·综述·

分化型甲状腺癌 ^{131}I 显像假阳性的原因分析

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【摘要】 分化型甲状腺癌患者 ^{131}I 全身显像及 SPECT 显像对于判定病情、决定下一步治疗方案具有重要意义。然而，显像有时会出现假阳性结果，即异常浓聚灶并不是残留的甲状腺组织或甲状腺癌转移灶。系统全面地了解这些假阳性分布及原因有助于图像的准确判读，更可避免患者后续不必要或过大剂量的 ^{131}I 治疗。笔者就分化型甲状腺癌 ^{131}I 全身显像假阳性情况分布、特点及其可能的机制展开综述。

【关键词】 分化型甲状腺癌；碘放射性同位素；全身显像；体层摄影术，发射型计算机，单光子；假阳性

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Analysis of the false positive findings on ^{131}I whole-body scan in differentiated thyroid cancer *Nan Nan, Zhu Xiaohua*

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【**Abstract**】 ^{131}I whole-body scan and SPECT imaging in patients with differentiated thyroid cancer can provide information regarding metastasis and prognosis, and assist in treatment planning. However, false positive uptake, which is not residual thyroid tissue or metastases, is sometimes encountered. Unless recognized as a false positive, ^{131}I uptake may result in diagnostic error and lead to administration of an unnecessary therapeutic dose. This review discussed various possibilities of false positive uptake on ^{131}I whole-body scan, as well as the underlying causes and mechanisms.

【**Key words**】 Differentiated thyroid carcinoma; Iodine radioisotopes; Whole body scan; Tomography, emission-computed, single-photon; False positive

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大部分分化型甲状腺癌的残留组织及转移灶均有摄取 ^{131}I 的功能，因此，分化型甲状腺癌患者 ^{131}I 全身显像有助于分析病情和评价疗效，进而指导下一步治疗方案的制定[1]。异常 ^{131}I 浓聚灶往往提示体内存在甲状腺癌的残留组织或转移灶，但首先需要排除假阳性 ^{131}I 摄取。近年来假阳性 ^{131}I 摄取时有报道，正确认识这些假阳性情况有助于避免对患者不必要的治疗。根据 ^{131}I 潜在的摄取机制，将假阳性 ^{131}I 摄取情况分为 4 类，具体如下。

1 生理性摄取

1.1 头面部：鼻部、泪腺及唾液腺、口咽

假阳性 ^{131}I 摄取在鼻部表现为热鼻征，即鼻子出现 ^{131}I 浓聚。鼻咽部摄取 ^{131}I 与其黏膜内的钠碘同向转运体（sodium iodide symporter，NIS）蛋白相关，之后黏膜分泌物排入鼻腔使鼻部显影。^{131}I 也可被泪腺摄取，并随泪液排出[2]。在唾液腺也有 ^{131}I 的正常浓聚，包括腮腺、颌下腺和舌下腺，并被分

泌到口咽。放射性多为对称性分布[3]。^{131}I 在头面部浓聚的生理机制：鼻黏膜、泪腺及唾液腺含有针对 NIS 的 mRNA，可表达 NIS 蛋白，进而使得 ^{131}I 在其中浓聚[4]。

1.2 乳腺

假阳性 ^{131}I 摄取在哺乳期前后的妇女中多见，非哺乳期乳腺也可摄取，多呈弥漫性、对称性放射性分布增高[2]。对于单侧乳腺显像，平面影像上可能会被误认为是肺转移，如经常使用某一侧乳房哺乳会导致该侧的 ^{131}I 摄取增加，应注意询问哺乳史和哺乳习惯。^{131}I 在乳腺浓聚的生理机制：哺乳期的乳腺腺上皮细胞含有 NIS，具有很强的摄 ^{131}I 能力，使得 ^{131}I 可以逆浓度梯度从血液中转运至乳腺而使乳腺显影，且可通过乳汁排出。非哺乳期的乳腺摄碘机制不清[5]。

1.3 胸腺

假阳性 ^{131}I 摄取在胸腺的发生率较低，主要表现为纵隔部位弥漫性、哑铃状或箭头状放射性摄取；^{131}I SPECT/CT 融合显像提示浓聚灶的位置位于胸腺；CT 以胸腺增大为主要表现。特点：蓄积部位在纵隔；多数系在服用治疗剂量 ^{131}I 后出现；随治疗次数的增加胸腺蓄积也越明显。这与纵隔转移灶不同，纵隔转移灶随治疗次数的增加，病变部位摄取 ^{131}I 的能力逐渐减低[6]。^{131}I 在胸腺浓聚的生理机制：有研究者认为，在细胞水平上，^{131}I 能积聚于胸腺小体（Hassall 小体）退化所形成的滤泡样结构中[7]，这点已被放射自显影技术证实；在分子水平上，发现胸腺组织中有与 NIS 蛋白相似的人钠碘共聚体（human sodium iodide symporter，hNIS）蛋白，只是 hNIS 对 ^{131}I 的亲和力较低，所以胸腺摄取往往发生在 ^{131}I 治疗后全身显像后 3 d 以上的延迟显像中；由于胸腺摄碘能力弱于甲状腺组织，随着 ^{131}I 治疗后与其竞争的残余甲状腺及转移灶的减少，胸腺摄取更加明显[8]。

