

B01/S/b

**2013/14 NHS STANDARD CONTRACT
FOR BRACHYTHERAPY AND MOLECULAR RADIOTHERAPY (ALL AGES)**

SECTION B PART 1 - SERVICE SPECIFICATIONS

| | |
|----------------------------------|---|
| Service Specification No. | B01/S/b |
| Service | Brachytherapy and Molecular Radiotherapy (All Ages) |
| Commissioner Lead | |
| Provider Lead | |
| Period | 12 months |
| Date of Review | |

1. Population Needs

1.1 National/local context and evidence base

Brachytherapy is the delivery of radiation therapy using sealed sources which are placed as close to the site that is to be treated. Isotopes used in brachytherapy can be applied directly to the tumour by surface applicators, inserted into body cavities and tubular organs via specially designed delivery systems (intracavitary and intraluminal therapy) or inserted directly into a tumour (interstitial therapy).

Brachytherapy treatment is one option available to patients and has seen steady growth over the last few years. Increasingly patients have selected brachytherapy over alternative treatments and it is expected to continue to increase in popularity.

Improving Outcomes: A Strategy for Cancer (Department of Health, January 2011) sets out that:

“Access to radiotherapy is critical to improving outcomes and, to improve outcomes from radiotherapy, there must be equitable access to high quality, safe, timely, protocol-driven quality-controlled services focused around patients’ needs”.

In the treatment of a localised cancer, the advantage of brachytherapy is that it delivers high doses of radiation to the tumour and only relatively small amounts to surrounding normal tissue.

In order to reduce staff radiation exposure to the very low limits that are mandatory under *The Ionising Radiation Regulations (1999)*, brachytherapy equipment using

remote afterloading of sealed radioactive sources is used in the majority of procedures. Exceptions to this are some iridium wire interstitial implants and the permanent implantation of Iodine seeds (I^{125}) in the prostate.

Service provision and care pathways are informed by national and regional recommendations and guidelines.

2. Scope

2.1 Aims and objectives of service

The appropriate delivery of radiotherapy treatments to patients with cancer will ensure that the outcomes from treatment will meet the requirements of the five domains of the NHS Outcomes Framework.

The process of brachytherapy is complex and involves understanding of the principles of medical physics, radiobiology, radiation safety, dosimetry, radiation treatment planning, and interaction of radiation with other treatment modalities.

All forms of radiotherapy are part of an overall cancer management and treatment pathway. Decisions on the overall treatment plan must relate back to a multi-disciplinary team (MDT) discussion and decision.

This specification has been developed to ensure that the services being delivered offered high quality brachytherapy to patients by ensuring that:

- Accurate treatment is delivered in the context of a safety-conscious culture.
- Treatment is delivered within an evidence-based approach and according to locally agreed protocols.
- Strong clinical and operational governance arrangement exist.
- All patients with cancer who require brachytherapy (including urgent and palliative brachytherapy) as part of their treatment receive this in a timely manner.
- Information included in the mandated national radiotherapy dataset (RTDS) is collected and submitted according to national requirement.
- The department has robust mechanisms in place for monitoring treatment outcomes.
- The provider must participate in the national peer review programme for radiotherapy and defined audits within Peer Review should be produced and acted upon.

Where any brachytherapy is used concurrently with other treatments (such as external beam radiotherapy or chemotherapy), it should be integrated appropriately and scheduled to meet the patients' needs.

- Brachytherapy is accessible to all patients with cancer who *are suitable*

candidates regardless of gender, age, ethnicity, disability, religion or belief, sexual orientation or any other non- medical characteristics and available to all parts of England.

- Clinical trials, where appropriate, should be discussed with patients. Discussions shall be supplemented with written information.
- The provider department must participate in the national inter-departmental dosimetry audit pro programme (National audit of high dose-rate (HDR) brachytherapy (Joint IPEM WP & Interlace trial).
- The provider must comply with the dosimetry quality assurance requirements of UK Guidance on Radiation Protection Issues following Permanent Iodine-125 Seed Prostate Brachytherapy IPEM Report 106.

There is a requirement for providers to work as part of a Network Radiotherapy Group, working in collaboration with commissioners, to develop longer term plans.

Radiotherapy is usually given as an external beam treatment (the most common form) but outside the scope of this document.

