AAPM Task Group Report 303 endorsed by the ABS: MRI Implementation in HDR Brachytherapy—Considerations from Simulation to Treatment

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Disclosure Statement:

The Chair of this task group reviewed the required Conflict of Interest statement on file for each member of AAPM Task Group # 303 and determined that disclosure of potential Conflicts of Interest is an adequate management plan. Disclosures of potential Conflicts of Interest for each member of AAPM Task Group # 303 are found at the close of this document.

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Abstract:

The Task Group (TG) on Magnetic Resonance Imaging (MRI) Implementation in High Dose Rate (HDR) Brachytherapy - Considerations from Simulation to Treatment, TG 303, was constituted by the American Association of Physicists in Medicine's (AAPM's) Science Council under the direction of the Therapy Physics Committee, the Brachytherapy Subcommittee, and the Working Group on Brachytherapy Clinical Applications. The TG was charged with developing recommendations for commissioning, clinical implementation, and on-going quality assurance (QA). Additionally, the TG was charged with describing HDR brachytherapy (BT) workflows and evaluating practical consideration that arise when implementing MR imaging. For brevity, the report is focused on the treatment of gynecologic and prostate cancer.

The TG report provides an introduction and rationale for MRI implementation in BT, a review of previous publications on topics including available applicators, clinical trials, previously published BT related TG reports, and new image guided recommendations beyond CT based practices. The report describes MRI protocols and methodologies, including recommendations for the clinical implementation and logical considerations for MR imaging for HDR BT. Given the evolution from prescriptive to risk-based QA,[1] an example of a risk-based analysis using MRI-based, prostate HDR BT is presented.

In summary, the TG report is intended to provide clear and comprehensive guidelines and recommendations for commissioning, clinical implementation, and QA for MRI-based HDR BT that may be utilized by the medical physics community to streamline this process. This report is endorsed by the American Brachytherapy Society (ABS).

I. Introduction: Purpose, Goals, and Rationale for the Task Group

A. Brief description of MRI-based HDR brachytherapy requirements

Brachytherapy (BT) has a long history in the treatment of cancer, with its initial applications performed shortly after the discovery and isolation of radium from pitchblende by Pierre and Marie Curie in 1898. Two dimensional (2D) imaging was the mainstay for image guidance for many years, as radiographs provided sharp subject contrast and detail between objects with significantly different attenuation properties. However, due to the limited differences in attenuation between different soft tissue types, 2D kilovoltage (kV) imaging does pose limitations in developing optimal treatment plans, for instance in the case of intracavitary applications. As such, BT treatment plans were traditionally designed to deliver a desired dose to a reference point relative to the applicator geometry.

As computed tomography (CT) and magnetic resonance imaging (MRI) have become more widely available in clinics and hospitals, BT imaging has transitioned from the use of planar to volumetric imaging, in particular for high dose rate (HDR) and pulsed dose rate (PDR) approaches using afterloading technology. Relative to planar radiographs, volumetric images can potentially provide better visualization of tumors and adjacent normal tissues. Over the last two decades, there has been increasing interest in MRI either in conjunction with CT or ultrasound (US) through a multi-imaging modality approach, or alone for image guidance.[2,3] Compared with CT, MR images have superior soft tissue contrast resolution that has demonstrated clear advantages for clinical assessment and radiotherapy treatment planning.[4,5] MRI has also proven to be advantageous because it allows for improved organ at risk (OAR) sparing and dose escalation to targets, adaptive imaging protocols, and multi-planar scanning and reconstruction.[4,6,7] Additionally, MRI is non-ionizing and does not require the use of radiocontrast agents, which can cause severe reactions in some patients.[4] These reactions were previously associated with an allergy to iodine, however, studies now suggest the response is due to the high osmolarity of these agents versus an iodine-specific reaction.[8,9]

Essential considerations in developing and implementing MRI for HDR BT include: 1) an MRI scanner (shared or dedicated radiation oncology MRI simulator) that meets the criteria outlined in this report; 2) MR safe or conditional ancillary equipment (e.g., applicators/needles, immobilization devices, transport table, stirrups) to support the proposed workflows; 3) Well-defined and documented clinical, quality assurance and safety procedures for each workflow; and 4) Appropriately trained and credentialed staff, as outlined in this report, to guarantee the safety and efficacy of these workflows in the MR environment.

In general, BT workflows involve diagnosis/staging, placement of intracavitary applicator(s) and/or interstitial needles, simulation imaging, treatment planning, pre-treatment implant verification, treatment delivery, and review of dose delivery to ensure the treatment was delivered as planned. MRI can be incorporated during most of these key steps, but for the purpose of this report, recommendations focus on clinical workflows, MRI acquisition parameters, commissioning and on-going quality assurance (QA), and practical considerations when implementing MRI in HDR brachytherapy.

B. Intracavitary and interstitial applications for gynecological and prostate BT

Over the last decade, several advancements have been made in the application of MRI for gynecological (GYN) and prostate BT. The July 2017 issue of the *Brachytherapy* journal focused on the utilization of MRI from diagnosis to treatment assessment in LDR and HDR BT for prostate cancer. The articles in this issue noted the evolution of MRI in the management of prostate cancer and its potential by providing clinicians the tools to ensure high quality curative treatment for patients. Additionally, gaps of knowledge, technical challenges, and barriers to MRI implementation were identified in each step of the process to provide a roadmap for future MRI education, training, research, innovation, and commercialization in prostate BT. For prostate cancers, MRI has been shown to be a superior diagnostic tool for the evaluation of dominant intraprostatic lesions (DILs), extracapsular extension (ECE), seminal vesicle invasion, and neurovascular bundle involvement.[10] Also, compared with US, MRI can reduce uncertainties associated with simulation, treatment planning, and treatment delivery.[11]

For GYN cancers, the Groupe Européen de Curiethérapie – European Society for Radiotherapy & Oncology (GEC-ESTRO) recognized the significance of volumetric imaging in the movement toward three-dimensional (3D) treatment planning, namely for cervical cancer, with the formation of the GYN GEC-ESTRO work group.[12-15] In the twenty years since its creation, the work group has published a series of recommendations to assist in the standardization of image-based BT treatment planning. This has included the definition of a common language and means of delineating the target volumes (i.e., low risk clinical target volume (CTV), intermediate risk CTV, and high risk CTV for the definitive treatment of cervix cancer), discussions on issues related to applicator reconstruction, and suggestions on the appropriate MR imaging sequences for treatment planning. Although these recommendations are helpful, their scope is limited to the experience of a few key institutions from Europe, North American, and Asia, and for magnetic field strengths of ≤ 1.5 T. The published International Commission on Radiation Units and Measurements (ICRU) Report 89[16] provides a description of current, volumetric imaging of the cervix with the addition of 4D adaptive target concepts, and updated radiobiology and dose volume histogram (DVH) parameter reporting for targets and OARs. It contains clinical examples of MRI-based treatment plans from European, North American, and Asian centers.

The present report covers the assigned Task Group (TG) 303 charges focused specifically on GYN and prostate; however, the principles may be applicable to other treatment sites using intracavitary and/or interstitial applications. The Task Group was charged to:

1. Describe workflow processes when implementing MRI in HDR brachytherapy from simulation to treatment for common sites such as gynecologic and prostate.
2. Develop recommendations for brachytherapy-specific MRI acquisition parameters.
3. Develop recommendations for the commissioning and on-going QA of applicators and/or needles when MRI is utilized with HDR brachytherapy.
4. Evaluate practical considerations arising when implementing MRI in HDR brachytherapy
    a. MR safety awareness for patients and staff when using HDR applicators
    b. Logistical and economic considerations for initial program development and maintenance

c. Geometric uncertainty, dosimetric uncertainty, and MRI-specific imaging artifacts

The recommendations presented reflect clinical practice standards for AAPM and American Brachytherapy Society (ABS) members. Readers should be aware that as technologies and methods evolve, the recommendations presented here may become obsolete, and this report represents best practices based on the current technical knowledge of the authors.

The report is organized into sections and subsections based on topics of interest. Section I provides a brief introduction and rationale for the utilization of MRI within HDR BT workflows. Section II includes a list of nomenclature and abbreviations used throughout the report. Section III provides a review of literature of various approaches to MRI guided BT, available applicators, a review of gynecologic and prostate clinical trials, a review of BT related TG reports, and new image guided recommendations beyond CT-based practices. Section IV describes MRI protocols and methodologies, including recommendations for the clinical implementation and logical consideration for MRI guidance. Section V presents an example of risk-based analysis using MRI-based, prostate HDR BT as a use case. Section VI provides recommendations to medical physicists related to clinical commissioning, MRI safety, process QA, and logistic and economic considerations. Section VII outlines potential future developments in MRI guided BT. Lastly, Section VIII provides a brief summary of the intent of the TG report.

Terminology used in this report is modeled after that used in other TG reports: “shall” or “must” are used when the activity is required by various regulatory agencies, “recommend” is used when it is expected that the procedure should normally be followed as described. However, there may be instances where other issues, techniques or priorities could force modification of the recommended practice. The term “should” is used when it is expected that local analysis of the situation may change the way a particular activity is performed.

Specific commercial equipment, instruments, and materials are described in the current report to illustrate the necessary clinical procedures. Such identification does not imply recommendation or endorsement by the AAPM, nor does it imply that the identified device is necessarily the best available for these procedures.

II. Nomenclature and abbreviations

- 1D – one dimensional
- 2D – two dimensional
- 3D – three dimensional
- ABS – American Brachytherapy Society
- ACR – American College of Radiology
- ADC – apparent diffusion coefficient
- ANR – artifact-to-noise ratio
- AAPM – American Association of Physicists in Medicine
- ASTM – American Society for Testing and Materials
- BT – brachytherapy
- CT – computed tomography

- CTV – clinical target volume
- DCE – dynamic contrast enhanced
- DIL - dominant intraprostatic lesion
- DIR – deformable image registration
- DMBT – direction modulated brachytherapy
- DVH – dose volume histogram
- DWI – diffusion weighted imaging
- Dxcc – maximum dose to the most exposed xcc of a given organ at risk (e.g., 2cc volume)
- DXX or DXX% - minimum dose to XX or XX% of a target volume (e.g., 90%)
- EBRT – external beam radiotherapy
- EMBRACE - IntErnational study on MRI-guided BRachytherapy in locally Advanced CErvical cancer
- ECE – extracapsular extension
- EPI – echo planar imaging
- EQD2 – equivalent dose delivered in 2 Gy fractions
- ERC – endorectal coil
- ETL – echo train length
- FDG – fluorodeoxyglucose
- FIGO – International Federation of Gynecology and Obstetrics
- FMEA – failure modes and effects analysis
- FOV – field-of-view
- FSE – fast spin echo
- GEC-ESTRO – the Groupe Européen de Curiethérapie – European Society for Radiotherapy & Oncology
- GNL – gradient nonlinearity
- GTV – gross tumor volume
- GU – genitourinary
- GYN – gynecological
- HDR – high dose rate
- ICRU – International Commission on Radiation Units and Measurements
- IGABT – image guided adaptive brachytherapy
- IMBT – intensity modulated brachytherapy
- IsoFSE – isotropic fast spin echo
- kV - kilovoltage
- LDR – low dose rate
- MBDCA – model-based dose calculation algorithm
- mp-MRI – multi-parametric magnetic resonance imaging
- MR – magnetic resonance
- MRI – magnetic resonance imaging
- NRG – This is a national clinical trials network group. The acronym NRG is derived from the names of its parental groups, the National Surgical Adjuvant Breast and Bowel Project (NSABP), the Radiation Therapy Oncology Group (RTOG), and the Gynecologic Oncology Group (GOG)[17]
- OAR – organ at risk
- MAR – metal-artifact reduction

- PDR – pulsed dose rate
- PDW – proton density weighted
- PET – positron emission tomography
- PIBS – posterior-inferior border of the pubic symphysis
- PI-RADS – prostate imaging-reporting and data system
- pMRI – parallel magnetic resonance imaging
- PSI – prostate seed implant
- PTV – planning target volume
- QA – quality assurance
- QC – quality control
- qMRI – quantitative MRI
- QM – quality management
- QMP – qualified medical physicist
- RAPS – real-time applicator position monitoring system
- rBW – readout bandwidth
- RF – radiofrequency
- RPN – risk priority number
- ROI – region of interest
- RTOG – Radiation Therapy Oncology Group
- SAR – specific absorption rate
- SE – spin echo
- SNR – signal-to-noise ratio
- SPACE – sampling perfection with application optimized contrasts using different flip angle evolution
- T1W – T1 weighted
- T2W – T2 weighted
- TE – echo time
- TG – task group
- TPS – treatment planning system
- TR – repetition time
- TRUS – trans-rectal ultrasound
- VISTA – volume isotropic turbo spin echo acquisition
- VFL – variable flip angle
- US – ultrasound

III. Background: Review of literature on MRI utilization for HDR BT

A. Summary of various approaches

CT is the most commonly available imaging modality in radiation oncology, and is widely used for BT planning. While CT is adequate for OAR delineation, GYN and prostate target contours have been shown to be larger on CT as compared to MRI.[18,19] For GYN HDR, MRI is considered to be the gold standard for target volume delineation, facilitating dose optimization to the target and adaptive planning. For prostate HDR, use of MRI is not yet considered a standard-of-care due to resource and infrastructure needs, complexity of an MRI integrated workflow, and reimbursement.[3,20,21] New approaches for prostate HDR BT have incorporated

MRI for its improved visualization, which can be used to boost the prostate or intra-prostatic volumes, as adjuvant therapy as well as monotherapy.[5,22]

When considering the integration of MRI within an HDR BT workflow, one should review the intended utilization (e.g., diagnosis, tumor response, implant guidance, post implant assessment and adjustment, and/or treatment planning), the available technology, location of the imaging and therapy equipment, as well as the time and staff resources that may be available. There are different approaches to incorporating MRI into the BT workflow as described in Section IV.A.

Regardless of the approach, it is important for users to be aware of the available MRI technology, namely the field strength and geometry of the main magnetic, as well as the gradient strength and linearity as these properties can affect the implementation of MRI-based/-guided HDR BT.[19,23]

i. Open bore MRI with <1.5 T magnetic field strength

Open MRI scanners are designed to allow the patient to lie between the two magnetic poles. Compared to cylindrical bore MRI scanners, they may offer greater patient comfort (reduced claustrophobia), greater accessibility to patients especially during interventional procedures, accommodation of larger patients, and greater variability in patient positioning. In terms of BT, the open configuration may be of particular interest for the guidance of interstitial implants, as it allows for direct access to the patient. The use of an open MRI unit has been reported for MRI-guided interstitial GYN BT.[24,25] As described in these references, the open MRI unit is located in a surgical suite and has a 60 cm bore with a 56 cm gap producing a field of 0.5 T. However, the use of open MRI systems is not widespread and no longer commercially available due to their limited field strength (≤ 1.2 T), which results in lower image quality (e.g., lower signal-to-noise ratio (SNR), lower contrast and contour sharpness, lower resolution), large geometric distortions due to field inhomogeneity and gradient nonlinearity, and greater motion artifacts due to the longer acquisition times compared to their closed bore counterparts.[5,19,23,26] For the duration of this report, the discussion will be limited to the use of closed bore MRI scanners alone or in combination with other imaging modalities, which will be termed as a multi-imaging modality approach.[27]

ii. Closed bore MRI with 1.5 T or 3.0 T magnetic field strength

Closed-bore MRI scanners at 1.5 T or 3.0 T are now widely available. The scanners have a cylindrical design with a standard central bore averaging 60 cm, with 70 cm systems becoming more prevalent and larger bore diameters now being introduced commercially (e.g., 80 cm). Even with wide bore scanners, accommodating the lithotomy position for implantation is difficult. To address this issue, several potential imaging workflows are presented in Section IV.A.

Both 1.5 T and 3.0 T are equally available commercially, and both provide images with sufficient quality for GYN and prostate BT. However, there is increasing interest in 3.0 T systems as they provide a higher SNR (i.e., SNR is proportional to the square of the static magnetic field strength), increased spatial resolution, shorter scan times, improved contrast-to-noise ratio,[28] and higher quality functional imaging (e.g., diffusion and perfusion). Additionally, 3.0 T systems come with increased safety considerations for patients and devices in terms of heating and translation/torque. Changing from a 1.5 T to 3.0 T system should not be done without re-evaluating the equipment and safety procedures in the workflow, due to the enhancement of

magnetic susceptibility artifacts, chemical shift artifacts, standing wave effects, and the heating potential observed for 3.0 T systems (see Section IV.G). Additionally, this change will result in T1 lengthening that will require modifications of some pulse sequences. It should also be noted that SAR goes approximately as $B0^2$ in tissue which can make it difficult to stay within the Normal Operating Mode (<2 W/kg) for a 3.0 T scanner when the same parameters need to be managed for anesthetized patients and patients whom SAR is limited due to implant conditions for safety.

The use of MR imaging from closed bore MRI-linacs with magnetic field strengths of < 1.5 T has been investigated for cervical HDR BT.[29] However, this implementation is still developing, and as such, is outside the scope of this report.

iii. Multi-imaging modality approach: MRI/Ultrasound (US), MRI/CT

Few radiation oncology clinics have a dedicated MRI scanner. Others may have to rely on diagnostic radiology departments to coordinate MR imaging for their BT patients. Even for those departments with a dedicated MRI(s), not all BT planning simulations may be performed on the MRI due to the designed procedural workflow, logistical, and reimbursement issues. In these scenarios, a multi-imaging modality approach may be selected that utilizes multiple imaging modalities such as MRI and US or MRI and CT for image guided brachytherapy. There are several permutations that may be used to integrate MR imaging into the BT workflow (see Section IV.A), each exploiting the superior soft tissue contrast of MRI compared to CT and US to better visualize the pelvic anatomy and identify the target tissues. Examples of multi-modality approaches include MRI-informed BT and MRI-based BT.[19] During MRI-informed BT, diagnostic or pre-implant simulation MR images may be reviewed during the implant procedure to help guide needle placement, and reviewed and/or fused with the planning CT or US to assist with the delineation of the target. In the case of MRI-based BT, an MRI and CT dataset may be acquired following applicator/needle placement and registered based on the applicator/needles.

B. Applicators and needles in the MR environment

The earliest examples of the application of MRI-based GYN BT were from the GEC-ESTRO working group, which provided recommendations for intracavitary tandem and ovoids and tandem and ring BT for the treatment of cervical cancer.[12-15] Since that time, MRI-conditional hybrid applicators, i.e., combined intracavitary-interstitial applicators like the Vienna,[30] Utrecht,[31] and Venezia[32] applicators have become commercially available for GYN HDR BT. Although not as common, there are also examples of MRI-based HDR BT for post-operative endometrial cancers using vaginal single or multi-channel cylinders and for inoperable endometrial using Heyman capsules or tandem(s) and/or cylinders.[33-35] Examples of template-based interstitial needle implants using, for example, the Syed-Neblett template, have been published for MRI-guided GYN BT.[24,25] There are also examples of more customized applicators, including a 3D-printed vaginal template or hybrid applicator,[36] a modified tandem and colpostat,[37] and custom-built MRI-conditional metallic alloy tandem applicator[38] for MRI-based BT in cervical cancer. With regard to prostate cancer, an example of MRI-guided placement of an interstitial implant using a custom perineal template has been published for the treatment with HDR BT.[39] For MRI-based interstitial GYN and prostate implants, needles made of plastic or non-ferromagnetic metals (e.g., titanium) are typically used. Before use, the conditions in which the applicator/needle(s) were tested should be reviewed (see Section G.ii).

C. Review of current MRI BT clinical trials

i. Prostate BT

Clinical prostate cancer trials combining HDR and MRI are fairly limited; most trials are ongoing or in their early stages. Based on a search of the Clinicaltrials.gov website using the terms MRI, HDR, and prostate cancer, several actively accruing studies have been identified and summarized in Table 1. The goal of TG 303 is to provide the medical physics community with guidance and the tools to clinically implement MRI safely into the prostate HDR workflow, and hence increase participation in clinical trials in this specialty. The ABS has endorsed this report since it is critical for clinical trials in this area.

ii. Gynecologic BT

For GYN cancer, the ICRU has updated their classical 1985 report 38[40] with ICRU report 89.[16] The updated report provides an excellent description on the use of volumetric imaging (MRI and CT) for cervical cancer with the addition of 4D adaptive target concepts, updated radiobiologic dose assessment, and recommended DVH parameters for targets and OARs.[16] Several of the updated guidelines were based on GEC-ESTRO recommendations,[12-15] taking into account the ABS consensus guidelines for locally advanced carcinoma of the cervix[2,41] and the state of the art for clinical implementation as well as research oriented approaches. MR imaging was introduced into clinical practice to assist in identifying the optimal implant technique (e.g., intracavitary, interstitial, hybrid intracavitary/interstitial) and allows for improved visualization of targets and OARs for treatment planning. Several centers from different regions of the world reported excellent feasibility and promising clinical results.[42-44]

The prospective EMBRACE I (An IntErnational study on MRI-guided BRachytherapy in locally Advanced CErvical cancer) multicenter protocol, which recorded MRI-based treatment planning parameters and outcomes, and the retrospective retroEMBRACE allowed a comprehensive analysis of the advantages of Image Guided Adaptive Brachytherapy (IGABT).[45] Outcome data with MRI-based planning and optimized treatment strategies are excellent in limited and well responding tumors demonstrating improved local control and decreased morbidities in comparison to historical 2D planning methods. Key findings include an improvement in overall survival by 10% when compared to traditional cohorts across all FIGO stages, as well as up to a 50% decrease in major morbidities.[46] The late rectal morbidity appears to be lower when D2cc ≤ 65 Gy versus ≥ 75 Gy EQD2, and the bladder morbidity appears lower when D2cc ≤ 80 Gy versus ≥ 90 Gy EQD2, even though the high risk CTV is dose escalated with IGABT.[47] Recently, Pötter *et al.* published on the mature EMBRACE I findings for 1341 patients, 1251 whom were analyzed for morbidity outcomes.[48] Across all FIGO stages, the 5 year local control, pelvic control, overall survival, and disease-free survival was 92%, 87%, 74%, and 68%, respectively. Of note, although the local control findings were similar across FIGO stages, the disease-free and overall survival differed significantly. Further, the grade 3 -5 morbidities were observed in 14.6% of patients, although per organ morbidities were limited, ranging from 3.2-8.5%.

A summary of on-going clinical trials utilizing MRI and HDR brachytherapy for the treatment of patients with cervical cancer is presented in Table 2.

D. Review of existing Task Group reports on HDR and MRI

The AAPM has historically provided guidelines for commissioning and QA related to HDR BT. TG 41 described remote afterloader technology;[49] TG 56 introduced a code of practice for BT physics including QA for HDR remote afterloading units and HDR treatment planning and evaluation;[50] TG 59 provided recommendations on safe HDR BT delivery;[51] TG 40 included comprehensive QA guidelines of BT;[52] and TG 53 presented comprehensive QA and commissioning for treatment planning systems (TPS), including BT.[53] Although these TG reports provide a conceptual framework for use of MR images in BT, they focus on technical issues related to 2D image-based BT procedures. The significant advancements in clinical use of MR images such as MRI-guided implants, MRI-based treatment planning, delivery, and verification in HDR BT have eclipsed the previous TG reports as the implementation of MRI in BT has been financially prohibitive in years past.

Task Group reports that address the use of MRI include MRI Subcommittee TG 1,[54] TG 118,[55] and TG 132.[56] MRI Subcommittee TG 1[54] presented recommendations on the general aspects of performing acceptance tests, commissioning, routine QA, and phantoms for MRI scanners. The tests recommended by TG 1 for acceptance, commissioning, and QA of MRI scanners should be performed prior to implementing the recommendations of the current report. TG 1 also provides recommendations for acceptable MRI phantom materials, designs, and analysis procedures, which can be referenced when developing MRI BT QA phantoms[57,58] for applicator commissioning to assess their reconstruction accuracy. Task Group 118[55] introduced the use of parallel imaging in MRI in terms of its technology, applications, and quality control (QC). TG 118[55] addressed the issue of delays to acquire MRI data within a clinically reasonable timeframe, and the introduction of parallel MRI (pMRI) allowing physicians to assess large volumes of MRI data in a time-efficient manner. The use of pMRI is still in the pioneering stage in radiotherapy with few studies conducted on its application.[59] As the use of mp-MRI in BT (e.g., the incorporation of diffusion-weighted imaging [DWI][60,61]- and dynamic contrast enhanced [DCE]-MRI[62]) is investigated, the application and QC of pMRI may also be considered after implementing MRI in an HDR BT program. Task Group 132[56] described the use of image registration, fusion algorithms and techniques in radiotherapy, including current approaches and recommendations for QA and QC of rigid and deformable image registration (DIR) processes, in the context of external beam radiotherapy.[56] This TG[56] is beneficial as a reference when primary MRI datasets are registered to secondary 3D image dataset for treatment planning or HDR delivery through rigid registration or DIR. In this scenario, registration could follow the geometry-based metric formalism of TG 132, in which at least three points are defined along the *in situ* applicators in both sets of images. Registration is then performed to minimize the sum of squared differences between corresponding points to align the applicators in the images. However, in the context of MRI-based HDR BT, commissioning and QA aspects of 3D image registration as a secondary dataset for treatment planning or HDR delivery were not specifically addressed in TG 132.

