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核医学影像设备进展

洪浩, 耿建华*

国家癌症中心, 国家肿瘤临床医学研究中心, 中国医学科学院北京协和医学院肿瘤医院核医学科, 北京 100021
* 联系人, E-mail: gengjean@163.com

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摘要 近年来, 国家对医疗机构配置大型医疗设备、医疗设备生产及医用同位素行业发展大力支持, 核医学科及核医学影像设备得到了快速发展. 伴随着核医学发展及临床需求的逐渐提高, 以SPECT/CT、PET/CT、PET/MR为关键代表的核医学影像设备的装机量逐年增长, 特别是国产核医学影像设备的装机量增长更加迅速. 同时, 随着核医学成像技术的不断更新, 更多先进的核医学影像设备投入临床使用, 更多新技术如以碲锌镉为代表的半导体探测器技术、全环设计SPECT/CT成像技术、长轴向视野全身PET/CT成像技术等逐渐成熟并应用于临床, 推动核医学影像技术迈向新的高度, 助力临床精准医疗. 本文通过调研综述近年来核医学影像设备的现状以及核医学影像技术的研究进展, 展望其未来发展方向.

关键词 核医学, 影像设备, 单光子发射计算机断层扫描, 正电子发射断层扫描

2021年《医用同位素中长期发展规划(2021–2035年)》发布, 预示未来我国核医学发展潜力巨大. 中华医学会核医学分会《2024年全国核医学现状普查结果简报》[1]显示, 我国核医学影像设备的装机量增长迅速. 伴随核医学进步及核医学影像设备发展, 核医学SPECT/CT、PET/CT、PET/MR影像设备得到了快速发展, 技术更新加快. 为此, 本文调研综述核医学影像设备的现状, 介绍核医学影像设备技术进展, 展望其发展方向.

1 SPECT/CT影像设备的发展

单光子发射计算机断层扫描(single photon emission computed tomography, SPECT)影像设备是核医学科功能影像诊断的基础设备. 利用新的技术手段, 提高SPECT设备的空间分辨率和灵敏度, 是当前临床SPECT研究的总体趋势.

1.1 SPECT设备准直技术的改善

准直器是传统SPECT影像设备成像的关键部件, 其功能是限制入射γ射线的方向, 用于成像的空间定位. 其对射线的限制又称机械准直, 机械准直特点使得SPECT成像的重要指标——空间分辨率及灵敏度, 只能顾此失彼, 限制了SPECT设备技术发展[2,3]. 传统准直器按形状可分为平行孔、针孔、发散孔和汇聚孔等类型. 当前几何形状机械准直研究, 尤其是运用多针孔放大技术的多针孔准直器研究, 成为SPECT设备的重要研究方向. 多针孔准直器结合高固有分辨率在临床应用中潜力较大, 适用于利用大视野探测器针对小器官及小物体成像. 该技术已在人体心脏、小动物SPECT显像中应用, 最先进的小动物SPECT系统甚至可以达到0.25 mm的空间分辨率[4,5]. 我国永新医疗2018年推出的国内首台可变角双探头SPECT, 其关键技术就是与清华大学工程物理系合作研发的多针孔准直器显像技术, 填补了国内空白. 同时, 该技术还运用于永新医疗自主研发的Insight四维定量SPECT/CT, 该设备于2023年11月获得国家药品监督管理局批准上市, 整体性能指标已达到国际先进水平. 另外, 机械准直器

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的其他方面如狭缝板条准直器、编码孔径准直器，通过改进准直器的几何结构提升设备性能是SPECT设备的另一研究方向[3,6]. 为了消除机械准直对SPECT设备分辨率和探测效率的影响，清华大学Ma等人[7]提出了(探测器)自准直SPECT成像技术. 该技术核心是利用空间分布的敏感探测器取代传统准直器，自准直设置能够使探测器执行准直和探测的双重功能，无需再安装准直器, 提高了探测效率.

