From CT to MR: Clinical Experience and Evaluation of MR-Only Simulation for Radiotherapy Planning of Brain Lesions

Jeffrey C.F. Lui, M.Sc.

Department of Clinical Oncology, Queen Elizabeth Hospital, Hong Kong

Introduction

Magnetic resonance imaging (MRI) has become an integral component of external beam radiotherapy (EBRT) treatment planning due to its exceptional soft-tissue contrast. This is particularly useful in delineating tumors and organs at risk (OARs) in the brain and head-and-neck region. Moreover, MRI offers functional images that may potentially provide additional information for EBRT planning. However, the absence of electron density information in MR images necessitates the registration to CT images for subsequent radiation dose calculation. This process is time-consuming, and multimodality image registration with different frames of reference is never perfect. Differences in patient setup position and anatomical changes between CT and MRI scans further increase the errors, which ultimately compromise the overall accuracy of treatment planning [1].

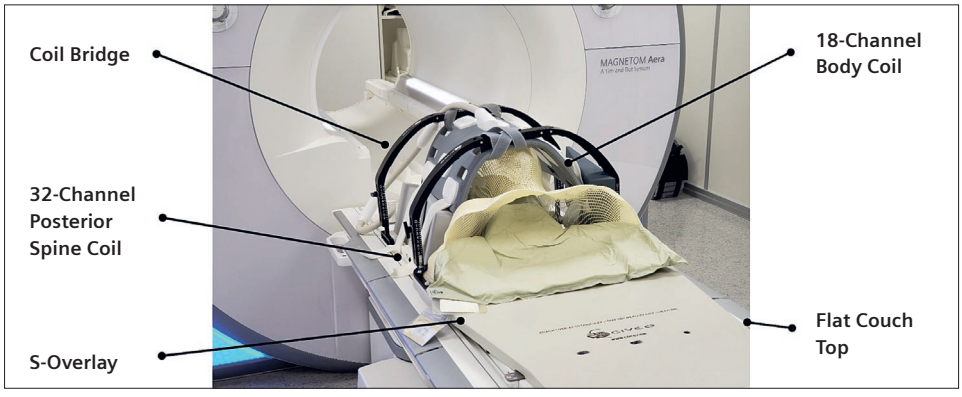
MR-only simulation was developed to address these challenges. MR-generated synthetic CT (sCT) images, also referred to as pseudo-CT images, are created by using a dedicated pulse sequence to provide the necessary CT numbers in dose calculation [2, 3], thus eliminating the need for a separate CT simulation. These sCT images can also be used for treatment setup verification against cone beam CT (CBCT) or orthogonal planar images using sCT digitally reconstructed radiographs (DRRs) [4].

Since 2020, our center has implemented MR-only simulation in EBRT planning for brain lesions [5]. In 2022, we adopted the VB60 *syngo*.via RT Image Suite deep learning-based sCT reconstruction algorithm. In this article, we present our experience with setting up MR simulation, and evaluating radiation dose calculation by the sCT images generated with the deep-learning algorithm. We hope to share practical tips on implementation, and to show the benefits of the technique.

