Novel ⁶⁸Ga-FAPI PET/CT offers oncologic staging without COVID-19 vaccine-related pitfalls

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ABSTRACT

In the setting of ongoing COVID-19 vaccination, vaccine-related tracer uptake in locoregional lymph nodes has become a well-known issue in tumor staging by ¹⁸F-FDG PET/CT. ⁶⁸Ga-FAPI PET/CT is a new oncologic imaging tool that may overcome this limitation.

Methods: We assessed post-vaccine, head-to-head and same-day ¹⁸F-FDG and ⁶⁸Ga-FAPI-46 PET/CT findings in a series of 11 patients from a large prospective imaging registry. All patients with documented tracer uptake in locoregional lymph nodes on PET/CT or PET/MRI, following vaccination within 6 weeks, were eligible for investigation.

Result: Significant visual lymph node uptake adjacent to the injection site was noted in 11/11 (100%) patients with ¹⁸F-FDG PET/CT versus 0/11 (0%) with ⁶⁸Ga-FAPI PET/CT. ¹⁸F-FDG detected 73% and ⁶⁸Ga-FAPI PET/CT 94% of all tumor lesions.

Conclusion: In this case-series study, ⁶⁸Ga-FAPI showed its potential to avoid ¹⁸F-FDG-PET/CT post-vaccination pitfalls and presented superior tumor localization.

INTRODUCTION

Since the outbreak of the COVID-19 pandemic in 2019 and the start of global mass vaccination in November 2020, several clinical studies have addressed the issue of reactive tracer accumulation in locoregional lymph nodes and upper arm muscles (1). At local sites, ¹⁸F-FDG is taken up by immune cells responding to the mRNA inflammatory stimulus (2–4). This observation is concerning as vulnerable groups, such as oncologic patients, undergo both regular booster shots and medical imaging. False positive findings on ¹⁸F-FDG PET due to uptake in inflammatory cells may trigger false management decisions.

⁶⁸Ga-FAPI PET/CT is a novel imaging test directed at cancer-associated fibroblasts in the tumor stroma. Due to its unique mechanism targeting only activated fibroblasts and subtypes of cancer-associated fibroblasts, ⁶⁸Ga-FAPI PET/CT may be able to avoid false positive postvaccine uptake. ⁶⁸Ga-FAPI PET/CT has emerged as a potential alternative to ¹⁸F-FDG PET/CT in many tumor types and may avoid locoregional pitfalls caused by vaccination. Here we assess, same-day head-to-head post-vaccine ¹⁸F-FDG and ⁶⁸Ga-FAPI PET/CT uptake in patients from a large prospective registry of oncologic imaging collected during the ongoing mass vaccination campaign in Germany.

METHODS

We selected 11 patients with ⁶⁸Ga-FAPI and ¹⁸F-FDG PET/CTs (May 2021 to April 2022) from our prospective database, which is part of a large prospective observational study (NCT04571086). Enrollment is offered to all patients who undergo ⁶⁸Ga-FAPI-46 PET in our Department. 11 patients met the following criteria: (a) same-day ⁶⁸Ga-FAPI and ¹⁸F-FDG PET for oncologic staging/restaging with ¹⁸F-FDG at least 4 hours after ⁶⁸Ga-FAPI PET, (b) ⁶⁸Ga-FAPI and/or ¹⁸F-FDG tracer uptake of local soft tissue or nodes with visual positive target-tobackground ratio on PET/CT, (c) COVID-19 vaccination within 6 weeks (d) no change in treatment between PET and vaccination (Figure 1).

The study was approved by the ethics committee (20-9485-BO and 19-8991-BO) and all patients gave written consent for enrollment into a prospective observational trial (NCT04571086).

Lymph nodes were considered positive when demonstrating visual focal uptake above background. Visual readings were performed by two nuclear medicine physicians in consensus. The median injected dose was 333 MBq [IQR 245-421] for ¹⁸F-FDG and 102 MBq [IQR 79-125] for ⁶⁸Ga-FAPI. Follow up data included imaging and clinical information. All patients fasted for 6 hours before the ¹⁸F-FDG scan and blood glucose (<200 mg/dl) was measured. Descriptive statistics are provided. An ANOVA-test was applied for assessing differences in standardized uptake value (SUV) among the different time frames after vaccination. The SUV was measured in the center of each lymph node, determined on fused PET/CT images.