Improved imaging with CT and MR imaging has allowed image-guided brachytherapy (IGBT). Some of the principles of volume-based dosimetry used in external beam radiotherapy can now be applied to brachytherapy. These include: defining a high risk CTV (clinical target volume), defining OAR (organs at risk) using dose constraints, optimising the plan, 3D image manipulation. Providers unable to deliver this type of treatment, where recommended by national guidelines, should develop plans to make this available within the next 12 months and where this is not possible providers, in consultation with the commissioners, should offer patients the opportunity to receive this treatment at an alternative provider.

To determine the minimum number of patients that would justify a brachytherapy service in a centre, the following should be taken into account:

- The cancer network demand for the service, and the availability or need for a similar service in adjacent networks.
- The number of patients needed to maintain expertise in each site specific discipline (note 2007 RCR Guidance “The Role of Brachytherapy Afterloading.” www.rcr.ac.uk)
- The standards within the guidance “Implementing IGBT for cervix cancer in the UK” should be followed. (RCR 2009 MRI based IGBT for cervix cancer)
- The role and development of afterloading brachytherapy services in the United Kingdom (2012) www.rcr.ac.uk/publications.aspx?PageID=149&PublicationID=376
- Cost-effectiveness
- The place of such a service in the research and development of brachytherapy

It is expected that trusts providing radiotherapy meet (and continue to meet) the requirements below:

- Brachytherapy services should be network based and configured to meet the needs of patients.

- Brachytherapy should only be carried out at centres with direct access to appropriate surgical oncology expertise for multi-disciplinary patient assessment and treatment.
- Each provider of a network service is expected to provide surgical and non-surgical oncological care according to nationally agreed standards.
- Networks are expected to have cross-network arrangements for the provision of highly specialist treatments that are provided regionally or nationally.
- The total brachytherapy caseload should exceed 50 cases per year as a minimum in each centre offering the service.
- The team should include at least two clinical oncologists three physicists (two Medical Physics Experts (MPE)) and three radiographers (see The role and development of afterloading brachytherapy services in the United Kingdom (2012) www.rcr.ac.uk/publications)
- 62 day and 31 day waiting time requirement to include all radiotherapy treatments.
- It is expected that the workload standards below are met within a 12 month period.
- It is expected that all clinicians within the service will contribute to studies and clinical trials.

For the purpose of setting standards in workload for the training and maintenance of experience in brachytherapy it is divided into three modality areas:

- Gynaecological intracavitary brachytherapy.
- Intestinal and intraluminal therapy (excluding prostate).
- Low dose-rate LDR I¹²⁵ seed prostate implantation.

There are two additional modality sites:

- Interstitial HDR prostate brachytherapy
- Skin surface HDR Brachytherapy

Gynaecological intracavitary brachytherapy

It is expected that:

- The intra-uterine applicator insertion is carried out by an appropriately trained clinical oncologist with relevant competencies.
- Vault brachytherapy applicators may be inserted by appropriately trained clinicians, nurses or radiographers after assessment by a specialist clinical oncologist and following assessment.*
- To maintain clinical oncologist expertise there should be a minimum of ten intra- uterine insertions per centre per year and each oncologists should attend six or more insertions and dosimetry reviews per year.

Interstitial and intraluminal therapy (Excluding prostate cancer HDR)

It is expected that:

- Ten patients per year of each technique are treated per centre as a minimum.

- Individual clinicians should ensure continued practical experience.
- Oncologists delivering brachytherapy either perform or attend more than five applicator insertions and dosimetry reviews per year in each of the low throughput techniques (head and neck interstitial implants, breast and intraluminal treatments in the bronchus, oesophagus and rectum).

Interstitial LDR prostate brachytherapy

In 2006, the Department of Health recommended the establishment of ^{125}I seed implantation services on the basis of a minimum catchment population of 1.5 million:

- To maintain expertise a minimum caseload of 25 patients per year per centre moving to 50 per year per centre by 2014 is expected.
- More **than** five implants per year per clinical oncologist.

In line with the RCR publication in 2012, plans should be in place to concentrate this activity to meet the expectation that each oncologist should be performing 25 cases per year. It is expected that centres delivering brachytherapy will develop plans during 2013 to meet this requirement.

* The Role and Development of Afterloading Brachytherapy Services in the United Kingdom (2012.): www.rcr.ac.uk/publications

Interstitial HDR Prostate Brachytherapy

It is expected that:

- At least 10 patients per year are treated per centre
- Individual clinicians and physics staff should ensure continued practical experience.
- All forms of radiotherapy are part of an overall cancer management and treatment pathway.
- Decisions on the overall treatment plan must relate back to an MDT discussion and decision.

