FDG-PET/CT investigation of the pathology of a SARS-CoV-2 VSV pseudotype and its role as an oncological imaging confounder

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Background and Aims

- SARS-CoV-2 has led to 608 million infections and 6.5 million deaths (Sep 19, 2022)[1]
- Estimated that at least 11% of Canadians and 27% of Americans have been infected
- Infection and vaccination seen to interfere with clinical FDG-PET scans[2]
- Fluoro-2-deoxy-D-glucose (FDG) preferentially taken up by cells with increased glucose metabolism[3,4]
- COVID-19 inflammation mimics cancer FDG uptake patterns
- COVID-19 is a CL3 pathogen → Expensive and difficult to work with
  - VSVΔG S expresses the spike protein of COVID-19 to facilitate early research

Goal: Characterize imaging and biological features of infection with VSV expressing SARS-CoV-2 spike.

Methods

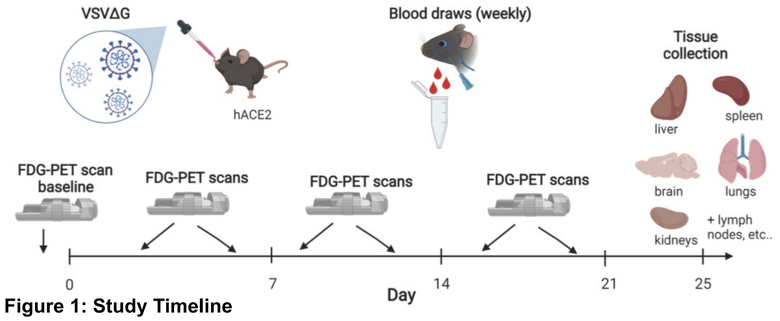
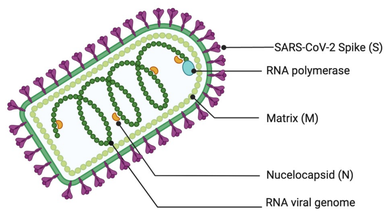
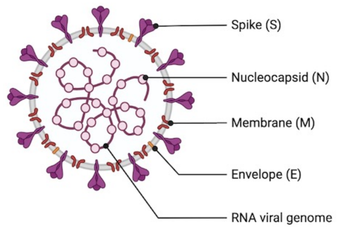


Figure 1: Study Timeline

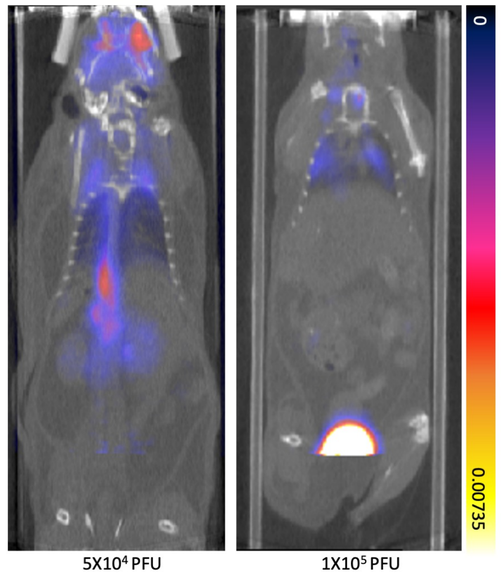
Experimental Design

- **Mouse model:**
  - K-18-hACE2 mice (C57BL/6 background)
  - Express human ACE2 under control of the K18 promotor
  - Directed expression to epithelial tissues, mimics human ACE2 distribution
- **Biological analysis:**
  - Samples: weekly and terminal blood, terminal organ collection
  - Flow cytometry for immune phenotyping
  - Level of GFP+ cells as marker of infection level
- **Groups:**
  - Low titre: 5X10^4 PFU
  - High titre: 1X10^5 PFU
  - Mock infection: 1X PBS
  - Naïve control
- **FDG-PET/CT:**
  - 500μCi injection 30 minutes prior to scan
  - 70kVp CT
  - Imaging 2X weekly
- **Virus model:**
  - VSVΔG S (GFP+)
  - Pseudotype virus expressing the S protein of COVID-19
  - Intranasal administration to mimic human route of infection





