


CASE REPORT

Benefits of respiratory navigation aided MRI in case of large abdominal tumors of canines: A case study

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Funding information

János Bolyai Research Fellowship, Grant/Award Number: BO/00313/14/4

Key Clinical Message

Magnetic resonance imaging using respiratory navigation technique can be the number one diagnostic method determining operability of large-sized abdominal tumors of dogs. This technique eliminates motion artifacts and makes possible the visualization of the origin and extent of the tumor and of the possible abdominal metastases.

KEYWORDS

abdominal tumor, dog, magnetic resonance imaging, respiratory navigation technique

1 | INTRODUCTION

Abdominal masses of small animals are primarily examined usually by ultrasonography. It may occur that ultrasonography reveals the presence of a large-size soft tissue mass in the abdomen, but it is unable to give the exact location, size, and origin of it. In such a case, further examinations are recommended such as computed tomography (CT) or magnetic resonance imaging (MRI). MRI provides soft tissue contrast that is far superior to that of provided by CT. Compared to ultrasound, MR is not a “real-time examination,” but image quality does not depend on the examiner. It also provides better three-dimensional distribution of an abnormality since it allows imaging of any view (sagittal, transversal, dorsal, or oblique planes) without the need of subject reposition. In

addition, MRI is noninvasive and it is ionizing radiation-free. Furthermore, allergic reactions are much less frequent against the contrast agent (gadolinium-based contrast material) that is used for MR examination compared to the iodine contrast agent used in CT.

Still, magnetic resonance imaging is mainly applied to the central nervous system and there have been only a few reports on abdominal lesions in veterinary practice. The evaluation of the abdominal and pelvic organs of dogs with MRI is a complex interaction of many factors but ultimately success or failure of the examination is reliant upon obtaining sequences free of motion-related artifacts caused by respiratory and peristaltic motion. Historically, ultrasound and CT have been the imaging modalities of choice for evaluation of the dogs' abdomen due to four main factors: access, ease of

incorporation into the clinical diagnostic profile, speed, and a greater capacity to avoid motion. There have been numerous attempts over the years to compensate for the various types of motion within the abdomen during MR imaging. The earliest and most simple form of motion correction was to average out the phase-related ghosting by acquiring data with multiple averages. The problem with this method is scan time, which increases with each additional average. Respiratory gating/triggering have been proven to be very successful in obtaining T2-weighted images of a very high diagnostic standard, but they ultimately require the patient to breathe in a regular pattern to obtain scan efficiency and motion-artifact-free images.

Attempts to implement more sophisticated motion insensitive sequences have been limited by system hardware and reconstruction times. With the improvement of coils and gradients, motion artifacts could be reduced by obtaining scans in breath-holds. This was fine for humans (adult), but not for sedated dogs.

By using respiratory navigation technique, these problems can be eliminated.¹ Respiratory navigation technique means “that the scanner is triggered to acquire data only when the diaphragm is in the most cranial position following expiration. When inspiration begins, the data acquisition is suspended.” With the respiratory navigation technique, there is no image blurring at all what is needed to visualize the functional attachment between the gastrointestinal organs wall and an expansive abdominal mass. This technique is superior compared to CT examination, especially for the evaluation of the alimentary organs due to the far better soft tissue contrast of the MR images. Compared to humans, dogs are not willing to drink the contrast material that is necessary to outline the lumen of the gastrointestinal organs on CT. Due to that and the lack of abdominal fat, which is a natural contrast of the abdomen, the soft tissues and their fluid content on the CT images will have all the same gray shade.

There are two recently published case reports, which are comparing the benefits of MRI and CT examinations in case of abdominal masses in dogs.

