核医学成像技术
在质子重离子放疗剂量监测中的应用

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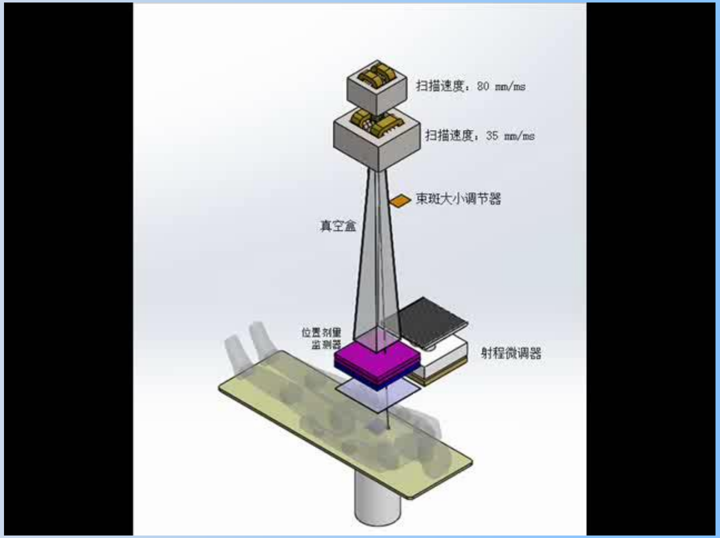
2019/7/20

