Clinical Implementation and Evaluation of MR-only Radiotherapy Planning for Brain Tumors

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Introduction

Over the past decades, magnetic resonance (MR) imaging has been increasingly used to improve delineation of targets to be irradiated and organs at risk (OAR) to be avoided. In 2020, the list of clinical scenarios where MR is not considered useful is shorter than the list of sites where it is felt to provide benefit. This being said, for most uses of MR in radiotherapy planning, the level of evidence for clinical benefit is weak. Although it can often be demonstrated that physician segmentations will be altered by the use of MR, it is not often proven that these changes result in more cures or better quality of life. As adoption of MR planning increases, the quality of the evidence will likely improve.

An impediment to a more widespread use of MR in radiotherapy is the need to obtain both MR and CT images for treatment planning. In such a workflow the MR is used for tissue segmentation and the CT for treatment planning. In the combined workflow, image registration is required to align the images from both modalities. Target volumes and OARs defined in the MR image can then be transferred to the CT dataset, with which plan optimization and dose calculation are performed. The electron density information required for accurate dose calculation and reference images used for patient positioning are obtained from CT.

The challenges from a combined MR and CT workflow include:
- Accurate image registration between MR and CT. Small inaccuracies in registration will translate into systematic error throughout the treatment course.
- Patient scheduling. Scheduling patients on two different devices (CT and MR) can be burdensome on the patient and the healthcare institution. As time elapses between the images, anatomy can change (bladder filling as an example) and image registration may suffer.
- Financial issues. In bundled reimbursement schemes both imaging procedures may not be reimbursed presenting a burden to the institution. In schemes where both procedures are reimbursed, the additional imaging procedures and imaging devices represent a potentially unnecessary financial burden on the healthcare system as a whole.

An analogous situation existed after the introduction of CT simulation. Many patients underwent CT simulation followed by conventional fluoroscopic simulation. Today, most fluoroscopic simulators have been sold for scrap metal and, when necessary, digitally reconstructed radiographs are produced using CT images. A future can be imagined where CT scanners also disappear from radiation oncology departments.

In contrast to other disease sites, the use of MR for delineation in the management of brain tumors is not controversial. Many brain targets and organs at risk are

1 Example of patient positioning for MR Brain acquisition for radiation therapy planning on 1.5T MAGNETOM Aera.

simply not visible on CT – this is the case, for example, of small brain metastases and the hippocampal regions of the temporal lobes. In narrow indications, such as Gamma Knife radiosurgery, MR-only planning has been used in routine clinical practice for decades. This adoption of MR-only planning for frame-based radiosurgery has been facilitated by the absence of image-guidance, dose calculations which ignore tissue inhomogeneities and external MR fiducials which provide some measure of geometric quality assurance. In the more widespread implementation of MR-only planning, one must account for:

- Reference images for image guidance (CT or digitally reconstructed radiographs)
- Dose calculations which take into account electron density
- Quality assurance of the geometric integrity of varied MR images

Synthetic CT (sCT) provides images generated from MR scans that emulate CT images regarding electron density information and geometric representation. The images contain different Hounsfield units (HU) for different materials and these HU can be converted to electron density in the treatment planning system (TPS) using a calibration curve. The purpose of sCT images is to provide the same dose calculation accuracy as with CT images, enabling MR-only radiotherapy planning without needing additional CT images. Synthetic CT is now commercially available for both the brain and pelvis. After evaluating the pre-clinical version of this software, we have begun the clinical implementation of the commercial version and describe our experience herein.

Clinical workflow

The first step in the MR-only workflow is patient immobilization. In our workflow, the curved MR table is rendered flat using a custom insert. A commercial overlay is placed on the insert. In order to identify the treatment table in the treatment planning system, we lay a small slab of gel on the MR couch top. The patient lies on the table and is positioned straight using the sagittal in-room laser. The thermoplastic mask is heated outside the MR room and the warm mask impressionned on the patient. Although it is possible to use external fiducials or the laser bridge to mark an isocenter on the patient, we chose to use the tip of the nose as our reference. We feel that this is simple and accurate for our practice where every treatment fraction is preceded by a cone beam CT. Using an in-house plastic

bridge, 2 flex small 4 coils are placed on each side of the head and a body 18 long above the patient. In addition, 2 rows of the spine 32 posterior coil are typically used for a total of 34 coil elements (Fig. 1).

