Glomerular filtration rate with MDCT

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Outline

• Functional parameter definition
• Tools :
  – EBCT
  – Spiral CT
  – MDCT
• Modeling methods
  – Gamma variate
  – Patlak
• Experimental data
The challenge of renal functional evaluation
Renal Functional Imaging

- CT SCAN/EBCT MDCT
- MRI
- PET

- Non invasive evaluation
- Split renal function
- Absolute quantification
Renal Functional parameters

Tissue Injury

- Blood Flow Perfusion
- Oxygen content
- Oxydative metabolism
- GFR

REDUCTION

Glomerular Filtration Rate

CT, MR → MR BOLD → PET → CT, MR

CT, PET
• Gamma variate:
  » Glomerular filtration rate
  » Renal blood flow
  » Renal perfusion
Electron Beam Computed-Tomography

- EBCT cardiac and renal functional imaging
  - Cortical and medulla volume
  - Regional blood flow, tissue perfusion
  - Glomerular filtration rate

- Split renal function

- Few evaluation in humans
  - Breath control
EBCT: Principles

- High temporal resolution
- Good spatial resolution
- Multi slices
Noninvasive measurement of concurrent single-kidney perfusion, glomerular filtration, and tubular function

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Received 16 February 2001; accepted in final form 18 May 2001
INJECTION VVC: 0.5 mL/kg, 15 mL/s

EBCT: gamma variate

Krier et al AJP, 2001
INJECTION VVC: 0.5 mL/kg, 15 mL/s
Krier et al. AJP, 2001
# Distinct Renal Injury in Early Atherosclerosis and Renovascular Disease

Alejandro R. Chade, MD; Martin Rodriguez-Porcel, MD; Joseph P. Grande, MD, PhD; James D. Krier, MS; Amir Lerman, MD; J. Carlos Romero, MD; Claudio Napoli, MD, PhD; Lilach O. Lerman, MD, PhD

## Table 2. Basal Single-Kidney Hemodynamics and Function in Normal, HC, RAS, and HC+RAS Pigs

<table>
<thead>
<tr>
<th></th>
<th>Normal (n=7)</th>
<th>HC (n=7)</th>
<th>RAS (n=6)</th>
<th>HC+RAS (n=7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume, mL</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cortex</td>
<td>100.4±6.2</td>
<td>95.1±5.7</td>
<td>55.2±15.3†</td>
<td>75.2±4.1†</td>
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<tr>
<td>Medulla</td>
<td>45.4±2.3</td>
<td>41.8±6.9</td>
<td>24.7±6.6†</td>
<td>30.3±3.3†</td>
</tr>
<tr>
<td>Renal blood flow, mL/min</td>
<td>534.0±49.1</td>
<td>499.5±44.5</td>
<td>266.9±99.9*</td>
<td>364.7±54.5*</td>
</tr>
<tr>
<td>Glomerular filtration rate, mL/min</td>
<td>70.8±4.3</td>
<td>60.3±3.1</td>
<td>31.8±11.1*</td>
<td>50.4±3.5*</td>
</tr>
<tr>
<td>Perfusion, mL·min⁻¹·g⁻¹</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cortex</td>
<td>4.11±0.33</td>
<td>4.36±0.43</td>
<td>3.27±0.62†</td>
<td>3.31±0.33†</td>
</tr>
<tr>
<td>Medulla</td>
<td>2.63±0.33</td>
<td>3.13±0.66</td>
<td>2.91±0.17</td>
<td>2.34±0.34‡‡</td>
</tr>
<tr>
<td>Papilla</td>
<td>2.38±0.33</td>
<td>2.59±0.55</td>
<td>1.99±0.43</td>
<td>2.42±0.76</td>
</tr>
</tbody>
</table>

Values are mean±SEM.

*P<0.05 vs normal; †P<0.05 vs HC, ‡P<0.05 vs RAS.

