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3T MR-based treatment planning for radiotherapy of brain lesions

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Purpose. *The aim of this work is to develop a complete treatment planning procedure for radiation therapy of intracranial lesions based solely on 3T magnetic resonance imaging (MRI), i.e. MRI simulation.*
Methods. *The proposed 3T MR-based radiotherapy treatment planning procedure consists of converting the MR images into CT-like images by assigning electron density information (related to CT values) to organ structures. Firstly, the 3D distortion field present in the MR volumes is determined and rectified by using an in-house developed distortion correction method. The MR volumes are segmented into anatomical structures, i.e. brain, bone and scalp, by using a combination of the »Profile« and »Autocontouring« tools available on Pinnacle (Philips Medical Systems) treatment planning system (TPS). Bulk electron density values are assigned to the 3D volumes in Pinnacle by overriding their default MR values. Once the MR images contain the target volume along with the electron density information, they are ready to be used for dose calculations. The resulting CT+MR and MR only based plans were compared in terms of isodose distributions and dose-volume histograms (DVHs). For plan ranking we use a tumor-control probability (TCP)-based procedure for heterogeneous irradiation, which does not require the knowledge of radiobiological parameters.*
Results. *For all patients investigated, the 3T MR only and CT+MR-based plans are in good agreement in terms of isodose distributions, DVHs and TCPs (within 1%) following our clinical criteria.*
Conclusions. *The proposed 3T MR only based treatment planning procedure performs as good as the standard clinical procedure that relies on both CT and MR studies. MRI simulation can significantly reduce the patient treatment cost and save staff and machine time, and avoid any errors that may be associated with the image fusion process.*

Key words: brain neoplasms – radiotherapy; radiotherapy planning, computer-assisted

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Introduction

Magnetic resonance imaging (MRI) is the imaging modality of choice for the delineation of target volumes used for radiation treatment planning (RTP) due to its superior soft-tissue contrast. Presently, knowledge of electron density of the images is requi-

red for treatment planning dose calculations. In practice, the electron density of a limited number of tissue types (*e.g.*, lung, bone, soft-tissue) is required in this process. For intracranial lesions, due to lack of electron density information in the magnetic resonance (MR) images, image fusion of CT and MR data sets along with CT-based dose calculations have become a standard treatment planning procedure. Ideally, the treatment planning process should rely solely on the information generated by the MR image studies, *i.e.* MRI simulation.[1] Using such a procedure, the CT imaging sessions and the image fusion process would become redundant. This would significantly reduce the patient treatment cost and save staff and machine time. Furthermore, the patient would not be exposed to unnecessary radiation (as insignificant as it may be when compared to doses received in radiation treatment) and the errors associated with the image fusion process would be avoided.

It is known that the MR images are affected by distortions that alter the accurate representation of anatomical structures, *i.e.* spatial location and relative intensity. Image distortions are due to system-related and object-induced effects. The system-related distortions are generated by inhomogeneities in the main magnetic field and gradient non-linearities whereas the object-induced distortions are sourced in susceptibility and chemical shift variations in the sample. To be used for MRI simulation, the images have to be corrected to a degree that is acceptable for RTP, *i.e.* spatial resolution accuracy less than 2 mm.

The data on MRI simulation for intracranial lesions are rather scarce. Beavis *et al.*[2] used a basic approach for 1.5T MR images-based RTP. The authors considered no inhomogeneities corrections and the distortions corresponding to a typical field of view of a brain patient as being negligible. To accurately measure the 3D distortions, it is required to have a phantom that contains a large number of control points to properly sample the volume of interest and a robust algorithm to map the control points and determine the distortions along all three axes. Beavis *et al.* used a phantom with a design that gives a limited number of control points and would allow to determine 2D distortion only, *i.e.* (x,y) plane. Recently, Wang *et al.*[3] performed a MR distortion correction study on various 1.5T MRI scanners and found that the total 3D distortion can be up to 6 mm in a sphere with a radius of 100 mm (relevant to brain studies). Therefore, more studies need to be performed to develop an accurate and robust MR-based RTP for intracranial lesions that takes into account the distortions and inhomogeneities present in the MR images. MRI simulation was also investigated for prostate patients by different authors.[4,5] The authors showed that MR data sets that are corrected for distortion and assigned bulk densities to organ structures can successfully replace the CT images for treatment planning. The advent of 3T MR systems offers superior image quality to facilitate delineation of tumor and organs at risk.