2.2 Service description / care pathway

Radiotherapy is the safe use of ionising radiation to treat people who have cancer. The aim of radiotherapy is to deliver as high a dose of radiation as possible to the cancerous tumour/s whilst sparing the surrounding normal tissues. Brachytherapy is a form of radiotherapy and is often used on its own or as part of a treatment plan including surgery or chemotherapy, or both.

An indication for radiotherapy is defined as ‘a clinical situation in which radiotherapy is recommended as the treatment of choice on the basis of evidence that including radiotherapy leads to superior clinical outcome compared to alternative treatments (including no treatment),’ (Barton & Delaney 2003 *Radiotherapy in Cancer Care: estimating optimal utilisation from a review of evidence based clinical guidelines*).

A high quality brachytherapy service should ensure that:

- The delivery of accurate treatment is the responsibility of all staff and each department must develop a safety-conscious culture as demonstrated by reporting to the National Reporting and Learning Service (NRLS).
- Regular reviews should be conducted to ensure that protocols remain up to date, and that staffing levels and skills mix are appropriate for the numbers of patients treated and complexity of treatments delivered .
- Up to date management guidelines should be followed where appropriate

Good multi-disciplinary working with clear communication is essential and such a culture must be actively developed. Patients and staff should be encouraged to question and raise concerns to which the provider is required to respond. When a clinically significant incident occurs, it is essential that the patient is informed and offered appropriate support. It is also important to offer support to the staff involved in such an incident.

Each department must have an ISO 9000 Quality system for reporting and analysing errors. The lessons learnt should be fed back to the staff in multidisciplinary meetings. It is required that the radiotherapy pathway coding system set out in 'Towards Safer Radiotherapy' is used to aid the sharing of information and learning between centres through the NRLS.

Commissioners should be informed of clinically significant errors reported to patients as reported under the IRMER regulations.

There should be a systematic approach to monitoring of late toxicities from brachytherapy in place.

Information should be made available on local outcomes to treatment to help inform patients who are considering management options for their cancer.

It is imperative that the service is compliant with the Ionising Radiation (Medical Exposure) Regulations (IR(ME)R) 2000. These regulations (which now also include the Ionising Radiation (Medical Exposure) (Amendment) Regulations 2006) are legislation intended to protect the patient from the hazards associated with ionising radiation. Major errors within radiotherapy are reported under IR(ME)R and investigations are conducted under criminal law and under the threat of caution.

IR(ME)R is flexible and allows for a wide variety of practices to be undertaken as long as they are clearly justified. It is imperative that roles and responsibilities are clearly set out in procedures and that everyone understands their individual roles. Responsibility for compliance with IR(ME)R rests with the employer and all entitled duty holders as defined in the regulations.

The employer should be considered to be the chief executive unless an alternative individual has been formally designated as the employer. Under IR(ME)R, the employer is legally responsible, when establishing practices for the safe delivery of radiotherapy, for ensuring that robust procedures exist including those listed in

Schedule 1,(Regulation (4(1))). It is usual for the detailed implementation of IR(ME)R to be delegated to an appropriate professional. Providers need to demonstrate compliance with IR(ME)R and show clear lines of authority from the professional leads to the employer as the employer's responsibility cannot be delegated under IR(ME)R.

As brachytherapy involves the use of radioactive sources, some of which are classified as high activity sources, to ensure protection of the staff and general public, providers must show compliance with the Ionising Radiation Regulations (IRR 1999) and the High Activity Sealed Sources (HASS) 2005 regulations.

Referral

The service forms part of the pathway of cancer care for patients and it has been developed with formal links to the relevant multi-disciplinary teams in mind. The pathways must be reviewed formally on a regular basis and also adhere to the local network guidelines. User and carer involvement is an important step in this process.

Patients on any radiotherapy pathway should have been discussed at an appropriate MDT. Referrals for brachytherapy are made to a Consultant Clinical Oncologist who is a member of that MDT. In some circumstances, onward referral to another provider may be appropriate.

It is essential that an individual consultant retains the responsibility for overall patient care across the whole pathway and will provide care when a patient is using a separate discrete radiotherapy service, and retains overall responsibility for the management of side effects and complications. A consultant practitioner (such as an appropriately trained and identified registered therapeutic radiographer working at consultant level) may provide the link between the radiotherapy service and the multi-disciplinary team.

