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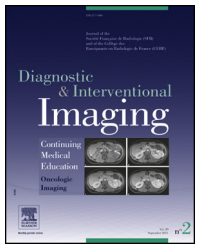

CONTINUING EDUCATION PROGRAM: FOCUS...

Perfusion imaging in renal diseases

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KEYWORDS
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Renal obstruction;
Renal tumors

Abstract Functional imaging of the kidney using radiological techniques has a great potential of development because the functional parameters, which can be approached non-invasively, are multiple. CT can provide measurement of perfusion and glomerular filtration but has the inconvenient to deliver irradiation and potentially nephrotoxicity due to iodine agents in this context. Sonography is able to evaluate perfusion only but quantification remains problematic. Therefore, MR imaging shows the greatest flexibility measuring blood volume and perfusion as well as split renal function. The main applications of perfusion imaging of the kidney are vascular diseases, as renal artery stenosis, renal obstruction and follow-up of renal tumors under antiangiogenic therapy. However, full clinical validation of these methods and the evaluation of their clinical impact are still often worthwhile.

Renal perfusion and glomerular filtration rate (GFR) are major functional parameters, which are involved in many parenchymal diseases and used to monitor the renal function. Getting an easy, reliable and reproducible access to these data, in conjunction with precise morphological information, would significantly improve the patient care in nephrology. For example, actually, measurement of perfusion in clinics is not reliable and no reference method is available for patients. In clinical practice, non-invasive and accurate measurement of renal blood flow or perfusion may become important for the evaluation of renal artery stenosis or nephropathies with microvascular involvement, to help in monitoring intravascular interventions, to characterize renal tumors and follow them after antiangiogenic therapies. Similarly, GFR is used as an index of functioning renal mass, representing the sum of filtration rates in each functioning nephron. Fall of GFR may be the earliest and only clinical sign of renal disease and its serial monitoring allows estimating the severity

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and following the course of kidney diseases. If measurement of GFR with radiological techniques remains a challenge for the future, measurement of the differential renal function is now available for clinical routine.

Contrast agents and technical issues

Sonography

Third generation of ultrasound contrast agents (USCA) are composed of microbubbles, containing a gas with a low diffusibility, stabilized by a shell, with a mean diameter range between 1 and 5 microns [1] Once injected into the blood circulation, these bubbles have a mono-compartment distribution, purely intravascular, without interstitial diffusion or glomerular filtration. The gas is eliminated via the respiratory system. This pharmacokinetics characterizes these agents as real blood pool agents, particularly appropriate for the evaluation of renal perfusion. However, there are major constraints making quantification process difficult with US: the response of both anatomical structures and microbubbles to an ultrasound beam is complex, which requires using contrast-specific imaging modes based on the enhancement of the non-linear response from bubbles; quantification is also mainly affected by shadowing which results from inaccurate correction of both tissue and microbubble attenuation. Variation in attenuation across the image at a given depth is not accounted for by time-gain compensation (TGC). Secondly, there is no linear relationship between the concentration of the agent and the intensity of the received signal. Third, even if imaging protocols require a sonication with low mechanical indexes, an unpredictable part of microbubbles are destroyed within the imaging plane, in both the analyzed tissue and the feeding vessels. Some mathematical models were proposed to compensate for this effect [2,3]. This is why such dynamic studies require applying quantification processes to non-compressed data, such as the true raw data, which can be available on certain systems. In such conditions, the application of functional renal US in humans has shown a large development in semi-quantitative evaluation of renal tumor perfusion [4].

Renal signal-time curves obtained with these agents are characteristic of non-diffusible agents with only a vascular peak followed by recirculation (Fig. 1).

CT

Iodine contrast agents used for X-rays can be considered as glomerular tracers as ^{99m}Tc-DTPA or ^{51}Cr-EDTA are used in nuclear medicine, they are freely filtered at the first pass by the glomeruli without any tubular secretion or reabsorption. The linear relation between the level of attenuation and the contrast agent concentration is a great advantage, facilitating modelisation. Axial acquisitions with CT allow including both kidneys (for comparison) and aorta to take into account the arterial input function [5,6]. There are several limitations making CT poorly available for the quantitative evaluation of renal function: nephrotoxicity of iodine agents in patients with decreased renal function, the induced radiation dose due to the necessary continuous irradiation during acquisition requiring the application of all dose reduction methods and the impossibility to include the entire kidney in the volume using the axial transverse plane (4 to 6 cm covered).

MR imaging

Regular low-molecular-weight gadolinium (Gd) chelates are still the only extrinsic agents used in clinical imaging [7,8]. As iodine contrast agents, they can also be considered as glomerular tracers. However, their role in the evaluation of renal function shows some limitations: first, as the other mentioned agents, they are also freely diffusing into the interstitium, compartment which is usually neglected in most pharmacokinetic models; second, the relationship between signal intensity (SI) and concentration is highly complex, inducing concomitant reduction of T1 and T2 (or T2*), which is not the case for radioactive agents or iodine compounds.

Concentration of agent can be calculated by the linear relationship to the R1 relaxation rate and the specific relaxivity of the agent (r):

$$C = (R1 - R1_0)/r$$

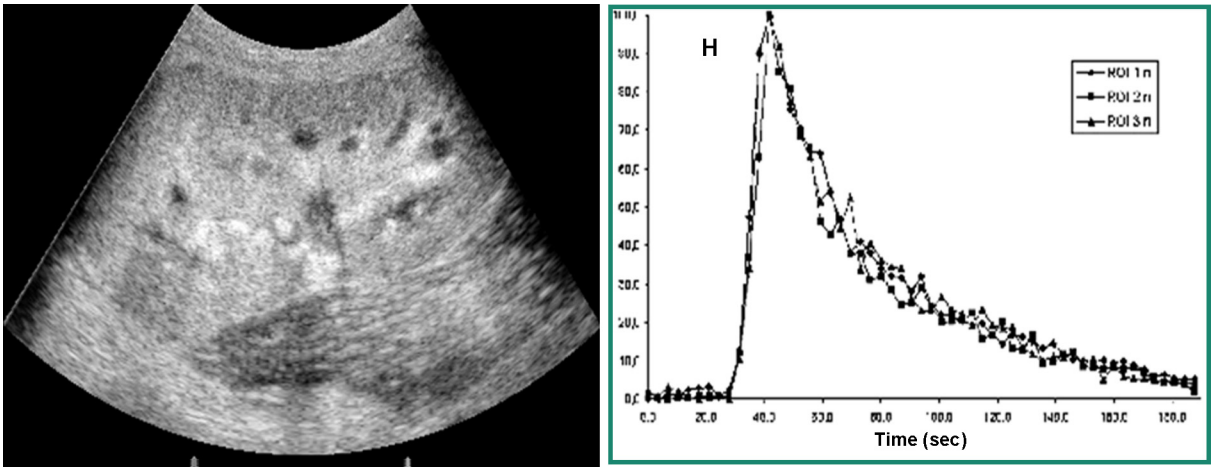

Figure 1. Typical signal-time curve obtained in a normal kidney transplant after injection of non-diffusible microbubbles. Courtesy of Dr J.M. Correas, Necker Hospital, Paris.

