

SOFIE

From start to clinic

Fibroblast Activation Protein (FAP) Inhibitors as Biomarkers in Oncology, Fibrotic Disease, and Cardiovascular Disease

Informa Connect: Radiopharmaceuticals and Imaging

3/14/23

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Theranostics

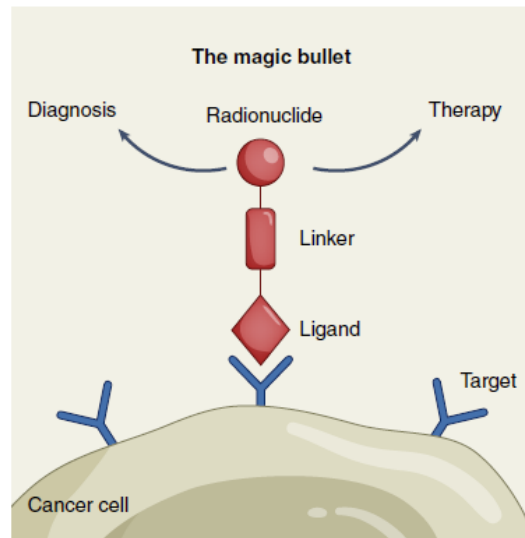
Diagnostic: PET imaging to Select patients whose cancer cells have the targeted protein. Short-lived radionuclide ^{68}Ga or ^{18}F

Treatment: Molecular targeted radio-ablation of cancer or cancer associated cells

Long-lived radionuclide ^{177}Lu , ^{225}Ac , ^{212}Pb or other beta or alpha particle emitters

WHY?

- *See where the drug is goes throughout the body and how it is cleared from the target and the rest of the body*
- *Select patients based on having a specific target protein for therapy*
- *Monitor treatment response*



The magic bullet. Theranostics target unique properties of cancer cells using different radionuclides for diagnosis and treatment. Credit: Marina Spence/Nature Medicine

Carrie Arnold Nature News 2022



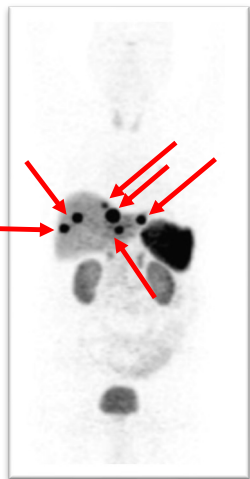
Theranostics: Recent Successes

Target: Somatostatin Receptor

Disease: Neuroendocrine Tumors

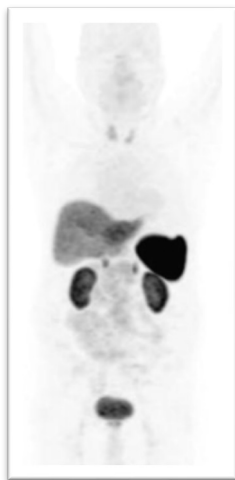
PET Imaging Probe is ^{68}Ga -DOTATATE

Treatment Probe is ^{177}Lu -DOTATATE



**BEFORE
TREATMENT**

^{177}Lu -DOTATATE
Treatment



**AFTER
TREATMENT**

F. Giesel (U of Heidelberg), K. Herrmann (U of Essen), W. Fendler (UCLA), J. Czernin (UCLA)

Target: PSMA

Disease: Castration Resistant Prostate Cancer

PET Imaging: ^{68}Ga -PSMA-11

Treatment: ^{177}Lu -PSMA-617



**BEFORE
TREATMENT**

PSA = 2,923 ng/ml

^{177}Lu -PSMA-617
Treatment



**AFTER
TREATMENT**

PSA < 0.1 ng/ml

F. Giesel (U of Heidelberg), K. Herrmann (U of Essen), W. Fendler (UCLA), J. Czernin (UCLA)

tumors



Next promising target? FAP (Fibroblast Activation Protein)

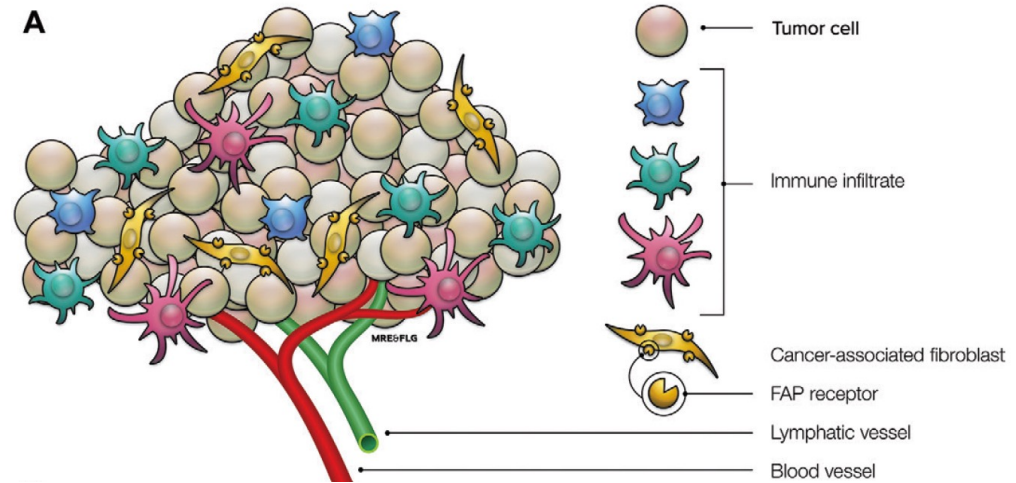
Activated Fibroblasts express high levels of FAP

Fibroblasts become activated during wound repair and regeneration. Malignant tumors are recognized as “wounds that do not heal”

Among all the stromal cells, **cancer-associated fibroblasts (CAFs)** are dominant populations in the tumor microenvironment

FAP is highly expressed on the surface of CAFs

FAP is a great target due to its overexpression in most of the cancer types (90%) with low or no expression in normal tissue

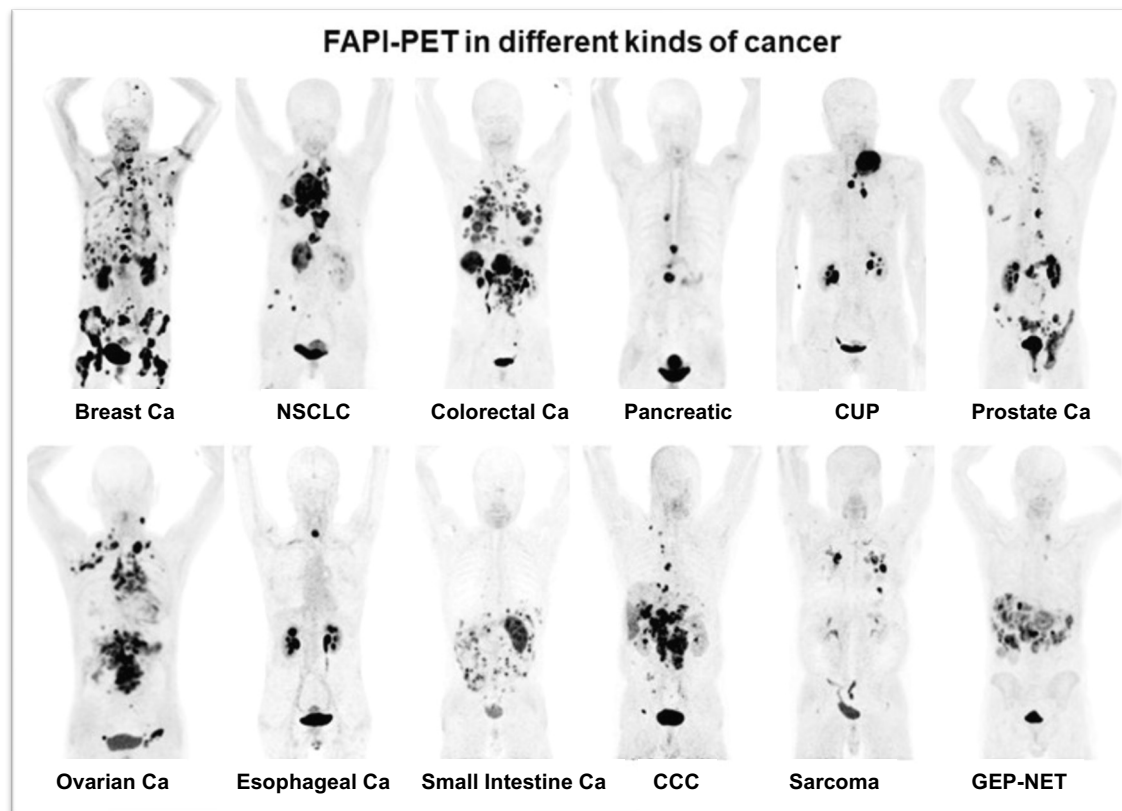


Mori Y, Dendl K, Cardinale J, Kratochwil C, Giesel FL, Haberkorn U. FAPI PET: Fibroblast Activation Protein Inhibitor Use in Oncologic and Nononcologic Disease. *Radiology*. 2023 Jan 3;220749. doi: 10.1148/radiol.220749. Epub ahead of print. PMID: 36594838.