Patient Pathways reflect three generic types:

- Permanent implant
- Temporary implant without anaesthetic
- Temporary implant with anaesthetic

2.3 Population covered

The service outlined in this specification is for patients ordinarily resident in England or otherwise the commissioning responsibility of the NHS in England (as defined in Who pays?: Establishing the responsible commissioner and other Department of Health guidance relating to patients entitled to NHS care or exempt from charges). Note: for the purposes of commissioning health services, this EXCLUDES patients who, whilst resident in England, are registered with a GP Practice in Wales, but INCLUDES patients resident in Wales who are registered with a GP Practice in England.

Specifically, it includes brachytherapy treatments delivered to adult patients for whom brachytherapy has been deemed an appropriate treatment and who have agreed to

receive this treatment. Typically, patients requiring any form of radiotherapy will have been discussed at least once at an MDT. Note paediatric brachytherapy is an appropriate clinical treatment but is carried out in highly specialised centres only.

The service should be accessible to all patients with cancer who require this treatment regardless of gender, age, ethnicity, disability, religion or belief, sexual orientation or any other non-medical characteristics.

2.4 Any acceptance and exclusion criteria

Appropriate education and continuing education of professionals directly involved in brachytherapy procedures should be given a high priority. Training should include quality assurance, planning, treatment delivery and verification technologies and techniques.

Safety considerations should also be included in the training for these new techniques. The training of professionals should involve the 'normal' and 'unusual' circumstances likely to occur in the process.

The service must comply with current legislation and local and national policies and standards in relation to Equality and Diversity. The Provider will ensure that the service offered is respectful and must not discriminate on grounds of age, gender, sexuality, ethnicity or religion. The service should be sensitive to the needs of people whose first language is not English and those with hearing, visual or learning disabilities.

The Provider will facilitate compliance with the Disability Discrimination Act (2005) by ensuring that all reasonable adjustments are made to remove the barriers to access by disabled people.

The Provider will comply with Equalities legislation including the Race Relations (Amendment) Act 2000 and Equalities Act 2006 and aim to meet the individual needs of the service users irrespective of race, disability, gender, religion/belief, age and sexual orientation.

The Provider has a duty to include people with learning difficulties in its activities, and should recognise they may need more support and preparation in order to access services.

Information supplied about the service must be sensitive, clear and professional and in formats appropriate to the needs of users and potential users of the service.

The Provider should consider accessibility and accessability of the facilities available for the service, such as ease of access, privacy, comfort and include these issues in audits of patient satisfaction.

Any exclusion criteria

This specification does not cover the use of External Beam Radiotherapy, molecular RT unused (Radio-pharmaceutical), Protons, intra-operative radiotherapy and treatments using unsealed radioactive sources. These treatments are subject to some additional requirements to the principles identified within this specification.

Independencies

Patients will often require general anaesthesia. This will necessitate support from theatres and anaesthetics service. As with all radiotherapy, medical physics experts (MPE) are essential in all stages of the process.

3. Applicable Service Standards

3.1 Applicable national standards e.g. NICE, Royal College

The Royal College of Radiologists – standards and guidelines

The role and development of afterloading brachytherapy services in the United Kingdom (2012)

www.rcr.ac.uk/publications.aspx?PageID=149&PublicationID=376

Quality assurance practice guidelines for transperineal LDR permanent seed brachytherapy of prostate cancer (2012)

www.rcr.ac.uk/publications.aspx?PageID=149&PublicationID=377

Implementing image-guided brachytherapy for cervix cancer in the UK

www.rcr.ac.uk/publications.aspx?PageID=149&PublicationID=297

UK Guidance on Radiation Protection Issues following Permanent Iodine- 125 Seed Prostate Brachytherapy IPEM Report 106
IRMER 2000 (Medical Exposure Regulation)

ICRP (International Commission Radiation Protection) IPEM (Institute of Physics, Engineering in Medicine)

“Joint Council for Clinical Oncology (1993) *Reducing Delays in Cancer Treatment: Some Targets*. London: Royal College of Physicians”

The RCR sets out clear guidance on waits for radiotherapy that goes beyond the mandatory cancer waits. These reflect good practice guidance and should be the standard of care where possible. They recommend:

- No patients waiting longer than 28 days for radical treatment.
- The overall treatment time should not be prolonged by delay in the provision of brachytherapy and special provision should be made to cover holidays, theatre servicing and source replacement.

Quality Standards and Governance

The service will comply with the relevant and current quality standards. This are defined in 'The role and development of afterloading brachytherapy services in the United Kingdom available on the Royal College of Radiologists website.