For each clinical scenario, an MR protocol needs to be assembled around the sequences required for sCT. We chose to start our clinical implementation with whole-brain radiotherapy using hippocampal avoidance. This clinical scenario was chosen based on its incidence (not too common, not too rare), the low total dose and delivery via conventional linear accelerators. The MR protocol for this indication includes, in addition to localizer and quality assurance sequences, five sequences. The following sequences are required to generate sCT images of the brain: T1 VIBE Dixon, T2 SPACE, PETRA, FLASH Gradient Echo with "Time of Flight generated contrast" [2] (Fig. 2). For hippocampal avoidance an MPRAGE sequence is added.

The acquisition of the four sequences takes approximately 14 minutes on our MAGNETOM Aera[1] (1.5T) and is reported to last a similar time on a MAGNETOM Sola (1.5T) – 9 minutes with the MAGNETOM Vida (3T). We send the images to the hospital PACS and *syngo*.via. In *syngo*.via, the sCT image set is generated. Prior to being sent to our contouring server with the MPRAGE dataset, the sCT is inspected for aberrations or artefacts. The target and organs at risk are segmented by the physician before the case moves to dosimetry. The structure sets and images are sent to planning (in our case, this is the same platform as contouring) and the radiation plan is optimized.

Quality assurance

Once the images are acquired, the quality assurance sequences are reviewed for geometric accuracy quality control. For geometric quality assurance control, two sets of axial images are acquired in opposed frequency axis pushing the distortions each to one side. The bandwidth is reduced to amplify the distortion. The two sets of images are compared. The goal is to find distortion coming from the patient: surgical clip, dental implant, air, etc. Basic B_0 and gradients quality control are performed weekly on phantom and annually for exhaustive QC.

A first dosimetric quality assurance is performed by comparing plans with and without heterogeneity corrections before sending the plan to the linear accelerator. At the first treatment session, the sCT is visually compared to the cone-beam CT (CBCT). After the first treatment session, the dose is recalculated on the CBCT as a final quality control step.

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[1]*MR protocols for Synthetic CT generation are works in progress for MAGNETOM Aera, they are currently under development and not for sale in the U.S. and in other countries. Their future availability cannot be ensured.*
MR protocols for Synthetic CT generation for 1.5T MAGNETOM Sola and 3T MAGNETOM Vida are clinically released.

Clinical implementation

In the process of clinical implementation, we chose to limit the use of sCT to a specific clinical scenario. In our clinic, the scenarios are formalized in radiation care plans – a total of approximately 30 for central nervous system cases and 40 for head and neck cases (without counting relevant palliative and lymphoma care plans). These care plans are made up of elements and are associated with various tasks. We modified the care plan for whole-brain radiotherapy with hippocampal avoidance to include sCT and the implementation was seamless for the physicians in our practice. In the process of implementation, the first patients had both an sCT and a conventional planning CT. Once we were comfortable that we had sampled the range of possible results (this required between 10 and 20 cases), the conventional CT was omitted.

Pitfalls

Although not specific to sCT, the distortion in the MR images is not uniform and will be greater near the sinuses. This does not have a significant impact in the care of patients with whole-brain radiotherapy but should be kept in mind for patients with lesions in or near the sinuses.

We have occasional cases in which a gel was used on the head support to increase patient comfort. This gel has led to unusual behavior of the sCT algorithm (Fig. 3) where bone is added between the patient and head support. This underlies the need to manually inspect all images. As well automatic segmentation tools which function on CT may not function on the sCT – this is the case of our automated brain segmentation tool.

## Clinical evaluation of synthetic CT dose calculation accuracy

In our initial evaluation of the dose accuracy of patients treated with sCT, the clinical plan generated with the sCT is delivered virtually on the conventional CT and the dose compared through 3D subtraction and superimposed dose volume histograms.

Our observations after analyzing seven patients are that the derived dose is similar (typically within 2%) using sCT as compared to CT. The discrepancies seen result in slightly less dose being delivered to the patient – likely as a result of a thinner skull on the sCT.

