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Investigation of a method for generating synthetic CT models from MRI scans of the head and neck for radiation therapy

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Abstract

MR images often provide superior anatomic and functional information over CT images, but generally are not used alone without CT images for radiotherapy treatment planning and image guidance. This study aims to investigate the potential of probabilistic classification of voxels from multiple MRI contrasts to generate synthetic CT ("MRCT") images. The method consists of (1) acquiring multiple MRI volumes: T1-weighted, T2-weighted, two echoes from a ultra-short TE (UTE) sequence, and calculated fat and water image volumes using a Dixon method, (2) classifying tissues using fuzzy c-means clustering with a spatial constraint, (3) assigning attenuation properties with weights based on the probability of individual tissue class being present in each voxel, and (4) generating a MRCT image volume from the sum of attenuation properties in each voxel. The capability of each MRI contrast to differentiate tissues of interest was investigated based on a retrospective analysis of ten patients. For one prospective patient, the correlation of skull intensities between CT and MR was investigated, the discriminatory power of MRI in separating air from bone was evaluated, and the generated MRCT image volume was qualitatively evaluated. Our analyses showed that one MRI volume was not sufficient to separate all tissue types, and T2-weighted images was more sensitive to bone density variation compared to other MRI image types. The short echo UTE image showed significant improvement in contrasting air versus bone, but could not completely separate air from bone without false labeling. Generated MRCT and CT images showed similar contrast between bone and soft/solid tissues. These results demonstrate the potential of the presented method to generate synthetic CT images to support the workflow of Radiation Oncology treatment planning and image guidance.

1. Introduction

While Magnetic Resonance Imaging (MRI) scans have been widely used for contouring in radiotherapy due to their superior soft tissue contrast as compared to Computed Tomography (CT) scans, they have rarely been used in isolation for support of Radiation Oncology procedures including treatment planning and image guidance. Primary reasons for the use of CT include beliefs about geometric integrity and precision in mapping Relative Electron Density (RED) for dose calculations. Typically, MR images have been aligned to CT images to transfer soft-tissue contrast information seen on MRI into the CT-based patient representation for treatment planning. In addition to using significant resources, such a transfer could potentially induce systematic errors due to registration uncertainties.

Interest is emerging to solely use MRI for radiotherapy treatment planning and image guidance. To achieve this goal, MRI must support the complete workflow currently in place with CT, including generation of electron density maps as well as images to facilitate patient positioning at the treatment unit. To address these issues, some investigators have manually identified segments of low intensity using T1-or T2-weighted MR images, and assigned bulk density to these segments to generate pseudo-CT images for treatment planning (Jonsson *et*

al 2010, Lambert *et al* 2011, Lee *et al* 2003) or digitally reconstructed radiographs (DRRs) for image guidance (Chen *et al* 2007). Atlas-based methods have aimed to apply reference CT images as electron density maps to individual MR images based on alignment between the two (Dowling *et al* 2012, Greer *et al* 2011, Stanescu *et al* 2008). However, the atlas-based methods ignore the differences of anatomy and electron density between individuals.

In more individualized approaches, investigators have utilized the characteristics of tissue presented on certain MR images, such as T1-weighted (Barra and Boire 2000, Zaidi *et al* 2003) or fat/water images (Kim *et al* 2012) to automatically segment various tissue types, but separation of bone from air has been challenging due to its short T2/T2*. Recently, ultra-short echo time (UTE) sequences were developed to visualize tissues with very short T2, such as bone (Robson *et al* 2003, Catana *et al* 2010, Keereman *et al* 2010). In addition, Kim *et al* (2012) and Berker *et al* (2012) showed that segmentation from multiple MRI volumes with various contrasts, such as UTE and fat/water images, generated results closer to CT images compared to acquiring only one source of MRI contrast. Johansson *et al* (2011) used a Gaussian mixture regression model to link the voxel values in CT images to the voxel values in images from MRI sequences, and showed the potential of using voxel-based methods to generate continuous CT-density information from MR images to represent the variation of tissue density in a human body. However, the degeneracy of the fitted relationship between signal intensities of CT and MRI, particularly at -1000 and 0 Hounsfield Units (HUs), presents challenges to use the method.