The AAPM and GEC-ESTRO TG 192 Report[63] briefly discussed aspects of MRI guidance for prostate cancer but their discussions are limited to robotic prostate seed implant (PSI) LDR BT and were focused on the introduction of MRI-guided robotic BT systems for prostate cancer. This report did not address commissioning, QA, and QC aspects of MRI-based HDR programs.

E. New recommendations beyond CT based practices

According to the 2014 ABS practice pattern survey,[18] the utilization of MRI in GYN HDR BT has increased in North America from 2% in 2007 to 34% in 2014. Additionally, within this timeframe, an increase in volume-based target delineation (i.e., high risk CTV) from 14% to 52% was observed. Recommendations for MRI and volume-based treatment planning have largely been based on the guidance of GEC ESTRO,[12-15] which are based on experience with magnetic field strengths of 1.5 T and lower. However, the use of higher magnetic fields, i.e., 3.0 T, has been reported in the literature.[58,64,65] Further, given the availability of universal health care in many European countries, reimbursement, which can play a significant role in healthcare decisions in the United States, was not factored into the recommendations of GEC ESTRO. As a result, there is a clear need for additional recommendations beyond those applicable to standard CT-based HDR BT to address MRI integration in the HDR BT workflow.

IV. Clinical implementation of MRI for HDR BT

A. General Workflows from Simulation to Delivery

The general workflow of prostate and GYN HDR BT procedure involves six steps, with various permutations in the order of execution: (1) disease staging/patient selection, (2) applicator(s)/needle(s) placement, (3) treatment simulation, (4) treatment planning, (5) treatment delivery, and (6) post-treatment response assessment/surveillance. For steps #2-5, where physicists have relatively heavier involvement, the traditional imaging modality has been CT and/or US, and is reflected in many of the professional society guidance reports.[50-53] MRI, on the other hand, had been limited in its use but the evidence of its usefulness is accumulating, especially for target volume delineation during steps #2-4. Various approaches to incorporating MRI into the BT workflow have been proposed, and Wang *et al*.[19] broadly categorized them as MRI-informed, MRI-based, and MRI-guided. It should be noted that the implementation of MRI into HDR BT will require expertise and efforts from multiple disciplines (e.g., anesthesia, radiology, radiation oncology) before a safe clinical workflow may be established. Since open bore MRI scanners are no longer commercially available, the following discussion will be limited to workflows utilizing closed bore MRI scanners.

In MRI-informed BT, diagnostic MRI and/or pre-implant MRI simulation images may be used to guide needle placement for interstitial implants and target delineation for treatment planning. This may be achieved by reviewing MR images in the operating or BT suite during the implant procedure, and/or by importing and registering the pre-implant MRI dataset with the planning CT or US images. This approach has been described for both GYN[23,66,67] and prostate HDR BT.[19,68] However, care must be taken when utilizing this approach due to anatomical variations and deformations introduced when comparing datasets acquired at different time points with and without the presence of the applicator(s)/needles. Deformations may also be introduced if the tabletop used during the diagnostic MRI differs from the planning CT (e.g., curved versus flat). An additional margin of error should be considered to account for these uncertainties.

For MRI-based BT, the most common approach in North America involves the acquisition of MRI alone or with CT datasets following applicator/needle placement (often guided by US for

GYN[69] and prostate[5,21]) and registration based on the applicator/needles. This multi-modality imaging approach is often utilized when MRI access is limited. For example, in the case of GYN BT, the MRI is commonly acquired early in the BT process (e.g., during the first treatment fraction), and registered to CT images for subsequent treatment fractions.[5,23,70-72] The MRI dataset is used for target delineation, while the CT is typically used for applicator reconstruction and to define the critical structures (Figures 1 and 2). However, care must be taken when using this approach due to potential variations in the position of the applicator as well as the anatomy as a result of organ, patient, and applicator motion as the patient is transferred between the two imagers. An additional margin of error should be considered to account for these uncertainties. Users should also be cautious of the differences in the presentation of the applicator(s) between imaging modalities. As shown in Figure 1, a gap is visible at the tip of the tandem on CT due to the presence of a cervical sleeve, but appears uniformly hypo-intense on the corresponding MRI, highlighting a potential pitfall of using MRI-only for tandem localization with a sleeve (challenges are detailed in section IV.B and C). Further, the applicator is easier to discern on CT than MRI, especially for metallic applicators and at higher field strengths.

The ideal and recommended clinical approach for MRI-based BT would involve MRI only simulations for each HDR treatment fraction. Unlike the multi-modality approach, patient transfers are kept at a minimum using an MRI only approach, thereby minimizing uncertainties associated with applicator and organ motion, as well as uncertainties related to image registration. Further, the superior soft tissue resolution of MRI compared to CT allows for the clear delineation of the tumor from neighboring pelvic tissue (e.g., cervix, uterus, parametrium, vaginal tissue).[16] This approach is routinely used in Europe and some academic centers in North America, however, due to resource and financial constraints, has not gained wide acceptance in North America.[5,71]

Finally, in MRI-guided BT, the applicator and needle insertion are guided intraoperatively in the MRI/operating room. The initial experience with using a 0.5 T MRI during prostate LDR BT was reported by the Dana Farber Cancer Institute, where 318 men were treated from 1997 through 2007 using an intraoperative real-time MRI guided BT technique targeting only the peripheral zone of the gland.[73] The rationale for this resource-intensive approach included better visualizations of the gross tumor and prostate boundaries than TRUS where uncertainties remain at the anterior aspect of the gland because of echogenic artifacts created by implanted catheters, sacrificing workflow efficiency in the hopes of improving accuracy. Therefore, this approach is best suited for salvage BT or dose escalation to DILs. This approach has been shown to be feasible at several specialty centers, with overall procedure times of 4-5 hours.[73,74] Ménard *et al.*[39] and Murgic *et al.*[75] reported MRI-guided needle insertion approaches for patients treated with prostate HDR BT in which the patient is positioned in the decubitus and frog-legged positions, respectively, then moved into the bore of the scanner for imaging, and removed for needle insertion and/or adjustments. For GYN BT, the Medical University of Vienna first reported using MRI-guided applicator and needle insertions for difficult cases involving extensive disease where patients were moved into and out of the magnet bore between insertions using a 0.35T MRI.[76] Several other workflows for BT with the patient in the bore of the scanner for imaging, and then withdrawn from the bore for implantation have been published in literature.[39,75,77] Kapur *et al.*[77] described an MRI-guided insertion workflow for interstitial gynecologic BT, in which the patient is in the lithotomy position with their pelvis outside of the scanner bore for

needle placement, and then with their legs partially down for imaging. Needle adjustments were performed by the physician reaching inside the scanner bore to access the patient. More recently, Anderson *et al.*[78] described an MRI-guided needle insertion technique using T2 weighted (T2W) MR images with a short scanning time in an interventional radiation oncology MRI-BT suite. Such MRI-guided insertion techniques are resource-intensive, requiring access to an MRI system with trained operators, MRI safe/conditional equipment (e.g., needles, template, anesthesia equipment, stretchers, etc.) and an anesthesia team familiar with MRI restrictions on anesthesia equipment.[75]

The incorporation of MRI into any of the six steps above, or in combination thereof, is feasible and has been proposed in workflows in the past, irrespective of fractionation schedules. It is up to the individual institution to assess their infrastructure and personnel to determine the best workflow to implement. If MRI is available, but not housed within the department, an MRI-informed or MRI-based approach of using CT-MRI fusion to guide the treatment planning becomes the best option for patient care.

B. Brachytherapy-specific MR imaging acquisition parameters

The development of an imaging protocol consisting of MRI acquisition sequences is dependent on several factors, including the technical specifications of the MRI unit, patient preparation, and MRI-safety of the BT applicator(s); the last of which in turn affects the interaction between imaging and the applicator(s) leading to heating effects, image distortions, and artifacts. A combination of phased-array RF receive coils is often utilized. Typically, the patient is positioned above a posterior array coil, integrated into the scanner couch, which provides posterior signal. Prior to imaging, an anterior array coil is positioned over the patient and lightly secured with straps. In general, the highest element density coil combination is desired to maximize SNR and acceleration. Use of RF coil bridges to support the coil above the patient is usually unnecessary for MRI-based BT because deformation of the surface anatomy is not a concern.

Acronyms and definitions of 3D fast spin-echo pulse sequences from the major MRI vendors are shown in Table 3. These vendor optimized and highly accelerated acquisition sequences permit the collection of high-resolution, T2W volumetric images with isotropic voxels within clinically acceptable scan times. One dimensional (1D) or 2D parallel imaging and partial Fourier techniques are often used to reduce acquisition times. The 3D fast spin echo (FSE) sequences utilize very long echo trains with non-selective refocusing pulses of (typically) variable flip angles to reduce tissue heating.[79] Compared to multi-slice 2D sequences, images acquired with 3D sequences with isotropic resolution can be reformatted into any arbitrary plane with relatively little loss of image quality, permitting BT-eye-view reconstructions, illustrating the geometry between the image orientation in patient and the applicator,[80] from a single acquisition. However, at this time the flip angle schedules of the refocusing pulses used in 3D FSE variable flip angle (VFL) are designed using spin models with assumed relaxation times which may not be representative of the relaxation times of tissues in the pelvis.[79] Consequently, the T2 contrast on 3D FSE VFL images is often altered compared to conventional, multi-slice 2D FSE images. Table 4 compares the advantages and disadvantages of 2D and 3D FSE VFL sequences for BT planning, and Table 5 provides a set of generalized 2D and 3D FSE VFL scan parameters (e.g., repetition time [TR], echo time [TE], echo train length [ETL], and readout bandwidth [rBW]) for 1.5 and 3.0

T systems for GYN and prostate BT. Beyond establishing the desired field-of-view (FOV) and spatial resolution, adapting sequences to BT also includes both increasing the rBWs to reduce applicator-induced distortions arising from magnetic susceptibility differences and controlling for gradient nonlinearity-induced distortions. Susceptibility causes distortions in the local magnetic field (B0), and the resulting shifts in spin frequency cause shifts and distortions along the frequency encoding or readout direction. To control for applicator or needle induced geometric distortions, it is advisable to set sequence rBWs to twice the fat-water shift at a particular magnetic field strength (e.g., 440Hz at 1.5T and 880Hz at 3.0T).[81] It should be noted that such a high rBW will result in substantial loss of SNR (approximately 30% or more). Therefore, increases in the number of signal averages, use of phase and slice oversampling, or reduction in parallel imaging acceleration factors may be required to recover SNR.[82,83] Each of these changes will increase the scan times. To minimize unnecessary SNR loss and scan time increases, the rBW should be tailored based on an estimated maximum susceptibility induced distortion map. This can be obtained by acquiring a B0 map of the applicator or needles during MRI-based BT commissioning. The rBW can then be determined using Equation 1, where f_0 is the system frequency, and Readout FOV and Readout Matrix Size are the desired FOV and matrix sizes, respectively.

Equation 1:

$$Readout\ BW\ \left(\frac{Hz}{pixel}\right) = \frac{Max\ \Delta B0(ppm) *\ f_0(MHz) * Readout\ FOV\ (mm)}{Permissible\ Shift\ Along\ Readout\ (mm) * Readout\ Matrix\ Size}$$

Gradient nonlinearity (GNL)-induced distortions are expected to be small for MRI-based BT because of the close proximity of the target volumes to the MRI scanner isocenter. GNL distortions can be further minimized by ensuring that the center of the prescribed imaging volume matches the MRI scanner isocenter along the table direction. In addition, vendor-provided 3D gradient distortion correction should be applied prior to using the images for treatment planning.[84] It should be noted that wider and shorter bore systems generally demonstrate larger GNL distortions, particularly in the z-direction. GNL corrections are performed by warping the reconstructed image slice or volume, and thus have certain limitations. Such corrections rely on lower order models of the gradient field which tend to be less accurate in regions away from isocenter. Blurring and residual distortions following correction may result from use of these algorithms. However, for the purposes of prostate and GYN brachytherapy discussed in this report, the fortuitous small and isocentric centralization of targets diminishes the severity of these GNL effects.

3D FSE based metal-artifact reduction (MAR) sequences have become more widely available and faster in recent years, and have been successfully applied to MRI of titanium applicators.[65] These sequences were found to improve visualization of the tandem tip on both T2W- and proton density weighted (PDW)-MRI sequences, with a significant reduction in the blooming artifact at the tip of the tandem in PDW-MRI.[65] Due to the altered tissue contrast, in all of these

studies, PDW-MRI was recommended as an addition to, and not as a substitute for, standard T2W-MRI to improve visualization of the applicator.

Other sequences have also been utilized for improved reconstruction of the applicator and/or detection of seeds or markers. These include 3D T1 weighted (T1W) gradient echo sequences such as VIBE or LAVA,[57,83] or 3D phase cycled steady-state free precession sequences such as CISS, FIESTA-C, or balanced FFE.[83,85] These sequences are generally fast compared to 3D FSE VFL sequences but produce less desirable contrast of the anatomy and lesion unless used with contrast agents.

C. Applicator/needle commissioning and reconstruction

When considering the selection of BT applicators that will be used in a clinical workflow involving MR imaging, the qualified medical physicist (QMP) must verify the device is safe in a high magnetic field environment. Details on safety risks and testing are provided in Section IV.G. As a component of applicator commissioning, the QMP should review and be familiar with the applicator's instruction for use and the conditions in which the applicator is safe for use within an MRI environment (see Section IV.G.ii). Additionally, regardless of whether an MRI and its associated protocols are fully optimized for diagnostic purposes or for external beam to serve as a secondary image dataset, during clinical commissioning MR images and protocols should be cautiously validated in terms of geometric accuracy for plastic and/or metal applicator(s)/needles (as discussed in Section IV.B). The level of distortions and general image artifacts such as truncation, aliasing, magnetic susceptibility,[38] and chemical shift artifacts[86] should be validated for the specific array coils used in the presence and absence of applicator(s)/needles.

Commissioning should also include an evaluation of the reconstruction accuracy of the applicator(s) intended to be used in an MRI workflow. Applicator reconstruction can be affected by distortions and susceptibility-related artifacts. The first issue is a valid concern in both plastic and titanium applicators/needles, as distortion levels of 1-2 mm around the active dwell positions of a GYN intracavitary applicator could cause > 2 mm uncertainties in applicator reconstruction.[16] On the other hand, susceptibility-related artifacts are an issue for non-ferromagnetic metallic applicators/needles, and their incidence increases as the magnetic field strength increases.[5] The evaluation of applicator/needle reconstruction accuracy on MRI requires the use of a specialized QA phantom since the applicator/needles need to be embedded in tissue-equivalent materials (e.g., Agarose gel[87]) to be identified on an imaging dataset. The phantom should be composed of an MRI safe material (as discussed in Section III.D) that can fixate the applicator. The phantom should also include a coordinate system independent of the applicator that is used to register the MRI dataset(s) acquired with the applicator to the gold standard imaging dataset (e.g., CT).[57,58] In-house MRI-QA phantoms designed for intracavitary applicators[57,88] or needles[88] have been described in the literature, as have techniques to evaluate the accuracy of applicator reconstruction using CT and MR imaging. In the absence of a specialized phantom, a water filled plastic container (e.g., small storage tote) can be used. The applicator(s) should be immobilized in the container (e.g., with tape) and care should be taken when transferring the container between the CT and MRI scanner. Details of applicator reconstruction commissioning for 3D image (e.g., CT or MR images) based treatment

planning are described in Hellebust *et al*.[15] For 1.5 - 3.0 T MRI scanners, applicator reconstruction uncertainty of less than 2 mm is achievable.[15,16,57,58] If the uncertainty exceeds 2 mm, efforts should be taken to improve the image quality such as reducing the slice thickness, optimizing MRI sequences to minimize artifacts or distortion, and/or using MRI markers (i.e., catheters containing MRI contrast agents that may assist with applicator reconstruction). Example CT and MR images acquired during the commissioning of a plastic and titanium ring and tandem applicator set are shown in Figure 3. Recent advances have led to increasing commercial availability of 3D zero TE or ultra-short TE imaging methods. These sequences are able to acquire signal from very short T2 spins and are robust against distortions and signal loss caused by acute susceptibility. While these sequences have been marketed for bone imaging, they have also been shown to preserve signal near devices such as deep brain stimulators [Ramani], suggesting possible future applications in applicator or needle reconstruction.

Currently, most vendors provide a library of 3D applicator models for rigid applicators that includes the detailed geometry and material of each applicator. Applicator libraries have been shown to be more accurate and efficient than manual applicator reconstruction on volumetric imaging,[15] but should be used only after they have been properly commissioned.[16] Commissioning should be performed using a specialized phantom or water filled container, as described above, to evaluate the geometric accuracy of the model.

The use of MRI contrast agents has been investigated to improve intracavitary applicator[37,57,88] or needle[88] reconstruction for plastic[37,57] and titanium[88] devices. The following MRI marker contrast materials have been investigated for MRI-based BT using plastic applicators: $CuSO_4$ solution,[57] saline,[37] cobalt-chloride complex contrast (C4),[88,89] Vitamin E,[88] 1% Agarose gel,[88] Conray-60 (Mallinckrodt Medical, Pointe-Claire, QC, Canada),[88] and fish oil.[88] These markers cannot be visualized in titanium applicators due to magnetic susceptibility artifacts.[57] The choice of an MRI-marker agent should be determined based on the MRI sequence (e.g., T1W- or T2W-MRI) used for applicator reconstruction. For instance, $CuSO_4$[57,88] and C4[88] are recommended when T1W-MRI are used for applicator reconstruction, while saline[37,88] is recommended for T2W-MRI. Since $CuSO_4$, C4, and saline are liquids, care should be taken to examine the vessel holding the MRI agent as leakage or evaporation of the agent will introduce additional uncertainty in applicator reconstruction (as shown in Figure 4). MRI-marker catheters are commercially available for plastic intracavitary applicators which may be filled with saline for T2W-MRI (Elekta, Inc., Stockholm, Sweden) or are filled with C4 for T1W- or T2W- MRI (C4 Imaging LLC, Doylestown, PA, USA). Users should follow the vendor's instructions for use in preparing MRI line markers and include these instructions in their standard operating procedures. Caution should be used in the application of saline- and water-based markers as signal may be too weak for visualization in small diameter lumens. Example images of a commercially available marker in a plastic ring and tandem applicator are shown in Figure 5. Efforts have been made to explore the use of MRI-marker agents for interstitial HDR BT using plastic needles and presented more than 100% hyper-signals with $CuSO_4$ and saline on T1W- and T2W- MRI, respectively.[88]

Plastic applicators/needles have also been reconstructed on MRI in the absence of markers. Care must be taken when relying on MR images alone for applicator reconstruction should air pockets be present in the anatomy at the tip of the applicators/needles or in locations where

applicators or needles cross. Additionally, in the case of needles, the user will need to verify if the needle obturator is MR conditional, if not, it must be removed prior to imaging. If MRI alone is used to reconstruct the needle and the user intends to leave the obturator in place during scanning, the tip offset should be evaluated both with and without the obturator when commissioning the needle for clinical use.

For titanium-based applicators/needles, no MRI-marker agent is feasible due to susceptibility artifacts.[57,88] An MRI-marker flange for titanium intracavitary applicators was proposed for use with its 3D-modeled applicator library to improve the applicator reconstruction accuracy.[88] Further, for these applicators, image quality can be improved by optimizing MRI sequences and acquisition techniques to minimize artifacts or distortion. This is of particular importance for a 3.0 T MRI scanner as the artifact-to-noise ratio (ANR) is proportional to the main magnetic field,[90] thus the ANR of a 3.0 T MRI is theoretically twice that of 1.5 T scanner.[90] The ANR is also proportional to the voxel size, so the clinically feasible smallest slice thickness should be considered. When isotropic reconstruction is achievable in a 1.5 T or higher strength MRI, the slice thickness should be maintained at < 2 mm, especially when MR images will be used for applicator reconstruction. If possible, a T2W-MRI protocol should be developed for use in contouring and applicator reconstruction with an approximate 1-mm isotropic pixel size (1 mm x 1 mm x 1 mm). For cervical cancer HDR BT, standard T2W-MRI has acceptable tumor-tissue contrast, but has poor uterus-tandem contrast making tandem localization on MR images somewhat challenging. One approach for BT imaging of titanium applicators is to incorporate PDW-MRI sequences, which use a very short TE and a very long TR compared to T2W-MRI, yielding images with high SNR and less susceptibility artifact.[91] The use of PDW-MRI, versus T2W-MRI, for titanium tandems, has been shown to significantly improve uterus-tandem contrast and reduce blooming of the tandem diameter.[91] PDW sequences are comparable in length to T2W-MRI scans (i.e., on the order of 5 – 10 minutes). Due to the high signal in PDW-MR images, the slice thickness for 2D image acquisition protocols can be reduced. Para-sagittal acquisitions of 2.5 mm slice thickness for PDW versus 5 mm thickness for T2W-MRI, have been shown to yield higher quality reconstructed views of the titanium tandem as well as the plastic ovoid caps.[92]

The impact on dosimetric indices and DVHs (e.g., D2cc and D90, for OARs and targets, respectively) due to uncertainties in the applicator/needle reconstruction in 3D image guided cervical BT has been well characterized by various investigators.[93-97] In general, the overall conclusion is that if the reconstruction error is within ±2 mm, the major dosimetric indices for both the target and OARs remain within 1-2%, on average, with variations of up to σ=1-3% for individual cases, and with the magnitude being larger for OARs than targets. This is due to the geometric location of the OARs that generally are in higher dose gradient regions. Individual findings include Schindel *et al.*[93], who simulated the applicator shifts and concluded that to avoid a greater than 10% variation in the relevant dosimetric indices, the reconstruction uncertainty should be managed to be less than 3 mm. Tanderup *et al.*[94] also simulated the shifts in the applicator position and found that the mean changes were less than 4% per mm for both OARs and targets in all directions including rotations, except in the anterior-posterior direction where a mean change of 5 ± 1% per mm, in terms of the D2cc to the bladder and rectum, were observed. De Leeuw *et al.*[95] studied applicator shifts for PDR ^{192}Ir-based BT and found that the magnitude of the dosimetric impact was similar to those reported by Tanderup *et al.*[94] and

Schindel *et al.*[93] and, confirmed the impact to be more severe on OARs than targets. These finding for OARs and targets were also confirmed by Deufel *et al.*[97]

It is worth noting that dosimetric uncertainties related to other geometric uncertainties (e.g., afterloader source positioning uncertainty) have been estimated to be up to 4% for OARs (D2cc) and the target (D90).[96] The authors have further reported that the overall uncertainty for a treatment course, accounting for uncertainties in the source calibration, dose and DVH calculation, geometry, contouring, and intra- and interfraction variability, may be on the order of 12% for targets and 21 – 26% for the OARs.

For interstitial prostate HDR BT, the reconstruction uncertainties due to slice thickness were evaluated for CT-based treatment planning. Under a realistic needle reconstruction error scenario where all catheters were randomly distributed within the space, dose uncertainties of 0.7 – 1.7% were reported.[98] A similar uncertainty is expected in the case of interstitial GYN HDR BT, as the reconstruction accuracy of interstitial needles due to slice thickness is irrelevant of the pelvic target. Acquiring MR images in multiple planar orientations (e.g., axial, sagittal, and coronal) can help reduce this specific source of uncertainty.

Given applicator reconstruction uncertainties of < 2mm are achievable,[15] which would allow dosimetric indices for the target and OARs to remain within 1 – 2%,[93-97] Task Group 303 recommends an applicator reconstruction accuracy of ≤ 2 mm.