6 (55%) Patients underwent imaging on a Siemens Biograph Vision and 5 (45%) on a mCT device. SUVpeak was selected based on phantom cross-calibration for the PET/CT devices to achieve reproducible results.

RESULTS

Patient characteristics are shown in Supplemental Table 1. Following database screening, 11 patients (5 men and 6 women) were included. Mean age was 44 years [IQR 34-54]. 3 (27%) underwent PET for staging and 8 (73%) for restaging. 5 (45%) patients had sarcoma and 6 (55%) patients had carcinoma. Considering combined findings from ⁶⁸Ga-FAPI and ¹⁸F-FDG scans, 3 (27%) patients showed primary lesions only, 1 (9%) patient showed locoregional lesions, and 7 (64%) patients showed distant metastases. Distant metastatic disease was noted in visceral organs, bone, or soft tissue in 5 (45%), 1 (9%), or 1 (9%) patients, respectively. In

total, the thoracic cavity was tumor-free in 7 (64%) patients. Two (18%) of 11 patients had a thoracic primary, i.e., lung (n=1) and breast cancer (n=1) before chemotherapy, which have a higher likelihood of axillary nodal involvement (Supplemental Table 2).

10 (91%) patients received BNT162b2 vaccine and 1 (9%) patient mRNA1273 vaccine at a median interval of 19 [IQR 8-30] days before PET/CT. 11 (100%) patients demonstrated focal ¹⁸F-FDG tracer uptake in axillary lymph nodes on PET/CT; none of the patients had focal ⁶⁸Ga-FAPI uptake. Details are listed in Supplemental Table 3. Uptake (SUV) at different times after vaccination in Figure 2A demonstrates highest ¹⁸F-FDG accumulation in lymph nodes 2-4 weeks post-vaccination (ANOVA p=0.002), while no increase in uptake on ⁶⁸Ga-FAPI was observed at any of the time points (Figure 2B, ANOVA p=0.79).

Imaging follow-up data at an average of 120 days [IQR 44-196] confirmed reactive nodal uptake in all patients: Decrease in uptake was documented in all 4 (100%) lymph nodes of the patient who underwent a follow-up ¹⁸F-FDG PET/CT (n=1). A decrease in lymph node size was documented for all patients (on CT n=5 (100%), ultrasound n=4 (100%)). One patient underwent a biopsy confirming reactive lymphoid hyperplasia with no evidence of malignancy (Supplemental Figure 1). Further tracer accumulation at the injection site in the deltoid muscle was detected in 5 (45%) patients (Supplemental Figure 2.2). Another patient showed generalized tracer accumulation in the bone marrow on ¹⁸F-FDG PET in addition to splenic uptake above liver uptake, indicating reactive bone marrow and splenic activation by a vaccineinduced immune response (Supplemental Figure 3). According to combined ¹⁸F-FDG and ⁶⁸Ga-FAPI PET/CT reports, none of the patients had tumor involvement of the arm or axillary lymph nodes. One patient with breast cancer demonstrated new bone metastases 4 years after initial therapy. Local recurrence was not noted, and focal nodal uptake was seen ipsilateral to vaccination and contralateral to the former tumor site. The combined analysis of ⁶⁸Ga-FAPI and ¹⁸F-FDG scans detected in total 102 (100%) tumor lesions (primary 6 (6%), locoregional 26 (25%), distant nodal 10 (10%), lung 7 (7%), liver 18 (18%), bone 28 (27%), soft tissue 7 (7%)). Lesion Detection efficacy was higher for ⁶⁸Ga-FAPI versus ¹⁸F-FDG PET (96 (94%) vs. 74 (73%)). ⁶⁸Ga-FAPI PET detected additional tumor lesions in the lung (7 (100%) vs. 5 (71%)), liver (17 (94%) vs. 9 (50%)) and bone (28 (100%) vs. 23 (82%)). The superior efficacy was based on higher detection rate in 3 patients with different tumor entities (ovarian cancer, solitary fibrous tumor, breast cancer). There was no ¹⁸F-FDGpositive, ⁶⁸Ga-FAPI-negative primary tumor lesion (Supplemental Table 4).

Representative images are shown for all included patients in Supplemental Figure 1 to 11.