1.2 SPECT设备探测器的优化

SPECT设备传统探测器主要是掺铊碘化钠[NaI(Tl)]闪烁晶体探测器，其光电转换效率低、能量分辨率差. 近年来, 闪烁探测器出现了新的晶体材料如溴化镧($LaBr_3$)晶体、硅酸钇镥(lutetium yttrium orthosilicate, LYSO)晶体、钆铝镓石榴石(gadolinium aluminum gallium garnet, GAGG)晶体. GAGG晶体具有高光产额、高阻挡本领、快衰减时间、无本底辐射和不潮解特性, 成为SPECT设备探测器的热门闪烁晶体[4]. 除了闪烁探测器，1996年碲锌镉(cadmium zinc telluride, CZT)探测器问世，以CZT为代表的半导体探测器技术逐渐成熟并在核医学成像设备中得到应用，成为SPECT设备发展过程中的“里程碑”. 与传统SPECT比较，CZT探测器更紧凑、能量分辨率更高、重量更轻[8]. 近年来, CZT半导体探测器应用技术有了新突破, 如双能探头技术、专用集成电路(application specific integrated circuit, ASIC)技术、深度学习技术和电荷损失补偿技术等, 其在核医学各领域应用越来越广泛, 已有多款CZT-SPECT设备在全身、骨骼和心脏领域成功应用[9~11]. 传统SPECT设备多为双探头或三探头，灵敏度低. 为提高SPECT设备的灵敏度, 环形SPECT、整环或全环SPECT系统设计成为新的研究发展方向. 近期的一个进步是用半固定和多头环形几何结构取代传统SPECT探头, 每个头独立前后移动并可旋转运动, 以便每个头都能面向对象并减少未使用的探测器部件的数量[12]. Huh等人[13]提出了一种使用像素化CZT和能量优化平行块准直器模版组成的可变孔径全环SPECT系统，可减少采集时间并提高灵敏度. Huh等人[14]还设计了一款配有宽能钨准直器的CZT全环SPECT扫描仪，可将能量范围扩展到250 keV，且使用^{99m}Tc和^{177}Lu预测灵敏度是目前最先进SPECT系统的两倍. 2024年，光脉医疗率先在国内安装了首台360°全环设计SPECT/CT “VERITON-CT”，是全球首款数字化全环SPECT/CT设备，检查时间大大缩短，诊断效率大大增加. 目前最新技术SPECT是基于CZT的3D全环SPECT系统，有两个品牌(StarGuide, GE Healthcare和Veriton, Spectrum Dynamics, 以色列)已上市[15], 但CZT材料的制造成本一直是制约设备量产的最大瓶颈. 另外, 器官高分辨成像专用的多类型准直器在多针孔准直器、Slit-Slat准直器成熟应用基础上，西门子和通用电器(GE)等公司又提出超薄准直器设计，可进一步减轻探头承重[16]. 同时，针对通用SPECT系统不能在各个器官上得到最佳成像效果的问题，近年来多种针对某些具体器官的专用SPECT系统也被研发出来，如心肌灌注显像的IQ·-SPECT技术、乳腺SPECT成像扫描技术和乳腺专用伽马射线成像技术等[4]，光脉医疗和GE推出了数字化CZT SPECT心脏专用机，光脉医疗的心脏专用机D-SPECT在全球心脏专用SPECT设备市场的占有率超55%.

1.3 其他

随着硬件设备、物理校正、图像重建算法等技术进步，SPECT/CT定量技术在不断进步，开启了SPECT SUV参数新时代，可以定量测定MBF(心肌血流量)和CFR(冠状动脉血流储备), 对骨骼的炎症性、肿瘤性疾病进行诊断及疗效评估[17,18]. 同时，人工智能(artificial intelligence，AI)技术被用于SPECT图像的去噪和分辨率改进、衰减图生成和校正、图像重建，有望改进定量SPECT成像相关方法, 进而缩短患者扫描时间[19,20].

2 PET/CT设备进展

PET/CT设备是医学影像设备中最为先进的分子影像设备之一，可同时获得PET功能影像和CT解剖影像，对疾病的早期诊断、病程分期、疗效判断、预后评价及药效研究等起着重要作用[21]. 近年来，PET/CT设备装机量增长迅速，技术发展迅速，全数字PET技术成为未来PET设备的一个发展方向[22]. 国产PET/CT在我国市场上的机型已远超进口机型，国内PET/CT企业已有近十家，2023年以联影医疗产品为代表的国产PET/CT在我国装机中占据44.71%份额[23,24].

