Evaluation of a lung tumor autocontouring algorithm for intrafractional tumor tracking using low-field MRI: A phantom study

Jihyun Yun  
Department of Physics, University of Alberta, 11322 – 89 Avenue, Edmonton, Alberta T6G 2G7, Canada and Department of Oncology, Medical Physics Division, University of Alberta, 11560 University Avenue, Edmonton, Alberta T6G 1Z2, Canada

Eugene Yip  
Department of Oncology, Medical Physics Division, University of Alberta, 11560 University Avenue, Edmonton, Alberta T6G 1Z2, Canada

Keith Wachowicz, Satyapal Rathee, Marc Mackenzie, and Don Robinson  
Department of Medical Physics, Cross Cancer Institute, 11560 University Avenue, Edmonton, Alberta T6G 1Z2, Canada and Department of Oncology, Medical Physics Division, University of Alberta, 11560 University Avenue, Edmonton, Alberta T6G 1Z2, Canada

B. G. Fallone  
Department of Physics, University of Alberta, 11322 – 89 Avenue, Edmonton, Alberta T6G 2G7, Canada; Department of Medical Physics, Cross Cancer Institute, 11560 University Avenue, Edmonton, Alberta T6G 1Z2, Canada; and Department of Oncology, Medical Physics Division, University of Alberta, 11560 University Avenue, Edmonton, Alberta T6G 1Z2, Canada

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Purpose: The first aim of this study is to investigate the feasibility of online autocontouring of tumor in low field MR images (0.2 and 0.5 T) by means of a phantom and simulation study for tumor-tracking in linac-MR systems. The second aim of this study is to develop an MR compatible, lung tumor motion phantom.

Methods: An autocontouring algorithm was developed to determine both the position and shape of a lung tumor from each intrafractional MR image. To initiate the algorithm, an expert user contours the tumor and its maximum anticipated range of motion (herein termed the Background) using pretreatment scan data. During treatment, the algorithm processes each intrafractional MR image and automatically contours the tumor. To evaluate this algorithm, the authors built a phantom that replicates the low field contrast parameters (proton density, $T_1$, $T_2$) of lung tumors and healthy lung parenchyma. This phantom allows simulation of MR images with the expected lung tumor CNR at 0.2 and 0.5 T by using a single 3 T scanner. Dynamic bSSFP images (approximately 4 images per second) are acquired while the phantom undergoes a series of preprogrammed motions based on patient lung tumor motion data. These images are autocontoured off-line using our algorithm. The fidelity of autocontouring is assessed by comparing autocontoured tumor shape and its centroid position to the actual tumor shape and its position.

Results: The algorithm successfully contoured the shape of a moving tumor model from dynamic MR images acquired every 275 ms. Dice’s coefficients of $>0.96$ and $>0.93$ are achieved in 0.5 and 0.2 T equivalent images, respectively. Also, the algorithm tracked tumor position during dynamic studies, with root mean squared error (RMSE) values of $<0.55$ and $<0.92$ mm for 0.5 and 0.2 T equivalent images, respectively. Autocontouring speed is approximately 5 ms for each image.

Conclusions: Dice’s coefficients of $>0.96$ and $>0.93$ are achieved between autocontoured and real tumor shapes, and the position of a tumor can be tracked with RMSE values of $<0.55$ and $<0.92$ mm in 0.5 and 0.2 T equivalent images, respectively. These results demonstrate the feasibility of lung tumor autocontouring in low field MR images, and, by extension, intrafractional lung tumor tracking with our laboratory’s linac-MR system. © 2012 American Association of Physicists in Medicine. [DOI: 10.1118/1.3685578]

Key words: intrafraction motion management, lung tumor tracking, linac-MR, MRI guidance, lung tumor phantom

I. INTRODUCTION

Image-guided radiotherapy (IGRT) promises improved targeting and delivery of highly conformal radiation dose to tumors. Using IGRT, interfractional variations due to daily patient positioning errors or changes in anatomy can be monitored and minimized.1 A problem still emerges, however, when treating mobile tumors such as those occurring in lung.
Lung tumors are often difficult to treat due to their potential for large ranges of motion and deformation over time. Various studies have shown that lung tumors may move up to 50 mm in superior–inferior (SI), 15 mm in anterior–posterior (AP), and 10 mm in left–right (LR) directions during normal breathing.\(^2\)\(^-\)\(^4\) Volume changes up to 20% and rotations up to 50° with respect to each axis have also been reported.\(^5\) Unfortunately, a method of directly imaging and tracking lung tumors during actual radiation delivery does not presently exist, and this presents potential limitations to accurate radiotherapy treatments.

Currently, available commercial systems deal with this problem by indirect tracking methods using several types of tumor surrogates. For example, the Varian real-time position management (RPM) system (Varian Inc., Palo Alto, CA)\(^6\) uses a single external surrogate, whereas Cyberknife (Accuray Inc., Sunnyvale, CA)\(^7\) requires both internal and external surrogates. The 4D localization system (Calypso Medical, Seattle, WA)\(^8\) uses electromagnetic transponders called “beacons” as internal surrogates, and the real-time tumor-tracking radiation therapy (RT-RT) system (Hokkaido University, Sapporo, Japan)\(^9\) requires internal seeds and orthogonal kV imaging to perform tumor tracking. In addition to these commercial systems, several groups are actively researching real-time (i.e., intrafractional) tumor tracking systems.\(^10\)-\(^13\)

Despite the wide variety of techniques currently in use, all current tracking methods remain based on indirect tracking through the use of internal or external tumor surrogates. Reliance on surrogates, however, has been shown to be problematic for accurate tumor tracking for the following reasons: (1) Utilizing internal surrogates requires invasive procedures, and these implanted surrogates have been known to migrate from their initial positions during the course of the radiation treatment\(^14\) and (2) Tracking with external surrogates must rely on ambiguous correlations between internal tumor motion and external surrogate displacement.\(^15\) More importantly, any deformation of tumor shape is completely unknown during treatment.

Due to the indirect nature of these tracking mechanisms, the shape and position of the tumor must be inferred from the location of the surrogates used. Therefore, extended regions surrounding the lesion must be irradiated in order to ensure sufficient target coverage,\(^16\) which includes the uncertainty caused by poor correlation between tumor position and surrogates. This approach, however, can result in (1) unacceptable medical complications due to excessive normal tissue irradiation adjacent to the tumor\(^17\) or (2) poor disease control caused by limiting the therapeutic dose necessary to avoid those complications.