(Fibroblast Activation Protein Inhibitor)-**FAP**I family of compounds

SNMMI Image of the Year 2019

“A single radiotracer can identify nearly 30 types of cancer, allowing for new applications in noninvasive diagnosis, staging and treatment, according to research presented at the 2019 Annual Meeting of the Society of Nuclear Medicine and Molecular Imaging (SNMMI). This honor goes to a team of researchers at University Hospital Heidelberg, Germany, showcasing the efficacy of the FAPI radiotracer.”

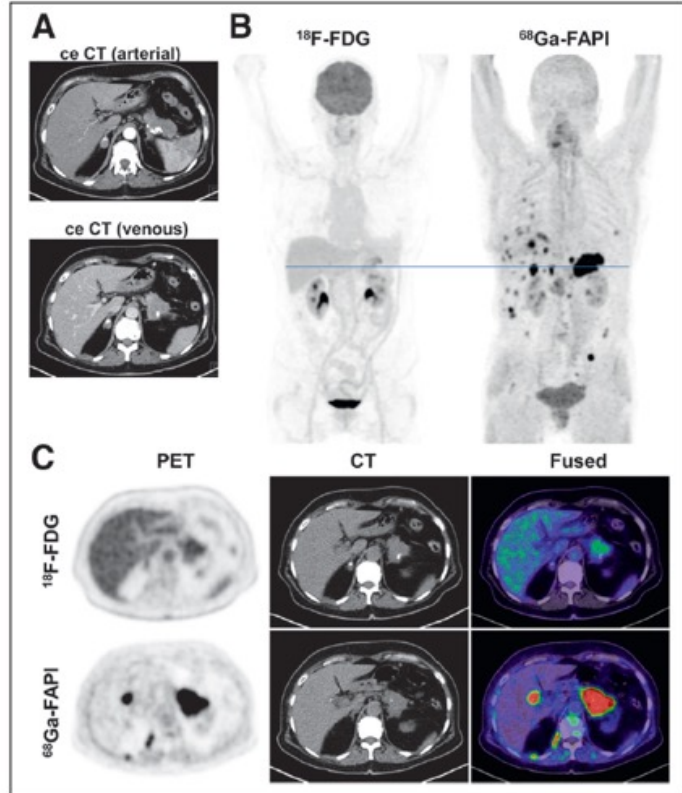


SOFIE holds diagnostic/companion diagnostic right of use for FAPI family of compounds

JNM Best Clinical Article in 2021

Impact of ^{68}Ga -FAPI PET/CT Imaging on the Therapeutic Management of Primary and Recurrent PDAC

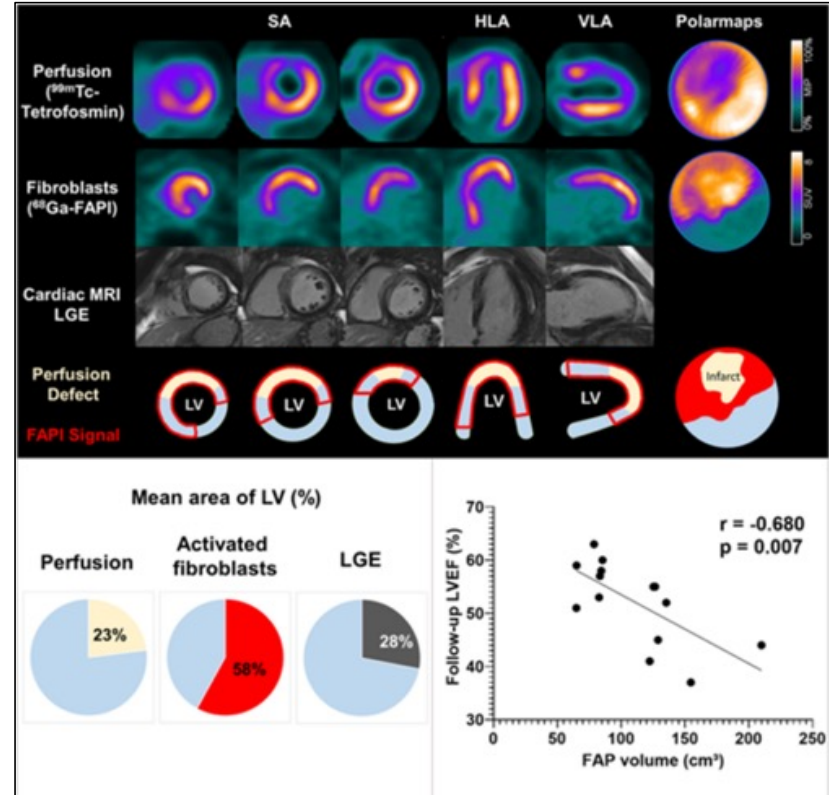
^{68}Ga FAPI PET/CT results led to changes in TNM staging in 10 of 19 patients



Röhrich M, Naumann P, Giesel FL, Choyke PL, Staudinger F, Wefers A, Liew DP, Kratochwil C, Rathke H, Liermann J, Herfarth K, Jäger D, Debus J, Haberkorn U, Lang M, Koerber SA. Impact of ^{68}Ga -FAPI PET/CT Imaging on the Therapeutic Management of Primary and Recurrent Pancreatic Ductal Adenocarcinomas. J Nucl Med. 2021 Jun 1;62(6):779-786

SNMMI Image of the Year 2022

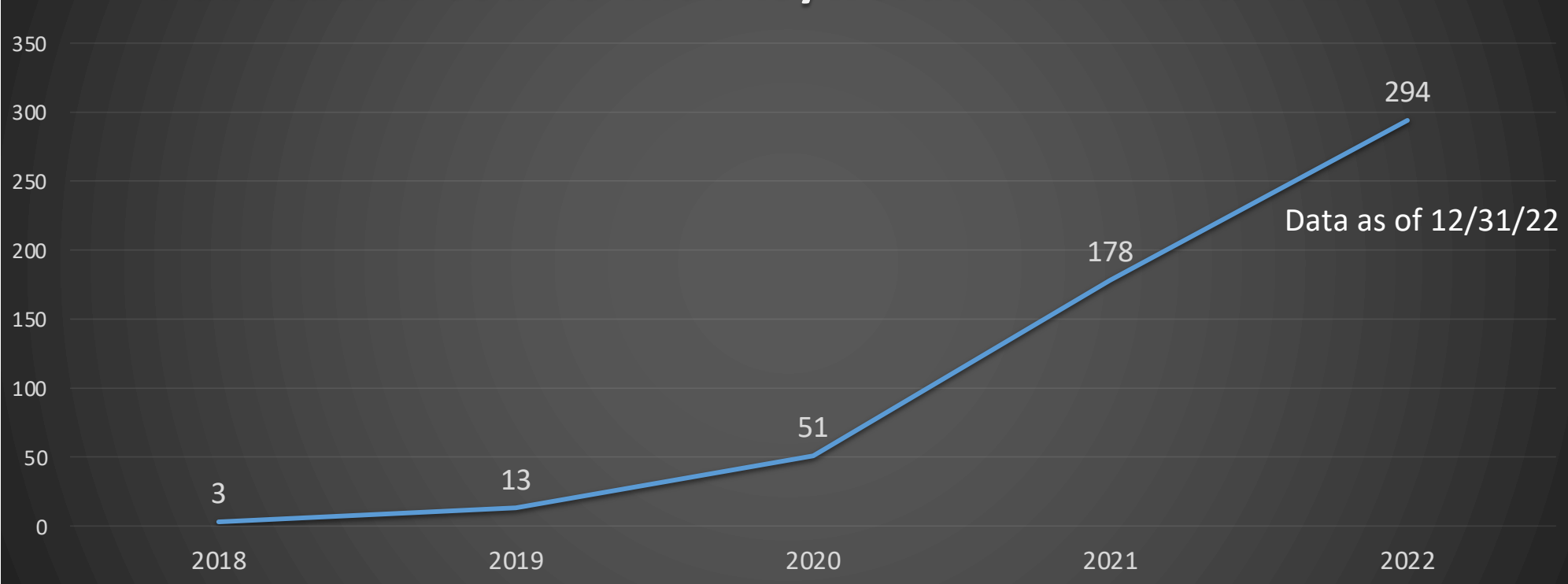
Representative case with acute anterior wall myocardial infarction: ^{68}Ga FAPI-46



Johanna Diekmann, James Thackeray, Thorsten Derlin, Christoph Czerner, Tobias Ross, and Frank Bengel, Department of Nuclear Medicine, Hannover Medical School, Hannover, Niedersachsen, Germany; and Tobias Koenig, Jonas Neuser, Andreas Schaefer, Jochen Tillmans, and Johann Bauersachs, Department of Cardiology and Angiology, Hannover School of Medicine, Hannover, Niedersachsen, Germany.

