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IMAGING

医学影像对辐射探测的需求

——PET相关辐射探测技术探讨

王 超

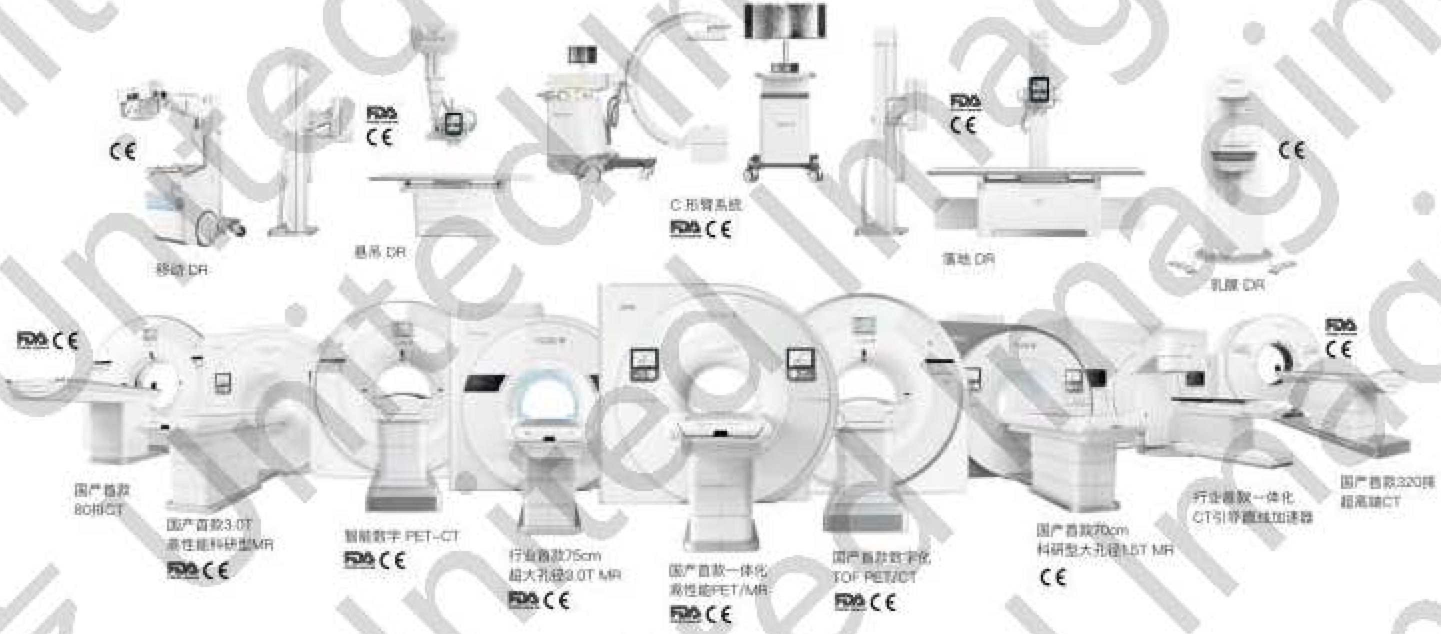
2022.8.7 合肥

常见医学影像模态

The first x-ray image produced by Roentgen depicting his wife's hand and ring. (From Wikipedia)

- Conventional radiography (X-ray);
- Fluoroscopy;
- Angiography;
- Mammography;
- Computer tomography (CT);
- Ultrasound and Doppler-ultrasound;
- Magnetic resonance imaging (MRI);
- Gamma Camera
- Single Photon Emission Computed Tomography(SPECT)
- Positron emission tomography (PET);
- Thermal imaging;
- Micro biopsy

- Contrast Resolution
- Spatial Resolution
- Noise
- Tempo Resolution



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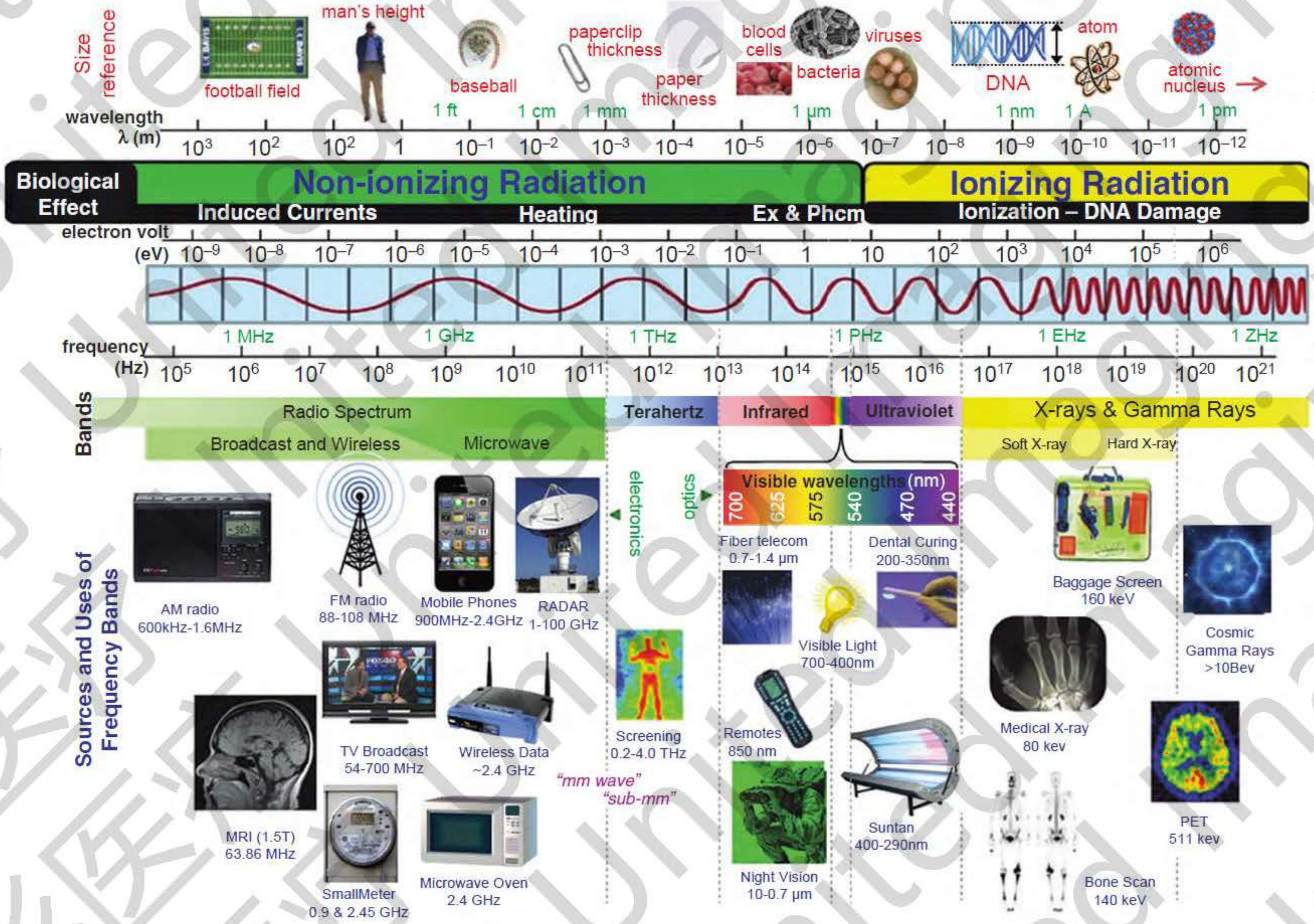
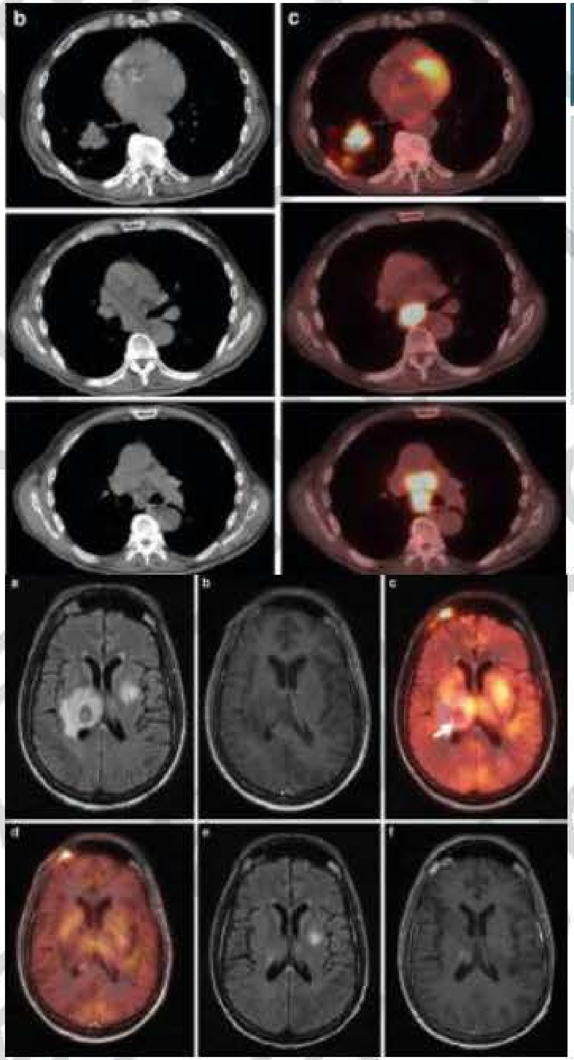
ELECTROMAGNETIC RADIATION SPECTRUM



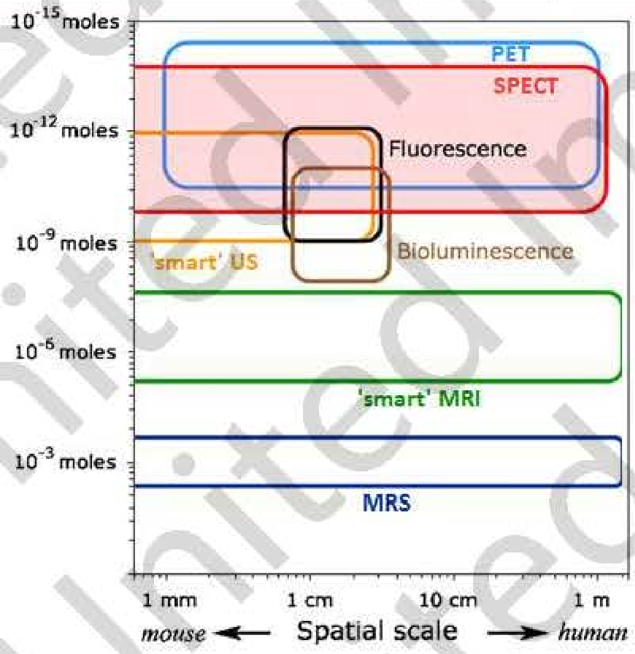
主流医学影像如XR、CT、SPECT、PET等都以辐射探测技术为基础

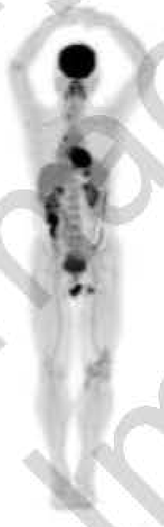
常见模态

多模态互补,“1+1>2”



MRI	CT	PET
• 解剖影像，反映原子核分布，也可进行一些分子影像。 • 扫描速度较慢，无电离辐射 • 孔径小且长，扫描体验较差。 • 软组织分辨率高， • 在肺部、骨骼等部位上存在短板	• 解剖影像，反映密度差异，可提供准确的电子密度分布图 • 扫描速度快，辐射剂量较高 • 在骨骼、血管相关病变显示上具有突出优势 • 软组织分辨率不如磁共振MRI。	• 分子影像，反映代谢、受体、转运等信息 • 高灵敏度,高特异性,高定量准确性 • 扫描速度较慢，辐射剂量较高 • 在体三维影像，但图像分辨率较低。 • 读片门槛较高，依赖医生经验。





