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Implementation of High Dose Rate Brachytherapy in Limited Resource Settings

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IMPLEMENTATION OF
HIGH DOSE RATE BRACHYTHERAPY
IN LIMITED RESOURCE SETTINGS

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IMPLEMENTATION OF HIGH DOSE RATE BRACHYTHERAPY IN LIMITED RESOURCE SETTINGS

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FOREWORD

Cancer is a leading cause of death globally. The World Health Organization reports that 7.6 million people died of cancer in 2012 and mortality continues to increase. It is estimated that it will reach 11.4 million deaths annually by 2025 if action is not taken. More than 70% of all cancer related deaths occur in low and middle income countries (LMICs), where resources for prevention, diagnosis and treatment are limited or non-existent. In high income countries, approximately 50% of new cases of cancer require radiotherapy at least once. Because of the specific types of cancer, the advanced nature of the cases at diagnosis and a lack of resources, the proportion of new cases that require radiotherapy is likely to be much higher in LMICs.

There has recently been increased demand from Member States for the IAEA to provide assistance, including the provision of radiation sources and equipment for establishing radiotherapy programmes for the treatment of cancer. Increased demand from LMICs for high dose rate (HDR) brachytherapy equipment has resulted from the discontinuation of the limited production of low dose rate equipment. In addition, some types of cancer (typically affecting the cervix, oesophagus and nasopharynx) which are suitable for treatment with brachytherapy are more frequent in LMICs. In this context, HDR brachytherapy may be the only practical solution to treat numerous patients successfully.

Brachytherapy using remote afterloading of a single HDR source was developed in the 1970s. After its introduction in clinics, the system spread rapidly among developed countries and has become a highly desirable modality in cancer treatment. The technique has also gained popularity in LMICs.

The HDR radioactive sources are produced with high specific activity. This results in an HDR to the tumour and shorter treatment times. The high specific activity simultaneously results in a smaller source (a so called microsource, approximately 1 mm in diameter), which can be easily inserted into tissue through a thin delivery tube, known as interstitial treatment, or into body cavities, known as intracavitary or endoluminal treatment.

Another advantage of HDR brachytherapy is the ability to change dwell times (i.e. the time a source remains in one position) of the stepping source, which allows dose distributions that closely match the target volume.

This publication is intended as a guide to help radiation oncologists, medical physicists and hospital administrators planning to introduce HDR remote afterloading systems. The publication supplements the IAEA publication Setting Up a Radiotherapy Programme: Clinical, Medical Physics, Radiation Protection and Safety Aspects, and will facilitate the implementation of this new brachytherapy technology, especially in LMICs. The operation and use of the system is beyond the scope of this publication.

The IAEA officers responsible for this publication were E. Rosenblatt and E. Fidarova of the Division of Human Health.

CONTENTS

1. INTRODUCTION

1.1. BACKGROUND

Brachytherapy (BT) is the administration of radiation therapy by placing radioactive sources adjacent to, or into, tumours or body cavities. Readers should refer to the IAEA publication Setting Up a Radiotherapy Programme: Clinical, Medical Physics, Radiation Protection and Safety Aspects for general guidelines on high dose rate (HDR) BT facilities [1].

With BT, a high radiation dose can be delivered locally to the tumour, with rapid dose fall-off in the surrounding normal tissue. In the past, BT was mostly performed with radium or radon sources. Currently, the use of artificially produced radionuclides is rapidly increasing, such as ^{198}Au, ^{60}Co, ^{137}Cs, ^{125}I, ^{192}Ir, ^{103}Pd and ^{103}Ru.

A relatively new technological approach is electronic BT, in which the radiation source is not an encapsulated radioactive isotope (radioisotope BT) but a miniature electronic X ray source that produces low energy radiation at an HDR.

Based on the implant loading technique, BT can be performed as:

— Manual loading;
— Manual afterloading;
— Remote controlled afterloading.

Based on the location of the implant, BT can be:

— Superficial (sources placed in contact with the skin or a skin tumour);
— Intracavitary (sources placed into natural body cavities, e.g. the uterine cavity);
— Interstitial (sources placed into tissues or tumours, e.g. the prostate).

Based on how the radioactive sources are removed, BT implants can be:

— Temporary (sources are inserted and later removed);
— Permanent (sources are inserted and left in place for the remainder of their active life).

According to the dose rate of the sources used, BT can be:

— Low dose rate (LDR);
— Medium dose rate (MDR);

— High dose rate (HDR);
— Pulsed dose rate (PDR).

The dose rate is defined in International Commission on Radiation Units and Measurements (ICRU) Report 38 [2]. An HDR means more than 12 Gy/h, although the usual dose rate delivered in practice is approximately 100–300 Gy/h.

1.2. OBJECTIVE AND SCOPE

The focus of this publication is the practical implementation of HDR BT for the management of tumours in different localizations. Guidance provided here, describing good practices, represents expert opinion but does not constitute recommendations made on the basis of a consensus of Member States.

1.3. DEVELOPMENTS IN BRACHYTHERAPY TECHNOLOGY

BT came into use soon after the discovery of radium by Marie Curie in 1898. S.W. Goldberg and Efim Semenovich London used it to treat facial basal cell carcinomas with surface applicators in 1903, and interstitial afterloading techniques were developed in the same year. Before the 1950s, radioactive material was generally inserted directly into the tumour ('hot loading'). Although BT was effective, it suffered from the major disadvantage of exposing the medical caregivers to radiation. This disadvantage and the advent of high voltage teletherapy for deep seated tumours led to a decline in the use of BT in the 1950s.

'Manual afterloading' was introduced to reduce the radiation exposure hazard by first inserting hollow needles or tubes with dummy catheters into the tumour and then loading the radioactive material through the tubes, thus increasing the accuracy and reducing the radiation exposure to caregivers.

Sievert first proposed the concept of 'remote controlled afterloading' in 1937 [3]. In this technique, hollow tubes are inserted into or close to the tumour and are connected to the radioactive material, which is housed in a shielded container. By remote control, the radiation source is driven through the transfer cables into the tumour, thus eliminating radiation exposure to personnel. Other systems include:

— A system using the concept of remote controlled BT [4];
— An oscillating source system [5];
— A system using ^{60}Co sources [6];
— An afterloading system with ^{60}Co [7];

— A remote afterloader using a single ^{192}Ir source that was mainly used for intracranial implants [8].

Although the earlier HDR machines had a limited number of channels (1–3), current models offer up to 40 channels to allow the treatment of larger tumour volumes at one time. Another development was the introduction of stepping source radiation in some systems to allow the optimization of treatment plans by varying the dwell times [9]. Currently, more than 1000 HDR units exist worldwide, including almost 400 in low and middle income countries [10].

2. HIGH DOSE RATE BRACHYTHERAPY COMPONENTS

2.1. TREATMENT UNIT

BT has been used as an integral part of cancer treatment for almost a century. It has been enhanced with the development of afterloading devices and new radioisotopes, as described in Section 1. Currently, BT is characterized by technical innovations such as:

(a) Increasing the number of channels in remote afterloading units;
(b) Developing radioactive microsources;
(c) Developing new algorithms for computerized treatment planning and dosimetry;
(d) Improving imaging methods and introducing sectional imaging.

These advances have shifted BT procedures to outpatient management and have increased the number of BT procedures that can be performed in a single day. An adequately shielded room and a remote afterloading device to avoid directly exposing the operators are essential components of an HDR facility.

A remote afterloading system consists of a pneumatically or motor driven source transporting system that automatically transfers a radioactive source between a shielded safe and each treatment applicator [11]. These systems were first designed for use in gynaecological BT, but more recent models have also been designed to be used for other sites.

The HDR remote afterloading systems need to comply with international standards of safety and quality, such as those of the International Electrotechnical Commission or the International Organization for Standardization ISO 9000 [12, 13].

Commercially available HDR afterloading units consist of the following components:

— HDR radioactive source;
— Afterloader device (treatment unit);
— Control console;
— Applicators and X ray catheters;
— Treatment planning system (TPS).

2.2. HIGH DOSE RATE RADIOACTIVE SOURCE

A radioisotope with high specific activity is required to simultaneously achieve the HDR and small source size required for intracavitary and interstitial BT. Iridium-192 is widely used for HDR BT because it has high specific activity (330 MBq/mm), relatively low gamma energy (average 0.375 MeV) and a relatively short half-life (73.8 d).

Currently, most HDR remote afterloaders use a single ^{192}Ir source with an activity of approximately 370 GBq. The active length of the source is approximately 3.5 mm, and the active diameter is 0.5 mm. The encapsulated source is approximately 5 mm long (some sources may be up to 10 mm long) and less than 1.5 mm in diameter; these dimensions vary with different commercial models. The source is welded to the end of a drive cable (see Fig. 1), transferred to programmed locations in the applicators (dwell positions) and held in place for the programmed duration (dwell times) using a motor driven system.
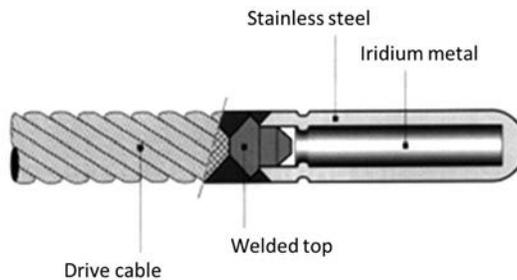
FIG. 1. Iridium-192 source for HDR BT (courtesy of Nucletron, Netherlands).

2.3. AFTERLOADER DEVICE

An afterloader device is a mobile machine that requires little floor space. The essential requirements for its design are:

(a) A shielded safe (main source container) to hold the source when not in use;
(b) A stepping motor;
(c) A source transferral and positioning feedback system;
(d) Several channels for source transport;
(e) An indexer to allow automatic transfer of the source cable between the different transfer tubes;
(f) Transfer tubes to connect the device to the applicators.

The safety system, which ensures safe operation of the device, includes:

(a) An automatic path check of the applicator and the transfer tube with a check cable;
(b) A means of sensing the source position and timing of its motion;
(c) A built-in radiation detector (e.g. a Geiger–Müller counter) to ensure that the source has returned to the safe;
(d) Backup batteries to remove the source in the event of power failure and for saving treatment data;
(e) Emergency systems to return the source to the safe.

A detailed description and specifications for HDR afterloading devices are available in appendix XI of Ref. [1].

2.4. CONTROL CONSOLE

The control console, located outside the treatment room, operates the afterloader, shows the source position on the display as the treatment progresses and prints out a treatment report. The treatment plan can be transferred to the control console through a direct link with the treatment planning computer, using a floppy disk or done manually. The control console has a microprocessor to automatically correct the dwell times for decay and is simple to operate.

2.5. APPLICATORS

Almost all applicators designed for LDR manual afterloading have been redesigned for HDR use, with a mechanism to connect them through the transfer tubes to the afterloader device. The connection has mechanical interlocks to ensure that the applicator is correctly positioned and connected to the transfer tubes. The interlocks prevent incorrect connections. Typically, the applicators for HDR have thinner tubes. When connected, the applicator, transfer tubes and afterloader device become a closed system, which prevents dislodging of the source within the patient's body or exiting into the air before reaching the target region.

There are three categories of applicators: intracavitary, intraluminal and interstitial (see Table 1). Each category has a specific connector or transfer tube to connect it to the treatment unit.

Specific transfer tubes for intracavitary applicators are designed to have the same overall length but different interlocks for each treatment channel to avoid connection errors. There is a variety of intracavitary applicators for HDR treatment. Some applicators are made of stainless steel for durability, and are suitable for X ray simulation. Others are made of materials (e.g. carbon fibre) that do not produce artefacts on computed tomography (CT) or magnetic resonance imaging (MRI). Some intracavitary applicators (e.g. Fletcher type) are rigid without a fixed geometry and, therefore, require individualized treatment planning for a patient. A fixed geometry applicator (e.g. a ring applicator) allows standard dose distribution planning prior to insertion, but dwell time optimization can be used to adapt to 3-D image guided individual dosimetry.

Intraluminal applicators are usually connected directly to the treatment unit using a specific adapter. These applicators can be blind ended, disposable, flexible tubes with a diameter of 5 or 6 French[1], or they can have a specific design (e.g. an oesophageal applicator). If a single catheter technique is used, then the treatment planning is simple and can be performed in advance. With multiple catheters (e.g. catheters placed at a bronchial bifurcation), individual planning should be performed.

Interstitial applicators can be rigid or flexible. The rigid stainless steel needles have different lengths and require specific transfer tubes. The needles can be reused after sterilization. Using a template for implantation with a fixed predetermined geometry allows the use of standard dose distributions. The thin, flexible, disposable plastic tubes require different transfer tubes.

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[1] One French is equal to ⅓ mm.

TABLE 1. CHARACTERISTICS OF THE MOST COMMONLY USED APPLICATORS

Category	Type	Preplan	Reusable	Clinical sites
Intracavitary	Ring applicator	Yes	Yes	Gynaecology
	Fletcher	No	Yes	Gynaecology
Intraluminal	Lumen catheter	Yes	No	Lung, oesophagus, bile duct
	Oesophageal applicator	Yes	Yes	Oesophagus
Interstitial	Rigid templates	Yes	Yes	Pelvis, breast
	Needles alone	No	Yes	Head and neck, breast
	Plastic tubes	No	No	Head and neck, soft tissue, breast

A more recent development is the redesign of the intracavitary applicators (ring and ovoid types) to allow combined insertions with interstitial needles to adapt the dose distribution to possible parametrial extensions of the tumour.

2.6. TREATMENT PLANNING SYSTEM

A TPS is typically supplied as part of an afterloading treatment unit. Following data input, it completes the dose calculation in a few minutes and transfers the programme to the treatment unit. The general requirements for a TPS are presented in Ref. [1].

A TPS basically consists of:

(a) An input device for simulation images (e.g. digitizer) or CT/MRI;
(b) A password controlled source strength input;
(c) A 3-D reconstruction of source channel geometry;
(d) An algorithm for source dwell position placement within each channel;
(e) Graphic implant visualization in 2-D (axial, sagittal and coronal) and optional 3-D;
(f) Dwell time calculations;
(g) A dose distribution algorithm;
(h) Potential for optimization;

(i)   Calculation of dose volume histograms (optional 3-D) and a plan for evaluation parameters;

(j)   A documentation and display method (e.g. printer);

(k)   A method to transfer the plan to the treatment unit.

The initial purchase contract is to include update support for hardware and software.

3. INFRASTRUCTURE

This section focuses on the operational and clinical aspects of the infrastructure. Setting up an HDR unit requires an investment of capital and human resources. A new HDR BT programme should consider the current and future projected patient volume, case mix, existing infrastructure, radiation safety and available human resources. Staff members should be trained in technical and radiobiological aspects and be supported by an experienced radiation oncologist and medical physicist during the initial procedures.

Before installing a BT unit, four steps of the treatment sequence need to be considered:

(1)   Applicator/catheter placement;

(2)   Imaging (simulation and localization);

(3)   Treatment planning;

(4)   Treatment delivery.

Ideally, the applicator insertion, radiograph generation and HDR treatment should be performed in a dedicated BT suite so that the patient does not need to be moved. If such a facility does not exist, each step can be performed in a different room. Options include transferring patients either from the operating room or a procedure room in the department to the simulator for radiograph generation or a CT (or MRI) scanner for 3-D imaging. However, it is preferable to minimize patient movement by performing the individual procedures within a short distance of the HDR unit treatment room. It is especially important that movement of the patient is kept to a minimum after the localization radiographs have been obtained.

3.1. BUILDING

3.1.1. Infrastructure required for applicator/catheter placement

This room functions similarly to an outpatient surgery room and is suitable for various interventions, such as endoscopy, percutaneous insertion of catheters or gynaecological applicator placement. Factors to be considered include the availability of:

(a) Sufficient space for both the BT team and any other medical or surgical teams that will be involved in the procedure;
(b) An adjustable and mobile table with stirrups that is ideally X ray compatible;
(c) Instruments for minor surgery;
(d) A cart with disposable supplies;
(e) A storage cabinet for HDR applicators and other accessories;
(f) Surgical lights, anaesthesia equipment and patient telemetry (desirable);
(g) A clean water supply and sink;
(h) Sterilization equipment;
(i) Endoscopic equipment, when needed.

3.1.2. Infrastructure required for localization radiographs

If the treatment room is separate from the applicator placement room, the size of the shielded treatment room needs to be adequate to allow localization radiographs to be obtained on the treatment table to minimize patient movement. Portable X ray equipment can be used, or preferably, dedicated X ray equipment (e.g. C-arm) should be installed. If X ray equipment is not available in the treatment room, there should be sufficient space to allow the patient to be transported on a stretcher to the simulator. In addition to the X ray equipment, there should be a device (e.g. a simulation box) available if semi-orthogonal films are used for dosimetry. The X ray equipment is to comply with the size (dimensions) of the simulation box. The voltage settings should be sufficient to image overweight patients adequately.

3.1.3. Infrastructure required for the treatment planning room

The hardware for treatment planning could be remote or adjacent to the control console. The only requirements are space and the power supply. A device for an uninterruptable power supply with a voltage regulator should be considered as part of the hardware.

It is desirable to have the TPS near the treatment room because it tends to improve efficiency and communication for on-line procedures.

3.1.4. Infrastructure required for the treatment room

An appropriately shielded room needs to be used for the HDR unit. Generally, when using an ^{192}Ir source, a concrete wall equivalent to 4 cm of lead (i.e. 35 cm thick) is required. However, the precise thickness depends on the room design, the workload and the local regulations. There should be a direct vision or closed circuit observation system. The control console should be just outside the treatment room. The requirement for the treatment room is described Refs [14–16]. A typical simple plan for an HDR BT room is shown in Fig. 2.

