Reproducibilities and responses to food intake of GFR measured with chromium-51-EDTA and iohexol simultaneously and independently in normal subjects

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Abstract

Background. The aim was to evaluate the reproducibility of glomerular filtration rate (GFR) measured with iohexol and its response to food in a direct and independent comparison with Cr-51-ethylenediaminetetraacetic acid (EDTA), and examine the influence of two different whole body scaling parameters, body surface area (BSA) and extracellular fluid volume (ECV).

Methods. Fasting and non-fasting GFR were measured in 20 normal volunteers using Cr-51-EDTA and iohexol, simultaneously injected into opposite arms. In 10, the fasting study was repeated. Venous samples obtained bilaterally 20, 40, 60, 120, 180, and 240 min after injection were assayed for indicator injected contralaterally—Cr-51-EDTA by well-counting and iohexol by X-ray fluorescence. GFR scaled to BSA was measured from six samples (GFR/BSA6) and from the last three (GFR/BSA3). GFR scaled to ECV was calculated as the mean transit time of marker using six samples (GFR/ECV6) or the last three (GFR/ECV3).

Results. GFR/BSA3 was reproducible (coefficient of variations of 7.4% for Cr-51-EDTA and 7.6% for iohexol). Using Cr-51-EDTA, GFR/ECV3 (9.1%) and GFR/ECV6 (7.7%) were as reproducible as GFR/BSA3 and GFR/BSA6 (both 8.1%). However, GFR/ECV3 measured with iohexol had poorer reproducibility (16.8%). Food resulted in an increase in scaled GFR of about 5 ml/min but this was statistically significant only with respect to GFR/BSA (measured with Cr-51-EDTA or iohexol) and not GFR/ECV.

Conclusions. Measured with Cr-51-EDTA, but not iohexol, GFR/ECV was as reproducible as GFR/BSA. GFR/BSA, measured with Cr-51-EDTA or iohexol, but not GFR/ECV, significantly increased after food.

Keywords: Cr-51-EDTA; extracellular fluid volume; glomerular filtration rate; iohexol; X-ray fluorescence
and BSA 1.48–2.09 (1.77) m²] with no history of allergy

...to ECV in both one-compartment and two-compartment

GFR, we also examined the reproducibility of GFR scaled

ues measured with Cr-51-EDTA. Because of the potential

and scaled to BSA and ECV against the corresponding val-

are generally restricted to correlation analysis of

simultaneously and independently com-

low physiological stimuli, such as a meal [17–19]. Whilst

able and non-toxic in the required doses [7]. Moreover, it

because it is non-radioactive, stable, cheap, easily avail-

need to be known, significantly simplifying the procedure.

To be described as near-ideal, it is essential to show that

filtration marker is reproducible in its measurement of

and is easily able to show changes in GFR that fol-

physiological stimuli, such as a meal [17–19]. Whilst

the reproducibilities of GFR based on both iohexol [20,21] and

and Cr-51-EDTA [22,23] have previously been separately

have generally been restricted to correlation analysis of

simultaneously measured GFR in patient cohorts with wide

ranges of renal function.

With the aim of further testing the reliability of not only

iohexol for measuring GFR but also the alternative scaling

variable, ECV, we simultaneously and independently com-

pared the reproducibilities of GFR measured with iohexol

and scaled to BSA and ECV against the corresponding val-

ues measured with Cr-51-EDTA. Because of the potential

advantages of ECV as a whole body scaling parameter for

GFR, we also examined the reproducibility of GFR scaled
to ECV in both one-compartment and two-compartment

scenarios.

Methods

Subjects

Twenty healthy volunteers [7 male, 13 female; age range

30–59 (median 45); body mass index 18–34 (22) kg/m²

were all studied twice, once fasting and once non-fasting.

Ten volunteered for a second fasting study. For each subject,

the two or three studies were completed within 6 weeks.

All measurements were commenced at the same time in

the morning, the non-fasting measurement after breakfast.

Volunteers were instructed to fast from midnight until the

completion of the GFR measurement the following day.

For the non-fasting study, volunteers were asked to follow

their usual breakfast routines. All volunteers gave informed

consent. The study was approved by the local research ethics

committee and by the Administration of Radioactive Sub-

stances Advisory Committee of the United Kingdom.