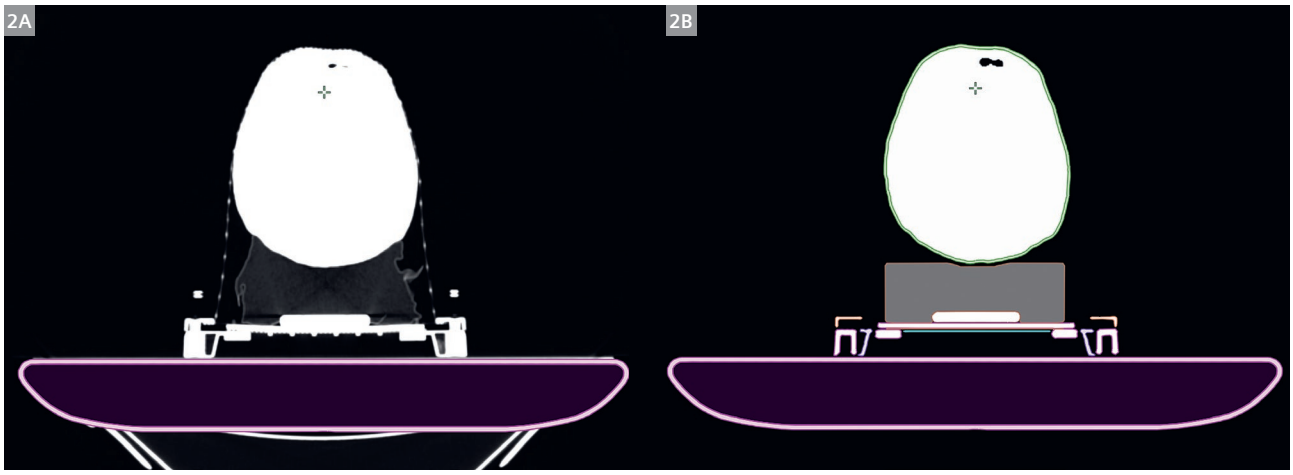
Setup of MR-only simulation

In our center, MR simulation was performed in a 1.5T MRI system (MAGNETOM Aera, Siemens Healthineers, Erlangen, Germany). The system was equipped with an MRI RT Pro option, which included an MRI-compatible external laser system (DORADOnova MR3T, LAP GmbH Laser Applikationen, Lüneburg, Germany), a flat couch top with coil bridges for RT positioning, additional flex coils for imaging, and an MRI simulation software package (VB60, *syngo*.via RT Image suite, Siemens Healthineers, Forchheim, Germany) to generate sCT images in EBRT treatment planning for brain lesions.

Patients were positioned in the treatment position using the same immobilization device and imaging isocenter as in ordinary CT simulation (Fig. 1). An 18-channel body flex coil was used to cover the scan region. A coil bridge was employed to support the weight of the flex coil and secure its position relative to the thermoplastic



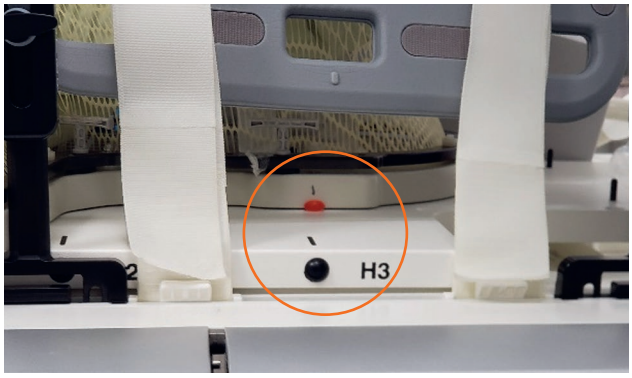
1 Patient setup for MR-only simulation.



2 Immobilization devices in planning CT **(2A)** and manually contoured immobilization devices in sCT **(2B)**.

mask. Additionally, a posterior spine coil was utilized to ensure sufficient signal reception at the posterior part of the brain. For all patients, the Type-S™ Overlay board (CIVCO Medical Solutions, Coralville, IA, USA) with thermoplastic masks, Provil spacer (Kulzer GmbH, Hanau, Germany), and head-and-neck Vac-Lok™ cushions were used. All the immobilization devices were thoroughly checked for MRI compatibility.

Due to the weak MR signal of the immobilization devices, they are not visible in the MR images (and thus in the subsequent sCT images). This has to be taken care of in treatment planning because the immobilization devices introduce attenuation to the radiation beam in EBRT. Consequently, during treatment planning, the immobilization devices must be manually added from a template, which was created by delineating the structure on a prior CT image, with bulk density assigned (Fig. 2) [5]. While the template can be created and stored in the treatment planning system for all subsequent patients, the exact location of the immobilization devices has to be determined for each patient, by utilizing MR-visible markers located on the Type-S™ Overlay (Fig. 3). These markers are visualized using an in-house-defined T1 SE sequence with a large field of view, and it shows the location to assign immobilization devices in the sCT.



