Dose Calculation on Synthetic CT and Related Patient-Specific Quality Assurance for MR-Only Radiotherapy Planning for the Male Pelvic Region

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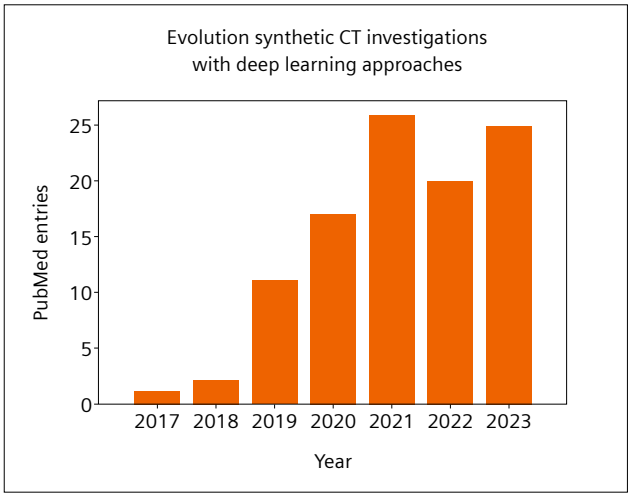
Introduction

Radiation therapy (RT) planning is classically based on computed tomography (CT). This derives from the fact that the CT voxel values, i.e., Hounsfield units (HU), have a monotonic correlation with the electron density, which in turn is required for the dose calculations in RT plans [1]. Improved results may be achieved with dual-energy CT (DECT) [2]. Nonetheless, while CT and DECT imaging are the preferable methods for performing dose calculations, additional imaging modalities have been introduced to the RT workflow during the past decades to improve the identification and contouring of target volumes and organs at risk (OAR). The use of positron emission tomography (PET) and magnetic resonance (MR) imaging as additional modalities is nowadays the standard of care for multiple treatment sites [3, 4]. In particular, the use of MR for RT is currently rapidly expanding, partly driven by the clinical introduction of hybrid MR-linac systems [5, 6]. Target and OAR contouring is therefore preferably performed on the MR data, exploiting the superior soft-tissue contrast and functional information acquired using dedicated sequences. The use of the CT data during treatment planning is then limited to dose calculation. In order to simplify the workflow and reduce the patient's radiation exposure, replacing the planning CT examination with "synthetic CT" (sCT) derived from the MR data has been proposed [7]. This would pave the way for MR-only RT planning. The seminal work by Han in 2017 has demonstrated the superiority of deep learning (DL) approaches for converting MR to sCT [8]. Figure 1 shows the rapid and steady expansion of this research field. Several commercial solutions are now available, and the value of sCT for dose calculation and matching to cone beam CT (CBCT) or kV imaging on image-guided RT (IGRT) linacs for patient positioning has been reported [9–12]. Novel challenges and dedicated solutions have been described for performing MR simulations in the RT position, including immobilization equipment [13]. Quality assurance guidelines are available for MR scanners used in RT applications [14], but only limited experience is available in the literature for patient-specific quality assurance of sCT data generated with DL approaches [15]. In this report, we focus on the clinical commissioning of the dose calculation and the implementation of patient-specific quality assurance for this task.



1 Evolution of the research field[1] of deep learning-generated synthetic computed tomography for radiotherapy planning.

[1]*"Search query: (""synthetic ct"" or ""sct"" or ""pseudo ct"" or ""synthetic computed tomography"" or ""pseudo computed tomography"") and (""radiotherapy"" and ""dose"") and (""deep learning"" or ""neural network"" or ""artificial intelligence"")"*

