PET-Guided Histological Characterization of Myocardial Infiltrating Cells in a Rat Model of Myocarditis

Rudolf A. Werner[1,2,3], Hiroshi Wakabayashi[1,2], Roland Jahns[2,4], Süleyman Ergün[5], Valerie Jahns[2,6], Takahiro Higuchi[1,2]

1. Department of Nuclear Medicine, University Hospital Wuerzburg, Wuerzburg, Germany;
2. Comprehensive Heart Failure Center, University Hospital Wuerzburg, Wuerzburg, Germany;
3. Interdisciplinary Center for Clinical Research, Else-Kröner-Forschungskolleg, University Hospital Wuerzburg, Wuerzburg, Germany;
4. Interdisciplinary Bank of Biomaterials and Data Wuerzburg (ibdw), University Hospital Wuerzburg, Wuerzburg, Germany
5. Institute for Anatomy and Cell Biology, University Wuerzburg, Germany.
6. Department of Pharmacology, University Hospital Wuerzburg, Wuerzburg, Germany.

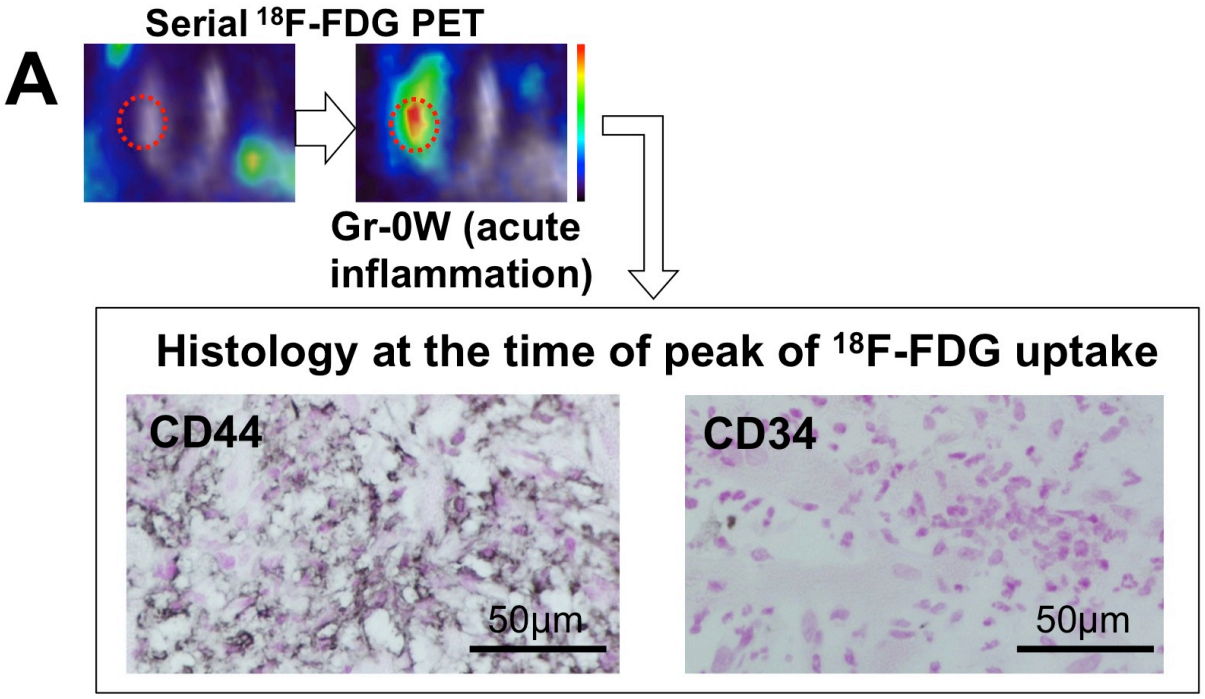
ABSTRACT

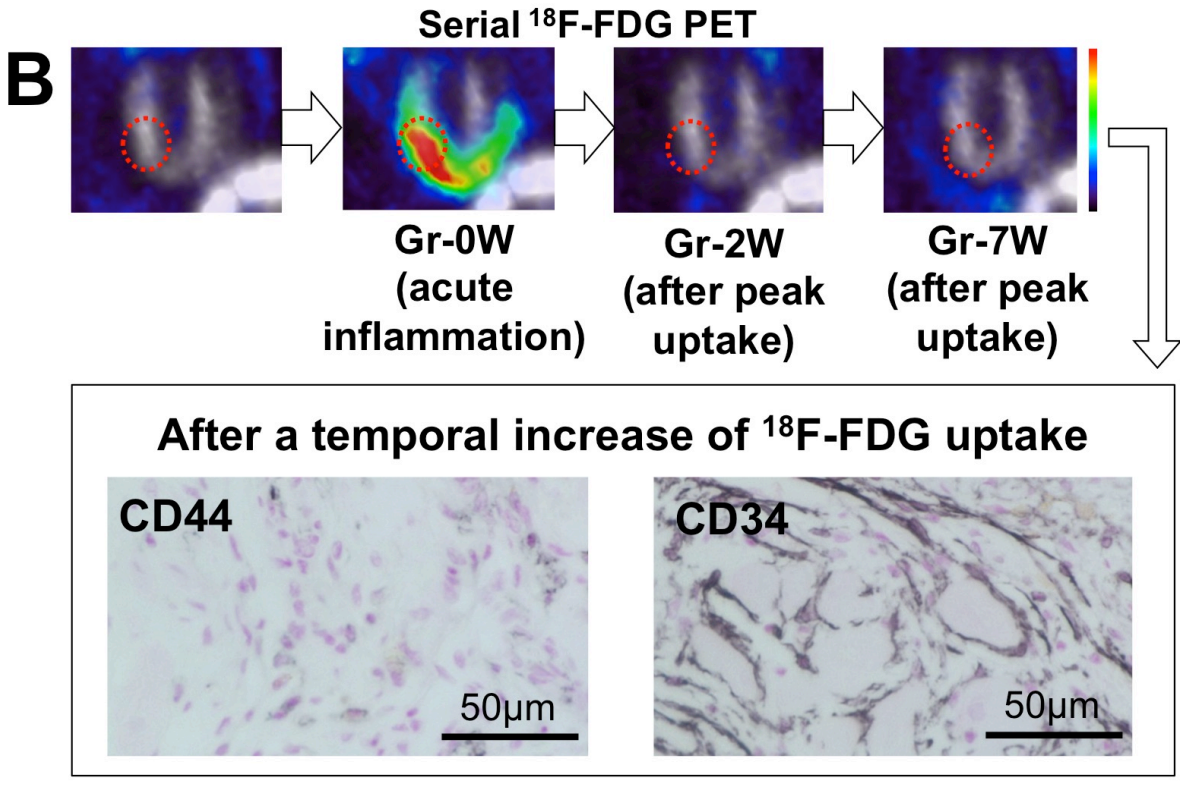
Background: Serial non-invasive inflammatory imaging would provide better understanding of subsequent histological findings. The aim of this study is to elucidate the dynamic cellular expression of adhesion molecules in acute autoimmune myocarditis in association with the prior time course of inflammatory activities identified by serial ^{18}F-FDG imaging.

Methods: Autoimmune myocarditis was induced in Lewis rats by immunizing with porcine cardiac myosin emulsified in complete Freund's adjuvant. First, serial ^{18}F-FDG PET imaging (2,3,4,5 and 10 weeks after immunization) was performed to determined the time course and feasibility of monitoring acute cardiac inflammation. Next, based on the individual results of serial ^{18}F-FDG imaging, animals were assigned for three inflammatory stages: acute inflammation (Gr-0W) as well as 2 weeks (Gr-2W) and 7 weeks (Gr-7W) after the peak of acute inflammation, respectively. Histological analysis at each stages was conducted for adhesion markers (CD44 and CD34).

