What parameters should be measured and why & QC
(researcher's view)

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Renal scintigraphy

- 99mTc-DTPA is used for 40 years
  *first laboratory SPECT images produced by Anger, Muehllechner and Wetzel*
- 99mTc-DMSA is used for 36 years
  *first clinically useful x-ray CT designed by Hounsfield and Cormack*
- 99mTc-MAG3 is used for 24 years
  *first PET clinical applications for the brain and heart described by Phelps, Mazziotta, Hoffman and Schelbert*
What's new?

- **detection devices** - *availability of double-head gamma cameras makes simultaneous detection of renal studies in opposite projections easy* - activity thus can be measured more accurately

- **computers** - *make complex and extensive calculations and simulations fast and feasible in clinical practice*

- **storage media** - *large database of anonymous, clinically validated data for development of analytical and data processing methods can be done*

- **models of renal scintigraphy** - *avoid regression techniques with unknown error of prediction and limited applicability*
Why renal data for quantitative analysis should be recorded in opposite projections (geometric mean)

• relative (split) renal function is independent of individual kidney depth
• attenuation depends on body thickness (rather than on kidney depth) that can be estimated more accurately
• transmission factors for attenuation correction can be measured using $^{57}$Co or $^{99m}$Tc flood source (it is accurate, simple, fast, and easy)
• due to feasible AC & SC, renal activity for assessment of renal clearance can be measured more accurately
• exception = small children (proximity of anterior detector)
Transmission measurement

\[ D = \ln\left(\frac{I_1 f}{I_2}\right) / -\mu \]
Accuracy of measurement in posterior view and geometric-mean image

Taylor's gamma-camera method in posterior projection with kidney-depth correction

mean abs. error of prediction (Taylor's > Russells' method)
30 (25 - 35) ml/min

Taylor's gamma-camera method in geometric mean with transmission factors

24 (20 - 28) ml/min
Why it is important to include the heart in the FOV

• vascular background in the kidney ROI is higher than extravascular background (especially during uptake) and its subtraction is thus more important
• Patlak-Rutland plot, renal output efficiency, deconvolution for calculation of renal retention function and the measurement of transit times - all require the heart ROI time-activity curve
• clearance methods based on the measurement of renal activity & NORA also need vascular background subtraction in order to produce accurate results
Accuracy of measurement without and with vascular background subtraction

Taylor's gamma-camera method without vascular background subtraction

mean abs. error of prediction (Taylor's > Russells' method)
34 (28 - 40) ml/min

Taylor's gamma-camera method with vascular background subtraction

mean abs. error of prediction (Taylor's > Russells' method)
24 (20 - 28) ml/min
$y = 0.748x + 0.051$

$r = 0.986$

by courtesy of Cyril C. Nimmon
Why Patlak - Rutland plot?

• it automatically corrects for vascular background that is important to subtract

\[
R(t) = k \int P(t) dt + hP(t) + qB(t)
\]

\[
\frac{R(t)}{P(t)} = k \int \frac{P(t) dt}{P(t)} + h
\]

\[
y = kx + h
\]
$R(t) = 1.16 \times \int P(t) dt + 0.478 \times P(t)$

$k = 1.16$

$k = \text{slope of Patlak-Rutland plot}$
Why renal transit time(s)?

• many studies demonstrate that TT is a sensitive indicator of abnormal renal function
• many studies that *do not* demonstrate TT usefulness suffer from technical flaws
• whole-kidney TT is a sensitive quantitative index of renal uptake, transit and outflow
• parenchymal TT is more difficult to measure but potentially much more useful
• TT is the only parameter completely avoiding the effect of vascular "input function" and, in consequence, the effect of contralateral kidney
$k = \text{plateau height of renal RF}$
UK audit and analysis of quantitative parameters obtained from gamma camera renography

A.S. HOUSTON,* D.R. WHALLEY, J.V. SKRYPNIUK, P.H. JARRITT, J.S. FLEMING and P.S. COSGRIFF

Institute of Physics and Engineering in Medicine (IPEM) Nuclear Medicine Software Working Party, York

Nuclear Medicine Communications, 2001, 22, 559–566

180 responses from 81 hospitals in the UK
10 renal studies (5 DTPA, 5 MAG3 in adult patients)
Distribution of the whole-kidney MTT in 10 patients
(x-axis = WK-MTT/10 [s], y-axis = number of hospitals)
Probable range for whole kidney mean transit time values determined by reexamination of UK audit studies
Cyril C. Nimmon\textsuperscript{a}, John S. Fleming\textsuperscript{b} and Martin \v{S}\'amal\textsuperscript{c}

Nuclear Medicine Communications 2008, 29:1006–1014
mean transit time = area under renal retention curve divided by the height of its plateau

If maximum value of the retention function is used instead of plateau, mean transit time is too short.
Why renal output efficiency?

