



ALMA MATER STUDIORUM  
UNIVERSITÀ DI BOLOGNA

ARCHIVIO ISTITUZIONALE  
DELLA RICERCA

## Alma Mater Studiorum Università di Bologna Archivio istituzionale della ricerca

Comparison of sonographic and CT findings for the identification of renal nodules in dogs and cats

This is the final peer-reviewed author's accepted manuscript (postprint) of the following publication:

*Published Version:*

Rossi, F., Gianni, B., Marconato, L., Sabattini, S., Caleri, E., Mattolini, M., et al. (2023). Comparison of sonographic and CT findings for the identification of renal nodules in dogs and cats. *VETERINARY RADIOLOGY & ULTRASOUND*, 64(3), 439-447 [10.1111/vru.13219].

*Availability:*

This version is available at: <https://hdl.handle.net/11585/960760> since: 2024-02-23

*Published:*

DOI: <http://doi.org/10.1111/vru.13219>

*Terms of use:*

Some rights reserved. The terms and conditions for the reuse of this version of the manuscript are specified in the publishing policy. For all terms of use and more information see the publisher's website.

This item was downloaded from IRIS Università di Bologna (<https://cris.unibo.it/>).  
When citing, please refer to the published version.

(Article begins on next page)

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26

**ULTRASONOGRAPHIC AND CT FINDINGS IN 39 CANINE AND FELINE KIDNEYS WITH RENAL NODULES**

**Key words:** kidney, metastases, small animals

**Conflict of interest disclosure:** the authors have no conflict of interest to declare.

**Previous presentation or publication disclosure:** the preliminary results of the present study have been presented at the ECVDI online meeting 2021.

**EQUATOR network disclosure:** no EQUATOR network checklist was used.

**Abstract:**

Ultrasonography (US) and Computed Tomography (CT) are used to diagnose neoplastic and non-neoplastic focal renal lesions; however, comparative studies between these two diagnostic tools are lacking. The aim of this retrospective study was to evaluate evaluate and compare the US and CT features of confirmed focal renal nodules in a group of animals.

Imaging studies of animals with mono- or bilateral renal nodules smaller than 3 cm that underwent both US and CT were reviewed. Animals with renal cysts and infarcts were excluded. Recorded features included, for both modalities, shape, size, number, localization, margins, renal profile; for CT only, attenuation (HU) and pattern of enhancement; for US only echogenicity, echostructure and rate of visibility. Final diagnosis was obtained by cytology or histopathology.

Using CT, lesions were identified in 39/39 (100%) kidneys of 18 dogs and 7 cats. Most lesions were multiple, cortical, well defined, iso-attenuating (pre-contrast), hypo-attenuating and moderately enhancing (post-contrast).

Using US, lesions were identified in 29/39 (74%) kidneys. Overall, 9 (31%) lesions were

27 poorly visible; 10 (26%) kidneys appeared normal; in 17 (59%) organs, lesions' number was  
28 underestimated. Isoechoic, non-protruding lesions were difficult to identify by US.  
29 Final diagnoses included metastatic disease (n=16), infiltration by feline lymphoma (n=4),  
30 primary neoplasia (n=3), and non-neoplastic benign lesions (n=2).  
31 In the current case series, both US and CT showed renal nodules, however US failed to  
32 diagnose or underestimated the number of inflammatory and neoplastic nodules in a  
33 significant number of cases compared to CT.

34

### 35 **1. Introduction:**

36 Focal renal nodules are uncommonly reported in small animals, primary renal neoplasia  
37 being the most frequent cause of renal nodules or masses.<sup>1-6</sup> Renal metastases are rare in  
38 people, with a reported incidence ranging from 2.36 to 12.6%, with carcinomas being the  
39 most common tumors (80%) spreading to the kidneys.<sup>7,8</sup> Little information is available in  
40 veterinary medicine regarding renal metastases. A single case report describes renal  
41 metastases in a dog with nasal condrosarcoma<sup>9</sup>, whereas in cats with lymphoma the kidneys  
42 can be infiltrated and a nodular pattern is commonly described.<sup>10,11</sup>

43 Benign nodules are even more rare in small animals. Renal adenomas have been described;  
44 however, there is a grey zone in the differentiation with well-differentiated carcinomas.<sup>4</sup>  
45 Finally, non-neoplastic lesions like granulomas, abscesses or haemorrhage are occasionally  
46 diagnosed.<sup>3</sup>

47 Diagnostic imaging plays a fundamental role in investigating kidney diseases:  
48 ultrasonography (US) is the first approach in clinical practice, however Computed  
49 Tomography (CT) is becoming more and more popular especially in large dogs and in  
50 patients where the sonographic window is suboptimal. A diagnostic multimodal approach is  
51 also preferred in human beings, where CT, MRI and PET-CT have shown a higher  
52 diagnostic accuracy in demonstrating renal disease compared to US.<sup>8,12,13,14</sup>

53 In veterinary medicine, comparative studies are lacking; in a single investigation including  
54 different abdominal conditions, CT was superior in lesion detection compared to US in dogs  
55 over 25 Kg; however, renal nodules were not included.<sup>15</sup>

56 **The aim of this descriptive cross-sectional retrospective study was to evaluate and compare**  
57 **the US and CT features of focal renal nodules confirmed by cytology or histopathology in**  
58 **dogs and cats.**

59

## 60 **2. Material and Methods**

### 61 ***Study population and imaging analysis***

62 Dogs and cats with a final diagnosis of uni- or bilateral, single or multiple renal nodules,  
63 undergoing both abdominal US and a pre- and post-contrast CT study of the abdomen at  
64 the Clinica Veterinaria dell'Orologio between 2012 and 2021, were identified from the  
65 database from one of the authors (XX).