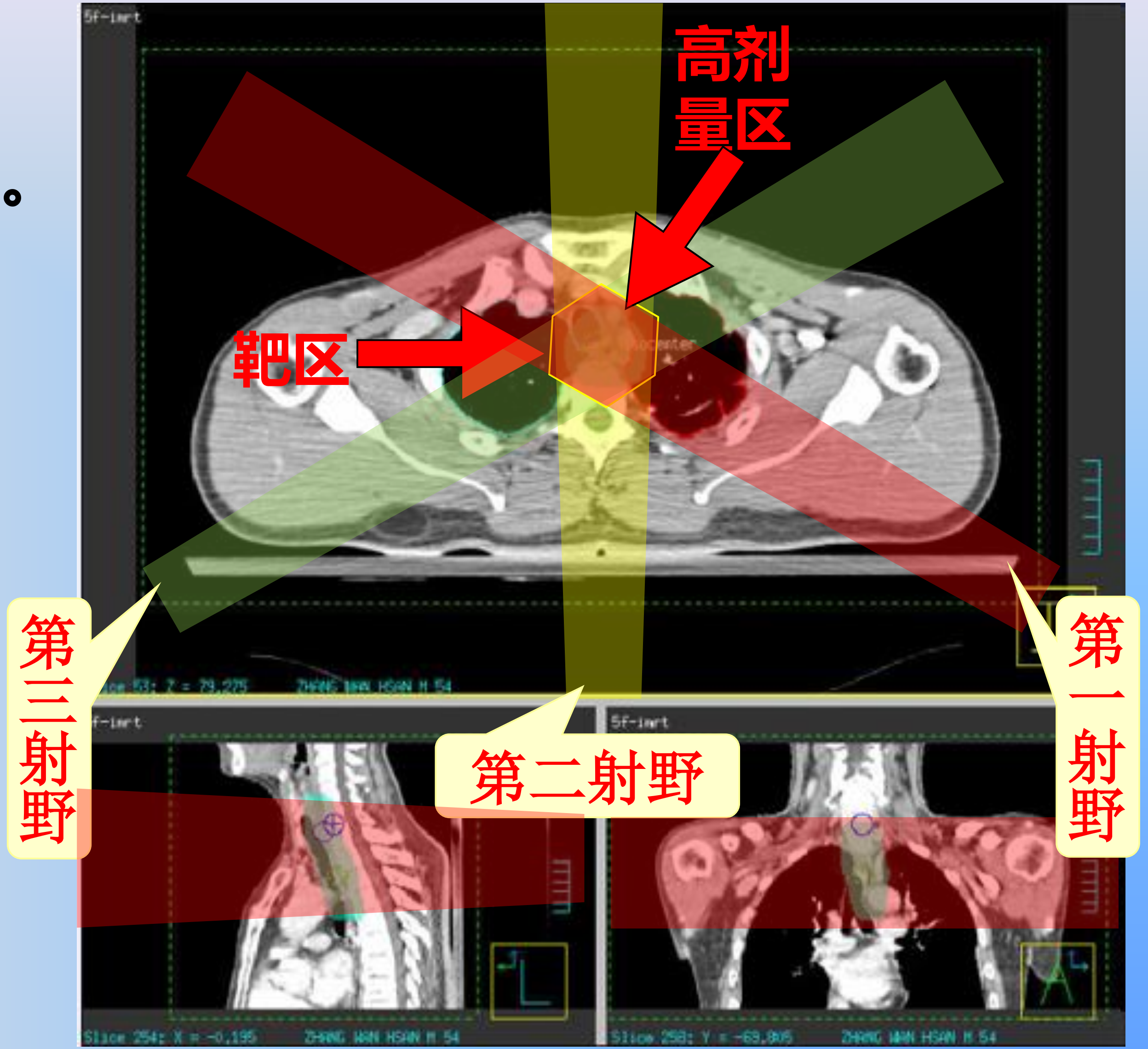


常规放射治疗

常规放疗属于远距离放射治疗，需使用高能X射线。

它以强度均匀、形状规则的辐射野为基础。为使肿瘤得到比周围组织高的照射剂量，每次从2～3个不同角度照射。

主要的装置是钴-60治疗机和直线加速器。

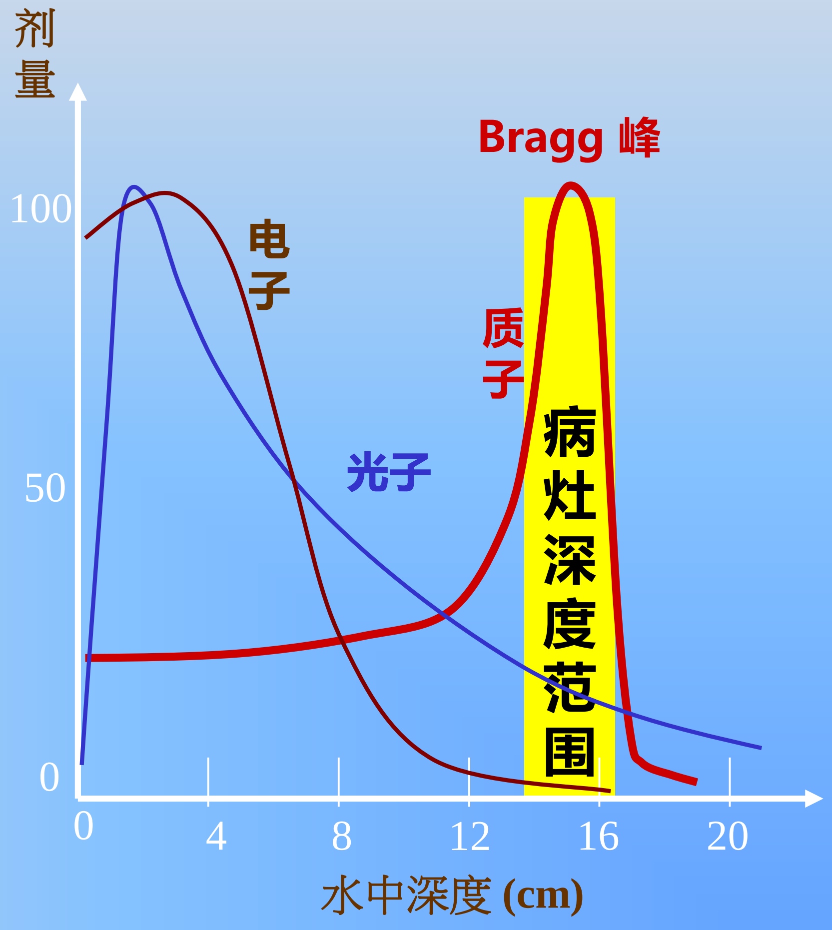


食管癌放射治疗

质子和重离子治疗

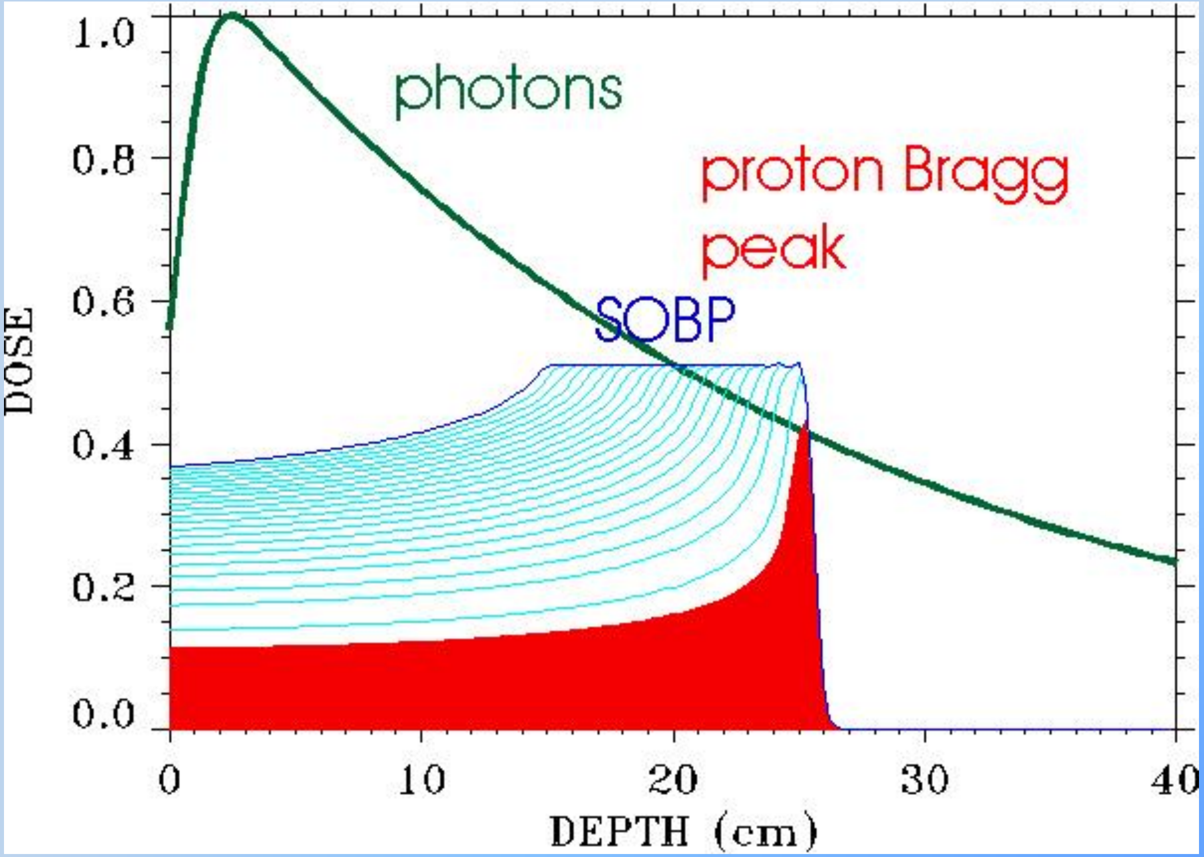
γ和X射线在人体中的剂量随入射深度增加而呈指数衰减，大部分能量都释放到靠近表皮的正常组织中，深部的肿瘤得不到足够的剂量。

高能质子和带电重离子进入人体后会逐渐减速，但与原子的核外电子作用却在增大，在终点附近与电子的作用最大，将大部分能量释放出来，这个发生最高剂量的区域叫作“Bragg峰”。

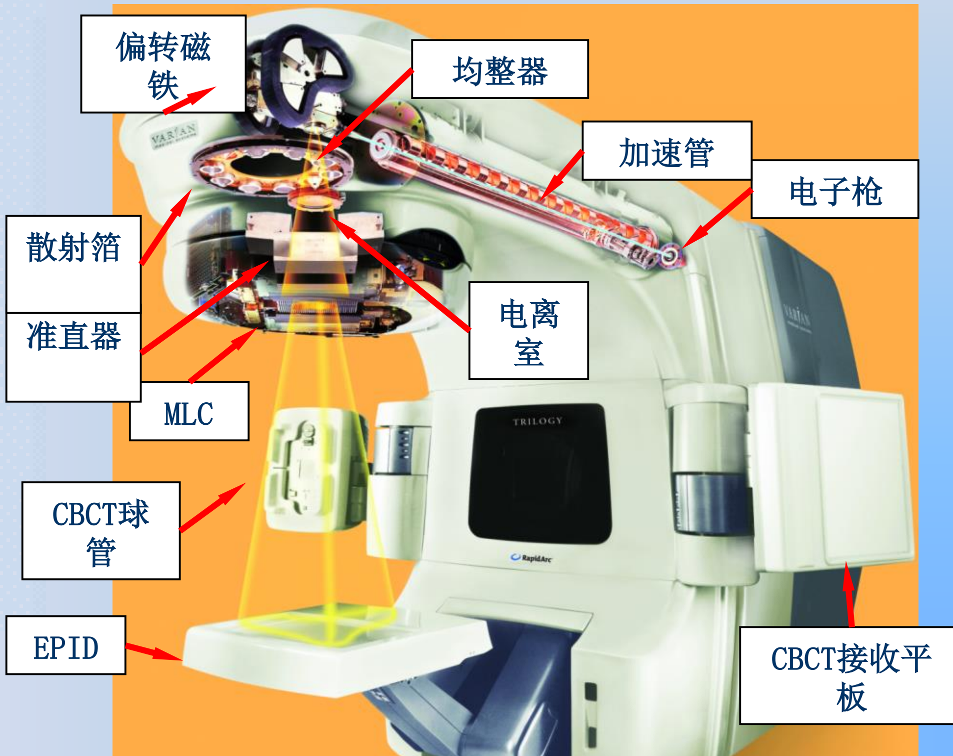


质子和带电重离子的**能量**及其在人体内经过的**组织密度**决定了Bragg峰的位置，这使得医生能够控制最大剂量区的深度，使之精确地覆盖整个肿瘤。如果进行多方向、多射野的治疗，施加到正常组织的剂量可以更低，而在束流重叠处的剂量可以大大增加。

质子和重离子治疗对靠近重要器官的肿瘤有特别的意义。如眼部黑色素瘤、颅内肿瘤、动静脉畸形、垂体瘤、前列腺瘤、脊索瘤、软骨肉瘤、头颈和子宫瘤。



医用电子直线加速器



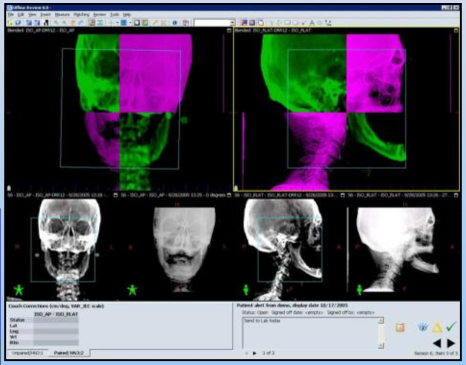
偏转磁铁
均整器
加速管
电子枪
散射箔
准直器
电离室
MLC
CBCT球管
EPID
CBCT接收平板
TRILOGY

电子射野影像装置（EPID）

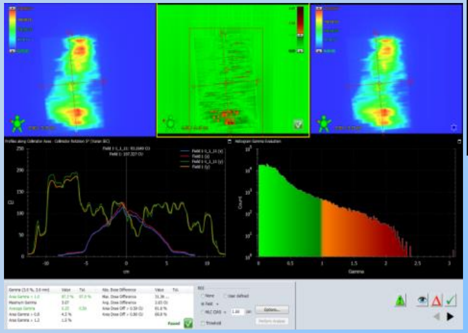
电子射野影像装置

EPID的临床应用

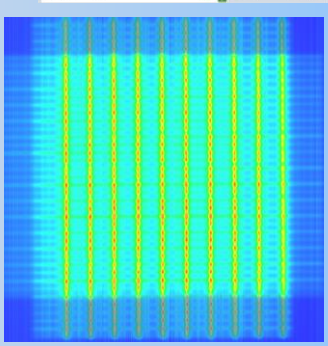
位置验证

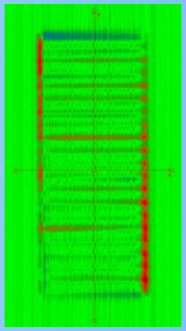


剂量验证



加速器的质控





质子重离子治疗

- **缺点：射程偏差导致目标靶区剂量不足，健康组织辐照风险**

常见造成射程偏差的因素[1]

