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Bench to bedside:
translational nuclear medicine research and clinical theranostics in PUMCH

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Peking Union Medical College Hospital, Beijing, China.

The 23rd International Conference on Cyclotrons and their Applications (CYC2022)
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PUMCH

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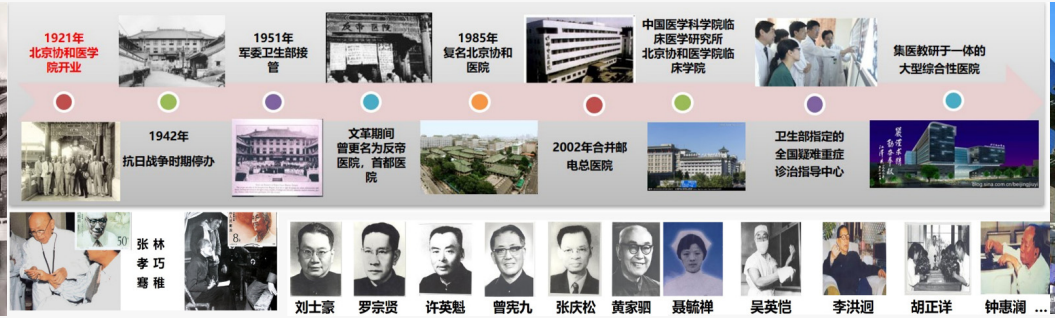
- **Peking Union Medical College Hospital** was founded by the Rockefeller Foundation in 1921.
- Over the past 100 years, PUMCH has been leading the advances of modern medical sciences in China, and being ranked 1 in the nation since 2009 to 2022.
- **PUMCH motto: Precision, Perseverance, Diligence, and devotion**



Nuclear Medicine in PUMCH

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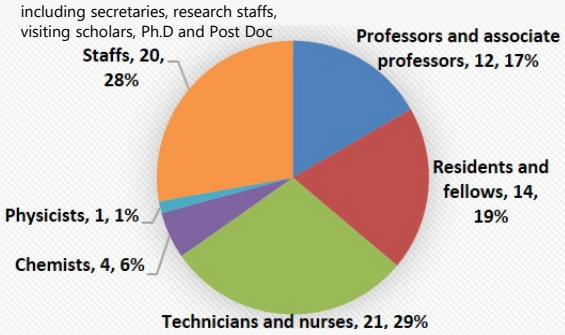
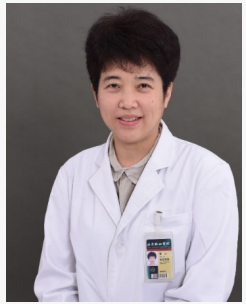
Faculties and staffs of NM (2021)

- Nuclear Medicine department was founded in **1958**
- Equipment for imaging: 2 PET/MR, 5 PET/CT, 8 SPECT/CT and 2 SPECT. Equipment for radiopharmaceutical synthesis and research: 1 Cyclotron, 1 Micro PET, 2 Generator (^{99}Mo-^{99m}Tc/^{68}Ge-^{68}Ga) and 10 hot cell.
- 1 ward(10beds) for radionuclide therapy
- More than 50 research projects
- More than 10 isotopes and 90 radiopharmaceuticals are employed to support clinical and research work.
- **Ranked 1# in in all China's NM department since 2015 to 2022.**



Clinical work per year in NM department (case)

	2019	2020	2021	2022（1-10）
PET scan	11127	9248	12871	10678
SPECT scan	23248	17250	21406	17056
Nuclide therapy	4245	2189	3722	2619
radioimmunoassay	64681	39993	60432	44452
^{13}C breath test	66228	29006	53836	46226



Director: Pro. Huo Li

Radiopharmaceuticals for clinical and research imaging

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	^{18}F (Since 1998)		^{68}Ga (Since 2012)	^{99m}Tc (Since 1980s)	^{13}N/^{11}C (Since 1998)	^{131}I (Since 1958)
1	^{18}F-FDG	^{18}F-FES	^{68}Ga-DOTA-TATE	^{99m}Tc-DTPA	^{13}N Ammonia	^{131}I
2	(S)-^{18}F-FBFP	^{18}F-FEL	^{68}Ga-DOTA-RGD	^{99m}Tc-MAA	^{11}C Acetate	^{131}I-MIBG
3	L-5-(2-[^{18}F]fluoro ethoxy)tryptophan	^{18}F-FECH	^{68}Ga-DOTA-EB	^{99m}Tc-MDP	^{11}C Choline	
4	Al^{18}F-PSMA-617	^{18}F-FDS	^{68}Ga-NOTA-PRGD2	^{99m}Tc-MIBI	^{11}C Methonine	
5	Al^{18}F-NOTA-LM3	^{18}F-FDDNP	^{68}Ga-NEB	^{99m}Tc-OCT	^{11}C-β-CFT	
6	Al^{18}F-NOTA-FAPI-04	^{18}F-FCH	^{68}Ga-DOTA-Nerotension	^{99m}Tc-SC	^{11}C-PIB	
7	^{8}F-Fluoroacetate	^{18}F-Fallypride	^{68}Ga-BMV101	^{99m}Tc-PYP	^{11}C-HFC	
8	^{18}F-β-CFT	^{18}F-DPA-714	^{68}Ga-CXCR4	^{99m}Tc-ECD		
9	^{18}F-XTR004	^{18}F-BPA	^{68}Ga-DOTA-TATE-RGD	^{99m}Tc-HIDA		
10	^{18}F-T807（Fluorine-18 flortaucipir）	^{18}F-AV45（Fluorine-18 florbetapir）	^{68}Ga-DOTA-EB-TATE	^{99m}Tc-DMSA		
11	^{18}F-SFB-VEGF	^{18}F-AV1（Fluorine-18 florbetaben）	^{68}Ga-DOTA-BBN-RGD	^{99m}Tc-HSA		
12	^{18}F-P1OP	^{18}F-Al-NOTA-TATE	^{68}Ga-DOTA-TMVP1	^{99m}Tc-GSA		
13	^{18}F-MK6240	^{18}F-Al-NOTA-PRGD2	^{68}Ga-exendin4	^{99m}Tc-RGD		
14	^{18}F-MFBG	^{18}F-Al-NOTA-EB	^{68}Ga-R01	^{99m}Tc-CNDG		
15	^{18}F-L-DOPA	^{18}F-92	^{68}Ga-JR11	^{99m}Tc-FAPI		
16	^{18}F-FP-CIT	^{18}F-1799	^{68}Ga-FAPI	^{99m}Tc-H-PoFP$_2$		
17	^{18}F-FPA	^{18}F-MK6240	^{68}Ga-PSMA			
18	^{18}F-FMISO	^{18}F-FP-CIT	^{68}Ga-DOTA-LM3			
19	^{18}F-FLT	^{18}F-FET	^{68}Ga-RM26			
20	^{18}F-FHBG		^{68}Ga-FSDD$_3$I			
21			^{68}Ga-3BP-227			