D. Patient-transfer systems

When a HDR patient-transfer system, such as the hover-based Zephyr (Diacor, Inc., Salt Lake City, Utah) or Symphony™ (Qfix Inc., Avondale, PA) systems, or a removal table top/trolley (Philips MR Therapy, Vantaa, Finland), is used to transfer a patient from the procedure suite/operating room to the MRI scanning room or vice versa, the degradation of the MR image quality due to the presence of the transport system should be verified by a QMP. The quality evaluation should also be performed using practical patient separations from the coils. The receiver coils detect signals emitted by spins in the patient's anatomy; reducing the distance between the coils and the region of interest increases SNR, improving the overall image quality. However, geometric uncertainties caused by general image artifacts as described above are challenging for medical physicists to quantify even using phantoms. Image quality in the presence of these devices has not yet been quantitatively assessed. As such, *in vivo* validation may be required, namely by acquiring CT and MR images with the applicator in place before transitioning to MRI-based BT treatment planning.

E. Target and OAR Delineation using MRI

The geometric accuracy of patient anatomy produced from MR images is critical when MRI is intended to be used for HDR treatment planning. MRI scan protocols must be optimized in terms of image quality for target and OAR delineation as well as applicator/needle reconstruction (as discussed in Section IV.B). Distortions due to the inhomogeneity of the static magnetic field and/or nonlinearities in the gradient coils should be evaluated, along with vendor-supplied correction algorithms to minimize these distortions. System related distortions are known to increase with increasing distance from the MRI isocenter,[81,99,100] and with increasing field

strength.[101] Thus the geometric accuracy should be maximized in the region of dosimetric interest by positioning this anatomical region at the center of the magnet,[84,102] while optimizing the scan protocol. On a modern 3.0T scanner, maximum residual mean distortions of 3.2 mm were found at a radial distance of 25 cm,[100] which may be considered clinically acceptable in the setting of prostate or GYN BT, if the pelvis is appropriately aligned in the MRI scanner. The magnetic susceptibility distribution of the patient and applicator/needles can potentially result in local geometric distortions if a non-optimized imaging protocol is used. These local distortions are independent of the position of the applicator/tandem and magnet isocenter. Geometric accuracies may be assessed using commercially available phantoms such as the QUASAR™ MRID3D (Modus Medical Devices Inc. London, ON N6H 5L6, Canada), Magphan RT (Image Owl, Inc., Greenwich, NY), or GRADE (Spectronic Medical AB, Helsingborg, Sweden). Equation 1 in Section IV.B. provides guidance on how an imaging protocol can be adjusted to minimize susceptibility-induced geometric distortions.

i. Delineation of GYN structures

Clinical contouring definitions and considerations of target volumes on MR images for treatment planning of cervical cancer have been well documented.[14,16] These standard definitions for a series of different gross tumor volumes (GTVs), CTV, and planning target volumes (PTVs) can be translated, merged, and further elaborated for adaptive BT in cervical cancer to account for changes in the target volume and anatomical changes of the OARs over the course of radiotherapy.[14,16,103] Additionally, these concepts can be applied to other adaptive gynecological BT when MRI-based treatment planning is intended. Clinicians must follow the different target volume definitions as reported when the high tumor contrast resolution of MR images is intended to deliver adaptive BT. For instance, the high risk CTV is defined at the time of BT and should include the residual tumor, cervix, and surrounding tissue with potential microscopic disease.[16] MR imaging may be utilized for contouring and treatment planning in a number of different clinical scenarios as described in Section IV.A. Whenever contouring is performed on MR images with the intention of adaptive BT, the use of T2W-MR images is recommended.[16,104]

With regard to anatomic MR imaging for GYN intracavitary BT, GEC-ESTRO describes the use of multi-planar T2W-MRI acquired with pelvic anterior coils as the “gold standard” for tumor and critical structure visualization and as having sufficient contrast for applicator definition based on their experience with 0.2-T and 1.5-T MRI units, with the use of complementary MRI sequences (e.g., contrast-enhanced T1W or 3D isotropic scans) to be considered optional.[13] Thus, T2W sequences are considered by GEC-ESTRO to be a mandatory sequence for BT, with emphasis on spin echo (SE) and fast spin echo (FSE) techniques to reduce image acquisition time and maintain image quality in the presence of local field inhomogeneities (e.g., presence of the BT applicator(s)). General scan protocol parameters are provided in Table 5. However, these scan protocols may require further optimization depending on the receiver coil hardware available for a specific scanner. GEC-ESTRO recommends obtaining images that are oriented orthogonal and parallel relative to the applicator axis (e.g, para-axial, para-sagittal, para-coronal), with imaging extents to capture at least the entire cervix, uterine corpus, vagina, and parametria, and OARs.[13] It should be noted that the recommendations from GEC-ESTRO Working Group IV[13] are based on the experience of a limited number of centers and on the evidence from a limited amount of clinical imaging data. For example, with multiplanar acquisitions, the reformatting

may also result in the loss of image quality.[105] With 3D imaging, one has the ability to reconstruct images in any plane. Although considered optional by GEC-ESTRO, 3D T2W imaging is also recommended with the understanding that this will generally lead to increased scanning time, which increases artifacts due to motion. Thus, the GEC-ESTRO recommendations may be used to provide a good starting point for MRI sequence development but will probably require some fine-tuning by the use of complementary sequences based on the particular applicator type and MRI scanner available.

There are no standard recommendations with regard to quantitative MR imaging (qMRI) for GYN intracavitary BT; however, the utility of qMRI has been explored by different centers. It has been suggested that quantitative imaging may further improve the accuracy of target and sub-volume target delineation.[105] With DWI one can identify areas of restricted water diffusion as areas of high cellularity, e.g., tumors versus normal tissues. The utility of DWI and the derived apparent diffusion coefficient (ADC) map has been used for tumor visualization and therapy response in cervical cancer.[60,61] Target volume borders can appear with more distinct edges on ADC maps than on T2W-MRI.[106] For pre-therapy ADC maps, with no applicator in place, regions with more restricted water diffusion have been shown to correspond to areas of increased metabolic activity on ^{18}F-fluorodeoxyglucose-positron emission tomography (^{18}F-FDG-PET) images.[61] However, DWI is typically acquired with echo planar imaging (EPI) sequences, which are prone to geometric distortion and severe susceptibility artifacts, especially in regions near the applicator. Thus, it is generally recommended that for BT imaging, DWI should be used as a supplement to, but not in place of, T2W imaging.[5,92,106,107] It should be noted that alternative DWI sequences, such as segmented EPI and single-shot TSE, may be used to reduce geometric distortions in diffusion weighted images and apparent diffusion coefficient maps.[108] Additionally, most sequences do not suffer from the severe susceptibility induced distortions seen with EPI sequences, and other qMRI methods such as DCE-MRI (discussed below) would not require such geometric corrections.

In a combined approach using multi-parametric imaging, anatomic T2W-MRI is supplemented with qMRI (e.g., DWI, DCE-MRI, and ^{18}F-FDG-PET) reducing inter-observer variability in the delineation of the GTV.[62] With DCE-MRI one can identify areas of homogeneous enhancement as small cervical tumors or areas surrounded by an enhancing rim as large necrotic tumors. In this multi-parametric approach, DCE-MRI was most often used to modify the GTV contour, and was found to be particularly helpful in visualizing residual disease involving the myometrium.[62] Given the data on the importance of dose to the GTV for local control, it has been suggested that the role of multi-parametric imaging for tumor delineation may expand in the future.[109,110]

The use of anterior array coils wrapped around the pelvis is considered standard for diagnostic pelvic MR imaging, and is also recommended for BT imaging. The appropriate placement of these coils on the patient are key to artifact reduction and acceleration of the 3D FSE techniques discussed in this TG. Intracavitary (i.e., rectal or vaginal) coils, although useful for the visualization of small tumors, are not recommended for BT imaging due to the deformations in organ shape after MR imaging and coil removal which would lead to uncertainties between the planned and delivered dose. An exception to this recommendation can be made for endorectal coils (ERCs) if the coil remains in place through treatment.

Additional items to consider are patient preparation prior to MR imaging, including the administration of antispasmodic agents, e.g., glucagon, to reduce artifacts due to bowel motion[13] and the use of packing soaked or filled with an MRI contrast agent such as diluted gadolinium, US gel, or saline water.[111,112] Gauze or balloon-based packing may be used to increase the separation between the BT applicator and OARs, as well as to enhance the visualization of the vagina and cervix.[41,111]

ii. Delineation of prostate structures

Contouring on MR images for treatment planning of the prostate has been well documented in the literature.[20,21,113] While US and CT are still the standard imaging modalities used in the United States,[114] MRI-based planning has recently gained interest due to the superior soft tissue contrast and resolution of MRI versus CT and US. The improved resolution results in smaller variability of prostate volumes on MR, especially when compared to CT-based prostate volumes which are larger than MRI and US, given uncertainties in the prostate boundaries on CT images near the seminal vesicles and apex of the prostate.[115-118] Prostate HDR monotherapy,[119-121] salvage,[122-124] and DIL focal treatment[125] planning can benefit from MR imaging. Utilizing MR imaging, intra-prostatic tumors, macroscopic ECE involvement, or seminal vesicle invasion can be identified and delineated.[10] Additionally, MRI allows for the visualization of the prostate-bladder interface, prostate-rectal interface, neurovascular bundles, and the genitourinary diaphragm, allowing for the avoidance of radiosensitive structures surrounding the target. Hydrogel is being utilized at some centers to increase the distance between the prostate and rectal wall, to minimize dose to the rectum.[126,127] They present as a hyperintense structure on T2W sequences.[128] Multi-parametric MRI has been used along with US-based HDR real-time planning for the treatment of intermediate- and high-risk patients.[125,129]

Although MR imaging can improve the delineation of structures, large interobserver contouring variabilities have been reported using both CT and T2W-MR images. This variability can result in large standard deviations of the prostate D90 (17 – 23%).[130] Although contouring variability may be due in part to poor soft tissue visualization on CT, the interobserver differences on MRI suggest that additional guidelines and training in contouring are necessary when integrating MRI into the clinical workflow.

The role of MRI for HDR prostate BT is less standardized, yet evolving as an area of investigation.[5,22,39,131] A multi-parametric approach including both anatomic T1W and T2W-MRI and the use of quantitative imaging sequences, DWI, DCE, and less frequently MRI spectroscopic imaging, is being increasingly recognized as a standard approach in a diagnostic setting.[5,132] With regard to anatomic imaging for prostate HDR BT, T2W-MRI sequences provide adequate visualization of the prostate gland as well as discrimination between peripheral and central zones. An endorectal coil may be used for staging of prostate lesions for better visualization of intraprostatic lesions, especially for low tesla MRI scanners (e.g., ≤ 1.5 T).[133] However, the use of an endorectal coil is not recommended for HDR prostate BT if it will be removed prior to treatment as its presence would introduce uncertainties in planned versus delivered dose due to organ deformation.[134] As an alternative, supplementing T2W-MRI with DWI and DCE in a multi-parametric approach for prostate HDR BT can improve the identification of intraprostatic lesions for sub-volume boosting or recurrent lesions after external beam radiotherapy for salvage

treatment.[135-138] Additionally, glucagon can be used to reduce bowel peristalsis and motion-related artifacts.[10]

F. Heterogeneities for calculations

The general commissioning considerations for model-based dose calculation algorithms (MBDCAs) for BT are detailed in TG 186.[139] At present, to perform a heterogeneity-corrected dose calculation, a CT dataset is required to account for the composition of various tissues in the patient. However, an MRI dataset can also be used with MBDCAs with the assignment of tissue material as water and regions of interest (ROIs) of air, such as air in rectum, which is feasible on MRI since air produces a hypointense (dark) signal.[140] For high energy sources such as ^{192}Ir, such simplified tissue assignment is acceptable.[139] It should be noted that the most critical factor is the patient skin interface (backscatter contribution to scatter) and the applicator material which can be accurately modeled in most commercial TPS using solid applicator models.[141,142]

For unshielded plastic GYN applicators, minimal dosimetric changes were found using MBDCA relative to the standard TG-43 formalism (a reduction of 2.1 +/- 1.1% to Point A as defined in ICRU 38,[40] 2.6 +/- 0.9% to the target D90, and 2.1 +/- 0.3% to the OARs).[143] For the prostate, dose predictions using MBDCAs for ^{192}Ir HDR sources have minimal impact on the dose distribution relative to those predicted by TG-43 (in water).[142]

The use of MRI-conditional shielded applicators in MR images has been commercially available owing to the advances in intracavitary applicators such as a Fletcher CT/MRI shielded applicator (Elekta, Inc.).[144]

Heterogeneity corrected dose calculations on MR images should be cautiously performed by: 1) only accounting for high density shielding material while assuming all water conditions,[144,145] 2) assigning bulk densities to individual segmented structures,[140] or 3) converting MR images into a synthetic/substitute/pseudo CT using a voxel,[146-148] atlas,[149,150] or multi-imaging modality approach.[151,152]

G. Safety considerations

The MRI safety guidelines presented here are not comprehensive but are intended to supplement and emphasize relevant points in the American College of Radiology (ACR) manual on MR safety and standards for medical device use in MRI.[153-155] MRI safety should be overseen by a QMP with an expertise in MRI physics.

i. Procedure room equipment

MRI safety of ancillary equipment and devices used during the procedure should be considered. Hospital gowns with ties and/or plastic snaps should be used if the patient is expected to undergo MR imaging during any stage of the clinical workflow. Equipment used for patient monitoring, anesthesia, medication, etc. need to be validated for use in MRI, and should be kept within vendor specifications. As well, changes to applicator imaging characteristics and heating susceptibility may occur when attached to immobilization devices. This topic will be addressed further in an upcoming Task Group report, TG 334 (a guidance document to using radiotherapy immobilization devices and accessories in an MRI environment).

ii. Applicator, needles, patient positioning systems

The main safety risks from the Radio-Frequency (RF) used under MR are tissue heating and burns.[156,157] Shellock's book[156] provides an excellent review of RF heating under MR. Titanium-based intracavitary applicators can be used for MRI-based and MRI-guided HDR BT,[38,58,64,158] along with plastic-based applicators. For commercially available non-ferromagnetic metallic applicators, it is strongly recommended that QMPs verify the device is labeled MRI-conditional, review the conditions in which it was tested (e.g., field strength, spatial gradient, RF fields, maximum specific absorption rate (SAR)),[159] and that the applicator(s) is(are) used in accordance with the vendors instructions for use. If the applicator has been deemed MRI conditional for a different magnetic field than one intends to use (e.g. 1.5-T versus 3.0-T MRI), its clinical use is not recommended.[58] If its clinical use needs to be pursued, the commissioning procedures should follow the recommended American Society for Testing and Materials (ASTM) International guidelines[160-162] for RF induced heating[161] and applicator displacement[160] and torque[162] under the MRI conditions intended for clinical use. Users should also be aware of whether the needle obturator is MR conditional, and under what conditions. If the obturator is not MR conditional or the user is unsure, the obturator should be removed from the needle(s) prior to MR imaging. Before an in-house intracavitary applicator undergoes MR imaging and is used clinically, additional tests, regardless of the material composition of the applicator(s), should be performed, including sterilization-capability and biocompatibility. Users should be mindful when using metal-based needles such as titanium needles for MRI-based BT, even if the needle is FDA-approved and labeled MRI-conditional. Again, the MRI conditions in which the needles were tested should be verified by a QMP. Additionally, care should be taken when implanting metallic needles. Should the needle tips come in close proximity or touch one another, unexpected RF induced heat induction may occur.[163] The use of plastic needles is recommended for MRI-based or MRI-guided HDR BT (Figure 2).

One should be cautious of the presence of metallic objects, even outside of the patient during MRI scans. For instance, when a hover based HDR patient-transfer system (e.g., Zephyr) is used, its metal side rails should not come into contact with the patient's arms. Kim *et al.*[164] reported an incident in which metal side rails touching a patient's arm during an MRI scan induced third degree skin burns. As such, all metallic objects on the patient-transfer system should be removed before an MRI is initiated.

There are also some safety concerns with regard to patient positioning that are particularly important when working with large patients, or with patients whose limbs are not aligned straight with the bore. It should be noted that RF energy radiates from the whole-body RF coil in the bore and thus thermal effects are greatest at the bore wall. Although the gradient and RF coils may themselves grow warm and contribute a thermal load with sustained use, RF deposition also increases with greater proximity to the RF coil. Thus, pads are typically available to prevent bore contact and to ensure some displacement from the bore wall. Care must also be taken by the MR technologist to prevent skin-to-skin contact of the hands, feet, and/or limbs, since the limbs can form large conductive loops that may result in thermal injuries.[153,154] Additionally, the external components of the applicators, specifically metallic applicators, should be padded to prevent applicator-to-skin, applicator-to-applicator, or other conductor contact during MRI imaging.

iii. Patient immobilization and transfer considerations

To perform MRI-guided implants or MRI-based treatment planning, a patient typically needs to be transferred between the MRI and HDR therapy rooms, unless MRI simulation and HDR delivery can be performed in a single room. Inherently, there are concerns related to potential applicator/needle displacement. The immobilization approaches may differ depending on the applicator used and fall into two categories: patient immobilization and applicator fixation. Patient immobilization in an MRI environment can be challenging due to the limited bore size but can be achieved using small leg ramps as a substitute for stirrups. Such ramps should be made of an MRI safe plastic material, should have a low profile to minimize the distance between the patient and the coil and keep the patient's knees from touching the bore of the scanner. An example of a commercially available ramp is the CT/MRI Slessinger board (Radiation Products Design, Inc., Albertville, MN). This approach may be useful for interstitial prostate as well as GYN cases, for which an external applicator fixation device is not available. For instance, for cervical BT, tandem and ovoids or tandem and ring applicators are often initially secured with vaginal packing such as gauze or vaginal balloons.[165] The Slessinger board can also be outfitted with an optional MR conditional GYN applicator fixation device. Additional applicator immobilization may be provided by a portable applicator supporting device (see Figure 1B. in Bou-Zeid *et al.*[166]) that is not secured to a table but to the patient's body. An articulating applicator clamp with baseboard that is positioned below the patient has also been used. However, additional precautions may be required with such devices as the applicator can inadvertently move and harm the patient should they move (e.g., in response to a cough/sneeze) or as a result of unintended movements during a patient's transfer. Intracavitary applicators can also be secured to a hover-based device with similar patient safety concerns.

The degree of applicator displacement due to patient transfers is still being investigated.[166-169] Most of the studies[166-169] use surrogates for the cervix such as bony anatomy on x-rays[166,168,169] or patient-infrared markers[166,167] on the skin surface to measure an applicator displacement due to the patient transfer. Gerszten *et al.*[169] reported up to a 12 mm applicator displacement even when using an applicator immobilization device. Bou-Zeid *et al.*[166] suggested a maximum applicator displacement of 6.7 mm (2.0 ± 1.5 mm) based on a real-time applicator monitoring system when using an in-house applicator-immobilization system, including a portable tandem and ovoids securing device and a modified transfer board. Andrew *et al.*[168] reported a 2.3 – 3.4 mm tandem and ovoid displacement on x-ray radiographs, and found that the use of a hover based patient transfer system resulted in a statistically significant reduction in the displacement of the applicators ($p < 0.01$). Although some simple applicators (e.g., vaginal cylinders) can be implanted on a hover-based transfer system, this may be challenging with more complex applicators (e.g., tandem and ovoids, tandem and ring) that may require greater accessibility and visibility for proper applicator placement (e.g., placement of the intrauterine tandem). Alternatively, the applicator can be implanted on a conventional procedure table and afterward, the patient can be transferred. Without using a conventional procedure table, the applicators can be implanted using a modified hover-based table system. Thus, a patient can remain on the hover device for the duration of the procedure.

The use of a hover mattress (e.g., HoverMatt®, Hovertech International, Allentown, PA), or a slide board is often employed as a means for efficient patient transport between simulation and

treatment tables. Precautions should be taken when using such a transfer device on patients with interstitial implants to ensure the needles are not displaced during the transfer, or transferring patients whose applicator(s) is(are) immobilized with an external fixation device clamped to the transport device. An attractive approach to minimize applicator displacement employs a dockable MRI table (e.g., Tim dockable table,[170] Siemens Healthineers, Henkestr. 127, 91052 Erlangen), or a removable table top/trolley (Philips MR Therapy, Vantaa, Finland) transport system. These systems allow for the transport of the patient in the simulation position without the need for moving the patient to a different table for treatment. However, these are vendor specific and may not be available on all scanner models. Please note, considerable applicator displacements can be introduced if a transfer device needs to be inserted under a patient after the implant procedure. These displacements may be corrected at time of simulation, therefore the insertion and removal of the transfer device after simulation is not recommended. Additionally, caution should be exercised when using a hover mattress since the pump is not MR safe. The device should not be operated in zone IV (MRI scanner room) unless an extra-long, MR safe hose is used.

The consideration of improved workflow using immobilization/transport devices should be weighed against possible degradation of MR image quality. The table and pads can inherently separate the patient in distance from the posterior array built into the MR table leading to SNR loss. Another issue may result from the metal railing in tables such as the Zephyr, which if left in for imaging present not only a potential safety hazard, but the conductivity of the rails can lead to issues with image quality. Positioning devices should be tested by a QMP for MRI safety before incorporation into an MRI workflow.

iv. Setup verification prior to HDR treatments

Treatment setup verification is an integral part of the procedure workflow. To ascertain the treatment geometry conforms to the planned geometry, pre-treatment imaging is recommended for each treatment fraction for a multi-fraction, single implant workflow or when there is a substantial delay between planning simulation and treatment (Figure 6). This will also require the establishment of action thresholds and remediation procedures in case a discrepancy is observed. To do so efficiently, it is recommended that fiducial markers implanted in the target volume be used as references to assess applicator or catheter displacement. If fiducial markers are used, they should be placed prior to the planning simulation by a physician. Bony references and other anatomical surrogates (such as Foley balloons) are not recommended as they do not provide information on the position of the applicator with respect to the target. Markers that have been evaluated for CBCT, CT, kV, MV, US, and MRI include gold markers, gold coils, and polymer markers.[171,172] The appropriate fiducial marker will be dependent on the imaging strategy employed, which in turn will be largely determined by the availability of imaging devices. Setup verification is recommended when a patient transfer is required as part of the treatment workflow, and in anticipation of unplanned events such as accidental patient movement or disturbance of the applicator.

Ideally, the treatment setup would be verified through the use of 3D imaging. A volumetric scan would be used to confirm the position of the applicator with respect to the patient's targeted anatomy, OARs, and fiducial markers. While MRI re-imaging prior to each fraction may not be logistically practical, and CT scans provide inferior target visualization compared to MRI,

CT does provide superior applicator, fiducial marker, and OAR visualization. The planning and treatment image set would be registered, e.g., based on the fiducial markers, and the distance between applicator/needle tip(s) and the markers would be used to assess the implant displacement.

If a diagnostic quality CT is unavailable, kV CBCT may be used to assess applicator to fiducial marker consistency. However due to the low soft tissue contrast of CBCT, re-planning in case a displacement is observed may require re-simulating the patient. MV-based treatment verification adds to this challenge due to poor of visualization of titanium or plastic MRI conditional or safe applicators and similar low-Z objects.

In some clinics, the HDR treatment room may be equipped with 2D imaging only. While 3D imaging is preferred over fluoroscopy/x-ray imaging in assessing applicator displacement relative to the target and neighboring OARs,[173] some clinics utilized 2D imaging modality as an alternative when 3D imaging is unavailable (see Figure 6E).

H. Logistical and economic considerations

Before integrating MRI within the HDR BT workflow, discussions should be held with the institution's finance department and the radiation oncology department administrator to seek the appropriate funding for initial and ongoing program maintenance. It is advantageous to hold these meetings early in the planning process to determine the required initial capital investment, and ongoing expected costs (e.g., FTE of MRI technologists, vendor related contracts). The department should be familiar with the appropriate charge codes when MRI is added to the clinical workflow, and develop a financial model with a conservative workload of patients to predict revenue streaming. Anderson *et al.*[78] described the introduction of MRI logistics and financial hurdles they encounter. They concluded the integration of MRI into the HDR workflow is feasible with a sustainable financial structure if basic elements are formally introduced in collaboration with other departments (e.g., infection control, anesthesia, radiology) for GYN tandem and ovoid and later for interstitial HDR. A novel billing structure was created for their clinical environment, and was only possible after several iterations.