66 Approval by an institutional animal care and use committee or institutional review board was  
67 not required.

68 Inclusion criteria were: 1. At least one renal nodule visible in US or CT, defined as a round  
69 to oval, vascularized cortical or medullary lesion with any type of echogenicity or CT  
70 perfusion pattern focally disrupting the normal renal parenchyma 2. Abdominal US and CT  
71 examination performed within one week 3. A complete set of diagnostic quality ultrasound  
72 images and videos representing all parts of one or both kidneys available for review and 4.  
73 Final diagnosis of the renal lesion/lesions obtained by conclusive cytology or histopathology.  
74 Animals with renal masses with a diameter over 3 cm, simple renal cysts and renal  
75 infarctions were excluded from the study. Nodules were defined as single solid focal lesions  
76 of any echogenicity or CT perfusion pattern. According to the Bosniak classification used in  
77 human radiology, simple renal cysts were diagnosed in CT as well-marginated, fluid-  
78 attenuating (0-20 Hounsfield Units, HU), non-enhancing homogeneous lesions with a

79 hairline-thin wall and confirmed in US as round to oval, anechoic, homogeneous, smooth  
80 and sharply demarcated thin wall structures associated with distal acoustic enhancement  
81 and surrounded by normal renal parenchyma.<sup>16,17</sup> Renal infarctions were recognized as  
82 wedge-shaped, cortical broad-based, hyperechoic bands in US and as wedge-shaped  
83 parenchyma perfusion defect, with or without a cortical rim sign, without mass effect, or  
84 major peri-renal fat stranding lesions in CT, eventually associated with irregular shape and  
85 focal cortical atrophy in the chronic phase.<sup>18,19</sup>

86 Signalment information including age, breed, sex, and body weight were obtained from the  
87 medical records.

88 Decisions regarding case selection and the review of the CT and US studies were made by  
89 a second year ECVDI resident (XX). The same author and an European College of  
90 Veterinary Diagnostic Imaging (ECVDI) board-certified radiologist (XX) recorded the US and  
91 CT findings independently. US images and videos were analysed first, followed by the CT  
92 studies, A consensus was found in case of initial disagreement. The CT images were  
93 evaluated using an open-source dedicated DICOM viewer software (Horos version 168  
94 3.3.6, Horosproject.com) and displayed using soft tissue window (window level 50 HU,  
95 window width 350 HU) for medium frequency and bone window (window level 300 HU,  
96 window width 1500 HU) for high frequency reconstruction algorithm. The second algorithm  
97 was used to identify the site of lesion's mineralization. Multiplanar reconstructions (dorsal,  
98 sagittal, and transverse) were used to evaluate all studies.

99 For both modalities and for each kidney, recorded images features were: lesions' number  
100 (divided in 3 groups: single, between 2-6 and over 6 lesions), size (nodule largest diameter,  
101 <1 cm or  $\geq 1$ ), shape (round or oval), margins (well-defined or irregular), location (cortical,  
102 medullary or both) and renal profile (normal or deformed).

103 Only for CT, the minimum, maximum, median ( $\pm$  SD) attenuation of the largest lesion,  
104 expressed in HU was measured in the pre- and post-contrast series including the entire

105 lesion; moreover, the enhancement pattern (homogeneous, heterogeneous, rim) was  
106 evaluated.

107 Only for US, the B-mode echogenicity (iso-, hypo or hyperechoic compared to the  
108 surrounding renal cortex or medulla), the echo-structure (homogeneous or heterogeneous)  
109 and, if available, the Color or Power Doppler pattern (hypo- or hypervascular lesions) were  
110 evaluated. If Doppler was used, the lesion and part of the surrounding normal kidney were  
111 included in the Color Doppler box, and the two regions were subjectively compared. Lesions  
112 were considered hypervascular if with similar or higher vessel conspicuity to the kidney was  
113 present and hypovascular if lower vessel density was observed. Finally, the visibility of all  
114 renal lesions recognized in CT were compared with the sonographic appearance and  
115 classified in 3 categories: 1. clearly visible (immediate, excellent visualization in US because  
116 of evident altered echogenicity or evident renal profile deformation), 2. poorly visible (unclear  
117 lesion, with mild changes of cortical/medullary echogenicity or echostructure and poor renal  
118 profile deformation) and 3. not visible (normal cortical/medullary echogenicity and  
119 echostructure, no deformation of the renal profile).

120 Other additional relevant CT findings, including abdominal lymphadenopathy, presence of  
121 lesions in other abdominal organs or in any additional examined body parts were annotated.

122 The final diagnosis was recorded. In case of renal metastasis, information on the primary  
123 extra-renal cancer (type, location, presence of other sites of metastases) was registered.

124 The study hypotheses were that a higher number of lesions was visible in CT and that  
125 lesions' US features (especially size, echogenicity, deformation of the renal profile) and  
126 location (right versus left kidney) influence their visibility in US.

### 127 **Statistical analysis**

128 The statistical analysis was performed by a veterinary researcher with experience in medical  
129 data analysis (SS). Descriptive statistics were used to summarize demographic information  
130 and lesion characteristics. When appropriate, data sets were tested for normality by use of

131 the D'Agostino and Pearson omnibus normality test. No data had normal distribution and  
132 were therefore expressed as median (range).

133 The difference on the number of nodules detected in US compared with CT for each kidney  
134 was assessed with Wilcoxon matched pairs signed rank test.

