Effect of pulse sequence parameter selection on signal strength in positive-contrast MRI markers for MRI-based prostate postimplant assessment

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Purpose: For postimplant dosimetric assessment, computed tomography (CT) is commonly used to identify prostate brachytherapy seeds, at the expense of accurate anatomical contouring. Magnetic resonance imaging (MRI) is superior to CT for anatomical delineation, but identification of the negative-contrast seeds is challenging. Positive-contrast MRI markers were proposed to replace spacers to assist seed localization on MRI images. Visualization of these markers under varying scan parameters was investigated.

Methods: To simulate a clinical scenario, a prostate phantom was implanted with 66 markers and 86 seeds, and imaged on a 3.0T MRI scanner using a 3D fast radiofrequency-spoiled gradient recalled echo acquisition with various combinations of scan parameters. Scan parameters, including flip angle, number of excitations, bandwidth, field-of-view, slice thickness, and encoding steps were systematically varied to study their effects on signal, noise, scan time, image resolution, and artifacts.

Results: The effects of pulse sequence parameter selection on the marker signal strength and image noise were characterized. The authors also examined the tradeoff between signal-to-noise ratio, scan time, and image artifacts, such as the wraparound artifact, susceptibility artifact, chemical shift artifact, and partial volume averaging artifact. Given reasonable scan time and manageable artifacts, the authors recommended scan parameter combinations that can provide robust visualization of the MRI markers.

Conclusions: The recommended MRI pulse sequence protocol allows for consistent visualization of the markers to assist seed localization, potentially enabling MRI-only prostate postimplant dosimetry.

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Key words: MRI, marker, prostate, brachytherapy

1. INTRODUCTION

In low-dose-rate (LDR) prostate brachytherapy, radioactive seeds are permanently implanted into the prostate to treat prostate cancer. Higher quality prostate implants are associated with better patient outcomes following brachytherapy.¹ Dose-volume parameters generated from postimplant dosimetric assessment are widely used as metrics to estimate the implant quality. The accuracy of dose-volume parameters depends on the accuracy of localizing the radioactive seeds and contouring the anatomical volumes on postimplant images. Therefore, postimplant imaging is crucial for ensuring the quality of the implant.

The two main imaging modalities used for postimplant imaging are computed tomography (CT) and magnetic resonance imaging (MRI). CT is useful for identifying the location of the seeds, but presents difficulties for delineating the prostatic capsule^{2,3} and normal tissue may be mistaken for prostate.⁴ Prostate delineation on MRI is associated with less interobserver contouring variability compared to CT,^{2,3} but definitive seed localization remains the main challenge preventing widespread use of MRI as a single-imaging modality for postimplant dosimetry.^{5,6}

MRI-based postimplant dosimetry may be realized by detecting positive-contrast MRI markers next to the seeds and extrapolating the seed positions from marker positions.⁶ The markers do not distort radiation dose,^{7,8} have low toxicity,⁹ and the MRI relaxation properties of the marker-filling material have been well characterized.¹⁰ A pulse sequence with the optimal combination of MRI scan parameters needs to be defined to obtain high marker visibility while balancing against other conflicting factors (such as image acquisition time, spatial resolution, and image artifacts) to provide the best images for postimplant dosimetry, given the significant time and cost associated with MRI.

In the current study, we investigated several user-adjustable scan parameters to determine which parameters yield the most consistent and high-signal visualization of the markers. We investigated the effects of varying flip angle (θ), number of excitations (NEX), receiver bandwidth (BW), field-of-view (FOV), slice thickness (Δz), and encoding steps ($N_x \times N_y$) on the marker's signal strength, image noise level, signal-to-noise ratio (SNR), and spatial resolution. In addition, we noted relevant conflicting factors that may advise against using the parameter value optimized for highest marker signal. A comprehensive and practical understanding of scan parameter adjustments' impact on image quality is important to acquire high-quality postimplant MRI scans for accurate dosimetric assessment.

2. METHODS

Since systematically testing the effects of 70 different scan parameter combinations on patients is not feasible, we performed the testing using a prostate phantom. We implanted a multimodality prostate phantom (Model 053-MM for ultrasound, CT and MRI; CIRS, Norfolk, VA) with 66 MRI markers (Sirius; C4 Imaging, Houston, TX) and 86 dummy seeds in

stranded seed-marker combination using 20 needles (Fig. 1). The phantom was imaged using a 3T MRI scanner [GE Discovery MR750 with 50 mT/m amplitude and 200 T/(m/s) slew rate; GE, Waukesha, WI] and an eight-channel torso coil (GE, Waukesha, WI) with a 3D fast radiofrequency-spoiled gradient recalled echo (FSPGR) sequence, under various combinations of scan parameters. The scan parameters varied here were θ , NEX, BW, FOV, Δz , and $N_x \times N_y$. Echo time (TE) was optimized as the minimum achievable TE to acquire a full echo in the frequency-encoding direction and repetition time (TR) was automatically minimized. We systematically studied the marker signal as a function of each parameter of interest by keeping all other parameters constant at baseline values (Table I).