Clinical Governance systems and policies should be in place and integrated into organisational governance with clear lines of accountability and responsibility for all clinical governance functions and Provider should produce annual Clinical Governance reports as part of NHS England reporting system.

- The provider is required to undertake annual patient surveys and develop and implement an action plan based on the findings.
- Patients should receive the right treatment, at the right time, in the right place, which, where possible, will be as close to home as practicable.
- Patients must receive clear written guidance when consenting to treatment to include the treatment intent, prognosis and potential complications associated with their treatment with clear instructions who to contact if they need advice outside working hours and how to proceed in the event of a medical emergency.
- The service should be able to demonstrate effective clinical leadership and decision making.
- Co-ordination of brachytherapy services in each centre should be by a lead Clinical Oncologist for Brachytherapy who should be clinically involved in the provision of the service.
- For patients receiving treatment with external beam by an oncologist other than that providing the brachytherapy, there should be clear protocols, case conferences and regular meetings between the clinicians involved.
- The service should be audited in terms of process, quality and clinical outcomes.
- A brachytherapy theatre suite should provide comprehensive facilities for anaesthesia and resuscitation, imaging (static and real time) and access to treatment planning in addition to treatment delivery.
- Every patient should be assessed for analgesia and anaesthesia.
- Patients requiring imaging not available at the place of insertion of the applicators should not be transferred over long distances within the centre as the applicators could be displaced.
- An annual audit should be undertaken to review activity within the centre and by clinician to demonstrate compliance with the activity standards.
- Appropriate Administration of Radioactive Substances Advisory Committee (ARSAC) certificates must be in place.

| 4. Key Service Outcomes | | | | |
|---|--|------------------|--|-------------------------------|
| Performance Indicator | Indicator | Threshold | Method of measurement | Consequence of Breach |
| Waits: First Definitive Treatment (part of whole RT service) | % of patients waiting less than or equal to 62 days | 96% | CWT-db | National Requirement Breached |
| Waits: Subsequent Treatment (part of whole RT service) | % patients waiting less than or equal to 31 days | 94% | CWT-db | National Requirement Breached |
| Total activity by centre Gynaecological intracavitary brachytherapy Interstitial and intraluminal therapy LDR I ¹²⁵ seed prostate implantation Interstitial HDR prostate brachytherapy Skin Surface HDR brachytherapy | Minimum 50 / year Minimum 10 intrauterine pts per year Minimum 10 pts per year Minimum 25 pts per year Minimum 10 pts per year Minimum 5 pts per year | | | |
| RCR within 28 days | | | | |
| Quality Compliance with National Cancer Peer Review | % compliance plus number of immediate risks or serious concerns | | CQuINS | Governance issue |
| Patient experience | Number of patients reporting positively through cancer patient | 83% | CPES via Cancer Commissioning Toolkit. | |

| | | | | |
|--|---|--------------------------|-------|--|
| | experience survey | | | |
| Unscheduled delays to Treatment | All patients in category 1 must not have their treatment delayed or interrupted | 95% of the group treated | Audit | |
| Cross-sectional imaging should be used | Intrauterine and interstitial brachytherapy placement and 3D planning | | | |

Interim for adoption from 01/10/13

**2012/13 NHS STANDARD CONTRACT
FOR MOLECULAR RADIOTHERAPY (MRT) FOR TUMOURS**

SECTION B PART 1 - SERVICE SPECIFICATIONS

| | |
|----------------------------------|--|
| Service Specification No. | B01/S/b |
| Service | Molecular Radiotherapy (MRT) for tumours |
| Commissioner Lead | |
| Provider Lead | |
| Period | 12 months |
| Date of Review | |

1. Population Needs

The text is drawn almost exclusively from the recent British Institute of Radiology report 23 “Molecular Radiotherapy in the UK: Current Status and Recommendations for Further Investigation” of the BIR Molecular Radiotherapy Working Party 2011.

Molecular radiotherapy (MRT) is the treatment of disease with radiopharmaceuticals. As with external beam radiotherapy, MRT offers the advantage of delivering high radiation doses to a specific target and sparing healthy organs from serious side effects; however in common with chemotherapy the treatment is generally delivered systemically with systemic side effects. With modern imaging techniques, a system of dosimetry has the potential to plan and deliver optimised treatments, maximising therapeutic advantage within dose limits to organs at risk.

