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# PET/CT 显像在头颈部肿瘤中的临床应用进展

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［摘要］ 头颈部肿瘤是常见的恶性肿瘤之一，由于其位置深在且复杂，临床上主要采用根治性放疗或同期放化疗。早期疗效评价对肿瘤治疗决策的制定具有重要的指导意义。传统的物理学技术已经不能够满足对疾病早期做出诊断的需求。PET/CT作为一种无创的功能成像技术，能够在解剖结构改变之前探测到包括增殖、凋亡及乏氧等在内的多种生物学信息的变化，在头颈部肿瘤中的应用日趋广泛。该研究综述了PET/CT显像在头颈部肿瘤中的临床应用进展。

［关键词］ 头颈部肿瘤；PET/CT；临床应用进展
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［**Abstract**］ Head and neck carcinoma (HNC) is one of the common malignancies in the world. Because of its deep location and complicated surroundings, patients usually receive definitive radiotherapy or concurrent chemoradiotherapy. Early prediction has significant importance to guide physicians in making treatment decisions. Traditional imaging techniques have obvious limitations. However, positron emission tomography (PET), as a non-invasive functional imaging, allows quantitative assessment of many biologic processes before the anatomic changes, such as proliferation, apoptosis and hypoxia. PET/CT is more and more widely used in HNC nowadays. This article reviewed the advances of clinical application of PET/CT in HNC in this paper

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［**Key words**］Head and neck carcinoma; PET/CT; The advances of clinical application

头颈部肿瘤是临床上常见的恶性肿瘤之一，乙醇、吸烟和人类乳头瘤病毒感染是头颈部肿瘤的主要诱发因素。常见的头颈部肿瘤主要有甲状腺癌(thyroid carcinoma，TC)、头颈部鳞癌(head and neck squamous cell carcinoma，HNSCC)和鼻咽癌(nasopharyngeal carcinoma，NPC)等；头颈部肿瘤位置多深在，周围解剖结构复杂，临床上主要的治疗方式是根治性放疗或同期放化疗。临床常用的检测手段，如内镜、CT及MRI等，均为物理学检查手段，仅能反映解剖学的变化。PET/CT是一种功能成像的核医学技术，与传统成像技术相比，可以进一步从分子水平反映肿瘤的生化和代谢，能够对原发和转移病灶进行定性、定量分析，评估治疗疗效，监测预后和随访等。

## 1 PET/CT显像在TC中的应用进展

TC近10年发病率有明显上升趋势，因此对该疾病的早期诊断和疗效预测具有重大的临床指导价值。

### 1.1 甲状腺结节良、恶性的鉴别

除传统的超声检查外，临床上对于甲状腺结节多采用穿刺的细胞学结果进行良、恶性鉴别，但仍有部分患者无法获得确定性诊断。Merten等[1]通过对细胞学上定义不确定的甲状腺结节进行系统性调查发现，甲状腺结节PET显像表现为阴性，即标准摄取值(standard uptake value，SUV)小于等于5，那么肿瘤为恶性的可能性较低，阴性预测值可达94%。PET/CT是一项非侵袭性的检查，可以降低患者误切甲状腺的概率。Wang等[2]通过对5个数据库7项研究的Meta分析发现，$^{18}$F-FDG PET或PET/CT鉴别甲状腺结节良、恶性的汇总灵敏度和特异度分别为89%和55%。Vriens等[3]的研究结果也显示，$^{18}$F-FDG PET对于细针穿刺细胞学检查病理不能确诊的甲状腺结节鉴别的汇总灵敏度和特异度分别为95%和48%。由此可见，PET有望用于细胞学检查无法确诊患者进一步治疗决策的制定。

### 1.2 甲状腺髓样癌中的诊断价值

甲状腺髓样癌(medullary thyroid carcinoma，MTC)起源于甲状腺滤泡旁细胞，占所有TC比例不足10%，但是恶性程度比较高的一种TC类型。有回顾性研究对比分析了$^{18}$F-FDG PET/CT与$^{111}$In-Octreotide SPECT在转移性MTC中的作用，发现$^{18}$F-FDG PET/CT在诊断准确率及发现淋巴结转移病灶方面具有明显优势，而$^{111}$In-Octreotide SPECT在发现骨转移方面价值更大[4]。此外，有研究提示，无论基于患者还是病灶的灵敏度，$^{18}$F-FDG PET/CT都最高，$^{99m}$Tc-Octreotide次之，$^{99m}$Tc-MIBI最低[5]。

