Supplemental Material

Characteristic (n=18)	Median	(Range)	n	(%)
Gender				
Male			12	(67)
Female			6	(33)
Age (years)	56	(31-73)		
Tumor entity				
Colorectal			3	(17)
Pancreas			3	(17)
Prostate			3	(17)
Bladder			2	(11)
Lung			2	(11)
Kidney			2	(11)
Sarcoma			2	(11)
Skin			1	(6)
Suspicious lymph node region				
pelvis			6	(33)
abdomen			6	(33)
mediastinum			3	(17)
axilla			2	(11)
inguinal			1	(6)
Time between PETs (days)	2	(0-22)		
Time between PET and Biopsy (days)	24	(1-164)		
Active tumor therapy at time of PET:				
None			14	(78)
Chemo			4	(22)

Supplemental Table 1: Patient Characteristics

Tumor characteristics		N	(%)
Indication:			
Staging		9	(50)
Restaging		9	(50)
Extent:			
No disease		0	(0)
Locoregional disease only		11	(61)
Distant metastatic disease		7	(39)
Metastatic regions:	lymph node	4	(22)
	bone	1	(6)
	visceral	5	(28)

Supplemental Table 2: Tumor characteristics (n=18 patients)

Tumor extent was tabulated based on combined findings from ^{18}F-FDG PET and ^{68}Ga-FAPI PET along with clinical information.

Supplemental Table 3: Individual patient data for lymph node assessment (n=18 patients)

| Patient No. | Tumor | | | | | Lymph node | | | | | | | |
| | Entity | SUV_{peak} | | Region | Histology | ^{18}F-FDG | | | | ^{68}Ga-FAPI | | | |
		^{18}F-FDG	^{68}Ga-FAPI			Visual[1]	TBR_{muscle}	SUV_{max}	SUV_{peak}	Visual[2]	TBR_{muscle}	SUV_{max}	SUV_{peak}
1	Bladder cancer	4.3	4.4	pelvis	benign	negative	1.4	0.8	0.8	negative	0.4	0.5	0.3
2	Prostate cancer	11.6	36.0	pelvis	benign	negative	3.5	1.6	1.4	negative	1.1	0.9	0.6
3	Renal cancer	6.1	3.2	renal	benign	negative	4.1	1.9	1.6	negative	0.6	1.0	0.6
4	Lung cancer	3.9	6.6	lung	benign	negative	1.0	0.7	0.5	negative	0.6	0.7	0.7
5	Rectal cancer	35.0	11.7	mesentery	benign	negative	2.8	2.7	2.3	negative	0.4	0.8	0.7
6	Sarcoma	19.4	8.6	inguinal	benign	positive	12.1	7.6	4.6	negative	0.7	1.6	0.8
7	Prostate cancer	5.4	12.2	pelvis	benign	negative	3.2	2.6	2.4	negative	0.7	1.0	0.9
8	Prostate cancer	10.6	14.7	pelvis	malignant	negative	3.0	1.5	0.8	positive	1.6	2.0	1.3
9	Pancreatic cancer	4.4	16.0	peripancreatic	benign	negative	3.3	2.4	2.0	negative	1.2	2.5	1.6
10	Bladder cancer	4.2	4.3	pelvis	benign	positive	8.2	7.4	3.3	negative	1.3	2.2	1.6
11	Pancreatic cancer	1.8	2.1	mesentery	malignant	negative	3.5	2.0	1.4	positive	2.3	2.4	1.8
12	Rectal cancer	3.8	6.4	axilla	benign/ reactive[3]	positive	23.6	14.4	10.5	negative	0.8	2.7	1.8
13	Lung cancer	20.2	19.6	lung	benign	positive	11.4	5.4	3.1	negative	1.2	3.0	2.1
14	Pancreatic cancer	3.5	3.3	peripancreatic	malignant	positive	5.5	3.8	2.4	positive	2.4	3.9	2.3
15	Melanoma	11.5	6.2	inguinal	malignant	positive	12.3	6.6	2.7	positive	3.1	4.9	3.0
16	Sarcoma	12.9	9.1	mesentery	benign/ inflammatory[4]	positive	29.2	13.2	10.0	positive	3.2	4.6	3.5
17	Colon cancer	8.9	5.3	lung	malignant	positive	15.9	9.1	6.9	positive	6.6	5.1	4.2
18	Renal cancer	5.0	3.2	pelvis	malignant	positive	12.3	6.7	4.4	positive	5.0	12.4	7.5