DISCUSSION

The COVID-19 pandemic is active globally with an estimated 12.8 billion vaccine doses given and 627.1 million registered infections (accessed October 21, 2022) (5). Vaccines aim to decrease COVID-19 spread and severe disease, protecting vulnerable groups, including cancer patients (*6*). Repeat vaccinations have been endorsed by the CDC and many national infection agencies (*7*). Thus, most cancer patients underwent 3 vaccinations within the last year (*7*). Based on current knowledge of decreasing protection over time and the emergence of new variants, vaccination at least annually is the likely scenario (*8–10*). For vulnerable groups, repeat COVID-19 vaccination will come in addition to annual flu shots.

Post-vaccination lymph node uptake on ¹⁸F-FDG PET has been demonstrated in prior case reports/series on COVID-19 and flu vaccine for a variety of tumor entities (*1–4,11–16*). Increase in annual vaccination will put oncologic patients at considerable risk of false positive ¹⁸F-FDG PET findings. Here we confirm ¹⁸F-FDG uptake within 6 weeks of vaccination in a case series of oncologic patients. Non-specific ¹⁸F-FDG uptake will adversely influence staging and restaging

procedures of oncology patients (*3*). Patients are at risk of false positive lymph node findings when undergoing ¹⁸F-FDG PET/CT within 6 weeks of vaccination. Therefore, PET/CT appointments for patients at risk must be planned carefully with consideration of any vaccination. In addition, bone marrow uptake was seen in one patient pointing to additional pitfalls in patients with myeloproliferative disease (*2*).

The regulation of fibroblast activation protein alpha (FAPα) in cancer is not completely understood. TGFbeta, associated with epithelial–mesenchymal transition, angiogenesis, or immune suppression, participates in the upregulation of FAPα expression, suggesting a lower susceptibility of ⁶⁸Ga-FAPI PET to acute inflammation (*17*). Fittingly, none of the patients demonstrated focal ⁶⁸Ga-FAPI uptake in locoregional lymph nodes post vaccination. In addition, ⁶⁸Ga-FAPI PET demonstrated higher detection efficacy when compared to ¹⁸F-FDG PET/CT both for locoregional and distant staging. Tumor detection was based on the PET/CT findings; however, lesions were not verified by imaging follow-up and findings are limited by a low sample size. Superior detection for ⁶⁸Ga-FAPI versus ¹⁸F-FDG PET is in line with previous reports on carcinoma of unknown primary, sarcoma, and breast carcinoma imaging (*18*). Our findings indicate that ⁶⁸Ga-FAPI PET delivers oncologic staging with equal or superior accuracy when compared with ¹⁸F-FDG PET, however with no risk of false diagnosis post vaccination (*19*).

An ongoing prospective trial at our institution aims to assess accuracy and correlation with histopathology for various types of cancer (clinicaltrials.gov, NCT05160051). Our study is limited by low number of patients and low histopathologic confirmation rate for lymph node findings.

Conclusion

Increased annual vaccinations are expected for vulnerable groups, including cancer patients. ¹⁸F-FDG may trigger costly follow-up investigations and false management decisions. In our study, ⁶⁸Ga-FAPI PET, a promising novel imaging tool, avoided post-vaccination lymph node and bone marrow pitfalls and provided accurate oncologic staging. ⁶⁸Ga-FAPI PET should be assessed as an alternative to ¹⁸F-FDG PET in ongoing (NCT05160051) and future prospective studies.

CONFLICT OF INTEREST DISCLOSURES

Katharina Lueckerath reports fees from SOFIE Bioscience (consultant) and Enlaza Therapeutics (consultant).

Rainer Hamacher is supported by Clinician Scientist Program of the University Medicine Essen Clinician Scientist Academy (UMEA) sponsored by faculty of medicine and Deutsche Forschungsgemeinschaft (DFG) and has received travel grants from Lilly, Novartis and PharmaMar as well as fees from Lilly and PharmaMar.

Jens T. Siveke received honoraria as consultant or for continuing medical education presentations from AstraZeneca, Bayer, Bristol-Myers Squibb, Eisbach Bio, Immunocore, Novartis, Roche/Genentech, Servier; his institution receives research funding from Bristol-Myers Squibb, Celgene, Eisbach Bio, Roche/Genentech; he holds ownership and serves on the Board of Directors of Pharma15, all outside the submitted work.

Benedikt M. Schaarschmidt received a research grant from PharmaCept for an undergoing investigator-initiated study not related to this paper.