2.1 PET闪烁晶体技术进展

PET用闪烁晶体材料技术进步较快, 并向快衰减时间、高光输出、高密度和强化学稳定性的晶体方向发展[22]. 早期使用的闪烁晶体有碘化钠(NaI)、锗酸铋

(bismuth germanate oxide, BGO)、硅酸钆(gadolinium orthosilicate, GSO)等, 目前使用的闪烁晶体有硅酸镥(lutetium orthosilicate, LSO)、硅酸钇镥(LYSO)等. LSO和LYSO性能相当, LYSO闪烁晶体是当前临床PET系统最为主流的晶体材料, 综合性能优越, 时间分辨率高, 推动了PET领域飞行时间(time of flight, TOF)等先进技术发展, 并降低了图像噪声, 提高了信噪比和图像质量[25,26]. 近年来, LYSO:Ce(铈掺杂硅酸钇镥)晶体不断受到国内外科研机构关注, 闪烁性能和生长技术不断提高, 高性能LYSO:Ce晶体成为当前PET设备研究领域最为广泛应用的闪烁晶体. 国内全数字PET Digit-MI930、国外西门子Vision临床PET设备采用性能优化的LYSO:Ce、LSO:Ce闪烁晶体, 实现了249、225 ps时间分辨率性能[27,28]. LYSO:Ce晶体加工特性良好, 用0.32 mm像素晶体阵列构建小动物PET, 中心处空间分辨率可达0.6 mm[29]. 但是, LYSO:Ce晶体仍有许多问题和挑战有待解决, 如LYSO:Ce晶体闪烁发光数学模型不明确、闪烁发光的调制难以精确控制等.

2.2 PET小晶体块技术进展

小晶体块是PET探头的重要组件, 其表面积的大小直接影响PET的空间分辨率, 表面积越小, 则该设备的空间分辨率越高. 随着技术的进步, 临床中小晶体块表面积已由最初的4.0 mm×4.0 mm~6.5 mm×6.5 mm, 下降到最小可达2.35 mm×2.35 mm[26].

2.3 PET光电转换器技术进展

PET系统中的光电转换器件将闪烁晶体输出的低能光信号转换为电信号. 随着电子技术的发展, 光电转换器由传统的光电倍增管(photomultiplier tube, PMT)发展到雪崩光电二极管(avalanche photodiode, APD), 再到基于半导体工艺的硅化光电倍增器(silicon photo-multiplier, SiPM). 其中, 雪崩光电二极管仅见于早期开发的PET/MR设备. SiPM具有增益高、时间分辨率高、工作电压低、探测效率高、对磁场不敏感等特点, 已成为目前PET主流产品包括PET/MR设备在内光电转换器的首选. SiPM制作工艺不断进步, 通道微型化、将SiPM后端的信号通过ASIC或现场可编程门阵列(field programmable gate array, FPGA)进行处理等措施, 进一步将SiPM性能推进至其物理极限, 提高了PET整机性能[30,31], 我国医疗企业2016年发布国内首台自主研发的ScintCare PET-CT, 采用SiPM且核心部件国产率90%以上, 打破了PET-CT生产长期被国外企业垄断的状况. 当前SiPM单光子时间分辨率普遍在100 ps左右, 而TOF-PET系统时间分辨率在达到10 ps时无需进行复杂重建, 可直接从TOF信息中恢复出PET图像, 因此SiPM物理性能还无法满足新兴应用领域对光电转换器的高性能要求[32]. 随着半导体制作工艺的不断进展, 将数字逻辑集成到SiPM内, SiPM输出数字信号, 标志着数字SiPM (digital SiPM, dSiPM)的到来, dSiPM将PET探测的信息数字化提高到新水平. 但dSiPM尚处于起步阶段, 发展潜力巨大, 技术门槛、经济成本均较高, 大规模商业化还未实现, 仅有少数几家公司推出dSiPM, 如Vereos PET/CT系统则采用了dSiPM技术[32].