The procedures can be complex and can require significant input from a number of disciplines including clinical oncology (and sometimes medical oncology), nuclear medicine, medical physics, radio-pharmacy and nursing. MRT is generally minimally invasive, incurs few side-effects and can achieve impressive clinical outcomes. It is particularly attractive in cancers which take up the radiopharmaceutical and in some of these cancers there are sometimes few therapeutic alternatives. The technique exhibits great potential and is often highly cost-effective. In the UK, the use of MRT is marked by significant variation in practice due to differing views on clinical applications, availability of expertise, lack of capacity to undertake individual dosimetry assessments, investment and development in the field, lack of ‘ownership’ and hitherto a lack of national policy or service specification. The commonest practice is radioiodine for thyroid cancer; hospital activity varies between 5 and 150 cases per year; centralisation of MRT should be considered to improve expertise, widen its applications and ensure quality standards.

2. Scope

Malignant Thyroid Disease

Rationale

Radioiodine-131 as Sodium Iodide has been used to treat differentiated thyroid cancer (DTC) since the 1940s and is used worldwide. Considerable expertise is required to manage particular patient groups including those with limited mobility, mental health problems, renal dialysis, colostomy/urostomy /urinary catheter and young patients.

Indications

The ablation of thyroid remnant following total or near-total thyroidectomy. Additional administrations may be required in patients with adverse histopathological indicators (positive resection margins and involved lymph nodes) and for therapy of unresectable nodal or distant metastatic disease.

Radiopharmaceutical

Radioiodine-131 as Sodium Iodide.

Technique

Oral administration, usually as capsule. Liquid form if medically indicated. At present in the UK, empirical activities are routinely prescribed rather than individualised activities based on imaging and dosimetry.

Guidelines

2009 ATA Guidelines for radioiodine therapy of differentiated thyroid cancer

Royal College of Physicians Guidelines for the management of thyroid cancer
http://www.rcplondon.ac.uk/sites/default/files/documents/management-_thyroid-cancer-guideline.pdf

Adult Neuro-endocrine Tumour

Rationale

The evidence for using radionuclide therapy in neuro-endocrine tumour management is mainly derived from small, non-randomised single institution studies that are often retrospective. These studies usually include patients with a number of different pathological types of NET, with varying disease burdens and with a variety

of previous therapies and performance status.

Indications

These treatments are used in the setting of locally advanced or metastatic disease where the aim of treatment is symptom palliation rather than cure.

Radiopharmaceuticals

Iodine-131 labelled meta-iodobenzyl guanidine (mIBG) has been used for over 20 years. More recently a number of peptide analogues of somatostatin have been developed, radio labelled with Yttrium-90, Indium-111 and Lutetium-177.

Technique

Intravenous administration over several cycles. There is currently no national or international consensus on the optimal radiolabelled somatostatin peptide or radioligand combination or on the administered activity for therapy, interval between therapies or method of response evaluation. There are currently significant variations in clinical practice, referral patterns and access to these radionuclide therapies across the UK. The activity (quantity) of radiopharmaceutical administered per treatment, the interval between treatments and the cumulative administered activity vary significantly.

Guidelines

EANM procedure guidelines for ¹³¹I-meta-iodobenzylguanidine (¹³¹I-mIBG) therapy
http://www.eanm.org/publications/guidelines/gl_radio_ther_benzyl.pdf

ENETS Consensus Guidelines for the Standards of Care in Neuroendocrine Tumors: Peptide Receptor Radionuclide Therapy with Radiolabeled Somatostatin Analogs
http://www.enets.org/guidelines_tnm_classifications.html&OPEN=menu,14
[Neuroendocrinology 2009;90:220–226](http://www.enets.org/guidelines_tnm_classifications.html&OPEN=menu,14)

NCCN Clinical practice guidelines in Oncology Neuroendocrine tumours v1.2011
http://www.nccn.org/professionals/physician_gls/pdf/neuroendocrine.pdf

UKNETwork for neuroendocrine tumours
Guidelines for the management of gastroenteropancreatic neuroendocrine (including carcinoid) tumours *Gut* 2005;54;1-16
http://www.bsg.org.uk/images/stories/docs/clinical/guidelines/liver/pan_net.pdf

Haematological Malignancies and disorders

Rationale

Radionuclides were first used in the 1940s to treat leukaemia. Haematopoietic tissues are inherently radiosensitive and tumour cells derived from them retain the relative

radio-sensitivity of the original tissue. Theoretically these malignant conditions are ideal candidates for MRT.

