Original Paper

nephron
Physiology

Nephron Physiol 2004;96:p99–p104
DOI: 10.1159/000077380

Received: June 23, 2003
Accepted: February 9, 2004

# A New Method of Color Doppler Perfusion Measurement via Dynamic Sonographic Signal Quantification in Renal Parenchyma

Thomas Scholbach[a] Ingo Dimos[a] Jakob Scholbach[b]

[a]Kinderklinik am Städtischen Klinikum 'St. Georg', und [b]Sektion Mathematik, Universität Leipzig, Leipzig, Deutschland

**Key Words**
Tissue perfusion · Color Doppler sonography · Healthy children

**Abstract**
***Objective:*** Perfusion quantification of tissues is an important goal to evaluate the state of blood supply of an organ. We developed a method to quantify tissue perfusion via color Doppler signal quantification from sonographic videos and applied this to describe renal parenchymal perfusion in healthy kidneys. ***Method:*** Color Doppler sonographic videos of renal perfusion from both kidneys of 87 healthy children (age 2 weeks to 16 years) were recorded under defined conditions. Perfusion data (color hue, color area) were measured in a standardized region of interest automatically. Signal intensity was calculated as whole ROIs (regions of interest) mean flow velocity (cm/s) encoded by color Doppler signals during one full heart cycle. ***Results:*** Normal signal intensity values are: 1.86 cm/s in the region encompassing central 50% of the renal cortex and 0.56 cm/s in the peripheral 50% of the renal cortex. These differences are significant. Signal intensity of both kidneys did not differ. ***Conclusion:*** Signal intensity of cortical tissue in healthy kidneys was quantified noninvasively from color Doppler signal data in an easily accomplishable manner with new measurement software. Normal values for this technique have been calculated. Possible further applications might be all situations, where perfusion changes could be expected like inflammation, renal insufficiency, vascular diseases and tumors.



## Introduction

Quantification of organ perfusion is an important issue for many decisions in clinical medicine. Perfusion changes due to various pathophysiologic influences as well as due to physiologic stimuli, inflammation, functional adaptation, tumor growth are known to be accompanied by increased perfusion. Organ insufficiency, tissue damage, scarring may be examples for decreased perfusion. To characterize such pathophysiologic phenomena it would be very helpful to have a bedside method to quantify tissue perfusion.

We present a new method of perfusion quantification from image data of color Doppler sonographic videos. This is applied to signal quantification in renal parenchyma.

KARGER

Fax + 41 61 306 12 34
E-Mail karger@karger.ch
www.karger.com


1660–2137/04/0964–0099$21.00/0

Accessible online at:
www.karger.com/nep

PD Dr. med. habil. Thomas Scholbach
Kinderklinik am Städtischen Klinikum 'St. Georg'
Delitzscher Strasse 141
DE–04229 Leipzig (Germany)
Tel./Fax +49 341 9093615, E-Mail thomas.scholbach@sanktgeorg.de

