

# Renal complex cysts in adults: contrast-enhanced ultrasound

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## Abstract

Contrast-enhanced ultrasound (CEUS) has been proved to be a useful imaging modality to characterize complex renal cysts using the Bosniak classification in a similar way as Computed Tomography (CT). CEUS helps not only in the characterization of complex cysts detected on baseline US but also in the characterization of indeterminate cystic lesions on CT or Magnetic Resonance (MR).

**Key words:** Renal cysts—Renal cell carcinoma—Contrast-enhanced ultrasound—Kidney

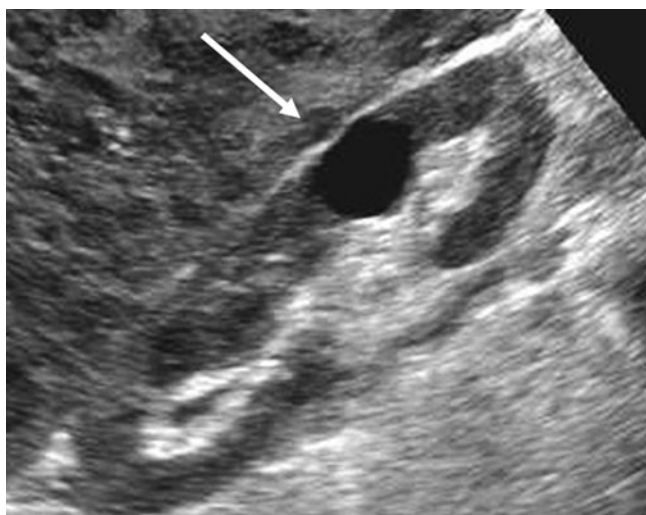
## Background

Renal cysts are collections of urine-like fluid enclosed by a continuous layer of epithelial cells. Renal cysts derive from nephrons and collecting ducts and progressively enlarge as a consequence of epithelial proliferation and transepithelial fluid secretion [1]. Renal cysts are very common in adults; approximately 50% of the population aged > 50 years develop renal cysts [2]. Ultrasound (US) is the most frequently used imaging technique for several abdominal purposes. US detection of renal cysts is very frequent in clinical practice because of the increasing use of imaging modalities and the continuous improvement of US equipments' quality. Benign renal cysts can be simple or complex (secondary to inflammation, infection or hemorrhage) [3]. On baseline US, a simple cyst is defined by the presence of a hairline-thin wall and anechoic content without septa, calcifications or solid components (Fig. 1). When a simple renal cyst is detected no further imaging examinations are necessary. Nonetheless, up to 8% of renal cysts may show a complex pattern [4] defined by the presence of increasing intracystic echogenicity, calcifications, at least one intracystic septum, wall thickening or solid nodules (Fig. 2). When a complex cyst is detected, baseline US is

not reliable enough to differentiate between benign cysts and the 10% of renal cell carcinomas (RCC) that may appear as complex cystic lesions. In these cases, further examination with computed tomography (CT) or magnetic resonance (MR) following administration of a contrast agent is usually required for characterization of the lesion. The administration of a contrast agent is essential since enhancement of solid components is the most specific sign suggesting malignancy (Fig. 3) [5, 6].

## Bosniak classification of renal cysts

Benignancy or malignancy of complex cysts can be suggested depending on their imaging characteristics. The Bosniak classification is the most widely accepted classification of complex cysts and it was initially based on CT findings providing criteria for deciding whether a complex cyst should be surgically explored. This classification was published in 1986, [7] and modified later [8], and several studies have corroborated its usefulness using single CT, multidetector CT or even MR [9–12]. The Bosniak classification correlates the malignant potential of the cysts depending on several features: thickness of cystic wall, number and thickness of intracystic septa, presence of mural solid nodules, enhancement of septa and nodules, and calcifications. Nonetheless, the presence of cystic calcifications is no longer considered a relevant feature to differentiate between benign and malignant renal cysts [13] since both types of lesions may show calcifications. Whereas the presence of thickened irregular septa, thickened irregular wall, and especially enhancing intracystic solid lesions are predictors of malignancy [10], and are usually key factors indicating surgical treatment instead of follow-up [14, 15]. The Bosniak classification is a practical guide for the management of renal cysts and includes 5 categories (I, II, IIf, III, and IV) ordered in increasing probability of malignancy. Surgery is recommended for III and IV categories, whereas category IIf means follow-up of lesions that present not enough features to be considered benign unless a follow-up



**Fig. 1.** Simple cyst detected on baseline US with anechoic content, without wall thickening, septa or solid nodules.

confirms that the lesion remains stable. Initially, a follow-up study at 6 months and repeated after 1 year was considered enough to establish that the lesion was benign as long as the lesion remained stable [16]. Nowadays, however, due to the slow growth rate of some low-grade RCCs, a 3–5 year follow-up is recommended to assure benignancy of a complex cyst [17, 18].

## Contrast-enhanced US of renal cysts

Currently, US performed after the administration of a contrast agent and the use of contrast specific software allows a real-time evaluation of the kidney vascularization during corticomedullary, nephrographic, and excretory phase [19–21]. CEUS has several advantages: it is cost-effective, can be performed at the bedside and can be administered to patients with renal failure [22]. One of the features of CEUS with respect to CT and MR is that US contrast agents are strictly intravascular (they remain within the blood pool). Several studies have demonstrated that CEUS can provide useful information of the microvascularization of renal tumors [23, 24], as has been described with tumors in other organs [22, 25–27]. When exploring renal cysts, CEUS is extremely sensitive in revealing even the tiny capillaries that feed hair-line septa. This fact can explain why several authors have found CEUS sensitivity higher than CT depicting the cystic wall and septa vascularity [28–30]. Moreover, evaluation in real time can also help in the evaluation of cysts with several confluent septa that may mimic a solid mass. Another advantage of CEUS is lack of radiation that makes it very helpful in the follow-up of cysts. As drawbacks CEUS has some limitations: cysts cannot be well visualized in obese patients or in depth kidneys, and bowel gas or ribs make kidney visualization difficult. Another

limitation of US is the presence of diffuse or large wall calcifications that may hamper the visualization of possible deeper enhancing nodules or intracystic septa, because of back shadowing of the calcifications.