There are three major options for HDR treatment unit arrangements:

(a) Treatment room for the HDR unit and shared use of existing operating or procedure rooms and imaging systems, such as a simulator: Patient transport (between the operating room, imaging room and treatment room) reduces efficiency and compromises immobilization of the applicator system.

(b) Treatment room for both applicator insertion and treatment, with the imaging being performed elsewhere: Conditions for anaesthesia and sterility might require a significant investment. In addition, other medical staff (e.g. gynaecologic oncologists and anaesthesiologists) should provide medical services outside their usual venue. As above, patient transport (between the operating room, imaging room and treatment room) reduces efficiency and hinders immobilization of the applicator system.

(c) Integrated BT suite: This option integrates a dedicated imaging system in the treatment room to option (b). This option is the most efficient, requiring no transport of the patient between steps.

Procedures and required patient transportation according to the arrangement of the HDR BT unit are described in Table 2.
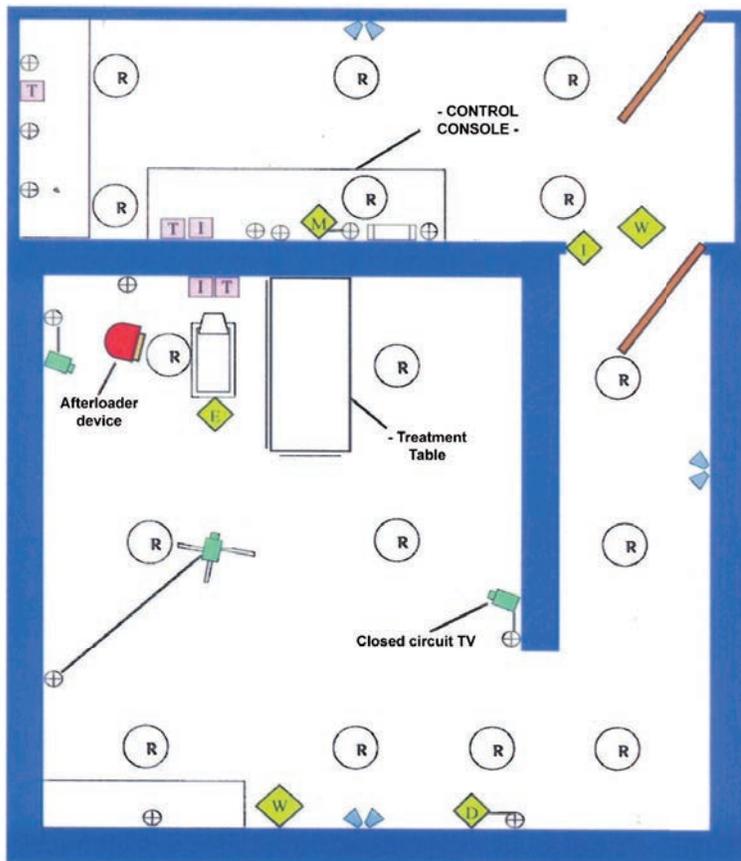
R	62.580 Main Room Lighting	W	63.561 Warning Light
◁▷	62.037 Emergency Lighting	F	63.637 Emergency Off Switch
T	67.113 Telephone	I	63.562 Safety Door Interlock Switch
I	67.069 Intercom	D	63.297 Radiation Detector
⊕	69.462 Electrical Power Receptacle	M	63.297 Radiation Monitor

FIG. 2. Typical floor plan of treatment and control room.

TABLE 2. ROOM ARRANGEMENT AND PROCEDURES

Procedure	Option (a)	Option (b)	Option (c)
Anaesthesia	Procedure room	Treatment room	Integrated suite
Applicator insertion	Procedure room	Treatment room	Integrated suite
Imaging	Imaging room	Imaging room	Integrated suite
Treatment	Treatment room	Treatment room	Integrated suite
Applicator removal	Treatment room or procedure room	Treatment room	Integrated suite
Patient recovery	Recovery room	Recovery room	Recovery room

Note: Option (a) — shared procedure room; shared imaging room; and treatment room. Option (b) — treatment room; and shared imaging room. Option (c) — integrated suite.

3.2. EQUIPMENT FOR RADIATION SAFETY AND SOURCE HANDLING

Every BT facility should have the following equipment:

(a) A storage container in the treatment room to serve as an emergency source container in case of failure of the afterloader in retracting the source;
(b) Long handled forceps;
(c) An easily accessible portable radiation survey meter and an area radiation monitor;
(d) Emergency instructions.

3.3. IMAGING

Reconstruction and dosimetry of treatment depend on the system used for obtaining images. Three methods can be defined, although the most simple (level 1) is appropriate in most clinical situations.

3.3.1. Level 1: Conventional radiographs

X ray films can be obtained using mobile equipment inside the shielded room (e.g. C-arm fluoroscopy unit) or equipment fixed to the ceiling or walls. This method produces semi-orthogonal films, as used in LDR BT. This reconstruction method with non-isocentric equipment requires a methodology (e.g. a simulation box) that permits a semi-orthogonal reconstruction by taking nearly orthogonal films (not necessarily 90° positions). If this technique is used, high voltage equipment, which allows lateral exposure of the pelvis for gynaecological treatments, is necessary.

3.3.2. Level 2: Simulator

Having a simulator for external radiotherapy not only allows conventional radiographs to be taken but also trustworthy orthogonal films. In addition, other easier reconstruction techniques, such as isocentric or variable angles, which may be required under special circumstances, can be used.

3.3.3. Level 3: Computed tomography and magnetic resonance imaging

Axial slices from a CT scan or MRI permit not only the reconstruction of the applicator but also the 3-D target and the organ at risk volumes. A 3-D approach requires the use of CT and/or MRI compatible applicators.

3.4. TREATMENT PLANNING PROCEDURE

The TPS needs to be fast and versatile to control the remote afterloader. In low and middle income countries, both level 1 and level 2 imaging devices (e.g. simulation with conventional or CT simulators) can be used for 90% of cases requiring BT. If good quality assurance is in place, these procedures can be performed with confidence without CT or MRI simulation, 3-D reconstruction or sophisticated planning systems.

The hardware and software needed to cope with the different degrees of dosimetric complexity are directly related to such complexity. Peripheral devices for printing (e.g. plotters or printers) and inputting images are needed. The latter can be achieved by means of digitizers or scanners. Ideally, the images can be uploaded from the diagnostic machine, either through a direct internet connection or through some magnetic or optical device that can store information. Once the images are on the worktable, the radiation oncologist

should indicate to the physicist the volumes to be treated, the doses to be applied and the surrounding organs at risk.

The simplest treatment plan uses a single catheter with the dose prescribed at a specified radius. Standard treatment plans for intracavitary treatment with fixed geometry applicators are more complex, followed by intracavitary treatment with non-fixed geometry applicators and optimized treatment plans. Multiplanar, rigid, interstitial applications with optimized treatment planning are used for breast or prostate cancer. Treatment planning involving optimization for multiplanar, flexible, interstitial or combined intracavitary interstitial applications is the most challenging. Optimally, data from the clinical examination, supplemented by one or several imaging modalities (e.g. CT, MRI or ultrasound imaging) are used to define the target volume and optimize the treatment plan to deliver a high dose to the tumour while minimizing the dose to normal tissue [17, 18].

3.5. SPARE PARTS

All commonly used spare parts should be stored in the department if they are not immediately available from a service centre.

3.6. OTHER REQUIREMENTS

The BT facility also needs hospital support, such as a clinical laboratory, sterilization facilities, examination rooms, recovery/monitoring rooms, anaesthesiologist services and air-conditioning.

4. PERSONNEL REQUIREMENTS AND TRAINING

The primary prerequisite for the development of an HDR BT facility is an adequate number of staff. A multidisciplinary team needs to be organized. A radiation oncologist, a medical physicist, a radiation therapist (radiation therapy technologist, RTT) and nursing staff are the minimum personnel required.

Depending on the workload, more nurses, radiation oncologists and RTTs may be added. Introduction of an HDR afterloader might increase the workload of a department considerably owing to a wider disease spectrum to treat. Thus, an increase of personnel in proportion to the workload should be a critical consideration.

4.1. PERSONNEL

4.1.1. Radiation oncologist

The radiation oncologist is responsible for the overall procedure because BT is a medical treatment. They need to be properly accredited according to the States' regulations.

Specific radiation oncologist responsibilities in the treatment planning process are [1]:

(a) Patient evaluation;
(b) Protocol selection and treatment prescription;
(c) Applicator insertion;
(d) Review of imaging;
(e) Defining target volumes and organs at risk;
(f) Treatment plan evaluation and approval;
(g) Applicator removal;
(h) Evaluation of tumour response and side effects;
(i) Patient follow-up.

4.1.2. Medical physicist

The medical physicist needs to be accredited in dosimetry according to the State's regulations.

Specific medical physicist responsibilities are [1, 19]:

(a) Specification of therapy equipment, assuring its radiation safety;
(b) Acceptance testing, commissioning and quality assurance of therapy equipment;
(c) Establishment of dose calculation procedures;
(d) Establishment of technical aspects of treatment planning and treatment procedures;
(e) Verification of source positioning;
(f) Checking of patient set-up, including applicator positioning;
(g) Provision of supervision, evaluation and optimization of treatment planning;
(h) Establishment and supervision of quality assurance procedures in BT regarding delivery of the treatment, radiation safety, quality control and regulatory compliance;
(i) Supervision of maintenance of therapy equipment.

The physicist should participate in the preparation of the patient after the applicator has been inserted and prior to obtaining the aforementioned images because the dummies (i.e. X ray marker wires) should be positioned in the applicators as specified by the technique used during this preparation. If catheters are used, they should be measured and identified. It is also necessary either to select the angles of the radiographic images or to select planes in the event of CT or MRI.

4.1.3. Radiation therapist

Responsibilities and team roles of a radiation therapist (or RTT) are described in Refs [1, 19]. RTTs should have credentials according to local regulations.
RTTs are involved in or are responsible for:

(a) Patient data acquisition;
(b) Patient positioning and immobilization;
(c) Simulation and/or localization and plan verification;
(d) Checking applicators and specific accessories;
(e) Connecting applicators to the afterloader with the help of transfer tubes;
(f) Delivering the treatment;
(g) Monitoring each treatment from the console;
(h) Recording the treatment;
(i) Assisting the medical physicist with various aspects of the quality assurance programme and radiation safety.

4.1.4. Radiation oncology nurse

The radiation oncology nurse in the BT unit is in charge of:

(a) Assisting the radiation oncologist during applicator insertion and removal;
(b) Monitoring patients during and after procedures;
(c) Assisting the radiation oncologist in counselling patients and families regarding BT procedures;
(d) Assisting the radiation oncologist in counselling patients and families regarding BT side effects and their management;
(e) Cleaning, sterilizing and storing BT applicators and specific accessories.

4.2. TRAINING

There are two main areas in which adequate training of staff is required:

(a) Principles and practice of BT in general and of HDR BT in particular;
(b) Operation of the particular model of the HDR remote afterloading system being used to prevent possible errors and promptly to identify and correct any errors that may occur.

4.2.1. Radiation oncologist

If the radiation oncologist has experience in LDR BT, additional training is required in HDR specific features, such as dose prescription, HDR radiobiology, insertion techniques and emergency procedures. HDR intracavitary, intraluminal or interstitial applicators are quite similar to those used in LDR, so the radiation oncologist only needs to become familiar with them. The radiation oncologist should be trained to place the applicators quickly and precisely. Updated radiobiology knowledge is required to select the treatment protocols and fractionation. The linear quadratic model could be used to develop HDR protocols in conjunction with published experiences on outcomes and morbidity. The radiation oncologist should be trained in all emergency procedures.

A radiation oncologist without experience in LDR BT requires training in general BT principles. Subsequently, the radiation oncologist needs to be trained in each site specific HDR BT technique. It is not necessary to have previous LDR BT experience to be trained in HDR BT.

4.2.2. Medical physicist

The physicist needs to be trained in the use of the HDR planning system (a necessary tool in the use of HDR equipment) and should become thoroughly familiar with applicator image reconstruction and the optimization tools used in the treatment planning system. Training in equipment use, security systems and emergency procedures is mandatory. Physicists also need to be trained in the basic principles and procedures of radiation protection.

Preferably, the radiation oncologist and the physicist should be trained at a BT centre that treats similar types of cancer. Hands-on training is desirable. During the initial phase of working with HDR BT, the support of an experienced physician and physicist is very useful for achieving the objectives with confidence and for good quality assurance.

4.2.3. Radiation therapists and nurses

The RTTs and nurses can be trained for HDR BT procedures by the radiation oncologist and the medical physicist. Radiation safety instruction and emergency procedures are essential elements to be covered.

4.3. EMERGENCY PROCEDURES

Concise and easily understandable emergency plans needs to be in place before starting an HDR BT programme. The main potential contingencies to take into consideration are:

— Dislodged sources;
— Stuck sources;
— Contamination;
— Accidental exposures.

Readers are referred to IAEA publications in which emergency procedures are described [1, 20].

5. QUALITY ASSURANCE

Quality assurance is essential for obtaining the best achievable tumour control, avoiding unnecessary side effects, and accurately and safely performing HDR BT. Quality assurance is extremely important because HDR BT procedures are performed quickly, with high doses given in a short time period, with little opportunity for correction.

The quality assurance programme should include clinical aspects of HDR BT:

— Patient selection criteria;
— Dose determination and specification;
— Fractionation;
— Quality of insertion;
— Definition of tumour/target volumes;
— Organs at risk.

The programme should also include physical aspects of dosimetry: checks of the computer information input, source strength and doses at different distances. The imaging protocols should be checked for appropriateness, quality and acquisition parameters (e.g. orthogonal or oblique acquisition angles).

The quality assurance for HDR BT can be divided into the following categories:

(a) Treatment unit;
(b) Planning system;
(c) Imaging;
(d) Patient treatment procedure.

Developing a quality assurance programme is beyond the scope of this publication. For a detailed description, please refer to Refs [1, 21, 22].

5.1. QUALITY ASSURANCE OF THE TREATMENT UNIT

This programme consists of a set of tests to be performed periodically to verify the proper function of the treatment unit.

5.1.1. Daily tests

These tests take approximately ten minutes and can be performed by an RTT. The following components need to be checked daily before starting the treatment of the first patient of the day:

— Emergency systems to withdraw the source into the safe;
— Door interlocks on the treatment room;
— Interrupt button on the control console;
— Emergency stop button;
— Interrupting the power supply;
— Source positioning;
— Room radiation monitors;
— Indicator lights;
— Source activity.

5.1.2. Monthly tests

Applicators should be checked with regard to their integrity, internal shields, welds and joints. Movement of the source to the desired location in the applicator should be confirmed.

5.1.3. Quarterly tests (with each ^{192}Ir source change)

With the use of ^{192}Ir sources, the source is customarily changed every three to four months to account for its radioactive decay. A quality assurance programme should then be designed in which check-ups relating to the exchange procedure are performed. For sources with a different half-life and, thus, a different interval of exchange, an extensive quality assurance test frequency of at least three times annually should be performed. A service level agreement with the vendor needs to specify the frequency of support by an experienced service engineer.

During the quarterly tests, the source strength needs to be calibrated using well type chambers that are specifically designed for this purpose or with Farmer style ion chambers. Using the latter, an interpolated technique for deriving a calibration factor for ^{192}Ir should be used. The well type chamber should be calibrated at a standard laboratory every second year. During this two year interval, the stability of the well type chamber can be verified using a long lived radioactive source, such as a ^{137}Cs source [23].

The positional accuracy of a new source should be tested, possibly by testing the ability of the unit to drive the source to a desired position in the applicator within ±1 mm precision. This precision can be tested using autoradiography with external markers or a 'check ruler' device [21, 22].

Procedures for quality control steps, frequencies, tolerances and procedures are described in Refs [21, 22].

5.2. QUALITY ASSURANCE OF THE BRACHYTHERAPY PLANNING SYSTEM

Quality assurance of the planning system basically consists of verifying the reconstruction quality and the accuracy of the dose calculation. The quality of the dosimetry is closely linked to the reconstruction technique used and to the image acquisition system of the planning software.

The quality of the reconstruction can be tested by performing the reconstruction of fixed geometry applicators or using a phantom to determine the accuracy of the X ray marker coordinates. This test should be performed for each reconstruction method in clinical use in the software (e.g. orthogonal, isocentric or CT).

The accuracy of dose point calculations can be tested by matching them with manual calculations or independent computer calculations. A comparison of calculations with published values is mandatory. For TG-43 based algorithms, the American Association of Physicists in Medicine (AAPM) has prepared consensus dosimetry datasets for use in BT treatment planning systems (TPSs). These datasets are often incorporated into TPS software vendors as 'silver' machine data, analogous to external beam treatment planning, and are also used in practice for treatment planning for patients in clinical trials. Typically, there is more than one dosimetry publication on a given BT source model and different possible interpretations on how to clinically implement treatment planning dosimetry parameters. For guidance on choosing a dataset for clinical use, see the following data sources:

(a) AAPM recommended consensus data from the TG-43, TG-43 update and TG-43U1S1 reports and any subsequent publications on LDR and HDR sources [23–25];

(b) Data from the joint AAPM/Radiological Physics Center Source Registry and other sites and original publications should be used to check for agreement. Such services are available from the Carleton Laboratory for Radiotherapy Physics and from the European Society for Radiotherapy and Oncology.

A comparison with other users or user groups should be performed if the required data are not easily accessible to the user.