治疗计划中的设定误差	CT图像伪影 CT图像转换误差 治疗方案计算近似误差
治疗过程与治疗计划的偏差	病人的摆位偏差 体内器官的运动 肿瘤形态变化 ……

➡

- **解决途径：**
  - **设置安全边界[2]**

    MD Anderson：3.5% + 3 mm

    ->导致健康区域辐照风险
  - **治疗过程监测**

    PET

    瞬发光子成像

    ->通过探测治疗过程中产生的次级粒子实现对射程和剂量的实时监测

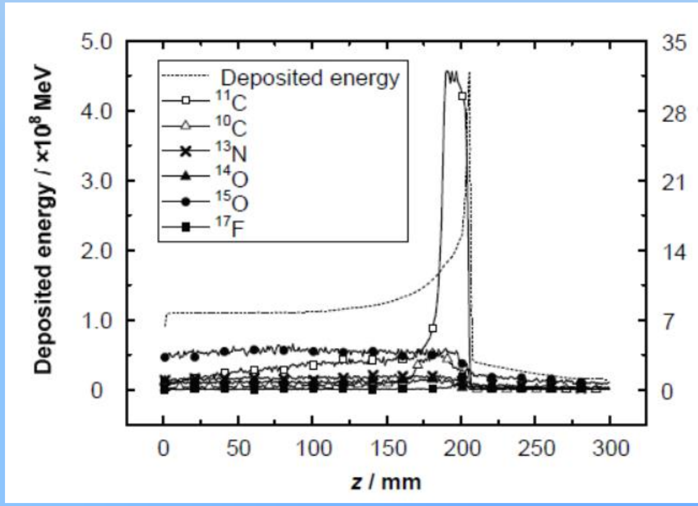
[1] Smeets J., 2012　[2] Harald P., 2012

PET射程监测原理

- 质子、重离子射束径迹上产生C-11，N-13和O-15等正电子核素，可用PET监测其空间分布，进而推测Bragg峰位置

Radionuclide	Half live (min)	Nuclear reaction channels / Threshold energies (MeV)
^{15}O	2.037	$^{16}O(p,pn)^{15}O$/16.79
^{11}C	20.385	$^{12}C(p,pn)^{11}C$/20.61,
		$^{14}N(p,2p2n)^{11}C$/3.22,
		$^{16}O(p,3p3n)^{11}C$/59.64
^{13}N	9.965	$^{16}O(p,2p2n)^{13}N$/5.66,
		$^{14}N(p,pn)^{13}N$/11.44
^{30}P	2.498	$^{31}P(p,pn)^{30}P$/19.7
^{38}K	7.636	$^{40}Ca(p,2p2n)^{38}K$/21.2

质子治疗中产生的主要正电子核素[1]

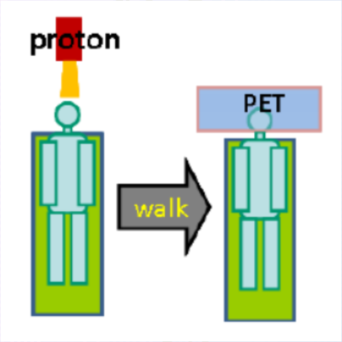


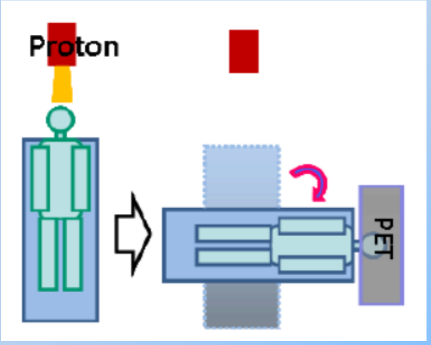
^{12}C重离子在水介质中沉积能量和正电子核素分布图[2]

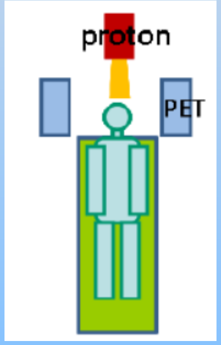
[1] Beebe-Wang J, et.al, 2003
[2] Jing Wu, et al., 2010

PET射程监测方案

- **Off-line PET**
- **In room PET**
- **In-beam PET**







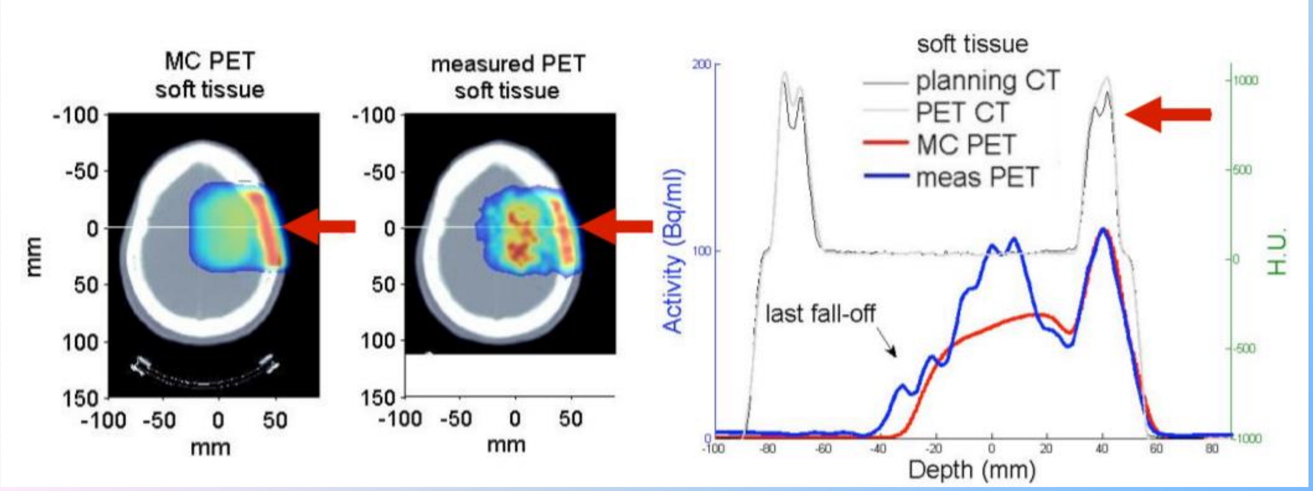
✓成熟的PET/CT系统
✓可以与治疗计划中的CT融合
✓可靠的衰减校正
×成像时间延迟长
×核素生物学清除

✓成像延迟平均2.5分钟
✓价格相对低
✓图像质量好
×图像融合误差

✓数据获取无延迟
✓活度高
×专用PET系统
×价格昂贵
×技术要求高
×成像存在伪影

Off-line PET：临床偏差分析

- 生物学清除



通过蒙特卡罗模拟和实验PET测量数据得出生物学清除效应对PET射程监测造成的偏差:

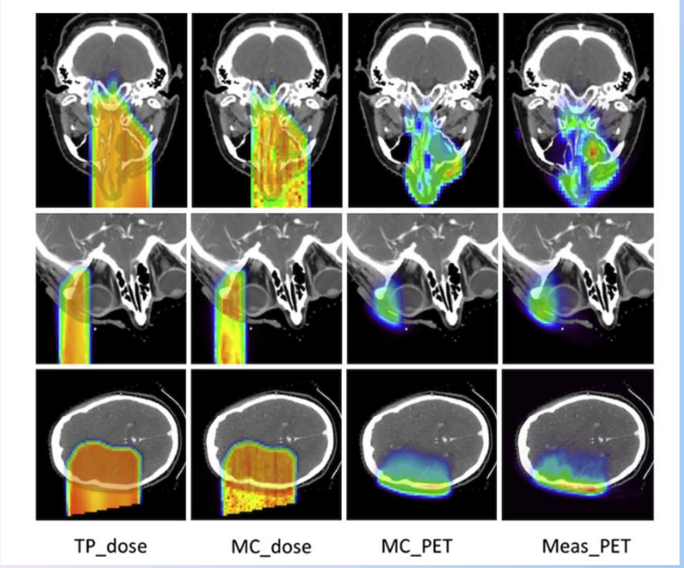
Bone:
2.4 mm
Bone/soft tissue：
2.2 mm
Soft tissue：
4.3 mm