135 The effects of species, sex, kidney side (right vs left), nodule location (cortical vs medullary),  
136 number of nodules (single vs multiple), nodule largest diameter ( $\geq 1$  vs  $< 1$  cm), nodule shape  
137 (round vs oval) and final histologic diagnosis (non-neoplastic lesion, primary renal tumor,  
138 metastatic tumor) on the possibility to detect renal nodular lesions were evaluated with  
139 Fisher's exact test. The effects of dogs' body weight on the possibility to obtain a correct US  
140 diagnosis was evaluated with Mann-Whitney U test.

141 Data were analyzed by use of commercial software programs (SPSS Statistics v. 26, IBM,  
142 Somers, NY). P values  $\leq 0.05$  were considered significant.

143

### 144 **3. Results**

#### 145 **3.1 Clinical demographic data**

146 Fifty-three animals with renal nodules that underwent both CT and US were initially  
147 identified. Twenty-eight cases were excluded because the renal lesions were not sampled  
148 (n=23) or cytology was inconclusive (n=5). Finally, the study population included 39 kidneys  
149 (22 right and 17 left) from 25 animals (18 dogs and 7 cats).

150 All cats were domestic shorthair; 2 of them were castrated males and 5 spayed females.

151 Median age was 15 years (range 5-21.2), and median weight was 5 Kg (range 3.1-6.7).

152 Mixed-breed dogs represented the majority (n=7), whereas purebred dogs included one  
153 each of the following: German Shepherd, Boxer, Dalmatian, Epagneul Breton, Chihuahua,  
154 English Setter, Cocker Spaniel, Labrador Retriever, Maltese, Beagle and Giant Schnauzer.

155 Median age was 11.2 years (range 6-18), and median weight 19.5 kg (range 3.3-40). There  
156 were 8 spayed females, 4 intact females, 4 intact males and 2 castrated males.

157 Final diagnoses were obtained in 23 cases by cytology (in 19 cases by US-guided fine  
158 needle aspiration and in 4 cases by combined CT/US guidance) and in 2 cases by  
159 histopathology (by US-guided tru-cut biopsy in one case and after nephrectomy in the  
160 second case). The combined CT/US approach was performed in 4 animals where US failed  
161 to visualize the nodules, by sampling the area where the lesion was visualized in CT.  
162 Following diseases were diagnosed: 2 (8%) non-neoplastic benign lesions (1 inflammatory  
163 granulomatous nodule, 1 nodular hyperplasia), 2 (8%) primary renal neoplasia (1 adenoma,  
164 1 primary canine lymphoma), 5 (20%) feline lymphoma (1 bilateral renal lymphoma, 2 nasal  
165 and 2 multicentric lymphomas with renal involvement), and 16 (64%) metastatic lesions.  
166 Among the latter, there were 12 carcinomas (4 canine pulmonary, 3 canine thyroid, 1 canine  
167 mediastinal neuroendocrine, 1 canine adrenal, 1 feline retrobulbar, 1 canine apocrine, 1  
168 canine metastatic cancer of unknown primary (MCUP), 2 sarcomas (1 canine histiocytic  
169 sarcoma, 1 canine hemangiosarcoma) and 2 melanomas (1 canine digital and 1 canine  
170 pharyngeal). Metastases were solitary (n=5/16, 31%) or multiple (n=11/16, 69%), bilateral  
171 (n=9/16, 56%) or unilateral (n=7/16, 44%). In 7/16 (44%) of these patients, the kidney was  
172 the only metastatic site, whereas in the remaining 9 cases metastases were found also in  
173 the lung, pleura, liver, subcutis, muscles, lymph nodes and bones.

### 174 **3.2 Imaging techniques**

175 US of the kidneys was performed with one of the following units: Esaote My Lab 30 Vet,  
176 Esaote Megas CVX, Esaote My Lab 70Vet, Esaote MyLab™ X8 platform, using either a  
177 electronic microconvex 5-7,5 MHz or a linear 5-13 MHz probe. In 10/26 cases (38,5%), a  
178 first abdominal US examination was performed by the referral veterinarian before the CT  
179 study: in 6/10 of them the kidneys were evaluated as normal, whereas single (n=2) or  
180 multiple (n=2) renal lesions were recognized in the other 4 animals; all lesions were  
181 confirmed in CT. In all animals, the kidneys were scanned by US under general anaesthesia  
182 immediately following the CT study, with the further aim of sampling the renal lesions found

183 in CT. Each kidney was scanned in longitudinal and transverse plane after clipping the area  
184 of interest, with the patient in lateral or dorsal recumbency. Grey-scale images were  
185 obtained in all cases, Color and/or Power Doppler was performed in 13 animals.

186 CT studies were performed in sternal recumbency under general anaesthesia. In all animals,  
187 a total-body CT was acquired, the scan including cranially the entire head and caudally the  
188 proximal half of the hind limbs. Two different CT units were used: a 16-slice multidetector  
189 CT (Brightspeed S, GE Healthcare, Medical Systems, Milan, Italy) and a 64-128  
190 multidetector CT (Optima 660, GE Healthcare, Medical Systems, Milan, Italy). Technique  
191 settings for the scans were: slice thickness range from 0.65 to 2.5 mm, matrix size of 512 x  
192 512, field of view ranging between 200-500 mm, kVp 100-120, mAs 99-400, and pitch  
193 0.9375-1.75.

194 A pre-contrast and a post-contrast study was always performed, after the administration of  
195 a water-soluble iodinated contrast medium (Ioversol, Optiray 300, Guerbet S.p.A, Milan),  
196 injected intravenously using a power injector (OptiVantage®DH, Guerbet S.p.A, Milan), at a  
197 dose range of 450-600 mg/l/kg.

