

## Prostate magnetic resonance imaging at 3 Tesla: Is administration of hyoscine-N-butyl-bromide mandatory?

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**RESULTS:** Comparison of anatomical details between the two cohorts showed no statistically significant difference ( $3.9 \pm 0.7$  vs  $4.0 \pm 0.9$ ,  $P = 0.54$ , and  $3.8 \pm 0.7$  vs  $4.2 \pm 0.6$ ,  $P = 0.07$ ) for both readers. There was no significant advantage regarding depiction of local and iliac lymph nodes ( $3.9 \pm 0.6$  vs  $4.2 \pm 0.6$ ,  $P = 0.07$ , and  $3.8 \pm 0.9$  vs  $4.1 \pm 0.8$ ,  $P = 0.19$ ). Motion artefacts were rated as "none" to "few" in both groups and showed no statistical difference ( $2.3 \pm 1.0$  vs  $1.9 \pm 0.9$ ,  $P = 0.19$ , and  $2.3 \pm 1.1$  vs  $1.9 \pm 0.7$ ,  $P = 0.22$ ). Overall image quality was rated "good" in average for both cohorts without significant difference ( $4.0 \pm 0.6$  vs  $4.0 \pm 0.9$ ,  $P = 0.78$ , and  $3.8 \pm 0.8$  vs  $4.2 \pm 0.6$ ,  $P = 0.09$ ).

**CONCLUSION:** The results demonstrated no significant effect of HBB administration on image quality. The study suggests that use of HBB is not mandatory for MRI of the prostate at 3.0 Tesla.

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### Abstract

**AIM:** To evaluate the value of administration of hyoscine-N-butyl-bromide (HBB) for image quality magnetic resonance imaging (MRI) of the prostate.

**METHODS:** Seventy patients were retrospectively included in the study. Thirty-five patients were examined with administration of 40 milligrams of HBB (Buscopan®; Boehringer, Ingelheim, Germany); 35 patients were examined without HBB. A multiparametric MRI protocol was performed on a 3.0 Tesla scanner without using an endorectal coil. The following criteria were evaluated independently by two experienced radiologists on a five-point Likert scale: anatomical details (delineation between peripheral and transitional zone of the prostate, visualisation of the capsule, depiction of the neurovascular bundles); visualisation of lymph nodes; motion related artefacts; and overall image quality.

**Key words:** Butylscopolamine; Buscopan; Motion artefacts; Magnetic resonance imaging; Prostate cancer; 3 Tesla

**Core tip:** The study demonstrated no significant effect of hyoscine-N-butyl-bromide (HBB) (butylscopolamine) administration on image quality of prostate magnetic resonance imaging (MRI) at 3.0 Tesla without using an endorectal coil. The results suggest that the use of HBB is not generally mandatory for MRI of the prostate.

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## INTRODUCTION

Magnetic resonance imaging (MRI) is an emerging modality for detection and staging of prostate cancer. To date, multiparametric imaging protocols for MRI of the prostate apply morphological high-spatial resolution T2-weighted sequences complemented by functional imaging techniques: diffusion weighted imaging, dynamic contrast-enhanced imaging, and MR-spectroscopy. A mandatory next step for further acceptance of this technique is to simplify and to standardize the MR-protocols for prostate MRI.

A majority of MR-studies of the prostate are performed with glucagon or hyoscine-N-butyl-bromide (HBB, butylscopolamine) because administration of an anti-peristaltic drug is recommended for many oncologic MR-examinations of the pelvis<sup>[1,2]</sup>. The rationale behind it consists of motion reduction of prostate surrounding structures (bladder, rectum, and small bowels) that may cause motion related artefacts which potentially degrade signal-to-noise ratio (SNR) and image quality. However, a recent study by Wagner *et al.*<sup>[3]</sup> found no benefit for HBB in prostate MRI at 1.5 Tesla. The authors contended that the prostate is located in the lower pelvis, between pelvic floor muscles, bladder and rectum, distant to small bowel structures, and thus it is not affected by peristaltic artefacts. Consequently, they suggested waiving of spasmolytic drug administration. At present, MRI of the prostate at 3.0 Tesla is becoming the state-of-the art examination, because the increased field strength at 3.0 Tesla potentially improves image quality by increased SNR<sup>[4,5]</sup>. Nevertheless, non-significant artefacts due to peristaltic bowel motion on 1.5 Tesla MR imaging may become more exaggerated on 3.0 Tesla MR imaging and result in reduced image quality.