Ken Herrmann reports personal fees from Bayer, personal fees and other from Sofie Biosciences, personal fees from SIRTEX, non-financial support from ABX, personal fees from Adacap, personal fees from Curium, personal fees from Endocyte, grants and personal fees from BTG, personal fees from IPSEN, personal fees from Siemens Healthineers, personal fees from GE Healthcare, personal fees from Amgen, personal fees from Novartis, personal fees from ymabs, personal fees from Aktis Oncology, personal fees from Theragnostics, personal fees from Pharma15, outside the submitted work.

Wolfgang P. Fendler reports fees from SOFIE Bioscience (research funding), Janssen (consultant, speakers bureau), Calyx (consultant), Bayer (consultant, speakers bureau, research funding), Parexel (image review) and AAA (speakers bureau) outside of the submitted work.

All disclosure were outside of the submitted work.

All other authors have nothing to disclose.

AUTHOR CONTRIBUTIONS

Wolfgang P. Fendler and Tristan T. Demmert had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: Wolfgang P. Fendler, Tristan T. Demmert

Financial support: Ken Herrmann, Wolfgang P. Fendler

Supervision: Wolfgang P. Fendler

Administrative, technical, or material support: Tristan T. Demmert, Ines Maric, Kelsey L. Pomykala, Katharina Lueckerath, Rainer Hamacher, Ken Herrmann, Wolfgang P. Fendler

Acquisition, analysis, or interpretation of data: Tristan T. Demmert, Ines Maric, Wolfgang P. Fendler

Manuscript writing: Wolfgang P. Fendler, Tristan T. Demmert, Kelsey L. Pomykala

Critical revision of the manuscript for important intellectual content: Tristan T. Demmert, Ines Maric, Kelsey L. Pomykala, Katharina Lueckerath, Rainer Hamacher, Ken Herrmann, Wolfgang P. Fendler

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Wolfgang P. Fendler, Tristan T. Demmert

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None

Key Points:

QUESTION: Can ⁶⁸Ga-FAPI PET prevent COVID-19 vaccine-related reactive lymph node uptake?

PERTINENT FINDINGS: We compared ¹⁸F-FDG and ⁶⁸Ga-FAPI PET/CTs acquired on the same day within 6 weeks of COVID19 vaccination in 11 oncology patients. While ¹⁸F-FDG was visually positive in 11 patients, ⁶⁸Ga-FAPI showed no vulnerability to vaccine-related tracer uptake in any patients, but higher tumor detection efficacy. Additionally, the tracer-uptake intensity of ¹⁸F-FDG was time-dependent to the vaccination interval, ⁶⁸Ga-FAPI was visual negative at all time points.

IMPLICATIONS FOR PATIENT CARE: ⁶⁸Ga-FAPI avoids vaccine-associated reactive lymph node uptake and is therefore superior to ¹⁸F-FDG in tumor staging in the period up to 6 weeks after COVID-19 vaccination.

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FIGURES

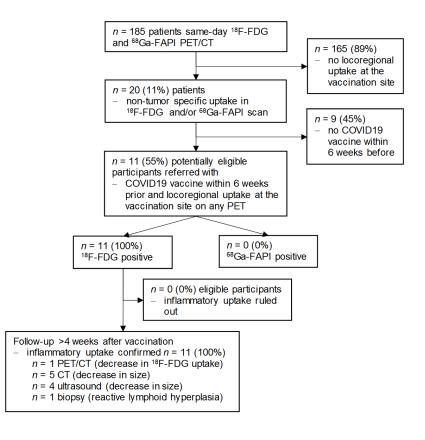


Figure 1. Patient Flow Diagram

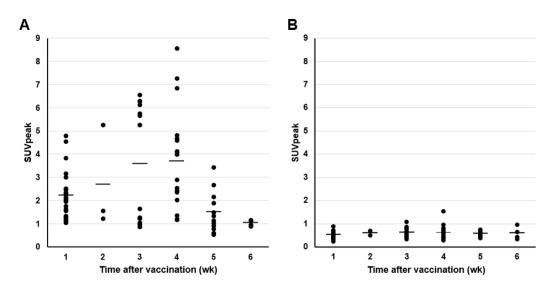
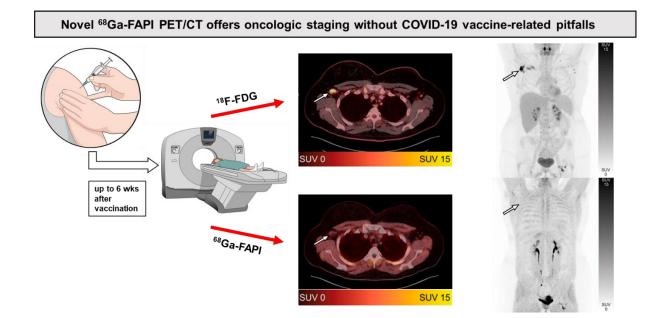