Filtration markers

Cr-51-EDTA (Amersham Health, Bucks, UK) was diluted
with benzyl alcohol containing sodium chloride solution
(1% by volume, benzyl alcohol, 0.75% by weight, NaCl) to
make a stock solution with a concentration of 1 MBq/ml.

Iohexol (Omnipaque 300; Amersham Health, Bucks, UK)
was delivered in 20 ml vials containing 300 mg iodine/ml.

Syringes were weighed before and after drawing up the

markers. Two millilitres of the Cr-51-EDTA stock with an
activity of ~2 MBq and 19 ml iohexol, containing 5.7 g
iodine, were injected.

Administration of markers

The markers were injected i.v. in close sequence in separate
arms. The time half way through injection was noted as
the time of injection. The Cr-51-EDTA usually took <5 s
to administer but the larger volume of viscous iohexol took
up to 30 s to inject. The volume of administered Cr-51-
EDTA was measured from the total weight drawn up into
the syringe assuming no post-injection residue and a density
of the Cr-51-EDTA solution of 1 g/ml. The syringes containing
the marker were flushed several times with saline to ensure
complete administration of the weighed amount.

Blood sampling

In addition to a baseline sample, 10-ml blood samples were

taken from both lines nominally at 20, 40, 60, 120, 180
and 240 min after marker administration. Approximately
3 ml of liquid was withdrawn from the line and discarded
prior to the collection of each blood sample. The mid-time
point time of sampling was taken as the sampling time.

Line patency was maintained with heparin-saline. The samples
were transferred from the syringe into heparinized glass

tubes, centrifuged at 800–1000 g for 15 min and plasma

separated.

Sample analysis

Each marker was assayed in samples contralateral to the
side of injection.

$^{51}$Cr-EDTA. For each stock solution of Cr-51-EDTA,
1:1000 diluted standards were prepared. Aliquots of
plasma, standards and water (as a blank) were counted
in an automatic gamma counter (Wallac 1480 ‘Wizard 3’,
Turku, Finland) for 1000 s with an energy window suitable
for Cr-51. Appropriate corrections were made for counter
dead-time and background.

Iohexol. Iohexol was assayed by X-ray fluorescence. In
order to calibrate the analyser (Oxford Instruments; Lab-
X3500; www.oxinst.com), a series of seven plasma stan-
dards were prepared containing iohexol concentrations of
0, 0.34, 0.69, 1.03, 1.36, 1.72 and 3.39 g/l (Figure 1). For
each sample, a holder was assembled in which the sample
is separated from the irradiation beam and the detector by
t a taut piece of 6 µm thick film. Three millilitres of the
sample was transferred to the sample holder immediately
prior to analysis. Once the sample was inside the analyser,
air was displaced from the measuring chamber by helium
gas to prevent emission of characteristic X-rays from argon
in the air or absorption of the characteristic X-rays from
the iodine by argon. The sample was irradiated for 300 s,
the X-ray target being palladium, the voltage 9 kV and the
tube current 100 µA. The average counts per second (cps)
was reported using an energy window that was optimized
for the L-characteristic X-rays from iodine at ~4–5 keV.
For each sample, the irradiation was repeated three times to confirm the reproducibility of the measurement, the average of the three being used. For each subject, the cps from the baseline blood sample from that subject on that day was used to correct the other sample measurements before using the calibration to obtain an absolute concentration of iohexol. The effective precision of the iohexol assay (i.e. in the range of plasma concentrations encountered; Figure 1) was estimated to be 4.9%.

Data analysis

Curve fitting. The plasma time–concentration curves for both markers were bi-exponential between 20 and 240 min. No samples were obtained before 20 min; otherwise the clearance curve would have been a triple exponential [24]. A bi-exponential fit to the six-sample curve was therefore performed using firstly a two-stage curve-stripping procedure and secondly iterative fitting. In the two-stage curve stripping procedure, the fast and slow exponentials were stripped in the conventional way. The fast exponential was then subtracted from the last three sample concentrations and a second slow exponential fitted to the resulting values. This was then subtracted from the initial three sample concentrations to give a second fast exponential. The zero-time intercepts of fast and slow exponentials extracted by these two curve-fitting procedures were denoted by $A$ and $B$, respectively, and the corresponding rate constants by $\alpha_1$ and $\alpha_2$.

