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Re: Increased ^{18}F-2-Fluorodeoxysorbitol (^{18}F-FDS) Activity in a Pituitary Spindle Cell Carcinoma

Mehrbod S. Javadi[1], **Alvaro A. Ordonez**[2,3], and **Sanjay K. Jain**[2,3]

[1]Russell H. Morgan Department of Radiology and Radiological Science, Johns Hopkins University School of Medicine, Baltimore, MD, USA

[2]Center for Infection and Inflammation Imaging Research, Johns Hopkins University School of Medicine, Baltimore, MD, USA

[3]Department of Pediatrics, Johns Hopkins University School of Medicine, Baltimore, MD, USA

To the Editor

We read the report by Cheng *et al* describing ^{18}F-2-fluorodeoxyglucose (^{18}F-FDG) and ^{18}F-2-fluorodeoxysorbitol (^{18}F-FDS) PET to differentiate malignancy from inflammation in a 33-year old woman with a pituitary spindle cell carcinoma.[1] Li *et al* were the first to synthesize ^{18}F-FDS, and reported visualization of both glioblastoma xenografts (U87MG) as well as inflammatory foci in mice, at early time-points after tracer injection.[2] It appears that the strong implication by Cheng *et al* that ^{18}F-FDS has the potential to differentiate malignancy from inflammation is admirable in enthusiasm but may be factually inconsistent with the current state of the art.

Cheng *et al* reported PET SUVmax of 4.73 (^{18}F-FDG) and 1.49 (^{18}F-FDS) respectively, at the site of the pituitary spindle cell carcinoma.[1] However, Li *et al* reported that ^{18}F-FDS exhibits very poor *in vitro* uptake by mammalian cells – 0.1% for ^{18}F-FDS versus up to 40% for ^{18}F-FDG in U87MG cells.[2] There are no transporters for ^{18}F-FDS entry into mammalian cells and the substitution of the hydroxyl group by fluorine at the 2C-position completely abrogates the recognition by mammalian enzymes.[3] Moreover, Li *et al* visualized tumors and inflammation in mice by ^{18}F-FDS PET in the context of high background at earlier time points after tracer injection (5–60 min). Therefore, given the lack of specific-uptake mechanisms, they suggested that increased blood flow and leaky vasculature were responsible for visualization of xenografts (U87MG) as well as inflammatory foci.[2] These findings are also consistent with the data by Weinstein and Ordonez *et al* who also demonstrated the lack of ^{18}F-FDS uptake in healthy mammalian or cancer cells.[4] Interestingly, Weinstein and Ordonez *et al* reported substantial (~1000-fold higher than mammalian cells) and specific uptake of ^{18}F-FDS in Gram-negative bacteria (Enterobacteriaceae). At 120 min after ^{18}F-FDS injection in mice, infectious foci due to these bacteria were clearly visualized by PET, but no appreciable signal was noted at the sites of (sterile) inflammation or U87MG brain xenografts.[4] Furthermore, dynamic ^{18}F-FDS

Corresponding author: Sanjay K. Jain, M.D., 1550 Orleans Street, CRB-II, Rm 1.09, Baltimore, MD 21287, Tel: 410-502-8241, Fax: 410-614-8173, sjain5@jhmi.edu.

PET studies in mice with U87MG brain tumors demonstrated some initial signal, which however dissipated 60–120 min after tracer-injection.

In conclusion, ^{18}F-FDS may be useful to detect infectious foci due to Enterobacteriaceae.[4] While the sensitivity and specificity of this technique in the clinical setting remains to be determined, it is likely that ^{18}F-FDS uptake at the sites of sterile inflammation and malignancy (as demonstrated by Cheng *et al*), is consistent with a non-specific blood pool effect; that is, capillary leak at the site of inflammation or malignancy.

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