On-line radiotherapy-MR systems, which have been proposed by several groups,\(^18\)-\(^21\) may overcome these difficulties by providing direct, intrafractional MR images of tumors without the need for surrogates. Our laboratory reported the first integrated radiotherapy-MR system known as a linac-MR.\(^19\) This system can provide 2D intrafractional MR images including a beam’s eye view depicting the plane of largest tumor motion.

Time consuming, manual contouring of tumor shape would effectively negate the potential advantages of fast tumor imaging. Thus a rapid and reliable tumor autocontouring algorithm is required in order to perform useful intrafractional tumor tracking. This algorithm must detect tumor shape and position in each intrafractional MR image during treatment, thus allowing for appropriate intrafractional radiation beam adjustment.

In this study, we investigate the feasibility of online autocontouring of tumor in MR images by means of a phantom and simulation study. This investigation is focused primarily on the requirements for lung tumor autocontouring in low field MR images, at 0.2 and 0.5 T. The development of an MR compatible, lung tumor motion phantom is also presented.

II. MATERIALS AND METHODS

Section II A describes our autocontouring algorithm. Section II B describes the fabrication of an MR compatible motion phantom incorporating a lung tumor like target imbedded in lung analogue materials, which is used to simulate lung tumor MR images at low fields. These images are used to evaluate the tracking performance of our algorithm, which is detailed in Sec. II C.

II.A. Lung tumor autocontouring algorithm

An autocontouring algorithm was developed to determine both the position and shape of a lung tumor from each intrafractional MR image. The algorithm was developed in accordance with the following scenario: (1) A pretreatment, dynamic MR scan is performed with the treatment unit (i.e., linac-MR), using the same MR sequence and patient setup intended for treatment. (2) During treatment, the linac-MR will provide 2D intrafractional, dynamic MR imaging of a lung tumor. The plane of MR imaging will be selected to visualize the maximum tumor dimensions for the beam’s eye view. (3) MR images will be acquired at an imaging rate of 3–4 fps. This rate is the minimum requirement for lung tumor tracking based on AAPM Task Group 76 report,\(^22\) which recommended less than 500 ms time delay (including 100–200 ms beam repositioning time) between acquisition of tumor position and beam repositioning in order to take clear advantage of real-time tracking over other tracking methods. To satisfy this, the tumor position must be updated approximately every 300 ms, which is the imaging rate assumed in this study.

Figure 1 illustrates the step-by-step autocontouring processes. In Fig. 1, steps 1–3 describe the pretreatment processes that must occur in preparation for the autocontouring session during treatment (Sec. II A 1). Steps 4–14 describe the main algorithm (Sec. II A 2). Each step of the algorithm is examined using an example lung tumor MR image obtained from a previous study.\(^23\) This image was acquired at 1.5 T with a half-Fourier single-shot turbo-spin-echo sequence, and reprinted in Fig. 2(a) with permission from Eur. J. Radiol. 29, 152–159 (1999). © 1999 Elsevier.
II.A.1. Pretreatment processes (steps 1-3)

In step 1, the pretreatment process commences with the acquisition of pretreatment images. A single image is chosen from these images as an input for steps 2 and 3. This image should be the one image of the series that is least impacted by motion artifacts, often an image at the end of an exhale period.

II.A.1.a. Algorithm initiation (step 2). In step 2, an expert user draws two contours on the pre-treatment image: (1) the lung tumor on the image, which we call a standard region of interest (ROI\textsubscript{std}) as shown in Fig. 2(b), and (2) the region covering the maximum anticipated range of tumor motion, which is herein after referred to as the “Background” as shown in Fig. 2(c). This may be determined by observing the maximum extension tumor movement from the pretreatment MR images over several breathing cycles. During autocontouring, the algorithm expects that the tumor will reside within the Background region of each MR image. Therefore, the pretreatment image must be taken by the treatment unit (e.g., linac-MR) to have the most similar patient anatomy, image size, resolution as

![Fig. 1. Flow chart for overall autocontouring processes.](image)

![Fig. 2. Algorithm initiation (step 2 in Fig. 1). (a) Pretreatment image (b) ROI\textsubscript{std} contour (c) Background contour (d) Background mask.](image)
the one that will be acquired during the autocontouring session. A binary mask (an array of ones and zeros) called “Background mask” is generated as shown in Fig. 2(d), where the delineated region has a pixel value of one.

II.A.I.b. Parameter optimization (step 3). Prior to the autocontouring session for each patient, the following five parameters must be chosen: (1) the scaling factor $f$ in the histogram shifting (HS) algorithm,\textsuperscript{24} (2) kernel size $s$ in the HS algorithm,\textsuperscript{24} (3) unit matrix size $u$ of smoothing filter, (4) number of smoothing operations, and (5) number of dilation operations. The HS algorithm\textsuperscript{24} is used for edge detection or edge enhancement within an image, which performs the following transformation with the choice of 2 parameters $f$ and $s$:

$$X_{k,l}' = X_{k,l} - [f \times \min(X_{\text{kernel}(i,j)})],$$

where $X_{k,l}'$ is the new gray level of the center pixel of a kernel at $(k,l)$, a kernel size $s$ is determined by step 3, $X_{k,l}$ is the original gray level of the center of the kernel located at $(k,l)$. $f$ is the scaling factor between 0 and 1, determined by step 3. $\min(X_{\text{kernel}(i,j)})$ is the minimum pixel value within the kernel $X_{i,j}$ (centered at $k,l$) covering all $(i,j)$ within the size $s$.

These five parameters are optimized in step 3. This is to determine a set of parameters that if the autocontouring is performed with these parameters, the autocontoured tumor shape will be the closest to the tumor shape contoured by an expert user. The parameters vary depending on the MR image characteristics such as signal intensity, contrast, resolution, etc. Therefore, the pretreatment image used in parameter optimization must be taken by the treatment unit (e.g. linac-MR) to have the most similar image characteristics as the one that will be acquired during the autocontouring session.

