Practical guidelines of online MR-guided adaptive radiotherapy

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ABSTRACT

The first magnetic resonance (MR)-guided radiotherapy system in Japan was installed in May 2017. Implementation of online MR-guided adaptive radiotherapy (MRgART) began in February 2018. Online MRgART offers greater treatment accuracy owing to the high soft-tissue contrast in MR-images (MRI), compared to that in X-ray imaging. The Japanese Society for Magnetic Resonance in Medicine (JSMRM), Japan Society of Medical Physics (JSMP), Japan Radiological Society (JRS), Japanese Society of Radiological Technology (JSRT), and Japanese Society for Radiation Oncology (JASTRO) jointly established the comprehensive practical guidelines for online MRgART. These guidelines propose the essential requirements for clinical implementation of online MRgART with respect to equipment, personnel, institutional environment, practice guidance, and quality assurance/quality control (QA/QC). The minimum requirements for related equipment and QA/QC tools, recommendations for safe operation of MRI system, and the implementation system are described. The accuracy of monitor chamber and detector in dose measurements should be confirmed because of the presence of magnetic field. The ionization chamber should be MR-compatible. Non-MR-compatible devices should be used in an area that is not affected by
INTRODUCTION

The first magnetic resonance (MR)-guided radiotherapy system in Japan was installed in May 2017, and implementation of online MR-guided adaptive radiotherapy (MRgART) using this system began in February 2018. Online MRgART benefits from high soft-tissue contrast offered by MR-images (MRI) compared with X-ray imaging (such as computed tomography), and provides high accuracy with respect to patient positioning and beam delivery to the tumor. Moreover, real-time monitoring of tumor and the surrounding organs at risk (OARs) helps improve the safety of adaptive radiotherapy (ART) based on anatomical structures, shapes, and tumor volume during radiotherapy as well as prior to treatment.

Owing to the co-installation of the MR system in the radiotherapy room, there are several essential physical, technological, and clinical considerations for online MRgART which are not applicable to conventional radiotherapy. Inadequate quality assurance (QA) and quality control (QC) checks can lead to unexpected outcomes, toxicity, and accidents. Because of the specific requirements for safe operation of MR systems, online MRgART should be performed according to the guidelines for the safe operation for clinical implementation of MRI published by the Japanese Society for Magnetic Resonance in Medicine (JSMRM).

Advanced techniques such as intensity-modulated radiation therapy (IMRT), stereotactic body radiation therapy (SBRT), image-guided radiotherapy (IGRT), and motion management technique, are used in online MRgART. Treatment accuracy in MRgART is achieved as long as each technology is safely performed. The following guidelines should be referred to meet the equipment and operational requirements for these fundamental technologies: guidelines for IMRT, SBRT, IGRT, and motion management or their updates [2–6], published by the Japanese Society for Radiation Oncology (JASTRO) and the related societies. It is necessary to sufficiently examine and verify the physical, technical, and clinical aspects of online MRgART prior to its clinical implementation.

Against this background, the associated five societies, JSMRM, Japan Society of Medical Physics (JSMP), Japan Radiological Society (JRS), Japanese Society of Radiological Technology (JSRT), and JASTRO have launched the project to establish the comprehensive practical guidelines for online MRgART. These guidelines specify the requirements for clinical implementation of online MRgART with respect to personnel, equipment, institutional environment, practice guidance, and QA/QC. Online computed tomography-guided ART is not subject to these guidelines owing to the insufficient knowledge and clinical experience about the physical, technical, and clinical aspects at the time of formulating this guideline. In future work, the scope of this guideline should be extended with consideration of domestic situation about clinical implementation of online computed tomography-guided ART.

DEFINITION OF ONLINE MR-GUIDED ADAPTIVE RADIOTherapy

The prerequisite technology for online MRgART is online ART as well as MR-guided radiotherapy and ART. Online MRgART is defined by combinations of three technologies: (i) MR-guided radiotherapy; (ii) online ART; and (iii) accurate control of beam delivery through continuous real-time direct monitoring of the tumor/target by MRI during irradiation to ensure conformity of the treatment delivered with the treatment plan created immediately before treatment. The MRgART allows for instantaneous reduction or modification of the treatment area, which is expected to confer clinical benefits, namely enhancing treatment outcome by higher dose to the tumor, reducing the risk of adverse events by dose reduction to surrounding normal organs, and clinical implementation of safer hypofractionation.

MR-guided radiotherapy is defined as radiotherapy performed with availability of MRI for measurements and correction of patient positioning; these technologies are specified in IGRT guideline as one of the IGRT techniques [4].

ART is defined as radiotherapy in which a new treatment plan is created based on three-dimensional medical images of the patient acquired during the radiotherapy session. This is done when there is a concern that the initial treatment plan may result in insufficient dose to the target or increased dose to surrounding organs due to tumor shrinkage or changes in patient weight that may occur during radiotherapy.