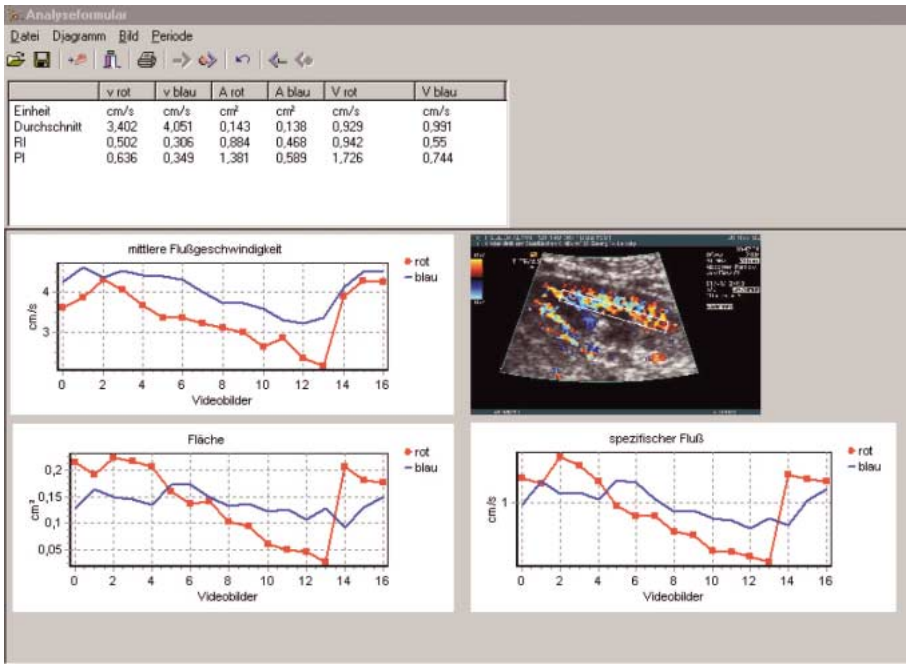


**Fig. 1.** Illustration of signal quantification in a kidney – in the lower part of the picture 3 diagrams and a color Doppler image are displayed. The color image is the first of a video sequence. Here a parallelogram is placed between the outer border of medullary pyramids and the renal surface encompassing proximal 50% of this region. Lateral borders were set to define the area fed by one interlobar artery. The three diagrams show changes of relevant perfusion parameters during one heart cycle: red lines refer to red color Doppler pixels – blue lines to blue pixels. The left upper diagram displays change of perfused area, left lower diagram changes of mean flow velocity and the right lower diagram demonstrates changes of specific flow, which is calculated from area and mean flow velocity.

## Aim

In healthy children renal parenchymal perfusion was to be quantified by means of a new technique of dynamic color Doppler signal quantification.

## Patients

87 healthy children and adolescents (2 weeks to 16 years old, mean 6.6 years, mean body height: 101 cm (50–167 cm), mean body weight 19 kg (3–49 kg)) without history of renal disease, without acute nephritis (based on clinical and laboratory data: no lumbar pain, no fever, no complaints during voiding, no pathologic urine specimen, no elevated creatinine, no elevated C-reactive protein) and with normal renal ultrasound (no scars, renal volume within normal range for weight and height, no hydronephrosis) were included. Patients had been sent for abdominal ultrasound examination to clarify abdominal discomfort and pain.

## Method

*Color Doppler Sonography*

Color Doppler sonographic investigations of the kidneys were performed with a 4–8 MHz curved array probe and a Sequoia ultrasound equipment (Acuson, Mountainview, Calif., USA). Transducer aperture was 44 mm with zenith height of 4 mm. Longitudinal and transverse sections of the kidneys were recorded. Care was taken to investigate vessels that run straight towards the transducer. To achieve this, the mid-segment of renal parenchyma was enlarged to such a size that the central 20 mm of the transducer aperture mapped the region of interest (ROI). This way an angle correction of the Doppler signal could be avoided. Presetting of the ultrasound equipment has fundamental importance. Always the same color Doppler frequency (7 MHz) was chosen for investigation. Otherwise no comparison of measurements is possible. Color gain was fixed by the presetting and never changed. To avoid aliasing color flow velocity settings were changed if necessary. Maximum color flow velocity was 4.3–8.6 cm/s.

*Dynamic Color Doppler Tissue Perfusion Measurement*

With a recently developed software [1] a dynamic (with regard to changes of flow during the heart cycle) quantification of color Doppler signals was carried out. Digital color Doppler sonographic videos (DICOM format) form the basis of measurements. The software calculates color pixel area and flow velocity – encoded by each pixel and displayed as a color scaling bar on screen – inside a region of interest of a video sequence. This way a quantification of blood flow inside the investigated tissue is achieved. Videos with movement artifacts were excluded from perfusion quantification.

