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Research article

Efficacy of butylscopolamine in obtaining clear MR image for intensity-modulated radiotherapy for prostate cancer



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ABSTRACT

Purpose: The use of butylscopolamine in magnetic resonance imaging (MRI) of the prostate is controversial in the context of diagnostic imaging where local invasion and the presence of metastases are evaluated. However, in radiation oncology, MRI is performed as part of the simulation process, and the objectives differ to the diagnostic setting. MRI is primarily used for accurate target delineation; hence, the use of an agent to reduce intestinal peristalsis and increase image quality may be beneficial. The impact of butylscopolamine on MRI for radiation oncology purposes has not previously been described. The aim of this study was to evaluate the efficacy of butylscopolamine in MRI acquired for radiation oncology simulation of the prostate.

Methods and materials: In total, 67 patients were enrolled in this study. Thirty-five patients received intramuscular injection of butylscopolamine (group A) and 32 patients did not (group B). Visualization of the prostate outline and detection of fiducial gold markers (GMs) in the prostate were evaluated on MRI. Two blinded radiation oncologists (ROs) and one radiation technologist (RT) scored the image quality of the detection of prostate outline and recognition of GMs in the prostate on a scale of 1–5 (1 = poor; 5 = excellent), and the results were evaluated using Mann–Whitney *U* test and $p < 0.05$ was considered as statistically significant.

Results: On MRI, group A was statistically superior to group B in terms of fiducial marker detection by two ROs ($p < 0.01$). However, there was no significant difference in RT scoring. Furthermore, on MRI, group A was statistically superior to group B in terms of the detection of the prostate outline by an RT.

Conclusions: Butylscopolamine is effective with respect to detection of the prostate outline and GM recognition (without endorectal coil). The addition of butylscopolamine is simple and cost efficient. We recommend the use of butylscopolamine routinely to obtain good MR images, particularly in the detection of GMs.

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Introduction

The use of radiotherapy for prostate cancer is increasing and so is the demand for accuracy with the advent of intensity-modulated radiotherapy (IMRT) and volumetric arc therapy (VMAT). The accurate delineation of the prostate is paramount to high quality radiotherapy. However, contouring the prostate outline using only computed tomography (CT) imaging is difficult; therefore, computed tomography (CT) and magnetic resonance imaging (MRI)

registration with the insertion of a fiducial gold marker (GM) in the prostate gland increases precise registration [1–6].

A set of MRI sequences require approximately 15–20 min. During the scan, the prostate can move as a result of movement in the rectum [7]. However, diagnostic MRI targets not only the prostate but also other organs, such as the iliac lymph node and neurovascular bundle. In the setting of IMRT, the visibility of the prostate outline and GM is very important. The aim of this study was to evaluate usefulness of butylscopolamine to reduce the bowel movement. Movement of the prostate reduced if rectal movement is limited; thus, we hypothesize a resultant improvement in the image quality.

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Methods and materials

This clinical trial was approved by the internal review board; the study was registered with the national UMIN–Clinical Trial Registration (No. 24804). Sixty-seven patients were enrolled in this study from September 2015 to October 2016. All patients provided written informed consent. We did not randomly assign the patients. We sequentially assigned them into two groups based on time. Of these, 35 patients were administered an intramuscular injection of butylscopolamine (Buscopan®; Boehringer Ingelheim International GmbH, 55216 Ingelheim am Rhein, Germany) between February 2016 and October 2016, and the remaining 32 patients did not receive butylscopolamine between September 2015 and January 2016. We retrospectively evaluated patients who did not receive butylscopolamine (group B) and prospectively evaluated those who did (group A). The characteristics of the patients are shown in Table 1. Patients with glaucoma, diabetes, and heart disease were excluded from this study based on physicians' interviews. Butylscopolamine was administered immediately before MRI examination. CT and MRI were acquired 3 weeks after GMs implantation to refrain from prostate edema.

Types of GMs

There were two types of GMs:

Gold Anchor: 0.5% iron-containing, 0.28 mm in diameter, 10 mm in length [Gold Anchor™ (GA); Naslund Medical AB, 14139 Huddinge, Sweden]. VISICOIL: 0.35 mm in diameter and 10 mm in length [VISICOIL (VIS); RadioMed Corporation, Bartlett, TN, USA]. Needle size was 22G for Gold Anchor and 19G for VISICOIL.