In the pattern survey of the ESTRO physics workshop [7], ARTs are classified into four categories according to their techniques:

1. Offline ad hoc replanning: A new treatment plan is created based on tumor shrinkage and other factors.
2. Protocolled offline replanning: The decision of replanning is taken by pre-defined action levels or clinicians’ decision on geometric deviations observed by either IGRT or scheduled surveillance scans.
3. Online plan library: The most appropriate plan is selected, based on deviation in anatomy observed by IGRT, from a library of available treatment plans covering several scenarios of tumor motion.
4. Daily online replanning: The optimum treatment plan is created immediately prior to treatment based on the day-to-day changes in the patient’s anatomical condition.

Online ART in this guideline indicates technique no. 4) in the above list. This technique entails a series of processes, including acquisition of three-dimensional images, contouring based on the images,
creation of a new treatment plan, verification, and irradiation, while the patient is placed on the treatment couch.

**INDICATIONS FOR ONLINE MR-GUIDED ADAPTIVE RADIOTHERAPY**

Both IGRT and online ART technology used for online MRgART are applicable to any disease that is treated by radiotherapy with X-rays. These technologies are especially suitable for localized solid malignancies that are in close proximity to risk organs and require high dose prescription. The clinical benefits of IGRT have been demonstrated, and its costs are covered by health insurance in Japan. In addition, online MRgART, compared with conventional IGRT using X-rays, allows continuous monitoring of 3-dimensional internal anatomy of the target and surrounding normal organs during irradiation (intra-fraction) without the use of fiducial markers. This may lead to new indications for radiotherapy for diseases in which conventional radiotherapy was not considered indicated (including benign diseases). Some issues regarding online ART remain unclear, i.e. which diseases are appropriate for its use, how often it is needed, and how it should be used in comparison with offline post-therapy adaptation (corresponding to techniques 1) and 2) defined by ESTRO physics workshop referred to in section "DEFINITION OF ONLINE MR-GUIDED ADAPTIVE RADIOTHERAPY"). Currently ongoing domestic and overseas studies are expected to help address these questions. In one overseas report, online ART was performed in 28.5% of sites and 67.7% of treatments [8]. According to a domestic report, 49% of treatments were reported to be performed by online ART [9]. Overseas multicenter prospective clinical trials have been conducted for various tumor sites, including brain tumor, breast cancer, lung cancer, esophageal cancer, head and neck cancer, pancreatic cancer, prostate cancer, rectal cancer, liver cancer, bile duct cancer, bladder cancer, kidney cancer, uterine cancer, oligo-metastasis and other solid cancers [10].

However, the following absolute contraindications should be noted: (i) patients with contraindications to MRI such as those with implantable cardiac defibrillators and cochlear implants, (ii) patients affected by claustrophobia, and (iii) patients who have difficulty in remaining immobilized for a prolonged time period (40 to 60 minutes) [11].

**EQUIPMENT REQUIREMENTS FOR ONLINE MR-GUIDED ADAPTIVE RADIOTHERAPY**

The equipment required for online MRgART include the online MRgRT system and the peripheral devices (QA tool, devices related to radiotherapy). The online MRgRT system integrates the radiotherapy system and MRI system with a shared patient couch, and treatment planning system are connected to this system. The following requirements must be met.

**Online MR-guided adaptive radiotherapy system**
The radiotherapy and MRI system for online MRgART should satisfy the following requirements.

**Radiotherapy system**
1. X-rays produced by a linear accelerator.
2. Availability of IMRT.
3. Minimization of the magnetic field effect of the MRI system on the radiotherapy system.
4. Availability of the MR images in the treatment planning system.
5. Monitoring of tumor and surrounding normal organs by MRI.
6. The phantom for evaluation of MRI quality should offer evaluation of signal-to-noise ratio (SNR) and uniformity for MRI.

**Magnetic field effect**
- The magnetic field effect is minimized using a magnetic field of the MR system within specified range to maintain treatment accuracy. A proper clinical target volume (CTV)-planning target volume (PTV) margin should be considered, if necessary.
- Availability of the MR images in the treatment planning system.
- The phantom for evaluation of MRI distortion should be able to evaluate distortion within the clinically used scan range.

**Peripheral radiotherapy equipment**
Peripheral radiotherapy equipment which should be used for online MRgART are provided below. When these and other similar devices are used in clinical practice, peripheral radiotherapy equipment (immobilization, QA tool) in subsection "Safety aspects of peripheral radiotherapy equipment (immobilization and QA tool)" should be referred to ensure safety.

**QA tools**
1. No heat should be generated in the solid phantom by radiofrequency (RF) during MR scans. The phantom should be designed to avoid unnecessary air gap, when stacking slabs of a phantom.
2. The motion phantom should be MR-compatible.
3. The dosimeter and radiation detector should be MR-compatible.
4. Electrometer can be utilized outside the treatment room. The utilizing electrometer inside treatment room potentially influence MR image quality. The utilizing it inside treatment room is allowed as long as institutions confirm that it does not influence on MR image quality.
5. An independent dose calculation system to verify treatment plan and gather plan information from the treatment planning system. Verification of the modified treatment plans in online ART should be possible prior to treatment.
6. The phantom for evaluation of MRI distortion should be able to evaluate distortion within the clinically used scan range.
7. The phantom for MRI quality should offer evaluation of signal-to-noise ratio (SNR) and uniformity for MRI.

