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

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**<sup>11</sup>C-glyburide PET imaging unveils the negligible brain penetration of glyburide in human**

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**Contribution**

<b>Name</b>	<b>Location</b>	<b>Role</b>	<b>Contribution</b>
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.<sup>1</sup> 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 <sup>11</sup>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.<sup>2</sup>

## 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  $^{11}\text{C}$ -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  $^{11}\text{C}$ -glyburide (60 minutes repeated whole-body scans).  $^{11}\text{C}$ -glyburide brain distribution ( $V_{\text{T-brain}}=0.023 \text{ mL}\cdot\text{cm}^{-3}$ ) was estimated using the Logan graphical analysis and the metabolite-corrected arterial input function.