In the present study, we investigate a 3T MR-based treatment planning procedure that relies on converting the MR images into CT-like images by assigning electron density information which is typically associated to CT values, to organ structures. The first step in the process is to correct the raw MR images for 3D geometrical distortions by applying a novel distortion correction procedure. The next step is to segment the volumes of interest into anatomical structures by using a semi-automatic method, *i.e.* brain, bone and scalp, required for dose calculations. Each volume is assigned a particular electron density before the data is used for dose calculations. The resulting CT+MR and MR only based plans

are compared in terms of isodose distributions, dose-volume histograms, and tumor-control-probability (TCP) modeling.

Materials and methods

We have evaluated the proposed MR-based treatment planning procedure by using 3T MR clinical studies to compare MR and CT+MR-based treatment plans. The flowchart of the procedure is presented in Figure 1.

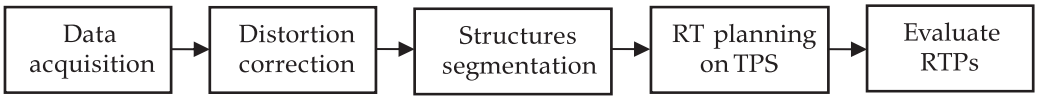


Figure 1. MR only based treatment planning procedure for RT of intracranial lesions.

Data acquisition

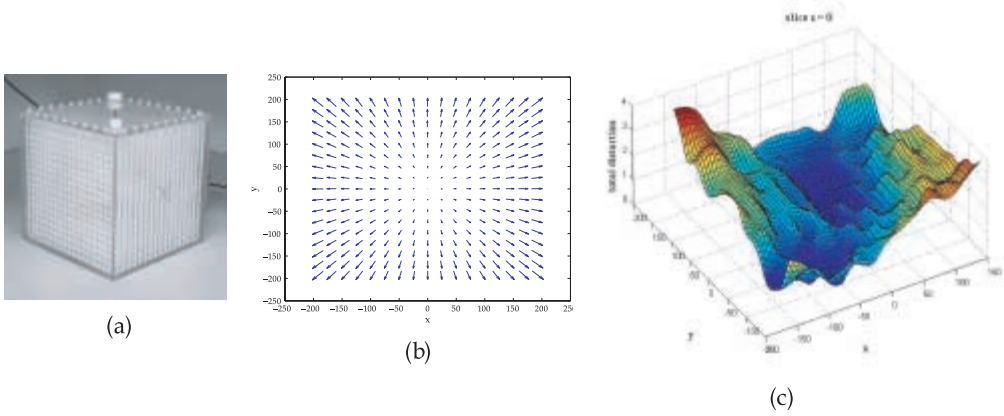
Data was acquired for each subject on a PQ 5000 CT (Philips Medical Systems) and a 3T Intera (Philips Medical Systems) MR scanner. The 3T clinical sequence consists of a 3D T1 TFE protocol with TE/TR/α 4.1/8.8/8°, field of view 240x240 mm^2 scanned on a 256x256 matrix in-plane, 125 partitions, each 1 mm and no gap. This MR sequence is used clinically for diagnostic and treatment planning of brain patients.

Distortion correction

Our technique is based on acquiring and comparing CT and MR scans of a 3D phantom filled with mineral oil consisting of parallel plastic grids 1 cm equally distributed inside the phantom (Figure 2a). We took three MR axial scans using the T1-weighted typical clinical sequence with the phantom positioned in such a way that the grid sheets were parallel to the transversal, saggital and corronal planes, respectively. The data sets were reconstructed using the scanner's software in the transversal, saggital and corronal plane to resemble grid-like structures in the MR images. CT axial scans (PET-CT Gemini, Philips Medical Systems) of the phantom was also acquired and reformatted to generate 3 data sets, *i.e.* transversal, saggital and corronal that would match the corresponding MR data sets. The 3D CT datasets are considered distortion-free, an accepted assumption in the field. To correct for object-induced distortions such as susceptibility, we acquired additional MR scans with reversed read gradient as per the technique described by Chang *et al.*[6]

The image analysis of all 3D data sets is performed automatically using our software developed in Matlab. Our algorithm determines the CT and MR control points, defined by the intersection of the grid crosses with the planes of the sheets surface. This is done sequentially by a) setting a threshold on the histogram for each image low enough to resemble the entire grid structure, b) applying 1D Gaussian blurring kernels along the x and y-axis to generate control point »blobs«, *i.e.* areas containing the control points, c) applying a watershed technique to isolate each »blob« in the images and d) determining the center of mass of each »blob« to obtain the coordinates of each control point.