Indications

Malignancies derived from haematological tissues are a heterogeneous group of disorders and include the lymphomas, (non-Hodgkin's [NHL] and Hodgkin's disease [HD]), acute and chronic leukaemias, and multiple myeloma. In addition there is a group of conditions characterised by an increased growth of components of bone marrow, the myeloproliferative disorders (MPDs), which include polycythaemia rubra vera (PRV), essential thrombocythaemia (ET) and myelofibrosis (MF). Although not strictly malignant these are clonal disorders requiring treatment to prevent complications such as stroke, haemorrhage and thrombosis. They can also progress to a more malignant phenotype.

Radiopharmaceutical

Yttrium-90 labelled Zevalin (Ibritumomab Tiuxetan) is used for the treatment of follicular NHL. It uses an anti-CD20 monoclonal antibody to target the CD20 antigen present on B-lymphocytes.

Phosphorus-32 has been used for several decades to treat Myeloproliferative Disorders (MPD). The use has diminished however, for some patients, particularly the elderly, infrequent administration is still used.

Technique

Intravenous administration.

Guidelines

NCCN Guidelines Clinical practice guidelines in Oncology Non Hodgkin's Lymphomas http://www.nccn.org/professionals/physician_gls/pdf/nhl.pdf

EANM procedure guideline of radio-immunotherapy for B-cell lymphoma with 90Y- radiolabeled ibritumomab tiuxetan (Zevalin®) http://www.eanm.org/publications/guidelines/gl_radio_ther_radioimmun.pdf

EANM procedure guideline for 32P phosphate treatment of myeloproliferative diseases http://www.eanm.org/publications/guidelines/gl_radio_ther_32p.pdf

Palliation of Bone Metastases

Rationale

Radiopharmaceuticals have been established as an effective agent for bone pain palliation since 1990. However, there are very scarce data on cost-effective evaluation of radionuclide treatment for metastatic bone pain. At present radionuclide

therapy targeted against bone metastases can only be considered palliative, although anecdotal evidence suggests that a therapeutic benefit may also be gained.

Indications

Bone pain is experienced by up to 90% of patients with Castration Resistant Prostate Cancer (CRPC) in the later phases of their disease. A significant body of evidence exists for the use of bone-seeking radionuclide therapy in CRPC.

Radiopharmaceuticals

A range of radiopharmaceuticals have been used to treat bone metastases. Two commercially available products are in relatively common use in the UK. These are: Strontium-89 Metastron (Strontium Chloride) and Samarium-153 Quadramet (Samarium Lexidronam). A recent pivotal randomised controlled trial has demonstrated a survival benefit compared to placebo for the alpha emitter Radium-223 Alpharadin. This is the first radiopharmaceutical to demonstrate survival benefit in CRCP. (Radium Chloride) has been shown to be effective.

Technique

Intravenous administration of empirical activities. Administration of these radiopharmaceuticals tends to be standardised by manufacturers' guidelines. The challenge now is to develop strategies that will elicit optimal therapeutic response.

Guidelines

EANM procedure guideline for treatment of refractory metastatic bone pain
http://www.eanm.org/publications/guidelines/gl_radio_treatment.pdf

Intra-Arterial Treatment of Liver Tumour, Selective Internal Radiation Therapy

Rationale

This treatment is used for primary and secondary tumours within the liver.

Indications

Studies have shown a good response in primary liver tumours and neuroendocrine tumours. In metastatic colon cancer there is evidence that this radiopharmaceutical should be combined with chemotherapy.

Radiopharmaceutical

Two forms of Yttrium-90 particulates are used. Theraspheres consist of ^{90}Y incorporated into small silica beads. SIR-spheres consist of ^{90}Y adhered to resin beads.

Technique

Administration requires interventional radiology as the spheres must be administered directly into the common, right or left hepatic artery via an angiographic catheter under radiological control. Therapy angiograms are performed to determine the blood supply to the tumour and the rest of the liver. Most of the liver has a joint arterial supply while tumours are supplied only by the hepatic artery and its branches. Any vessels, such as the gastroduodenal artery and other branches not leading to the tumour, are then embolised. At the end of the procedure a small volume of $^{99}\text{Tc}^m\text{MAA}$ is administered to check for shunting to the lungs and spill into the stomach or other organs. Treatment activities are determined according to the patient body surface area, the size of the tumour, the size of the normal liver and the degree of any shunt.