Measurement of GFR based on all six samples. GFR was calculated from $A$, $\alpha_1$, $B$ and $\alpha_2$ using the following conventional formula that equates clearance to the quotient of injected marker divided by the area under the clearance curve between times zero and infinity:

$$GFR = \frac{\text{injected activity or dose}}{(A/\alpha_1) + (B/\alpha_2)}.$$  

(1)

Using the equation of Du Bois and Du Bois [25] to compute BSA from subject height and weight, GFR was then scaled to $1.73 \text{ m}^2$ to give GFR/BSA6.
Measurement of GFR based on the final three samples. A single exponential with intercept \( B' \) and rate constant \( \alpha'_2 \) (to be distinguished from \( B \) and \( \alpha_2 \) based on six-sample fitting) was fitted to the last three sample points. The reciprocal of \( B' \) is the one-compartment distribution volume, \( V_d' \). Slope–intercept GFR was then calculated as the product of \( \alpha'_2 \) and \( V_d' \) and scaled to 1.73 m². It was corrected for the one-compartment assumption using second-order polynomials (of the form \( y = A + Bx + Cx^2 \)) based on the relations between one-compartment and two-compartment GFR to give GFR/BSA3. The formula for iohexol (in which \( \alpha'_2 = 0 \)) based on the relations between one-compartment and two-compartment GFR to give GFR/BSA3. The formula for iohexol (in which \( \alpha'_2 = 0 \)) was derived from our own database of 110 iohexol clearances in which \( \alpha_2 = 1.0022 \) and \( C = -0.00131 \). Mean marker residence time in the ECV using six samples. Any individual molecule of indicator within the extracellular fluid (assumed to be the same as the indicator's distribution volume) will wait a certain amount of time before undergoing glomerular filtration. The mean waiting time of all the molecules, i.e. transit time (\( T \)), can be calculated from the following equation [27]:

\[
T = \frac{(A/[\alpha_1]^2) + (B/[\alpha_2]^2)}{(A/\alpha_1) + (B/\alpha_2)}.
\]

The reciprocal of \( T \) is the rate at which the ECV is ‘turned over’ by GFR and is therefore a measure of GFR that is already scaled to ECV. This scaled version of GFR is denoted by GFR/ECV or, as it was based on six samples, GFR/ECV6. Multiplication of GFR (ml/min) by \( T \) (min) gives ECV (ml). ECV was then scaled to a BSA of 1.73 m².

Measurement of mean marker residence time in the ECV using the last three samples. The variable \( \alpha'_2 \) (with units of \( \text{min}^{-1} \)) is also an estimate of GFR/ECV (ml/min/ml = \( \text{min}^{-1} \)), which, as it was based on the three samples between 2 and 4 h, was denoted by GFR/ECV3. As for GFR/BSA3, GFR/ECV3 also needs correcting for the one-compartment assumption. For iohexol data, GFR/ECV3 was therefore corrected using a second-order polynomial derived from our own database of 110 iohexol clearances in which \( A = 0 \), \( B = 1.0526 \) and \( C = 5.17 \). With respect to Cr-51-EDTA, correction for the one-compartment assumption was based on \( \alpha'_2 \) using a formula in which \( A = 0 \), \( B = 1 \) and \( C = 15.4 \), similar to that reported by Peters et al. [28].

Statistics

Reproducibility. Estimates of repeatability were made from within-subject variance for the volunteers who had repeat fasting measurements. The within-subject variance (CV) was calculated from the residual mean square from one-way analysis of variance [29]:

\[
CV = \left( \frac{\Sigma(x_1 - x_2)^2/2n}{\Sigma x_1 + \Sigma x_2)/2n} \right)^{0.5}
\]

where \( x_1 \) and \( x_2 \) refer to first and second measurements and \( n \) is number of paired measurements.

Comparison of repeatability between different methods and markers was made from the \( F \)-test on the variance of the differences between repeat measurements.

The standard deviation (SD) of the differences between repeat measures of GFR approximates to \(((\text{SD of the real differences})^2 + 2(\text{measurement error})^2)^{0.5} \).