Image processing was performed in MATLAB 8.1.0 (The Mathworks, Inc., Natick, MA). On the magnitude reconstructed images, we recorded the maximum signal intensities for each of the 66 markers to calculate the average and standard deviation of the marker signal intensity. We plotted average marker signal against the various scan parameters, with error bars denoting the marker signal standard deviation. We also recorded the standard deviation of a 50×50 (2500 pixels) rectangular region-of-interest without artifacts in air, per the National Electrical Manufacturers Association (NEMA)¹¹ image noise evaluation method 4. The SNR was calculated as the ratio of average marker signal intensity to the standard deviation in air. We plotted marker SNR against the various scan parameters, with error bars denoting propagated uncertainty from the marker signal. All signal, noise, or SNR values were normalized to the signal, noise, or SNR values obtained using baseline imaging parameters.

Image resolution refers to the pixel size of the output image. In-plane spatial resolution depends on the FOV and the number of encoding steps, while through-plane spatial resolution depends on the slice thickness. To determine whether there was a significant relationship between a certain scan parameter versus signal, noise, or SNR, we performed a linear regression t -test at significance level = 0.01 with the null hypothesis that the slope parameter of a simple linear regression model was zero against the alternative hypothesis that the slope was not zero. The assumptions made were that signal, noise, or SNR has a linear relationship to a certain scan parameter, independent of the scan parameter, has the same probability distribution standard deviation, and roughly normally distributed.

3. RESULTS

3.A. Flip angle, θ

The signal is strongly dependent on θ , following the trend predicted by the spoiled gradient recalled echo sequence equation:

$$\hat{\rho} = \rho_0 \sin \theta \frac{(1 - e^{-TR/T_1})}{(1 - e^{-TR/T_1 \cos \theta})} e^{-TE/T_2^*}. \quad (1)$$

From Fig. 2(a), the θ that provided the highest marker signal was 14° , while noise was not significantly affected by θ (slope = -0.0019 , $p = 0.0554$). Owing to the constancy in

FIG. 1. Materials used in our study. (a) Dummy seeds and MRI markers. (b) Seed-marker strand. (c) Implanted CIRS multimodality prostate phantom. (d) MRI scan of the prostate phantom acquired with baseline scan parameters. (e) Zoomed-in view of the prostate. The seeds appear as hypointense voids while markers appear as hyperintense spots. (Scale denotes 1 cm.)

noise levels across varying θ , the marker's SNR reflects the measured marker signal, and the θ that provided the highest marker SNR was 12° [Fig. 2(b)]. TE, TR, and scan time were longer at larger θ [Fig. 2(c)]. At very small and very large θ , the marker SNR was reduced [Fig. 2(d)].

3.B. Number of excitations, NEX

Except at NEX = 1 where the signal was lower, the average signal was not significantly affected by varying NEX (slope = -0.0022 , $p = 0.0188$), while the average noise was reduced by $1/\sqrt{\text{NEX}}$ [Fig. 3(a)]. SNR was thus improved by $\sqrt{\text{NEX}}$ [Fig. 3(b)]. Varying NEX did not affect TE and TR, but scan time was proportionally increased [Fig. 3(c)]. Since noise was reduced at higher NEX, image quality was improved at higher NEX [Fig. 3(d)].

3.C. Bandwidth, BW

For BW ≥ 244.14 Hz/pixel, the signal increased with $\sqrt{\text{BW}}$; for BW < 244.14 Hz/pixel, the measured signal was greater than expected, with increasing signal at smaller BW until 162.77 Hz/pixel, then decreasing signal at smaller BW [Fig. 4(a)]. Narrower BW was associated with lower noise [Fig. 4(a)]. SNR decreased with increasing BW and then

leveled off starting at 244.14 Hz/pixel [Fig. 4(b)]. At BW < 244.14 Hz/pixel, increasing BW decreased TR and scan times, while at BW ≥ 244.14 Hz/pixel, increasing BW increased TR and scan times; at BW < 162.77 Hz/pixel, increasing BW decreased TE [Fig. 4(c)]. At very narrow BW, SNR was higher but prominent marker displacement in the frequency-encoding direction due to chemical shift artifact was observed [Figs. 4(d) and 5]. At narrower BW, the shift artifact observed in the frequency-encoding direction was greater (Fig. 5). For BW ≥ 122.07 Hz/pixel, the mean marker displacements were < 1 mm; for BW ≥ 325.508 Hz/pixel, the mean marker displacements were < 0.2 mm (Fig. 5). At wider BW, chemical shift and susceptibility artifacts were reduced.