Two case examples are illustrated in Figures 4 and 5. In the more favorable example, the mean target dose is within 0.1% and the minimum target dose within 2%. In an unfavorable case, the mean dose is still within 2% and the minimum dose within 4%. In both cases the direction of the discrepancies is the same with the patients likely receiving slightly less dose than planned.
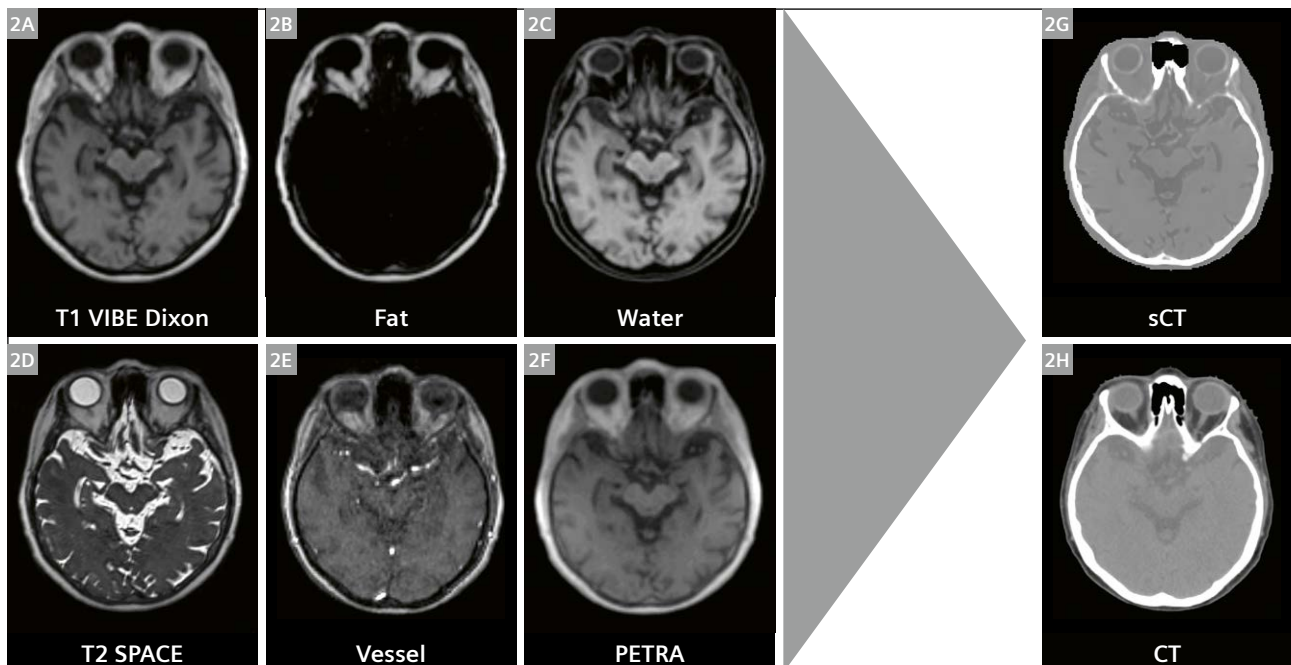