where $R1_0$ is the bulk R1 in the tissue without contrast agent. In principle, this means that a pre-contrast measurement of R1 should be performed before injection of the contrast agent.

Measurement of relative values of perfusion (tumor vs normal kidney or one kidney vs the other) does not require converting changes in SI into changes in R1. Only absolute values calculation requires this calculation (mainly for GFR).

Measurement of renal perfusion based on other types of contrast agents, such as larger Gd chelates or iron oxide particles or on displacement of water protons (spin-labeling) will not be discussed here because they do not have agreement for clinics for the former, or are not fully available for the latter.

With dynamic CT and MRI, the signal-time curve obtained within the renal parenchyma with these diffusible contrast agents is characteristic with three discernible phases (Fig. 2): a vascular phase with a tight upslope and an early peak, a glomerulotubular phase with a slow uptake (the agent being filtered) and a slowly descending excretory phase.

Functional parameters

Renal flow rate

Renal blood flow (RBF), or flow rate, refers to the global amount of blood reaching the kidney per unit time normally expressed in mL/min. This parameter is usually measured on a renal artery or a renal vein. Measurement of renal flow rate is based on the product of mean velocities in the renal artery and its section area. The cine phase-contrast MR method is able to sample intra-arterial velocity profile and to quantify the renal blood flow in each renal vessel without injection of contrast agent. This technique is well described in the literature [9—11]: it is based on the encoding of phase shifts of flowing spins along either one direction, perpendicular to the vessel of interest, or in all the three directions. For accurate measurements in the human arteries, the imaging plane is usually positioned 10 to 15 mm downstream from the ostium, where respiratory movements are minimal, and perpendicularly to the renal artery (Fig. 3).

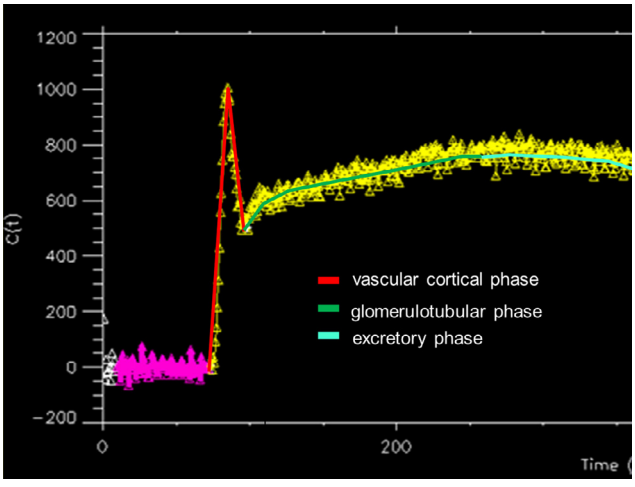

Figure 2. Typical signal-time curve obtained in a normal kidney transplant after injection of diffusible Gd chelate showing a vascular phase (red), a glomerulotubular phase (green) and an excretory phase (blue).

Renal perfusion

Renal perfusion refers to the blood flow that passes through a unit mass of renal tissue (mL/min/g) in order to vascularize it and exchange with the extravascular space. The degree of perfusion depends on both the arterial flow rate and local factors, such as regional blood volume and vasoreactivity. Renal perfusion parameters, as renal blood volume (RBV) and renal blood flow (RBF) can then be measured. These calculations are possible with dynamic contrast-enhanced methods using CT or MRI.

Technical requirements

Arterial input function (AIF): in order to compensate for the non-instantaneous bolus injected into the blood, quantification requires an accurate sampling of the vascular phase of the enhancement with a high temporal resolution to measure the AIF within the suprarenal abdominal aorta, far from the entry volume to avoid inflow artifacts (Fig. 4) [8]. If the AIF is not taken into account, only semi-quantitative parameters as maximal signal change (MSC), time to MSC (T_{MSC}) or wash-in and wash-out slopes can be measured for comparison from right to left kidney, from cortex to medulla or from one territory to another, or for follow-up of the patients [12—14].

With MRI, pulse-sequences used must have a heavy T1-weighting: gradient-echo sequences or sequences with a non-selective magnetization preparation are preferred, combining with very short TR/TE and low flip angles. Concentration of Gd within the kidney can be very high

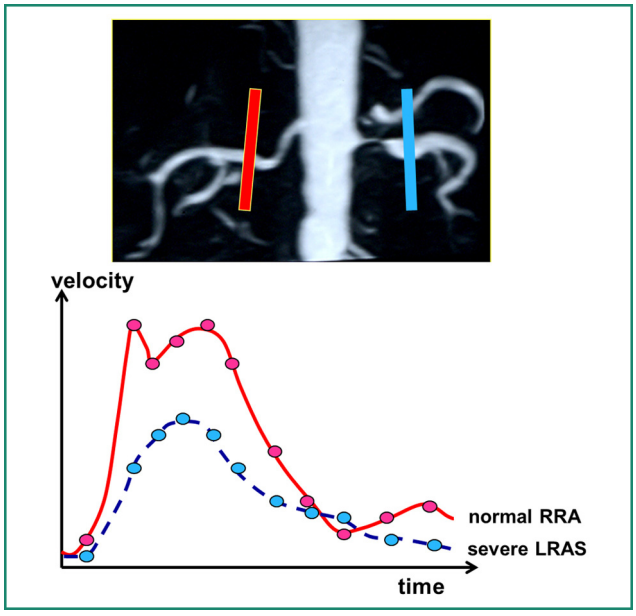

Figure 3. Technique of cine phase-contrast on renal arteries in a patient with left renal artery stenosis. Acquisition planes are positioned after each ostium, perpendicular to the arterial lumen. The velocity—time curve from the left renal artery (blue) is damped compared to the normal right one (red).