3.D. Field-of-view, FOV

Smaller FOV was associated with increased signal, but also increased noise [Fig. 6(a)]. SNR was slightly higher at smaller FOV [Fig. 6(b)], at the expense of longer scan times [Fig. 6(c)]. Using smaller FOV, spatial resolution was improved [Fig. 6(d)].

3.E. Slice thickness, Δz

Using smaller Δz , the signal was higher but the noise was also higher [Fig. 7(a)]. Therefore, over varying effective $\Delta z \leq 1.5$ mm (reconstructed marker's active length), there was no significant change in SNR (slope = -0.0376 , $p = 0.2707$) [Fig. 7(b)]. Using thin slices did not affect TE and TR, but to cover the same volume, more slices and longer scan times were needed [Fig. 7(c)]. The partial volume artifact was more severe at larger Δz [Fig. 7(d)].

3.F. Encoding steps, $N_x \times N_y$

Encoding steps relate directly to the number of pixels in the x and y directions. At higher $N_x \times N_y$, the signal was higher, but the noise was also higher [Fig. 8(a)]. The SNR increased with $N_x \times N_y$, but leveled off beyond 320×320 , where the acquisition pixel size is smaller than the marker's active cross-section [Fig. 8(b)]. Higher $N_x \times N_y$ required longer TR, and scan time increased proportionally [Fig. 8(c)]. The in-plane resolution is greater with higher $N_x \times N_y$ [Fig. 8(d)].

Increasing N_x increased the signal, but the noise increased as well [Fig. 9(a)]. SNR increased with increasing N_x , but leveled off beyond 320×320 , where the acquisition pixel size

TABLE I. Scan parameters investigated (baseline values are bolded).

Scan parameters	
θ°	4, 8, 12, 14, 16, 18, 20 , 22, 30, 40, 50, 60
NEX ^a	1, 2, 3, 4, 5, 6, 7, 8 , 9, 10, 15, 20, 25
BW ($\pm$ kHz)	19.23, 31.25, 41.67, 50.00, 62.50, 83.33 , 90.91, 100.00, 111.10, 125.00, 142.86
FOV (cm) ^b	8, 10, 12, 14 , 16, 18, 20
Δz (mm) ^c	1, 1.2, 1.4, 1.6, 2 , 3, 4, 5, 6, 7, 8, 9, 10
$N_x \times N_y$ ^d	140 $\times$ 140, 160 $\times$ 160, 160 $\times$ 256, 192 $\times$ 192, 224 $\times$ 224, 256 $\times$ 160, 256 $\times$ 192, 256 $\times$ 224, 256 $\times$ 256 , 320 $\times$ 320, 320 $\times$ 256, 384 $\times$ 256, 384 $\times$ 384, 512 $\times$ 256, 512 $\times$ 512
TE (ms)	2.3
TR (ms)	5.9
Scan time (min)	7.3

^aHalved due to phase oversampling.

^bSquare FOV.

^cInterpolated to half the specified Δz .

^dInterpolated to 512 $\times$ 512.

FIG. 2. The effect of varying flip angle on: (a) normalized marker signal and normalized image noise, (b) normalized marker SNR [theoretical line plotted according to Eq. (1)], (c) TE, TR, and scan times, and (d) visual appearance of images. (NEX = 8, BW = ± 83.33 kHz, FOV = 14 cm, Δz = 2 mm, $N_x \times N_y$ = 256×256 .)

was smaller than the marker's active cross-section [Fig. 9(b)], but scan time increased proportionally [Fig. 9(c)]. The markers were still visible at low N_x , but image resolution was poor [Fig. 9(d)].

Increasing N_y increased the signal proportionally and increased the noise by $\sqrt{N_y}$ [Fig. 10(a)], resulting in a net $\sqrt{N_y}$ increase in SNR [Fig. 10(b)], at the expense of proportional increase in scan time [Fig. 10(c)]. The in-plane resolution at high N_y was better [Fig. 10(d)].