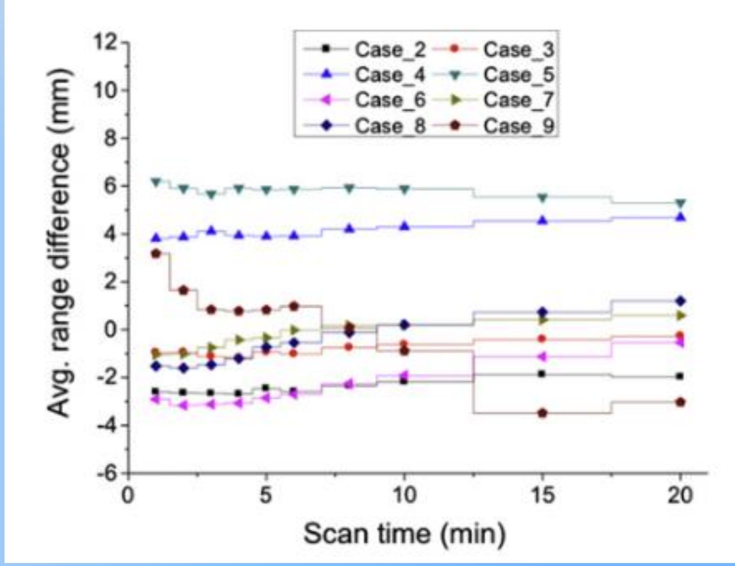
A Knopf, et al., 2019

In-room PET：临床应用

- 9个病人： 质子治疗 + in-room PET
- Geant4 蒙特卡罗模拟结果作为金标准

- 研究了不同扫描时间对射程精度的影响



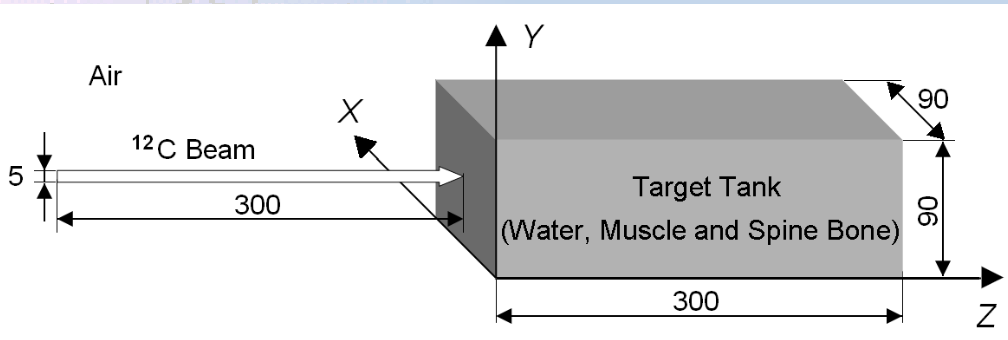


- 模拟与PET测量的平均射程差在2mm以内

- 潜在最佳的扫描时间在5分钟

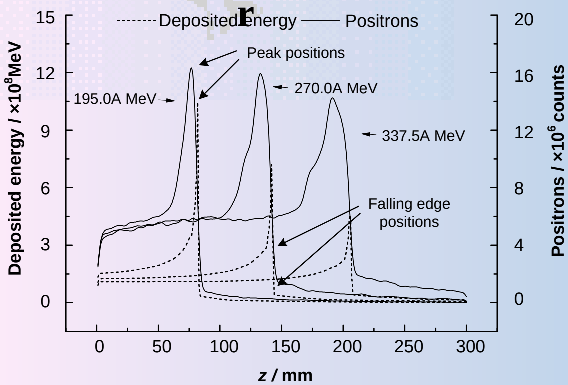
Chul Hee Min, et al., 2012

使用In-beam PET监控重离子癌症治疗的GATE模拟研究

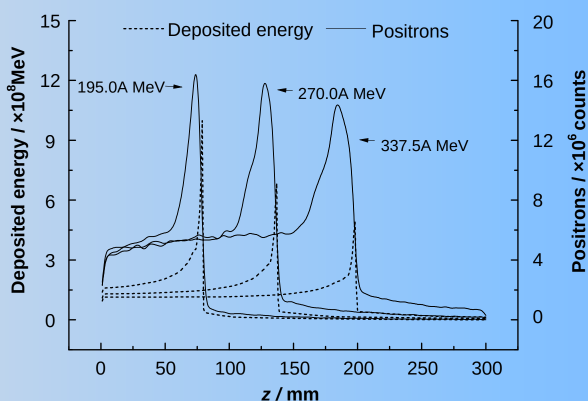


- 模拟了不同能量的C-12射束与不同物质相互作用时的剂量分布和正电子分布
- C-12剂量和正电子在入射方向上的分布具有高度相关性: Bragg峰和正电子峰的下降沿在1mm的误差范围内