The expected timeline to develop a budget/business plan may stretch over a month, however, equipment purchase, and commissioning will take considerably longer. Prior to developing a business model, the QMP and physician with other relevant BT staff members (e.g., nursing, therapists, dosimetrists, administration) should meet with infection control, the MR imaging nurse manager, anesthesia, and clinical engineering to develop a workflow and define the workspace. Most departments perform the applicator insertion outside the MRI vault, hence, following the TG-100[1] methodology, a fishbone diagram should be developed with inputs from all stakeholders. This is highly recommended to ensure that all key elements required for patient care are considered. If the procedure is performed within a hospital environment, the anesthesia department usually has MRI conditional monitors and equipment for other patient populations that require anesthesia while undergoing MR imaging, otherwise these costs will need to be included in the operating and maintenance budget.

Workflow can also impact the cost structure. Kim *et al.*[174] has reported on the experience of a single center performing MRI-based HDR for cervical cancer patients. They divided the procedure into four key steps based on where the procedure was performed: (1) applicator

insertion under sedation, (2) MR imaging, (3) planning, and (4) treatment delivery. The reported mean total procedure time was 149.3 min (SD 17.9, ranges 112–178), and the mean procedure times and range for each section (expressed in minutes) were (1) 56.2 (28.0–103.0), (2) 31.0 (19.0–70.0), (3) 44.3 (21.0–104.0), and (4) 17.8 (9.0–34.0), respectively. In this setting, the authors stated that the combined mean procedure time for MR imaging and planning was 63.2 min, compared to 137.7 min during their initial implementation/learning phase in 2007–2008 ($p < 0.001$). Of note, the authors stressed the importance of seeking input and working with a skilled and multidisciplinary team to achieve an efficient clinical workflow.[174]

V. Risk based analysis

The inclusion of MRI guidance requires several changes to the current BT paradigm. Such changes include modifications in workflow, equipment, training, documentation, policies and procedures, and potentially personnel/staffing. In considering the effects to patient safety and QA, one way to examine the risk associated with a new or modified process is through failure mode and effects analysis (FMEA). An FMEA comprises three key steps including process mapping, the collection of failure modes, and the scoring/ranking of those failure modes. The output of an FMEA is a list of ways in which a process can fail, prioritized based on risk. This list can be used to better distribute QA resources, create new checklists, and/or educate staff. At a deeper level, the output of an FMEA can be used along with other tools such as fault tree analysis to potentially create new safeguards or re-design a process to improve quality and safety.[1,175,176]

In order to demonstrate this technique for an MRI-based BT procedure, an FMEA was performed for a representative use case, MRI-based, high dose rate BT of the prostate (MRI-$HDR_{Prostate}$). Sample FMEA's for GYN BT are available for review in several publications.[177,178] The process map for this example was based on the procedures as performed by one of the TG members at their local institution. The chosen workflow is best categorized as single fraction prostate HDR after the reversal of anesthesia. This workflow, as opposed to one where the entire procedure is performed intraoperatively, requires several patient transfers over the course of many hours. As such, there is an increased need for verification imaging, which in this workflow includes a CT scan after the patient recovers from anesthesia followed immediately by fluoroscopy once the patient has been transferred to the treatment room. This scenario is likely applicable to a broader audience as many institutions do not have MRI available within the department to facilitate intraoperative treatment.

The process map for an MRI-based, high dose rate prostate BT procedure can be found in Figure 7. There are eight steps which represent the high level sub-processes. These include patient assessment, implantation, MRI simulation, treatment planning, plan review, pre-treatment actions/QA, treatment, and post-treatment actions/QA. Within these sub-processes, several subsequent actions have been outlined including items such as catheter insertion, image sequence selection, and contouring. The process map was used to guide the collection of failure modes, which were submitted by six physics TG members with relevant experience. Collectively, the team identified 63 failure modes (see Table 6).

The collected failure modes represent instances in which requirements to the MRI-HDR$_{Prostate}$ process are not being met. In effect, they are the anti-functions to the proper actions needed for a successful outcome. In each case, the reason the failure occurred and the potential impact to the patient, staff, and the process itself were also identified. The three variables scored within an FMEA, occurrence (O), severity (S), and detectability (D), are related to these cause and effect mechanisms. Accordingly, occurrence is defined as the likelihood a failure mode occurs given a specific cause. Detectability is defined as the likelihood of not detecting a failure mode after it has happened but before the effects take place. And severity is defined simply as the magnitude of the effect considering aspects such as injury, cost, delays, etc. In each case, a higher score indicates that a failure mode is more likely to occur, less likely to be detected, and have more severe consequences. For this study, these three items were scored individually by the six team members using guidelines defined by AAPM TG 100.[1] The median scores were then used to determine the risk priority number (RPN) of each failure mode, i.e., RPN = O x S x D.

Table 6 highlights the top ranked failure modes according to RPN. The first item on the list relates to target contouring which is a commonly identified error pathway in radiation oncology risk assessment.[177,179,180] The elevated RPN is driven by high scores for detection and severity indicating that the failure mode is not easily identified and capable of causing serious harm to the patient. The difficulty in detection is related to the fact that target contouring is a high level, knowledge-based action where the information and experience involved in the decision making process are not widely distributed. While in this setting the QMP is not optimally suited to detect subtle errors, familiarity with the planning process should allow for the discovery of obvious mistakes if the QMP is actively looking for them. Additionally, institutional controls such as peer review should be encouraged, and it is always prudent to verify that contours provided by a trainee are critically reviewed by an attending physician.

Three prominent failure modes more specific to the current process are “needles crossed/doubled/swapped”, “calcification/artifact mistaken as needle tip”, and “needle tip/path not correctly defined.” These errors dealing with needle misidentification are closely related where the first two errors could additionally function as a cause for the latter. In any case, the end result is an implant model that does not accurately reflect the implant geometry. The causes associated with these failure modes are many including a sub-optimal implant, poor image quality, lack of training, and anatomical masking whereby a calcification is mistaken for a needle tip. Using FMEA as a guide, quality controls are primarily based in prevention or detection (a third option would be mitigation). Thus, in terms of preventing needle misidentification, quality measures addressing causal factors include proper commissioning of imaging protocols as discussed in Section IV.A, the critical review of MRI scans immediately after acquisition, and error training that familiarizes users with challenging situations where misidentification is likely to occur. In terms of detection, an independent review by a QMP should be performed, preferably within the planning system itself, as opposed to a review that relies on documentation alone.

Another top failure mode specific to the chosen workflow is the movement of needles during transport. As detailed in Figure 7, the patient is transferred from surgery to MRI, from the MRI to holding, from holding to CT, and from CT to treatment. During this route, any deviation in needle position will introduce changes not reflected in the MRI-based treatment plan. In terms

of prevention, immobilization is important as well as the use of a suitable transfer mechanism such as a hover device, removable couch top, or portable mattress that can be transferred with the patient. In terms of detection, imaging for quality control purposes is built into the workflow at two specific time points, at CT that takes place after recovery from anesthesia and at planar x-ray acquisition that takes place immediately prior to treatment within the HDR suite. It is important not only to image the patient but also to develop protocols for registration and review.[56] As noted previously, error training can help familiarize users as to how images appear when needle movement has occurred. The QMP and attending physician should be responsible for detecting needle movement, and needle corrections, if needed, should be performed by the physician.

Data import and selection represent another type of action associated with several highly ranked failure modes. Here, the error often takes the form of slips, lapses, or misinterpretation of information. Since import and selection typically occur at the beginning of a process, it can be difficult to detect an error if the system does not make the origin/nature of the data apparent at subsequent time points. In these situations, it is prudent to document whenever important information enters the system or is selected as a key item. An example of this practice is the labeling of the planning MRI with relevant identifiers such as scan type, date, and/or intended use at the time of import. It can also be helpful to screen capture the import window showing exactly which scan is being brought into the system. The image can then be added to the plan documentation as a way to make this key item visible to a reviewer.

To summarize, this FMEA is put forth as an example of how to conduct a prospective risk assessment for an MRI-based BT procedure. It is important to keep in mind that there are many ways to perform both FMEA and MRI-based BT. Failure modes which may be relevant in the current workflow may not be applicable to every clinic and vice versa. It is therefore important for each clinic to map their own processes and assess risk within their own clinical setting. Users are encouraged to periodically review previously reported medical events released by the Nuclear Regulatory Commission,[181] and summarized in publications,[182,183] as part of continuous quality improvement of their BT program. As demonstrated in Table 6, a significant source of these events are due to human errors, especially in situations of time pressures. To minimize the risk of these events, members of the care team should perform a time-out, and verify the patient's identity and that the HDR administration is in accordance with the treatment plan (10 Code of Federal Regulations § 35.41).

VI. Recommendations to the medical physicists

A. Clinical commissioning tasks

During the initial discussions of MRI integration into an HDR clinical workflow, a QMP should assume a leading role and assist in the formation of a multidisciplinary team. Additionally, given the expertise in Radiology departments with MRI, either contacting and working with experts in Radiology (e.g., radiologists, MR physicists) and/or including them in the multidisciplinary team to discuss possible workflow options and safety processes, and develop scanning protocols may prove to be helpful. The formed team will determine the proper resources for the safe implementation of MRI, as well as the appropriate MRI workflow for this implementation (e.g.,

MRI-informed, MRI-based, or MRI-guided) based on access to the MRI, resources, and staffing. Perhaps the easiest form of integration is an MRI-informed approach using diagnostic or pre-implant MR images to guide applicator needle placement and/or target segmentation. This may be accomplished by reviewing the MR images immediately preceding or during implant, or by reviewing the MRI dataset with the planning CT. However, at this time, the Task Group does not recommend fusing the MRI dataset in the absence of applicators and/or needles with the planning CT or US (i.e., in the case of prostate BT) due to the potential for large uncertainties between imaging datasets with and without applicators. Although an MRI only approach is preferred as discussed in Section IV.A, if it is not feasible, the next approach to MRI integration, in terms of increasing level of complexity, is the MRI-based approach. Ideally, this approach would involve an MRI acquisition for each treatment fraction. However, in some cases the MRI dataset is only acquired for one treatment fraction, and registered to all subsequent CTs based on the same applicator(s) to help delineate the target.[71] In the United States, this approach is feasible in most clinics and is recommended if MRI-only workflows are not available. However, it should be noted that this approach of a single MRI for patients treated with GYN malignancies may not be well-suited to clinics that deliver BT early on in conjunction with external beam therapy, due to tumor shrinkage early in the course of irradiation, thus requiring MRI for multiple fractions to capture the changing target volume over the course of BT.[92] The ideal and most complex MRI approach is MRI-guided BT. In this workflow, the applicator and/or needles are implanted using real-time MRI guidance. In the United States, only a few centers have currently adopted this approach due to its time and resource demands. As such, the Task Group does not address specific recommendation for this workflow.

Commissioning and Workflow Recommendations:

- For MRI-based and MRI-guided approaches, geometric and dosimetric uncertainties should be evaluated during clinical commissioning. The geometric accuracy should be maximized in regions of greatest dosimetric interest. High resolution CT images should be used as the gold standard for comparison.
- Image degradation due to patient immobilization or transfer devices should be evaluated both in phantom and *in vivo.*
- Acquisition time should be optimized to reduce the risk of motion blurring (ideally, the acquisition time for each MRI sequence should be approximately 5 minutes).
- Intracavitary (i.e., rectal or vaginal) coils are not recommended for BT imaging due to organ deformations introduced by the coil during MR imaging, which would lead to uncertainties between the planned and delivered dose. In the case of ERCs, an exception to this recommendation can be made in workflows where the coil remains in place through treatment delivery.
- Anterior array coils positioned around the pelvis are recommended for MR imaging for GYN and prostate BT.
- A rectal enema or antispasmodic agents (e.g., glucagon, buscopan) may be used prior to MR imaging to reduce peristalsis and motion induced artifacts.
- Gauze or balloon-based packing soaked or filled with MRI contrast (e.g., gadolinium, US gel, saline, sterile water) is recommended to increase the separation between the

BT applicator and OARs, as well as enhance the delineation between structures (e.g., the vagina and cervix).

- Bladder filling should be consistent between planning simulation and treatment, and should be well tolerated by the patient.
- If images show significant motion artifacts, the sequence(s) should be repeated.
- Vendor-provided gradient distortion correction and optimization of bandwidth should be utilized to ensure geometric fidelity of the MRI dataset.
- Work with an MRI physicist and/or vendor to optimize pulse sequences; 3D sequences with isotropic resolution of ≤ 2 mm are recommended for target delineation. In the absence of such 3D isotropic sequences, 2D T2W FSE acquired at ≤ 5 mm slice thicknesses[15] and with < 1mm in-plane resolution are recommended if acquired using multiple scan orientations (e.g., axial, sagittal, coronal).
- Acquisition of multiparametric MRI, including T2W-MRI, DWI, and DCE is recommended for HDR prostate BT to improve the identification of intraprostatic lesions.
- MRI-based applicator reconstruction commissioning and validation should follow the recommendations of Hellebust *et al*.[15] and ICRU 89.[16,104] Applicator reconstruction uncertainties should be ≤ 2 mm. If the uncertainties exceed 2 mm, efforts should be made to improve quality (e.g., reduce slice thickness, optimize MRI sequences to minimize artifacts and distortions, use MRI specific markers). When available, and following commissioning, use of 3D applicator models is recommended.
- If available, verification imaging is recommended when a patient transfer is required as part of the treatment workflow to account for potential patient movement or disturbance of the applicator(s). The dosimetric significance of this potential motion remains controversial, and is dependent on the type of implant (e.g., intracavitary versus interstitial), sedation, and the immobilization equipment utilized.[184-187] For instance, motion can be minimized with tighter packing although this may require the administration of anesthesia.
- Develop a plan with an MRI physicist and/or vendor to ensure SAR limits are not exceeded in special situations such as when a patient is anesthetized/sedated or has an implanted device.
- Work with an MRI physicist and /or vendor to develop a QA program for the MRI scanner (e.g., image quality, image geometry, image transfer integrity, orientation).

B. MRI safety essential considerations

Care should be taken when considering a transition to a higher field strength MRI scanner (e.g., 1.5 to 3 T) for BT patients. It is imperative that commissioning tests be performed with the relevant BT equipment and accessories, in phantom, to ensure patients may be safely imaged with the existing equipment at a higher magnetic strength. Commissioning will require a review and re-optimization of the imaging sequences since the level of susceptibility artifacts can become substantial for certain sequences, such as diffusion weighted imaging.[188] Also, the presence of metal (e.g., titanium applicators) can enhance magnetic susceptibility artifacts and heating at higher magnetic field strengths; therefore, the use of plastic applicators is preferred. Lastly, the user should investigate whether their applicators/needles are labeled MRI safe or MRI conditional at 3.0 T. Not all devices that have been tested at 1.5 T have been tested at higher

magnetic fields,[189] and a device deemed MRI conditional under one environment (e.g., field strength) may not be safe to scan in another.[159] To expedite this process, it may prove helpful to consult with colleagues in Radiology. Below is a summary of the TG MRI safety recommendations as it relates to MRI integration in HDR BT. This list should be used to compliment the recommendations and requirements found in the ACR manual on MR safety.[155]

MRI Safety Recommendations:

- Establish a checklist for screening patients and equipment prior to each MRI scan (example forms are available on acr.org or mrisafety.com).[190,191]
- Transition from 1.5 T to 3.0 T should not be done without repeating safety and image optimization tests as described in Section IV.
- Ensure checks are in place to ensure MRI safe or conditional applicators are used for BT implants, and that applicators and all ancillary devices to be introduced specifically for the BT workflow are used in accordance with the vendor instructions for use.
- Members of the care team requiring access to the MRI suite should receive MRI safety training and annual refreshers to ensure they can safely practice near and/or in the MRI vault. Additionally, they should also receive the appropriate BT procedure specific training as this may be a non-standard image guided procedure.
- Ensure all members of the care team are appropriately screened before entering zone III or IV.
- Vendor provided or approved padding should be used to prevent the patient from coming into direct contact with metallic objects, even outside of the bore, and the bore wall during MRI scans to reduce the risk that the patient may experience thermal induced effects.
- Care should be taken to prevent skin-to-skin contact of limbs during MRI scans to prevent thermal injuries.
- Hearing protection should be provided to the patient and personnel remaining in the MRI room during imaging. If the patient is anesthetized, proper placement should be checked by the team.
- MR conditional ancillary equipment needed for specific or special BT workflows should be kept separate from non-MR conditional equipment and labeled appropriately. Screening of equipment just prior to use on day of procedure is advised to help minimize potential for errors.
- Patients who are sedated or anesthetized should be scanned in Normal Operating Mode (<2 W/kg whole body limit). Work with an MRI physicist and/or vendor to verify that SAR limits are not exceeded for the different clinical sequences that have been developed, especially when scanning at 3T.
- Patients with implanted devices should be scanned in accordance with the MR conditions provided by the device manufacturer, which may be stricter than the Normal Operating Mode and/or limit scanning to lower field strengths. Work with an MRI physicist and/or vendor to verify that SAR limits are not exceeded for the different clinical sequences that have been developed, especially when scanning at 3T. Further adjustments may be necessary to address possible artifacts induced by implanted devices. If safety and image quality requirements cannot be met, then another modality may need to be considered.

C. Quality Assurance

Traditionally, recommendations for QA have been issued in publications as a series of prescriptive guidelines, with suggested frequencies and tolerances. However, with the increasing complexity of radiotherapy planning and delivery techniques, alternative approaches to QA have been considered.[1] As BT physicists new to MRI will seek guidance to its integration to HDR BT, the Task Group has provided recommendations for traditional QA, as well as the AAPM TG-100 Report approach.

i. Traditional HDR BT Program QA

The Task Group recommends that clinics continue to perform their standard imaging and HDR BT QA in accordance with federal/state regulations and professional society recommendations. In addition, several additional QA tests should be performed to ensure the safe integration of MRI into the BT workflow.[192] Table 7 provides a list of suggested QA procedures and frequencies to perform specifically when MRI is integrated into the HDR clinical workflow. For a comprehensive list of QA tests recommended for MR simulators, please refer to TG 284.[192]

ii. QA considerations for MRI integration with HDR BT

The Task Group recommends that each clinic follow the AAPM TG-100 Report methodology for process mapping, failure mode collection, scoring, and analysis as demonstrated in Section V for an MRI-$HDR_{prostate}$ workflow. Safety barriers should be used to address high priority failure modes and include mechanisms for both prevention and detection. A number of barriers were identified during the current FMEA analysis in Section V. Several of these apply universally to other workflows involving HDR BT and/or MRI.

<u>Recommendations on Safety Barriers:</u>

- Radiation oncologist contouring remains a critical and often overlooked aspect of treatment planning. The QMP should actively look for contouring errors and encourage robust peer review and trainee supervision.
- Needle/catheter digitization is a crucial step in any HDR BT workflow. The following safety barriers are recommended:
  - If MRI markers are used for plastic applicators, the marker should be inspected prior to use to verify the integrity of the marker, and the absence of air bubbles in critical locations of the marker (e.g., marker tip).
  - Critical review of planning images by physician and physicist prior to removing patient from the MRI table. The QMP involved in the procedure should be familiar with the types of applicators used and how these applicators present in both normal and abnormal scenarios.
  - Secondary review of applicator digitization should be performed by an independent QMP or a certified medical dosimetrist prior to resuming planning.
- Whenever implantation and delivery are performed in separate locations, applicator movement during transport is a major concern. Robust immobilization is

recommended as well as the use of a dedicated transfer device such as a portable mattress, hover unit, or removable couch top. A pre-treatment imaging protocol should be implemented to define image acquisition sequences, registration, and validation of applicator(s) positioning.

- All data imported and selected for use during treatment planning should be made visible to an independent reviewer through descriptive labeling, the use of screen captures, or other suitable mechanisms.
- While not specifically highlighted among the top failure modes, other routine safety barriers specific to current FMEA example apply such as verification of the:
  - Treatment length;
  - Plan transfer from treatment planning system to treatment control station;
  - Source model (i.e., if multiple models are commissioned in the TPS);
  - Source strength;
  - Afterloader (i.e., if multiple afterloaders are available in a clinic);
  - Template alignment; and
  - Plan normalization and prescription.

Additionally, an independent secondary dose calculation should be performed.[51,52]

D. Logistical and economic considerations

Before integrating MRI into a BT practice, it is important for the BT team to meet with all relevant stakeholders both within and outside of the department.

Recommendations on Logistics and Economics

- Brachytherapy team should meet with parties outside of the department (e.g., radiology, anesthesia, infection control, clinical engineering) to develop a workflow and identify resource needs and workspaces.
- Discussions on finances should be initiated with department administrators early in the planning phase to ensure appropriate funds.
- Team should review and be familiar with the relevant charge codes that should be captured with the use of MRI within the BT workflow.
- Charges should be periodically reviewed and updates made, when necessary (e.g., introduction of new bundle payments).

VII. Potential future development in MRI-guided BT

Interests in MRI-integrated BT suites, equipped with both RF and radiation shielding for simultaneous MR imaging and treatment delivery, are increasing as the field recognizes the value and convenience of having an MRI available at the time of BT implants.[193] Figure 8 illustrates an example setup where a typical afterloader is placed just outside the 5 Gauss line to ensure proper functioning of electronics, especially what drives the ^{192}Ir source. In addition, towards true integration, Beld *et al.*[194] proposed a prototype of an MRI-conditional HDR

afterloader design that properly shields the electronics from RF, and contains a plastic source cable. If this line of research is successful, one day, it may be possible to observe real-time MR imaging while the HDR treatment is delivered, much like an MRI-linac system.[195] This may also allow real-time visualization of source positions with respect to patient anatomy.

VIII. Summary

The Task Group presented a series of recommendations to ensure the successful implementation of MRI for HDR BT. Recommendations have been provided on potential workflows, simulation imaging, treatment planning, and pre-treatment verification for those centers that are integrating MRI into their HDR program, and to support centers with existing programs. MRI safety considerations were discussed, and a risk based analysis was provided for an MRI-guided prostate HDR workflow. Although these recommendations have been limited to gynecologic and prostate BT, many may be applicable to other disease sites.

Disclosure Statement

The members of AAPM Task Group # 303 listed below disclose the following potential Conflict(s) of Interest related to subject matter or materials presented in this document.

K-P. Hwang receives research funding from General Electric Healthcare.

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FIGURES CAPTIONS:

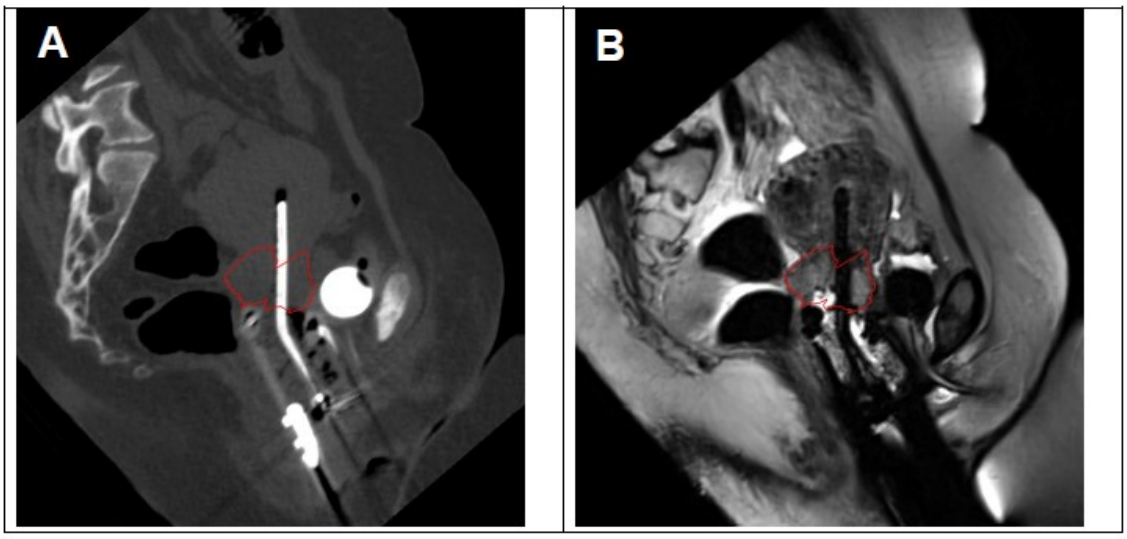


Figure 1. Sagittal view of a GYN patient with a titanium tandem and ring applicator set, including a rectal retractor on (A) CT (Philips Brilliance large bore CT) and (B) MRI (sagittal 2D T2W FSE sequence acquired on a 3.0T Siemens Skyra MRI scanner). The high risk CTV is depicted in the red contour.

