Cancer Care Ontario
Action Cancer Ontario

Imaging Strategies for Definitive Intracavitary Brachytherapy of Cervical Cancer

Recommendation Report

A project developed by the The Ontario Gynaecological Community of Practice (CoP) of the Radiation Treatment Program of Cancer Care Ontario:
Imaging for cervix brachytherapy and moving towards CT/MRI access

Report Date: June 2014

Ontario
Cancer Care Ontario
Action Cancer Ontario

CONTENTS

1. INTRODUCTION

Scope

These recommendations suggest various imaging strategies for the definitive treatment of cervical cancer, utilizing intracavitary brachytherapy. In this document, best practice recommendations will be outlined, discussing the roles of various imaging modalities and stratifying them in terms of clinical evidence for cervix brachytherapy. The necessary resources required to implement each strategy successfully will be documented. In doing so, these recommendations provide a long-term direction for image guided brachytherapy (IGBT) of cervical cancer in the province of Ontario.

Intended Users

These recommendations are targeted towards radiation oncologists, physicists, dosimetrists and radiation therapists for the purpose of IGBT of cervical cancer. The recommendations may be useful in the development of new, and improvement of already established, image guided cervical brachytherapy programs in Ontario. These recommendations can also be used to identify and improve access to personnel with core expertise in the implementation and maintenance of IGBT programs for cervical cancer.

Development of Recommendations

The recommendations have been developed by the "Imaging for Cervix Brachytherapy and Moving Towards CT/MRI Access" Working Group, which was established by the Radiation Treatment Program - Gynaecology Community of Practice (CoP) for Ontario. Current clinical practice and peer-reviewed literature have been considered during the development process.

The final recommendations report was formulated as follows:
Based on clinical evidence from peer-reviewed literature.
Consideration was given to current IGBT practices and resources for cervical cancer within the province (See Appendix A – summary of current state of IGBT in Ontario).

2. BEST PRACTICE RECOMMENDATIONS FOR IMAGE GUIDED BRACHYTHERAPY (IGBT) OF CERVICAL CANCER

It is the recommendation of the Ontario gynaecological CoP that the use of volumetric imaging is the best practice for cervix brachytherapy treatment planning. Furthermore, MR imaging must be a component of any imaging strategy implemented to ensure informed clinical decisions. These recommendations assume that ultrasound is routinely used to guide the insertions of the uterine applicators and to prevent perforations [1, 2]. Given these recommendations, this document defines MR/CT volumetric imaging strategies for IGBT of cervical cancer based on their impact in improving clinical outcomes and reducing toxicities as reported in available peer-reviewed literature. Best practices suggest the following ranking in order of most recommended to least recommended strategy (please see subsequent sections for full discussion):

1. **MR image guided adaptive brachytherapy**: MR images are acquired at each insertion for the purposes of treatment planning.

2. **MR-CT Hybrid planning**: MR images are acquired for the first fraction, followed by subsequent CT imaging.
   Pre-first-fraction MR imaging: MR images are acquired with applicator in place, then MR images are used for treatment planning, and subsequent fractions use fused MR and CT images for conformal avoidance.
   Post-first-fraction MR imaging: CT images are used for treatment planning and delivery, then MR images are acquired with applicator in place, and subsequent fractions use fused MR and CT images for conformal avoidance.

3. **MR aided CT based planning**: CT images are acquired at each insertion for the purposes of treatment planning.
   Diagnostic and pre-brachytherapy MR: In addition to CT images, diagnostic MR and pre-brachytherapy (<5days) MR images (i.e. post-external beam radiation therapy MR images), are available to inform treatment planning.
   Diagnostic MR: In addition to CT images, diagnostic MR only is available to inform treatment planning.

2.1. MR image guided adaptive brachytherapy

Preamble

MR guided adaptive brachytherapy has recently been endorsed by the GEC-ESTRO as the preferred method of delivering brachytherapy for cervical cancer. It is generally accepted that MR images provide superior soft tissue resolution in comparison to CT and ultrasonography imaging. This improved soft tissue resolution enables the determination of cervical tumour size, extent and location [3-13]. Moreover, the delineated tumour on MR images more accurately represents the true target volume as compared to clinical exam or CT imaging [4, 6, 12, 14]. The use of repeated imaging and planning at each brachytherapy fraction tracks the topographical changes that result from the target volume shrinking, thereby ensuring coverage of the target volume while also limiting dose to the organs at risk [4, 14].

Furthermore, there have been results from mono-institutional prospective clinical trials that demonstrate clear improvements in local control with limited treatment-associated morbidity [9-11]. The first of these trials by Pötter et al. demonstrates high control rates of 95-100% at 3 years for limited disease (IB1/IIB proximal less than 4-5) with G3+G4 late morbidity rates of less than 5%. For more advanced disease (IB2, IIB more than 5 cm, IIB) local control rates of 85-90% can be expected with G3+G4 morbidity rates of less than 5%[9]. These improvements in local control are expected to translate into improvements in overall survival [9-11, 13, 15]. The promise of MR guided adaptive brachytherapy has led to the creation of an ongoing multicentre study on this topic: EMBRACE (www.clinicaltrials.org, www.embracestudy.dk). EMBRACE started accrual in 2008 from 30 participating institutions internationally and by the end of 2013 is expected to have accrued a total number of 1000 patients.

The implementation of an MR guided adaptive brachytherapy protocol for locally advanced cervical cancer is recognised as being challenging for most radiation therapy programs [7]. MR image guided adaptive brachytherapy (MR IGABT) optimally incorporates the latest in volumetric imaging to effectively treat locally advanced cervix cancer, as such this should be the ultimate goal as IGBT practices evolve within each cancer program. The following sections discuss some of the challenges and their proposed solutions, and provide resources for centres that would like to implement an MR IGABT program.

2.1.1 Imaging Equipment / Software

Appropriate imaging is critical throughout the treatment chain for brachytherapy of the cervix cancer. The different stages where imaging is necessary include guidance for applicator placement and verification of immobilization, contouring of target volumes and OARs, and geometric reconstruction of the applicators.

2.1.1.1 Verification of applicator placement and immobilization:

Ultrasonography should be used to guide the placement of the intra-uterine applicator intra-operatively and limit perforations [1, 2, 16]. Once the applicators have been placed, it is important to ensure immobilization of the applicator during the patient transfers between applicator insertion, MR imaging and treatment delivery. For centers in the process of implementing volumetric planning, imaging may be necessary to verify applicator immobilization; ultrasound or radiographic imaging devices available in the HDR suite can be used for this purpose. This practice may be discontinued once adequate experience and confidence has been established in the applicator immobilization during patient transfer.

2.1.1.2 MRI Scanner Access:

Typically, radiation oncology teams have limited experience with MR imaging, making the implementation of an MR IGABT program challenging. To increase the possibility of success and allow for future program development, a close collaboration with diagnostic radiology is encouraged. Such a partnership should be based on a common vision focused on improving the quality of care delivered to cervix brachytherapy patients. As part of the dialogue, it is important to stress the vital role diagnostic imaging can play to improve current treatment planning processes to the benefit of cervix brachytherapy patients. As a natural component of this collaboration, the development of programs centered on research as well as interdisciplinary mentorship should be fostered. This will not only strengthen the inter-departmental partnership but also ensure continued quality improvement and advancement. MRI access is recognized by the gynaecological community of practice as being a limiting factor in the implementation of MR IGABT. As such, three solutions that have already been implemented within the province are presented below:

1. The first approach is a multidisciplinary collaboration with the local radiology department whereby a diagnostic MR may be used for imaging cervix brachytherapy patients. Such a partnership will afford the radiation oncology program the opportunity to leverage and benefit from the expertise of MR radiologists, physicists, and technologists. A challenge with implementing this strategy is scheduling MR scan time on an already taxed clinical scanner. However, this can be achieved by either setting aside dedicated radiation therapy timeslots or by booking MR timeslots that have been scheduled at the time of the patient's first external beam radiation therapy treatment. This approach poses the additional challenge of having to transport patients to the radiology department safely, while maintaining patient and applicator positioning. Another issue is that it may be difficult to establish this collaboration given that resources are already stretched within each program. It is recommended that hospital administration be made aware of the clinical significance of an MR IGABT program, and thereby their support and endorsement can be used to facilitate the initiation of such collaborations.
2. The second approach is to make use of a dedicated radiation therapy MRI simulator. Challenges associated with implementing this strategy are that a dedicated radiation therapy MRI is a

significant infrastructure cost, and one that may not be achievable by most provincial programs in the immediate future. However, as the costs of MR scanners decrease and its use in radiation therapy becomes ubiquitous, a dedicated radiation therapy MR scanner may become more feasible. An additional challenge is that the expertise required to commission and operate an MR scanner does not traditionally exist within a radiation therapy program. This can be addressed by consultations with MR radiologists, physicists and technologists, or members of the gynaecological CoP who have experience in implementing such strategies.