2 Image sets required to generate the sCT. The T1 VIBE Dixon sequence **(2A)** produces the fat and water images **(2B, C)** and the T2 SPACE sequence (**2D**, with an isotropic voxel size of 1 mm) is run to visualize the brain anatomy and morphology. The T2 SPACE sequence defines the resolution of the Synthetic CT output. The FLASH sequence **(2E)** is used to make sure that a vessel is not misclassified as bone and PETRA (**2F**, an ultra-short echo-time sequence sensitive to bone), is used as an override mask to correct voxels incorrectly identified as air.
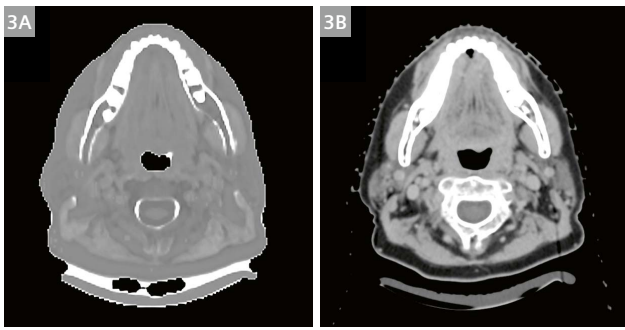
3 sCT artefact resulting from an immobilization device (**3A**: sCT and **3B**: CT).
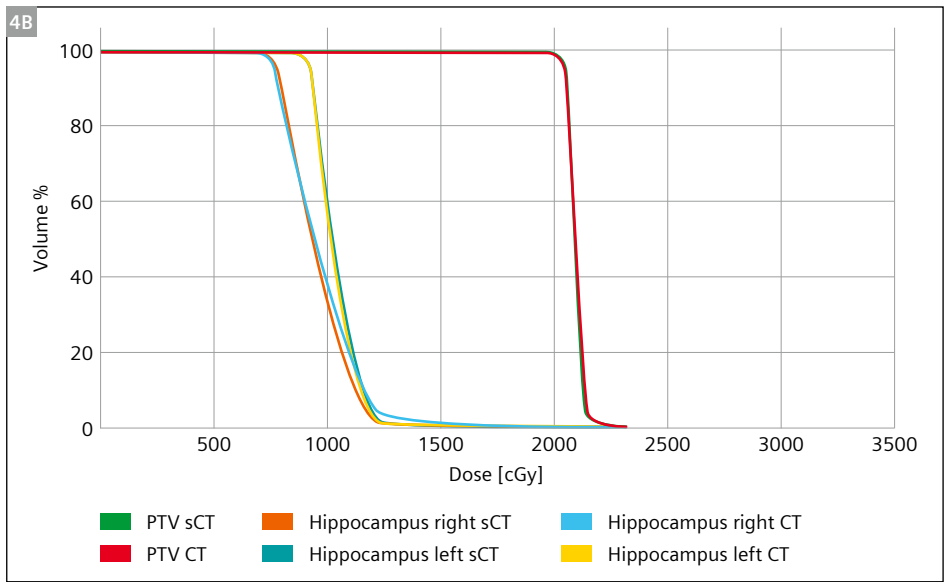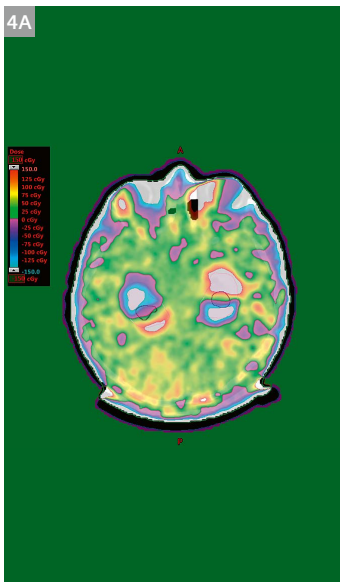
4 Dose subtraction and dose volume histograms from a clinical case.
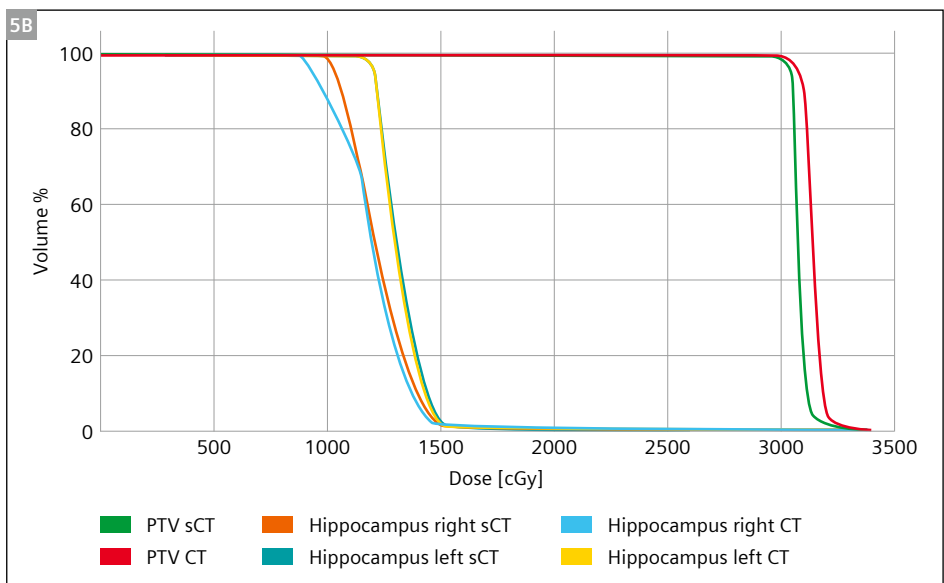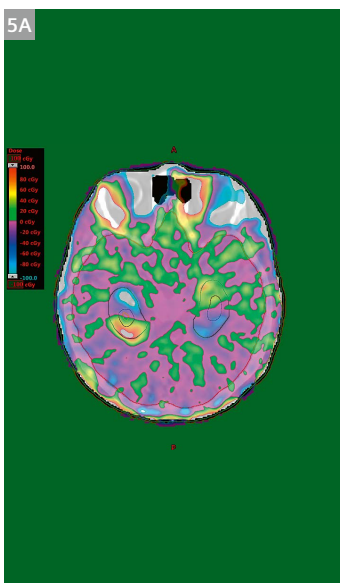
5 Dose subtraction and dose volume histograms from a clinical case.

Discussion

We have begun the clinical implementation of MR-only planning with the Siemens sCT protocol. Our preliminary evaluation is that this process allows a feasible and dosimetrically satisfactory workflow for whole-brain treatments. Our next step is to expand the use of this technology to other higher-dose brain treatments (high-grade gliomas are expected to be next). The MR-only workflow does add additional quality control steps which will hopefully be streamlines in the future. In the medium term, we plan to investigate the use of generative adversarial network (machine learning) generated images in an attempt to accelerate our workflow and improve accuracy.

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