Mijin Kim et al found that postcontrast MRI was superior to CT in terms of soft tissue resolution in case of splenic hemangiosarcoma.² The authors concluded that MRI allowed differentiation between large-sized tumors and neighboring normal structures. Their results suggest that MRI might be a useful tool to visualize large-size splenic tumors and so improve the accuracy of diagnosis.²

Another case study of a canine mesenteric lymphoma reported that postcontrast MRI gave more information for the clinician than CT.³ Yasuda et al examined a dog with an abdominal mass, that was detected by ultrasound examination, using a dual-slice CT scanner and a 1.5 T MR imaging system.³ In this study, the lesion was assumed to be a single mass of large tumor based on the images obtained from the

dynamic CT scan with iodine contrast material. The subsequently produced three-dimensional CT angiography gave the same result. In contrast, the mass was found to be a complex tumor with adhesion to the gut on the gadolinium-enhanced T1-weighted MR images. The exploratory laparotomy confirmed the result of the MR examination. In conclusion, MRI gave more details of the lesion than CT or ultrasonography.

These results suggest that MRI is a useful tool to visualize large-sized abdominal masses and to improve the accuracy of diagnosis. However, Kim et al stated that when a mass grows large enough to compress the neighboring structures, its origin may be difficult to determine even with the standard MR sequences.²

According to another study about imaging abdominal lesions in dogs by Clifford et al, MRI can give valuable information about the location and extent of hepatic and splenic lesions, which can help the surgeon to assess the feasibility of surgical resection and accurately differentiate benign from malignant lesions.⁴ Clifford says that MRI currently is the modality of choice for characterizing hepatic lesions in human patients based on the interpretation of the lesion's signal intensity and morphology on precontrast T1-weighted (T1W), T2-weighted (T2W), and postcontrast T1W images.⁴ It is important because liver is a primary site of hematogenous metastasis of gastrointestinal tumors.

The purpose of the present study was to determine the effects of respiratory navigation technique on diagnostic quality of MRI in a dog with a large abdominal mass. Our aim was to see whether MRI with respiratory navigation technique is able to show the origin and exact location of the tumor compared to the ultrasound examination and to give valuable data to judge operability.

2 | MATERIALS AND METHODS

A five-year-old dog, a neutered female Hungarian vizsla, visited the local veterinary clinic with the main complaints of polyuria and polydipsia. Because of the symptoms, the veterinarian first decided to rule out the possibility of Cushing's disease using laboratory blood work. On the blood work results, the lactate dehydrogenase level was high, suggesting neoplastic or inflammatory process. Following abdominal palpation, ultrasound examination was carried out and an approximately 8 cm large mass was found in the right cranial- and midabdomen.

It was not possible to determine the origin of the mass by its location or by its tissue type characteristics seen on ultrasound. Therefore, aspiration cytology sample was taken from the mass and anaplastic carcinoma was revealed, which could stem from either an intestinal organ or the ovary. The dog was neutered and had no clinical signs that would indicate the disease of the gastrointestinal tract.

Before considering surgery, the clinician decided to send the dog further for a CT or MR examination. The radiologist suggested an abdominal MR examination using respiratory navigation technique to give the exact location and extension of the abdominal mass. CT was not considered to define the origin, extent, and geometry of the mass because the MR imaging using respiratory navigation technique is much more superior due to its soft tissue contrast compared to CT. And during MR examination, plane can be set freely while for the evaluation of structures with CT reconstruction images needed. These reconstruction images in the different planes are made from the cross-sectional CT images but lose detail. Furthermore, MR does not use ionizing radiation and better to detect metastasis in the omentum, mesenteries, peritoneal surface, retroperitoneum, and liver and then CT.

The weight of the dog was 25 kg at the time of the MR investigation. The examination was performed using a 3 Tesla magnet (Siemens Magnetom Trio a Tim System, Erlangen, Germany). Before scanning, the dog was sedated via a 22 G intravenous catheter (Vygonüle V Luer-Lock; Laboratoires pharmaceutiques VYGON, France) that was placed to the lateral saphenous vein of the right front limb. The dog was premedicated with medetomidin-hidroklorid (0.5 mL Narco Start 1 mg/mL AUV, Le Vet BV, Hollandia). Following premedication, anesthesia was induced with 2 mg/ttkg propofol iv (FRESENIUS KABI Deutschland GmbH, Germany). For the contrast-enhanced MRI examination, gadobutrol (Gadovist 1.0 mmol/mL, Bayer) was used at the dose of 0.1 mL/ttkg followed by 5 mL saline flush, in a bolus.