In step 3, an ROI delineated by an expert user (ROI$_{std}$) is compared to an autocontoured tumor shape (ROI$_{auto}$) obtained from the same MR image. Dice’s coefficient ($D$) is used as a measure of similarity, which is defined as:

$$D = 2 \times \frac{\text{Area}(\text{ROI}_{std} \cap \text{ROI}_{auto})}{\{\text{Area}(\text{ROI}_{std}) + \text{Area}(\text{ROI}_{auto})\}}. \quad (1)$$

The goal of optimization is to maximize $D$ as the following:

1. Autocontouring occurs with different possible combinations of the 5 parameters from: $f = 1, 0.95, \ldots, 0.5, s = 10, 15, \ldots, 30\%$ of ROI$_{std}$ size, $u = 3 \times 3$ or $5 \times 5$, number of smoothings $= 0, 1, \ldots, 20$, number of dilations $= 0, 1, \ldots, 20$.

2. From the autocontouring process performed with each combination, an ROI$_{auto}$ is determined. A $D$ value is calculated between the ROI$_{auto}$ and ROI$_{std}$.

3. The combination of parameters that produces the maximum $D$ ($D_{\text{max}}$) is chosen as the optimum combination. Typical $D_{\text{max}}$ values of 0.93–0.95 are achieved at the end of parameter optimization.

II.A.2. Main algorithm (steps 4–14)

After the pretreatment processes are completed, the main algorithm is applied to each intrafractional MR image to contour the tumor. This is an automated process requiring no further input from the user.

II.A.2.a. Background extraction (steps 4–6). Step 4 describes the acquisition and reconstruction of intrafractional MR images by the linac-MR system. Each image will be fed into the algorithm on-line in step 5. In step 6, the algorithm extracts the Background region from the image input as shown in Fig. 3. Subsequent processing from step 7–14 assumes that the tumor will reside within the Background [Fig. 3(c)] during autocontouring.

II.A.2.b. Determination of approximate tumor position (steps 7 and 8). The Background contains a tumor as well as a large amount of undesirable anatomy surrounding the tumor (e.g., blood vessels, normal lung parenchyma, etc). Steps 7 and 8 are implemented to minimize the undesirable anatomy presented to the subsequent steps (steps 9–14), so that the interference from the surrounding anatomy can be minimized in determination of the tumor shape. Also, because the subsequent steps are applied only to the result of step 8 that could be considerably smaller than the entire Background, less computing time is required.

In step 7, a fast normalized cross-correlation (FNCC)\textsuperscript{25} is applied between the ROI$_{std}$, i.e., a portion of Fig. 2(b) enclosed by ROI$_{std}$ contour, and the Background shown in Fig. 3(c). In step 8, a square portion of the Background [Fig. 3(c)] is extracted, where the center of the square is located at the coordinate of the maximum correlation coefficient. The size of this square is user adjustable, but calculated to match 120% of the ROI$_{std}$ size as a default. This is a conservative approach for minimizing the influence of the surrounding anatomy on the subsequent steps.

![Fig. 3. Background extraction (step 6 in Fig. 1). (a) Each MR image, (b) Background mask from step 2, and (c) Background (extracted by multiplying each MR image and the Background mask.)](image-url)
assumption based on a study by Plathow et al.\textsuperscript{5} that provides an adequate coverage for tumor volume changes during autocontouring. The coordinate of the maximum correlation coefficient indicates an approximate tumor position within the Background. However, this may not exactly be the center of the tumor, because the tumor shape in each MR image is expected to change during treatment, whereas the ROI\_std stays the same. Hence, the coordinate of the maximum correlation coefficient may not always coincide with the center of the tumor.

\section*{II.A.2.c. Determination of tumor shape (steps 9–14).}
The output of step 8 is shown in Fig. 4(a), which is a square portion (240\% of the ROI\_std size) extracted from the Background. This is referred as the “most probable tumor region.” In this report, 240\% is chosen for better visualization of the surrounding anatomy of the tumor and the results of subsequent steps [Figs. 4(b)–4(f)]. The following steps are applied to the output of Step 8 to determine the tumor shape:

1. In Step 9, the HS algorithm\textsuperscript{24} is applied to the most probable tumor region for edge enhancement. The result is shown in Fig. 4(b).

2. In Step 10, a pixel threshold method is used to transform Fig. 4(b) into a binary mask as shown in Fig. 4(c). A pixel threshold value is calculated by the Otsu’s method\textsuperscript{26} which finds an optimal threshold from a gray-level histogram that will maximize the separation between the two classes such as background and objects. There is no other parameter involved in this step. The result of thresholding undergoes a morphological closing\textsuperscript{27} operation in step 11.

3. The result of step 11 is shown in Fig. 4(d), which contains many isolated pixel clusters in addition to the tumor. In step 12, the algorithm determines only the tumor shape and rejects other pixel clusters. This occurs by selecting the pixel cluster containing the coordinate of maximum correlation coefficient obtained from step 7, which represents the most likely position of the tumor. The result is shown in Fig. 4(e).

4. In step 13, a final tumor shape is determined by applying morphological smoothing and dilation operations.\textsuperscript{27} A unit matrix size $u$ for the smoothing filter, the number of smoothing, and the number of dilation operations was predetermined from step 3.

5. In step 14, the outer edge of the tumor shape is delineated by applying a morphological gradient operation.\textsuperscript{27} A typical result is shown in Fig. 5(c) for the sample image used in this report.

\section*{II.B. Simulating low field contrast-to-noise ratio (CNR) of lung tumor in a clinical 3 T system}
To evaluate the performance of our autocontouring algorithm, phantom images were acquired which would best reflect the image quality characteristic of lung tumor MR images at low fields with special attention to contrast-to-noise ratio (CNR). Further, as our laboratory’s linac-MR designs are based on low field MR systems (0.5 and 0.2 T), the performance of our autocontouring algorithm must be evaluated in these situations. Hence, a series of experiments were devised to image a special lung contrast phantom in a high-field clinical scanner (Achieva 3 T, Philips Medical Systems, Andover, MA), which could then be used to simulate the relative signal levels and relaxation behaviors of a lung tumor and normal lung parenchyma at arbitrarily chosen lower fields.
II.B.1. MR contrast parameters and CNR

The ability to distinguish two different types of tissues in an image is largely dependent on CNR. In the case of a lung tumor, even if the contrast between lung tumor and normal lung parenchyma is substantial, excessive noise can hamper clear distinction of the tumor. Also, even if the noise is low, it will be difficult to make a clear distinction of the tumor with insufficient contrast.