The accuracy of input and output devices, the transfer of the plan to the control console and the consistency of the printed output should also be tested. The quality assurance tests on the planning system should be repeated after any significant software change.

The medical physicist should document the source of the BT dosimetry parameter data and provide the rationale for why a given dataset and web site tabulation were chosen.

5.3. QUALITY ASSURANCE OF THE TREATMENT PROCEDURE

The objective is to verify each BT step during each patient treatment. This treatment has the following components:

(a) Consistency and accuracy of the prescription;
(b) Applicator placement or catheter implantation;
(c) Simulation and localization images;
(d) Treatment planning and calculations;
(e) Treatment delivery and verification;
(f) Documentation.

For complete dose specification and documentation of BT treatments, the following points are necessary according to ICRU Reports 38 [2] and 58 [26]:

— Description of volume;
— Description of method and technique;
— Specification of source strength;
— Description of source distribution and source pattern;
— Reference dose and dose distribution;
— Fractionation.

With the introduction of modern 3-D based imaging, planning and dosimetry procedures in BT, it is advised that the recently published recommendations on dose and volume specifications in this field are closely followed [27–30].

Establishing standardized protocols and policies for common treatments reduces the chances of mistakes. For this reason, centres should initially perform only simple procedures, using fixed geometry applicators and standard planning. For each treatment, the following items need to be checked:

— Source strength matches the strength used in the calculation and the one indicated at the treatment unit;
— Proper source localization is programmed;
— Programmed dwell times match the plan;
— Positions match the plan;
— Dose per fraction matches the prescription.

The quality control of the treatment itself consists of verifying the positioning of the applicator in the patient, the connection of connecting tubes between applicators and the treatment unit and the presence of staff controlling the treatment at the control console. For each treatment, the completion

of the quality control tests should be documented by signature, and the personnel responsible for performing them should be recorded.

6. RADIATION SAFETY

6.1. RELEVANT RADIATION SAFETY STANDARDS AND RELATED DOCUMENTS

Safety requirements on the use of radiation for BT are defined by States' regulations. International harmonization is provided by IAEA safety standards. This harmonization is recognized in the statutory IAEA functions to establish or adopt standards of safety for protection of health and to provide for the application of these standards (Article III, The Statute of the International Atomic Energy Agency).

For activities relating to this report, the relevant radiation safety requirements are contained in IAEA Safety Standards Series No. GSR Part 3, Radiation Protection and Safety of Radiation Sources: International Basic Safety Standards [20], published in 2014 and cosponsored by the European Commission, the Food and Agriculture Organization of the United Nations, the IAEA, the International Labour Organization, the OECD Nuclear Energy Agency, the Pan American Health Organization, the United Nations Environment Programme and the World Health Organization. GSR Part 3 contains principal requirements covering all practices, including uses of radiation in medicine, agriculture, industry, research and teaching, and intervention in the event of accidents or chronic exposure situations, such as from residues from past activities [20]. Detailed requirements are provided in GSR Part 3, with specific requirements for medical applications in section 3, on planned exposure situations [20].

Recommendations on how to comply with the requirements of GSR Part 3 are also given [20]. In GSR Part 3, the responsibility for patient safety is shared by the government, regulatory body, licensee or registrant and manufacturers [20]. However the primary responsibility for protection and safety for patients lies with the health care professional responsible for administration of the radiation dose (i.e. the radiological medical practitioner). The regulatory body needs to provide guidance on how certain regulatory requirements are to be fulfilled for various practices. It is not feasible to reproduce detailed safety requirements here. However, a few pertinent issues are highlighted.

6.1.1. Government responsibilities

Governments are responsible, either through their actions or through the actions of others as required by laws, for protecting the public and the environment. Having an active regulatory programme that performs all these activities (authorization, inspection and enforcement) is essential to ensure the safe and secure use of radiation in medicine. Government responsibilities are to establish and maintain the legal and regulatory framework, establish regulations and guides, and perform inspections and enforcement actions.

6.1.2. Regulatory body responsibilities

Within governments, regulatory bodies have two important objectives. The first objective is to protect public health and ensure safety by preventing unsafe practices and the use of unsafe equipment. The second objective is to promote safe and effective practices and equipment that will enhance public health and safety. These objectives are accomplished by establishing regulations, conducting inspections and applying enforcements accordingly. In general, the types of regulation that are of concern for HDR BT apply to authorization, justification, optimization and dose constraints.

6.1.2.1. Authorization

Regulatory bodies are responsible for authorizing the use of radioactive materials. This authorization is given after the regulatory body has reviewed the necessary information to support the activity and has performed the necessary assessment of the activity from a safety and security perspective. Registrants or licensees need to be aware of the specific requirements for medical exposure in their country. Registrants or licensees will be expected to comply with all requirements and refer to specific State regulations.

6.1.2.2. Justification

The introduction of a new source of radiation that can change the likelihood of exposure needs to be justified to assure that the detriments of possession and use of the device are outweighed by individual and societal benefits. In medicine, the use of radiation brings more benefit than harm. The responsibility to assess this lies with health authorities in conjunction with appropriate professional bodies. For individual patients, it is to be performed in consultation with the radiation medicine practitioner and the referring medical practitioner.

6.1.2.3. Radiation protection and optimization

The dose to the patient should be sufficient for treatment, but it should not exceed the amount of radiation needed. In radiotherapy, a radiation dose which is too low could be just as detrimental as one which is too high. The consequence would be that the patient does not benefit from the treatment.

6.1.2.4. Dose constraints

Dose constraints and diagnostic reference levels are used to optimize protection and safety. Dose constraints are used to control occupational and public exposure but not to set dose limits. Non-compliance with the constraint should lead to an investigation and follow-up actions.

In HDR, these constraints may be the dose limit for members of the public who are housed in a room adjacent to the therapy room, necessitating additional shielding of the shared wall, or they could be the administrative requirements that the radiation oncologist, medical physicist or RTT need to leave the room prior to treatment and to evaluate the patient via remote visual technology (cameras). There are no specific dose constraints for patients in therapy, but the radiation oncologist should rely on the recommendations of professional organizations that have established acceptable dose ranges.

The requirements vary from State to State. In some States, few or none of these requirements may be in place, making importation of radiation generating devices or sources difficult to obtain and potentially unsafe. Potential registrants or licensees may need assistance in promoting the development of these regulatory requirements to obtain the desired equipment.

6.1.3. Registrant or licensee responsibilities

Registrants and licensees will need to establish and implement technical and organizational measures for the types of activity they are performing. The licensee (usually the manager of the institution) can delegate functions relating to radiation protection and safety while retaining the overall responsibility. An efficient way of delegating is by establishing a radiation protection programme and a committee to supervise compliance with the programme. The programme should consist of all issues relating to radiation protection requirements, including:

(a) Definition of responsibilities;
(b) Administrative requirements;

(c)   Requirements for occupational exposure, medical exposure, public exposure and emergency exposure situations.

Registrants and licensees may need to establish a radiation protection or safety committee and to appoint a radiation protection officer who is qualified to perform tasks associated with protection and safety.

An additional component that is especially important in radiotherapy is the quality assurance programme, which ensures good practice and radiation protection of the staff, patients and the public. Experience has shown that the frequency of accidental exposures is related to the absence or inadequacy of an established quality assurance programme in the department.

6.1.4. Manufacturer responsibilities

The regulatory body needs to approve HDR equipment before its installation for clinical use. Manufacturers will need to submit protection and safety standards, engineering performance reviews, quality standards and function specifications and information on the display and operational systems. The regulatory body should consider equipment that meets the standards of the International Organization for Standardization and the International Electrotechnical Commission. Some States may defer approval of equipment to certification provided by other States that have established standards, such as the medical device approval process of the Medicines and Healthcare Products Regulatory Agency, in the United Kingdom. This agency is responsible for safeguarding public health by ensuring that medical devices work and are acceptably safe. Successful manufacturers are identified with a seal of approval called an accreditation mark [15].

6.2. SAFETY AND SECURITY OF RADIATION DEVICES

Security is important and should be considered in the same way as safety in the use of radioactive sources in medicine. However, safety and security measures need to be designed so that they do not compromise the safe use of the device and vice versa.

Prior to the possession and use of radiation sources, a safety and security assessment should be completed by the registrant or licensee and reviewed by the regulatory body. Safety assessments are required at different stages of equipment acquisition (initial siting design, manufacture, construction, assembly and commissioning) and use (maintenance, annual checks and decommissioning). The level of assessment is commensurate with the level of risk associated

with the use of the radiation device. For HDR equipment, a safety assessment needs to be performed prior to use. The registrant or licensee will need to perform a safety assessment as part of the design process to assure that the planned shielding is adequate for the protection of workers, the public and the environment. A second safety assessment would be needed to validate that the actual shielding plan was adequate. This assessment would require surveys of the area surrounding the treatment room and calculations of exposure based on, for example, hours of operation. In addition, an independent verification of radiotherapy equipment should be performed prior to use. The regulatory body may also perform an inspection of the facility to verify compliance.

For radioactive sources, a security assessment should be performed to prevent unauthorized access and removal of sources. A security assessment should be a review of the registrant's or licensee's security equipment, training and procedures that deter, delay and detect a security breach, and unauthorized access or removal of material.

Excessive regulations, or an absence of them, can prohibit access to radiotherapy. The State's regulatory infrastructure needs to be in place to balance safety and security, effectiveness, the need for medical radiation practices and access to therapy. Coordination and support of the government, the regulatory body, the licensee or registrant and manufacturers are encouraged.

6.3. ACCIDENTAL EXPOSURE IN HIGH DOSE RATE BRACHYTHERAPY

6.3.1. Causes of accidental exposure in radiotherapy

The following events were identified and reported in Safety Reports Series No. 17, Lessons Learned from Accidental Exposures in Radiotherapy [31]:

(a) Errors in the calibration of radiotherapy sources;
(b) Errors in the preparation of input parameters;
(c) Errors in acceptance tests and commissioning or lack of tests of both radiation sources and treatment planning systems;
(d) Maintenance errors;
(e) Communication errors, transmission of information, misunderstanding of prescriptions and protocols, or use of obsolete protocols;
(f) Errors in the identification of the patient and treatment site;
(g) Dislodging of the HDR BT sources;
(h) Sources left inside the patient's body.

6.3.2. Prevention and mitigation of accidents

To prevent accidental exposure, it is crucial to identify what can happen and which treatments can be performed. Human mistakes and equipment faults in HDR BT can lead to a harmful situation when there is a difference between prescribed and delivered doses. Working procedures should be planned to prevent these situations.

The maintenance of HDR BT devices is a radiation safety related issue. In other areas of radiotherapy, complex electronics and mechanics have caused severe accidents. Therefore, it is necessary to develop a strategy for the maintenance and servicing of HDR BT devices with sufficient resources.

The quality assurance programme needs to incorporate sufficient double and independent checks of all safety critical parameters, such as the commissioning of the machine, source calibration, the treatment plan and the delivery of the dose to the patient.

Numerous measures can be taken by the registrant or licensee to minimize the possibility of medical errors. Some of these measures are described in GSR Part 3 [20], such as:

(a) Providing information and training to workers;
(b) Developing and maintaining adequate operating procedures and inventory procedures;
(c) Reviewing and maintaining occupational worker reports;
(d) Performing daily, monthly, annually and after servicing tests on equipment, including mechanical, hardware and software checks [15].

6.3.3. Investigation of accidental exposure

The requirements of GSR Part 3 [20] with regard to the investigation of accidental medical exposure are:

(a) To calculate or estimate the doses received and their distribution within the patient;
(b) To indicate the corrective measures required to prevent the recurrence of such an incident;
(c) To implement all corrective measures that are under the responsibility of the registrant and licensee;
(d) To submit a written report that states the cause of the incident and includes all relevant, required information to the regulatory authority as soon as possible after the investigation or as otherwise specified by the regulatory authority;

(e)   To inform the referring medical practitioner, the patient or the patient's legally authorized representative of the unintended or accidental medical exposure.

7. COSTS

The increasing popularity and widespread applications of BT are a direct consequence of its effectiveness in the cure or palliation of various forms of cancer. Similarly, the increasing dependence of BT on complex technology leads to a corresponding increase in costs.

7.1. ECONOMIC ANALYSIS

Health care economic analyses attempt to relate explicitly the additional cost of an intervention to its extra benefit. These analyses encompass classic approaches such as cost minimization analysis, cost effectiveness, cost utility and cost benefit, each with its different characteristics.

In many ways, economic analyses are a natural evolution towards a more structured way of considering how policy decisions on health care are made. The choice of an analysis method should consider the method's consistency with the economic nature of the specific question. The intervention is usually evaluated relative to an alternative form of treatment. Economic analyses are therefore comparative incremental analyses.

7.2. COST EFFECTIVENESS ANALYSIS

Cost effectiveness analyses relate the additional cost to its incremental impact on any clinically relevant measure of benefit [32]. Because one of the primary uses of an economic analysis is to allocate limited resources among diverse interventions, 'benefit' needs to be measured in units that are universally applicable to all interventions. 'Years of life saved' is the most commonly used measure of benefit. Thus, when calculating 'cost effectiveness', only cost and survival need be measured. A treatment's cost effectiveness ratio is calculated by dividing its incremental cost by its incremental impact on survival compared with the most reasonable alternative treatment. The result of this rate is then expressed in dollars per years of life saved. Interventions that cost less than an additional US $50 000 per year of life saved are considered cost effective.

The concept of cost effectiveness incorporates two concepts: effectiveness and cost. To be cost effective, an intervention has to be at least as effective as the alternative and should be cheaper, in the sense that the additional cost for years of life saved is less than US $50 000. Interventions that have a clinical benefit in terms of palliation or quality of life but do not improve survival should not be evaluated using the cost effectiveness method. For these types of intervention, the 'cost utility' method may be more appropriate because its results are expressed in quality adjusted life years (QALYs).

7.3. INITIAL COST ANALYSIS

The initial cost analysis of a health programme is especially relevant in States with limited resources. Unfortunately, enormous differences between low and middle income countries make it difficult to extrapolate an overall cost analysis based on the data from high income countries. A detailed analysis of the various economic factors and variables that influence the establishment of an HDR BT programme is beyond the scope of this publication. Table 3 summarizes the main items that should be considered.

TABLE 3. ITEMS FOR COST CONSIDERATION

Category	Items	Remarks
Capital costs	Room	With air conditioning
	Recovery room	None
	Shielding	Adapted to the type of source used (more shielding is needed for Co-60)
	Treatment equipment	Afterloader
		Applicators/accessories
		TPS
	Imaging equipment	C-arm/simulator/CT/MRI (subject to availability in the hospital)
		Film developer (if not digital imaging)
	Quality assurance equipment	Check position ruler
		Absolute source calibration system (well chamber based or phantom based, electrometer)
		Autoradiography for commissioning

TABLE 3. ITEMS FOR COST CONSIDERATION (cont.)

Category	Items	Remarks
	Autoclave for sterilization	None
	Anaesthesia workstation	None
	Treatment table/chair	None
	Long term equipment replacement	Replacement of afterloader/TPS/imaging
Operational costs	Source replacement	Every 3–4 months for Ir-192 Every 5 years for Co-60
	Maintenance contract	None
	Applicators/accessories	Regular CT/MRI compatible
	Anaesthesia	Consumable materials Anaesthetic agents Patient telemetry
	Hospitalization (bed stay)	Cost of hospital bed/day
	Other consumable materials	Catheters, gauze, tape, etc.
	Sterilization	Costs of external service
	Imaging (if not digital)	Film and chemical reagents
	Overhead costs	Electricity, water and heating Air-conditioning maintenance Cleaning
	Staffing	Radiation oncologist Medical physicist Radiation therapist Nurse Anaesthesiologist Other specialists required
	Training and continuing professional education	Courses, seminars, international and national meetings, fellowships

Note: CT — computed tomography; MRI — magnetic resonance imaging; TPS — treatment planning system.

7.4. ADDITIONAL COST ANALYSIS

Consideration should also be given to the development and implementation, operational and decommissioning, or disposal costs associated with HDR. The development and implementation costs are the fixed costs for construction, staff training, procurement of the device and source, and corresponding safety and quality assurance equipment. These costs will include any additional security enhancement costs. The security costs could be considerable and should be taken into consideration at the development stage. The operational costs are the costs associated with providing the services, including basic utilities, personnel, procurement of new sources, disposal of used sources, patient specific equipment such as catheters, daily and weekly checks, continual staff training and education, and maintenance costs. As the unit ages, the maintenance costs will likely increase. The final cost is the decommissioning cost, when the unit is no longer operational or supported by the manufacturer, and the equipment and sources need to be correctly disposed of.

Cost effectiveness studies in BT have been mainly performed in developed countries [33–38]. Their findings indicate that BT is a cost effective modality in the specific clinical scenarios studied. However, these findings are difficult to extrapolate to low middle income countries. Reliable cost data are indispensable for these computations and for guiding discussions on reimbursement settings between the radiation oncology community (the users) and government parties and insurance companies (the payers).

7.5. STRATEGIES FOR REDUCING COSTS

The choice of a radioactive source is an important factor when considering the HDR programme costs. HDR devices with ^{60}Co or ^{192}Ir sources are currently available. The miniaturization of the ^{60}Co sources, making them the same size of previously used ^{192}Ir sources, was a clear and significant step towards more cost effective BT [39]. However, ^{60}Co requires more cost allocations for shielding of the treatment suite than for a room with an ^{192}Ir source afterloader. From the frequency of source replacement perspective, ^{60}Co offers a great advantage because it has a half-life of 5.27 years compared with 73.8 days for ^{192}Ir. Therefore, this form of HDR BT has been promoted in recent years [40].

