standing Committee who drew up this document: Professor Val Lewington and Dr Di Gilson.

This document has been published on the websites of the Royal College of Physicians (RCP) and The Royal College of Radiologists (RCR). Details of the publication will be made known to the relevant ICSCNM constituents: the Clinical Oncology Faculty of the RCR, the Royal College of Physicians of London, the Royal College of Physicians and Surgeons of Glasgow, the Royal College of Physicians of Edinburgh, the Royal College of Pathologists and the British Nuclear Medicine Society (BNMS), so that they can inform their members as appropriate.

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1. Aims

This document aims to:

- Provide guidance for clinical teams delivering molecular radiotherapy and focuses on medical staff
- Define the roles and key responsibilities of specialists involved in delivering molecular radiotherapy
- Emphasise the importance of training, skills and maintenance of competence for all staff involved in caring for patients receiving molecular radiotherapy
- Describe the requirement for close liaison within a skilled multiprofessional team and appropriate infrastructure to ensure high-quality molecular radiotherapy service provision
- Identify the specialists required in multidisciplinary teams delivering specific molecular radiotherapy treatments.
2. Introduction

A 2011 survey of molecular radiotherapy in the UK demonstrated significant geographic disparities in treatment availability and differences in practice between specialist centres.² Taken with previous surveys, these data highlight the importance of practice guidelines to drive consistent standards of care in the UK.

The complex infrastructure requirements of a high-quality service limit the delivery of molecular radiotherapy to hospitals that provide specialist expertise. Centres delivering molecular radiotherapy for malignant disease, for example, will also provide comprehensive diagnostic facilities, systemic therapy and radiotherapy services.

Close liaison between all staff involved in managing patients undergoing molecular radiotherapy is a prerequisite for the delivery of a high-quality service. The training, competence and commitment of non-medical members of the molecular radiotherapy team are pivotal to high-quality service provision, but lie beyond the scope of this document.

Compared with external beam radiotherapy, cytotoxic chemotherapy and biological therapies for cancer, molecular radiotherapy is applicable to a relatively small number of patients. It is, nevertheless, an effective treatment for specific groups of patients and as healthcare commissioning changes, it is essential that the funding allocation for molecular radiotherapy safeguards access for all patients who might benefit from this form of treatment.
3. Safe patient care and treatment: clinical, legal and administration responsibilities

Team and individual responsibilities

Several clinicians may be involved with the care of an individual patient. Local protocols should be developed to facilitate close collaboration and clear communication pathways between members of the molecular radiotherapy team and referring specialists.

The principle of working in teams complies with the General Medical Council (GMC) document Good Medical Practice. Individuals working within a team remain accountable for their own professional conduct and for the care they provide. Care should only be delivered by doctors who have the appropriate training, knowledge and skills. The number of clinicians who have relevant expertise within the team must be sufficient to provide prospective cover, and robust arrangements should be in place to ensure continuity of high-quality care.

All staff involved in the care of patients receiving molecular radiotherapy must be appropriately trained and ensure that their knowledge and skills remain up to date through continuing medical education and professional development. It is essential that the volume of molecular radiotherapy work undertaken by staff is sufficient to maintain the necessary level of competence to deliver the highest standards of care.

Shared care between the referring specialist and clinician responsible for prescribing and delivering molecular radiotherapy should be underpinned by written protocols that specify the responsibilities of individual specialists involved in delivering treatment, immediate post-treatment care and supervising follow-up clearly. The doctor responsible for administering molecular radiotherapy must be satisfied that the patient is fit to proceed with therapy on the day of treatment administration and that robust arrangements for ongoing care are in place.

Molecular radiotherapy should be administered by appropriately trained staff who are used to handling unsealed sources and are experienced in radiation protection.

In centres where it is difficult for clinicians to maintain competence in managing uncommon conditions, referral to another unit that has a higher specialist workload should be considered. Molecular radiotherapy for very rare malignancies, for example neuroendocrine tumours (mIBG or peptide receptor radiotherapy [PRRT]), should be limited to centres supported by a relevant tumour-specific, multidisciplinary team that has expertise in delivering these treatments. It is the responsibility of all clinicians prescribing molecular radiotherapy to work collaboratively on a national/European level to optimise therapy protocols and pool outcome data for rare diseases.