3 Fiducial marker (orange circle) for visualizing the position of the immobilization devices.

Evaluation of the dosimetric accuracy of the sCT

As part of the software commissioning process, a study was conducted to evaluate the dosimetric accuracy of the sCT generated by the deep learning-based reconstruction algorithm before its implementation in clinical practice. For this evaluation, a group of eight patients with brain lesions scheduled to undergo Volumetric Modulated Arc Therapy (VMAT) was selected. The prescription dose for the Planning Target Volume (PTV) in these patients ranged from 45 Gy to 60 Gy, delivered over 25 to 33 fractions. All patients underwent MR simulation using the aforementioned imaging setup and preparation process. Prior to MR-only simulation, routine planning CT simulation was performed using the same immobilization system.

VMAT treatment plans were generated for all eight patients using 6 MV photon beams. These plans were optimized on the planning CT images using a treatment planning system (Eclipse 16.1, Varian Medical Systems, Palo Alto, CA, USA). The target dose was assigned based on the oncologist's prescription, and dose constraints were applied in accordance with relevant published guidelines. Dose calculation was based on the Analytical Anisotropic Algorithm (AAA) available in the planning system. Subsequently, the optimized VMAT plans, along with the treatment parameters, were transferred to the sCT, and radiation dose was recalculated with the same dose grid and CT–relative electron density calibration curve as in the planning CT. The doses calculated using the planning

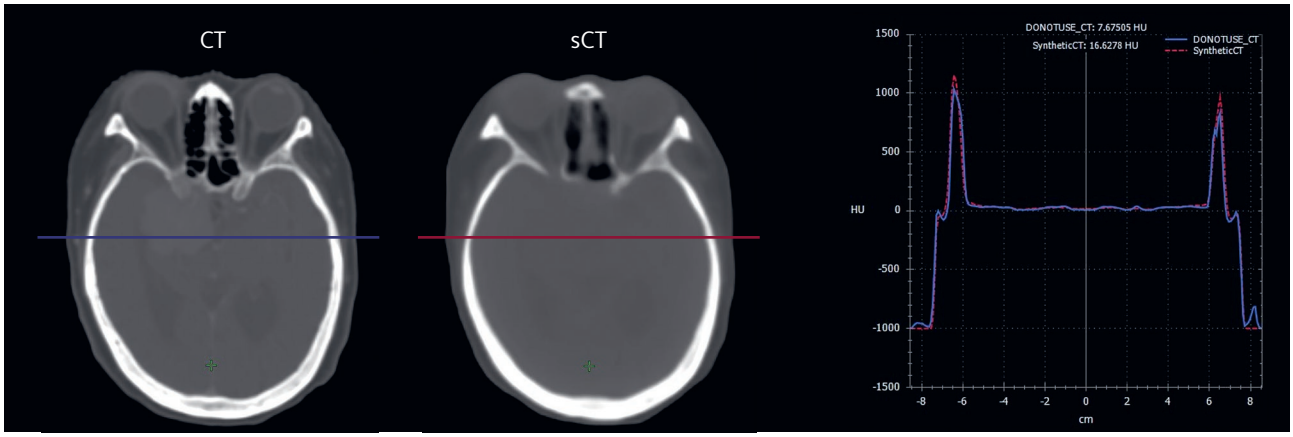
CT and sCT were then compared by analyzing the Dose-Volume Histograms (DVH) and other clinically relevant parameters. The Wilcoxon signed-rank test was performed between the parameters calculated by sCT and planning CT. Bonferroni correction was applied to avoid inflating the type-I error probability in these statistical tests.

