Technical Aspects of MR-only Radiotherapy

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Introduction

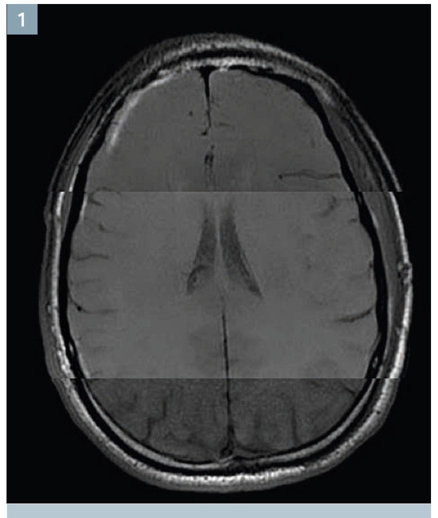
Magnetic resonance imaging (MRI) has emerged as a key component in modern radiotherapy. The superior soft tissue contrast compared to computed tomography (CT) allows for increased accuracy in the definition of both target and organs at risk [7] using commonplace sequences [29]. Functional imaging techniques, primarily diffusion-weighted imaging and dynamic contrast enhanced imaging, are currently studied as a means of identifying areas within a tumor that require a higher dose in dose-painting trials [41]. Several current studies also aim to evaluate the possibilities of early treatment response assessment using MRI [25], which could enable treatment adaptation. At present, the main rationale of integrating MRI into the radiotherapy workflow is the gain in accuracy in target volume definitions. For several major patient groups, MR imaging is preferable from a medical point of view, i.e. for tumor definition [5, 27, 30]. CT or CT equivalent information is still, however, required for the technical aspects of treatment planning such as:

- accurate dose calculations, which depend on knowledge of the attenuation properties of the tissue measured in a CT exam and
- generation of reference images which are used for patient positioning based on in-room X-ray imaging.

Therefore, it is common practice to acquire both CT and MR data and align these image series in the same coordinate system, or frame of reference, through image registration.

The MR data is used to define the target volume and the CT data to plan the treatment and serve as a reference for patient positioning. This workflow is, however, not optimal for several reasons. Besides the increase in cost and workload when using multiple imaging modalities, there is also an introduction of additional geometrical uncertainty due to the image registration.

Image registration is commonly performed at many clinics in order to align two image sets within a common frame of reference. Depending on the purpose of the image registration and the properties of the available image data, the registration can be performed in several ways. Mutual information rigid registration, based either on the full image volume or a smaller sub-volume, is available in most clinical treatment planning systems. For prostate cancer cases, where gold fiducial markers are commonly used, landmark registration methods can be employed in order to co-register MRI data to the planning CT. Manual registration, which is a robust but time-consuming method, is also an option. Regardless of method, image registration is a tricky business for several reasons. First off, for clinical cases we never know the correct alignment of two images, which makes it difficult to assess the uncertainties of a specific method. Phantom studies and purely digital experiments are unlikely to reflect the full complexity of the clinical case. Secondly, and related to the aforementioned problem, is the lack of robust quality measures for individual registrations. Finally, the task may actually be close to impossible, regardless of registration method. An example could be a prostate case without implanted fiducial markers. MRI is the imaging modality of choice for target definition, due to the greater soft tissue contrast. The prostate behaves much in the same way as other soft tissue tumors, i.e. its position in the body is not fixed and the spatial relation to surrounding bony anatomy may vary. This implies that a sub-volume based registration algorithm would be suitable in order to avoid any negative influence the surrounding anatomy may have on the registration. Although there are limited references regarding the matter, it is reasonable to assume that the limited soft tissue contrast in, and in close proximity to, the prostate gland in the CT image set would degrade the quality of a multi-modal sub-volume registration. In other words, the reason that soft tissue registrations between MR and CT images will be associated with substantial uncertainties is exactly the same reason why we need MR image data to begin with; we lack sufficient anatomical information on soft tissue in the CT images. For the sake of balance, it should be said that for some indications, such as intracranial lesions, including larger volumes in the registration is not associated with any added uncertainty since the soft tissue is relatively fixed with respect to the bony anatomy. Even in those cases, however, image registration uncertainty is still a factor to consider. Ulin et al. [42] investigated the clinical variability of MR-CT registrations for one patient with an intracranial lesion for 45 clinics. The analysis revealed a standard deviation of 2.2 mm, which only accounts for the variability among the observers. There may still be a systematic component on top of this.