Radiopharmaceuticals for clinical and research therapy

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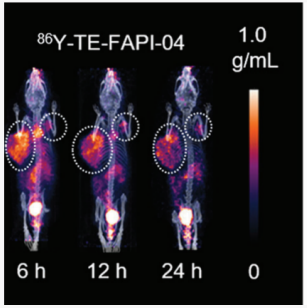
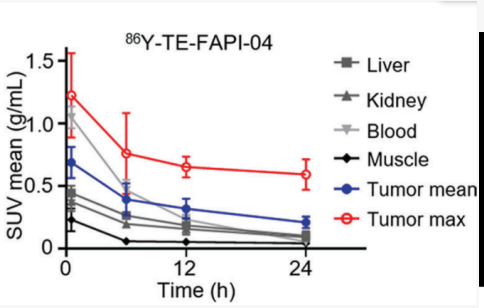
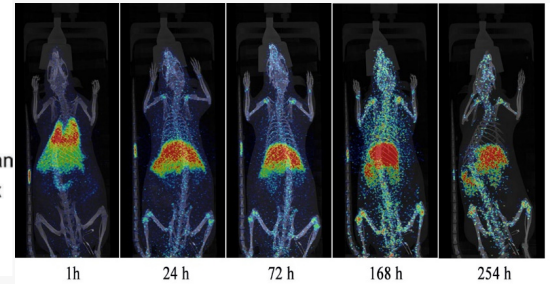
- For preclinical research: ^{188}Re, ^{89}Zr, ^{64}Cu, and ^{86}Y.
- For radionuclide therapy:

^{131}I	^{177}Lu (Since 2017)	^{90}Y (Since 2002)	^{89}Sr	^{223}Ra	^{32}P
^{131}I-MIBG ^{131}I	^{177}Lu-PSMA ^{177}Lu-EB-PSMA ^{177}Lu-TATE ^{177}Lu-EB-TATE	^{90}Y-TATE			

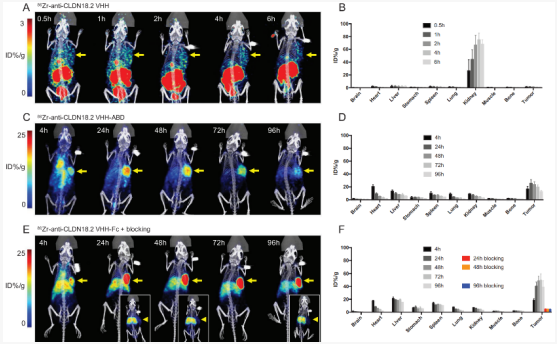




Whole-body microPET/CT imaging of ^{89}Zr-oxine EPCs in health rats.



^{89}Zr-anti-CLDN18.2 VHH



- Ding, Jie; et al. 86Y-Labeled Albumin-Binding Fibroblast Activation Protein Inhibitor for Late-Time-Point Cancer Diagnosis. Molecular Pharmaceutics, 2022, 19(9): 3429-3438.
- Hu Guilan, et al. Development and comparison of three (89)Zr-labeled anti-CLDN18.2 antibodies to noninvasively evaluate CLDN18.2 expression in gastric cancer: a preclinical study. *Eur J Nucl Med Mol Imaging, 2022, 49(8): 2634-2644.
- 42. Yimin Liu; et al; Evidence of accumulated endothelial progenitor cells in the lungs of rats with pulmonary arterial hypertension by 89Zr-oxine PET imaging , Molecular Therapy-Methods & Clinical Development, 2020. May 3;17:1108-1117

NM translational research stay ahead of the NET theranostic curve

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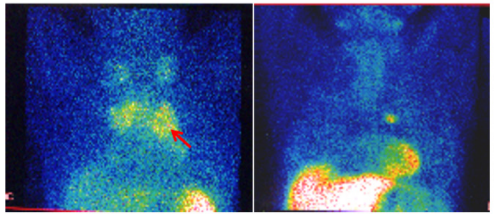
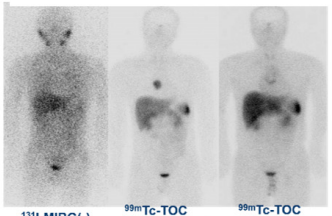
Series translational nuclear medicine research on somatostatin receptor

^{111}In-DTPA-D-Phe^{1}-octreotide (1996)



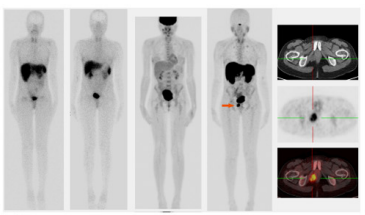
^{111}In-octrotide ^{99m}Tc-MIBI

^{99m}Tc-HYNIC-TOC (2001)



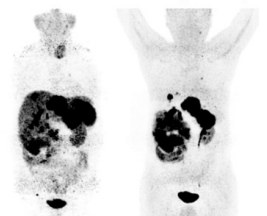
^{131}I-MIBG(-) ^{99m}Tc-TOC (preoperative) ^{99m}Tc-TOC (postoperative)

^{68}Ga-DOTATATE (2010)



^{99m}Tc-TOC (-) FDG PET (-) ^{68}Ga-DOTATATE PET/CT

^{68}Ga-DOTA-JR11 (2018)

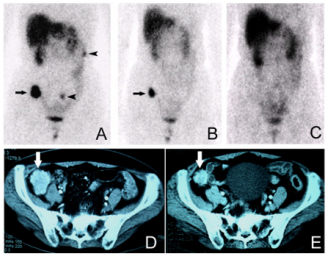


^{68}Ga-DOTA-TATE ^{68}Ga-DOTA-JR11

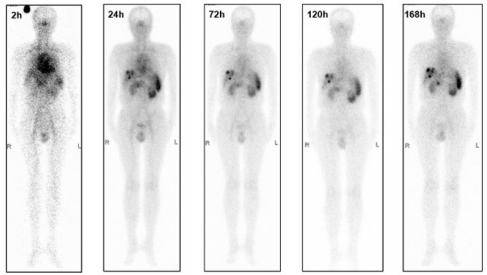
^{90}Y-TATE (2002)

Unique in China:

^{99m}Tc-HYNIC-TOC scan guiding PRRT of ^{90}Y-TATE



^{177}Lu-DOTATATE (2017)



Representative images of a 62y-old male patient at 2, 24, 72, 120 and 168h after intravenous administration of ^{177}Lu-DOTA-EB-TATE (19.5mCi)

^{68}Ga-DOTA-TATE PET/CT监测^{177}Lu-DOTATATE治疗疗效

NM translational research stay ahead of the NET theranostic curve

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Series translational nuclear medicine research on somatostatin

2020年第6期
Featured article and cover image

2021年第10期
Featured article and cover image

Translational medicine is critical for complex severe and rare diseases.