The dosimetric comparison revealed excellent agreement between dose calculated in the sCT and the planning CT. The mean dose difference between the planning CT and sCT in terms of PTV D_{95} and D_{max}, across the eight patients was found to be -0.1% and -0.3%, respectively. Similarly, the mean dose differences for all relevant OAR structures were within 0.2 Gy. The average calculated dose differences between the planning CT and sCT for PTV and OARs are summarized in Table 1. No statistically significant difference was found. These results agree with the findings from the literature [6] that evaluated the same deep learning sCT algorithm in brain lesions.

Furthermore, the CT numbers derived from the sCT exhibited good agreement with those obtained from the planning CT images. Figure 4 illustrates the CT number profile for a representative patient, demonstrating a close match between the two images.

Dosimetric parameters	Mean difference (Range)		*P-value*
Target (%)			
PTV D_{max}	-0.3	(0.4 to -2.5)	0.844
PTV D_{95}	-0.1	(0.5 to -0.2)	0.742
OAR (cGy)			
Spinal cord D_{max}	-0.6	(0.5 to -2.3)	0.148
Brainstem D_{max}	13.4	(47.4 to -4.7)	0.039
L len D_{max}	-0.4	(9.7 to -5.3)	0.383
R len D_{max}	1.7	(12.8 to -4.7)	0.383
L optic nerve D_{max}	-3.4	(18.0 to -35.0)	0.641
R optic nerve D_{max}	-10.0	(7.8 to -80.6)	0.742
Optic chiasm D_{max}	-5.0	(12.5 to -49.2)	0.735
L eye D_{max}	7.5	(22.5 to 0.2)	0.008
R eye D_{max}	5.9	(29.1 to -10.3)	0.250
L cochlea D_{mean}	16.2	(83.3 to -2.3)	0.078
R cochlea D_{mean}	17.3	(67.8 to -2.5)	0.176

Table 1: Mean dosimetric differences (planning CT minus sCT) of eight patients.
PTV, planning target volume; L, left; R, right*** *P* = < 0.0038** is considered statistically significant after Bonferroni correction for multiple comparisons.



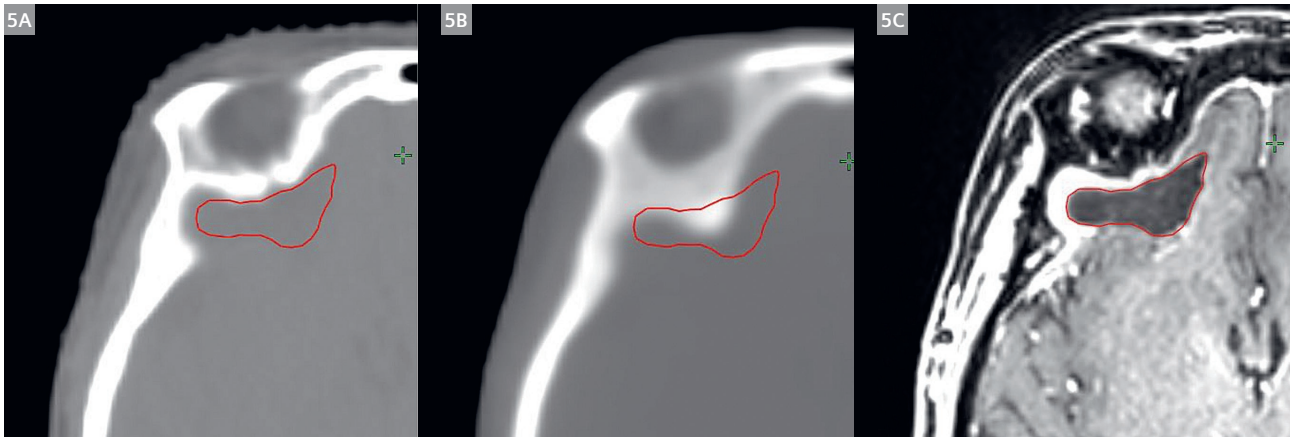
4 The planning CT (left), sCT (middle), and CT number profiles (right) of the planning CT (blue line) and sCT (red dotted line). It demonstrates good agreement between planning CT and sCT.