In this study, we investigated the potential of probabilistic classification of MRI voxels from multiple contrasts to create synthetic CT. We developed a method that potentially supports the mixing of tissue types within a voxel, and further took advantage of the composition of tissue in the immediate vicinity to regularize the assignment of probabilistic membership. We investigated the relationship of MRI contrasts to bone density, and evaluated the ability of this method to generate patient representations that support the workflow of Radiation Therapy that CT scans are otherwise used for.

2. Methods and materials

We performed preliminary studies to evaluate the feasibility of this method. First, we investigated the capability of each MR image contrast type to differentiate the (tissue) materials of interest. This was done by retrospective analysis, approved by the institution review board, of 10 patients who had brain MRI and CT scans for routine treatment planning purposes. Second, we investigated the correlation of bone intensities between CT and MR, using data acquired from a patient under an institution review board-approved prospective protocol. All MR and CT images were acquired using a large-bore 3T MR scanner (Skyra, Siemens Medical Systems, Erlangen, Germany) and CT simulator (Brilliance, Philips), respectively. In addition, we evaluated the ability of UTE images to directly discriminate air and bone, and qualitatively evaluated MRCT images versus CT for one patient.

2.1. Image acquisition

In the retrospective study, routine clinical brain MRI images, including 3D volumetric T1-weighted magnetization-prepared rapid gradient echo sequence and 3D T2-weighted turbo spin echo, acquired using a 20 channel head and neck coil, were analyzed. T1-weighted images were acquired with TE/TR/TI = 2.5/1900/900 ms, flip angle = 9°, and voxel size $\approx 1.25 \times 1.25 \times 0.9$ mm³. T2-weighted images were acquired with TE/TR/TI = 387/5000/1800 ms, flip angle = 120°, and voxel size $\approx 0.47 \times 0.47 \times 3.3$ mm³. In-phase and out-phase images of water and fat MR signals were used to calculate water and fat components using a Dixon method (Dixon 1984), with voxel sizes of $1.17 \times 1.17 \times 3.9$ mm³. All MR images were

corrected on-line for gradient non-linearity-caused spatial distortion. For CT image acquisition, the whole brain region for these patients was scanned with slice thickness of 1–3 mm and in-plane pixel size $\approx 0.6 \times 0.6 \text{ mm}^2$. The CT images were aligned with the MR images (the T1-weighted image volume was used for CT-MR alignment). All images were reformatted as axial cuts with a voxel size of $0.9 \times 0.9 \times 1 \text{ mm}^3$.

In the prospective study, a patient was scanned in the RT position with an immobilization mask, using a combination of an 18-channel anterior surface coil and a posterior 4-channel coil. MR and CT acquisition parameters were similar to those routinely used in the clinic and described for the first study. In addition, an investigational UTE sequence with dual echoes was used to generate two sets of image volumes. The UTE images were acquired with TR = 7.66 ms, TE = 0.06 (UTE1) and 4.46 (UTE2) ms for the first and second echoes, flip angle = 12° , and voxel size $\approx 1.41 \times 1.41 \times 1.41 \text{ mm}^3$. In these images, blood flow yielded dark voxels, which would be interpreted as false positive indications for bone. To improve the accuracy in classifying bone, 2D multi-plane time-of-flight (TOF) angiography was acquired (TE/TR = 4/8.6 ms and flip angle = 20°) providing “vessel” images in which large blood vessels demonstrated higher signal intensity than the surrounding brain. All MR image volumes were acquired in the sagittal orientation except the angiography which was acquired in the axial plane. All MR images were acquired within 12 minutes. A total of seven MRI and one CT volumes were thus acquired for the patient, and, after rigid alignment of the CT volume to the MRI T1-weighted image volume, all image volumes were reformatted in axial orientation with a voxel size of $1 \times 1 \times 1 \text{ mm}^3$ (Figure 1).