The dog was in dorsal recumbence throughout the MR examination.

T2-weighted and T1-weighted pre- and postcontrast MRI sequences were made. The acquisition parameters are disclosed in Table 1.

Images were stored on the local PACS system and evaluated using a Siemens Leonardo Multi-modality Workstation (Siemens, Erlangen, Germany) by a veterinary radiologist.

2.1 | Histopathology and immunohistochemistry

Following surgical excision, the tumor was stored in 8% buffered formaldehyde solution at room temperature for 24 hours. After conservation, tumor sections were prepared for histopathological examination and stained with routine hematoxylin and eosin (H&E) solution.

The mitotic index was defined by counting the number of mitoses per high power field (HPF, 400×) by careful analyses of 50 HPF.

The following immunohistochemistry markers were used for completing the pathological diagnosis: vimentin for detecting the presence of mesenchymal cells; α -smooth muscle actin (α -SMA) for detecting smooth muscle; anti-S-100 protein for detecting melanomas, schwannomas, neurofibromas, peripheral nerve sheath tumors, paraganglioma stromal cells, histiocytoma, and clear cell sarcomas; c-Kit (CD117) for detecting gastrointestinal stromal tumor and/or mast cell tumors; CD31 and claudin-5 for detecting hemangiosarcomas; Ki-67 for the detection of proliferative cells.

The slides for the immunohistochemical reaction were deparaffinized in xylene and graded ethanol. After antigen retrieval (Target Retrieval Solution, DAKO, Glostrup, Denmark, pH 6; microwave oven for 30 minutes), the deparaffinized sections were treated with primary antibodies

TABLE 1 Parameters of the MRI sequences used with respiratory navigation technique

Sequence	T2 haste COR with RN	T2 haste AXI with RN	T2 haste SAG with RN	T1 AXI native with RN	T1 AXI postcontrast with RN
Repetition time (ms)	2000	2000	2000	1500	1500
Echo time (ms)	86	90	86	2.5	2.5
Length of acquisition (min:s)	2:11	2:11	2:11	1:46	1:46
Slice thickness (mm)	3	3	3	3.5	3.5
Interslice gap (mm)	0.6	0.9	0.6	0.7	0.7
Field of view	300 × 300	370 × 370	300 × 300	285 × 380	285 × 380
Echo train length	256	256	256		
Matrix	256 × 320	256 × 320	256 × 320	157 × 256	157 × 256
Number of slices	40	40	40	37	37
NEX (number of excitation)	1	1	1	1	1
Flip angle	150°	150°	150°	20°	20°
Scout TR (ms)	150	150	150	150	150
Accept window (mm)	±2	±2	±2	±2	±2

Axi: axial; Cor: coronal; Haste: half-Fourier acquisition single-shot turbo spin echo; RN, respiratory navigation technique; Sag: sagittal.

including vimentin (diluted 1:100, mouse monoclonal, DAKO), α -smooth muscle actin (α -SMA) (diluted 1:8000, mouse monoclonal, Sigma), anti-S-100 protein (diluted 1:50, rabbit polyclonal, DAKO), anti-c-Kit (CD117) (diluted 1:100, rabbit polyclonal, DAKO), Ki-67 (diluted 1:100, mouse monoclonal, DAKO), CD31 (diluted 1:80, mouse monoclonal, DAKO), and claudin-5 (diluted 1:100, mouse monoclonal, Zymed Inc, San Francisco) at room temperature for 60 minutes. Immunohistochemical staining was performed using the streptavidin-peroxidase procedure. Antigen-bound primary antibody was detected using standard avidin-biotin immunoperoxidase complex (DAKO LSAB2 Kit). The chromogen substrate was diaminobenzidine (DAB). Mayer's hemalaun was used for counter-staining. For negative control, the slides were stained with the omission of primary antibody. The external positive controls were canine fibroma for vimentin, canine leiomyoma for α -SMA, canine peripheral nerve sheath tumor for S-100 protein, canine mast cell tumor for c-Kit, canine hemangiosarcoma for CD31, claudin-5, and Ki-67.