全身三维成像

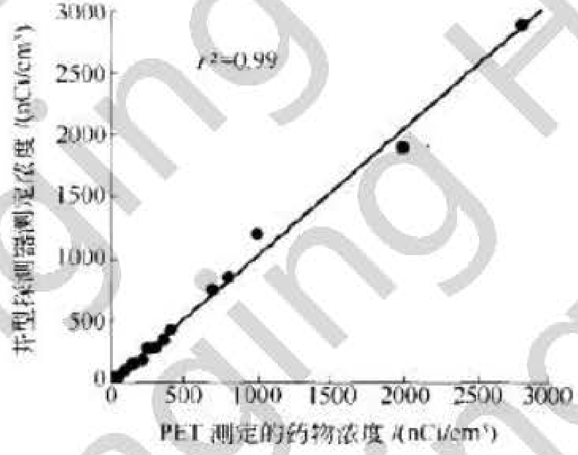
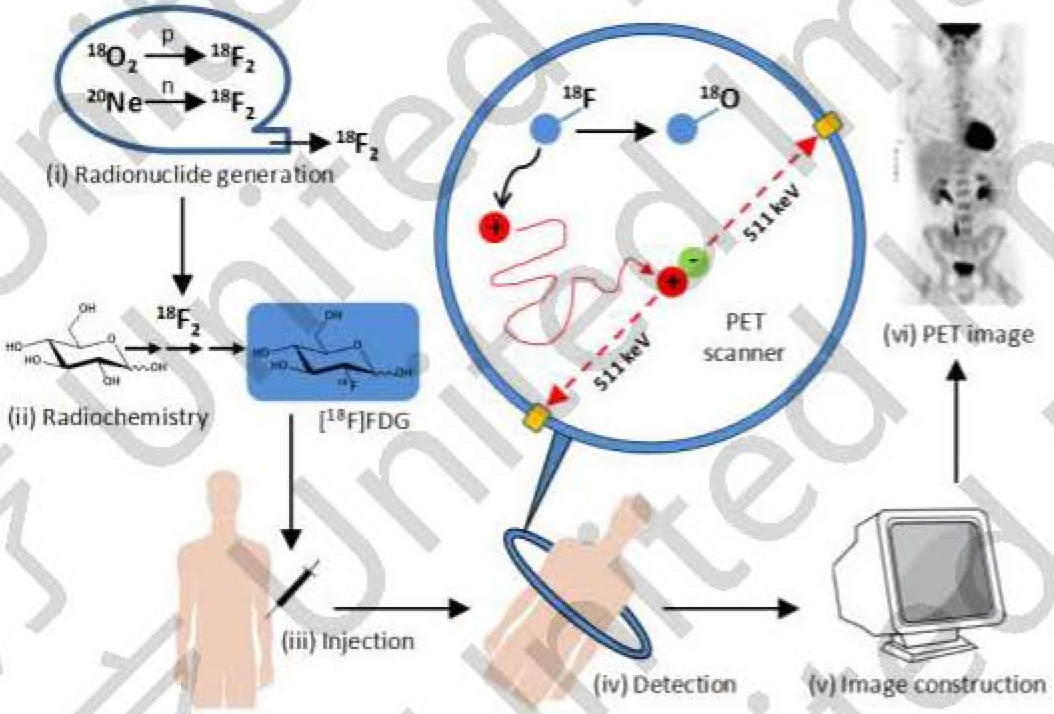


图 46-1 PET 测定的药物浓度与井型探测器直接测定组织标本结果的比较

PET成像原理



① 核素生产：使用回旋加速器生产出放射性物质

② 放化合成：通过化学反应，将放射性物质标记到目标分子上，即为放射性药物

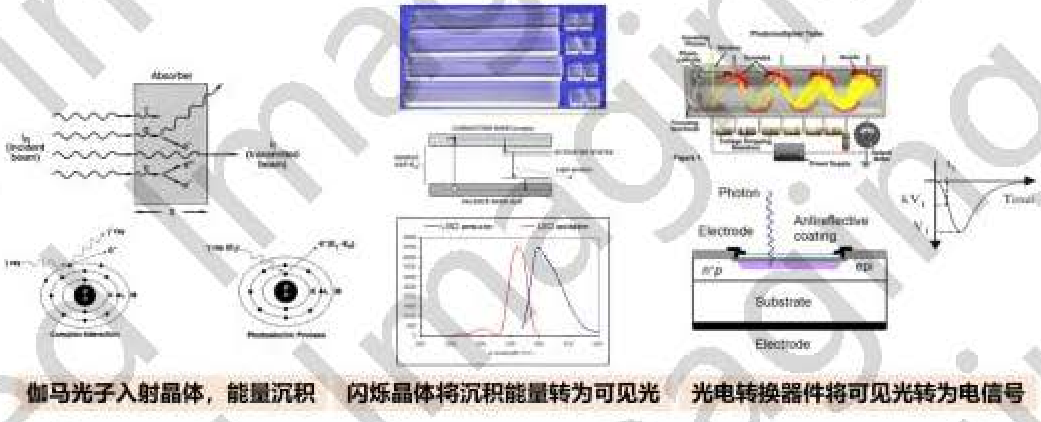
③ 药物注射：将放射性药物注射入人体

④ 信号探测：人体内的放射性药物不断衰变，衰变的核素放出正电子，与人体内电子相遇湮灭后，放出相背飞行的伽马光子对，被PET探测器环探测到符合事例

⑤ 图像重建：通过专用算法处理探测到的信号

⑥ PET图像：图像重建产出PET图像，即放射性药物在人体内的分布图像

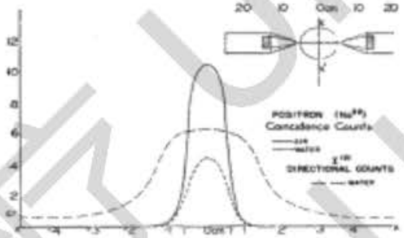
PET关键器件：探测器



PET发展史

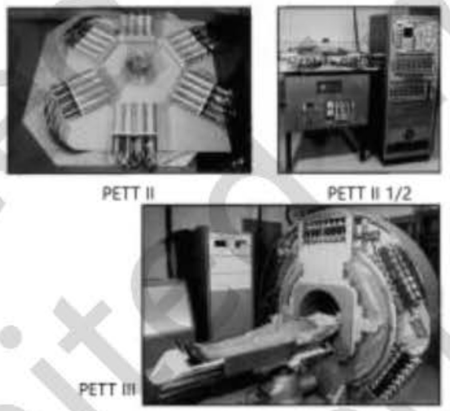
Gordon L. Brownell

William H. Sweet



1950s

- Na-22成像试验

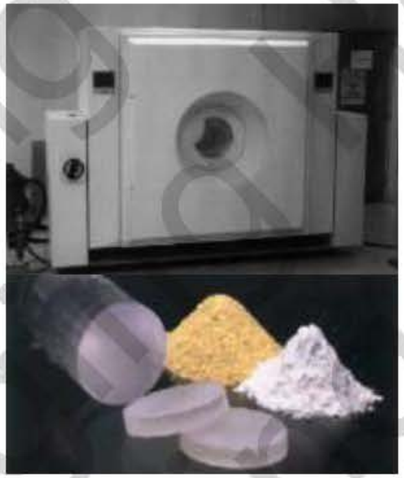


1970s

- PET产品
- 实现图像重建

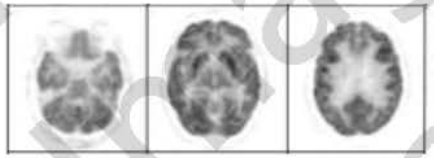
1980s

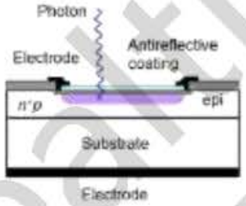
- BGO晶体PET
- Block探测器



1990s

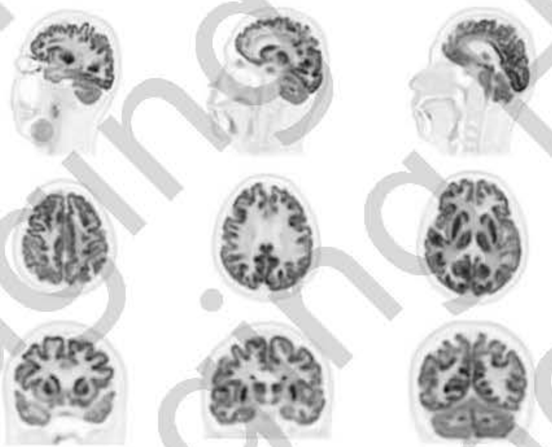
- LSO晶体TOF-PET
- PET/CT





2010s

- SiPM代替PMT



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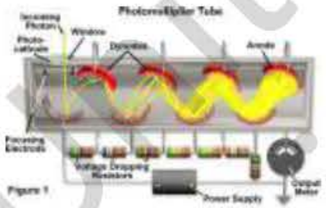
技术趋势 | SiPM替代PMT