The results are:

- Area (A) of depicted vessels inside the ROI (average of one whole heart cycle) (these measurements are not presented here).
- Mean flow velocity (v) inside the ROI (average of one whole heart cycle) (results not given here).
- Indices of changes of these parameters during the heart cycle (not further outlined).
- A measure of flow quantity inside called *signal intensity* (F) of the ROI (calculated by multiplication of vessels area (A) and mean velocity (v) in the ROI ($A_{ROI}$)).

$$F = A \cdot v / A_{ROI} \text{ [cm/s]}$$

Figure 1 shows presentation of flow data with three diagrams displaying changing flow velocities during heart cycle (upper left) chang-

ing perfused area inside the ROI (lower left) and the calculated specific perfusion (lower right diagram) in an example of renal perfusion. The ROI is outlined as white parallelogram in the sonographic image (upper right).

Prior to measurement images are calibrated with respect to distance and color hue. A 1-cm distance according to image markers was assigned first. Maximum velocity values encoded by the end of the color bar were read in next. The color bar must be symmetric, i.e. both ends of the color bar must indicate the same color value. A linear progression of velocity values from zero to the given maximum value was correlated with red and blue color hues automatically. This way each hue was assigned a specific velocity value. Each pixel inside ROI was then compared with the hues from the color bar and its specific flow velocity value was read out.

The ROI was chosen in the renal parenchyma in the area between the outer border of medullary pyramids and the kidney surface (fig. 2) to comprise interlobular arteries into investigation and to omit arcuate arteries. The ROI was chosen in a way to contain vessels running in symmetric distribution pattern to the transducer. A parallelogram was placed to enclose a complete vascular segment fed by one interlobar artery. Digital videos (DICOM format) containing 25–50 images and at least one full heart cycle were recorded. The velocity range of color depiction was adjusted to minimize aliasing in the ROI.

Mean values of colored area and mean flow velocity are calculated automatically by reckoning average values of all pixels inside one single image's ROI and averaging these values for all images encompassing one full heart cycle which is detected automatically by the software. These averaged values of flow velocity and area from a whole heart cycle inside ROI are used for calculation of signal intensity (F). It defines the mean flow velocity of the whole ROI as if the ROI was homogeneously perfused with one velocity.

We carried out measurements at different levels inside the parallelogram which defined the ROI. The ROI was divided into two segments encompassing proximal (p50) and distal (d50) 50% of the cortex (see fig. 2: green area: p50; blue area: d50).

*Statistical Analysis*

Means of groups were compared by the Mann-Whitney U test. p values <5% were regarded statistically significant. To investigate correlation Pearson's correlation coefficient was calculated with the same significance assumptions.

## Results

73% of the videos were without movement and breathing artifacts and allowed perfusion quantification.

Normal range of perfusion at various levels inside renal parenchyma is given in table 1. Significant differences have been calculated between proximal and distal cortical signal intensity. Between both kidneys no significant differences of perfusion were found (results not shown). Moreover, no significant differences existed between measurements in longitudinal and transverse orientation of the kidneys during investigation (results not shown).

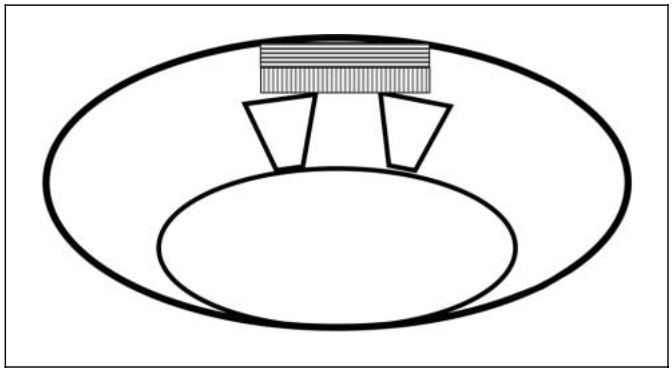

**Fig. 2.** Schematic placement of the ROI and measurement regions; p50 – green area: proximal 50% of the ROI. d50 – blue area: distal 50% of the ROI.