[1]Visuality was defined as: positive if SUVmax > Percist and negative if SUVmax < Percist.
[2]Visuality was defined as: positive if SUVmax > (SUV_{mean} of muscle (^{68}Ga-FAPI) +2x SD) and negative if SUVmax < (SUV_{mean} of muscle (^{68}Ga-FAPI) +2x SD).
[3]Reactive presenting as immune response to a vaccination 3 weeks before PET.
[4]Inflammatory presenting as sarcoid-like lymph nodes.

Supplemental Table 4: Tumor detection efficacy for ^{18}F-FDG and ^{68}Ga-FAPI PET/CT (n=18 patients). Tumor locations were assessed separately for ^{18}F-FDG and ^{68}Ga-FAPI and for 7 regions.

	overall detection N	^{18}F-FDG N	(%)	[64]Ga-FAPI N	(%)
Patient level detection of tumor	18	18	(100)	18	(100)
Total N of lesions	89	85	(96)	85	(96)
Primary	18	18	(100)	18	(100)
Local nodal	40	39	(98)	40	(100)
Distant nodal	22	22	(100)	18	(82)
Lung	3	3	(100)	3	(100)
Liver	4	1	(25)	4	(100)
Bone	1	1	(100)	1	(100)
Other	1	1	(100)	1	(100)
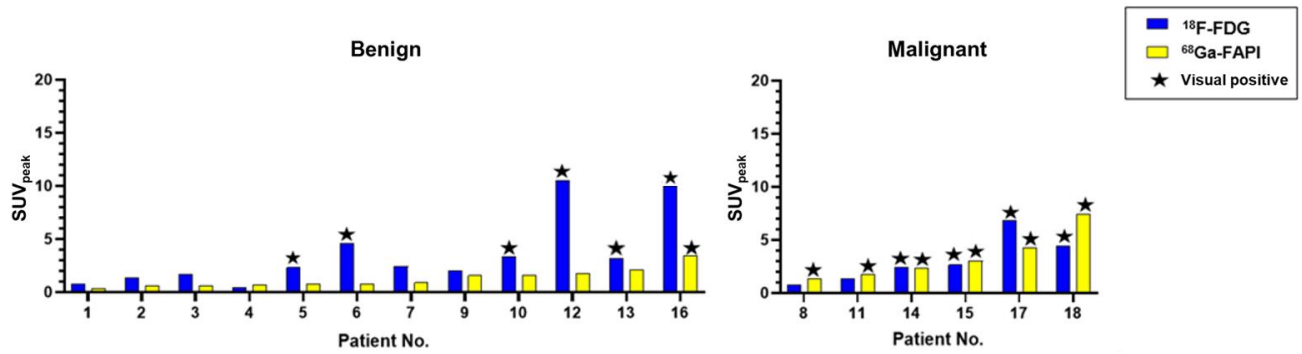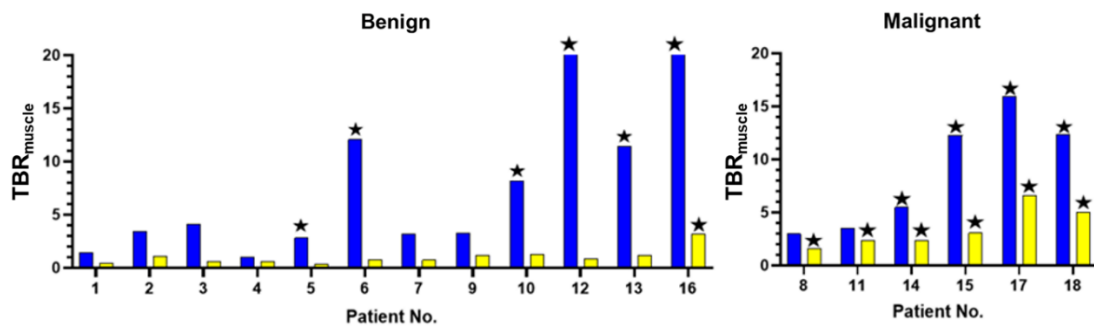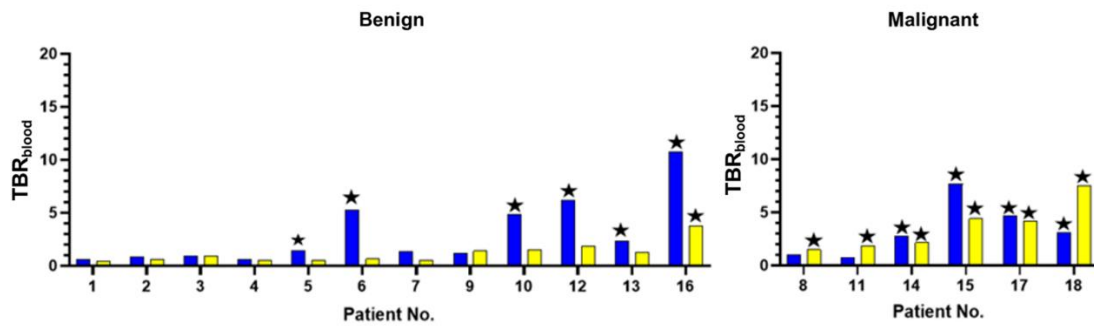
Supplemental Figure 1: Individual lymph node assessment (n=18 patients, one lymph node per patient)