## Bosniak classification using CEUS and correlation with findings on CT

Due to its sensitivity to detect microvascularization of the cysts' septa and walls, CEUS can be used to classify renal cysts depending on the probability of malignancy of the Bosniak classification [21], as described in the study of Ascenti of 44 asymptomatic complex cystic masses [29]. CEUS classification also distinguishes renal cysts in the same 5 Bosniak categories (Table 1) and features of every group can be compared to the typical enhancement and morphological features described on CT since CEUS and CT reveal similar findings in most complex cysts.

### *Bosniak I*

A Bosniak I cyst or simple cyst with 0% probability of malignancy is a cyst with a hairline-thin wall, and anechoic content without septa, calcifications or solid components and with no enhancement after intravenous contrast agent injection (Fig. 4) which entails no further investigations.

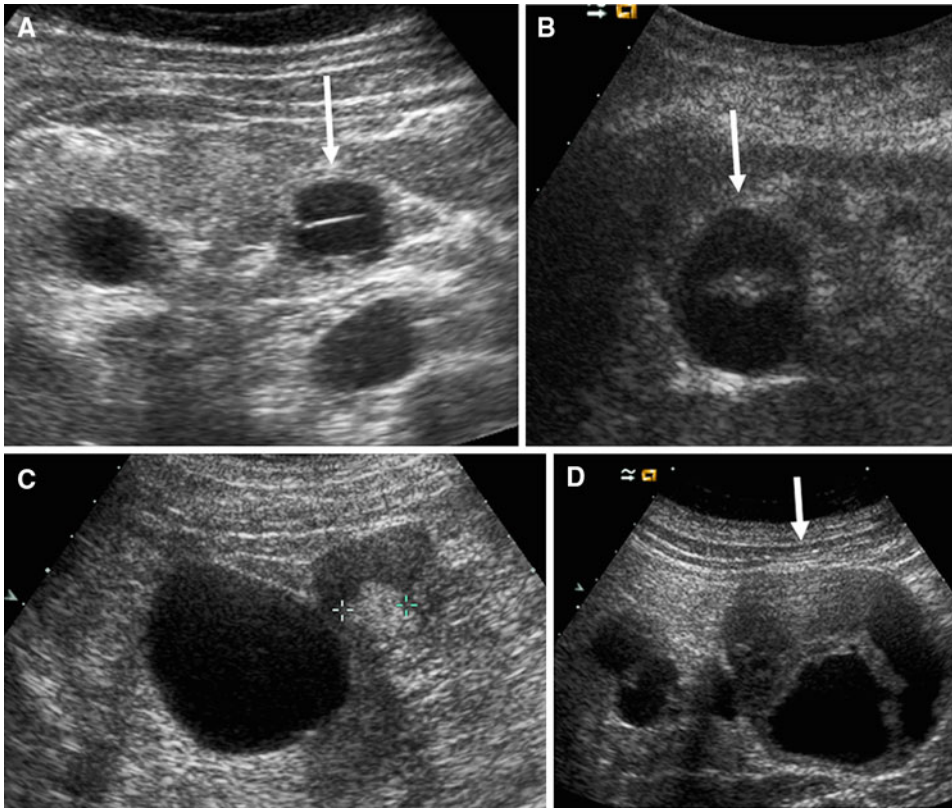
### *Bosniak II*

A Bosniak II renal cyst with also an estimated 0% probability of malignancy is a cyst that may contain few hairline-thin septa, fine calcifications in a short segment of the wall or slightly thickened calcification. It may show minimal enhancement “just perceived” of the septa without soft-tissue nodular enhancement. All these findings correlate with the same findings using CT (Fig. 5). Nevertheless, the detection of microbubbles traveling in the septa is much more common using CEUS than using CT and this should not be misdiagnosed as a sign of malignancy unless accompanied by thickening of the septa.

When using the Bosniak CT classification, uniformly hyperdense cysts smaller than 3 cm without enhancement are also included in this category.

### *Bosniak II<sub>f</sub>*

A Bosniak II<sub>f</sub> cyst, where “f” indicates need for follow-up imaging, and with an estimated 5% probability of malignancy, is a renal cyst with multiple hairline-thin septa, smooth minimal thickening of the wall or septa and thick or nodular calcifications. CEUS and CT may show minimal enhancement “just perceived” of the septa, but without soft-tissue nodular enhancement (Fig. 6). According to the Bosniak CT classification, uniformly



**Fig. 2.** Various complex cysts on baseline US. **A** Cyst with a hair-line septum (*arrow*). **B** Cyst with a thickened septum. **C** Cyst with an intracystic solid nodule. **D** Cyst with hyperechoic content partially filling the cystic cavity.

hyperdense cysts larger than 3 cm without enhancement are also included in this category. Frequently, those hyperdense cysts on CT have features of simple cysts on US and are low-graded to Bosniak I grade, consequently, with a change in the management. Bosniak IIf cysts are considered benign but need to remain stable at follow-up.

