1. **Introduction**

Intraoperative radiotherapy (IORT) typically involves the delivery of a single high dose of radiation as part of a surgical procedure [1]. This novel therapy has the potential to provide benefit for a number of treatment sites. Direct surgical visualisation of the tumour bed and mobilisation of organs at risk (OAR) can allow dose escalation or re-treatment where external beam radiotherapy (EBRT) isn’t possible, or as in the case of breast cancer, can be delivered instead of the boost dose or as an alternative to whole breast radiotherapy (WBRT) – a treatment which is most commonly associated with IORT in the UK.

Intra-operative devices fall into two main categories:

- Low energy kilovoltage units, such as INTRABEAM (Carl Zeiss Surgical) and Xoft Axxent (iCAD), consisting of compact mobile 50kV x-ray sources with shaped applicators to conform the patient tissue to the dose distribution (spherical, cylindrical etc.).
- Electron-only linear accelerators (linacs), such as Mobetron (IntraOp Medical), NOVAC and LIAC (Sordina), with a typical energies of 4-12MeV and a range of cylindrical applicators to direct the beam, and shields to reduce exit dose.

Experience of IORT has been gained for numerous indications, including colorectal, gynaecological and brain tumours. Despite this, in the UK, IORT has been predominantly associated with partial breast irradiation guided by two phase-III randomised trials: the TARGIT A study [2] and the ELIOT study [3]. The studies have not been without controversy, with TARGIT criticised in particular for a lack of long term follow-up. Moreover, this trial data is machine specific, indicating the need to clinically validate other commercially available devices against existing evidence. National registries of all treated patients may provide additional data. Further discussion of the clinical aspects of breast IORT can be found elsewhere [4].

The content of these guidelines is designed to provide guidance on medical physics service support for new and existing providers of IORT. Particular emphasis is given to partial breast irradiation with regard to staffing models, radiation protection and system dosimetry. Intraoperative Electron Radiotherapy (IOERT) is also currently being established in the UK and therefore some relevant guidance for this service is also included.
2. **Use of ionising radiation in healthcare**

By law, under the Ionising Radiation Medical Exposure Regulations 2000 / 2018 (IRMER), *Medical Physics Experts* (MPEs) must be closely involved in every therapeutic medical exposure. The MPE must be contracted full-time to the radiation employer and available at all times in radiotherapy practices [5]. Radiotherapy delivery must be prescribed and authorised by a designated and qualified *Practitioner*, usually an oncologist. Treatment delivery requires a minimum of two trained *Operators* to provide independent verification of treatment parameters. For EBRT this is traditionally undertaken by therapeutic radiographers with physics support available on site. Additionally, under the Ionising Radiation Regulations 1999 / 2017, hospitals must appoint a *Radiation Protection Adviser* (RPA) where ionising radiations are in use.

IORT systems represent a paradigm shift in treatment delivery, often taking radiotherapy units out of the radiotherapy department into a clinical environment where staff will have much less familiarity with the required safety precautions, and also potentially taking radiotherapy out of the major centres into smaller hospitals with no prior infrastructure for the highly specialist modality of radiotherapy treatment. Although beneficial for patients who could avoid lengthy commute times for daily fractionated therapy at specialist radiotherapy centres, the use of these devices requires caution and careful consideration to ensure that the appropriate legislation is adhered to and the required skill sets are available for service delivery.

3. **Staffing models**

There are four potential models for implementation of IORT:

1) **Large acute cancer centre** - Treatments are delivered on site at an existing large radiotherapy centre. This has the advantage of greater economies of scale in resources available to support the technique, expertise in radiation delivery and facilities for further treatment if necessary. Despite this, there may be more demand for theatre time and a heavy routine workload.

2) **Small but established radiotherapy centre** - a smaller centre may have more flexibility to accommodate this new technique, but may also have fewer staff and so commissioning time may be prolonged. Also, studies of cost equality by NICE for INTRABEAM supposed a centre delivering at least 100 treatments per year to a catchment area of in excess of 1 million [6], so it may be more economical to concentrate units in large and geographically diverse centres.

