Received:
17 August 2017

Revised:
18 October 2017

Accepted:
07 November 2017

<https://doi.org/10.1259/bjr.20170601>

Cite this article as:

Mao Y, Mu J, Zhao J, Zhao L, Xin X. The value of superb microvascular imaging in differentiating benign renal mass from malignant renal tumor: a retrospective study. *Br J Radiol* 2018; **91**: 20170601.

FULL PAPER

The value of superb microvascular imaging in differentiating benign renal mass from malignant renal tumor: a retrospective study

YIRAN MAO, MS, JIE MU, MS, JING ZHAO, MS, LIHUI ZHAO, MS and XIAOJIE XIN, BS

Department of Ultrasound Diagnosis and Treatment, Tianjin Medical University Cancer Institute and Hospital, National Clinical Research Center for Cancer, Key Laboratory of Cancer Prevention and Therapy, Tianjin's Clinical Research Center for Cancer, Tianjin, China

Address correspondence to: Dr Xiaojie Xin
E-mail: xinxiaojie@163.com

Objective: This study is to evaluate the value of superb microvascular imaging (SMI) in assessing renal tumour vascularity and in differentiating benign from malignant renal tumours.

Methods: Patients with pathologically confirmed renal mass who underwent colour Doppler flow imaging (CDFI) and SMI examination between October 2016 and March 2017 were retrospectively analysed. Patients were classified into benign renal mass group and malignant tumour group according to their pathological results. The vascularity, vascular distribution and vessel morphology obtained from the two scanning methods were analysed and compared between the two groups.

Results: 53 patients with renal tumour were enrolled into the study, including 11 cases of benign renal tumours and 42 cases of malignant ones. SMI showed significant difference in vascularity between the two groups; CDFI showed

no statistical difference. Compared with CDFI, SMI showed significantly higher grade in malignant tumour ($p < 0.001$), and no significant difference ($p = 0.421$) in benign mass. According to CDFI, there is no statistical difference in vascular distribution and vessel morphology ($p = 0.432$, $p = 0.122$) between the two groups, while SMI method showed significant difference ($p < 0.05$) between the two groups. SMI was significantly more sensitive and accurate than CDFI.

Conclusion: Comparing with CDFI, SMI could effectively detect vascularity, vascular characteristics and distribution and annular blood flow in renal tumour. SMI appears more sensitive and precise in distinguishing benign renal mass from malignant tumour.

Advances in knowledge: SMI seems potentially valuable in evaluating renal tumour vascularity and in differentiating benign from malignant renal tumours.

INTRODUCTION

Renal masses are considered as a heterogeneous group of tumours ranging from benign masses to cancers that can be indolent or aggressive.^{1,2} Although renal cell carcinoma affects about 65,000 new patients each year, the incidence of suspected malignant renal masses is unknown. Besides, approximately 20% of surgically removed renal masses are benign, and more than 6000 benign renal masses are resected each year according to the report of the USA.^{1,3} All solid renal masses are suspicious for renal cell carcinoma, but the incipient symptoms of renal mass are not typical. With increasing trend of renal mass incidence, it is important to make an early diagnosis to distinguish benign renal mass from malignant tumour.⁴

The genesis of microvessels and microvascular architecture is closely associated with tumour growth, infiltration, metastasis, staging and prognosis.⁵ The characteristics of

tumour microvessel are important in differentiating benign tumour from malignant ones. Besides, the blood flow state in tumour has great meaning in differentiating benign renal mass from malignant tumour. Currently, renal tumour vascularity could be evaluated using non-contrast-enhanced ultrasonography, e.g. colour Doppler flow imaging (CDFI), and contrast-enhanced imaging methods. CDFI is useful in assessing tumour vascularity, which, however, is limited in detecting the microvasculature and blood flow of low-velocity. And the overlap of CDFI in renal mass has interrupting effect on diagnosis.⁶ Superb microvascular imaging (SMI) is a new Doppler ultrasound technique and is informative for evaluating very slow blood flow state, which allows for imaging microvessels with low velocity in the absence of a contrast agent.⁷ SMI has been reported to be used in diagnosing breast tumours and liver lesions,^{8,9} with advantages in detecting low-velocity blood flow over CDFI.

As far as we know, there is no clinical report about SMI technology in evaluating microvascular characteristics of renal mass. To assess the value of SMI in evaluating renal tumour vascularity and in differentiating benign from malignant renal tumours, we retrospectively reviewed and compared the vascularity and vessel characteristics between SMI and CDFI.