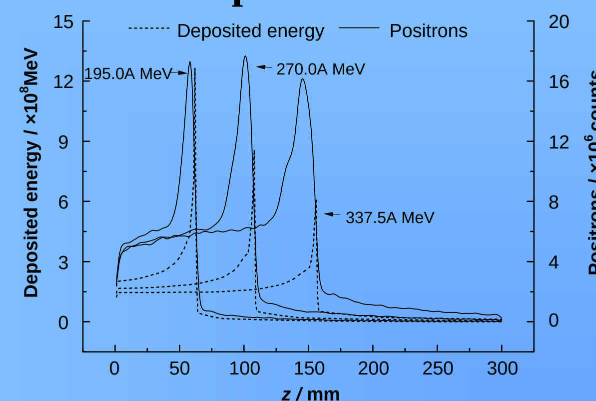
Water



Muscle

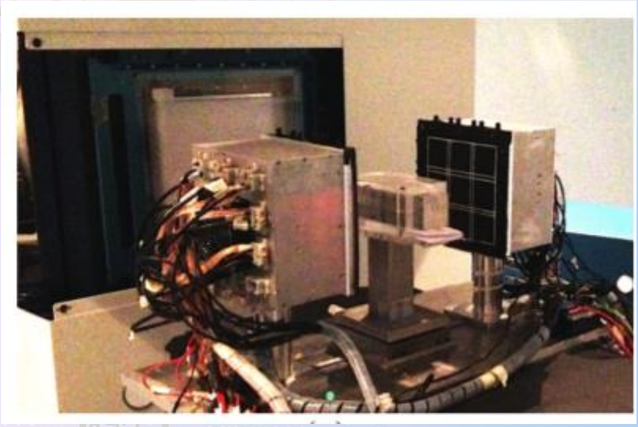


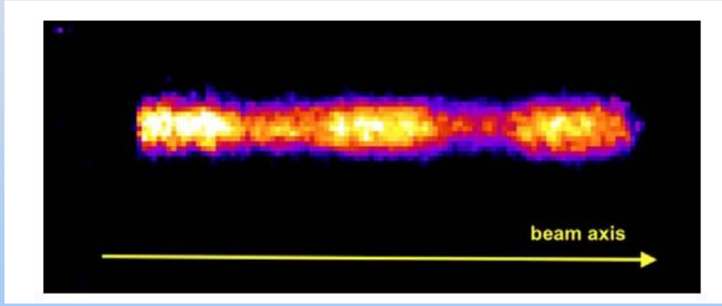
Spine bone



Jing Wu, et al., 2010

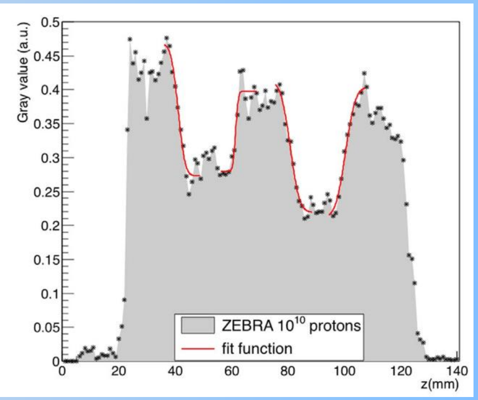
In-beam PET: DoPET

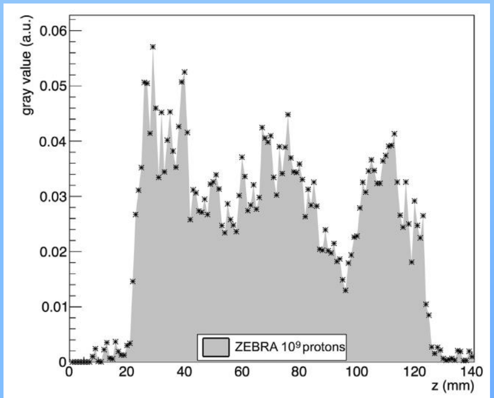




10^{10}质子PET成像

DoPET系统
•双探头：LYSO
•9个模块组成一个探头
•23 x 23 晶体阵列
•3ns 符合时间窗

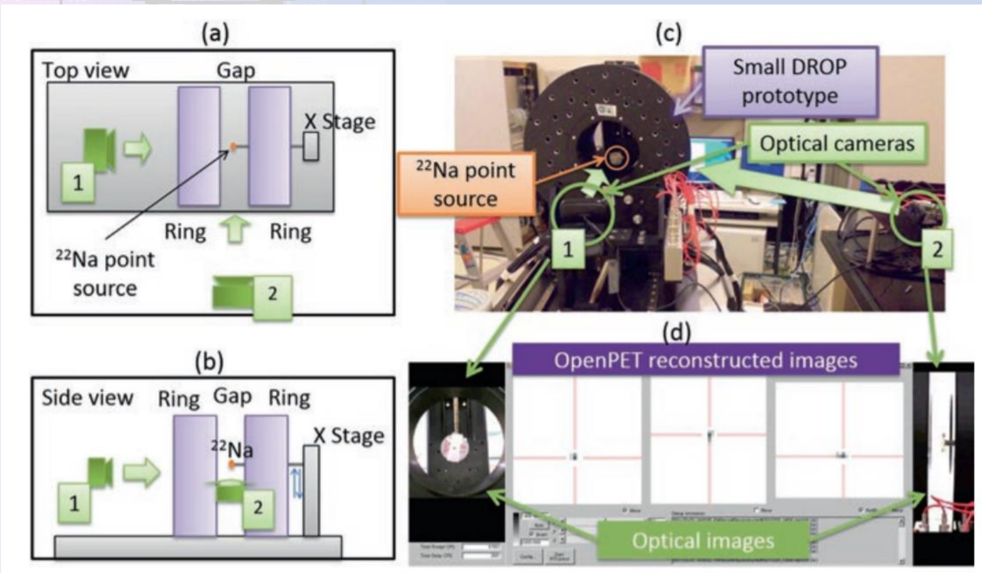




不同质子数目下的PET图像分布：
监控射程精度受噪声影响较大

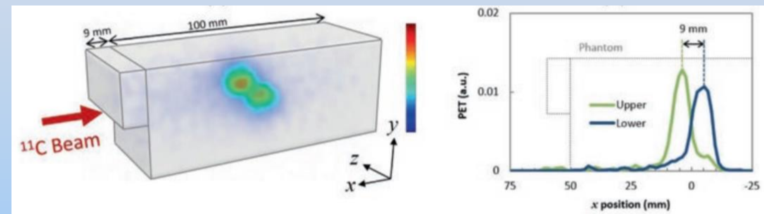
V Rosso, et al. 2016

In-beam PET: Open PET

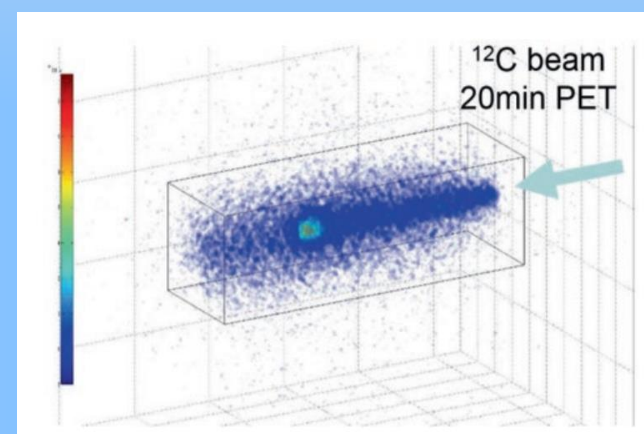


双环Open PET系统

- 16x16x4 GSOZ
- 4 层DOI探测器
- 64 通道PMT



^{11}C笔形束实验

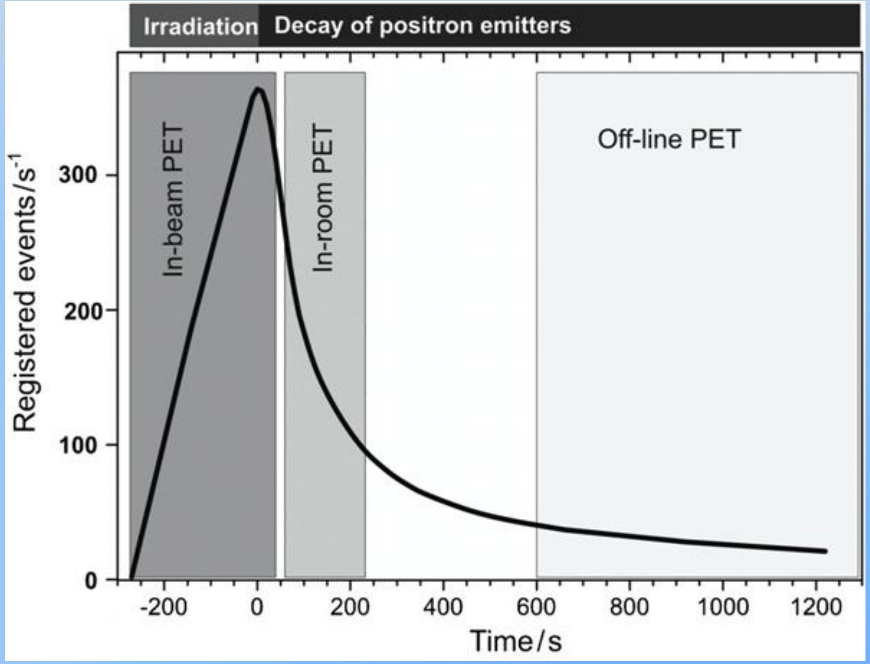


^{12}C离子束20分钟PET成像结果

Taiga Yamaya, et al., 2015

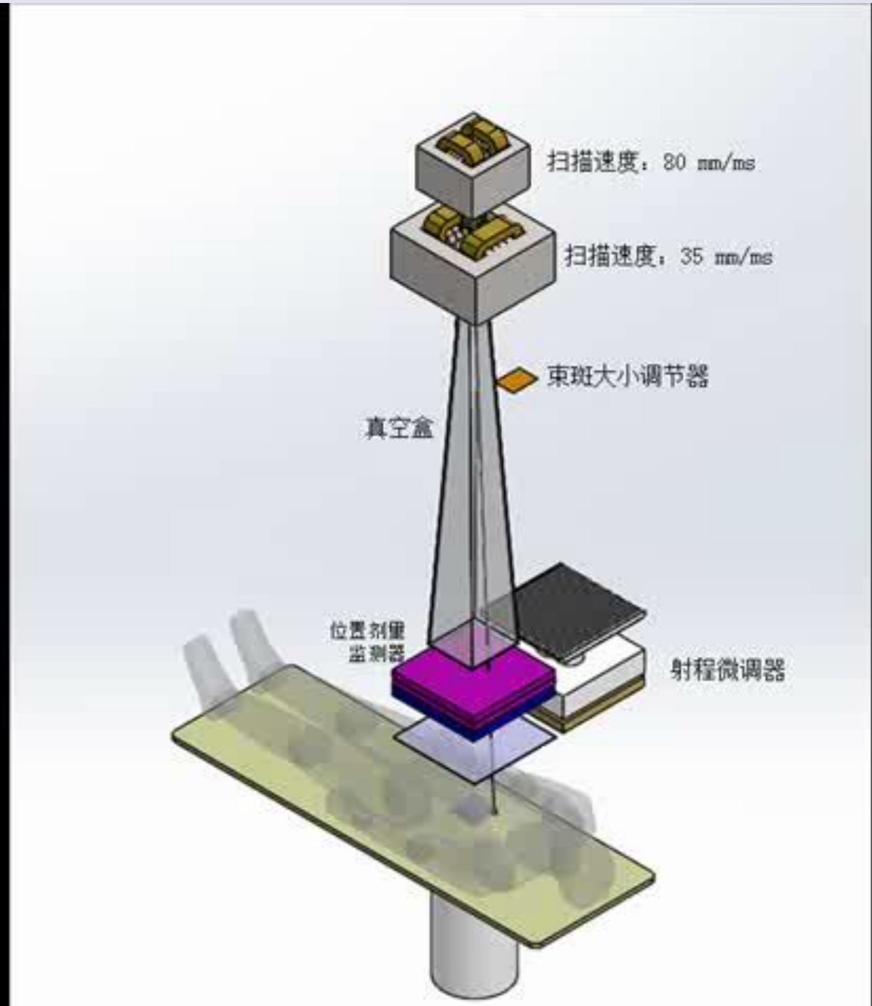
PET射程监测小结

- 三种PET监测方案是在质子治疗（正电子核素产生）的不同时间进行监测， off-line PET的收集信息时间过晚导致大多数短半衰期核素已衰变，in-beam PET的探测时刻最及时，同时没有再定位误差，因而in-beam PET的图像活度高，射程监测精度也高，对于质子重离子射程的检测误差可控制在1 mm以内。



瞬发γ光子监测

- 实时监测？
- 剂量监测？

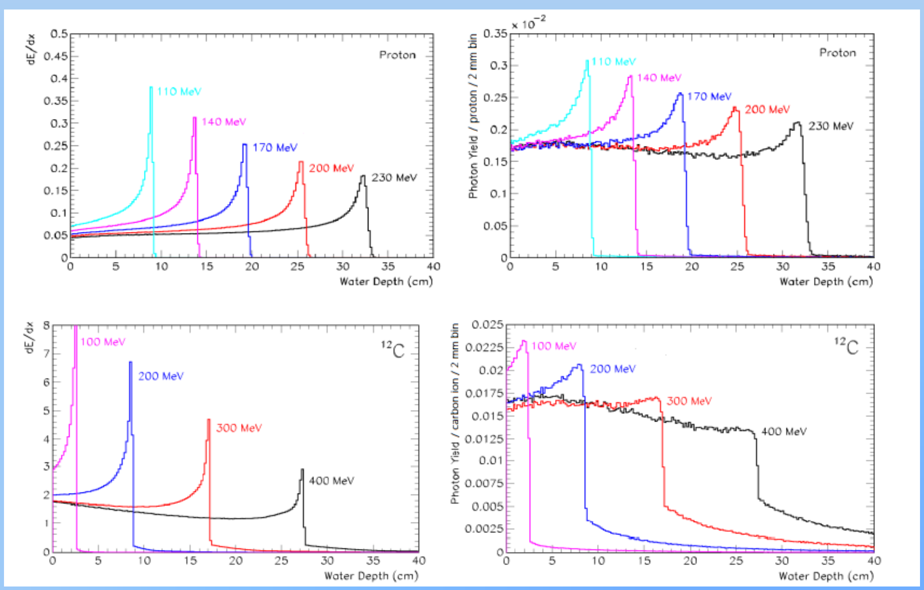

扫描速度：80 mm/ms
扫描速度：35 mm/ms
束斑大小调节器
真空盒
位置剂量
监测器
射程微调器

瞬发光子成像原理

- 质子、重离子轰击原子核使其激发，并**瞬时**（10^{-19}~10^{-9}s）退激产生瞬发光子，瞬发光子分布与粒子能量沉积分布**空间相关度高**

质子治疗中产生的常见瞬发光子能量[1]