Chade et al Circulation, 2001
Figure 1. a, Basal intratubular concentration in normal (n=7), HC (n=7), RAS (n=6), and HC+RAS (n=7) pigs. *P<0.05 vs normal and HC, †P<0.05 vs RAS. b and d, Change in RBF in response to ACh (b) and SNP (d). *P<0.05 vs baseline. c, Change in GFR in response to ACh. *P<0.05 vs baseline, †P<0.05 vs normal.
PATIENTS

Hypertension

Unilateral RAS with FMD

MR or Conventional angiography

« Hemodynamically significant » US
Results: Regional Volumes

- Stenosis
- Kidney
- Contralateral

Regional volume (cm³)

Cortex

Medulla

*
Results: Blood Flow

- Stenosis
- Kidney
- Contralateral

Regional Blood Flow (mL/min)

- Cortex
- Medulla

* Denotes statistical significance
Results: Perfusion

Regional perfusion (mL/min/g)

- Stenosis
- Kidney
- Contralateral

Cortex
Medulla
Results: GFR

- Stenosis
- Kidney
- Contralateral
Non-invasive evaluation of bilateral renal regional blood flow and tubular dynamics during acute unilateral ureteral obstruction

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Pelaez et al NDT, 2005

Fig. 1. Comparison of renal cortical time density curves at baseline and 90 min after AUUO. The first peak represents the vascular cortical curve while the second and third peaks are the proximal and distal cortical tubular curves. The profile of the curve obtained
Fig. 2. Changes in RBF, GFR, C-RBF and M-RBF in the obstructed (○) and contralateral kidney (●) at baseline and 30 and 90 min after the onset of acute unilateral ureteral obstruction in pigs. *P<0.06 vs baseline.
MDCT : Principles

Vs EBCT
Identical parameters
Assessment of Renal Hemodynamics and Function in Pigs with 64-Section Multidetector CT: Comparison with Electron-Beam CT

Daghini et al, Radiology, 2007
Figure 1: Representative renal CT images and corresponding TACs obtained from one pig by using electron-beam CT and 64-section multidetector CT. (a, b) Transverse CT images of hilar region of both kidneys, obtained with (a) multidetector CT and (b) electron-beam CT 1 week apart show manually traced region of interest in the renal cortex (white arrow) and medulla (black arrow). (c–f) Representative cortical and medullary TACs obtained with (c, e) multidetector CT and (d, f) electron-beam CT.
<table>
<thead>
<tr>
<th>Measurement</th>
<th>Electron-Beam CT</th>
<th>Multidetector CT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cortical Perfusion ([mL ⋅ min⁻¹]/cm²)</td>
<td></td>
<td></td>
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<tr>
<td>Baseline</td>
<td></td>
<td></td>
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<tr>
<td>All kidneys (n = 16)</td>
<td>3.9 ± 0.2</td>
<td>3.6 ± 0.2</td>
</tr>
<tr>
<td>Stenotic kidney (n = 2)</td>
<td>2.9 ± 0.6</td>
<td>3.2 ± 0.4</td>
</tr>
<tr>
<td>Contralateral (n = 2)</td>
<td>4.0 ± 0.7*</td>
<td>3.8 ± 0.8*</td>
</tr>
<tr>
<td>Acetylcholine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All kidneys (n = 16)</td>
<td>5.1 ± 0.3†</td>
<td>4.8 ± 0.3†</td>
</tr>
<tr>
<td>Stenotic kidney (n = 2)</td>
<td>3.7 ± 0.3</td>
<td>3.6 ± 0.07</td>
</tr>
<tr>
<td>Contralateral (n = 2)</td>
<td>4.5 ± 0.4</td>
<td>4.2 ± 0.5</td>
</tr>
<tr>
<td>Medullary perfusion ([mL ⋅ min⁻¹]/cm²)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>3.7 ± 0.5</td>
<td>2.9 ± 0.4</td>
</tr>
<tr>
<td>Acetylcholine</td>
<td>5.0 ± 0.4†</td>
<td>4.5 ± 0.4†</td>
</tr>
<tr>
<td>RBF ([mL ⋅ min⁻¹])</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>484.9 ± 50.5</td>
<td>469.1 ± 47.8</td>
</tr>
<tr>
<td>Acetylcholine</td>
<td>636.1 ± 64.1†</td>
<td>644.4 ± 64.1†</td>
</tr>
<tr>
<td>GFR ([mL ⋅ min⁻¹]/cm²)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>79.8 ± 8.8</td>
<td>77.6 ± 8.3</td>
</tr>
<tr>
<td>Acetylcholine</td>
<td>99.1 ± 11.7†</td>
<td>104.6 ± 12.6†</td>
</tr>
<tr>
<td>Cortical volume (cm³)</td>
<td>103.2 ± 8.7</td>
<td>111.2 ± 8.8†</td>
</tr>
<tr>
<td>Medullary volume (cm³)</td>
<td>20.1 ± 1.6</td>
<td>22.1 ± 1.6†</td>
</tr>
</tbody>
</table>

Note.—Data are mean ± standard error of the mean.