Hence, purpose of the study was to evaluate the value of administration of HBB for image quality in prostate MRI at 3.0 Tesla.

## MATERIALS AND METHODS

### Patients

This retrospective, single institutional study was approved by local ethics committee. Patients were included into the study from October 2010 to June 2011. All patients were referred for prostate MRI from the university hospital by the department of urology with clinical suspicion of prostate cancer. Patients with prior radiation therapy or adjuvant hormone ablative therapy were not included into the study. The standard MR-protocol provided administration of HBB. HBB was not administered in the presence of contraindications such as glaucoma, cardiac arrhythmia and/or ischemic heart disease, myasthenia gravis, and apparent benign prostatic hyperplasia with potential urinary retention<sup>[6]</sup>. Patients who used their car after the examination did not receive HBB for safety reasons. The data of the included patients were transferred into pseudonymous data and allocated to a database into

a HBB-group and into a non-HBB-group. Then, the patients in both groups were sorted according to age in an ascending sequence and into 5-year intervals. To avoid a selection bias, a random number generator software function was used (Excel; Microsoft, Redmond, WA, United States): first, a patient was selected out of the HBB-group. Then, a patient from the non-HBB-group was randomly drawn out of the corresponding age-interval. In total, two datasets with 35 patients from each group were generated (Figure 1). Finally, the resulting groups were tested for statistically significant age difference.

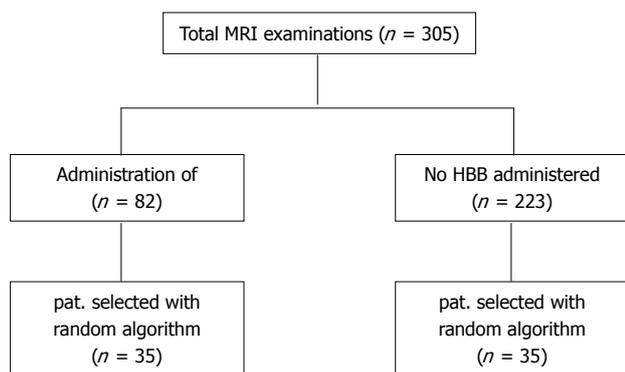
### Imaging technique

Patients in the HBB group were administered 40 mg of drug approved HBB (Buscopan®; Boehringer, Ingelheim, Germany) by a venous access directly before the examination. All examinations were performed on a 3.0 Tesla scanner (Siemens Magnetom Trio; Siemens Healthcare, Erlangen, Germany) using the manufacturer standard multi-channel body coil and integrated spine phased-array coil. The MR-protocol started with T2-weighted half-fourier acquisition turbo spin echo localizer sequences. An transverse T1-weighted 3-dimensional gradient echo sequence (FLASH-3D) was obtained for lymph node staging and detection of haemorrhage with the following imaging parameters: repetition time (TR): 6.66 ms, echo time (TE): 2.55 ms, echo train length: 1, averages: 1, section thickness: 3 mm, no intersection gap, matrix: 317 × 512, field of view: 24 cm × 35 cm, acquisition time: 1:40 min. Sequences included high-spatial resolution T2-weighted turbo spin echo MR imaging in the transverse and coronal plane with the following imaging parameters: TR: 5120 ms, TE: 143 ms, echo train length: 13, averages: 4, section thickness: 3 mm, no intersection gap, matrix: 254 × 448, field of view: 21.2 cm × 30.0 cm, acquisition time: 4:14 min. Axial diffusion-weighted images were acquired using a single-shot echo-planar imaging pulse sequence: TR 12500 ms, TE 65 ms; averages, 4; matrix size, 176 × 176; FOV 450 × 306 mm<sup>2</sup>; slice thickness, 5 mm; parallel imaging GRAPPA factor 2; b-values: 0, 50, 100, 150, 200, 250, and 800 s/mm<sup>2</sup>. Three orthogonal diffusion directions were acquired. ADC maps were implicitly calculated on the scanner with the standard software provided by the manufacturer using all measured b-values.

DCE was performed with a high-spatial resolution T1-weighted 3-dimensional gradient echo sequence with a temporal resolution of 9.9 s: TR 4.42 ms, TE 2.2 ms; flip angle 15°; matrix size 176 × 265, FOV 400 × 275 mm<sup>2</sup>; slice thickness 1.5 mm. As contrast agent, weight-adjusted (0.1 mmol/kg) gadobutrol (Gadovist®; Bayer Healthcare, Leverkusen, Germany) was administered.