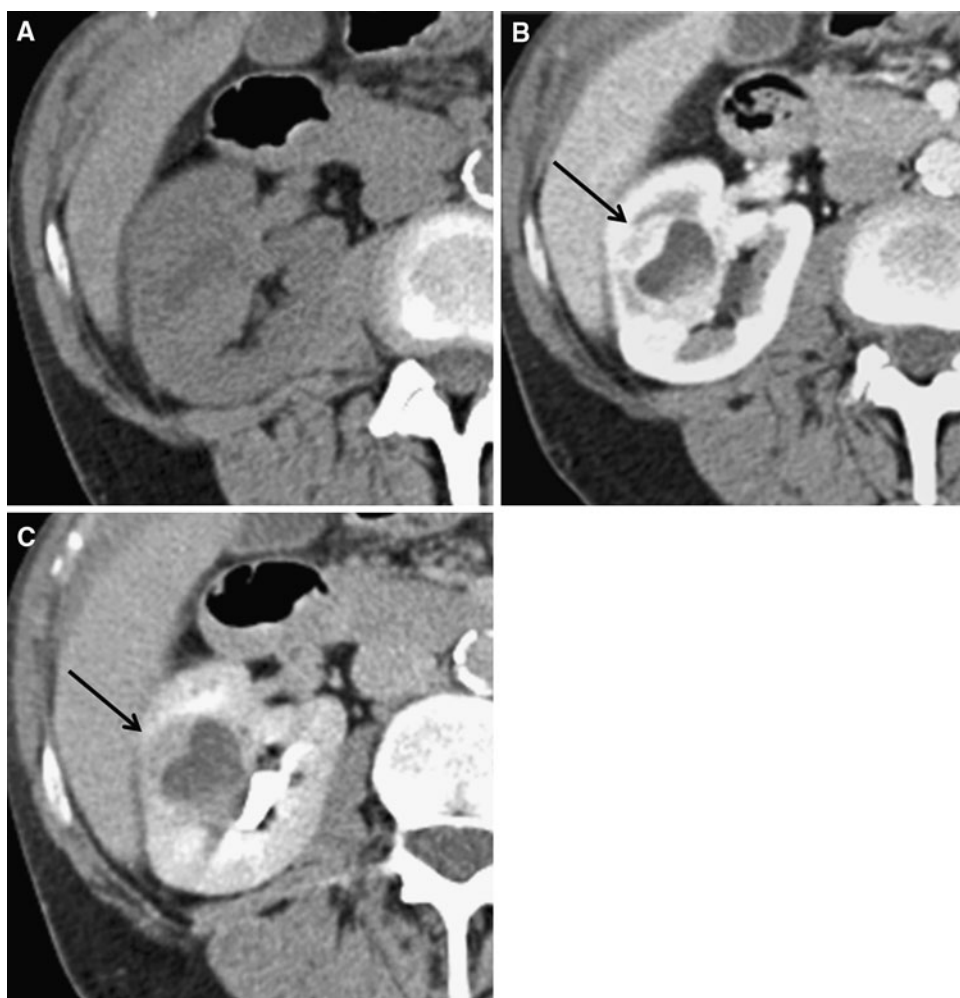
### *Bosniak III*

A Bosniak III cyst, with an estimated 50%–70% probability of malignancy, is an indeterminate mass that includes complicated hemorrhagic or infected cysts, multilocular cystic nephromas and cystic RCC. Using CEUS, a Bosniak III cyst may contain thickened irregular wall or septa with enhancement after the administration of contrast agent (Fig. 7). Cysts with measurable smooth enhancing thickened wall or septa are also included in this category but they are more suggestive of inflammatory or hemorrhagic cyst. No enhancing solid masses are detected.

### *Bosniak IV*

A Bosniak IV cyst, with an estimated 95%–100% probability of malignancy, is a clear malignant cystic mass with the presence of soft-tissue enhancing mass independent of the wall or septa (Fig. 8), which can be demonstrated using CEUS or CT.

In clinical practice, with all imaging modalities there are no problems to include cysts correctly into category I and IV, but difficulties arise in differentiating between category II and III and in recommending surgery or conservative follow-up. This is due to the difficulties to define the millimeters of septa and wall thickness as well as to differentiate apparently thickened and irregular walls and septa from walls or septa thinner and more regular. Although there is an excellent correlation of the features of complex cysts features using CEUS with those using CT, there are some differences. Several studies have suggested that CEUS performs better than CT in the detection of cyst vascularity [29, 30] as has been also described using MRI [6]. Especially, CEUS may demonstrate more septa, thickening of the wall or septa and subtle nodular enhancement than CT. This may lead to an upgrade of the Bosniak classification that can represent a change in the surgical management. In this sense, the study of Park [30] showed an upgrade of category in 8 out of 31 cysts (26%). Similarly, Clevert showed an upgrade of 7 out of 37 cysts when evaluated with CEUS (19%), with an upgrade from II to IIF in 5 patients (1/3 of Bosniak II cysts), and with an increase of clearly malignant cysts (Bosniak IV) in 2 patients [31]. The detection of additional septa does not involve a significant change in the management since it only represents an upgrade from I to II or from II to IIf. However, the detection of solid lesions or more thickened enhancing



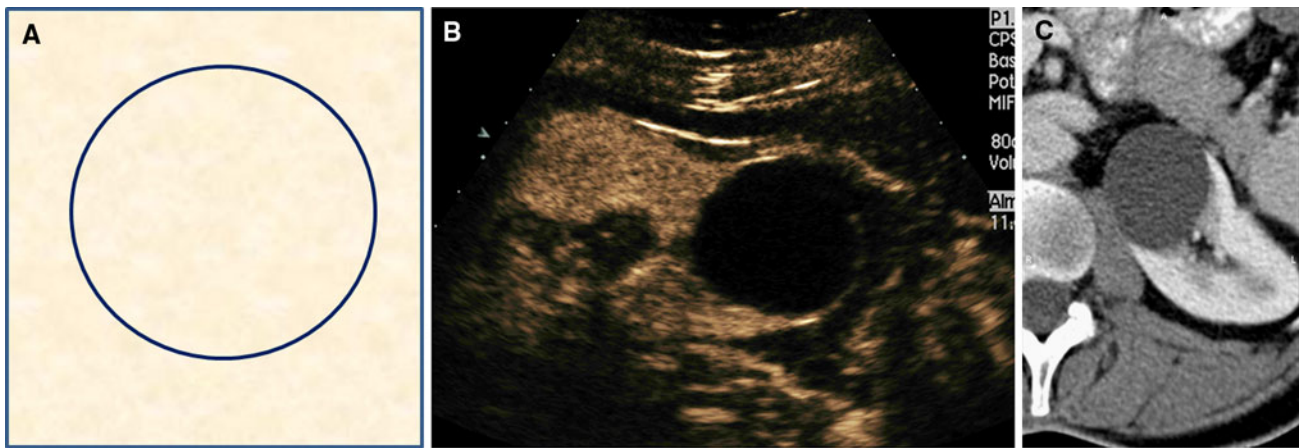
**Fig. 3.** Cystic RCC diagnosed by CT. **A** Unenhanced, **B** nephrographic phase-enhanced and **C** excretory phase-enhanced axial CT scans reveal complex cystic mass of right kidney with enhancing nodule (*arrow*) and a thickened enhancing posterior wall.