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PUMCH, national center for complex, severe and rare diseases

- Pro. Xiaoqian Zhang , famous professor and internist in China.
- He diagnosed the first case of tumor-induced osteomalacia (TIO) in China, a rare paraneoplastic syndrome clinically characterized by bone pain, fractures and muscle weakness.
- TIO lesions are typically small, benign mesenchymal tumors that may be found in bone or soft tissue, anywhere in the body. Locating the tumor is critical, as complete removal is curative.
- However, localization of the lesion is challenging. Only 30% are superficial and can be palpated, while the remaining 70% are impalpable.
- Step wise locating of the culprit lesions is critical for the patients with TIO

SSTR2 imaging help localize TIO

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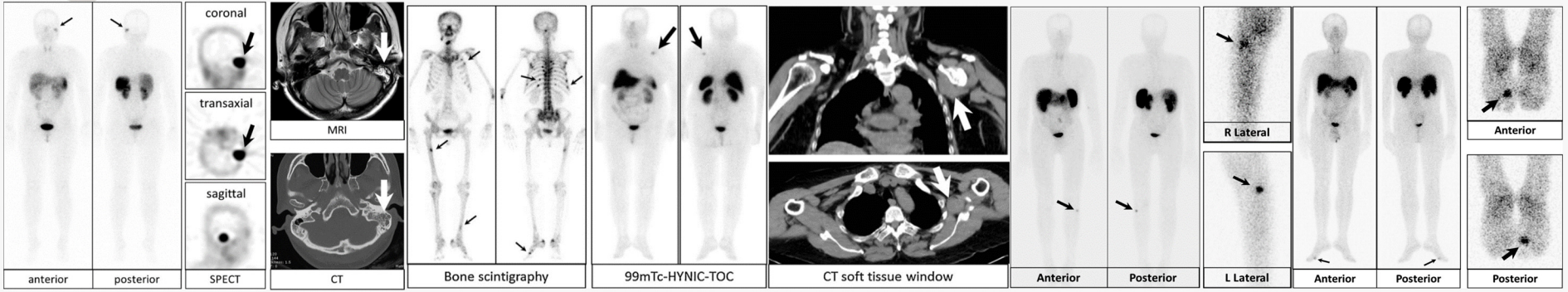

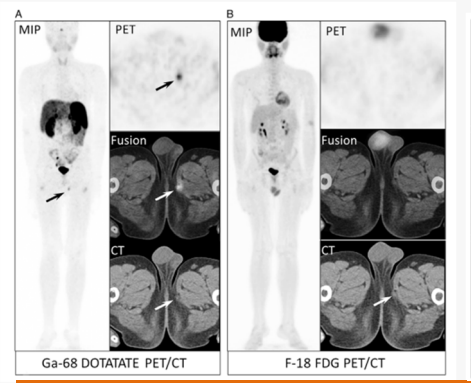

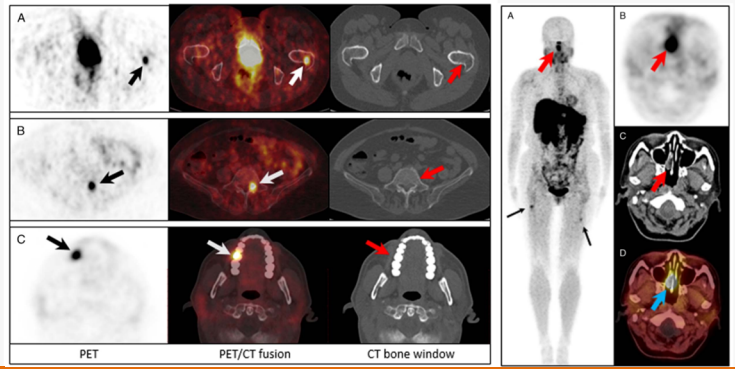

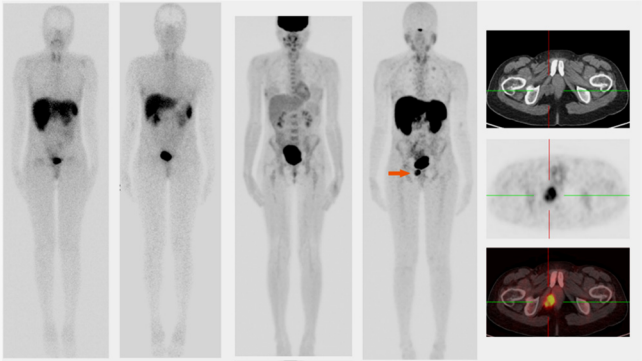

^{68}Ga-DOTATATE PET (+) FDG (-) ^{68}Ga-DOTATATE PET (+) ^{99m}Tc-TOC (-) FDG (-) ^{68}Ga-DOTATATE PET (+)

SSTR2 imaging help localize TIO

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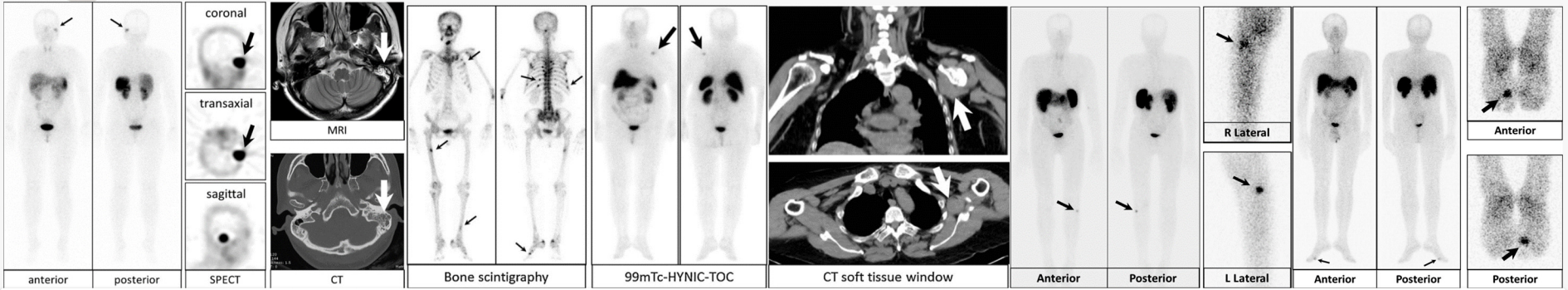
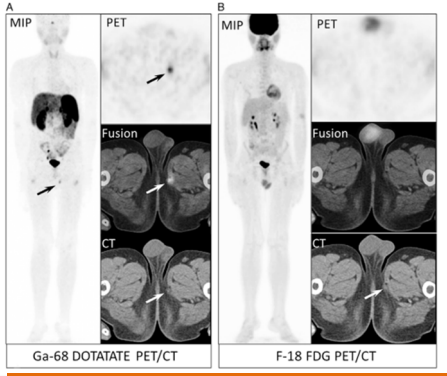
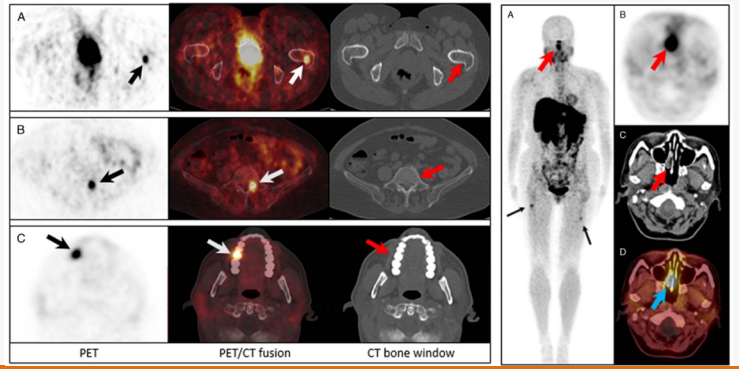