Workflow for MR-only simulation of brain lesions

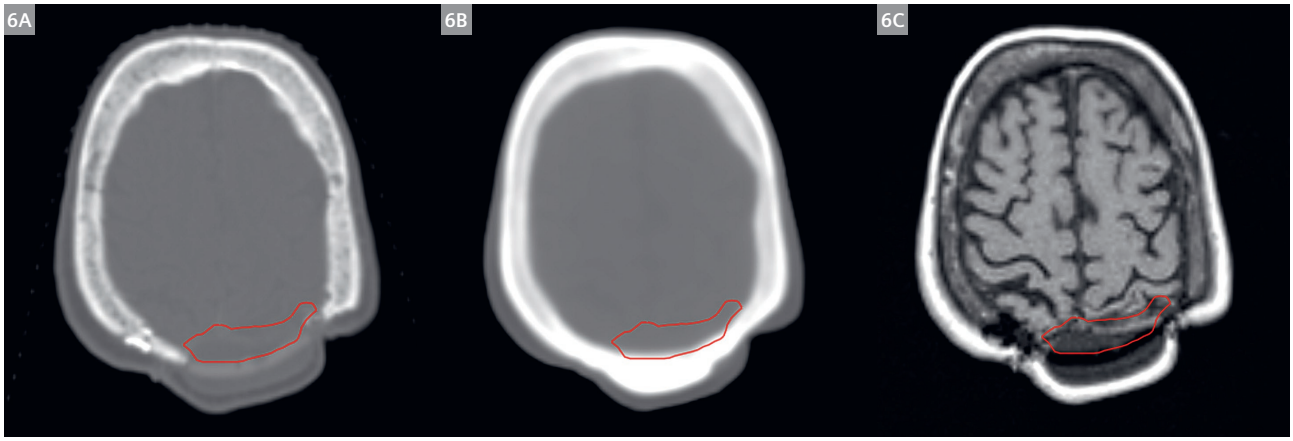
Following the dosimetric validation of the sCT, a standardized workflow for MR-only simulation of brain lesions was established, as described in the following

The patient setup described above was performed. The pulse sequence of MR-only simulation starts with the T1 VIBE sequence, required for sCT reconstruction, and the in-house-defined T1 SE sequence, which captures the position of the MR-visible marker on the couch top. The total duration for these two pulse sequences is approximately 6 minutes. Subsequently, other pulse sequences acquired for delineation of tumors and OARs are performed. The total time for the whole simulation process is typically 20 minutes.

After acquiring the T1 VIBE sequence, *syngo*.via automatically generates the sCT, with the reconstruction process taking approximately 5 minutes. The quality of the reconstructed sCT is then evaluated by the physicist and oncologist to determine its suitability for MR-only treatment planning. One critical assessment is to identify reconstruction artifacts that could impact dose calculation accuracy. Although in most cases, the quality of the sCT is acceptable, artifacts were identified in a few very special cases. An example of these artifacts is tissue mislabeling. Figure 5 shows a portion of hypo-intensity tissue near the skull incorrectly reconstructed as bone in the sCT. Figure 6 shows another patient who underwent craniotomy with synthetic fiber for cranioplasty. The synthetic fiber and the adjacent metal implants are incorrectly reconstructed as bone. When these reconstruction artifacts are located within or near the target volume, dosimetric accuracy may be affected. As a conservative approach, the MR-only treatment planning workflow is not used in such cases.