Specialized publications have shown that HDR BT offers cost effective advantages for centres with a significant load of patients with gynaecological malignancies [41]. The advantages are not very pronounced in departments that treat fewer than 300 patients per year. Estimations show that an HDR BT machine

working at full capacity can treat over 700 patients annually, including interstitial procedures.

The introduction of HDR BT has allowed treatments to be administered in minutes rather than days, replaced hospital admissions by ambulatory treatments and, very often, eliminated the need for spinal or general anaesthesia. Together, these changes result in more cost effective BT. The equivalence of HDR versus LDR in terms of clinical outcomes and toxicities has already been established in level 1 evidence studies performed in developed and developing countries [42–44].

The concept of accelerated partial breast irradiation (APBI) in selected patients, in which either interstitial catheters or the balloon technique can be used, allows the treatment of a limited volume of the breast in a patient with early low risk breast cancer in five days [45]. This technique is resource sparing and cost effective. However, the long term toxicity of APBI is still a matter of discussion, and more follow-up data are required.

7.6. CERVICAL AND PROSTATE CANCER

Another strategy to reduce costs relies on the use of shorter fractionation schedules with fewer fractions. In the case of cervical cancer, three fractions of 8.0 Gy or two fractions of 9.0 Gy have been proven to be effective and safe [42, 43], and the IAEA is testing them against more protracted fractionations in two randomized trials.

With an ever increasing focus on health care costs, making the best use of the available resources is a key consideration in today's health care systems [46]. Total health care costs for cancer in the United States of America were an estimated US $93.2 billion in 2008 [47]. Despite the widespread use of radiotherapy in cancer care, however, it accounts for a relatively small percentage of overall health care costs. In the United Kingdom, radiotherapy comprises less than 10% of the budget, compared with over 15% for chemotherapy and more than 30% for surgery [48]. In Sweden, radiotherapy accounts for approximately 5% of cancer costs. Although the actual costs for external beam radiation therapy (EBRT) increased by 16% between 1991 and 2001, the number of fractions delivered increased by 37%, so the cost per fraction was actually reduced [49].

As pressure on resources intensifies, reductions in overall treatment length along with an increased use of outpatient based treatment are effective ways to reduce costs and provide more efficient utilization of resources. In cervical cancer, for example, HDR BT offers reduced treatment times compared with LDR BT, allowing treatment on an outpatient basis and reducing the time spent in hospital from approximately one week to one day [50, 51].

A survey in Australia and New Zealand showed that the use of HDR BT for cervical cancer exceeded the number of procedures of LDR BT, with the installation of more HDR units indicating a continuing trend away from LDR BT [52]. The use of HDR BT has also increased in the United States of America, and has become increasingly popular in the developing world [53]. The increased dosing flexibility that HDR BT provides also allows treatments to be better tailored to the individual patient, reducing dosage to adjacent organs at risk and thus providing potential benefits in terms of reduced morbidity. Maximizing the use of existing advanced BT equipment, such as a remote afterloader, could also lead to efficiency savings because the costs per patient treated are reduced. Together, the use of 3-D image based BT and advanced, computerized dose optimization algorithms means that BT can provide a highly conformal treatment, delivering the desired radiation dose in a targeted and precise manner.

To generate an accurate picture of the costs of a particular therapy, cumulative costs need to be considered over several years to ensure that factors such as side effects and the need for subsequent therapy are included. An analysis of patients with newly diagnosed prostate cancer in the United States of America showed a wide variation in total treatment costs over five and half years, with BT among the cost effective options (US $35 143) and EBRT among the most expensive options (US $59 455). When subdivided by risk group, treatment costs rose with increasing risk, although EBRT was still consistently more costly than BT in each group [54].

The Institute for Clinical and Economic Review, United States of America, recently considered the comparative value of radical prostatectomy, BT, intensity modulated radiation therapy (IMRT) and proton therapy for treating low risk prostate cancer [55]. The assessment considered both the clinical effectiveness and the initial and lifetime costs of the different options. Although clinical effectiveness was considered comparable between radical prostatectomy, BT and IMRT, the comparative values differed.

In two recent analyses, cost effectiveness models were used to evaluate the potential efficacy gains associated with the increased radiation doses delivered by IMRT and proton beam therapy for patients with intermediate risk prostate cancer. One assessment suggested that IMRT was cost effective over 3-D conformal radiotherapy, although the incremental cost effectiveness value for IMRT (US $40 101 per QALY) was near the upper limit of what is considered cost effective (US $50 000 per QALY) [56]. The other study suggested that proton beam therapy was not cost effective compared with IMRT [57]. The combination of BT and EBRT provides an alternative approach to increasing treatment dose and has proved effective in intermediate and high risk patients with prostate cancer. Both IMRT and proton therapy are associated with substantial capital and

maintenance costs. The lower infrastructure and usage costs of BT suggest that BT plus EBRT may prove a more cost effective treatment strategy in intermediate and high risk patients with prostate cancer.

In a systematic review of the clinical and cost effectiveness of emerging technologies for early localized prostate cancer by the University of Sheffield, United Kingdom, no relevant cost effectiveness studies could be identified [37]. An economic model was developed to explore the potential cost effectiveness of newer treatments. Owing to the lack of disease free survival data for both treatments included in the review and for traditional treatments, cost effectiveness estimates were based on the impact of adverse events on QALYs. Owing to the paucity of evidence related to adverse events for the majority of interventions, the cost effectiveness assessment was restricted to BT, 3-D conformal radiotherapy and cryotherapy compared with standard treatments (prostatectomy and 2-D radiotherapy).

Of the new treatments included in this analysis, only cryotherapy appeared not to be potentially cost effective compared with traditional treatments, and this was due to the associated high incidence of impotence. However, this economic analysis was based on the assumption that newer and traditional treatments are equally effective in terms of survival, and results are sensitive to the estimates of adverse events and utility values.

A study in France compared the cost effectiveness of transperineal seed BT versus radical prostatectomy in a prospective economic study [35]. In 435 men with localized prostate cancer, a similar cost profile was found for both modalities, but with different health related quality of life and side effect profiles. The transperineal seed approach requires the purchase of a new batch of ^{125}I or ^{103}Pd seed for each individual patient. In contrast, HDR BT for prostate cancer can be performed with the same unit and source that is available for gynaecological or other sites, thereby sparing resources.

In an economic study on 1436 patients with low and intermediate risk prostate cancer, the combination of hypofractionated EBRT and HDR BT was more cost effective compared with protracted fractionation with IMRT [58]. Reimbursement levels were always higher for IMRT and had comparable patient outcomes. No differences in biochemical failures or local recurrences were noted at five years between these modalities. While there was a significant decrease in the overall survival with IMRT and LDR compared with the HDR regimens, no difference in the cause specific mortality existed. In this study, which involved low and intermediate risk prostate cancer patients, the reimbursement for IMRT was found to be significantly higher than that for other treatment regimens, despite their comparable five year biochemical control and cause specific survival.

In summary, direct and indirect evidence suggests that HDR BT is cost effective in the treatment of cervical cancer in centres that have a high turnover of patients with this disease. In prostate cancer, HDR BT is resource sparing compared with the seed technique. Quality cost effectiveness studies are needed.

8. COBALT-60 HIGH DOSE RATE BRACHYTHERAPY

Cobalt-60 is not a new radionuclide for BT use. In fact, the first generation of remotely controlled HDR afterloaders (Ralston and Cathetron) was developed using ^{60}Co. Because of the relatively large diameter of the source (3 mm), the diameter of the applicators was also large and required insertion under general or spinal anaesthesia and admission of the patient to the hospital ward.

Until recently, the manufacture of microsources for HDR afterloading was possible only for ^{192}Ir. Modern technology allows the production of sufficiently high specific activity ^{60}Co sources with geometrical dimensions that are identical to a micro ^{192}Ir source. One such ^{60}Co source currently available has an active length of 3.5 mm and a diameter of 0.5 mm. It is encapsulated in a stainless steel capsule 1 mm in diameter.

The main physical characteristics of ^{192}Ir and ^{60}Co used in HDR BT are given in Table 4.

TABLE 4. PHYSICAL CHARACTERISTICS OF ^{192}IR AND ^{60}CO AS RADIONUCLIDES FOR BRACHYTHERAPY [23]

Radionuclide	Average energy of γ rays (MeV)	Half-life	Air kerma rate constant (μGy·m^2/GBq·h)	Initial activity (GBq)	Tenth value layer for concrete (cm)
Ir-192	0.375	73.8 days	108	370	11.3
Co-60	1.25	5.27 years	309	74	20.6

The application of Monte Carlo simulations and the TG-43 formalism of the American Association of Physicists in Medicine (AAPM) to a ^{60}Co source revealed that, for the same contained activity, the air kerma rate of a ^{60}Co source is higher than for an ^{192}Ir source by a factor of 2.8. Because of the lower maximum

specific activity value of the ^{60}Co source compared with ^{192}Ir, the initial dose rate of a commercial source will be lower. The decay of the source strength, however, is much smaller with the ^{60}Co source [39, 59].

The radial dose function for the ^{192}Ir source provides somewhat higher values compared with the ^{60}Co source (<2% for a radius of <20 cm). Similarly, anisotropy is slightly different for the two radionuclides contained in commercial HDR sources. Nevertheless, in solid tissue, both sources lead to an almost identical dose distribution. There are only minimal differences between the dose distributions of ^{192}Ir and ^{60}Co for the irradiation of cervical carcinoma [59]. The reason is that the inverse square law is responsible for the largest part of the dose gradient around the sources. The requirement of more room shielding for the application of ^{60}Co sources is explained by the much higher value of the average energy of the gamma rays [59].

There are potential logistical advantages of ^{60}Co sources, although the afterloader would operate with only 33% of the initial source activity compared with the generally applied ^{192}Ir sources. Using typical intervals for replacement due to decay, 25 source exchanges are required for ^{192}Ir for one exchange of the ^{60}Co source, which results in reduced operating costs. However, these comparisons are only valid provided that the mechanical stability of the afterloader and the source capsule allows extended use at such a magnitude [59]. A physics analysis supports that a time saving of approximately 40% can be achieved with ^{60}Co in comparison to ^{192}Ir [60].

Individual treatment times for ^{60}Co sources are almost within the variation of times for ^{192}Ir sources. However, over five years, the total clinical irradiation time is approximately 20% longer for a ^{60}Co source and approximately 46% longer in the worst case scenario (during the fifth year of the ^{60}Co source) [60].

9. ELECTRONIC BRACHYTHERAPY

Electronic BT is a relatively new technological approach in which the radiation source is not an encapsulated radioactive isotope (radioisotope BT) but instead is a miniature electronic X ray source that produces low energy radiation at an HDR. The source is a disposable miniaturized X ray tube of approximately 2.2 mm in diameter and has an operating potential of up to 50 kV. It is integrated into a water cooled, flexible probe assembly that, in turn, is connected to a high voltage cable which is directed into the lumen of the applicator and enables the controller to step the source to preprogrammed dwell positions within the applicator. The power to the source reaches a maximum of 15 W. When the

source is active, the radiation output is 0.6 Gy/min at 3 cm from the source axis as measured in water [38]. Several variables can be manually controlled, including the operating voltage of the anode (penetration depth), the beam current (dose rate), the dwell positions within the applicator and the time at each dwell point. Therefore, the electronic source can be intensity modulated to mimic the penetrations and dose rate characteristics of several isotopes, such as ^{125}I, ^{192}Ir and ^{103}Pd. Source specifications according to AAPM TG-43 (BT dosimetry formalism) as well as TG-56, TG-59 and TG-61 have been applied.

The scope of US Food and Drug Administration approval for marketing this device has so far been restricted to postoperative breast cancer treatment. A commonly used dose fractionation schedule is that of the RTOG-NSABP-0143 trial, which is 3.4 Gy in ten fractions delivered twice daily. Confirmatory radiographic imaging is performed at the time of each fraction. However, the system can be potentially useful for vaginal BT, intraoperative BT or other situations. Advantages include the fact that the low energy obviates the need for special room shielding compared with standard HDR BT sources. Personnel can wear lead aprons, and patients can be draped with lead sheets.

Advantages of electronic BT in terms of the efficacy or patient outcome are as yet unproven. There are minimal clinical data available from single institution studies, and none has had a significant follow-up. Accepted quality assurance standards do not yet exist. Thus, individual centres could inadvertently admit systematic errors in the calibration or treatment delivery processes. Because the device is a source of ionizing radiation, its use should be regulated in the same way as other radiation emitting devices. Properly trained professionals can take advantage of the potential treatment planning features of the system and ensure appropriate administration in a safe manner.

10. CURRENT APPLICATIONS OF
HIGH DOSE RATE BRACHYTHERAPY

Surgery, radiation therapy and chemotherapy, or a combination thereof, are used to treat, and potentially cure, cancer. BT is a critical component of radiation therapy treatment in the primary and adjuvant setting for many malignancies. HDR BT has replaced LDR BT with the exception of permanent seed implants for early stage prostate cancer.

The advantages of HDR include outpatient treatment, patient convenience, elimination of radiation exposure to staff and dose optimization. PDR BT is another treatment option that is employed by some centres. The choice of radiation

modality used depends on the frequency and site of the disease, the efficacy and duration of the treatment, the equipment available, the expertise of the therapeutic staff team and institutional traditions, and the radiation safety considerations.

The incidence of cancer types varies around the globe and is linked to socioeconomic and demographic factors. For example, cervical cancer is often the most common malignancy in many low and middle income countries (LMICs), whereas prostate and breast cancer are the most common malignancies in high income countries. Because of the accessible location of these tumours, BT represents a good therapeutic option. For cervical cancer, BT is mandatory for curative management and has been used successfully for decades. The rationale for using BT in prostate cancer includes the possibility of dose escalation, convenience and high cure rates for early stage disease. For appropriately selected patients, breast BT can be used as adjuvant monotherapy rather than using external beam radiation. For some women, this approach could increase the rate of breast preservation owing to it having a markedly shorter treatment duration, and it could be a resource sparing strategy for high volume radiotherapy centres. BT continues to have a role in the treatment of the head and neck, oesophageal, lung and endometrial cancers. Other sites amenable to BT include bile duct, rectal, anal, vaginal and soft tissue malignancies.

The initial cost of HDR equipment is relatively high. However, the capacity to treat more patients with little incremental costs, coupled with the versatility of the HDR machine, can overcome the higher cost and demonstrate an economic advantage.

The main advantages of HDR BT versus LDR BT include [41]:

(a) Elimination of radiation doses to caregivers and visitors.
(b) Elimination of source preparation and transportation.
(c) Treatment times are shorter, resulting in:
   (i) No need for hospitalization (outpatient treatments);
   (ii) Less patient discomfort and lower risks of thromboembolism because prolonged bed rest is eliminated;
   (iii) Possibility of treating patients who might not tolerate long periods of isolation;
   (iv) Reduced risk of applicator movement during therapy;
   (v) Possibility of lower doses to the bladder and rectum through rigorous packing, the use of a rectal retractor (if possible) and immobilization;
   (vi) Higher throughput of patients in busy departments.
(d) The smaller tandem diameter — 3.2 mm compared with 6.4 mm for LDR BT — reduces the need for cervical dilatation and the need for general or spinal anaesthesia.
(e) Improved dose distribution through dose optimization.

(f) Integration (overlapping) of EBRT and HDR BT, which can lead to shorter overall treatment duration and potentially better tumour control because accelerated repopulation can be minimized [61].

There is also a potential disadvantage of increased labour intensity for the radiation oncologist and physicist.

A routine HDR BT application follows four steps:

(1) Insertion of applicators;
(2) Imaging;
(3) Planning;
(4) Treatment.

A relatively brief summary that describes the use of HDR BT for a variety of malignancies follows. Treatment protocols are beyond the scope of this publication, and the reader is referred to standard textbooks or reviews for further details [17, 62–65].

10.1. UTERINE CERVICAL CANCER

The incidence of cervical cancer is high, exceeding an age standardized rate of 30 per 100 000 in many LMICs, and it constitutes the most common malignancy in some countries [66]. Early stage cervical cancer can be successfully treated by either primary radical surgery or radiotherapy, with cure rates of above 80% for stage IB-1 disease. Advanced stage cervical cancers (stage IB-2 and above) should be treated with concurrent chemoradiation or radiotherapy alone because surgically treated patients will invariably require postoperative radiation with higher late toxicity rates. When 2-D BT is used, the cure rates for locally advanced disease (stages IIB and IIIB) are approximately as high as 70% and 50%, respectively [67]. For medically fit patients who can be reliably followed, concurrent chemotherapy should be considered because survival can be improved by as much as 12% [68–74].

BT is mandatory for the curative treatment of all invasive cervical cancers [75–79]. Gynaecological BT can account for up to 100% of the BT practice in some LMICs. HDR machines are capable of treating larger numbers of patients, owing to the short treatment times.

Depending on the tumour volume and extent, as well as the risk of lymph node involvement, BT is usually combined with EBRT. For very early stage disease (stage IA), when surgery is not performed, BT can be used as an exclusive treatment [76, 80]. In most cases, it is used as an intracavitary procedure, and

in selected cases, it can be a combined intracavitary interstitial implant or an interstitial implant only.

Radiobiological models, retrospective studies, randomized trials and a meta-analysis have shown equivalent effectiveness in terms of the local control and late complications between LDR and HDR BT [42, 44, 50, 81–85].