4. DISCUSSION

To obtain the desired image contrast, the user has the capability to adjust several parameters of a pulse sequence,

depending on the suitability to the specified pulse sequence template file, variations in imaging technique implementation, and hardware performance limits. In this study, we examined all user-adjustable scan parameters of the spoiled gradient recalled echo pulse sequence on a GE 3T scanner in normal scanning mode. All markers were detected on images acquired using the scan parameter combinations examined, but the extent of the marker visibility and conspicuity varied depending on the selected scan parameter combinations. The scan parameters should be chosen based on evaluating the trade-offs between marker visibility, resolution, scan time, and artifacts. The extent of marker visibility and image quality due to variations of θ , NEX, BW, FOV, Δz , and $N_x \times N_y$ were evaluated.

FIG. 3. The effect of varying number of excitations on: (a) normalized marker signal and normalized image noise, (b) normalized marker SNR, (c) TE, TR, and scan times, and (d) visual appearance of images. ($\theta = 20^{\circ}$, BW = ± 83.33 kHz, FOV = 14 cm, Δz = 2 mm, $N_x \times N_y$ = 256×256 .)

FIG. 4. The effect of varying bandwidth on: (a) normalized marker signal and normalized image noise, (b) normalized marker SNR, (c) TE, TR, and scan times, and (d) visual appearance of images. Both the chemical shift artifact (black arrows) and seed susceptibility artifact (white arrows) were reduced with increasing bandwidth. ($\theta = 20^\circ$, NEX = 8, FOV = 14 cm, $\Delta z = 2$ mm, $N_x \times N_y = 256 \times 256$.)

4.A. Flip angle, θ

θ is the angle at which the magnetization vector is flipped from the longitudinal axis of the main magnetic field. The signals acquired at $\theta = 12^\circ$ (angle providing greatest signal) and $\theta = 14^\circ$ (angle providing greatest SNR) were not significantly different ($p = 0.4799$). The measured θ that provided the greatest signal was not significantly lower than the theoretical $\theta_E = 16.48^\circ \pm 1.08^\circ$ ($p = 0.2538$). The lower signal measurements [Fig. 2(a)] may be due to nonuniform excitation, that is, radiofrequency field inhomogeneity leading to spatial variation of the flip angle. Smaller θ , characteristic of gradient echo sequences, allows for shorter TR and thus shorter scan times [Fig. 2(c)].

Contrast agents, such as that encapsulated in the marker, interact with nearby hydrogen protons, facilitating the magnetization recovery of the hydrogen protons and shortening the T_1 of the material, resulting in a bright appearance on T_1 -weighted images.¹² Together with TR and the intrinsic T_1 , θ affects the

extent of T_1 -weighting. For $\theta < 12^\circ$, the marker signal falls off very quickly, and becomes similar in signal intensity to the prostate, making the markers less conspicuous [Fig. 2(d)]; hence we do not recommend using $\theta < 12^\circ$. Conversely, for $\theta > 12^\circ$, the reduced regrowth of the longitudinal magnetization may have reduced the signal, but even at very large flip angles up to $\theta = 90^\circ$, the marker signal remained higher than the prostate signal such that the markers can still be visualized [Fig. 2(d)]. Nevertheless, for mean signal reduction of no more than 10% of the maximum marker signal, we recommend not using $\theta > 20^\circ$. Future studies in patients may focus on the contrast separation between the marker and true prostate tissue (see Fig. 1 of the Supplementary material¹⁴ for our prediction that contrast separation would be greatest at $\theta = 17.42^\circ$, using marker¹⁰ $T_1/T_2 = 163.81/102.01$ ms and the literature values¹³ for human prostate $T_1/T_2 = 1597/74$ ms; see Fig. 2 of the Supplementary material¹⁴ for the contrast-to-noise ratio plots based on prostate phantom measurements).

4.B. Number of excitations, NEX

The NEX is the number of times the signal is averaged. However, since we selected the phase-oversampling option (doubled N_y to reduce wrap artifact), NEX was reduced by half to preserve scan time. The signal drop at NEX = 1 [Fig. 3(a)] was most likely due to phase-oversampling requiring the use of fractional NEX imaging where only about half of k -space was sampled. Using more NEX, noise was reduced [Fig. 3(a)], thereby increasing SNR by $\sqrt{\text{NEX}}$ [Fig. 3(b)], consistent with theory. Since NEX is the number of times the scan is repeated, scan time proportionally increases with NEX [Fig. 3(c)]. Therefore, even though the signal using more NEX is greater, it may not be clinically feasible, as the lengthened scan time increases the likelihood of patient motion artifacts. Very high NEX (NEX ≥ 15) has diminishing returns, whereby further

FIG. 5. Shift artifact. At narrower bandwidths, the marker displacement in the frequency-encoding direction due to the chemical shift artifact is greater.

