

## Brain SPECT-CT versus 8 FDG PET scan

I would like to express my appreciation for the publication of Chen et al. that has piqued my interest. This research delves into the potential usefulness of total body PET scans in Long Covid patients.<sup>1</sup> It appears that the whole-body PET scans you conducted did not provide any meaningful information despite the presence of widespread symptoms associated with Long Covid.

Verger, Guedj, and their team effectively utilised Brain PET Scans to reveal areas of cerebral hypometabolism in patients experiencing symptoms such as fatigue, cognitive impairment, and memory impairment associated with Long Covid.<sup>2 3</sup>

Given the limitations of requesting Brain PET Scans as a general practitioner in Belgium, I opted to request more readily available brain scans such as Technetium SPECT CT scans. Surprisingly almost all clinically severely affected patients (33 out of 38 requested scans) demonstrate a blood flow disorder when undergoing the requested brain scans (Technetium SPECT CT scans).<sup>4</sup>

Binding of the technetium tracers is dependent on cerebral blood flow. Tc-99m is used for brain perfusion studies because of its high first-pass extraction fraction and high affinity for the brain<sup>5</sup>

According to research conducted by Douglas Kell and colleagues, the transport of oxygen at a capillary/cellular level may be hindered by various factors, including fibrin amyloid microclots, platelet hyperactivation/aggregation, and widespread endothelitis. These factors can result in impaired oxygen transport, which may contribute to the symptoms experienced by Long Covid patients<sup>6</sup>. Charfeddine and colleagues have also conducted research on endothelial dysfunction in Long Covid patients.<sup>7</sup>

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<sup>1</sup> Chen, Linda L., et al. "Investigating the Potential Added Value of [18F]FDG-PET/CT in Long COVID Patients with Persistent Symptoms: A Proof of Concept Study." *Nuclear Medicine Communications*, Mar. 2023, <https://doi.org/10.1097/MNM.0000000000001689>.

<sup>2</sup> Verger, Antoine, et al. "Visual Interpretation of Brain Hypometabolism Related to Neurological Long COVID: A French Multicentric Experience." *European Journal of Nuclear Medicine and Molecular Imaging*, vol. 49, no. 9, July 2022, pp. 3197–202, <https://doi.org/10.1007/s00259-022-05753-5>.

<sup>3</sup> E, Guedj, and Horowitz T. "Brain Metabolic PET Findings on the Long-Term Effects of COVID-19." *Journal of Nuclear Medicine : Official Publication, Society of Nuclear Medicine*, vol. 63, no. 9, 2022, <https://www.ncbi.nlm.nih.gov/pubmed/35906093>.

<sup>4</sup> Jamouille, Marc, et al. "Follow-Up of a Cohort of Patients with Post-Acute COVID-19 Syndrome in a Belgian Family Practice." *Viruses*, vol. 14, no. 9, Sept. 2022, p. 2000, <https://doi.org/10.3390/v14092000>.

<sup>5</sup> M, Koyama, et al. "SPECT Imaging of Normal Subjects with Technetium-99m-HMPAO and Technetium-99m-ECD." *Journal of Nuclear Medicine : Official Publication, Society of Nuclear Medicine*, vol. 38, no. 4, 1997, <https://www.ncbi.nlm.nih.gov/pubmed/9098207>.

<sup>6</sup> Kell, Douglas B., et al. "A Central Role for Amyloid Fibrin Microclots in Long COVID/PASC: Origins and Therapeutic Implications." *The Biochemical Journal*, vol. 479, no. 4, Feb. 2022, pp. 537–59, <https://doi.org/10.1042/BCJ20220016>.

<sup>7</sup> Charfeddine, Salma, Hassen Ibn Hadj Amor, et al. "Long COVID 19 Syndrome: Is It Related to Microcirculation and Endothelial Dysfunction? Insights From TUN-EndCOV Study." *Frontiers in Cardiovascular Medicine*, vol. 8, Nov. 2021, p. 745-758, <https://doi.org/10.3389/fcvm.2021.745758>.

It is probably possible to establish a relationship between the endothelial dysfunction observed in Long Covid patients, the presence of microclots, and the blood flow disturbances detected on SPECT-CT scans.

Research conducted recently by South African and Tunisian scientists has demonstrated therapeutic success in treating Long Covid patients using anticoagulants.<sup>8 9</sup>

As far as I am aware, there is currently no direct comparison study available that evaluates the diagnostic utility of SPECT-CT versus PET Scan for brain exploration. Both techniques have their own strengths and limitations and are used in different clinical contexts. SPECT-CT is readily available and can provide valuable information about regional cerebral blood flow, while PET Scan offers superior spatial resolution and the ability to measure metabolic activity in the brain. However, both techniques require further validation for their use in the diagnosis and management of Long Covid-related neurological symptoms.

Comparing the diagnostic value of 8FDG PET Scan and Technetium SPECT-CT in Long Covid patients could be a valuable research endeavour. A direct comparison study would be useful in determining the relative diagnostic performance of these imaging techniques in identifying neurological symptoms associated with Long Covid. Such a study could help to inform clinical practice and aid in the development of effective diagnostic and treatment strategies for Long Covid patients.

The use of Technetium SPECT-CT scans could potentially be a more cost-effective and environmentally-friendly alternative than the 8FDG PET scan. Additionally, by reducing the demand for 8FDG PET Scan, we could lower the burden on healthcare systems and reduce the need for the production and disposal of radioactive materials used in 8FDG PET Scan.

Sincerely

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<sup>8</sup> Gert J Laubscher, M Asad Khan, Chantelle Venter et al. Treatment of Long COVID symptoms with triple anticoagulant therapy, 21 March 2023, PREPRINT (Version 1) available at Research Square [<https://doi.org/10.21203/rs.3.rs-2697680/v1>]

<sup>9</sup> Charfeddine, Salma, Hassen Ibnhadjamor, et al. "Sulodexide Significantly Improves Endothelial Dysfunction and Alleviates Chest Pain and Palpitations in Patients With Long-COVID-19: Insights From TUN-EndCOV Study." *Frontiers in Cardiovascular Medicine*, vol. 9, 2022, <https://www.frontiersin.org/articles/10.3389/fcvm.2022.866113>.