2.4 PET系统探测器模块进展

PET系统探测器模块是PET系统的关键部件, 根据探测器输出信号类型可分为模拟探测器和数字探测器. 传统探测器通常为模拟探测器, 主要由闪烁晶体、光电转换器件和模拟信号处理板块封装在一起组成; 模拟探测器需将模拟信号转换为数字信号后才输入计算机运算[33]. 随着光电转换器件及微电子技术等的发展, 数字探测器设计被提出. 数字探测器采用集成电路设计, 即大规模采用ASIC或者FPGA技术, 输出包含光子能量、位置和时间信息的数字信号. 目前数字探测器设计的数字化程度不同, 但随着集成度和数字化程度逐渐提高, 有望提高PET系统的整体性能[34]. 国产NeuEra系列PET/CT搭载自主研发的64通道PET专用ASIC芯片, 使系统性能达到国际先进水平, TOF时间分辨率达到180 ps级别. 国外对TOF PET ASIC领域的研究和开发进展显著, 主要集中在提高时间分辨率、降低功耗和增强集成度方面. 最新影像设备西门子Bio-graph Vision PET/CT系统采用高灵敏度探测器, 集成定制ASIC以优化TOF功能, TOF时间分辨率可达214 ps.

2.5 轴向视野技术进展

轴向视野的大小与PET灵敏度密切相关, 轴向视野越大, 则PET系统的灵敏度越高. 目前商用PET/CT设备轴向视野多在15~35 cm范围, 小的轴向视野范围制约了PET系统的探测效率和灵敏度[35]. 计算机模拟显示当轴向视野范围从20 cm提升到200 cm时, 灵敏度可提升40倍[36]; 对于能基本覆盖的单一脏器进行PET/CT扫描, 当轴向视野增加到200 cm时, 灵敏度可提升4~5

倍[35]. 联影医疗和美国加州大学Davis分校(UC Davis)合作研发出长轴向视野全身PET/CT (total-body PET/CT)设备uExplorer应用于临床, 并于2019年4月安装在复旦大学附属中山医院, 该设备最大轴向视野可达到194 cm[37,38]. 增加PET轴向视野范围, 可有效提高PET的灵敏度. 同时, 全身PET/CT提供的灵敏度增益, 可为众多研究和临床应用开辟新的可能, 如低剂量显像、快速显像、全身动态等. 目前, 轴向视野100~150 cm的多款长轴PET/CT也相继问世.

2.6 飞行时间(TOF)技术进展

TOF技术是通过测量两个湮灭光子到达探测器的飞行时间差来确定湮灭事件位置, 基于新一代晶体和光电转换基础实现, 代表PET技术的发展方向, 近年来具有TOF能力的PET发展迅速. TOF PET与非TOF PET比较, 具有更低的噪声和更高的病变对比度, 可以提供更好的图像质量[39]. 随着临床对TOF技术重视, NEMA NU2-2018质量控制标准增加了TOF时间分辨率指标, 并规范了其测试方法[40]. 早期PET无TOF技术, 第一代TOF-PET扫描仪使用的是氟化铯(CsF)或氟化钡(BaF)闪烁体, 可实现450~750 ps的TOF时间分辨率, 但晶体的检测效率和光输出较低; 第二代TOF-PET扫描仪使用的是掺铈硅酸镥(LSO:Ce)和其他镥(Lu)基闪烁体, 可实现450~600 ps的TOF时间分辨率, 且具有更高的灵敏度和空间分辨率; 第三代TOF-PET系统为全身TOF-PET系统, 基于硅光电倍增管(SiPM)实现了200~382 ps的时间分辨率, 且灵敏度大幅提升, 国内联影医疗、东软医疗等PET生产厂家先后发布最新PET/CT设备TOF时间分辨率突破200 ps. TOF PET系统的光电传感器由PMT升级为SiPM再到dSiPM, 促进了TOF分辨率的提高, TOF分辨率的提高又促进了图像重建技术的开发[41,42]. 最近的研究热点主要在探测材料阶段, 旨在寻找与标准闪烁材料不同但射线发射过程更快的探测材料, 但目前研究材料511 keV γ射线的光子产率低[43]. Turtos等人[44]为提升TOF PET探测器性能提出了一种新型探测器结构概念, 即将互补特性材料结合在异质结构或超导闪烁体中的TOF PET异质结构概念.