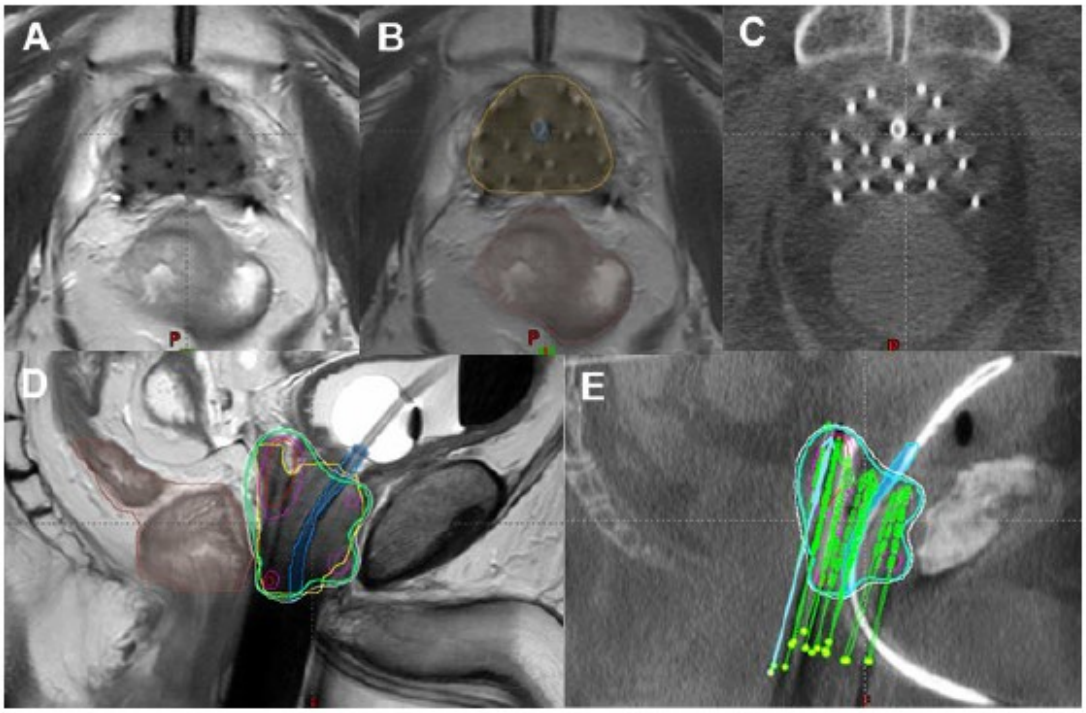


Figure 2. Mid-gland axial and sagittal views of a patient with a prostate HDR implant on (A) & (D) MRI and (C) & (E) intraoperative CBCT, respectively. The registration of the two datasets, with a 50% MRI-CT blending in the axial view is depicted in (B). The MRI dataset (axial and sagittal T2 sequences obtained with the patient under general anesthesia, using a 3.0T Philips Ingenia MRI scanner) is used for target delineation, while the CT is typically used for applicator reconstruction.

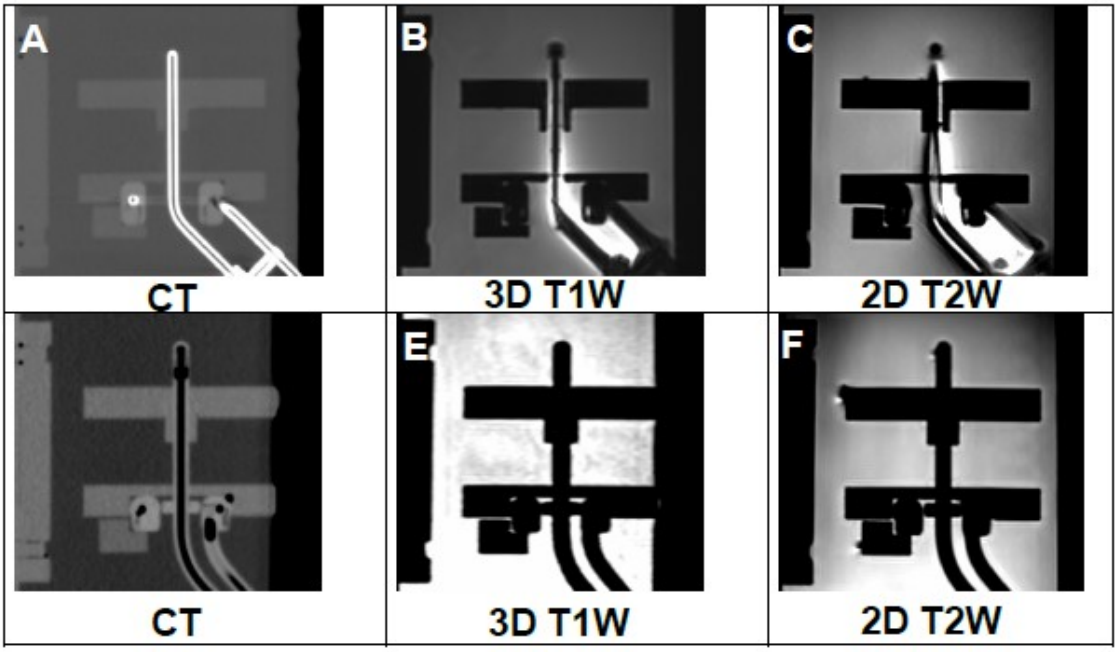


Figure 3. Sagittal view of a (A-C) titanium and (D-F) plastic ring and tandem applicator set in an in-house phantom designed for applicator reconstruction commissioning on (A&D) CT (Philips Brilliance large bore CT), (B&E) 3D T1W images (3.0T Siemens Skyra MRI), and (C&F) 2D T2W images (3.0T Siemens Skyra MRI).

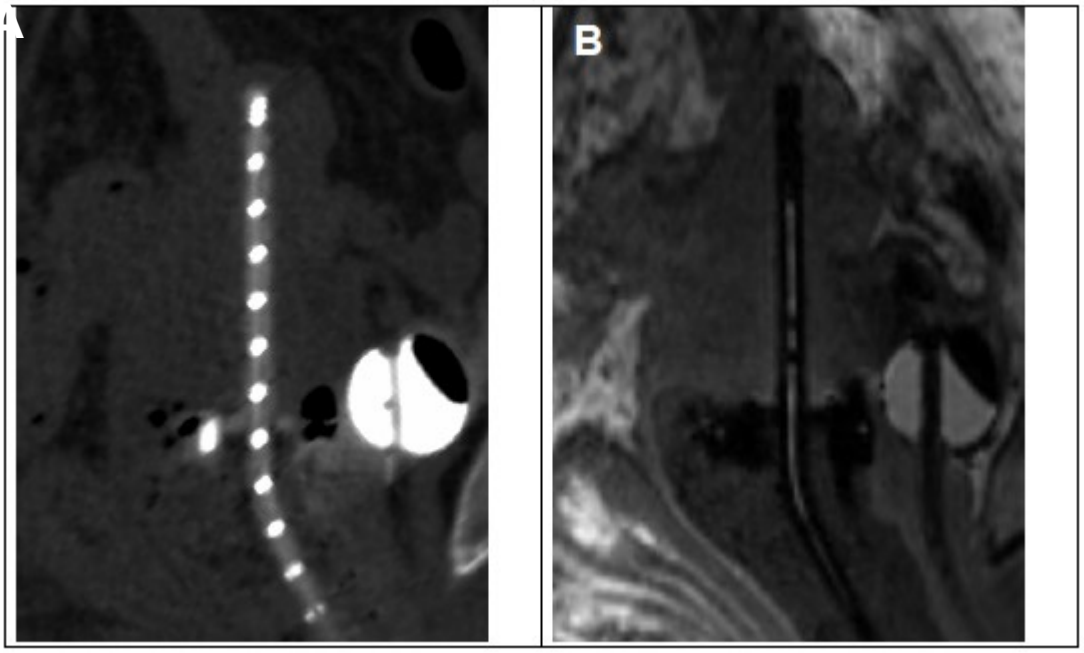


Figure 4. Sagittal MRI images on A) CT (Philips Brilliance large bore CT) and B) 3D T1W MPRAGE MRI (3.0T Siemens Skyra MRI) of a plastic ring and tandem applicator *in vivo*. To visualize the lumen of the ring and tandem applicators, an x-ray marker wire and an in-house fabricated marker filled with gadolinium-doped water was inserted in the applicators during CT and MRI acquisition, respectively. The absence of a hyperintense signal at the tip of the tandem on MRI versus CT, is an indication of the presence of air-bubbles in the MRI marker. (Please note, given the contrast agent used for the in-house marker, it was not visible on T2W images. If a marker with a T2W contrast is used, a similar void may be expected in the presence of an air-bubble.)

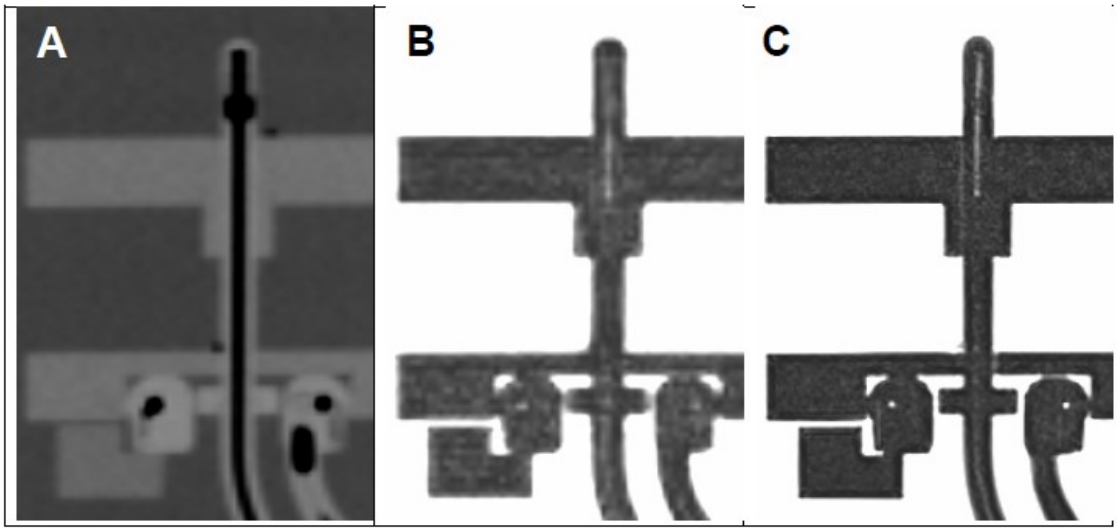
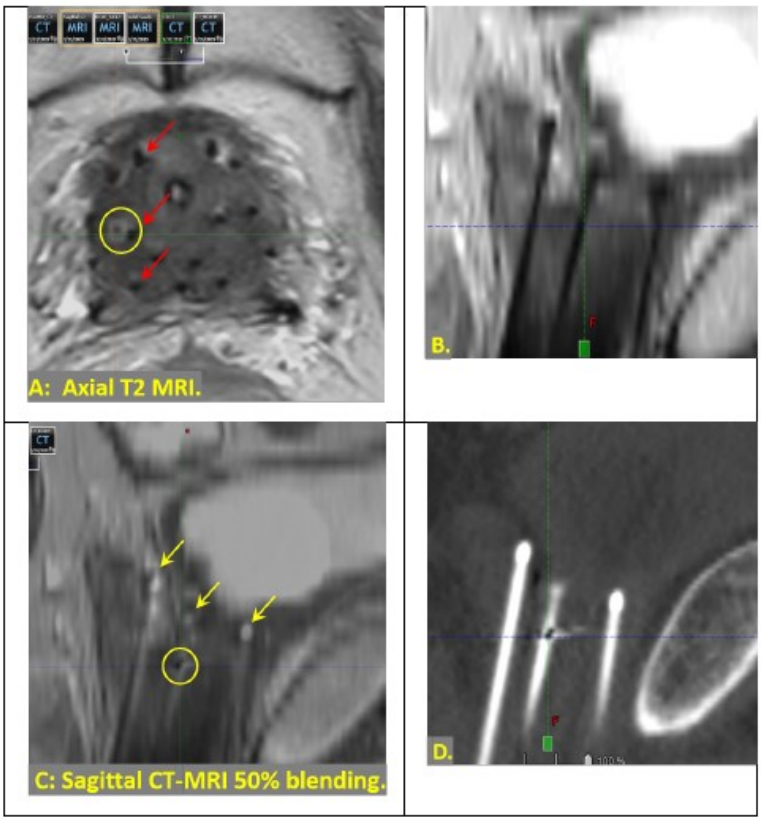


Figure 5. Sagittal images of a plastic ring and tandem applicator set in an in-house phantom using (A) CT (Philips Brilliance large bore CT), (B) 3D T1W, and (C) 2D T2W images (3.0T Siemens Skyra MRI) during the evaluation of a commercially available MRI marker (C4 Imaging LLC, Doylestown, PA, USA). The presence of the marker in the MR images allows the lumen of the ring and tandem applicators to appear hyperintense on the MR imaging sequences.



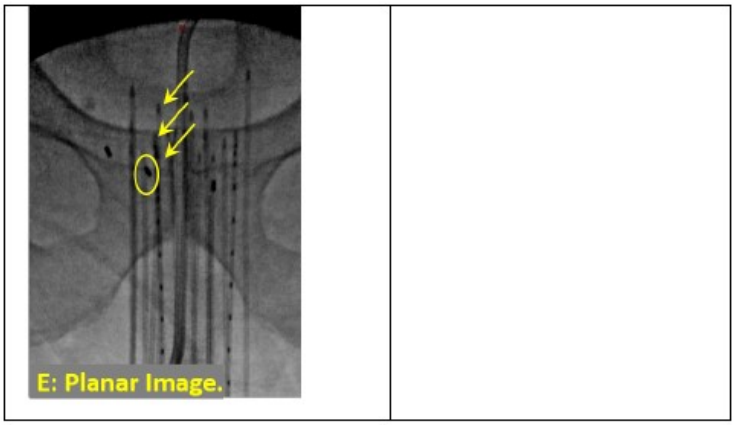


Figure 6: Example images acquired during implant and pre-treatment for a multi-fraction, single implant workflow as described in the risk-based analysis in Section V. An intraoperative planning (A & B) T2W-MRI [(A) axial and (B) sagittal T2W-MRI] was registered to (D) a pre-treatment, post recovery CT using implanted fiducial markers. The circles denote one of the fiducial markers and arrows point to needles. The needle tip positions were then confirmed to coincide between CT and MRI, as shown in (C) a 50:50 blended view. Artifacts from the marker reconstruction on the sagittal image is seen on CT only. After the patient is transferred to the treatment vault, (E) a planar x-ray image is taken to verify the distance from the selected needle tips to the respective fiducial markers has not changed.

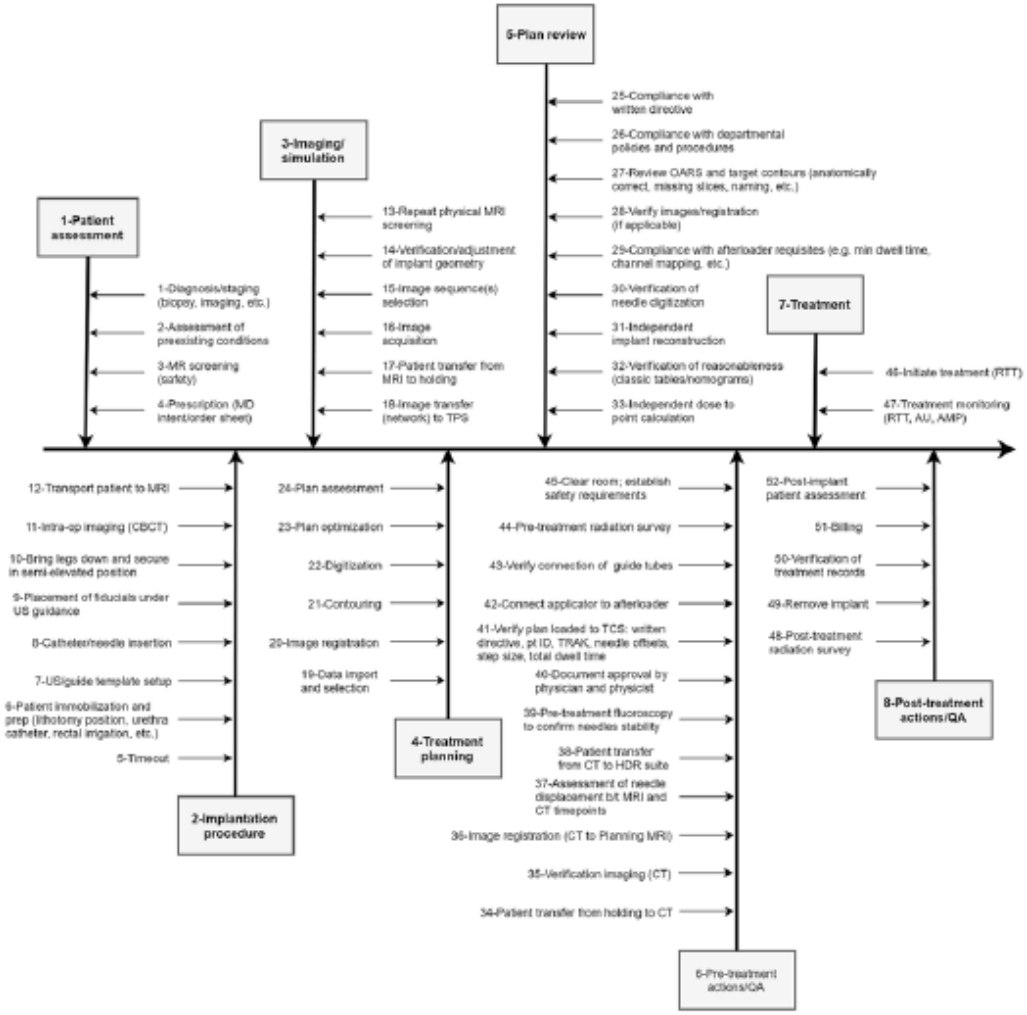


Figure 7: Process map for an example MRI-based, prostate HDR BT detailed in Section V.

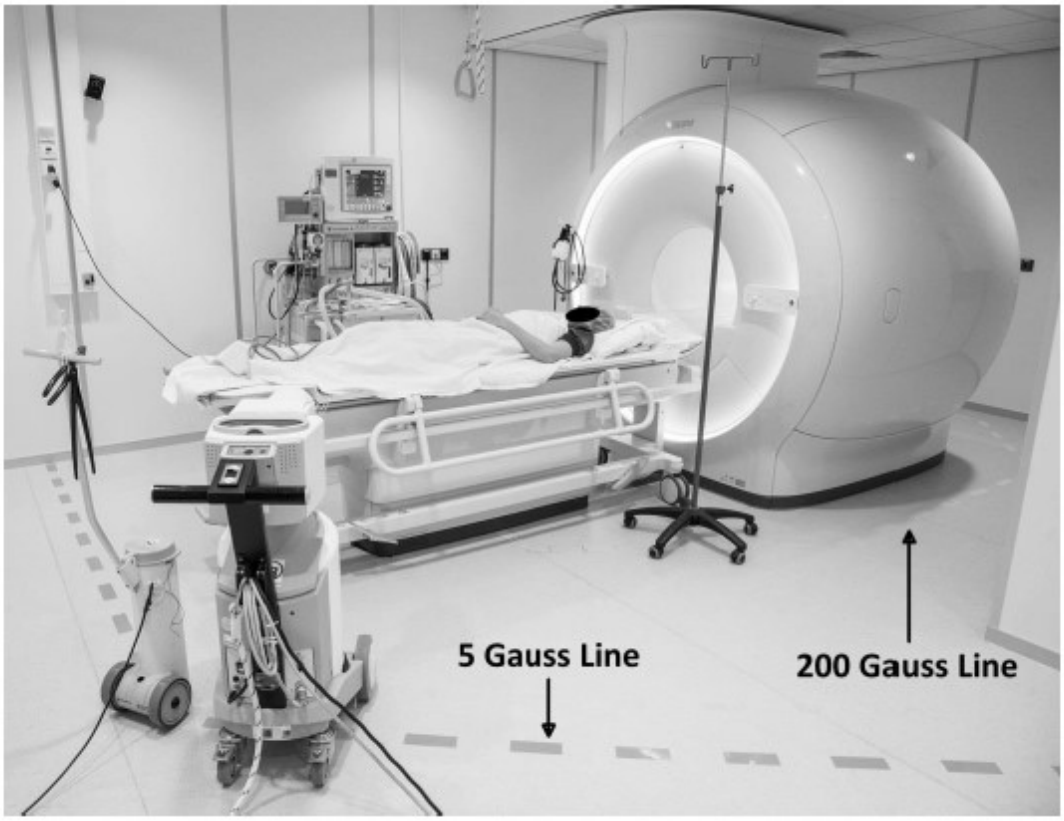


Figure 8. An MRI-HDR BT-integrated suite at the University of Medical Center Utrecht, Utrecht, the Netherlands. Note that MRI-conditional anesthesia cart is available in-room enabling a wide range of treatment procedures. Picture courtesy of Dr Rien Moerland.[193]

IX. References

1. Huq MS, Fraass BA, Dunscombe PB, et al. The report of Task Group 100 of the AAPM: Application of risk analysis methods to radiation therapy quality management. *Medical Physics.* 2016;43(7):4209-4262.
2. Viswanathan AN, Beriwal S, De Los Santos J, et al. The American Brachytherapy Society Treatment Recommendations for Locally Advanced Carcinoma of the Cervix Part II: High Dose-Rate Brachytherapy. *Brachytherapy.* 2012;11(1):47-52.
3. Pugh TJ, Pokharel SS. Magnetic resonance imaging in prostate brachytherapy: Evidence, clinical end points to data, and direction forward. *Brachytherapy.* 2017;16(4):659-664.
4. Dirix P, Haustermans K, Vandecaveye V. The Value of Magnetic Resonance Imaging for Radiotherapy Planning. *Seminars in Radiation Oncology.* 2014;24(3):151-159.
5. Tanderup K, Viswanathan AN, Kirisits C, et al. Magnetic resonance image guided brachytherapy. *Semin Radiat Oncol.* 2014;24(3):181-191.
6. Gay S, Chen N, Burch J, et al. Multiplanar Reconstruction in Magnetic Resonance Evaluation of the Knee: Comparison with Film Magnetic Resonance Interpretation. *Investigative Radiology.* 1993;28(2):142-145.
7. Bruno F, Arrigoni F, Mariani S, et al. Advanced magnetic resonance imaging (MRI) of soft tissue tumors: techniques and applications. *La radiologia medica.* 2019;124(4):243-252.
8. Schabelman E, Witting M. The Relationship of Radiocontrast, Iodine, and Seafood Allergies: A Medical Myth Exposed. *Journal of Emergency Medicine.* 2010;39(5):701-707.
9. Sicherer SH. Risk of severe allergic reactions from the use of potassium iodide for radiation emergencies. *Journal of Allergy and Clinical Immunology.* 2004;114(6):1395-1397.
10. Venkatesan AM, Stafford RJ, Duran C, et al. Prostate magnetic resonance imaging for brachytherapists: Anatomy and technique. *Brachytherapy.* 2017;16(4):679-687.
11. Blanchard P, Pugh TJ, Mahmood U, et al. MRI Simulation for LDR prostate brachytherapy: Can we replace ultrasound with MRI for treatment planning? Comparison of pre-planning, day 0, and day 30 MR dosimetry *Brachytherapy.* 2016;15(3):S57.
12. Potter R, Haie-Meder C, Van Limbergen E, 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. *Radiother Oncol.* 2006;78(1):67-77.
13. Dimopoulos JC, Petrow P, Tanderup K, 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.* 2012;103(1):113-122.
14. Haie-Meder C, Potter R, Van Limbergen E, et al. Recommendations from Gynaecological (GYN) GEC-ESTRO Working Group (I): concepts and terms in 3D image based 3D treatment planning in cervix cancer brachytherapy with emphasis on MRI assessment of GTV and CTV. *Radiother Oncol.* 2005;74(3):235-245.