Mounting interest and growth of publications with FAPI

Publication counts with keywords "FAPI" and "PET"



FAP as a biomarker for FAP expression

What is a biomarker?

Live visualization and quantitation of FAP expression in humans

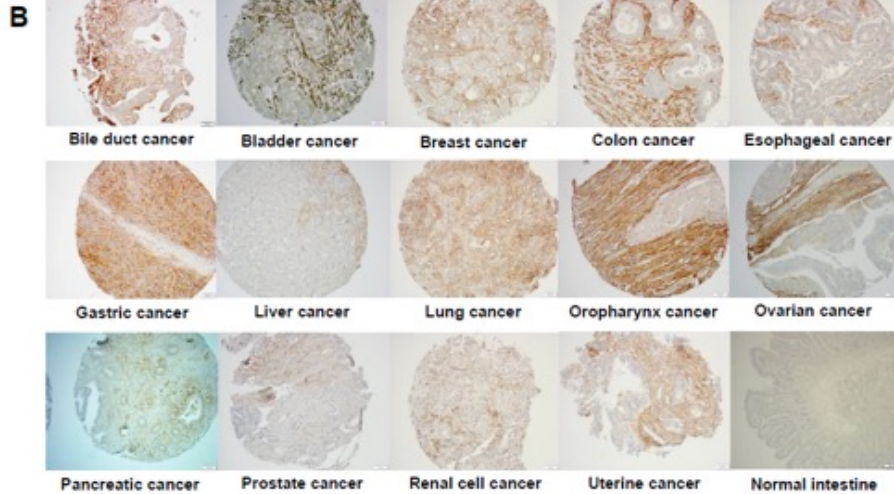
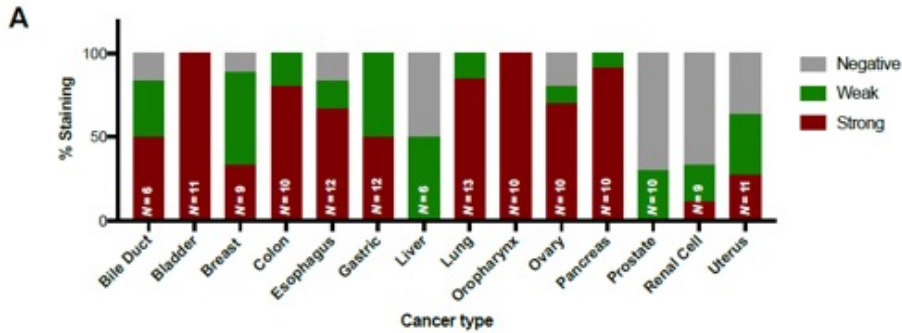
Why is this of value?

- Early diagnosis
- Disease staging
- Management of care
- Companion diagnostic
 - Enrich percent responders in therapy trials
 - Patient selection assay for effective therapy
- Treatment monitoring

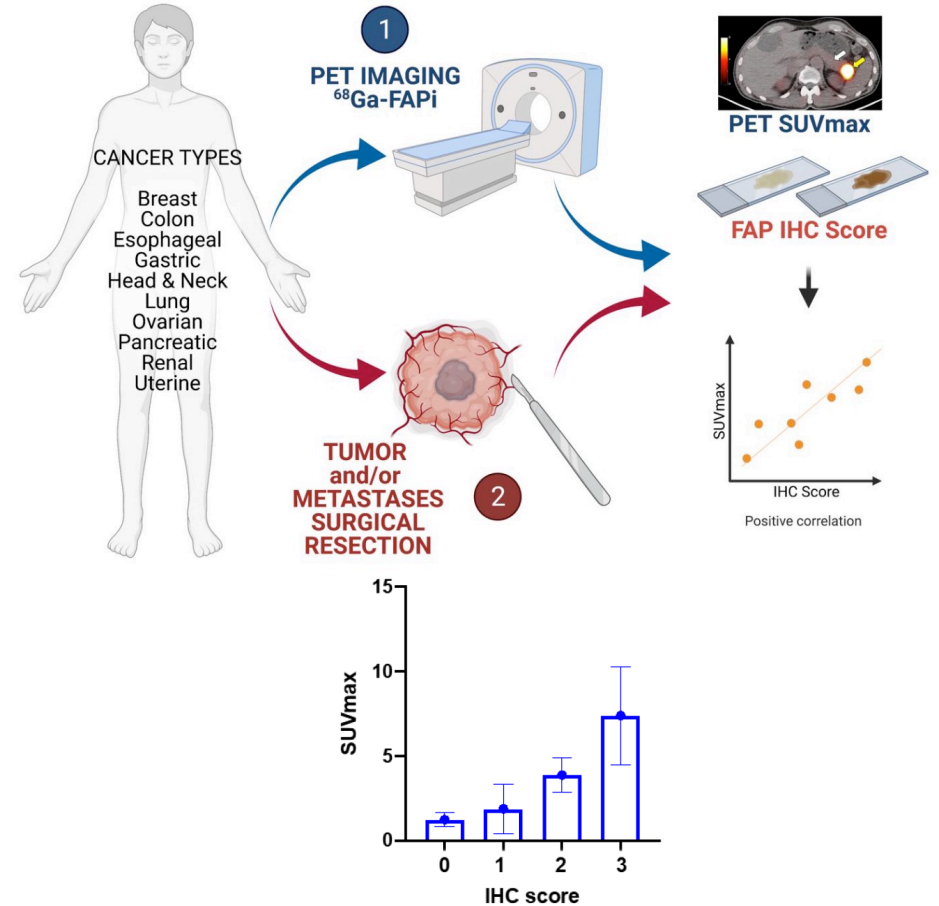


FAP expression and PET signal validation

Correlation between FAP immunohistochemistry score and ^{68}Ga -FAPi-46 PET SUVs across cancer and non-cancer tissues



Mona et al. doi: 10.2967/jnumed.121.262426



CARDIOVASCULAR DISEASE

Myocardial Fibrosis in systemic sclerosis

BACKGROUND

Myocardial fibrosis (MF) is a factor of poor prognosis in systemic sclerosis (SSc). Direct in-vivo visualization of fibroblast activation as early readout of MF has not been feasible to date.

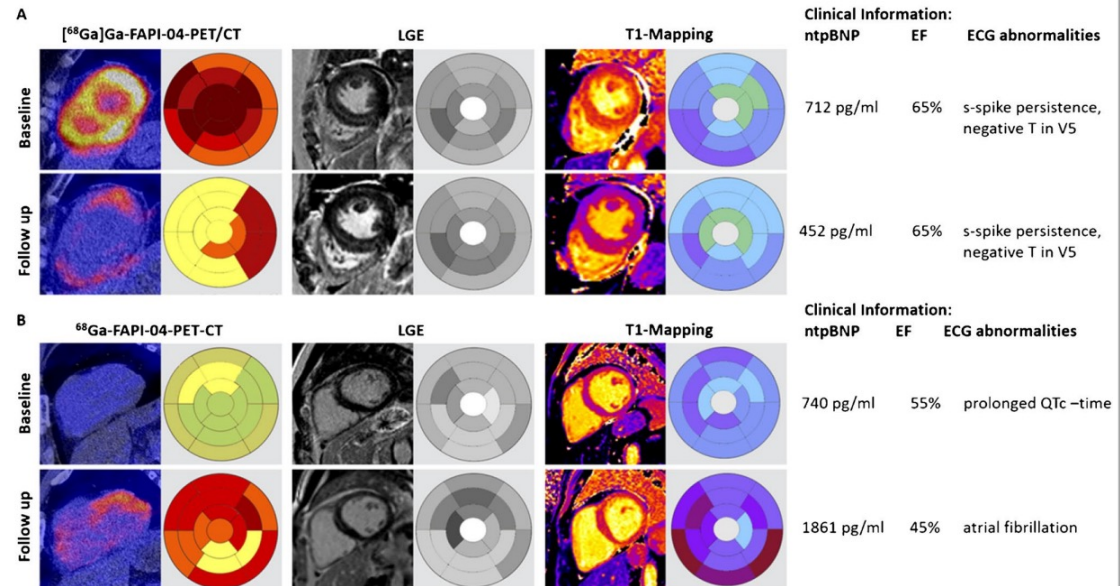
RESULTS

Sequential FAPI PET-CT dynamic changes of uptake associated with changes in the activity of myocardial fibrosis, while cMRI parameters remained stable after regression of molecular activity.