Results: Serial ^{18}F-FDG PET imaging revealed focal and temporal increased tracer uptake in the heart peaked at around week 3 in average and decreased rapidly. Localization of CD68 positive cell infiltrations and ^{18}F-FDG uptake signals were well correlated ($R=0.91$, $P<0.0001$). To be noted, the cardiac inflammation after the immunization was highly variable between individual animals inlcuding no inflammatory induction in 3/23 (13%). Based on the serial individual ^{18}F-FDG findings, different stages of cardiac inflammatory tissue samples were successfully identified (Gr-0W n=4, Gr-2W, n=5, Gr-7W, n=5). High CD44-expressing cells were observed in the entire inflammatory lesions of Gr-0W and decreased time dependently in Gr-2W and Gr-7W. On the other hand, CD34 positive cells were scarce and only observed in the margins in Gr-0W, while strong expression was seen in the sample tissue of Gr-2W and Gr-7W.

Conclusions: Acute autoimmune myocarditis was successfully induced in Lewis rats and monitored by non-invasive serial ^{18}F-FDG PET imaging. Furthermore, histological characterization of adhesion molecules at different stages of inflammation guided by individual ^{18}F-FDG uptake signals was conducted. Preclinical longitudinal imaging of EAM rats might pave the way for a deeper understanding of the pathogenetic mechanisms involved in autoimmune myocarditis.





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