METHODS AND MATERIALS

Patients

This study was approved by the ethics committee of the hospital and the signed informed consents were obtained from all patients. The clinical data of the patients with pathologically confirmed renal mass who underwent CDFI and SMI examination between October 2016 and March 2017 were retrospectively analysed. The inclusion criteria were that patients older than 18 years old, pathologically confirmed renal mass and patients without having chemotherapy. The exclusion criteria were patients that had not undergone surgery or biopsy. Patients were classified into benign renal mass group and malignant tumour group based on their pathological results.

Examination method

All ultrasound examinations were performed using Aplio 500 (Toshiba Medical Systems, Tokyo, Japan). The sonographic scanning was done by two radiologists (about 6 years of clinical experience in sonography and CDFI and 6 months in SMI). Greyscale, CDFI and SMI examination were completed, which took about 15–25 min.

At least two orthogonal greyscale images of each solid mass were obtained. The radiologists recorded the conventional ultrasound characteristics of the tumour that included the lesion size, shape, orientation, margin, boundary and echo pattern. Then, two orthogonal images of each mass were scanned slowly with CDFI. The CDFI examination was performed under the following parameters: the colour velocity scale at 9.8 cm s^{-1} , the wall filter at 50–100 Hz, the colour gain was adjusted adequately in order to avoid the background colour and detect small vessels. The region of interest (ROI) involved the tumour and its adjacent normal tissue (1 cm). The scanning was completed with the patients holding breath. The signal was considered as one real blood flow signal on ultrasonography when an arterial flow pattern showed on CDFI or SMI. The lesion vascularity on the richest vascular images was recorded. Similarly, SMI was done and obtained in two patterns including greyscale and colour. SMI examination was performed under the following mode: the colour velocity scale at 1.5–2.0

cm s^{-1} , the colour frequency at 5–7 MHz and the vascular information was enhanced by adjusting the time smooth.

Imaging analysis

The vascularity, vascular distribution and vessel morphology in renal mass were evaluated. The vascularity of the renal tumour was visualized and recorded by CDFI and SMI. Conforming to Adler's method, the vascularity was subjectively determined as absent (Grade 0), minimal (Grade 1), moderate (Grade 2) and marked (Grade 3). The amount of blood flow shown in ROI was assessed as the following. Generally, if there were one or two pixels contained blood flow (usually <1 mm in diameter), then it was determined as minimal. When a main vessel was visualized in the area and/or 3–4 pixels were shown, the amount of blood flow was considered as moderate. It was judged as having marked vascularity when ≥ 5 pixels or ≥ 2 main vessels were visualized.¹⁰

Vascular distribution includes the peripheral type in which the signal of blood flow was detected in the tumour margin, the central type with blood flow signal in the centre of tumour and the mixed type which shows blood flow signal in both centre and margin of tumour. Vessel morphology includes (1) none, without any clear blood flow signal; (2) dotted or linear, in which the blood flow signal could be detected as the shape of dot or line; (3) arbourization with blood flow distributed in arbourization within tumour; (4) irregular, in which the tortuously and disorderedly distributed blood flow was detected in tumour. Besides, whether there existed the annular blood flow in the tumour was also recorded.

All histopathological specimens were reviewed by an experienced pathologist after surgery or biopsy.

Statistical analysis

Statistical analysis was performed using SPSS 22.0 (SPSS Inc, Chicago, IL). Data were presented as mean $\pm$ standard deviation for continuous variables, and frequencies with percentages for categorical variables. The comparison of categorical variables between the two groups were performed using χ^2 test and Fisher's exact test, and that of continuous variables using independent *t*-test. *p* value <0.05 indicated statistically significant.

RESULTS

53 patients (average age of 55.8 ± 9.9 , range of 23–75 years; 38 males and 15 females) with renal tumour (maximum diameter of 5.08 ± 2.82 , range of 1.3–15.0 cm; 27 in left side and

Table 1. Comparison of renal tumour vascularity based on Adler's method between the benign group (11 cases) and the malignant group (42 cases)

Grade	CDFI				SMI			
	0	1	2	3	0	1	2	3
Benign (cases per percentage)	4/36.4%	4/36.4%	3/27.3%	0/0.0%	3/27.3%	4/36.4%	2/18.2%	2/18.2%
Malignant (cases per percentage)	6/14.3%	15/35.7%	16/38.1%	5/11.9%	0/0.0%	1/2.38%	10/23.8%	31/73.8%
χ^2	3.213				14.794			
<i>p</i>	0.323				0.001			

CDFI, colour Doppler flow imaging; SMI, superb microvascular imaging.