3. The third approach is to establish a close partnership with the radiology department, whereby the MR is a shared resource. Similar to the first approach, the expertise already present in the radiology department can be leveraged to benefit the radiation oncology program. The challenge of properly implementing this type of framework is to ensure that the radiation oncology program can provide sufficient funding to offset the initial investment and operating costs of the MR suite. Given that only a fraction of the MR suite time will be dedicated to the radiation oncology program this approach may be more fiscally achievable rather than a dedicated MR simulator.

2.1.1.3 Image Reconstruction Software:

It is necessary to have an image reconstruction software that is capable of manipulating and transferring the MR datasets across a secure local network to the treatment planning system (TPS). This software needs to maintain the fidelity of imaging and demographic information during this transfer. Reconstruction software is conventionally found alongside the MRI scanner, and usually have rudimentary image processing capabilities, which are sufficient to manipulate standard T1 and T2 weighted axial imaging. In addition to these datasets, para-transverse, para-coronal, and para-sagittal images must also be transferred to the TPS [7, 8]. For 3D imaging sequences with isotropic voxel sizes, additional software may be required to re-slice the data sets into a data format that can be interpreted by the TPS [17-19].

2.1.2 Treatment equipment and software

2.1.2.1 Remote Afterloader:

In order to deliver treatments a remote afterloader is required. There are multiple vendors available for the remote afterloader on the market, principally Nucletron (an Elekta subsidiary) and Varian.

2.1.2.2 CT-MR Compatible Applicators:

Since treatment planning is required at each brachytherapy fraction, the applicators must be in place during imaging. As such, these applicators must be constructed from CT-MR compatible materials such that they pose no safety risk to the patient nor do they cause excessive artefact impairing their visualization. There are two main classes of CT-MR compatible applicators: plastic systems made out of polyetheretherketone (PEEK) and fluorinatedethylenepropylene (FEP); and systems made out of titanium [8, 18, 19]. Of the two systems, titanium applicators produce susceptibility artefacts that are not evident in the MR images of the plastic systems [18, 19]. While titanium applicators are physically smaller; which makes them easier to insert and more comfortable for patients, specialized strategies need to be developed to address the distortions they may introduce on applicator reconstruction and/or target delineation in the vicinity of the applicator.

2.1.2.3 Treatment Planning System and Fusion Software:

Since MR IGABT represents a departure from standard point-based treatment planning, the TPS used must be able to provide tools for contouring, catheter reconstruction, automated optimization, and dose-volume histogram analysis on 3D image datasets. As part of MR IGABT, there are several MR datasets that are acquired and used for treatment planning. Therefore, if image fusion capabilities do not already exist within the TPS, additional image processing software is recommended [17-19].

2.1.3 Quality Assurance (QA) equipment and protocols

2.1.3.1 Applicator Reconstruction:

Standard applicator commissioning and acceptance has been outlined in AAPM recommendations from Task Groups 40, 53, and 56, CAPCA as well as CPQR documents [20-24]. However, these pre-clinical commissioning steps are designed for radiographic imaging and do not adequately account for the specific requirements of MR imaging [25]. Specifically, standard dummy markers used in CT or radiography are not visible on or compatible with MR imaging. Therefore, special fluid-containing catheters may be required to visualize the internal lumen of the applicators such that they are visible in the MR datasets [19]. Specific strategies for catheter reconstruction have been reviewed and summarized by Hellebust et al [19]. A catalogue of applicator reconstruction techniques can be found in their supplementary data [19]. If necessary CT images can be used to reconstruct the applicators and subsequently be fused with the MR datasets [7, 8, 19]. Reconstruction errors can lead to significant misrepresentation of the delivered dose. As such, any technique used to reconstruct applicators must be validated and reconstruction uncertainties minimized [19].

2.1.3.2 Quality Assurance Program:

Each centre should maintain a periodic QA program for applicator imaging and reconstruction methods. Initial commissioning and periodic QA of contouring, source modeling, and dose calculations should be performed. Standard guidelines for applicator commissioning and QA requirements are available in AAPM Task Group reports 40, 53, and 56, CAPCA as well as CPQR documents [20-24].

2.1.4 Imaging protocol considerations

The standard MR dataset that is conventionally imported into the TPS for the purpose of treatment planning is a T2 weighted transverse dataset. In addition, images with orientations parallel and orthogonal to the axes of the applicator should be transferred to accurately reconstruct the applicator and thereby localize source dwell positions in relation to target volumes and OAR. The recommended imaging orientations are para-transverse, para-coronal, and para-sagittal [7, 8, 19]. In general, slice thickness should be less than 5 mm. Geometric distortions and susceptibility artefacts inherent in MR images must be evaluated before introducing a new imaging sequence into the treatment planning workflow. If necessary CT images can be used to reconstruct the applicators and subsequently be fused with the MR datasets [7, 8, 19]. Please refer to see Appendix B, Figure 1 for example of a patient care pathway for MR-IGABT.

2.1.5 Contouring

GEC-ESTRO has provided a comprehensive set of contouring guidelines, and it is recommended that these be followed, as this will facilitate contouring uniformity across the province [6]. At the start of an

MR IGABT program it is advised that contouring be performed in consultation with an MR radiologist to benefit from their experience in pelvic MR image interpretation.

2.1.6 Treatment planning

In cervix brachytherapy, correct applicator placement and proper dose optimization are vital for calculation and delivery of a conformal dose distribution. The failure to perform custom treatment planning for individual fractions may compromise the target dose coverage and increase risk of exceeding the tolerance doses of the OAR [26, 27]. Therefore, treatment planning should be performed at each brachytherapy fraction. The treatment plan should begin with a standard loading pattern and can then be further optimized through manual or graphical optimization techniques to cover the target volume or spare OAR[6, 24, 26, 28]. Caution should be exercised when optimizing standard plans using automated techniques. Small iterative changes to the standard plan should be made and after each iteration the dose distribution should be reviewed with respect to doses to ICRU 38 reference points as well as DVH parameters related to OAR sparing and target coverage[9-11, 29-33]. The recommendation of the gynecological communities of practice is that target coverage takes priority over OAR sparing during plan optimization.

2.1.6.1 Dose volume histogram parameters for plan optimization:

Evidence relating dose volume parameters to tumour control and toxicities was collected through an environmental scan and iterative search of the literature. 20 documents were identified as being most recent, relevant and comprehensive. The recommendations of the Gynae CoP working group are to support the dose volume parameters outlined in the EMBRACE Protocol. The EMBRACE protocol states that the reporting of dose volume parameters is to follow the GEC ESTRO Recommendations in a uniform way. The suggested values below are for reference only. Due to the lack of maturity in the available data, these recommendations should be used in concert with clinical judgment and with updated data if and when such becomes available.

The following plan optimization goals are recommended by the working group:

HR-CTV or Point A the EQD2 to point A or D90 doses should be between 80-96 Gy.
IR-CTV the EQD2 to D90 should be between 60-75 Gy.

Rectum the EQD2 dose to D2cc < 70-75 Gy

Bladder the EQD2 to D2cc < 90 Gy

Sigmoid the EQD2 to D2cc < 75 Gy

2.1.7.1 Treatment plan optimization:

During volumetric brachytherapy treatment planning it may become apparent that the standard “pear-shaped” distribution[26, 29, 34] is not ideal for a specific patient’s anatomy; therefore, modifications to the standard plan may be considered. It is reiterated that any changes to the standard plan should be done cautiously, whilst monitoring doses to the target in addition to the OAR. Two scenarios where changes to the standard plan may be appropriate are discussed below:

1. OAR dose(s) are below suggested tolerance DVH parameters:
   In this scenario, the dose distribution of the standard treatment plan, when applied to a patient's specific anatomy, affords the possibility to escalate the dose to the target volume while sparing the OAR(s). The compromise between dose escalation and a minor increase in potential toxicities should be based on clinical judgement and discussions with the patient.
2. OAR dose(s) are at or exceed suggested tolerance DVH parameters:
   In this scenario, the dose to the OAR(s) using the standard plan are at or exceed the suggested tolerance levels. To reduce the risk of toxicity while maintaining a good probability of local control, the standard plan may be altered to reduce the dose to the offending OAR(s). Clinical judgement based on tumour size from MR and clinical exam must be used to ensure that sufficient target coverage is achieved. It necessitates repeating that the recommendation of the gynecological communities of practice is that target coverage takes priority over OAR sparing during plan optimization.