### 198 **3.3 Imaging characteristics of renal nodules**

199 Table 1 summarizes US and CT findings of renal nodules.

200 US identified lesions in 21/25 (84%) animals and 29/39 (74%) kidneys, 12 on the left kidney  
201 and 17 on the right kidney. Renal lesions were bilateral in 8/21 (38%) animals and unilateral  
202 in 13/21 (62%); nodules were single in 18/29 cases (62%, 6 left and 12 right), between 2-6  
203 in 6 cases (21%, 4 left and 2 right) and over 6 in 5 cases (17%, 2 left and 3 right).

204 The median maximum diameter was 1.2 cm (range 0.4-2.9). In 18/29 (62%) cases, the  
205 biggest lesion visualized in US was over 1 cm, whereas in 11/29 (38%) was smaller than 1  
206 cm.

207 The shape was round in 25 (86%) nodules and oval in 4 (14%). Margins were well-defined  
208 (n=19, 66%) or ill defined (n=10, 34%). The nodules were located in the cortex in 24 kidneys  
209 (83%) and in the medulla in 5 (17%).

210 Lesions were mostly hypoechoic (n=18, 62%), less frequently hyperechoic (n=8, 28%) or  
211 isoechoic (n=3, 10%); the echotexture was mostly heterogeneous (n=20, 69%), less  
212 frequently homogeneous (n=9, 31%), deforming (n=18, 62%) and non-deforming (n=11,  
213 38%) the renal capsule.

214 The sonographically detectable nodules were most frequently single (62%), hypoechoic  
215 (62%), heterogeneous (69%), deforming (62%) and well-defined (66%).

216 Color-Doppler was available for 13 animals, in 2 of them Power-Doppler was also used. In  
217 the cases where the lesion was already clearly visible in grey-scale (n=9), Doppler was  
218 considered useful to evaluate lesion's vascularisation. Overall, nodules were mostly  
219 hypovascular (n=6, 46%) except for 3 hypervascular metastases (23%) from thyroid  
220 carcinomas, where a net of thin uniformly distributed vessels was visible in the lesion. In the  
221 4 cases (30.8%) with poorly visible nodules, Color Doppler did not improve their  
222 visualization.

223 CT identified focal renal lesions in 25/25 animals (100%) and 39/39 kidneys (100%). Lesions  
224 were distributed almost equally in the two kidneys, 22 (56%) on the right side and 17 (44%)  
225 on the left side. In 12/39 (31%) cases, lesions were single, in 16/39 (41%) cases 2-6 nodules  
226 were identified, and in 11 cases (28%) there were more than 6 lesions.

227 Lesions' shape was mostly round (n=32, 82%) and less frequently oval (n=7, 18%).

228 Mean maximum diameter was 1.5 cm, with 14/39 (36%) kidneys having nodules smaller  
229 than 1 cm, 14/39 (36%) over 1 cm and 11/39 (28%) nodules of both categories.

230 The nodules had mostly well-defined margins (n=36, 92%), cortical location (n=36, 92%)  
231 and deformed the renal profile in 18 (46%) cases. The mean attenuation was 35.8 HU in the  
232 native scan and 78.24 HU after contrast administration. Compared to the surrounding cortex,

233 all nodules were markedly hypoattenuating post contrast. The enhancement was  
234 homogeneous in 24/39 kidneys (62%), heterogeneous in 13/39 (33%) and ring-type in 2  
235 (5%).

### 236 **3.4 Comparison of sonographic and CT findings**

237 In CT, renal nodules were clearly visible in all kidneys; in the post-contrast scan they were  
238 strongly hypoattenuating to the surrounding cortex. There were no cases where US  
239 identified renal lesions and CT did not.

240 US identified renal nodules in 29/39 kidneys (74%) and 21/25 patients (84%). Within the 29  
241 kidneys with sonographically detected lesions, the number of visualized lesions was the  
242 same as in CT for 12 (41%) cases and underestimated in 17 (59%) ( $P < 0.001$ ). Among  
243 identified nodules, lesions were considered poorly visible in 9 (31%) kidneys and 7 (33%)  
244 patients, and clearly detectable in 20 (69%) kidneys and 14 (67%) patients. The distribution  
245 of the identified nodules between right and left side was not significantly different in both the  
246 total group and the dogs group.

247 Compared to CT, lesions were not detected by US in 10/39 kidneys (26%). In one dog,  
248 bilateral nodules were missed, whereas in 3 cases (2 dogs and 1 cat) one kidney was normal  
249 but the contralateral was affected; all these 4 animals had a primary neoplasia (3 carcinomas  
250 and 1 melanoma) and were staged negative with US. In other 5 dogs, one kidney was  
251 considered normal but nodules in the contralateral kidney were identified. Table 2  
252 summarizes the CT features of the 10 nodules undetected in US.

253 The median weight of dogs with visible renal lesions (either clearly or poorly visible) in US  
254 was significantly lower compared with that of dogs with undetected renal lesions (16.0 kg vs  
255 29.5 kg, respectively;  $P = 0.032$ ).

256 No significant effect of species, sex, kidney side, nodule location, number of nodules, nodule  
257 size, nodule shape and final histologic diagnosis on the possibility to detect renal nodular  
258 lesions was identified. Isoechoic, non-protruding lesions were difficult to identify by US.

259

260 **Discussion**

261 This study first describes the US and CT features and prevalence in a group of dogs and cats with  
262 confirmed renal nodules. In clinical practice, both techniques are used to scan the abdomen in  
263 oncologic patients, with the aim of identifying parenchymal lesions compatible with metastases.