西门子Siemens　通用电气GE　飞利浦Philips　联影United Imaging

PMT



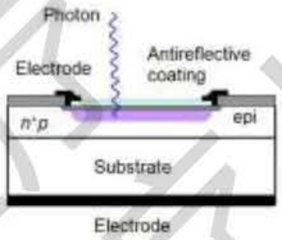
540ps

555ps

495ps

486ps

SiPM



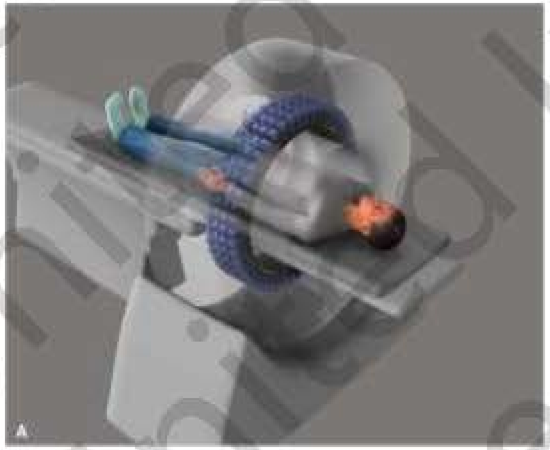
214ps

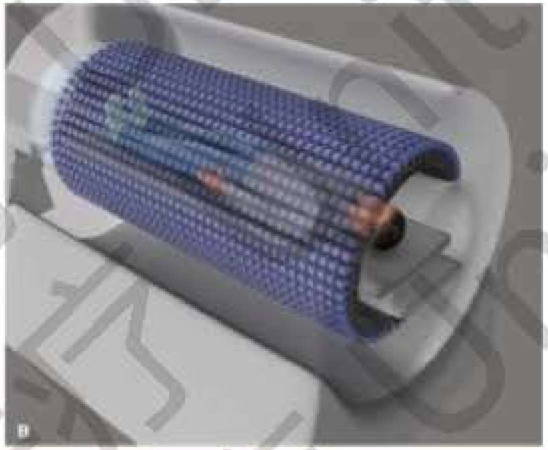
375ps

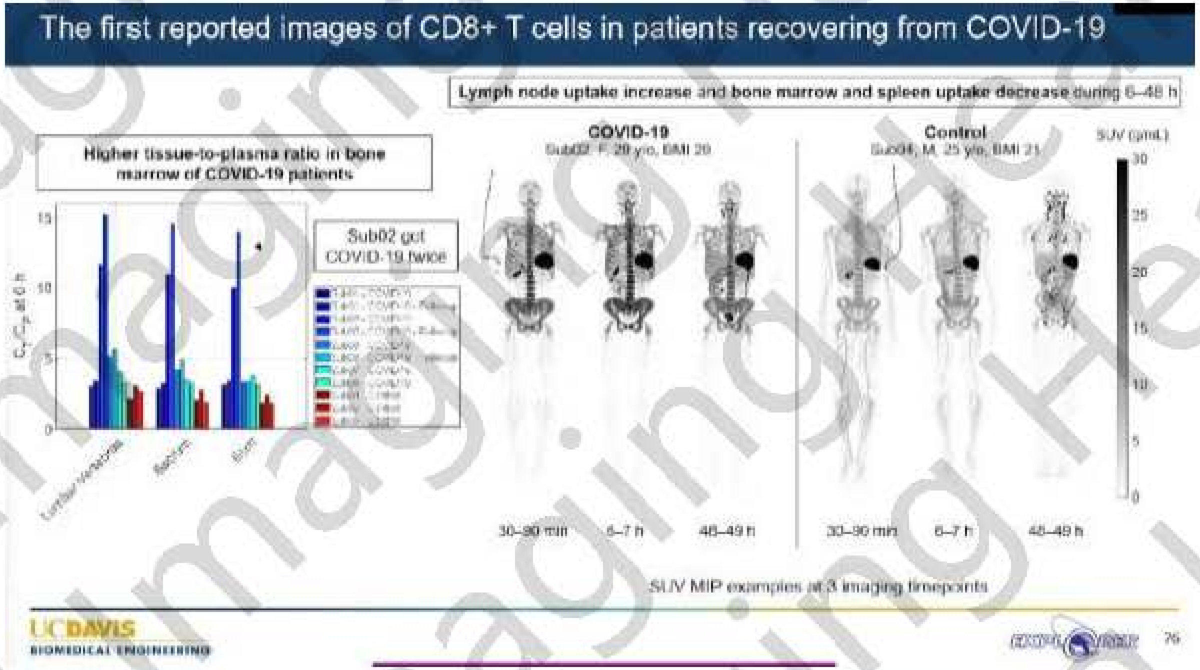
345ps

196ps

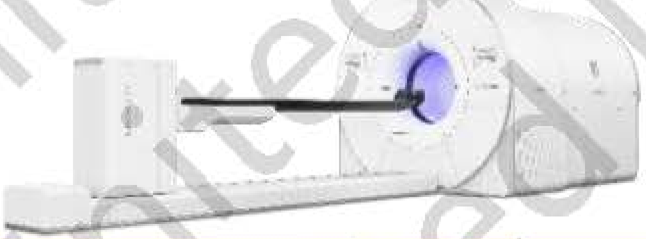
技术趋势 | Total body PET







2m PET
uEXPLORER
2018.12



1m PET
Quadra
2021.3

图像质量极佳，临床上可进行极速/低剂量扫描，科研可全身动态成像，实现药代、毒理、细胞追踪等尖端研究

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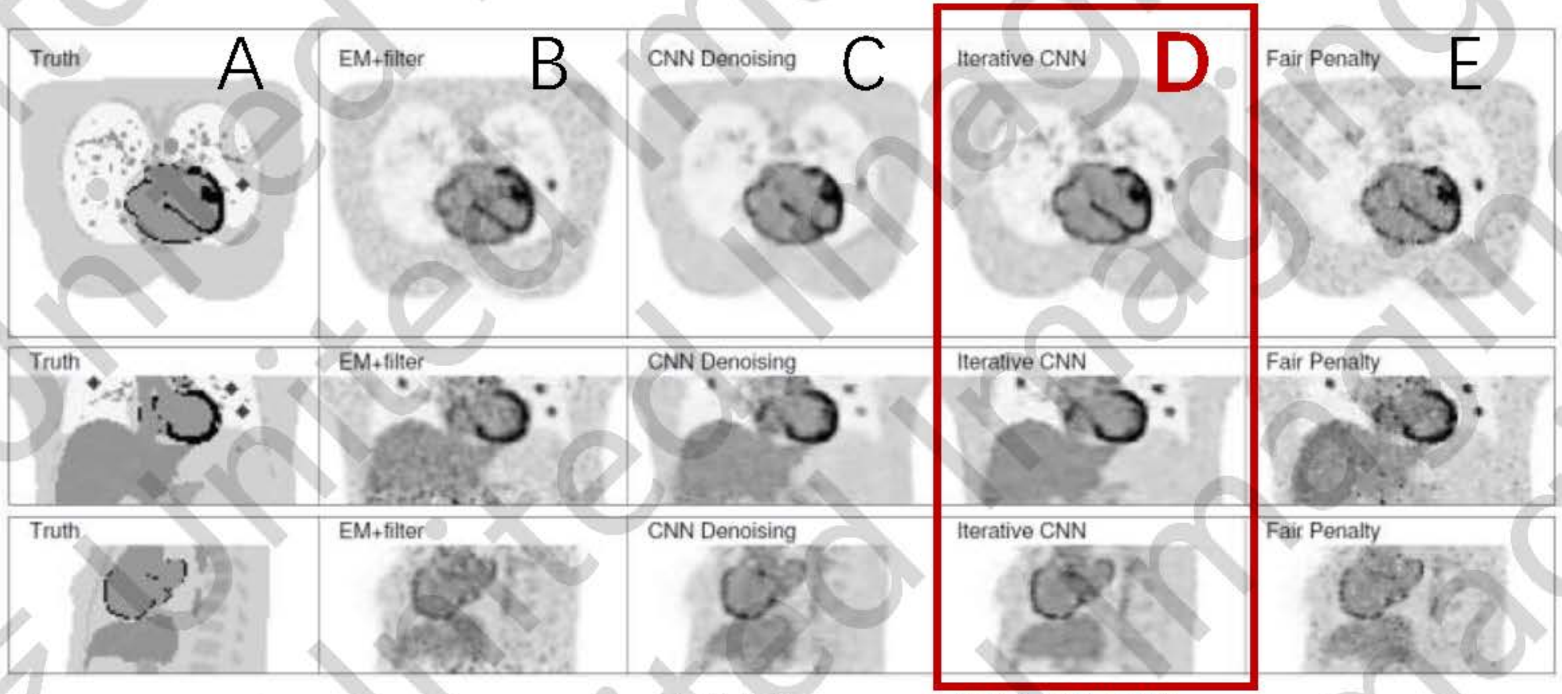
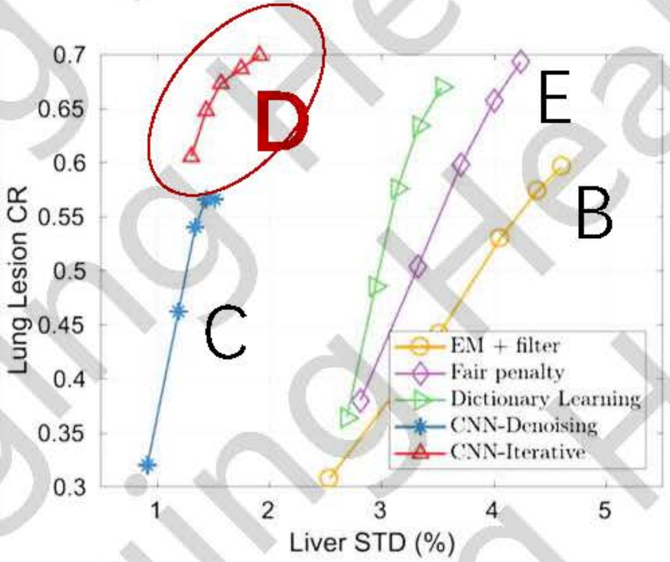
技术趋势 | Deep Learning 技术



Ground Truth　OSEM+filter　AI图像降噪　AI降噪内嵌迭代过程　ROSEM

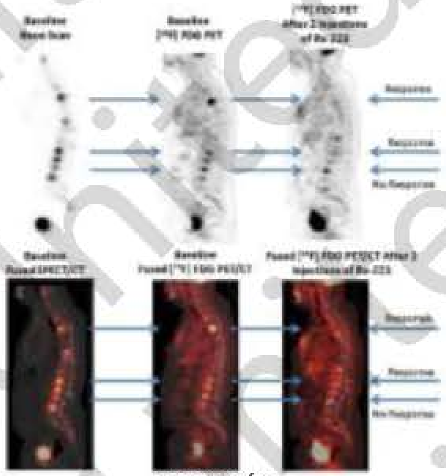


- 与PSF、TOF、正则化方法类似，AI迭代重建为进一步了提升图像质量（对比度提升、降噪效果提升、分辨率提升等）

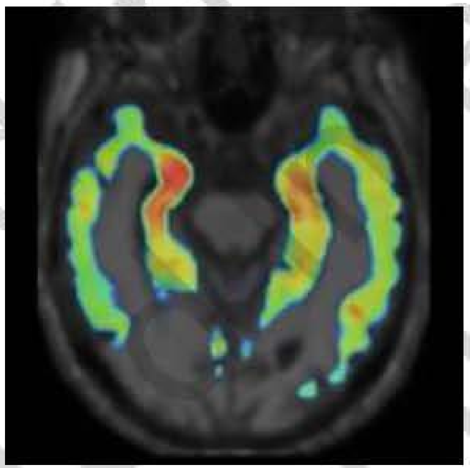
K. Gong et al., "Iterative PET Image Reconstruction Using Convolutional Neural Network Representation," in IEEE Transactions on Medical Imaging, vol. 38, no. 3, pp. 675-685, March 2019, doi: 10.1109/TMI.2018.2869871.
Reader A J , Corda G , Mehranian A , et al. Deep Learning for PET Image Reconstruction[J]. IEEE Transactions on Radiation and Plasma Medical Sciences, PP(99):1-1.

技术趋势 | 新探针

美国核医学年会历年 The image of the year

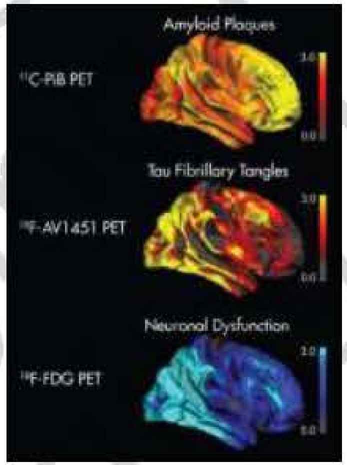


2013年

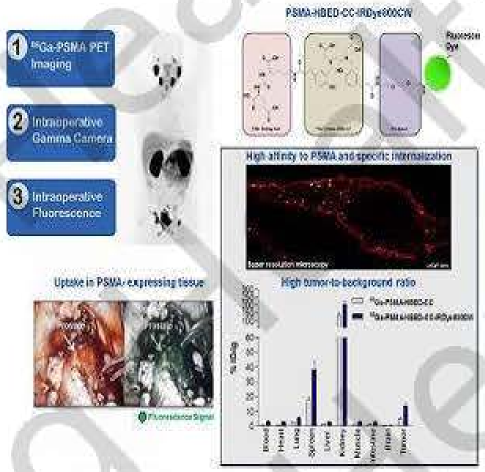


2014年

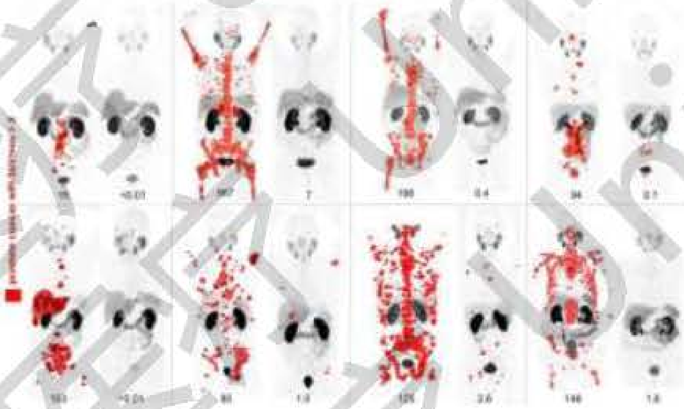
2015年



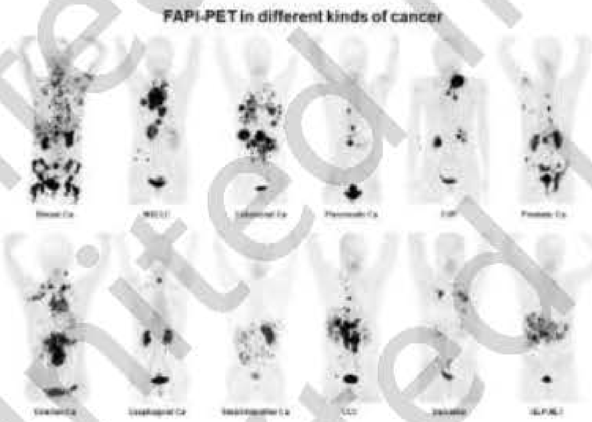
2016年



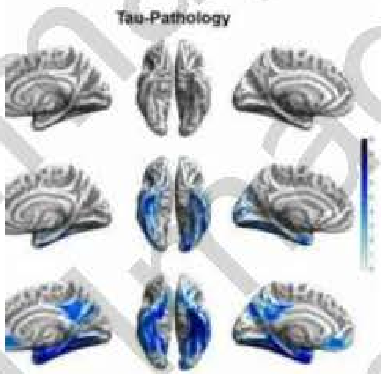
2017年



2018年



2019年



2020年

2021年

PET技术的发展趋势

- ✓ PET轴向视野不断拓宽，比如Total-body PET-CT，可以单床覆盖人体全身；
- ✓ L(Y)SO闪烁晶体占据主流，晶体尺寸不断变小，处理工艺更精细，系统空间分辨率逐步提升；
- ✓ 随着SiPM光电转换器件的发展成熟，PET探测器已进入全面SiPM-based时代；
- ✓ ToF飞行时间分辨率不断提升，最新商用PET已突破200ps；
- ✓ 设备智能化质控和智能化状态监控，设备的可用性更佳，减少了对操作者的辐射；
- ✓ 图像重建智能化技术不断发展，在降噪、提升图像质量、以及伪影校正等多方面有较大的提升；
- ✓ 新探针使用逐步得到推广。

长轴PET技术 Total-body PET

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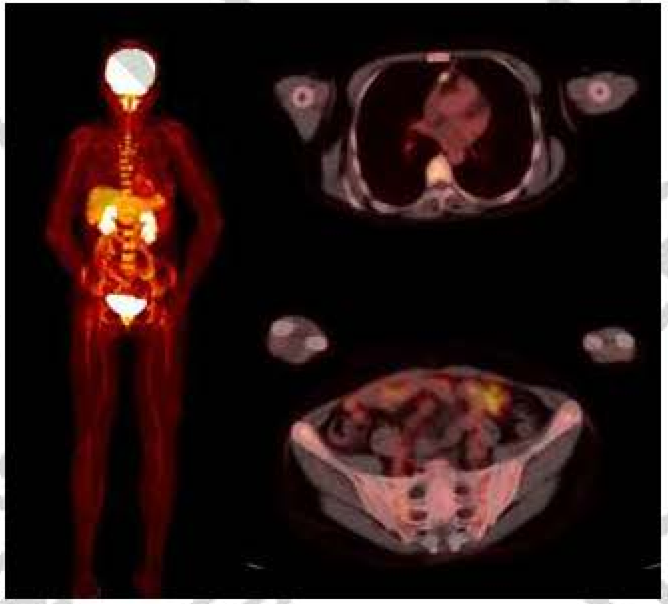
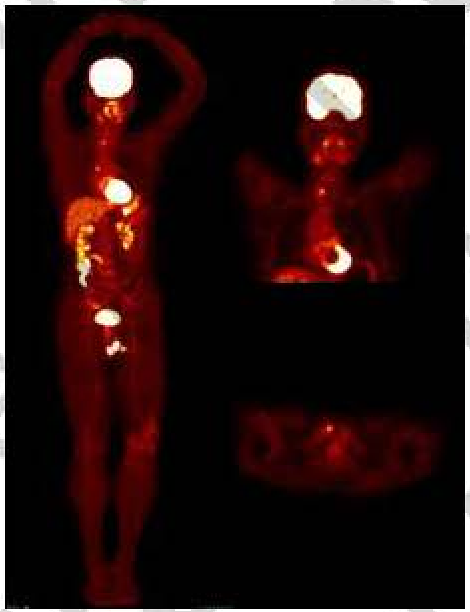
传统PET的局限性