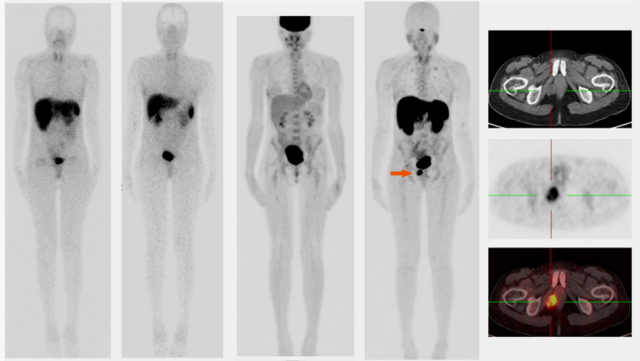
^{99m}Tc-HYNIC-TOC SPECT imaging



^{68}Ga-DOTATATE PET (+) FDG (-)



^{68}Ga-DOTATATE PET (+)



^{99m}Tc-TOC (-) FDG (-) ^{68}Ga-DOTATATE PET (+)

A series of translational research work promote MDT for complex, severe and rare diseases

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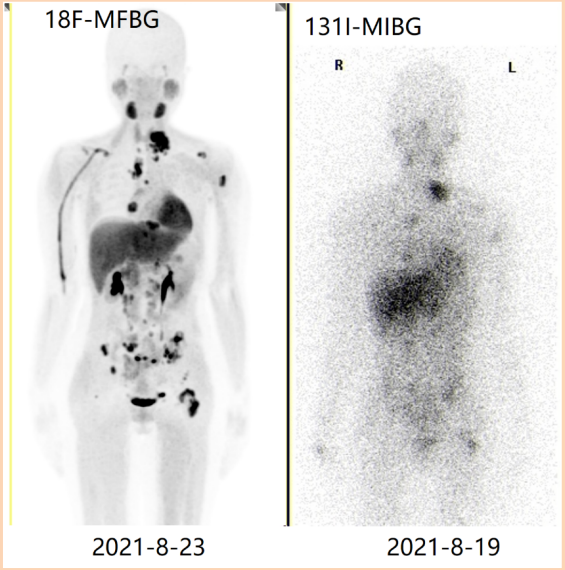
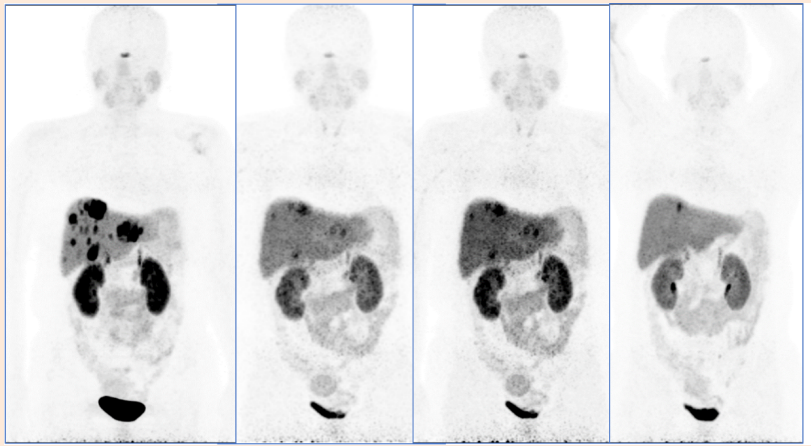


^{18}F-MFBG shows higher sensitivity than ^{131}I-MIBG in staging primary pheochromocytoma and metastasis.



^{177}Lu TATE for patient with advanced GEP NET

Cohort study on insulinoma detection and localization with GLP-1 receptor imaging

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Data from PUMCH (~300 patients)

JNM The Journal of NUCLEAR MEDICINE

Glucagon-Like Peptide-1 Receptor PET/CT with ^{68}Ga-NOTA-Exendin-4 for Detecting Localized Insulinoma: A Prospective Cohort Study

Yaping Luo, Qingqing Pan, Shaobo Yao, Miao Yu, Wenming Wu, Huadan Xue, Dale O. Kiesewetter, Zhaohui Zhu, Fang Li, Yupei Zhao and Xiaoyuan Chen

	Sen	Spe	Acc	PPV	NPV
^{68}Ga-exendin-4	99.1%	100%	99.4%	100%	98.2%
CT	80.7%	83.7%	81.6%	92.6%	63.2%
MR	78.9%	77.3%	78.6%	92.3%	51.5%
BUS	79.2%	80.0%	79.3%	95.0%	44.4%
SSTR	22.8%	97.9%	47.3%	95.8%	38.1%

Cohort study on insulinoma detection and localization with GLP-1 receptor imaging

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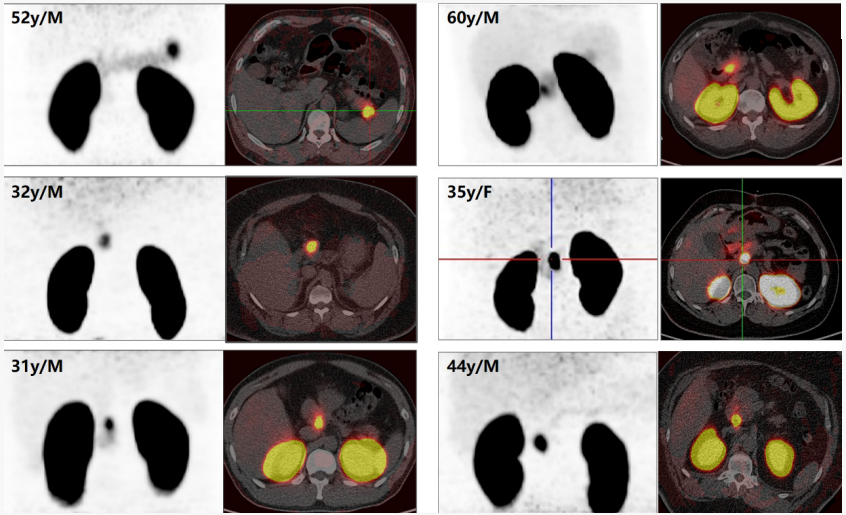

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	Sen	Spe	Acc	PPV	NPV
^{68}Ga-exendin-4	99.1%	100%	99.4%	100%	98.2%
CT	80.7%	83.7%	81.6%	92.6%	63.2%
MR	78.9%	77.3%	78.6%	92.3%	51.5%
BUS	79.2%	80.0%	79.3%	95.0%	44.4%
SSTR	22.8%	97.9%	47.3%	95.8%	38.1%

Characterization the functional status of Adrenocortical Masses using CXCR4 receptor imaging