3 | RESULTS

3.1 | Findings of the ultrasound examination

A mass of 8 cm diameter with mixed echogenicity was found in the cranial abdomen via ultrasound examination. It was surrounded by the liver, spleen, stomach, and colon. The structure of the liver was normal. The capsule of the spleen was well determined. The echogenicity of the spleen, liver, and renal cortex—compared to each other—was normal. The shape and structure of the right and left kidneys were also normal and they were not in contact with the mass. The adrenal glands could not be visualized. The stomach was pushed toward the left and compressed by the mass. Its wall could only partly be seen. Enlarged lymph nodes were not found in the abdomen. Fine-needle aspiration of the mass was made for cytological examination.

3.2 | Cytology

The cytological report states that the sample contains only a very few cells. Among the few macrophages, there are scarcely some moderately large round cells. These cells are 2-3 times of the red blood cells, and their cytoplasm is narrow, basophil, and granulated. Their nuclei are large, round, and granulous. Based on these very few cells, a suspicion of anaplastic carcinoma, which may originate from the intestine or the ovarium, occur.

3.3 | MRI findings

T2-weighted sagittal, dorsal and axial images, native and postcontrast T1-weighted sagittal and axial images were prepared with respiratory navigation technique.

On the T2-weighted sagittal images, the mass was heterogeneous considering its structure and had mainly low signal intensity. It was well demarcated except for a 2 cm length near the gastric wall see Figures 1 and 2. Both left and right kidneys were normal considering their size, signal

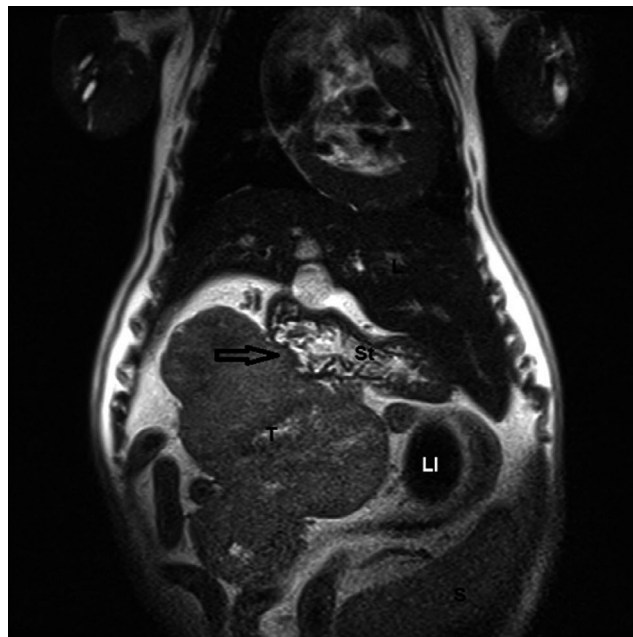


FIGURE 1 Dorsal T2-weighted image of the abdomen. Arrow: the area where not possible to separate the mass from the gastric wall. L: liver; LI: large intestine; S: spleen; St: stomach; T: tumor