The use of rigid applicators limits the extent to which a standard plan may be altered to three optimization strategies. Additional flexibility for optimization can be achieved through the introduction of an interstitial component to the cervix brachytherapy program. However, this is a specialized technique and requires specific training and expertise from the brachytherapy team, which is out of the scope of this document. The three optimization strategies available with rigid applicators are discussed below:

1. Scaling the dose distribution: The prescription dose can be increased/decreased in an iterative fashion to scale the size of the entire distribution. In effect, this modification will expand or contract the dose distribution while retaining the original shape of the standard plan.
2. Scaling relative applicator weighting: This optimization strategy changes the relative contribution of the ring/ovoids with respect to the intra-uterine tandem. Altering the weighting of the ring/ovoids will immediately impact the doses to surrounding OAR(s), in particular the vaginal mucosa, and therefore OAR(s) doses should be evaluated closely.
3. Manipulating individual dwell weights: Altering the activation state or dwell weights of individual dwell positions has the effect of distorting the shape of the standard plan. Scenarios where this technique may be used include: in the event that the intra-uterine tandem is situated beyond the target or has perforated the uterus, individual dwell positions can be inactivated. Additionally if the target volume exhibits laterality, the weighting on one side of the ring/ovoid can be increased relative to the contra-lateral side. While this strategy affords the most freedom for optimization, it also may have unpredictable consequences if multiple changes are made simultaneously. Therefore, it is preferred that small incremental changes are made to the standard plan with careful evaluation of target and OAR doses after each iteration.

2.1.7 Personnel

Standard personnel required for a brachytherapy program include board certified radiation oncologists, radiation therapy medical physicists, radiation therapists, dosimetrists, anesthesiologists, and nurses [1, 24]. For an MR IGABT program, it is recommended that the team be supplemented with individuals who have key expertise in the area of MR imaging. These include a board certified MR radiologist, an MR technologist, and an MR medical physicist. It is recommended that an MR radiologist be consulted, especially at the outset of a new MR IGABT program to help interpret and establish comfort with analysing the MR datasets. An MR technologist is required in order to operate the MR scanner and

ensure efficient and safe patient throughput. It is suggested that an MR physicist be consulted in order to optimize the imaging sequences to suit the particular applicator and situation at each cancer centre. However, using the validated sequences presented by Nag et al.[7] and discussed in the supplement to the GEC-ESTRO recommendations [8, 19] may be sufficient.

2.1.8 Training

Opportunities for practice enhancement and training should be provided to all personnel involved in the brachytherapy program. Workshops dedicated to the implementation of MR IGABT are available through the European Society of Radiotherapy & Oncology and through the American Brachytherapy Society. Some cross-over training is necessary for radiation therapists interacting with MR technicians in the simulation capacity of an MR suite. Similarly, MR technicians need to understand the brachytherapy treatment process so that imaging decisions can be made in an informed and cooperative manner.

2.2. MR-CT Hybrid planning

Preamble

As a first step towards MR image guided adaptive brachytherapy, MR images can be used in concert with CT imaging to clarify both target and avoidance volumes. Creative solutions can be found in work-flow models and in the patient care path to fit the patterns of care of the treating centre, while incorporating the wealth of information available from MR images. If CT is already being used for volumetric planning and conformal avoidance, MR imaging can be integrated into the process without significant disruption, to add additional soft tissue information in a hybrid approach.
Example treatment paths include:

1. The treating centre proceeds normally with applicator insertion, CT imaging and planning. Parallel to the planning stage, the patient is sent to the local MR imaging suite for image acquisition. When ready, the MR image set is fused to the CT and contours can be added or adjusted based on MR information. The plan is finalized only after all imaging information is available. This process is repeated for every insertion (see Appendix B, Figure 2).
2. The treatment path outlined in the first example above is used for the first insertion only. For subsequent fractions, the first insertion MR is fused to the current CT image, matching applicator geometry. This is particularly useful in the case of small tumours where sufficient information can be provided by a single MR image set[35].
3. In the case where it is not feasible to acquire an MR image before treatment occurs, an MR image is acquired after the first treatment is delivered, but before the applicators are removed. In this way, the subsequent CT images can be fused to the patient's anatomy with the applicators in place.

2.2.1 Imaging Equipment / Software

As described in the previous section, 2.1.1, appropriate imaging is critical through the treatment chain. In this variation, imaging equipment is expanded to include access to a CT simulator.

2.2.1.1 Verification of applicator placement and immobilization:

Briefly, ultrasonography should be used to guide the placement of the intra-uterine applicator intra-operatively and the applicators should be immobilized, as described in 2.1.1.1.

2.2.1.2 CT Simulator Access:

When the patient is ready to be transported after applicator insertion, they are taken to the cancer centre's CT simulator suite for imaging during a scheduled appointment time. Preferably large bore CT scanners with a flat tabletop (couch) should be used to obtain images for post-insertion treatment planning.

2.2.1.3 MR Scanner Access:

Access to a MRI suite is a similar problem with solutions as described in section 2.1.1.2.

2.2.1.4 Image Reconstruction Software:

It is necessary to have access to software that can import and fuse CT and MR data sets, while maintaining fidelity of imaging and demographic information during transfer.
Because this schema recommends planning primarily on the CT data set, the MR should be the secondary image set, fused to the primary CT image. All other comments regarding image reconstruction addressed in 2.1.1.3 are relevant.

2.2.2 Treatment equipment and software

Please see section 2.1.2

2.2.3 Quality Assurance (QA) equipment and protocols

2.2.3.1 Applicator Reconstruction:

Further to the discussion in 2.1.3.1, it is recommended in this schema that the applicator set be delineated on the CT image set, as it is a more reliable modality for this task than MR [36].

2.2.3.2 Quality Assurance Program:

Please see section 2.1.3.2

2.2.4 Imaging protocol considerations

2.2.4.1 CT Imaging:

With the help of therapists trained in CT simulation, the patient is transferred to the CT simulator couch by using a technique that enables a smooth transition from to the imaging table. A nurse or therapist should protect the ends of the applicators during the slide. When on the treatment couch, the patient should be set up such that the pelvic anatomy is in a repeatable position for subsequent imaging and treatment. This can be accomplished by various methods: two such approaches include the placement of pillows under their knees or through a a pelvic tilt to flatten the small of the back against the couch A

small amount of CT contrast can be placed through the catheter and into the bladder to aid in contouring. The therapists should then align the patient to lasers, so that an MR image can be more readily fused to this image.

CT imaging should be acquired at a CT slice thickness of ≤ 3 mm so that the applicator tips can be more accurately identified, because the applicators are in a plane perpendicular to the acquired axial slices. The imaging extent should extend at least 2-3 cm beyond the fundus, usually to the pelvic brim, and to about the midpoint of the vagina. The applicators, seen in the CT scout image, can be used as a guide.

The images are then exported to the planning system.

2.2.4.2 MR Imaging:

The patient should be set up such that their pelvic position is reproduced from CT imaging as this will aid in producing an image set that is similar to the CT sim image and make fusion easier, whether the MR hardware is a simulator or not. If it is a MR sim, tattoos should be aligned to lasers, and the flat-top couch should make fusion more accurate. However, because we are most concerned with matching a volume in the centre of the pelvis, a non-flat couch should not overly impede a successful fusion.

The image volume should be similar to that acquired for CT simulation.

Total scan time for MR imaging is longer than that for CT, and the Radiation Oncology department should coordinate with the attending diagnostic radiologist to ensure that an efficient imaging session is prescribed. As mentioned above in section 2.1.4, a True Axial T2 image set is what is necessary for fusion with the CT planning image set. If Radiology requires additional scans to make diagnostic comments, these should be kept to a minimum to expedite the planning and treatment process.

It is recommended that an attending diagnostic radiologist participate in the process, from image set prescription, as well as either expedient annotation of the T2 image sets, or through education of radiation oncology.

2.2.4.3 Patient Transport and Bed Transfer Between and At Imaging Suites:

If the MR suite is some distance from the brachytherapy suite, consideration must be made for the time of transport of the patient, and any accompanying staff. If staff are to be removed from the brachytherapy department to attend the patient through the MR Sim process, the department needs to account for their absence. As indicated in Figures 1 and 2, transport of the patient can also be a significant factor in the efficiency of the care path. In addition, with the addition of MR imaging in a CT workflow, two additional patient transfers are required to move the patient on and off the MR couch. However, fusing two scans that are separated by a transport and two transfers, can give the clinician confidence in the stability of the applicator's geometry. As indicated in the patient care path of Figure 1, the first task upon image fusion is to assess applicator stability.

2.2.5 Contouring

There are two clear advantages to using the CT image set as the core image for planning. First, it is ubiquitous in the radiation therapy department, and is easily accessible for image acquisition so that planning can be expedited. Also, due to its ubiquity, radiation oncologists are familiar with contouring on CT image datasets.

In terms of soft tissue tumours, MR has been shown to be clearly superior to CT in determining extent of cervical disease, as well as the normal uterine tissue[13]. CT and MR provide very similar results for contouring bladder, rectum, sigmoid colon and vagina[8], so it may be the clinician's preference to use the familiarity of CT to delineate these tissues.