2.2. Image data analyses

2.2.1. Tissue contrast on various MRI image types—To investigate the capability of each MR image contrast-type to differentiate the (tissue) materials of interest, data from the 10 patients was analyzed. Using an in-house software environment for functional image analysis (FIAT), MR and CT image volumes were spatially aligned to the T1-weighted image volume using a rigid registration method and mutual information as a metric. Regions of interest (ROIs) were defined within tissues that were clearly identified, and which contained primarily one of the following classes of tissue/material each: (1) bone (occipital bone), (2) fat (external layer of fat beneath the skin), (3) fluid (aqueous humor in the eyes), (4) white matter (WM), (5) grey matter (GM), and (6) air (maxillary sinuses) (Figure 2). The ROI of bone was initially defined on CT images using a threshold of 1000 HU (i.e. little or no mixing of bone with other tissues), and manually modified using MR images to reduce the influence of image registration errors and partial volume effects in CT images and thus ensure that the region consisted primarily of bone. The ROI of fat was initially defined on MR fat images and modified using the other MR image volumes to increase the likelihood that the voxels contained within consisted of primarily fatty tissue. The ROIs of fluid, WM, GM, and air were initially defined on T1-weighted images and then were modified using the other image volumes to ensure that they primarily consisted of their respective tissues. The volumes encompassed by these ROIs varied between tissue types and patients, with a range of $5.4 \times 10^2 - 2.3 \times 10^4 \text{ mm}^3$. The average and standard deviations of intensities within each ROI were calculated for each patient and image type. For each individual patient, a t-test was performed to investigate the ability of various image contrasts in distinguishing different material types from the material of interest.

2.2.2. Tissue classification for synthetic CT generation—Synthetic CT generation is based on a series of steps (Figure 3). First, multiple contrast MRI volumes spanning the volumes of interest are placed in a common frame of reference. T1-weighted, T2-weighted FLAIR, UTE with echoes at TE of 0.06 (UTE1) and 4.6 ms (UTE2) as well as calculated fat and water image volumes (from a 2-point Dixon technique (Dixon 1984)) are included in

this example to differentiate the major tissue types of bone, fat, solid tissue, fluid and air. In this pre-processing step, all MRI volumes are spatially aligned to the T1-weighted volume if indicated. The skin surface is extracted in order to define the volume of interest for classification.

Probabilistic tissue classification is achieved via fuzzy c-means (FCM) clustering with a spatial constraint. The FCM algorithm assigns voxels of the images a probability of belonging to a class. A membership probability can be between zero and one, with one indicating a 100% probability and zero denoting no probability of a given voxel to belong to a specific class. In FCM clustering analysis, a dataset $\{x_k\}_{k=1}^N \subset R^d$ from d image volumes is classified into c prototype classes to obtain probability memberships and class centroid vectors by minimizing an objective function. The objective function (J_m) that we use includes a spatial constraint as (Chen and Zhang 2004):

$$J_m = \sum_{i=1}^c \sum_{k=1}^N u_{ik}^m \|x_k - v_i\|^2 + \alpha \sum_{i=1}^c \sum_{k=1}^N u_{ik}^m \|\bar{x}_k - v_i\|^2 \quad (1)$$

where u_{ik} represents the fuzzy membership of the k th voxel (x_k) to the i th prototype class (v_i), $m \in [1, \infty]$ is an exponent of the fuzzy membership, $\bar{x}_k$ is a mean or median of the neighbors within a specified kernel around x_k , and α is a weighting factor for the spatial constraint. The spatial constraint could reduce the influence of noise, improve spatial connectivity of classification results, and reduce the impact of residual small local movement not resolved by image registration. The solutions to minimize the objective function are,

$$u_{ik} = \frac{(\|x_k - v_i\|^2 + \alpha \|\bar{x}_k - v_i\|^2)^{-1/(m-1)}}{\sum_{j=1}^c (\|x_k - v_j\|^2 + \alpha \|\bar{x}_k - v_j\|^2)^{-1/(m-1)}} \quad (2)$$

$$v_i = \frac{\sum_{k=1}^n u_{ik}^m (x_k + \alpha \bar{x}_k)}{(1 + \alpha) \sum_{k=1}^n u_{ik}^m} \quad (3)$$

