



True GFR Measurement

precise, affordable, and rapid



1. Nephrolyx Medical Advisory Board

- Prof. Dr. M. van der Giet, Berlin, Germany
- Prof. Dr. E. Cavalier, Liège, Belgium
- Prof. Dr. P. Delanaye, Liège, Belgium
- Prof. Dr. D. Goldsmith, London, UK
- Prof. Dr. J. Prowle, London, UK

2. Publication by Nephrolyx and Medical Advisory Board

- Key review paper on True GFR measurement in clinical practice
Delanaye P, Ebert N, Melsom T, Gaspari F, Mariat C, **Cavalier E**, Björk J, Christensson A, Nyman U, Porrini E, Remuzzi G, Ruggenenti P, Schaeffner E, Soveri I, Sterner G, Eriksen BO, Bäck SE. **Iohexol plasma clearance for measuring glomerular filtration rate in clinical practice and research: a review. Part 1: How to measure glomerular filtration rate with iohexol?** Clin Kidney J. 2016
<https://pubmed.ncbi.nlm.nih.gov/27679715/>
- The original study which started the development of the Iohexol method in Berlin
Schaeffner ES, Ebert N, Delanaye P, Frei U, Gaedeke J, Jakob O, Kuhlmann MK, Schuchardt M, Tölle M, Ziebig R, **van der Giet M**, Martus P. **Two novel equations to estimate kidney function in persons aged 70 years or older.** Ann Intern Med. 2012
<https://pubmed.ncbi.nlm.nih.gov/23027318/>
- The predecessor method of our commercial offering is described.
Schweinsberg V, Eckelt S, Schulz AM, Arlt M, Schumann M, **van der Giet M**, Tauber R, Binscheck-Domaß T, Kießling P. Enhanced specificity due to method specific limits for relative ion intensities in a high-performance liquid chromatography - tandem mass spectrometry

method for iohexol in human serum. Clin Chem Lab Med. 2020

<https://pubmed.ncbi.nlm.nih.gov/32069224/>

- Highlights the challenges of computing GFR from Iohexol measurements, which was the rationale behind our offering of a dedicated nephrology calculation platform.

Pottel H, Schaeffner E, Ebert N, **van der Giet M, Delanaye P**. Iohexol plasma clearance for measuring glomerular filtration rate: effect of different ways to calculate the area under the curve. BMC Nephrol. 2021.

<https://pubmed.ncbi.nlm.nih.gov/33952185/>

- Additional publications on request

3. National and International Guidelines

- Suggests using additional tests such as Iohexol clearance measurement when estimated GFR is less accurate, or treatment decisions are impacted.

Kidney Disease: Improving Global Outcomes 2012 - Clinical practice guideline for the evaluation and management of chronic kidney disease

- Iohexol is listed among the gold standard external filtration markers which should be used to determine renal function when pharmacokinetic studies are mandated.

European Medicines Agency (EMA) Committee for Medicinal Products for Human use (CHMP) 2015 - Guideline on the evaluation of the pharmacokinetics of medicinal products in patients with decreased renal function

- The UK national guidelines on CKD endorse Iohexol Clearance as the gold standard for evaluation of GFR in CKD patients.
- The German national guideline on CKD describes Iohexol Clearance as a gold standard for kidney function measurement but is currently not used due to a lack of commercial methods.

Deutsche Gesellschaft für Nephrologie (DGfN), Deutsche Gesellschaft für Klinische Chemie und Laboratoriumsmedizin e. V. (DGKL) 2021 - Interdisziplinäre S2k-Leitlinie: Rationelle Labordiagnostik zur Abklärung Akuter Nierenschädigungen und Progredienter Nierenerkrankungen

4. Technical Publications

- Publication on the External Performance Validation at CHU Liege
Cavalier E, Delanaye P, Ferrante N, Peeters S, Le Goff C – Validation of Iohexol Determination by the Nephrolyx UPLC-UV Assay, the first commercially available method to measure glomerular filtration rate – In Kidney diseases and transplantation, urinalysis – Clinical Chemistry and Laboratory Medicine (CCLM) 2023
<https://doi.org/10.1515/cclm-2023-7052>
- Le Goff C, Peeters S, **Cavalier E** 2023 – External Performance Validation of Nephrolyx UHPLC method at CHU Liege
- **Nephrolyx** GmbH, 2022 – Analytical performance validation for CE mark
- **Nephrolyx** External Quality Assessment (EQA) via Equalis AB (Sweden) – Ring Trial Results

5. Other Relevant Publications

Further relevant publications are listed below:

- Initial study demonstrating the use of Iohexol as a contrast agent with superior safety properties.
Aakhus T, Sommerfelt SC, Stormorken H et al. Tolerance and excretion of Iohexol after intravenous injection in healthy volunteers. Preliminary report. Acta Radiol Suppl 1980; 362:131–134
- During 15,147 GFR measurements, only one treatment-related event of moderate intensity was identified
Gaspari F, Thakar S, Carrara F, Perna A, Trillini M, Aparicio MC, Diadei O, Ferrari S, Cannata A, Stucchi N, Ruggenenti P, Remuzzi G, Perico N. Safety of Iohexol Administration to Measure Glomerular Filtration Rate in Different Patient Populations: A 25-Year Experience. Nephron. 2018;140(1):1–8. <https://pubmed.ncbi.nlm.nih.gov/29772565/>

- Review publication on Iohexol use for GFR measurement from a laboratory perspective.