2.2.6 Treatment planning

Using a CT-MR hybrid approach could allow for an efficient use of hospital resources, while enriching the data for the brachytherapy planning process. The CT image set may be easier to acquire within the cancer care program than an MR image set, and the planning process can therefore begin quickly in the patient care path. This reduces the urgency of acquiring an MR image set, and allows for the use of MR imaging resources that are perhaps not as conveniently located to the brachytherapy treatment area. Challenges would still include the physical location of the MR suite and co-ordination with the diagnostic radiology department, but there is a clear benefit to including the soft-tissue imaging data from MRI.

We recommend, in this scheme, that treatment planning on the CT data set proceed until the MR images are available. When fused, a HR-CTV can be outlined, and the organs at risk contours be evaluated. The plan can then be adapted to appropriately avoid the organs at risk, and the prescription dose coverage of the target can be evaluated.

The dose-volume histogram parameters required for this IGBT protocol have been described in section 2.1.6.1. The treatment plan optimization strategies have been described in section 2.1.6.2

2.2.7 Personnel

In addition to the standard personnel required for this schema described in 2.1.7. For a CT imaging, it is recommended that the team be supplemented with radiation therapists who have key expertise in the area of CT simulation.

2.2.8 Training

In addition to the suggested training in section 2.1.8 some cross-over training is necessary for radiation therapists interacting with MR technicians/MR certified radiation therapists in the simulation capacity of an MR suite. Similarly, MR technicians need to understand the brachytherapy treatment process so that imaging decisions can be made in an informed and cooperative manner.

2.3. MR aided CT based planning

Preamble

In gynaecological oncology, MR imaging is considered the ideal modality for accurate delineation of tumors of uterine cervix [1, 3-13, 26]. MR imaging provides both superior soft tissue contrast and enhanced anatomical details in comparison to Computed Tomography (CT) imaging for pelvic anatomy. Despite the established superiority of MR imaging, access to MR imaging for cervix brachytherapy remains a serious limitation. International surveys of patterns of practices show that radiography and CT based planning remain the dominant approaches to image guidance for cervix brachytherapy [37-39]. Several RT centres worldwide have reported on use of CT based treatment planning practices in cervical brachytherapy [40-46]. American Brachytherapy Society (ABS) consensus guidelines report that CT imaging, although a less sensitive compared to MRI, can estimate cervical diameter and afford meaningful clinical information [26]. CT imaging is considered acceptable for delineating the organs at risk (OAR) such as bladder, rectum and sigmoid colon. Differences between CT and MR drawn OAR contours have been found to be insignificant both in terms volume and in treatment planning dosimetry [12].

In order to promote best practices it is the recommendation of the Ontario gynaecological CoP workgroup that cancer centres with radiography based cervix brachytherapy programs, transition towards CT based volumetric planning approach [37]. The methodologies used in MR based contouring protocol may provide a framework for CT image-guided brachytherapy (CT-IGBT) of cervical cancer [12]. The following sections discuss some of the challenges and their proposed solutions, and provide resources for centres that would like to implement a CT-IGBT program.

2.3.2 Imaging Equipment / Software

Appropriate imaging is critical throughout the treatment chain for brachytherapy of the cervix cancer. The different stages where imaging is necessary include guidance for applicator placement and verification of immobilization, contouring of target volumes and OARs, and geometric reconstruction of the applicators.

2.3.2.1 Verification of applicator placement and immobilization:

Briefly, ultrasonography should be used to guide the placement of the intra-uterine applicator intra-operatively and the applicators should be immobilized, as described in 2.1.1.1.

2.3.1.2 CT Simulator Access:

Please see section 2.2.1.2.

2.3.2.3 Image Reconstruction Software:

It is necessary to have a DICOM compatible image reconstruction software that is capable of manipulating and transferring CT image datasets used in treatment planning process across a secure local network to the TPS. This software needs to maintain the fidelity of imaging and demographic information during this transfer.

2.3.3 Treatment equipment and software

Please see section 2.1.2

2.3.4 Quality Assurance (QA) equipment and protocols

2.3.4.1 Applicator Reconstruction:

CT imaging provides the optimal image datasets for applicator reconstruction. The geometric distortions that are evident in some MR image sequences are not evident in CT datasets. CT compatible dummy markers and applicators should be used to digitize the applicators as well as identify the first dwell position. Some treatment planning systems (TPS) offer applicator models that can be accurately overlaid on to the volumetric reconstruction of the imaged anatomy. These virtual models should be carefully examined at the time of TPS commissioning

2.3.4.2 Quality Assurance Program:

Each centre should maintain a periodic QA program for applicator imaging, digitization and reconstruction methods. In addition to the above, initial commissioning and periodic QA of contouring, source modeling, and dose calculations should be performed. Standard guidelines for applicator commissioning and QA requirements are available in AAPM Task Group reports 40, 53, 56, and CAPCA and CPQR documents [20-24]. AAPM Task Group report 66 provides QA guidelines for the CT simulators [47].

2.3.5 Imaging protocol considerations

Diagnostic MR images may be used to aid in delineating the target volumes on the planning CT images during CT-based volumetric treatment planning of cervical brachytherapy. The following sub-sections provide guidelines for MR and CT imaging for CT-IGABT:

2.3.5.1 MR Imaging:

The workgroup recommends the following MR imaging for CT-IGABT:
Ideally, pre-brachytherapy MR images within 5 days of the first insertion, should be acquired to inform CT based treatment planning. If this is not achievable, pre-EBRT diagnostic MR images may also be used to aid in CT based treatment planning. For a patient care path example on how to implement this protocol see Appendix B, Figure 3.

Please refer the Section 2.1.4 Imaging Protocol Considerations for additional details on MR imaging protocols.

2.3.5.2 Planning CT Imaging:

Volumetric treatment planning must be performed for each individual applicator insertion. CT images should be acquired after the applicator has been placed and should be used for treatment planning.

The imaged anatomy should include the entire applicator length and all volumes of interest for treatment planning. It is recommended that the imaging cover the anatomical region extending from the iliac crest to the ischial tuberosities [40]. Appropriate contrast agents could be used to aid in accurate delineation of volumes of interest e.g. bladder and rectum. This working group recommends a contiguous acquisition of CT slices of thickness $\leq$ 3 mm [26, 27, 40, 43]. An inter-slice separation less than or equal to the slice thickness should be used to avoid loss volumetric information on target, OARs and proper reconstruction of applicators,

2.3.6 Contouring

In CT based volumetric treatment planning contouring and dosimetric calculations are performed on the planning CT images. The following two sub-sections provide recommendations for the delineation of target and OAR structures:

2.3.6.1 Target Delineation:

While a direct fusion between diagnostic MR images and planning CT datasets is not advised for target and OAR delineation, a *reference* high-risk volume (HRV-CT) may be inferred on the planning CT images from the diagnostic MR and the clinical exam. The HRV-CT is purely a reference volume to monitor dose in a high-risk region; thus must not be used for optimization of the dose distribution.

2.3.6.2 OAR Delineation:

Published reports show insignificant differences between OAR volumes and dose to the OARs for CT and MR based treatment planning [12]. Therefore, planning CT images can be used to accurately delineate OARs such as rectum, bladder and sigmoid colon. Use of suitable contrast agents during the CT imaging improves accuracy in contouring of OARs.

2.3.7 Treatment planning

For the CT based schema, the Point A dose should be reported even if volumetric treatment planning techniques are used. Given that in this schema it is difficult to accurately delineate the target volumes on the CT dataset, it is imperative that target coverage (Point A doses) not be compromised to spare the OAR.

The dose-volume histogram parameters required for this IGBT protocol have been described in section 2.1.6.1. The treatment plan optimization strategies have been described in section 2.1.6.2

2.3.8 Personnel

The standard personnel required for this schema described in 2.2.7

2.3.9 Training

The suggested training required for this schema are as described in 2.2.8.

3. CONCLUSION

This report represents a key opportunity to gather, analyze and make recommendations on best practices for the definitive treatment of cervical cancer, utilizing intracavitary brachytherapy. This recommendation report has provides provincial evidence-guidance to Ontario's cancer centres and improve the care of cancer patients who receive intracavitary brachytherapy during their treatment. This report will be reviewed on a regular basis to determine whether the information is still accurate and relevant to current practice and revised accordingly.

For general inquiries regarding this report, please contact: eric.gutierrez@cancercare.on.ca or RTP@cancercare.on.ca.

ACKNOWLEDGEMENTS

This report was developed with the assistance of the Imaging for Cervix Brachytherapy and Moving Towards CT/MRI Access Community of Practice Leadership Group: Ananth Ravi PhD, MCCPM; Anthony Fyles, MD, FRCPC; Kathleen Surry, PhD, MCCPM; Wendy Wells BSc MRT(T); Chandra Joshi PhD, DRP, DABMP, MCCPM; Melanie Davidson, PhD, MCCPM and the Radiation Treatment Program: Eric Gutierrez, MRT(T), CMD, BSc; Elizabeth Murray, MA; Padraig Warde, MB, MRCPI, FRCPC.