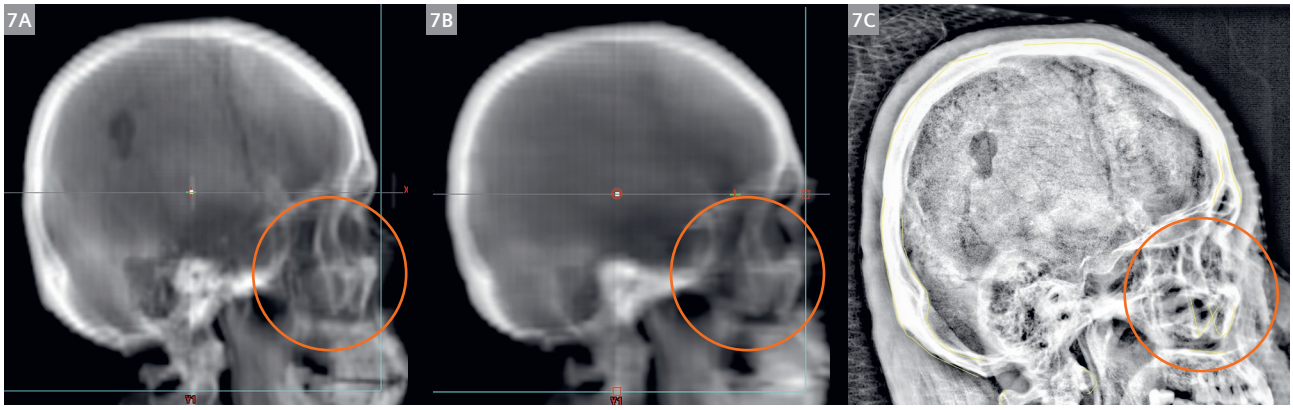
5 The images from the planning CT **(5A)**, sCT **(5B)**, and T1-weighted MR **(5C)** of a sample patient. The red region of interest indicates the Gross Target Volume (GTV) of the patient. In the sCT image, there is incorrect reconstruction where a portion of soft tissue inside the GTV is mistakenly reconstructed as bone.



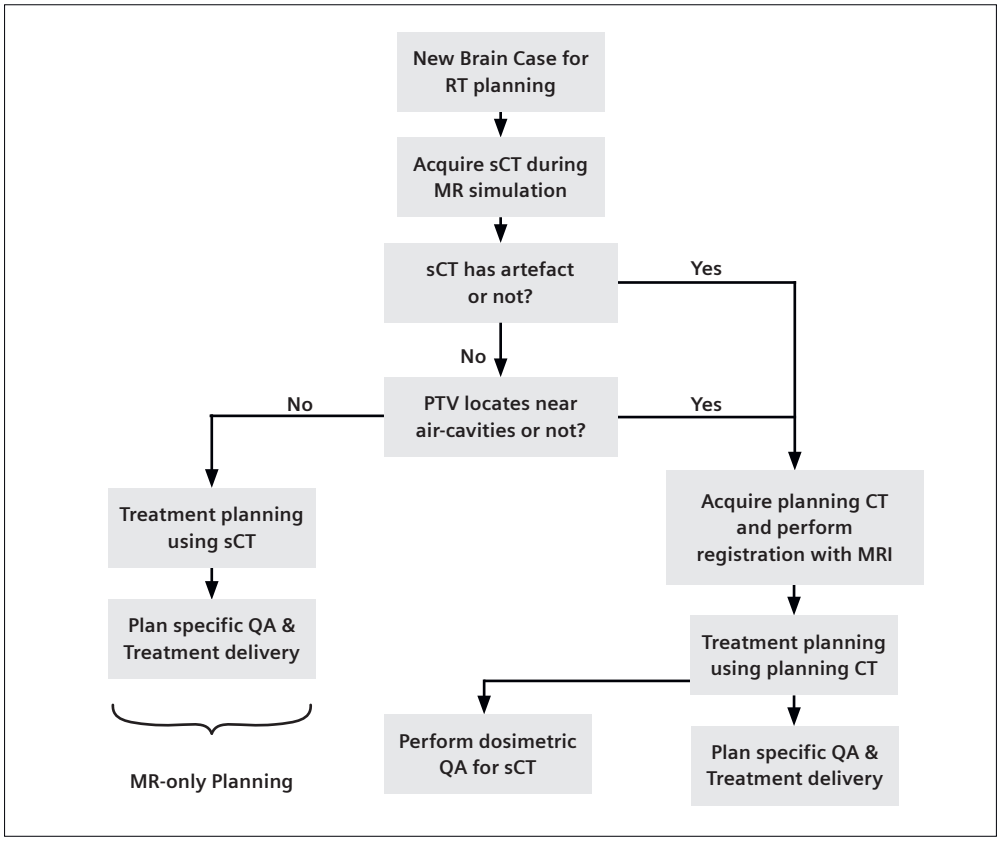
6 The images from the planning CT **(6A)**, sCT **(6B)**, and T1-weighted MR **(6C)** of a sample patient. The red region of interest indicates the GTV of the patient. The sCT image shows incorrect reconstruction where the synthetic fiber and metal implants near the GTV for skull repair are mistakenly labeled as bone.