* P ≤ .05 vs stenotic kidney.
† P ≤ .05 vs baseline.
‡ P ≤ .05 vs electron-beam CT.
Figure 2: (a, b) Correlation and (c, d) Bland-Altman plots describe the relationship between electron-beam CT and multidetector CT values of (a, c) GFR and (b, d) RBF, obtained under basal conditions (□) and during vasodilation (◆).

Daghini et al, Radiology, 2007
14 patients with ARAS
14 patients with EH
MRI BOLD for oxygen content
MDCT study

Gloviczki et al, Hypertension 2010
GFR ??

Gloiczki et al, Hypertension 2010
Spiral CT Scanner

- Patlak: Glomerular filtration rate
Use of Contrast-Enhanced Computed Tomography to Measure Clearance Per Unit Renal Volume: A Novel Measurement of Renal Function and Fractional Vascular Volume

Yoshito Tsushima, MD, Martin J. K. Blomley, MB, Shoichi Kusano, MD, and Keigo Endo, MD

Fig 1. For each kidney, ROIs were drawn over the entire kidney. The ROIs were drawn as large as possible to allow for regional variations. Care was taken to exclude vessels and fatty tissue from the ROIs. ROIs were also drawn within the abdominal aorta.

Fig 2. Patlak plot will be linear with gradient $\alpha/V$, and y axis intercepts fvv.

Tsushima et al, AJKD 99
Use of Contrast-Enhanced Computed Tomography to Measure Clearance Per Unit Renal Volume: A Novel Measurement of Renal Function and Fractional Vascular Volume

Yoshito Tsushima, MD, Martin J. K. Blomley, MB, Shoichi Kusano, MD, and Keigo Endo, MD

Fig 5. There was a significant positive correlation between global contrast clearance and blood clearance of creatinine ($y = 0.64x + 29.20; n = 24; r = 0.87; P < 0.0001$).
DETERMINATION OF GLOMERULAR FILTRATION RATE PER UNIT RENAL VOLUME USING COMPUTERIZED TOMOGRAPHY: CORRELATION WITH CONVENTIONAL MEASURES OF TOTAL AND DIVIDED RENAL FUNCTION

YOSHITO TSUSHIMA, MARTIN J. K. BLOMLEY, KAZUHIKO OKABE, KIYOTAKA TSUCHIYA, JUN AOKI AND KEIGO ENDO

From the Department of Imaging, Imperial College School of Medicine, Hammersmith Hospital, London, United Kingdom, and Departments of Radiology and Urology, Motojima General Hospital and Department of Diagnostic Radiology and Nuclear Medicine, Gunma University Hospital, Gunma, Japan

Fig. 1. Renal regions of interest excluding vessels and fatty tissue. Regions of interest in abdominal aorta

Tsushima et al, AJR 01
Fig. 2. A, correlation between relative GFR measured by functional CT and that estimated by radioisotope (RI) renography ($^{99m}$Tc-DTPA) in 24 cases ($y = 0.98x + 2.13$, $r = 0.97$, $p < 0.0001$). B, comparison of relative GFR measured by renography and functional CT. Mean difference is $-0.9$ percentage points with 95% CI $-8.7$ to $6.9$.
Fig. 1.—74-year-old man with bladder carcinoma obstructing both ureters; he was treated with percutaneous nephrostomy on right and left sides. CT scan obtained during parenchymal phase shows one region of interest delineating parenchyma of right kidney (outlined in white) and second region of interest inside aortic lumen (outlined in black).
Glomerular Filtration Rate Measured by Using Triphasic Helical CT with a Two-Point Patlak Plot Technique

Figure 1. Graph shows aortic attenuation curve of a 64-year-old patient. Four clusters of data points were measured with CT. The area under the curve was determined graphically.

Figure 2. Graph shows two-point Patlak plot of left and right kidney of a 36-year-old woman. Each point is calculated from the input function \( b(t) \) and net kidney attenuation \( K(t) \), both solely measured with triphasic CT. The lower pair of points represent data from the arterial scan, and the higher pair of points represent data from the parenchymal scan. CT clearance was determined from the slope of the line connecting the points and was then corrected for hematocrit levels. GFR as calculated with the two-point Patlak plot was 53 mL/min for the right kidney and 59 mL/min for the left kidney and yielded a total GFR of 112 mL/min. As a reference, GFR was measured in this patient with iopromide plasma clearance, which resulted in 99 mL/min.