DISCLAIMER

- This recommendation report was developed by a working group of the Gynecological Cancers Community of Practice of the Radiation Treatment Program of Cancer Care Ontario. The working group was comprised of gynecological cancers radiation treatment professionals belonging to the disciplines of radiation oncology, medical physics, and radiation therapy. The material presented in this recommendation report illustrates the consensus reached among members of the Gynecological Cancers Community of Practice and may not reflect current practice at all Ontario cancer centres. All approaches to treatment are subject to clinical judgment and actual practice patterns may not follow the material outlined in this report.
- This recommendation report may not reflect all the available scientific research and is not intended as an exhaustive report. CCO and Gynecological Cancers Community of Practice members assume no responsibility for omissions or incomplete analysis resulting from this recommendation report. It is possible that other relevant scientific findings may have been reported since completion of this recommendation report. This recommendation report may be superseded by an updated publication on the same topic.
- This recommendation report is not a clinical guideline or practice standard, and was not developed in collaboration with CCO's Program in Evidence-Based Care (PEBC). Evidence-based guidelines for Gynecological are available through the PEBC.
- This recommendation report is intended to be used for informational purposes only, by radiation treatment professionals. It is not intended to constitute or be a substitute for medical advice and should not be relied upon in any such regard. Any person seeking to apply this recommendation report is expected to use independent medical judgment in the context of

individual clinical circumstances or seek out the supervision of a qualified clinician. CCO and Gynecological Cancers Community of Practice members make no representation or guarantee of any kind whatsoever regarding the content, use, or application of this recommendation report and disclaim any responsibility for its application or use in any way.

COPYRIGHT

APPENDIX A

Summary of Current State of Assessment for Image Guided Brachytherapy of Cervical Cancer

Figure 1: Utilization of ultrasound (US) for applicator placement. Reasons given for lack of routine adoption of US imaging included: no access to a suitable US system (necessitating special Gyn consult when US required), impression that US does not provide useful information and US had not been considered for applicator placement. *1 of 3 centres only used US for patients without a Smit sleeve.

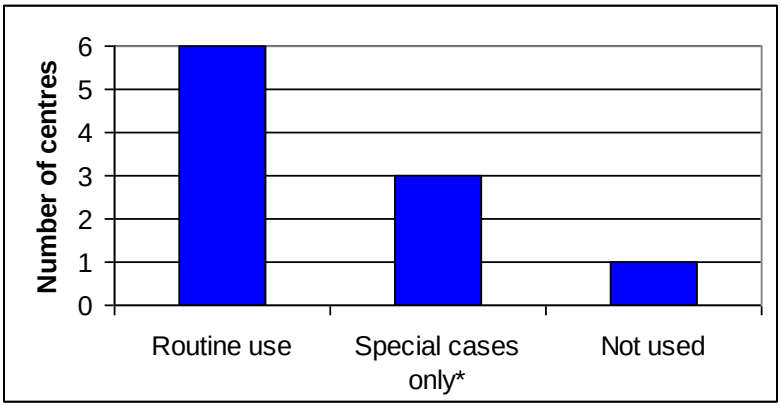


Figure 2: Strategies for applicator immobilization. *Foley balloon fitted over tandem filled with 30cc saline/contrast.

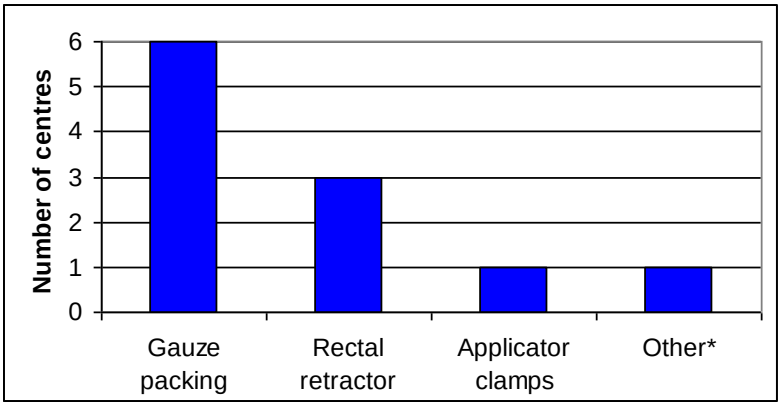


Figure 3: Imaging modality used for treatment planning. * 1 centre uses CT and MRI for first fraction, followed by CT for subsequent fractions, and another centre uses CT for first fraction, followed by orthogonal x-ray imaging for subsequent fractions.

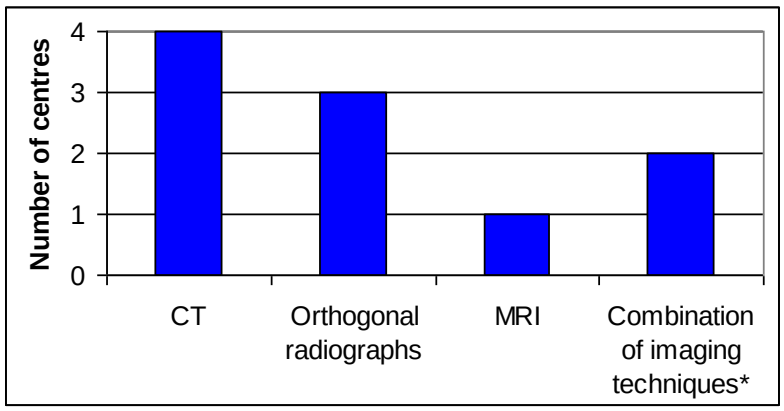


Figure 4: Access to diagnostic MR images, either taken prior to EBRT or within 5 days of first HDR brachytherapy session. 6 of the 10 centres polled have indicated that diagnostic MRI images are sometimes used to inform treatment planning (2 of 10 do this routinely).

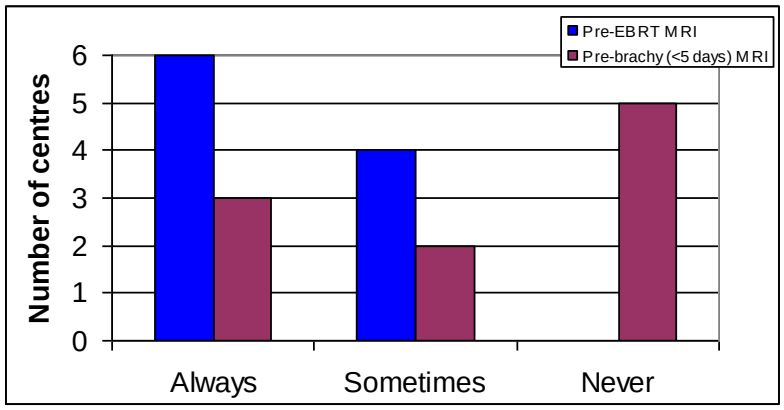


Figure 5: Dose / fractionation schedules. 1 centre delivers 2 fractions with a single insertion (all others perform an applicator insertion for each fraction)

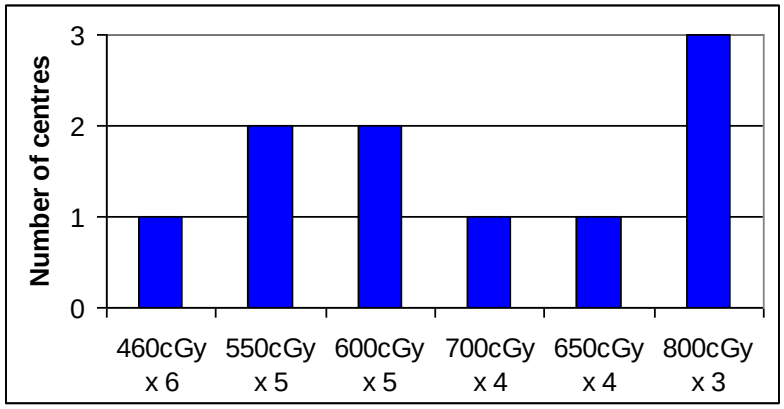


Figure 6: Verification of applicator position following treatment planning, prior to treatment