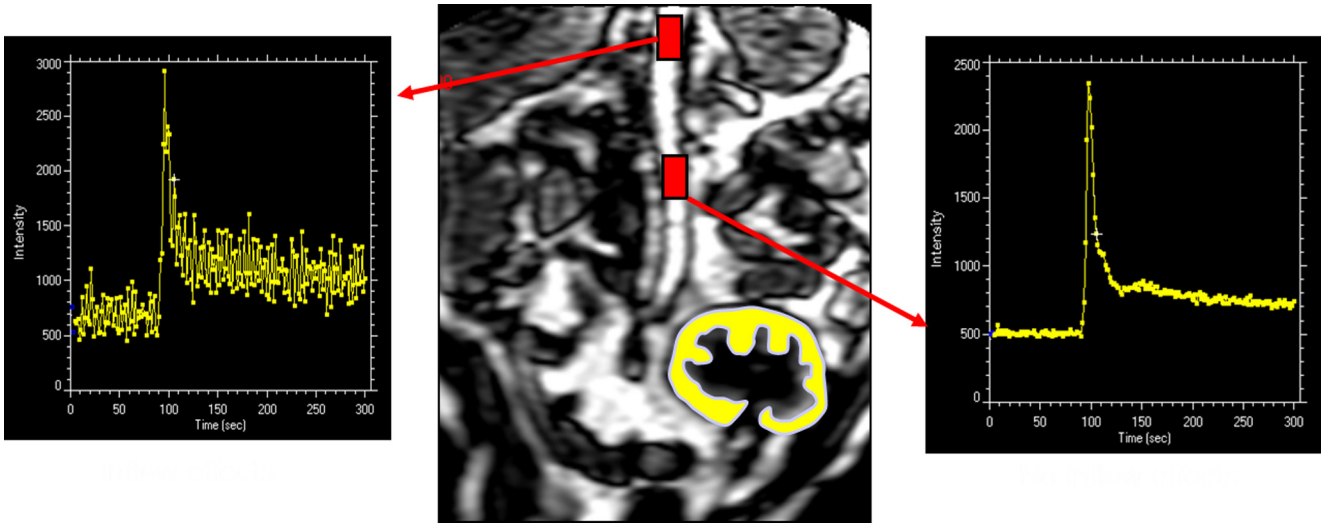

Figure 4. When an arterial input function (AIF) is used with MRI, the ROI has to be placed above renal arteries for native kidneys and on the lower aorta for transplanted kidneys. If positioned too high into the volume, it can be hampered by inflow artifacts.

due to water reasbsorption in the proximal convoluted tubule and in the medulla. Therefore, to avoid T2* contribution to the signal, the injected dose must be lowered between 0.025 mmol/kg and 0.05 mmol/kg, and the patient should be well hydrated [15]. An oblique-coronal plane, passing through the long axis of the kidneys, has to be preferred to an axial plane because with the later, movement correction, when necessary, is more difficult and the AIF can be severely impaired by inflow effects within the aorta.

With CT, conversion of densities into contrast concentration is straightforward whereas with MRI, this conversion is more hazardous. With the latter, if conversion is not made, only relative values of perfusion (rRBV and rRBF) can be extracted, making only comparative studies possible (one kidney/the other; one area/another area; follow-up of treatments for tumors).

Models

Calculated concentration—time curves must then be processed using specific mathematical models (Fig. 5) [16]. Dujardin et al. [17,18] generalized the tracer kinetic theory from intravascular to diffusible tracers using deconvolution, which is a model-free approach. From ROI drawn on the aorta and on the renal cortex, tissue concentration—time course has to be deconvolved pixel by pixel with the flow corrected aortic time course, resulting in an impulse response function (IRF). This method allows getting intrarenal maps of RBF, as maximum of IRF, RBV, as the time integral of the IRF over the available time interval, and MTT as the ratio RVD/RBF. Others used a two-compartment model, giving access to RBV, RBF and additional parameters, such as GFR, for renal diseases (see below) or tissue permeability, for tumors.

Post-processing methods

When only perfusion is required, dynamic CT or MR acquisitions can be short in time, compatible with a single breath hold, because one needs only the first renal pass. However, when complementary parameters are necessary, as permeability or GFR measurements, movement correction must be applied because they require longer acquisition times. Several methods have been proposed [19] but not always available commercially (Fig. 6).

Measurement of split renal function

Semi-quantitative evaluation of renal function, as split (or differential) renal function is sufficient in urological management of most uropathies, mainly obstructive. However, it is usually not useful in daily assessment and follow-up of renal diseases. In the nephrologic field, it can be required when a reduced renal function is associated with renal asymmetry, in renovascular diseases, before renal surgery, if renal function is altered or before renal biopsy. The split renal function (given in percentage) corresponds, for each kidney, to the product:

$$RF\,(\%) = RF/RF_{total} \times 100$$

where RF_{total} is the sum of RFs of both kidneys.

In clinical routine, the split renal function is still measured using nuclear medicine with glomerular (^{99m}Tc-DTPA) or tubular (^{99m}Tc-MAG3) agents. Two methods are promoted for that purpose: either the calculation of areas under the filtration curves or Rutland—Patlak plots:

- using dynamic contrast-enhanced MR imaging, Rohrschneider et al. [20] obtained calculations of the percentage of the single-kidney ''activity'' comparable to those derived with gamma camera scintigraphy, using areas under the filtration curves:
  $RF = AUC\,(mm^2) \times S\,(mm^2)$
  where AUC corresponds to the area under the glomerulotubular segment of the time—intensity curve and S is the ROI area (Fig. 7).