Subparts are introduced as in (A) with the SUV_{peak}, in (B) with the TBR_{muscle} and in (C) with the TBR_{blood}.
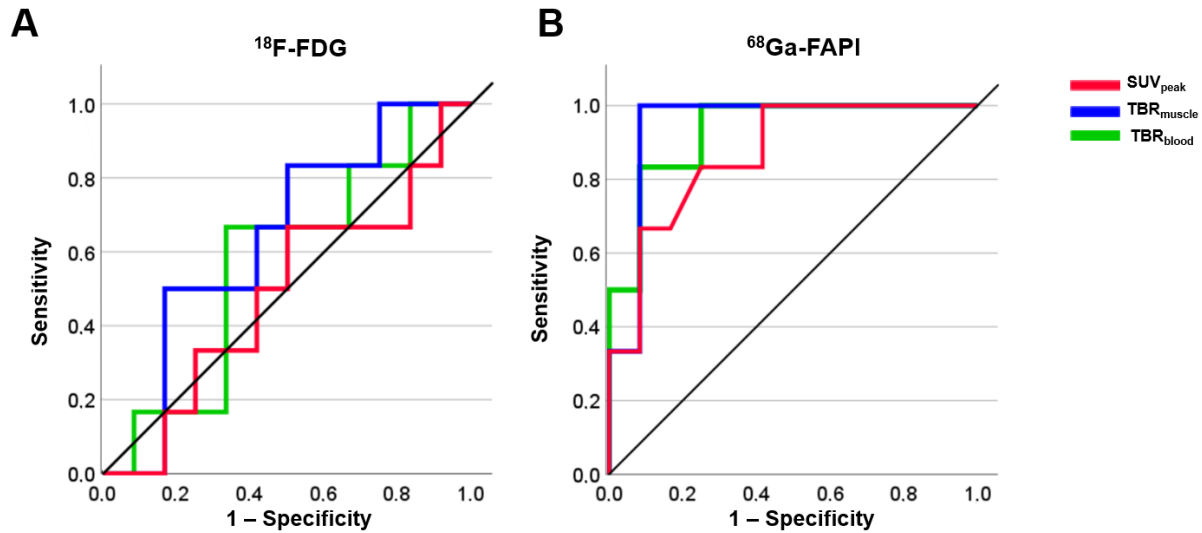
**Supplemental Figure 2: ROC-Analysis for ^{18}F-FDG and ^{68}Ga-FAPI**

A: For ^{18}F-FDG the Overall Model Quality was <0.5 for SUV$_{peak}$ (0.2), TBR$_{muscle}$ (0.4) and TBR$_{blood}$ (0.3) and therefore a cut-off not useful.

