Comparison of computed tomographic and cytological results in evaluation of normal prostate, prostatitis and benign prostatic hyperplasia in dogs

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Article Info	Abstract
	Prostate gland can be structurally evaluated by computed tomography (CT) with taking advantages of tomographic feature and post-contrast parenchymal changes. The current examination initiated to determine association between computed tomographic and cytological results in evaluation of canine prostate. Thirty mature male dogs were included and under gone by both CT and fine needle sampling of prostate. The cytology and CT examination results showed 18/30 (60.00%) and 15/30 (50.00%) normal prostate, 5/30 (16.66%) and 4/30 (13.33%) prostatitis and 7/30 (23.33%) and 11/30 (36.66%) benign prostatic hyperplasia, respectively. Moderate agreement has been found between cytology and final diagnosis based on pre-contrast CT images, however fair agreement was existed between cytological diagnosis and final CT interpretation according to post-contrast and both pre- and post- contrast CT series. Additionally, the internal iliac lymph node length showed statistically significant difference in prostatitis compared to normal and benign hyperplastic prostates in this study. In conclusion, the fair and moderate associations between cytology and final diagnosis based on CT images should be considered and they can be used in further investigations and clinical examinations. Also, using internal iliac lymph node length to differentiate prostatitis with normal and benign hyperplastic prostates can be used efficiently in diagnosis to choose the best method of management and have a proper follow up and prognosis.

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مقایسه نتایج برش نگاری رایانه ای و سلول شناسی در ارزیابی پروستات طبیعی، التهاب پروستات و هایپرپلازی خوش خیم پروستات در سگ ها

چکیده

ساختار غده ی پروستات را می توان با استفاده از برش نگاری رایانه ای (CT) با بهره جستن از خصوصیات مقطعی و تغییرات پارانشیمی آن بعد از تزریق ماده ی حاجب مورد ارزیابی قرار داد. مطالعه ی حاضر جهت بررسی ارتباط نتایج حاصل از CT و سلول شناسی در ارزیابی پروستات سگ طرح ریزی گردید. سی قلاده سگ نر بالغ وارد مطالعه شدند و پروستات آن ها مورد بررسی CT و نمونه برداری قرار گرفت. نتایج سلول شناسی و CT به ترتیب نشان داد که ۱۸/۳۰ (۶۰/۰۰ درصد) و ۱۵/۳۰ (۵۰/۰۰ درصد) دارای پروستات طبیعی، ۵/۳۰ (۱۶/۶۶ درصد) و ۴/۳۰ (۱۳/۳۳ درصد) مبتلا به التهاب پروستات و ۷/۳۰ (۲۳/۳۳ درصد) و ۱۱/۳۰ (۳۶/۶۶ درصد) مبتلا به هیپرپلازی خوش خیم پروستات بودند. توافق متوسطی بین سلول شناسی و تشخیص نهایی بر اساس تصاویر CT پیش از تزریق ماده حاجب مشاهده گردید، این در حالی است که توافق ضعیفی بین تشخیص سلول شناسی و تفسیر CT نهایی با توجه به تصاویر بعد از تزریق ماده حاجب و هر دو نوع تصویر قبل و بعد از تزریق ماده حاجب وجود داشت. همچنین، طول عقده لنفاوی ایلیاک داخلی اختلاف معنی داری را در التهاب پروستات در مقایسه با با پروستات های طبیعی و مبتلا به هیپرپلازی خوش خیم در این مطالعه نشان داد. ارتباطات ضعیف و متوسط بین سلول شناسی و تشخیص نهایی بر اساس تصاویر CT می تواند مدنظر قرار گیرد و این امر می تواند در مطالعات آتی و معاینات بالینی مورد استفاده قرار گیرد. همچنین، توجه به طول عقده لنفاوی ایلیاک داخلی جهت تفریق التهاب پروستات با پروستات های طبیعی و مبتلا به هیپرپلازی خوش خیم می تواند به گونه ای موثر در تشخیص به کار گرفته شود، تا بهترین روش جهت مدیریت انتخاب شود و پیگیری و پیش آگهی مطلوب فراهم گردد.