Hackstein et al, Radiology 05
Glomerular Filtration Rate Measured by Using Triphasic Helical CT with a Two-Point Patlak Plot Technique

Figure 3. Graph shows correlation of total GFR measured with two-point Patlak plot \(GFR(CT)\) and plasma clearance in 48 patients. Correlation coefficient \(r\) was 0.899 and SD was 12.2 mL/min. The solid line represents linear correlation \(y = 14.8 + 0.83x\), and the dashed line represents line of identity.

Figure 4. Graph shows results of Bland-Altman test. The differences between plasma clearance and GFR as calculated with the two-point Patlak plot \(GFR(CT)\) are plotted against their means. The dashed line represents mean difference \((d = -1.2\) mL/min\), and the solid line represents limits of agreement \((d \pm 2 SD, -27.1\) to 24.6 mL/min\).
Patlak GFR

• Correlation between GFR Patlak and
  - Creatinine clearance
  - EDTA scintigraphy

• BUT
  - ROI cortex AND medulla
  - No comparison with reference method

Dawson, Invest Radiol, 1993
Miles, Br J Radiol, 1999
Tsushima, AJKD, 1999
Hackstein, Eur Radiol, 2001
Comparison of Mathematical Models for Assessment of Glomerular Filtration Rate with Electron-Beam CT in Pigs

Daghini et al, Radiology, 2007
Comparison of Mathematical Models for Assessment of Glomerular Filtration Rate with Electron-Beam CT in Pigs

Daghini et al, Radiology, 2007

**Figure 3**

- PATLAK $r=0.12$
- PATLAK modified $r=0.75$
- Gamma Variate $r=0.79$
Comparison of Mathematic Models for Assessment of Glomerular Filtration Rate with Electron-Beam CT in Pigs

PATLAK Gamma Variate -12+/-10

PATLAK modified -29+/- 12

Gamma Variate -12+/-10

Daghini et al, Radiology, 2007
Summary CT

Most powerful method
GFR, RBF, Perfusion, ICT, Volume

But

Remain invasive
Contrast media toxicity
Validation of Renal Perfusion and Glomerular Filtration Rate measurement with MDCT and low rate CM Injection.

Sandrine LEMOINE, Laurent JUILLARD
Aim

• Validation of the measurement of
  – Cortical perfusion
  – Glomerular filtration rate
    using MDCT

• With a low rate CM injection (3mL/s) and using a peripheral vein injection

• Using the gamma variate modeling

• Using fluorescent microspheres as a reference for RBF and Inulin clearance for GFR
Images dynamiques sur 144 secondes au niveau d’une coupe du porc n°6 après injection de dopamine. Une image toutes les secondes les 30 premières secondes puis une image toutes les 6 secondes.
Materiel et Methods

Régions d'intérêt tracée manuellement
Vascular = Perfusion

Proximal peak = GFR

Gamma variate
Materiel et Methods

- 10 pigs
- Protocole:

- Dopamine
  - 10 µg/kg/min
- Dopamine + SSI
  - 10 µg/kg/min
- Angiotensine II
  - (500ng/kg/min)
- MDCT: PERF 1 GFR 1
- MDCT: PERF 2 GFR 2
- MDCT: PERF 3 GFR 3

MS 1 = Perf 1
MS 2 = Perf 2
MS 3 = Perf 3

DFG 1
- Urine + blood
DFG 2
- Urine + blood
DFG 3
- Urine + blood

Sacrifice
Results Perfusion

Perfusion scanner
Perfusion microsphères

Dopamine
Dopamine +
Angiotensine II

Perfusion (mL/min/g)
Results Perfusion

![Graph showing the correlation between perfusion measurements with the scanner and with microspheres. The equation is y = 0.8421x + 0.2496, with R^2 = 0.8758 and R = 0.93. The p-value is less than 0.0001.](image)
Results Perfusion

- 0.2 +/- 0.3 mL/min
Results GFR gamma variate

\[ R^2 = 0.0006 \]

Corrélation entre les mesures de DFG mesurée avec la clairance de l’inuline et avec le scanner.
Corrélation entre les mesures de DFG mesurée avec la clairance de l'inuline et avec le scanner.

Results GFR Patlak

\[ y = 0.4844x + 13.186 \]

\[ R^2 = 0.4192 \]

GFR Inulin (mL/min) vs GFR Patlak (mL/min)
Conclusion

Most powerful functional imaging modality for quantitative assessment of renal performance

Limits: CM toxicity and high rate injection for gamma variate

Low rate injection: compartmental modeling to be tested for GFR