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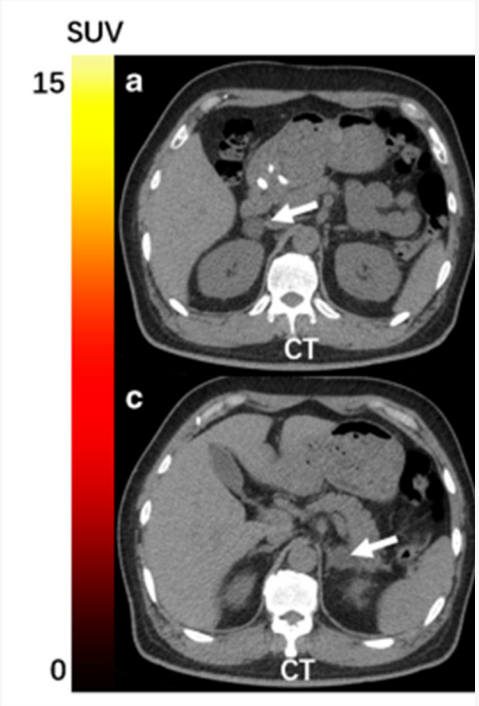
^{68}Ga-pentixafor PET/CT determine aldosterone-producing adenoma



Huo L, Ding J, et al. Eur J Nucl Med Mol Imaging(2020) https://doi.org/10.1007/s00259-020-04722-0

Characterization the functional status of Adrenocortical Masses using CXCR4 receptor imaging

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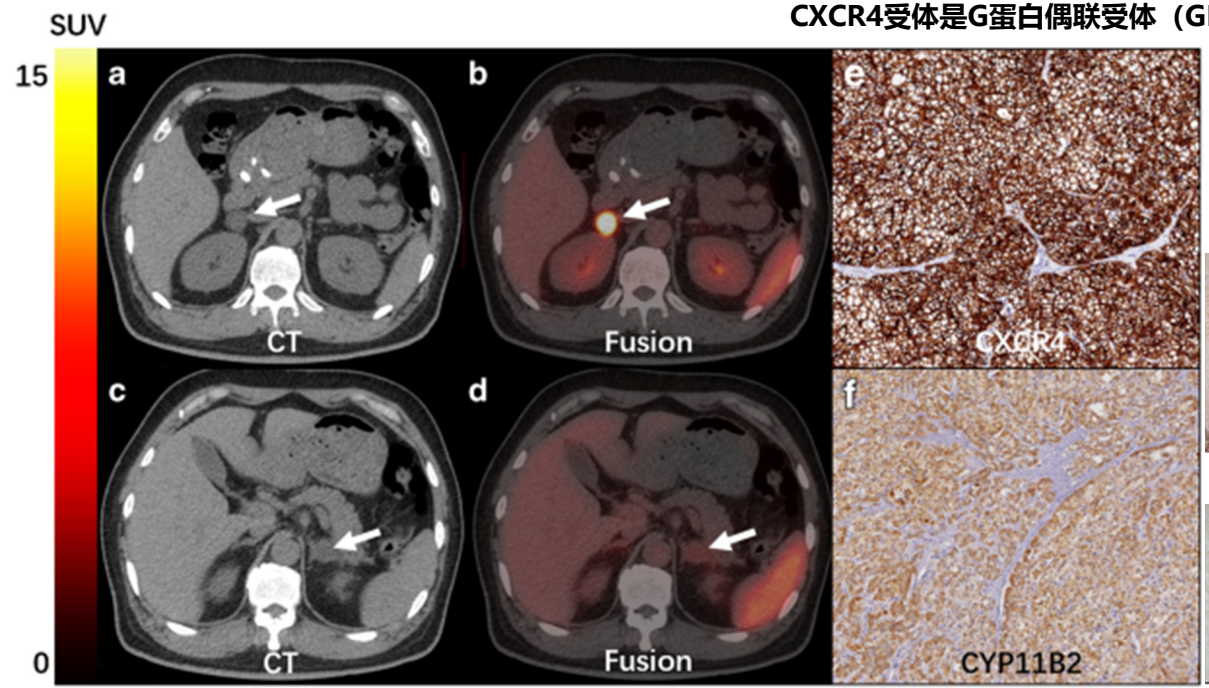
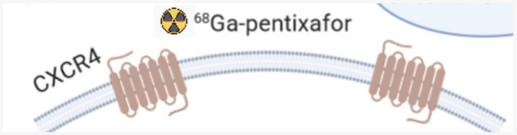


CXCR4受体是G蛋白偶联受体（GPCR），^{68}Ga-pentixafor与CXCR4受体特异性结合



Huo L, Ding J, et al. Eur J Nucl Med Mol Imaging(2020) https://doi.org/10.1007/s00259-020-04722-0

Non-invasive NM technology to help diagnose and classify cardiac amyloidosis

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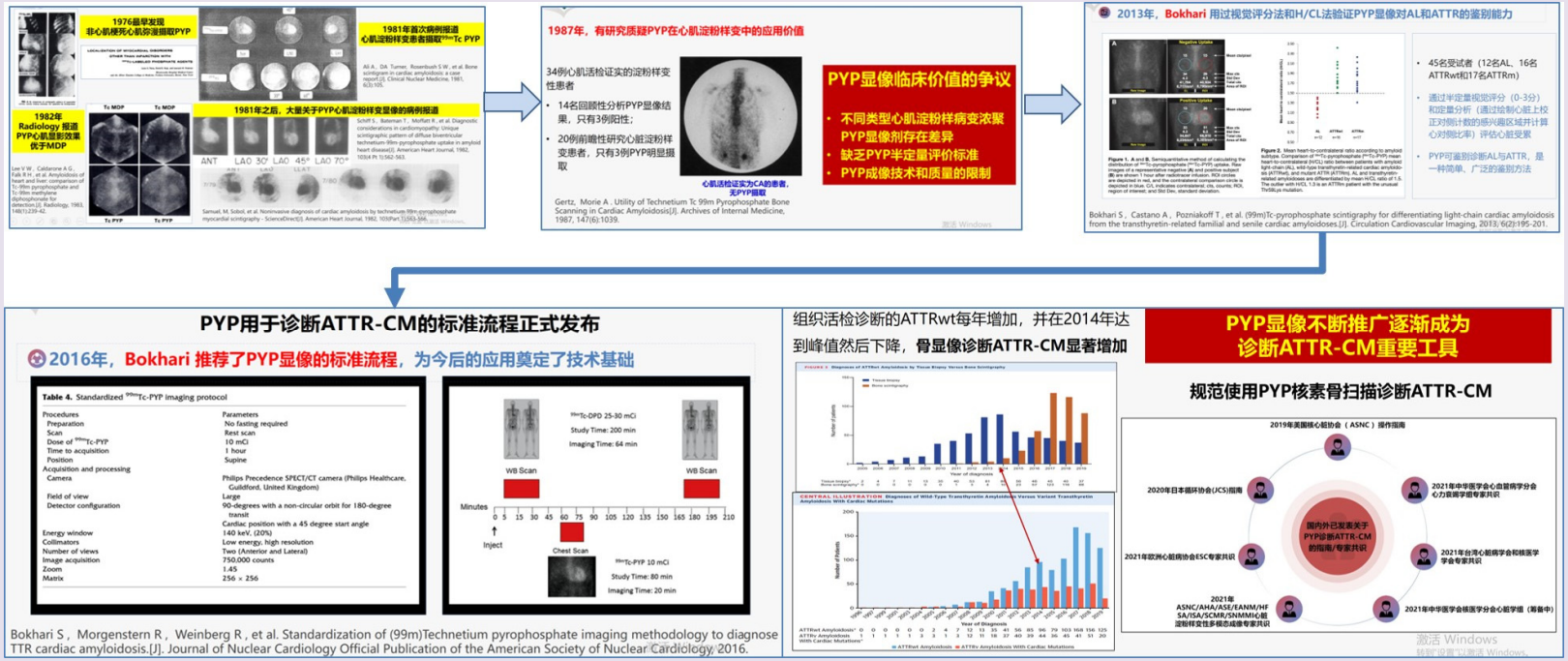
^{99m}Tc-PYP were employed for Cardiac amyloidosis diagnosis and classification since 1970s