Another assessment is the proximity of the PTV to air cavities. In sCT, bony structures near air cavities, such as in the sinus cavities, are generally not as clearly revealed as in the planning CT. Although our dosimetric evaluation indicates that the dose deviation caused by this issue is insignificant (discussed in below section), the clarity of bony features in such regions in the sCT-generated DRR may be degraded as shown in Figure 7. In our center, we tend to exclude these cases from MR-only simulation, until more experience is gained to show its effect on image-guided treatment verification [7].

If the physicist and oncologist determined that the MR-only workflow is not preferred for a patient, arrangements were made for CT simulation. For quality assurance of the sCT reconstruction algorithm, regular dosimetric comparisons were performed between the planning CT and sCT on patients who had obtained both. The dose difference was compared to the results obtained from our previous evaluation study, in order to check for consistency.



7 The images from planning CT DRR **(7A)**, sCT DRR **(7B)**, and the kV image **(7C)** of a patient. The bony features in the orange circle are less detailed in the sCT DRR.



8 Workflow for MR-only planning of brain cases in our center.

Clinical experience with an MR-only treatment planning workflow

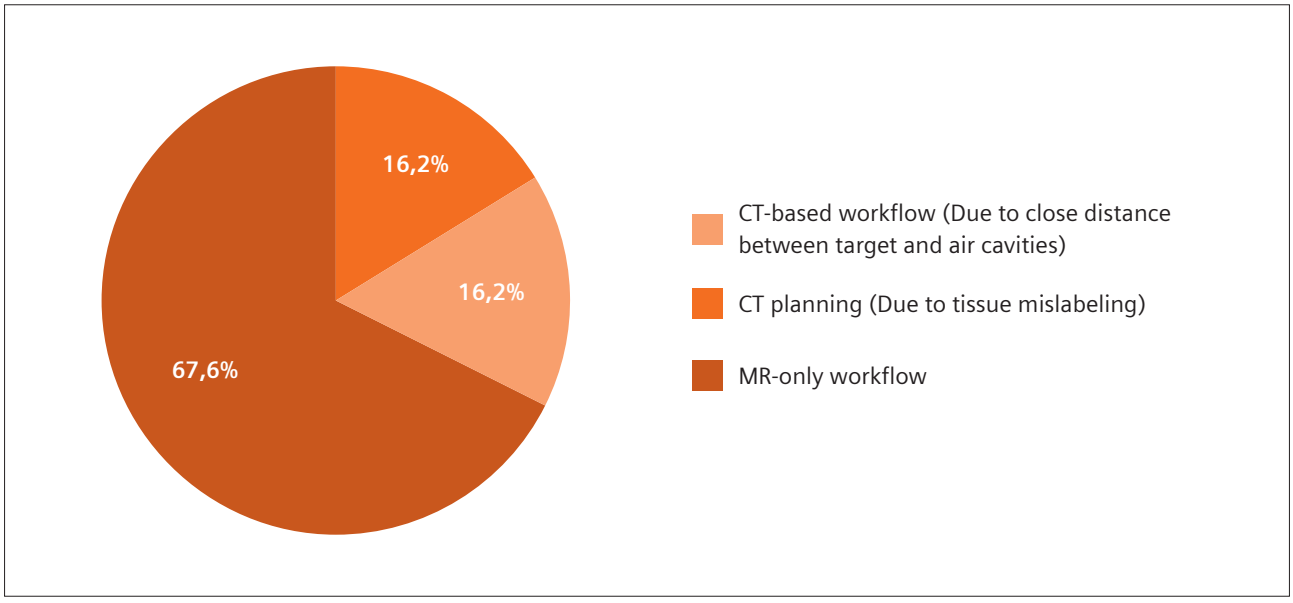
Since the commissioning of the deep learning MR sCT algorithm in September 2022, our center has conducted MR-only simulations on 37 patients with brain lesions. Among these patients, 25 (67.6%) were assigned to undergo the MR-only treatment planning workflow, while 12 patients (32.4%) were assigned to follow the traditional CT-based workflow. Figure 9 presents the distribution of treatment planning workflows used for patients who underwent MR simulation.