瞬发光子能量 MeV	反应过程	退激过程	平均寿命 s
2.124	$^{12}C(p, x)^{11}B^*$	$^{11}B^*$2.125->g.s.	5.5×10^{-15}
2.313	$^{14}N(p,p')^{14}N^*$ $^{16}O(p,x)^{14}N^*$	$^{14}N^*$2.313->g.s.	9.8×10^{-14}
4.444	$^{12}C(p, 2p)^{11}B^*$ $^{14}N(p,x)^{14}B^*$	$^{11}B^*$4.445->g.s.	5.6×10^{-19}
5.298	$^{16}O(p,x)^{15}N^*$	$^{15}N^*$5.299->g.s.	1.2×10^{-14}
6.129	$^{16}O(p, p')^{16}O^*$	$^{16}O^*$6.130->g.s.	2.7×10^{-11}

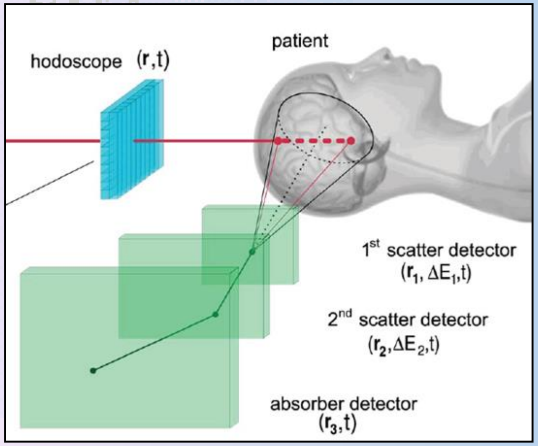


粒子能量沉积（左）和瞬发光子产生分布（右）：上方为质子束入射水中情况，下方为碳离子入射水中情况[2]

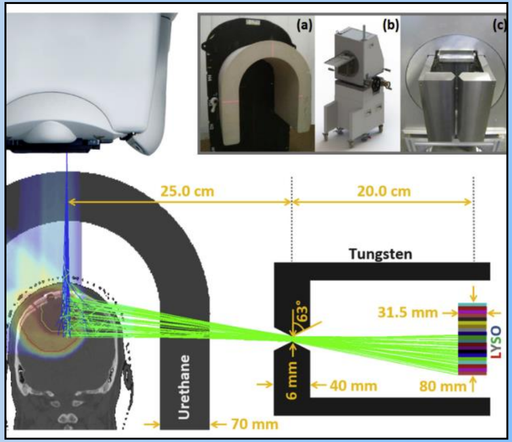
[1] Kozlovsky, et.al, **2002** **[2] Smeets J., 2012**

瞬发光子成像技术

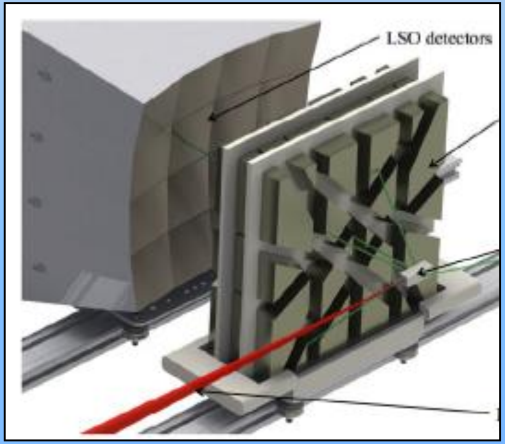
康普顿相机



单缝准直伽马相机

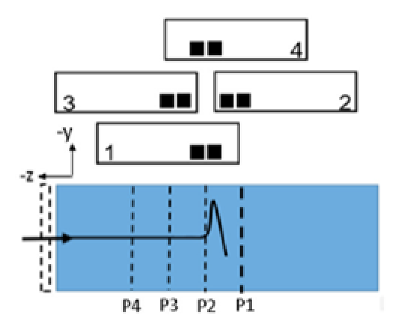


多缝准直伽马相机



康普顿相机

- **系统实现**



Polaris J 探测器（H3D Inc.)

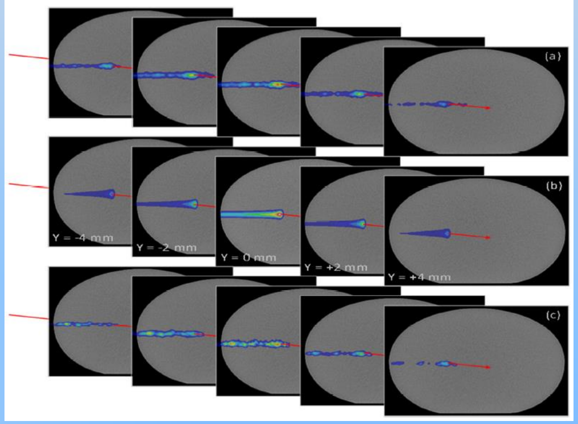
四个探测器 + 同步符合计数模块

每个探测器包含2×2个CZT晶体模块

每个晶体模块包含11×11根晶体

晶体尺寸 2 × 2× 1.5 cm³ (1,2) 2 × 2 × 1 cm³ (3,4)

- **成像效果评估**



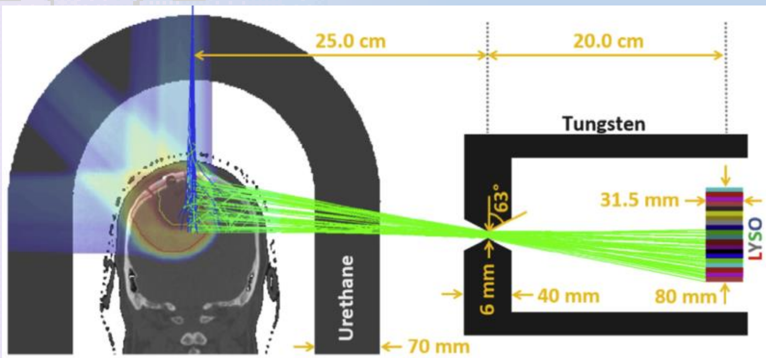
(a) 6.29×10⁸个质子子入射时瞬发光子图像, (b)质子剂量分布, (c) 1×10⁸个质子入射时瞬发光子图像