Modern commercially available applicators come in different designs (ovoid type with or without shielding, ring type) and with different names, which mainly represent traditional schools (Manchester style, Henschke style or Fletcher style). Table 5 presents the most salient characteristics of available BT applicator models, and Fig. 3 shows some examples.

TABLE 5. BRACHYTHERAPY APPLICATORS USED IN THE TREATMENT OF CERVICAL CANCER

Applicator model	Characteristics
Tandem and ring	Carries two radioactive lines: one in the rigid intrauterine tandem and the other in a ring shaped part that is placed against the cervix
	Intrauterine tubes come in different lengths and angles (30°, 45° or 60°)
	Ring is available in different diameters (26, 30 or 34 mm)
Henschke	Vaginal colpostats are hemispherical in shape
	Vaginal sources lie approximately parallel to the axis of the intrauterine tube
Fletcher	Includes an intrauterine tube and two cylindrical colpostats
	Vaginal sources lie in the fornices, perpendicular to the axis of the vagina
	Intrauterine tube comes in various angulations Vaginal colpostats come in various sizes
Manchester	Includes one intrauterine tube and two ovoid shaped vaginal colpostats
	In modern HDR models, a clamp fixes the position of the ovoids relative to the intrauterine tube
Moulage	Method was developed at the Institut Gustave Roussy, France, and constitutes the construction of an individualized mould (*moulage*), made of liquid plaster and acrylic, to maximize individual anatomical adaptation
	Afterloading catheters are placed in the mould according to the individual tumour topography

TABLE 5. BRACHYTHERAPY APPLICATORS USED IN THE TREATMENT
OF CERVICAL CANCER (cont.)

Applicator model	Characteristics
Joslin–Flynn	Ovoid alignment in relation to the vagina is similar to the Henschke applicator
	Rectal retractor enables limitation of the dose to the rectum
	Tenaculum forceps can be used to grip the cervix and to hold the applicator in the correct position
CT/MRI compatible models	All of the above applicator models are available in CT/MRI compatible versions
	These models are made of plastic and carbon fibre, which makes them compatible with CT and MRI scans
	CT and MRI scans are performed on the patient with the applicator in place, which allows 3-D treatment planning based on the images and volume delineation
Syed–Neblett template	Two plastic plates are joined by screws that tighten to fix in place up to 38 stainless steel needles
	Six additional needles can be placed around the central cylinder
	This applicator can be used for interstitial techniques only or for combined interstitial and intracavitary techniques
Martinez universal perineal interstitial template	This approach uses an interstitial template that has needles at various depths and angulations
	Treatment can be adapted to various tumour volumes in the pelvis, using HDR optimization
	This method has been adapted for use with HDR remote afterloading units and modern image based treatment planning
Vienna applicator	Modification of the tandem and ring model, in which needles can be inserted laterally through holes in the ring carrier. This applicator is CT/MRI compatible and could be useful to cover proximal parametrial extension of tumours
Vaginal cylinders	Designed to treat the mucosa of the vaginal wall at the vaginal cuff or at various lengths. These cylinders are commercially available in different diameters and lengths

Note: CT — computed tomography; HDR — high dose rate; MRI — magnetic resonance imaging.

Note: CT — computed tomography; MRI — magnetic resonance imaging; MUPIT — Martinez universal perineal interstitial template.

FIG. 3. Some BT applicators used in the treatment of cervical cancer (courtesy of Nucletron, Netherlands).

10.1.1. Insertion

The insertion of the LDR and MDR applicators with tandem diameters of 6–7 mm requires cervical channel dilatation and, therefore, general or spinal anaesthesia. Light to moderate sedation with or without topical anaesthesia or paracervical nerve block can be used to anaesthetize patients who are undergoing HDR BT because of the smaller (3.2 mm) tandem diameter [86, 87].

It should be noted that the tandem diameter of CT/MRI compatible applicators for HDR BT is larger; therefore, adequate anaesthesia should be considered. It is critical that the patient is adequately sedated, which allows proper applicator placement and retraction of the bladder and rectum using vaginal packing, to move this normal tissue away from the high dose region.

The patient is placed in the lithotomy position. A careful pelvic examination is required to determine the disease extent and regression compared with the initial examination and to determine the applicator type and size. The results of the examination should be documented using a clinical diagram. After the preparation of the vulva, perineum and vagina with iodine solution or an equivalent, a Foley catheter is inserted using a sterile technique and is filled with 7 mL of diluted radio-opaque solution. A vaginal speculum is introduced that has adequate exposure of the cervix. If feasible, seed markers should be placed in both the anterior and posterior cervical lips for radiographic visualization. Additional seed markers should be placed in the most inferior extent of the disease that involves the vagina.

When necessary, sharp pointed forceps (tenaculum) can be placed on the anterior cervical lip to straighten out the uterine canal, which facilitates uterine sounding and minimizes the risk of uterine perforation. A uterine sound is used to measure the depth of the uterine cavity and to determine its position. Dilatation of the external cervical orifice (cervical os) is performed when required. The curvature angle and length of a tandem should match the uterine position, as determined by sounding.

Some centres routinely use an intrauterine stent — a Smit sleeve (see Fig. 3) — which is fixed with stitches to the cervix or upper vagina. The stent stays in place for the whole course of BT and is removed after the last BT session. The intrauterine stent carries a small metal ring that facilitates the localization of the cervical os in the radiographs and prevents uterine perforations.

Pelvic ultrasound, if available, can be very useful to facilitate tandem placement and repositioning for patients with distorted anatomy. Bimanual rectal and abdominal examination should be performed regularly to define clinically the position of the uterus and to guide the insertion based on the uterus position assessment.

After inserting the intrauterine tandem, colpostats or a ring applicator are placed gently in the vaginal fornices. In general, the ovoids or caps of the largest possible diameter are preferred because a better dose distribution in depth can be achieved. The ovoids should fit snugly without compromising the packing. In the case of the ring applicator, a ring/cap with an adequate diameter is used. The cap should always be used to minimize the risk of vaginal necrosis. The tandem should be bisecting the ovoids on both the lateral and anterior–posterior view for optimal geometry (Figs 4 and 5).

Depending on the model used, the vaginal and uterine applicators could be fixed to one another (see Fig. 3). Since the tandem and ring applicator has a fixed geometry, a reproducible dose distribution between applications is possible, which could obviate the need to plan subsequent insertions. Libraries (atlases) of dosimetry for the standard loading of the tandem and ring are available.

The rectum is packed away using either a rectal retractor or a radio-opaque gauze, which also stabilizes the applicators. Similarly, the bladder is packed away with radio-opaque gauze using pick-up forceps.
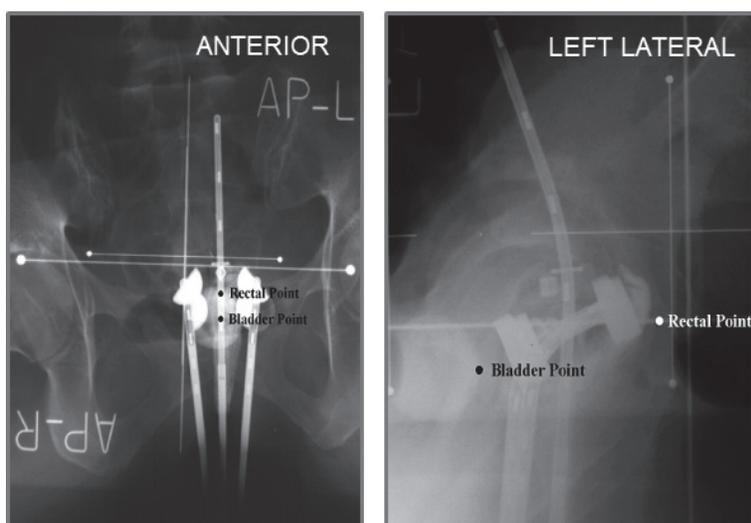
Note: The following elements can be identified: tandem, vaginal ovoids with their shielding, metal ring in the external os, bladder Foley balloon, posterior vaginal packing, and rectal and bladder calculation points. AP-L — anteroposterior left; AP-R — anteroposterior right.

FIG. 4. Anterior and lateral localization radiographs following insertion of applicators for HDR BT.
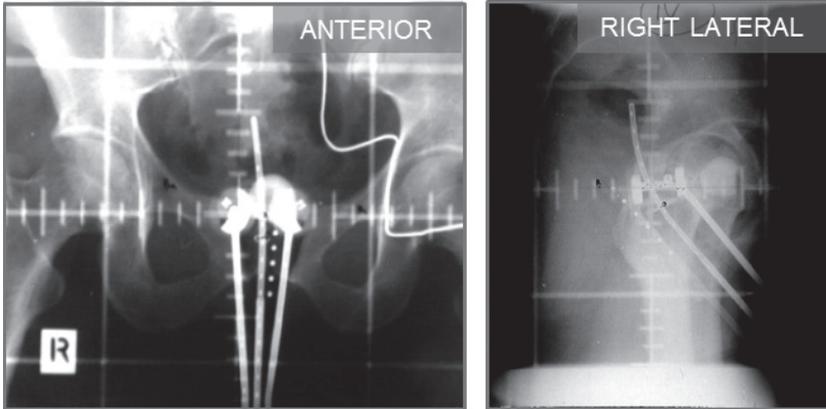
Note: The white dots indicate the position of a flat rectal retractor.

FIG. 5. Anterior and lateral radiographs following insertion of applicators for HDR BT.

For patients with a narrow vaginal anatomy, with which the introduction of standard size ovoids or the ring is not possible, a tandem and cylinder should be used. For patients with extensive vaginal disease, with which a tandem and cylinder cannot be used, the best option is an interstitial implant combined with intracavitary placement of an intrauterine tandem.

For the tandem and ring applicator, defined standard configurations with specific loading patterns for each applicator (dwell positions and times) have been generated and are available in the 'library plan' of the TPS [88, 89]. However, some intracavitary applicators (e.g. the Fletcher type) are rigid, but do not have a fixed geometry. These applicators require an individual treatment plan for each insertion.

Fixed geometry applicators such as a tandem and ring should be used because it simplifies and expedites the treatment planning process and also reduces the chance of error. Because multiple HDR fractions are required for treatment, applicator position reproducibility is most important. For treatment planning based on sectional imaging, CT/MRI compatible ovoid or ring type applicators are available.

The Vienna applicator is a tandem and ring applicator that allows the transvaginal placement of interstitial needles into the proximal parametrium through drillings in the ring. Improved dosimetry and pelvic control have been demonstrated with this applicator for patients who have bulky tumours with parametrial infiltration [90–92].

10.1.2. Imaging

10.1.2.1. Level 1: Conventional radiology

X ray films are taken with either a mobile unit or a C-arm, using a reconstruction box to produce orthogonal films for planning. High voltage equipment allows adequate lateral exposure when needed.

10.1.2.2. Level 2: Simulator

This level allows orthogonal films to be taken in which variable isocentric angles and reconstruction techniques can be used.

10.1.2.3. Level 3: Computed tomography and magnetic resonance imaging

Axial slices from a CT scan or MRI permit not only the reconstruction of the applicator, but also delineation of the tumour and target volumes as well as of the organs at risk [89, 93].

Ideally, the applicator insertion, radiograph generation and treatment should take place in a dedicated BT suite, which avoids transportation of the patient. However, this approach is not always possible. Adequate vaginal packing or external immobilization devices should be used to minimize applicator movement [94–96]. In any case, the patient should remain in a supine position, and movements between the stages of imaging and treatment delivery should be minimized.

10.1.3. Treatment planning

The total dose, dose schedule and time pattern for each individual patient should be unambiguously prescribed, recorded and signed by the radiation oncologist in the BT chart. As a minimum, the radiation oncologist should specify the dose per fraction given to point A (see Figs 6–8), the number of fractions, the technique to be used and the time dose pattern. Limiting criteria for the maximal doses or dose rates to be given to the anterior rectal mucosa and to the bladder trigon should be well defined.
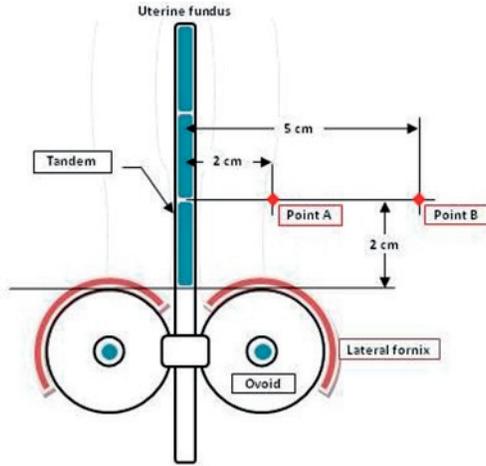
Note: The duration of the irradiation is based on the dose rate at point A, which is located 2 cm superior to the applicator surface and 2 cm lateral to the cervical canal.

FIG. 6. Localization of point A for a tandem and ovoid applicator.
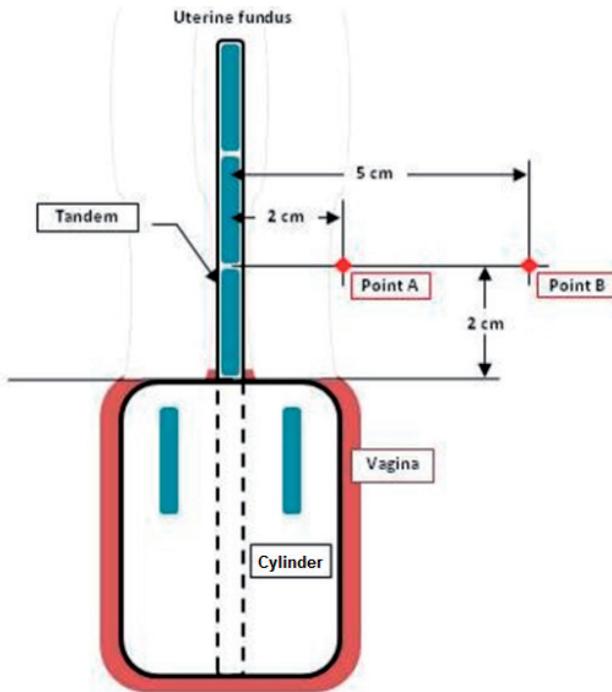
FIG. 7. Localization of point A for a tandem and vaginal cylinder application, which is 2 cm superior to the upper face of the ring and 2 cm lateral to the cervical canal.
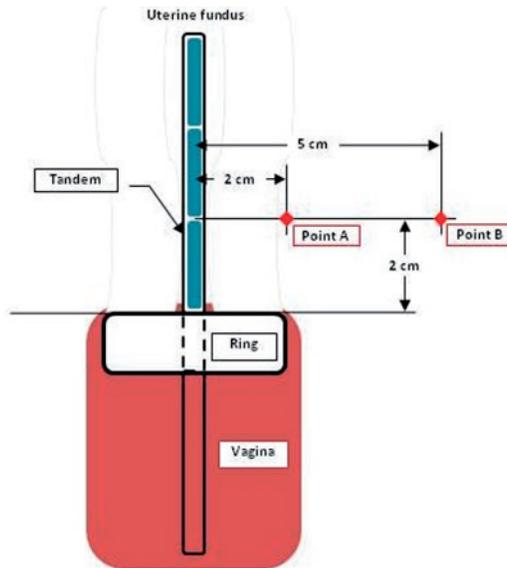
FIG. 8. Localization of point A for a tandem and ring application, which is 2 cm superior to the applicator surface and 2 cm lateral to the cervical canal.

During the subsequent phases of imaging, treatment planning and treatment delivery, the radiation oncologist should work in close consultation with the medical physicist to obtain an acceptable treatment plan.

Because of the very high dose gradient that surrounds the radioactive sources (approximately 10% per millimetre), there has been difficulty in expressing the dose used in intracavitary BT. There are many different methods that are used by various centres to prescribe and calculate the dose of a BT implant. Most methods prescribe an absorbed dose to point A, as per the Manchester system; others have defined different new points or variations from the original point A [97–100].

Regardless of the system used, each centre should be consistent when reporting the doses to the tumour and normal tissue. The use of dose volume histograms is encouraged. In addition, the radiobiological equivalences for different dose rates need to be accounted for.

Recommendations on the dose and volume specifications for reporting intracavitary gynaecological BT were published by the ICRU in 1985 [2]. More recently, important changes have taken place in the field of BT, such as the widespread use of HDR techniques and the development of image based treatment planning. A new ICRU report on gynaecological BT is in preparation [100].

10.1.4. Reporting

In centres that practice HDR BT with 2-D planning (planning based on a pair of orthogonal radiographs), the recording and reporting of BT applications are conducted by following a combination of criteria, which are described in the Manchester system and ICRU Report 38 [2] (see Figs 9–11):

(a) Dose to point A;
(b) Dose to the lateral pelvic point;
(c) Dose to the ICRU rectal point;
(d) Dose to the ICRU bladder point.

Limitations are set for doses to the critical organs: less than 70% of the prescribed point A to the rectum and less than 80% to the bladder, if possible. With adequate packing, these goals are typically achieved.