$^{18}$F-DOPA PET/CT作为基于受体的成像技术，有望用于高度怀疑术后复发患者的诊断；在基于患者的分析中，其灵敏度可达75.6%[6]。近年来，关于MTC生长抑素受体成像的研究逐渐增多， Treglia等[7]回顾性分析评价了$^{18}$F-DOPA、$^{18}$F-FDG和$^{68}$Ga-生长抑素受体类似物在检测MTC复发方面的应用，发现$^{18}$F-DOPA PET/CT在三者之中最具优势。PET/CT在复发、转移MTC中诊断价值的Meta分析见表1[8-10]。

**表 1 PET/CT或PET在复发、转移甲状腺髓样癌诊断中的Meta分析**

**Tab. 1 The Meta-analysis of PET/CT or PET in diagnosis of recurrent/metastatic MTC**

| Year | Authors | *N* | Included literatures | Included databases | Results | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | Pooled Se/% | 95%CI | Pooled Sp/% | 95%CI |
| 2016 | Haslerud, et al[8] | 2 639 | 34 | 5 | 79.4* | 73.9-84.1* | 79.4* | 71.2-85.4* |
| 2016 | Caetano, et al[9] | 958 | 20 | 4 | 84.0*, 93.0# | 84.0-97.0# | 84.0*,81.0# | 69.0-90.0# |
| 2012 | Cheng, et al[10] | 815 | 15 | 2 | 68.0*, 69.0# | 64.0-72.0*<br>64.0-74.0# | | |

*: Pooled sensitivity/specificity of PET; #: Pooled sensitivity/specificity of PET/CT

### 1.3 核素治疗中的价值

如果$^{18}$F-FDG PET/CT显像表现为高摄取灶，那么一般表现为对放射性碘的摄取则较低，与转移病灶无$^{18}$F-FDG摄取的患者相比3年死亡率明显升高[11]。只有少数文献[12]报道甲状腺癌转移病灶对$^{131}$I和$^{18}$F-FDG同时有摄取的现象，表明转移病灶呈现分化良好的与去分化的肿瘤细胞共同存在的状态。

$^{124}$I PET/CT在具有碘吸收功能的TC中具有评价预后的作用。Pont等[13]对20例患者在$^{131}$I放射性消融治疗前行$^{124}$I PET/CT显像，$^{131}$I放射性消融治疗后行$^{131}$I SPECT/CT显像。$^{124}$I PET/CT与$^{131}$I平面和SPECT/CT显像结果相比，其中15%的患者TNM分期提高，主要是由于SPECT/CT的空间分辨率和灵敏度较低，即使注射较高的放射性剂量，假阳性率依旧高于PET/CT。Ruhlmann等[14]则通过治疗中的显像取代治疗后的$^{131}$I显像，其结果显示，在以病灶为中心的分析中，共发现227处转移灶，其中$^{124}$I PET探测到98%的病灶，$^{131}$I则为99%，一致率为97%(221/227)，并且发现1%的治疗剂量用作诊断剂量一致率较高。有文献支持在诊断方面，$^{131}$I治疗前$^{124}$I PET显像与治疗后$^{131}$I成像相比具有优势[13]，但也有报道不支持以上研究结果[15-16]，故目前对此仍存在较大争议。

### 1.4 甲状腺偶发瘤的检出

Hagenimana等[17]回顾性分析了进行$^{18}$F-FDG PET/CT检查的40 914例患者，其中探测到甲状腺偶发瘤的发生率为0.74%。Yang等[18]对15 948例非甲状腺疾病的患者进行$^{18}$F-FDG PET/CT的回顾性研究则提示偶发瘤的检出率高达3.1%。当表现为局灶性$^{18}$F-FDG摄取，且$SUV_{max}$极高，或出现钙化的现象时，那么很有可能是甲状腺恶性肿瘤，需要进一步的检查。

## 2 PET/CT显像在HNSCC中的应用进展

HNSCC在全球发病率和死亡率中占较大比例，对于手术不能切除的病灶，主要采取根治性放疗伴或不伴化疗，其中肿瘤对放疗敏感与否是HNSCC重要的预后和预测因子。

### 2.1 诊断、分期、再分期

HNSCC是头颈部肿瘤中最常见的病理类型，其发生远处脏器转移的概率虽然仅4%~25%，但远处转移是HNSCC的主要死因[19]，一旦探测到远处脏器转移，期望存活率仅有4.4~7.3个月[20]。一系列的Meta分析提示，$^{18}$F-FDG PET/CT在HNSCC中的汇总灵敏度为48.3%~89.3%，特异度为86.2%~98.0%(表2)，具有一定的诊断价值[21-24]。