In MRI, the relationship between CNR and $B_0$ (polarizing magnetic field strength) is generally complex. CNR is also closely related to signal–to–noise ratio (SNR) as:

$$\text{CNR} = \frac{S_T - S_N}{\sigma} = (\text{SNR}_T - \text{SNR}_N), \quad (2)$$

where $S_T$ and $S_N$ refer to the MR signal of lung tumor and normal lung parenchyma respectively, and $\sigma$ is the noise measured as the standard deviation of a region with uniform background signal. SNR$_T$ and SNR$_N$ are the signal to noise ratios for the tumor and normal parenchyma, respectively. The difference between $S_T$ and $S_N$ arise from several factors intrinsic to tissue type, including NMR relaxation parameters that vary in a nonlinear fashion with respect to $B_0$.

One of the contributions to signal difference (i.e., contrast) in Eq. (2) is relative proton density (PD). PD for lung parenchyma is reported to be roughly 0.2–0.35 relative to muscle,28 whereas PD of lung tumor is very similar to muscle at 1.04.29 From these values, one can infer that the lung parenchyma will have a relative PD to tumor of 0.19–0.34. This large difference contributes to the high inherent contrast in the imaging of solid lung tumors. Other intrinsic factors such as the spin–spin relaxation times ($T_2$), spin-lattice relaxation times ($T_1$), and $T_2^*$ relaxation times also affect contrast to a certain extent depending on sequence type, chosen parameters (TE/TR), and the strength of $B_0$.

Investigations into NMR relaxation times of lung tumor and normal lung parenchyma, and their dependencies on $B_0$ have been published in the literature30 as the following:

(1) At lower magnetic field strengths, $T_1$ for normal lung parenchyma and lung tumor are expected to be $455 \pm 86$ and $372 \pm 185$ ms at 0.2 T ($\Delta T_1$ of 83 ms) respectively, compared to $599 \pm 114$ and $532 \pm 271$ ms at 0.5 T ($\Delta T_1$ of 68 ms), and $829 \pm 157$ and $826 \pm 421$ ms at 1.5 T ($\Delta T_1$ of 3 ms).30 Therefore, from the point of view of $T_1$ alone, the shorter $T_1$ at lower fields offer a relative signal enhancement due to the more rapid recovery of longitudinal magnetization. Also, the greater difference in $T_1$ between the two tissues ($\Delta T_1$) at low fields may lead to more favorable tumor contrast.

(2) $T_2$ for normal lung parenchyma and lung tumor are quite similar, $79 \pm 29$ and $68 \pm 45$ ms respectively, and have only minor dependencies on $B_0$.30

(3) $T_2^*$ for normal lung parenchyma is known to be significantly longer at lower fields31 and may lead to increased signal for some sequences. As solid lung tumors are less sensitive to susceptibility effects that arise from air-tissue interfaces, they will have a considerably higher $T_2^*$ compared to lung parenchyma,32 and are likely to be less sensitive to change in $B_0$. Nevertheless, our dynamic MR sequence of choice, balanced steady state free precession (bSSFP), is largely independent of $T_2^*$, so its impact will be limited.33

$B_0$ affects SNR, and, by extension, the CNR in MR images [Eq. (2)]. MR signal is proportional to $B_0^2$ due to two complementary factors:34 (1) the difference in population of the two spin states increases linearly with $B_0$ and (2) the increase of Larmor frequency ($\propto B_0$) generates greater flux in MR coils by Faraday induction. However, MR noise is also known to be dependent on Larmor frequency.34 MR noise arises from resistance in the coils and electronics ($\propto B_0^2$), and resistance from the body ($\propto B_0$).34 For our range of $B_0$ (scaling down from 3 T to 0.5/0.2 T), body noise ($\propto B_0$) is likely to be the dominant source of noise.35 Thus, if the effects of different relaxation times can be accounted for in each tissue type (i.e. built into a phantom), a general assumption may be made that SNR$_T$ and SNR$_N$ (and therefore CNR) will vary linearly with $B_0$.

Our approach was to build a lung phantom that replicates the low field (0.2 and 0.5 T) $T_1$ and $T_2$ values of lung tumor and normal lung parenchyma in the 3 T environment. This phantom would also have a correct relative PD between tumor and normal parenchyma. As the appropriate contrast parameters were built into the phantom, images acquired using a 3 T MRI with this phantom will yield the correct low field contrast even if the MR sequence parameters (such as flip angle, TR/TE) are changed. Because these images have correct low field contrast, CNR may be scaled down to the appropriate levels at 0.2 and 0.5 T by the addition of Gaussian noise.

II.B.2. Phantom construction

Our phantom and its experimental setup are shown in Fig. 6. The phantom contains a moving lung compartment within a thorax region. A lung tumor model is located approximately at the center of the lung compartment, and this model is surrounded by simulated normal lung parenchyma. The lung compartment is driven by a programmable motor using a rigid aluminum rod (grounded to the wave-guide), creating 1D motion along the axis of the cylindrical lung compartment similar to the dominant superior–inferior motion of lung tumors.

The lung compartment of the phantom contains two different tissue equivalents, a solid lung tumor and normal lung parenchyma. The idea of creating a specific tissue-equivalent MR phantom is not new. Methods have been devised for creating MR phantoms that can simulate relaxation and dielectric properties of various tissues in the body at 1.5 T.36 However, building a lung parenchyma equivalent phantom is particularly challenging because of its low PD. In general, this cannot be achieved by using standard phantom materials such as solutions, gels and aqueous media. Our lung parenchyma equivalent requires a low relative PD (approximately 0.3) compared to the tumor. To achieve this,
plastic beads (ColorFill vase fillers, ~2 mm diameter) that contribute no MR signal are mixed with porcine skin gelatin in a 70:30 ratio by volume. The resulting mixture has the relative PD similar to lung parenchyma. This is verified by performing a PD-weighted (short TE and long TR) scan on the phantom and comparing the signal of the tumor region and parenchyma regions. \(T_1\) and \(T_2\) relaxation parameters are modified by doping the gelatin with MR contrast agents.

