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Evaluation of P-glycoprotein function at the blood–brain barrier using [¹⁸F]MC225-PET

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P-glycoprotein (P-gp) is an ATP-dependent efflux transporter located at the blood–brain barrier (BBB), involved in the transport of a variety of neurotoxic substances out of the brain. Alterations in P-gp function play an essential role in the pathophysiological mechanisms underlying neurodegenerative disorders. The most widely used tracer to measure BBB P-gp function in vivo is (*R*)-[¹¹C]verapamil [1]. However, (*R*)-[¹¹C]verapamil is an avid P-gp substrate, and its low uptake hampers the measurement of increases in P-gp function. In order to overcome this limitation, [¹⁸F]MC225 was developed as a novel PET tracer to measure P-gp function in vivo. [¹⁸F]MC225 is a weaker P-gp substrate and has shown higher brain uptake than (*R*)-[¹¹C]verapamil at baseline in preclinical studies [2]. This may facilitate the evaluation of both increases and decreases in P-gp function.

In addition, the longer half-life of fluorine-18 enables the use of [¹⁸F]MC225 in centers without an onsite cyclotron.

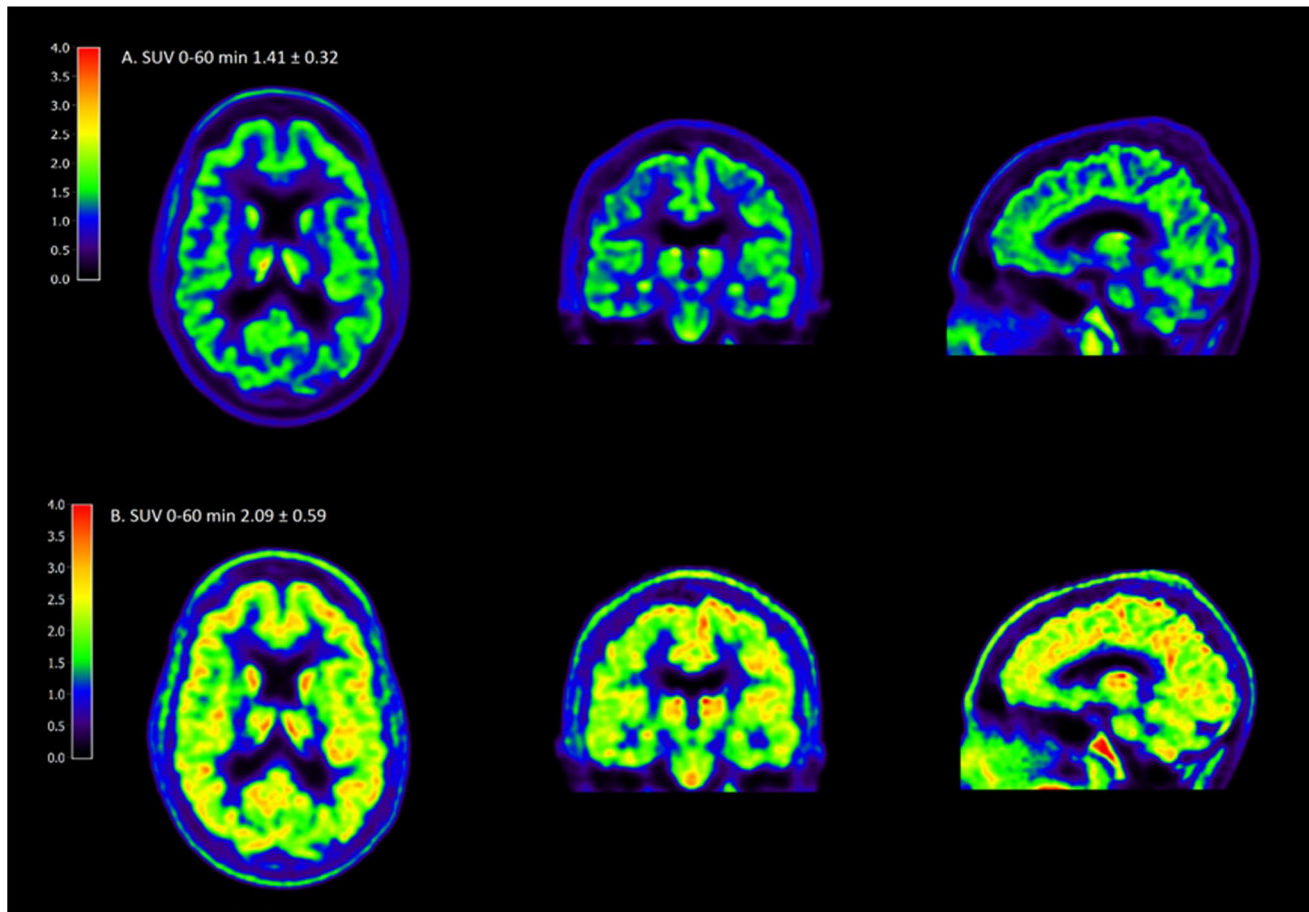
These standardized uptake value (SUV) images show one of the first [¹⁸F]MC225 PET brain scans in a healthy human subject in both unblocked (A) and blocked (B) P-gp state. Blocking was achieved by continuous intravenous administration of the specific P-gp inhibitor cyclosporin (2.5 mg/kg/h), starting 30 min prior to the scan. Quantitatively, the whole brain grey matter volume of distribution V_T changed from $V_T = 4.38$ at baseline to $V_T = 5.48$ after cyclosporin administration, showing higher uptake at baseline levels compared with previously described data of [¹¹C]verapamil ($V_T = 1.28$ at baseline, $V_T = 2.00$ after P-gp inhibition) [3], illustrating [¹⁸F]MC225 as a promising tracer to measure BBB P-gp function in humans.

This article is part of the Topical Collection on Image of the month.

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Declarations

Ethics approval and informed consent All procedures performed involving the human participant were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from the patient.

Competing interests GL received a research grant from Siemens Healthineers for appointing a PhD candidate. The other authors declare no competing interests.

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