**Table 1.** Bosniak classification of renal cysts using CEUS

Category	Probability of malignancy (%)	Features
I	0	No echoes within the mass, and sharply marginated smooth walls No septa, calcifications or solid components No enhancement after intravenous contrast agent injection
II	0	It may contain few hairline-thin septa, fine calcifications in a short segment of the wall or slightly thickened calcification. It may show minimal enhancement “just perceived” of the septa without soft-tissue nodular enhancement
IIf	5	It may contain multiple hairline-thin septa, smooth minimal thickening of the wall or septa and thick or nodular calcifications. It may show minimal enhancement “just perceived” of the septa, but without soft-tissue nodular enhancement
III	50–70	It may contain thickened irregular or smooth wall or septa with measurable enhancement. No solid enhancing lesions are present
IV	95–100	It may contain soft-tissue enhancing mass independent of the wall or septa

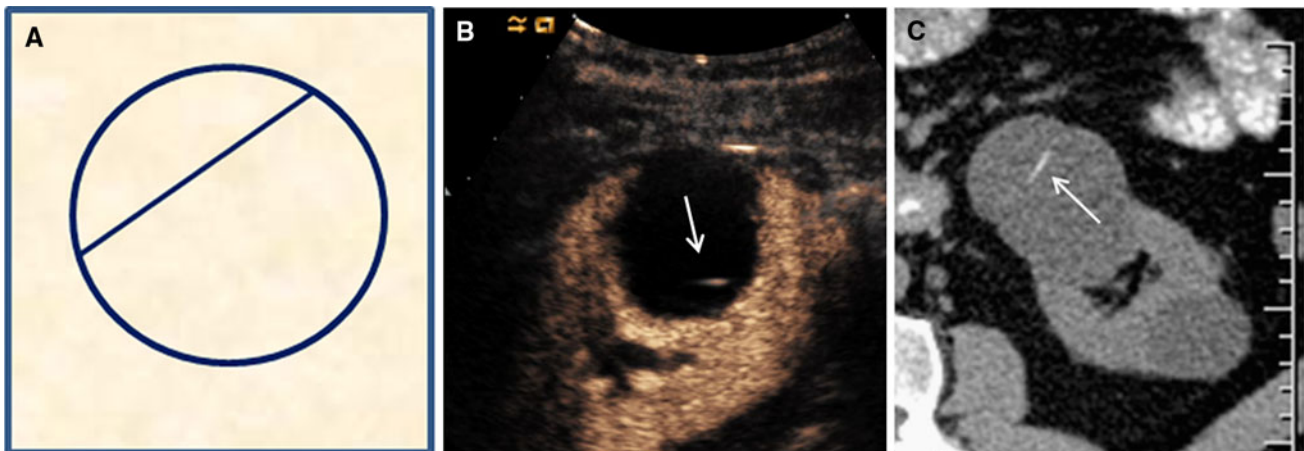
septa represents an important change, with a tendency to upgrade category II lesions to categories III or IV. An important question is how to manage those cases in which the cyst appears benign using CT but appears more complex using CEUS. It is advisable to send to the operating room all cysts that have been upgraded to category IV due to CEUS findings. Nonetheless, it is wise

to be cautious with cysts upgraded to group III, because up to now, there is not enough experience using CEUS with longer follow-up or surgery in IIf or Bosniak III cysts. Additional studies including more patients are necessary to prove if the CEUS upgrade to group III represents a non-desirable increase of false positive cystic RCCs due to the detection of irregular or thick septal or



**Fig. 4.** Bosniak I cyst. **A** Schema of a simple cyst using CEUS. **B** A simple cyst using CEUS is defined as a mass with anechoic content with a hair-line thin wall, and without septa, calcifications, solid components, or enhancement. **C** Same

characteristics (liquid density, hair-line thin wall, absence of septa or solid components) are shown in another simple cyst on CT.



**Fig. 5.** Bosniak II cyst. **A** Schema of a Bosniak II cyst. A fine septum is identified. **B** CEUS of a Bosniak II cyst shows a fine septum (*arrow*) with enhancement. **C** Same finding is detected using CT (*arrow*).

wall enhancement in benign cysts. In these Bosniak III cysts, other possibilities instead of surgery have been proposed. Although surveillance and biopsy are not widely accepted as alternative options [2, 18, 32] these approaches may be useful in some cases in order to avoid resection of benign cysts.

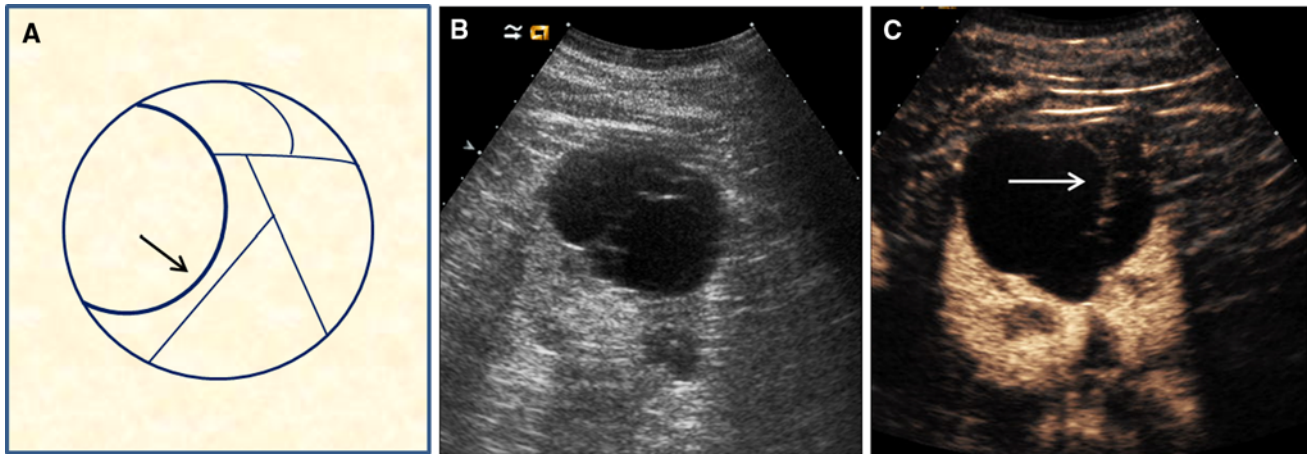
### Utility of CEUS in the clinical practice. Clinical scenarios

In our routine clinical practice, we are using CEUS to characterize complex cysts found on conventional US, but also to further investigate indeterminate masses found on CT/MR. In our institution, we use the standard dose of 2.4 mL of US contrast agent approved in Europe for radiological clinical purposes (Sonovue, Bracco),

which is composed of sulfur hexafluoride microbubbles stabilized with a phospholipid shell, plus a 10 mL of flush of a saline solution.