The ICRU rectal reference point is determined on a lateral radiograph. On the lateral radiograph, an anteroposterior line is drawn from the lower end of the intrauterine source position or from the middle of the intravaginal source positions. The rectal reference point is located along this anteroposterior line, 5 mm posterior to the posterior vaginal wall.
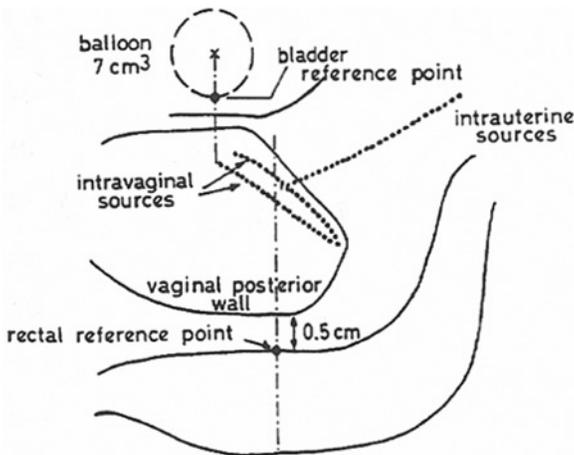
FIG. 9. Definitions for rectum and bladder reference points (reproduced from Ref. [2] with permission courtesy of the ICRU, United States of America).

Note: On the left side is an anterior view and on the right side is a left lateral view. L. COM: left common iliac, L. EXT — left external iliac; L. PARA — left para-aortic; R. COM — right common iliac; R. EXT — right external iliac; R. PARA — right para-aortic.

FIG. 10. Determination of the anatomical location of the pelvic and low para-aortic lymph node groups (lymphatic trapezoid) (reproduced from Ref. [2] with permission courtesy of the ICRU, United States of America).

FIG. 11. Determination of the right (RPW) and the left (LPW) pelvic wall reference points in the anteroposterior (AP) and lateral radiographs (reproduced from Ref. [2] with permission courtesy of the ICRU, United States of America).

The bladder dose is reported at the ICRU bladder point. A Foley catheter with a balloon filled with 7 cm^3 of diluted radio-opaque fluid is used. The catheter is pulled downwards to bring the balloon against the bladder neck. On the lateral radiograph, an anteroposterior line is drawn through the centre of the balloon, where this line intersects the posterior balloon surface.

There is evidence that supports the existence of a correlation between rectal complications and the dose to the ICRU rectal reference point [101]. In contrast, the bladder reference point was found to be reproducible but does not correlate well with bladder complications. A number of studies demonstrated that the ICRU reference points for the bladder and rectum underestimate the maximum organ dose when compared with the CT based dose assessment [102–104].

The actual maximum bladder dose, in most cases, is significantly higher than the ICRU reference point and is usually located more superiorly. Hence, a second bladder point (defined by Gerbaulet et al. [105]) usually yields a more realistic maximal bladder dose [106]. This point is located 1.5 cm superior to the ICRU point, as defined on the lateral radiograph.

Reporting at level 3 is characterized by individualized techniques that are usually complex and often evolving (e.g. 3-D image based BT). The applicators, relevant tumour/target volumes and organs at risk are defined using sectional imaging (CT or MRI) [27, 93, 107]. This approach also enables 3-D dose distributions to be obtained and dose volume histograms to be generated.

10.1.5. Time dose pattern

The dose contribution to point A from BT needs to be reduced when changing from LDR to HDR because of the dose rate effect [108, 109]. Studies have demonstrated increased late complications when the dose rate effect is not considered [110, 111]. Commonly used fractionation schedules are listed in Table 6.

10.1.6. Vaginal cylinders

In situations in which there is a narrow vaginal anatomy, it might not be possible to insert even the smallest colpostat. In addition, for patients with stage IIIA tumours, the disease might not be adequately covered with colpostats. In both cases, a vaginal cylinder should be used rather than colpostats, along with the intrauterine tandem (see Figs 3–7).

TABLE 6. COMMONLY USED HIGH DOSE RATE SCHEDULES AFTER WHOLE PELVIS EXTERNAL BEAM RADIATION THERAPY[a]

No. of fractions	Dose per fraction (Gy)	Total tumour dose EQD_2 (Gy)	Total rectum dose EQD_2[b] (Gy)
2	9	74.5	69.4
3	8	82	74.9
4	7	85.7	77

[a] Total EBRT dose is 46 Gy in 23 fractions.
[b] Assuming 70% of the dose at point A.

Rectal and vaginal mucosal tolerance needs to be respected to minimize the risk of a rectovaginal or vesico vaginal fistula. A macroscopic residual tumour after initial EBRT is treated with 80–90 Gy EQD_2, while a vagina that has been involved at diagnosis, but which has no signs of macroscopic disease at the time of BT, is treated with 60–70 Gy EQD_2. These doses are prescribed to the vaginal surface, and additional vaginal dose points should be calculated at a 5 mm depth from the cylinder surface.

10.1.7. Interstitial implants

Interstitial BT might be required in the treatment of advanced primary cervical carcinomas, with extensive parametrial or vaginal involvement.

Interstitial techniques can be divided into pure interstitial and combined intracavitary–interstitial, as in the case of the Vienna applicator (see Fig. 3) [90, 91]. Blunt interstitial needles are placed into the parametria through holes in the ring, which serve as a template for guidance. The dosimetry of an implant for the Vienna applicator is based on the intracavitary dose distribution, which has a dose contribution from the interstitial needles that is limited to approximately 10%. Currently, tandem ovoid type applicators are available with the same option for being combined with interstitial needles [112, 113].

The pure interstitial approach implies the use of template systems that are designed to assist in preplanning and to guide and secure the position of the needles in the target volume. All of these systems rely on pelvic examination to help in guiding the location and depth of the needle placement. The most commonly used template systems are: the Syed–Neblett device, the modified Syed–Neblett device and the MUPIT (see Fig. 3).

Some of these templates have incorporated a central cylinder that allows for the placement of intracavitary radioactive sources. Usually, all of the interstitial techniques require special training.

10.2. ENDOMETRIAL CANCER

Although adjuvant pelvic irradiation does not improve survival for intermediate risk or high risk early stage endometrial cancer patients, it reduces the rate of local recurrences, at a net positive cost compared with no postoperative therapy [114–117]. According to the results of the PORTEC-2 (postoperative radiation therapy for endometrial carcinoma) trial, it appears to be reasonable that adjuvant pelvic irradiation can be replaced by vaginal BT alone in high intermediate risk patients [118]. Ideally, the HDR BT scheme to be used is three to four fractions of 5–7 Gy each, which is prescribed weekly at 5 mm from the surface of the cylinder (vaginal vault mucosa) [119, 120].

For stages II and above, BT is given after postoperative EBRT as a boost to the vaginal vault. Ideally, the scheme to be used is three fractions of 5 Gy each, with one fraction per week prescribed at 5 mm from the surface of the cylinder [119].

Medically inoperable endometrial carcinoma can be treated with curative intent using radiotherapy alone. A double tandem intrauterine two channel HDR applicator (see Fig. 12), with or without a vaginal cylinder (see Fig. 13), or a Simon–Heyman applicator are used to deliver a boost radiation dose to the uterus [64].

FIG. 12. Rotte 'Y' applicator (courtesy of Nucletron, Netherlands).

FIG. 13. Martinez endometrial applicator (courtesy of Nucletron, Netherlands).

EBRT to the whole pelvis of up to 46–50 Gy over 23–25 fractions should be given along with two to three intracavitary applications of 6–7 Gy each [120]. Different dose specification points can be used depending on institutional practices [119].

10.3. VAGINAL CANCER

Early superficial lesions of less than 5 mm in depth are amenable to be exclusively treated using intracavitary BT [121]. Following EBRT (45–50 Gy over 23–25 fractions), vaginal BT is given as a boost to the primary tumour. If a major or complete response is achieved, then BT is given through a vaginal surface applicator, which is usually a multichannel device to avoid the uninvolved surface of the vagina. A total dose of 20–28 Gy in fractions of 3–8 Gy at a 5 mm tissue depth is usually given. When gross residual disease persists after EBRT, an interstitial implant through a perineal template should be used (see Table 6) [64, 121].

Special caution is required when treating primary vaginal cancer with HDR BT, due to the high risk of severe late complications such as vaginal wall necrosis and fistulas [64, 121].

10.4. BREAST CANCER

Since 1990, conservative treatment has been widely accepted as the best therapeutic option for the management of stages I and II breast cancer patients [122]. Lumpectomy and axillary dissection followed by postoperative radiation therapy to the whole breast achieve the same overall survival and local control as radical surgery. Conservative treatment does not increase the risk of developing cancer in contralateral breast, and cosmetic results are undoubtedly superior [123–126].

Conservative treatment should be avoided when any of the following clinical conditions is present [127]:

(a)   First two trimesters of pregnancy;
(b)   Prior radiotherapy to the same breast region;
(c)   Multiple primary tumours in different quadrants of the breast;
(d)   Extensive calcifications with malignant or indeterminate appearance throughout the breast.

In addition, while not being a formal medical contraindication, some patients who live in areas remote from centres that offer multidisciplinary treatment should not be treated conservatively [128, 129].

The locoregional conservative treatment for stage I and II breast cancer always includes postoperative radiation therapy. Otherwise, the local failure risk triples [123, 129]. The vast majority of recurrences develop near the lumpectomy site [123]. Therefore, there has been increasing interest to investigate whether irradiation of the tumour bed with some margin would provide the same results as treatment of the entire breast volume. This option, which is even more conservative than the current adjuvant standard, is known as partial breast irradiation.

10.4.1. Accelerated partial breast irradiation

Accelerated partial breast irradiation (APBI) is the treatment of the tumour bed with a high dose per fraction by completing the entire local postoperative course in five days or less [45].

A wide variety of APBI techniques have been described [45, 130–136]:

(a)   EBRT with photons, electrons, protons or combinations thereof:
   (i) 2-D EBRT;
  (ii) 3-D EBRT;
 (iii) IMRT;

(iv) Intraoperative radiation therapy.
(b)   HDR BT:
     (i) Interstitial multicatheter;
     (ii) Intracavitary using an inflatable balloon.

There is no consensus on recommendation of one BT technique over the others [133]. Most long term results are available from single institution studies using multicatheter interstitial high dose rate brachytherapy (MI HDR BT) [45, 133–135].

Several prospective randomized studies that compare APBI with whole breast irradiation were started in the early 2000s, but a longer follow-up is required before definitive conclusions can be drawn [137, 138]. Preliminary results demonstrate that, with a proper technique and strict criteria of patient selection, APBI provides excellent local control and cosmesis [139–152].

Not all candidates for conservative treatment are suitable for postoperative APBI [45, 134, 153, 154]. Patient selection includes patient dependent factors, histopathology findings, lymph node status and prior treatment characteristics (see Table 7). Despite some minor discrepancies between the Groupe Européen de Curiethérapie (GEC)–European Society for Radiotherapy and Oncology (ESTRO) recommendations and American Society for Therapeutic Radiology and Oncology (ASTRO) consensus statement, there is general agreement that only the patients who have a low risk for local recurrence should receive APBI outside of investigational studies [45, 134].

TABLE 7. ASTRO AND GEC–ESTRO CRITERIA FOR LOW RISK PATIENTS

	Factors	ASTRO (2009)	GEC–ESTRO (2010)
Patient	Age	≥60 years	>50 years
	BRCA1/BRCA2 mutation	Not present	—[a]
Pathologic	Tumour size	≤2 cm	≤3 cm
	T stage	pT1	pT1–pT2 (≤3 cm)
	Surgical margin	Negative (≥2 mm)	Negative (≥2 mm)
	Histologic grade	Any	Any
	Lymphovascular space invasion	Not allowed	Not allowed

TABLE 7.   ASTRO   AND   GEC–ESTRO   CRITERIA   FOR   LOW   RISK PATIENTS (cont.)

	Factors	ASTRO (2009)	GEC–ESTRO (2010)
	Oestrogen receptor status	Any	Any
	Multicentricity	Unicentric only	Unicentric only
	Multifocality	Clinically unifocal (microscopic multifocality is allowed) with a total size ≤ 2 cm	Unifocal only
	Histology	Invasive ductal carcinoma Mucinous carcinoma Tubular carcinoma Colloid carcinoma	Invasive ductal carcinoma Mucinous carcinoma Tubular carcinoma Colloid carcinoma Medullary carcinoma
	Pure ductal carcinoma in situ	Not allowed	Not allowed
	Extensive intraductal carcinoma	Not allowed	Not allowed
	Associated lobular carcinoma in situ	Allowed	Allowed
Nodal	N stage	pN0 (i$^-$, i$^+$)	pN0
	Nodal surgery	Sentinel lymph node biopsy Axillary lymph node dissection	Sentinel lymph node biopsy Axillary lymph node dissection
Treatment	Neoadjuvant chemotherapy	Not allowed	Not allowed

Note: ASTRO — American Society for Therapeutic Radiology and Oncology; ESTRO — European Society for Radiotherapy and Oncology; GEC — Groupe Européen de Curiethérapie.

[a] —: data not available.

10.4.2. Multicatheter interstitial high dose rate brachytherapy

The most experience and the best documented long term follow-up results have been accumulated on the BT technique that involves the placement of interstitial catheters to the tumour bed. Although certain variations and preferences among different groups exist, interstitial insertion is usually performed under local anaesthesia between the fourth and sixth week after the lumpectomy. During the lumpectomy procedure, radio-opaque clips should be carefully placed to mark the surgical margins because this information is important for BT planning. The accumulation of secretions should be avoided to keep the postsurgical cavity closed until the BT date [149]. Fine needle aspirations are usually sufficient to drain seromas.

The first step in the interstitial BT is simulation with a special template in place to define the entry and exit points of the guiding needles (see Fig. 14).
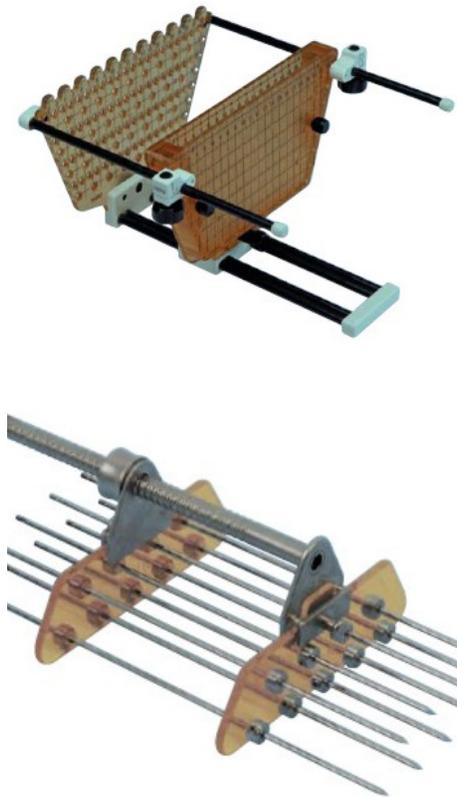
FIG. 14. Templates for interstitial breast BT (courtesy of Nucletron, Netherlands).

Basic dosimetry is performed according to the rules of the Paris system. The planning target volume (PTV) includes the lumpectomy cavity with reference to the radio-opaque markers with a 1–2 cm margin. The PTV should be covered by the 100% isodose, considering that the skin should not receive doses greater than 60% of the prescribed dose [149]. A preplan is designed from a 3-D reconstruction that combines conventional images or volumetric images (CT or MRI), if available [153].

After the preplan is approved by the therapy team, needles are inserted while maintaining a 15 mm distance between them [149]. In general, the needles are inserted in two or three parallel planes, with an arrangement that aims for an adequate PTV spatial coverage (see A of Fig. 15).

The replacement of needles by plastic catheters follows. A fixation button is placed at the end of each catheter, which prevents any possible displacement (see B of Fig. 15) [149]. Different radioactive sources can be used according to the institutional protocol and availability.

The most common MI HDR BT schedules for APBI uses two daily fractions with a minimum break of six hours between treatments. The full treatment is delivered in four to five days (see Table 8) [133, 140, 149].
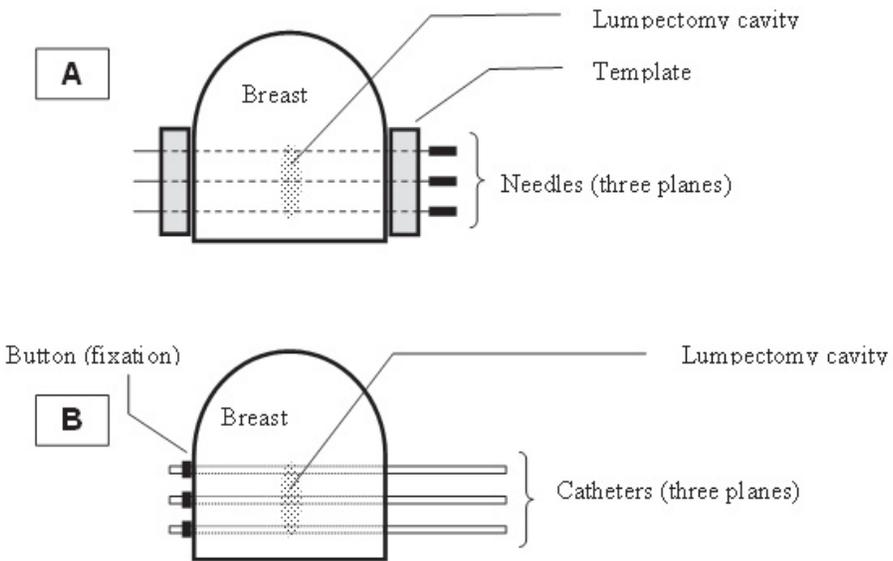
FIG. 15. A: Axial schematic representation of an interstitial BT implant for partial breast irradiation, with template and needle placements. B: Three catheter planes in an arrangement that replaces the needles.