2.7 图像重建技术进展

早期PET图像传统重建方法有用于图像2D重建的滤波反投影法(filtered back-projection, FBP)、最大似然-期望最大法(maximum likelihood-expectation maximization, ML-EM)、有序子集最大期望值算法(ordered subsets expectation maximization, OSEM)等. FBP是解析算法, 抗噪声能力差; 后两种重建算法属于迭代法, OSEM最为常用, 对ML-EM的迭代方程细微改进后提高了图像重建速度, 缺点是噪声大. 后又在OSEM算法基础上加入各种校正, 生成最新的贝叶斯惩罚似然算法(Bayesian penalized likelihood, BPL)[45]. 后来PET图像重建采用3D重建算法, 例如: 3D重建的重组法、3D重投影算法(three dimensional reprojection, 3DRP)、3D迭代重建算法. 2D图像重建速度快, 效率高; 3D图像重建数据量大, 会产生空间偏差, 对硬件要求高[46]. 随着PET技术的进步, 又出现了TOF技术、基于点扩展函数(point spread function, PSF)的高清重建技术、呼吸门控技术等应用于图像的重建. 随着人工智能在医学图像领域的应用, 基于深度学习的PET图像重建技术如端到端重建、基于正则化的迭代重建等技术成为PET成像领域的又一个研究热点, 多数国产设备已应用了这些新技术[47].

3 PET/MR设备进展

PET/MR设备集成了正电子发射断层扫描(positron emission tomography, PET)和磁共振成像(magnetic resonance imaging, MRI)的优势, 代表了医学成像技术的巅峰[48]. 国内一体化PET/MR设备主要是联影医疗、通用电气(GE)、西门子医疗三个品牌[23,24]. 但PET/MR在临床上应用尚处于初级阶段, 随着技术的进步, 其在临床中应用将更加广泛.

3.1 结构设计进展

随着磁场兼容性PET探测材料的发展, PET/MR设备结构设计先后经历双机房分体式设计、单机房分体式设计、集成一体化PET/MR设计三个发展阶段. 前两个阶段PET与MR数据分开采集且设备占用面积大, 到一体化PET/MR设备阶段才真正意义上实现了PET与MR的同时间、同空间、同步成像. 一体化PET/MR设备结构又分为分离式、嵌入式及插入式三种类型, 目前临床主流PET/MR设备多为一体化设计. 随着TOF技术的进步, 又推出了具备TOF功能的一体化PET/MR系统[49]. 我国联影医疗uPMR 790被业界称为首台“时空一体”超清TOF PET/MR设备, 填补了我国在高端医疗设备最尖端领域的空白.

3.2 硬件结构的进步

首先是探测器技术发展. 为解决PET与MR的兼容性问题, 新型闪烁晶体如硅酸镥(LSO)、硅酸钇镥(LYSO, LBS)闪烁晶体在临床推广, 有效改善传统闪烁晶体如硅酸镥钆、硅酸钆等磁敏感性高, 影响MR磁场均匀性产生伪影的问题. 其次是光电转换器件的不断改进. 早期PET光电转换器件PMT受磁场影响无法在PET/MR系统中使用, 后来对磁场不敏感的雪崩光电二极管(APD)被研制成功替代了PMT, 诞生了第一台PET/MR一体机Biograph mMR, 但APD时间分辨率差, 不能使用TOF技术. 目前新的光电转换器件SiPM逐渐取代APD, SiPM具有体积小、灵敏度高、时间分辨率好等特点, 促进PET整体性能提高, 助力一体化TOF PET/MR系统研发. SiPM对温度比较敏感, 随着温度空间技术发展, 该问题已得到解决. 另外, 磁共振的扫描线圈也取得进展, 从正交线圈到表面线圈、相控阵表面线圈, 再到近期一体化相控阵表面线圈, 实现了扫描范围从头顶到脚的全身MR扫描, 同时一体化透明体线圈在PET/MR中使用, 优化了PET图像质量[50,51].