TAKEAWAY

FAPI uptake visualizes fibroblast activation in SSc-related myocardial fibrosis and can serve as a diagnostic option to monitor cardiac fibroblast activity.

Assessment of myocardial fibrosis in patients with systemic sclerosis using [68Ga]Ga-FAPI-04-PET-CT



Treutlein, C et al. Assessment of myocardial fibrosis in patients with systemic sclerosis using [68Ga]Ga-FAPI-04-PET-CT. Eur J Nucl Med Mol Imaging (2022).

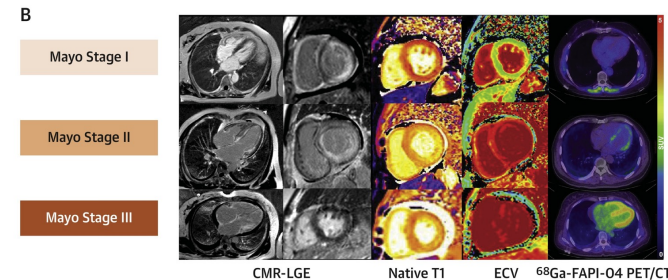
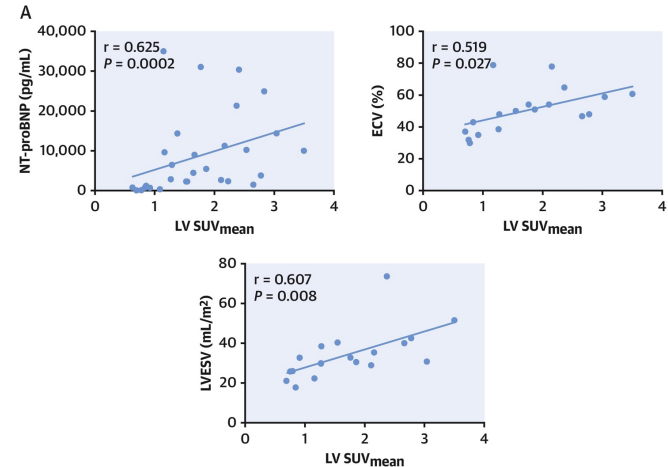
Amyloid light chain (AL) Cardiac Amyloidosis

BACKGROUND: Systemic amyloid light chain (AL) amyloidosis is the most common type of amyloidosis, leading to cardiomyocyte necrosis and interstitial fibrosis. To date, cardiac fibroblast and cardiac amyloidosis phenotype activities have not been mapped out in the myocardium.

STUDY: 30 consecutive patients with biopsy-proven AL amyloidosis were enrolled prospectively

TAKEAWAY: FAPI PET/CT detects myocardial fibroblast activation in patients with AL CA in correlation with myocardial remodeling. It can provide complementary information on cardiac biological characterization and staging of disease.

CENTRAL ILLUSTRATION: Fibroblast Activation PET in AL CA



Wang X, et al. J Am Coll Cardiol Img. 2022;15(11):1960-1970.

⁶⁸Ga-FAPI-04 uptake was significantly correlated with clinical biomarkers (Mayo stage and N-terminal pro-brain natriuretic peptide), interventricular septal thickness, left ventricular ejection fraction (LVEF), LV end-systolic volume, extracellular volume, and LV global strain ($P < 0.05$).

Immune-mediated disease

- Crohn's Disease

- Arthritis

- IgG4 Disease

Crohn's Disease

BACKGROUND

Differentiation between active intestinal inflammation and fibrosis has implications for treatment.

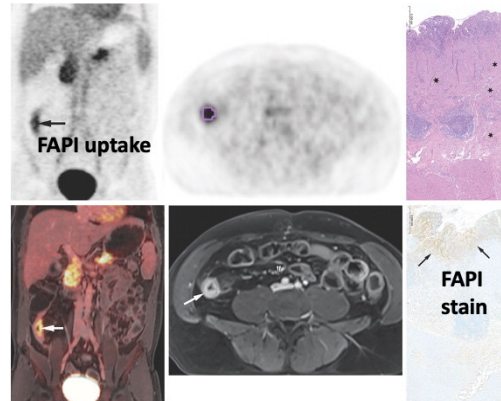
PURPOSE

To evaluate the predictive value of FAPI PET/MR for the assessment of bowel wall fibrosis in Crohn's disease.

TAKEAWAY

Higher FAPI uptake at PET/MR is associated with histopathologically assessed bowel wall suggesting diagnostic potential for treatment decisions.

Evaluation of Intestinal Fibrosis with ^{68}Ga -FAPI PET/MR Enterography in Crohn Disease



- Prospective study of 14 participants with Crohn disease; 28 of 51 bowel segments were fibrotic at histologic examination (14 moderate, 14 severe).
- The maximum standardized uptake value (SUV_{max}) at ^{68}Ga -FAPI PET/MR enterography was higher in bowel with fibrosis than without (mean, 7.6 vs 2.0) ($P < .001$).
- Bowel with more severe fibrosis had a higher uptake than bowel with moderate fibrosis (SUV_{max} , 8.9 vs 6.2, $P = .045$).

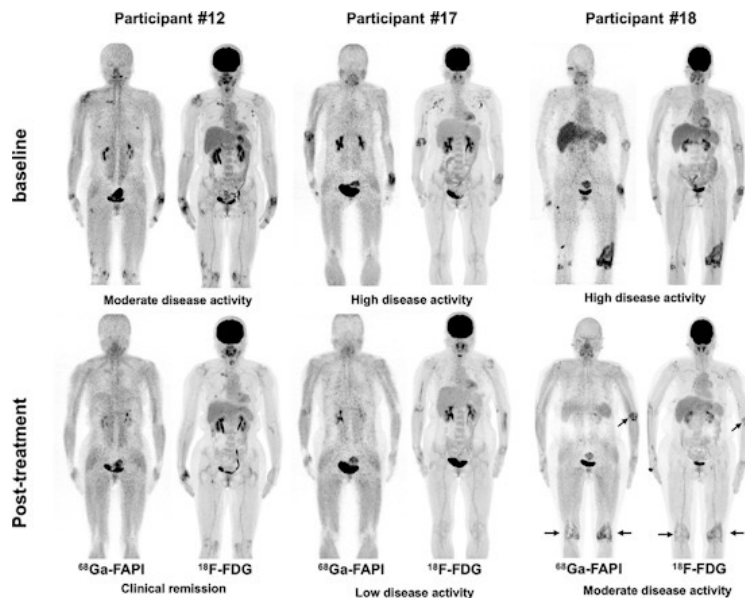
Scharitzer M et al. Published Online: February 28, 2023
<https://doi.org/10.1148/radiol.222389>

Radiology

Rheumatoid Arthritis

PURPOSE: In rheumatoid arthritis, fibroblast-like synoviocyte cells, which overexpress FAP. This is a feature that can be leveraged to improve imaging assessment of disease.

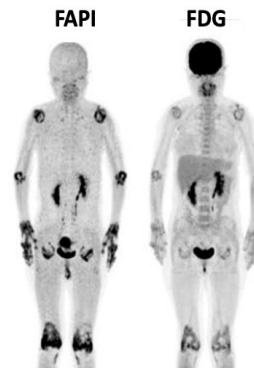
RESULTS: In rheumatoid arthritis subjects undergoing FAPI PET/CT, the extent of joint involvement correlated with clinical and laboratory variables of disease activity and showed a greater amount and degree of affected joints than at fluorine 18 fluorodeoxyglucose PET/CT.



FAPI-PET shows promise in patients with RA

By Will Morton, AuntMinnie.com staff writer March 2, 2023

^{68}Ga -FAPI PET/CT for Rheumatoid Arthritis: A Prospective Study



- Prospective study of 20 participants with moderate to severe rheumatoid arthritis (RA) who underwent PET/CT with ^{68}Ga -FAPI and FDG.
- The number of affected joints and degree of uptake at PET correlated with clinical assessment and C-reactive protein levels ($P < .05$).
- The maximum standard uptake value of the most affected joint was higher with ^{68}Ga -FAPI than with ^{18}F -FDG (9.5% vs 5.9%, respectively; $P < .001$).