International journey of NM imaging application in cardiac amyloidosis



Non-invasive NM technology to help diagnose and classify cardiac amyloidosis

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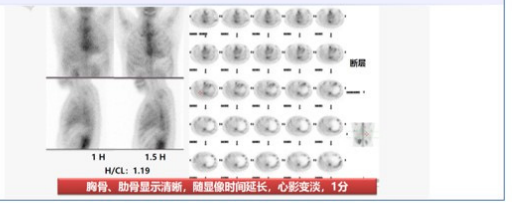
NM technology is well-accepted for ATTR-CM diagnosis and treatment in China since 2019

2019.1.25 First international exchange meeting

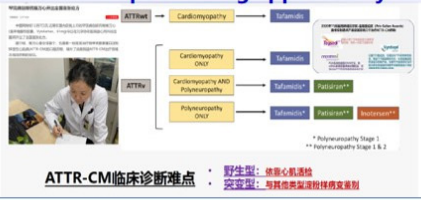
2019.3.14 Health control imaging



2019.8.30 First patient with wild-type ATTR in China

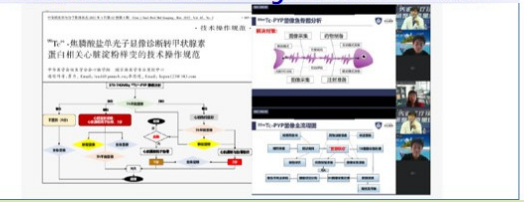
2020.8 Serve as routine examination project

2020.10 ATTR-CM therapeutic drug approved by CFDA



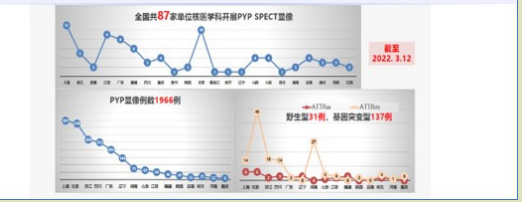
2021.12 ATTR-CM therapeutic drug included in NDRL

2021.12 Consensus for ATTR-CM diagnosis with PYP scan



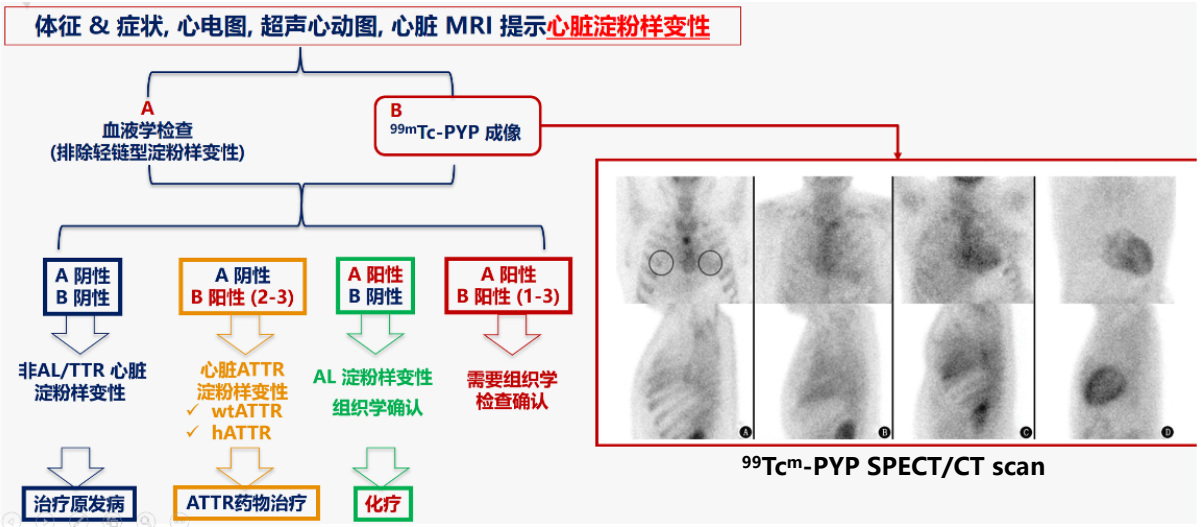
Over 30 speeches for PYP scan promotion

Over 100 hospitals applied PYP scan for ATTR-CM



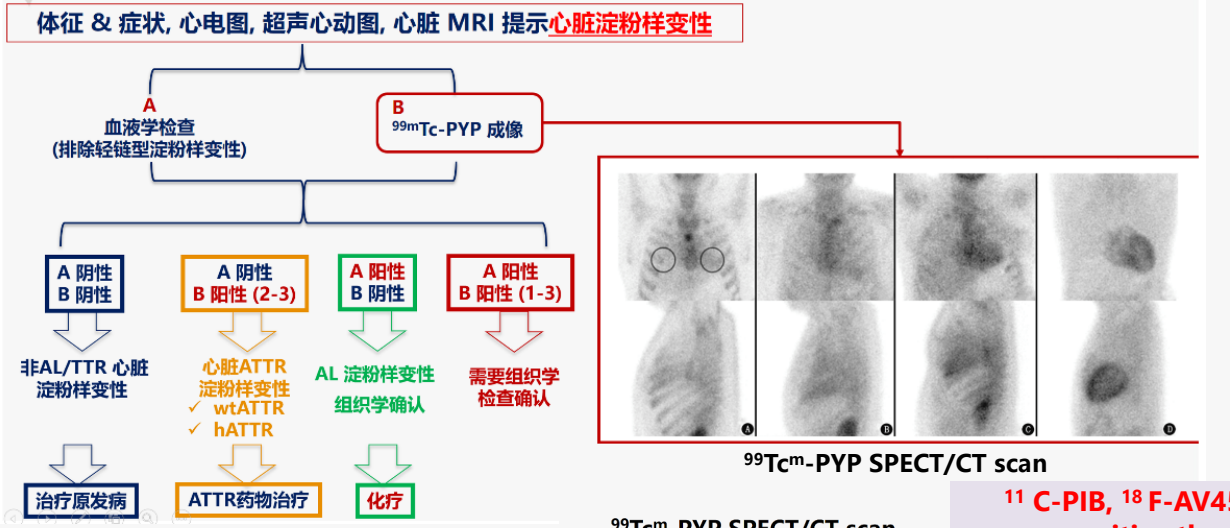
Development of NM technology to improve ATTRm diagnosis sensitivity and AL-CM risk assessment