Figure 2. SUVpeak over time for n=78 locoregional lymph nodes for (A) ¹⁸F-FDG (ANOVA p=0.002) and (B) ⁶⁸Ga-FAPI (ANOVA p=0.791) PET/CT.

The average SUVpeak for week 1 through 6 was 2.2, 2.7, 3.6, 3.7, 1.5, 1.0 for 18 F-FDG (A) and 0.5, 0.6, 0.6, 0.6, 0.6 for 68 Ga-FAPI (B) PET, respectively.

Graphical Abstract



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ONLINE MATERIAL

Supplemental Table 1. Patient Characteristics (n=11)

Supplemental Table 2. Tumor stage by combined ¹⁸F-FDG and ⁶⁸Ga-FAPI PET/CT in

11 patients

Supplemental Table 3. Non-tumor specific uptake

Supplemental Table 4. Tumor detection efficacy for ¹⁸F-FDG vs. ⁶⁸Ga-FAPI PET/CT

(n=11 patients)

Supplemental Figure 1-11. ¹⁸F-FDG PET/CT and ⁶⁸Ga-FAPI PET/CT images in all 11 patients

TABLES

Characteristic	Mean [IQR]	N (%)					
Gender							
Male		5 (45)					
Female		6 (55)					
Age (years)	44 [34-54]						
Indication for PET/CT							
Sarcoma (SFT)		2 (18)					
Ovarian carcinoma		1 (9)					
Pleomorphic sarcoma		1 (9)					
Sarcoma		1 (9)					
Colorectal carcinoma		1 (9)					
Breast carcinoma		1 (9)					
Prostate carcinoma		1 (9)					
Lung carcinoma		1 (9)					
Urothelial carcinoma		1 (9)					
Myxofibrosarcoma		1 (9)					
Type of mRNA vaccine							
BNT162b2		10 (91)					
mRNA1273		1 (9)					
Time between vaccine and PET/CT (days)							
	19 [8-30]						
Concominant tumor therapy							
at PET							
None		6 (55)					
Radionuclide		1 (9)					
Chemo		2 (18)					
Immune		3 (27)					

Supplemental Table 1. Patient Characteristics (n=11)

Characteristic	Ν	(%)	
Indication			_
Staging		3	(27)
Restaging		8	(73)
Extent			
No disease		0	(0)
Primary tumor			
only		3	(27)
Locoregional dise			
only		1	(9)
Distant			
metastatic:	nodal		(27)
	bone	1	(9)
	organ	5	(45)

Supplemental Table 2. Tumor stage by combined ¹⁸F-FDG and ⁶⁸Ga-FAPI PET/CT in 11 patients

Patient No.	Tumor			Injection site		Axillary & Adjacent Nodes					Distant Nodes, Spleen, BM		
	Entity	SUVpeak		185 500	8°0 5451	¹⁸ F-FDG		68Ga-FAPI					
		¹⁸ F-FDG	68Ga-FAPI	¹⁸ F-FDG	⁶⁸ Ga-FAPI visual	visual	Ν	SUVpeak	visual	Ν	SUVpeak	¹⁸ F-FDG	⁶⁸ Ga-FAPI
1	Ovarian	4.1	4.7	positive	negative	positive	12	2.2	negative	0	0.7	negative	negative
2	Sarcoma (SFT)	3.3	11.7	positive	negative	positive	4	2.1	negative	0	0.7	negative	negative
3	Pleomorphic sarcoma	3.9	1.8	positive	negative	positive	12	4.8	negative	0	0.5	positive*	negative
4	Sarcoma	1.0	2.5	positive	negative	positive	2	2.7	negative	0	0.7	negative	negative
5	Colorectal	3.8	6.0	positive	negative	positive	12	9.1	negative	0	1.5	negative	negative
6	Sarcoma (SFT)	4.4	8.1	positive	negative	positive	8	6.6	negative	0	1.1	negative	negative
7	Breast	2.1	4.0	positive	negative	positive	1	1.5	negative	0	0.9	negative	negative
8	Prostate	10.1	12.0	positive	negative	positive	2	2.9	negative	0	0.4	negative	negative
9	Lung	20.2	18.8	positive	negative	positive	5	1.9	negative	0	0.9	negative	negative
10	Urothelial	7.1	5.3	positive	negative	positive	12	3.4	negative	0	0.9	negative	negative
11	Myxofibrosarcoma	4.4	4.0	positive	negative	positive	4	1.6	negative	0	0.7	negative	negative
Sum (%) or Median [IQR]	-	4.1 [0-9.4]	5.3 [0.2-10.4]	11 (100%)	0 (0%)	11 (100%)	74	2.7 [1.1-5.9]	0 (0%)	0	0.7 [0.4-1.0]	1 (9%)	0 (0%)