Results



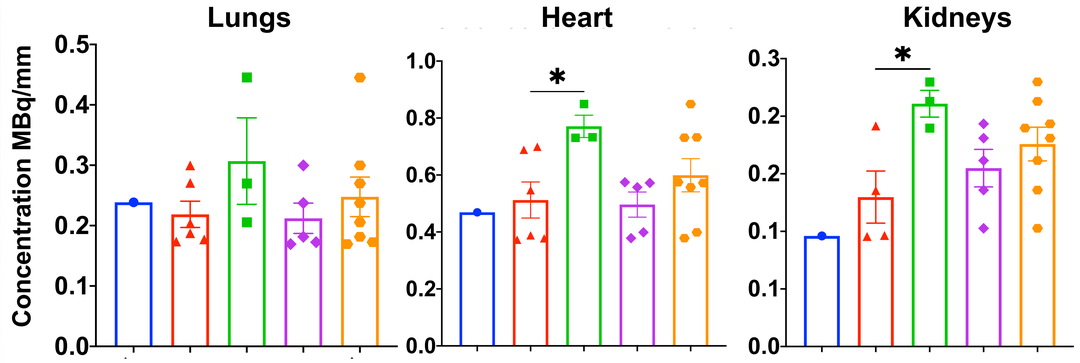


Figure 2:The heart and kidneys of infected mice show significantly higher FDG uptake than those of control and mock infected mice. A) FDG-PET/CT images from a mouse in the low titre infection (5X10^{4}PFU) and high titre infection (1X10^{5}PFU) groups, taken on days 6 (low titre) and 5 (high titre). In both mice there are regions of increased FDG uptake in the lungs, with the low titre mouse also showing high uptake in the kidneys. These imaging features were not present in control animals. Data was obtained using a 30 minute PET scan from the Cubresa NuPET BIO with 500μCi of FDG left to uptake for 30 minutes. CT images were obtained using a Trifoil CT at 70kVp with a magnification of 1.36**. B)** Levels of FDG uptake in the heart, kidneys, and lungs for control and infected mice. **(*P<0.05)**

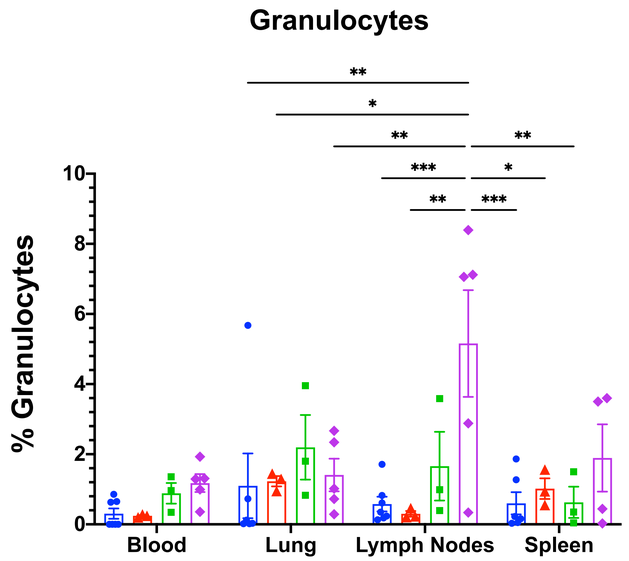


Figure 4: Increase in granulocytes in infected groups in the lungs and lymph nodes. Granulocytes were defined as CD11c+ Ly6C- Ly6G+ live single cells. In the lymph nodes there were marked increases in the levels of these cells between infected and control mice, with increases also seen between the same groups in the lungs, spleen and blood. **(*P<0.05, **P<0.01, *** P<0.001)**

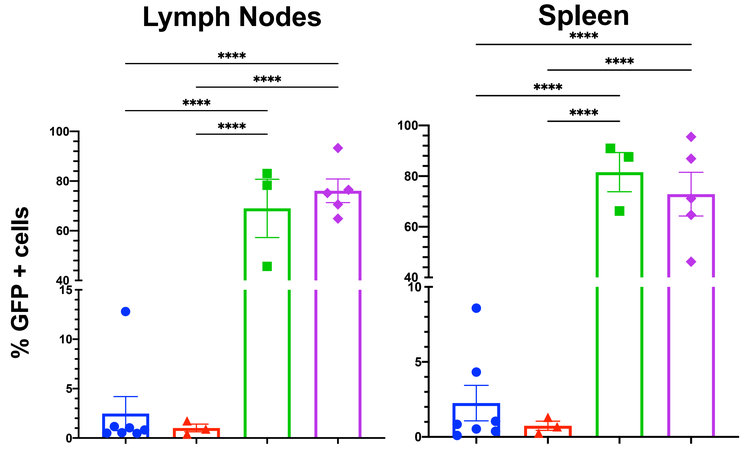


Figure 3: Levels of GFP+ cells increased significantly in infected groups. The VSVΔG S pseudovirus is GFP positive. The presence of more GFP+ cells in infected groups supports the potential of using GFP level as a marker of infection. **(*P<0.05, **P<0.01, *** P<0.001)**

Conclusions & Future Directions

CONCLUSIONS

- GFP levels can be used as markers of VSV infection
- Higher granulocytes are likely infiltrating neutrophils - they have been linked to increased FDG uptake[5,6]
- Corresponds to FDG uptake & granulocytes in lungs
- Increased FDG uptake in infected groups indicates a possible role of the virus as an imaging confounder

FUTURE WORK

- Compare pseudotype model to SARS-CoV-2
- Test in male mice to investigate sex-based differences
- Test the impact of vaccination on imaging features and disease pathology
- Test the potential of FDG-PET/CT to monitor vaccine induced pathology
- Test the impact of (co-)infection with a common cold hCoV on imaging features
- Investigate imaging changes of infection in mice implanted with the E0771.lmb breast cancer cell line

References and Acknowledgements

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