北京协和医院
PEKING UNION MEDICAL COLLEGE HOSPITAL

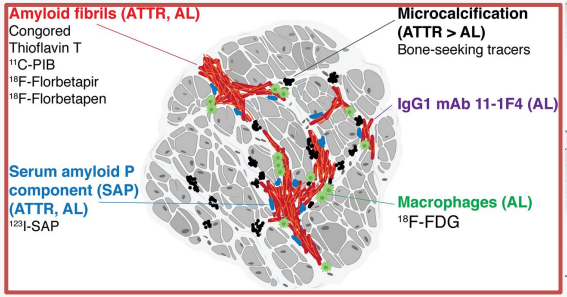


Development of NM technology to improve ATTRm diagnosis sensitivity and AL-CM risk assessment

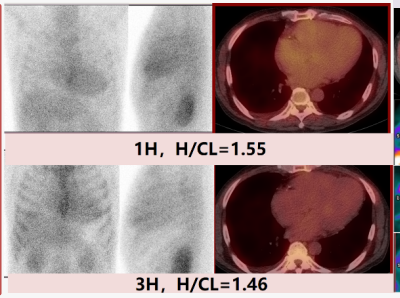
北京协和医院
PEKING UNION MEDICAL COLLEGE HOSPITAL



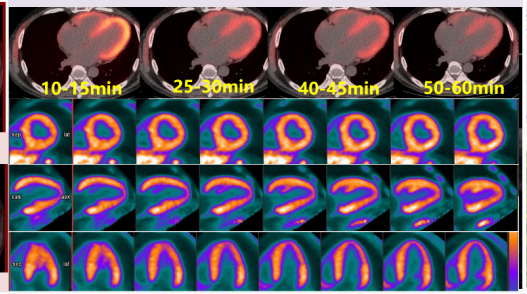
$^{99}Tc^{m}$-PYP SPECT/CT scan

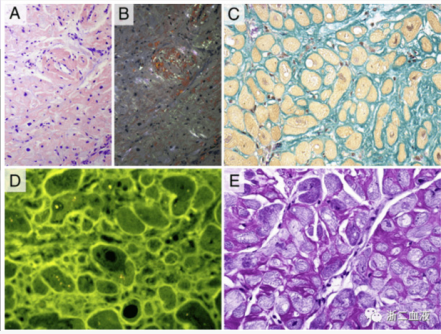


$^{99}Tc^{m}$-PYP SPECT/CT scan



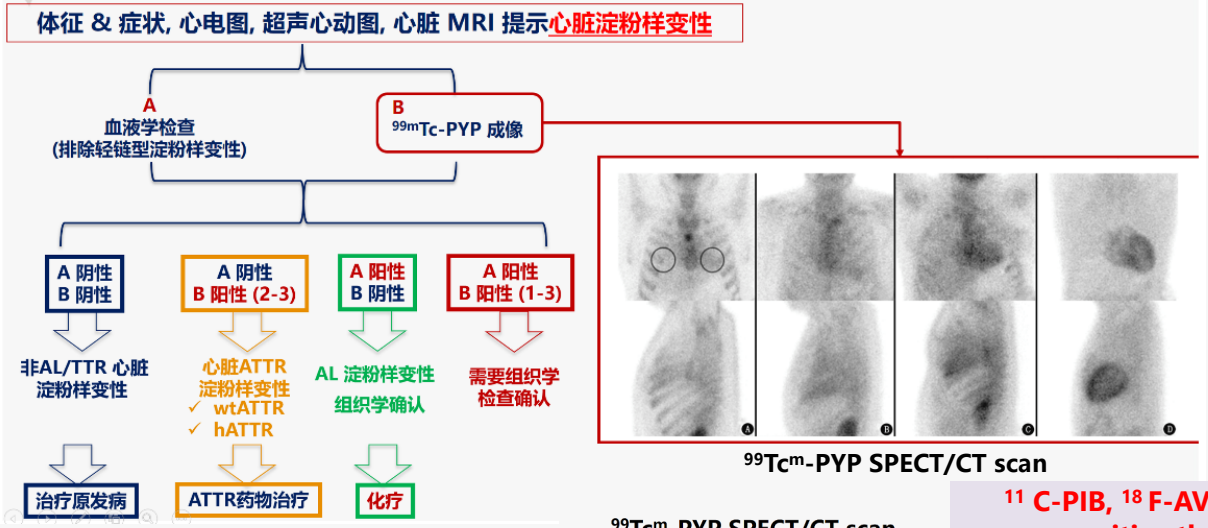
^{11}C-PIB, ^{18}F-AV45 PET/CT scan
more sensitive than PYP for ATTRm





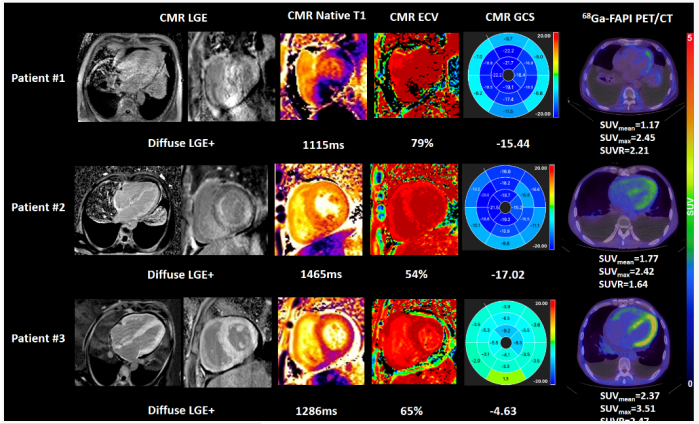
Development of NM technology to improve ATTRm diagnosis sensitivity and AL-CM risk assessment

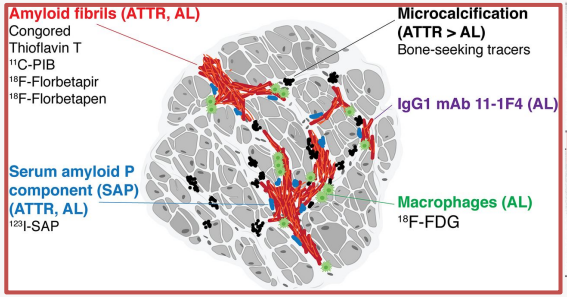
北京协和医院 PEKING UNION MEDICAL COLLEGE HOSPITAL