Supplemental Table 3. Non-tumor specific uptake

*Diffuse bone marrow uptake - SUVpeak 3.4

	overall detection N	¹⁸ F-FDG N (%)	⁶⁸ Ga-FAPI N (%)
Patient level detection of			
tumor	11	11 (100)	11 (100)
Total N of detected tumor			
lesions	102	74 (73)	96 (94)
Primary lesion	6	6 (100)	6 (100)
Local nodal	26	20 (77)	21 (81)
Distant nodal	10	8 (80)	10 (100)
Lung	7	5 (71)	7 (100)
Liver	18	9 (50)	17 (94)
Bone	28	23 (82)	28 (100)
Other	7	3 (43)	7 (100)

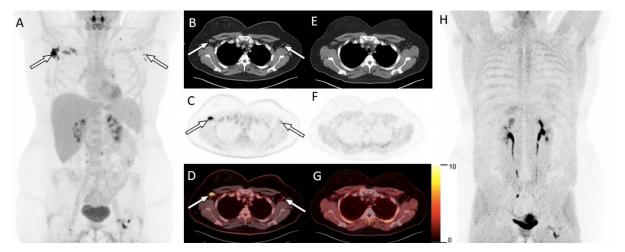
Supplemental Table 4. Tumor detection efficacy for ¹⁸F-FDG vs. ⁶⁸Ga-FAPI PET/CT (n=11 patients)

FIGURES

Supplemental Figure 1-11. ¹⁸F-FDG PET/CT and ⁶⁸Ga-FAPI PET/CT images in all 11 patients

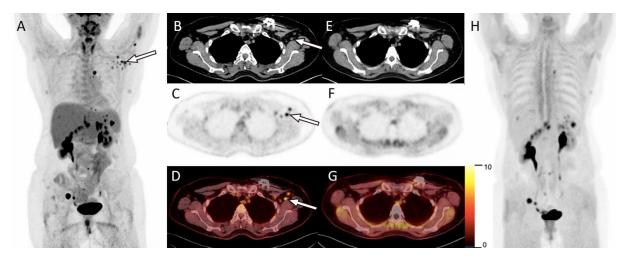
¹⁸F-FDG (A-D) and ⁶⁸Ga-FAPI (E-H) Maximum intensity projection images (MIP) of the PET/CT scan (A, H), axial CT (B, E), PET (C,

F), PET/CT (D, G) are shown.



Supplemental Figure 1. Patient 1, female, 32 y

Tumor stage: Colorectal cancer, R0 resection with locoregional and distant metastases. PET uptake in the vaccination region: ¹⁸F-FDG positive (n=12 lymph nodes, arrow) vs. ⁶⁸Ga-FAPI negative (bilateral findings after vaccination on right side followed by a biospy confirming reactive lymphoid hyperplasia)

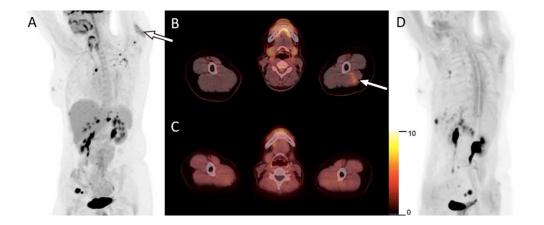


Supplemental Figure 2.1. Patient 2, female, 49 y

Tumor stage: Ovarian cancer, R0 resection with locoregional and distant metastases.