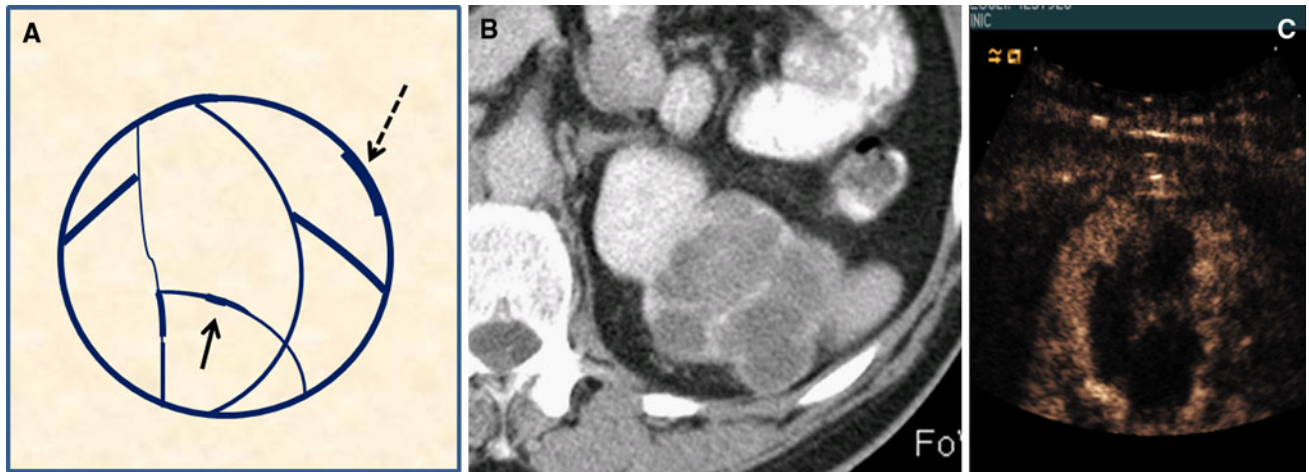
### *Characterization and follow-up of complex cyst found on conventional US*

In clinical practice, when a complex cyst is detected on baseline US another imaging modality after the administration of a contrast agent is recommended to evaluate the enhancement of the wall, septa and possible soft-tissue nodules. Nowadays, CEUS can be used as the first imaging technique to evaluate the behavior of complex cysts. Moreover, if CEUS is performed right after the detection of the complex cyst on baseline US, the time to arrive at a diagnosis is reduced avoiding patient distress



**Fig. 6.** Bosniak IIc cyst. **A** Schema of a Bosniak IIc cyst. Cyst with several septa or minimal smooth thickening of septum (arrow) or wall. **B** US of complex cyst shows multiple hair-line

septa. **C** CEUS shows perceived enhancement of of the hair-line septum without nodular enhancement.



**Fig. 7.** Bosniak III cyst. **A** Schema of a Bosniak III cyst. Cyst with several irregular enhancing and thickened septa (arrow) or irregular thickening of the wall (discontinuous arrow). **B** CT

of a Bosniak III cyst with irregular enhancing thickening of wall and septa. **C** Same finding was detected on CEUS study. A cystic RCC was confirmed after surgery.

while waiting for a new radiological study. CEUS can confirm the suspected Bosniak grade, can low-grade the suspected category if no enhancement of septa or enhancing solid components are detected, or upgrade if detection of more septa/enhancement of septa/enhancement of solid areas is present (Figs. 9, 10, 11). Recent studies have demonstrated the high accuracy of CEUS in the characterization of baseline complex cysts [28, 31]. In the study of Quaia et al., CEUS performed better than CT in the diagnosis of malignancy in complex cystic renal masses, with similar diagnostic confidence between CEUS and CT [28].

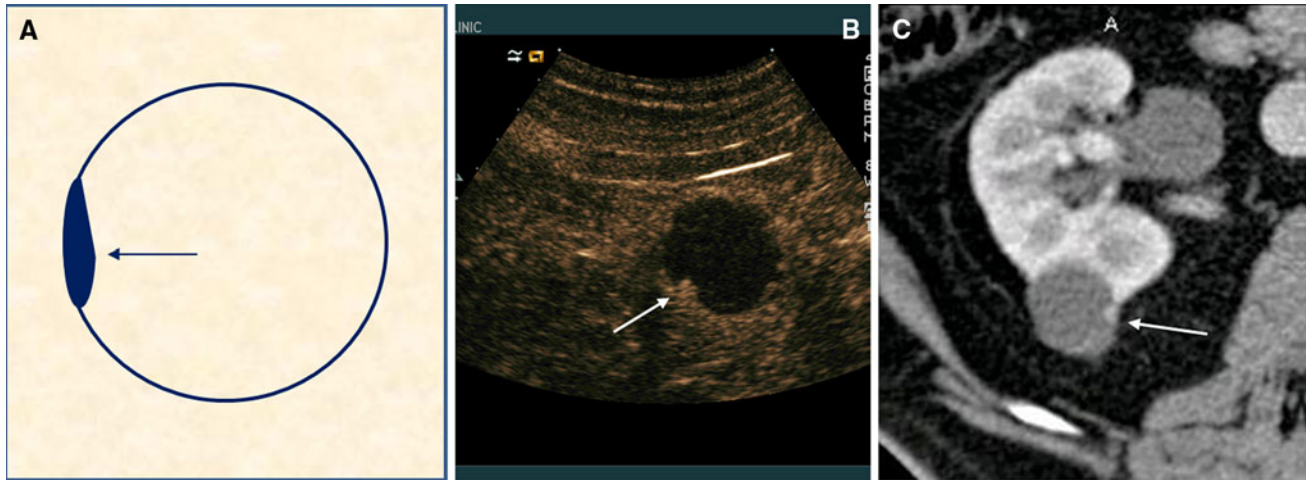
CEUS can be also used instead of CT for the follow-up of Bosniak IIc cysts to detect any morphologic changes such as thickening of septa, appearance of a

solid nodule or contrast-enhanced modifications indicative of progression of the disease with the benefits of a reduction of cost and radiation. In the follow-up, the increase of size might not represent a suspicious criterion of progression because benign cysts can also grow [33].