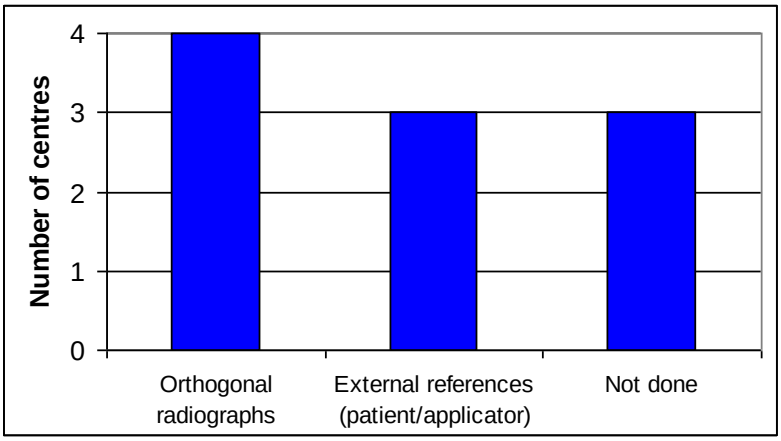
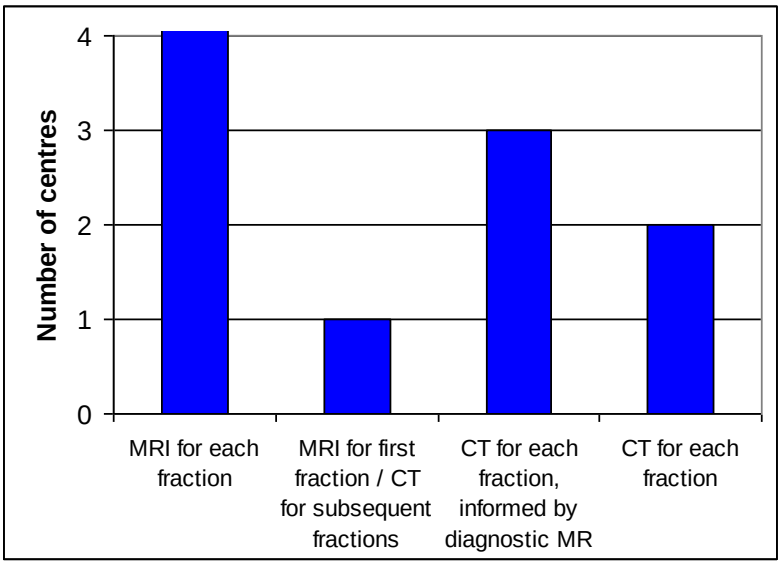


Figure 7: Target image guidance strategy to be implemented within the next 5 years. 2 additional centres have been included as they plan on starting an HDR cervix brachytherapy treatment program within this time frame.