واژه های کلیدی: برش نگاری رایانه ای، سگ، سلول شناسی، غده پروستات

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Introduction

The canine prostate is a main sexual gland in male dogs that can be affected by several diseases with overlapping clinical signs. Accurate diagnosis of prostatic diseases requires different diagnostic imaging procedures as well as complete physical examination. Although prostatic size can be evaluated by transrectal digital palpation, diagnostic imaging modalities such as computed tomography (CT) can ease prospective evaluation of the prostate and adjacent pelvic structures in addition to parenchymal evaluation. Recently CT is considered as a useful diagnostic imaging modality in veterinary medicine which avoids superimpositions of the structures in reproductive system and caudal abdomen evaluations.[1]

The CT image of a normal prostate (NP) gland has a homogenous well-defined appearance with a soft tissue density of 40-70 Hansfield Unit (HU) and 90-150 HU in pre- and post- contrast images, respectively. Symmetrical or asymmetrical prostatomegaly and heterogeneous parenchyma are presented as CT features of benign prostatic hyperplasia (BPH), prostatitis (PI) and neoplasia. These common CT features may be associated with lymph-adenopathy in PI, bone and lung metastasis in neoplasia and parenchymal mineralization in both conditions.[2]

In addition to all the physical examinations, diagnostic imaging procedures and available laboratory tests in veterinary medicine, histopathology is considered as a gold standard in evaluation of the prostatic disorders. According to the strong agreement between histo-pathological and cytological results, it is reliable to take advantages of cytology for the investigation of prostatic diseases. Cytology is a less invasive and an easier method with lower costs providing the results in a short time.[3]

To the best of the author's knowledge, there is no available study in evaluating the association between the CT and cytological results in canine prostates. In this prospective study, we assessed the association between computed tomographic and cytological findings and results in canine prostate evaluations.

Materials and Methods

The study design and ethical approval was obtained by Faculty of Veterinary Medicine, University of Tehran, Tehran, Iran (No. 749, 1394/04/14). The CT images of thirty intact mature mixed large breed dogs were assessed in this study prospectively in a random inclusion if the dogs were scanned for non-related diseases to urogenital system but the pelvic region was considered in the images. All the CT exams were taken with same protocol (kVp: 130, MAS: 80, slice thickness: 1.25, rotation time: 0.8 and pitch: 2) in dorsal recumbency and the same scanner (SiemensSomatom® two detectors; Siemens, Erlangen, Germany) under general anesthesia using 5.00 mg kg^{-1}

ketamine (Alfasan, Woerden, Netherlands) and 0.25 mg kg^{-1} Diazepam (Caspian Tamin Pharmaceutical Co., Rasht, Iran), intravenously. The patients without post-contrast images (320 mg mL^{-1} Iodixanol; GE Health care, Dublin, Ireland) were excluded during screening. The images were anonymized separately in pre- and post- contrast images and then reviewed by the experienced national board certified veterinary radiologist using Somaris/Syngo® software (version 5.5; Siemens AG, Berlin, Germany) in transverse images and multi planar reconstruction. The dogs were categorized into NP, PI and BPH based on subjective evaluation (Fig. 1) including presence of symmetrical or asymmetrical enlargement, heterogeneous parenchyma, enlarged iliac lymph nodes, detectability of median sulcus and related abnormalities within the pelvic region.[2] Prostatic length, width and height (Fig. 2), prostatic area at the level of median sulcus (Fig. 2) and internal iliac lymph nodes length (Fig. 2), width and height were measured using hand-drown and ruler tools in objective evaluation phase of study in both pre- and post-contrast images. The mean, maximum (Max), minimum (Min) and standard deviation (SD) of HU have been obtained automatically by software evaluated for hand-drawn area marked at the level of median sulcus. The length of the 7th lumbar vertebra (L7L) was measured in sagittal pre-contrast images (Fig. 2).
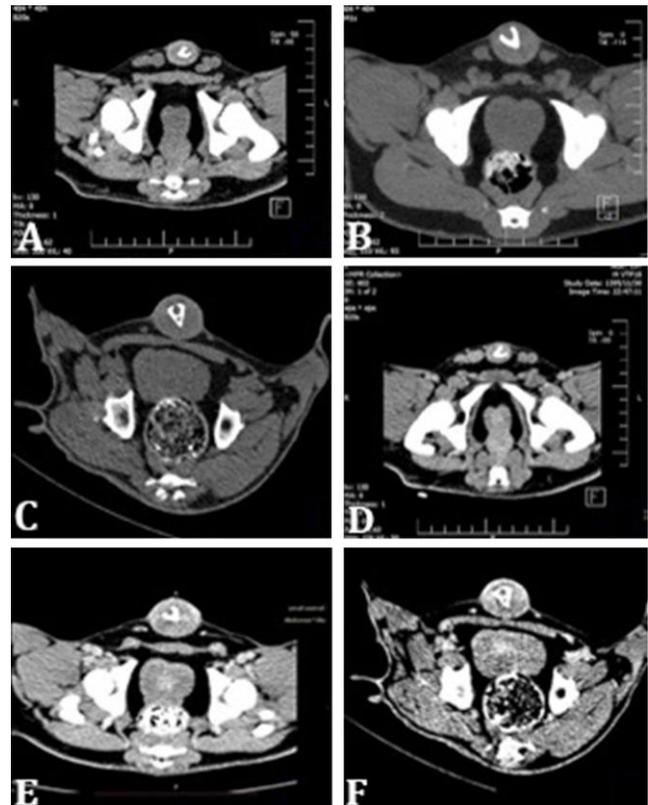