### 2.2 疗效预测

$^{18}$F-FDG PET/CT通过对代谢活性进行定量分析，能够在评估HNSCC预后及疗效预测方面提供有价值的信息。有研究对2 692例头颈部肿瘤患者进行了回顾性分析，发现转移肿瘤的$^{18}$F-FDG $SUV_{max}$与HNSCC患者的生存结果具有明显相关性[20]。另有研究提示，$^{18}$F-FDG $SUV_{max}$除可用于预后判断外，其与临床TNM分期亦具有很好的相关性[25]。此外，对64例咽癌患者的回顾性研究结果表明，治疗前代谢肿瘤体积(metabolic tumor volume，MTV)大于13.6 mL是复发的唯一预测指标[26]。

表 2 PET/CT或PET在原发HNSCC中的Meta分析

**Tab. 2 The Meta-analysis of PET/CT or PET in primary head and neck squamous cell carcinoma**

| Year | Authors | *N* | Included literature | Included databases | Results | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | Pooled Se/% | 95%CI | Pooled Sp/% | 95%CI |
| 2016 | Liao, et al[21] | – | 73 | 2 | 48.3* | 30.9-66.1* | 86.2* | 76.9-92.1* |
| 2015 | Xi, et al[22] | 1 431 | 12 | 2 | 85.0# | 66.0-94.0# | 98.0# | 96.0-99.0# |
| 2014 | Rohde, et al[23] | 987 | 9 | 3 | 89.3# | 83.4-93.2# | 89.5# | 82.9-93.7# |
| 2011 | Gupta, et al[24] | 2 335 | 51 | 2 | 79.9Δ | 73.7-85.2Δ | 87.5Δ | 85.2-89.5Δ |

*: Pooled sensitivity/specificity of PET; #: Pooled sensitivity/specificity of PET/CT; Δ: Combined sensitivity/specificity of PET or PET/CT

2.3 第二原发肿瘤的检出

16.3%的头颈部肿瘤具有发生第二原发肿瘤的倾向，故第二原发恶性肿瘤是一个重要的预后影响因子。一旦探测到第二原发肿瘤，患者预后多不佳，因此早期探测出该病灶尤为迫切。它是治疗失败及分期低的HNSCC患者死亡的主要原因，而且该肿瘤好发的部位多预后较差，如食管。$^{18}$F-FDG PET/CT探测第二原发肿瘤的灵敏度和阳性预测值分别为91%和69%[27]，故能在第二原发肿瘤早期探测到异常，为后续治疗提供最佳机会。

2.4 个体化治疗决策的制定

早期的报道[28-30]只研究了$^{18}$F-FDG PET/CT在HNSCC诱导化疗1个疗程后的治疗效果，而没有根据结果辅助个体化治疗方案的制定。近些年，随着个体化治疗决策概念深入人心，有研究对比了功能MRI和$^{18}$F-FDG PET/CT在HNSCC诱导化疗1个疗程后的早期疗效评价的价值，结果表明MTV和病灶总糖代谢(total lesion glycolysis，TLG)可对诱导化疗后进行放化疗的结果进行早期预测，有望将患者进行分层并进行个体化治疗[31]。

## 3 PET/CT显像在NPC中的应用进展

3.1 诊断、分期和再分期

NPC是起源于鼻咽上皮细胞的恶性肿瘤，好发于中国南部，以未分化的病理类型居多。多数患者起病隐匿，确诊时多已为局部晚期患者，90%的患者已发生淋巴结转移，5%~10%的患者发生远处转移[32]。虽然NPC对放化疗非常敏感，但仍有7%~13%的患者治疗后有残余病灶持续存在。发生局部和远处复发后，患者预后显著下降。因此，早期发现残留和复发病灶对预后具有非常重要的意义。

$^{18}$F-FDG PET/CT对NPC残留或复发的诊断价值见表3[33-37]。此外，有Meta分析比较了$^{18}$F-FDG PET/CT、$^{201}$TI/$^{99m}$Tc-SPECT和MRI的诊断价值，SPECT的诊断灵敏度和特异度分别为85%和81%，MRI为77%和76%，而PET/CT可达90%和93%，故在早期探测残余和复发病灶方面，$^{18}$F-FDG PET/CT更具优势[33]。