辐射剂量**偏大**　扫描时间**偏长**　图像信噪比**偏低**

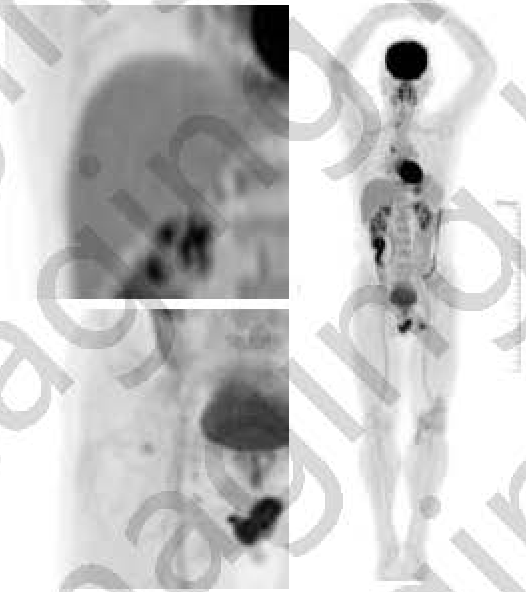
2m PET：两米轴向视野、超高灵敏度、**全身**动态成像



1/40注射剂量

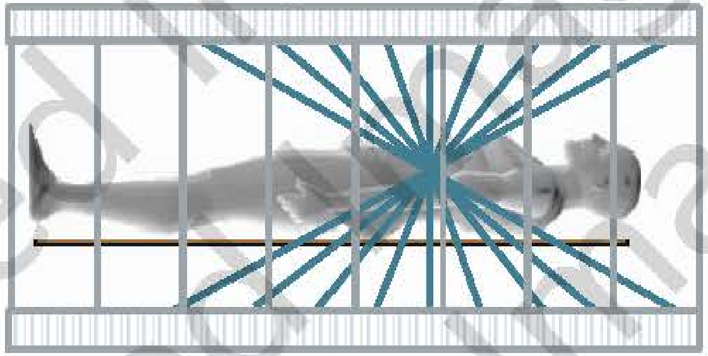


1/40扫描时间



>5倍信噪比

2m PET创新点及挑战

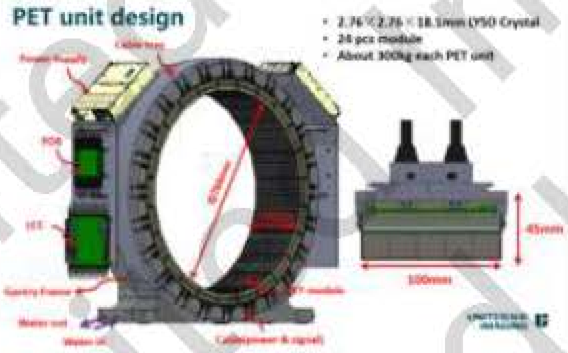


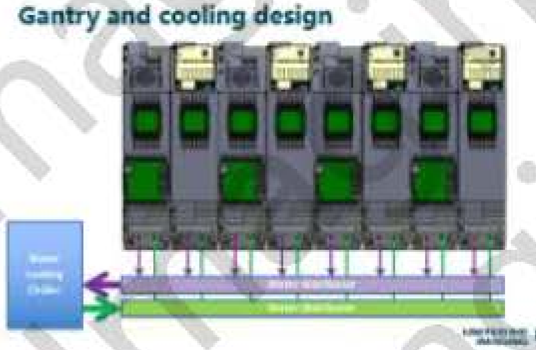
uEXPLORER

- 多单元结构
- 跨单元符合
- 分布式架构

两米超长轴向视野	超高灵敏度	全身动态采集
探测器结构设计	海量数据处理	定量准确性
多单元性能一致	超高计算量	
运输、安装和维护		

创新系统设计


PET unit design
2.76 × 2.76 × 18.1mm LYSO Crystal
24 pcs module
About 300kg each PET unit
100mm


Gantry and cooling design


Distributed Recon for 2mPET
Target reconstruction: 5 minutes

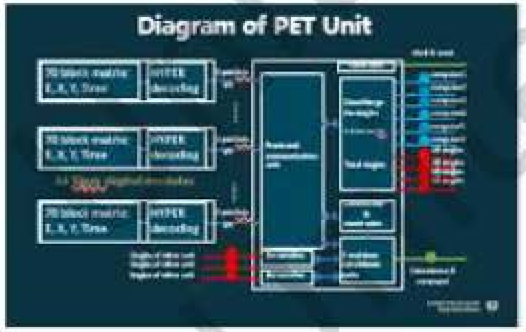
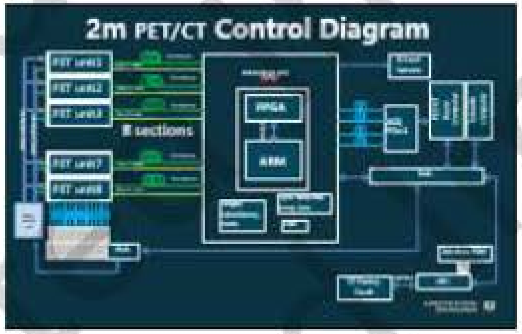
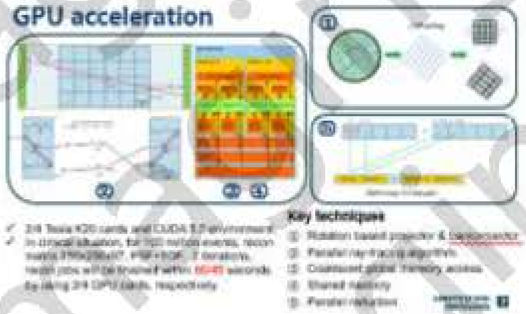


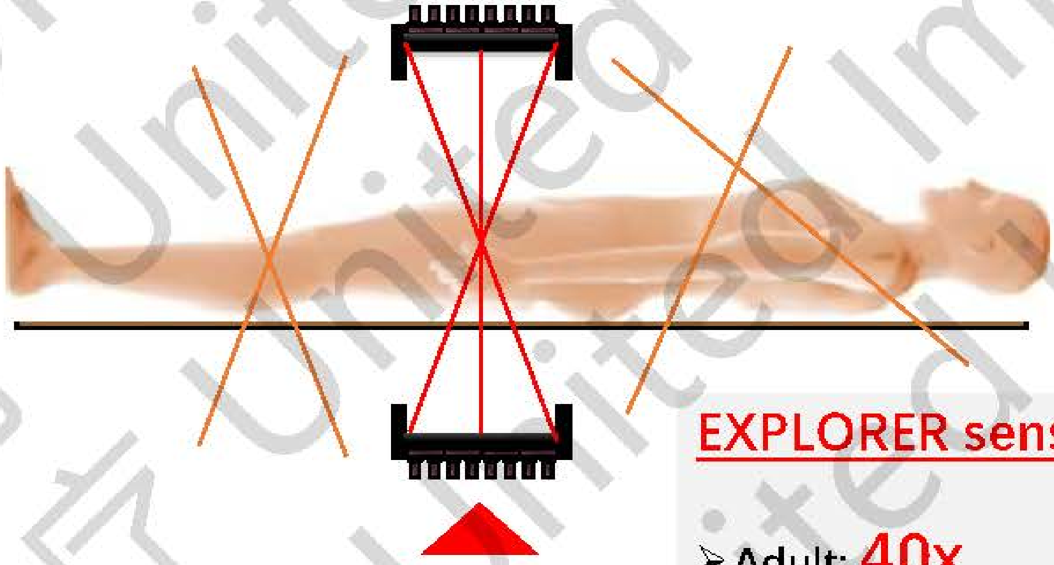
Diagram of PET Unit


2m PET/CT Control Diagram
8 sections
FPGA
ARM


GPU acceleration
Key techniques

Comparing to Conventional Scanners

CONVENTIONAL PET

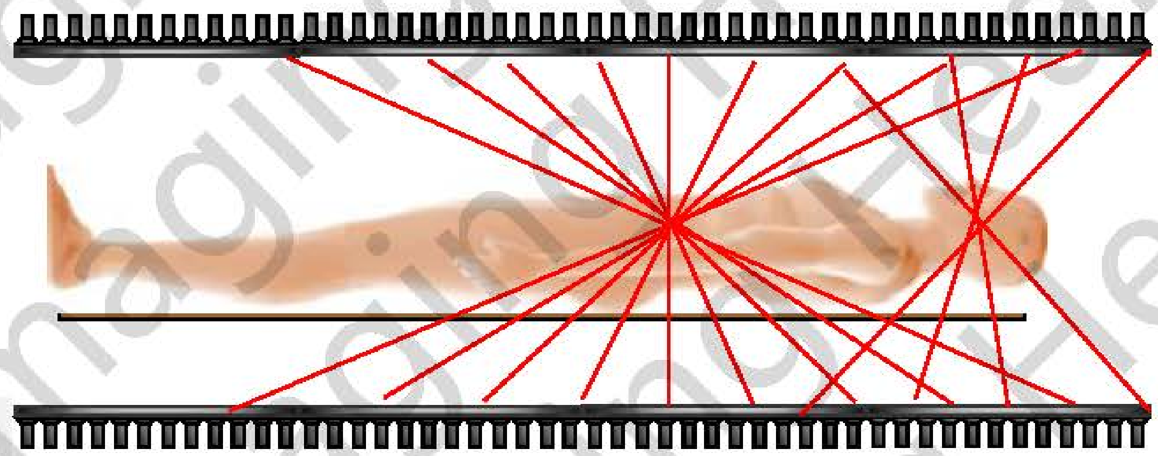


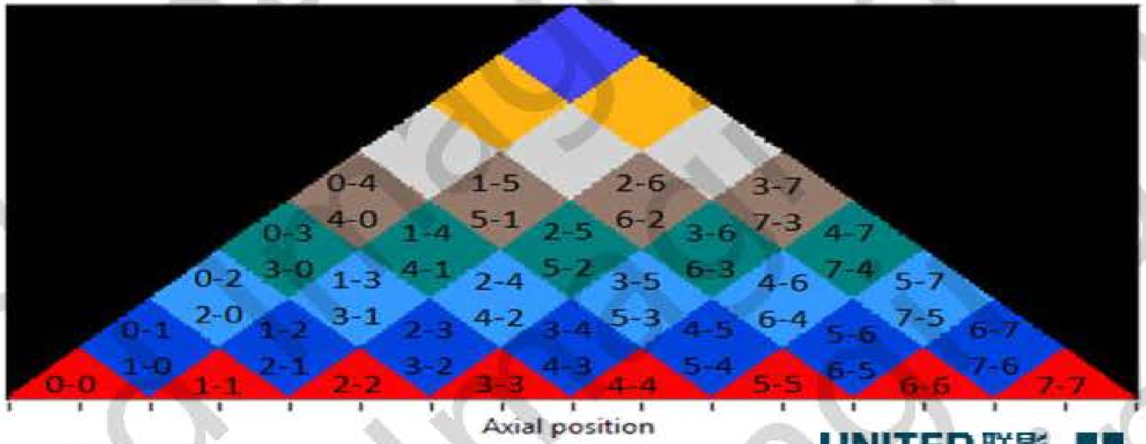
UIH uMI 780	1.60%
Siemens mCT	1.02%
Discovery 710	0.75%
Philips Vereos	0.57%

