



A Novel Immunoassay-Based System that Accurately Measures GFR in Patients with CKD, Transplantation Recipients and Potential Living Donors

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OBJECTIVE

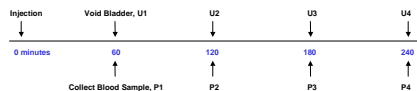
This is the first human clinical study designed to compare functional immunoassay technology (FITTM) GFR measurements to those obtained by an FDA approved diagnostic test to measure GFR, (Sodium Iothalamate I-125, Glofil®).

EXPERIMENTAL PROTOCOL

The investigation was performed in 20 subjects (14 males), ranging from 30-71 years in age. Two subjects were healthy volunteers, 8 subjects were diabetics, 12 subjects received a kidney transplant and 1 subject received a liver transplant.

All subjects received Lugol's solution before the start of the study to block thyroidal uptake of I-125. The height and weight of each subject was measured and subjects were encouraged to drink water throughout the study.

Glofil (10 µCi) and Magnevist® (Gd-DTPA, 10 µl/kg) were intravenously administered to each subject at the start of the study. After injection, blood and urine samples were collected.



The exact time of each blood and urine collection was recorded and the volume of each urine collection measured. Blood was collected in serum separation tubes without anticoagulant and centrifuged within one hour. Serum creatinine was also measured to estimate GFR using the MDRD correction equation (eGFR).

DATA ANALYSIS

Glofil GFR values obtained by the UV/P method were considered the gold standard. FIT-GFR values obtained by UV/P and by the blood clearance method and eGFR values were directly compared to Glofil UV/P GFR values using the analysis of Bland and Altman.

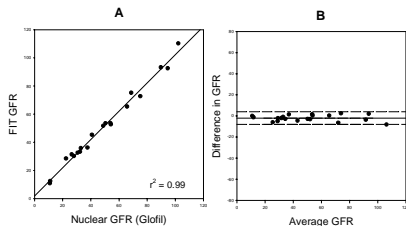


Figure 1: A) UV/P FIT and Glofil GFR values (ml/min/1.73m²), $y = 1.85 + 1.00x$; $r^2 = 0.99$. B) The difference against the mean for FIT GFR values, 95% of the patients fell within 20% of the clinical standard.

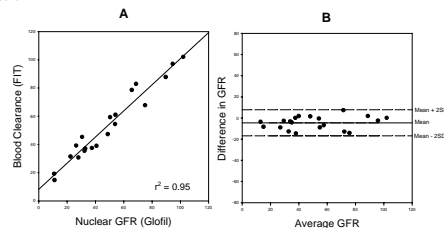


Figure 2: A) FIT-GFR values (ml/min/1.73m²) via the blood clearance method and Glofil GFR values (ml/min/1.73m²) via UV/P method, $y = 8.22 + 0.93x$; $r^2 = 0.95$. B) The difference against the mean for FIT GFR values, 75% of the patients fell within 20% of the clinical standard.

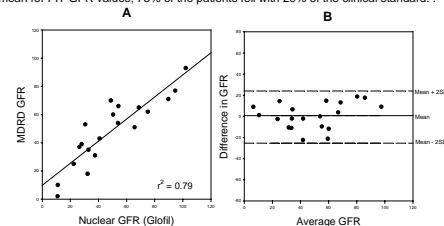


Figure 2: A) eGFR values (ml/min/1.73m²) and Glofil GFR values (ml/min/1.73m²) calculated by UV/P method, $y = 9.87 + 0.78x$; $r^2 = 0.78$. B) The difference against the mean for eGFR values, 45% of the patients fell within 20% of the clinical standard.

RESULTS

The FIT-GFR test provides comparable results to the FDA approved diagnostic test (Figures 1-2). The nephrology practice guidelines recommend that patients with chronic kidney disease (CKD) be classified into one of five stages based on eGFR. If the FDA approved GFR test is used as the clinical standard, FIT-GFR values correctly classify patients with a high degree of precision, see Tables 1-2. In contrast, eGFR compared poorly to the FDA approved test (Figure 3), with half of the subjects being misclassified by eGFR (Tables 1 and 2).

Table 1: The accuracy of different methods to correctly classify patients into CKD stage using Glofil GFR values as the clinical standard. FIT-GFR values obtained by UV/P are in blue, FIT-GFR values obtained by the blood clearance are in green, and the MDRD eGFR values are in red.

Stage of CKD	Correctly Classified	Misclassified into A higher stage	Misclassified into A lower stage
I (>90 ml/min/1.73m ²)	1, 0, 0	N.A.	0, 1, 1
II (60-90 ml/min/1.73m ²)	3, 3, 2	0, 0, 0	0, 0, 1
III (30-59 ml/min/1.73m ²)	9, 8, 5	2, 1, 3	0, 0, 1
IV (15-29 ml/min/1.73m ²)	1, 0, 1	0, 3, 2	0, 0, 1
V (<15 ml/min/1.73m ²)	2, 2, 2	0, 0, 0	N.A.

Table 2: The deviation from the CKD stage is listed for those misclassified. For example, if Glofil provides a GFR of 45 ml/min/1.73m² and the test method provides a GFR of 63 ml/min/1.73m², the deviation outside the CKD stage III is 4 ml/min/1.73m². FIT GFR values obtained by UV/P are in blue, FIT GFR values obtained by the blood clearance are in green, and the eGFR values are in red.

Stage of CKD	Deviation from CKD stage (ml/min/1.73m ²)			
	>2	>5	>10	>15
I (>90 ml/min/1.73m ²)	0, 0, 1	0, 0, 1	0, 0, 1	0, 0, 1
II (60-90 ml/min/1.73m ²)	0, 0, 1	0, 0, 1	0, 0, 0	0, 0, 0
III (30-59 ml/min/1.73m ²)	0, 0, 3	0, 0, 3	0, 0, 2	0, 0, 0
IV (15-29 ml/min/1.73m ²)	0, 1, 2	0, 1, 2	0, 0, 1	0, 0, 0
V (<15 ml/min/1.73m ²)	0, 0, 0	0, 0, 0	0, 0, 0	0, 0, 0

CONCLUSION

The FIT-GFR test provides an accurate measurement of GFR and eliminates all previous analytical barriers associated with alternative methods.