15. Hellebust TP, Kirisits C, Berger D, 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.* 2010;96(2):153-160.

16. ICRU Report No. 89. Prescribing, Recording, and Reporting Brachytherapy for Cancer of the Cervix. *Journal of the ICRU.* 2013;13(1).

17. Curran WJ, DiSaia PJ, Wolmark N. NRG Oncology Research Opportunities within the New National Clinical Trials Network. *Seminars in oncology.* 2014;41(5):553-555.

18. Grover S, Harkenrider MM, Cho LP, et al. Image Guided Cervical Brachytherapy: 2014 Survey of the American Brachytherapy Society. *Int J Radiat Oncol Biol Phys.* 2016;94(3):598-604.

19. Wang J, Tanderup K, Cunha A, et al. Magnetic resonance imaging basics for the prostate brachytherapist. *Brachytherapy.* 2017;16(4):715-727.

20. Blanchard P, Menard C, Frank SJ. Clinical use of magnetic resonance imaging across the prostate brachytherapy workflow. *Brachytherapy.* 2017;16:734 - 742.

21. Buus S, Rylander S, Hokland S, et al. Learning curve of MRI-based planning for high-dose-rate brachytherapy for prostate cancer. *Brachytherapy.* 2016;15(4):426-434.

22. Hoskin PJ, Rojas AM, Ostler PJ, et al. Dosimetric predictors of biochemical control of prostate cancer in patients randomised to external beam radiotherapy with a boost of high dose rate brachytherapy. *Radiother Oncol.* 2013;110(1):110-113.

23. Damato AL, Viswanathan AN. Magnetic Resonance-Guided Gynecologic Brachytherapy. *Magn Reson Imaging Clin N Am.* 2015;23(4):633-642.

24. Viswanathan AN, Cormack R, Holloway CL, et al. Magnetic resonance–guided interstitial therapy for vaginal recurrence of endometrial cancer. *International Journal of Radiation Oncology*Biology*Physics.* 2006;66(1):91-99.

25. Viswanathan AN, Szymonifka J, Tempany-Afdhal CM, et al. A prospective trial of real-time magnetic resonance–guided catheter placement in interstitial gynecologic brachytherapy. *Brachytherapy.* 2013;12(3):240-247.

26. Enders J, Rief M, Zimmermann E, et al. High-Field Open versus Short-Bore Magnetic Resonance Imaging of the Spine: A Randomized Controlled Comparison of Image Quality. *PLoS ONE.* 2013;8(12):e83427.

27. Beriwal S, Kannan N, Kim H, 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. *Clinical Oncology.* 2011;23(10):685-690.

28. Wood R, Bassett, K., Foerster, V., Spry, C., and Tong, L. *1.5 Tesla Magnetic Resonance Imaging Scanners Compared with 3.0 Tesla Magnetic Resonance Imaging Scanners: Systematic Review of Clinical Effectiveness.* Available from: https://www.ncbi.nlm.nih.gov/books/NBK174456/.

29. Ko HC, Huang JY, Miller JR, et al. Novel use of ViewRay MRI guidance for high-dose-rate brachytherapy in the treatment of cervical cancer. *Brachytherapy.* 2018;17(4):680-688.

30. Kirisits C, Lang S, Dimopoulos J, et al. The Vienna applicator for combined intracavitary and interstitial brachytherapy of cervical cancer: Design, application, treatment planning, and dosimetric results. *International Journal of Radiation Oncology*Biology*Physics.* 2006;65(2):624-630.

31. Nomden CN, de Leeuw AAC, Moerland MA, et al. Clinical Use of the Utrecht Applicator for Combined Intracavitary/Interstitial Brachytherapy Treatment in Locally Advanced Cervical Cancer. *International Journal of Radiation Oncology • Biology • Physics.* 2012;82(4):1424-1430.

32. Walter F, Maihofer C, Schuttrumpf L, et al. Combined intracavitary and interstitial brachytherapy of cervical cancer using the novel hybrid applicator Venezia: Clinical feasibility and initial results. *Brachytherapy.* 2018.

33. Schwarz JK, Beriwal S, Esthappan J, et al. Consensus statement for brachytherapy for the treatment of medically inoperable endometrial cancer. *Brachytherapy.* 2015;14(5):587-599.

34. Owrangi AM, Jolly S, Balter JM, et al. Clinical implementation of MR-guided vaginal cylinder brachytherapy. *J Appl Clin Med Phys.* 2015;16(6):490-500.

35. Chapman CH, Prisciandaro JI, Maturen KE, et al. MRI-Based Evaluation of the Vaginal Cuff in Brachytherapy Planning: Are We Missing the Target? *Int J Radiat Oncol Biol Phys.* 2016;95(2):743-750.

36. Lindegaard JC, Madsen ML, Traberg A, et al. Individualised 3D printed vaginal template for MRI guided brachytherapy in locally advanced cervical cancer. *Radiotherapy and Oncology.* 2016;118(1):173-175.

37. Perez-Calatayud J, Kuipers F, Ballester F, et al. Exclusive MRI-based tandem and colpostats reconstruction in gynaecological brachytherapy treatment planning. *Radiotherapy and Oncology.* 2009;91(2):181-186.

38. Soliman AS, Owrangi A, Ravi A, et al. Metal artifacts in MRI-guided brachytherapy of cervical cancer. *J Contemp Brachytherapy.* 2016;8(4):363-369.

39. Menard C, Susil RC, Choyke P, et al. MRI-guided HDR prostate brachytherapy in standard 1.5T scanner. *Int J Radiat Oncol Biol Phys.* 2004;59(5):1414-1423.

40. Chassagne D, Dutreix A, Almond P, et al. Dose and Volume Specification for Reporting Intracavitary Therapy in Gynecology. *Journal of the International Commission on Radiation Units and Measurements.* 1985;ICRU 38:1-23.

41. Viswanathan AN, Thomadsen B. American Brachytherapy Society consensus guidelines for locally advanced carcinoma of the cervix. Part I: General principles. *Brachytherapy.* 2012;11:33-46.

42. Potter R, Georg P, Dimopoulos JC, 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.* 2011;100(1):116-123.

43. Lindegaard JC, Fokdal LU, Nielsen SK, et al. MRI-guided adaptive radiotherapy in locally advanced cervical cancer from a Nordic perspective. *Acta Oncol.* 2013;52(7):1510-1519.

44. Mahantshetty U, Krishnatry R, Hande V, et al. Magnetic Resonance Image Guided Adaptive Brachytherapy in Locally Advanced Cervical Cancer: An Experience From a

Tertiary Cancer Center in a Low and Middle Income Countries Setting. *Int J Radiat Oncol Biol Phys.* 2017;99(3):608-617.

45. Pötter R, Tanderup K, Kirisits C, et al. The EMBRACE II study: The outcome and prospect of two decades of evolution within the GEC-ESTRO GYN working group and the EMBRACE studies. *Clinical and Translational Radiation Oncology.* 2018;9:48-60.

46. Fokdal L, Sturdza A, Mazeron R, et al. Image guided adaptive brachytherapy with combined intracavitary and interstitial technique improves the therapeutic ratio in locally advanced cervical cancer: Analysis from the retroEMBRACE study. *Radiother Oncol.* 2016;120(3):434-440.

47. Mazeron R, Fokdal LU, Kirchheiner K, et al. Dose-volume effect relationships for late rectal morbidity in patients treated with chemoradiation and MRI-guided adaptive brachytherapy for locally advanced cervical cancer: Results from the prospective multicenter EMBRACE study. *Radiother Oncol.* 2016;120(3):412-419.

48. Pötter R, Tanderup K, Schmid MP, et al. MRI-guided adaptive brachytherapy in locally advanced cervical cancer (EMBRACE-I): a multicentre prospective cohort study. *The Lancet Oncology.* 2021;22(4):538-547.

49. Glasgow GP, Bourland DJ, Grigsby PW, et al. *Remote Afterloading Technology.* College Park, MD

50. Nath R, Anderson LL, Meli JA, 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.* 1997;24(10):1557-1598.

51. Kubo HD, Glasgow GP, Pethel TD, et al. High dose-rate brachytherapy treatment delivery: Report of the AAPM Radiation Therapy Committee Task Group No. 59. *Med Phys.* 1998;25(4):375-403.

52. Kutcher GJ, Coia L, Gillin M, et al. Comprehensive QA for radiation oncology: Report of AAPM Radiation Therapy Committee Task Group 40. *Med Phys.* 1994;21(4):581-618.

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

54. Jackson EF, Bronskill MJ, Drost DJ, et al. *Acceptance Testing and Quality Assurance Procedures for Magnetic Resonance Imaging Facilities: Report of MR Subcommittee Task Group I.* College Park, MD 2010. Available from: https://www.aapm.org/pubs/reports/RPT_100.pdf.

55. Yanasak N, Clarke G, Stafford RJ, et al. *Parallel Imaging in MRI: Technology, Applications, and Quality Control: The Report of AAPM Task Group 118.* College Park, MD

56. Brock KK, Mutic S, McNutt TR, et al. Use of image registration and fusion algorithms and techniques in radiotherapy: Report of the AAPM Radiation Therapy Committee Task Group No. 132. *Medical Physics.* 2017;44(7):e43-e76.

57. Haack S, Nielsen SK, Lindegaard JC, et al. Applicator reconstruction in MRI 3D image-based dose planning of brachytherapy for cervical cancer. *Radiother Oncol.* 2009;91(2):187-193.

58. Kim Y, Muruganandham M, Modrick JM, et al. Evaluation of artifacts and distortions of titanium applicators on 3.0-Tesla MRI: feasibility of titanium applicators in MRI-guided

brachytherapy for gynecological cancer. *Int J Radiat Oncol Biol Phys.* 2011;80(3):947-955.

59. Miquel ME, Blackall JM, Uribe S, et al. Patient-specific respiratory models using dynamic 3D MRI: preliminary volunteer results. *Phys Med.* 2013;29(2):214-220.

60. Harry VN, Semple SI, Gilbert FJ, et al. Diffusion-weighted magnetic resonance imaging in the early detection of response to chemoradiation in cervical cancer. *Gynecol Oncol.* 2008;111(2):213-220.

61. Olsen JR, Esthappan J, DeWees T, et al. Tumor volume and subvolume concordance between FDG-PET/CT and diffusion-weighted MRI for squamous cell carcinoma of the cervix. *Journal of Magnetic Resonance Imaging.* 2013;37(2):431-434.

62. Han K, Croke J, Foltz W, et al. A prospective study of DWI, DCE-MRI and FDG PET imaging for target delineation in brachytherapy for cervical cancer. *Radiotherapy and Oncology.* 2016;120(3):519-525.

63. Podder TK, Beaulieu L, Caldwell B, et al. AAPM and GEC-ESTRO guidelines for image-guided robotic brachytherapy: report of Task Group 192. *Med Phys.* 2014;41(10):101501.

64. Sun W, Bhatia SK, Jacobson GM, et al. Target volume changes through high-dose-rate brachytherapy for cervical cancer when evaluated on high resolution (3.0 Tesla) magnetic resonance imaging. *Practical Radiation Oncology.* 2012;2(4):e101-e106.

65. Rao YJ, Zoberi JE, Kadbi M, et al. Metal artifact reduction in MRI-based cervical cancer intracavitary brachytherapy. *Phys Med Biol.* 2017;62:3011-3024.

66. Trifiletti DM, Libby B, Feuerlein S, et al. Implementing MRI-based target delineation for cervical cancer treatment within a rapid workflow environment for image-guided brachytherapy: A practical approach for centers without in-room MRI. *Brachytherapy.*14(6):905-909.

67. Pötter R, Federico M, Sturdza A, et al. Value of Magnetic Resonance Imaging Without or With Applicator in Place for Target Definition in Cervix Cancer Brachytherapy. *International Journal of Radiation Oncology • Biology • Physics.* 2016;94(3):588-597.

68. Maenhout M, Peters M, van Vulpen M, et al. Focal MRI-Guided Salvage High-Dose-Rate Brachytherapy in Patients With Radiorecurrent Prostate Cancer. *Technology in Cancer Research & Treatment.* 2017;16(6):1194-1201.

69. Davidson MT, Yuen J, D'Souza DP, et al. Optimization of high-dose-rate cervix brachytherapy applicator placement: the benefits of intraoperative ultrasound guidance. *Brachytherapy.* 2008;7(3):248-253.

70. GEC-ESTRO. *A European study on MRI-guided brachytherapy in locally advanced cervical cancer (EMBRACE).* Available from: https://www.embracestudy.dk/.

71. Nesvacil N, Potter R, Sturdza A, et al. Adaptive image guided brachytherapy for cervical cancer: a combined MRI-/CT-planning technique with MRI only at first fraction. *Radiother Oncol.* 2013;107(1):75-81.

72. Harkenrider MM, Shea SM, Wood AM, et al. How one institution overcame the challenges to start an MRI-based brachytherapy program for cervical cancer. *Journal of Contemporary Brachytherapy.* 2017;9(2):177-186.

73. D'Amico AV, Tempany CM, Schultz D, et al. Comparing PSA outcome after radical prostatectomy or magnetic resonance imaging-guided partial prostatic irradiation in select patients with clinically localized adenocarcinoma of the prostate. *Urology.* 2003;62(6):1063-1067.

74. Menard C, Pambrun JF, Kadoury S. The utilization of magnetic resonance imaging in the operating room. *Brachytherapy.* 2017;16(4):754-760.

75. Murgic J, Chung P, Berlin A, et al. Lessons learned using an MRI-only workflow during high-dose-rate brachytherapy for prostate cancer. *Brachytherapy.* 2016;15(2):147-155.

76. Kirisits C, Schmid MP, Nesvacil N, et al. Chapter 19: Medical University of Vienna, Vienna, Austria. In: Song WY, Tanderup K, Pieters BR, eds. *Emerging technologies in brachytherapy*. Boca Raton, FL: CRC Press, Taylor & Francis Group; 2017.

77. Kapur T, Egger J, Damato A, et al. 3-T MR-guided brachytherapy for gynecologic malignancies. *Magn Reson Imaging.* 2012;30(9):1279-1290.

78. Anderson R, Armour E, Beeckler C, et al. Interventional Radiation Oncology (IRO): Transition of a magnetic resonance simulator to a brachytherapy suite. *Brachytherapy.* 2018;17(3):587-596.

79. Busse RF, Hariharan H, Vu A, et al. Fast spin echo sequences with very long echo trains: design of variable refocusing flip angle schedules and generation of clinical T2 contrast. *Magn Reson Med.* 2006;55(5):1030-1037.

80. Potter R, Kirisits C, Fidarova E, et al. Present status and future of high-precision image guided adaptive brachytherapy for cervix carcinoma. *Acta Oncol.* 2008;47:1325-1336.

81. Liney GP, Moerland MA. Magnetic resonance imaging acquisition techniques for radiotherapy planning. *Semin Radiat Oncol.* 2014;24(3):160-168.

82. Bernstein M, K. King, and X. Zhou. *Handbook of MRI Pulse Sequences.* 1st edition ed. Burlington, MA: Elsevier Academic Press; 2004.

83. Ma J, Moerland MA, Venkatesan AM, et al. Pulse sequence considerations for simulation and postimplant dosimetry of prostate brachytherapy. *Brachytherapy.* 2017;16(4):743-753.

84. Paulson ES, Erickson B, Schultz C, et al. Comprehensive MRI simulation methodology using a dedicated MRI scanner in radiation oncology for external beam radiation treatment planning. *Med Phys.* 2015;42(1):28-39.

85. Jan JWL, Bas WR, Cornelis ATVdB, et al. MR guidance in radiotherapy. *Physics in Medicine & Biology.* 2014;59(21):R349.

86. Krupa K, Bekiesinska-Figatowska M. Artifacts in magnetic resonance imaging. *Pol J Radiol.* 2015;80:93-106.

87. Mitchell MD, Kundel HL, Axel L, et al. Agarose as a tissue equivalent phantom material for NMR imaging. *Magn Reson Imaging.* 1986;4(3):263-266.

88. Schindel J, Muruganandham M, Pigge FC, et al. Magnetic resonance imaging (MRI) markers for MRI-guided high-dose-rate brachytherapy: novel marker-flange for cervical cancer and marker catheters for prostate cancer. *Int J Radiat Oncol Biol Phys.* 2013;86(2):387-393.

89. Frank SJ, Stafford RJ, Bankson JA, et al. A novel MRI marker for prostate brachytherapy. *Int J Radiat Oncol Biol Phys.* 2008;71(1):5-8.

90. Merkle EM, Dale BM. Abdominal MRI at 3.0 T: the basics revisited. *AJR Am J Roentgenol.* 2006;186:1524-1532.

91. Hu Y, Esthappan J, Mutic S, et al. Improve definition of titanium tandems in MR-guided high dose rate brachytherapy for cervical cancer using proton density weighted MRI. *Radiation Oncology.* 2013;8(1):16.

92. Zoberi JE, Garcia-Ramirez J, Hu Y, et al. Clinical implementation of multisequence MRI-based adaptive intracavitary brachytherapy for cervix cancer. *Journal of Applied Clinical Medical Physics.* 2016;17(1):121-131.

93. Schindel J, Zhang W, Bhatia SK, et al. Dosimetric impacts of applicator displacements and applicator reconstruction-uncertainties on 3D image-guided brachytherapy for cervical cancer. *J Contemp Brachytherapy.* 2013;5:250-257.

94. Tanderup K, Hellebust TP, Lang S, et al. Consequences of random and systematic reconstruction uncertainties in 3D image based brachytherapy in cervical cancer. *Radiotherapy and Oncology.* 2008;89(2):156-163.

95. De Leeuw AAC, Moerland MA, Nomden C, et al. Applicator reconstruction and applicator shifts in 3D MR-based PDR brachytherapy of cervical cancer. *Radiotherapy and Oncology.* 2009;93(2):341-346.

96. Tanderup K, Nesvacil N, Potter R, et al. Uncertainties in image guided adaptive cervix cancer brachytherapy: impact on planning and prescription. *Radiother Oncol.* 2013;107(1):1-5.

97. Deufel CL, Tian S, Yan BB, et al. Automated applicator digitization for high-dose-rate cervix brachytherapy using image thresholding and density-based clustering. *Brachytherapy.* 2020;19(1):111-118.

98. Kim Y, Hsu IC, Lessard E, et al. Dose uncertainty due to computed tomography (CT) slice thickness in CT-based high dose rate brachytherapy of the prostate cancer. *Med Phys.* 2004;31:2543-2548.

99. Walker A, Metcalfe P, Liney G, et al. MRI geometric distortion: Impact on tangential whole-breast IMRT. *Journal of applied clinical medical physics.* 2016;17(5):7-19.

100. Adjeiwaah M, Bylund M, Lundman JA, et al. Quantifying the Effect of 3T Magnetic Resonance Imaging Residual System Distortions and Patient-Induced Susceptibility Distortions on Radiation Therapy Treatment Planning for Prostate Cancer. *International Journal of Radiation Oncology*Biology*Physics.* 2018;100(2):317-324.

101. Pappas EP, Alshanqity M, Moutsatsos A, et al. MRI-Related Geometric Distortions in Stereotactic Radiotherapy Treatment Planning: Evaluation and Dosimetric Impact. *Technology in cancer research & treatment.* 2017;16(6):1120-1129.

102. Brunt JNH. Computed Tomography–Magnetic Resonance Image Registration in Radiotherapy Treatment Planning. *Clinical Oncology.* 2010;22(8):688-697.

103. Tan LT, Tanderup K, Kirisits C, et al. Image-guided Adaptive Radiotherapy in Cervical Cancer. *Seminars in Radiation Oncology.* 2019;29(3):284-298.

104. Kim Y, Kim Y, Todor D, et al. Recommendations on 3D image-based treatment planning, dosimetry and quality management for HDR intracavitary brachytherapy: Report of AAPM Task Group No. 236; Part II: Intracavitary Gynecological Brachytherapy. *In progress.*

105. Petric P, Hudej R, Rogelj P, et al. Comparison of 3D MRI with high sampling efficiency and 2D multiplanar MRI for contouring in cervix cancer brachytherapy. *Radiology and Oncology.* 2012;46(3):242-251.

106. Esthappan J, Ma DJ, Narra VR, et al. Comparison of apparent diffusion coefficient maps to T2-weighted images for target delineation in cervix cancer brachytherapy. *J Contemp Brachytherapy.* 2011;3(4):193-198.

107. Haack S, Pedersen EM, Jespersen SN, et al. Apparent diffusion coefficients in GEC ESTRO target volumes for image guided adaptive brachytherapy of locally advanced cervical cancer. *Acta Oncol.* 2010;49(7):978-983.

108. Schakel T, Hoogduin JM, Terhaard CHJ, et al. Technical Note: Diffusion-weighted MRI with minimal distortion in head-and-neck radiotherapy using a turbo spin echo acquisition method. *Medical Physics.* 2017;44(8):4188-4193.

109. Dyk P, Jiang N, Sun B, et al. Cervical Gross Tumor Volume Dose Predicts Local Control Using Magnetic Resonance Imaging/Diffusion-Weighted Imaging—Guided High-Dose-Rate and Positron Emission Tomography/Computed Tomography—Guided Intensity Modulated Radiation Therapy. *International Journal of Radiation Oncology*Biology*Physics.* 2014;90(4):794-801.

110. Tanderup K, Fokdal LU, Sturdza A, et al. Effect of tumor dose, volume and overall treatment time on local control after radiochemotherapy including MRI guided brachytherapy of locally advanced cervical cancer. *Radiother Oncol.* 2016;120(3):441-446.

111. Tanderup K, R. Pötter, J. Lindegaard, C. Kirisits, I. Juergenliemk-Schulz, A. de Leeuw, I. Fortin, K. Kirchheiner, D. Georg, R. Nout, Y. Seppenwoolde, W. Dörr, T. Liederer, and L. Tee Tan. *Image guided intensity modulated External beam radiochemotherapy and MRI based adaptive BRAchytherapy in locally advanced CErvical cancer - EMBRACE-II.* Available from: https://www.embracestudy.dk/.

112. Swanick CW, Castle KO, Rechner LA, et al. Optimizing packing contrast for MRI-based intracavitary brachytherapy planning for cervical cancer. *Brachytherapy.* 2015;14(3):385-389.

113. Citrin D, Ning H, Guion P, et al. Inverse treatment planning based on MRI for HDR prostate brachytherapy. *Int J Radiat Oncol Biol Phys.* 2005;61(4):1267-1275.

114. Yamada Y, Rogers L, Demanes DJ, et al. American Brachytherapy Society consensus guidelines for high-dose-rate prostate brachytherapy. *Brachytherapy.* 2012;11(1):20-32.

115. Debois M, Oyen R, Maes F, et al. The contribution of magnetic resonance imaging to the three-dimensional treatment planning of localized prostate cancer. *Int J Radiat Oncol Biol Phys.* 1999;45(4):857-865.

116. Rasch C, Barillot I, Remeijer P, et al. Definition of the prostate in CT and MRI: a multi-observer study. *Int J Radiat Oncol Biol Phys.* 1999;43(1):57-66.

117. Smith WL, Lewis C, Bauman G, et al. Prostate volume contouring: a 3D analysis of segmentation using 3DTRUS, CT, and MR. *Int J Radiat Oncol Biol Phys.* 2007;67(4):1238-1247.

118. Christie DRH, Sharpley CF. How Accurately Can Prostate Gland Imaging Measure the Prostate Gland Volume? Results of a Systematic Review. *Prostate Cancer.* 2019;2019:6932572.

119. Demanes DJ, Martinez AA, Ghilezan M, et al. High-Dose-Rate Monotherapy: Safe and Effective Brachytherapy for Patients With Localized Prostate Cancer. *International Journal of Radiation Oncology*Biology*Physics.* 2011;81(5):1286-1292.

120. Zamboglou N, Tselis N, Baltas D, et al. High-Dose-Rate Interstitial Brachytherapy as Monotherapy for Clinically Localized Prostate Cancer: Treatment Evolution and Mature Results. *International Journal of Radiation Oncology*Biology*Physics.* 2013;85(3):672-678.

121. Demanes DJ, Ghilezan MI. High-dose-rate brachytherapy as monotherapy for prostate cancer. *Brachytherapy.* 2014;13(6):529-541.