*Complex cyst vs. solid tumor found in CT/MR*

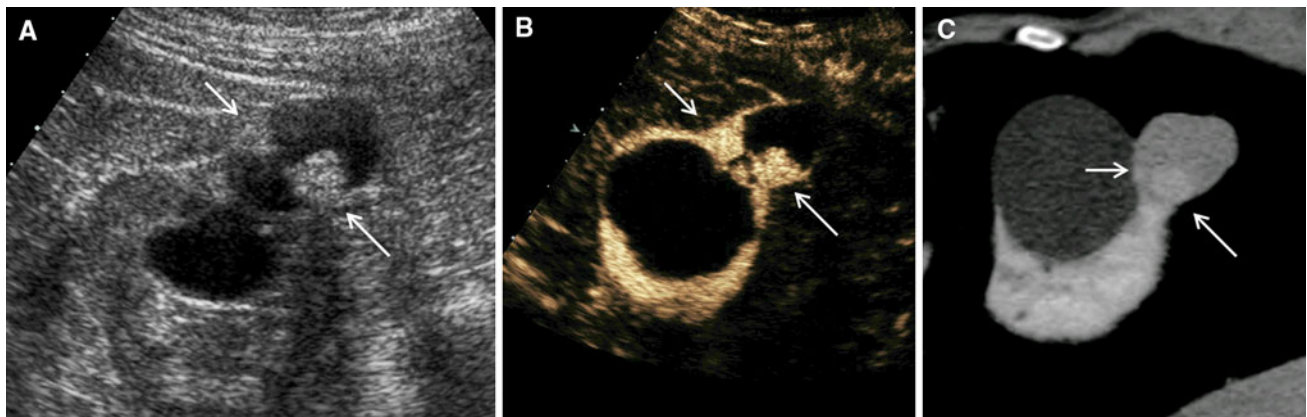
In a different scenario, when CT or MRI are performed, indeterminate kidney masses suggesting complex cysts can be detected very often. This situation can be found due to different causes:

- a) CT studies without contrast agent (i.e., renal insufficiency, allergy to iodinated contrast agents), studies without a baseline phase (many abdominal CT



**Fig. 8.** Bosniak IV cyst. **A** Schema of a Bosniak IV cyst. Cyst with a solid enhancing intracystic lesion (arrow). **B** CEUS of a Bosniak IV cyst shows a very small enhancing nodule

suggesting cystic RCC (arrow). **C** The solid enhancing nodule (arrow) was confirmed using CT (nephrographic phase).

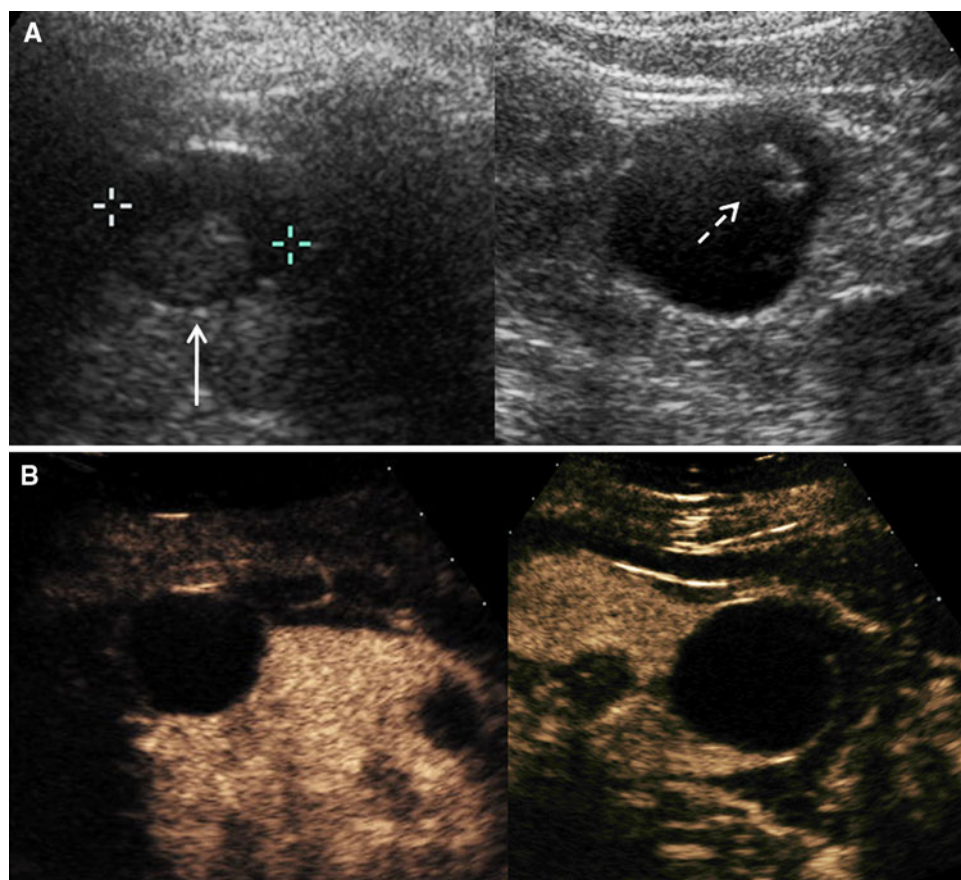


**Fig. 9.** Incidental complex cyst found in a 75-year-old man. **A** On baseline US, several bilateral simple cysts and one complex cyst with two solid areas (arrows) in the left kidney are detected suggesting Bosniak IV. **B** CEUS was performed confirming the presence of two solid lesions (arrows) with