1 Top 40 Hz/pixel, mid 100 Hz/pixel, bottom 400 Hz/pixel. Notice differences in signal-to-noise but especially geometrical differences.

In summary, MR imaging has been shown to increase the geometrical accuracy in the definition of target volume. The challenge today is to make sure that we can radiate this target volume in an accurate and precise manner. This problem can be reduced into several sub-problems, e.g. control over geometrical distortions in the MR images; differences in the patient setup in the MR scanner compared to treatment; and registration uncertainties introduced when MR and CT data is placed in the same coordinate system. In this article we provide a brief overview of the current knowledge regarding geometrical distortions and patient setup in the radiotherapy context and describe the problems and proposed solutions for MR only radiotherapy.

MR image distortions

Geometric distortions in MR images can be caused by the system itself, from nonlinearities in the magnetic gradients or inhomogeneities in the static magnetic field. Nonlinearities in the gradients can be characterized and corrected using spherical harmonics expansions of the fields generated by the gradient coils and can be accurately corrected using software supplied by the MR vendors.

Distortions can also be caused by the imaged object in the form of chemical shift or magnetic susceptibility artefacts. Image distortions due to susceptibility effects and chemical shift in conventional MR imaging are inversely proportional to the gradient field strength, so that stronger gradients will minimize such distortions at a cost of more image noise. Phantom studies have shown the residual distortion for clinical sequences to be within 1 mm [18, 31]. Object-induced distortion effects have also been investigated in clinical data and the effect proved to be small for internal structures relevant for prostate treatments [28]. In general, anatomical imaging sequences using relatively high bandwidths reduce distortions caused by susceptibility effects and chemical shift to an acceptable level for radiotherapy [26, 40]. Methods using post-processing corrections [35] or special modes of acquisition [6] have also been studied.

Some MR protocols are more sensitive to geometric distortions, echo planar imaging being one example. Such sequences can display significant geometric distortions due to susceptibility effects, and must be handled with care when used for radiotherapy purposes.