Clinical workflow for RT planning

Imaging data acquisition

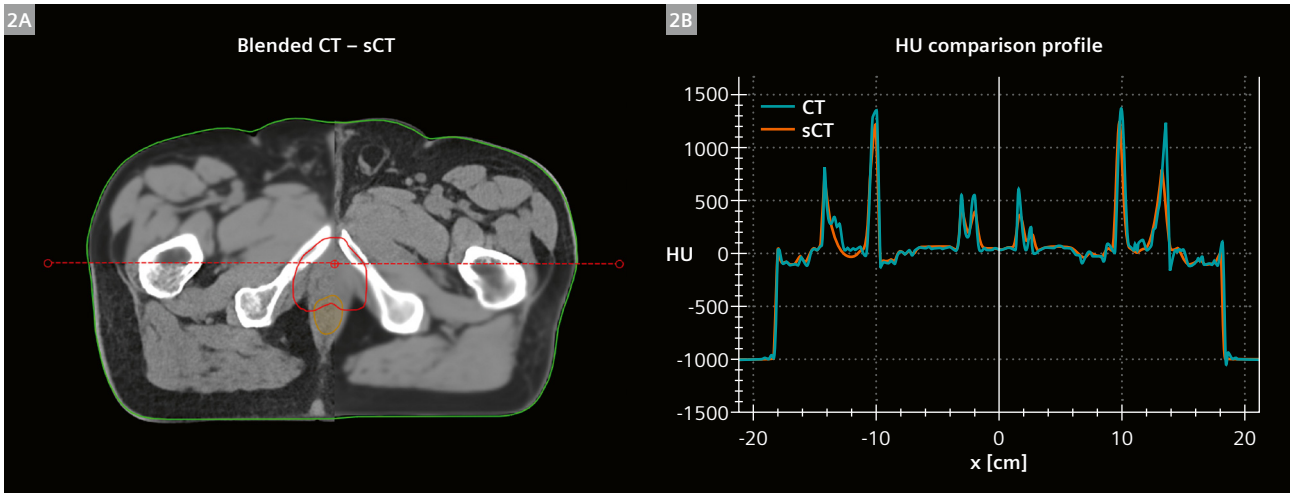
CT and MR data acquisition is the first task to be completed for the treatment-planning workflow. If eligible for MR examinations, male patients referred for pelvic RT at the Radiation Oncology Department of University Hospital Zurich are examined for both modalities in the RT treatment position. This setup includes a flat table top, flex body coils fixed on arcs to avoid compressing the abdomen and deforming the patient contour, and knee and feet rests to achieve reproducible patient positioning. MR simulations are performed on a 1.5T MAGNETOM Sola scanner (Siemens Healthcare, Erlangen, Germany), and CT simulations are performed on a SOMATOM Definition AS scanner (Siemens Healthcare, Forchheim, Germany). The MR examination includes sequences dedicated to diagnostics and contouring, adjusted to our institutional requirements (T1 StarVIBE, T2 turbo spin echo, diffusion-weighted imaging). Siemens Healthineers provided sequences for sCT generation (T1 VIBE/Dixon). The total examination time ranges from 30 to 45 minutes. The latter is acquired with a native resolution of 1.6 mm in-plane and 2 mm slice thickness with transversal orientation. The coverage is up to half of the L1 vertebral body and includes couch markers positioned posterior to the patient. All sequences are acquired with activated 3D distortion correction and cardinal slice directions (transversal, sagittal, or coronal) without any tilt angles. The data is then sent to the hospital's PACS and the department's treatment planning system (TPS) for diagnostic reporting and RT treatment planning, respectively.

Synthetic CT generation

The MR Dixon scans are reconstructed directly at the scanner to produce four 3D images: in-phase, opposed-phase, water, and fat. The first two reconstructions are provided as input data for *syngo*.via RT Image Suite VB60 (Siemens Healthineers, Erlangen, Germany) to generate an sCT with continuous HU values matching the anatomy of the MR Dixon. Acquiring the dedicated sequence requires up to 5 minutes, which is similar for the sCT reconstruction, which sums up to a total time burden of up to 10 minutes. The process is performed while the patient is still inside the bore for the acquisition of additional diagnostic sequences. Therefore, if artifacts (e.g., due to erroneous FOV positioning) or uncommon anatomies (e.g., excessive rectal filling) are observed in the Dixon and sCT, these can be repeated at the end of the examination without requiring an additional appointment for the patient. A prompt inspection of the sCT reconstruction can be performed directly at the scanner using *syngo*.via RT Image Suite. Figure 2 shows a comparison with the planning CT performed in the Aria Eclipse V16.1 TPS (Varian, a Siemens Healthineers Company, Palo Alto, CA, USA).