**Immobilization and related devices**
(1) A patient immobilization device whose safety during MR scans had been confirmed should be used.
(2) Infusion stand and patient monitoring device should be MR-compatible. For non-MR-compatible devices, safety during MR scans should be ensured.
(3) Immobilization and related devices brought into the treatment room should not influence the magnetic field.
(4) Ferromagnetic material detector should be installed at the entry point of the treatment room.
(5) Patient transfer devices, e.g. wheelchairs and stretchers, should be MR-compatible.

STAFFING AND FACILITY REQUIREMENTS AND PRACTICAL GUIDELINES FOR ONLINE MR-GUIDED ADAPTIVE RADIOThERAPY

Online MRgART involves the use of fundamental technologies and implementation structure for SBRT, IGRT, and IMRT. Therefore, substantial experience and systems for safe implementation of SBRT, IGRT, and IMRT are a prerequisite for safe clinical implementation of online MRgART. Additionally, the assigned medical personnel should have sufficient education, knowledge, and skills for treatment planning and verification of each treatment fraction. Moreover, they should be well trained with respect to the safety aspects of operating the MR system. The implementation structure is described in this section. Besides, for implementation of MR-guided non-ART, the "guideline of IGRT 2019 [4]" or its updated version should be referred to.

Staffing requirement

Staffing requirement mentioned in the national regulations for implementing IMRT is an essential prerequisite. The additional staffing requirements for online MRgART are described in this subsection.

Full-time physician or dentist exclusively in charge of radiation therapy or diagnostic imaging

More than two physicians or dentists exclusively in charge of radiotherapy and one physician exclusively in charge of image diagnostic shall be assigned. The inclusion of dentists is unique to Japan. At least one physician in radiotherapy shall have a specialized license in radiation oncology certified jointly by the JASTRO and JRS. The physician exclusively in charge of diagnostic imaging shall have a specialized license in diagnostic radiology certified by the JRS.

Full-time radiological technologist exclusively in charge of radiotherapy

A full-time radiological technologist in charge of radiotherapy (more than 5 years’ experience) shall be assigned. He/she shall have a specialized license in radiotherapy, certified by the Japan professional accreditation board for radiotherapy technologists.

Full-time nurse exclusively in charge of radiotherapy

One full-time nurse in charge of radiotherapy shall be assigned. He/she is recommended to have a specialized license in radiotherapy nursing, certified by the Japanese Nursing Association.

Technologist exclusively in charge of QA/QC for equipment related to radiotherapy, treatment plan verification, and technical support for treatment planning

One staff member exclusively in charge of QA/QC of equipment related to radiotherapy, treatment plan verification, and technical support for treatment planning (more than 5 years’ experience) shall be assigned. He/she shall be a licensed medical physicist certified by the Japanese board for medical physicist qualification.

Staff for MR safety

One full-time staff member for MR safety shall be assigned. He/she is recommended to have a specialized license for safety control in MRI, certified by the Japan authorize organization for MR technological specialist.

Institutional requirements

The national regulations related to institutional requirements for implementing IMRT and IGRT shall fulfilled. In addition, the institution shall qualify the following minimum criteria for treatment.

(1) More than 10 SBRT patients per year.
(2) More than 50 IMRT patients per year.
(3) More than 50 IGRT (based on tumor matching) patients per year.

Practical guidelines

Basic policy

To ensure treatment accuracy and safety, the following recommendations should be complied with.

(1) The QA/QC program for equipment related to online ART should be established and meticulously conducted at each facility. The results should be recorded in disclosable documents.
(2) Clinical procedures describing the role of each professional for online ART, institutional guidelines for treatment planning for each disease and for MR safety should be established. Online ART should be performed according to these procedures and guidelines, and all treatment records should be available as disclosable documents. The treatment plan guideline should specify the criteria of dose constraints for OARs.

Implementation structure

The following staffing requirements are recommended for online MRgART.

(1) One physician exclusively in charge of radiotherapy should be assigned for modifying the treatment volume and providing approvals for treatment plan and patient positioning.
(2) Two radiological technologists exclusively in charge of radiotherapy (preferably full-time) should be assigned for modifying treatment position and its confirmation.
(3) One nurse should be assigned for promptly responding to an emergency or a patient’s request. The patient should be monitored during modification of treatment position and treatment plan.

(4) One technologist for QA/QC should be assigned for equipment related to radiotherapy, treatment plan verification, and technical support for treatment planning.

Use of MRI system for diagnostic purpose
Diagnostic MR scans performed using this system should include the treatment sites. It is recommended that the MRI system should be used only for assessment of sites associated with radiotherapy such as tumor characteristics and functional diagnosis for patients undergoing radiotherapy.

Education and training system for involved personnel
The personnel involved in implementing online MRgART should be adequately educated about the system characteristics and operation. It is recommended that the appointed personnel should be those who have already been trained at an institution that has adequate capacity and clinical experience, or should undergo training courses provided by such institutions.

GUIDELINES FOR SAFE OPERATION IN MRI
To ensure safety in MRI system, the operation of MRI should be performed according to the guidelines for safe operation of clinical MRI [1], published by the JSRMRI, and related guidelines [2–6]. The subject of this guideline is not for radiotherapy practices. Therefore, a part of the description in the guideline, should be translated as follows.