布拉格峰位置偏移小于3mm

E Draeger, et.al, **2018**

单缝准直相机

- **系统实现**



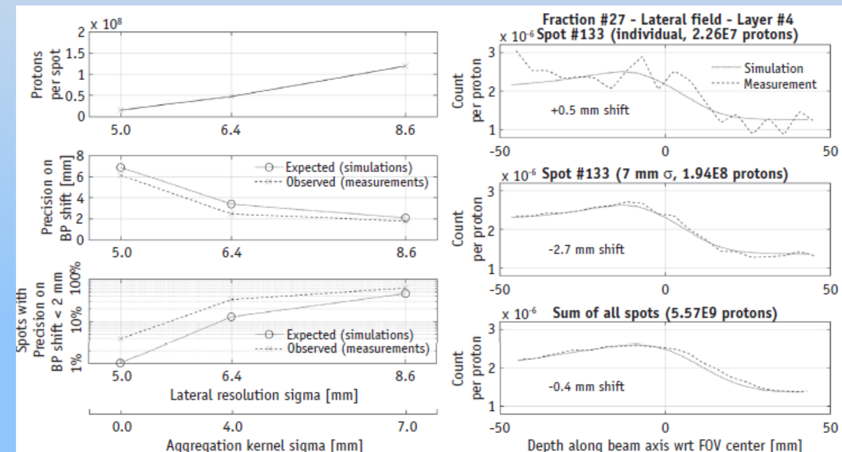
准直器

- **材料：钨**
- **厚度：40 mm**
- **刃口宽度：6 mm**

探测器

- **2×20 LYSO晶体**
- **晶体尺寸：100 × 4× 31.5 mm³**

- **成像效果评估**



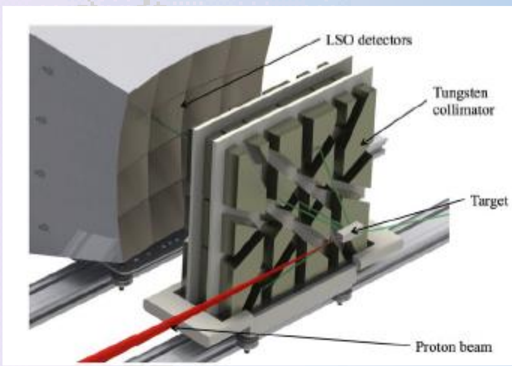
对于6个治疗方案，不同入射位置

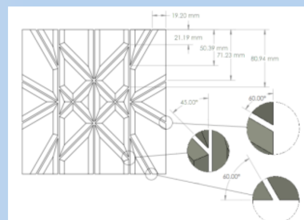
位置偏移均小于2mm

Yunhe Xie, et.al, 2018

多缝准直相机

- 系统实现





准直器

- 材料：钨
- 尺寸：20 × 20× 7.5 cm^3
- 刃口宽度：2 mm
- 刃口张角：20°

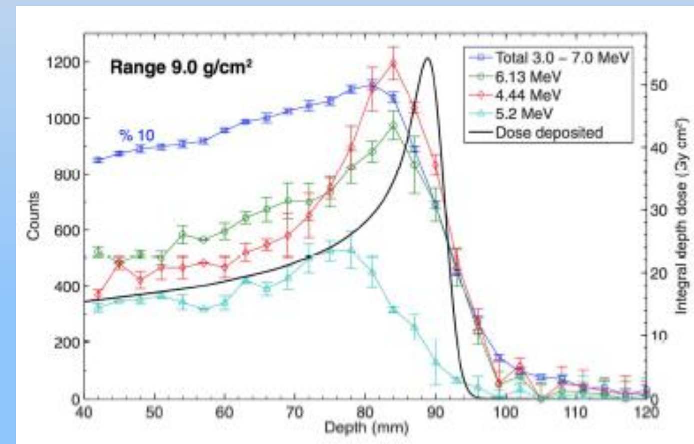
探测器

•4×4 LSO晶体

•模块包含 12×12根晶体

•晶体尺寸：4 × 4× 20 mm^3

- 成像效果评估



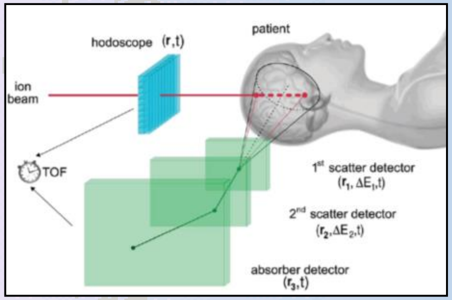
布拉格峰定位精度（探测到位置对实际变化的灵敏度）小于1mm

布拉格峰位置偏移小于1.6mm，优于康普顿相机和单缝准直相机

Ready John, 2016

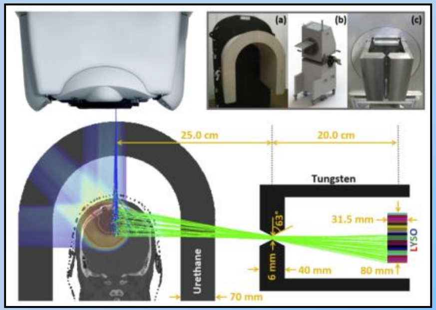
瞬发光子成像技术小结

康普顿相机[1]



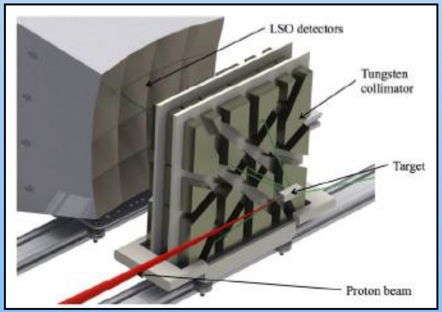
- ✓ 三维成像
- ✓ 高探测效率
- x 算法及系统实现复杂
- x 高计数率导致随机事件

单缝准直相机[2]



- ✓ 分辨率较高
- ✓ 技术简单
- x 探测效率低
- x 仅适用于一维射程监测

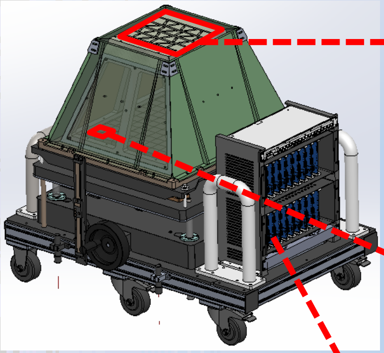
多缝准直相机[3]



- ✓ 三维成像
- ✓ 分辨率较高
- ✓ 探测效率较高
- x 系统设计复杂

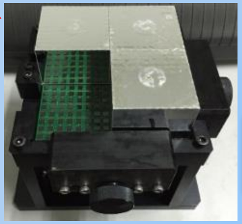
[1] E Draeger, et.al, **2018** **[2] Yunhe Xie, et.al, 2018** **[3] Ready John, 2016**

PGI 系统设计-清华



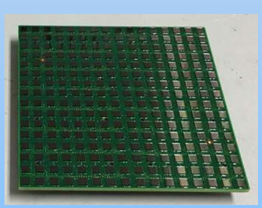
Schematic diagram

Multi-slit collimator based on Tungsten alloy



Detector based on BGO and SiPM

BGO block and SiPM board (back)



SiPM board (front)

ASIC based detector readout

Assembled real system

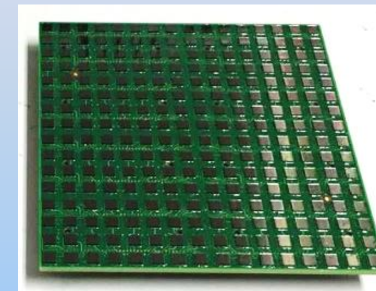
Data acquisition electronics

Digital processing board for AD and data acquisition

Detector design based on BGO and SiPM

Detector module

BGO block

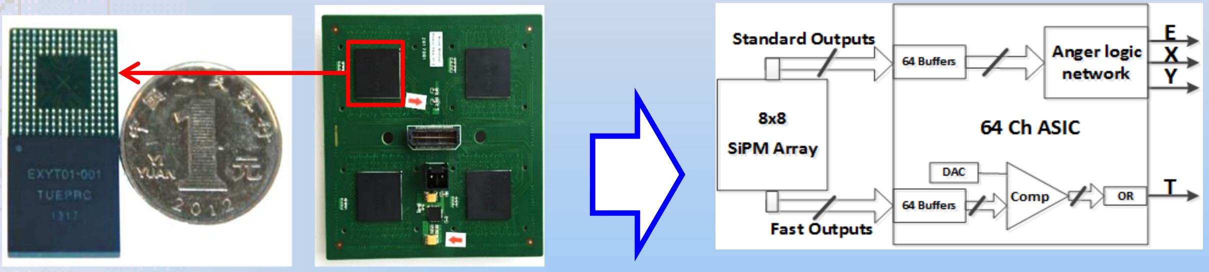


SiPM array

- Crystal pixel size: 3.5 mm $\times$ 3.5 mm $\times$ 30 mm
- 30 mm BGO: ~60% detection efficiency for 2~8 MeV gamma
- BGO block size: 12 $\times$ 12, SiPM array size: 8 $\times$ 8
- Each detector module contains 2 $\times$ 2 BGO blocks
- Whole system: 6 $\times$ 5 detector modules used

System electronics design

- Detector readout electronics



Detector readout based on customized ASIC-EXYT

- Data acquisition electronics

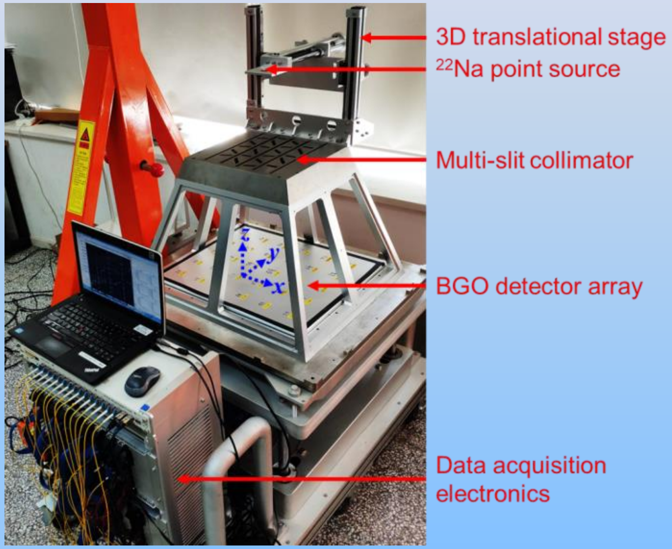
Digital processing board (DPB)

- 12-bit, 80 MHz ADC for digitization of E, X and Y signals from ASIC
- Each DPB handles 2 detector modules
- Total 15 DPBs used for the whole PGI system

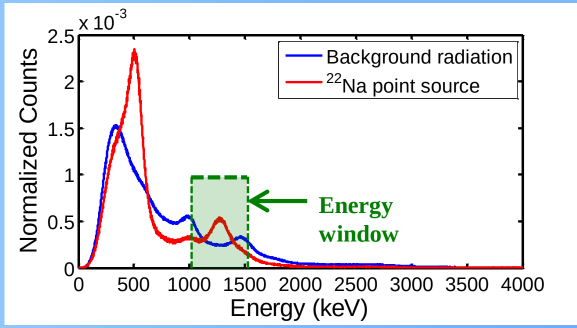
Zhu, Xuezhou, et al. IEEE Transactions on Nuclear Science 2016