Figure 1. Images of a patient with hamartoma in the left side. (a) Two dimension ultrasound. It shows moderately strong echo in its clear boundary and homogenous echo in the internal part. (b–c) Colour Doppler flow imaging (b) and superb microvascular imaging (c) images show dotted or linear signals peripherally and centrally, and Adler Grade 2.

26 in right side) were enrolled into the study, including 11 cases of benign renal tumours and 42 cases of malignant ones according to pathological results. All patients had single renal mass. The benign group included 7 cases of angiomyolipoma, 3 cases of renal acidophil tumour and 1 case of nephrophthisis; the malignant group included 37 cases of renal clear cell carcinoma, 4 cases of chromophobe cell tumour and 1 case of mucinous carcinoma.

According to CDFI, there is no statistical significance in vascularity based on Adler's method between the benign group and the malignant group (Table 1 and Figure 1). SMI shows significant difference between the two groups. Comparing with CDFI, SMI showed significantly higher grade in malignant tumour ($\chi^2 = 41.034$, $p < 0.001$), and no significant difference ($\chi^2 = 3.523$, $p = 0.421$) in benign renal mass.

The vascular distribution of the two groups is showed in Table 2. According to CDFI, there is no statistical difference in vascular distribution (Figure 2) and vessel morphology ($\chi^2 = 1.786$, $p = 0.432$; $\chi^2 = 5.684$, $p = 0.122$) between the two groups, while SMI method showed significant difference ($\chi^2 = 11.150$, $p = 0.002$; $\chi^2 = 18.061$, $p = 0.000$) between the two groups. In detecting annular blood flow (Figure 3), the two ultrasonography methods showed statistical difference in benign tumour group and malignant tumour group ($\chi^2 = 5.479$, $p = 0.016$; $\chi^2 = 11.662$, $p = 0.001$). SMI is more sensitive than CDFI in detecting annular blood flow in malignant mass ($\chi^2 = 8.052$, $p = 0.004$).

Table 3 summarizes the sensitivity, specificity, positive predictive value, negative predictive value and accuracy of the two methods. SMI was significantly more sensitive and accurate than CDFI.

Table 2. Vascular distribution and vessel morphology in the benign group (11 cases) and the malignant group (42 cases)

	CDFI		SMI	
	Benign	Malignant	Benign	Malignant
Vascular distribution				
Peripheral type	6 (54.5%)	15 (35.8%)	6 (54.5%)	4 (9.5%)
Central type	3 (27.3%)	11 (26.2%)	2 (18.2%)	6 (14.3%)
Mixed type	2 (18.2%)	16 (38.1%)	3 (27.3%)	32 (76.2%)
Vessel morphology				
None	4 (36.4%)	6 (14.3%)	3 (27.3%)	0 (0.00%)
Dotted or linear	3 (27.3%)	10 (23.8%)	3 (27.3%)	1 (2.38%)
Arbourization	4 (36.4%)	14 (33.3%)	3 (27.3%)	12 (28.6%)
Irregular	0 (0.00%)	12 (28.6%)	2 (18.2%)	29 (69.0%)
Annular blood flow				
Yes	0 (0.00%)	15 (35.7%)	1 (9.09%)	28 (66.67%)
No	11 (100%)	27 (64.3%)	10 (90.91%)	14 (33.33%)

Colour Doppler flow imaging, CDFI; superb microvascular imaging, SMI.

Figure 2. Images of a patient with renal clear cell carcinoma in the right side. (a) Two dimension ultrasound. It shows moderately strong echo in its unclear boundary and inhomogenous echo in the internal part. (b) Colour Doppler flow imaging image shows dotted or linear signals peripherally, and Adler Grade 2. (c) superb microvascular imaging image shows irregular signals peripherally and centrally, and Adler Grade 3.