In cases where the traditional CT-based workflow was chosen, we performed dosimetric comparisons between the sCT and the subsequently acquired planning CT. For cases with a close distance between the target and air cavities (6 out of 37), the mean dose difference in PTV D_{95} and D_{max} was 0.0% and -0.3%, respectively. The mean dose difference for all relevant OAR structures was within 0.5 Gy. The dosimetric accuracy of such cases showed good agreement between sCT and planning CT, consistent with the result of our previous evaluation study during commissioning as demonstrated in the previous section.

Despite the excellent dosimetric agreement in sCT, our center adopted a rather conservative and safe approach to incorporate the technique, especially during this early phase of adoption. As described before, reduced sharpness in bony structures near air cavities in the sCT-reconstructed DRR is currently a factor that we consider. The exact impact of this issue is unknown and will be investigated in future studies. It is expected that the impact will be minimized as we gather more experience in the image verification process. Centers routinely using cone beam CT (CBCT) instead of planar kV images for verification may also experience less impact [8].

For cases with tissue mislabeling near the target (6 out of 37), the mean difference for PTV D_{95} and D_{max} was 0.2% and 0.1%, respectively. The mean dose difference for all relevant OAR structures was within 0.1 Gy. Again, the dosimetric accuracy of such cases showed good agreement and was consistent with the results of our previous evaluation study.

Although the dosimetric impact in such cases is generally acceptable, it is worthwhile noting that the dosimetric comparison in this article was performed using the Eclipse AAA dose algorithm. The adoption of more sophisticated algorithms with dose-to-medium as the calculation quantity, such as the Acuros XB and Monte Carlo algorithms, may increase the dose difference in the bone and soft-tissue mislabeling regions [9, 10]. This is because under the same dose fluence, the dose-to-bone is systematically lower than the dose-to-soft-tissue [11], which is expected to increase the dosimetric perturbation in regions of bone and soft-tissue mislabeling. This area is worth looking into for future applications.



9 Distribution of treatment planning workflows used for patients who underwent MR-only simulation in our center.

Conclusion

The new deep-learning sCT reconstruction algorithm has been successfully integrated into our MR-only simulation workflow for brain lesions. The implementation of this workflow simplifies the radiotherapy workflow, and spares patients unnecessary CT simulations. It also eliminates the need for CT and MR image registration, thereby mitigating the associated uncertainties. At this point in time, we intend to continue careful case evaluations to ensure we identify the appropriate candidates for this approach. As we gain more confidence, the workflow will become applicable to more patients.

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Contact

Jeffrey C.F. Lui, M.Sc.
Medical Physicist
Department of Clinical Oncology
Queen Elizabeth Hospital
30 Gascoigne Road, KLN
Hong Kong
lcf767@ha.org.hk