HAL
open science

# $^{11}$C-glyburide PET imaging unveils the negligible brain penetration of glyburide in humans

Solène Marie, Claude Comtat, Fabien Caillé, Laurent Becquemont, Michel Bottlaender, Nicolas Tournier

## To cite this version:

Solène Marie, Claude Comtat, Fabien Caillé, Laurent Becquemont, Michel Bottlaender, et al.. $^{11}$C-glyburide PET imaging unveils the negligible brain penetration of glyburide in humans. Neurology, In press, 92 (17), pp.813-814. 10.1212/WNL.0000000000007378 . hal-03883039

**HAL Id: hal-03883039**

**https://hal.science/hal-03883039v1**

Submitted on 2 Dec 2022

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

# $^{11}$C-glyburide PET imaging unveils the negligible brain penetration of glyburide in human

Solène MARIE (Pharm D)[1,2,3], Claude COMTAT (PhD)[1], Fabien CAILLÉ (PhD)[1], Laurent BECQUEMONT (MD, PhD)[2,4], Michel BOTTLAENDER (MD, PhD)[1], Nicolas TOURNIER (PharmD, PhD)[1,*]

1. Imagerie Moléculaire In Vivo, IMIV, Institut des sciences du vivant Frédéric Joliot, Direction de la Recherche Fondamentale, CEA, Inserm, CNRS, Univ. Paris-Sud, Université Paris Saclay, CEA-SHFJ, Orsay, France
2. Hôpital Bicêtre, APHP, Le Kremlin Bicêtre, France
3. Faculté de Pharmacie, Université Paris-Sud, Châtenay-Malabry, France.
4. Department of Pharmacology, University Paris Sud, faculty of medicine Paris Sud, INSERM UMR-1178, CESP, Le Kremlin Bicêtre, France

* Corresponding author

nicolas.tournier@cea.fr

CEA, DRF, JOLIOT, Service Hospitalier Frédéric Joliot, Orsay,

4, place du Général Leclerc, F-91401, France

Phone number: +33 1 69 86 77 12 Fax number: +33 1 69 86 77 68

**Title:** 88 characters (including space)

**Word count**

- Body manuscript: 100 words
- 1 figure
- 2 references
- Figure legend: 50 words

**Study funding**

Supported by the french national research agency (IsotoPK, ANR-16-CE17-0011-001)

**Disclosure**

Dr. Solène MARIE reports no disclosure, Dr. Claude COMTAT reports no disclosure, Dr. Fabien CAILLÉ reports no disclosure, Pr. Laurent BECQUEMONT reports no disclosure, Dr. Michel BOTTLAENDER reports no disclosure, Dr. Nicolas TOURNIER reports no disclosure.

**Contribution**

| Name | Location | Role | Contribution |
|---|---|---|---|
| Solène MARIE (Pharm D) | CEA/SHFJ | Author | Analyzed the data; wrote the manuscript; study supervision |
| Claude COMTAT (PhD) | CEA/SHFJ | Author | Major role in the acquisition of data |
| Fabien CAILLÉ (PhD) | CEA/SHFJ | Author | Radiotracer production; Major role in the acquisition of data |
| Laurent BECQUEMONT (MD, PhD) | Paris Sud University | Author | Major role in the acquisition of data; revised the manuscript for intellectual content |
| Michel BOTTLAENDER (MD, PhD) | CEA/SHFJ | Author | Design and conceptualized study. Major role in the acquisition of data |
| Nicolas TOURNIER (PharmD, PhD) | CEA/SHFJ | Author | Design and conceptualized study; drafted the manuscript for intellectual content |

**Article**

Kimberly and coworkers reported the beneficial effects of intravenous glyburide on the clinical outcome of brain edema.[1] We developed the carbon-11 radiolabeled analogue of glyburide to study the body distribution of this compound using PET imaging (Fig. 1A). In a healthy subject, the brain distribution of $^{11}$C-glyburide matched the cerebral blood volume suggesting negligible blood-brain barrier (BBB) penetration (Fig. 1B, 1C). This clinical observation corroborates preclinical findings suggesting that local changes in BBB structure and function are required for targeted delivery and favorable effects of glyburide to the injured brain tissue while minimizing potential side effects to the healthy brain.[2]

**Study Registration**

EudraCT 2017-001703-69

**References**

1. Kimberly WT, Bevers MB, von Kummer R, et al. Effect of IV glyburide on adjudicated edema endpoints in the GAMES-RP Trial. Neurology. 2018;91:e2163–e2169.
2. Kurland DB, Tosun C, Pampori A, et al. Glibenclamide for the Treatment of Acute CNS Injury. Pharmaceuticals. 2013;6:1287–1303.