Guidelines

EANM procedure guideline for the treatment of liver cancer and liver metastases with intra-arterial radioactive compounds

http://www.eanm.org/publications/guidelines/EANM_liver_treatment_guidelines_2012.pdf

Children and Young People, Malignant Thyroid Disease

Rationale

Radioiodine-131 as Sodium Iodide has been used for many decades in children with differentiated thyroid cancer in much the same way as it is in adults.

Indications

Post-operative remnant ablation and cancer therapy.

Radiopharmaceutical

Radioiodine-131 as Sodium Iodide.

Technique

Oral administration, usually as capsule. Liquid form if medically indicated. There is no clear guidance about how administered activities should be adjusted for differences in body weight or surface area.

Children and Young People, Neuroblastoma

Rationale

Neuroblastoma has been regarded as an ideal disease for treatment with MRT as it is highly radiosensitive compared with many other cancer types, and is often widely disseminated, making systemic therapy in addition to local treatment essential.

Indications

Iodine-131 labelled meta-iodobenzyl guanidine (mIBG) has been recognised for 25 years as a valuable palliative treatment.

Radiopharmaceutical

Iodine-131 labelled meta-iodobenzyl guanidine (mIBG).

Technique

Intravenous administration.

3. Applicable Service Standards

The European Directive Euratom 97/43¹ specifies that: "For all medical exposures of individuals for radiotherapeutic purposes exposures of target volumes shall be individually planned; taking into account that doses of non-target volumes and tissues shall be as low as reasonably achievable and consistent with the intended radiotherapeutic purpose of the exposure". MRT in Benign Thyroid Disease would be compatible with Service Level 1 of BIR Report 23.

For other MRT procedures, higher service levels need to be defined to determine the resources and expertise required to deliver particular MRT procedures. These would be compatible with Service Level 2 of BIR Report 23 because of requiring highly-shielded in-patient facilities, scanning or dosimetry; or compatible with Service Level 3 of BIR Report 23 because of requiring in-house preparation of the radiopharmaceutical or using the radiopharmaceutical for a new indication.

4. Key Service Outcomes

Therapeutic response and toxicity from MRT treatments are sometimes unpredictable. It is likely that one major cause of this is that patients receive a very wide range of absorbed doses that are not subsequently calculated. This is in stark contrast to external beam radiotherapy with its standardised dosimetry; the need to avoid undue toxicity leads to all patients being treated according to the dose limiting criteria of normal tissues, identified in clinical trials. Individualised treatment using MRT, based on accurate dosimetry obtained using standardised protocols, would in many cases enable higher activities and absorbed doses to be delivered where this may achieve improved tumour control. It would also prevent unnecessarily high

activities to be administered, which would minimise late toxicity.

A number of dosimetry studies have demonstrated that patient response is determined by absorbed dose rather than by administered activities. With recent improvements in availability of dosimetry software and advances in Monte-Carlo based dosimetry, there is now the prospect of accurate patient-specific treatment planning. Pre-therapy planning would indicate on a patient-by-patient basis when a therapeutic ratio would not be sufficient to justify treatment.

International bodies are now producing guidelines on advanced dosimetry based on best practice MIRDPamphlet No. 16: Techniques for Quantitative Radiopharmaceutical Biodistribution Data Acquisition and Analysis for Use in Human Radiation Dose Estimates <http://interactive.snm.org/docs/MIRD16.pdf>.

EANM Dosimetry Committee guidance document: Good practice of clinical dosimetry reporting: www.eanm.org/publications/guidelines/EANM_guidance_document_good_dosimetry_reporting.pdf

Prospective data collection studies for all therapies are essential to determine the range of absorbed doses currently being delivered and to determine correlations between absorbed doses, response and toxicity.

Many therapies, particularly those involving radiolabelled somatostatin analogues or antibodies, are expensive. The range of current practice indicates that the most cost-effective protocols are not being followed. Few centres have substantial numbers of patients and very few undertake MRT in children and young people.

To improve efficiency and to encourage the properly planned development and utilisation of MRT in tumours, a limited number of fully-equipped and resourced centres of excellence with satellite centres should be promoted. Principal treatment centres should be identified for children and young people with protected suites and parent sleeping areas situated on paediatric oncology wards. Treatment of children and young people outside such recognised centres should not be undertaken.

The centres need to be overseen by a national multi-disciplinary body which would champion clinical service delivery, education and training, and research. This should include critical evaluation of clinical needs, patient groups and the development of protocols.



Interim for adoption from 01/10/13