DISCUSSION

Renal cancer tissue can secrete a variety of vascular active substances for the induction of angiogenesis.¹¹ Renal benign and malignant neoplasm have great difference in microvessel quantity, structure and distribution. In most malignant tumour, there is a great genesis of blood vessels that are characterized with wide and irregular diameters, distortion, deformation, dense clumps and even arteriovenous fistula. While in benign tumour, angiogenesis is relatively slow with relatively regular vessels and less branches.¹² In this study, 76.2% malignant tumour showed peripherally or centrally distributed vascular distribution; 54.5% benign mass showed no blood flow or peripherally distributed. As for vessel morphology, 97.6% malignant tumour showed dendritic or irregular, while in the benign mass group, 54.6% showed linear or dendritic shape.

SMI has more advantages than CDFI in detecting and showing low-velocity blood flow and clear vascular characteristics and distribution. SMI could show clear images of blood flow with low velocity of $1.5\text{--}2.0\text{ cm s}^{-1}$ according to our clinical experience and previous report. In this study, according to Adler method, malignant renal tumour group showed higher grade than benign mass group, with 31 cases (73.8%) of Grade 3, 10 cases (23.8%) of

Grade 2 and 1 case (2.4%) of Grade 1 in malignant group, and 2 cases (18.2%) of Grade 3, 6 cases (54.6%) of Grade 1–2 and 3 cases (27.3%) of Grade 0 in benign group. CDFI usually fails to evaluate low-velocity blood flow ($3\text{--}5\text{ cm s}^{-1}$) signals in small vessels ($<1\text{ mm}$) owing to the limitation of its angular dependency and poor signal-to-noise ratios.^{9,13} Thus, SMI seems to possess higher predictive sensitivity and precision than CDFI.

As SMI is sensitive in detecting low-velocity blood flow, it might contribute to a misdiagnosis in benign renal tumour when it contains rich blood. In this study, there are four cases of benign renal tumour with vascularity Grade 2–3, among which three cases have hamartoma and one case has renal acidophilic tumour. Li et al reported that 85% acidophilic adenoma are rich in blood supply.¹⁴ The manifestation of rich blood flow in hamartoma can be seen as it sometimes has plenty of blood vessels. In this condition, we must combine with other examination methods to make a right judge.¹⁵

Renal cell carcinoma is usually enveloped by pseudocapsule, an annular tissue containing fibrous tissue and capillary vessel and located between the tumour and normal renal tissue. And the annular enhancement in ultrasound image is a distinctive character.¹⁶ In this study, SMI showed there are 28 cases (66.67%)

Figure 3. Images of a patient with renal clear cell carcinoma in the right kidney. (a) Colour Doppler flow imaging image shows dotted signal of blood flow in the internal and peripheral part of the mass. (b, c), superb microvascular imaging images show new vessels tortuously extruding into the internal part of mass, and annular blood flow in the periphery of the mass (as the arrow shows).

Table 3. Diagnostic sensitivity and specificity of CDFI and SMI in renal tumour

	Sensitivity	Specificity	Positive-prediction value	Negative-prediction value	Accuracy
CDFI	73.81	63.64	88.57	61.11	71.70
SMI	92.86	45.45	86.67	62.5	83.02

CDFI, colour Doppler flow imaging; SMI, superb microvascular imaging.

of annular blood flow in malignant group and 1 case (9.09%) in benign group. Compared with CDFI, SMI showed more sensitivity in detecting annular blood flow. In the benign case with annular blood flow, the pathological result showed it was acidophilic cell tumour, immune-histochemical suggested it was acidophilic cell adenoma. The neoplasm was in the middle of the right kidney, with maximum diameter of 2.8 cm, and showed blood flow signals in the peripheral and internal part of the tumour. We supposed the annular blood flow might be resulted from the extrusion of neoplasm to the surrounding renal blood vessels.

As far as we know, this is the first study that have applied SMI in distinguishing benign renal mass from malignant renal tumour. During SMI examination, it is critical that the patients hold breath to minimize the negative effect of breathing. The greyscale mode of SMI could show blood flow in more direct and clearer way according to our clinical experience. Although SMI has

advantages over CDFI in detecting vascularity, blood flow and vessel morphology, it still has limits. For example, the renal mass in the distant end of the kidney is easily influenced by intestinal gas during the scanning, which may result in artefact in the ROI.

There are some limitations in this study. Firstly, SMI is rarely reported to be used in kidney tumours and our experience is limited in applying SMI to evaluate vascular characteristics and distribution in renal tumour. Secondly, the sample size is small, especially the benign cases. Further clinical study with a large sample is necessary to draw a more solid conclusion.

In conclusion, comparing with CDFI, SMI could effectively detect vascularity, vascular characteristics and distribution and annular blood flow in renal tumour. Thus, SMI appears to be more sensitive and precise in distinguishing benign renal tumour from malignant tumour.