The lung tumor model is a shaped plastic container (40 mm diameter and 0.3 mm wall thickness) filled with a MnCl\(_2\) and CuSO\(_4\):5H\(_2\)O solution. Two different shapes are fabricated; an ideal, spherical tumor shape, and a more realistic, non-spherical tumor shape. An aqueous solution (approximately 100% water) is used in this study as the solid tumor equivalent, even though a real tumor, similar to tissue,\(^{29}\) contains only ~75% water.\(^{37}\) This will result in overestimation of SNRT by 33%. Also, as previously explained, our simulated normal lung parenchyma has correct relative PD to the tumor. Therefore, both SNRT and SNRN is overestimated by 33%, and this will be compensated by adding additional Gaussian noise in the post-processing steps explained later in this report.

Specific concentrations of MnCl\(_2\) and CuSO\(_4\):5H\(_2\)O are required to achieve the \(T_1\) and \(T_2\) relaxation times for 0.5 and 0.2 T as reported by Bottomley \textit{et al.}\(^{30}\) These are: (1) for lung tumor model, 0.020 and 0.016 g/l of MnCl\(_2\) in de-ionized water to generate the equivalent 0.5 and 0.2 T relaxation times respectively; and (2) for normal lung parenchyma, 0.0125 g/l MnCl\(_2\) gel/plastic bead mixture generating 0.5 T relaxation times, and 0.016 g/l MnCl\(_2\) + 0.06 g CuSO\(_4\):5H\(_2\)O gel/plastic mixture producing 0.2 T relaxation times. In addition, 3.6 g/l NaCl is added to all solutions to simulate the electric conductivity of tissues.\(^{38}\) To simulate the “body noise,” the thoracic cage is filled with substantial amounts of materials that have similar electric conductivity to the body. Approximately 121 of generic MR tissue phantom solution (1.25 g/l CuSO\(_4\):5H\(_2\)O + 3.6 g/l of NaCl) is used to simulate coil loading in realistic situations.\(^{38}\)

Relaxation times are determined from experiments in 3 T MRI as the following: (1) \(T_1\) times are measured with a \(T_1\) mapping algorithm using inverse recovery sequence (TE = 11 ms and TR = 1400 ms) with 6 different delay times (\(\tau\) = 100, 200, 300, 400, 500, 600 ms) and (2) \(T_2\) relaxation times are measured with a 32 echo multi-spin-echo sequence (TE = 6.2, 12.4, 18.6 ms, TR = 1048 ms). In Table I, the measured relative PD and relaxation times of our phantom are compared to reported values in the literature.\(^{30}\)

\begin{table}[h]
\centering
\begin{tabular}{lccccc}
\hline
 & \multicolumn{2}{c}{Lung tumor} & \multicolumn{2}{c}{Normal lung parenchyma} \\
 & Literature & Measured & Literature & Measured \\
\hline
\(T_1\) & 372 ± 185 (Ref. 30) & 352 & 455 ± 86 (Ref. 30) & 470 \\
\(T_2\) & 69 ± 45 (Ref. 30) & 67 & 79 ± 29 (Ref. 30) & 83 \\
Relative PD to tumor & N/A & N/A & 0.19–0.34 (Refs. 28 and 29) & 0.27 \\
\hline
\(T_1\) & 532 ± 271 (Ref. 30) & 519 & 599 ± 114 (Ref. 30) & 604 \\
\(T_2\) & 69 ± 45 (Ref. 30) & 61 & 79 ± 29 (Ref. 30) & 97 \\
Relative PD to tumor & N/A & N/A & 0.19–0.34 (Refs. 28 and 29) & 0.30 \\
\hline
\end{tabular}
\caption{MR contrast parameters for 0.2 T (top) and 0.5 T (bottom) contrast phantoms, measured at 3 T.}
\end{table}

II.C. Dynamic MR Study: Evaluation of autocontouring and tracking performance

A series of dynamic studies were performed with the phantom to evaluate the autocontouring algorithm in low field images. In this study, dynamic MR imaging was performed with 3 T MRI replacing the role of linac-MR in step 4 in Fig. 1. Also, autocontouring was performed off-line after a session of dynamic MR imaging was completed.
For the 0.2 T contrast parameters, we created two separate lung compartments differing in tumor shape: a spherical tumor model, and another with an elongated, irregularly shaped tumor model. The same procedure is repeated with the 0.5 T contrast phantom. Hence, the study was performed with four different lung compartments in total. In each case, the lung compartment was moving inside of the thoracic cage during the scan.

The lung compartment was driven in accordance with four different predetermined motion patterns during the dynamic study. The motion patterns used in our dynamic studies are shown in Fig. 7. The first pattern is a sine wave of 40 mm peak-to-peak amplitude and a period of 4 s. This pattern was created to simulate very large amount of regular, predictable lung tumor motion. The other three patterns were obtained from three different patient datasets. Suh et al. analyzed thoracic and abdominal tumor motions from 42 patients using Cyberknife Synchrony (Accuray Incorporated, Sunnyvale, CA). This group provided us with clinical data containing 3D lung tumor positions that were estimated and recorded with a temporal frequency of 25 Hz during actual treatments. Because lung tumors show the largest motions in the superior–inferior (SI) direction, we selected three lung tumor motion patterns that incorporated relatively large SI motions, approximately 15 mm amplitude on average, and with varying periods. Each study took approximately 3 min, and the patterns represent 1D motion of lung tumor in the SI direction.

To provide an independent, reference measurement of tumor position, an optical encoder (model #: AEDR-8300-1Q2, Avago technologies, San Jose, CA) was attached to the thoracic cage as shown in Fig. 6. Paired with the encoder, a reflective code strip (resolution: 180 lines per inch) is attached to the moving compartment that contains the tumor model. Because all other parts of the phantom are stationary, and the tumor model is fixed in the lung compartment, any change in the tumor position in the SI direction is measured by the encoder as a change in counts (1 count ≈ 0.035 mm).

II.C.1. MR imaging sequence

For each motion pattern, we performed the following two MR scans in order: (1) a high resolution turbo-spin-echo (TSE) scan acquired when the tumor is stationary in its starting position, followed by (2) a dynamic bSSFP scan while the tumor is undergoing motion.