Luo Y et al. Published Online: February 28, 2023
<https://doi.org/10.1148/radiol.222052>

Radiology

IgG4 disease

Key messages

What is already known about this subject?

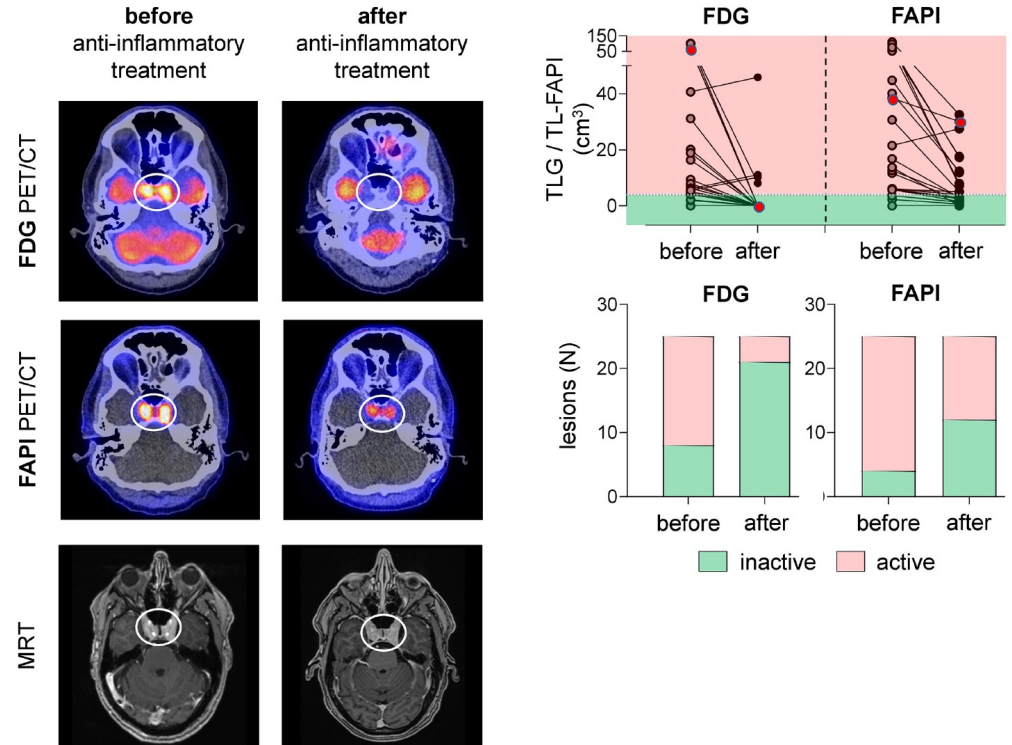
- How to distinguish inflammatory from fibrotic activity in human immune-mediated disease in vivo.

What does this study add?

- Positron emission tomography (PET) for fibroblast-activation protein (FAP) permits the discrimination of inflammatory from fibrotic activity in fibroinflammatory diseases such as IgG₄-related disease.

How might this impact on clinical practice or future developments?

- FAP-specific PET/CT currently represents the only available non-invasive imaging modality that can specifically visualise fibrotic activity independent from inflammation.



Schmidkonz C et al. Disentangling inflammatory from fibrotic disease activity by fibroblast activation protein imaging. Ann Rheum Dis. 2020 Nov.

FIBROTIC DISEASE

- Liver
 - Lung
-

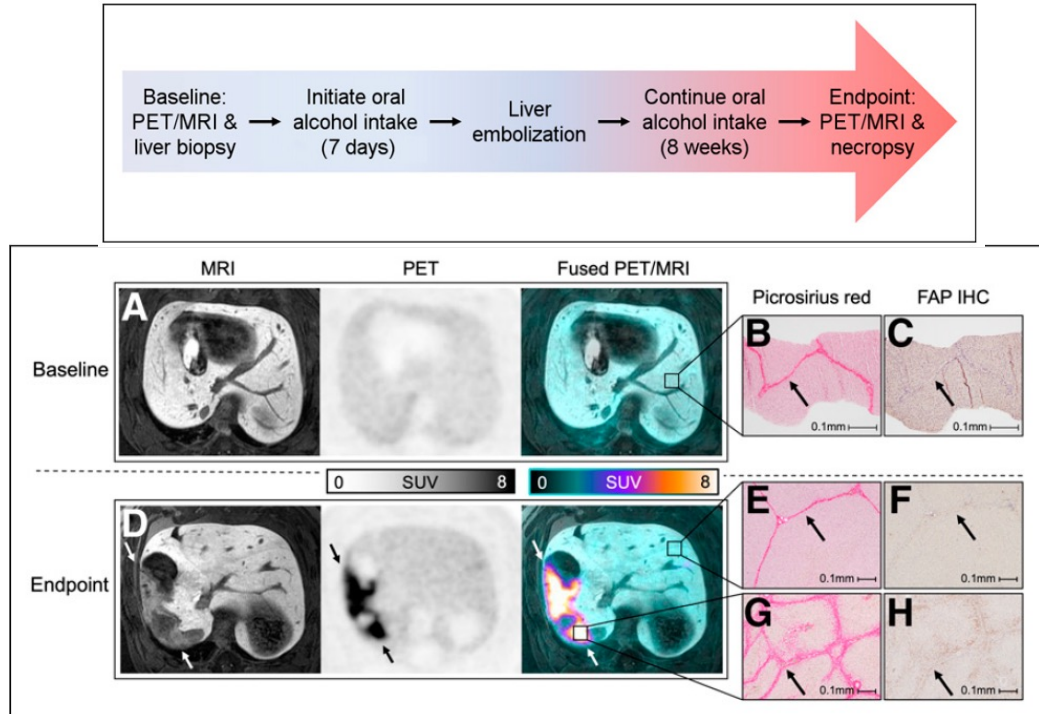
Liver Fibrosis

QUESTION: Is there potential for ^{68}Ga -FAPI PET in staging liver fibrosis?

RESULTS: This animal study demonstrated a direct correlation between quantitative liver ^{68}Ga -FAPI uptake on PET and both histologic measures of liver fibrosis.

TAKEAWAYS: The strong correlation between liver FAPI uptake and the histologic stage of liver fibrosis suggests FAPI PET is a promising assay that can achieve noninvasive and accurate staging of fibrosis throughout the entire liver.

Staging Liver Fibrosis by Fibroblast Activation Protein Inhibitor Positron Emission Tomography in a Human-sized Swine Model



Pirasteh A. et al. Staging Liver Fibrosis by Fibroblast Activation Protein Inhibitor PET in a Human-Sized Swine Model. *J Nucl Med.* 2022 Dec

Interstitial lung diseases (ILDs)

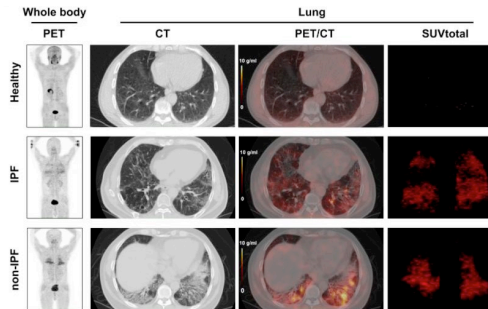
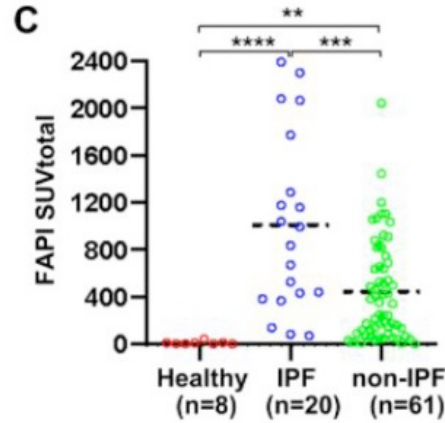
QUESTION: Is ^{68}Ga -FAPI PET/CT a potential new imaging method for patients with fibrotic interstitial lung diseases (fILDs)?