REFERENCES

- Kutikov A, Fossett LK, Ramchandani P, Tomaszewski JE, Siegelman ES, Banner MP, et al. Incidence of benign pathologic findings at partial nephrectomy for solitary renal mass presumed to be renal cell carcinoma on preoperative imaging. *Urology* 2006; **68**: 737–40. doi: <https://doi.org/10.1016/j.urology.2006.04.011>
- Thompson RH, Hill JR, Babayev Y, Cronin A, Kaag M, Kundu S, et al. Metastatic renal cell carcinoma risk according to tumor size. *J Urol* 2009; **182**: 41–5. doi: <https://doi.org/10.1016/j.juro.2009.02.128>
- Lane BR, Babineau D, Kattan MW, Novick AC, Gill IS, Zhou M, et al. A preoperative prognostic nomogram for solid enhancing renal tumors 7 cm or less amenable to partial nephrectomy. *J Urol* 2007; **178**: 429–34. doi: <https://doi.org/10.1016/j.juro.2007.03.106>
- Pierorazio PM, Patel HD, Johnson MH, Sozio SM, Sharma R, Iyoha E, et al. Distinguishing malignant and benign renal masses with composite models and nomograms: a systematic review and meta-analysis of clinically localized renal masses suspicious for malignancy. *Cancer* 2016; **122**: 3267–76. doi: <https://doi.org/10.1002/cncr.30268>
- Pluda JM. Tumor-associated angiogenesis: mechanisms, clinical implications, and therapeutic strategies. *Semin Oncol* 1997; **24**: 203–18.
- Zhang H, Zhao Y. Clinical study on angiogenesis of renal cell carcinoma. *Chin J Ultrasonogr* 2003; **12**: 172–3.
- Xiao XY, Chen X, Guan XF, Wu H, Qin W, Luo BM. Superb microvascular imaging in diagnosis of breast lesions: a comparative study with contrast-enhanced ultrasonographic microvascular imaging. *Br J Radiol* 2016; **89**: 20160546. doi: <https://doi.org/10.1259/bjr.20160546>
- Lee DH, Lee JY, Han JK. Superb microvascular imaging technology for ultrasound examinations: Initial experiences for hepatic tumors. *Eur J Radiol* 2016; **85**: 2090–5. doi: <https://doi.org/10.1016/j.ejrad.2016.09.026>
- Ma Y, Li G, Li J, Ren W-dong, Ren WD. The diagnostic value of superb microvascular imaging (SMI) in detecting blood flow signals of breast lesions. *Medicine* 2015; **94**: e1502. doi: <https://doi.org/10.1097/MD.0000000000001502>
- Adler DD, Carson PL, Rubin JM, Quinn-Reid D. Doppler ultrasound color flow imaging in the study of breast cancer: preliminary findings. *Ultrasound Med Biol* 1990; **16**: 553–9. doi: [https://doi.org/10.1016/0301-5629\(90\)90020-D](https://doi.org/10.1016/0301-5629(90)90020-D)
- Sandlund J. *Angiogenesis in human renal cell carcinoma: hypoxia, vascularity and prognosis*. Umea, Sweden: Faculty of Medicine Radiation Sciences, Umea University; 2007. pp. 11–12.
- Sun X, Zhao Y, Sun X. The imaging of renal tumor by color doppler ultrasound. *Chinese Journal of Ultrasound Diagnosis* 2003; **4**: 45–6.
- Schroeder RJ, Bostanjoglo M, Rademaker J, Maeurer J, Felix R. Role of power Doppler techniques and ultrasound contrast enhancement in the differential diagnosis of focal breast lesions. *Eur Radiol* 2003; **13**: 68–79. doi: <https://doi.org/10.1007/s00330-002-1413-3>
- Li QH, Hou J, Yan FH. The imaging manifestations of renal oncocytoma with correlation of pathology. *Chin J Radiol* 2008; **42**: 97–9.
- Gao B. Significance of color doppler ultrasonography for differentiating benign and malignant renal neoplasms. *J Pract Med Imag* 2008; **9**: 183–5.
- Liu L, LF D, Li F. Specificity analysis of peritumoral hyper-enhanced rim in diagnosis of renal tumors using contrast-enhanced ultrasound. *J Chin Ultrasound in Med* 2012; **14**: 603–5.