Effect of food intake. The difference between fasting and non-fasting GFR was evaluated for all measures of GFR using the paired Student \( t \)-test. For volunteers with two fasting measurements, the difference was based on the first of the two.

Results

Curve stripping versus iterative fitting

Six-sample GFR based on iterative fitting was less reproducible than six-sample GFR based on two-stage curve fitting, whether scaled to BSA or ECV (results not shown). Six-sample GFR and ECV values are therefore reported only for two-stage curve stripping.

Scaling ECV

ECV showed a marginally better correlation with BSA than with its more traditional scaling parameter, body weight (results not shown). Mean fasting ECV/BSA was 13.5 (SD 1.0) L for Cr-51-EDTA and 13.2 (1.5) L for iohexol. Mean non-fasting ECV/BSA was 13.7 (1.5) L for Cr-51-EDTA and 13.6 (1.7) L for iohexol, not significantly different from fasting values. To obtain GFR/ECV numerically comparable with GFR/BSA, GFR/ECV (measured with either Cr-51-EDTA or iohexol) was therefore multiplied by 13.500.

Reproducibility

Measured with Cr-51-EDTA, there were no significant differences between the reproducibilities of GFR/BSA3, GFR/BSA6, GFR/ECV3 and GFR/ECV6 (Table 1). For iohexol, however, the within-subject variances of GFR/ECV3 and GFR/ECV6 were both significantly higher \((P < 0.05) \) than GFR/BSA3, but not GFR/BSA6. The within-subject variances of GFR/ECV3 and GFR/ECV6 based on iohexol were both significantly higher than the corresponding variances recorded with Cr-51-EDTA, but there were no significant differences between the two markers with respect to GFR/BSA3 and GFR/BSA6.

The changes between the two separate, simultaneous and independent measurements of fasting GFR values based respectively on Cr-51-EDTA and iohexol correlated with each other (Figure 2), although not significantly with respect to GFR/ECV3, indicating that the variation between the two measurements partly reflects real changes in filtration function.

Effect of a light meal

Food intake consistently resulted in small increases in GFR values but these were significant only when scaled to BSA (Table 2). The corresponding food-induced changes in GFR
Table 1. Reproducibilities of fasting GFR/BSA (ml/min/1.73 m²) and GFR/ECV (ml/min/13.5 l) measured on two separate occasions in 10 normal subjects with Cr-51-EDTA and iohexol

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Mean difference between replicates</th>
<th>SD of differences</th>
<th>Within subject standard deviation</th>
<th>CV%</th>
</tr>
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<tbody>
<tr>
<td><strong>Cr-51-EDTA</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GFR/BSA3</td>
<td>88.2</td>
<td>0.4</td>
<td>9.7</td>
<td>6.5</td>
<td>7.4</td>
</tr>
<tr>
<td>GFR/BSA6</td>
<td>89.9</td>
<td>2.4</td>
<td>10.6</td>
<td>7.3</td>
<td>8.1</td>
</tr>
<tr>
<td>GFR/ECV3</td>
<td>88.7</td>
<td>5.8</td>
<td>10.4</td>
<td>8.1</td>
<td>9.1</td>
</tr>
<tr>
<td>GFR/ECV6</td>
<td>92.4</td>
<td>5.4</td>
<td>8.9</td>
<td>7.1</td>
<td>7.7</td>
</tr>
<tr>
<td><strong>Iohexol</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GFR/BSA3</td>
<td>83.8</td>
<td>0.6</td>
<td>9.5</td>
<td>6.4</td>
<td>7.6</td>
</tr>
<tr>
<td>GFR/BSA6</td>
<td>84.4</td>
<td>1.9</td>
<td>12.9</td>
<td>8.7</td>
<td>10.4</td>
</tr>
<tr>
<td>GFR/ECV3</td>
<td>87.5</td>
<td>5.9</td>
<td>21.1*</td>
<td>14.8</td>
<td>16.8b</td>
</tr>
<tr>
<td>GFR/ECV6</td>
<td>87.8</td>
<td>5.4</td>
<td>17.0*</td>
<td>12.0</td>
<td>13.2b</td>
</tr>
</tbody>
</table>

*Significantly different compared with corresponding variable measured with Cr-51-EDTA.

bSignificantly different compared with GFR/BSA3 (iohexol).