Data post-processing for the TPS

The reconstructed MR and sCT data are transferred to MIM (MIM Software Inc, Cleveland, OH, USA) for post-processing, and then to the Aria Eclipse TPS for treatment planning. All data transfers are automated and performed via DICOM node. Aria stores the incoming DICOM data as

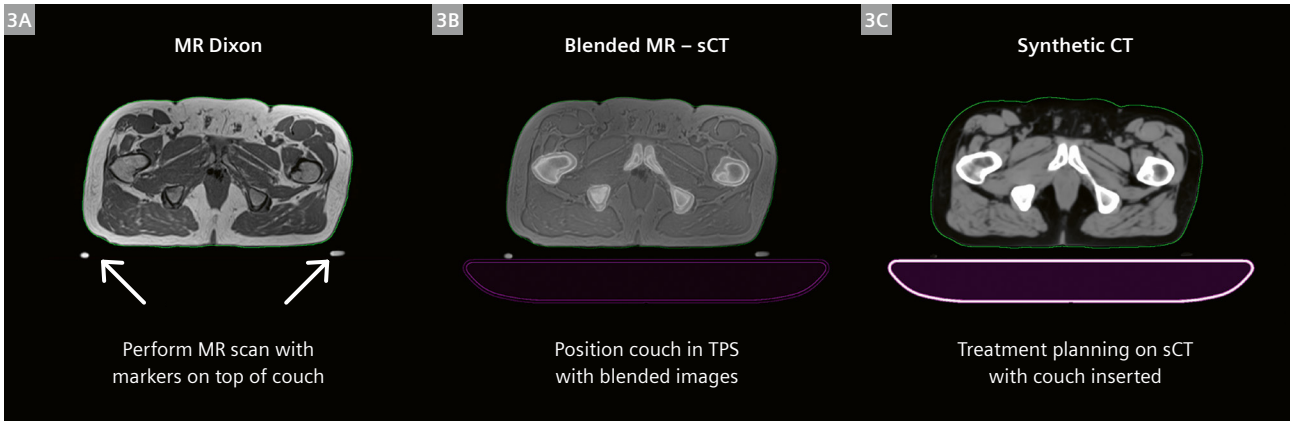


2 Comparison of sCT and planning CT data with checkerboard blending of the two images **(2A)**. The PTV contour is reported in red. The line profiles with corresponding HU values in the left-to-right patient direction through the PTV are shown **(2B)**.

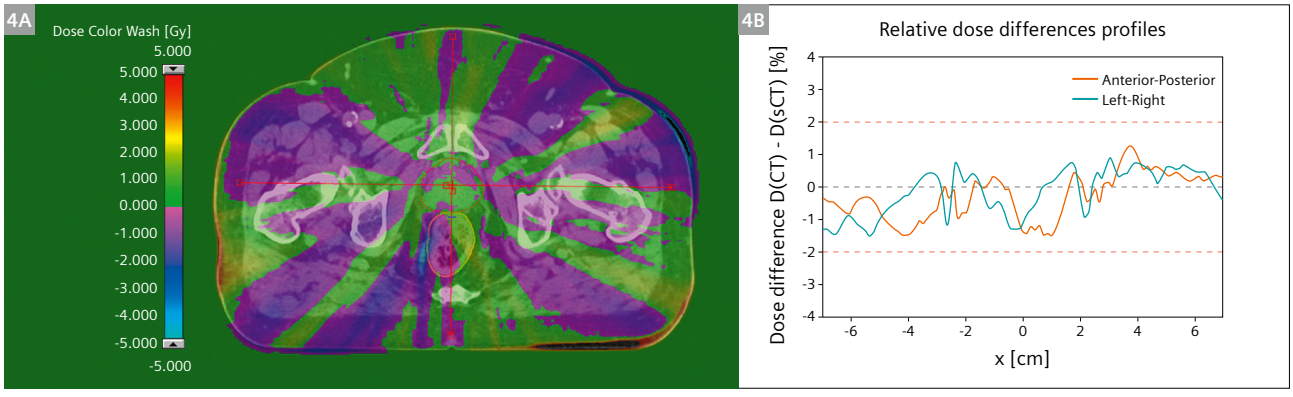
2D slices, and the generation of the 3D volumes for selected sequences is automated by assigning an RTStruct in MIM before the last DICOM node transfer. Further post-processing, such as renaming the 3D volumes according to institutional guidelines, is automated using ESAPI scripts developed in-house. The sCT is resampled to a resolution of 1 x 1 x 1 mm^3 in order to provide adequate and standardized resolution for support structures and contours in the TPS. The support structures include the IGRT linac couch top, which should be included at the correct location to calculate the shifts used during the daily positioning, to evaluate the clearance of the linac gantry rotation, and to compute the dose considering the couch attenuation. The procedure for correctly placing the support structure is shown in Figure 3. Finally, contouring is performed in the dedicated Aria application. The MR sequences and the sCT share the same frame of reference UID and are therefore intrinsically registered. Since there may be a time difference of up to 45 minutes between the first Dixon acquisition and the last diagnostic MR sequence, physiological changes (e.g., bladder filling) or patient movement (e.g., relaxation of the dorsal and gluteal muscles) might occur. In such cases, the MR dataset is extracted from the frame of reference, registered to the Dixon and sCT by an experienced radiation oncologist, and then used for contouring. The structure set is always assigned to the sCT.

