Validation of network-based correlation analysis with [^{11}C]glyburide whole-body PET

Abigail F. Hellman[1], Paul S. Clegg[1], Solène Marie[2], Nicolas Tournier[2], Adriana A. S. Tavares[3,4]

(1) School of Physics and Astronomy, University of Edinburgh, Edinburgh, United Kingdom
(2) Université Paris-Saclay, CEA, Inserm, CNRS, BioMaps, Service Hospitalier Frédéric Joliot, Orsay, France
(3) University/British Heart Foundation (BHF) Centre for Cardiovascular Science, The Queen's Medical Research Institute, University of Edinburgh, Edinburgh, United Kingdom
(4) Edinburgh Imaging, University of Edinburgh, Edinburgh, United Kingdom

Network analysis is a form of correlation analysis that is particularly useful in performing whole-body studies with positron emission tomography (PET), as it provides a way to quantify the similarities and differences in the data from a range of organs and patients. Network analysis was performed on dynamic whole-body PET with [^{11}C]glyburide in humans, with and without infusion of rifampicin [1]. Glyburide is a substrate of several Organic Anion-Transporting Polypeptides (OATPs), which are proteins that control the uptake of drugs into the liver, although OATP expression in other organs has been reported. Rifampicin is a strong OATP inhibitor that has been shown to decrease the body's ability to eliminate glyburide [1].

Time-activity curves (TACs) in kBq/mL from several organs of interest were used to perform network analysis with the Pearson correlation coefficient employed as the linear correlation measure. In the liver, network analysis was able to differentiate the control and rifampicin-treated groups (Fig. 1A). In this network, each node represents an average TAC from the liver of one patient (Fig. 1C), and the edges between nodes represent significant correlations. The edges are colour-coded to the strength of the Pearson value, showing stronger, more dense correlations within the control group.

Additionally, network analysis was performed on static PET data (Fig. 1B), where each node represents a patient curve comprised of the average activity in each organ at equilibrium (Fig. 1D). With the static data, network analysis was able to separate the control and treatment groups into two components. This is highly dependent on the liver though and removing it from the curves leads to reduced differentiation.

Overall, network analysis is sensitive to the differing uptake of [^{11}C]glyburide throughout the body under normal and rifampicin-treated conditions. It provides confirmation that the control and treatment groups differ largely through the uptake in the liver, which is the predominant site of OATP function.

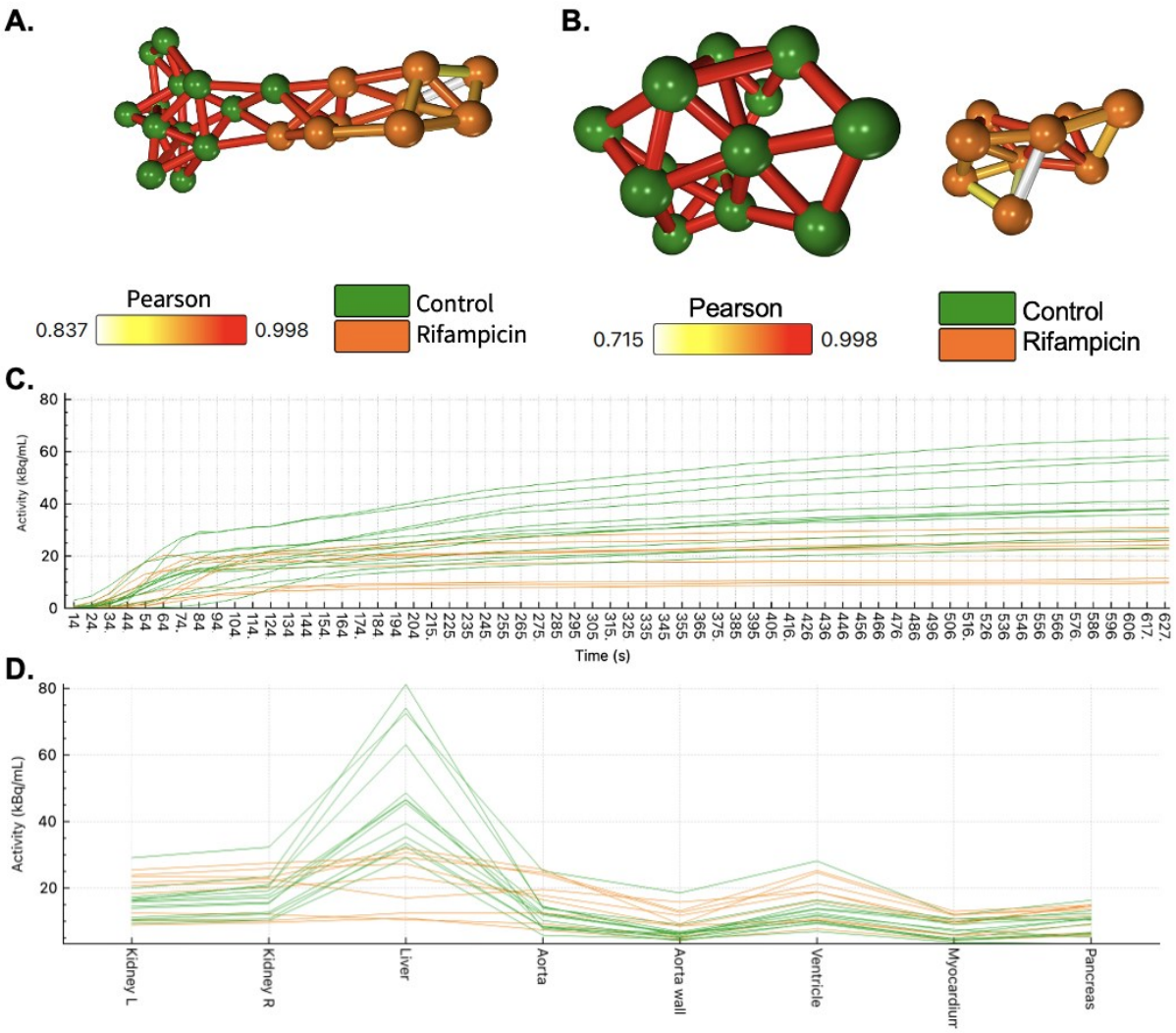

Figure. 1. A. Liver-specific multi-subject network derived from [^{11}C]Glyburide PET TACs **B.** comparing control subjects to those treated with rifampicin. **C.** Multi-subject network derived from static [^{11}C]Glyburide PET data **D.** comparing control and rifampicin-treated subjects.

References:

(1) Marie S, Breuil L, Chalampalakis Z, Becquemont L, Verstuyft C, Lecoq AL, et al. *[^{11}C]glyburide PET imaging for quantitative determination of the importance of Organic Anion-Transporting Polypeptide transporter function in the human liver and whole-body.* Biomed Pharmacother. 156, 113994 (2022). DOI: 10.1016/j.biopha.2022.113994.