APPENDIX B

Patient Care Path for each IGBT strategy

Legend to Flow Chart Shapes

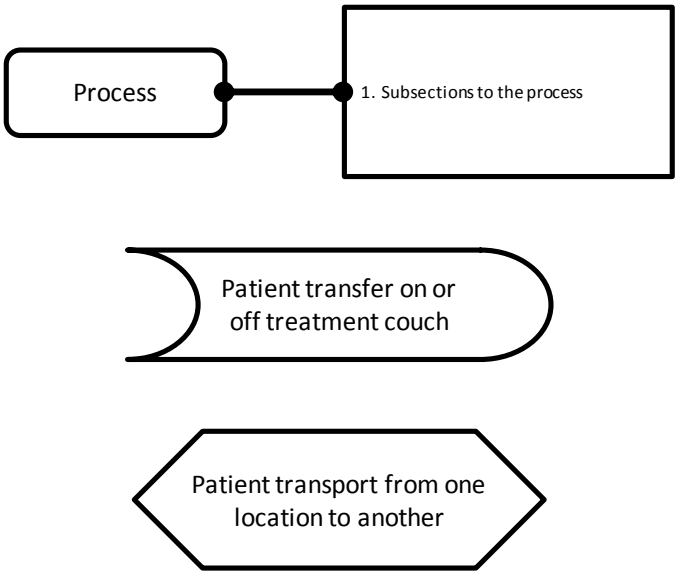


Figure 1: Patient Care Path Example MR for Planning

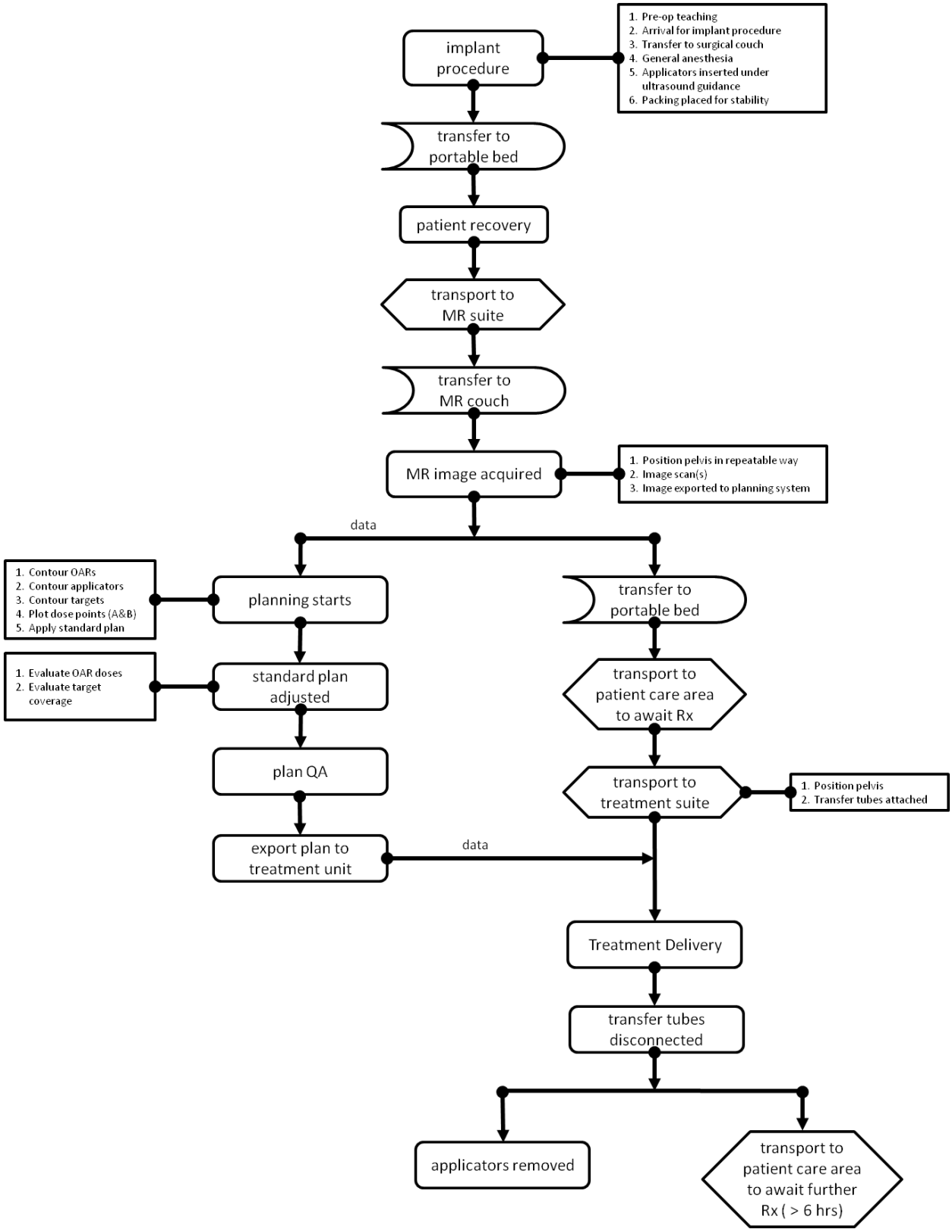


Figure 2: Patient Care Path Example CT and MR Fusion for Planning

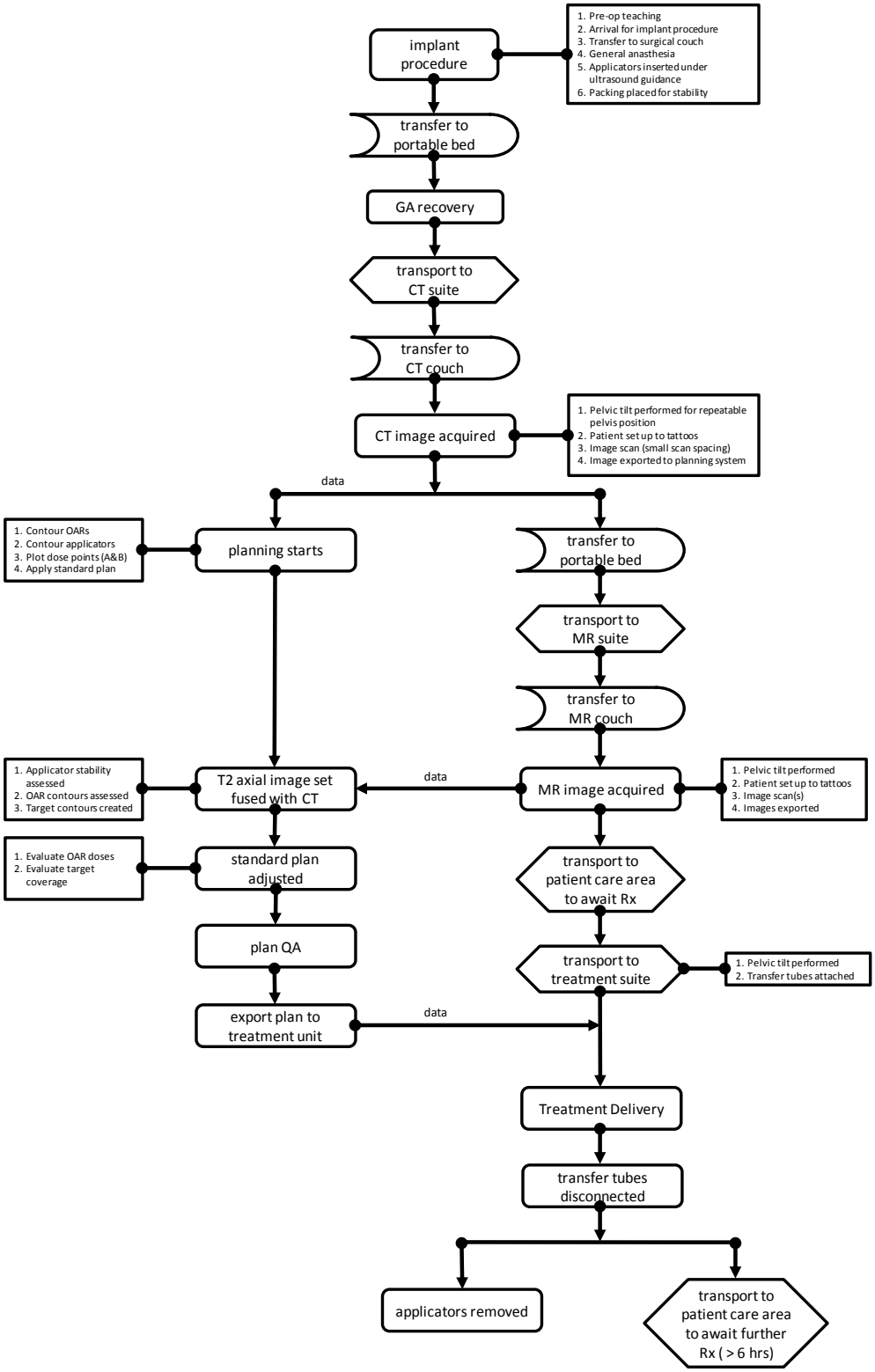
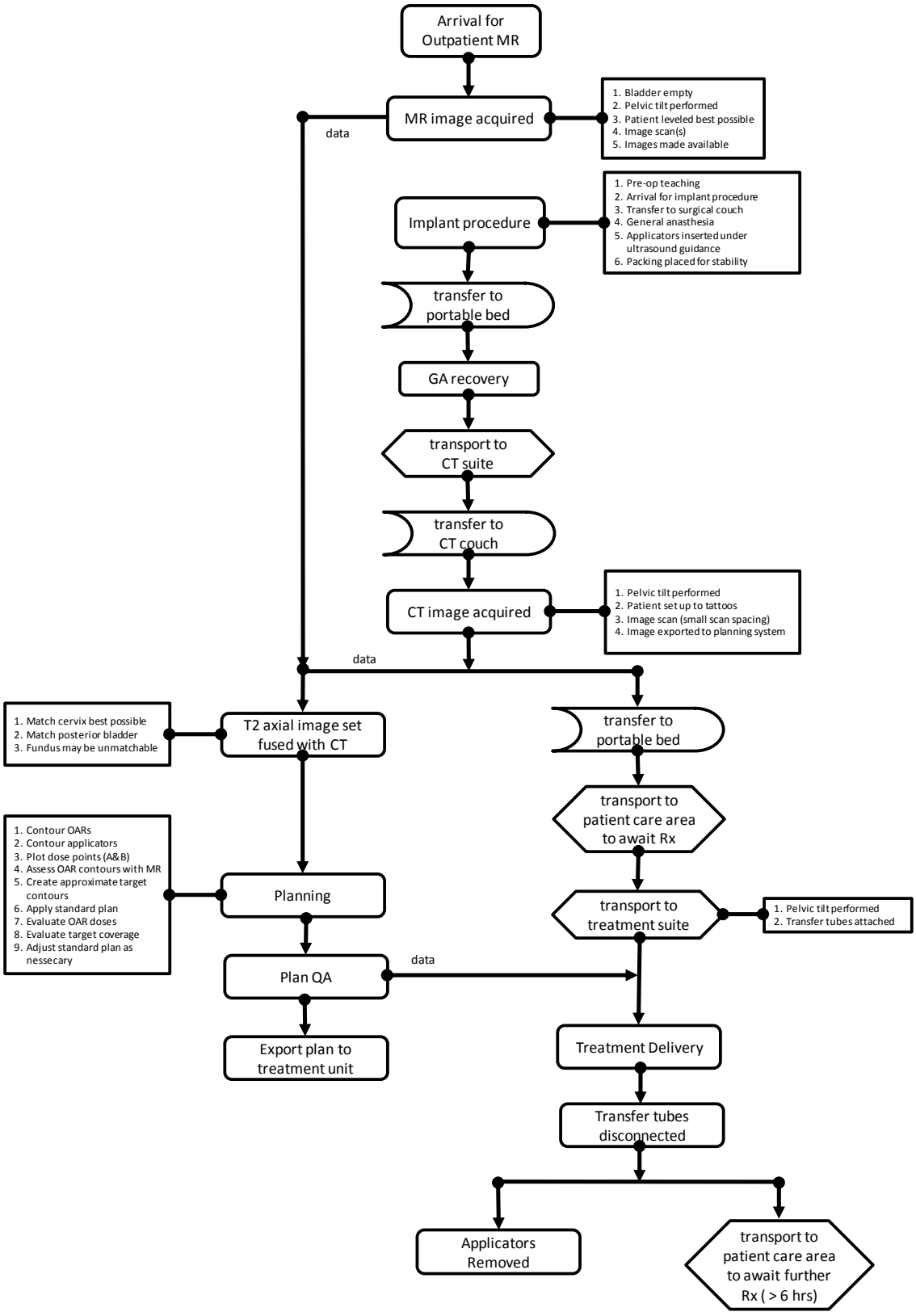


Figure 3: Patient Care Path Example Diagnostic MR and CT Planning



REFERENCES

1. G. Morton *et al.*, "Delivery of brachytherapy for cervical cancer: organisational and technical advice to facilitate high-quality care," Clin.Oncol.(R.Coll.Radiol) 22 (7), 605-614 (2010).

2. S. Van Dyk *et al.*, "Conformal brachytherapy planning for cervical cancer using transabdominal ultrasound," Int.J.Radiat.Oncol.Biol.Phys. 75 (1), 64-70 (2009).

3. J. C. Dimopoulos *et al.*, "Systematic evaluation of MRI findings in different stages of treatment of cervical cancer: potential of MRI on delineation of target, pathoanatomic structures, and organs at risk," Int.J.Radiat.Oncol.Biol.Phys. 64 (5), 1380-1388 (2006).

4. J. C. Dimopoulos *et al.*, "Inter-observer comparison of target delineation for MRI-assisted cervical cancer brachytherapy: application of the GYN GEC-ESTRO recommendations," Radiother.Oncol. 91 (2), 166-172 (2009).

5. J. C. Dimopoulos *et al.*, "Recommendations from Gynaecological (GYN) GEC-ESTRO Working Group (IV): Basic principles and parameters for MR imaging within the frame of image based adaptive cervix cancer brachytherapy," Radiother.Oncol. 103 (1), 113-122 (2012).

6. C. Haie-Meder *et al.*, "Recommendations from Gynaecological (GYN) GEC-ESTRO Working Group[star, open] (I): concepts and terms in 3D image based 3D treatment planning in cervix cancer brachytherapy with emphasis on MRI assessment of GTV and CTV," Radiotherapy and Oncology 74 (3), 235-245 (2005).

7. S. Nag *et al.*, "Proposed guidelines for image-based intracavitary brachytherapy for cervical carcinoma: report from Image-Guided Brachytherapy Working Group," Int.J.Radiat.Oncol.Biol.Phys. 60 (4), 1160-1172 (2004).

8. R. Pötter *et al.*, "Recommendations from gynaecological (GYN) GEC ESTRO working group (II): Concepts and terms in 3D image-based treatment planning in cervix cancer brachytherapy--3D dose volume parameters and aspects of 3D image-based anatomy, radiation physics, radiobiology," Radiotherapy and Oncology 78 (1), 67-77 (2006).