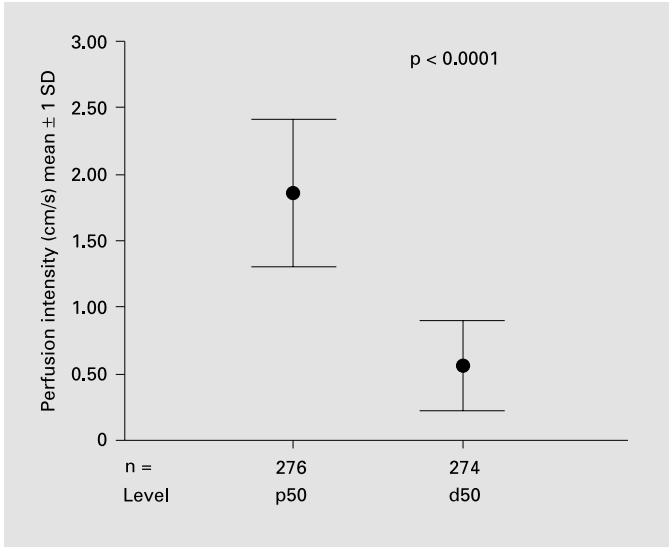


**Fig. 3.** Significant differences of tissue signal intensity exist at various levels inside renal cortical parenchyma (central cortex – p50; peripheral cortex – d50). Bars show mean values and standard deviation of the mean from 87 patients with 276 and 274 measurements (Mann Whitney U test: $p < 0.0001$).

**Table 1.** Tissue signal intensity at various levels inside renal cortical parenchyma

| Signal intensity, cm/s | | |
|---|---|---|
| Level | Median | Standard deviation |
| p50 | 1.857 | 0.557 |
| d50 | 0.511 | 0.333 |

## Discussion

Evaluation of perfusion is of interest in many situations. Normal perfusion is a prerequisite of normal function of an organ. On the other hand, perfusion will be changed to react to pathophysiologic stimuli. This may be to preserve normal function despite damage of functional tissue or this may be simply a consequence of loss of adaptation to pathophysiologic influences. The latter may be observed in infarction, mechanical tissue damage, venous congestion or decreasing blood pressure. Examples for functional adaptation could be spreading vessels in tumors, in compensatory organ growth due to loss of sister organ (nephrectomy), bacteria, radiation which may lead to an inflammatory increase of perfusion.

Therefore, a method measuring perfusion in a simple and reliable way is clinically important. In physiologic literature perfusion is defined as volume of blood passing through an organ in a certain time (ml/s). In physiological experimental settings ex vivo preparations are in use. These allow direct flow measurements (i.e. electromagnetic or volumetric) and moreover weighing the organ's mass. This approach to perfusion is blocked in most clinical circumstances when neither a direct measurement of blood volume nor the mass or exact volume of an organ can be defined.

Nevertheless, it is obvious that in a certain vasculature perfusion is determined by the cross-sectional area (A) of the vasculature and velocity (v) of flow. Both parameters are directly proportional to intensity of perfusion. Perfusion is displayed as color in color Doppler sonography. Important parameters are color hue to encode a pixel's frequency shift (displayed as flow velocity after automatic calculation according to the Doppler equation), color spectra (red or blue) to encode flow direction and area of color pixel to define extension of perfused area.

Increase in perfused area as well as increase of flow velocity result in increase of blood volume or perfusion of a given structure. Although we cannot (yet) measure simultaneously volumes and flow of a volume of interest, we can depict flow in planar projections familiar to us as ultrasound images. This offers the possibility to measure flow not in a volume (as physiologists do) but we can measure color pixel area and their velocity values in an imaging plane. Therefore, we must in clinical practice deviate from the traditional experimental approach. To obtain an impression of perfusion sonographers estimate the colored area and the color hue approximately. Description of perfusion is done roughly as low, medium or strong. This estimation has to take into account the presetting of the ultrasound machine because the same color hue may represent quite different flow velocities when the color calibration at the beginning of the ultrasound investigation differs from the investigation before. Therefore, it needs long experience with ultrasound to estimate perfusion quality in tissues only roughly. Hence such an estimation is of limited clinical use. Reports of different sonographers are in most cases not comparable. Nevertheless, imaging conditions are comparable in most situations. Therefore, if an investigator is scanning kidneys he or she will strive to optimize ultrasound presetting in a certain manner: the organ will be found in a similar depth in many patients, the vasculature is similar in kidneys from different patients and so it is possible in most patients to use the same transducer, Doppler frequency, wall filter and gain. What we wanted to achieve was to quantify color information from the images displayed on screen and so to give more reliable information about important flow parameters. If a software could measure color hue (resp. flow velocity) of a pixel and pixel area, could calculate in a region of interest mean flow velocity of the whole ROI and could repeat these measurements for a whole heart cycle under predefined and fixed imaging presetting, a more reliable and refined estimation of perfusion should become possible.

