Author’s response to reviews

Title: The independent indicators for differentiating renal cell carcinoma from renal angiomyolipoma by contrast-enhanced ultrasound

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Author’s response to reviews:

Dear editor,

According to the comments, we have revised the manuscript. The detailed changes are appended below.

1. “Renal cell carcinoma (RCC), one of the most lethal urological malignancies, originates in the renal tubular epithelium of the urinary system.” has been changed to “Renal cell carcinoma (RCC) originates from the renal tubular epithelium and is one of the most lethal urological malignancies.” (Line 2, page 2)

2. “Though CUS is a readily available, inexpensive, non-invasive, and non-ionizing imaging modality, it has limited use when attempting to differentiate between RCC and AML” has been changed to “Though CUS is non-ionizing, non-invasive, readily available and inexpensive, it is limited in attempting to differentiate RCC from AML” (Line 10, page 2)

3. “Therefore, a safe and accurate imaging modality is needed to differentiate between RCC and AML, and Contrast-enhanced ultrasound (CEUS) using microbubble-based contrast agents has garnered increasing attention in this regard.” has been changed to “Therefore, a safe and accurate imaging method is needed for differential diagnosing RCC from AML, and microbubble-based contrast-enhanced ultrasound (CEUS) has garnered increasing attention in this field.” (Line 12, page 2)

4. “This single-institution retrospective study was approved by the ethical committee of Huadong hospital,” has been changed to “This was a single-institution retrospective study. This study was approved by the Review Board of Huadong Hospital,” (Line 5, page 3)

5. “Both CUS and CEUS were performed by a single radiologist (C.L.) at our institution with 17 years of experience in abdominal US and 13 years in CEUS.” has been changed to “Both CUS and CEUS were performed by a single radiologist (C.L.) with 17 years of experience in abdominal US and 13 years in CEUS at our institution.” (Line 17, page 3)

6. “Both CUS and CEUS were performed by a single radiologist (C.L.) at our institution with 17 years of experience in abdominal US and 13 years in CEUS. The examinations were performed using an
ultrasound scanner (4C1 probe, 3–5 MHz, mechanical index &lt;0.10, Aplio500, Toshiba Medical Systems, Otawara, Japan). Initially CUS was conducted to obtain the position, shape, echogenicity, size, margins, homogeneity, and orientation of the tumor, then color Doppler flow imaging (CDFI) was used to assess the blood flow of the tumor. The depth of the renal lesions was all less than 10 cm in this study. Optimal scanning containing both mass and normal adjacent renal parenchyma was selected, and the system was then switched to contrast imaging mode using (contrast pulse sequence) CPS technology. The US contrast agent used in this study was SonoVue (Bracco, Milan, Italy), a sulfur hexafluoride (SF6)-filled microbubble which was stabilized by phospholipids. The SonoVue freeze-dried powder was shaken with 5ml of normal saline, and a dose of 1.6–2.4ml contrast agent, which was chosen individually depending on the weight, height, and age of the patient, was administered into the antecubital vein in a bolus fashion, followed by 5-ml saline flush. The timer and video recorder were started and the contrast agent was injected simultaneously. All patients were required to maintain slow shallow breathing, and checked in real time for at least 3 minutes. If a tumor was incompletely assessed, a second injection was repeated 15 minutes after the first injection. The single images and video clips of CUS and CEUS were stored in the local hard drive for subsequent analysis.” has been changed to “Both CUS and CEUS were performed by a single radiologist (C.L.) with 17 years of experience in abdominal US and 13 years in CEUS at our institution. The examinations were performed using an ultrasound scanner (4C1 probe, 3–5 MHz, mechanical index &lt;0.10, Aplio500, Toshiba Medical Systems, Otawara, Japan). Initial CUS was conducted to obtain the position, shape, echogenicity, size, margins, homogeneity, and orientation of the tumor. Then color Doppler flow imaging (CDFI) was used to assess the blood flow of the tumor. Subsequently, optimal section containing both renal lesion and normal adjacent parenchyma was selected, and the ultrasound scanner was switched to CEUS mode. The US contrast agent of SonoVue (Bracco, Milan, Italy), a sulfur hexafluoride (SF6) microbubble stabilized by phospholipids, was used in this study. The freeze-dried powder of SonoVue was shaken with 5.0 ml of normal saline into suspension. According to the weight, height, and age of the patients, a dose of 1.6–2.4ml of this suspension was individually administered into the antecubital vein in a bolus fashion, followed by a flush of 5.0 ml saline. At the time of contrast agent injection, the keys of the timer and video recorder were pressed simultaneously. Maintain slow shallow breath was required for all patients, and each dynamic contrast image was observed at least 3 minutes. If a tumor was incompletely assessed, a second injection was repeated 15 minutes after the first injection. The single images and video clips of CUS and CEUS were stored in the local hard disk for subsequent analysis.” (Line 17, page 4)

7. “The images and video clips saved on the local hard drive were reviewed in random by two independent radiologists (D.X.H. and Z.J.), both blinded to the pathological results. Both radiologists had more than 10 years of experience in abdominal US and 8 years in reading CEUS images.” has been changed to “The images and video clips saved on the local hard disk were independently reviewed in random by two radiologists (D.X.H. and Z.J.), both blinded to the pathological results. Both radiologists had more than 10 years of experience in urinary US and 8 years in reading CEUS images.” (Line 14, page 4)

8. “The CEUS characteristics included the degree of peak enhancement, the homogeneity of enhancement, the perilesional rim-like enhancement and the “wash in” and “wash out” pattern. The normal renal cortex adjacent to the tumor was used as the control for comparison of the enhancement. The degree of tumor peak enhancement was classified as hyper-, iso-, and hypo-enhancement. The homogeneity at peak enhancement was classified as homogeneous, which was defined as a lesion completely enhancing without any defects, and heterogeneous, which was defined as a lesion with unenhanced areas, regardless of various enhancement degrees. The perilesional rim-like enhancement becoming more distinct in the late phase was considered to represent the presence of a pseudocapsule,
which was classified as with or without. Both the wash in and wash out of contrast in renal masses were described as fast, synchronous, or slow. ” has been changed to “Referring to the normal renal cortex adjacent to renal mass, the enhancement characteristics of renal mass were analyzed. The CEUS features included the enhancement intensity at peak time, the homogeneity of enhancement, the perilesional rim-like enhancement and the “wash in” and “wash out” mode. The enhancement intensity at peak time was described into hyper-, iso-, and hypo-enhancement. The homogeneity at peak enhancement was classified into homogeneous and heterogeneous. The homogeneous was defined as a renal mass with uniform enhancement, and the heterogeneous was defined as a renal mass with inconsistent enhancement. The perilesional rim-like enhancement, more distinct in the late phase of enhancement, was classified as present or absent. Both the “wash in” and “wash out” of renal masses contrast enhancement were classified as fast, synchronous, or slow.” (Line 18, page 4)

9. “Fig 2. A 85-year-old man with clear cell renal carcinoma.” has been changed to “Fig 2. A case of clear cell renal carcinoma.” (Line 6, page 16)

10. “Fig 3. A 22-year-old man with renal angiomyolipoma .” has been changed to “Fig 3. A case of renal angiomyolipoma.” (Line 15, page 16)

11. Our manuscript is a single, final, clean version that does not contain any tracked changes, comments, highlights, strikethroughs or text in different colours. All relevant tables/figures/additional files are clean versions. All figures, tables and additional/supplementary files are cited within the text.