FIG. 6. The effect of varying field-of-view on: (a) normalized marker signal and normalized image noise (vertical line denotes the marker's active cross-section), (b) normalized marker SNR, (c) TE, TR, and scan times, and (d) visual appearance of images. ($\theta = 20^\circ$, NEX = 8, BW = ± 83.33 kHz, $\Delta z = 2$ mm, $N_x \times N_y = 256 \times 256$.)

increases in NEX did not yield significant gain in SNR but scan time still scaled proportionally. Limiting to scan times under 10 min, we recommend using $NEX \leq 10$.

4.C. Bandwidth, BW

BW is the signal sampling rate. For narrow BW (BW < 162.77 Hz/pixel), the sampling time was longer and the TE required was longer [Fig. 4(c)], resulting in more T_2 decay and the subsequent drop in signal [Fig. 4(a)]. Theoretically, signal increases with $\sqrt{BW}$, since bandwidth is the signal sampling rate, at smaller bandwidth, the sampling time is longer,

and the TE required is longer, resulting in more T_2 decay, hence lower signal. However, for BW < 244.14 Hz/pixel, the measured signal being greater than the theoretical prediction [Fig. 4(a)] may be due to the increased TR [Fig. 4(c)]. Generally, narrow BW is associated with lower noise [Fig. 4(a)], the effects of which may outweigh that of increased T_2 decay, thus SNR was improved [Fig. 4(b)]. Theoretically, SNR is proportional to $1/\sqrt{BW}$, as narrower bandwidths allow less noise to pass through.¹² We observed that images acquired with narrow BW had high SNR [Fig. 4(b)], but long scan times [Fig. 4(c)]. Scan times were <10 min for 122.07 Hz/pixel $\leq BW \leq 433.984$ Hz/pixel [Fig. 4(c)].

FIG. 7. The effect of varying slice thickness on: (a) normalized marker signal and normalized image noise (vertical line denotes the marker's reconstructed active length), (b) normalized marker SNR, (c) TE, TR, and scan times, and (d) visual appearance of images. ($\theta = 20^\circ$, NEX = 8, BW = ± 83.33 kHz, FOV = 14 cm, $N_x \times N_y = 256 \times 256$.)

FIG. 8. The effect of varying encoding steps on: (a) normalized marker signal and normalized image noise (vertical line denotes the marker's active cross-section), (b) normalized marker SNR, (c) TE, TR, and scan times, and (d) visual appearance of images. ($\theta = 20^\circ$, NEX = 8, BW = ± 83.33 kHz, FOV = 14 cm, $\Delta z = 2$ mm.)

At narrower BW, there was less noise and higher SNR, while at wider BW, there were less susceptibility artifacts and chemical shift artifacts.¹² For the highest SNR with scan time <10 min and mean marker shift <0.2 mm, we recommend using BW = 325.508 Hz/pixel (± 83.33 kHz). The effect of the shift artifact on dosimetry depends on the seed localization method. If the marker locations were used to extrapolate to the seed locations, the shift extent must be accounted for; if the markers were simply used to confirm that the negative-contrast voids adjacent to positive-contrast markers are seeds, the shift artifact would be less consequential.

4.D. Field-of-view, FOV

The FOV is the area from which the signal is sampled in the defined scan plane. It may be specified in the frequency- and phase-encoding directions on the image. In this study, the FOV refers to a square FOV (full phase FOV). The use of a small FOV corresponded to small voxel sizes. Theoretically, smaller voxel sizes have less spins in the voxel resulting in lower signal. However, we observed higher signal [Fig. 6(a)] and SNR [Fig. 6(b)] at smaller FOV. This is most likely due to the small size of the markers causing the partial volume effect to dominate, whereby higher resolution images allow

FIG. 9. The effect of varying frequency-encoding steps on: (a) normalized marker signal and normalized image noise (vertical line denotes the marker's active cross-section), (b) normalized marker SNR, (c) TE, TR, and scan times, and (d) visual appearance of images. ($\theta = 20^\circ$, NEX = 8, BW = ± 83.33 kHz, FOV = 14 cm, $\Delta z = 2$ mm, $N_y = 256$.)