Fig. 1. Pre-contrast and post-contrast images of **A** and **D)** normal prostate, **B** and **E)** benign prostatic hyperplasia and **C** and **F)** prostatitis, respectively.
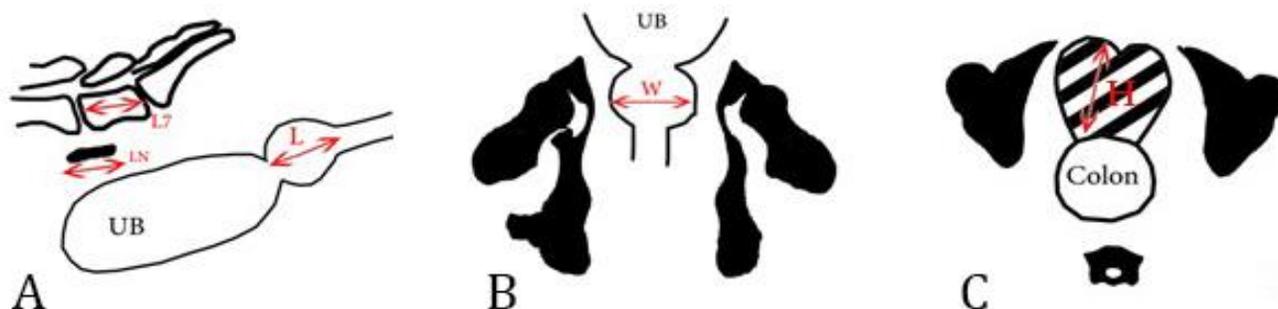
Fig. 2. Schematic figure of multi planar reconstruction computed tomographic images of prostate gland of a dog. **A)** Sagittal; **B)** Dorsal and **C)** Transverse plans. L: Length of prostate; W: Width of prostate and H: Height of prostate. Prostatic area at the level of median sulcus was measured by hand-drown tool of Somaris/Syngo 5.5 software and calculating area is indicated with straight area. UB: Urinary bladder; LN: Internal iliac lymph node length which was measured on para-sagittal plane image after multi planar reconstruction of images; L7: Length of 7th lumbar vertebra.

The CT guided fine needle aspiration (FNA) was done to take cytological samples. The samples were taken under CT guidance with needle gauge 21 from ventral approach lateral to prepuce avoiding prostatic urethra under the same anesthesia which was used for CT scanning with owner's permission. The slides were prepared with squash technique and fixed with ethanol before staining with Giemsa. The slides were anonymously labeled by the laboratory technician and sent for national board certified veterinary clinical pathologist for evaluation. The cases were categorized into NP, BPH and PI based on the presence of normal cells, anisocytosis and neutrophils, respectively (Fig. 3).[4]

A single dose Tramadol (Caspian Tamin Pharma-ceutical Co., Rasht, Iran) 0.40 mg kg^{-1} was prescribed for elimination of possible visceral pain.

Statistical analyses were done by SPSS (version 19.0; IBM, Chicago, USA). The data were described by mean ± SEM. The qualitative data (presence of symmetrical or asymmetrical enlargement, heterogeneous parenchyma, enlarged iliac lymph nodes, detectability of median sulcus, related abnormalities within the pelvic region, final CT diagnosis and cytological diagnosis) were analyzed by Chi-Square test. The analyses of quantitative data (prostatic length, width and height, prostatic area at the level of median sulcus, internal iliac lymph nodes length, width and height, Min; Max and SD of HU and L7L) were done by

Pearson coefficient correlation, one-way ANOVA and LSD post hoc tests. A p-value less than 0.05 was statistically considered significant.