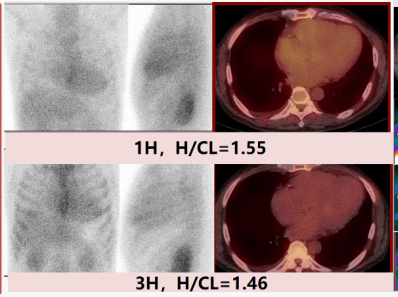
99Tcm-PYP SPECT/CT scan

68Ga-FAPI for risk assessment

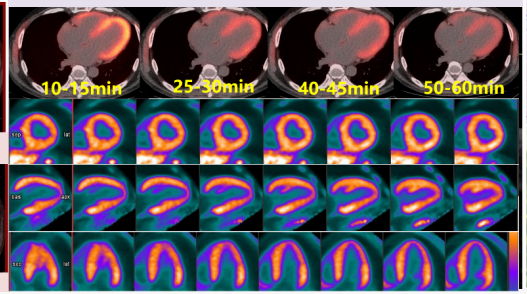


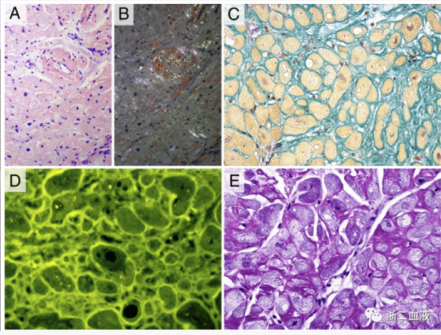


99Tcm-PYP SPECT/CT scan



11 C-PIB, 18 F-AV45 PET/CT scan more sensitive than PYP for ATTRm





Set up translational corporation platform with clinical department in PUMCH

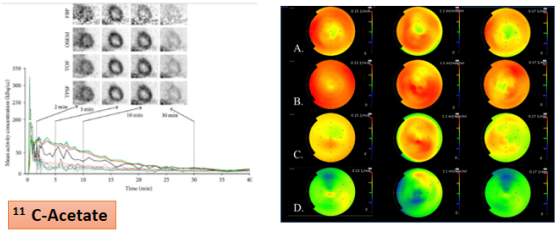
北京协和医院
PEKING UNION MEDICAL COLLEGE HOSPITAL

Hematology, cardiology, endocrinology and neurology department

一、酒精性心肌病

主要合作人：林雪、方理刚（心内科）
刘帅（北京理工大学）
张辉（清华大学）

国内率先利用PET动态图像计算心肌耗氧量等动力学参数，发现饮酒与心肌损伤关系



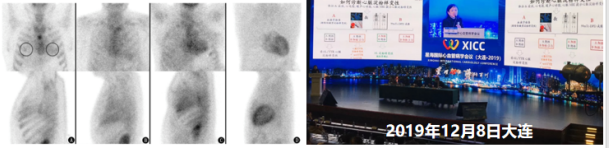
^{11}C-Acetate

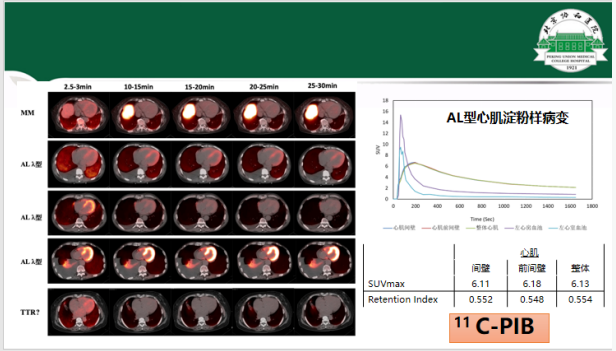
二、心肌淀粉样病变

主要合作人：田庄、张抒扬（心内科）
李剑（血液内科）
王怡宁（放射科）
许百灵（美国哥伦比亚密苏里大学）

- 国内率先建立ATTR心肌淀粉样变显像和图像分析方法，成为科室特色检查项目
- 推广与培训，在全国建立8个研究中心
- 编写共识；
- 开展高水平科研工作，解决临床问题

^{99m}Tc-PYP

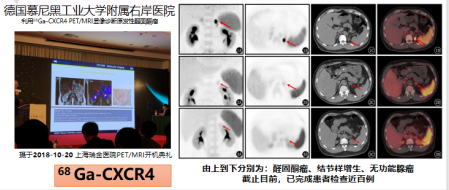




^{11}C-PIB

三、原醛所致高血压

主要合作人：窦宏霞、夏维波（内分泌）
张玉石、文进、杞志卿（泌尿外科）



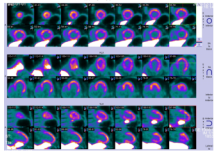
由上到下分别为：腹肉腺瘤、结节样增生、无功能腺瘤
截止目前，已完成患者检查近百例

^{68}Ga-CXCR4

四、其他心肌病与心衰

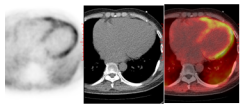
主要合作人：林雪、方理刚、陈末（心内科）
杨华昊、郑文洁、张文（免疫科）

心肌炎症



^{68}Ga-DOTATATE

心衰与心肌重构

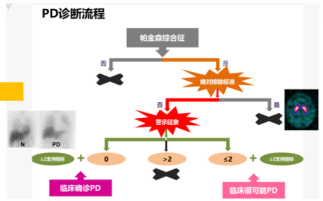


^{68}Ga-FAPI

五、心脏交感神经显像与PD

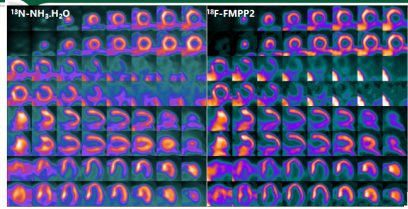
主要合作人：徐丹、王含（神经内科）

^{131}I-MIBG



六、国产新药临床转化

主要合作人：钱浩，刘颖娴，沈珠军（心内科）
赵作全、方伟（骨外医院）
许百灵（美国哥伦比亚密苏里大学）



Collaboration with universities, institutions, companies and government for NM translational research in PUMCH

北京协和医院
PEKING UNION MEDICAL COLLEGE HOSPITAL

PUMCH NM (图像采集与诊断)

Nuclide production

CHINA NATIONAL NUCLEAR CORPORATION

Radiopharmaceutical

- Beijing Xiantong International Pharmaceutical Technology Co., Ltd.
- Yantai Dongcheng Biochemicals Co.,Ltd.
- Peking university
- Standford university
- Beijing Normal University
- Fuwai hospital, CAMS.
- Huayi Technology Co., Ltd

Image data analysis

- Tsinghua University
- Beijing Institute of Technology
- Institute of Automation, Chinese Academy of Sciences
- Nanjing University of Aeronautics and Astronautics
- Medical college of University of Vienna
- Finland national PET center

Quality control

National center for nuclear medicine quality control

Bench to Bed, characteristic of NM translational research work in PUMCH

北京协和医院
PEKING UNION MEDICAL COLLEGE HOSPITAL

Strengthening basic research and developing new theranostic tracer for renal cell carcinoma.