(1) ‘Physician, radiological technologist, and medical technologist, and nurse’ → ‘Physician, radiological technologist, and medical technologist, nurse, and medical physicist’ according to subsection ‘Staffing requirement’.

(2) ‘MRI examination’ → ‘MR scans’ 1’

*1: The ‘MR scans’ in this guideline include MRI for IGRT and treatment planning as well as for diagnostic examination. The safe operation of MRI in radiation oncology department is described as follows.

Safety management system in radiation oncology department
A safety management team should be established within the institution to manage MRI safety according to the safety management system described in the guidelines for safe operation of clinical MRI [1]. This team should consist of a radiation oncologist involved with radiotherapy, radiological technologist or medical technologists, nurse, and medical physicist, etc. It is recommended that this team be integrated with the safety management team in the diagnostic imaging department.

Quality control in MRI system
Image quality should be monitored at the start and end of work. Regular maintenance should be performed according to the safe operation for clinical implementation of MRI [1]. It should be confirmed whether the monitor and lighting in the treatment room, the measurement devices related to radiotherapy, and the related devices (immobilization, insulating tool) do not affect the MR image quality (subsection “Acceptance and commissioning”) for evaluation of image quality. The potential effect of changing the treatment parameters, gantry angles, and multi leaf collimator locations, as well as beam delivery and dose measurements, on the quality of MRI during treatment should be ruled out [12, 13].

Safety management during treatment
During imaging, a towel or dedicated insulating tool should be used to avoid current loops created by contact between both hands or both feet. When moving the couch, collision between the immobilization equipment and the treatment machine should be avoided. Since the patient stays in the magnetic field for a longer time, attention should be paid to heat generated by RF pulse and peripheral nerve stimulation by changes in the gradient magnetic field. The specific absorption rate (SAR, W/kg) and change in magnetic field per unit time (db/dt) should be confirmed. It is necessary to educate the patient about the means of communication during any emergency situation and he/she should be cautioned about heat generated during MR scans. In particular, the patient should be carefully monitored in the primary level management operation mode. Primary level management operation mode is the operation mode in MRI for one or several outputs which potentially lead to physiological stress requiring medical management (JIS Z 495114) [14].

Safety aspects of peripheral radiotherapy equipment (immobilization and QA tool)
When bringing the related devices into the MR-guided radiotherapy room, checklist for entering the treatment room [15], published by Japan Medical Imaging and Radiological Systems Industries Association, is useful. Table 1 shows the other notable devices. Some of these are compatible with MR. The MR-compatible devices should be used as far as possible.

Metallic materials (radiation shielding block) are prohibited in the treatment room. It should be confirmed in advance that the immobilization device used during treatment does not generate heat by RF pulse, considering that they will be imaged for a long time. In particular, carbon, which is commonly used as a material for immobilization devices, is conductive and generate heat by RF pulse. Therefore, use of carbon material in immobilization device should not be allowed.

When bringing the QA tool into the treatment room, the presence of magnetic materials in the QA tool should be excluded by ferromagnetic material detector in order to prevent projectile or missile events. When non-MR-compatible QA tool with electronic devices such as digital thermometers is brought into the treatment room, the QA tool should be used in an area that is not affected by the static magnetic field (for example, an area outside the five Gauss line), and its operation as well as its potential effect on image quality should be checked. Even the MR-compatible QA tools should be periodically checked for their potential effect on image quality and operation before use.
Table 1. Checklist for notable peripheral equipment or devices before bringing them into treatment room

- **During treatment**
  - Prohibited equipment
    - Metals (radiation shielding blocks, contacts for eye lens shielding, etc.)
    - Skin markers with metallic components
    - Equipment that needs to be checked for influence
    - Patient immobilization device
    - Bolus
    - Mouthpiece
    - In vivo dosimeter

- **During QA/QC**
  - Equipment that needs to be checked for influence
    - Ruler
    - Level
    - Thermometers
    - Barometer
    - Electrometer
    - Signal cable
    - Ionization chamber
    - Multidimensional detectors
    - Survey meters

- **Other dosimeters** (dosimetry films, glass dosimeters, etc.)
  - Water phantom
  - Solid phantom
  - Other equipment
  - Device of hospital information system, etc. (including monitors)
  - Stretcher
  - Wheelchair
  - Infusion stand

* These are already MR-compatible products that are allowed in the treatment room.

**TREATMENT PLANNING**

Online MRgART can be expected to confer clinical benefits as the pretreatment plans can be adapted to the actual condition of the patient at the time of treatment. However, some caution should be exercised so as not to inordinately increase the treatment time owing to the time constraints in clinical practice. To ensure safety, treatment planning should be done as follows.

**Establishment of institutional guidelines for treatment planning**

Confirmation when implementing online adaptive radiotherapy

The process in online MRgART is different from that in conventional treatment. To implement MRgART, it is desirable to prepare manuals and procedures, and to conduct rehearsals prior to clinical implementation. The expected increase in treatment time is liable to lead to increasing patient burden. It is recommended that targets should be set with respect to treatment time. Moreover, after the clinical implementation, continuous analysis should be conducted to identify the time-consuming processes in order to improve the treatment efficiency.