264 In the current study, 16% of animals with renal lesions were staged negative with US and,  
265 among patients with sonographically identified lesions, there was a significant  
266 underestimation of the number of nodules compared with CT. Renal lesions were clearly  
267 identified by contrast CT, regardless of their size, because of the evident hypoattenuating  
268 appearance compared to the surrounding cortex. The strong cortical enhancement in CT is  
269 produced by the sum of the vascular component (contrast medium in the renal vascular bed)  
270 and the filtration process (contrast medium filtered from the renal glomeruli to the tubules);  
271 the distortion of the vascular pattern and of the filtrating structures in the nodule can explain  
272 the marked hypoattenuating aspect.<sup>8</sup>

273 The second study hypothesis was also confirmed. In US, the hypo- or hyperechogenicity,  
274 the heterogeneous echostructure and the deformation of the renal profile were the most  
275 useful features to visualize the nodules, whereas isoechoic, non-protruding nodules were  
276 undetectable, even if multiple. In the category of poorly visualized nodules, the majority of  
277 them were non-protruding and their presence was suspected because of the subtle changes  
278 in echogenicity compared to the homogeneous surrounding cortex. This result suggests  
279 that cortical renal lesions may be difficult to visualize by US and that a complete and  
280 accurate evaluation of the entire cortex is necessary, especially when renal lesions are  
281 suspected.

282 It is interesting to note that the number of nodules did not increase the US performance.  
283 Among the 10 cases with sonographically undetectable lesions, 7 had multiple nodules  
284 identified by CT.

285 Surprisingly, the location of the nodules (right versus left kidney) did not affect the US  
286 performance; our hypothesis was that the more cranial location of the right kidney could  
287 increase the risk of missing renal lesions, however this was not confirmed in both the total  
288 group, and the dogs group. On the contrary, the weight of the animals significantly influenced  
289 the nodules visibility, since the median weight was significantly lower in the group of dogs  
290 with visible nodules (16 kg vs 29.5 kg). The dog size is recognized to be a limitation in  
291 ultrasound, since the increased skin-organ distance requires lower frequencies to be used,  
292 leading to a decreased image quality.<sup>15</sup> This might have affected the possibility to visualize  
293 ill-defined cortical nodules. By contrast, CT is not influenced by dog size and this could be  
294 one of the reasons explaining the better performance.

295 In this study, renal nodules always showed some enhancement, and this is an important  
296 feature to distinguish vascularized nodules from renal cysts.<sup>14,20</sup> The CT enhancement  
297 pattern was mostly homogeneous (61.5%); however, heterogeneous/ring type nodules were  
298 likewise well represented (38.5%), without any significant correlation with the histologic type.  
299 The small number of primary neoplasia and inflammatory lesions makes the comparison  
300 between different types of nodules not reliable. Indeed, this was not the goal of this study,  
301 and the exclusion of renal lesions bigger than 3 cm represents a bias and explains why  
302 primary cancer was under-represented here. Our goal was to compare the performance of  
303 US and CT in the challenging situation of small cortical renal lesions. Sampling the nodules  
304 remains the only way to obtain a definitive diagnosis.

305 In this study, a high number of renal nodules were represented by renal metastases (17/25  
306 animals, 68%). The majority of primary tumours were carcinomas followed by melanomas  
307 and sarcomas; lung and thyroid carcinomas were over-represented. Metastatic nodules

308 were most commonly cortical, multiple and bilateral. In 7 patients, kidneys were the only  
309 metastatic sites; therefore, the detection of these lesions was crucial for a correct staging.  
310 In 4 cases, renal nodules were missed in US and the abdomen was considered normal,  
311 whereas CT showed them clearly.

312 In human medicine, renal metastases are considered a rare entity with a reported incidence  
313 variable between 2.36% and 12,6% in autopsies studies of cancer patients.<sup>7,8,21-22</sup> Similarly  
314 to our study, the most common primary location is the lung (43.7%), followed by colorectal  
315 region (10.6%), small intestine (6%), breast (5.3%), soft tissue (5.3%), thyroid (5.3%), and  
316 unknown primary (5.3%).<sup>7,8,14</sup> The kidney cortex is a common site for haematogenous  
317 metastases from highly vascularized tumours. Because of the high vessel density of the  
318 glomeruli, the cortex is an ideal area for entrapment and proliferation of tumour emboli.<sup>23</sup> CT  
319 is the preferred modality for the diagnostic work-up, even though pathognomonic imaging  
320 characteristics for renal metastases versus primary neoplasia have not been recognized,  
321 rather the suspected diagnosis is based on the history of a known primary and the  
322 knowledge about the disease biology and behaviour.<sup>7,8,14,20,,23,24,26</sup> Fine-needle aspiration  
323 or, less frequently, tissue core biopsy is used to confirm the suspected diagnosis.<sup>7,8</sup>

324 Detection of renal metastases is often incidental without symptoms referable to the kidneys,  
325 therefore very important since it influences treatment and survival.<sup>7,14</sup> In veterinary medicine,  
326 there is lack of information about the prevalence, clinical presentation and prognosis of  
327 animals with renal metastases. This study shows that in the presence of a primary tumour  
328 and multiple renal nodules, this scenario should be considered very likely, especially if the  
329 primary tumour is a lung or thyroid carcinoma. In these patients, CT is indicated for staging  
330 purposes, followed by sampling by FNA or biopsy. If the abdominal staging is performed by  
331 ultrasound, every subtle change in the renal cortex must be identified and the clinician must  
332 be aware of a possible false-negative result.