Results

Thirty cases in the present study had mean ± SD weight of 25.49 ± 3.80 kg. The results showed 18/30 (60.00%) NP and 12/30 (40.00%) involved prostates based on cytology results and 15/30 (50.00%) NP and 15/30 (50.00%) involved prostates according to CT examination (Fig. 1).

There were no significant statistical associations between cytology and prostatic parenchymal appearance ($p = 0.05$ and $p > 0.05$; Table 1), prostate size ($p > 0.05$; Table 1) and detectability of median sulcus ($p > 0.05$; Table 1) in pre- and post-contrast images respectively during subjective evaluation. However, the association between cytology and internal iliac lymph node size was statistically significant in pre- and post-contrast images ($p < 0.001$ and $p < 0.05$, respectively).

The associations between cytology and final diagnosis based on pre-contrast ($p < 0.001$; κ value = 0.42, $p < 0.05$, moderate agreement), post-contrast ($p < 0.001$; κ value= 0.38, $p < 0.05$, fair agreement) and both image series ($p < 0.001$; κ value= 0.38, $p < 0.05$, fair agreement) were also statistically significant.
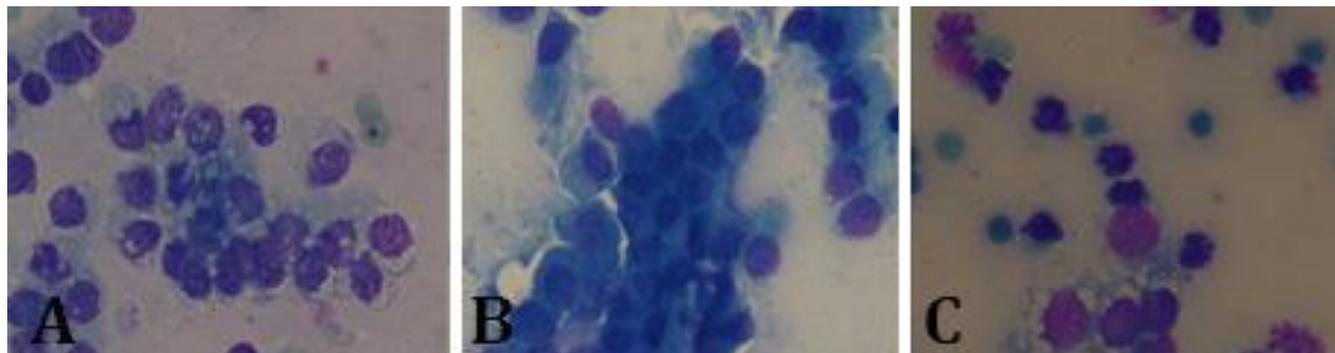

Fig. 3. Cytology images of **A)** normal prostate, **B)** benign prostatic hyperplasia and **C)** prostatitis, (Giemsa, 100×).

Table 1. Crosstabs in evaluation of the association between cytology and prostatic parenchymal evaluation, size and median sulcus in plain and post-contrast images.

Parameters		Cytology			Total
		Normal	Benign prostatic hyperplasia	Prostatitis	
Prostatic parenchyma	Homogeneous count plain	14	5	1	20
	Homogeneous count post-contrast	11	4	1	16
	Heterogeneous count plain	4	2	4	10
	Heterogeneous count contrast	7	3	4	14
Size	Normal count plain	10	4	2	16
	Normal count post-contrast	11	4	2	17
	Enlarged count plain	8	3	3	14
	Enlarged count post-contrast	7	3	3	13
Median sulcus	Detectable count plain	17	4	4	25
	Detectable count post-contrast	16	5	3	24
	Deteriorated count plain	1	3	1	5
	Deteriorated count post-contrast	2	2	2	6

Statistical correlations were detected between measured area and prostatic height ($p = 0.000$ and $p = 0.000$), length ($p = 0.001$ and $p = 0.001$) and width ($p < 0.001$ and $p = 0.000$) in pre- and post-contrast images, respectively (Table 2). No statistical difference was found among mean HU, measured area, Min HU, Max HU, SD and prostatic length; width and height, with different prostatic conditions in both pre- and post-contrast images ($p < 0.05$). Only the internal iliac lymph node length showed statistical difference in post-contrast images ($p < 0.05$) among different groups of cases. The differences in internal iliac lymph node length between NP and PI groups and PI and BPH groups were statistically significant ($p < 0.05$), while there was no statistical difference between NP and BPH groups ($p > 0.05$; Table 2). The differences among L7L values in normal and diseased prostatic conditions were not statistically significant ($p > 0.05$; Table 2).