Equation (1) can be used to optimally classify MRI data from each individual patient, but this process is computationally intensive. If sufficient similarity of intensity values across the population of patients scanned with the same protocol exists, the classification process for a new patient can be sped up by using the averaged prototype vectors of the tissue classes found in a sample of patients.

The probabilities of tissue class memberships are then used to assign properties of interest. For the purpose of radiation therapy treatment planning, relative attenuation properties are assigned with weights based on the probability that each class exists at a given location. The probability-weighted sum of the attenuation properties of each voxel yields an attenuation map, which can for example produce a synthetic CT (MRCT) volume.

In order to appreciate the stability of intensities across scanning sessions, FCM-based classification was performed using FIAT software for each of the 10 retrospective patients individually, and the resulting optimized intensity values for each tissue/material class in each image type were compared.

2.2.3. Correlation between CT and MR intensity values in bone—To investigate the correlation of bone intensities between CT and MR in the presence of other tissue, CT images were used to define a bone region with intensity between 250 and 2050 HU in the

skull. This region was divided into 12 ROIs binned with intensity widths of 150 HU each. The average intensity within each ROI was compared between CT and MR image volumes from the prospective patient.

2.2.4. Discriminatory power in separating air from bone—To further evaluate the ability of various MR image types to discriminate air from bone, receiver operating characteristic (ROC) evaluation was performed on data from the prospective protocol patient. CT images were used to define the “true” air (defined as intensity < -400) and bone ROIs (intensity > 200). As opposed to the higher threshold applied to define bone for feasibility of FCM, the threshold of 200 included voxels in which bone potentially mixed with other tissues. Intensity thresholds were applied to the voxels of the T1-weighted, T2-weighted, UTE1, and UTE2 MR image volumes within these ROIs to label bone (intensity above threshold) versus air (intensity below threshold). The number of voxels labeled as air in MR images at a given threshold and located within air region defined in CT images was divided by the total number of voxels labeled as air from CT, yielding the true positive rate (sensitivity). The number of true bone voxels mislabeled as air voxels at the same MRI threshold was divided by the total number of bone voxels identified on CT to yield the false positive rate (1-specificity). ROC curves of true positive rates vs. false positive rates were generated by varying the thresholds across the range of image intensities on the T1-weighted, T2-weighted, UTE1, and UTE2 image volumes, respectively. The areas under the ROC curves (AUC) were compared for these different MR image volumes.

2.2.5. MRCT generation and evaluation—Six of the seven MR image volumes (T1-weighted, T2-weighted, UTE1, fat, water and “vessel”) from the prospective protocol patient were used to generate MRCT image volumes and MRCT-derived DRR images (in this instance using a projection program written in MATLAB (Mathworks, Natick, MA)) for comparison with CT and CT-derived DRR images (UTE2 provided no additional useful information, and thus was not included). First, intensity inhomogeneity corrections were applied using a N4 bias field correction algorithm (Tustison *et al* 2010) implemented in an image analysis software environment (SLICER, surgical processing laboratory, Brigham and Women’s Hospital, Boston, MA). Next, the skin surface was extracted as the union of contours extracted from T1-weighted, T2-weighted, fat and water images using intensity thresholds of 20, 10, 10, and 70, respectively. This surface was then cleaned up using morphologic operations (filling holes, erosion and dilation). Next, an air mask within the skin surface was generated using UTE1 images with an intensity threshold that was selected based on the ROC analysis to optimally remove air from classification. This air mask not only contained air but also partial fluid regions, such as eyes, due to low signals of fluid in UTE1 images. To address this issue, the air mask was modified by automatically removing those voxels that clearly represented tissue on water images, where air and water were clearly separable (as seen in Table 1). Third, a vessel mask was generated using “vessel” images with an intensity threshold that separated flowing blood from bone.