3.2 疗效预测

Yang等[38]利用局部晚期NPC患者治疗前$^{18}$F-FDG PET/CT显像的异质性数据评估患者的生存期，结果表明，肿瘤和淋巴结的异质性指数越低，无进展生存期越长。Shi等[39]还对比了$^{18}$F-FLT和$^{18}$F-FDG PET/CT对NPC放化疗疗效的监测价值，新辅助化疗前后分别进行两种显像剂显像，治疗后$^{18}$F-FLT、$^{18}$F-FDG PET $\sum SUV_{max}$均较治疗前有明显下降，但$^{18}$F-FLT与常规的$^{18}$F-FDG显像相比，并无明显优势。Chen等[40]研究则发现，放疗中$^{18}$F-FDG $SUV_{mean}$与局部病灶复发或引起死亡有显著相关性。

由此可见，$^{18}$F-FDG PET/CT有关的指标$SUV_{mean}$、$SUV_{max}$及MTV在NPC预后评估中可发挥重要作用。虽然TNM和CT都已用于评估预后，但是由于肿瘤的放射敏感性不同，单纯依赖TNM和CT并不能精确反应放疗结果，而PET/CT从分子水平反映肿瘤的功能改变，能够更早期、更准确地反映疗效变化。

表 3 PET/CT或PET在诊断残余/转移鼻咽癌的Meta分析

Tab. 3 The Meta-analysis of PET/CT or PET in diagnosis of residual/metastatic nasopharyngeal carcinoma

| Year | Author | *N* | Included literature | Included databases | Results | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | Pooled Se/% | 95%CI | Pooled Sp/% | 95%CI |
| 2016 | Zhou, et al[34] | 1 253 | 23 | 7 | 93$^{\Delta}$ | 91-95$^{\Delta}$ | 87$^{\Delta}$ | 84-89$^{\Delta}$ |
| 2016 | Wei, et al[33] | 957 | 17 | 3 | 90$^{\#}$ | 85-94$^{\#}$ | 93$^{\#}$ | 90-95$^{\#}$ |
| 2016 | Chen, et al[35] | 2 413 | 23 | 3 | 95$^{\#}$ | 93-97$^{\#}$ | 76$^{\#}$ | 71-80$^{\#}$ |
| 2015 | Shen, et al[36] | 1 203 | 26 | 8 | 92$^{\#}$ | 89-94$^{\#}$ | 87$^{\#}$ | 84-90$^{\#}$ |
| 2014 | Shen, et al[37] | 2 396 | 18 | 7 | 89$^{\Delta}$ | 86-91$^{\Delta}$ | 96$^{\Delta}$ | 95-96$^{\Delta}$ |

#: Pooled sensitivity/specificity of PET/CT; Δ: Combined sensitivity/specificity of PET or PET/CT

3.3 放疗计划的制定

传统的预后因子能够提供临床信息，却不能预测治疗疗效；新型的预后因子致力于将危险组进行分层，从而根据患者的实际情况制定个体化的治疗方案。其中应用比较广泛的危险因子有$SUV_{max}$、MTV、TLG、吸烟状态、化疗与否、肿瘤大小、肿瘤部位及转移与否等[41]。

## 4 PET/CT在不明原因头颈部肿瘤中的应用进展

临床上患者有时以颈部不明原因肿块就诊[42]，该类型肿瘤占所有肿瘤的0.5%~10.0%，占头颈部肿瘤的1.0%~4.0%，但随着影像学技术的发展，这一比例在逐渐下降，其中2.0%~5.0%为鳞状细胞癌颈部淋巴结转移的患者。形态学检查(超声、CT、MRI)对头颈部淋巴结转移原发病灶检出率仅9%~23%，对模棱两可的放射学影像结果结合内镜活组织检查检出率也仅提高到60%。

传统形态学的检查对隐蔽性高和其他类型肿瘤(如淋巴瘤、黑色素瘤)不易探测出。如今$^{18}$F-FDG PET/CT作为传统影像学技术的补充，在寻找原发灶中发挥着不可替代的作用，其检出率为27%~68%[43-44]。

## 5 PET/CT的局限性

$^{18}$F-FDG PET/CT是核医学上常规使用的检查，但是其灵敏度(35%~71%)和阳性预测值(38%~50%)有限[45]。$^{18}$F-FDG与糖酵解有关，炎性反应、感染病灶、近期接受病理检查或发生坏死的淋巴结，放疗病灶均易出现假阳性[46]。其次，PET/CT价格昂贵。

随着卫生保健支出的大幅上升，医务工作者迫切需要对卫生保健资源进行评估来提升资源的分配。PET/CT在头颈部肿瘤治疗中的经济效益已获肯定，有望充分发挥其价值用以改善患者的预后。

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