Carrara F, Gaspari F. GFR measured by Iohexol: the best choice from a laboratory perspective. *J Lab Precis Med* 2018

- Systematic review of studies measuring GFR using exogenous markers, finding that Iohexol and ⁵¹Cr-EDTA plasma clearance have demonstrated sufficient accuracy for GFR measurement.

Soveri I, Berg UB, Björk J, Elinder CG, Grubb A, Mejare I, Sterner G, Bäck SE; SBU GFR Review Group. Measuring GFR: a systematic review. *Am J Kidney Dis.* 2014 Sep;64(3):411-24. doi: 10.1053/j.ajkd.2014.04.010. Epub 2014 May 17. PMID: 24840668.

- HPLC method for measuring Iohexol in plasma shows excellent linearity and sample stability of 9 days.

Castagnet, S., Blasco, H., Vourc'h, P., Benz-De-Bretagne, I., Veyrat-Durebex, C., Barbet, C., ... Andres, C. R. (2012). Routine Determination of GFR in Renal Transplant Recipients by HPLC Quantification of Plasma Iohexol Concentrations and Comparison With Estimated GFR. *Journal of Clinical Laboratory Analysis*, 26(5), 376–383. doi:10.1002/jcla.21537

6. Publications About Specific Patient Populations & Indications

- Iohexol Plasma clearance was found to be accurate when compared to Iohexol urine clearance in 9 cirrhotic patients.

Carrier P, Destere A, Giguet B, Debette-Gratien M, Essig M, Monchaud C, Woillard JB, Loustaud-Ratti V. Iohexol plasma and urinary concentrations in cirrhotic patients: A pilot study. *World J Hepatol.* 2022 Aug 27;14(8):1621-1632. <https://pubmed.ncbi.nlm.nih.gov/36157874/>

- Iohexol plasma clearance was considered the gold standard in a longitudinal study over 7 years regarding measurement of GFR in HIV positive and negative patients.

Lucas, Gregory M. MD, PhDa; Atta, Mohamed G. MD, MPHa; Zook, Katie BAa; Vaidya, Dhananjay MBBS, PhDa; Tao, Xueting MHSa; Maier, Paula BSb; Schwartz, George J. MDb Cross-Sectional and Longitudinal Performance of Creatinine- and Cystatin C-Based Estimating Equations Relative to Exogenously Measured Glomerular Filtration Rate in HIV-Positive and HIV-Negative Persons, *JAIDS Journal of Acquired Immune Deficiency Syndromes*: December 1, 2020 - Volume 85 - Issue 4 - p e58-e66 doi:10.1097/QAI.0000000000002471

- In the ICU setting, GFR can be reliably estimated by plasma iohexol clearance in unstable critically ill patients.

Salmon-Gandonnière C, Benz-de Bretagne I, Mercier E, Joret A, Halimi JM, Ehrmann S, Barin-Le Guellec C. Iohexol clearance in unstable critically ill patients: a tool to assess glomerular filtration rate. Clin Chem Lab Med. 2016

<https://pubmed.ncbi.nlm.nih.gov/27166722/>

- Study validating the use of iohexol plasma clearance for use in children.

Schwartz GJ, Furth S, Cole SR, Warady B, Muñoz A. Glomerular filtration rate via plasma iohexol disappearance: pilot study for chronic kidney disease in children. Kidney Int. 2006 Jun;69(11):2070-7.

- Study assessing the viability of iohexol measurements in dialysis patients, which found that GFR is overestimated in cases of GFR < 15 ml/min/1.73qm.

Shafi T, Levey AS, Inker LA, Schwartz GJ, Knight C, Abraham AG, Eckfeldt JH, Coresh J. Plasma Iohexol Clearance for Assessing Residual Kidney Function in Dialysis Patients. Am J Kidney Dis. 2015 Oct;66(4):728-30.

- Study showing the viability of using iohexol measurements in stable kidney transplant recipients with a GFR 47.4 +/- 16.3.

Riff, Camille, Besombes, Joesvin, Gatault, Philippe, Barbet, Christelle, Büchler, Matthias, Blasco, Hélène, Halimi, Jean-Michel, Barin-Le Guellec, Chantal and Benz-de Bretagne, Isabelle. "Assessment of the glomerular filtration rate (GFR) in kidney transplant recipients using Bayesian estimation of the iohexol clearance" Clinical Chemistry and Laboratory Medicine (CCLM), vol. 58, no. 4, 2020, pp. 577-587.

<https://doi.org/10.1515/cclm-2019-0904>

- Iohexol is unlikely to affect the clinical pharmacokinetics of carboplatin, paclitaxel, gemcitabine, or other agents used in combination with carboplatin treatment. Thus, measuring GFR using iohexol for carboplatin dosing is not expected to alter the safety or efficacy of such chemotherapy.

Joshi A, Guo J, Holleran JL, Kiesel B, Taylor S, Christner S, Parise RA, Miller BM, Ivy SP, Chu E, Venkataramanan R, Beumer JH. Evaluation of the pharmacokinetic drug-drug interaction potential of iohexol, a renal

filtration marker. Cancer Chemother Pharmacol. 2020 Oct;86(4):535-545. <https://pubmed.ncbi.nlm.nih.gov/32948918/>

7. Contact

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