The probabilities of voxels within the skin surface (excluding air and vessel masks) containing each of 5 classes (fat, fluid, GM, WM, bone) were determined using FCM clustering analysis. Two different combinations of input image volumes were tested for FCM classification: (1) four inputs: T1-weighted, T2-weighted, fat and water images, and (2) five inputs: T1-weighted, T2-weighted, fat, water, and UTE1 images. A weighting factor (α) of 3.8 was used for the spatial constraint, and a fuzzy exponent (m) of 1.6 was used. The five classes were chosen to represent the main tissue types in a head. Based on ICRU report 46 (1992), physical density values of fluid, fat, WM, GM and adult cranium are 0.95, 1, 1.04, 1.04 and 1.61 g/cm³. Applying these values with the inverse of the HU to relative electron density calibration curve from our treatment planning system yielded CT numbers assigned to individual tissue types of -98, -12, 14, 14, and 1139 HU. In addition, a CT

number of 14 HU (the same as brain tissue) was assigned to the voxels within the vessel mask. The MRCT image volumes were then generated by multiplying the probability of each voxel being represented in each class by the attenuation value of that class and summing the result across all classes.

The correlation of bone intensities between CT and MRCT image volumes was investigated using the 12 ROIs previously generated from the intensity range of 250 to 2050 from the treatment planning CT scan.

A dose calculation comparison was performed using a commercial treatment planning system (Eclipse 11.0, Varian, Palo Alto CA). A clinical target volume (CTV) was created and a stereotactic radiosurgery plan was designed to treat this target using 9 non-opposed and non-coplanar beams. Dose calculations were performed using the analytical anisotropic algorithm (AAA) with a grid size of 2.5 mm on both CT and MRCT images with heterogeneity corrections as well as on CT images without heterogeneity corrections. Dose distributions and dose volume histograms were compared between these plans and using the same monitor units (MUs).

3. Results

3.1. Tissue contrast on various MRI image types

Mean intensities and standard deviations of T1-weighted, T2-weighted, fat and water images within the ROIs of the six material types (bone, fat, fluid, WM, GM, and air) were measured for each of the 10 patients. Figure 4 shows the intensity values and variations of one patient as an example.

The results of the t-tests to determine the ability of each image type to separate two tissue classes for each patient are given in Table 1. Bone could not be separated from air by using any of the four image types for any patient, due to its low signals on these conventional MRI images. Bone also could not be separated from fluid using T1-weighted images alone, because fluid has a long T1, resulting in a low intensity on T1-weighted images. In fat images, only fat could be separated from other types of tissue but other types of tissue could not be separated from each other.

For these 10 patients, separate FCM optimization was performed on each patient, using the T1-weighted, T2-weighted, fat, and water images. The mean values and standard deviations of the prototype class intensities are shown in Figure 5.

3.2. Correlation between CT and MR intensity values in bone

For all MRI scan volumes (T1-weighted, T2-weighted, UTE1, UTE2, Fat, Water), MR signal intensities decreased as CT numbers increased within the CT-defined bone volume when CT numbers were smaller than 1600 in the protocol patient (Figure 6). The bone signal intensity was highest on UTE1 images but lowest on the T2-weighted images (Figure 6 (a)), indicating that UTE1 is more sensitive to bone signals. However, normalization (Figure 6 (b)) reveals that, for this scanning configuration, UTE1 images had the shallowest slope but T2-weighted images had the sharpest slope, indicating that UTE1 images likely do not aid T2-weighted imaging in discriminating bone density, which will be tested in 3.4.