PET uptake in the vaccination region: ¹⁸F-FDG positive (n=12 lymph nodes, arrow) vs. ⁶⁸Ga-

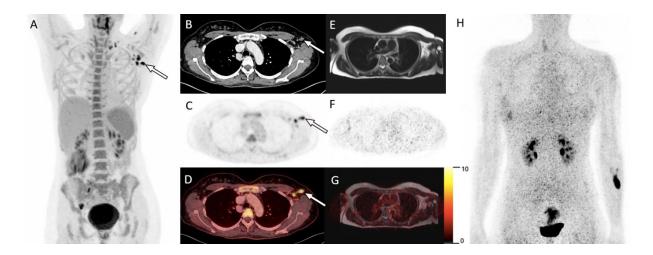
FAPI negative



Supplemental Figure 2.2.

Same patient showing additional deltoid muscle uptake on ¹⁸F-FDG¹⁸ (SUV_{peak} 2.3, arrow).

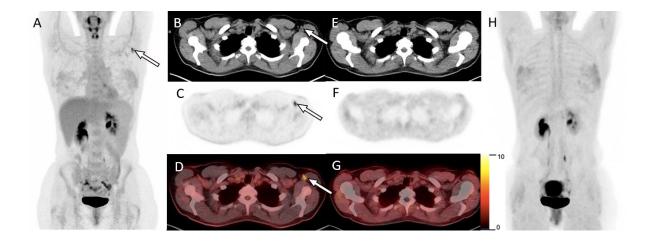
¹⁸F-FDG (A, B) and ⁶⁸Ga-FAPI (C, D), MIP (A, D), PET/CT (B, C)



Supplemental Figure 3. Patient 3, female, 42 y

Tumor stage: Undifferentiated pleomorphic sarcoma (UPS), primary lesion with one locoregional metastasis.

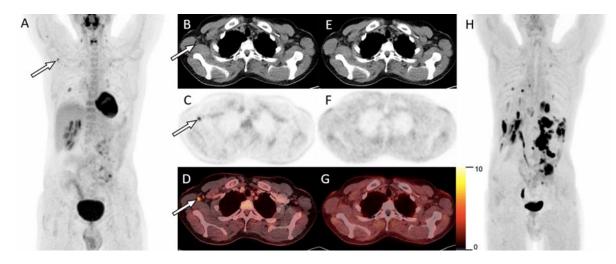
PET uptake in the vaccination region: ¹⁸F-FDG positive (n=11 lymph nodes, arrow) vs. ⁶⁸Ga-FAPI negative



Supplemental Figure 4. Patient 4, female, 39 y

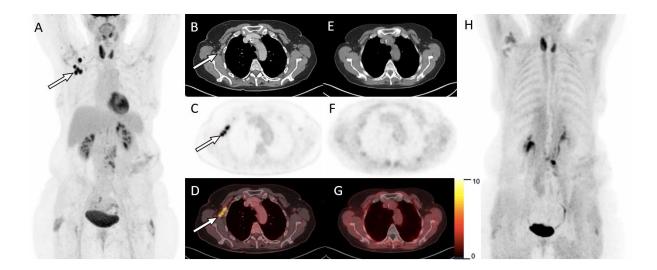
Tumor stage: Low grade myxoid liposarcoma, primary lesion with no metastases.

PET uptake in the vaccination region: ¹⁸F-FDG positive (n=2 lymph nodes, arrow) vs. ⁶⁸Ga-FAPI negative



Supplemental Figure 5. Patient 5, male, 36 y

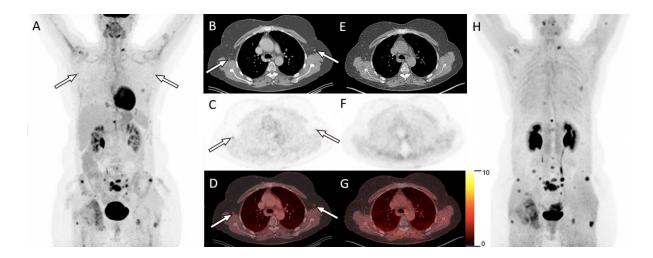
Tumor stage: Solitary fibrous tumor, R0 resection with locoregional and distant metastases. PET uptake in the vaccination region: ¹⁸F-FDG positive (n=4 lymph nodes, arrow) vs. ⁶⁸Ga-FAPI negative



Supplemental Figure 6. Patient 6, female, 57 y

Tumor stage: Solitary fibrous tumor, primary lesion with no metastases.