A TSE scan (FOV = 40 × 40 cm, voxel size = 0.4 × 0.4 × 4 mm, 5 slices, TE = 87 ms, TR = 1798 ms) was chosen as a reference scan due to its high SNR, very high resolution, and minimal susceptibility to artifacts. The high resolution of this scan allows for visualization of the thin walls (~0.3 mm) of the tumor model, allowing the true shape of the tumor to be easily contoured. The middle slice that covers the largest extent of the tumor is contoured manually and considered as a standard shape in this study.

For dynamic imaging, we used a 2D bSSFP sequence acquired at ~4 fps (identical FOV to TSE scan: 40 × 40 cm, 3.1 × 3.1 × 20 mm, TE = 1.1 ms, TR = 2.2 ms, dynamic scan time = 275 ms) in the coronal plane. Imaging parameters are selected to balance between CNR and spatial resolution while maintaining the imaging speed requirements of ~4 fps. The imaging plane is chosen so that the tumor is near isocenter where distortion is minimized. Prior to each dynamic acquisition, an external synchronization pulse is sent to the optical encoder. Using this pulse, the optical encoder records the position of the tumor at the mid-point of each dynamic scan when the signal acquisition is occurring.

Fig. 7. Motion Patterns used to drive lung compartment. A sine pattern (upper left) and three lung tumor motion patterns from patient data.
at the center of k-space. The first images of the dynamic scans are acquired prior to the commencement of motion, with the phantom in the same position as the reference TSE scan. These images are visually inspected to ensure alignment with the high-resolution TSE image.

MR images were acquired with a six channel Philips torso coil. As parallel imaging is not used in this experiment, noise is approximately uniform in the image. Noise is measured as the standard deviation of each individual image in a 10 × 10 pixel region in the corner of the image containing no signal. To ensure there is no positive noise bias, noise is measured in the real and imaginary images and averaged, rather than measured in the magnitude images only.

II.C.2. Image post processing (CNR modification)

Gaussian noise is added to the images acquired on the 3 T scanner in order to reflect the lower CNR at 0.5 and 0.2 T. Downscaling of CNR from 3 T images could be achieved by amplifying the measured background noise by a factor of 6 and 15 for 0.5 and 0.2 T images, respectively. As mentioned previously, noise is increased by another 33% to account for the difference in absolute PD between real solid tumors and the aqueous tumor model used in our phantom. Combining these two corrections, noise amplification factors of 8 and 20 were applied to simulate the 0.5 and 0.2 T images, respectively. Assuming statistical independence, the standard deviation of the added noise can be derived from the standard deviation of measured noise,

\[
\langle N \cdot \sigma_{\text{meas}} \rangle^2 = \sigma_{\text{meas}}^2 + \sigma_{\text{added}}^2, \tag{3}
\]

\[
\sigma_{\text{added}} = \sqrt{N^2 - 1} \cdot \sigma_{\text{meas}}, \tag{4}
\]

where \( N \) is the noise amplification factor and \( \sigma_{\text{meas}} \) and \( \sigma_{\text{added}} \) are the standard deviation of the measured and added noise, respectively. Noise is independently measured and amplified in the real and imaginary images and combined to generate the magnitude image. After noise addition, the image is interpolated to a 256 × 256 matrix prior to autocontouring.

II.C.3. CNR measurements

At the end of each dynamic scan (~3 min), an extra set of 100 dynamic images is acquired. This was performed when the phantom is stationary, located at the last position of the motion pattern. As a result, 16 different sets of images (2 tumor models × 2 field strengths × 4 motion patterns = 16 sets) were obtained, each set containing 100 images. Using these, CNR is measured for each set. The mean pixel values in the regions of interest within the tumor and the surrounding tissue were taken, as the value of \( S_T \) and \( S_N \) in Eq. (2), respectively. Noise is measured as the standard deviation of pixels in a 10 × 10 region in the corner of the real and imaginary images. This noise measurement is performed after noise has been added for CNR modification, but prior to the 256 × 256 interpolation.

II.C.4. Data analysis

For each dynamic study (~600 images), the post processed images are fed into the autocontouring algorithm offline. These images are autocontoured with the following parameters: (1) 0.2 T images \((f = 0.6, s = 11 \times 11, u = 5 \times 5, 9\) smoothings, 0 dilations), (2) 0.5 T images \((f = 0.7, s = 11 \times 11, u = 5 \times 5, 9\) smoothings, 0 dilations). There are no considerable changes in these values for both field strengths. The algorithm returns an autocontoured tumor shape and its centroid from each image, and these results were used to evaluate the autocontouring and tracking performance of our algorithm. The following two steps (Secs. II C 4 a and II C 4 b) were applied to each dynamic study.

II.C.4.a. Contour shape fidelity. To evaluate the quality of the contours generated from the autocontouring algorithm, we first manually contoured the tumor in a reference TSE scan Fig. 8. From this manual contour, a binary mask was generated, and considered as a standard tumor shape. The optical encoder readings were used to linearly translate this mask, generating a standard set of masks that corresponds to the standard tumor shape in each dynamic image. Similarly,

FIG. 8. First row, from left to right: (1) High Resolution, static TSE scan (spherical tumor, middle slice) for reference. (2) Lower resolution, dynamic bSSFP scan (noise added, 0.5 T equivalent). (3) High Resolution, static TSE scan (non spherical tumor, middle slice). (4) Lower resolution, dynamic bSSFP scan (noise added, 0.5 T equivalent). Second row: equivalent images for 0.2 T experiments.
a set of autocontoured masks is produced from the autocontouring algorithm.

The autocontoured mask has lower resolution (256 × 256) than the manually contoured mask (1024 × 1024). For comparison, the low resolution mask is resampled to 1024 × 1024 resolution using the nearest neighbor method, which maintains the pixilated appearance of the low resolution image. We performed one-to-one comparison of the tumor shape between the two sets of masks, and their similarities are evaluated by calculating Dice’s coefficient as previously described in Sec. II A 1 b [Eq. (1)].

II.C.4.b. Centroid position accuracy. We also evaluated the algorithm’s ability to accurately determine and track the centroid position of a moving tumor. First, we determined an initial centroid position of the tumor from a high resolution image. This image was acquired when the tumor was located on its initial position of the motion pattern, and the tumor shape was manually contoured. The initial centroid position served as the reference point (i.e., zero count) for optical encoder reading. Second, the tumor position change during each dynamic acquisition was continuously recorded by the encoder. As previously explained, the encoder reads the tumor position when the signal acquisition is occurring at the center of k-space. Third, the centroid position of the tumor in each dynamic image was determined by the autocontouring algorithm. Last, a one-to-one comparison of the centroid position of the tumor in each image was made between the encoder reading and the result from our algorithm.