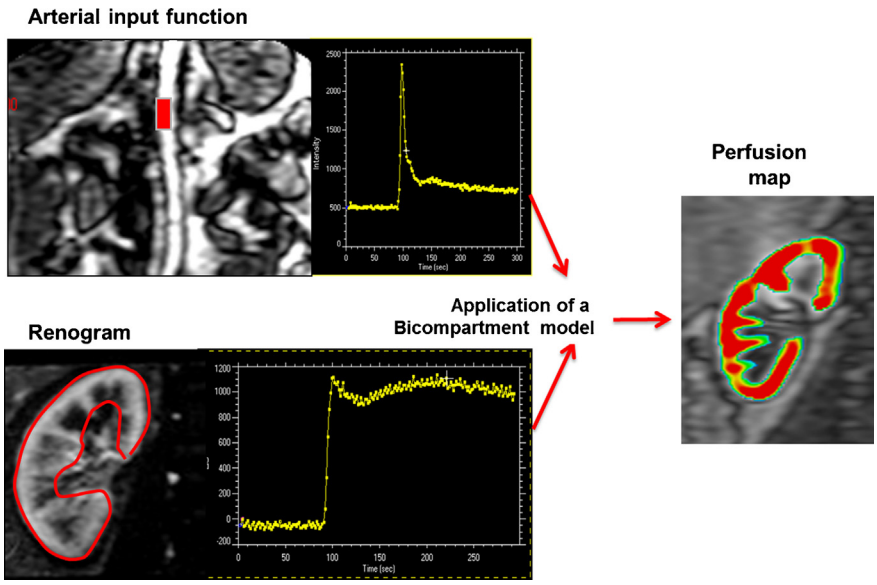

Figure 5. Two-compartments model. From the cortical signal intensity—time curve and from the AIF, a two-compartment model can be applied on voxel-by-voxel basis. We can obtain maps of perfusion (in mL/g/min) and vascular volume (in %).

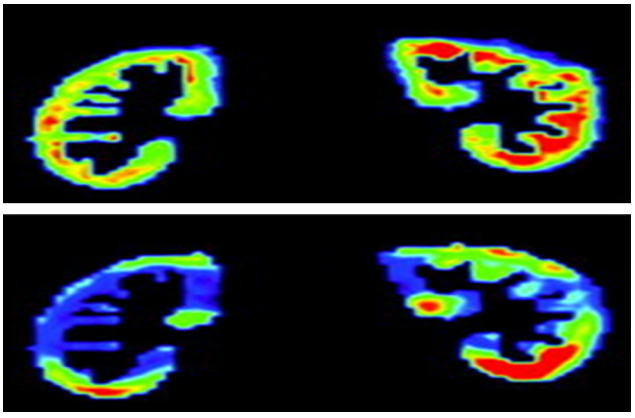

Figure 6. Impact of movement correction on functional maps: corrected maps (above) versus non-corrected maps (bottom) Reprinted with permission from Denis-de-Senneville et al., JMRI 2008;28:970—8.

- the Rutland—Patlak plot technique is a graphical method based on a two-compartmental model with the assumptions that the rate of change of concentration in the kidney during the clearance phase is constant if the amount of contrast agent is taken into account during this period [21]. The assumption that no contrast agent leaves the ROI during the sampling period may justify theoretically the use of ROIs encompassing both cortex and medulla. The model is realized as a *x*—*y* plot using the ratio of the renal concentration/aortic concentration plotted against the ratio of the integral of aortic concentration/aortic concentration. When applied to the second phase of the signal intensity—time curve (glomerulotubular uptake), this plot leads to a straight line, with a slope proportional to the renal clearance, and an intercept with the *y*-axis proportional to the cortical blood volume (Fig. 8).

Measurement of GFR

Whereas the level of GFR is the best index for monitoring chronic kidney diseases (CKD), measurement of glomerular filtration is difficult to obtain accurately in routine. Estimated renal clearance has several limitations [22]:

- variations of plasma creatinine level are around 10%;
- some tubular secretion may lead to the overestimation of GFR, particularly in advanced renal failure;
- there is a reduction of creatinine excretion with age-related to a decrease in skeletal muscle mass;

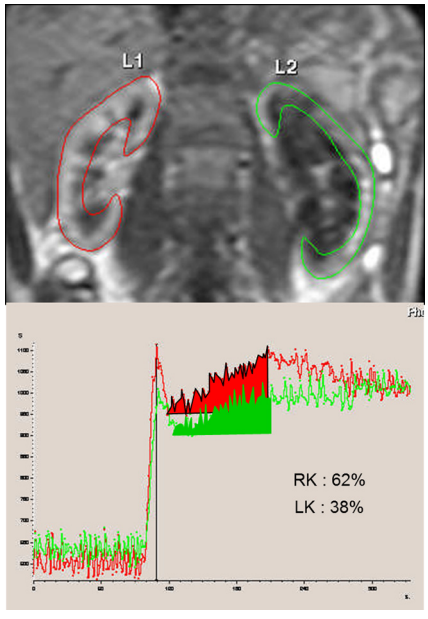

Figure 7. Measurement of the differential renal function, in a patient with a left hydronephrosis, using the method of areas under the glomerulotubular phase.

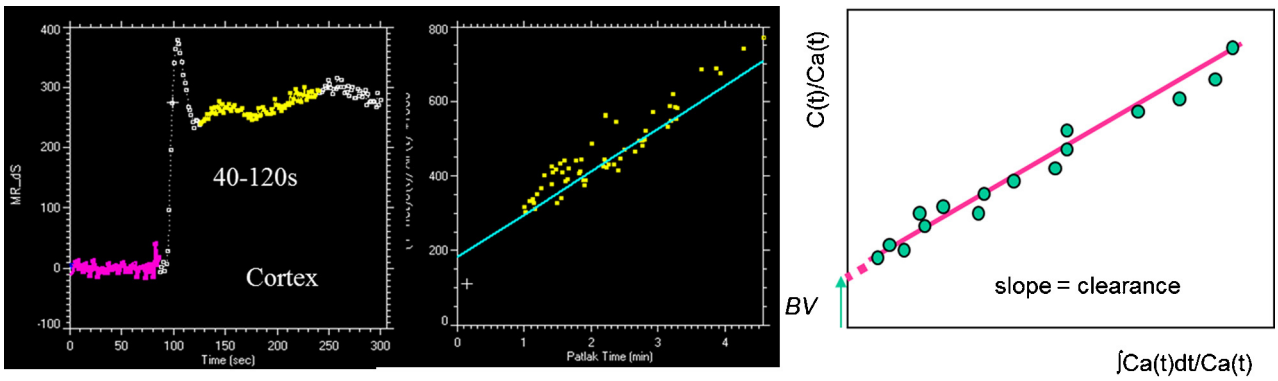

Figure 8. Principle of the Patlak—Rutland method. Based on the AIF and on the signal intensity—time curve from the renal cortex, the time points corresponding to the glomerulotubular phase are selected. The Patlak plot shows a good alignment of points. The slope corresponds to filtration and the intersection with vertical axis corresponds to blood volume (%).