122. Tisseverasinghe SA, Crook JM. The role of salvage brachytherapy for local relapse after external beam radiotherapy for prostate cancer. *Transl Androl Urol.* 2018;7(3):414-435.

123. Murgic J, Morton G, Loblaw A, et al. Focal Salvage High Dose-Rate Brachytherapy for Locally Recurrent Prostate Cancer After Primary Radiation Therapy Failure: Results From a Prospective Clinical Trial. *Int J Radiat Oncol Biol Phys.* 2018;102(3):561-567.

124. Tharmalingam H, Hamada M, Tsang YM, et al. Salvage High-Dose Rate (HDR) Brachytherapy as a Treatment for Locally Recurrent Prostate Cancer after Primary Radiation Therapy. *International Journal of Radiation Oncology • Biology • Physics.* 2018;102(3):e118-e119.

125. Crook J, Ots A, Gaztanaga M, et al. Ultrasound-planned high-dose-rate prostate brachytherapy: dose painting to the dominant intraprostatic lesion. *Brachytherapy.* 2014;13(5):433-441.

126. Strom TJ, Wilder RB, Fernandez DC, et al. A dosimetric study of polyethylene glycol hydrogel in 200 prostate cancer patients treated with high-dose rate brachytherapy±intensity modulated radiation therapy. *Radiotherapy and Oncology.* 2014;111(1):126-131.

127. Yeh J, Lehrich B, Tran C, et al. Polyethylene glycol hydrogel rectal spacer implantation in patients with prostate cancer undergoing combination high-dose-rate brachytherapy and external beam radiotherapy. *Brachytherapy.* 2016;15(3):283-287.

128. Sheridan AD, Nath SK, Huber S, et al. Role of MRI in the Use of an Absorbable Hydrogel Spacer in Men Undergoing Radiation Therapy for Prostate Cancer: What the Radiologist Needs to Know. *American Journal of Roentgenology.* 2017;209(4):797-799.

129. Gomez-Iturriaga A, Casquero F, Urresola A, et al. Dose escalation to dominant intraprostatic lesions with MRI-transrectal ultrasound fusion High-Dose-Rate prostate brachytherapy. Prospective phase II trial. *Radiother Oncol.* 2016;119(1):91-96.

130. De Brabandere M, Hoskin P, Haustermans K, et al. Prostate post-implant dosimetry: interobserver variability in seed localisation, contouring and fusion. *Radiother Oncol.* 2012;104(2):192-198.

131. Frank SJ, Mourtada F, Crook J, et al. Use of magnetic resonance imaging in low-dose-rate and high-dose-rate prostate brachytherapy from diagnosis to treatment assessment: Defining the knowledge gaps, technical challenges, and barriers to implementation. *Brachytherapy.* 2017;16(4):672-678.

132. Barentsz JO, Richenberg J, Clements R, et al. ESUR prostate MR guidelines 2012. *Eur Radiol.* 2012;22(4):746-757.

133. Pugh TJ, Frank SJ, Achim M, et al. Endorectal magnetic resonance imaging for predicting pathologic T3 disease in Gleason score 7 prostate cancer: implications for prostate brachytherapy. *Brachytherapy.* 2013;12(3):204-209.

134. Albert JM, Swanson DA, Pugh TJ, et al. Magnetic resonance imaging-based treatment planning for prostate brachytherapy. *Brachytherapy.* 2013;12(1):30-37.

135. Haider MA, Chung P, Sweet J, et al. Dynamic contrast-enhanced magnetic resonance imaging for localization of recurrent prostate cancer after external beam radiotherapy. *Int J Radiat Oncol Biol Phys.* 2008;70(2):425-430.

136. Bauman G, Haider M, Van der Heide UA, et al. Boosting imaging defined dominant prostatic tumors: a systematic review. *Radiother Oncol.* 2013;107(3):274-281.

137. Groenendaal G, Borren A, Moman MR, et al. Pathologic validation of a model based on diffusion-weighted imaging and dynamic contrast-enhanced magnetic resonance imaging for tumor delineation in the prostate peripheral zone. *Int J Radiat Oncol Biol Phys.* 2012;82(3):e537-544.

138. Menard C, Iupati D, Publicover J, et al. MR-guided prostate biopsy for planning of focal salvage after radiation therapy. *Radiology.* 2015;274(1):181-191.

139. Beaulieu L, Carlsson Tedgren A, Carrier JF, et al. Report of the Task Group 186 on model-based dose calculation methods in brachytherapy beyond the TG-43 formalism: current status and recommendations for clinical implementation. *Med Phys.* 2012;39(10):6208-6236.

140. Lambert J, Greer PB, Menk F, et al. MRI-guided prostate radiation therapy planning: Investigation of dosimetric accuracy of MRI-based dose planning. *Radiother Oncol.* 2011;98(3):330-334.

141. Mikell JK, Klopp AH, Gonzalez GM, et al. Impact of heterogeneity-based dose calculation using a deterministic grid-based Boltzmann equation solver for intracavitary brachytherapy. *Int J Radiat Oncol Biol Phys.* 2012;83(3):e417-422.

142. Rivard MJ, Venselaar JL, Beaulieu L. The evolution of brachytherapy treatment planning. *Med Phys.* 2009;36(6):2136-2153.

143. Jacob D, Lamberto M, DeSouza Lawrence L, et al. Clinical transition to model-based dose calculation algorithm: A retrospective analysis of high-dose-rate tandem and ring brachytherapy of the cervix. *Brachytherapy.* 2017;16(3):624-629.

144. Price MJ, Jackson EF, Gifford KA, et al. Development of prototype shielded cervical intracavitary brachytherapy applicators compatible with CT and MR imaging. *Medical Physics.* 2009;36(12):5515-5524.

145. Rivard MJ, Melhus CS, Granero D, et al. An approach to using conventional brachytherapy software for clinical treatment planning of complex, Monte Carlo-based brachytherapy dose distributionsa). *Medical Physics.* 2009;36(6Part1):1968-1975.

146. Johansson A, Karlsson M, Nyholm T. CT substitute derived from MRI sequences with ultrashort echo time. *Med Phys.* 2011;38(5):2708-2714.

147. Korhonen J, Kapanen M, Keyrilainen J, et al. A dual model HU conversion from MRI intensity values within and outside of bone segment for MRI-based radiotherapy treatment planning of prostate cancer. *Med Phys.* 2014;41(1):011704.

148. Edmund JM, Kjer HM, Van Leemput K, et al. A voxel-based investigation for MRI-only radiotherapy of the brain using ultra short echo times. *Phys Med Biol.* 2014;59(23):7501-7519.

149. Sjolund J, Forsberg D, Andersson M, et al. Generating patient specific pseudo-CT of the head from MR using atlas-based regression. *Phys Med Biol.* 2015;60(2):825-839.

150. Dowling JA, Lambert J, Parker J, et al. An atlas-based electron density mapping method for magnetic resonance imaging (MRI)-alone treatment planning and adaptive MRI-based prostate radiation therapy. *Int J Radiat Oncol Biol Phys.* 2012;83(1):e5-11.

151. Gudur MS, Hara W, Le QT, et al. A unifying probabilistic Bayesian approach to derive electron density from MRI for radiation therapy treatment planning. *Phys Med Biol.* 2014;59(21):6595-6606.

152. Siversson C, Nordstrom F, Nilsson T, et al. Technical Note: MRI only prostate radiotherapy planning using the statistical decomposition algorithm. *Med Phys.* 2015;42(10):6090-6097.

153. Kanal E, Barkovich AJ, Bell C, et al. ACR guidance document on MR safe practices: 2013. *J Magn Reson Imaging.* 2013;37(3):501-530.

154. Greenberg TD, Hoff MN, Gilk TB, et al. ACR guidance document on MR safe practices: Updates and critical information 2019. *J Magn Reson Imaging.* 2020;51(2):331-338.

155. Kanal E, Greenberg TD, Hoff MN, et al. *ACR manual on MR safety.* Reston, VA. Available from: https://www.acr.org/-/media/ACR/Files/Radiology-Safety/MR-Safety/Manual-on-MR-Safety.pdf.

156. Shellock FG. *Reference Manual for Magnetic Resonance Safety, Implants, and Devices: Edition 2017.* Los Angeles, CA: Biomedical Research Publishing Group; 2017.

157. Hartwig V, Giovannetti G, Vanello N, et al. Biological effects and safety in magnetic resonance imaging: a review. *Int J Environ Res Public Health.* 2009;6:1778-1798.

158. Nixon E, Kim Y, Kearney WR, et al. HDR brachytherapy tandem and ovoid titanium applicator safety assessment in 3T MRI. *Brachytherapy.* 2008;7(2):135-136.

159. Woods TO. Standards for Medical Devices in MRI: Present and Future. *J Magn Reson Imaging.* 2007;26:1186 -1189.

160. International A. ASTM F2503-05 Standard Practice for Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment. West Conshohocken, PA: ASTM International; 2005.

161. International A. ASTM F2052-06 Standard Test Method for Measurement of Magnetically Induced Displacement Force on Medical Devices in the Magnetic Resonance Environment. West conshohocken, PA: ASTM International; 2006.

162. International A. ASTM F2213-06 Standard Test Method for Measurement of Magnetically Induced Torque on Medical Devices in the Magnetic Resonance Environment. West Conshohocken, PA: ASTM International; 2006.

163. Murbach M, Zastrow E, Neufeld E, et al. Heating and Safety Concerns of the Radio-Frequency Field in MRI. *Current Radiology Reports.* 2015;3(12):45.

164. Kim Y, Chesnut D, Wagner BS, et al. Ferromagnetic Metal Side-Rails on Air-Hover HDR Patient Transport Table Can Cause Severe Skin Burns to Patients During MR Simulation for Brachytherapy. *International Journal of Radiation Oncology*Biology*Physics.* 2017;99(2, Supplement):E556-E557.

165. Rockey WR, Bhatia SK, Jacobson GM, et al. The dosimetric impact of vaginal balloon-packing on intracavitary high-dose-rate brachytherapy for gynecological cancer. *J Contemp Brachytherapy.* 2013;5(1):17-22.

166. Bou-Zeid W, Bauer C, Kim Y, et al. Clinical validation of a real-time applicator position monitoring system for gynecologic intracavitary brachytherapy. *Biomed Phys Eng Express.* 2016;2:045008.

167. Xia J, Waldron T, Kim Y. A Real-Time Applicator Position Monitoring System (RAPS) for High-Dose-Rate Intracavitary Brachytherapy. *Med Phys.* 2013;40:465.

168. Andrew M, Kim Y, Ginader T, et al. Reduction of applicator displacement in MR/CT-guided cervical cancer HDR brachytherapy by the use of patient hover transport system. *J Contemp Brachytherapy.* 2018;10(1):85-90.

169. Gerszten K, Faul C, Kounelis S, et al. The Impact of Adjuvant Radiotherapy on Carcinosarcoma of the Uterus. *Gynecologic Oncology.* 1998;68(1):8-13.

170. Siemens Healthineers. Magnetom Skyra - Transforming 3T productivity. 2010; https://static.healthcare.siemens.com/siemens_hwem-hwem_ssxa_websites-context-root/wcm/idc/groups/public/@us/@imaging/@mri/documents/download/mdaw/ndq3/~edisp/mri-magnetom-skyra-usa-product-brochure-00308805.pdf.

171. Chan MF, Cohen GaN, Deasy JO. Qualitative evaluation of fiducial markers for radiotherapy imaging. *Technology in cancer research & treatment.* 2015;14(3):298-304.

172. Osman SOS, Russell E, King RB, et al. Fiducial markers visibility and artefacts in prostate cancer radiotherapy multi-modality imaging. *Radiation Oncology.* 2019;14(1):237.

173. Erickson BA, Bittner NHJ, Chadha M, et al. The American College of Radiology and the American Brachytherapy Society practice parameter for the performance of radionuclide-based high-dose-rate brachytherapy. *Brachytherapy.* 2017;16(1):75-84.

174. Kim H, Houser CJ, Kalash R, et al. Workflow and efficiency in MRI-based high-dose-rate brachytherapy for cervical cancer in a high-volume brachytherapy center. *Brachytherapy.* 2018;17(5):753-760.

175. Ford EC, Gaudette R, Myers L, et al. Evaluation of safety in a radiation oncology setting using failure mode and effects analysis. *Int J Radiat Oncol Biol Phys.* 2009;74(3):852-858.

176. Rath F. Tools for developing a quality management program: proactive tools (process mapping, value stream mapping, fault tree analysis, and failure mode and effects analysis). *Int J Radiat Oncol Biol Phys.* 2008;71(1 Suppl):S187-190.

177. Mayadev J, Dieterich S, Harse R, et al. A failure modes and effects analysis study for gynecologic high-dose-rate brachytherapy. *Brachytherapy.* 2015;14(6):866-875.

178. Richardson S, D. Scanderbeg, and J. Swamidas. FMEA for brachytherapy. In: Song WY, K. Tanderup, and B.R. Pieters, ed. *Emerging technologies in brachytherapy*: CRC Press, Taylor & Francis Group; 2017.

179. Poder J, Brown R, Howie A, et al. A risk-based approach to development of ultrasound-based high-dose-rate prostate brachytherapy quality management. *Brachytherapy.* 2018;17(5):788-793.

180. TG275. Strategies for effective physics plan and chart review in radaition therapy *In progress.*

181. Nuclear Regulatory Commission. Event Notification Reports. https://www.nrc.gov/reading-rm/doc-collections/event-status/event/.

182. Richardson S. A 2-year review of recent Nuclear Regulatory Commission events: What errors occur in the modern brachytherapy era? *Practical Radiation Oncology.* 2012;2(3):157-163.

183. Thomadsen BR, Erickson BA, Eifel PJ, et al. A review of safety, quality management, and practice guidelines for high-dose-rate brachytherapy: Executive summary. *Practical Radiation Oncology.* 2014;4(2):65-70.

184. Nesvacil N, Tanderup K, Hellebust TP, et al. A multicentre comparison of the dosimetric impact of inter- and intra-fractional anatomical variations in fractionated cervix cancer brachytherapy. *Radiotherapy and Oncology.* 2013;107(1):20-25.

185. Mazeron R, Champoudry J, Gilmore J, et al. Intrafractional organs movement in three-dimensional image-guided adaptive pulsed-dose-rate cervical cancer brachytherapy: Assessment and dosimetric impact. *Brachytherapy.* 2015;14(2):260-266.

186. Meerschaert R, Nalichowski A, Burmeister J, et al. A comprehensive evaluation of adaptive daily planning for cervical cancer HDR brachytherapy. *J Appl Clin Med Phys.* 2016;17(6):323-333.

187. Kandasamy S, Reddy KS, Nagarajan V, et al. Inter-fraction variation in interstitial high-dose-rate brachytherapy. *Journal of Radiotherapy in Practice.* 2015;14(2):143-151.

188. Haack S, Kallehauge JF, Jespersen SN, et al. Correction of diffusion-weighted magnetic resonance imaging for brachytherapy of locally advanced cervical cancer. *Acta Oncol.* 2014;53(8):1073-1078.

189. Wood R BK, Foerster V, Spry C, and Tong L. *1.5 Tesla Magnetic Resonance Imaging Scanners Compared with 3.0 Tesla Magnetic Resonance Imaging Scanners: Systematic Review of Clinical Effectiveness: Pilot Project* Ottawa. Available from: https://www.ncbi.nlm.nih.gov/books/NBK174467/pdf/Bookshelf_NBK174467.pdf.

190. American College of Radiology. Safety Screening Form for MR Procedures. https://www.acr.org/Clinical-Resources/Radiology-Safety/MR-Safety. Accessed May 18, 2022, 2022.

191. Shellock FG. Magnetic Resonance (MR) procedure screening form for patients http://www.mrisafety.com/images/PreScrnF.pdf. Accessed March 18, 2022, 2022.

192. Glide-Hurst C, E. Paulson, K. McGee, N. Tyagi, Y. Hu, J. Balter, and J. Bayouth. Task group 284 report: magnetic resonance imaging simulation in radiotherapy: considerations for clinical implementation, optimization, and quality assurance. *Medical Physics.* 2021;48(7):e636-670.

193. Song WY, Tanderup K, Pieters BR. Section III: Brachytherapy Suites. *Emerging technologies in brachytherapy*: CRC Press: Taylor & Francis Group; 2017.

194. Beld E, Seevinck PR, Schuurman J, et al. Development and Testing of a Magnetic Resonance (MR) Conditional Afterloader for Source Tracking in Magnetic Resonance Imaging-Guided High-Dose-Rate (HDR) Brachytherapy. *Int J Radiat Oncol Biol Phys.* 2018;102(4):960-968.

195. Mutic S, Dempsey JF. The ViewRay System: Magnetic Resonance–Guided and Controlled Radiotherapy. *Seminars in Radiation Oncology.* 2014;24(3):196-199.

196. NCT00913939. MRI-Guided HDR Brachytherapy for Prostate Cancer. 2009; https://clinicaltrials.gov/ct2/show/NCT00913939. Accessed December 1, 2019.

197. NCT02342054. Prospective Phase II Trial of Single Fraction Real-time High-Dose-Rate Brachytherapy in Patients With Low and Intermediate Risk Prostate Cancer. 2014; https://www.clinicaltrials.gov/ct2/show/NCT02342054. Accessed December 1, 2019.

198. NCT03424694. HDR Brachytherapy Used as Monotherapy for Low and Intermediate Risk Prostate Cancer: a Phase II Randomized Trial. 2015; https://clinicaltrials.gov/ct2/show/NCT03424694. Accessed December 1, 2019.

199. NCT02623933. MRI Assisted Focal Boost Integrated With HDR Monotherapy Study in Low and Intermediate Risk Prostate Cancer Patients (MARS). 2015; https://clinicaltrials.gov/ct2/show/NCT02623933. Accessed December 1, 2019.

200. NCT04523896. HDR Brachytherapy combined with Stereotactic Ablative Prostate Radiotherapy for Patients With Intermediate and High-risk Prostate Cancer: Phase II clinical trial. 2020; https://clinicaltrials.gov/ct2/show/NCT04523896. Accessed March 29, 2022.

201. NCT01583920. Pilot study of focal salvage HDR prostate brachytherapy 2020; https://clinicaltrials.gov/ct2/show/NCT01583920. Accessed March 29, 2022.

202. GEC-ESTRO. *Image guided intensity modulated External beam radiochemotherapy and MRI based adaptive BRAchytherapy in locally advanced CErvical cancer (EMBRACE-II).* Available from: https://www.embracestudy.dk/.

203. NRG Oncology. NRG-GY006: A Randomized Phase II Trial of Radiation Therapy and Cisplatin Alone or in Combination with Intravenous Triapine in Women with Newly Diagnosed Bulky Stage IB2, Stage II, IIIB, or IVA Cancer of the Uterine Cervix or Stage II-IVA Vaginal Cancer https://www.nrgoncology.org/Clinical-Trials/Protocol-Table.

204. NRG Oncology. NRG-GY017: Anti PD-L1 (Atezolizumab) as an Immune Primer and Concurrently with Extended Field Chemoradiotherapy for Node Positive Locally Advanced Cervical Cancer https://www.nrgoncology.org/Clinical-Trials/Protocol-Table.

205. clinicaltrials.gov. Optimizing Brachytherapy Application and Delivery With MRI Guidance for Gynecologic Cancer. https://www.clinicaltrials.gov/ct2/show/NCT03277469?term=brachytherapy%2C+MRI&cond=Gynecologic+Cancer&draw=2&rank=1. Accessed March 31, 2022.

206. Prisciandaro J, Hadley S, Jolly S, et al. Development of a brachytherapy audit checklist tool. *Brachytherapy.* 2015;14(6):963-969.

207. MRISafety.com. Screening Form. http://www.mrisafety.com/ScreeningForm.html. Accessed January 13, 2020.

208. Pei-Jan Paul Lin TJB, Caridad Borras, Gerald Cohen, Robert A. Jucius, Robert J. Kriz, Edward L. Nickoloff, Lawrence N. Rothenberg, Keith J. Strauss, Theodore Villafana, Robert K. Cacak, Joel E. Gray, Thomas N. Hangartner, R. Edward Hendrick, Raymond P. Rossi. *AAPM Report No. 39: Specification and acceptance testing of computed tomography scanners.* College Park, MD. Available from: https://www.aapm.org/pubs/reports/detail.asp?docid=38.

209. Klein EE, Hanley J, Bayouth J, et al. Task Group 142 report: Quality assurance of medical acceleratorsa). *Medical Physics.* 2009;36(9Part1):4197-4212.

210. Bissonnette J-P, Balter PA, Dong L, et al. Quality assurance for image-guided radiation therapy utilizing CT-based technologies: A report of the AAPM TG-179. *Medical Physics.* 2012;39(4):1946-1963.

Table 1. A summary of on-going clinical trials utilizing MRI and HDR brachytherapy for the treatment of patients with prostate cancer.

Title	Description	Ref
MRI-guided HDR BT for prostate cancer (NCT00913939)	Evaluate technical and clinical performance of MRI-guided prostate HDR BT.	[41]
Prospective Phase II trial of single fraction real-time High-Dose-Rate BT in patients with low and intermediate risk prostate cancer (NCT02342054)	Evaluate safety, tolerance, and impact on quality of life of single fraction, 19 Gy prostate HDR BT in patients with low and intermediate risk prostate cancer. The trial involves the acquisition of T2 axial, pre-implant MR images that are imported and fused with planning transrectal US images.	[42]
HDR brachytherapy used as monotherapy for low and intermediate risk prostate cancer: a Phase II Randomized Trial (NCT03424694)	Phase II randomized trial evaluating HDR BT in 1 versus 2 fractions as monotherapy for the treatment of low and intermediate risk prostate cancer. In one arm of this study, patients receive a single fraction of 19.5 Gy, while in the second arm, patients receive a total of 29 Gy delivered in 2 fractions separated by 6 hours with a single implant. The implant is performed under US guidance, but the treatment plan is optimized based on post-implant MR imaging.	[43]
MRI assisted focal boost integrated with HDR monotherapy study in low and intermediate risk prostate cancer patients (MARS) (NCT02623933)	Pilot study investigating the feasibility and toxicities of an integrated focal boost using whole gland prostate HDR BT. Patient eligibility is determined by multi-parametric MRI (mp-MRI) to identify the dominant intraprostatic lesion (DIL), which is fused with the preplanning US dataset. The prescribed dose is 19 Gy to the whole gland and 22.5 Gy to the MRI visible lesion delivered in a single HDR fraction.	[44]
HDR brachytherapy combined with stereotactic ablative prostate radiotherapy for patients diagnosed with intermediate and high-risk prostate cancer: Phase II clinical trial (NCT04523896)	Phase II study intended to access the impact on quality of life and tolerability of combining HDR BT and stereotactic radiotherapy in the treatment of prostate cancer. Patients on this study receive a single HDR fraction of 15 Gy to the followed by 5 fractions of 5 Gy (total dose of 25 Gy) to the prostate with stereotactic radiotherapy 2 – 4 weeks following BT.	[46]
Pilot study of focal salvage HDR prostate brachytherapy (NCT01583920)	Pilot study investigating the feasibility and toxicities (e.g., acute and late urinary and rectal, biochemical disease-free survival, quality of life) associated with focal HDR BT. In this single arm study, patients will receive 2 fractions of HDR BT to the prostate of 13.5 Gy each, spaced 1 week apart.	[47]

Table 2. A summary of on-going clinical trials utilizing MRI and HDR brachytherapy for the treatment of patients with gynecologic cancer.