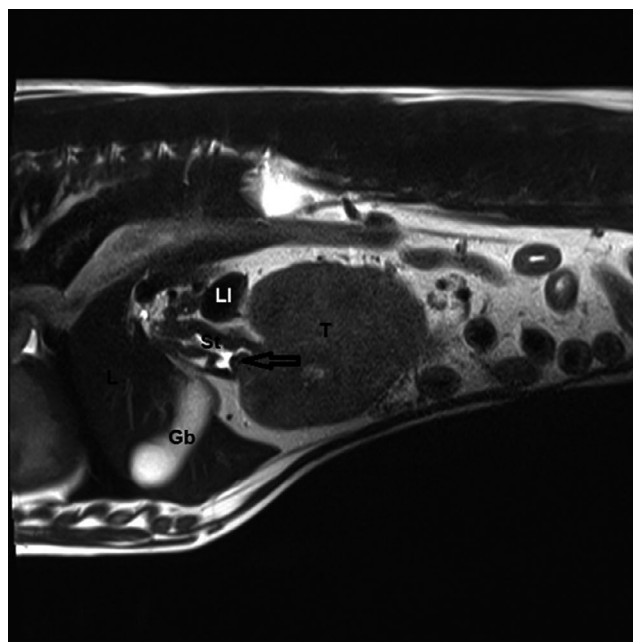


FIGURE 2 Sagittal T2-weighted image of the abdomen. Arrow: the area where not possible to separate the mass from the gastric wall; L: liver; Gb: gall bladder; LI: large intestine; St: stomach; T: tumor

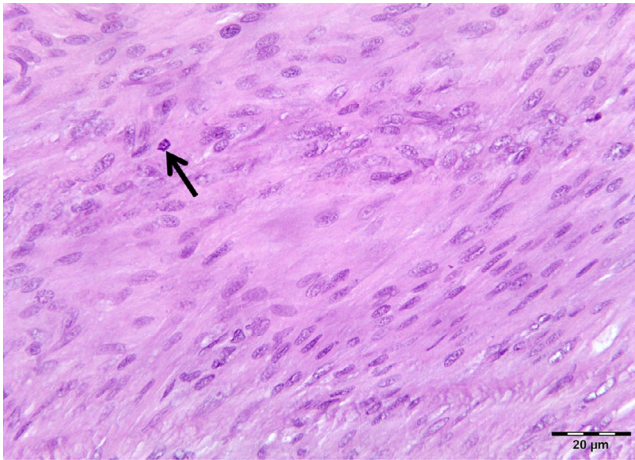


FIGURE 3 Histopathological picture of the tumor with mitotic neoplastic cell (arrow), H.-E., 400 \times

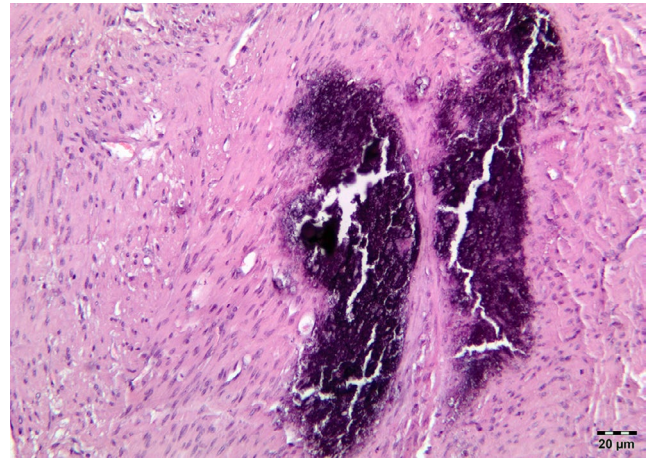


FIGURE 4 Necro-calcification in the parenchyma of the tumor, H.-E., 200 \times

intensity, and shape. Spleen was also normal in appearance. Both, the left and right adrenal glands were well determined, normal.

Postcontrast T1-weighted images were also prepared in two (sagittal and axial) orientations. On the postcontrast images, the tumor was well determined. It was clearly separated from the liver, spleen, intestines, kidneys, and adrenal glands. But it was not possible to demarcate the borderline between the mass and the gastric wall on a 2 cm length in the right midabdomen.

The MRI examination reconfirmed the suspicion of intestinal origin of the mass. Signs of metastasis in the abdomen were not found.