3.3. Discriminatory power in separating air from bone

Figure 7 shows “true” air and bone regions defined on CT images, and air and bone regions defined on UTE1 images using example thresholds of 50, 100 and 200. With a threshold of 50, the masked air region was smaller than the “true” air region, (21% true positive rate) but only 0.1% of bone was mislabeled as air (false positive). As the threshold was increased, the

masked air region increased in coverage of the CT-identified air voxels, but more bone was also mislabeled as air. In Figure 8, ROC curves generated by continuous threshold adjustment show that UTE1 had the greatest discriminatory power (AUC of 0.961), followed by T1 (AUC 0.882), UTE2 (AUC 0.845), and T2 (AUC 0.764).

3.4. MRCT generation and evaluation

Figure 9 shows the correlation between CT intensities and bone memberships as well as MRCT intensities within 12 CT-intensity bins when using 4 (T1-weighted, T2-weighted, fat, water) and 5 (T1-weighted, T2-weighted, fat, water, UTE1) image volumes as input to the FCM classifier. When the CT intensity was 1150 or below, the bone memberships and MRCT intensities correlated linearly with CT intensities ($R^2=0.99$, slope = 0.8 for MRCT vs. CT) for either 4 or 5 inputs (without or with UTE1 as input). Incorporating UTE1 images in the classifier did not change classification results, indicating UTE1 did not drive the bone classification. Bone memberships and MRCT intensities reached a plateau at 1150, and began to decrease as CT intensity increased beyond 1600. Of note, the total volume of CT intensities above 1600 HU was less than 0.1% (less than 0.6 cc), of the total skull volume (607 cc), indicating likely minimal impact of these regions on uses of attenuation values such as DRR generation and dose calculation for multiple-beam treatment plans.

MRCT images (Figure 10) show similar contrast between bone, fluid and solid tissue compared to CT images. Some small volumes of air in the sinuses and ear canals were misclassified as bone. The threshold selected to generate the air mask was 100 on UTE1 images, which resulted in sensitivity of 74% (true positive rate) and specificity of 98% (1-false positive rate) based on the ROC analysis (Figure 8), i.e. a specific bias towards labeling more air as bone as opposed to labeling more bone as air. The DRR generated from MRCT images (Figure 10 (e) and (f)) was similar to that of CT images. The projections of bony edges in the skull can be clearly visualized.

Neither the dose distributions nor the DVHs from heterogeneous calculations on CT and MRCT images (Figure 11) show significant differences between calculations. As expected, a difference was found between calculations with and without heterogeneity corrections.

4. Discussion

A method using FCM classification of multiple MRI volumes to yield synthetic CT ("MRCT") images has been presented and evaluated in the brain region. This method has been shown to distinguish tissues/materials that contribute significantly to attenuation variations seen on CT with reasonable accuracy. Generation of a mask to separate air from bone using UTE images was shown to involve tradeoffs of sensitivity versus specificity. MRCT images present contrast sufficiently similar to CT images to support routine use in Radiation Oncology treatment planning and image guidance, although large scale studies will be needed to extensively explore the accuracy of MRCT compared to CT for the broad workflow of radiation therapy applications in the head.

The presented method differs from previous studies (Berker *et al* 2012, Catana *et al* 2010, Chen *et al* 2007, Dowling *et al* 2012, Keereman *et al* 2010, Kim *et al* 2012, Lambert *et al* 2011, Stanescu *et al* 2008, Zaidi *et al* 2003) in that it classifies each voxel with a probability membership of belonging to the specific tissue class, assigns the tissue attenuation property to each tissue class, and then generates synthetic CT images through a weighted sum of attenuation properties, rather than simple segmentation with bulk density assignment. Our method uses multiple MR image volumes with differential tissue contrasts as input. Johansson *et al* (2011) generated synthetic CT images using a Gaussian mixture regression model with fitting intensities of T2-weighted and UTE MR image volumes to CT intensity

values. As opposed to directly mapping MR voxel intensities to individual CT intensities (which may suffer from significant degeneracy), our method utilized individual intensity features on MRI to classify a limited number of tissues/materials, and assigned individual attenuation properties to each class, permitting attenuation assignment for voxels composed of combinations of two or more material types with varying concentrations.