Table 2. Fasting (first in those having two fasting studies) and non-fasting values of GFR/BSA (ml/min/1.73 m²) and GFR/ECV (ml/min/13.5 l) measured in 20 normal subjects with Cr-51-EDTA and iohexol

<table>
<thead>
<tr>
<th></th>
<th>Mean fasted</th>
<th>Mean increase after food intake</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cr-51-EDTA</strong></td>
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<td></td>
</tr>
<tr>
<td>GFR/BSA3</td>
<td>87.9</td>
<td>4.9</td>
<td>0.0045</td>
</tr>
<tr>
<td>GFR/BSA6</td>
<td>89.3</td>
<td>4.6</td>
<td>0.0067</td>
</tr>
<tr>
<td>GFR/ECV3</td>
<td>88.4</td>
<td>2.9</td>
<td>0.086</td>
</tr>
<tr>
<td>GFR/ECV6</td>
<td>92.2</td>
<td>3.2</td>
<td>0.052</td>
</tr>
<tr>
<td><strong>Iohexol</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GFR/BSA3</td>
<td>85.1</td>
<td>3.8</td>
<td>0.023</td>
</tr>
<tr>
<td>GFR/BSA6</td>
<td>83.8</td>
<td>5.7</td>
<td>0.011</td>
</tr>
<tr>
<td>GFR/ECV3</td>
<td>83.3</td>
<td>5.6</td>
<td>0.10</td>
</tr>
<tr>
<td>GFR/ECV6</td>
<td>87.8</td>
<td>5.0</td>
<td>0.092</td>
</tr>
</tbody>
</table>

Fig. 2. Relations between corresponding individual fractional changes in GFR values simultaneously measured with Cr-51-EDTA and iohexol between the first and second fasting measurements in 10 normal subjects.

Fig. 3. Relations between corresponding individual fractional changes in GFR values simultaneously measured with Cr-51-EDTA and iohexol between the non-fasting and fasting measurements in 20 normal subjects (the first in the 10 normal subjects who had two fasting measurements).

Discussion

Many previous studies assessing the accuracy of GFR measurement against a gold standard have not performed the measurements in a truly independent fashion. The novelty of this study is that complete independence was assured with respect to both the reproducibility and effect of food studies. Although this was a cohort of normal volunteers, average GFR was surprisingly low. We have no reason, however, to suspect any measurement errors as the mean
ratio of slope–intercept GFR, e.g. given by the two indicators in all 50 paired studies was 1.037 (SD 0.063).

**Reproducibility**

Reproducibility studies of Cr-51-EDTA and iohexol are scarce, and we could find no direct comparisons between them. Since chronic kidney disease (CKD) is slowly progressive, reproducibility is a key element for any clinical measure of its rate of progression. There is an underlying diurnal variation in GFR [30–33] as well as changes in response to external stimuli, e.g. exercise [34] and food intake [9–11]. The diurnal rhythm in GFR, which reflects changes in circulating atrial natriuretic peptide rather than arterial pressure [32], is represented differently by insulin and creatinine clearances [35,36].

**Food intake**

A protein-rich meal causes an increase in GFR of about 25% [18,19] but in the current study we observed a general increase much less than this because the meal was generally lighter. As our intention was to compare iohexol and Cr-51-EDTA in a paired fashion, there was no need to standardize the meal. Moreover, a light meal, resulting in a more modest increase in GFR, is more discriminatory.

**Reliability of iohexol**

There have been several previous comparisons between iohexol and Cr-51-EDTA for measuring GFR [7–14], although they have not compared the two markers in a truly independent fashion by basing their clearances on separate sets of blood samples drawn from separate sites after simultaneous administration of markers via separate lines or directly compared their reproducibilities, as we have done here.

In the current study, the coefficients of variation did not differ significantly between the two indicators, at least with respect to the conventional slope–intercept approach (i.e. GFR/BSA3). By showing a significant correlation between individual changes in fasting GFR measured by the two markers simultaneously and independently, it is evident that a considerable proportion of the variability between sequential measurements was the result of real changes in GFR.