TABLE 8. COMMON FRACTIONATION SCHEMES USED IN MULTICATHETER INTERSTITIAL HIGH DOSE RATE BRACHYTHERAPY FOR ACCELERATED PARTIAL BREAST IRRADIATION

No. of fractions	Dose per fraction (Gy)	Total dose (Gy)	Length of treatment (days)
10	3.4	34	5
8	4	32	4
7	4.33	30.3	4

10.4.3. Intracavitary high dose rate brachytherapy

Intracavitary BT is the second most common HDR technique for APBI. The best investigated applicator is MammoSite, a special catheter that is placed inside the surgical cavity (see A of Fig. 16) [136]. The end of the catheter is equipped with an inflatable balloon, which fits tightly in the postoperative cavity (see B of Fig. 16). The applicator can be placed during the lumpectomy procedure or later, as an outpatient approach [132, 155].
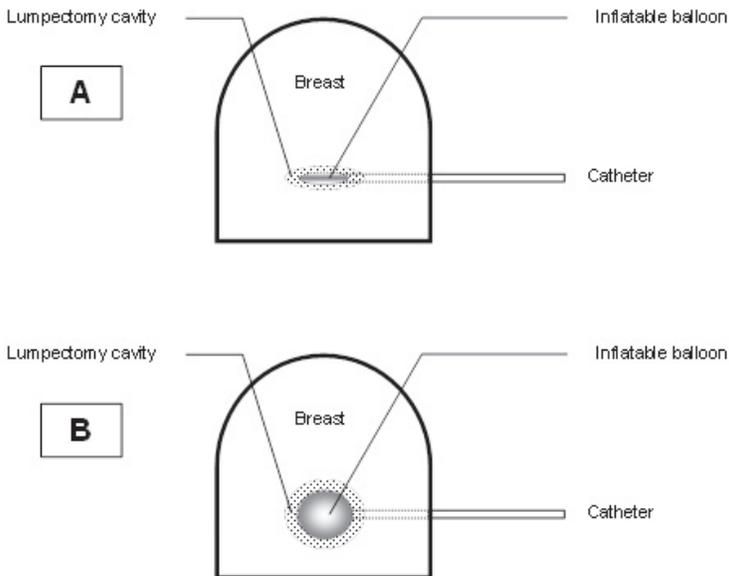

FIG. 16. A: Axial schematic representation of intracavitary BT for APBI with catheter placement. B: Cavity shape after the balloon is inflated.

Typically, treatment is delivered in ten fractions, with 3–4 Gy per fraction over five consecutive days. The dose is prescribed at 1 cm from the balloon surface [155, 156]. MammoSite breast HDR BT should not be used in postoperative cavities that are located less than 1 cm from the skin because the cosmetic results might be poor [136].

10.5. OESOPHAGEAL CANCER

Oesophageal cancer incidence presents large geographical differences, which are mostly attributable to different environmental conditions, social habits and hereditary factors.

The best identified risk factors are:

(a)   Tobacco and alcohol (Europe and North America);
(b)   Chewing tobacco and betel (India);
(c)   Hot beverages (northern Argentina, southern Brazil and Uruguay);
(d)   Nutritional (micronutrient) deficiencies, pickled vegetables, nitrosamine rich foods, mycotoxins (Central Asia, China and southern Africa);
(e)   Opium residues (Islamic Republic of Iran);
(f)   Pipe stem residues (South Africa);
(g)   Genetic factors (Japan, US Japanese, east and south-east Asia) [66].

Although an increased number of adenocarcinomas of the lower third of the oesophagus has been reported in Western countries, the most common histologic pattern worldwide is squamous cell carcinoma, which originates in the middle and lower third of the thoracic oesophagus [66]. Survival of oesophageal cancer remains poor (the five year survival rate is approximately 16% in the United States of America and 10% in Europe) [66]. Most cases are presented at an advanced stage, therefore treatment becomes mostly palliative. HDR BT has been used for the treatment of oesophageal cancer, either alone or in combination with EBRT [157–164].

Surgical palliation techniques of resection and bypass have been progressively replaced by endoluminal approaches performed using modern endoscopic technology. Oesophageal dilation offers prompt results in relieving dysphagia, but the effect lasts no more than four weeks. This procedure is generally used to insert a self-expandable metal stent, for which the palliative effect lasts five to six months. Neodymium-YAG (yttrium aluminium garnet) laser therapy is useful to treat dysphagia from tumours of the mid-oesophagus, although multiple procedures could be necessary to obtain satisfactory results with a variable duration of response of one to three months [164].

The HDR technique is relatively simple because a single line catheter is used for BT. The insertion is performed under sedation after surgical dilation and biopsy. Treatment is usually given using an intraoral access and a nasogastric tube or a special oesophageal applicator [165]. The applicator of the largest possible diameter should be used to minimize the mucosal dose. The segment to be irradiated can be confirmed by fluoroscopy or endoscopy. Superior and inferior margins of 1–3 cm from the tumour should be included in the treatment length. Palliative BT is commonly performed in one or two fractions, to a total dose of 10–14 Gy prescribed at 5 mm from the applicator surface [157, 165].

Oesophageal fistula, tumours of the cervical part of the oesophagus and stenosis, which cannot be bypassed, are absolute contraindications for BT [157, 165].

A series of IAEA trials have shown a significant benefit of HDR BT for the palliation of pain and dysphagia. A recent multicentre randomized trial demonstrated that two fractions of 8 Gy at one per week, combined with 30 Gy EBRT in ten fractions, were superior to HDR BT alone. Concurrent chemotherapy has also been evaluated, but it should not be used, owing to a high rate of grade 3–4 toxicity [157, 164].

Because a high dose is delivered to the oesophageal mucosa, possible complications include development of an oesophageal ulcer, fistula or stricture [166].

10.6. HEAD AND NECK CANCER

Head and neck cancer incidence is variable in different regions worldwide and is highest in States such as China and India. The two main risk factors that are associated with head and neck cancer are tobacco and alcohol consumption, and the disease is three times more common in men [167, 168].

BT is potentially useful in the treatment of carcinomas that involve the lips, tongue, floor of the mouth, tonsils, oropharynx, hypopharynx, nasopharynx, paranasal sinuses and neck. The most common method for BT administration is a combination with EBRT, although BT has been demonstrated to be successful as a sole treatment in early lesions and superficial recurrences after EBRT [169–171].

HDR BT can be used as an intraoperative procedure that allows the displacement of critical structures, building specific protections and accessing complex anatomical regions. The treatment plan is usually chosen from an atlas that contains predesigned plans for different types of applicator [169, 171]. HDR BT requires special caution when treating lesions that are located near to bony structures owing to the relatively high risk of osteoradionecrosis [169, 171–173].

Factors that are associated with the risk of mandibular osteoradionecrosis in radiotherapy include:

(a) Treatment related factors:
     (i) Total radiotherapy dose;
     (ii) Biologically effective dose;
     (iii) Photon energy;
     (iv) BT dose rate;
     (v) Combination of external beam irradiation and interstitial BT;
     (vi) Volume of BT overdosage or reference volume;
     (vii) Field size;
     (viii) Dose per fraction;
     (ix) Short interval between fractions (but not hyperfractionated therapy in itself);
     (x) Volume of the horizontal ramus of the mandible irradiated with a high dose;
     (xi) Use of a single ipsilateral radiotherapy field;
     (xii) Use of unilateral wedge arrangements;
     (xiii) Bone surgery in the case of postoperative irradiation.
(b) Patient related factors:
     (i) Severe parodontitis;
     (ii) Poor oral hygiene;
     (iii) Alcohol and tobacco abuse;
     (iv) Bone inflammation;
     (v) Pretreatment dental status;
     (vi) Dental extraction after radiotherapy.
(c) Tumour related factors:
     (i) Tumour size or tumour stage;
     (ii) Association of the tumour with bone;
     (iii) Anatomic site of tumour (higher risk in molar and retromolar regions).

There are no standard recommendations regarding the total doses and fraction sizes to be prescribed in HDR BT for head and neck cancer. However, when HDR BT is used as a sole treatment, each fraction dose should be limited to 4–6 Gy, and it should be lowered to 2.4–4.5 Gy when the method is used as a boost. A general consensus exists about the interfraction period, which should be a minimum of six hours [169, 171].

10.6.1. Oral cavity

HDR BT can be used as a sole radical treatment to manage stage T1–T2 N0 carcinomas. Most schemes use six to twelve fractions of 4–6 Gy each [174, 175]. In combined treatments, an HDR BT boost (six to ten fractions of 2.4–4 Gy each) usually follows a complete course of EBRT (45–50 Gy). Doses given to the cervical nodes that need to be treated commonly reach 45–60 Gy [171, 176, 177].

10.6.2. Oropharynx

An HDR BT boost can be a useful component of the primary tumour treatment following a 50–60 Gy EBRT course [178]. Boost doses vary between 16 and 30 Gy, with fractions no more than 4.5 Gy each [169, 171]. Some authors report a potential benefit of HDR BT boost when treating locally advanced oropharynx and oral cavity tumours (stages T3–T4) [179, 180].

10.6.3. Lip

Tumours that have a diameter of less than 5 cm can be exclusively treated with local BT. It is not necessary to add prophylactic EBRT to lymphatic chains owing to the very low incidence of regional node metastases in this clinical context. As in other tumour localizations in the head and neck, most published studies report their results using LDR BT and PDR BT (see Table 9) [167, 171]. However, some retrospective data report similar local control and adverse event probabilities using LDR, PDR or HDR BT techniques [177].

Lesions of 5 cm or more in diameter should receive combined treatment with EBRT and BT. In the presence of bone involvement, a surgical procedure is preferred [167, 169, 171]. The same approach should be used in cases of tumour recurrence after primary radiation treatment.

10.6.4. Nasopharynx

The nasopharynx is a mucosa lined cuboid cavity surrounded by bony structures, blood vessels and nerves. BT indications are limited to those lesions that do not have deep invasion and that show minimal residual disease after EBRT (with or without chemotherapy) or as a treatment for the superficial recurrences that are limited to the cavity [171].

The most widespread HDR BT technique uses a silicon applicator that is adaptable to the nasopharyngeal vault (see Fig. 17) [169, 181, 182].

TABLE 9. SQUAMOUS CELL CARCINOMA OF THE ORAL CAVITY AND OROPHARYNX: SUMMARY OF METHODS AND RESULTS ACCORDING TO ANATOMICAL SITE

Anatomical site	Tumour characteristics	Safety margin	Dose	Results
Lip	T1–T3	5–10 mm	60–75 Gy LDR/PDR	LC: 90–95% Nc: 2–10%
Buccal mucosa	T<4 cm	5–10 mm	60–75 Gy LDR/PDR or Boost 25–30 Gy if 45–50 Gy EBRT	LC: 80–90% Nc: <10%
Mobile tongue	T1–T3	5 mm	60–75 Gy LDR/PDR or Boost 25–30 Gy if 40–45 Gy EBRT	LC: >90%. Nc: 10–20%
Floor of mouth	T1–T2, N0	>5 mm	65 Gy LDR/PDR or Boost 10–25 Gy if 46–50 Gy EBRT	LC: >90% Nc: 10–30%
Oropharynx	T<5 cm	>10 mm	LDR/PDR: Boost 25–35 Gy following 45–50 Gy EBRT HDR: Boost 21–30 Gy/3 Gy fractions or 21–24 Gy/4 Gy fractions following 45–50 Gy EBRT	Base of tongue: LC: T1–2 80–90%; T3–4 65–80% Nc: 25% Faucial arch: LC: T1–T2 up to 90%; T3 67% Nc: 20%

Note: EBRT — external beam radiotherapy; HDR — high dose rate BT; LC — local control rate; LDR — low dose rate BT; Nc — necrosis rate; PDR — pulsed dose rate BT.

FIG. 17. Rotterdam nasopharyngeal applicator (courtesy of Nucletron, Netherlands).

Ideally, the scheme to treat T1–T3 tumours is to use EBRT up to 60 Gy followed by an HDR BT boost of 18 Gy in six fractions (3 Gy each, commonly prescribed at 10 mm from the mucosal surface), which are given on three consecutive days. In T4 lesions, EBRT reaches 70 Gy and the HDR BT boost reaches 12 Gy (four fractions, 3 Gy each on two days) [169, 171, 181, 182]. It needs to be taken into account that HDR BT has a limited role in the management of deep invasive nasopharyngeal carcinomas, owing to the abrupt dose fall-off and the presence of multiple critical structures that are neighbouring the nasopharyngeal cavity. The target volume should not exceed 10 mm in depth [171].

Preliminary results from a multi-institutional study conducted by the IAEA[2] showed a lack of benefit in terms of local control when an HDR BT boost was added to EBRT as part of the treatment for locoregionally advanced T3–T4 nasopharyngeal carcinoma.

10.7. LUNG CANCER

Lung cancer remains a major health problem worldwide. Although the disease had a lower incidence over a hundred years ago, the widespread dissemination and availability of tobacco products has led to a rapid increase in the worldwide incidence and mortality of lung cancer. The best reported five year survival rates are only 15% in developed countries [66].

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[2] Coordinated Reasearch Project E3.20.23, Resource Sparing Treatment of Head and Neck Cancer.

For patients with stage III non-small-cell lung cancer and a reasonable performance status, the treatment of choice is concurrent chemoradiotherapy [183]. Approximately 40–50% of patients with lung cancer experience malignant airway occlusion. Retrospective data show a high response rate when HDR BT is used for palliation. Clinical end points are time to reaeration, success of reaeration and relief of post-obstructive symptoms, such as chest pain, shortness of breath, cough and haemoptysis [184]. The risk of fatal haemoptysis is approximately 10%, with some series reporting higher rates [185–187]. Risk factors include upper lobe lesions, which are in close proximity to the pulmonary artery, repeated endoscopies when HDR BT is performed weekly and retreatment after definitive EBRT. In addition, the irradiated volume has been identified as a major risk factor that concerns life threatening haemorrhage after endobronchial HDR BT [186].

The application is usually performed jointly with a pulmonologist and requires endobronchial placement of one or more small sized catheters (diameter of 5 or 6 French), using a flexible fibre optic bronchoscope. These catheters can be left in place for either a few hours or a couple of days, depending on the selection of fractionation schedules. The University of Wisconsin, United States of America, reported an approximate 80% palliating rate of obstructive symptoms when using a single placement followed by fractionated HDR BT over two days, with the catheter left in place. Four fractions of 4 Gy each were delivered twice daily to yield an LDR equivalent of 20 Gy [188]. Another feasible fractionated HDR BT schedule recommends a total dose of 18 Gy given in three fractions (6 Gy each) over two days, which results in a shorter duration of the catheter, and 20 Gy in four fractions of 5 Gy each at one per week [184]. The dose is prescribed at 10 mm from the source axis when small applicators are used or at 5 mm from the applicator surface for large applicators [189].

Some authors have retrospectively compared their results regarding the use of HDR versus LDR BT for endobronchial obstruction palliation. The results showed similar response rates in terms of symptom control and adverse effect incidences. Hence, they recommend that the HDR technique should progressively replace the LDR technique because the first offers advantages such as eliminating a hospital stay, improved convenience for the patient and radiation safety for personnel [185].

HDR BT is an effective palliative treatment for selected patients who suffer from symptomatic endobronchial central relapse after EBRT [190]. For these cases, 60–70% response rates have been reported, although the incidence of fatal adverse effects could be high [185].

In conclusion, HDR endobronchial BT effectively palliates malignant airway occlusion and should be considered, when feasible.

10.8. PROSTATE CANCER

Prostate cancer is a health issue not only for men in Western countries but for men worldwide — especially considering recent epidemiological trends. With the introduction of the prostate specific antigen (PSA) test, the total number of diagnosed prostate cancer cases has increased. Recently, the results of a large European trial showed a reduction in prostate cancer associated mortality, which was related to PSA screening [191]. However, a trial in the United States of America addressing the same subject did not report similar results [192]. Overdiagnosis and overtreatment are the most important adverse consequences of prostate cancer screening. The United States Preventive Services Task Force has recommended PSA screening for all men over the age of 75 years [193].

Dose escalation above 70 Gy has been proven to be beneficial in prostate cancer radiotherapy in consideration of higher cure rates with similar or lower incidences of late effects compared with standard radiation therapy. Dose escalation can be performed either with EBRT techniques (i.e. 3-D conformal radiation therapy, IMRT and proton beams) or with BT using temporary ^{192}Ir or permanent ^{125}I or ^{103}Pd seed implants [194–196].

The current standard of practice is to stratify patients according to predictive factors into risk groups because the risk group affects the outcome dramatically. For practical purposes, patients who have localized prostate cancer are usually divided into three risk groups: low, intermediate and high. Although there are many schemes that are proposed, National Comprehensive Cancer Network guidelines have been the most widely adopted in the United States of America (see Table 10) [197].

TABLE 10. NATIONAL COMPREHENSIVE CANCER NETWORK RISK STRATIFICATION

Risk level	Criteria
Low	T1–T2a and Gleason score 2–6 and PSA < 10 ng/mL
Intermediate[a]	T2b–T2c or Gleason score 7 or PSA = 10–20 ng/mL
High[a]	T3a or Gleason score 8–10 or PSA > 20 ng/mL
Locally advanced very high	T3b–T4
Metastatic	Any T N1 or any T, any N with M1

[a] Patients with multiple adverse factors can be shifted into the next higher risk group.

The optimal management of both localized and locally advanced prostate cancer remains controversial. Surgery, radiotherapy and hormonal therapy can be used alone or in combination to treat the different risk groups [198].

Theoretical advantages of BT in the form of temporary implantations include:

(a) Potential for 'boost-in-boost' radiation due to steep dose fall-off in the peripheral zone, which is the most common target location;
(b) A shorter learning curve compared with LDR implantations;
(c) No movement of the source in relation to the target volume within the time interval of radiation;
(d) More effective dose volume optimization potential of the stepping source technology;
(e) Potential of less toxicity due to the improved protection of risk areas, such as the urethra, rectum and bladder base as well as the penile bulb.