PERTINENT FINDINGS:

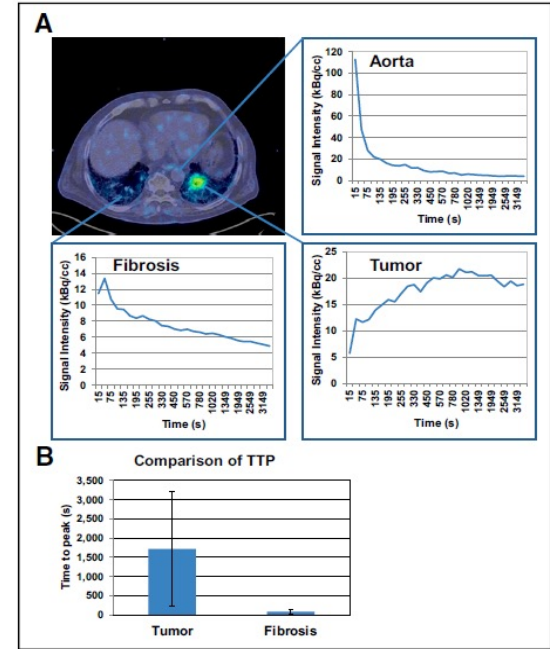
Fibrotic areas and tumor lesions both showed elevated ^{68}Ga -FAPI uptake but had different tracer kinetics.

TAKEAWAY

^{68}Ga -FAPI PET/CT is a promising imaging method for patients with fILDs and can be used for early diagnosis and selection of appropriate therapy and therapeutic window.