Dosimetric commissioning

Volumetric modulated arc therapy (VMAT) treatment plans are prepared in the Aria Eclipse V16.1 TPS (N = 10 patients in this study). The settings used are beam quality 6X, two full arcs with opposed gantry rotation and different collimator angles, activated jaw tracking, and dose-to-medium calculation with Acuros V16.1 using a 1.5 mm grid resolution and normalization on the PTV Dmean. The plans are



3 Procedure for support-structure positioning in the TPS. **(3A)** MR markers are placed on top of the flat couch during the MR simulation. **(3B)** The markers are visible in the blended MR-sCT view and can be used for the IGRT couch positioning. **(3C)** Treatment planning on the sCT can proceed with the IGRT couch correctly placed.

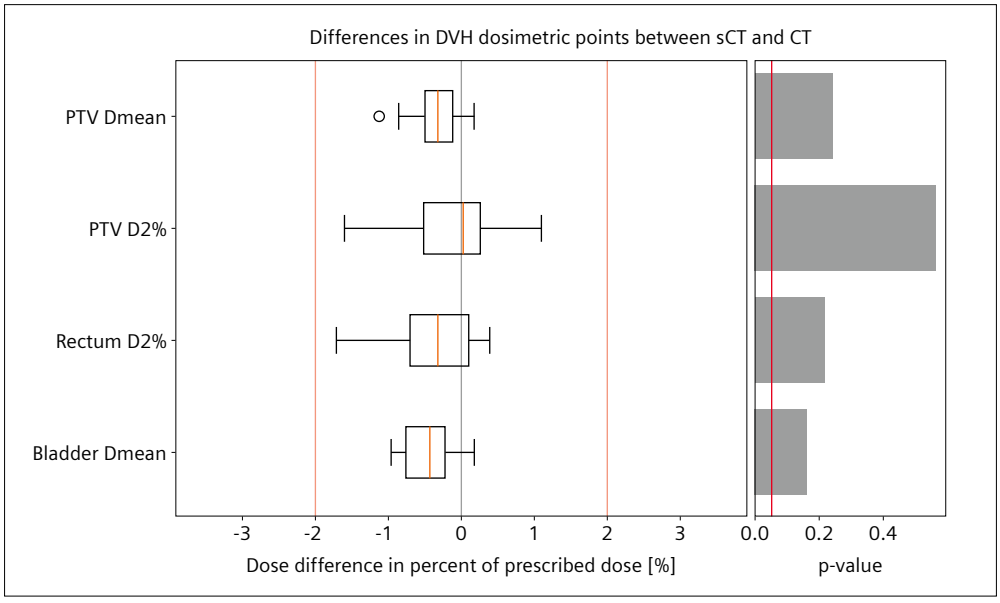


4 The point-wise absolute dose-difference map between the calculation on the CT and the sCT is shown for an example patient with prescription 5 x 7.25 Gy **(4A)**. Line profiles with the relative dose differences in the anterior-posterior and left-right direction crossing the PTV center are also reported **(4B)**. Reference horizontal lines at 0% and ± 2% relative deviations are reported in grey and red, respectively.