EXPLORER sensitivity

- Adult: **40x**
- Pediatric: 20x
- Brain: 5x
- Single organ: 5x

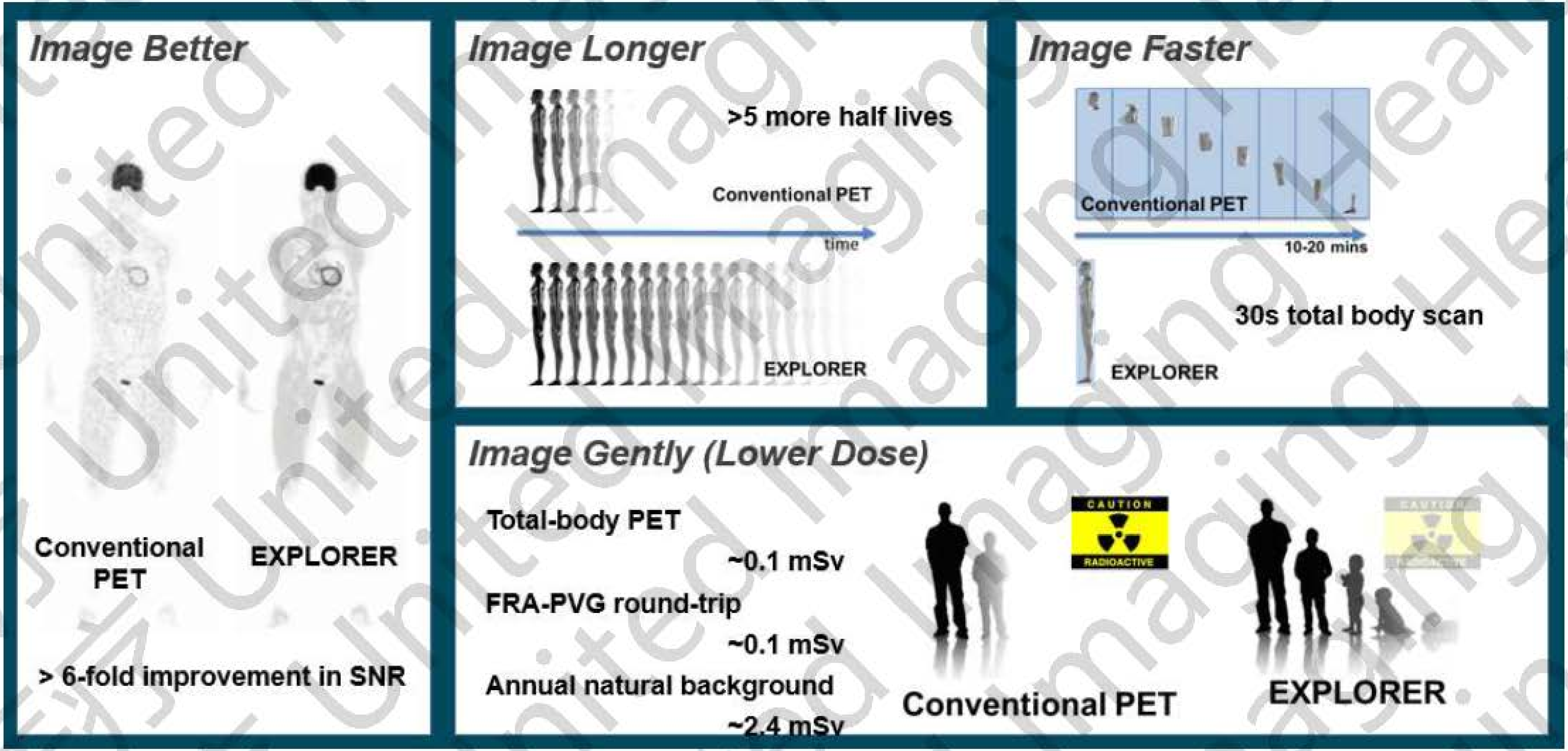
EXPLORER





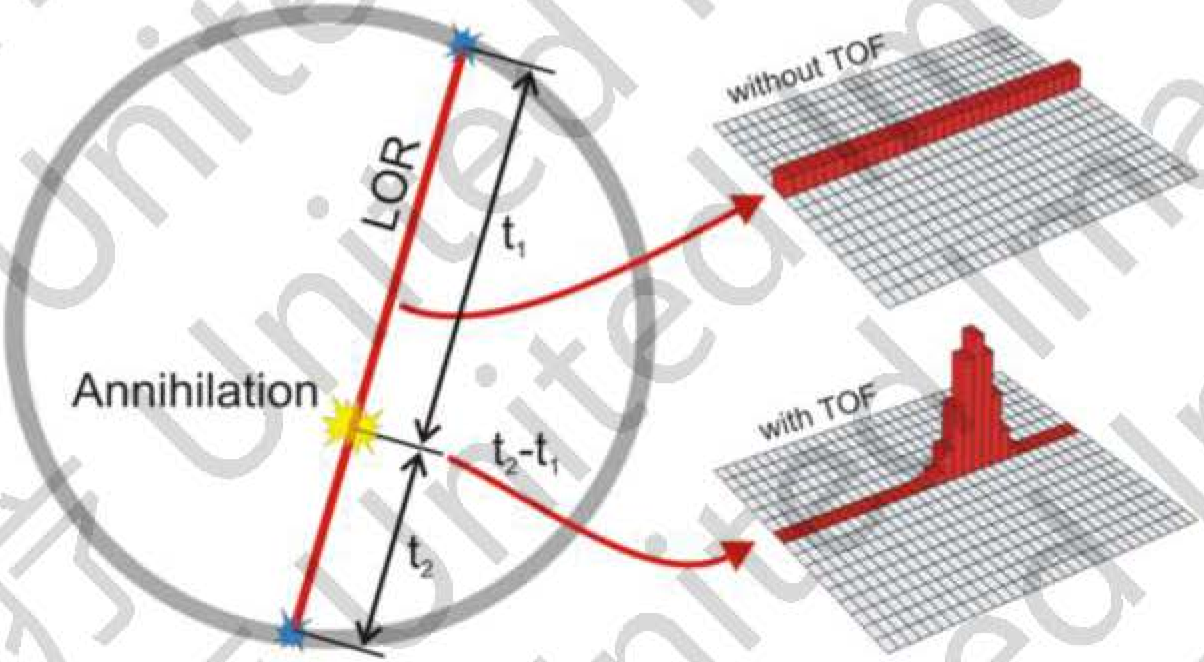
EXPLORER sensitivity

uEXPLORER Can



TOF-PET技术

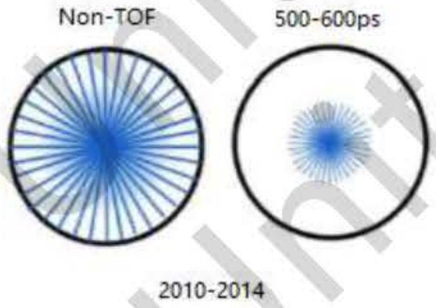
TOF-PET的优势

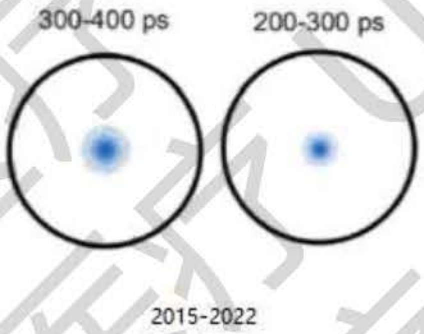


结节间距：2.3mm

商用PET系统的飞行时间分辨率

TOF





西门子Siemens	通用电气GE	飞利浦Philips	联影UIH
			
540ps	544ps	495ps	485ps
			
214ps	385ps	320ps	196ps

联影在TOF-PET上的工作

完成「十三五」科技部国家重点研发计划数字诊疗专项

开发下一代全数字高性能PET-CT整机系统

项目编号：2016YFC0104300　　密　级：公开

国家重点研发计划
项目任务书

项目名称：新一代临床全数字 PET/CT 整机系统研发

所属专项：数字诊疗装备研发

指南方向：新一代临床全数字 PET 成像系统

推荐单位：上海市科学技术委员会

专业机构：中国生物技术发展中心

项目牵头承担单位：上海联影医疗科技有限公司（公章）

项目负责人：安少辉

执行期限：2016 年 07 月 至 2020 年 12 月

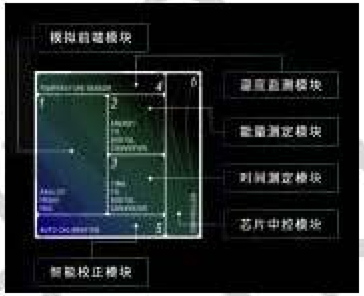
中华人民共和国科学技术部

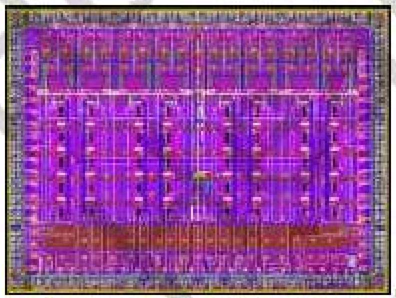
2016 年 07 月 26 日

联影在TOF-PET上的工作

全自主闪烁晶体工厂

自研PET探测器专用ASIC芯片





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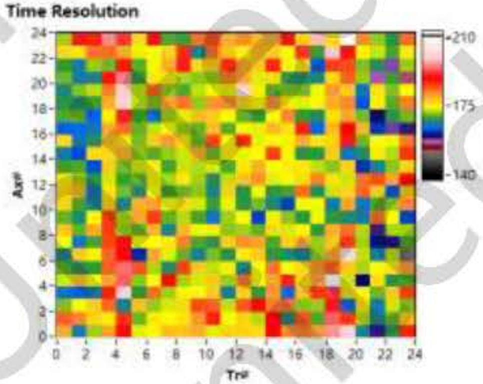
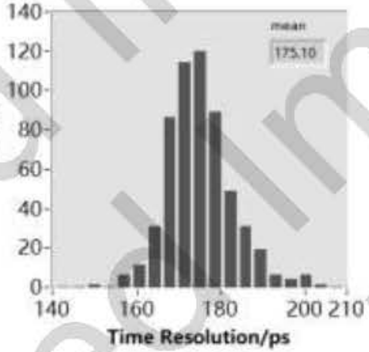
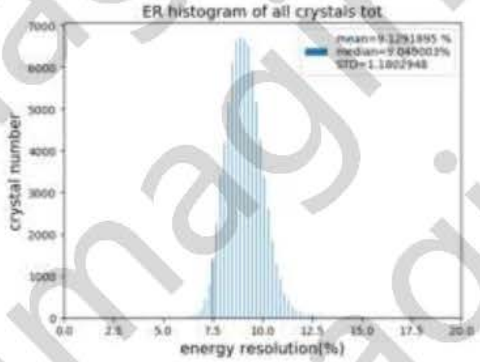
联影在TOF-PET上的工作

M-06-046 – Preliminary Performance evaluation of the PET detectors with UIH PET ASIC (#1273)

S. Chu, Z. Han, X. Wang, J. Ni, B. Liu, D. Bi, H. Xie, Z. Li, Q. Zhao, Y. Sun, S. An







2022最近进展：
Detector Performance
- CTR ~ 175ps
- ER ~ 9.5%

System Performance
- CTR ~ 188ps

M-11-01

Preliminary results of the performance characteristics for the new digital uMI Panorama PET/CT system (#1282)

Y. Liu[1], Y. Sun[1], Y. Wu[1], L. He[1], D. Hu[1], Y. Dong[1], S. An[1], Y. Ding[1], S. Chu[1], D. Bi[1]
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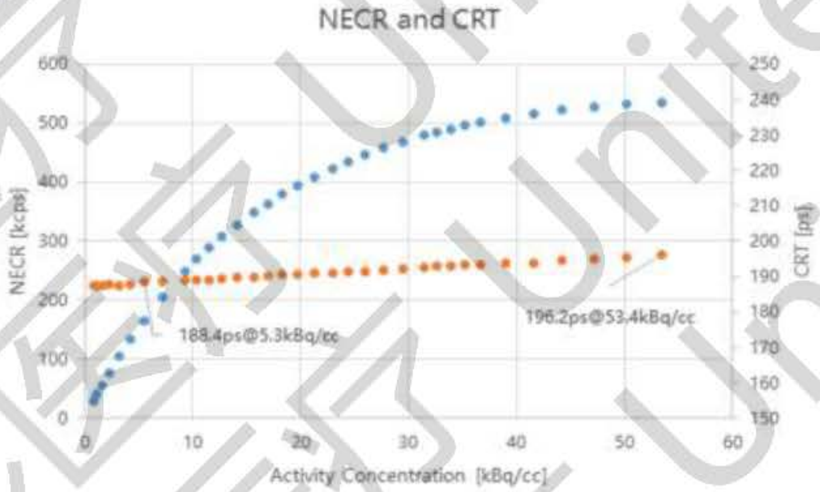

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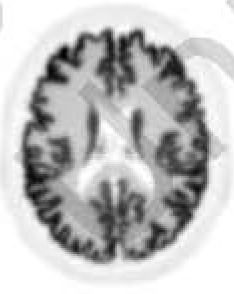
So What is NEXT?