3) **Small district hospital supported by existing radiotherapy centre** - staff travelling from the radiotherapy centre to the district hospital increases resources expended, but allows greater access for the patients to their local hospital. The same considerations for throughput also apply however. An MPE must be closely involved. Emphasis should be given on radiation protection training for staff who may have no prior experience.

4) **Privately run service** (to a private or NHS hospital) – for example, a portable service has been offered to some private centres in the UK. This allows use by hospitals without having to invest in their own capital equipment, but there should be clearly documented cooperation between employers.
Whatever model is followed, a period of equipment commissioning and staff training must be worked into the timescale prior to clinical implementation. In addition, funding of new technology should include dedicated staff for commissioning and initial installation. Although in the long term the resources required may be the same as for conventional (EBRT) treatment [6], in the short term extra physics staff will be needed to establish the service. Recruitment and training of these staff should be factored into the implementation time. It is also suggested that radiographers are used to provide the routine service. If the service is at a remote site, then one registered clinical scientist and one radiographer should be present. If on the same site, then two radiographers may be used as the operators, as long as a registered clinical scientist is available on site if needed. In all situations, an MPE must be closely involved, which in practice this means they should be contactable during treatment, either on- or off-site.

The typical time frame for delivery of INTRABEAM radiotherapy is ~ 25 – 40 mins, however the multi-professional team needs to be available for longer than this, typically 2- 3 hours per patient. This advice also applies to implementation of IOERT, although note there must be a suitably shielded facility accessible for commissioning, maintenance and quality assurance (QA) schedules.

4. Radiation protection and theatre assessment

Mobile IORT accelerators can be manoeuvred into any suitably sized theatre and therefore it is essential to consider the appropriate additional radiation protection required and any changes to local practices to ensure the safe delivery of radiation. The RPA must be consulted to advise on radiation protection requirements, including the designation of controlled and supervised areas. The following guidance is based upon three main references [7-9].

Prospective dose surveys should be performed in every operating theatre to be used for IORT, although reference data for diagnostic kilovoltage units may be used to estimate shielding by common materials. Environmental surveys should be repeated at regular intervals to confirm the sufficiency of protection measures for clinical patients. It may be prudent to designate the whole theatre as a controlled area, including any side rooms if they are difficult to restrict access to separately. Regard should be given to the local practices of the working theatres, including access routes for movement of IORT equipment and storage. Theatres should also have appropriate space for the safe mobilisation and positioning of equipment including room to place the equipment when idle, as not to interfere with surgical procedures.

Doors should be clearly signed and where possible locked to prevent unauthorised access. Appropriate training should be conducted for local theatre staff and Local Rules must be available. During irradiation, all non-essential staff should leave, with just the two operators and an anaesthetist remaining to monitor the patient. Personal electronic monitors (EPDs) may be distributed to provide a live dose measurement during the procedure. For kV
treatments at a typical operator position of 2m from the source, dose rates of <5mSv per hour should be achievable. Shielding sheets placed on the patient surface over the treatment area will reduce external dose rates by 95–99% and may be useful to keep doses as low as reasonably practicable, although should be placed with care as not to deform the treatment site after positioning of any applicator. For 50kV units, mobile lead screens >0.3mm in thickness will usually reduce transmitted radiation to effectively zero, however, scattered dose around the screen can still give small measured dose rates. Lead aprons could also be used but are cumbersome to wear and do not provide whole-body protection. Either way, no permanent modification of the theatre should be necessary.

Positioning of any lead screen should be discussed with the anaesthetist to allow appropriate access to necessary medical equipment. Relocation of anaesthetic equipment may be amenable to improved radiation protection according to room layout. Following placement of appropriate shielding sheets and mobile screens instantaneous dose rate adjacent to the operators should be confirmed either via EPD or a survey meter to confirm the efficacy of the positioning of the control measures. Another possibility would be to use an operating theatre which is already used for radiation procedures such as fluoroscopy. Specific risk assessments are still required for IORT, but the shielding is likely to be sufficient. In this case, operators may stand outside the main room, and observe through a window.