Management guidelines

Evidence-based management guidelines and protocols should be developed by the multidisciplinary team, reflecting published guidance for high-quality care. Multidisciplinary teams should develop clearly documented referral pathways to ensure equity of access and that patients are referred appropriately for consideration for molecular radiotherapy. Where possible, patients should be offered the opportunity to participate in clinical trials.
Decision to treat

Treatment decisions for patients with benign conditions will be made jointly by the referring clinician and by an appropriately trained, experienced specialist (Administration of Radioactive Substances Advisory Committee [ARSAC] certificate holder) in accordance with local and national guidance.

The treatment plan for patients with malignant disease should be discussed and agreed by the appropriate tumour-specific multidisciplinary team, in accordance with national guidance. The outcome of the multidisciplinary team meeting may be to recommend a specific radionuclide therapy, but the final decision and legal responsibility for treatment delivery rest with the ARSAC certificate holder.

Informed consent

Patients must give written informed consent for the treatment being delivered. The doctor taking consent must have the relevant training and experience of using the radiopharmaceutical prescribed and be able to discuss the aims and potential benefits, risks and side-effects of treatment. In practice, consent will usually be taken by the ARSAC certificate holder but this duty may be delegated, in writing, to another suitably trained doctor at the certificate holder’s discretion.

Patient fitness for treatment

The patient’s fitness to proceed with treatment safely, particularly where therapy requires a period of isolation for radiation protection reasons, must be assessed by the ARSAC certificate holder or by an appropriately trained doctor to whom the duty of assessment has been delegated. It may be necessary to delay molecular radiotherapy to allow time for significant co-morbidities to be treated or for radiation protection arrangements to be put in place. The reasons for any treatment delay, which might include a formal risk assessment, should be documented in the patient’s notes.

Responsibility for molecular radiotherapy administration

The clinician responsible for the delivery of molecular radiotherapy must possess an ARSAC certificate for the radiopharmaceutical being administered.4

Treatment delivery

All treatment will be delivered according to locally agreed protocols for molecular radiotherapy, in an appropriate facility, within designated areas for therapy handling and administration of radionuclides.

Unsealed radioactive sources should be handled in a safe, designated area that meets statutory requirements.

Outpatient therapies should be administered in a specified location. Delivery of inpatient molecular radiotherapy and subsequent care of radioactive inpatients should be undertaken in an appropriately designated room.5–7 Staff involved in caring for the patient should be familiar with radiation protection and with the condition being treated.

Dosimetry

Molecular radiotherapy is usually prescribed as a fixed activity or fixed activity adjusted for body mass or surface area. In the absence of randomised clinical trial evidence, activities are prescribed according to published experience supported by clinical judgement and specialist expertise within the multidisciplinary team. Where possible, patients should be recruited to clinical trials to establish whether prospective
dosimetry-based individual treatment planning improves outcomes. Personalised treatment planning is mandated in EU directive 97/43 Euratom (1997).®

Radiation protection

Under the Ionising Radiation (Medical Exposure) Regulations (IR(ME)R)®, the employer is responsible for radiation protection, but associated tasks are usually delegated to the clinician directing the exposure. The advice of a medical physics expert (MPE) with expertise in radionuclide therapy must be consulted when setting up a service. An MPE must be present for all administrations other than those for where a standard protocol is followed. For standard treatments, an MPE must be available on site or at least contactable. Systems must be in place for reporting, recording and responding to errors in delivery of radionuclide therapies.

The patient must be informed of radiation protection precautions that they should observe post-therapy in accordance with the local protocol. Oral radiation protection advice provided by the doctor taking consent should be reiterated by another suitably trained member of the molecular radiotherapy team (for example, medical physicist, clinical scientist, technologist or radiographer) and confirmed in writing.