B: For ^{68}Ga-FAPI the Overall Model Quality was >0.5 for SUV$_{peak}$ (0.7), TBR$_{muscle}$ (0.8) and TBR$_{blood}$ (0.8). The maximum Youden Index preserves a cut-off of 1.7 for SUV$_{peak}$ (Youden Index: 0.6), 1.4 for TBR$_{muscle}$ (Youden Index: 0.9), and 1.9 for TBR$_{blood}$ (Youden Index: 0.8).
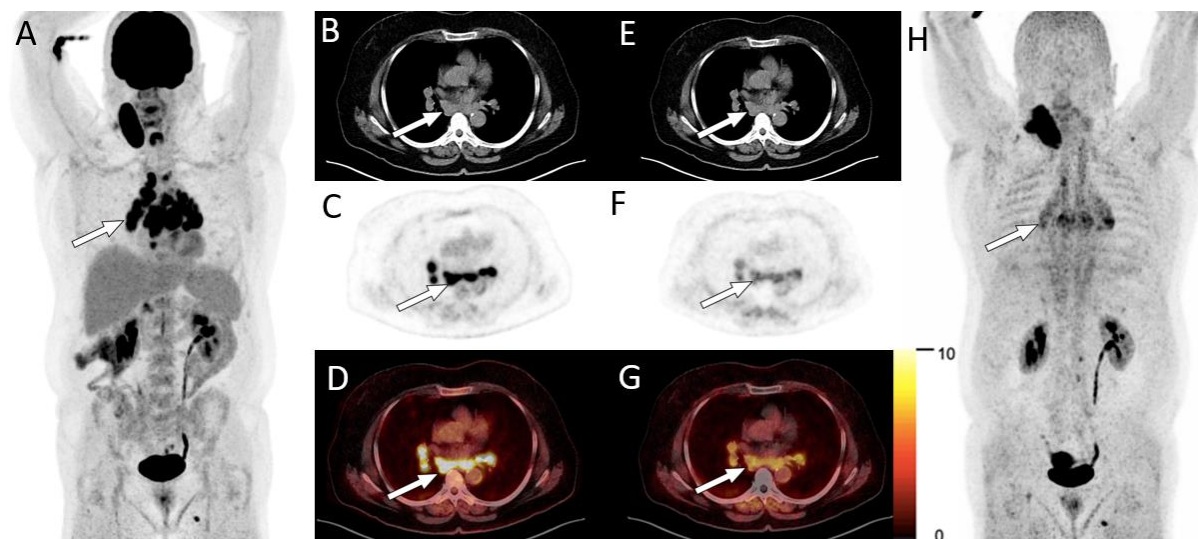
Supplemental Figures 3-5. ¹⁸F-FDG PET/CT and ⁶⁸Ga-FAPI PET/CT patient examples

The following images show examples of a true negative match, a false positive match as well as a true positive match.