### Imaging analysis

The acquired datasets were analysed by two board-certified radiologists with 5 and 12 years of experience in reading prostate MRI studies. Both radiologists were blinded to administration of HBB. The readers scored the cases independently and in random order on Likert five-point



**Figure 1** Flowchart of patient inclusion. Total of 70 patients were selected randomly out of the hyoscine-N-butyl-bromide (HBB) and the corresponding control group. MRI: Magnetic resonance imaging.

scales. First, anatomical details (delineation between peripheral and transitional zone of the prostate, visualisation of the capsule, depiction of neurovascular bundles) and visualisation of local and iliac lymph nodes were assigned on a five-point scale referring to imaging criteria described by Wagner *et al.*<sup>[3]</sup>: (1) non-diagnostic: structures cannot be evaluated; (2) poor visualization: heavily blurred appearance of structures; (3) moderate visualization: moderate blurring; (4) good delineation: slight blurring; and (5) excellent visualization: sharp delineation. Motion related artefacts in the prostatic area were scored on the following five-point scale: (1) no artefacts; (2) few artefacts; (3) moderate artefacts; (4) considerable artefacts; and (5) severely affected. Finally, the readers documented their perception of overall image quality: (1) non-diagnostic; (2) poor; (3) satisfactory; (4) good; and (5) excellent.

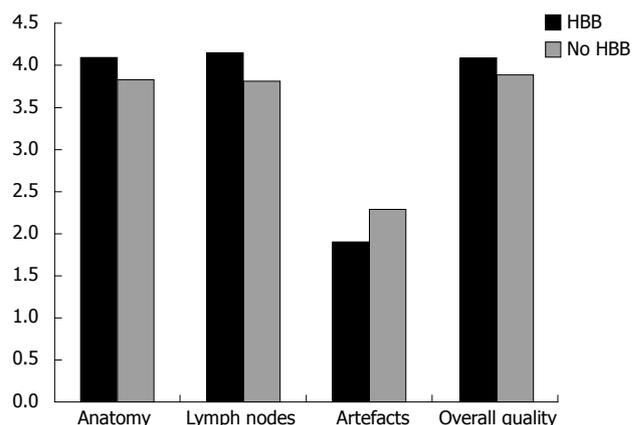
### Statistical analysis

A two-tailed Wilcoxon rank-sum test was used to determine significant difference between the two cohorts. Additionally, Bonferroni correction was applied. Weighted kappa ( $\kappa$ ) statistics were used for evaluation of interobserver agreement. The following intervals were defined for interpretation of the kappa values: 0.0-0.2 = poor, 0.21-0.4 = fair, 0.41-0.6 = moderate, 0.61-0.8 = substantial, 0.81-1.00 high to almost perfect agreement. A *P*-value of 0.05 or less was considered as statistically significant. All analyses were performed with SAS/STAT software (SAS Institute, Cary, NC, United States).

## RESULTS

### Patients

305 patients matched the predefined criteria. Out of this cohort 82 patients were eligible for administration of HBB and 223 patients did not receive HBB. The two resulting groups of 35 patients each showed no statistical difference regarding age distribution ( $P = 0.26$ ) with an average age in the HBB-group of 64.9 [95%CI: 62.4-67.4] and 67.0 years [95%CI: 64.7-68.6] in the non-HBB group, respectively.



**Figure 2** Average scores of the obtained imaging categories in both groups. No statistical significant difference could be obtained. HBB: Hyoscine-N-butyl-bromide.

### Imaging analysis

Qualitative analysis demonstrated good results regarding the scored criteria for both groups (Figure 2, Table 1). Comparison of anatomical details between the two cohorts showed no statistical significant difference ( $P = 0.54$  and  $P = 0.07$ ) for both readers. There was no statistically significant advantage regarding depiction of local and iliac lymph nodes ( $P = 0.07$  and  $P = 0.19$ ). Motion artefacts were rated as “no” to “few” in both groups. Analysis showed no statistical difference ( $P = 0.19$  and  $P = 0.22$ ) between the two groups. Two examples of the evaluated patient sets are demonstrated in Figure 3A and B. Scoring of overall image quality showed no significant difference ( $P = 0.78$  and  $P = 0.09$ ).