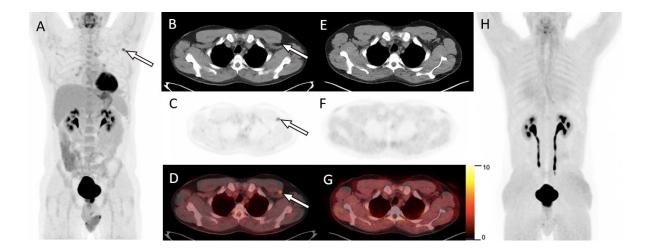
PET uptake in the vaccination region: ¹⁸F-FDG positive (n=8 lymph nodes, arrow) vs. ⁶⁸Ga-FAPI negative



Supplemental Figure 7. Patient 7, female, 44 y

Tumor stage: Breast cancer, prior lumpectomy, bone metastases.

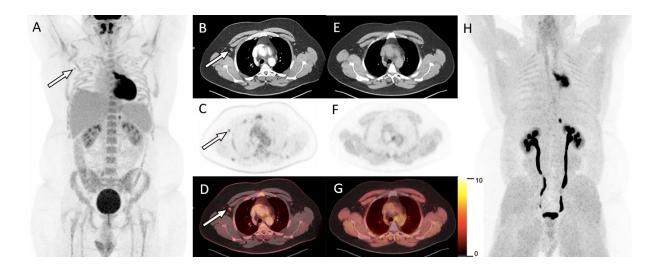
PET uptake in the vaccination region: ¹⁸F-FDG positive (n=2 lymph nodes, arrow) vs. ⁶⁸Ga-FAPI negative



Supplemental Figure 8. Patient 8, male, 47 y

Tumor stage: Prostate cancer, primary lesion with no metastases.

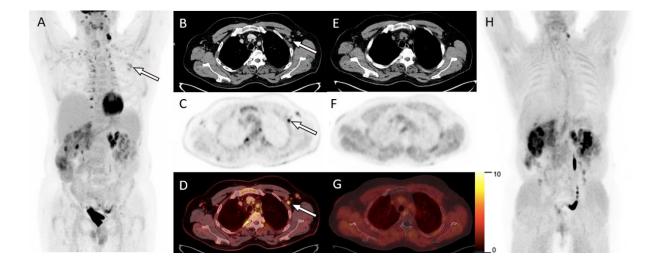
PET uptake in the vaccination region: ¹⁸F-FDG positive (n=2 lymph nodes, arrow) vs. ⁶⁸Ga-FAPI negative



Supplemental Figure 9. Patient 9, male, 39 y

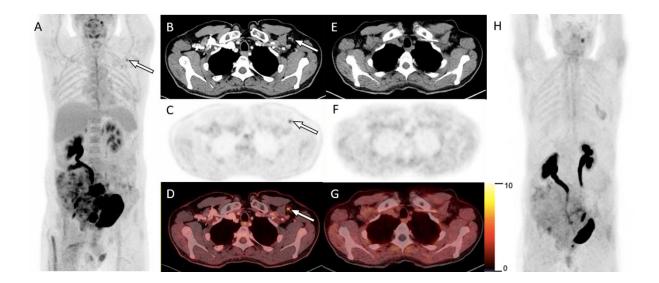
Tumor stage: Lung cancer, primary lesions with one distant metastasis.

PET uptake in the vaccination region: ¹⁸F-FDG positive (n=5 lymph nodes, arrow) vs. ⁶⁸Ga-FAPI negative



Supplemental Figure 10. Patient 10, male, 47 y

Tumor stage: Urothelial cancer, primary lesion with locoregional and distant metastases. PET uptake in the vaccination region: ¹⁸F-FDG positive (n=12 lymph nodes, arrow) vs. ⁶⁸Ga-FAPI negative



Supplemental Figure 11. Patient 11, male, 62 y

Tumor stage: Myxofibrosarcoma, primary lesion, left gynecomastia with no metastases.

PET uptake in the vaccination region: ¹⁸F-FDG positive (n=4 lymph nodes, arrow) vs. ⁶⁸Ga-FAPI negative