There are some disadvantages compared with the seed implant approach discussed in the literature:

— Because fractionation can occur with one implant, the needle to target relationship can change compared with the initial situation, so a high level of quality assurance is necessary before each application of radiation;
— Lack of comparative and prospective randomized studies on quality of life;
— Unclear cost compared with LDR treatments. However, in high workload centres, HDR monotherapy could have an economic advantage.

10.8.1. High dose rate brachytherapy as a boost

The most common application of temporary BT in prostate cancer is its use as a local dose escalation method that is complementary to external beam techniques. This combination allows lower normal tissue doses in the surrounding tissue and a very high local dose to the tumour. This treatment is indicated in intermediate or high risk cases that do not have nodal involvement or metastases. Indications, contraindications and commonly used dose schedules are available in the literature [199]. Fractions and doses are widely variable, but they are in the range 1–15 Gy to four fractions of 3 Gy.

Long term follow-up data confirm that the HDR boost combined with external beam radiation results in excellent biochemical control rates [200–204]. In experienced hands, a 67–78% biochemical relapse free rate is achievable with a genitourinary/gastrointestinal toxicity rate of 5–7% for greater than G3 complications. Usually, temporary BT causes the same level of erectile

dysfunction as permanent or LDR seed implants, which is approximately 30–40%. Urethral strictures (approximately 8% G2 or higher) are the most common treatment related injuries following HDR prostate BT. Both clinical and dosimetry factors appear to influence the risk of stricture formation [205, 206].

It is noteworthy that androgen deprivation has a role in conjunction with BT. The role of combining neoadjuvant androgen deprivation and permanent prostate BT was to reduce the prostate to a size suitable for optimal implantation. Ebara et al. [207] show that a three month course of the neoadjuvant luteinizing hormone releasing hormone agonist resulted in effective volume reduction of 32–35% for an enlarged prostate.

Temporary BT using stepping source technology does not require special source preparation and causes no post-implant radiation protection problems. It also allows fractionated treatment schedules as well as individual dose optimization and high delivery quality assurance. The only disadvantage compared with LDR permanent seed implants is the need for fractionation, which results in a higher workload for the department. On the other hand, there might be some cost benefits to HDR implants, which can be seen if one compares the costs of the LDR seeds (which are used once per patient) and the HDR treatment (which is given over a fixed time period). The costs of the radiation source and workforce in the HDR treatments are stable, while the growing number of implanted seeds purchased for each patient continues to add up. This benefit would be applicable in departments that have a high volume of implants.

10.8.2. High dose rate brachytherapy as monotherapy

HDR fractionated monotherapy for prostate cancer was introduced by Yoshioka et al. [208], and feasibility studies were published by Martinez et al. [209] and Martin et al. [210]. Standard fractionated EBRT (i.e. 3-D EBRT and IMRT) or permanent seed implantation are the most common methods for delivering radiotherapy in low risk patients. However, radiobiological considerations (very low α/β ratio of prostate cancer) suggest that hypofractionation could be an advantage due to much shorter treatment times and lower costs than those in IMRT and seed implants, with comparable outcome levels [211, 212].

HDR BT as monotherapy has indications that are very similar to those used for seed implantation, for patients with low risk prostate cancer. There is a difference in the fractionation approach: some groups use three to four implantations, while others use two implantations with three to four fractions. The dose per fraction varies in the range of 8.0–9.6 Gy in the peripheral zone. The time interval between the fractions needs to be a minimum of six hours. There are no published phase III clinical investigations that compare HDR monotherapy

with other radiotherapy methods. The available phase II studies suggest that there is an excellent biochemical response with no differences seen in acute and late toxicity between the dose schemes of 34 Gy in four fractions, 36 Gy in four fractions or 31.5 Gy in three fractions [213, 214].

Experienced groups report five year biochemical control rates of 91% (Phoenix definition, nadir + 2 ng/mL) and local control rates of 98.9% [215].

The incidence of BT relating to normal tissue injury could be minimized by using advanced technology or strict rectal dose constraints (V40 < 8 cm^3 and D5 cc > 27 Gy) as well as by keeping the volume of high dose areas low [216–218]. Rigorous quality assurance practices can avoid unplanned dosimetry changes between different fractions by using the same implant [219].

The role of antiandrogen treatment as a complementary approach to HDR monotherapy in prostate cancer has not yet been systematically investigated.

HDR fractionated monotherapy is still in its early development. The relatively small number of reported patient series and the relatively short follow-ups require regular updates to produce mature data. Therefore, evidence based consensus is required for generating dose and fractionation schedule guidelines for this type of prostate interstitial BT.

10.8.3. High dose rate brachytherapy as salvage treatment

HDR BT has been used as a salvage approach for isolated local recurrences after previous EBRT or permanent seed implantation [220, 221].

10.8.4. High dose rate prostate implantation technique

HDR implantation can be performed before or after EBRT because an insignificant prostate volume change is expected [222, 223]. However, individual variations can occur, and the effect of oedema should be considered when planning EBRT after single fraction HDR prostate BT [222].

In most cases, HDR implantation is performed under spinal or general anaesthesia with the patient in the lithotomy position. Data on the use of local anaesthesia with or without sedation is also available [224–226]. Different perineal templates can be used for needle guidance to obtain an optimal implant (see Fig. 18).

Prostate stepper template

Porter perineal applicator set

MUPIT applicator set
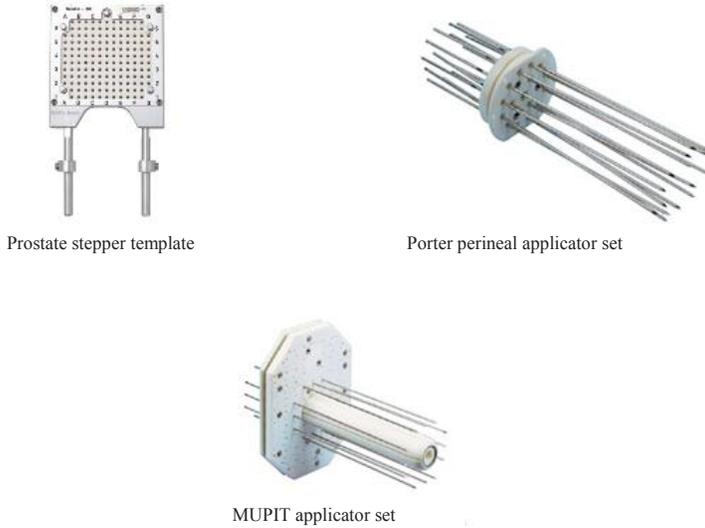
Note: MUPIT — Martinez universal perineal interstitial template.

FIG. 18. Applicators for prostate HDR BT (courtesy of Nucletron, Netherlands).

A transrectal ultrasound (TRUS) probe that is linked to a stepping unit is usually positioned as parallel as possible to the prostatic urethra. The apex and base of the gland need to be clearly identified. Fiducial markers are inserted into the apex and the base of the prostate to ensure quality control of any needle displacement during the treatment and to allow corrections whenever necessary [227].

Since real time TRUS based procedures can provide better prostate imaging quality than CT, and the procedure can be performed in the operating room within 10–15 minutes, this method is recommended in many existing guidelines [199]. Descriptions of both the TRUS based and CT based procedures are given below, and the steps of a TRUS based HDR implant procedure are detailed in Ref. [228].

Following adequate anaesthesia and positioning of the patient in the lithotomy position, a Foley catheter is introduced. The catheter can be filled with aerated gel for improved visibility on TRUS images.

After checking for potential pubic arch interference, as well as for prostate position projection to the perineal template grid on the screen of the TRUS machine, a 3-D TRUS volume is created. Imaging starts at half of the Foley balloon in the bladder and finishes at the penile bulb. Additional methods can help to define the geographical location of the intraprostatic tumour load (e.g. magnetic resonance spectroscopy image matching and Doppler TRUS)

and can influence the planned needle geometry within the prostate. Needles are implanted from the medial to the lateral section of the gland using axial TRUS image guidance.

The peripheral zone and detectable areas of capsule invasion are usually implanted with approximately 1 cm needle separation. If necessary, additional needles are used to cover the apical part of the prostate. In the case of base involvement, needle tips are inserted into the bladder because the first possible source position is approximately 6–8 mm behind the trocar tip of the needle. The implantation starts in the ventrodorsal direction, and right/left needles are implanted, one after the other, to avoid procedure related torsion of the gland. On the sagittal view, each needle is then forwarded to the base of the prostate under visual control.

After completing the implant procedure, a 3-D TRUS volume is created and analysed to control the needle geometry. It is easy to improve its geometry, if necessary. If the geometry of the implantation is acceptable, then the capture of 1.0 mm transverse images via a video connection from the TRUS unit to the planning computer is performed. The capture starts at least 5.0 mm cranial to the needle tips and ends 5.0 mm caudal from the apex. Delineation of the volumes of interest (prostate, rectum, bladder and urethra) is performed, and individual needle positions in the virtual 3-D volume are noted.

After creating an appropriate dose distribution, the needles are connected to the afterloading machine and radiation is given. After completing a fraction of the radiation treatment, the needles and any in vivo dosimetry devices are removed. Recommended dose constraints vary between different publications and are listed in the GEC–ESTRO temporary BT recommendations [199].

Alternatively, Slessinger et al. [223] describe the CT based HDR BT technique. TRUS is used to identify the prostate and to place gold marker seeds at the base and apex. With the stepper stabilizer and template in place, needle placement is performed at the largest cross-section of the prostate. Needles are placed to allow for peripheral coverage with approximately 1 cm needle spacing. In addition, two to four interior needles, depending on the prostate size, are placed midway between the urethra and the peripheral needles. Fluoroscopy and flexible cystoscopy are used to confirm adequate needle insertion depth. Once the needle implantation is completed, a template photograph is obtained in the operating room. A special CT compatible board can be used to move the patient from the operating room table to the CT table and to the hospital bed because a stable needle insertion depth requires leg movement to be minimized. CT scanning is performed once the patient is released from the recovery room. CT images (with diluted contrast filling the bladder) are obtained to evaluate and adjust the needle insertion depth to assure adequate coverage at the prostate base. Once the adjustments are complete, rectal contrast is introduced, the needle obturators

are withdrawn and 2.5 mm axial CT slices are acquired from the level of the mid-Foley balloon to the perineum. The needles contain only air and appear as dark spots on the CT images.

After the CT scan, the level at which the needles emerge from the template are marked to document the catheter position. The CT study is exported to the treatment planning computer. The radiation oncologist delineates the planning target, urethra and rectal dose points. Implant needle catheters are then reconstructed, and active dwell positions are selected. The maximum urethral dose is limited to 110% of the prescription dose based on the contoured volume, and the anterior rectal dose points at the rectal contrast interface are not allowed to exceed 75%. In addition, the volume that receives 125% and 150% of the prescribed dose should not be greater than 50% and 25% of the target volume, respectively. The total planned treatment time is verified using an independent method. A range of doses has been deemed to be acceptable. Slessinger et al. [223] recommend 9.5 Gy followed seven days later by another implant that delivers another 9.5 Gy when the BT is administered as a boost to supplement the external beam radiation. The patients who are treated with monotherapy receive six HDR treatment fractions (7 Gy/fraction). For monotherapy, the patient has two operating room procedures, each of which is associated with an operating room day treatment, and two fractions the following day, which are a minimum of six hours apart. The following day, before the treatments, radiographic imaging is obtained. Adjustments to the catheter insertion depth are made based on a comparison with the baseline orthogonal film set obtained shortly after the planning CT scan.

It is important to note that on completion of each treatment session, the patient is surveyed using a calibrated radiation instrument to confirm that the HDR source is safely stored.

A summary of the HDR implantation procedure is given in the following:

(a) A perineal template that will be used for needle guidance during the procedure is prepared.
(b) Following adequate anaesthesia and positioning of the patient in the lithotomy position, a Foley catheter filled with aerated gel is introduced.
(c) To create a 3-D TRUS volume, imaging for the volume starts at the half of the Foley balloon that is in the bladder and finishes at the bulb of the penis. Implantation of needles with approximately 1 cm of needle separation is performed from the medial to the lateral section of the gland, using axial TRUS image guidance. The implantation starts in the ventrodorsal direction, and right/left needles are implanted. On the sagittal view, each needle is then forwarded to the base of the prostate under visual control.

(d) Fluoroscopy and flexible cystoscopy are used to confirm an adequate needle insertion depth.

(e) Once the needle implantation is completed, a template photograph is obtained in the operating room. Imaging is performed after the procedure. The type of imaging depends on the BT technique:
— If the BT technique is ultrasound based, then a 3-D TRUS volume is created after the procedure. Corrections to the geometry can be performed at this point.
— If the BT technique is CT based, then a CT compatible board is used to move the patient from the operating room table to the CT table and to the hospital bed to maintain a stable needle insertion depth. CT scanning is performed, and adjustments can be made to the needle depth.

(f) The volumes of interest (prostate, rectum, bladder and urethra) are delineated. Implant needle catheters are then reconstructed, and active dwell positions are selected. Planning is performed based on 1 mm transverse images.

(g) Before each fraction, radiographic imaging is obtained. Adjustments to the catheter insertion depth are performed based on a comparison with the baseline orthogonal film set obtained shortly after the planning CT scan. Fiducial markers should be placed at the apex and base if this method of verification is used.

(h) The needles are connected to the afterloading machine, and radiation is administered. After completing the radiation treatment fraction, the needles and any in vivo dosimetry devices are removed.

(i) It is important to note that on completion of each treatment session, the patient is surveyed using a calibrated radiation instrument to confirm that the HDR source is safely stored.

10.9. OTHER SITES

HDR BT has also been used to treat soft tissue sarcomas, cancers of the bladder, urethra, bile duct, brain, skin, anus and rectum [17, 18, 65, 175, 229]. Because the use of BT in these sites is uncommon in low and middle income countries, these applications are not discussed in this publication.

11. CLINICAL ADVANCES IN HIGH DOSE RATE BRACHYTHERAPY

While current indications for HDR BT have been addressed in Section 10, some of the recent clinical advances in this field should be considered when planning a new HDR programme. One way to improve the therapeutic ratio of HDR BT is to deliver irradiation during surgery while the patient is still under anaesthesia. This technique (intraoperative HDR BT) allows radiosensitive normal tissue to be retracted or shielded during surgery, which lowers the radiation dose to normal tissue [175]. In addition, because irradiation is given under direct vision, the risk of a geographical miss is reduced. Best achievable tumour debulking is an aim. The tumour bed is irradiated using special intraoperative applicators with parallel HDR catheters embedded in them, at least 1 cm apart. The use of a fixed geometry applicator allows the patient to be treated without delay, using a preplanned atlas or library for the selected applicator. Doses of 10–20 Gy are usually given as a single fraction over 10–60 min. Ideally, the surgery should be performed in a shielded operating room with remote anaesthesia and a television monitoring system. Publications on intraoperative HDR BT in rectal cancer, soft tissue sarcomas, and head and neck cancer are available [230–239].

When starting a new programme, a shielded operating room with appropriate imaging facilities (e.g. mobile C-arm or mobile cone beam CT unit) should be integrated into the plan, if intraoperative HDR BT is considered. Because of the restricted availability of fully equipped and shielded operating rooms, only a limited number of institutions perform intraoperative HDR BT [175].

Some HDR devices are certified as transportable radioactive containers. This approach allows different hospitals to use an HDR afterloader on a shared basis in cases in which centres do not have a sufficient patient load to justify the purchase of individual devices.

The development of miniature sources allows for percutaneous interstitial BT through very thin needles (21 gauge). This approach could be of particular advantage for the treatment of lip, nose and eyelid tumours and for percutaneous image guided treatment of intrathoracic or intra-abdominal tumours.

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ABBREVIATIONS

AAPM	American Association of Physicists in Medicine
APBI	accelerated partial breast irradiation
ASTRO	American Society for Therapeutic Radiology and Oncology
BT	brachytherapy
CT	computed tomography
EBRT	external beam radiation therapy
ESTRO	European Society for Radiotherapy and Oncology
GEC	Groupe Européen de Curiethérapie
HDR	high dose rate
ICRU	International Commission on Radiation Units and Measurements
IMRT	intensity modulated radiation therapy
LDR	low dose rate
LMIC	low and middle income country
MDR	medium dose rate
MI HDR BT	multicatheter interstitial high dose rate brachytherapy
MRI	magnetic resonance imaging
MUPIT	Martinez universal perineal interstitial template
PDR	pulsed dose rate
PSA	prostate specific antigen
PTV	planning target volume
QALY	quality adjusted life year
RTT	radiation therapy technologist
TPS	treatment planning system
TRUS	transrectal ultrasound

CONTRIBUTORS TO DRAFTING AND REVIEW

Binia, S.	International Atomic Energy Agency
Engineer, R.	Tata Memorial Hospital, India
Fidarova, E.	International Atomic Energy Agency
Gilley, D.	International Atomic Energy Agency
Grundei, B.	Bayreuth Hospital, Germany
Hoskin, P.	Mount Vernon Cancer Centre, United Kingdom
Pellizon, A.	Hospital AC Camargo, Brazil
Petereit, D.	Rapid City Hospital, United States of America
Pötter, R.	Medical University of Vienna, Austria
Rosenblatt, E.	International Atomic Energy Agency
van der Merwe, D.	International Atomic Energy Agency
Venselaar, J.	Dr. Bernard Verbeeten Institute, Netherlands
Zubizarreta, E.	International Atomic Energy Agency

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