- finally, in acute or rapidly progressing renal failure, this technique provides inaccurate information when GFR is rapidly changing.

Measuring GFR with dynamic CT or MRI still requires evaluation and validation phases before translated in routine practice.

Clinical applications

The main clinical applications of perfusion measurements are renal vascular diseases. In assessment of renal tumors, both perfusion and extravascular leak are considered. The main clinical application of split renal function is chronic urinary obstruction.

Renal artery stenosis (RAS)

Diagnosis of RAS is now based on non-invasive techniques as Doppler sonography, CT- or MR-angiography. Considering grading the severity of narrowing, the reproducibility of this evaluation is not perfect, explaining some discrepancies in published results, and it is not a good predictor of functional improvement after revascularization. Several functional tests have been proposed in the past to characterize ''functional stenoses'' as captopril-scintigraphy or captopril-MRI. These approaches are not used routinely anymore. Therefore, measurement of renal blood flow or renal perfusion, added to the morphologic evaluation in the same examination, can assess the haemodynamic significance of stenoses. Schoenberg et al. [23] used first cardiac-gated phase-contrast flow measurement to complete morphological acquisitions. Agreement between the morphological degree of stenosis and changes in the pattern of the flow profile was first documented in animal and then, in human studies [10,11,24]. The loss of the early systolic peak was proposed as a sensitive indicator for the loss of the autoregulatory capacity and the onset of significant mean flow reduction. This flow measurement technique provided a functional grading of the degree of stenosis independent of the morphologic grading (Fig. 9). These observations were confirmed by a multicenter trial, showing a significant reduction in interobserver variability and an improvement of overall accuracy compared with DSA, with sensitivities and specificities exceeding 95%.

Evaluation of perfusion also provided quantified functional information in these patients (Fig. 10) [24]. Michaely et al. [14], first calculated semi-quantitative parameters, such as mean transit time (MTT), maximal upslope (MUS) of the curve, maximum SI, and time to SI peak (TTP) after a gamma variate fit of the signal intensity—time curve. Significant differences between patients without stenoses or with low-to-intermediate grade stenoses and patients with high-grade stenoses were found for each of these parameters (Fig. 10). Based on a small series of 27 patients, the same group evaluated the diagnostic accuracy of quantified renal perfusion in identifying and differentiating renovascular from renal parenchymal disease [16]. Measurement of MR perfusion yielded a sensitivity of 100% and a specificity of 85% utilizing an optimal plasma flow threshold value of 150 mL/100 mL/min, whereas single MRA achieved a sensitivity of 51.9% and a specificity of 90%. An example of quantification of renal perfusion in a case of left RAS is shown in Fig. 11.

Follow-up of RAS after revascularisation is another application of these quantitative functional studies, adding objective hemodynamic criteria to the morphologic analysis of the artery [7].

Renal obstruction

Technically, the acquisition mode is the same than for perfusion studies. However, injection of furosemide is now recommended just before the injection of Gd, at a dose of 1 mg/kg in neonates and 0.5 mg/kg in infants and adults. For the split renal function, comparison between both kidneys based on the Rutland—Patlak plot is preferred to measurement of areas under the curves (see above) (Fig. 12). A prospective multicentric study in France on 295 patients [25] showed that both techniques are equivalent for cases with mild to moderate pyelectasis but underestimated the values for highly dilated kidneys.

Grading obstruction by placing an additional region-of-interest on the pyelocaliceal system is more difficult because many factors of variability may occur, such as the level of split function, the volume of cavities, the degree of bladder filling...