Based on our current analysis, one MRI image volume is not sufficient to separate all major tissue types in the head. Differentiating bone from air is most challenging, and combining T1-weighted, T2-weighted, fat, and water images could not address this issue. Ultra-short TE images present higher signal intensities from bone relative to air than other image types, as demonstrated in the ROC analysis, and also noted by previous investigators (Robson *et al* 2003). While the UTE1 image studies here demonstrated increased intensity in the bone and enhanced contrast between bone and air, they still could not completely separate the two cleanly without false labeling. Possible causes of mislabeling include partial volume effects, image misalignment, artifacts, and noise. Barring other approaches to further enhance separation of air and bone, an appropriate tradeoff should be determined for selecting internal air regions on UTE1 based on the intended use (some examples are dose calculation and DRR generation). To avoid mis-classify a vessel as bone or air due to its low intensities on all MR images, a rapid TOF-like sequence was used to acquire “bright” vessels. Our investigations (Figures 6 and 9) indicate that T2-weighted images drive the bone density classification rather than UTE1 images. Our study indicates that combining the information from multiple MRI contrasts results in robust classification of tissue types. Future studies will further optimize inputs, contrasts and acquisition time for generating MRCT.

Our method of generating MRCT images was evaluated prospectively for a protocol patient. The generated MRCT and CT images showed similar contrast between bone and soft/solid tissue. Differentiation of air from bone on MRI was strongly dependent on the threshold used to generate the air mask. In future investigations, the nature of signal changes across intensity thresholds will be explored to further optimize air separation. When comparing MRCT bone intensity with bone CT number, a strong correlation was found for threshold of CT number less than 1150, indicating the potential for FCM classification to yield CT intensities that are reflective of changing bone density up to a point. Denser bone may be harder to define via this method, as it has a very short T2. It is possible to investigate adding a class of very dense bone, and this will be explored across a broad class of patients in the future. Even though the densest bone was less well-defined and some of the interfaces between air and bone were mis-classified, dose calculations on MRCT had no significant difference from those on CT with heterogeneity corrections. The MRCT-DRR was also comparable to the CT-DRR. These results suggest that our method can generate MRCT images to support current photon external beam treatment planning and image guidance techniques for radiotherapy.

MR images may suffer artifacts of non-uniform intensity across the same type of tissues, which may result in inaccuracy of tissue classification. Our study applied the N4 bias field correction to original MR images, and thus, the intensity of the generated MRCT images using these corrected images was more uniform across the brain region. Future investigations of bias field correction methods and normalization may improve intensity homogeneity, with impacts on material classification as well as bone-air separation.

Our initial retrospective test showed that MR intensity values were similar across the population of patients scanned with the same protocol (Figure 5). This result indicates the possibility of applying an average prototype vectors generated from a sample of patients to FCM classification for a new patient, which can reduce computation time in optimization.

Material types of interest in the head region include bone, air, fat, solid tissue (GM and WM) and fluid, representing different attenuation properties on CT images. GM and WM have similar intensities on CT images and in theory could be considered one class of tissue. However, because GM has different intensity compared to WM, most notably in the T2-weighted MR images used for classification, separating these two tissue types and assigning the same attenuation properties was found to be beneficial to improvement of the classification accuracy.

A number of interesting observations from this study have prompted additional directions in this area of research. Tradeoffs in fuzziness of classification, as well as sensitivity/specificity of bone/air separation are a subject of ongoing investigation. Additional areas of research include optimization of the MRI scan protocols to trade off scan time versus resolution and accuracy of classification, and studies of similar classification strategies outside of the head region.