• it provides similar information as renal transit times
• it is an obvious physiological measure of renal outflow
• many studies proved its clinical validity and usefulness in both adults and children
• it is easy to calculate also in post-voiding images
free outflow  
reduced outflow
\( k = 1.16 \)

\[
R(t) = 1.16 \times \int P(t) \, dt + 0
\]

\( k = \text{scale of zero-output curve} \)
**KKK** - providing the backgrounds are correctly subtracted

1. slope of Patlak-Rutland plot
2. height of the plateau of renal retention function, and
3. constant scaling the integral of the heart ROI curve so that it fits uptake part of the renogram

are all the same number, obtained in different ways from the same model, that can be used for QC purposes
Why not Patlak - Rutland plot?

• because there is potentially better, simpler, and more robust solution
• why not to apply multivariate regression on the complete equation?

\[ R(t) = k \int P(t)dt + hP(t) + qB(t) \]

observed renogram  heart ROI curve  background ROI curve
A multiple regression analysis for accurate background subtraction in $^{99}$Tcm-DTPA renography

G.W. MIDDLETON, W.H. THOMSON*, I.H. DAVIES and A. MORGAN

$$R(t) = k \int P(t) dt + hP(t) + qB(t)$$

- observed renogram
- heart ROI curve
- background ROI curve

pure renal curve in uptake period = zero output curve
A multiple regression analysis for accurate background subtraction in $^{99}$Tc$^m$-DTPA renography

G.W. MIDDLETON, W.H. THOMSON*, I.H. DAVIES and A. MORGAN

$$R_p(t) = R(t) - hP(t) - qB(t)$$

- **pure renal curve (all times)**
- **observed renogram**
- **heart ROI curve**
- **background ROI curve**
\[ k \int P(t)dt \]

\[ R_p(t) = R(t) - hP(t) - qB(t) \]
Middleton's equation

• does not account for the fact that both \( P(t) \) and \( B(t) \) are mixtures of vascular and extra-vascular background > implicit inaccuracy
• at worst it performs as well as traditional procedures
• usually, it performs much better because its result is independent of location and size of background ROI (it should not include kidneys, pelves, ureters, or bladder)
• it's performance can be improved by combination with Imbrie's factor analysis extracting real, observed (not hypothetical) curves from scintigraphic data
Fractional uptake rate (FUR)

= fraction of injected activity entering the kidney per unit time

Friday 14 May 2010, 15:20

Rutland M.
Glomerular filtration rate without blood sampling.
*Nucl Med Commun* 1983; 4:425-433

Rutland M., Que L., Hassan I.M.
"FUR" - one size suits all.
Reproducibility: ROIs drawn by 7 physicians

time-activity curves after background subtraction
(background ROIs not shown)
Differential renal function estimation by dynamic renal scintigraphy: influence of background definition and radiopharmaceutical

Meltem Caglar\textsuperscript{a}, Gonca Kara Gedik\textsuperscript{a} and Erdem Karabulut\textsuperscript{b}

\textbf{Nuclear Medicine Communications} 2008, 29:1002–1005

\textbf{FOR EXAMPLE:}

split function of hydronephrotic right kidney

= 51\% after subtraction of subrenal background

= 44\% after subtraction of lateral background
Table 2  Differences between DRF estimates with subrenal and perirenal BG subtraction

<table>
<thead>
<tr>
<th>Patients</th>
<th>n</th>
<th>Mean difference</th>
<th>Standard deviation</th>
<th>Median</th>
<th>Minimum</th>
<th>Maximum</th>
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<tbody>
<tr>
<td>No HN</td>
<td>9</td>
<td>5.33</td>
<td>4.24</td>
<td>6.00</td>
<td>−1.00</td>
<td>12.00</td>
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<tr>
<td>L HN</td>
<td>32</td>
<td>2.25</td>
<td>3.54</td>
<td>3.00</td>
<td>−7.00</td>
<td>8.00</td>
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<tr>
<td>R HN</td>
<td>26</td>
<td>7.96</td>
<td>5.24</td>
<td>7.00</td>
<td>−2.00</td>
<td>19.00</td>
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<tr>
<td>B HN</td>
<td>16</td>
<td>4.56</td>
<td>6.18</td>
<td>4.00</td>
<td>−2.00</td>
<td>25.00</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>83</strong></td>
<td><strong>4.81</strong></td>
<td><strong>5.25</strong></td>
<td><strong>4.00</strong></td>
<td><strong>−7.00</strong></td>
<td><strong>25.00</strong></td>
</tr>
</tbody>
</table>

B HN, bilateral hydronephrosis; DRF, differential renal function; L HN, left hydronephrosis; R HN, right hydronephrosis. Kruskal–Wallis test, $P<0.001$. 

