A discordant pattern of uptake on ^{68}Ga-PSMA PET/CT versus ^{18}F-fluciclovine PET/CT in radiation-induced hepatitis: implications for early post-radiotherapy imaging-based response assessment

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Abstract: A 62-year-old female patient with right-sided invasive lobular breast carcinoma (ILC) completed external beam radiotherapy 6 weeks before undergoing a ^{68}Ga-PSMA PET-CT and ^{18}F-fluciclovine PET-CT scan as part of an ongoing clinical trial (NCT04750473) assessing the performance of these molecular imaging modalities in ILC. The ^{68}Ga-PSMA PET-CT demonstrated a band-like area of increased radiotracer uptake in the dome of the right lobe of the liver anteriorly, while ^{18}F-fluciclovine PET-CT done a day later revealed photopenia in the

corresponding area of the liver. The external beam radiotherapy plan confirmed that the radiotherapy field overlaid the region of the hepatic discordant radiotracer uptake on the PET-CT scans.

Keywords: ^{68}Ga-PSMA PET, ^{18}F-fluciclovin PET, Radiation hepatitis, PET-based response assessment of radiotherapy, Lobular breast cancer

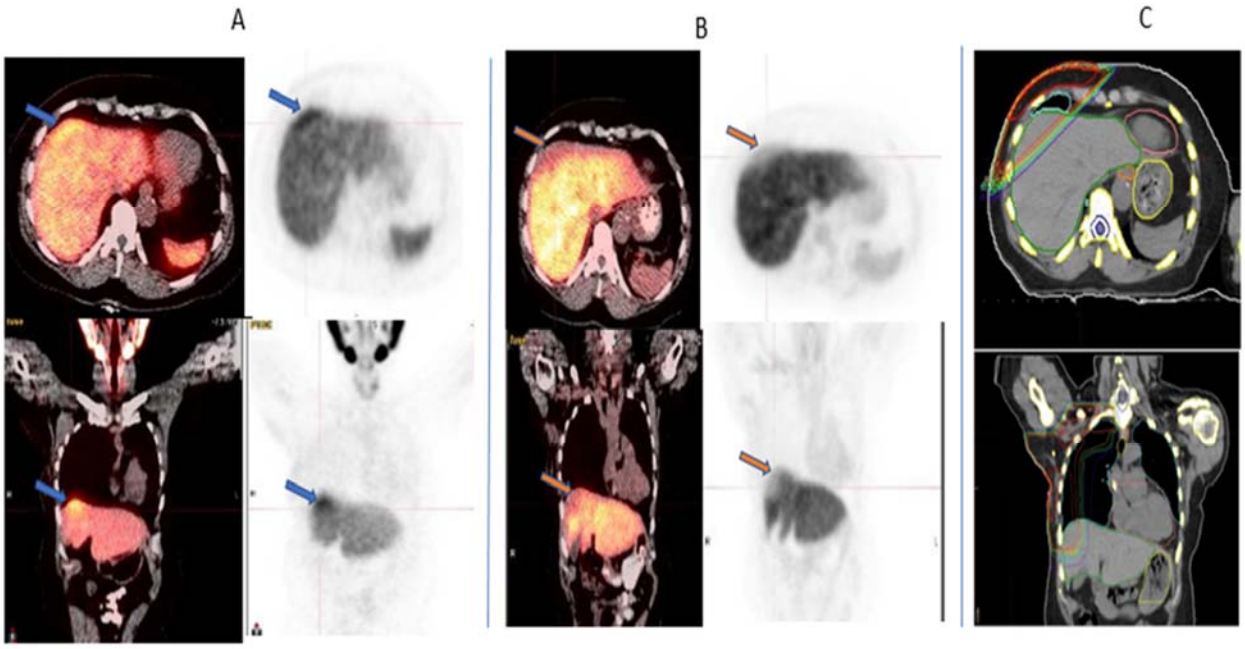

Figure 1: A 62-year-old female patient with right-sided invasive lobular breast carcinoma (ILC) completed external beam radiotherapy 6 weeks before undergoing a ^{68}Ga-PSMA PET-CT and ^{18}F-fluciclovine PET-CT scan as part of an ongoing clinical trial assessing the performance of ^{68}Ga-PSMA PET-CT and ^{18}F-fluciclovine PET-CT for staging and re-staging ILC. The ^{68}Ga-PSMA PET-CT demonstrated a band-like area of increased radiotracer uptake in the dome of the right lobe of the liver anteriorly (Blue arrows in A, axial and coronal fused PET/CT and PET images). ^{18}F-fluciclovine PET-CT done a day later revealed photopenia in the corresponding area of the liver (Red arrows B, axial and coronal fused PET/CT and PET images). The external beam radiotherapy plan confirmed that the radiotherapy field overlaid the region of the hepatic discordant radiotracer uptake on the PET-CT scans (C: axial and coronal CT radiotherapy planning images). This case illustrates the differences in the appearance of radiation-induced hepatitis on two different radiotracers approved for prostate cancer imaging. We hypothesize that the increased radiotracer uptake on the ^{68}Ga-PSMA PET may be explained by neovascularization which could occur in the liver tissue due to inflammation from the radiation. In distinction, the reduced uptake on ^{18}F-fluciclovine PET may be due to reduced amino acid utilization in radiation-damaged hepatic cells, reflecting diminished metabolism. Inflammation

accompanying post-radiation hepatitis has been previously reported on FDG PET-CT [1,2]. To our knowledge, the appearance of radiation-induced hepatitis on ^{68}Ga-PSMA and ^{18}F-fluciclovine PET-CT has not been previously reported. The discordant findings in this patient may have implications for post-radiotherapy response assessment using these radiotracers in the acute timeframe. Acute radiation-induced hepatitis occurs within 2 to 12 weeks after radiation damage to the liver [3]. Pathologic liver changes that predominate during this stage include portal and systemic venous congestion, thrombi within the sinusoids, perisinusoidal hemorrhages, reactive hyperemia, atrophy, and degeneration of hepatocytes [3]. Tissue hypoxia created by these vascular changes promotes neovascularization via the expression of angiogenic cytokines [4]. ^{18}F- fluciclovine is less prone to uptake in acute inflammatory cells such as granulocytes and macrophages [5]. This explains the photopenia seen on the ^{18}F-fluciclovine PET/CT images in this patient. Radiolabeled PSMA ligand uptake has been described in inflammation likely due to the presence of PSMA receptors in neovasculature associated with regeneration and repair [6-8]. The awareness of these findings, therefore, may find application in guiding the timing of PET-based response assessment post-radiotherapy.

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