FIG. 10. The effect of varying phase-encoding steps on: (a) normalized marker signal and normalized image noise (vertical line denotes the marker's active cross-section), (b) normalized marker SNR, (c) TE, TR, and scan times, and (d) visual appearance of images. ($\theta = 20^\circ$, NEX = 8, BW = ± 83.33 kHz, FOV = 14 cm, $\Delta z = 2$ mm, $N_x = 256$.)

partial volume objects that are smaller than the voxel size to be visible¹² [see Fig. 3(a) of the Supplementary material¹⁴ for the resolution at varying FOV]. Smaller voxels were more likely to contain signal from the marker only, resulting in higher signal; larger voxels succumbed to the partial volume artifact whereby marker and nonmarker signals were averaged out, resulting in lower signal [Fig. 6(a)] and lower visibility of the marker [Fig. 6(d)]. The acquisition pixel sizes using FOV = 10 cm and FOV = 12 cm were less than the marker's active cross-sectional area [Fig. 6(a)], and thus may be least subjected to the partial volume artifact. For a fixed BW (range of frequencies from one end to the other end of the image), decreasing the FOV requires a stronger gradient, and longer TR [Fig. 6(c)] owing to the limited gradient power, contributing to higher signal [Fig. 6(a)] but also longer scan times [Fig. 6(c)]. At smaller FOV, in-plane resolution was higher and the markers were more conspicuous [Fig. 6(d)].

Smaller FOV resulted in less partial volume artifact, but was more susceptible to the aliasing/wraparound artifact observed in the phase-encoding direction (see Fig. 4 of the Supplementary material¹⁴ for the wraparound artifact). Phase-oversampling only oversamples one-half of the FOV at each end in the phase-encoding direction, hence signals outside these limits may still wrap into the FOV. To prevent the wrap artifact, larger FOV could be used. However, if a smaller FOV is desired, the use of an endorectal coil may render the wrap artifact less prominent by confining signal reception in a smaller area. At our institution, to increase SNR in patients we sometimes use the Medrad endorectal coil (Bayer Healthcare LLC, Whippany, NJ), but this coil does not fit in the prostate phantom, hence all images in this study were acquired using an eight-channel torso coil (GE, Waukesha, WI) typically used for pelvic exams. Future evaluation of the marker using a smaller-diameter endorectal coil, such as the Sentinelle endorectal coil (Invivo, Gainesville, FL), could be performed in phantom or patients.

4.E. Slice thickness, Δz

Δz is the through-plane resolution. Images with effective $\Delta z = 1.5$ mm were interpolated from images acquired with input $\Delta z = 3.0$ mm, which is the filled length of the marker. This may be why there was no significant change in the SNR for varying effective $\Delta z \leq 1.5$ mm [Fig. 7(b)], but the SNR for effective $\Delta z > 1.5$ mm was statistically significantly lower due to partial volume averaging. At smaller Δz , the same marker could be seen traversing across more slices. The marker appeared brighter at smaller Δz [Fig. 7(d)] because the voxels with marker contain mostly signal from the marker. At very small Δz (effective $\Delta z < 0.7$ mm), the through-plane resolution was improved, but much longer scan time was required to cover the same volume [Fig. 7(c)] and miniscule bubbles in the marker may cause a disjointed artifact that can potentially confound accurate marker localization [see Fig. 5(a) of the Supplementary material¹⁴ for marker appearance across axial slices for varying Δz].

However, very large Δz resulted in the inability to discern marker versus seed due to low through-plane resolution [see Fig. 5(b) of the Supplementary material¹⁴ for the effect of very large Δz]. Extreme partial volume averaging artifact was observed for effective $\Delta z > 2.5$ mm, hence we did not report on the signal, noise, or SNR of the marker on those images. To minimize the disjointed artifact, partial volume artifact and for scan time < 10 min, we recommend effective Δz of 0.7–1.5 mm.

4.F. Encoding steps, $N_x \times N_y$

The frequency- and phase-encoding steps can be transformed to physical dimensions, as spatial locations are encoded by varying frequency and phase across the volume. Theoretically, larger pixel sizes are associated with higher SNR, but in our measurements we observed higher SNR using

smaller pixel sizes, most likely owing to dominance of the partial volume effect [see Figs. 3(b)–3(d) of the Supplementary material¹⁴ for the acquisition pixel sizes in relation to the marker's active cross-sectional area]. For images acquired with encoding steps $\geq 320 \times 320$, which corresponded to the acquisition pixel sizes being less than the marker's active cross-sectional area and minimal partial volume averaging effects, there was no statistically significant difference in SNR [Fig. 8(b)]. To examine the effect of varying $N_x \times N_y$ on signal, noise, and SNR [trend lines in Figs. 8(a) and 8(b)], we examined the effects of varying N_x and N_y separately. With higher $N_x \times N_y$, the in-plane resolution was greater, but scan time was longer [Fig. 8(c)]. Zero filling was used to allow for lower acquisition resolution but increased apparent displayed resolution, and since extra zeroes contain no signal or noise, zero filling should not affect SNR. Large $N_x \times N_y$ requires longer scan times; hence the zero filling process can be used to reduce scanning time without too much SNR loss. For the highest in-plane resolution with scan time < 10 min, we recommend a square 256×256 acquisition matrix (interpolated to 512×512).