Title	Description	Ref
Image guided intensity modulated external beam radiochemotherapy and MRI based adaptive brachytherapy in locally advanced cervical cancer (EMBRACE-II)	A prospective multi-institutional protocol utilizing state of the art treatment radiotherapy techniques in the treatment of cervical cancer, including MRI guided adaptive IMRT and BT to enhance local, nodal, and systemic control while minimizing normal tissue toxicity. The protocol intends to benchmark local, nodal, distant control and survival rates, morbidity, and quality of life.	[61]
A Randomized Phase II trial of radiation therapy and Cisplatin alone or in combination with intravenous Triapine in women with newly diagnosed bulky stage IB2, stage II, IIIB, or IVA cancer of the uterine cervix or stage II-IVA vaginal cancer (NRG-GY006)	Randomized phase II/III trial of "radiation therapy and cisplatin alone or in combination with intravenous triapine in women with newly diagnosed bulky stage IB2, II, IIIB, or IVA cancer of the uterine cervix or stage II-IVA vaginal cancer." For volume-based BT, a pelvic MRI (≤ 3 mm slice thickness) is required for either the first or second insertion with an MRI-conditional applicator. Subsequent insertions may use CT or MRI for planning.	[57]
Anti PD-L1 (Atezolizumab) as an immune primer and concurrently with extended field chemoradiotherapy for node positive locally advanced cervical cancer (NRG-GY017)	Phase I study whose primary objective is to determine whether differences in sequencing of atezolizumab and chemoradiation result in differential immune activation in cervical cancer patients with FIGO stages IB2/IIA with positive para-aortic nodes or stages IIB/IIIB/IVA with positive pelvic or para-aortic lymph nodes. The radiation component of this trial involves EBRT followed by LDR, PDR, or HDR BT. This trial requires volumetric imaging and encourages the use of volume-based treatment planning in accordance with GEC-ESTRO/EMBRACE II dose constraints.	[59]
Optimizing Brachytherapy Application and Delivery With MRI Guidance for Gynecologic Cancer	Research study designed to evaluate whether a real-time MR-tracking device will improve the placement of brachytherapy catheters for patients treated with gynecologic cancer.	[208]

Table 3: MRI vendor-specific 3D fast spin echo sequence acronyms and descriptions

Vendor	Acronym	Definition
Siemens	SPACE	Sampling Perfection with Application optimized Contrasts using different flip angle Evolution
GE	CUBE	(Not an acronym)
Philips	VISTA	Volume Isotropic Turbo spin echo Acquisition
Toshiba	3D MVOX	3D MultiVOXel
Hitachi	isoFSE	isotropic Fast Spin Echo

Table 4: Comparison between multi-slice 2D FSE and 3D FSE VFL sequences for MRI-based BT.

	Advantages	Disadvantages
2D FSE	• Standard, most familiar T2 contrast • High in-plane resolution • Can be oriented to oblique applicator geometry to maximize resolution of desired views	• Larger slice thickness • Multiple orthogonal views typically required, increasing scan time • Oblique acquisitions may require reformatting to generate straight axial, coronal, or sagittal image(s) prior to import into BT planning systems, resulting in decreased image quality • May require separate sequence for applicator reconstruction • Full 3D gradient nonlinearity (GNL) distortion correction may not be supported for 2D FSE sequences
3D FSE VFL	• Isotropic spatial resolution ($1mm^3$) • Permits easy reformatting into BT eye views • Permits easy applicator reconstruction • Permits full 3D GNL distortion correction	• T2 contrast often different from 2D FSE[1] • Motion sensitivity due to longer scan times

[1]The user should be advised that T2 contrast on 3D FSE VFL images may differ from that on 2D FSE images obtained diagnostically for detection/staging or obtained during MRI simulation for external beam target delineation. Though the 3D FSE images are optimal for applicator reconstruction, the altered 3D FSE VFL contrast may challenge interpretation of treatment related changes resulting from external beam when used alone and may require re-learning for contouring. Alternatively, a mixed-mode approach could be utilized in which the 3D FSE images serve as the reference and additional multi-planar 2D FSE images oriented to the applicator are acquired and used for delineation or verification of target contours. This approach maximizes the advantages of both 2D and 3D FSE VFL sequences at the cost of longer scan times.

Table 5: An example of generalized 2D/3D FSE VFL scan parameters for GYN and prostate BT from two institutions.

GYN BT (Institution 1, based on a 3.0 T Siemens Verio scanner)

	Slice Prescription [1]	TE (ms)	TR (ms)	Voxel Size (mm) [7]	ETL	Readout BW (Hz/pix)[5]	Scan Time (min)
2D FSE[2]	PA, PS, PC	85	2500	0.9x0.9x3.0	16	440/880	3
3D FSE VFL	Ax	85[3]	2500	1.0x1.0x1.5	300[4]	440/880	12[6]

GYN BT (Institution 2, based on a 3.0 T Philips Ingenia scanner)

	Slice Prescription [1]	TE (ms)	TR (ms)	Voxel Size (mm) [7]	ETL	Readout BW (Hz/pix)	Scan Time (min)
2D FSE[2]	Ax, Sag	100	4471	0.45x0.45x3.0	30	244.1	5:13

Prostate BT (Institution 2, based on a 3.0 T Philips Ingenia scanner)

	Slice Prescription [1]	TE (ms)	TR (ms)	Voxel Size (mm)[7]	ETL	Readout BW (Hz/pix)	Scan Time (min)
2D FSE[2]	Ax, Sag	100	5194	0.6x0.6x2.0	29	244.1	3
3D FSE VFL	Ax	245	1800	0.65x0.65x2.0	79	455.3	5:40

[1]Ax = Axial, Sag = Sagittal, and PA = Para-Axial, PS = Para-Sagittal, PC = Para-Coronal to Applicator for GYN

[2]Full 3D gradient non-linearity (GNL) correction may not be supported for 2D sequences.

[3]Effective TE reported for 3D FSE VFL

[4]Echo train duration reported for 3D FSE VFL

[5]Readout bandwidth reported for 1.5T/3.0T; Additional optimization to recover SNR may be required.

[6]Longer scan times may benefit from administration of antispasmodic agents to reduce motion.

[7]Use of in-plane and through plane interpolation and acceleration methods (e.g., partial Fourier and parallel imaging) can introduce blurring and artifacts and should be verified prior to clinical use.

Table 6. Failure modes identified by task group members for an example MRI-based, high dose rate BT of the prostate detailed in Section V.

Rank (process step#)	Subprocess #_description	Step description	Potential failure modes	Potential causes of failure	Potential effects of failure	O	S	D	RPN
1 (#21)	4—Treatment planning	Contouring	Target not completely contoured	Resident or trainee contours not reviewed, poor judgement, lack of peer review	Under-coverage of target leading to recurrance	4.0	8.0	5.0	160
2 (#22)	4–Treatment planning	Digitization	Needles crossed/doubled/swapped	Sub-optimal implant	Wrong dose distribution	3.5	7.0	6.0	147
3 (#1)	1—Patient assessment	Diagnosis/staging (biopsy, imaging)	Data entered incorrectly into EMR	Slip or lapse caused by inattention, distraction, etc.	Wrong treatment (i.e. treatment of patient with mets)	3.0	8.3	5.8	142
4 (#17)	3—Imaging/simulation	Patient transfer back to treatment room/OR	Needles move during transport	Patient makes large movement	Needle location different b/t planning and delivery - wrong dose distribution	5.0	7.0	4.0	140
5 (#22)	4—Treatment planning	Digitization	Needle tip/path not correctly defined	Poor image quality, lack of training or well defined procedure, anatomical masking	Wrong dose distribution	4.5	6.5	4.5	132
6 (#17)	3—Imaging/simulation	Patient transfer back to treatment room/OR	Needles move during trasport	Needles not secured properly	Needle location different b/t planning and delivery - wrong dose distribution	4.0	7.5	4.0	120
7 (#2)	1—Patient assessment	Assessment of pre-existing conditions	Incorrect or missing data	Relevant information not available, patient fails to report relevant pre-existing condition	Unsafe procedure, possible harm to patient	3.0	8.0	5.0	120

8 (#18)	3—Imaging/simulation	Image (network) transfer to TPS	Wrong timepoint or sequence dataset transferred to planning system	Confusion over time and date, mislabeling, distraction	Wrong or sub-optimal dose distribution	3.0	7.0	5.5	116
9 (#22)	4—Treatment planning	Digitization	Calcification/artifact mistaken as needle tip	Lack of training, sub-optimal imaging	Wrong dose distribution	4.0	7.0	4.0	112
10 (#19)	4—Treatment planning	Data import and selection	Wrong timepoint images imported	Confusion over time and date, mislabeling, distraction	Wrong or sub-optimal dose distribution	3.0	7.0	4.5	95
11 (#4)	1—Patient assessment	Prescription (MD intent/order sheet)	Documented prescription does not match intent	Slip or lapse caused by inattention, distraction, etc.	Wrong dose, wrong side	2.5	9.0	4.0	90
12 (#21)	4—Treatment planning	Contouring	Target over-contoured	Resident or trainee contours not reviewed, poor judgement, lack of peer review	Overdose to critical structure	3.5	7.3	3.5	89
13 (#14)	3—Imaging/simulation	Verification/adjustment of implant geometry	Implant not adjusted when necessary	Failure to interpret nature of developing problem - expectation bias	Inadequate location of needles leading to sub-optiml dose distribution	4.5	6.5	3.0	88
14 (#22)	4—Treatment planning	Digitization	Template coordinate incorrectly defined	Planner unfamiliar, lack of training	Wrong dose distribution	3.5	7.0	3.5	86
15 (#16)	3—Imaging/simulation	Imaging	Spatial distortion present in image	System not QA'd properly	Wrong location of needles leading to wrong dose distribution	2.5	6.0	5.5	83
16 (#4)	1—Patient assessment	Prescription (MD intent/order sheet)	Choice of prescription is incorrect for current use case	Resident or trainee enters rx, poor judgement, lack of peer review	Wrong dose	3.5	7.8	3.0	81
17 (#21)	4—Treatment planning	Contouring	Contour(s) missing slices	Slip or lapse caused by inattention,	Overdose to critical structure	3.0	7.0	3.5	74

				distraction, etc.					
18 (#14)	3—Imaging/simulation	Verification/adjustment of implant geometry	Implant geometry not critically reviewed	Lapse due to rushed procedure, lack of policy for critical review	Possible inadequate location of needles leading to sub-optimal dose distribution	4.5	6.5	2.5	73
19 (#23)	4—Treatment planning	Plan optimization	Not enough dwell location activated	Lack of training or well defined procedure	Wrong dose distribution	4.0	6.0	3.0	72
20 (#20)	4—Treatment planning	Image registration	Registration between the wrong two datasets	Mislabeling, similar names of patients, distraction	Wrong dose distribution	2.5	7.0	4.0	70
21 (#21)	4—Treatment planning	Digitization	Digitization does not extend beyond region of interest	Lack of training or well defined procedure	Wrong dose distribution	3.5	6.5	3.0	68
22 (#23)	4—Treatment planning	Plan optimization	Optimization goals incorrectly set or wrong parameters used.	Lack of training or well defined procedure	Wrong dose distribution	4.0	6.5	2.5	65
23 (#15)	3—Imaging/simulation	Image sequence(s) selection	Wrong MR sequence selected	Staff not familiar with appropriate sequences, lack of training or well-defined procedure	Inadequate MR scan - Wrong digitization of catheters	3.0	6.0	3.5	63
24 (#20)	4—Treatment planning	Image registration	Poor registration b/t planning MRI and verification CBCT	Registration not critically reviewed	Sub-optimal dose distribution, under-coverage of target, overdose to critical structure	3.0	7.0	3.0	63
25 (#16)	3—Imaging/simulation	Imaging	Patient moves during imaging	Patient uncomfortable	Artifacts present in MR images	6.0	3.5	3.0	63
26 (#10)	2—Implantation procedure	Bring legs down and secure in semi-elevated position	Needles not immobilized/secured.	Staff not familiar with appropriate immoblization, lack of training	Needles placed incorrectly leading to sub-optimal dose distribution	4.0	6.0	2.5	60
27 (#24)	4—Treatment planning	Plan assessment	Minimum dwell time required but not	Lack of training or	Sub-optimal plan	5.0	4.0	3.0	60

			observed	well defined procedure					
28 (#24)	4—Treatment planning	Plan assessment	Plan not modified when necessary	Poor judgement, lack of training, lack of peer review	Sub-optimal dose distribution	3.0	5.5	3.5	58
29 (#42)	6—Pre-treatment actions/QA	Connect applicator to afterloader	Transfer tube connected to wrong channel	Slip or lapse caused by inattention, distraction, etc., no double check	Wrong dose distribution	3.0	7.5	2.5	56
30 (#23)	4—Treatment planning	Plan optimization	Wrong prescription dose	Poor communication, poor documentation	Wrong dose	2.5	8.8	2.5	55
31 (#8)	2—Implantation procedure	Catheter/needle insertion	Needles penetrate bladder	Poor US guidance, lack of training	Possible needle placement inside bladder, overdose of critical structure	4.5	6.0	2.0	54
32 (#42)	6—Pre-treatment actions/QA	Connect applicator to afterloader	Wrong length of transfer tube	Slip or lapse caused by inattention, distraction, etc., no double check	Wrong dose	3.0	9.0	2.0	54
33 (#21)	4—Treatment planning	Digitization	Incorrect selection of implant geometry parameters	Planner not familiar with appropriate geometry, lack of training or well-defined procedure	Wrong dose distribution	3.0	7.0	2.5	53
34 (#13)	3—Imaging/simulation	MRI screening (repeat questionnaire and physical inspection)	Patient scanned on MR without being screened	Routine screening not performed, patient fails to report implant, etc.	Artifacts present in MR images, potential safety hazard	2.5	7.0	3.0	53
35 (#15)	3—Imaging/simulation	Image sequence(s) selection	Wrong MR sequence selected	Staff not familiar with appropriate sequences, lack of training or well-defined	Inadequate MR scan - MR must be repeated	3.5	2.5	6.0	53

				procedure					
36 (#7)	2—Implantation procedure	US/guide template setup	Template incorrectly aligned	Slip or lapse caused by inattention, distraction, etc., lack of well-defined procedure	Needles placed incorrectly leading to sub-optimal dose distribution	3.0	6.5	2.5	49
37 (#20)	6—Pre-treatment actions/QA	Image registration (CT-MR)	Poor registration b/t planning MRI and treatment CBCT	Registration not critically reviewed	Needle location different b/t planning and delivery - wrong dose distribution	3.0	6.5	2.5	49
38 (#21)	4—Treatment planning	Contouring	Non-target contoured as target	Resident or trainee contours not reviewed, poor judgement, lack of peer review	Overdose to critical structure	3.0	8.0	2.0	48
39 (#23)	4—Treatment planning	Plan optimization	Dwell positions set grossly outside target	Lack of training or well defined procedure	Wrong dose distribution	3.0	7.5	2.0	45
40 (#18)	3—Imaging/simulation	Image (network) transfer to TPS	Wrong patient dataset transferred to planning system	Mislabeling, similar names of patients, distraction	Wrong patient	2.0	8.5	2.5	43
41 (#24)	4—Treatment planning	Plan assessment	Dose constraints not met and not noticed	Slip or lapse caused by inattention, distraction, etc.	Overdose to critical structure	3.0	7.0	2.0	42
42 (#22)	4—Treatment planning	Digitization	Wrong offset assumed	Lack of training or well defined procedure	Wrong dose distribution	3.5	6.0	2.0	42
43 (#24)	4—Treatment planning	Plan assessment	Acceptance of plan that does not meet SOP	Poor judgement, lack of training, lack of peer review	Sub-optimal dose distribution	3.0	4.5	3.0	41
44 (#24)	4—Treatment planning	Plan assessment	Plan accidentally modified	Slip or lapse caused by inattention, distraction, etc.	Wrong dose distribution	3.0	6.5	2.0	39

45 (#21)	4—Treatment planning	Contouring	Contour(s) name does not match anatomy	Slip or lapse caused by inattention, distraction, etc.	Overdose to critical structure	2.5	7.3	2.0	36
46 (#6)	2—Implantation procedure	Patient immobilization and preparation (lithotomy position, urethra catheter, rectal irragation and prep)	Patient not fully immobilized	Staff not familiar with appropriate positioning, lack of training	Needles placed incorrectly leading to sub-optimal dose distribution	3.0	6.0	2.0	36
47 (#19)	4—Treatment planning	Data import and selection	Wrong patient images imported	Mislabeling, similar names of patients, distraction	Wrong patient	2.0	8.5	2.0	34
48 (#5)	2—Implantation procedure	Timeout	Timeout not performed	Lapse due to rushed procedure	Breakdown of QA procedures	2.0	4.0	4.0	32
49 (#22)	4—Treatment planning	Digitization	Wrong distal reference length	Lack of training or well defined procedure	Wrong dose distribution	4.0	8.0	1.0	32
50 (#12)	2—Implantation procedure	Transport patient to MRI	Stretcher/bed not MR compatible	No standardized procedure, staff not trained or unaware	Patient immoblization not maintained leading to movement of needles	2.0	7.5	2.0	30
51 (#7)	2—Implantation procedure	US/guide template setup	Selection of wrong template	Slip or lapse caused by inattention, distraction, etc., lack of well-defined procedure	Needles placed incorrectly leading to sub-optimal dose distribution	3.0	6.0	1.5	27
52 (#9)	2—Implantation procedure	Placement of fiducial markers under US guidance	Fiducial non MR compatible	Proper commissioning not performed, lack of policy and procedure for selection	Image artifacts genertated/image not usable	3.0	4.0	2.0	24
53 (#8)	2—Implantation procedure	Catheter/needle insertion	Needles/catheters not MR compatible	Proper commissioning not performed, lack of policy and procedure for selection	Image artifacts genertated/image not usable	3.5	4.5	1.5	24

54 (#51)	8—Post-treatment actions/QA	Billing	Incorrect billing codes applied	Lack of training or well defined procedure	Additional effort required to fix codes	4.5	1.0	4.0	18
55 (#24)	4—Treatment planning	Plan assessment	Physician fails to review treatment plan	Poor judgement, lack of peer review	Possible sub-optimal plan	2.0	4.5	2.0	18
56 (#21)	4—Treatment planning	Contouring	OAR contour(s) missing	Poor communication, lack of well defined procedure	Overdose to critical structure	2.0	8.0	1.0	16
57 (#51)	8—Post-treatment actions/QA	Billing	Billing codes not added	Lack of training or well defined procedure	Reduction in revenue	3.0	1.5	3.5	16
58 (#44)	6—Pre-treatment actions/QA	Pre-treatment radiation survey	Pre-treatment radiation survey not performed	Lack of well defined procedure, survey meter not available	Breakdown of QA procedures, possible confusion over presence of radioactivity	3.0	2.5	2.0	15
59 (#39)	6—Pre-treatment actions/QA	Pre-treatment fluoroscopy to confirm needles have not moved in transport	Flouroscopy not performed	Lack of well defined procedure, breakdown in communication	Needle location different b/t planning and delivery - wrong dose distribution	1.5	6.5	1.0	10
60 (#48)	8—Post-treatment actions/QA	Post-treatment radiation survey	Radiation survey not performed	Lack of well defined procedure, survey meter not available	Breakdown of QA procedures, possible confusion over presence of radioactivity	1.5	3.0	2.0	9
61 (#8)	2—Implantation procedure	Catheter/needle insertion	Pubic arch interference	Patient not properly pre-screened	Cacellation of case or incomplete coverage of target	2.5	3.5	1.0	9
62 (#6)	2—Implantation procedure	Patient immobilization and preparation (lithotomy position, urethra catheter, rectal irragation and prep)	Patient incorrectly positioned, i.e. legs down	Staff not familiar with appropriate positioning, lack of training	Needles placed incorrectly leading to sub-optimal dose distribution	1.5	4.5	1.3	8
63 (#49)	8—Post-treatment actions/QA	Remove implant	Second fraction intended to be delivered with same implant	Poor communication, poor documentati	Must repeat implant	1.5	4.5	1.0	7

				on					

Table 7. Recommended QA procedures, tolerances (where applicable), and frequency with which to perform these tasks when MRI is integrated into the HDR clinical workflow. Please note, in accordance with TG 100, users should develop a process map based on their individual workflow and perform a risk-based analysis to determine if additional checks should be performed. (TPS – Treatment Planning System)

Frequency	Procedure	Tolerances (if applicable)
Initial	Review instructions for use for proposed HDR applicators/needles (e.g., MRI safety, sterilization process and maximum number of cycles)	N/A
	Review imaging, HDR, and third-party vendor websites to verify whether customer bulletins have been released regarding applicators, software, or hardware	N/A
	Verify MRI safety of ancillary equipment (e.g., used for patient monitoring, anesthesia, medication delivery, patient transport/transfer, applicator immobilization devices), and write standard operating procedures for their use	N/A
	Optimize MRI pulse sequences in phantom and *in vivo*, and evaluate image artifacts and distortion and save sequence to MRI console, limiting write access	N/A
	Ensure BT staff receive MRI safety and appropriate procedure specific training[209]	N/A
	Verify a pre-MRI screening questionnaire has been developed[210]	
	Verify procedure for screening staff has been developed and is introduced to relevant BT staff. Screening should be performed for all staff entering zone III or IV.	N/A
	Commission relevant applicator models[17] in the treatment planning system, if applicable	N/A

	Commission image registration software, evaluate imaging data transfer, and rigid and/or deformable registration accuracy[69]	See TG 132 Tables IV and VI[69]
	Perform applicator reconstruction commissioning[16] and evaluate geometric and dosimetric accuracy for relevant HDR applicators compared with gold standard imaging (e.g., CT)	≤ 2 mm and < 8 – 10%,[106,107] respectively
	Evaluate MRI markers if planned for clinical use with plastic applicators	≤ 2 mm
	Perform end-to-end testing to evaluate workflow	N/A
	Develop policies and procedures for appropriate use of applicators in an MRI environment, imaging sequences, and QA prior to clinical implementation of MRI within the BT workflow	N/A
	Document clinical workflow and update checklists based on changes introduced with MRI integration	N/A
Each treatment day	Perform imaging QA per guidelines (e.g., CT,[211] MRI,[10,67] kV/MV images,[212] kV or MV-CBCT[212,213])	See references [10,67,211-213]
	Perform pre-implant check to ensure the appropriate applicator/needles was selected and that applicator/needles is/are MR safe or conditional	N/A
	Confirm pre-MRI screening questionnaire completed before start of procedure	N/A
	Perform physical screening before patient enters zone III	
	Prior to MR imaging, prevent skin-to-skin contact of the hands, feet, and/or limb, and bore contact	N/A
	If a non-ferromatic metal applicator(s)/needles implanted, verify applicator does not come in contact with	N/A

	patients skin and applicator tips do not cross	
	If applicable, verify the integrity of the MRI markers prior to MR imaging	N/A
Monthly	Perform imaging QA per guidelines (e.g., CT,[211] MRI, kV/MV images,[212] kV or MV-CBCT[212,213])	See references [10,211-213]
Each source exchange or quarterly	Review imaging and HDR vendor websites to verify whether new customer bulletins have been released regarding applicators, software, or hardware	N/A
Annual	Verify staff has completed annual MRI and radiation safety refreshers, as well as HDR emergency training	N/A
	Perform imaging QA per guidelines (e.g., CT,[211] MRI,[10,67] kV/MV images,[212] kV or MV-CBCT[212,213])	See references [10,67,211-213]
	Review policies and procedures, and if necessary updated	N/A
	Evaluate imaging data transfer and rigid and/or deformable registration accuracy[69]	See TG 132 Tables IV and VI[69]
	Review clinical workflows and checklists, update as needed	N/A
Software/hardware upgrades*	Review software/hardware releases to determine which software/hardware features should be tested post-upgrade	N/A
	With updates to MRI software/hardware, verify clinical pulse sequences in phantom and evaluate image artifacts and distortion to determine if adjustments are needed in imaging parameters	≤ 2 mm
	Evaluate imaging data transfer and rigid and/or deformable registration accuracy[69]	See TG 132 Tables IV and VI[69]
	Verify whether upgrade has affected relevant applicator models,[17] if so,	N/A

	applicator models may need to be recommissioned	
	Perform end-to-end testing to evaluate workflow	N/A
Purchase of new model of applicator/needles	Review instructions for use for relevant HDR applicators; if third party applicator or accessories, ensure compatibility with existing devices	N/A
	Verify MRI safety of relevant HDR applicators	N/A
	Optimize MRI pulse sequences in phantom and *in vivo*, and evaluate image artifacts and distortion	≤ 2 mm
	Commission applicator models,[17] if applicable	N/A
	Perform applicator reconstruction commissioning[16] and evaluate accuracy for relevant HDR applicators	≤ 2 mm
	Evaluate MRI markers if planned for clinical use with plastic applicators	≤ 2 mm
Safety Related Events	Imaging and treatment related variances or medical events should be investigated and reported to the appropriate state or federal agency within the required timeframe. Lessons learned from these events should be used to drive quality efforts and improvement within the program.	N/A

* If a diagnostic MRI is used in the BT workflow versus a dedicated MRI simulator, then regular communication should be established with MR physicists, MR technologist, or administrators to ensure the QMP and/or BT team is alerted when an upgrade is scheduled.