### Inter-reader evaluation

Evaluation of inter-observer agreement was moderate for all criteria (range:  $\kappa = 0.44$ -0.53) except for a fair result with  $\kappa = 0.37$  for assessment of overall image quality. However, a difference of more than one scale interval between the two readers occurred in only 3 of 280 scores (1.07%).

## DISCUSSION

The results demonstrated no significant effect of administration of HBB on visualisation of the prostate, iliac lymph nodes, periprostatic artefacts, and overall image quality. The findings correspond to the results of a study by Wagner *et al.*<sup>[3]</sup> at 1.5 Tesla with ERC that found no significant effect of intravenous or intramuscular administration of HBB for visualisation of the prostate, neurovascular bundles, pelvic lymph nodes, and overall image quality. Studies promoting the use of HBB for pelvic MRI emphasize the advantage of suppressing bowel peristalsis to reduce motion artefacts<sup>[4,7,8]</sup>, which is particularly the case in MR-sequences with long acquisition times such as T2w TSE sequences<sup>[9]</sup>. Nevertheless, motion artefacts were comparably low in both of our assessed

**Table 1** Qualitative evaluation using a five-point-scale

	Non-HBB group		HBB group	
	A	B	A	B
Prostate anatomy	3.9 ± 0.7	3.8 ± 0.7	4.0 ± 0.9	4.2 ± 0.6
Iliac lymph nodes	3.9 ± 0.6	3.8 ± 0.9	4.2 ± 0.6	4.1 ± 0.8
Related artefacts	2.3 ± 1.0	2.3 ± 1.1	1.9 ± 0.9	1.9 ± 0.7
Overall quality	4.0 ± 0.6	3.8 ± 0.8	4.0 ± 0.9	4.2 ± 0.6

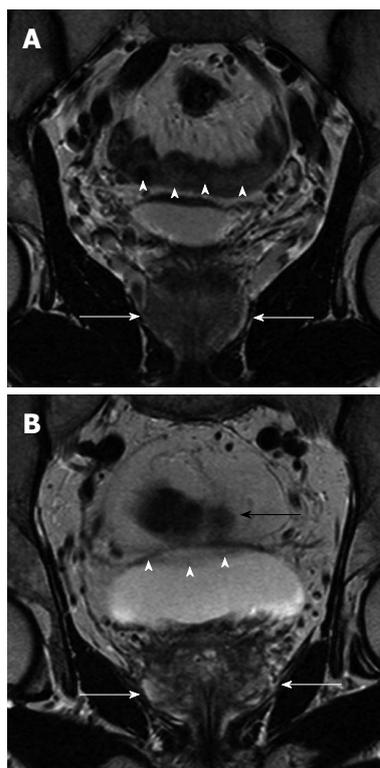
Data are expressed as mean ± SD. HBB: Hyoscine-N-butyl-bromide.

groups, which could be explained by the anatomical distance between the prostate and small bowel. Thus, the prostate is not directly affected by small bowel motion artefacts (Figure 3A and B). Choosing a posteroanterior phase-encoding direction, which sufficiently suppresses peristaltic artefacts caused by small and larger intestine, is an explanation for visualisation of iliac lymph nodes being marginally affected by administration of HBB<sup>[10]</sup>. In contrast to this study, an initial study by Johnson *et al*<sup>[11]</sup> found improved visualisation of the prostate in about 40% of the patients after HBB administration. However, the number of patients was considerably small with 23 men and there was no dedicated MR-protocol for prostate imaging at a 1.0 Tesla system.

In opposite to this study, Wagner *et al*<sup>[3]</sup> used an ERC for prostate imaging at 1.5 Tesla. To date, after introduction of 3.0 Tesla scanners, the increased SNR is frequently used to exclude the ERC from prostate examinations, mainly in order to prevent discomfort from patients and to avoid the additional costs for the ERC<sup>[12-17]</sup>. The use of an ERC provides a wide-ranging immobilization of the prostate in the lower pelvis, which contributes to reduction of motion related artefacts in that specific area<sup>[3]</sup>. On the other hand, the inflated ERC provides a mechanical stimulus for rectal motion artefacts that can hardly be suppressed by HBB. That is further the case for air that processes through the rectum during the examination. Nevertheless, studies at 1.5 Tesla found that image quality of prostate MRI without ERC to be equal to those with ERC without increased motion artefacts<sup>[5,12,13]</sup>. A few studies assessed the additional value of the use of an ERC for prostate MRI at 3.0 Tesla. These studies demonstrated an incremental benefit for image quality using an ERC<sup>[4,7,8]</sup>. However, it remains unclear if further improved SNR at 3.0 Tesla by an ERC improves diagnostic performance<sup>[9]</sup>.