333 There are some limitations, mainly due to the retrospective nature of this study.

334 A Doppler study of the kidney was available only for about half of the cases (13/25 animals).  
335 With nodules already clearly identified by grey-scale ultrasound, Doppler enabled to  
336 evaluate the abnormal vascular pattern; on the contrary, Doppler did not help to increase  
337 the visualization of poorly detected nodules. Moreover, if the kidneys were considered  
338 normal, this technique was not consistently used, therefore it is not possible to draw  
339 definitive conclusions regarding Doppler examination performance. Both Power Doppler and  
340 Contrast Ultrasound are used in humans to study focal renal lesions, with improved  
341 visualization of the vascular pattern and some utility in the differential diagnosis<sup>26,27</sup>.  
342 However, these techniques are used to investigate lesions already identified by grey-scale  
343 US, and a complete screening of both kidneys in each cancer patients would be time-  
344 consuming and not realistically possible. In cancer patients, CT combines the advantages  
345 to investigate the primary lesion and to perform a complete staging; renal metastases are  
346 quickly suspected in all vascular phases; in 12 of our 25 patients, bilateral, multiple  
347 vascularized renal nodules were detected; therefore, the diagnosis of metastatic diseases  
348 was already likely even before sampling.

349 **The two authors were blinded to CT when analysing the US images but not vice versa.**  
350 **However, lesions in CT were always obvious, whereas more difficult to detect in US in part**  
351 **of the cases, therefore this was not considered a bias.**

352 Other limitations are the limited numbers of primary neoplasia and inflammatory lesions,  
353 compared to the metastatic group, therefore a comparison between these categories was  
354 not possible. Finally, histopathology was available only for 2 cases and necropsy was not  
355 performed to confirm the CT findings. It is possible that also CT fails to diagnose renal  
356 lesions and that these are detectable only with histopathology after necropsy; a study having  
357 this method as gold standard is needed to evaluate and compare US and CT accuracy.

358

359 In conclusion, both US and CT are useful for the detection of renal nodules. Compared to  
360 CT, US failed to diagnose or underestimated the number of inflammatory and neoplastic  
361 nodules in a significant number of cases. Renal nodules were frequently represented by  
362 metastases, especially from lung and thyroid carcinomas, therefore CT can be considered  
363 an indicated tool for the abdominal staging.

364

## 365 **List of Authors Contributions**

### 366 **Category 1**

367 (a) Conception and Design: Author name (s) Federica Rossi, Beatrice Gianni

368 (b) Acquisition of Data: Author name (s) Federica Rossi, Beatrice Gianni, Elvanessa  
369 Caleri, Mirko Mattolini, Veronica Camosci, Gregorio Carozzi.

370 (c) Analysis and Interpretation of Data: Author name (s) Federica Rossi, Beatrice Gianni,  
371 Silvia Sabattini, Laura Marconato

### 372 **Category 2**

373 (a) Drafting the Article: Author name (s): Federica Rossi, Silvia Sabattini

374 (b) Revising Article for Intellectual Content: Author name (s): Federica Rossi, Beatrice  
375 Gianni, Silvia Sabattini, Laura Marconato, Elvanessa Caleri, Mirko Mattolini, Veronica  
376 Camosci, Gregorio Carozzi.

### 377 **Category 3**

378 (a) Final Approval of the Completed Article: Author name(s): Federica Rossi, Beatrice  
379 Gianni, Silvia Sabattini, Laura Marconato, Elvanessa Caleri, Mirko Mattolini, Veronica  
380 Camosci, Gregorio Carozzi

### 381 **Category 4**

382 (a) Agreement to be accountable for all aspects of the work in ensuring that questions  
383 related to the accuracy or integrity of any part of the work are appropriately investigated

384 and resolved: Author name (s): Federica Rossi, Beatrice Gianni, Silvia Sabattini, Laura  
385 Marconato, Elvanessa Caleri, Mirko Mattolini, Veronica Camosci, Gregorio Carozzi

386

## 387 **Bibliography**

- 388 1. Kent ACC , Constantino-Casas F , Rusbridge C, Corcoran BM, Carter M, Ledger  
389 T, Watson PJ. Prevalence of pancreatic, hepatic and renal microscopic lesions in  
390 post-mortem samples from Cavalier King Charles spaniels. *J Small Anim Pract*  
391 2016;57:188-93.
- 392 2. Bryan JN, Henry CJ, Turnquist SE, Tyler JW, Liptak JM, Scott A, SA, Sfiligoi G,  
393 Steinberg SJ, Smith AN, Jackson T. Primary Renal Neoplasia of Dogs. *J Vet Intern*  
394 *Med* 2006;20:1155–1160.
- 395 3. McAloney CA, Sharkey LC, Feeney DA, Seelig DM, Avery AC, Jessen CR.  
396 Evaluation of the diagnostic utility of cytologic examination of renal fine-needle  
397 aspirates from dogs and the use of ultrasonographic features to inform cytologic  
398 diagnosis *J Am Vet Med Assoc* 2018;252:1247-1256.
- 399 4. Baskin GB, De Paoli A. Primary renal neoplasms of the dog. *Vet Pathol* 1977;14:591-  
400 605.
- 401 5. Moe L, Lium B. Hereditary multifocal renal cystadenocarcinomas and nodular  
402 dermatofibrosis in 51 German shepherd dogs. *J Small Anim Pract* 1997;38:498-505.
- 403 6. Moe L, Lium B. Computed tomography of hereditary multifocal renal  
404 cystadenocarcinomas in German shepherd dogs. *Vet Radiol Ultrasound*  
405 1997;38:335-43.
- 406 7. Zhou C, Urbauer DL, Fellman BM, Tamboli P, Zhang M, Matin SF, Wood CG, Karam  
407 JA Metastases to the kidney: a comprehensive analysis of 151 patients from a tertiary  
408 referral centre. *BJU Int* 2016;117:775-82.