Responsibility for patient care following molecular radiotherapy

Local protocols should clearly document arrangements for the patient’s care following administration of molecular radiotherapy. The doctor prescribing treatment carries responsibility for the delivery of molecular radiotherapy and for any complications arising from that treatment; follow-up may be undertaken by this clinician (such as the ARSAC certificate holder) or by another appropriate doctor (for example, the referring clinician, an endocrinologist or general practitioner). This process must be clearly documented in the agreed local protocol and the ARSAC certificate holder must be satisfied that suitable arrangements for continuing care are in place before radiopharmaceutical administration.

Access to clinical trials

Clinicians should, where possible, provide the opportunity for patients requiring molecular radiotherapy to be included in well-designed clinical trials to strengthen the evidence for molecular radiotherapy and improve outcomes.
4. Recommended approaches for specific radionuclide therapies

Benign disease

**Radioiodine (\(^{131}\text{I}\)) for benign thyroid disease**
The extent to which nuclear medicine specialists, endocrinologists or clinical oncologists participate in the decision-making process and supervise treatment delivery should be agreed locally and clearly documented. Arrangements will vary between hospitals depending on the training and expertise of the medical staff. The ARSAC certificate holder is responsible for ensuring that written protocols are in place that are consistent with national guidance and best practice.\(^{10}\)

**Intra-articular therapy (radiation synovectomy)**
Decision-making with respect to the administration of intra-articular therapy may involve rheumatology, orthopaedic, haematology, musculoskeletal radiology, nuclear medicine or clinical oncology specialists. Aseptic cannulation of the joint space, drainage and administration of intra-articular radiopharmaceuticals may be performed by the ARSAC certificate holder, or by an appropriately trained doctor acting in accordance with the ARSAC certificate holder’s written directions. Protocols should clarify responsibility for patient preparation, for example, when treating patients with haemophilia, and for supervising aftercare with respect to immobilisation of the treated joint.

Malignant disease

**Radioiodine for differentiated thyroid cancer**
A treatment plan for all new patients with differentiated thyroid cancer should be discussed and agreed at an appropriate (head and neck cancer or thyroid cancer) multidisciplinary meeting. Local pathways for the management of thyroid cancer should be agreed in accordance with national guidance.\(^{11}\)

Patients should have ready access to all specialists who may contribute to their care (clinical oncologists, endocrinologists, nuclear medicine specialists and surgeons). Decisions regarding the administration of radioiodine may involve several members of the clinical team, with specialists in clinical oncology and nuclear medicine taking a lead role.

The management of patients with recurrent or metastatic disease should be discussed by the multidisciplinary team to ensure that all treatment options are considered.

**\(^{131}\text{I}-\text{meta Iodobenzylguanidine (\(^{131}\text{I mIBG}) for neuroendocrine tumours****
A treatment plan for neuroendocrine tumour (NET) patients should be discussed and agreed in an appropriate, specialist multidisciplinary team meeting. Patients should have ready access to all specialists who may contribute to their care (clinical oncologists, endocrinologists, medical oncologists, nuclear medicine specialists and surgeons).

Due to the rarity of these tumours and the relative complexity of \(^{131}\text{I mIBG} treatment, it is recommended that this therapy is provided by a small number of hospitals which offer specialist expertise and have the infrastructure to support treatment delivery. This necessitates the development of clear referral pathways to ensure that all appropriate patients have access to \(^{131}\text{I mIBG} treatment.

\(^{131}\text{I mIBG} therapy for children requires close co-operation between paediatric oncology and adult molecular radiotherapy teams – both of which should contribute to decisions about treatment in the context of a
paediatric cancer multidisciplinary team meeting. It is recommended that this treatment is only provided by a small number of hospitals that offer both molecular radiotherapy and paediatric oncology expertise in line with the National Institute for Health and Care Excellence (NICE) *Improving Outcomes Guidance for the Management of Children and Young People with Cancer.*

**Radiopeptide therapy for somatostatin receptor-positive neuroendocrine tumours (NETs)**

Treatment plans for all NET patients should be discussed and agreed in an appropriate NET multidisciplinary meeting. Local pathways for NET management should be agreed in accordance with published guidance.