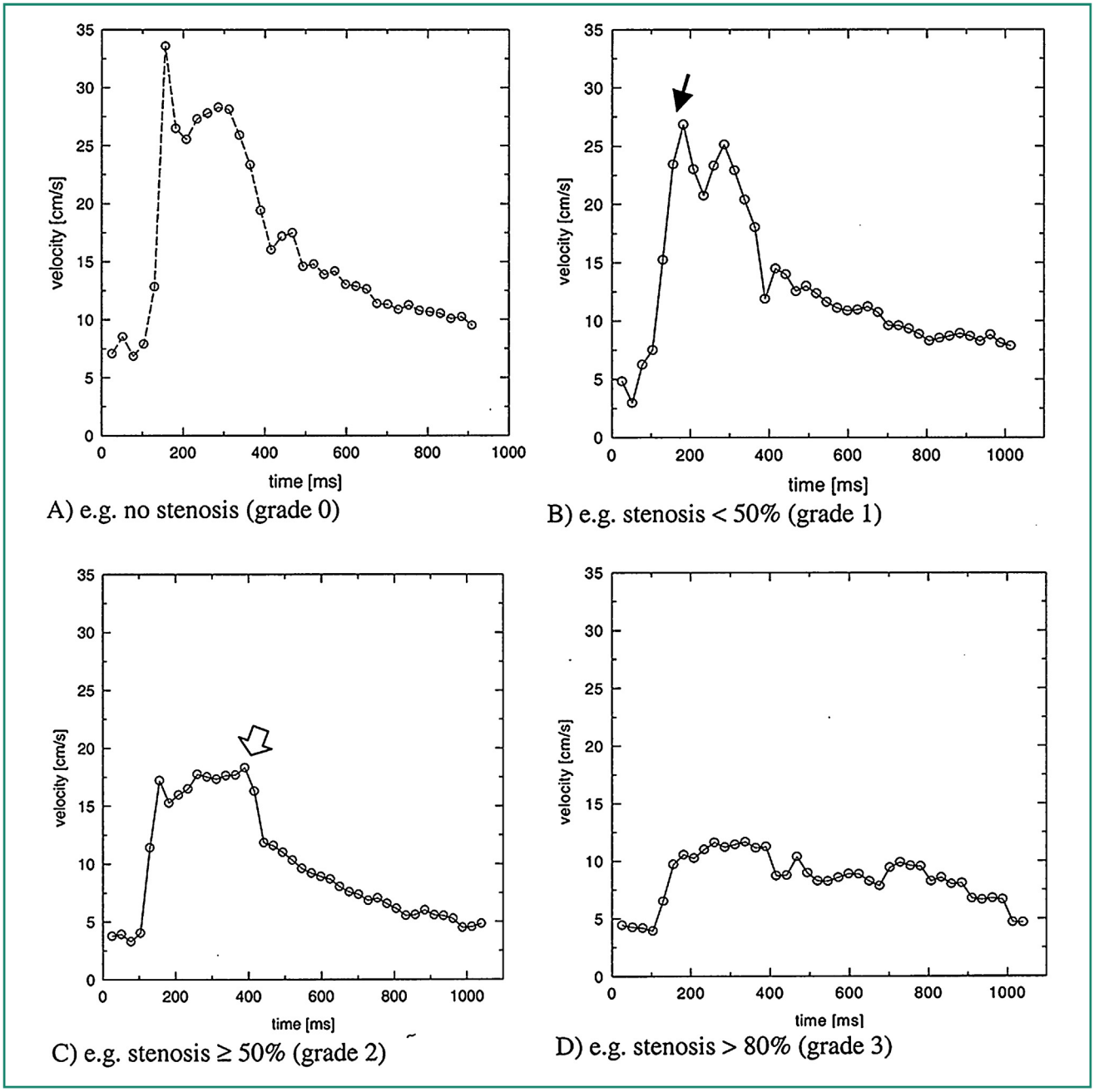

Figure 9. Cine phase-contrast flow curves for different degrees of renal artery stenosis. A. Normal flow profiles reveal a characteristic early systolic peak and a midsystolic maximum. B. Low-grade stenoses typically reveal only a partial loss of the early systolic peak (solid arrow). C. Moderate stenoses demonstrate an almost complete loss of the early systolic peak and a decrease of the midsystolic maximum (open arrow). D. High-grade stenoses have a featureless flattened flow profile.
Reprinted with permission from Schoenberg et al., J Am Soc Nephrol 2002;13:158—69.

Follow-up of renal tumors under antiangiogenic treatment

This application has emerged with the development of new targeted therapies as antiangiogenic drugs. Renal cancer is a major target for these treatments. The largest experience in that field was conducted with USCAs. Lassau et al. [26] defined the different pertinent parameters for such applications, such as the TTP, the AUC during the wash-in or the AUC during the wash-out with a low interoperator variability. They showed that this method was able to demonstrate the effect of antiangiogenic treatment as early as day 15 in metastatic renal cancer or day 3 for hepatocarcinomas, differentiating good and bad responders [27,28].

The same approach was validated with dynamic CT [29] providing discriminant quantified values of BF and BV between responders and non-responders after one cycle. An example of good response of a renal tumor after three cycles of antiangiogenic therapy is shown in Fig. 13.

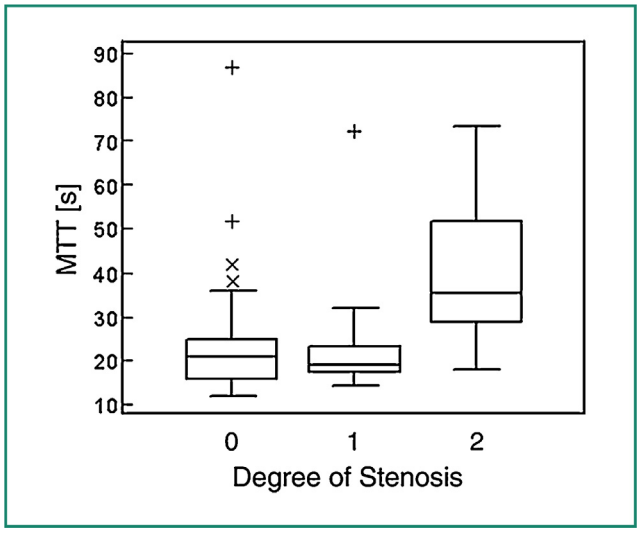

Figure 10. Semi-quantitative measurement of perfusion using mean transit time (MTT) in patients without (0) and with mild (1) or severe (2) renal artery stenosis.
Reprinted with permission from Michaely H.J. et al., Radiology 2006;238:586—96.

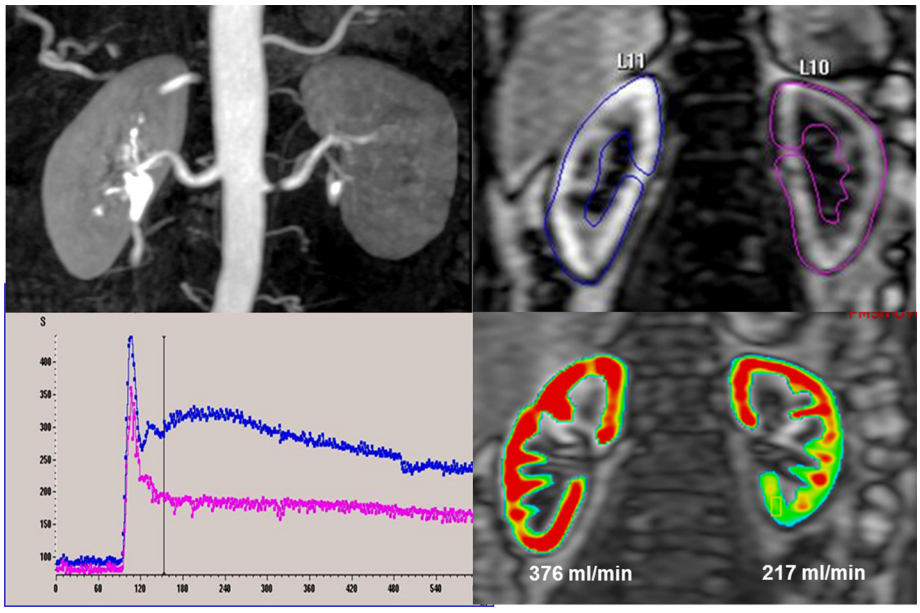

Figure 11. Quantification of renal perfusion in a patient with left renal artery stenosis. Signal intensity—time curves show the asymmetry. By applying a two-compartment model and taking into account the AIF, perfusion maps can be obtained, which demonstrate the asymmetry of vascularisation.