Nuclear Medicine Communications 2008, 29:1002–1005
Totally automatic definition of renal regions of interest from $^{99m}$Tc-MAG3 renograms: validation in patients with normal kidneys and in patients with suspected renal obstruction

Ernest V. Garcia$^a$, Russell Folks$^a$, Samuel Pak$^b$ and Andrew Taylor$^{a,b}$

Nuclear Medicine Communications 2010, 31:366–374
<table>
<thead>
<tr>
<th></th>
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<tr>
<td>good ROIs</td>
<td>235 / 323</td>
<td>172 / 194</td>
</tr>
<tr>
<td>no warning</td>
<td>73 %</td>
<td>89 %</td>
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<tr>
<td>no interaction required</td>
<td></td>
<td></td>
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<tr>
<td>good ROIs</td>
<td>52 / 323</td>
<td></td>
</tr>
<tr>
<td>with warning</td>
<td>16%</td>
<td></td>
</tr>
<tr>
<td>user check required</td>
<td></td>
<td></td>
</tr>
<tr>
<td>poor ROIs</td>
<td>32 / 323</td>
<td></td>
</tr>
<tr>
<td>with warning</td>
<td>10%</td>
<td></td>
</tr>
<tr>
<td>new ROIs required</td>
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<td></td>
</tr>
<tr>
<td>poor ROIs</td>
<td>4 / 323</td>
<td></td>
</tr>
<tr>
<td>no warning</td>
<td>1%</td>
<td></td>
</tr>
<tr>
<td>new analysis required</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
0 - 1 min  1 - 2 min  2 - 3 min  3 - 4 min

0 - 3 min  mean-time  factor images
Factor analysis of dynamic renal study

- It has not met original expectations - yet (for many reasons outside the scope of this lecture), factor-analysis-like methods can still be successful in the future, their potential is large.

- It can be used with benefit for semi-automatic measurement of relative renal function (it needs 2 whole-kidney and 1 heart ROI, no background ROIs).

- Factor images can be used as parametric images to guide manual definition of ROIs including parenchymal ROIs.
Department of Nuclear Medicine
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left kidney: parenchyma pelvis

parametric images

right kidney: parenchyma pelvis

individual fuzzy ROI maxima

dotted line = contralateral whole kidney curve

results

<table>
<thead>
<tr>
<th>Patient Identification</th>
<th>(Name, Date of Birth, etc.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type and Date of the Study</td>
<td>IM2.img</td>
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<table>
<thead>
<tr>
<th>rel. uptake (Patlak) [%]</th>
<th>WK-L</th>
<th>PA-L</th>
<th>WK-R</th>
<th>PA-R</th>
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<tbody>
<tr>
<td>75.6</td>
<td></td>
<td></td>
<td>24.4</td>
<td></td>
</tr>
<tr>
<td>rel. uptake (factor) [%]</td>
<td>75.3</td>
<td></td>
<td>24.7</td>
<td></td>
</tr>
<tr>
<td>max. value [cps]:</td>
<td>682</td>
<td>328</td>
<td>355</td>
<td>118</td>
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<tr>
<td>peak time [s]:</td>
<td>1170</td>
<td>190</td>
<td>1200</td>
<td>150</td>
</tr>
<tr>
<td>NORA(20) [%]:</td>
<td>198</td>
<td>58</td>
<td>172</td>
<td>39</td>
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<tr>
<td>ROE(20) [%]:</td>
<td>28</td>
<td>86</td>
<td>-1</td>
<td>90</td>
</tr>
</tbody>
</table>

version 5.7, July 2002
(c) M. Samal, Charles Univ. Prague, 2002
(c) H. Bergmann, IBMTP AkH Wien, 2002

11-14 May 2010
14th International Symposium on Radionuclides in Nephrourology
Which methods

- whole-kidney ROIs need no automation
- parametric images support definition of parenchymal ROIs
- Middleton regression equation
- fractional renal uptake (FUR)
- Kuruc's method for deconvolution
- renal output efficiency
- in the future - more automation and more accurate extraction of parenchymal curves