Electron-only linacs are typically fitted with beam stoppers, so the main consideration is scatter and leakage. Scattered electrons have limited penetration into typical wall materials. Some example environmental dose data has been published, but it is recommended to perform a survey of dose rates with the specific unit and operating theatre(s) and then limit the workload to achieve acceptable exposure levels. Workload calculations should include warm-up and daily QA checks as well as the number of expected patient treatments. Dose surveys should be performed at all available energies as the maximum dose rate in laterally and vertically adjacent rooms can occur at different energies and consideration should be given to the expected treatment sites in determining maximum permissible work load – N.B. instantaneous dose rates are likely to exceed 7.5µSv/hr in adjacent areas – it may be desirable to customise the unit to a reduced dose rate and increase beam stopper thickness. Detailed investigations for each unit suggest that typical workloads of a few patients per week can be safely accommodated in buildings of standard construction or that mobile shielding panels can be used instead of permanent shielding. Neutron exposure levels were found to be very low, even for energies above 10MeV. At minimum, safety devices such as warning signs, physical barriers or door interlocks are required.

Where a mobile electron linac is used in a standard operating theatre, it is likely that the unit will need to be relocated back to a shielded facility such as a traditional linac bunker for commissioning data collection and for planned maintenance and QA. It is important to consider the route (including weight capacity of lifts) between the theatre and the radiotherapy department (or other suitable shielded facility).
5. **Commissioning, dosimetry & QA**

Commonly kV IORT systems arrive pre-calibrated or potentially calibrated on-site by the manufacturer. Typically manufacturer specific hardware is available to conduct dosimetric commissioning but despite this, independent verification of dosimetry of radiotherapy systems is recognised best practice in the UK following a number of incidents where systematic errors caused by human error in dosimetry were exposed. It is recommended that, especially with new technologies such as this, there is an agreed programme of technical commissioning including independent measurement equipment, to ensure consistent, accurate and safe treatment. A recognised time allowance must be allowed for appropriate commissioning tests to be undertaken prior to commencement of any service. If theatre time is limited, commissioning and annual checks are better performed elsewhere in a shielded environment where available, e.g. a linear accelerator bunker.

Commissioning may be performed with a variety of independent equipment including traceable parallel plate secondary standard chamber, radiochromic film, thermoluminescence dosimetry and appropriate phantom material which must be compatible for the energy and modality. It is noted that reference dosimetry of kV IORT systems may deviate from the published IPEM codes of practice. Independent verification is not straightforward and subject to a number of uncertainties relating to positional accuracy of the detector and high dose gradients. An accuracy of 5-10% in absolute dosimetry may be acceptable. Empirical validation of the physical dose through clinical trials is required to validate the safety of such systems. External independent dose audit is strongly recommended, preferably by a department with experience in IORT. A recognised scheme of external audit for radiotherapy equipment exists and is overseen by IPEM.

Electron IORT systems need to be commissioned following a similar process to electrons on a conventional linac [9]. A modified scanning water tank may be required for data collection and particular attention should be paid to the position of the clinical axis when commissioning bevelled angled applicators.

Particular issues to note include:

- Systems may be provided with manufacturer dosimetry data, which must be independently verified.
- External audit is strongly recommended when commissioning a new unit, as with other radiotherapy modalities.
- The rapid fall-off of dose with depth results in the dominant uncertainties relating to positional accuracy of the detector (and require dosimeters with high spatial resolution). An accuracy of 5-10% in absolute dosimetry may be acceptable.
- Solid phantom materials must be water-equivalent at the appropriate energy ranges, which may not always be true for kilovoltage energies.
- Prescription to a point at depth in tissue (e.g. 6Gy at 1cm) is preferable to a point at the surface of spherical applicators, to minimise variation between units and allow more accurate verification by measurement [7].
• High dose rate electron beams lead to non-standard behaviour of dosimeters, such as recombination rate of ion chambers.
• Mobile electron accelerators do not evidence the same level of stability and a standard linac and QC tolerances need to be set accordingly.

In-vivo dosimetry is possible with various options for IORT including TLDs, radiochromic film, MOSFETs and optically stimulated luminescence detectors (OSLDs). These measurements may be helpful in monitoring skin dose or dose to any critical nearby structures.

References