All these tasks are accomplished by the software used for these measurements [1]. Until now only a few reports exist on quantitative color Doppler sonographic evaluations of renal perfusion. Most of them deal with velocity data solely and with parameters like RI derived from these raw data [2, 3]. Other methods used to evaluate (microvascular) perfusion are plethysmography, skin temperature and skin color measurements (thermometry and colormetry), laser Doppler investigations and capillaroscopy [4]. Most of these procedures have limitations rendering them restricted to surfaces like skin, visible mucosal layers or sites of operation or are restricted to extremities like plethysmography.

Another approach to sonographic perfusion estimation is application of sonographic contrast enhancers. After intravenous injection of such agents changes of contrast in organs can be observed. This contrast amplification depends on the amount of inflowing contrast enhancer carried by bloodstream and is therefore a measure of perfusion intensity. So-called wash-in-wash-out curves are in use to estimate perfusion in B-mode sonograms. Another possibility is to observe changes in coloration after contrast enhancer injection. Quantification of flow with such agents remains demanding. Local changes of contrast and coloration depend on many variables as (a) local concen-

tration of the agent, (b) its ability to circulate trough capillaries, (c) it's physical and chemical stability and (d) acoustic properties of investigated tissue. Many imponderabilities may fog a clear evaluation of perfusion: variables to (a) distribution in circulation, depending on blood volume and distribution in central and peripheral regions, heart rate and stroke volume; (b) particle size of agent, size of capillaries in the region of interest; (c) destruction of the enhancer by ultrasound, spontaneous disintegration, and (d) generation of harmonic backscatter from tissues interfering with harmonic echoes from contrast enhancers. Other obstacles are high costs of the agents, need of invasiveness and limited investigation time (spontaneous disintegration of enhancer). New developments like superharmonic imaging have been presented recently to overcome difficulties of contrast-to-tissue ratio [5]. In an animal study [6] an excellent correlation was found between cortical blood flow using contrast enhancer and invasively measured renal blood flow. These promising reports underline an ongoing interest to measure renal perfusion and the need of simple noninvasive and non-ionizing procedure to evaluate (renal) perfusion with the means of ultrasound. Venz et al. [7] describe a computer assisted evaluation of percentage of vessel-covered renal parenchyma (POV) analyzing power Doppler still images. They concluded that the evaluation of renal vessels by power Doppler images improves diagnostic accuracy for patients with renal allografts. Others demonstrated that semiautomated measurements resulted in improved signal-to-noise ratios in quantitative analysis of myocardial perfusion [8].

An important aspect of our new technique compared to precursors was to use videos encompassing at least one full heart action (we actually used clips of 3 s duration). Actual perfusion changes rapidly and in relevant degree throughout heart action. The extent of change depends on tissue and disease characteristics. An increase of blood flow of more than 100% from diastole to systole is not rare. So a reliable perfusion evaluation is not possible from single sonograms taken at undefined points during the heart cycle. Moreover, perfusion evaluation from single images is hampered because the changes of perfusion are not summed up. If always maximal systolic perfusion was recorded even in situations with the same perfusion at systolic peak, the overall perfusion could vary in substantial degrees at diastole and in-between. So we developed a technique to collect and average perfusion data from every single frame of a video encompassing time enough to record at least one full heart cycle.

73% of the videos recorded were artifact free and usable for perfusion quantification. With respect to the wide age span of our probands and inclusion of children below 1 year of age we regard this rate satisfactory. Movements produce color veils and frustrate reliable measurements. We investigated children and therefore might have found a rather high percentage of movement artifacts in our recordings. Nevertheless, signal quantification in a certain patient should always be possible after pacification. Our series included longitudinal and transverse sectional recordings. Here no significant differences were found (data not shown). This offers the opportunity to spend more time on the preparation of a single recording to place more emphasis on movement-free video recordings.