Although there was no significant effect of HBB administration on image in our study, the authors believe that there are indications for administration of an anti-peristaltic drug in MR of the prostate, *e.g.*, for patients with hyper-motile intestine or flatulence. In these cases, an anti-peristaltic drug can be administered subsequently after detection on initial T1- or T2-weighted sequences. Furthermore, it would be interesting to investigate the effect of an anti-peristaltic agent on spectral noise in MR-spectroscopy.

The study has some limitations. First, the study was



**Figure 3** The results demonstrated no significant effect of administration of hyoscine-N-butyl-bromide on visualisation of the prostate, iliac lymph nodes, periprostatic artefacts, and overall image quality. A: 54-year-old patient. Coronal T2w-TSE sequence after administration of hyoscine-N-butyl-bromide (HBB): Prostate capsule (arrows) and neurovascular bundles are well visualized. Central gland and peripheral zone can be differentiated. Bowel wall structures are sharply depicted without artefacts (arrowheads); B: 72-year-old patient after coronal T2w-TSE sequence without administration of hyoscine-N-butyl-bromide (HBB): Qualitative rating showed no significant difference in visualisation of prostate capsule (white arrow), differentiation between central and peripheral gland, and neurovascular bundle structures (black arrow). However, ill-defined and blurred small bowel loops with surrounding artefacts occurred (arrowheads) without affecting the prostate or periprostatic space.

performed in a retrospective design. A larger prospective study would substantiate the findings of this study. Secondly, there was no intra-individual comparison between HBB and no HBB administration. This methodical drawback was compensated by a sufficient number of patients and adjustment of the age characteristics in both patient groups. At present, there is no evidence for a difference between the HBB and the non-HBB group caused by a methodical bias.

In conclusion, the results of the study demonstrated no significant effect of HBB administration on image quality of prostate MRI at 3.0 Tesla without ERC. The results of the study suggest that the use of HBB is not mandatory for MRI of the prostate.

## COMMENTS

### Background

A mandatory next step for further acceptance for prostate magnetic resonance imaging (MRI) is to simplify and to standardize MR-protocols. Like many other oncologic MR-examinations of the pelvis, a majority of MR-studies of the

prostate are performed using an anti-peristaltic drug. However, recent studies indicate that the additional value of bowel motion suppressing agents is limited. Thus, purpose of this study was to evaluate the value of administration of an anti-peristaltic agent for prostate MRI at 3.0 Tesla.

### Research frontiers

A current topic of research consists of standardizing reading, reporting, and conduction of multiparametric MRI of the prostate. At present, for prostate MRI, there are different recommendations regarding the use of an anti-peristaltic agent for bowel motion suppression.

### Innovations and breakthroughs

A recent study by Wagner *et al.* found no benefit for administration of an anti-peristaltic agent for prostate MRI at 1.5 Tesla. However, a contrary study by Johnson *et al.* found improved visualisation of the prostate at 1.0 Tesla in about 40% of the patients after administration of an anti-peristaltic agent. Furthermore, the use of an endorectal coil may have an influence on prostate MRI. Currently, a major number of examinations at state-of-the-art 3.0 Tesla scanners are carried out without using an endorectal coil.

### Applications

The study demonstrated no significant effect of hyoscine-N-butyl-bromide (HBB) (butylscopolamine) administration on image quality of prostate MRI at 3.0 Tesla. The results suggest that the use of HBB is not generally mandatory for MRI of the prostate. This may help to further facilitate and to simplify prostate MRI.

### Terminology

HBB, an anti-peristaltic agent commonly used for suppression of bowel motion, *e.g.*, for pelvic imaging. Endorectal coils are used to gain increased signal from the prostate. However, modern pelvic phased-array surface coils deliver excellent signal, especially at higher field strengths. Therefore, many sites perform prostate MRI without using an endorectal coil.

### Peer review

The authors evaluated the role of administration of HBB in improving the image quality of MRI of the prostate at 3.0 Tesla. The results demonstrated no significant effect of HBB administration on image quality, and suggest that the use of HBB is not mandatory for MRI of the prostate at 3.0 Tesla. This is a direct and carefully-designed study with relatively large number of patients. The conclusion drew from the study is clear and convincing. The study was carried out thoroughly and the paper is written nicely.

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