9. R. Potter *et al.*, "Clinical impact of MRI assisted dose volume adaptation and dose escalation in brachytherapy of locally advanced cervix cancer," Radiother.Oncol. 83 (2), 148-155 (2007).

10. R. Potter *et al.*, "Clinical outcome of protocol based image (MRI) guided adaptive brachytherapy combined with 3D conformal radiotherapy with or without chemotherapy in patients with locally advanced cervical cancer," Radiother.Oncol. 100 (1), 116-123 (2011).

11. K. Tanderup *et al.*, "From point A to the sculpted pear: MR image guidance significantly improves tumour dose and sparing of organs at risk in brachytherapy of cervical cancer," Radiother.Oncol. 94 (2), 173-180 (2010).

12. A. N. Viswanathan *et al.*, "Computed tomography versus magnetic resonance imaging-based contouring in cervical cancer brachytherapy: results of a prospective trial and preliminary guidelines for standardized contours," Int.J.Radiat.Oncol.Biol.Phys. 68 (2), 491-498 (2007).

13. R. Potter *et al.*, "Image-guided adaptive brachytherapy for cervix carcinoma," Clin.Oncol.(R.Coll.Radiol) 20 (6), 426-432 (2008).

14. J. C. Dimopoulos *et al.*, "MRI assessment of cervical cancer for adaptive radiotherapy," Strahlenther.Onkol. 185 (5), 282-287 (2009).

15. K. Tanderup *et al.*, "Adaptive management of cervical cancer radiotherapy," Semin.Radiat.Oncol. 20 (2), 121-129 (2010).

16. M. T. Davidson *et al.*, "Optimization of high-dose-rate cervix brachytherapy applicator placement: the benefits of intraoperative ultrasound guidance," Brachytherapy 7 (3), 248-253 (2008).

17. A. A. De Leeuw *et al.*, "Applicator reconstruction and applicator shifts in 3D MR-based PDR brachytherapy of cervical cancer," Radiother.Oncol. 93 (2), 341-346 (2009).

18. S. Haack *et al.*, "Applicator reconstruction in MRI 3D image-based dose planning of brachytherapy for cervical cancer," Radiother.Oncol. 91 (2), 187-193 (2009).

19. T. P. Hellebust *et al.*, "Recommendations from Gynaecological (GYN) GEC-ESTRO Working Group: considerations and pitfalls in commissioning and applicator reconstruction in 3D image-based treatment planning of cervix cancer brachytherapy," Radiother.Oncol. 96 (2), 153-160 (2010).

20. B. Fraass *et al.*, "American Association of Physicists in Medicine Radiation Therapy Committee Task Group 53: quality assurance for clinical radiotherapy treatment planning," Med.Phys. 25 (10), 1773-1829 (1998).

21. G. J. Kutcher *et al.*, "Comprehensive QA for radiation oncology: report of AAPM Radiation Therapy Committee Task Group 40," Med.Phys. 21 (4), 581-618 (1994).

22. R. Nath *et al.*, "Code of practice for brachytherapy physics: report of the AAPM Radiation Therapy Committee Task Group No. 56. American Association of Physicists in Medicine," Med.Phys. 24 (10), 1557-1598 (1997).

23. Canadian Association of Provincial Cancer Agencies, "Standards for Quality Control at Canadian Radiation Treatment Centres: Brachytherapy Remote Afterloaders," 2012 (10/16), (2006).

24. Canadian Partnership for Quality Radiotherapy, "QUALITY ASSURANCE GUIDANCE FOR CANADIAN RADIATION TREATMENT PROGRAMS," 2012 (10/16), (2011).

25. C. Dempsey, "Methodology for commissioning a brachytherapy treatment planning system in the era of 3D planning," Australas.Phys.Eng.Sci.Med. 33 (4), 341-349 (2010).

26. A. N. Viswanathan *et al.*, "American Brachytherapy Society consensus guidelines for locally advanced carcinoma of the cervix. Part I: general principles," Brachytherapy 11 (1), 33-46 (2012).

27. M. T. Davidson *et al.*, "Image-guided cervix high-dose-rate brachytherapy treatment planning: does custom computed tomography planning for each insertion provide better conformal avoidance of organs at risk?" Brachytherapy 7 (1), 37-42 (2008).

28. S. Nag *et al.*, "The American Brachytherapy Society recommendations for high-dose-rate brachytherapy for carcinoma of the cervix," Int.J.Radiat.Oncol.Biol.Phys. 48 (1), 201-211 (2000).

29. International Commission on Radiation Units and Measurements, "Dose and volume specification for reporting intracavitary therapy in gynecology," ICRU Report 38 (3rd ed), (1985).

30. J. C. Dimopoulos *et al.*, "Dose-effect relationship for local control of cervical cancer by magnetic resonance image-guided brachytherapy," Radiother.Oncol. 93 (2), 311-315 (2009).

31. P. Georg *et al.*, "Correlation of dose-volume parameters, endoscopic and clinical rectal side effects in cervix cancer patients treated with definitive radiotherapy including MRI-based brachytherapy," Radiother.Oncol. 91 (2), 173-180 (2009).

32. P. Georg *et al.*, "Dose-volume histogram parameters and late side effects in magnetic resonance image-guided adaptive cervical cancer brachytherapy," Int.J.Radiat.Oncol.Biol.Phys. 79 (2), 356-362 (2011).

33. P. Georg *et al.*, "Dose effect relationship for late side effects of the rectum and urinary bladder in magnetic resonance image-guided adaptive cervix cancer brachytherapy," Int.J.Radiat.Oncol.Biol.Phys. 82 (2), 653-657 (2012).

34. A. N. Viswanathan *et al.*, "American Brachytherapy Society consensus guidelines for locally advanced carcinoma of the cervix. Part II: high-dose-rate brachytherapy," Brachytherapy 11 (1), 47-52 (2012).

35. N. Nesvacil *et al.*, "Adaptive image guided brachytherapy for cervical cancer: A combined MRI-/CT-planning technique with MRI only at first fraction," Radiother.Oncol. , (2012).

36. C. E. Pelloski *et al.*, "Comparison between CT-based volumetric calculations and ICRU reference-point estimates of radiation doses delivered to bladder and rectum during intracavitary radiotherapy for cervical cancer," Int.J.Radiat.Oncol.Biol.Phys. 62 (1), 131-137 (2005).

37. S. Pavamani *et al.*, "Image-guided brachytherapy for cervical cancer: a Canadian Brachytherapy Group survey," Brachytherapy 10 (5), 345-351 (2011).

38. L. T. Tan, "Implementation of image-guided brachytherapy for cervix cancer in the UK: progress update," Clin.Oncol.(R.Coll.Radiol) 23 (10), 681-684 (2011).

39. A. N. Viswanathan and B. A. Erickson, "Three-dimensional imaging in gynecologic brachytherapy: a survey of the American Brachytherapy Society," Int.J.Radiat.Oncol.Biol.Phys. 76 (1), 104-109 (2010).

40. S. Beriwal *et al.*, "Three-dimensional high dose rate intracavitary image-guided brachytherapy for the treatment of cervical cancer using a hybrid magnetic resonance imaging/computed tomography approach: feasibility and early results," Clin.Oncol.(R.Coll.Radiol) 23 (10), 685-690 (2011).

41. H. C. Kang *et al.*, "3D CT-based high-dose-rate brachytherapy for cervical cancer: clinical impact on late rectal bleeding and local control," Radiother.Oncol. 97 (3), 507-513 (2010).

42. H. Kim *et al.*, "Dosimetric analysis of 3D image-guided HDR brachytherapy planning for the treatment of cervical cancer: is point A-based dose prescription still valid in image-guided brachytherapy?" Med.Dosim. 36 (2), 166-170 (2011).

43. B. Wang *et al.*, "Image-guided intracavitary high-dose-rate brachytherapy for cervix cancer: A single institutional experience with three-dimensional CT-based planning," Brachytherapy 8 (2), 240-247 (2009).

44. L. T. Tan *et al.*, "Clinical impact of computed tomography-based image-guided brachytherapy for cervix cancer using the tandem-ring applicator - the Addenbrooke's experience," Clin.Oncol.(R.Coll.Radiol) 21 (3), 175-182 (2009).

45. M. Gao *et al.*, "3D CT-based volumetric dose assessment of 2D plans using GEC-ESTRO guidelines for cervical cancer brachytherapy," Brachytherapy 9 (1), 55-60 (2010).

46. C. Charra-Brunaud *et al.*, "Impact of 3D image-based PDR brachytherapy on outcome of patients treated for cervix carcinoma in France: results of the French STIC prospective study," Radiother.Oncol. 103 (3), 305-313 (2012).

47. S. Mutic *et al.*, "Quality assurance for computed-tomography simulators and the computed-tomography-simulation process: report of the AAPM Radiation Therapy Committee Task Group No. 66," Med.Phys. 30 (10), 2762-2792 (2003).