3.3 数据校正技术进展

运动校正用来减少因运动导致小病灶变模糊漏诊或病灶定位错误等情况发生. 传统PET/MR在PET和MR同步扫描时外置呼吸门控或心电监控等来减少运动伪影, 一体化TOF-PET/MR通过提供与呼吸周期不同时相匹配的MR衰减校正技术(MR attenuation correction, MRAC)来对呼吸运动伪影校正提高胸部图像质量. 最新一体化PET/MR还通过协同采集方式, 将生理运动信息纳入MR特殊序列采集中建立生理运动模型, 以指引PET的重建. 衰减校正的方法主要有分割法、图集法和基于透射数据重建法[52,53]. 随着衰减技术进步, 又出现了五组织分隔法、梯度增强磁场均匀法等[54]. 另外, 还有散射校正, 其校正方法包括能窗法、卷积法、物理模型法及AI模型法[53].

3.4 其他

TOF技术的应用使一体化PET/MR的整体扫描速度大幅提高. 人工智能技术在PET/MR的图像采集及图像重建中应用, 推动了核医学成像技术进步和精准医学发展[55].

4 展望

我国发布《"健康中国2030"规划纲要》和《医用同位素中长期发展规划(2021–2035年)》, 为中国核医学发展描绘了美好蓝图. 在国家政策的大力支持下, 核医学的发展将提速, 核医学影像设备的装机量将大幅提升. 随着影像技术的进步, 各种先进技术及先进设备将在核医学影像设备的诊疗中大量出现, 进而促进核医学诊疗技术的提高, 核医学影像设备将在医疗领域发挥越来越重要的作用.

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Summary for “核医学影像设备进展”

Advances in nuclear medicine imaging equipment

Hao Hong & Jianhua Geng*

Department of Nuclear Medicine, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100021, China
* Corresponding author, E-mail: gengjean@163.com

In recent years, the government has offered substantial support for the deployment of large-scale medical equipment in medical institutions, the production of medical equipment, and the development of the medical isotope industry. As a result, the nuclear medicine department and nuclear medicine imaging equipment have developed rapidly. Along with the development of nuclear medicine and the gradual increase in clinical needs, the installation of nuclear medicine imaging equipment represented by SPECT/CT imaging equipment, PET/CT equipment, and PET/MR equipment has been growing year by year. In particular, the number of installed domestic nuclear medicine imaging equipment has been increasing even more rapidly. This paper reviews the current situation of nuclear medicine imaging equipment through research, introduces the technical progress of nuclear medicine imaging equipment, and looks forward to its development direction.

As nuclear medicine imaging technology continues to be updated, more advanced nuclear medicine imaging equipment has been put into clinical use, and more new technologies have gradually matured and been applied to serve clinical practice, benefiting a wide range of patients. The collimation technology of SPECT equipment has developed from mechanical collimation to detector self-collimation, the detector is developing from traditional scintillation detectors such as lutetium silicate crystals to semiconductor detectors such as cadmium zinc telluride, and the technology progress such as physical correction and image reconstruction algorithm has greatly improved the spatial resolution and sensitivity of SPECT equipment. The research and development of PET scintillation crystals and the technological progress of small crystals block technology. The photoelectric converter has developed from the initial photomultiplier tube and avalanche photodiode to photoelectric multipliers and digital silicon photoelectric multipliers. The axial field of view has been continuously broken through from the traditional 15 to 35 cm and the current maximum can reach 194 cm. The time of flight is getting smaller and smaller. The improvement of image reconstruction technology and other performance technology and technological advancements have made all-digital PET technology a development direction of PET equipment in the future. The structural design of PET/MR equipment has evolved from a dual-room separate design to a single-room separate design and then to an integrated PET/MR design. The progress of hardware structure has solved the compatibility problem between PET and MR, and the data correction technology has been gradually improved, which will make the application of PET/MR in clinical more extensive.

Recently, China has released a series of major policies such as “Healthy China 2030” and the “Medium and Long-term Development Plan for Medical Isotopes (2021–2035)”, which has outlined a beautiful blueprint for the development of nuclear medicine in China, indicating that the potential for the development of nuclear medicine China is enormous in the future. With the strong support of national policies, the development of nuclear medicine will accelerate, and various advanced technologies and advanced equipment will be more widely used in the diagnosis and treatment of nuclear medicine imaging, which will promote the improvement of nuclear medicine diagnosis and treatment technology. Nuclear medicine imaging equipment will play an increasingly important role in the future medical field.

nuclear medicine, imaging equipment, single photon emission computed tomography, positron emission tomography

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