Image acquisition

All patients emptied their bowels before CT, MRI, and radiotherapy treatment as per the institutional practice. When gas got collected in the rectum during both planning and cone-beam CT and MRI examination, a nurse exhausted gas in a tube. The patients drank 200 ml of water 30 min before CT (Optima CT580; GE Medical Systems, Milwaukee, WI, USA) and MRI (Intera 1.5 Nova; Philips Medical Systems, Eindhoven, The Netherlands). We used the MR system Achieva Release 3.2 Level 1 3. Therefore, we do the body movement revision in MultiVane Method, and the MRI device does not support the Gradient Recall Echo method, we cannot cope with T2*3D-WI. Moreover, this causes prolongation of the imaging time because we cannot use SENSE together. MRI was performed within 20 min after CT. When urine is accumulated in the bladder, the radiation irradiated to the bladder wall decreases. If the bladder is swollen, then the intestinal tract moves to the head side.

Table 1
Basic characteristics of patients. A: Butylscopolamine-administered group ($n = 35$). B: Non-administered group ($n = 32$).

Group	A	B
Age (years)	72.3 (68–76)	76.1 (62–79)
Race	All Asians	All Asians
<i>Risk (D'Amico classification)</i>		
Low	2	6
Intermediate	12	9
High	21	17
Initial PSA (ng/ml)	21.1	14.8
Gleason score	7.4	7.1
Prostate volume (cc)	34.6	38.1
Hormone therapy	9	6
Chemotherapy	None	None

CT images were acquired as follows: 16-row detector CT; thickness: 1.25 mm; field of view: 40 cm × 40 cm; 120 kV; and 460 mA.

For MRI imaging, two sequences were imaged as follows: MRI was performed with 3 mm section thickness, no intersection gaps, and a 16 cm × 16 cm field of view using a cardiac coil in all cases.

T2-weighted imaging (T2-WI) comprised T2-weighted fast spin-echo. Repetition time (TR)/echo time (TE) range in milliseconds: 4000/80; number of averages (NA): 4; number of phase-encoding steps (PESs): 205; number of frequency-encoding steps (FESs): 256; and typical spatial resolutions (TPRs) of frequency/phase are 0.63/0.80.

T2* three-dimensional-weighted imaging (T2*3D-WI): T2*3D-weighted gradient echo (TR/TE/deltaTE; 37/14/7.3), NA: 2; PESs: 218, FESs: 272; and TPRs of frequency/phase are 0.55/0.54. The total acquisition time was approximately 15 min.

Evaluation of images

From the two sequences acquired, one was selected for analysis based on the visibility of GMs and the prostate. The evaluation points were the outline of the prostate and visibility of GMs on MRI. The radiotherapy equipment in our hospital is a Novalis Tx system (Varian Medical Systems, Inc., Palo Alto, CA, USA).

We estimated a recognition degree of the prostatic outline of CT and MRI as 1: poor; 2: slightly poor; 3: neutral; 4: marginally better; and 5: excellent. In theory, CT image does not affect butylscopolamine. We evaluated CT image for comparison with MRI. The impact of CT artifacts and MRI signal void in the presence of GMs was also rated by the observers. For degree of artifact on CT image, high score was regarded as less artifact, and degree of recognition of the GMs as a signal void in the MRI was scored as 1: poor; 2: slightly poor; 3: neutral; 4: marginally better; and 5: best visible. This study focused on MR image, especially the outline and GM detection. For example, when no signal void was found, it was assigned as score 1; in guidance with CT image, if GM was found, it was assigned as score 3; and when GM was clearly found on only MR image, it was assigned as score 5. GMs are inherently visible on CT, however, sometimes metal artefacts influence the prostate outline. The signal void on MRI by a metal component is important. If the signal void is not recognized on MRI, CT and MRI registration cannot be performed. We evaluated the signal void in MRI that occurred by including iron. The 0.5% of iron containing GM was well visualized compared with pure GM.

Comparison was conducted by two radiation oncologists (7 and 15 years' experience) and one radiation therapy technologist (10 years' experience). The radiation oncologists acquire the ability of the fundamental diagnostic radiologists by becoming a certified radiation oncologist in our country. Moreover, the radiation technologist in our study is a certified MRI specialist. The radiotherapy treatment plan is usually prepared by two radiation oncologist and a radiation technologist. Example of scores is as follows: In Fig. 1, outline in CT is assigned score 2, outline in MRI is assigned 4, artifact in CT is assigned 3, and signal void in MRI is assigned 4. In Fig. 2, outline in CT is assigned score 3, outline in MRI is assigned 3, artifact in CT is assigned 4, and signal void in MRI is assigned 2.

