[^{18}F]F-AraG PET Imaging Reveals Increased Gut T-Cell Activation in People With Long COVID

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BACKGROUND

- We hypothesize that people living with Long COVID have increased tissue T-cell activation compared with those who have fully recovered.

We previously demonstrated increased T-cell activation across tissues (e.g., bone marrow, spinal cord, lung parenchyma, pulmonary vasculature, nasal, pharyngeal colorectal) in people months to years following SARS-CoV-2 infection compared to participants imaged prior to the COVID-19 pandemic using a novel PET imaging tracer of T cell activation ([^{18}F]F-AraG). [Peluso, et al., Sci. Transl. Med. 2024] The relationships between persistent whole-body T-cell activation and various Long COVID (LC) clinical phenotypes, however, is not known.

METHODS

- We performed PET imaging on 65 individuals, months to years following initial COVID-19 infection and analyzed [^{18}F]F-AraG distribution across the whole body in those with and without Long COVID (LC). [^{18}F]F-AraG is a small-molecule guanosine analog PET tracer specific for activated T-cells (CD8 > CD4).

- Whole-body PET-CT imaging was performed ~50 minutes following [^{18}F]F-AraG iv injection (5mCi). Standardized uptake values (SUV) across tissue regions of interest in people with LC (n=51) at the time of imaging were compared with those who recovered rapidly after initial infection without residual symptoms (n=15).

- Non-parametric comparisons between LC phenotypes and SUV were performed adjusting for false discovery within tissue groups.

Infectious Disease Molecular Imaging

LIINC Long-term Impact of Infection with Novel Coronavirus

Non-invasive PET imaging revealed increased T-cell activation in colorectal tissues in participants with cardiopulmonary Long COVID and increased T-cell activation in skull base bone marrow in those with persistent olfactory dysfunction compared to fully recovered controls.

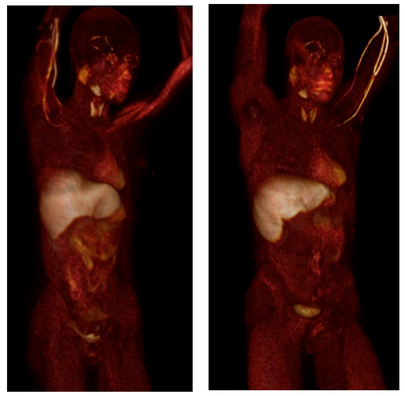
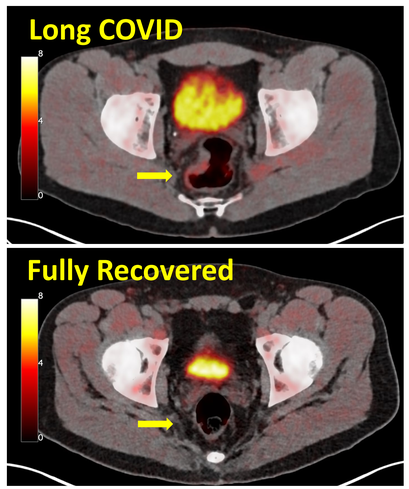


Figure 1: Examples of volume rendered PET images from participants with (left) and without (right) LC.



RESULTS

- We observed significantly higher rectosigmoid wall mean SUVs in people with LC versus fully recovered and in people reporting cardiopulmonary symptoms (n=37; i.e., cough, shortness of breath, heart rhythm abnormalities, chest pain; vs the 28 participants that did not report CP symptoms (0.78 vs 0.51, P=0.019; 0.84 vs 0.57, P=0.013, respectively).

- We observed significantly increased T-cell activation at the skull base bone marrow (peri-oropharyngeal) in people with lingering olfactory dysfunction.

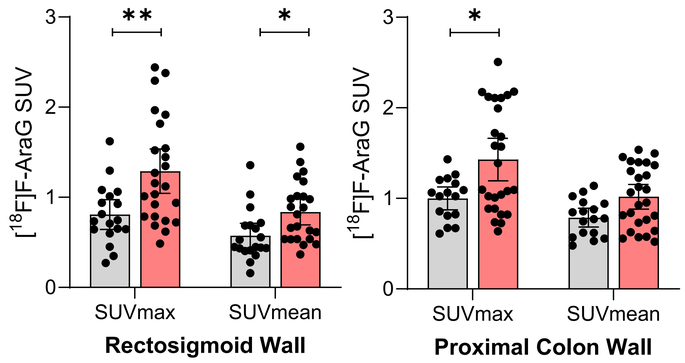


Figure 2: Increased gut wall [^{18}F]F-AraG uptake in people with cardiopulmonary LC Examples of axial PET-CT fused images from sample participants (left); tracer uptake values in colorectal tissues from people with (red) and without (gray) cardiopulmonary LC (top panels). *P<0.05, **P<0.01 by Kruskal-Wallis test with FDR correction.

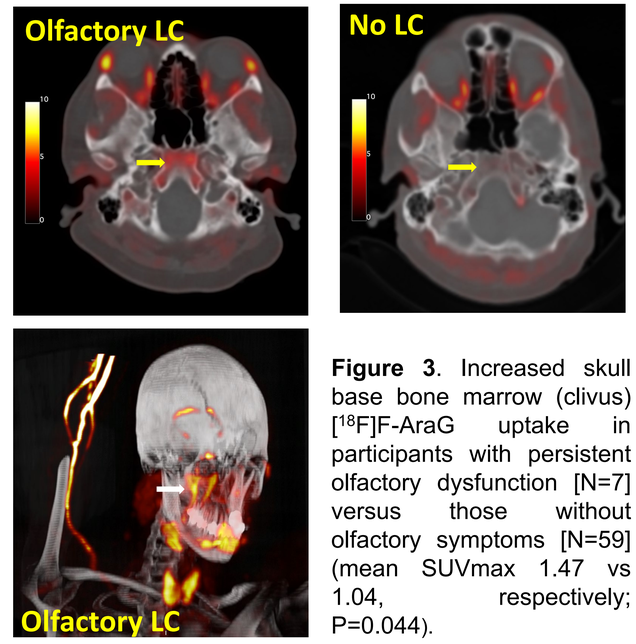


Figure 3. Increased skull base bone marrow (clivus) [^{18}F]F-AraG uptake in participants with persistent olfactory dysfunction [N=7] versus those without olfactory symptoms [N=59] (mean SUVmax 1.47 vs 1.04, respectively; P=0.044).

- There were no other significant differences observed across tissues in other LC phenotypes (including fatigue, sleep disturbances, musculoskeletal, gastrointestinal, neurocognitive) compared to fully recovered participants.

CONCLUSIONS

- Non-invasive PET imaging revealed increased uptake of T-cell activation in colorectal tissue in those with Long COVID versus those who fully recovered in unique anatomical regions.
- People with cardiopulmonary LC had higher T-cell activation measured by [^{18}F]F-AraG in colorectal wall tissue compared to those without LC and people with olfactory LC symptoms had higher skull base marrow tracer uptake than those without olfactory abnormalities.
- Our data suggest that the etiology of various LC clinical phenotypes is likely heterogenous and may need to be considered as different etiologic entities.

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