**Figure legend**
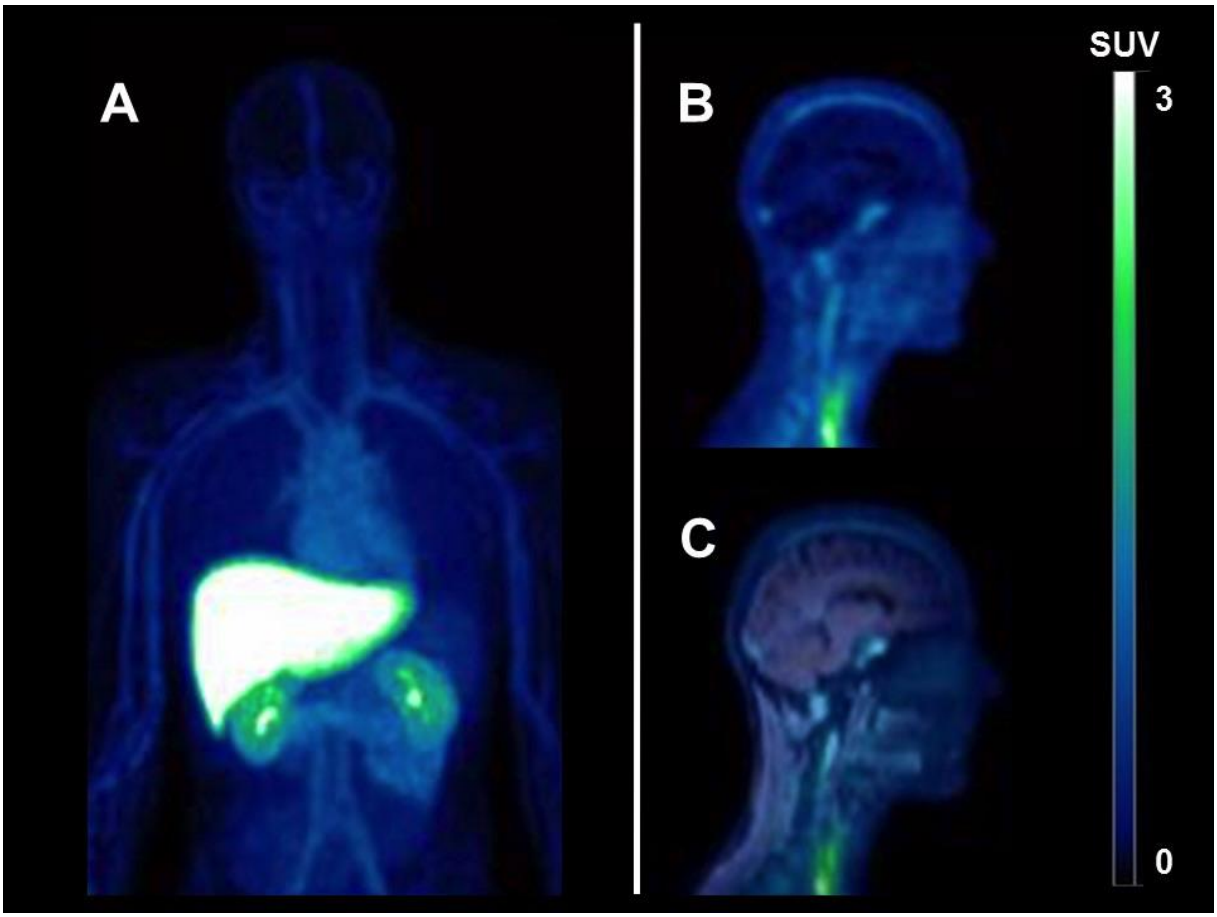
**Fig.1**: **Biodistribution of $^{11}$C-glyburide.** Summed PET projection (A), brain PET (B) and PET-MR fusion (C) images obtained in a 30-year-old healthy male subject after i.v injection of $^{11}$C-glyburide (60 minutes repeated whole-body scans). $^{11}$C-glyburide brain distribution ($V_{T\text{-}brain}$=0.023 mL.cm$^{-3}$) was estimated using the Logan graphical analysis and the metabolite-corrected arterial input function.