Discussion

Prostatitis and BPH commonly affect old intact male dogs of all breeds and according to some studies, middle to large breeds are prone to develop these disorders.[5-7] It is suggested to select diagnostic methods from less invasive to more invasive methods such as biopsy for diagnosis and management of prostatic disorders.[6]

Among all the diagnostic methods, guided FNA is presented as a reliable, cheap and quick method to evaluate the prostate gland, but it still has a mild invasive nature. According to high correlation between FNA and histopathology as a gold standard method, this study has been conducted to find an association between CT and FNA results to establish a reliable diagnosis and avoiding the invasion in addition to use advantages of computed tomographic imaging.[3,7,8]

Table 2. Descriptive objective data (HU: Hounsfield unit).

Index	No.	Minimum	Maximum	Mean	SEM	Standard Deviation
Area in plain images (cm²)	30	2	15	8.01	0.60	3.33
HU of area in plain images	30	26	54	40.06	1.51	8.28
MinHU of area in plain images	30	−131	−20	−77.40	4.52	24.76
MaxHU of area in plain images	30	65	158	119.10	4.27	23.42
SD of HU of area in plain images	30	14	33	23.28	0.83	4.58
Prostatic length in plain images	29	1	4	2.56	0.129	0.69
Prostatic width in plain images	30	1	5	3.49	0.17	0.93
Prostatic height in plain images	30	1	4	2.55	0.10	0.57
Lymph node length in plain images	28	1	3	1.78	0.10	0.55
Lymph node width in plain images	28	0	1	0.50	0.02	0.10
Lymph node height in plain images	28	1	1	0.97	0.03	0.17
Area in contrast images	30	2	14	8.07	0.61	3.36
HUA of area in contrast images	30	43	89	68.83	1.96	10.73
MinHU of area in contrast images	30	−106	7	−63.03	5.06	27.75
MaxHU of area in contrast images	30	−157	341	176.70	15.17	83.13
SD of HU of area in contrast images	30	20	39	29.32	0.93	5.12
Prostatic length in contrast images	30	1	4	2.58	0.12	0.68
Prostatic width in contrast images	30	1	5	3.49	0.17	0.93
Prostatic height in contrast images	30	1	4	2.55	0.10	0.57
Lymph node length in contrast images	29	1	3	1.66	0.07	0.40
Lymph node width in contrast images	29	0	1	0.46	0.01	0.08
Lymph node height in contrast images	29	0	1	0.98	0.03	0.20
Length of 7th lumbar vertebra (cm)	29	2	3	2.58	0.03	0.20

Recently, CT is become widely available in veterinary medicine for evaluation of the reproductive system, avoiding superimposed shadows and tomographic imaging in addition to the ability of parenchyma evaluation.[1] As CT features of prostatic disorders have not been reliably reported, the features used in the present study have been chosen based on case reports, ultrasonographic features and pathophysiological changes as well as normal reported CT appearance.[1,2]

Computed tomography evaluation of apparently normal dogs showed that 83.00% of the dogs had homogenous appearance in plain images and 75.00% in post-contrast images.[1] In the present study, 78.00% of the cytological NPs demonstrate homogenous appearance in plain images and 61.00% in post-contrast images. No association has been found in present study between parenchymal heterogeneity which was subjectively reported and has also been considered as SD of an objective index and final FNA result. Lee *et al.* and Kuhnt *et al.* have reported that heterogeneity may be a result of aging and fibrous formation that can affect the tissue structure and blood supply.[1,5] Although all the included cases were sexually and skeletally mature, age of the patients was not clear and was not considered in present study. The effect of age on heterogeneous reported glands cannot be ruled out and of course might affect association between CT and cytological result.

Above-mentioned changes associated with heterogeneous blood flow without cyst formation in normal aged dogs can be the reason of the present moderate to fair correlation between cytology and CT examination results.

Differentiation of capsule, glandular and parenchymal parts and median septum of prostate were not possible in any of the normal and abnormal groups in pre- and post-contrast images as it was reported by Lee *et al.* in apparently healthy dogs as a normal phenomenon in CT images.[1] Therefore, it is advised that changes in these parts should be considered as criteria for evaluation of prostate in further studies and especially in neoplasia which wasn't considered in current study.