MR imaging using immobilization equipment

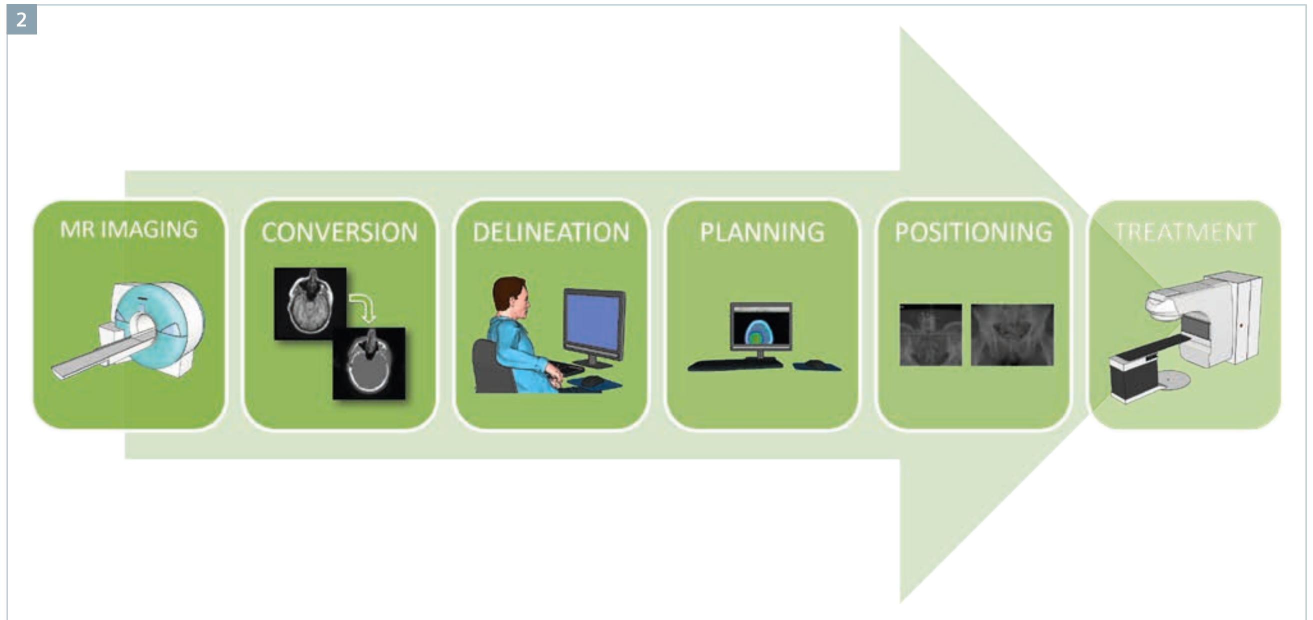
Planning CT scans are normally acquired using flat table tops to match the flat treatment couch used at the accelerator. The standard patient support is concave in most MRI scanners, although some have flat couches. The problem of concave patient supports is easily surmounted, either by manufacturing a flat table top insert at the hospital or by purchasing a commercial solution. Flat table tops are necessary if patient immobilization is to be used at the MRI scanner.

A more intricate problem is MRI compatibility of the immobilization equipment, both in material properties and size. MR safe materials must be used for base-plates, nuts, bolts and other fittings. A traditional plastic face mask for head and neck immobilization is normally constructed in MR safe materials; however, a standard MRI head coil will not be able to accommodate it. By using surface coils (i.e. flex coils) instead, imaging of the immobilized head and neck is possible, although a dedicated head coil still provide higher quality images [10]. When using surface coils for radiotherapy planning, care must be taken not to place the coils directly on the skin of the patient since the external anatomy may be distorted. Instead, the coils should be placed either hanging from a frame or on top of a holder close to the patient surface, without touching it. Nowadays, MRI compatible immobilization equipment and coil holders are commercially available.

MR-only radiotherapy[1]

In this article, we define MR-only radiotherapy as external beam radiotherapy where MR data is the only imaging information that is used for the planning and preparation of the treatment. Arguments for an MR-only workflow commonly include the avoidance of image registration in the planning stage of the treatment [1, 4, 8, 15, 18, 19, 20, 23, 31, 33, 39], reduced costs due to less imaging or a simplified workflow [1, 4, 8, 24, 39], and reduced exposure to unspecifically aimed radiation [4, 18, 39].

[1] Radiotherapy Planning where MR data is the only imaging information is ongoing research. The concepts and information presented in this article are based on research and are not commercially available. Its future availability cannot be ensured.



2 Simple schematic displaying the MR-only radiotherapy workflow. The difference from the traditional radiotherapy workflow is mainly the exclusion of CT imaging and registration and the addition of the conversion step.

Current methods of accurate dose calculations rely heavily on CT (or CT equivalent) information due to the relationship between Hounsfield units and electron density, and will probably continue to do so for the foreseeable future. Therefore, a reliable conversion method from MR information to CT equivalent information will be necessary for an MR-only workflow in radiotherapy. Several methods have been investigated by multiple research teams.