Following the MR examination, the dog was operated and the mass was removed. Metastatic lymph node was not found during the surgery.

3.4 | Histopathology and immunohistochemistry result

The surgically removed mass was sent to histopathological examination. The histopathology and immunohistochemistry report said that the neoplasm was highly cellular spindle cell tumor with moderate nuclear density, prominent nuclear palisading and scant cytoplasm, and without perinuclear vacuolization (Figure 3). Multifocal necro-calcifications were detected in the parenchyma of the tumor (Figure 4). Mitotic index was 5/50HPFs. Percentage of the necrosis in the section was mild (20%-25%). Tumor showed vimentin-, c-Kit-positivity, and α -SMA-, S-100 protein-, CD31-, claudin-5-negativity. The Ki-67-labeling index was 9%-10%. The endothelial cells of the tumor-induced microvessels showed CD31- and claudin-5-positivity. The histopathological diagnosis, based on the characteristics of the tissue, was high-grade canine gastrointestinal stromal tumor, originating from the gastric wall.

3.5 | Therapy

Computed tomography was used after the removal of the tumor to evaluate the entire body status for metastasis before treatment. CT is preferable compared to thoracic radiographs as there is no superimposition, and its resolution is superior. Also important that GISTs most commonly metastasize to the intra-abdominal soft tissues (omentum, mesenteries, and retroperitoneum).⁵ Hematogenous metastases commonly develop in the liver, and rarely in bones and lungs.⁶ Rarely seen sites of metastases are the peripheral soft tissues (arm, axilla, and abdominal wall). There was no tumor detected at any site.

The dog was treated with vincristine (0.75 mg/m² iv), doxorubicin (30 mg/m² iv.), and cyclophosphamide (150 mg/m² iv.), the “VAC” chemotherapy protocol in two cycles. It was followed with metronomic chemotherapy according to Elmslie: low dosage of cyclophosphamide (12.5 mg/m² orally) with etoposide (50 mg/m² orally), piroxicam (0.3 mg/kg orally), and famotidine (1 mg/kg orally).

Three and a half years after treatment, the dog is in good health and free of disease.

4 | DISCUSSION

A large tumor in the abdomen of a dog can be challenging for the clinicians. It is often difficult to determine the origin of these masses. Not to mention to answer the frequently asked question, whether it is operable or not. Our aim was to see whether MRI could provide more details about the origin and location of the tumor compared to ultrasound examination and give valuable data to answer operability.

In the literature, there are only two publications of similar cases, where the main indication of MRI was to evaluate the operability of the tumor. Mijin Kim et al found a large-sized

soft tissue mass caudodorsal to the liver by abdominal radiography without thoracic metastasis on radiographs.² They first examined a mass using ultrasound as in our case. Similar to us, they were not able to define the origin of the mass by ultrasonography. They followed the check-up using both CT and MRI. On CT, the mass was in contact with both the liver and the spleen. There was an enlarged mesenteric lymph node, a splenic nodule, and a pulmonary metastasis also proved by CT. The MRI clearly showed that the tumor originated from the head of the spleen. The mass was hyperintense on the T2-weighted images and hypointense on the T1-weighted images. It showed mild contrast enhancement. It was thought to be a splenic hemangiosarcoma that was later verified by the histopathological examination. The MRI confirmed the enlarged mesenteric lymph node and the splenic nodule as well.

Daiji Yasuda and co-authors published an article in 2004 about the examinations of a large-size intra-abdominal tumor with MRI.³ The tumor in the central abdomen was first recognized via radiography. On the lateral view, the mass was ventral to the kidneys. In this case, similar to Mijin et al, both CT and MRI examination were carried out.² The native CT analysis showed the location of the mass in the center of the abdomen, similar to the simple radiograph. The dynamic CT gave a diagnosis of a homogeneously enhancing single mass, with a size of a $3 \times 5 \times 5$ cm³. On the contrary, the MR revealed that the mass was a complex mass with adhesions to the ileum and cecum and identified an enlarged mesenteric lymph node. Histologically, the mass was lymphoma.