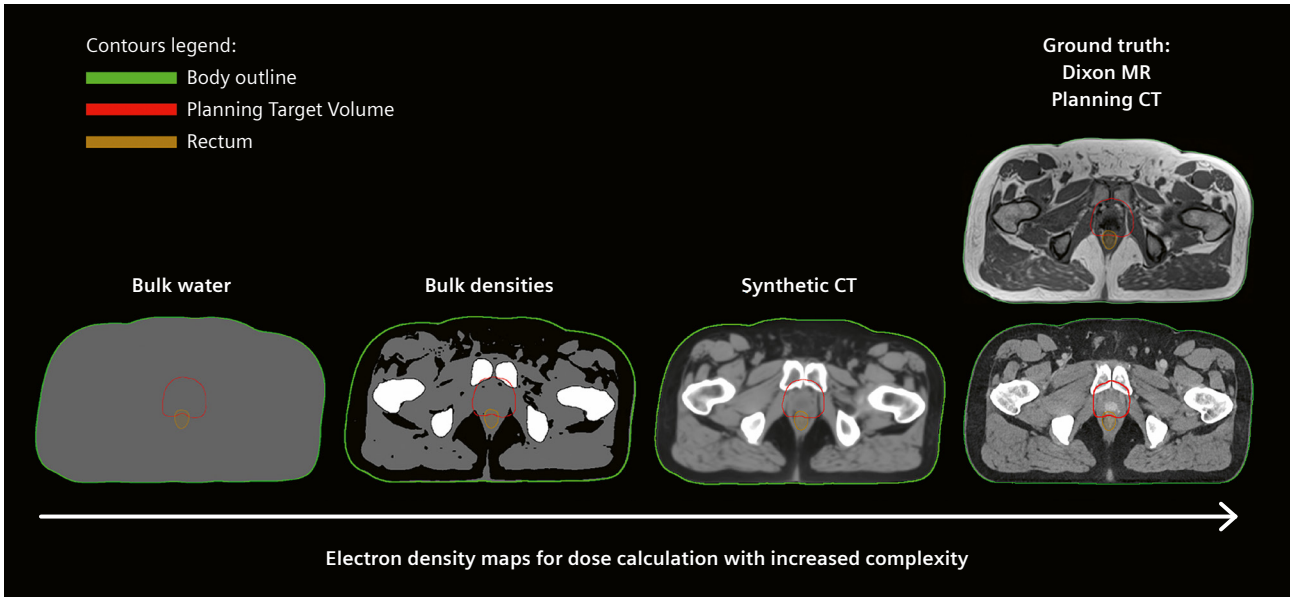
optimized on the sCT and rigidly copied and recalculated with a preset number of monitor units (MU) on the CT. Figure 4 shows a qualitative evaluation of the dose differences between the two calculations for an example patient. The quantitative analysis of multiple dose volume histogram (DVH) points is reported in Figure 5. The statistical analysis is performed with a Z-test (variance 1%, significance level p = 0.05, testing H_0: dose difference is 0%) in line with previous literature [16].

Patient-specific quality assurance

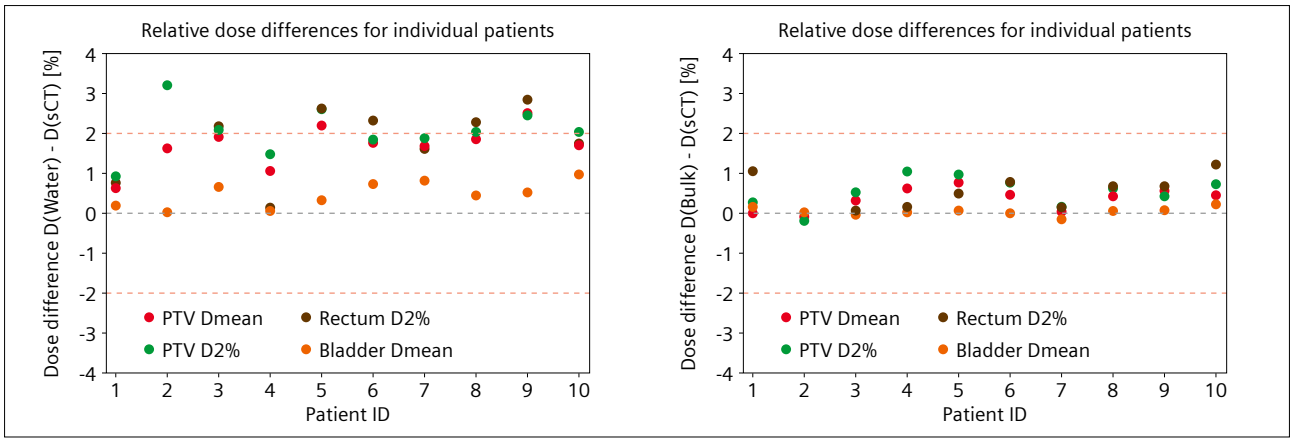
National and international recommendations for patient-specific quality assurance (PSQA) of intensity-modulated RT plans prescribe the use of independent secondary calculation software to verify the correctness of the MU to be delivered [17]. We use a similar approach for PSQA of the electron density map on which the dose is calculated, which in turn affects the number of MU predicted by the



5 Quantitative analysis of four DVH dosimetric points. The differences between dose calculation on sCT and CT are summarized with box plots (left). Reference vertical lines at 0% and ± 2% relative deviations are reported in grey and red, respectively. The statistical Z-test shows that all parameters are non-significantly (p = 0.05) different from zero (right).