The trends of signal, noise, and SNR were inferred from examining the trends of varying N_y only and varying $N_x \times N_y$. Since the frequency-encoding gradient is on during echo sampling, increasing the number of N_x (while keeping BW and sampling interval constant) increases the sampling time, thereby increasing TE, TR, and scan time [Fig. 9(c)]. For $N_x \geq 320$ where the partial volume artifact was minimal, SNR was not affected by varying frequency-encoding steps [Fig. 9(b)]. Although lower N_x shortens scan time [Fig. 9(c)], SNR [Fig. 9(b)] and in-plane resolution [Fig. 9(d)] were reduced due to partial volume averaging effects.

Theoretically, increasing N_y decreases the voxel size thus decreasing the SNR by $1/\sqrt{N_y}$. However, from our measurements, increasing N_y resulted in an increase in SNR by $\sqrt{N_y}$ [Fig. 10(b)]. We postulate that the trends in signal, noise, and SNR observed for varying N_y were heavily determined by the effects of partial volume averaging, whereby smaller voxel sizes contain a greater percentage of marker signals. For our measurements of varying N_y , all the acquisition pixel sizes were greater than the marker's active cross-sectional area; hence all these measurements were subjected to partial volume averaging effects. The 256×256 acquisition matrix yielded acquisition pixel size similar to the marker's active cross-sectional area. Reducing N_y is a common technique to reduce scan time [Fig. 10(c)]. Although lower N_y shortened scan time [Fig. 10(c)], SNR [Fig. 10(b)] and in-plane resolution [Fig. 10(d)] were reduced due to partial volume averaging effects.

In this study, we presented the impact of varying scan parameters on marker visualization and defined the scan parameters that led to best marker visualization. From the range of values we investigated, the highest MRI marker SNR was independently given by flip angle = 12° , NEX = 25 (scan time = 22.9 min), BW = ± 19.23 kHz (shift = 1.42 ± 0.37 mm), and FOV = 12 cm, 384×384 . However, the scan parameters that provided the highest MRI marker SNR may not be the best choice from a practical standpoint. Taking into consideration SNR, scan time, resolution, and artifacts, the recommended

scan parameters are listed in Table II. This phantom study gave us a practical understanding on the impact of scan parameter adjustments on marker visibility, image quality, and scan time, thus allowing for a more directed effort to be made for marker evaluation in patients.

The main limitation of this study is that not every possible combination of all the scan parameters was covered because it would be extremely laborious to acquire images and perform analysis for over 2×10^6 possible combinations of the six scan parameters we studied. Nevertheless, we presented all signal, noise, and SNR values normalized to that acquired using baseline scan parameters (bold font in Table I), so that different plots can be studied together to predict gains/losses in signal, noise, and SNR for the desired combination of scan parameters.

Another limitation of our study is that the metric used was signal instead of contrast, because this study is a phantom study, but contrast is dependent on the prostate and other tissues in the imaging volume. Measuring true contrast between marker and prostate is problematic due to interpatient variation, inpatient variation, scan time, and ethical considerations. Interpatient variation owing to differences in prostate T_1 and T_2 from patient to patient compels all measurements to be done in a single patient to be able to isolate the effect of scan parameter variation from interpatient variation. However, there is also inpatient variation, because different prostate zones exhibit different contrast and the presence of edema enhances regions within the prostate, resulting in the contrast measurements being affected by the marker position within the prostate. Statistics aside, looking at only a single marker in a specified location within the prostate for a single patient, the total continuous scan time of more than 11 h would raise patient discomfort and heating concerns. Our systematic evaluation of the effects on MRI marker signal for 70 different scan parameter combinations in this phantom study guided our evaluation of MRI marker visibility in actual prostate tissue in a separate patient study.

The scan parameter values affect the actual TE and TR used on the GE scanner used for this study. For instance, when changing only the BW at the scanner console in normal scanning mode, any change in signal was not due solely to the change of BW because the TE and TR changed as well [Fig. 4(c)], thus confounding direct prediction of signal behavior from equations and necessitating actual measurement of the signal, as was done in this study. This may be better controlled on other scanner manufacturer platforms.

TABLE II. Recommended scan parameters for high visualization of MRI markers, accounting for scan time, in-plane/through-plane resolution, and artifacts.