- 409 8. Mitnick CK, Bosniak MA, Rothberg M, Megibow AJ, Raghavendra BN, Subramanyam  
410 BR. Metastatic neoplasm to the kidney studied by Computed Tomography and  
411 Sonography. *Journal of Comput Assist Tomography* 1985;9:43-49
- 412 9. Hahn KA, McGavin MD, Adams WH. Bilateral renal metastases of nasal  
413 chondrosarcoma in a dog. *Vet Pathol* 1997;34:352-5.
- 414 10. Valdes-Martinez A, Cianciolo R, Mai W. Association between renal hypoechoic  
415 subcapsular thickening and lymphosarcoma in cats. *Vet Radiol Ultrasound* 2007;48:  
416 357–360.
- 417 11. Griffin S. Feline abdominal ultrasonography: what's normal? what's abnormal? The  
418 kidneys and perinephric space. *J Feline Med Surg* 2020;22:409-427.
- 419 12. Noone TC, Semelka RC, Chaney DM, Reinhold C. Abdominal imaging studies:  
420 comparison of diagnostic accuracies resulting from ultrasound, computed  
421 tomography, and magnetic resonance imaging in the same individual. *Magn Reson*  
422 *Imaging* 2004;22:19-24.
- 423 13. Yamazaki H, Kishida T, Noguchi G, Iwasaki H, Suganuma N, Masudo K, Nakayama  
424 H, Yamashita T, Yamanaka T, Sugawara Y, Matsubara Y, Kohagura K, Rino Y,  
425 Masuda M. Nephrectomy for Metastatic Kidney Tumor in Patients with Differentiated  
426 Thyroid Cancer: A Report of Two Cases. *Case Rep Endocrinol* 2018 Nov  
427 11;2018:7842792.
- 428 14. Choyke P, White EM; Zeman RK; Jaffe MK, Clark LR. Renal metastases.  
429 Clinicopathologic and radiologic correlations. *Radiology* 1987;162:359-363.
- 430 15. Fields EL, Robertson ID, Osborne JA, Brown JC Jr. Comparison of abdominal  
431 computed tomography and abdominal ultrasound in sedated dogs. *Vet Radiol*  
432 *Ultrasound* 2012;53:513-7.

- 433 16. Wood CG, Stromberg LJ, Harmath CB, Horowitz JM, Feng C, Hammond NA,  
434 Casalino DD, Goodhartz LA, Miller FH, Nikolaidis. CT and MR imaging for evaluation  
435 of cystic renal lesions and diseases. *Radiographics*. 2015;35:125-41.
- 436 17. Walter PA, Johnston GR, Feeney DA, O'Brien TD. Applications of ultrasonography in  
437 the diagnosis of parenchymal kidney disease in cats: 24 cases (1981-1986). *J Am*  
438 *Vet Med Assoc*. 1988;192:92-8.
- 439 18. Biller DS, Schenkman DI, Bortnowski H. Ultrasonic appearance of renal infarcts in a  
440 dog. *J Am Anim Hosp Assoc* 1991;27:370-2.
- 441 19. Sutthigran S, Saisawart P, Klaengkaew A, Horoongruang K, Chaivoravitsakul N, Komin  
442 K, Thanaboonnipat C, Choisunirachon N. Use of contrast-enhanced computed  
443 tomography to detect kidney infarction in dogs. *J Vet Intern Med* 2022;36:164-170.
- 444 20. Kang SK, Kim D, Chandarana H. Contemporary imaging of the renal mass. *Curr*  
445 *Urol Rep*. 2011;1:11-7.
- 446 21. Bracken RB, Chica G, Johnson DE, Luna M. Secondary renal neoplasms: an  
447 autopsy study. *Southern medical journal* 1979;72:806–807.
- 448 22. Agochukwu N, Huber S, Spektor M, Goehler A, Israel GM. Differentiating Renal  
449 Neoplasms From Simple Cysts on Contrast-Enhanced CT on the Basis of Attenuation  
450 and Homogeneity. *Am J Roentgenol* 2017;208:801-804.
- 451 23. Abrams HL, Spiro R, Goldstein N. Metastases in carcinoma; analysis of 1000  
452 autopsied cases. *Cancer* 1950;3:74–85.
- 453 24. Pagani JJ. Solid renal mass in the cancer patient: second primary renal cell  
454 carcinoma versus renal metastasis. *J Comput Assist Tomography*. 1983;7:444–448.
- 455 25. Bhatt GM, Bernardino ME, Graham SD. CT Diagnosis of Renal Metastases. *J*  
456 *Comput Assist Tomography* 1983;7:1032-1034.

457 26. Jinzaki M, Ohkuma K, Tanimoto A, Mukai M, Hiramatsu K, Murai M, Hata J. Small  
458 solid renal lesions: usefulness of power Doppler US. *Radiology* 1998;209:543-50.

459 27. Bertolotto M, Bucci S, Valentino M, Currò F, Sachs C, Cova MA. Contrast-enhanced  
460 ultrasound for characterizing renal masses. *Eur J Radiol.* 2018;105:41-48.