Lee *et al.* reported the correlations of the prostatic length and width with prostatic area which were also found in this study. However, in this study, the correlation between prostatic area and height is also reported and seemed logical. Thus, it is helpful to use prostatic dimensions for assessment of prostate area and size.[1]

No statistically difference was found between HU and final cytological diagnosis in our study. To the best of the author's knowledge, the only report of prostatic attenuation was presented in apparently normal dogs which was not confirmed cytologically or histopathologically.[1] Thus, HU as a represented of parenchymal changes in prostatic involvements requires more imaging and histological studies in both human medicine and animal models.

As the main drainage of the prostatic lymph is taking by the medial iliac lymph nodes, these lymph nodes were evaluated in the present study.[9] Since detecting pre-sacral and all pairs of medial iliac lymph nodes in CT exams is not possible, average measured height, width and length of detectable lymph nodes were considered in each patient.[10] The length of lymph nodes measured in post-contrast images is different between PI and BPH. Although the reactive lymph nodes routinely show an increase in width, this result can be used for differentiation of PI and BPH.

The length of the prostate was not correlated with cytological results. As the normal prostatic size varies with body size, 7th lumbar vertebra (L7) has been used as a body size presenter. However, no correlation has been detected in present study between prostatic dimensions and L7L.[11] Lee *et al.* have used sixth lumbar vertebra length and they have reported no correlation as well.[1]

As the urethra was considered in estimated prostatic area, we should be aware that it could affect the calculated mean, Max and Min of HU. Although this condition was same in all of the patients, it might be a source of error if there was any pathological condition within the urethra. Other limitation of this study was lack of some data about the patients such as age and exact breed which can have a direct influence on prostatic size and parenchymal appearance. At last, it is highly suggested to use pathological examination as a gold standard to evaluate both prostate and lymph nodes in larger group of patients in addition to covering the described limitations for next studies.

In conclusion, the association between cytology and final diagnosis based of CT images should be considered and it can be used in further investigations and clinical examinations. Moreover, using internal medial iliac lymph node length for differentiating PI with NP and BPH can be used efficiently in diagnosing to choose the best method of management.

Conflict of interest

The authors declare that there is no conflict of interest.

References

1. Lee KJ, Shimizu J, Kishimoto M, et al. Computed tomography of the prostate gland in apparently healthy entire dogs. J Small Anim Pract 2011; 52(3): 146-151.
2. Schwarz T, Rossi F, Saunders J. Genital tract. In: Schwarz T, Saunders J (Eds). Veterinary computed tomography. West Sussex, UK: John Wiley & Sons; 2011; 339-344.
3. Powe JR, Canfield PJ, Martin PA. Evaluation of the cytologic diagnosis of canine prostatic disorders. Vet Clin Pathol 2004; 33(3):150-154.

4. Raskin R, Meyer DJ. Canine and feline cytology. St. Louis, USA: Saunders Elsevier; 2010; 313-352.

5. Kuhnt NS, Harder LK, Nolte I, et al. Computed tomography: A beneficial diagnostic tool for the evaluation of the canine prostate? BMC Vet Res 2017; 13(1):123.

6. Paclikova K, Kohout P, Vlasin M. Diagnostic possibilities in the management of canine prostatic disorders. Vet Med 2006;51(1):1-13.

7. Smith J. Canine prostatic disease: A review of anatomy, pathology, diagnosis, and treatment. Theriogenology 2008; 70(3):375-783.

8. Noack G, Mortensson W, Robertson B, et al. Correlations between radiological and cytological findings in early development of bronchopulmonary dysplasia. Eur J Pediatr 1993; 152(12):1024-1029.

9. Suzuki T, Kurokawa K, Yamanaka H, et al. Lymphatic drainage of the prostate gland in canines. Prostate 1992; 21(4):279-286.

10. Beukers M, Grosso FV, Voorhout G. Computed tomographic characteristics of presumed normal canine abdominal lymph nodes. Vet Radiol Ultrasound 2013; 54(6):610-617.

11. Nyland TG, Mattoon JS. Peritoneal fluid, lymph nodes, masses, peritoneal cavity, great vessel thrombosis, and focused examinations. In: Mattoon JS, Nyland TG (Eds). Small animal diagnostic ultrasound. Philadelphia, USA: Elsevier Health Sciences 2015; 501-515.