Yang et al. AJRCCM 2023

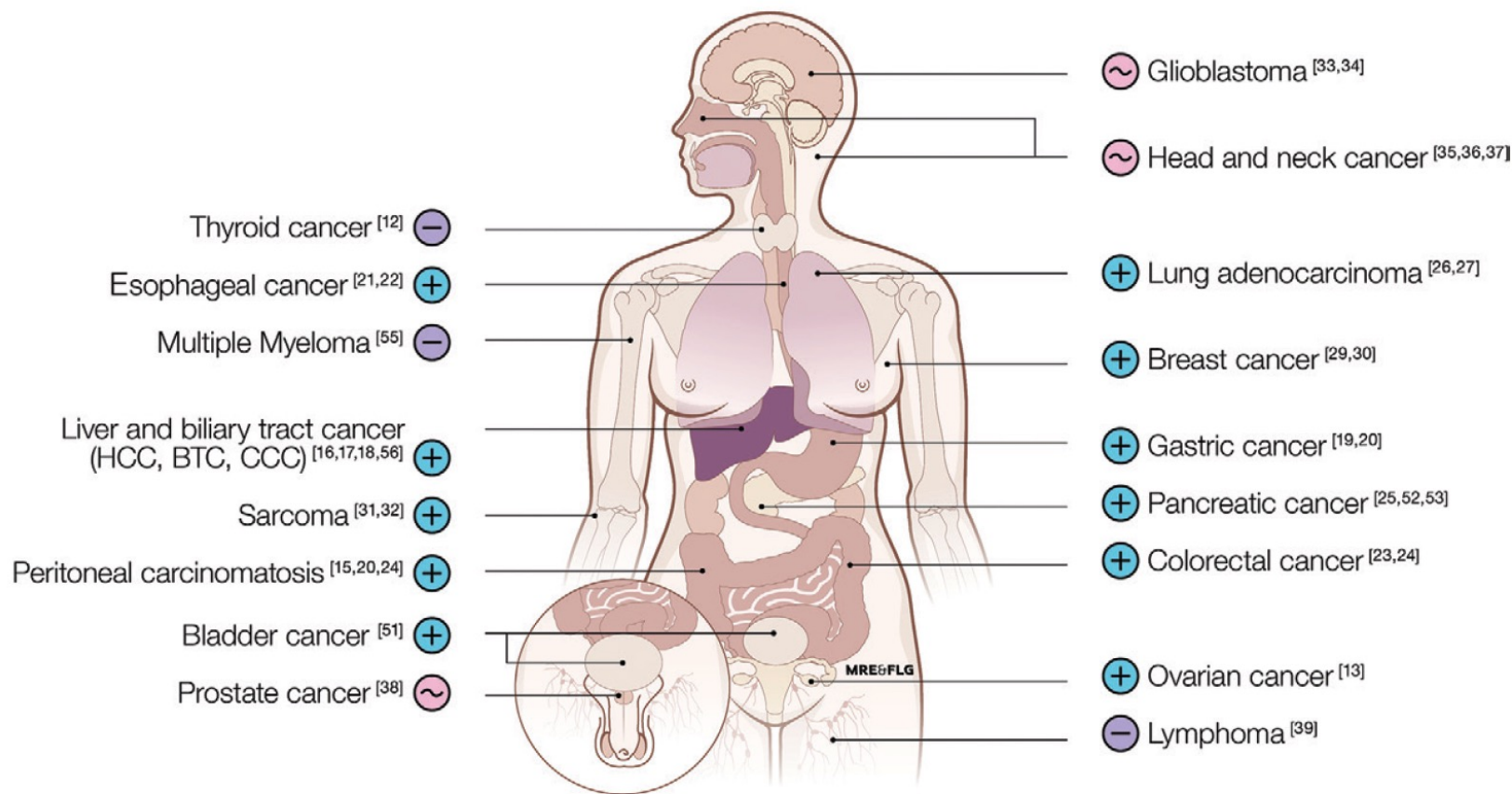


Rohrich et al. JNM 2022

IPF: Idiopathic pulmonary fibrosis

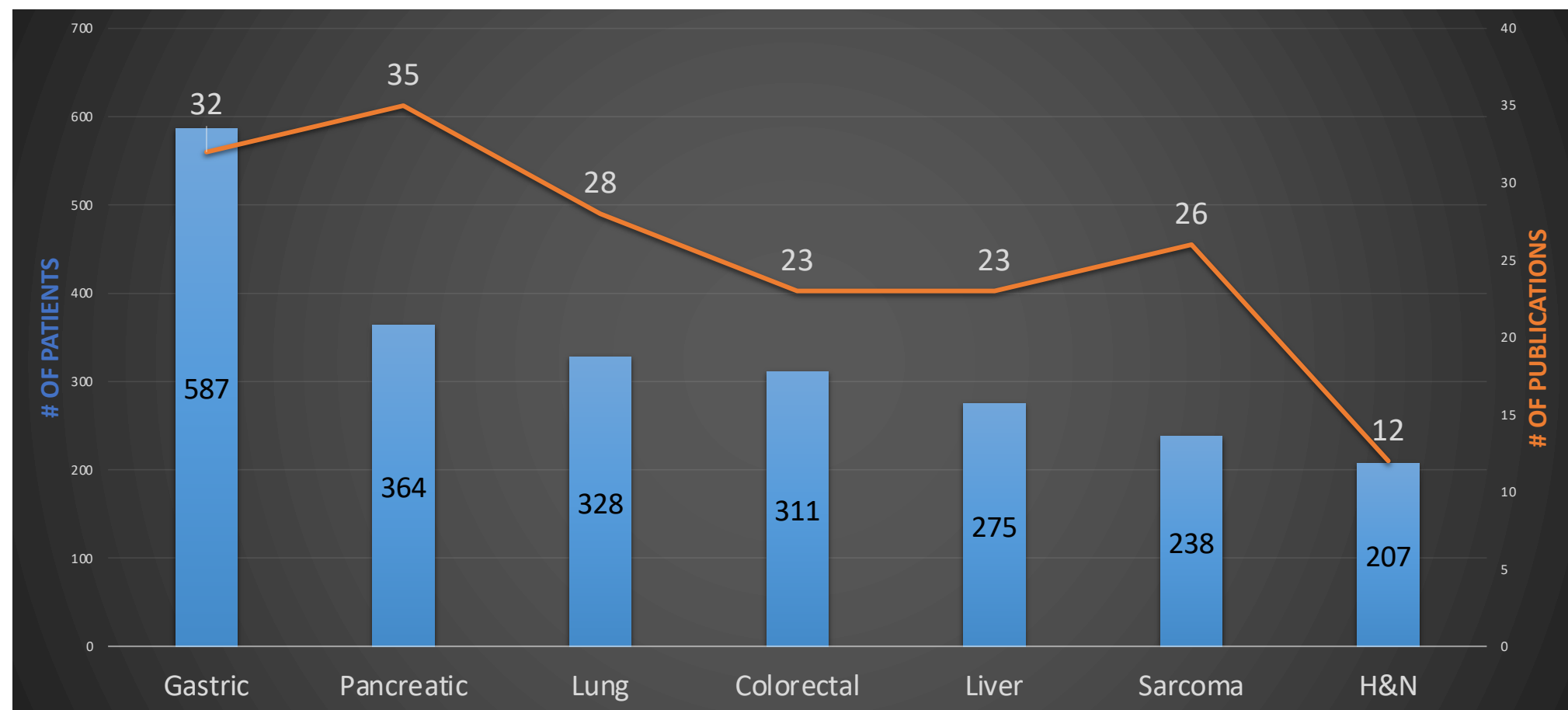
ONCOLOGY

Comparison of FAPI vs. FDG in oncological PET-imaging

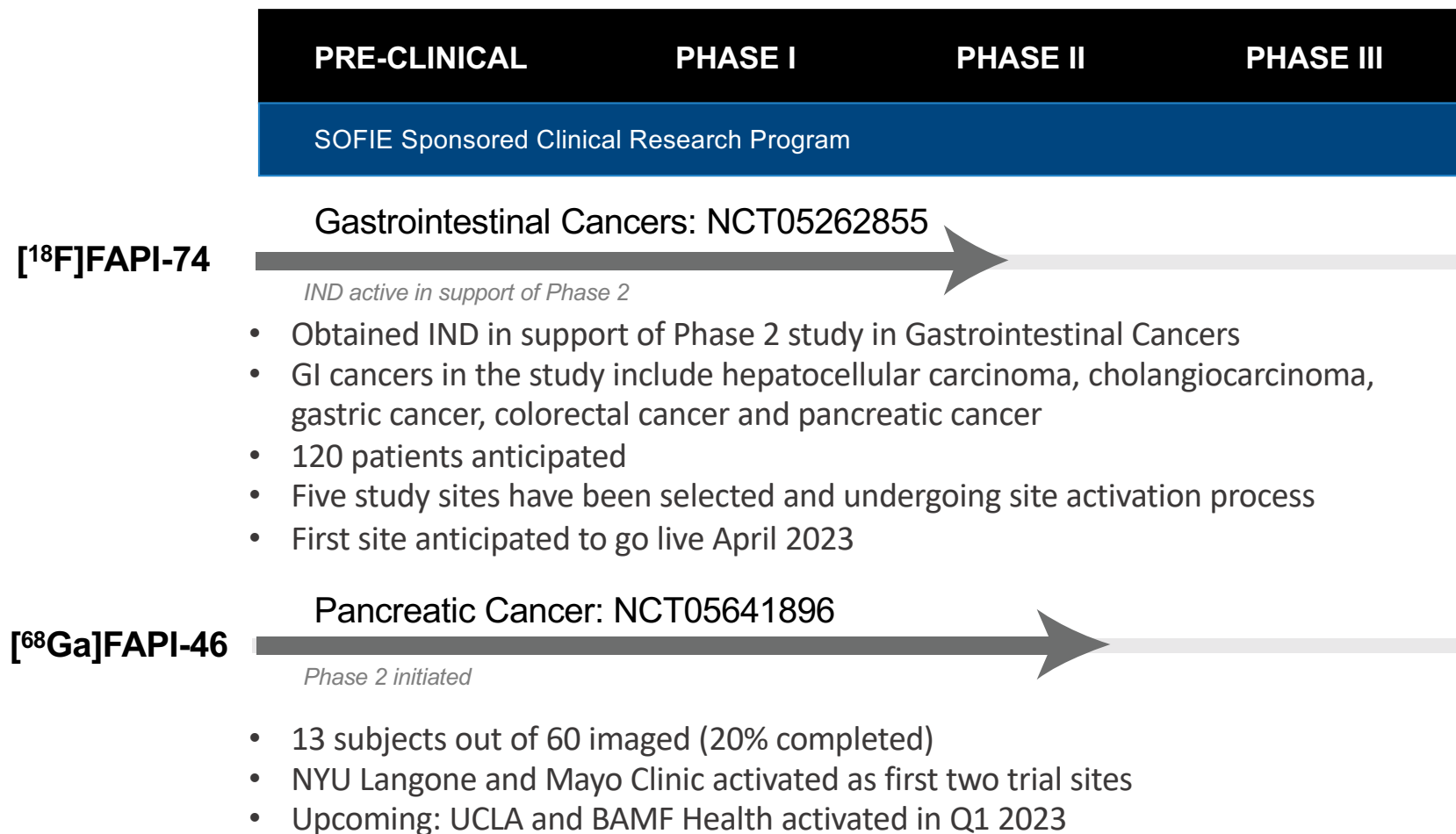


Publication analysis

Cancers with the highest # of patients (>200) reported with FAPI compounds



SOFIE's FAPI pipeline and progress update



SOFIE's Product Pipeline



Gastrointestinal Cancers: (NCT05262855)

[¹⁸F]FAPI-74

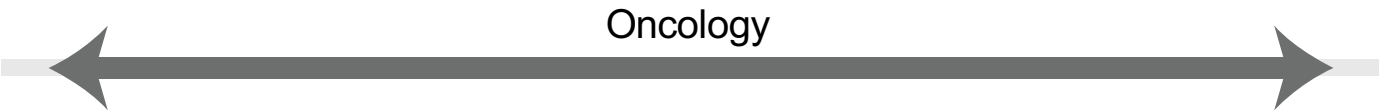


Pancreatic Cancer: (NCT05641896)