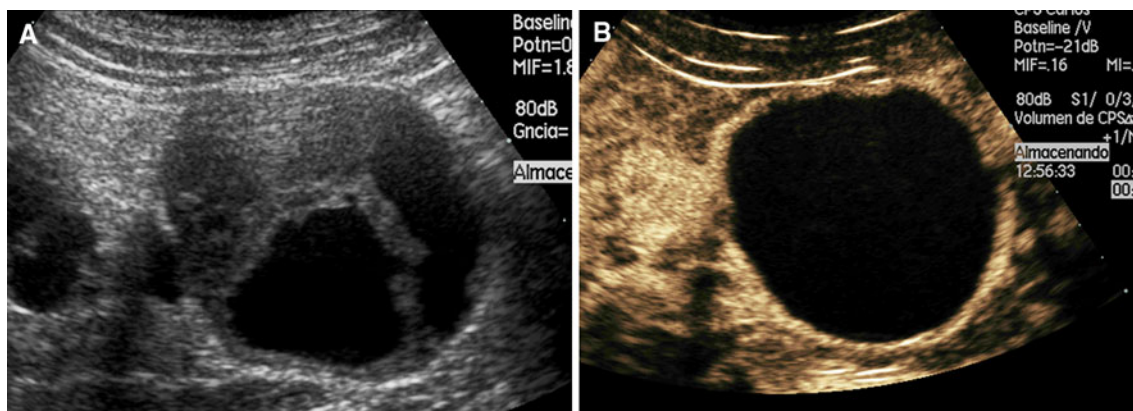
enhancement compatible with cystic RCC. A third small solid nodule not identified on baseline was also detected between the other two. **C** Conspicuity of the solid lesions (arrows) was lower on the CT study, even modifying the standard window of soft tissue.

protocols do not include a baseline phase: i.e., abdominal pain, follow-up of most abdominal neoplasias...). Nowadays, there are different CT technical protocols depending on the disease of the patient that only include some of the more common phases (unenhanced, arterial, venous, excretory phase), and in many cases the radiologist reviews the study after the patient has gone from the CT department. If a complex cyst is detected and if the CT study does not include a baseline phase or a contrast phase, it is impossible to know if the lesion enhances, unless the study had been performed in a dual-CT with the dual technique that obtains a baseline phase automatically

or if there are significant changes of attenuation between two enhanced phases [34]. When CT only includes an unenhanced phase, 20 HU is the upper limit acceptable of water density [33], thus, suspected cysts with higher density (over 20 HU) cannot be considered as simple cysts and need further examinations. It has been suggested that cysts measuring between 20 and 40 HU are proteinaceous cysts that will show characteristics of simple cysts on US and cysts measuring between 40 and 50 HU are usually hemorrhagic cysts that will appear heterogeneous and complex on US [33]. Moreover, it has been recently described that unenhanced homogeneous cysts over



**Fig. 10.** Patient with two complex cysts. **A** On baseline US a complex cyst with an intracystic solid lesion (*arrow*) suggesting Bosniak IV and another with a thickened septum (*discontinuous arrow*) suggesting Bosniak III. **B** Using CEUS no solid lesions nor thickened enhancing septa are identified being compatible with benign cysts.



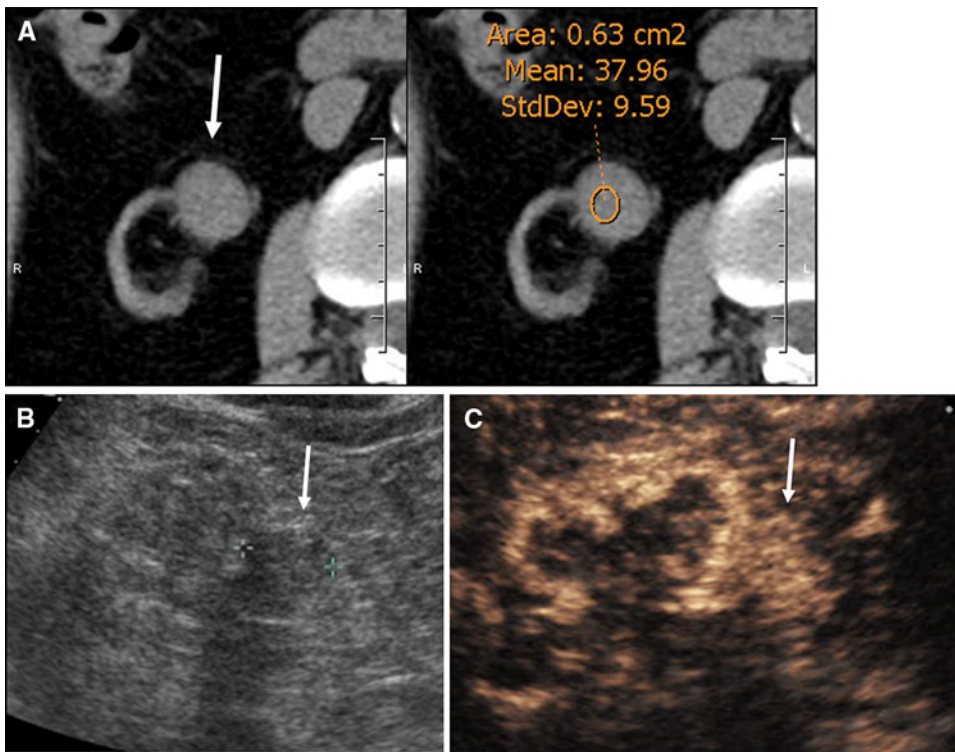
**Fig. 11.** Patient with a complex cyst. **A** Baseline US, the cystic cavity is partially occupied by echogenic material. **B** After the administration of contrast agent, a thickened

enhancing wall is detected without solid nodules or enhancing septa. The cyst was classified as Bosniak III and an inflammatory cyst was demonstrated on surgery.

70 HU have a 99% probability to be benign [35]. On the contrary, when the study does not include an unenhanced phase, some features such as the density and heterogeneity of the lesion or changes of density between different enhanced phases have been

described as useful to differentiate between complex cysts and solid tumors [34, 36, 37]. In spite of these suggestions, in clinical practice renal masses in unenhanced CT with density higher than 20 HU or doubtful enhancing masses in enhanced CT that do





**Fig. 12.** Patient in waiting list for kidney transplant, CT was required to evaluate the abdominal vessels. CT was performed without contrast agent due to renal failure. **A** A well defined lesion is identified in the lower pole of the right kidney (*arrow*). Density of the lesion (ROI) was 38 HU. **B** An US study was performed to evaluate the mass. Baseline US (*arrow*) could not assure if the lesion was solid or cystic. **C** CEUS showed enhancement of the lesion suggesting RCC that was confirmed after surgery.