This method currently involves the acquisition of multiple image types in order to classify tissue components. The length of scanning, while still relatively short, may raise new issues related to patient motion. Future work will include attempts at reducing the number of sequences or developing new ones to optimize contrast, as well as investigations of minimum spatial resolution for certain scans and other novel sampling methods to make scanning faster. Furthermore, the tools that synthesize CT representations from multiple images will need to be handled with sufficient robustness to operate successfully in busy clinical environments.

5. Conclusions

A method of using FCM classification on multiple MRI volumes has been presented and initially evaluated for protocol patients. This classification method can assign attenuation values to heterogeneous tissues. We did not find a single MRI image volume that could sufficiently differentiate all tissue types. UTE images increase differentiation of bone from air but currently tradeoffs between specificity and sensitivity exist. Using multiple MRI volumes permitted generation of synthetic CT (MRCT) images, from which MRCT-DRRs may provide sufficient information for the purpose of image guidance. The presented method of generating MRCT images is a potentially feasible step towards realizing radiotherapy based on MRI without CT.

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Figure 1.
(a) CT and (b)–(h) MR images for the prospective protocol patient.

Figure 2.
Example ROIs on T1-weighted images: (a) bone, (b) fat, (c) fluid, (d) WM, (e) GM, and (f) air.

Figure 3.
Overall scheme of using multiple MRI volumes to generate MRCT.

Figure 4.

An example of intensity variations for various tissue types on T1-weighted, T2-weighted, fat and water images. The error bar represents one standard deviation of tissue intensities within the ROI.

Figure 5.

Results from FCM classification of each of 10 patients. For each tissue/material type, the average optimized intensity value is shown as well as their standard deviations across the patient population (error bars).

Figure 6.

MR intensities for CT-defined ROIs within the skull for a patient scanned in a mask with an 18-channel anterior surface coil and a 4-channel posterior surface coil. (a) Absolute and (b) normalized intensities are shown.

Figure 7.

(a) Contours of air (magenta) and bone (white) generated from CT images using thresholds of < -400 and > 200 , respectively. Contours of air (yellow) are shown as generated from UTE1 images using threshold values of 50 (b), 100 (c) and 200 (d).

Figure 8. ROC curves and areas under the curves (AUC) for differentiation of air from bone using UTE1, T1-weighted, UTE2, and T2-weighted images.

Figure 9. Correlations between CT intensities and (a) bone memberships and (b) MRCT intensities for ROIs within bone when using four (T1-weighted, T2-weighted, fat, water) and five (T1-weighted, T2-weighted, fat, water, UTE1) image volumes as input.

Figure 10.

Axial (a) and sagittal images (c) through a MRCT image volume and corresponding cuts through the same patient's CT volume ((b) and (d)). Left lateral DRR images generated from MRCT (e) and CT (f).

(a)

(b)

Figure 11.

(a) An example cut of relative dose distributions on CT (left) and MRCT(right) with heterogeneity corrections. (b) DVHs (relative volume vs. relative dose) for both CT and MRCT with heterogeneity corrections and CT without heterogeneity corrections.

Table 1

Number of patients whose tissue contrasts in images are sufficient to separate material pairs (p-value < 0.05). The total number of patients tested was 10.

Material	T1-weighted	T2-weighted	Dixon_Fat	Dixon_Water
Differentiation from bone				
Air	0	0	0	0
Fat	10	10	10	4
Fluid	0	10	0	10
GM	10	10	0	10
WM	10	8	0	10
Differentiation from fat				
Bone	10	10	10	4
Air	10	10	10	10
Fluid	10	8	10	10
GM	10	10	10	10
WM	10	10	10	10
Differentiation from fluid				
Bone	0	10	0	10
Air	10	10	1	10
Fat	10	8	10	10
GM	10	10	2	9
WM	10	10	4	1