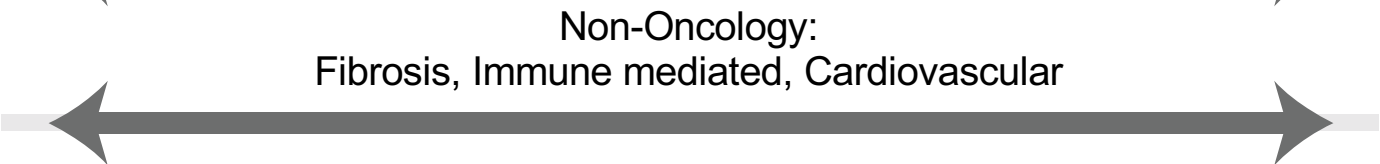
[⁶⁸Ga]FAPI-46

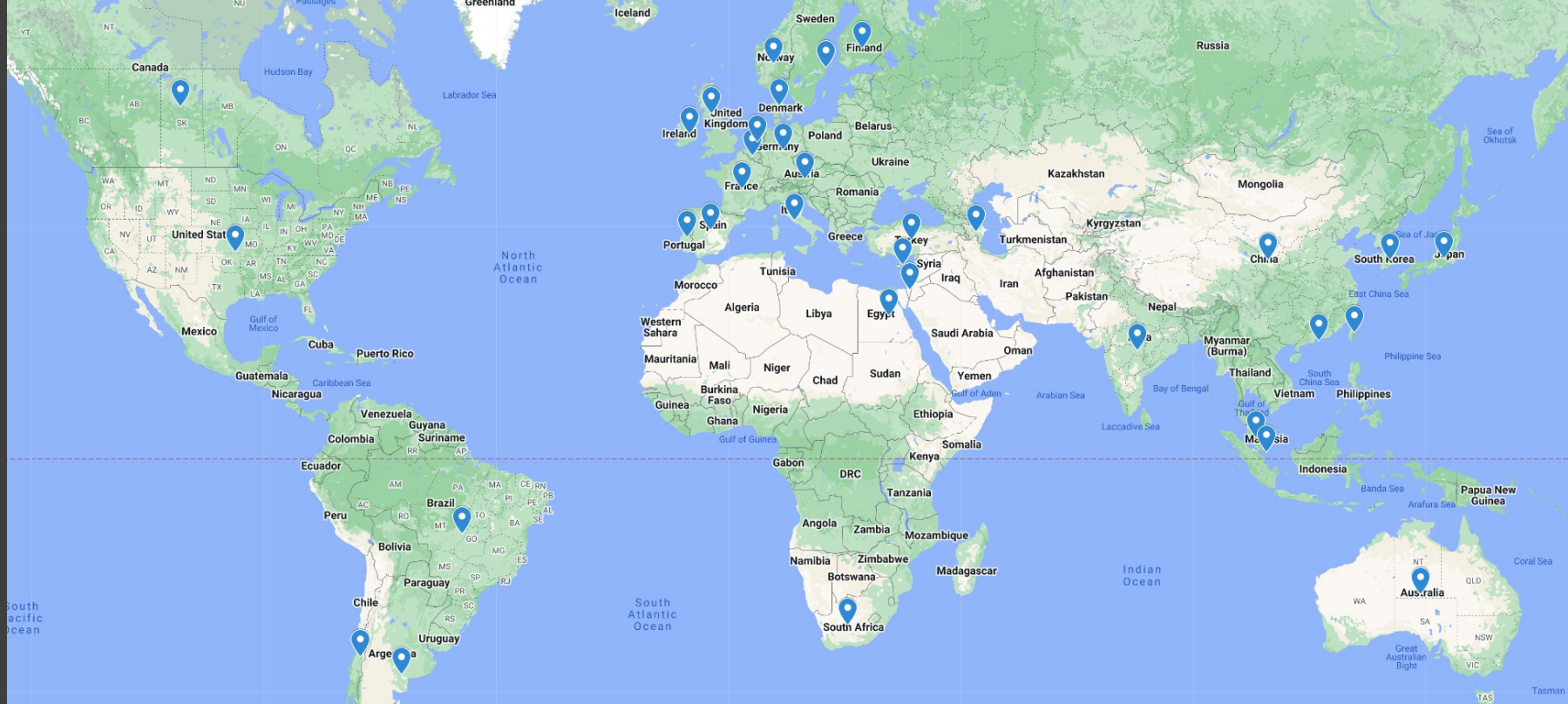


[¹⁸F]FAPI-74
[⁶⁸Ga]FAPI-46



[¹⁸F]FAPI-74
[⁶⁸Ga]FAPI-46

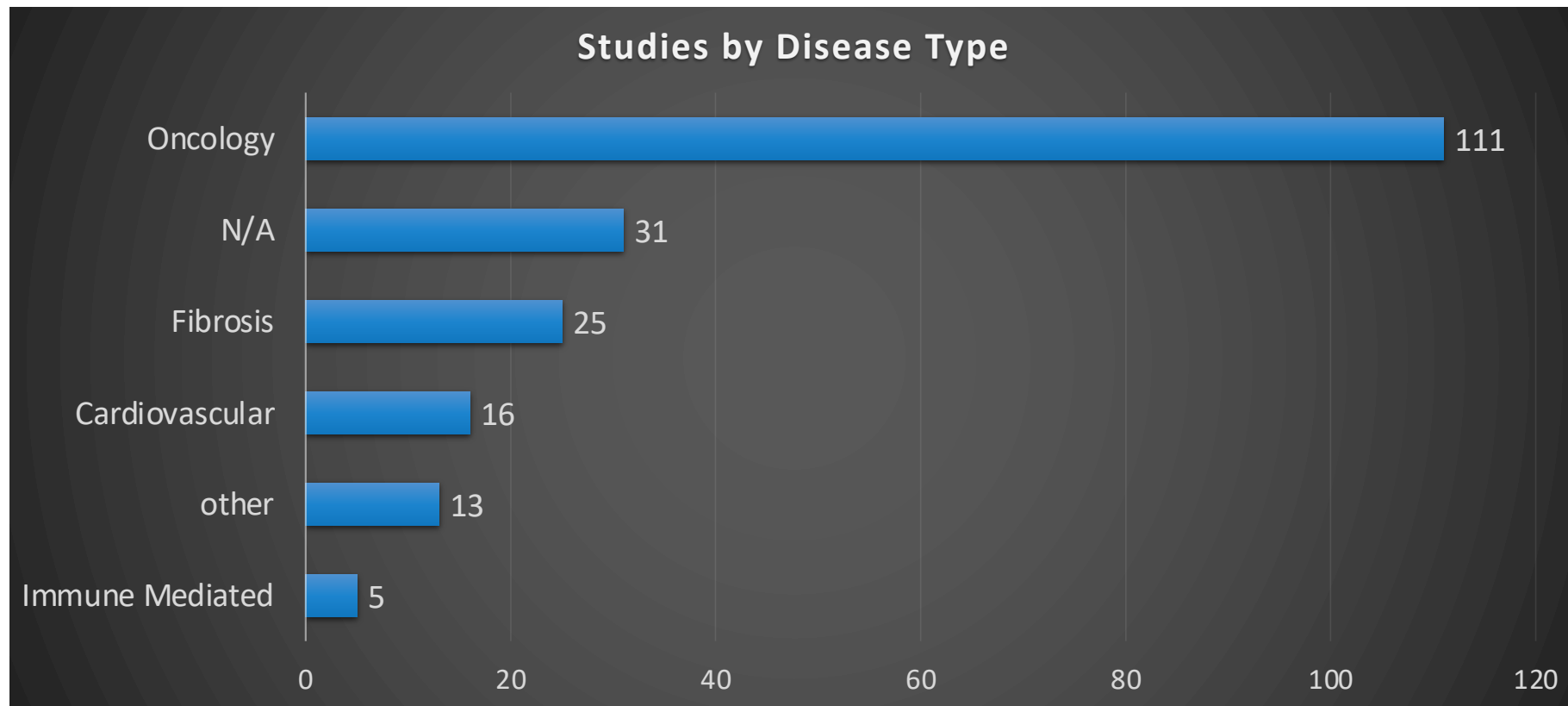




SOFIE's FAPI Global Outreach Program

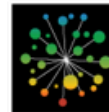
- 38 Countries and growing
- 201 research studies and growing
- 115 unique institutions and growing
- Compounds: [^{18}F]FAPI-74 and [^{68}Ga]FAPI-46

Studies with the FAPI probe by disease type

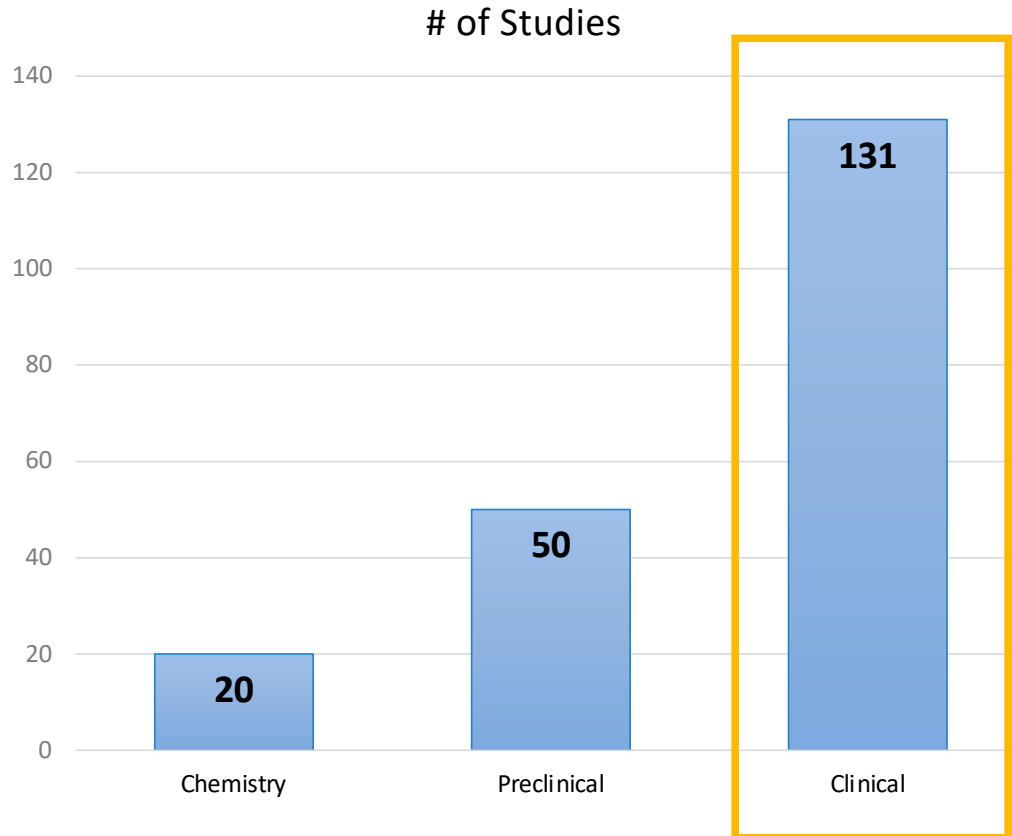


N/A: Chemistry or other studies with no specific disease indication

Other: Other clinical indications not captured



FAPI Global Outreach Patient Studies



6879

Total Planned Patients

1,082

Patients Imaged by Aug 2022





To improve patient outcomes by developing and delivering molecular diagnostics and therapeutics (theranostics). With our robust radiopharmaceutical production and distribution network, mature contract manufacturing services, and now, high value radiopharmaceutical intellectual property, we are poised to deliver on the promise of radiopharmaceuticals.



Our Pipeline

With over 50 years of passion and dedication for the future of PET, we have taken bold steps to advance the development of next generation radiopharmaceuticals.

[VIEW PIPELINE](#)



Partnership

We offer a range of contract manufacturing services to meet your clinical needs through our network and new Theranostics Center of Excellence.

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PET Education

We have created a multifaceted approach designed to strengthen the quality of PET programs in your practice and deliver enhanced care to your patients.

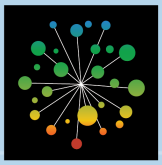
[LEARN MORE](#)



Our Network

We have 14 network sites committed to on-time delivery of radiopharmaceuticals to meet our clients' need in diagnosing and treating critical illnesses every day.

[FIND A PHARMACY](#)



SOFIE

From start to clinic

Thank you

3/14/23

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