10ps challenge

https://the10ps-challenge.org/

Non-TOF back-projection



TOF back-projection with 10ps FWHM CTR

190ps FWHM CTR Hoffman OSEM

Hoffman brain phantom simulated analytically without noise (courtesy: Johan Nuyts, University of Leuven)

Endorsements

Scientists

TOF-PET技术的瓶颈

主流PET探测系统结构：闪烁晶体L(Y)SO + SiPM + 读出

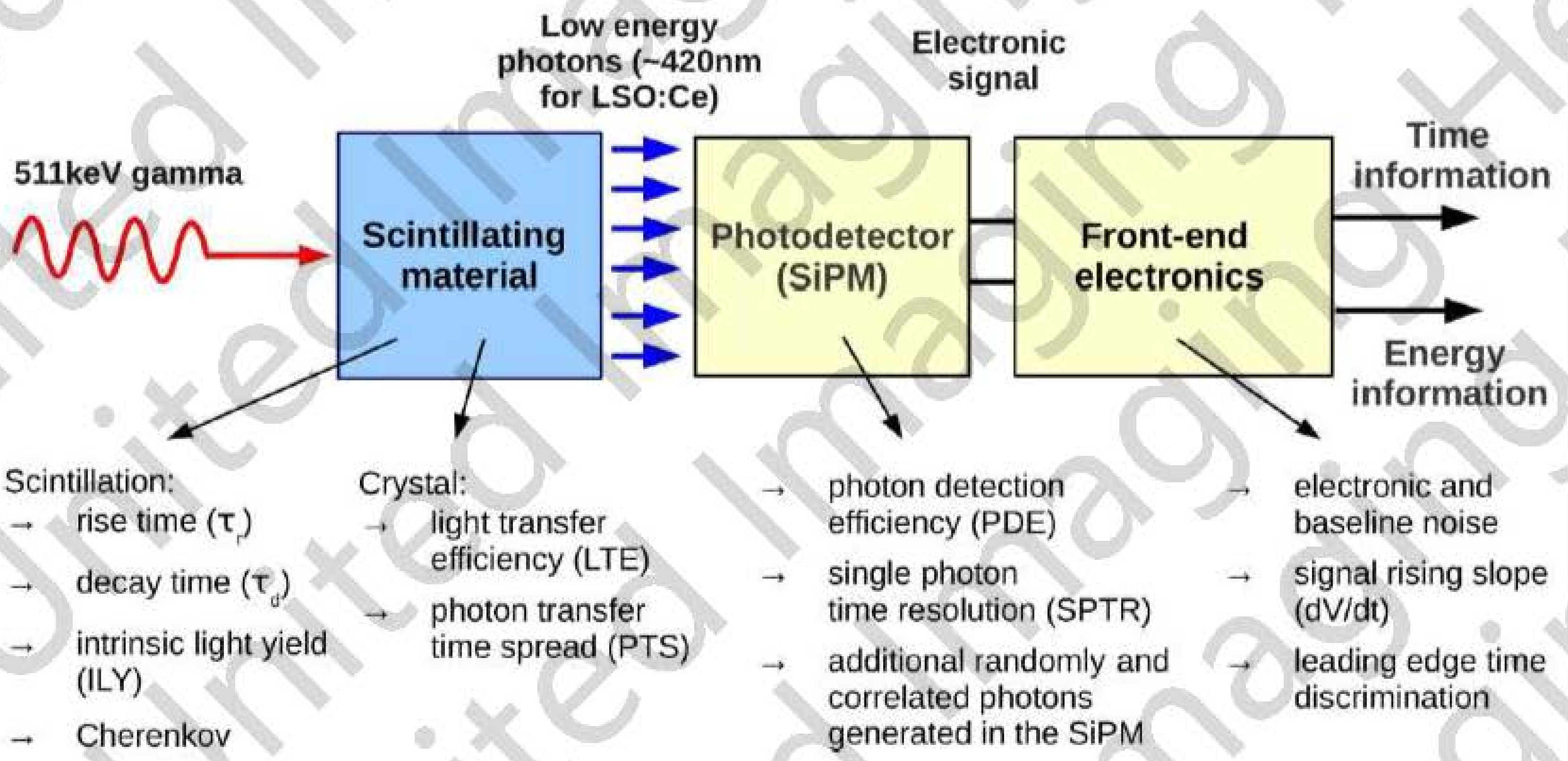


Figure 1. The three main building blocks of a typical TOF-PET detector (Acerbi and Gundacker, 2019).

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TOF-PET技术的瓶颈

TOF水平预测

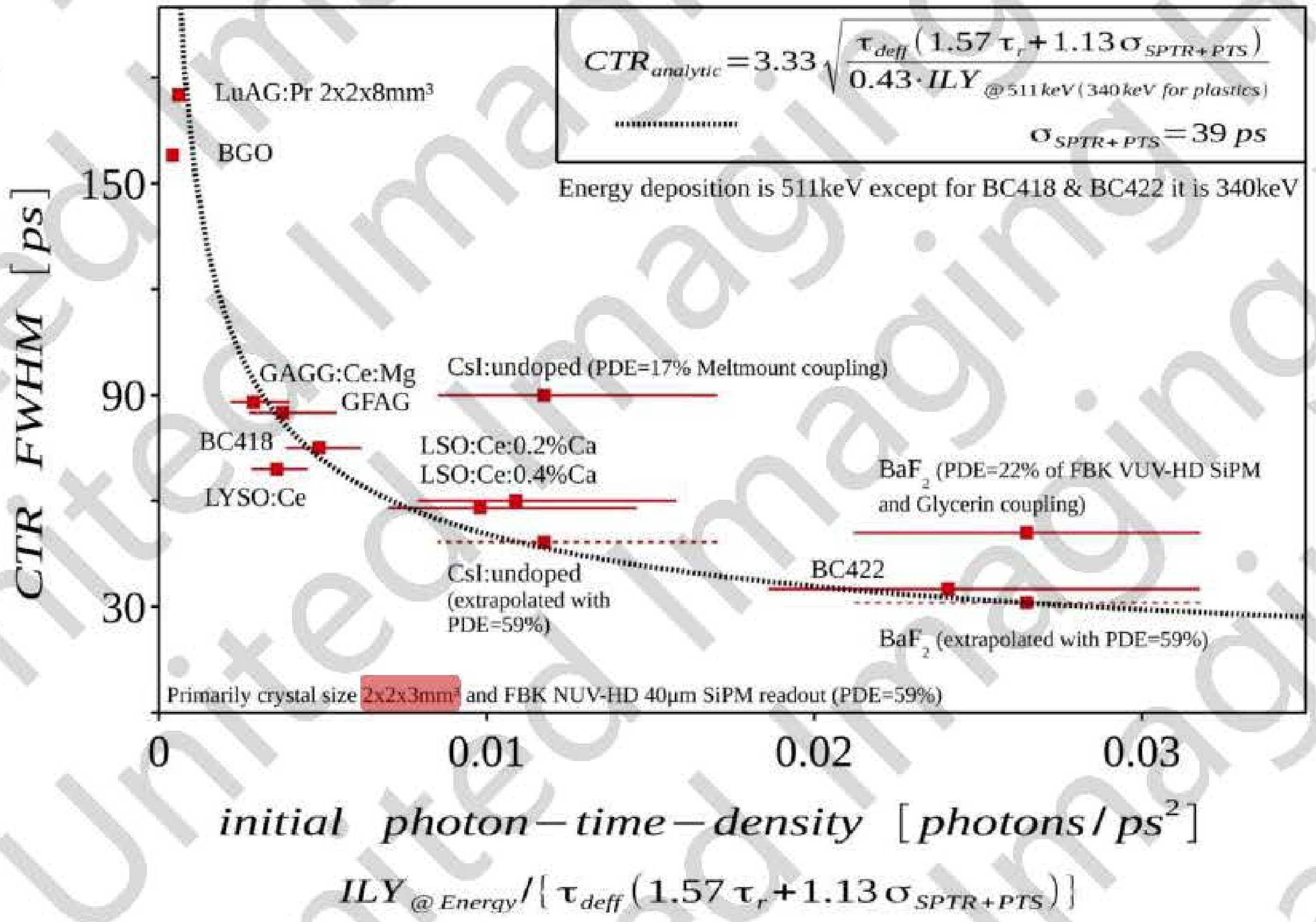


Figure 2. Measured CTR (*y*-axis) as a function of the scintillator intrinsic timing capability, given by the scintillation emission initial photon-time-density, on the *x*-axis. The black dashed line shows an analytic CTR model (Vinogradov 2018) only dependent on the scintillation kinetics and intrinsic light yield (ILY), taking into account the light transfer in the crystal and the SiPM SPTR and PDE. (Gundacker *et al* 2020).

TOF-PET技术的瓶颈

1、理想的晶体材料，光产额要尽量高，同时发光衰减时间尽量短，射线阻止能力较好，能量分辨率较好，性能稳定。L(Y)SO:Ce发光衰减时间一般会随着光产额的增加而增加，LaBr3:Ce各项性能较好，但极易潮解，易碎。

2、为了确保探测效率，晶体需要一定的长度(约20mm)，闪烁光子在晶体内传输时间的不确定性会增加定时误差较长的晶体还会引入严重的DOI(depth-of-interaction效应），进一步增加定时误差

3、光电器件的SPTR(Single Photon Timing Resolution)和PDE(Photodetection efficiency)对CTR的影响很大，虽然SiPM的不断提升，但对系统CTR的提升有限。

经典的长闪烁晶体+高速光电转换器的PET探测器架构，限制了TOF水平在100ps左右。

Achieving 10 ps coincidence time resolution in TOF-PET is an impossible dream
Medical Physics（July 2020 | Volume 47,Issue 7）

TOF-PET探测器进展

Direct positron emission imaging with Cerenkov radiator integrated MCP-PMTs

nature photonics
ARTICLES
https://doi.org/10.1038/s41566-021-00871-2
Check for updates

Ultrafast timing enables reconstruction-free positron emission imaging

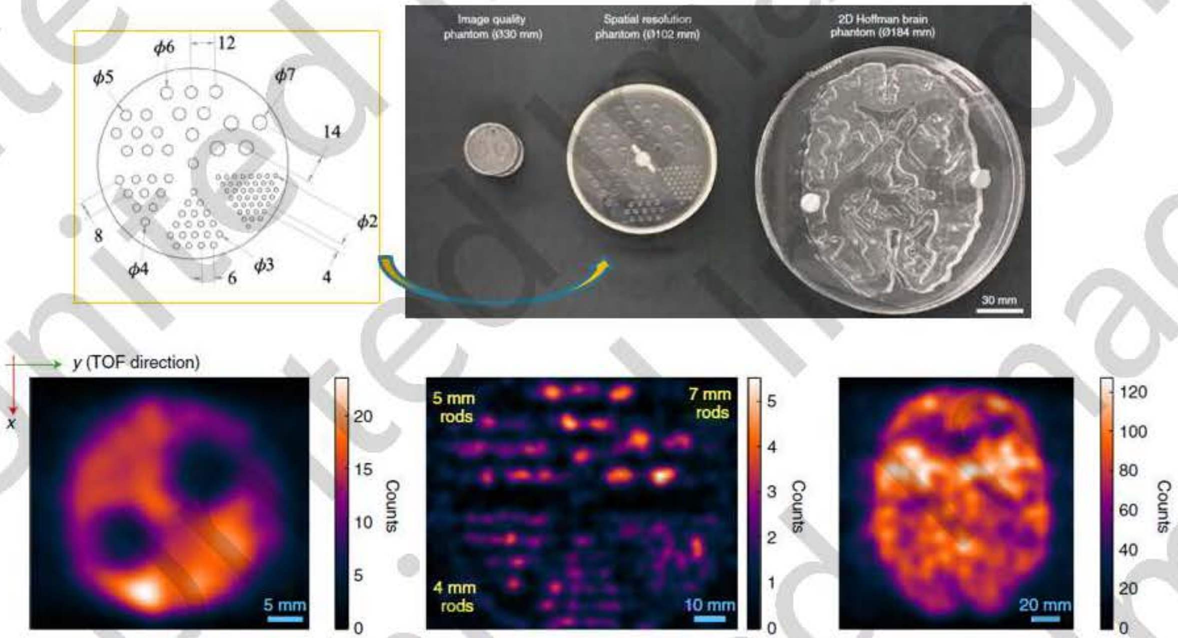
Sun Il Kwon[1,5], Ryosuke Ota[2,5], Eric Berg[1,5], Fumio Hashimoto[2], Kyohei Nakajima[3], Izumi Ogawa[3], Yoichi Tamagawa[3], Tomohide Omura[2], Tomoyuki Hasegawa[4] and Simon R. Cherry[1]✉

① Using **Cerenkov light** as the mechanism to achieve a fast timing signal. Light rise/decay time <10 ps

② **Integration of a Cerenkov radiator directly within the photosensor** to optimize light transport and photo-detection timing properties

③ Apply **convolutional neural network (CNN)** as a standalone algorithm to predict the timing information from the measured detector waveforms

Imaging results of dPEI



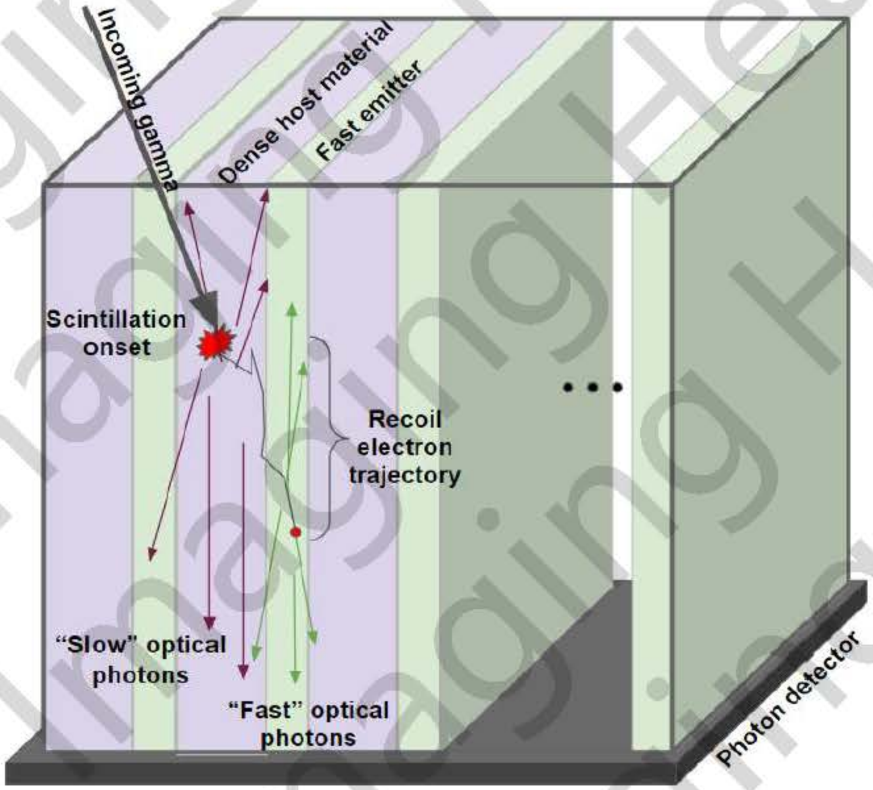
- 3 mm rods can be resolved, indicating a spatial resolution on the order of 4-5mm
- The spatial resolution is in line with timing response of **32 ps**

Limitations	Future solutions
• Low coincidence rate: ~1.65% • Long acquisition time: 2-34 minutes per measurement position, 4-24 hours for the whole image • High amount of radioactivity used: up to ~1000 MBq • MCP-PMT: bulky and small sensitive area	• Using a higher atomic number radiator such as PbF_2, BGO, HfO_2 • Increasing radiator thickness • Developing multi-channel detectors that can be tiled together, and then using multiple detectors arrays to increase geometric coverage and collection efficiency.