Policy of online adaptive radiotherapy

A policy document outlining the cases for whom online ART is indicated should be developed for each disease and should be shared within the radiotherapy department. It should also be developed for offline ART cases to prevent excessive use of online ART and ensure appropriate treatment. Additionally, for each case, radiation oncologists, radiological technologists, and medical physicists should discuss the clinical significance and key treatment-related issues (such as treatment time, body movement, etc.), and the radiation oncologist should finally approve the decision for online ART.

**Treatment planning**

**Patient immobilization**

It is assumed that use of online MRgART would necessitate prolonged maintenance of patient positions on the couch resulting in increasing patient burden. Comfort of the patient should be considered for immobilization to reduce patient burden.

**Image used in treatment plan**

The reference images for treatment planning should be MRI with high soft-tissue contrast as well as CT images. Attention should be paid to differences of the coils, patient positions, and the couch used for actual treatment.

**Registration accuracy in treatment planning**

The registration accuracy of planning MR and CT images should be evaluated.

**Personnel involved with delineation and treatment planning**

Delineation and treatment planning should be a collaborative effort involving radiation oncologist, radiological technologist, and medical physicist who are adequately trained in online MRgART.

**Assignment of relative electron density**

Assignment of relative electron density necessary for dose calculation involves proper relative electron density determined based on the types of organs or using deformed CT images using DIR to MRI. The confirmation items of this assignment at the commissioning are described in section "QA/QC".

**CTV-PTV margin**

The CTV-PTV margin differs according to the treatment site. Therefore, a proper margin for each treatment site should be considered. For online MRgART, the various uncertainties related to geometrical orientation of the margins should be considered to determine the optimum margins.

**Online MR-guided adaptive radiotherapy**

The subject of the delineation should be determined in advance for new treatment plan. Additionally, policy of assessment of dose volume histogram (DVH) and dose distribution in each treatment fraction should be determined in advance.
PATIENT POSITIONING AND TREATMENT

This section describes the important issues related to patient immobilization, positioning, and monitoring during treatment planning and treatment.

Patient immobilization

1. The safety aspects of MRI system described in section "GUIDELINES FOR SAFE OPERATION IN MRI". The safety of use of patient immobilization and related devices during MR scan should be confirmed. Due caution should be exercised to avoid collision of the immobilization device and the patient body with the bore in the machine and not to generate heating by loop area. Entry of any magnetic material is not allowed in the treatment room. Since some skin marker inks contain metals, they should be used only after confirming the safety of their heat generation.

2. General cautions for IGRT and MR scans should also be exercised. In particular, owing to the image distortion caused by non-uniform static magnetic field induced by the presence of the patient and type of image sequence, the target should be placed at the center of magnetic field or as near as possible.

3. Owing to the risk of unexpected increasing doses at the surface outside of the radiation field of head & neck and breast treatment by streaming of electrons to the outside of the radiation field due to magnetic field effect, use of bolus on the surface is recommended to reduce the surface dose [16, 17].

Patient positioning

1. When evaluating the position of organs using MRI, the image characteristics of various artifacts, such as chemical shift and magnetic susceptibility, which may cause misalignment, should be considered.

2. When MR-guided therapy is performed with reference to CT images, it is necessary to take into account the effect of patient positioning on the anatomical information because image contrast differs greatly between CT and MR.

Monitoring during treatment planning

The process from patient positioning including delineations and dose evaluation to the start of treatment is assumed to take a long time. Due attention should be paid to body movements and organ displacements during that time, and MR scan just before treatment is recommended to confirm appropriate positioning of the target.

Treatment

1. In online MRgART, appropriate location of the target and the surrounding OARs should be confirmed by obtaining MRI during irradiation.

2. In case of MR-guided motion management to the treatment sites, the accuracy of identifying the target site should be observed on the images at any time. The treatment should be immediately stopped in case of inaccurate tracking of the target. In addition, the beam control generally has a latency, and the time delay in processing and generating the MR image as well as the time delay generated in the treatment equipment should be considered.

QA/QC

Acceptance and commissioning

The following criteria in addition to the conventional procedures should be fulfilled in acceptance and commissioning of online MRgART system.

Dose output in radiotherapy system

The accuracy of the monitor chamber and detector in dose measurements should be confirmed because of the presence of magnetic field. The long-term stability of the monitor chamber should be evaluated not only at the time of commissioning, but also daily and regular QA/QC. Moreover, long-term changes in calibration factor and charge collected by the detector in measurements should be evaluated.

For assessment of dose-output accuracy of the monitor chamber, general test (dose rate dependency, reproducibility, linearity) is performed. Additionally, dosimetry audit is recommended prior to clinical implementation and at regular intervals. For calibration of dose output, MR-compatible chamber should be used. The longitudinal direction of the chamber should be parallel to the static magnetic field because presence of the magnetic field induces changes in the trajectory of scattered electrons resulting in significant changes of charge [18–24].

Reference beam data

Reference beam data is provided for beam modeling. If this is used in clinical practice, the guidelines for implementation of treatment machine and treatment planning system using reference beam data, published by the JSPM or updated is recommended [25].