Patients should have ready access to all specialists who may contribute to their care (cardiologists, clinical geneticists, clinical oncologists, endocrinologists, gastroenterologists, medical oncologists, nuclear medicine specialists, palliative care and surgeons). Decisions regarding the administration of radiopeptide therapy and radiopharmaceutical selection may involve several members of the clinical team, with specialists in clinical oncology and nuclear medicine taking a lead role.

Given the rarity of NETs and relative complexity of radiopeptide treatment delivery, particularly in patients with functioning NETs, it is recommended that this therapy is restricted to a small number of hospitals which offer specialist expertise and have the infrastructure to support high-quality, safe treatment delivery. This necessitates the development of clear referral pathways to ensure that all appropriate patients have access to radiopeptide treatment.

**Selective internal radioembolisation therapy (SIRT)**

SIRT is approved for the treatment of non-resectable, liver (predominantly colorectal) metastases and intrahepatic cholangiocarcinoma. Patients should be selected for SIRT by a hepatobiliary cancer multidisciplinary team. This requires close liaison between interventional radiologists and the colorectal cancer multidisciplinary team. It is recommended that eligible patients are offered the opportunity to be entered into clinical trials where possible.

Treatment decisions will involve several members of the clinical team including specialists in interventional radiology, oncology and nuclear medicine taking a leading role. It is recommended that this treatment is provided by hospitals that offer specialist expertise in all these areas.

**Treatment for bone metastases**

**Radium-223 dichloride (223RaCl2)**

223RaCl2 is approved for the treatment of skeletal metastases due to castrate resistant prostate cancer, following, or for those unable to have, docetaxel chemotherapy. Local treatment pathways should be developed by the multidisciplinary team, in accordance with published evidence, to ensure that all treatment options are considered for and are available to all appropriate patients with metastatic disease.

Treatment decisions are likely to involve specialists in oncology, nuclear medicine and palliative care. Written protocols should clarify responsibility for clinical supervision and monitoring between treatment cycles.

**Strontium-89 dichloride and samarium-153 Lexidronam**

Strontium-89 dichloride and samarium-153 Lexidronam treatments for bone pain palliation in patients with skeletal metastases should be discussed by the relevant, disease-specific multidisciplinary team. Treatment decisions should involve oncology, nuclear medicine and palliative care specialists.
**32P for haematological disorders**
Decisions about 32P therapy will involve the ARSAC certificate holder and a consultant haematologist with appropriate expertise in the management of myeloproliferative disorders. Treatment will be arranged in conjunction with the ARSAC certificate holder who may be a specialist in haematology or nuclear medicine, or a clinical oncologist.

**90Y-Ibritumomab tiuxetan**
90Y-Ibritumomab is licenced for use in adult patients with rituximab relapsed or refractory CD20+ follicular B-cell non-Hodgkin’s lymphoma (NHL), and as consolidation therapy after remission induction in previously untreated patients with follicular lymphoma. Patients should be discussed at an appropriate haematology multidisciplinary team meeting.

Treatment decisions are likely to involve clinical oncologists and/or nuclear medicine physicians and a lymphoma haemato-oncologist or medical oncologist. It is essential that appropriate follow-up and support are in place to manage post-treatment cytopaenias.
5. Summary

- The provision of molecular radiotherapy requires effective, cross-specialty collaboration and multidisciplinary teamwork.
- Legal responsibility for the administration of molecular radiotherapy rests with the doctor prescribing the treatment (the ARSAC certificate holder).
- The ARSAC certificate holder is responsible for ensuring that arrangements are in place for all aspects of the patient’s care during and after treatment with molecular radiotherapy.
- Molecular radiotherapy should be delivered in accordance with agreed written protocols that define the duties and responsibilities of all specialists involved in an individual patient’s management.
- Individual team members remain accountable for their own professional conduct and the standard of care they provide.
- Molecular radiotherapy for patients with rare malignancies should be managed by a small number of designated individuals working in specialist hospitals, capable of providing the expertise, patient throughput and infrastructure to support treatment.

Approved by the Royal College of Physicians Intercollegiate Standing Committee for Nuclear Medicine: 19 June 2014
Approved by the Clinical Oncology Faculty Board of The Royal College of Radiologists: 26 June 2014
References