Scan parameters	
FA (deg)	12–20
NEX	2–10 (halved due to phase oversampling)
BW (kHz)	± 83.33
FOV (cm)	14–16
Δz (mm)	1.4–3.0 (interpolated to 0.7–1.5)
$N_x \times N_y$	256×256 (interpolated to 512×512)

We reported the trends of scan times for varying scan parameters, as short image acquisition time is a priority, sometimes at the expense of spatial resolution and contrast. Using a gradient echo pulse sequence enables shorter TR and TE values, therefore reducing image acquisition time. The commonly cited drawback of gradient echo pulse sequences is increased susceptibility artifacts; but for postimplant dosimetry, the susceptibility artifact from the seeds result in a characteristic dumbbell appearance that could potentially be used to more definitively locate the seeds based on the distinct susceptibility patterns.¹⁵

Apart from CT-only or MRI-only postimplant dosimetry, another option is MRI-CT fusion, which capitalizes on seed identification on CT images, while still benefiting from soft tissue delineation on MRI scans. However, the accuracy of MRI-CT fusion depends on the registration technique (landmarks used for matching, fusion method, fusion algorithm parameters) and quality of the input data (MRI pulse sequence used, use of intravenous contrast, seed orientations, use of MRI endorectal coil, differences in table on the two imaging modalities, patient travel between CT and MRI scanners, time lapse between the two types of imaging, differences in bladder or rectal filling, pelvic tilt, and prostate edema).^{15–17} Moreover, optimal MRI-CT fusion can be time-consuming, and training of the radiation oncologist, dosimetrist, and/or physicist to identify the relevant anatomical landmarks is required.

MRI-only postimplant dosimetry may be realized using the MRI markers, but the caveats are that the markers can only be used for stranded applications and marker identification is currently done manually. Even with the use of the markers for MRI-based postimplant dosimetry, the true dose distribution may vary between scans due to motion of the internal structures, such as varying amounts of bladder/rectal displacements.¹⁷ This motion can be minimized by the use of glucagon and is reduced in the scanning duration.

To our knowledge, MRI-only postimplant dosimetry is currently not part of any routine clinical workflows. The pulse sequence recommended in this manuscript is for marker visualization toward MRI-only postimplant dosimetry using markers; others have explored pulse sequences for seed visualization toward MRI-only postimplant dosimetry without the use of markers. Dubois *et al.*¹⁸ and Moerland *et al.*¹⁹ first described seed localization on MRIs but lamented the difficulty in consistent seed localization on standard spin echo sequences. By taking advantage of the seeds' high magnetic susceptibility, recent efforts in seed visualization on MRI images include the use of an inversion-recovery with ON-resonant water suppression (IRON) prepulse to spectrally select off-resonant protons,²⁰ the use of ultrashort-TE sequences to preserve signal before rapid transverse dephasing,²¹ the postprocessing use of homodyne high-pass filters of various sizes,^{22,23} the use of susceptibility gradient mapping using the original resolution (SUMO) by filtering in *k*-space,²⁴ the use of a kernel deconvolution algorithm with regularized L_1 minimization²⁵ (the dipole kernel²⁶ and a nominal seed kernel²⁷ have been explored), as well as the use of center-out radial sampling with off-resonance reception (co-RASOR)

that moves the radial signal pile-up to the seed's center (using multiple acquisitions²⁸ and only a single acquisition²⁹). However, imaging susceptibility may be inconsistent across MRI slices, difficult to locate accurately, and more challenging in heterogeneous tissue.²³

Ultimately, MRI-only postimplant dosimetry allows for superior soft tissue contouring, no extraneous radiation dose, image-acquisition flexibility, and possible integration of functional imaging. Regardless of whether MRI-only postimplant dosimetry is achieved using markers⁶ or the other solutions^{18–29} described above, the next step is to explore the impact of MRI soft tissue contrast on the accuracy and precision of anatomical contouring on patient images, so as to examine the correlation of dose deposited in the prostate and normal tissue to tumor control and normal tissue complications. Ultimately, in future patient studies comparing MRI-only to MRI-CT fusion-based postimplant dosimetry, we need to evaluate the improvements in the accuracy and precision of contouring prostate and organs at risk, the accuracy and precision of seed localization, as well as the subsequent accuracy and precision of dose volume histogram parameters, apart from accounting from fusion uncertainties.

5. CONCLUSION

We have evaluated the effects of flip angle, number of excitations, bandwidth, field-of-view, slice thickness, and encoding steps on MRI marker SNR, scan time, resolution, and artifacts in a prostate brachytherapy phantom. The findings of this study may be used to guide MRI protocol development for high marker visibility to obtain useful postimplant dosimetry images in patients.

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CONFLICT OF INTEREST DISCLOSURE

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