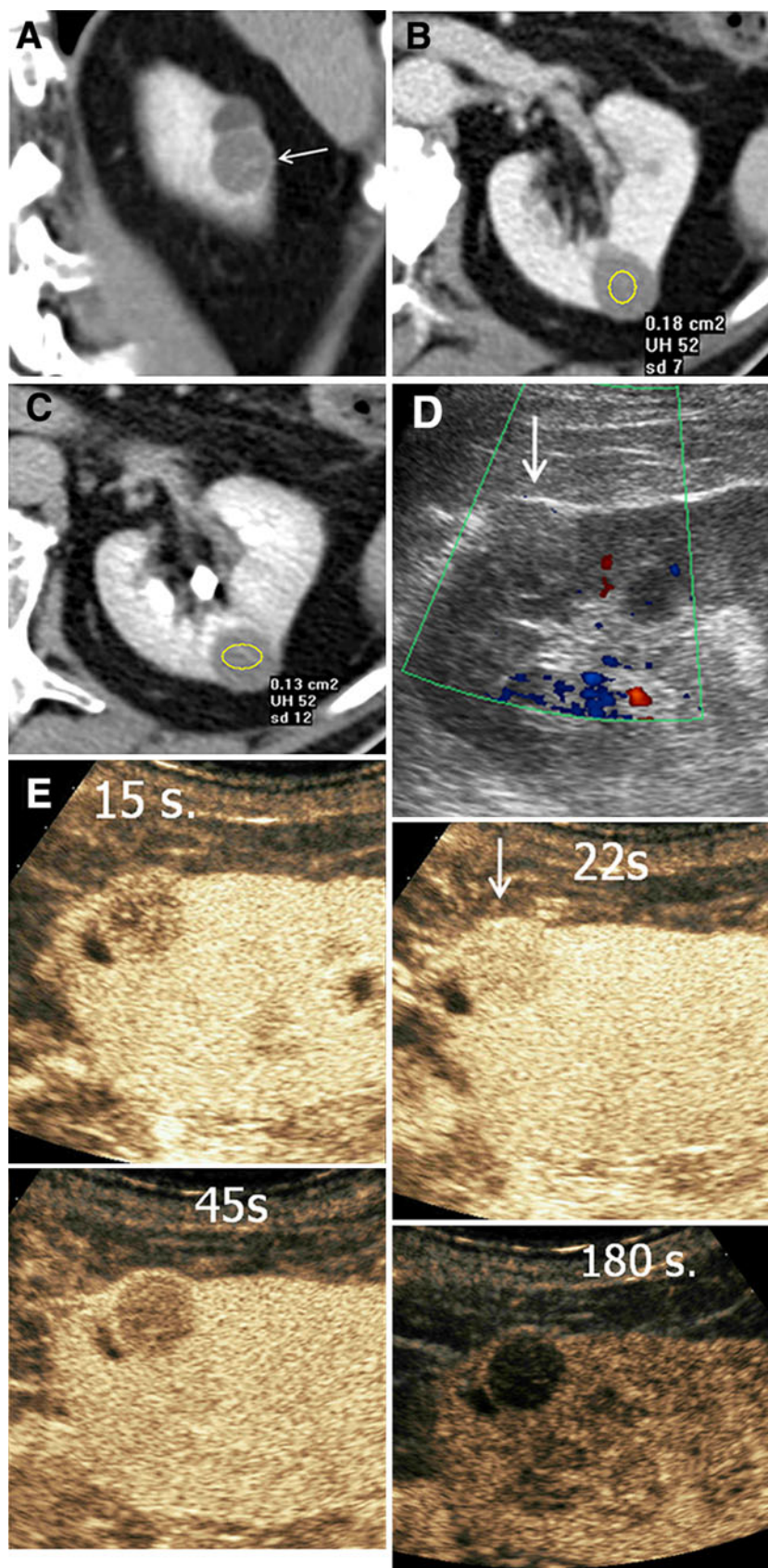
not include a baseline phase are usually reevaluated with a specific CT or MR (before and after administration of contrast agent) to confirm that the lesion is not RCC [2, 38]. In these cases, CEUS may be performed rather than reexamining the lesions with CT or MR (Fig. 12).

- b) Another common situation is the detection of a suspected complex cyst studied with unenhanced and enhanced CT with a non-conclusive enhancement. Enhancement of solid component is considered when attenuation increases by more than 15 HU [14], but there is no universal agreement about the correct threshold to identify enhancement with certainty using the most accepted range between 10 HU [4] and 20 HU [6, 33] depending on the authors. This non-conclusive enhancement can also appear in MR studies, especially if the lesions are hyperintense on T1. Independently of the cause of the non-conclusive enhancement on CT or MRI, CEUS can provide a rapid and accurate diagnosis of these indeterminate masses, differentiating between cysts and hypovascular renal masses usually corresponding to a low-grade (papillary or follicular) RCCs that can mimic renal cysts. In our experience, US has become a very

useful tool to characterize them. In some cases baseline US without the injection of contrast agent is enough to demonstrate the presence of a typical simple cyst [39]. If a simple cyst is not confirmed with baseline US, the administration of an US contrast agent shows definitive enhancement in cases of hypovascular tumors usually with tiny and sometimes very fast enhancement not clearly observed on CT (Fig. 13).

## Conclusions

CEUS is a very useful tool to characterize complex renal cysts found on baseline US with the advantage that it can be used in patients with renal insufficiency. The Bosniak classification is accurate for predicting malignancy using CEUS, and the presence of nodular septal or nodular wall enhancement and irregular thickening of the wall or septa are features suggesting malignancy. CEUS is also very helpful for further characterization of renal lesions with indeterminate enhancement at CT or MR.



**Fig. 13.** **A** Follow-up abdominal CT due to colon cancer in a 76-year-old patient. The study was performed without unenhanced phase following the protocol used in our hospital. A dense well defined lesion (*arrow*) is detected in the upper pole of the left kidney in contact with a simple cyst. There are no significant differences of the lesion density between the portal phase (**B**, 52 HU) and excretory phase (**C**, 52 HU) suggesting the presence of an hemorrhagic cyst. **D** Doppler study shows a possible solid mass but without color Doppler signal inside it (*arrow*). **E** CEUS demonstrates that the renal lesion is hypovascular during almost all phases except for a very rapid enhancement (*arrow*, at 22 s. after the administration of contrast agent). The lesion was removed and the final diagnosis was RCC.

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