Statistical analysis

The difference in observers' scores between the group administered butylscopolamine and the group without butylscopolamine was assessed using the Mann–Whitney *U* test. All statistical analyses of recorded data were performed using the Excel statistical software package (Excel-statistics 2015; Social Survey Research Information Co., Ltd., Tokyo, Japan).

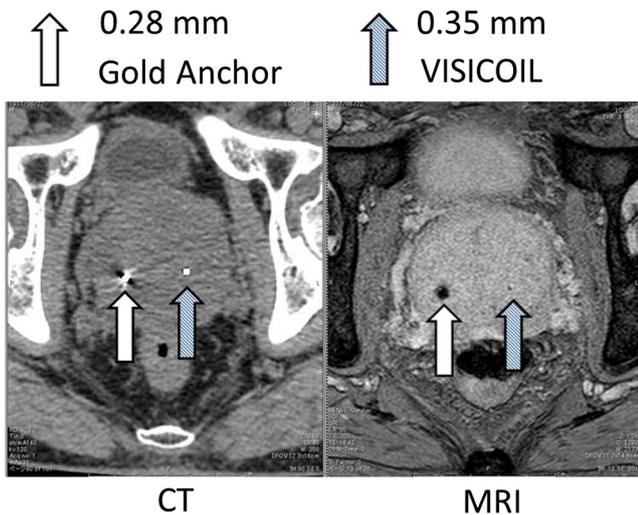


Fig. 1. An example of the butylscopolamine administered group. White arrow: Gold Anchor, 0.28 mm in diameter and spherical in shape. Arrow with diagonal lines: VISICOIL, 0.35 mm in diameter and linear in shape.

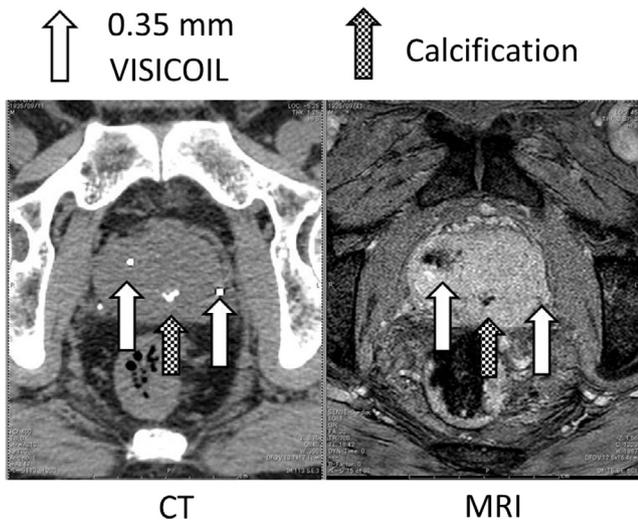


Fig. 2. An example of the non-butylscopolamine administered group. White arrow: VISICOIL, 0.35 mm in diameter and linear in shape. Arrow with a checkered pattern: Calcifications.

Table 2

Comparison of the patients with butylscopolamine administrated (A group) and the patients with butylscopolamine non-administrated (B group). A group $n = 35$, B group $n = 32$.

	Outline in CT	Outline in MRI	Artifact in CT	Signal void in MRI
<i>Radiation oncologist 1</i>				
A	2.21	3.64	3.11	3.67
B	2.45	3.21	3.02	2.71
<i>p</i> value	0.32	0.44	0.21	<0.01
<i>Radiation oncologist 2</i>				
A	2.81	3.15	3.06	3.59
B	2.35	2.92	2.34	2.24
<i>p</i> value	0.22	0.31	0.03	<0.01
<i>Radiation technologist</i>				
A	2.41	3.28	2.69	3.41
B	1.91	1.91	2.37	2.96
<i>p</i> value	0.28	<0.01	0.42	0.23

Abbreviations: CT, computed tomography; MRI, magnetic resonance imaging; Outline, Prostatic outline.

For the prostatic outline, a higher score indicated better depiction of prostate outline, outline is influenced by bowel motion.

For the CT artifact, a higher score indicated less artifact.

For signal void on MRI, a higher score indicated better marker visualization.

Statistical analysis was performed using the Mann-Whitney U test.

Bold values indicate where p value is <0.05 .