Couch attenuation

Carbon fiber couch with less attenuation of photon beams, which is used in conventional radiotherapy, is not allowed in the MRI system as it generates heat during MR scans. Therefore, glass fiber couch which does not generate heat is used. Such material has comparatively greater attenuation, and correction of couch attenuation should be applied during dose calculation in the TPS. The couch attenuation correction should be verified at the time of commissioning. Additionally, attenuation of the surface coil should also be measured, and the attenuation corrections should be done in the TPS system, etc., if necessary.

Image quality and distortion of MR

MRI is affected by distortion due to non-uniformity of static magnetic field. Image distortion should be evaluated within the clinically used range from isocenter to peripheral by using a phantom, and three-dimensional evaluation should be performed by placing the phantom in different axes [26]. Additionally, baseline for SNR and uniformity as reference data is determined using the dedicated phantom for image quality evaluation [27]. The influence of treatment environment (monitor, room lighting, devices related to radiotherapy) on image quality should also be verified.

Dose calculation accuracy in the treatment planning system (including using MRI)

The dose calculation accuracy in TPS system should be verified prior to clinical implementation. Treatment plans under simulated clinical
conditions, from simple to IMRT, should be created, and dose calculation accuracy should be evaluated through measurements. It should be also done for MRI available in dose calculation. Moreover, dose calculation accuracy for electron return effect should be evaluated using heterogeneous phantom.

Image registration (Rigid and non-rigid registration)

Image registration accuracy significantly influences the treatment accuracy of ART. Therefore, verification of rigid- and non-rigid- image registration accuracy is required. For evaluation of non-rigid registration accuracy, consistency between moving and fixed image should be confirmed. For evaluation, guidelines for clinical implementation of non-rigid image registration in radiotherapy 2018 or its updated version should be referred to [28].

Data communication and image storage

Online MRgART entails the use of a combination of different systems. Therefore, it should be verified whether matching image, positional, and planed information is correctly shared among the radiotherapy system, TPS, and MR system. These data should be appropriately managed and saved as recommended by the guidelines for the safety management of medical information systems and a guideline for KAKUTEI of image information [29, 30].

Assessment of overall treatment accuracy in online adaptive radiotherapy (End-to-end test)

Integrated radiotherapy system with MRI system (including TPS system) requires an independent positional accuracy test in both the systems and a comprehensive test to assess the consistency of the two coordinates. The former is performed as the acceptance test, and the latter is performed as an end-to-end test for comprehensive assessment of positional accuracy. Comprehensive assessment of treatment positional accuracy and dose calculation involves the entire series of procedures, i.e. planning imaging, importing images into the TPS, treatment planning, registration of planed information into the radiotherapy system, online ART using a phantom, independent verification, communication and sharing information between the entire system. The end-to-end test is performed not only at the time of commissioning, but also regularly after clinical implementation, to rule out any abnormalities in the overall system.

Organ motions

To perform radiotherapy with motion management by monitoring organ motions (target and surrounding normal organs), dose verification is conducted using a motion phantom as recommended in the guidelines for motion management in radiotherapy 2019 [3] and guidelines for clinical implementation of IGRT 2019 [4] or its updated version. Optimum motion management (breath-hold or free breathing) should be determined from the view of treatment accuracy, patient’s burden, and treatment efficiency.

Daily test, regular quality control

Daily test and regular QC for MRI system and online ART as well as general tests for TPS and treatment machine should be performed [2–4, 31, 32]. In addition, issues and improvements related to overall treatment procedure and improvements of procedures as well as regular QC in treatment machines should be discussed among the radiation oncologist, radiological technologist, nurse, and medical physicist. The process map to visualize the overall treatment workflow should be developed if necessary, and risk assessment of online ART should be regularly performed. Especially, higher risk events should be prevented by improving the workflow and processes [33]. For instance, a typical treatment process map was provided in the Supplementary Fig. 1.

Key recommendations for QA/QC program

1. Dose-output calibration in the radiotherapy system.
2. Dosimetric accuracy of monitor chamber in the radiotherapy system.
3. Geometrical accuracy in the radiotherapy system.
4. Consistency of coordinates of MRI and radiotherapy system.
5. Image quality and image distortion of MR.
6. Safety in MRI system.
7. Dose calculation accuracy in the TPS system (including using MRI).
8. Image registration accuracy (rigid and non-rigid).
9. Connection between radiotherapy (including TPS system) and MR systems.
10. End-to-end test in online ART.

Quality assurance in online adaptive radiotherapy

Dose verification should be performed for all patients in online ART according to the IMRT guidelines [2]. However, since image acquisition, treatment planning, and irradiation are carried out in a series while the patient is on the bed, dose verification using ionization chambers, films, or multidimensional detectors is difficult. Therefore, use of alternative dose verification tools that are confirmed to be reliable through commissioning can be used. A general method is to use an independent dose verification system. It is necessary to establish a system to ensure the safety of treatment plan within a limited time. The practical guidance is described below.