The resulting CT and MR 3D matrices of control points are registered to a common system of reference. The 3D CT control points matrix is considered to accurately describe our volume of interest as there is no spatial distortion in the CT images. We can estimate the distortion by determining the displacement of the MR points from the corresponding CT ones. As an example, Figure 2b and Figure 2c show a typical distortion vector distribution and total distor-



(a) (b) (c)

Figure 2. (a) phantom design; (b) typical distortion vector distribution; (c) sample graph of total distortion values.

tion values, respectively. Once we determined the 3D distortion field matrix, we can correct the raw images by applying spatial and pixel intensity interpolations.

Structures segmentation

We converted the MR data sets into CT-like images by assigning electron density information to organ structures. Namely, the head image slices were segmented into scalp, bone and brain by using a set of contouring tools available on Pinnacle (Phillips Medical Systems) treatment planning system. We found that the best structure delineation method was based on a combination of the »Autocontouring« and »Profile« tools. Threshold values of the structures of interest interfaces are quickly assessed using the »Profile« tool and inputted into the »Autocontouring« tool. Contours are automatically generated by placing a seed point reasonably close to the boundary of the region that needs to be delineated. These contours can be subsequently adjusted as desired using manual tools. The scalp-air interface of the entire volume, the scalp-bone and the bone-brain interfaces corresponding to the upper part of the skull can be automatically generated with little manual adjustment. For the lower part of the skull, due to a higher gradient of anatomical structures more manual adjustment of the automatically generated contours is required. Bulk electron density values, relevant to the delineated structures, were assigned to the 3D volumes in Pinnacle by overriding their MR default values *i.e.* 1 g/cm^3 to brain and scalp and 1.47 g/cm^3 to bone.

RT planning on TPS

We generated and compared CT+MR and MR only based treatment plans using clinical data. The treatment planning process was performed on Pinnacle. At the Cross Cancer Institute (CCI), the standard clinical procedure for radiotherapy of intracranial lesions consists of acquiring CT and MR studies and performing image fusion. In the image fusion process, the contours of the planning target volume (PTV) and organs-at-risk are drawn on the T1-weighted MR images and automatically generated on the corresponding CT images. These contours are required in order to use the CT images for treatment planning purposes. In our study, we had data available for 4 GBM (glioblastoma multiforme) patients scanned

on CT and 3T MR units. To compare the CT+MR and the MR only based plans, we built typical treatment plans using the CT+MR datasets and applied these plans to the MR images only by using the same beam arrangements, dose constraints and optimization parameters. To perform dose calculations on the MR images all structure contours (*i.e*. brain, bone, scalp and all other delineated structures) were assigned relevant bulk electron density values by using Pinnacle's override density feature.

Evaluate RTPs

The resulting CT+MR and MR only based plans were compared in terms of isodose distribution and DVHs. For plan ranking, we use a TCP-based procedure for heterogeneous irradiation, which does not require the knowledge of radiobiological parameters. Here we give a brief description of the method, which will be published in details in another study and was applied for plan ranking in.[7]

The Poisson based TCP model $TCP = e^{-N_3}$ is used, where N_s is the number of surviving clonogens, estimated by the single hit cell dose-response model as $N_s = N_o e^{-\alpha D}$ where N_o is the initial clonogen number and α is the radiosensitivity. As pointed out by Brahme[8], the mathematical form of the single hit model becomes identical to the LQ model in the case of the standard fractionation schemes (*n* fractions each delivering a dose *d*): $NS = N_s = N_o e^{-(\alpha D+\beta nd)D} = N_o e^{-\hat{\alpha}D}$, where is $\hat{\alpha}$ called adjusted radiosensitivity. Recently, it was shown that the adjusted radiosensitivity takes into account the repopulation as well.[9] For the plan ranking purposes, it is better to use the TCP model in terms of the survival fraction at 2 Gy (SF_2), because this parameter is confined in the interval [0,1].

$$TCP = e^{-N_o e^{-\hat{\alpha}D}} = e^{-N_o SF_2^{0.5D}}$$

In the case of heterogeneous irradiation one obtains:

$$TCP = e^{-\rho\sum V_i e^{-\alpha D_i}} = e^{-\rho\sum V_i SF_2^{0.5D_i}}$$

where represents the differential DVH using the absolute (not the relative) volume. The tumor cell density is presumed to be 10^9 cells/mm^3. This number is actually not very important because the plans ranked are for one and the same tumor site, hence having one and the same tumor cell density.