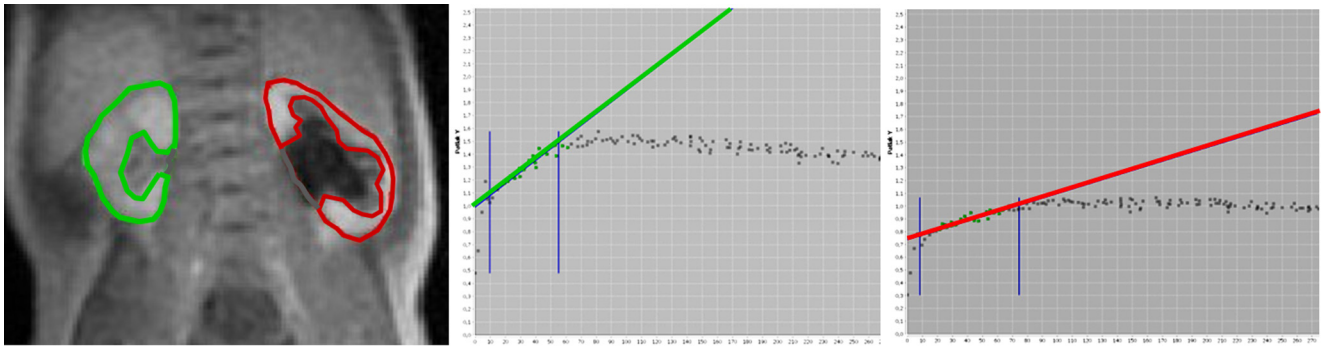

Figure 12. Patlak plots obtained in a child with left urinary obstruction. The anatomic image shows dilatation of the left pyelocaliceal system. The left plot (red) shows a lower slope corresponding to a lower filtration rate than the right (green). (Courtesy of M. Claudon, Nancy, France).

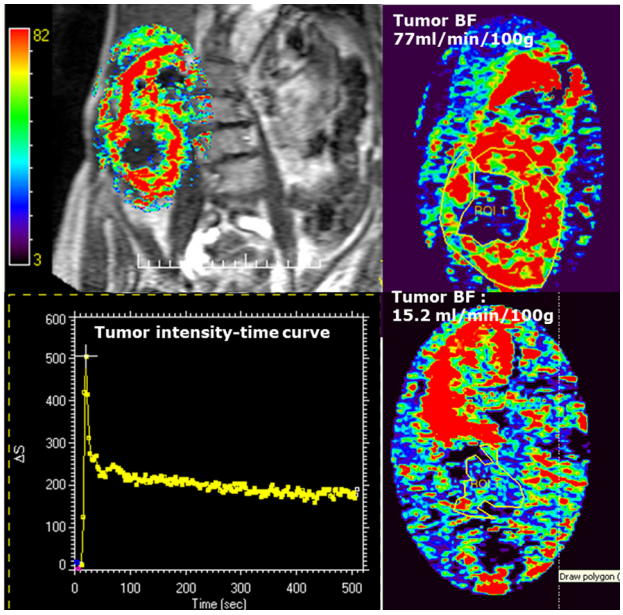

Figure 13. Perfusion maps in a patient with a metastatic renal tumor of the right lower pole, imaged before and after three cycles of antiangiogenic therapy. Functional maps show a decrease of perfusion values induced by treatment.

Conclusion

Evaluation of perfusion in kidney diseases is increasing in clinical routine. MR imaging provides more flexibility for measurement of blood flow, perfusion and split renal function without being nephrotoxic. CEUS and dynamic CT are probably more appropriate for evaluating response to antiangiogenic treatments. However, adapted post-processing software have still to be implemented on our MR systems to increase the diffusion of these techniques.

TAKE-HOME MESSAGES

General assessments

- Renal perfusion can be assessed semi-quantitatively and quantitatively.
- Quantitative measurements make inter-patient comparative studies more accurate.
- DCE-US allows semi-quantitative measurements only.
- DCE-CT and DCE-MRI allow both, semi-quantitative and quantitative measurements.
- DCE-CT and DCE-MRI allow measurement of both, perfusion and differential renal function.

Technical points

- Measurement of semi-quantitative parameters requires only SI changes within the kidney.
- Measurement of quantitative parameters requires also SI changes within abdominal aorta (AIF).
- DCE-US requires having access to raw data or linearized post-processed data.
- Movement correction by post-processing is required due to renal respiratory movements.
- In DCE-MRI, only a small dose of Gd (0.05 mL/kg) is required to avoid T2* effects within kidney.
- Rutland—Patlak plot is preferred for measurement of differential renal function.

Main results

- Measurement of renal blood flow improves the interobserver variability for diagnosis of significant RAS.
- A renal perfusion value < 150 Ml/min has a sensitivity of 100% for diagnosis of significant RAS.
- Functional studies provide unequivocal data on renal perfusion after revascularization.
- Measurement of differential renal function with scintigraphy and DCE-MRI provides equivalent results in renal obstruction.
- Response to antiangiogenic therapy can be evaluated early by perfusion studies in metastatic renal cell carcinoma.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

References

[1] Correas JM, Bridal L, Lesavre A, Mejean A, Claudon M, Helenon O. Ultrasound contrast agents: properties, principles of action, tolerance, and artifacts. Eur Radiol 2001;11:1316—28.
[2] Lucidarme O, Correas JM, Bridal SL, Berger G. Quantification of ultrasound contrast agent response: comparison of continuous wave Doppler and power Doppler to backscattered radiofrequency data. Ultrasound Med Biol 2001;27:1379—86.
[3] Lucidarme O, Franchi-Abella S, Correas JM, Bridal SL, Kurtisovski E, Berger G. Blood flow quantification with contrast-enhanced US: ''entrance in the section'' phenomenon—phantom and rabbit study. Radiology 2003;228:473—9.
[4] Dietrich CF, Averkiou MA, Correas JM, Lassau N, Leen E, Piscaglia F. An EFSUMB introduction into dynamic contrast-enhanced ultrasound (DCE-US) for quantification of tumour perfusion. Ultraschall in der Medizin 2012;33:344—51.
[5] Daghini E, Juillard L, Haas JA, Krier JD, Romero JC, Lerman LO. Comparison of mathematic models for assessment of glomerular filtration rate with electron-beam CT in pigs. Radiology 2007;242:417—24.
[6] Lemoine S, Papillard M, Belloi A, Rognant N, Fouque D, Laville M, et al. Renal perfusion: noninvasive measurement with multidetector CT versus fluorescent microspheres in a pig model. Radiology 2011;260:414—20.
[7] Attenberger UI, Morelli JN, Schoenberg SO, Michaely HJ. Assessment of the kidneys: magnetic resonance angiography, perfusion and diffusion. J Cardiovasc Magn Reson 2011;13:70.