1. Calculation accuracy in independent dose verification system should be verified through dose verification using a phantom at the time of commissioning. For at least the first 30 patients after the clinical implementation of online ART, post-dose measurement should be done at least once for each patient immediately after the start of the treatment session. Validity of the independent dose verification system should be evaluated by comparing with the results of post-dose measurement.
2. The safety of monitor unit and other equipment used in online ART should be confirmed using the independent dose verification system. Besides, non-ART, i.e. conventional IMRT required pre-treatment dose verification according to the IMRT guidelines [2]. In addition, it should also be applied for the original treatment plan in the online ART.
3. Guidelines for the acceptability of treatment when the results of the independent dose verification system exceed the criteria should be established in advance based on the results of the commissioning of the independent dose verification system.
(4) The decision to approve or dismiss the online ART based on the results of independent dose verification system is made after discussion among the radiation oncologist, radiological technologist, and the medical physicist. The final authority to approve vests with the radiation oncologist. Alternatively, the decision to approve or dismiss online ART should be based on the institutional guideline approved by radiation oncologist in advance.

(5) Safety in treatment plan for online ART should be confirmed by several persons, and results of confirmations should be recorded. A checklist is recommended for this purpose.

(6) Treatment plan information and actual treatment information after online ART should be recorded in the hospital information system.

The following items related to treatment plan are recommended in the checklist for online ART:

(1) Delineation accuracy
(2) Boolean operation for delineations
(3) Electron density used for dose calculation \(^\ast\)
(4) Dose prescription \((D_{\text{pres}}\), etc.)
(5) Dose distribution and DVH evaluation
(6) Comparison of planned information between original and revised treatment plan \(^\ast\)

\(^2\): If the deformed CT to daily MRI is used for dose calculation, the DIR accuracy such as body shape should be confirmed. If uniform electron density (bulk density) is applied to each delineation for dose calculation, it should be confirmed whether appropriate electron density is applied.

\(^3\): Dose distribution, DVH, treatment parameters (gantry angle, number of beams, delivered dose, MU, etc.)

**SUMMARY**

Five Japanese professional societies, JSMRM, JSMP, JRS, JSRT, JASTRO, jointly established a practical guideline for online MRgART. Integrated radiotherapy system with MR system has been developed and clinically implemented in Japan. Use of MR-guided radiotherapy has also begun in clinical practice. This guideline comprehensively covers the clinical and physical aspects related to appropriate and safe clinical implementation of MR-guided online ART. As mentioned in section “INTRODUCTION”, MR-guided online ART requires the use of fundamental technologies such as IMRT, SBRT, and IGRT; and motion management that is used in conventional radiotherapy. Considering the technological advances in IGRT, three societies, JSMP, JSRT, and JASTRO jointly published IGRT guidelines in May 2019. Continuing from IGRT guideline, the advances in radiotherapy have opened the prospects for wider clinical implementation of ‘ART’ which entails adaptation of the treatment plan taking into account the day-to-day changes in tumor size and changes in the patient’s body shape during the treatment session.

Online MRgART ‘is online ART,’ corresponding to ‘daily online replanning’ among the definitions of ‘ART’ under the technology of MR-guided radiotherapy. This guideline also includes a definition of ‘ART’. Additionally, the definition is not limited to IGRT based on MRI, but also applies to IGRT using other imaging techniques; thus, it is complementary to the IGRT guideline and this guideline.

**SUPPLEMENTARY DATA**

Supplementary data is available at RADRES Journal online.

**CONFLICT OF INTEREST**

There is no ethical problem with regard to this manuscript.

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**REFERENCES**

1. The Japanese Society for Magnetic Resonance in Medicine. Guidelines for safe operation of clinical MRI [authors’ translation].
2. Japanese Society for Radiation Oncology. Physical and technological guidelines of IMRT [author’s translation]. https://www.jastro.or.jp/customer/guideline/2016/10/IMRT2011.pdf (1 June 2022, date last accessed).

3. Japanese Society of Medical Physics, JH-PEBRG, Japanese Society of Radiological Technology, Japanese Society for Radiation Oncology. Guidelines of motion management in radiotherapy 2019 [author’s translation]. https://www.jastro.or.jp/medicalpersonnel/guideline/kokyu2019.pdf (June 1, 2022, date last accessed).

4. Japanese Society of Medical Physics, JSoRT, Japanese Society for Radiation Oncology. Guidelines of clinical implementation of IGRT 2019 [author’s translation]. https://www.jastro.or.jp/medicalpersonnel/guideline/igrt2019.pdf (1 June 2022, date last accessed).

5. Japanese Society for Radiation Oncology. Guidelines of SBRT [author’s translation]. https://www.jastro.or.jp/customer/guideline/2016/10/SRT.pdf (1 June 2022, date last accessed).

6. Japanese Society for Radiation Oncology, JRS, Japan High-Precision Beam Radiotherapy Group. A IMRT guideline 2008 [author’s translation]. https://www.jastro.or.jp/customer/guideline/2016/10/imrt.pdf (1 June 2022, date last accessed).

7. Bertholet J, Anastasi G, Noble D et al. Patterns of practice for adaptive and real-time radiotherapy (POP-ART) RT part II: Offline and online plan adaption for interfractional changes. Radiother Oncol 2020;153:88–96.

8. Henke LE, Contreras JA, Green OL et al. Magnetic Resonance Image-Guided Radiotherapy (MRIgRT): A 4.5-Year Clinical Experience. Clin Oncol (R Coll Radiol) 2018;30:720–7.

9. Inaba K, IiH, Nishio k aS et al. Initial experience of MR guided adaptive radiation therapy. J Clin Radiol 2018;63:1015–20.