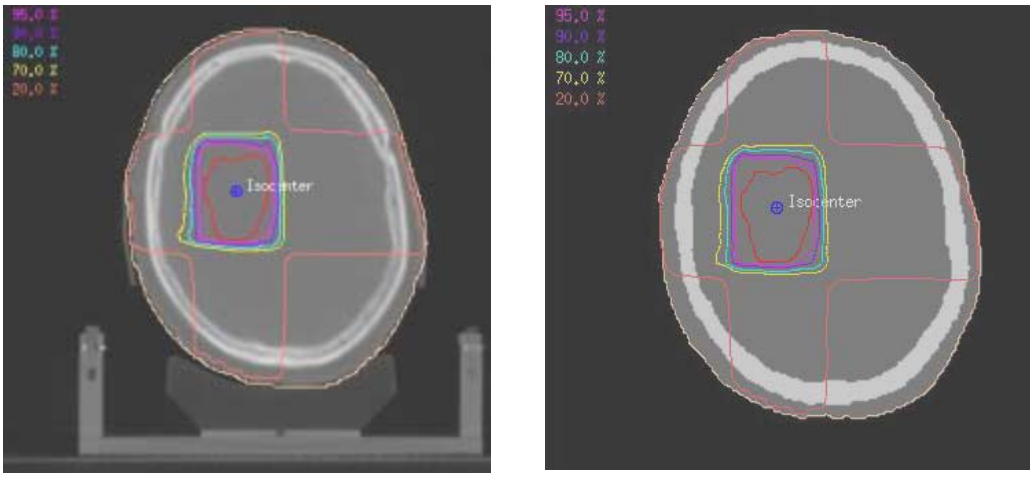
Let us have two plans, defined by a set of DVHs $\{V_i,D_i\}^I$ and $\{V_i,D_i\}^{II}$. The plan for which the tumor control probability is higher for each value of the parameter SF_2 is obviously the better one $TCP^I(SF_2 \mid \{V_i,D_i\}) > TCP^{II}(SF_2 \mid \{V_i,D_i\}) \forall SF_2$. The method is easily visualized graphically. Curves $TCP^I(SF_2 \mid \{V_i,D_i\})$ and $TCP^{II}(SF_2 \mid \{V_i,D_i\})$ are calculated and plotted for both plans. The far right curve will correspond to the better RT plan, producing the highest TCP.

Results and discussion

The total distortion for the standard 3T MR sequence used for brain patients in a volume relevant to brain studies, *i.e*. 20x20x20 cm^3, was found to be about 4 mm. Considering that the requirement for image spatial accuracy in radiation treatment planning is 2 mm, our distortion correction is applied to correct the patient MR images.The residual distortion determined after applying these transformations was found to be within one pixel resolution, *i.e*. 0.94 x 0.94 mm^2.

Figure 3a shows an example of the planning target volume (PTV) isodose distributions of RT plans based on CT+MR and MR only images, respectively. It can be seen that the two plans look very similar in terms of PTV isodose distributions and they are all in agreement with our clinical

(a)



CT+MR-based RT plan MR only based RT plan

(b)