Mean and standard deviation of the difference between the two (either positive or negative) are calculated from all the images within the motion pattern. Root mean square error (RMSE) is also calculated to give an indication of overall error as:

\[ e_{\text{RMS}} = \sqrt{\frac{\sum_{i=1}^{n} (y_{i,\text{centroid}} - y_{i,\text{encoder}})^2}{n}} \]

where \( y_{i,\text{centroid}} \) is the centroid position of the autocontoured tumor and \( y_{i,\text{encoder}} \) is the position of the tumor measured by the optical encoding device.

III. RESULTS AND DISCUSSION

III.A. Simulated lung tumor images with low field CNR

A close up view of the tumor and its surrounding tissue acquired using TSE and post processed bSSFP are shown in Fig. 8. As predicted, the thin wall of tumor container is visualized by the high resolution TSE scan to aid in manual contouring, but it is not detected in the bSSFP image to affect the autocontouring algorithm.

III.B. CNR of acquired images

After the images are acquired at 3 T, noise is added to generate 0.2 and 0.5 T equivalent images Fig. 9. The CNR of these images are shown in Table II. In summary, the measured CNR ranges from 10.3 to 12.3 for 0.5 T images and from 4.2 to 4.5 for 0.2 T images.

III.C. Contour shape fidelity

Dice’s coefficients for the phantom experiment are shown in Table III. Dice’s coefficient of > 0.96 is achieved in the

| Table II. CNR for spherical and non spherical tumor models in 0.5 and 0.2 T equivalent images. The standard deviation of the CNR is given in brackets. |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
|                 | 0.5 T CNR        |                 | 0.2 T CNR        |                 |
|                 | Spherical tumor  | Non spherical tumor | Spherical tumor  | Non spherical tumor |
| No motion       | 12.3 (0.9)       | 10.3 (0.8)      | 4.3 (0.4)       | 4.5 (0.4)        |
| Sine pattern    | 12.3 (1.0)       | 10.5 (0.9)      | 4.4 (0.3)       | 4.4 (0.4)        |
| Patient pattern 1 | 12.1 (1.0)       | 10.7 (0.8)      | 4.4 (0.4)       | 4.3 (0.3)        |
| Patient pattern 2 | 12.1 (1.0)       | 11.2 (0.8)      | 4.4 (0.4)       | 4.3 (0.3)        |
| Patient pattern 3 | 11.9 (0.9)       | 11.2 (0.9)      | 4.2 (0.4)       | 4.2 (0.4)        |
0.5 T equivalent images, and Dice’s coefficient of > 0.93 is achieved in the 0.2 T equivalent images. Approximately 5 ms was required for our algorithm to autocontour the tumor in each dynamic image. The algorithm was coded in LABVIEW 2011 (National Instruments, Austin, TX) and tested on 32 bit computer system (Windows 7, Intel i7-2600 k, 4 GB RAM).

### III.D. Centroid position accuracy

Differences between the centroid positions determined by autocontouring and those from the encoder reading are summarized in Table III. Mean and standard deviation represents the systematic and random errors in tumor tracking, while RMSE is a representation of overall error. RMSE of < 0.55 mm is achieved for 0.5 T equivalent images, whereas RMSE of < 0.92 mm is achieved for 0.2 T equivalent images.

### III.E. Discussion

Intrafractional tumor tracking, especially for lung tumor cases, is of considerable interest. Inspired by the current success of linac-MR systems, a recent study assessed the possibility of MR-based tumor tracking. However, to the best knowledge of the authors, this is the first study exploring the feasibility of intrafractional lung tumor tracking geared towards lower magnetic field strengths. The use of an autocontouring algorithm and an MR compatible lung tumor motion phantom also makes this a unique study.

Our phantom simulates the 0.2/0.5 T relaxation properties of lung tissues and diseased tissues in a 3 T scanner. Using the phantom we approximated the CNR of lung tumor MR images acquired in the 0.2/0.5 T at 4 fps from the well established relationship of $B_0 \times$ SNR and the addition of Gaussian noise. It should be noted that this experiment is not designed to determine the optimal field strength for the linac-MR, but to determine the feasibility of lung tumor autocontouring with images acquired at field strengths for different linac-MR designs (0.2 or 0.5 T).

To evaluate the accuracy of our algorithm, we reported Dice’s coefficient comparing the autocontoured tumor shapes and the standard ones. Simply reporting the total area of the autocontoured tumor shapes and comparing it to the total area of the standard ones is also a possible method of evaluation. However, this does not indicate whether the contours are actually overlapping, which is the most important criteria evaluating the autocontouring performance of our algorithm. We have found instances where two contours yielding a perfect agreement in terms of area comparisons, while not being near perfect in terms of contour comparisons. This may be the result of an overestimated edge in one region of the contour being compensated by an underestimated edge in a different region of the contour, which will produce misleading conclusions evaluating our algorithm. As Dice’s coefficient is determined primarily by the overlapping area, we have found that it is much more sensitive to these types of errors, and is a better indicator of shape fidelity.

Our algorithm achieved high fidelity of autocontoured tumor shape, Dice’s coefficients > 0.96 and > 0.93 in the 0.5 and 0.2 T equivalent images, respectively. Centroid tracking accuracy using our algorithm was measured in terms of...
RMSE values, which were < 0.55 and < 0.92 mm for the 0.5 and 0.2 T equivalent images, respectively. As expected, tumor tracking accuracy is improved by the higher CNR provided at 0.5 T. These results show that our autocontouring algorithm is successful in contouring the lung tumor model in both 0.2 and 0.5 T equivalent images acquired at 3 T with ~ 4 fps imaging rate.

The 0.2/0.5 T equivalent images represent an estimation, based on the best available information, of the achievable tumor CNR at low field scanners acquired at ~ 4 fps. Our results therefore suggest that autocontouring tumor will be feasible in both 0.2 and 0.5 T MR systems. However, there will be inherent variances between individual patients, as well as individual MR scanners and coils. Therefore, patient images that will be acquired at the actual linac-MR may have slightly different CNRs compared with our phantom-based 0.2/0.5 T equivalent images acquired in 3 T. Hence, investigating the autocontouring performance of our algorithm with patient images acquired with the linac-MR will be a subject of future studies.