6 Patient-specific quality assurance approach with independent electron density maps of increasing complexity.



7 Dose differences for individual patients and selected DVH dosimetric points between the investigated PSQA methods (water (i) left; bulk densities (ii) right) and the reference calculation on the sCT. Reference horizontal lines at 0% and ± 2% relative deviations are reported in grey and red, respectively.

DVH point	PTV Dmean	PTV D2%	Rectum D2%	Bladder Dmean
Relative deviations Water–sCT (Mean ± Stdev)	1.7 ± 0.51%	2.06 ± 0.6%	1.65 ± 0.98%	0.45 ± 0.31%
Relative deviations Bulk densities–sCT (Mean ± Stdev)	0.34 ± 0.27%	0.51 ± 0.37%	0.51 ± 0.41%	0.02 ± 0.1%

Table 1: Summary of the dose deviations observed between the investigated PSQA methods and the reference calculation on the sCT.

primary and secondary dose-calculation algorithms. The process is shown for an example case in Figure 6. The ground truth data is the Dixon MR and, when available, the planning CT. Four different models are evaluated to generate independent electron density maps: (i) bulk override of the patient body[2] with water, (ii) bulk overrides of four tissue classes[3] based on contours generated on the Dixon MR, (iii) synthetic CT, and (iv) the planning CT. The electron density maps (i) and (ii) are generated with a dedicated ESAPI script in Aria Eclipse V16.1. The electron density map (iii) is generated in *syngo*.via RT Image Suite VB60. The planning CT (iv) is not considered in the following, assuming that it is not available for PSQA in an MR-only RT context. For the N = 10 patients included in the study, the differences in dose calculation between (i) and (ii) and the synthetic CT (iii) are reported in Figure 7 and Table 1. The method (i) shows outliers above 2%, but none above 4%, and systematic positive dose deviations. The method (ii) does not lead to any outlier above 2%, and the average dose deviations are within 1%.

[2]Body contour defined on the Dixon MR.
[3]HU(Air) = -1000, HU(Bone) = +400, HU(Fat) = -75, HU(Soft tissue) = +7.

Discussion

The transition toward MR-only RT relies on the availability of high-quality sCT, which should replace the need for a planning CT examination. This study reports on the results of dose calculations obtained using MR data acquired on a 1.5T MAGNETOM Sola scanner and then used to generate sCT with continuous HU on the *syngo*.via RT Image Suite VB60 software. The qualitative evaluation of the HU reconstruction (Fig. 2) and dose maps (Fig. 4) show the high level of equivalence between sCT and CT. The quantitative analysis (Fig. 5) shows non-significant dose differences between calculations performed on sCT and CT. These results support the use of sCT for treatment planning and dose calculation in the context of MR-only RT, without the need for a planning CT examination. This study also evaluates the PSQA methods to be used to verify the quality of the dose calculation on sCT if the planning CT data is not available, i.e., after the go-live phase in the clinical MR-only RT implementation. The use of an easily implementable but naïve recalculation of the treatment plans on bulk water may be valuable for identifying potential outliers with large errors in the HU reconstruction of the sCT, which lead to dose deviations above 5%. A more resource-

intensive approach requiring the contouring of four tissue classes on the Dixon MR is a robust method for potentially identifying smaller reconstruction errors leading to dose differences within a 2% threshold. These results should be compared to typical limits for PSQA recommendations that require MU equivalence between the primary and secondary dose calculation engines to the 3% level [17]. Moreover, generating data with DL approaches leads to an sCT that is based on large amounts of data in the software's training phase, is realistic, and can be inspected with dedicated applications. However, it does not allow direct human interpretation of the underlying conversion processes of MR to sCT. On the other hand, in the case of dose differences during the PSQA process, adopting a method based on bulk densities allows human interpretability. This approach provides the simultaneous use of a data-driven method (sCT) for the RT plan, and a preparation- and knowledge-driven one (bulk densities) for PSQA [18], which we combine to achieve a robust clinical implementation. Furthermore, a comprehensive PSQA procedure should encompass the validation of data-transfer integrity between the MR scanner, TPS, and DL for sCT generation. This study does not address these particular aspects. The primary focus of the current investigation is the dose-calculation QA for sCT. Nevertheless, it is crucial to consider other QA aspects as well, such as sCT-to-CBCT or sCT-to-kV matching on an IGRT linac, end-to-end testing, and imaging QA for the MR scanner.

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