Other recent studies have assayed iohexol by HPLC [6,7,16,20]. Notably though, Brandstrom et al. [7] recorded correlation coefficients with Cr-51-EDTA that were similar for both XRF (0.95) and HPLC (0.92). They commented on the necessity of a minimum plasma iodine concentration of 0.06 g/l (which corresponds to an iohexol concentration of 0.27 g/l, less than our most dilute standard (see Figure 1).

GFR values measured with Cr-51-EDTA showed statistically more significant responses compared with iohexol in response to food. High protein meals act directly on the kidney to cause an increase in GFR, which should therefore correlate inversely with any simultaneous change in ECV. However, we previously observed a positive correlation [37], suggesting that for a light meal, with small increases in GFR, primary changes in ECV play a more important role in the GFR increment. This would explain why the increases in GFR/ECV were not significant.

**Three versus six samples**

The coefficients of variation did not differ significantly between three- and six-sample GFR measured with Cr-51-EDTA, with respect either to GFR/BSA or GFR/ECV. For iohexol, three-sample GFR was more reproducible when scaled to BSA but the opposite was seen scaled to ECV. There was little difference between three- and six-sample GFR with respect to response to food intake. In terms of both reproducibility and response to food intake, inclusion of the initial three blood samples seemed to offer no improvement. So although not necessarily more accurate than six-sample GFR, three-sample GFR provided good precision. This is presumably because the additional error generated by the inclusion of early samples is greater than the normal variation that exists in the parameters on which the first exponential is based. This may not of course apply to an abnormal population or to the elderly with their reduced muscle mass and possibly therefore also a reduced ECV.

**Reliability of scaling to ECV**

The mean transit time, $T$, and its approximation, the reciprocal of the terminal rate constant, represent the mean waiting time of individual molecules of marker in the extracellular fluid space compartment before filtration and are therefore measures of GFR that are already scaled to ECV. In other words, measuring GFR per unit ECV requires measurement only of their ratio, and not of their individual values. BSA for scaling GFR is largely historical and well entrenched but has nevertheless been criticized on several grounds, including sex differences in renal perfusion and gross differences in body size [1,38] and compared unfavourably with several alternatives, including ECV. In addition to technical convenience, ECV as a whole body scaling parameter offers the attraction of physiological validity [39], including an element of dependence of GFR on ECV [39–41]. Further advantages of the exclusive use of the terminal rate constant to measure GFR are the opportunity of the ‘real-time’ measurement of GFR (which allows the detection of instantaneous changes) [42,43] and convenience in the context of the remote measurement of GFR.

The coefficients of variation did not differ significantly between GFR values respectively scaled to BSA and ECV with respect either to three- or six-sample Cr-51-EDTA clearance. The slope–intercept technique, however, exposed a clearer response to food intake than scaling to ECV which could be explained by a simultaneous corresponding increase in ECV [37], limiting an increase in the ratio. Scaling to ECV also impaired reproducibility when iohexol was the marker.
Conclusion

GFR measured with iohexol has similar reproducibility to GFR measured with Cr-51-EDTA using three samples and the slope–intercept approach. Unless the volunteer’s weight changes significantly between paired measurements, reproducibility and response to food intake of unscaled GFR would, of course, be identical to BSA-scaled GFR, and some of the disadvantages of BSA as a scaling parameter, discussed above, would not be apparent in reproducibility and acute response studies such as the current one. When measured with Cr-51-EDTA, GFR/ECV was almost as reproducible as GFR/BSA, thereby in principle validating the slope-only technique. GFR/ECV measured with iohexol, however, was less reliable. A feature of the conventional slope–intercept technique that is usually taken for granted, but which relies on careful attention to technical detail, is the administered amount of indicator, errors in which are impossible to detect retrospectively. As far as a postal service is concerned, therefore, scaling to ECV would be highly favoured but critically dependent on the accuracy of the iohexol assay. Technology advances rapidly, and although previous experiences with XRF have shown it to be reliable, most authorities would agree that HPLC is the most accurate method for assaying iohexol and its unavailability to the current authors must be seen as a limitation in this study. We believe, however, that the results reported here provide a sound platform from which a postal service with iohexol could be developed. Whether it should be based on three or six samples awaits further work to confirm that three-sample GFR/ECV measured with iohexol and HPLC is as accurate as GFR/ECV measured with Cr-51-EDTA.

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Conflict of interest statement. None declared.

References


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