10. de Mol van Otterloo SR, Christodoulouas JP, Blezer ELA et al. The MOMENTUM Study: An International Registry for the Evidence-Based Introduction of MR-Guided Adaptive Therapy. Front Oncol 2020;10:1328.

11. Güngör G, SerbezI, Temur B et al. Time analysis of online adaptive magnetic resonance-guided radiation therapy workflow according to anatomical sites. Pract Radiat Oncol 2021;11: e11–21.

12. Cai B, Li H, Yang D et al. Performance of a multi leaf collimator system for MR-guided radiation therapy. Med Phys 2017;44:6504–14.

13. Michael Gach H, Curcuru AN, Wittland EJ et al. MRI quality control for low-field MR-IGRT systems: lessons learned. J Appl Clin Med Phys 2019;20:53–66.

14. Japanese Industrial Standards, MRISBsabp. Japanese Industrial Standards (JIS) Z 4951.

15. Japan Medical Imaging and Radiological Systems Industries Association. A Checklist for Entering Examination Room [author's translation]. https://www.jira-net.or.jp/anzenkanri/02_seizouha_nbaigo/02-03.html#02-03_2013_0701 (1 June 2022, date last accessed).

16. Park JM, Shin KH, Kim JI et al. Air-electron stream interactions during magnetic resonance IGRT: skin irradiation outside the treatment field during accelerated partial breast irradiation. Strahlenther Onkol 2018;194:50–9.

17. De-Colle C, Nachbar M, Mönich D et al. Analysis of the electron-stream effect in patients treated with partial breast irradiation using the 1.5 T MR-linear accelerator. Clin Transl Radiat Oncol 2021;27:103–8.

18. Malkov VN, Rogers DWO. Sensitive volume effects on Monte Carlo calculated ion chamber response in magnetic fields. Med Phys 2017;44:4854–8.

19. Meijsing I, Raaymakers BW, Raaijmakers AJ et al. Dosimetry for the MRI accelerator: the impact of a magnetic field on the response of a Farmer NE2571 ionization chamber. Phys Med Biol 2009;54:2993–3002.

20. O’Brien DJ, Roberts DA, Ib bott GS et al. Reference dosimetry in magnetic fields: formalism and ionization chamber correction factors. Med Phys 2016;43:4915–27.

21. Reynolds M, Fallone BG, Rathee S. Dose response of selected ion chambers in applied homogeneous transverse and longitudinal magnetic fields. Med Phys 2013;40:042102.

22. Smit K, van Asselen B, Kok JG et al. Towards reference dosimetry for the MR-linac: magnetic field correction of the ionization chamber reading. Phys Med Biol 2013;58:5945–57.

23. Spindeldreier CK, Schrenk O, Bakenecker A et al. Radiation dosimetry in magnetic fields with Farmer-type ionization chambers: determination of magnetic field correction factors for different magnetic field strengths and field orientations. Phys Med Biol 2017;62:6708–28.

24. van Asselen B, Woodings SJ, Hacket SL et al. A formalism for reference dosimetry in photon beams in the presence of a magnetic field. Phys Med Biol 2018;63:125008. https://iopscience.iop.org/article/10.1088/1361-6560/aac70e.

25. Japan Society of Medical Physics. Guidelines for Implementation of Treatment Machine and Treatment Planning System Using Reference Beam Data 2020 [author’s translation]. https://www.jsmp.or.jp/wp-content/uploads/guideline_beamdata.pdf (1 June 2022, date last accessed).

26. Weygand J, Fuller CD, Ib b ott GS et al. Spatial Precision in Magnetic Resonance Imaging-Guided Radiation Therapy: The Role of Geometric Distortion. Int J Radiat Oncol Biol Phys 2016;95:1304–16.

27. Tijssen RHN, Philippens MEP, Paulson ES et al. MRI commissioning of 1.5T MR-linac systems - a multi-institutional study. Radiother Oncol 2019;132:114–20.

28. Japanese Society for Radiation Oncology. Guidelines of Implementation of Non-rigid Registration in Radiotherapy 2018 [author’s translation]. https://www.jastro.or.jp/medicalpersonnel/guideline/dir_v3.pdf (1 June 2022, date last accessed).

29. Ministry of Health, LaW. Guidelines for the Safety Management of Medical Information Systems (Ver. 5.1) 2021 [author’s information]. https://www.mhlw.go.jp/content/10808000/000730541.pdf (1st June 2022, date last accessed).

30. Japanese Society of Radiological Technology, gKoiiast. Guidelines for KAKUTEI of Image Information 2014 [author’s translation]. https://www.jsrt.or.jp/97mi/content/guideline/kakutei_guideline_ver2.1.pdf (1 June 2022, date last accessed).

31. American College of Radiology Committee on Quality Assurance in Magnetic Resonance Imaging. 2015 Magnetic Resonance Imaging. https://www.acr.org/-/media/ACR/Files/Clinical-Re
32. Klein EE, Hanley J, Bayouth J et al. Task Group 142 Report: Quality Assurance of Medical Accelerators. *Med Phys* 2009;36:4197–212.

33. 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. *Med Phys* 2016;43:4209.