Comparison of ^{68}Ga-FAPI versus ^{18}F-FDG PET/CT for Initial Cancer Staging

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Take-Away Points

- Major Focus: To compare ^{68}Ga-FAPI, a fibroblast-activated protein inhibitor (FAPI) coupled with radioactive gallium 68, with fluorine 18 fluorodeoxyglucose (^{18}F-FDG) PET/CT.
- Key Result: In a direct comparison, ^{68}Ga-FAPI PET/CT outperformed ^{18}F-FDG PET/CT in sensitivity and specificity for primary, nodal, and metastatic lesion characterization across different tumor types.
- Impact: ^{68}Ga-FAPI PET/CT is safe, and initial studies show it is more accurate than ^{18}F-FDG PET/CT for oncologic staging. Additionally, coupled with its theranostic potential, ^{68}Ga-FAPI could become a widely used PET radiotracer in oncologic imaging in the future.

Currently, ^{18}F-FDG PET/CT is the workhorse of oncologic nuclear medicine. ^{18}F-FDG PET takes advantage of the propensity that most tumor cells consume high levels of glucose. However, accumulation of FDG by nonmalignant cells limits detection of cancer in tissue with high native glucose uptake, and not all cancer cells preferentially metabolize glucose. ^{18}F-FDG PET/CT lacks specificity, as activated immune cells in tumors or inflammatory lesions also accumulate the radiotracer. Fibroblast-activated protein is expressed at very low levels throughout the body; however, it is highly expressed on cancer-associated fibroblasts. Therefore, ^{68}Ga-FAPI PET/CT may be more specific for imaging tumors.

Chen et al compared the standard uptake value of cancer lesions in 75 patients with 12 different tumor types who underwent both scans within 1 week. A per-lesion analysis showed greater sensitivity of ^{68}Ga-FAPI PET/CT for primary lesions (98.2% vs 82.1%, $P = .021$), metastatic nodes (86.4% vs 45.5%, $P = .004$), and bone and visceral metastases (83.8% vs 59.5%, $P = .004$) than ^{18}F-FDG PET/CT, likely because of the higher tumor-to-background signal ratio for ^{68}Ga-FAPI. Biopsies of some discordant lesions did not find ^{68}Ga-FAPI PET/CT to be less specific than ^{18}F-FDG PET/CT. In this initial study, authors also present some intriguing findings that might be a harbinger of limitations in larger and more diverse populations. One primary pancreatic cancer was not found on ^{68}Ga-FAPI PET/CT, likely because of high uptake of the whole gland due to concurrent pancreatitis. ^{68}Ga-FAPI PET showed false-positive findings not seen with FDG, namely a bone lesion due to myelofibrosis, a mass-forming liver cirrhotic lesion, and pleural thickening caused by mycobacterial infection. These false-positive findings all share benign fibrosis.

With FAPIs being tested in clinical trials for cancer treatment, ^{68}Ga-FAPI PET/CT may be applied both for detecting cancer and selecting patients for treatment.

—Mateus Taveira

Highlighted Article

Chen H, Pang Y, Wu J, et al. Comparison of [^{68}Ga]Ga-DOTA-FAPI-04 and [^{18}F] FDG PET/CT for the diagnosis of primary and metastatic lesions in patients with various types of cancer. Eur J Nucl Med Mol Imaging 2020;47;1820–1832. doi: https://doi.org/10.1007/s00259-020-04769-z