¹⁸F-FDG **(A-D)** and ⁶⁸Ga-FAPI **(E-H)** maximum intensity projections (MIP) **(A, H)**, axial CT **(B, E)**, PET **(C, F)**, fused PET/CT **(D, G)** are shown. Arrows in CT images are pointing to the lymph nodes that were biopsied. If lymph nodes were rated positive, additional arrows are shown in the respective PET image.
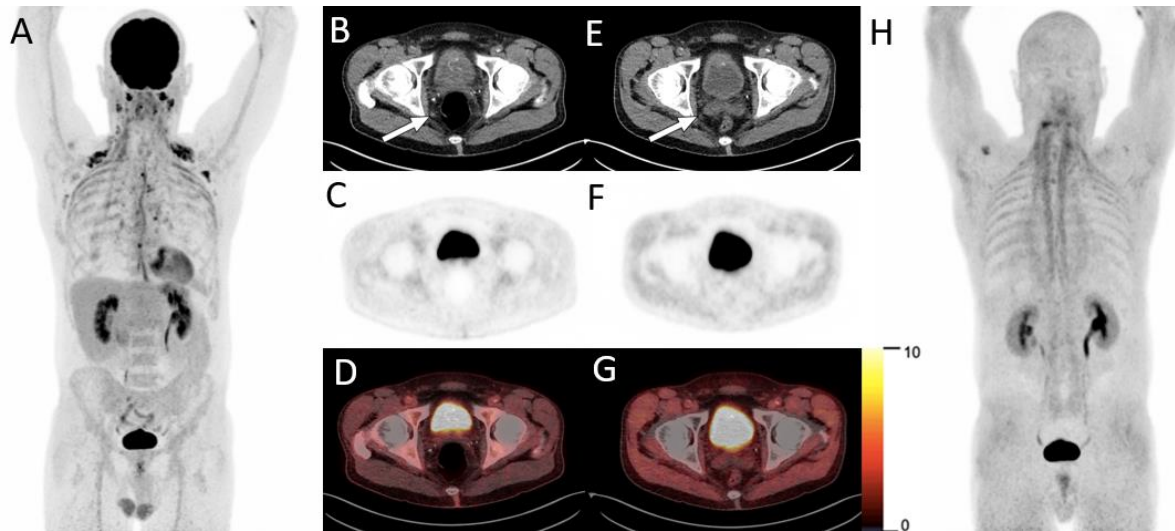
Supplemental Figure 3: Patient 1, male, 59 years, bladder cancer, restaging during chemotherapy showing a match of tracer-non-avid lymph nodes in ¹⁸F-FDG and ⁶⁸Ga-FAPI PET. Histopathology result: benign.

Supplemental Figure 4: Patient 16, female, 61 years, small blue round cell tumor of the neck, staging before therapy showing a match of tracer-avid lymph nodes in ^{18}F-FDG and ^{68}Ga-FAPI PET. Both tracers accumulate in a non-malignant lymph node affected by sarcoidosis but ^{18}F-FDG revealed a 7-times higher TBR$_{muscle}$ than ^{68}Ga-FAPI. Histopathology result: benign/inflammatory.
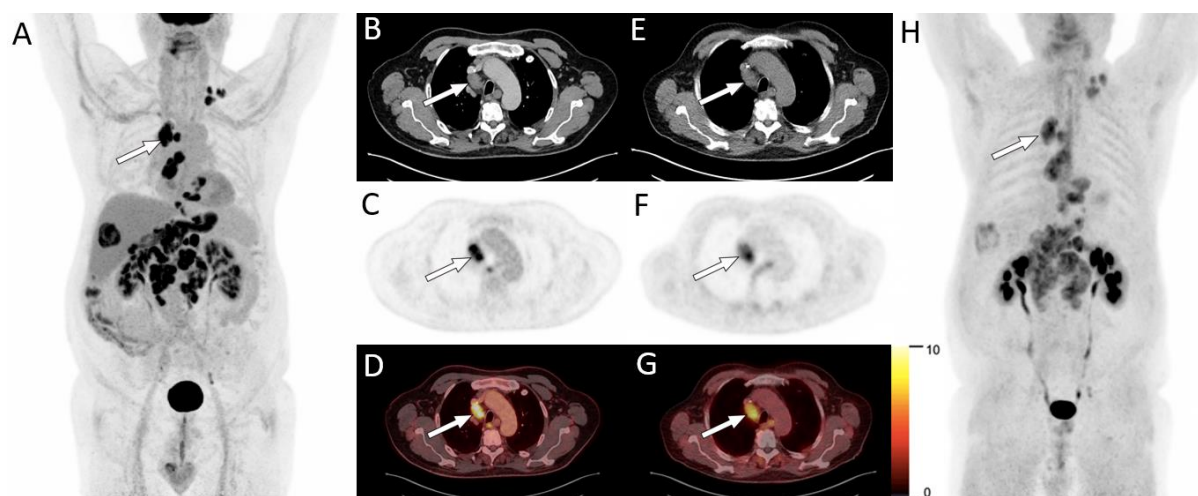
Supplemental Figure 5: Patient 17, male, 68 years, colorectal adenocarcinoma, **restaging during chemotherapy** showing a match of tracer-avid lymph nodes in ^{18}F-FDG and ^{68}Ga-FAPI PET. Histopathology result: malignant.