Manual bulk density assignment

A method that has been researched extensively is segmentation, i.e. dividing the image into classes with different attenuation properties. The simplest form of segmentation is to only use one tissue class and assign a bulk density to the entire patient, typically that of water or a mixture of adipose tissue and muscle. Even though this is an extremely simplified version of reality, it yields acceptable dosimetric results. Typical dosimetric differences from inhomogeneity corrected CT based dose calculations using this approach have been reported to be within 2-3% for prostate and intracranial target volumes [9, 17, 22, 23, 32, 33, 38]. A significant problem with this approach is that the traditional method of patient positioning at treatment depends on anatomical reference images that visualize bony anatomy. To overcome this issue, the number of tissue classes can be increased to include e.g. bone, soft tissue, lung tissue and air, and assign each tissue class an appropriate bulk density. In addition to making the creation of anatomical reference images possible, this also increases the dosimetric accuracy to around 1% for intracranial targets volumes [17, 22, 38] and between 1-2% for prostate treatments [17, 23].

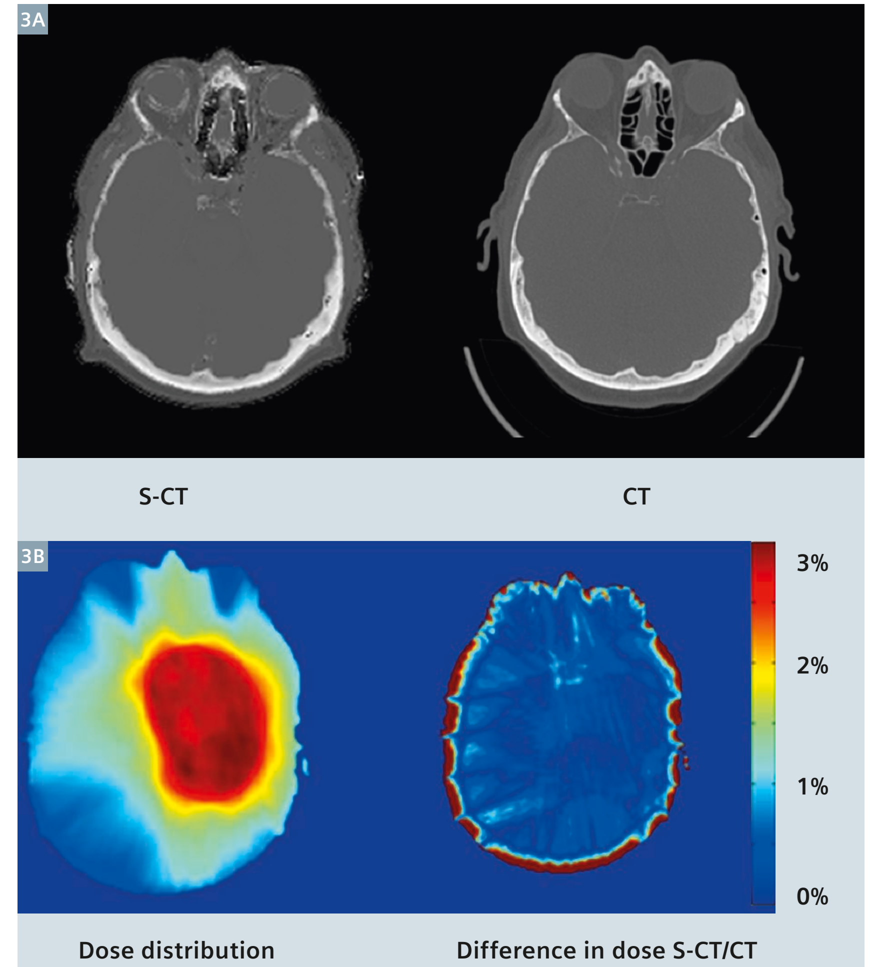
Although the dosimetric results are relatively accurate, the method of manual density assignment has problems – the method relies on the precision of the operator that defines the anatomy in the MR images. This is of limited importance in the dosimetric aspect, but may have substantial impact on the subsequently generated positioning references. Also, the method is so labor intensive and time consuming that it is not feasible for widespread clinical implementation. In order to accomplish such a development, automated conversion methods from MR to s-CT data are needed.