Meta-Scintillator

- Recoil electrons produced by 511keV γ loosing energy through a dE/dx process. For dense organic scintillators, the recoil electron range reaches up to around 500μm.
- Sampling pixel: first generation of composite metastructures, a high-Z host and a fast emitter, cut in layers with thicknesses of less than the recoil electron range and arranged in geometrically periodic alternating positions
- The fast material is driving the timing improvements, and the heavy scintillator provides the stopping power and energy resolution.

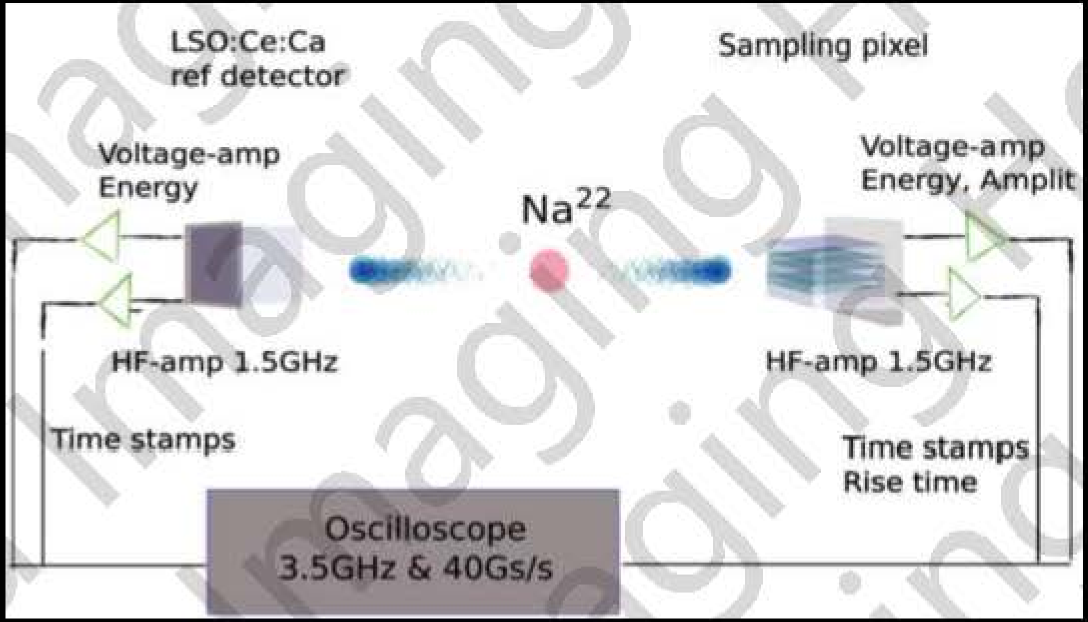
Schematic of sampling pixel



Plastic based metascintillators LYSO/BGO + BC422

Schematics and picture of the sampling pixels

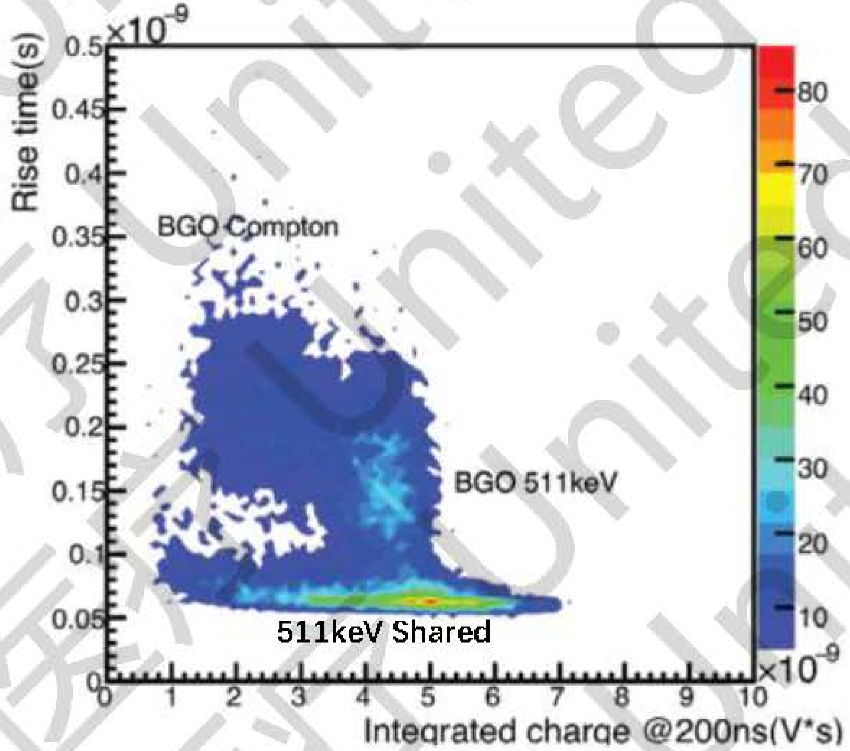
CTR measurement setup



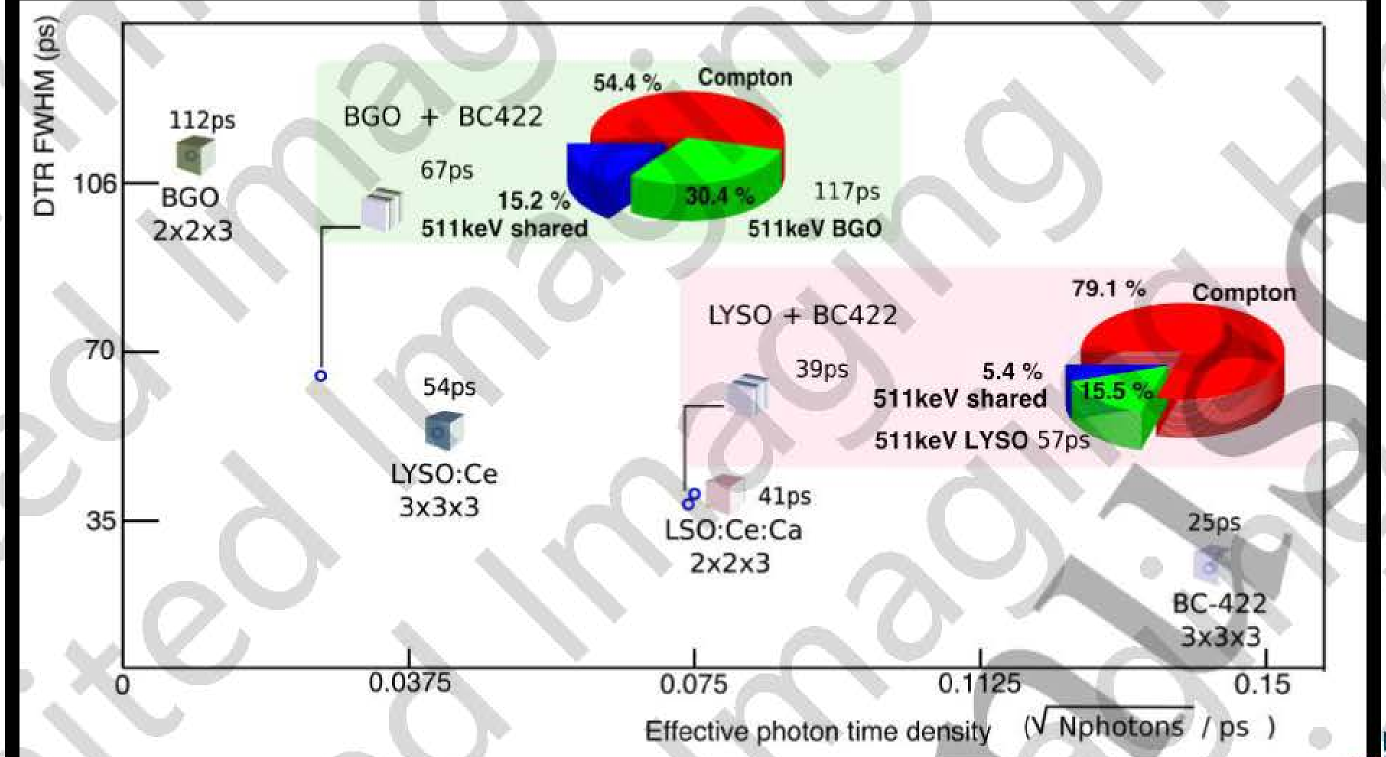
LYSO/BGO + BC422

- 511keV gamma detection efficiency reduced ~40% compared with bulk LYSO/BGO
- 511keV shared events: rise time < 100ps, DTR 67ps (equivalent CTR of 95 ps)

Integrated charge vs. rise time



Measured results



Nanocrystal based metascintillators
CdSe/CdS nanocomposite

- CdSe nanoplatelets: one of the materials with fastest radiative recombination times
- Intrinsic short-comings:
  - Lower stopping power
  - High self-absorption
  - Organic ligands needed for surface passivation

CdSe/CdS@PS1%: CdSe-based nanocomposite 1% weight concentration, uses polystyrene (PS) as a host matrix

CdSe/CdS + LYSO sampling pixel

Nanocrystal based metascintillators
CdSe/CdS nanocomposite

- CdSe/CdS@PS1%
- Emission centered at ~530nm
- ~100 photons /MeV

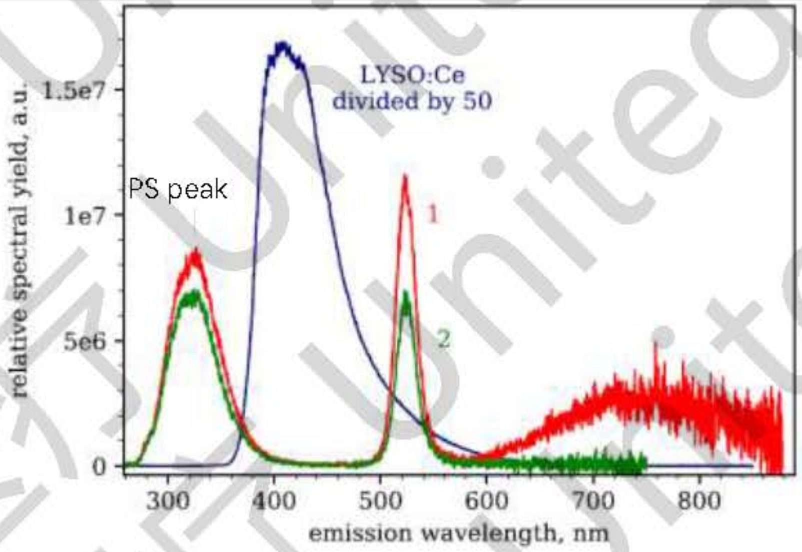
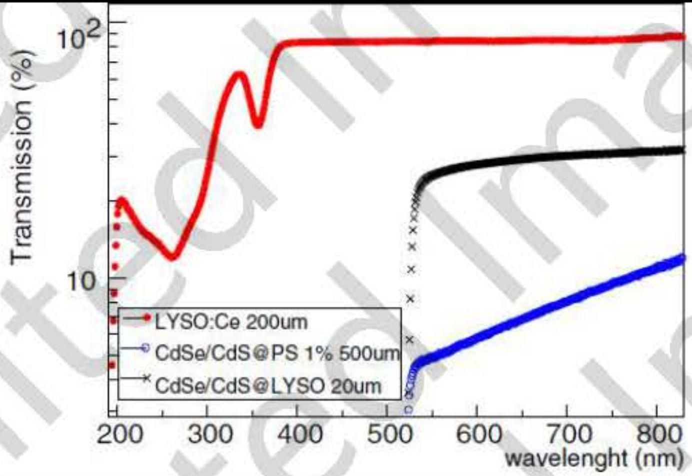
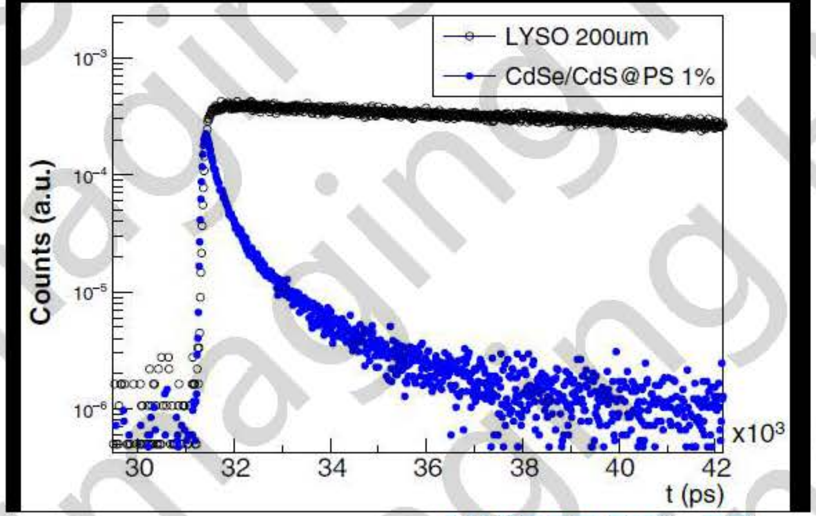