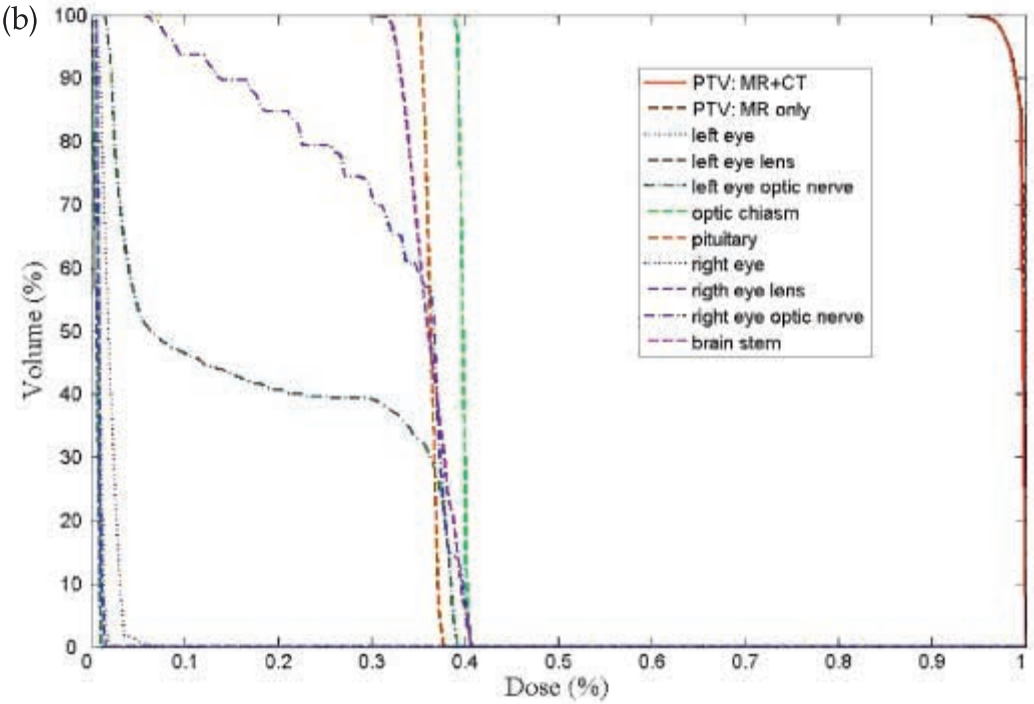


Figure 3. (a) Comparison of isodose distributions; (b) dose-volume histograms (DVHs) for the CT+MR and MR only based radiation therapy plans.

criteria, *e.g.* 95% isodose line coverage of the PTV. For all patients, we also compared the CT+MR and MR only based RT plans in terms of DVHs. Figure 3b depicts sample DVHs corresponding to the two plans of the same patient. For visualization purposes, we displayed only the DVHs of the organs-at-risk (*i.e.* eyes, eye lenses, optical nerve, pituitary gland, optic chiasm and brain stem) corresponding to the CT+MR-based plan only as they overlap with the corresponding DVHs generated for the MR only based plan. For all patients, we found that the differences are clinically insignificant (within 1%).

To evaluate the impact of the inhomogeneities on the treatment planning process, we compared the standard CT+MR based plans with and without non-homogeneity correction. The 3D skull contours were assigned bulk water electron density values, *i.e.* 1g/cm^3, for the plans that used non-inhomogeneity corrections. In the case of 3 patients, we found that the difference between the plans with and without the non-homogeneity correction was within 2%. For the 4th patient the discrepancy was 3% due to a large tumor volume and its location near the vortex, therefore the beams passed through a thicker layer of bone.

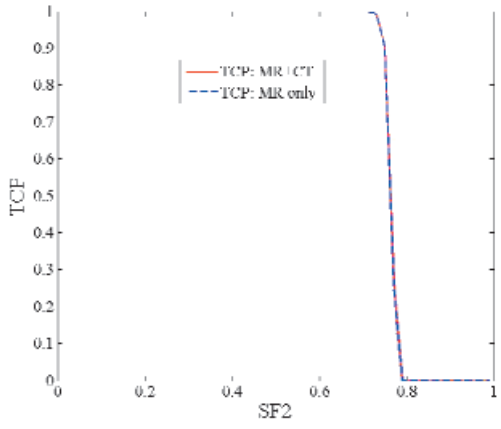


Figure 4. TCP-based radiation treatment plan ranking for CT+MR and MR only based plans.

Figure 4 shows a typical TCP-based RT plan ranking for the CT+MR and MR only based plans. It can be seen that there is a good agreement between the two plans. The differences are clinically insignificant (within 1%) for all patients investigated.

In this study, we investigated a treatment planning procedure for intracranial lesions based solely on 3T MRI data sets that consists of converting the MR images into CT-like images by assigning bulk electron density to segmented structure volumes, *i.e.* scalp, bone and brain. Before being used in the treatment planning process, the MR images were corrected for 3D geometrical distortions. We found that the MR-based treatment planning procedure performed as good as the current clinical procedure based on both the CT and MR data sets.

MRI has proven to be the best imaging modality for RTP target delineation. Increasing the magnetic field strength form 1.5 to 3 T results in an increase in the signal-to-noise ratio, which not only, simplifies the task of target delineation, but could improve the accuracy in delineating the 3D tumor and structures volumes.

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