Atlas methods

One method for automatically generating s-CT data is the combined MR-label image atlas. By deformably registering the atlas MR image to a new patient MR image and applying the resulting deformation field to the corresponding label image, a new image can be created based on the data in the label image. The label image can contain any information, e.g. CT or attenuation data. This approach has been used for attenuation correction applications in PET/MRI [37] as well as for dose calculation purposes in radiotherapy [8]. Atlas methods do not normally rely on tissue segmentation; instead, the full complexity atlas label image is warped onto the patient shape. Dosimetric results indicate accuracy comparable to bulk density assignment; for the radiotherapy application, Dowling et al [8] reported point dose differences between atlas label image and CT based calculations of about 2%. Atlas based methods are normally sensitive to atypical anatomy; e.g. in the study by Dowling et al., 2 out of 39 patients had to be excluded for this reason. Although atlas based methods are fairly robust and automatic, an argument can be made that the deformable image registration is associated with a considerable geometric uncertainty. This uncertainty is introduced into the treatment if the deformed label image is used to create the positing reference image and not solely for dose calculations.

Direct conversion

With the advent of ultra-short echo time imaging (UTE), interest has increased for direct conversion of MR image intensities to Hounsfield units. Since cortical bone appears as a signal void in traditional MR imaging, it has been impossible to distinguish it from air. UTE imaging samples the signal during the free induction decay, before the signal from cortical bone and other tissues with short T2 relaxation times has vanished [36], making it possible to discriminate such tissues from air. Even though UTE images renders signal from bone, it is not presently possible to find any single MR sequence which is directly convertible to Hounsfield units – more information is necessary. Several researchers have suggested using UTE sequences with several different echo-times to segment soft-tissue, air and bone [2, 3, 21]. This technique is fully automatic and preserves the geometric integrity of the input image. UTE images suffer from the same system related distortions as traditional MR sequences; however, the fast radial sampling makes it less sensitive to common object related distortions such as chemical shift and susceptibility effects. An alternative to the previously mentioned segmentation approach is to build a statistical model that relates MR voxel intensities to Hounsfield units [12, 34]. Such an approach yields an s-CT image with a continuous Hounsfield unit distribution, as well as making it possible to estimate the uncertainties in the conversion [13]. Recent studies compared dose calculations on s-CT data with CT data, and found statistically insignificant dose differences of less than ±0.5% for intracranial targets [14, 16].



3 Comparison between s-CT and CT **(3A)**. **(3B)** shows the planned dose distribution together with the percentage difference in dose when calculated on s-CT and CT.

It is also possible to combine segmentation methods with direct conversion. A recent study [19] investigated the accuracy of a conversion method were the pelvic bone structures were first delineated manually. These delineations then served as input for a direct conversion method which could successfully convert the image intensities from standard MRI sequences to Hounsfield units. When the entire remaining anatomy was set to a bulk density, all points within the prostate PTV were within ±1.3% of the dose calculated on the standard CT input data.

The atlas registration approach can also produce segmentations that can serve as input for a later stage direct conversion. Hoffman et al. [11], which employed this approach for attenuation correction of PET/MR images, demonstrated that the method could accurately predict the attenuation map of a patient from MR input data. No systematic differences were found between PET images corrected with s-CT data and actual CT data. These combined methods ease the demand on the local accuracy of the segmentation, since the final conversion is performed using direct voxel wise conversion.

Summary

Radiotherapy is a local treatment modality that is highly dependent on image guidance. Over the last decade there has been an increased clinical use of both MRI and PET to enable accurate delineation of the target volume. However, the radiotherapy workflow does still depend on CT information as the treatment planning softwares require attenuation data to be able to perform accurate dose calculation and to generate reference images for positioning. It has been shown that it is possible to generate CT equivalent information based on MR data, and with this technology it will be possible to abandon the CT in the future for those diagnoses where MR is the modality of choice for target delineation. Imaging in treatment position and risk of geometrical distortions are two other areas that need to be addressed when introducing an MR scanner in the radiotherapy environment.

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