461

462

463

464

465

466

467

468

469

470

471

472

473

474

475

476

<b>Renal nodules</b>		<b>CT (n=39)</b>	<b>US (n=29)</b>
<b>Accuracy US vs CT</b>			74%
<b>Number</b>	single	12 (30.8%)	18 (62.1%)
	>2 and < 6	16 (41%)	6 (20.7)
	>6	11 (28.2%)	5 (17.2%)
<b>Size</b>	mean	1,45	1,3
	< 1 cm	14 (35.9%)	11 (38%)

	> 1 cm	14 (35.9%)	18 (62%)
	< 1 cm and > 1 cm	11 (28.2%)	0 (0%)
<b>Shape</b>	round	32 (82%)	25 (86.2%)
	oval	7 (18%)	4 (13,8%)
<b>Margins</b>	well defined	36 (92%)	19 (65.5%)
	irregular	3 (8%)	10 (34.5%)
<b>Location</b>	cortical	36 (92%)	24 (82.8%)
	medullary	0 (0%)	5 (17.2%)
	cortical and medullary	3 - (8%)	0 (0%)
<b>Renal profile</b>	deformed	18 (46%)	18 (62%)
	not deformed	21 (54%)	11 (38%)
<b>Attenuation</b>	mean HU	Pre-contrast 35,8 Post-contrast 78,24	
	compared to the cortex	Pre-contrast isoattenuating - 32 (82%) Post-contrast hypoattenuating - 39 (100%)	
<b>Enhancement pattern</b>	homogeneous	24 (61,5%)	
	heterogeneous	13 (33.3)	
	ring	2 (5.2%)	
<b>Echogenicity</b>	Isoechoic		3 (10.4%)
	Hypoechoic		18 (62%)
	Hyperechoic		8 (27.6%)
<b>Echostructure</b>	Homogeneous		9 (31%)
	Heterogeneous		20 (69%)
<b>Color/Power Doppler (n=13)</b>	Hypovascular		6 (46%)
	Hypervascular		3 (23%)
	Non useful		4 (31%)

477 **Table 1.** CT and US feature of renal nodules. In CT (39 kidneys), renal nodules were mostly  
478 multiple, cortical, round, well marginated, not deforming the renal profile, isoattenuating in  
479 the native scan and hypoattenuating after contrast administration, homogeneously  
480 enhancing. US feature of 29/39 kidneys, showed that renal nodules were mostly cortical,  
481 single, round, with well-defined margins, deforming the renal profile, hypoechoic and  
482 heterogeneous.

483

484

485

486

487

488

489

490

491

492

493

494

495

496

497

498

499

500

501

502

<b>CT features of renal nodules non visible in US (total 10)</b>	
<b>Number</b>	
<i>Single</i>	3 (30%)
<i>&gt;2 and &lt;6</i>	5 (50%)
<i>&gt; 6</i>	2 (20%)

<b>Size</b>	
<i>&gt; 1 cm</i>	7 (70%)
<i>&lt; 1 cm</i>	3 (30%)
<b>Shape</b>	
<i>Round</i>	9 (90%)
<i>Oval</i>	1 (10%)
<b>Margins</b>	
<i>Well-defined</i>	10 (100%)
<b>Location</b>	
<i>Cortex</i>	10 (100%)
<b>Profile</b>	
<i>Non deforming</i>	10 (100%)

503

504

505 **Table 2:** Features of the nodules visible in CT and undetected in US. They were mostly  
506 multiple, over 1 cm in size, round, cortical, with well-defined margins and non-deforming the  
507 renal cortex.

508

509

510

511

		<b>CT</b>	<b>US</b>
<b>Accuracy</b>		100% (kidneys)	74% (kidneys)
		100% (patients)	84% (patients)
<b>Lesion's visibility</b>	Clearly visible	39 (100%)	20 (69%)
	Poorly visible		9 (31%)

	Not visible		10 (25,6%)
<b>Side</b>	Right	22 (all patients) 17 (dogs)	17 (all patients) 13 (dogs)
	Left	17 (all patients) 13 (dogs)	12 (all patients) 8 (dogs)
<b>Median weight of dogs with visible lesions</b>		29.5*	16*
<b>Number of visualized lesions - US versus CT</b>	Same number		12 (41%) <sup>^</sup>
	Less number		17 (59%) <sup>^</sup>

512

513           **\*P = 0.032**

514           **<sup>^</sup>P = 0.001**

515   **Table 3. Comparison between US and CT.**

516   US accuracy was 74% considering the kidneys and 84% the patients. In US, 31% of the  
517   lesions were poorly visible and 25,6% not visible. There was not significant difference  
518   between right and left side, however the median weight of dogs with visible lesions was  
519   higher in CT (29.5 versus 16 Kg; P=0.032). US underestimated renal lesions compared to  
520   CT in 59% of the kidneys (P=0.001)

521

522

523   **Figures Legends.**

524

525   **Fig. 1.** Example of a single renal nodule imaged with grey-scale US (A), Power Doppler (B)  
526   and CT (C, post-contrast, sagittal reformatted image). All images modality clearly showed

527 the nodule, with a high flow with Power Doppler and a moderate heterogeneous  
528 enhancement in CT. Final diagnosis was a metastasis arising from thyroid carcinoma.

529

530

531 **Fig. 2** Mixed breed dog with multiple bilateral metastases arising from a mediastinal  
532 neuroendocrine carcinoma. A,B: right kidney. C,D: left kidney. A,C: post-contrast CT  
533 images, sagittal reconstruction. B,D: US focused on the region where the nodules were  
534 visible in CT. On the right (A,B), renal nodules were clearly visible in CT and poorly visible  
535 in US. The nodule at the cranial pole of the left kidney was not visualized in US (C,D).

536

537

538