Results

MRI (Table 2 and Figs. 1 and 2): Based on the radiation oncologists' evaluation, the butylscopolamine group was statistically superior to the non-butylscopolamine group in terms of GM detection from signal voids visible on MRI. Based on the radiation technologist's evaluation, on MRI, the prostate outline in the butylscopolamine group was superior to that in the non-butylscopolamine group.

CT: The butylscopolamine group was statistically superior to the non-butylscopolamine group in terms of artifact on CT ($p = 0.03$) by one of the two radiation oncologists. The outline of prostate on CT was not significantly different between the groups. In terms of MR images, butylscopolamine was statistically influenced in recognition of GMs. On the other hand, CT image was only affected by the artifact of CT by scoring result of two radiation oncologists.

Discussion

Detection of GMs on MRI is critical of registration in the setting of IMRT. If the size of GM is larger, then precision of recognition becomes higher on MRI. However, precision of recognition may be lower due to an artifact appearing on CT if the metal volume is big. Therefore, it is more effective to use as small a GM as possible, and it is very useful if an ideal MRI image can be obtained with a small GM. However, CT acquisition time is not influenced by movement due to CT image is obtained 2 or 3 s.

Butylscopolamine for prostate imaging has been reported, but some reports indicate that butylscopolamine is unnecessary [7–10]. The reason for these results is that organs including the prostate, bladder, rectum, and lymph nodes are not different whether or not butylscopolamine is used. Diagnostic MR images are to examine invasion and metastasis around the organ; therefore, the field of view is wide. On the other hand, the reports from Dasda and Johnson showed that the administration of butylscopolamine is useful in the examination of pelvic MRI [11,12].

The present study is concerned with the imaging of the prostate specifically. In this context, butylscopolamine has been reported to improve image quality in pelvic malignancy; however, it doesn't impact on the prostate gland [7,8], because the prostate is imaged along with some structures such as bladder, small bowel and rectum. Wagner et al. reported a small utility of effect of butylscopolamine [7].

The simulation images can also encompass a large FOV the imaging is used for OAR contouring. If an endorectal coil is used, there is no need to use butylscopolamine. However, when better MR images are required, MR images of prostate are influenced by even a little movement during MRI examination. Furthermore, MR images should be obtained in a natural position (head–spine position) because the endorectal coil is not useful for IMRT.

Therefore, increasing the size of GM may increase visibility on MRI, but also increases artifact on CT and influences dose distribution. Raising the visibility of small GM is necessary for MRI if we consider these results.

We previously reported that MR sequence comparison study which is recognition of loose I^{125} radioactive seeds (Oncoseed; Nihon Mediphysics Co., Tokyo, Japan) in the prostate by comparing five MRI sequences [5]. From this knowledge, we could narrow the focus to include only the prostate, and we made the smallest field of view ($16\text{ cm} \times 16\text{ cm}$) and the best sequence of the MRI by comparing other MRI sequences. Therefore, we were able to depict a diameter by MRI in small GM of 0.28 mm and 0.35 mm in diameter. This thin needle used to insert GMs reduces the patient's pain, and also reduces the artifact on CT. Therefore, to obtain a clear MR image, we introduced butylscopolamine to reduce the movement of the rectum. Registration of CT and MRI for radiation treatment planning is easily performed with a clear image. With respect to the artifact on CT, we obtained a significant statistical difference. However, the time required to obtain a CT image is 10 s, whereas that required to obtain an MR image is 6 min; therefore, butylscopolamine is required.

In our retrospective analysis of GM by the examination of MR images, the rectum moved only in 5–6 min of MRI. Image quality strongly depends on motion in the natural position (without an endorectal coil) during MRI. Thus, poor images were seen even using a large size of GM without butylscopolamine. We recommend the use of butylscopolamine in MRI for natural positioning of the head and spine in IMRT.

Limitations

By decreasing the movement of the rectum, the depiction of GMs in the prostate increased. However, we noted the locations of GMs in CT images and identified the positions of GMs in MR images. This cognitive ability is related to an individual's medical ability. Rectal feces and gas can affect images, and there are uncertain parts in only 1–2 MR images.

Conclusions

When the focus is on only the prostate outline and GM recognition, butylscopolamine can assist in the detection of a small GM and the prostate outline. While the magnitude of the benefit is small, it is a useful technique to obtain good MR images at a low cost.

Compliance with ethical standards

Conflicts of interest: None.

Registered National Clinical Trial Systems: All patients provided written informed consent.

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