[8] Bokacheva L, Rusinek H, Zhang JL, Lee VS. Assessment of renal function with dynamic contrast-enhanced MR imaging. Magn Reson Imaging Clin N Am 2008;16(viii):597—611.
[9] Schoenberg SO, Bock M, Kallinowski F, Just A. Correlation of hemodynamic impact and morphologic degree of renal artery stenosis in a canine model. J Am Soc Nephrol 2000;11:2190—8.
[10] Schoenberg SO, Knopp MV, Bock M, Prince MR, Allenberg JR. Combined morphologic and functional assessment of renal artery stenosis using gadolinium enhanced magnetic resonance imaging [editorial]. Nephrol Dial Transplant 1998;13:2738—42.
[11] Schoenberg SO, Knopp MV, Londy F, Krishnan S, Zuna I, Lang N, et al. Morphologic and functional magnetic resonance imaging of renal artery stenosis: a multireader tricenter study. J Am Soc Nephrol 2002;13:158—69.
[12] Michaely HJ, Kramer H, Oesingmann N, Lodemann KP, Miserock K, Reiser MF, et al. Intraindividual comparison of MR-renal perfusion imaging at 1.5 T and 3.0 T. Invest Radiol 2007;42:406—11.
[13] Michaely HJ, Kramer H, Oesingmann N, Lodemann KP, Reiser MF, Schoenberg SO. Semiquantitative assessment of first-pass renal perfusion at 1.5 T: comparison of 2D saturation recovery sequences with and without parallel imaging. AJR 2007;188:919—26.
[14] Michaely HJ, Schoenberg SO, Oesingmann N, Ittrich C, Buhlig C, Friedrich D, et al. Renal artery stenosis: functional assessment with dynamic MR perfusion measurements—feasibility study. Radiology 2006;238:586—96.
[15] Rusinek H, Lee VS, Johnson G. Optimal dose of Gd-DTPA in dynamic MR studies. Magn Reson Med 2001;46:312—6.
[16] Attenberger UI, Sourbron SP, Schoenberg SO, Morelli J, Leiner T, Schoeppler GM, et al. Comprehensive MR evaluation of renal disease: added clinical value of quantified renal perfusion values over single MR angiography. J Magn Reson Imaging 2010;31:125—33.
[17] Dujardin M, Sourbron S, Luypaert R, Verbeelen D, Stadnik T. Quantification of renal perfusion and function on a voxel-by-voxel basis: a feasibility study. Magn Reson Med 2005;54:841—9.
[18] Dujardin M, Luypaert R, Vandenbroucke F, Van der Niepen P, Sourbron S, Verbeelen D, et al. Combined T1-based perfusion MRI and MR angiography in kidney: first experience in normals and pathology. Eur J Radiol 2009;69:542—9.
[19] de Senneville BD, Mendichovszky IA, Roujol S, Gordon I, Moonen C, Grenier N. Improvement of MRI-functional measurement with automatic movement correction in native and transplanted kidneys. J Magn Reson Imaging 2008;28:970—8.
[20] Rohrschneider WK, Hoffend J, Becker K, Clorius JH, Darge K, Kooijman H, et al. Combined static-dynamic MR urography for the simultaneous evaluation of morphology and function in urinary tract obstruction I. Evaluation of the normal status in an animal model. Pediatr Radiol 2000;30:511—22.
[21] Patlak CS, Blasberg RG, Fenstermacher JD. Graphical evaluation of blood-to-brain transfer constants from multiple-time uptake data. J Cereb Blood Flow Metab 1983;3:1—7.
[22] Prigent A. Monitoring renal function and limitations of renal function tests. Semin Nucl Med 2008;38:32—46.
[23] Schoenberg SO, Knopp MV, Bock M, Kallinowski F, Just A, Essig M, et al. Renal artery stenosis: grading of hemodynamic changes with cine phase-contrast MR blood flow measurements. Radiology 1997;203:45—53.
[24] Schoenberg SO, Rieger JR, Michaely HJ, Rupprecht H, Samtleben W, Reiser MF. Functional magnetic resonance imaging in renal artery stenosis. Abdom Imaging 2006;31:200—12.
[25] Claudon M, Durand E, Grenier N et al. Evaluation of dynamic contrast-enhanced magnetic resonance urography for the split renal function measurement in chronic urinary obstruction. Radiology [in press].
[26] Lassau N, Chapotot L, Benatsou B, Vilgrain V, Kind M, Lacroix J, et al. Standardization of dynamic contrast-enhanced ultrasound for the evaluation of antiangiogenic therapies: the French multicenter Support for Innovative and Expensive Techniques Study. Invest Radiol 2012;47:711—6.
[27] Lassau N, Koscielny S, Chami L, Chebil M, Benatsou B, Roche A, et al. Advanced hepatocellular carcinoma: early evaluation of response to bevacizumab therapy at dynamic contrast-enhanced US with quantification—preliminary results. Radiology 2011;258:291—300.
[28] Lassau N, Koscielny S, Albiges L, Chami L, Benatsou B, Chebil M, et al. Metastatic renal cell carcinoma treated with sunitinib: early evaluation of treatment response using dynamic contrast-enhanced ultrasonography. Clin Cancer Res 2010;16:1216—25.
[29] Fournier LS, Oudard S, Thiam R, Trinquart L, Banu E, Medioni J, et al. Metastatic renal carcinoma: evaluation of antiangiogenic therapy with dynamic contrast-enhanced CT. Radiology 2010;256:511—8.