System performance evaluation: experiment

- Assembled PGI system without radiation shielding components
- ^{22}Na point source (14.3 μCi, φ1.8 mm)
- Energy window: 1275 keV ± 20%
- Three different source positions, 10 min acquisition for each position
- 2 h background radiation acquisition for background counts correction
- Source-collimator distance: 250 mm, Collimator-detector distance: 375 mm
- FWHM resolution calculated for x and y directions from reconstructed images

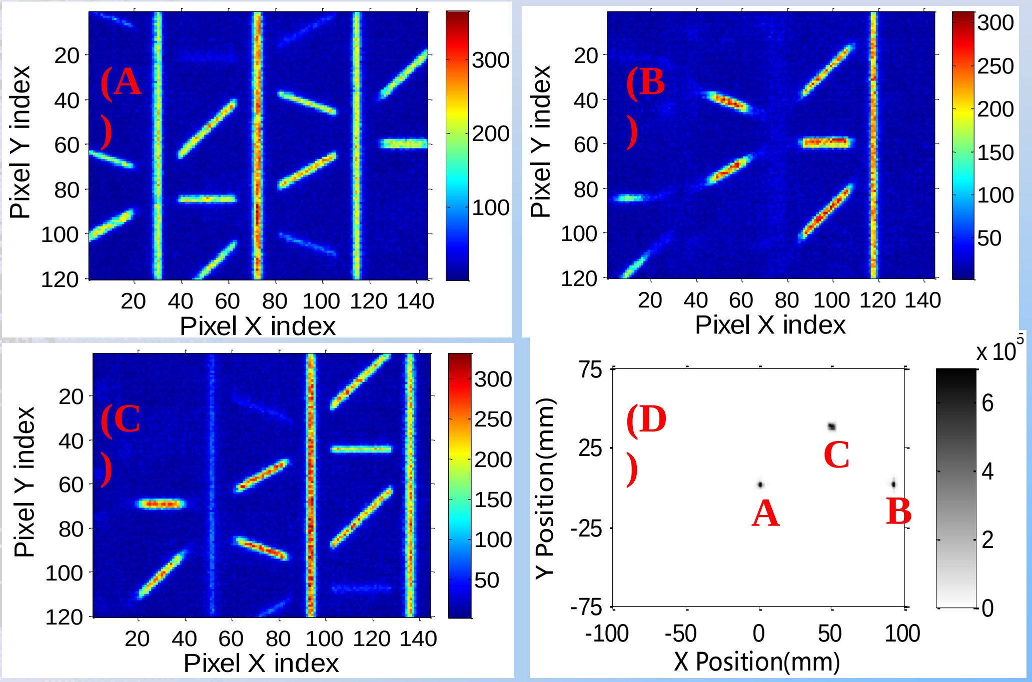


Measured background radiation projection



Measured energy spectrum

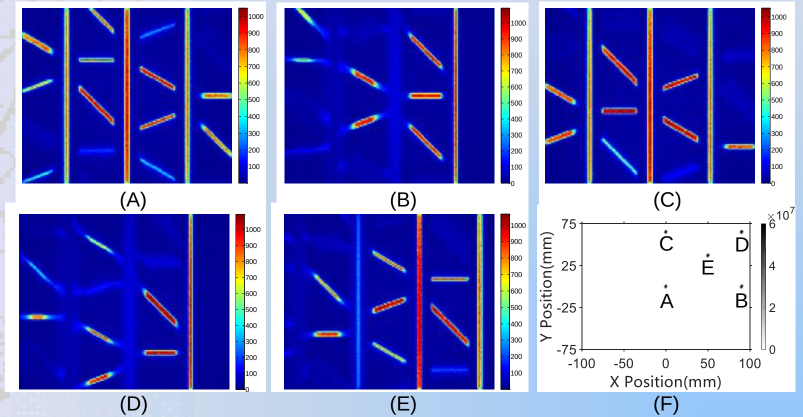
Results: point source experiments



SourceID		A	B	C
FWHM resolution (mm)	X direction	1.62	1.53	2.56
	Y direction	2.10	1.56	1.67

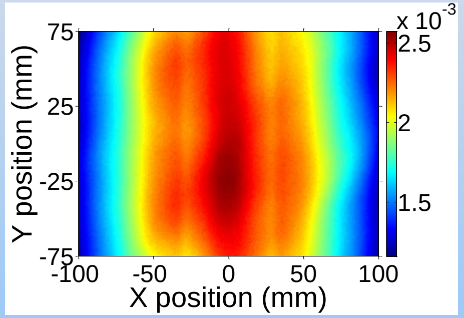
- A-C: measured point source projections for three different point source positions
- D: reconstructed point source images
- Achieved spatial resolution: ＜3mm

Results: proton beam simulations

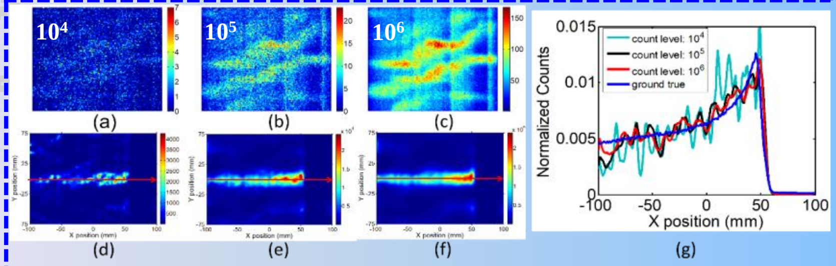


A-E: simulated projection for point sources A-E
F: reconstructed point source image
Average spatial resolution: 2.07 mm (X), 2.58 mm (Y)

System sensitivity map @4.44 MeV



0.251% @ FOV center
0.200% averaged over FOV



a-c: simulated projections at different count levels
d-f: reconstructed PG distribution
g: PG profile in x direction

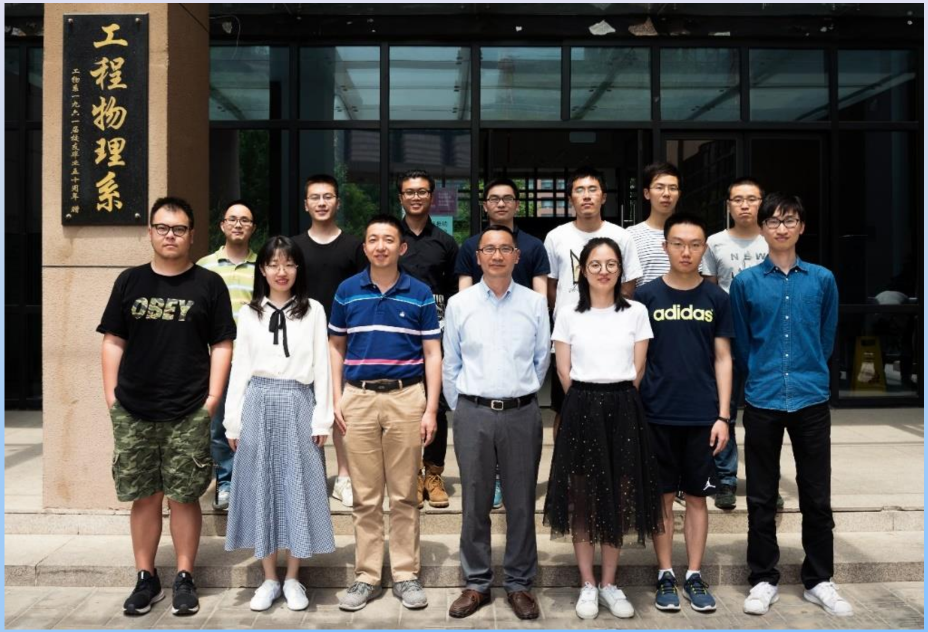
Count level	$MDEP_{bias}$ (mm)	$MDEP_{RMSE}$ (mm)
10^4	0.44	2.29
10^5	-0.04	1.45
10^6	0.29	0.76

- Improved RMSE with higher count level
- Good Bragg peak positioning performance even at 10^4 count level

Conclusions/Future work

- A PGI system for proton therapy monitoring
  - Multi-slit collimator
  - BGO + SiPM for 2-8 MeV prompt gamma detection
  - Hybrid system response modelling for image reconstruction
- Initial detector and system performance evaluation with Monte Carlo simulations and experiments demonstrate its feasibility for prompt gamma imaging
  - High sensitivity: 0.25% @ FOV center
  - High spatial resolution: <3 mm
  - Good Bragg peak positioning capability: 2.29 mm @10^4 counts
- Future work: system performance evaluation with high energy gamma isotopes and in real proton therapy facility

谢谢！



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  - National Key Research and Development (R&D) Plan of China (Grant ID. 2016YFC0105405)