Fig. 6 High-energy cathodoluminescence emission spectra of CdSe/CdS@PS 1% Curve (1) was recorded in the 0–200 µs time gate and curve (2) between 0 and 32 ns time window relative to the excitation pulse. The CL spectrum of LYSO:Ce was recorded in 0–200 µs time window

- Transmission of CdSe/CdS nanocomposite
- Very low transparency

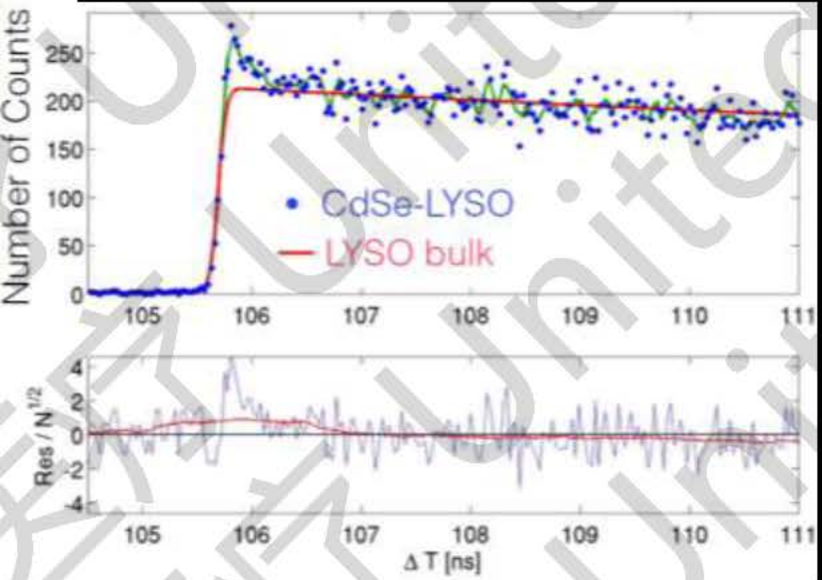


- CdSe/CdS@PS1% light output obtained in a time correlated single photon counting setup with 40 kV X-ray
- Rise time <1ps, time duration <1ns

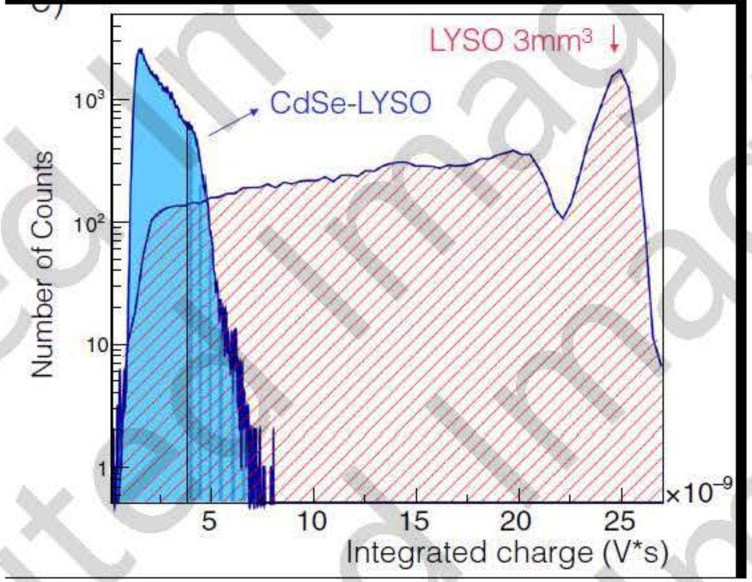


CdSe-LYSO sampling pixel results

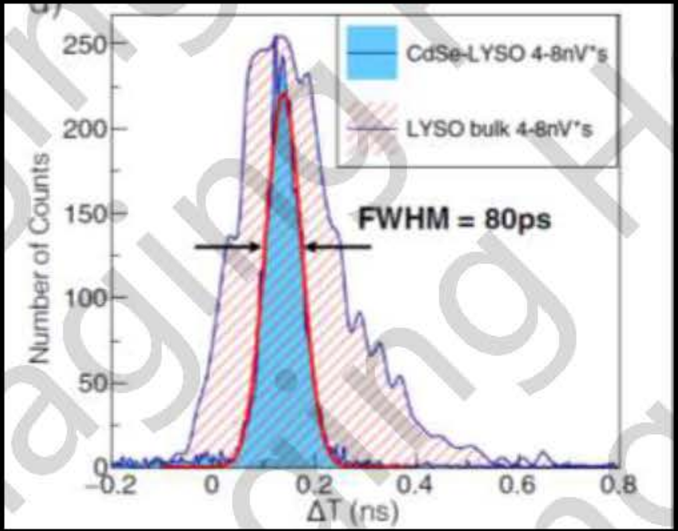
- Rise time measured in a time correlated single photon counting setup



- Energy spectrum obtained with a Na22 source
- CdSe-LYSO shows significantly decreased light output and poor energy resolution

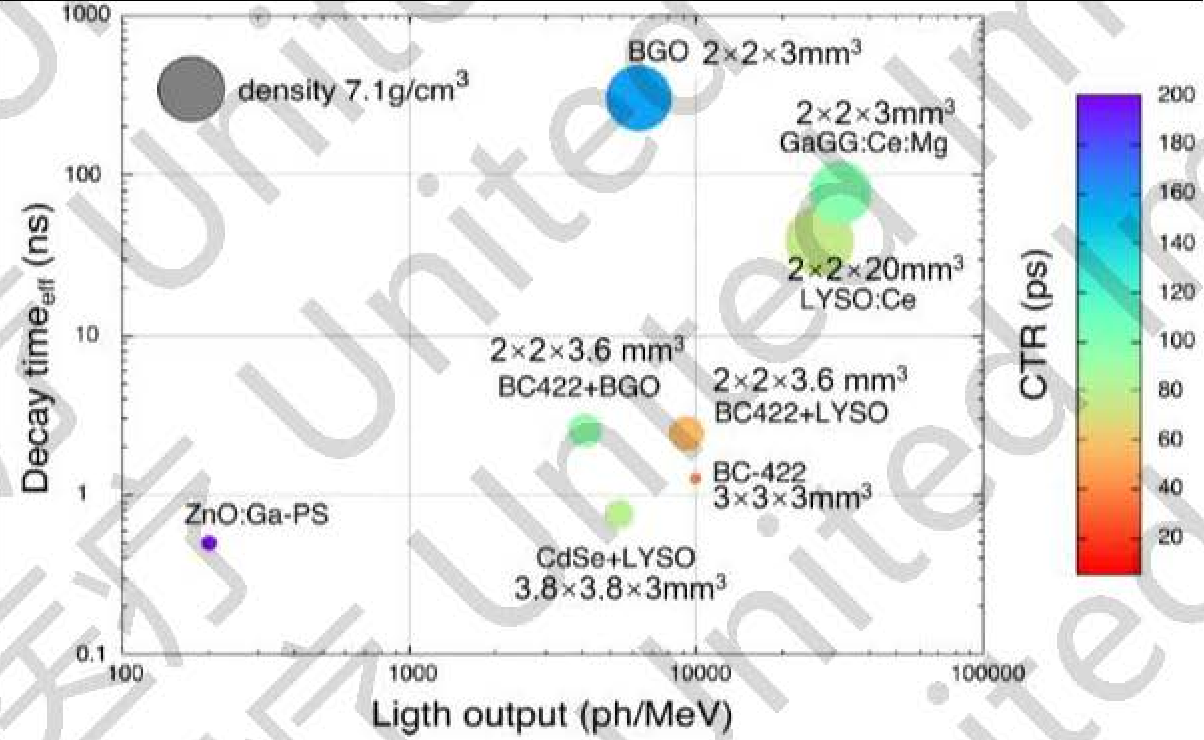


- Delay time distribution for all CdSe-LYSO events in coincidence with integrated charge higher that 4nV*s

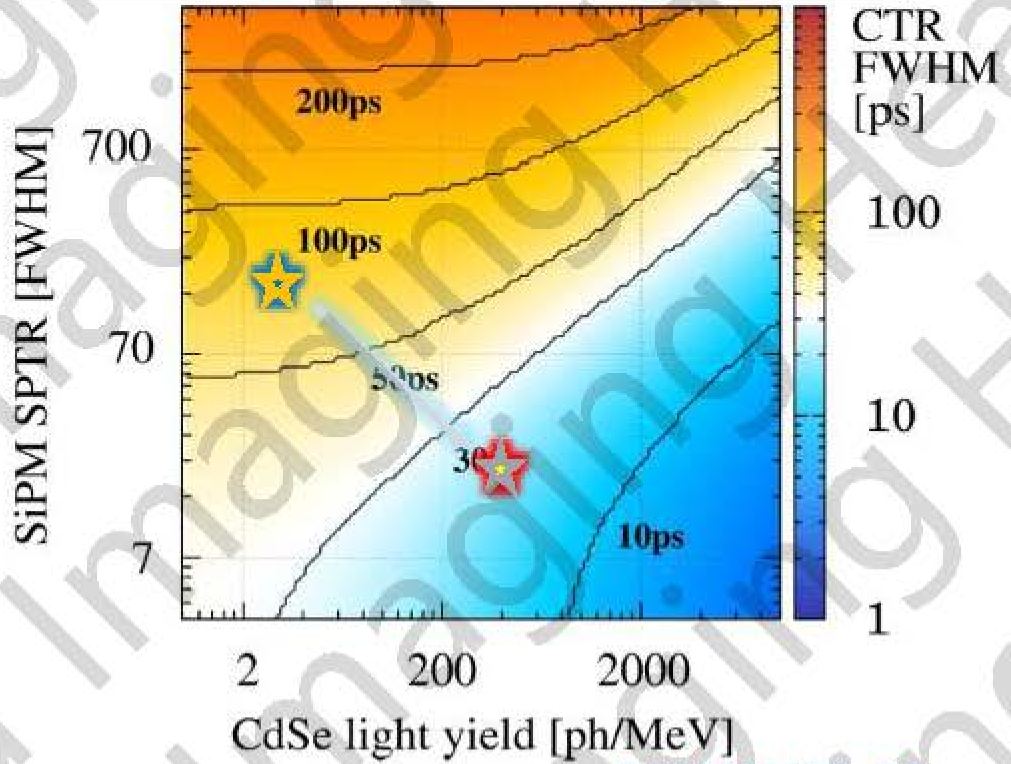


CTR values achieved with a first generation of sampling pixel detectors

- CTR values achieved with a first generation of sampling pixel detectors
- *Fast but low efficiency !*



- CTR lower bound of a hypothetical 2×2×3 mm³ meta-scintillator
- Is 10 ps possible?



Summary of Metascintillators

- Metascintillators have potential to enhance the timing performance of TOF-PET based on conventional inorganic crystal
- Published results show that 3mm length sampling pixels achieved CTR <100ps with greatly reduced 511keV gamma detection efficiency
- This approach has to overcome significant barriers relating to their deposition, orientation and ways to avoid self-absorption
- Increasing the total light yield of CdSe-based nanocomposite in a factor 100 provide with the photon-time density is critical to reach ultimate time resolution for a significant fraction of the events fully contained in the proposed hybrid pixel geometry
- Much efforts need to be made before it can be applied in PET scanners

Summary

- 提升探测器TOF水平和轴向长度是PET的发展趋势，全身PET/CT已经带来全新的应用
- PET探测系统的设计要兼顾探测效率，TOF时间分辨率，空间分辨率和能量分辨率等多项指标，同时要考虑可加工性、长期稳定性和成本
- 经过近10年发展，主流商用PET均采用L(Y)SO + SiPM的技术架构，目前已经达到了探测器180ps左右，系统200ps左右的水平
- L(Y)SO + SiPM的架构下，整机难以实现好过100ps的TOF水平
- 利用切伦科夫辐射光可以实现更好的TOF，但距离实用还有相当的距离
- 结合fast material 和 heavy scintillator的meta-scintillator可以提供较好的TOF性能和较好stopping power，但距离实用还有相当距离。

如果想要达到10ps的CTR，同时保持高探测效率 、空间和能量分辨率，需要创新的探测器材料、高度集成的光电器件和创新的信号处理方法。

- 希望能够和各位专家交流合作！

PASSION FOR CHANGE

United Imaging Healthcare Co., Ltd