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Title: PET imaging with [^{11}C]PBR28 and [^{18}F]FDG distinguishes macrophage from neutrophil lung inflammation

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Body: Introduction: Noninvasive methods for quantifying macrophage and neutrophil activation and recruitment in chronic obstructive pulmonary disease (COPD) would be highly useful in assessing the efficacy of anti-inflammatory therapies. Objective: To test whether positron emission tomography (PET) imaging with [^{11}C]PBR28 and [^{18}F]fluorodeoxyglucose ([^{18}F]FDG) could distinguish macrophage-dominant from neutrophilic inflammation in a mouse model of COPD. Methods: C57BL/6J mice inoculated with PBS or Sendai virus were imaged by microPET (Inveon or Focus 220, Siemens/CTI) with both [^{11}C]PBR28 and [^{18}F]FDG at Days 3 and 84 post-inoculation (p.i.). Regions of interest placed over the lungs determined the % injected dose per cc (%ID/cc) at 60 min. Lung sections were stained for TSPO ([^{11}C]PBR28 ligand), Ly6G (neutrophil marker) and CD68 (macrophage marker). Results: Only [^{18}F]FDG uptake increased significantly during acute illness at p.i. Day 3. Both [^{11}C]PBR28 and [^{18}F]FDG uptake increased significantly during chronic disease at p.i. Day 84. The [^{11}C]PBR28:[^{18}F]FDG ratio, calculated for each mouse, was no different between infected (1.9 ± 0.3) and uninfected mice (2.0 ± 0.4) at p.i. Day 3. This ratio increased significantly at p.i. Day 84 (3.1 ± 0.9) in infected mice compared to controls (1.7 ± 0.5). Lung sections showed macrophages with intense TSPO staining at p.i. Day 84. Conclusion: PET imaging with [^{11}C]PBR28 and [^{18}F]FDG quantitatively distinguishes macrophage-dominant from neutrophilic inflammation in a mouse model of COPD. This approach may be useful for monitoring the pulmonary macrophage burden in humans with COPD, thereby guiding emerging targeted anti-inflammatory therapies.