In both cases, laparotomy confirmed the results gained by MRI.

In our case, the 8 cm wide mass was found by ultrasonographic examination.

The result of the aspiration cytology taken from the mass was anaplastic carcinoma that may originate from the gastrointestinal tract or the ovarium. The dog was neutered; therefore, it had a small probability that the tumor grew from ovarian cells that may remain in the abdomen though it could not be entirely ruled out. For surgical intervention, it was important to localize the tumor including its origin. For this, the most up to date method, MRI examination with respiratory navigation technique was carried out. The mass was removed, and the histopathology examination gave the diagnosis of gastrointestinal stromal tumor (GIST). This was different from the result of the cytology examination that was carried out from the fine-needle aspiration sample taken during ultrasound examination. The large gastrointestinal stromal tumors can be centrally necrotic and cystic, containing hemorrhagic and necrotic materials or fluid. Furthermore, stromal calcifications may occur. The viable tumor is usually present only as a narrow peripheral rim.⁵ According to the MR images, this was the case in our patient and it explains the very few cells in the fine-needle aspiration sample. As this method

based on cytomorphological aspect of cells and tissue particles acquired using a fine needle, a mass that has only a narrow rim of cells can give a poor sample. One more reason, which explains the different results gained by cytology and histology, could be the fact that fine-needle aspiration is often more reliable to predict the malignicity of the tumor and then to define its exact type due to its low sensitivity to characterize.⁷ Contrary to cytology, for the histopathological examination, the whole tumor was available that made possible to determine its type. The diagnosis also explains the lack of gastrointestinal signs, as those GISTs that do not cause ulceration can grow into a large size without being noticed even in people.⁵

To provide the most accurate information regarding the large abdominal masses for surgical intervention and to search for metastasis, MRI examination with respiratory navigation technique is the choice. With this technique, good quality images are gained. Respiratory navigation technique for the reductions of motion artifacts is easier to implement in anesthetized dogs, as compared to breath-hold technique used by Yasuda et al³ The entire abdomen can be examined in different views that not only help to delineate the borders of the organs but also important to detect metastatic changes. The high resolution and excellent soft tissue contrast of the MR images, compared to ultrasonography and CT, makes it the method of choice in these cases. It is very helpful in determining the tumor configuration and its extensions and relationship with adjacent organs.

The MR examination using respiratory navigation technique should always be considered previous to surgical intervention in cases when the origin of an abdominal mass could not be determined by ultrasonography.

ACKNOWLEDGMENTS

The study was sponsored by János Bolyai Research Fellowship (BO/00313/14/4). The study was supported by the Hungarian Brain Research Program (2017-1.2.1-NKP-2017-00002) government-based fund, EFOP-3.6.2-16-2017-00008 "The role of neuro-inflammation in neurodegeneration: from molecules to clinics," the János Bolyai Research Scholarship of the Hungarian Academy of Sciences (G.P. and G.O.), PTE ÁOK-KA-2017-05 and PTE ÁOK-KA-2017-06.

AUTHOR CONTRIBUTION

MV: conceived of the presented idea and wrote the manuscript. JB: participated in developing the ideas, supervised the imaging works, and guided the writing processes and supervised the manuscript. GO: developed the theory and performed the MR imaging and wrote about its technical details. GP: developed the theory and wrote about the technical details of MRI together with Gergely Orsi. CJ: carried out

the histopathology and immunohistochemistry work and also wrote that part of the manuscript. PV: was responsible for the cytology work and also described it and supervised the manuscript. PB: supervised the project.

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How to cite this article: Vaskó M, Orsi G, Perlaki G, et al. Benefits of respiratory navigation aided MRI in case of large abdominal tumors of canines: A case study. *Clin Case Rep*. 2019;7:1071–1077. <https://doi.org/10.1002/ccr3.2115>