It is important to note that a very fast autocontouring speed (~ 5 ms for each image) is achieved in this study with a regular 32-bit computer system (Windows 7, Intel i7-2600k, 4 GB RAM). This is an important achievement as minimizing the time delay between tumor detection (i.e., imaging) and actual beam delivery is crucial to the success of a functional intrafractional tumor tracking system.

This study involves the evaluation of our algorithm. A phantom study with exact knowledge of the shape and position of the tumor model is required to validate the algorithm. An advantage of performing this type of phantom study is that it allows for a “gold-standard” measurement for both tumor shape and position, thus permitting the quantification of the autocontouring and tracking capabilities of the algorithm. This is not possible in a patient study mainly due to interobserver and intraobserver variability in contouring, and the difficulties associated with the exact independent determination of position of the tumor within a patient. After this study, patient studies can then be done.

The use of a virtual phantom, i.e., creating new images from an original one with the tumor motion and deformation, was considered to evaluate our algorithm. However, it was felt that more conclusive results would be obtained with an actual phantom instead. It would be difficult to properly simulate, in a virtual phantom, the variations in image characteristics, such as signal intensity, noise, contrast, and motion artifacts that would occur in realistic dynamic MR imaging. Furthermore, there would be some level of subjectivity in simulating tumor motion and deformation which would most probably introduce unrealistic characteristics of the tumor (e.g., sharp edges, etc). These would be difficult to adjust appropriately.

Although, the real phantom study we have reported demonstrated the possible applicability of low field linac-MR systems for the tracking of lung tumors, there still remain several issues that would need to be addressed in future studies:

1. Our phantom is limited to 1D motion in the SI direction, while tumors in patient often have a 3D motion trajectory. In current linac based treatments, as well as in future linac-MR based treatments using our laboratory’s designs, radiation beams rotate around the SI axis of the patient. Hence, if intrafractional MR imaging is performed from the beam’s eye view, the 2D imaging presented here may be sufficient for tumor tracking in SI and one more direction in that imaging plane. In this scenario, our algorithm can be used to detect in-plane changes in tumor position and adjust collimation accordingly.

However, a potential problem that can arise is through-plane tumor motion (motion orthogonal to the imaging plane). Tumors can potentially move out of the imaging plane. Although numerous studies have demonstrated that the largest lung tumor motions occur in SI directions, smaller motions in anterior–posterior and left–right directions could contribute to the out of the imaging plane motion.

Potential solutions to this problem include adjusting the slice thickness of the imaging plane to ensure the tumor remains in the imaging plane. Also, our CNR measurements suggest that at 0.5 T, there is potentially enough CNR (10.3–12.3) to allow image acceleration via various techniques such as parallel imaging. This opens up the possibility to perform intrafractional multislice or 3D imaging, which will be investigated in future studies.

2. Other factors may arise during clinical situations that are not addressed in this phantom study. Tumors may potentially rotate or change shape during respiratory motion. Also, during dynamic MR imaging, tumor contrast may fluctuate due to compression and expansion of lung between images. No current state of the art tumor tracking methods has the ability to account for these changes.

Nevertheless, our autocontouring algorithm deals with the possible deformations of the tumor shape, as well as interimage tumor contrast changes. Our algorithm contours each image individually without the need of a priori assumptions regarding tumor shape or contrast. The algorithm’s performance for autocontouring solid, moving tumors in low field dynamic MR imaging is reasonable with Dice’s coefficients > 0.96 and > 0.93 in 0.5 and 0.2 T equivalent images. However, the algorithm’s performance with shape deformations and contrast fluctuations in real patients’ images still require further investigation.

3. Our contrast phantoms, imaged in a 3 T MRI, and subsequent noise addition, resulted in an expected CNR of 4.2–4.5 and of 10.3–12.3 from 0.2 and 0.5 T systems, respectively. However, several factors can actually lead to an improvement in image quality in low field MRI. First, in our experiments, the flip angle is limited by specific absorption rate (SAR) safety limits due to the very short TR required for fast imaging. SAR is proportional to the square of the main magnetic field, so the diminished SAR at low fields will allow greater freedom in choosing flip angles. This may enhance the CNR in
bSSFP images. Second, banding artifacts, while not affecting the central area of the tumor in our scans, are clearly visible in the periphery of the image in 3 T. These banding artifacts will be considerably less severe in a low field MRI due to the improved local field homogeneity.

Geometric distortion is a potential problem for MRI based radiation therapy. Our experimental protocol is set up such that the optical encoder is calibrated to the reference scan. This is acquired prior to the dynamic scan, with the phantom located at the starting position of the dynamic scan. Because geometric distortion is spatially dependent, it is possible that the tumor shown in the MR image is misplaced from its actual position as the phantom moves. Nevertheless, the optical encoder reading is independent and not affected by geometric distortion. Therefore, any tumor positional error due to geometric distortion is encapsulated by our centroid error measurements reported in Sec. III D, which is < 0.92 mm for all measurements. Geometric distortion in our experiments is relatively minor, mainly because the tumor model trajectory of our phantom is located near the isocenter of the magnet where automatic shimming from the MR system could eliminate most of the magnetic field inhomogeneity. In a patient study where the tumor could be potentially located far from the isocenter of the magnet, i.e., left or right periphery of lung, geometric distortion might be considerably larger. In this case, a more sophisticated geometric distortion correction method will be required.

IV. CONCLUSION

We have developed a lung tumor autocontouring algorithm and evaluated its performance in low field MR images (0.2 and 0.5 T). In our experiments, the algorithm successfully contoured the shape of a moving tumor from dynamic MR images acquired at 275 ms intervals. Dice’s coefficients of > 0.96 and > 0.93 are achieved in 0.5 and 0.2 T equivalent images respectively, where autocontouring takes approximately 5 ms for each image. Also, the algorithm was able to track the tumor position during dynamic studies, with RMSE values of < 0.55 mm and < 0.92 mm for 0.5 and 0.2 T equivalent images, respectively. These results demonstrate the feasibility of lung tumor autocontouring in low field MR images, and, by extension, intrafractional lung tumor tracking with our laboratory’s linac-MRI systems.

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