We demonstrated a decline of specific perfusion from central to peripheral regions of renal parenchyma. This can be interpreted as an effect of vascular branching. At the level of the outer edge of renal medullary pyramids interlobar arteries enter the renal cortex and give rise to arcuate arteries. From these multiple interlobular arteries ascend, directed to the renal surface [9]. Many tiny arterial branches are directed from the trunk of these arteries and disperse the blood. At more peripheral levels of renal cortical parenchyma less blood is therefore passing through due to continuously tapering vessels. The reduction of blood flow from central to peripheral levels reflects therefore anatomical and functional aspects of vascularization inside cortical parenchyma. Investigations presented here allow a quantification of perfusion that may be interpreted as a functional description of an organ's vasculature.

Color Doppler sonographic measurements of signal intensity in the renal cortex in children do not yet exist. Until now perfusion measurements in the main feeding arteries are possible [10]. Such measurements can be used to evaluate renal function [11]. In some situations a global perfusion measurement is not sensitive enough to define impact of disease onto the kidney. Such cases could be partial destruction of the organ, double collecting systems and vesico-ureteral reflux into one part of the kidney, patients with local inflammation (focal bacterial nephritis), patients after kidney operation, local parenchymal damage and tumors. Ultrasonic delineation of the feeding arteries may be difficult due to anatomical peculiarities such as obesity, vascular variants, meandering vessels and others. Here, a tissue perfusion quantification would be very helpful.

Our measurements could form a starting point for comparisons of renal perfusion in a broad spectrum of diseases. Eventually not only perfusion but also its spatial distribution inside an organ may be used to diagnose and describe numerically diseases and functional changes in kidney diseases. This perspective needs to be confirmed by further studies. Hopefully, one day manufacturers will allow use of raw data stored inside their sonographic systems. This would pave the way for further refinements.


## Acknowledgement

We gratefully acknowledge Siemens AG, Nürnberg, Germany for contributing to the costs of printing this article.


## References


1 www.chameleon-software.de
2 Kondo A, Akakura K, Ito H: Assessment of renal function with color Doppler ultrasound in autosomal dominant polycystic kidney disease. Int J Urol 2001;8:95–98.
3 Frauscher F, Radmayr C, Klauser A, Helweg G, Amort B, zur Nedden D, Bartsch G: Wertigkeit des renalen Resistenz-Index bei Kindern mit vesikoureteralem Reflux. Ultraschall-Med 1999;20:93–97.
4 Carpentier PH: Methodes actuelles d'exploration clinique de la microcirculation. J Mal Vasc 2001;26:142–147.
5 Bouakaz A, Krenning BJ, Vletter WB, ten Cate FJ, De Jong N: Contrast superharmonic imaging: A feasibility study. Ultrasound Med Biol 2003;29:547–553.
6 Wei K, Le E, Bin JP, Coggins M, Thorpe J, Kaul S: Quantification of renal blood flow with contrast-enhanced ultrasound. J Am Coll Cardiol 2001;37:1135–1140.
7 Venz S, Kahl A, Hierholzer J, et al: Contribution of color and power Doppler sonography to the differential diagnosis of acute and chronic rejection, and tacrolimus nephrotoxicity in renal allografts. Transplant Int 1999;12:127–134.
8 Caiani EG, Lang RM, Caslini S, Collins KA, Korcarz CE, Mor-Avi V: Quantification of regional myocardial perfusion using semiautomated translation-free analysis of contrast-enhanced power modulation images. J Am Soc Echocardiogr 2003;16:116–123.
9 Platzer W (ed): Pernkopf Anatomie. Munich, Urban & Schwarzenberg, 1994.
10 Scholbach T: Color Doppler sonographic determination of renal blood flow in healthy children. J Ultrasound Med 1999;18:559–564.
11 Scholbach T: Changes of renal flow volume in the hemolytic-uremic syndrome: Color Doppler sonographic investigations. Pediatr Nephrol 2001;16:644–647.