1.4 肺部

肺部生理性摄取 ^{131}I 少见报道，李镜发等[9]及罗全勇等[10]曾报道了双肺弥漫性摄取，结合血清甲状腺球蛋白（thyroglobulin，Tg）水平、X 线胸片及 CT 检查，考虑为生理性摄取。肺部摄取 ^{131}I 的机制不清，可能与 ^{131}I 被肺泡上皮细胞摄取有关。罗全勇等[10]认为，由于 ^{131}I 扫描可以检出 X 线胸片、CT 等检查尚不能发现的微小转移灶，因此当胸片及 CT 无异常时，结合血清 Tg 水平评估是否有转移十分重要，如果 Tg 水平接近零，则转移的可能极小；如果 Tg 水平较之前有所升高，则应该密切随访。

1.5 肝脏

假阳性 ^{131}I 摄取在肝脏中较普遍，在高达 80% 的患者中可见假阳性 ^{131}I 摄取，图像表现为弥漫性、均质性和低强度摄取。^{131}I 剂量越高，给药与显像的时间间隔越长，肝脏放射活性摄取的频率和强度就越高。另外，有残留正常甲状腺或功能性转移灶存在时，肝脏也容易显影。^{131}I 在肝脏浓聚的生理机制：体内形成的放射性甲状腺激素及其他标记蛋白为肝脏代谢，常在肝内蓄积[3,11]。

1.6 胆囊和胆管

胆囊和胆管中的假阳性 ^{131}I 摄取少见报道。Seok 等[12]和 Carlisle 等[13]分别报道了胆囊和胆管的假阳性摄取，均未见病理性异常征象，考虑为生理性摄取，具体机制不清。

1.7 胃肠道

^{131}I 可经胃黏膜摄取至全身。大量饮水可减少 ^{131}I 在胃部的残留，同时胃液进入肠道，导致肠道显影，多见于结肠部位。显像时间越早胃肠道显影的几率越大。便秘患者因其胃肠蠕动较慢也易显影。胃肠道显影可能源于以下几种因素：吞咽的放射性唾液、胃黏膜的放射性分泌和肝内脱碘并经胆道排泌的甲状腺素[4,14]。异位的胃黏膜（Meckel 憩室、食管切除后或胸内胃食管吻合术后）[2]也可摄取 ^{131}I。

1.8 膀胱

尿液是 ^{131}I 排泄的主要途径，因此膀胱浓聚 ^{131}I 很常见。其影像形状及强度多变，是全身扫描放射性最高的部位，尤其是在 24~48 h。所以扫描前应鼓励患者排空膀胱[14]。

1.9 异位甲状腺

异位甲状腺也会出现 ^{131}I 的浓聚，其摄碘机制与颈部正常甲状腺相同。异位甲状腺可发生于舌下、胸腔、卵巢等部位，常见的是甲状腺舌管部位的异位甲状腺[15-16]。另有手术致甲状腺组织异位显影的情况，系经腋下入路的内镜甲状腺切除术使得甲状腺组织碎片播散所致[17]。

1.10 子宫

子宫中的假阳性 ^{131}I 摄取少见报道。月经期女性子宫可出现 ^{131}I 假阳性摄取[18]。Nishiyama 等[19]报

道了一例妊娠囊摄取 ^{131}I 的病例，其机制可能为 ^{131}I 从母体向胎儿运输及胎盘表达 NIS 蛋白。

2 病理性摄取

2.1 炎症

炎症性病变可以摄取 ^{131}I，如慢性胆囊炎[20]、皮脂腺炎、毛囊炎、非活动期的肺结核、类风湿性关节炎相关性肺疾病、支气管扩张[21-22]、慢性细支气管炎[23]、肺部感染、慢性鼻窦炎、牙龈炎、唾液腺炎、泪囊炎[24]、肺慢性炎症伴纤维化[25-26]、自体骨移植[27]、疫苗接种部位过敏反应性炎症[28]等。炎症性病变摄取 ^{131}I 的机制：可能是 ^{131}I 被炎症部位的白细胞有机化或吞噬 ^{131}I 标记的蛋白而储存在炎症部位，使得炎症病灶显影；也可能是炎症局部血管通透性增加，使 ^{131}I 渗出血管外而聚集于炎症部位。慢性胆囊炎浓聚 ^{131}I，与胆囊收缩功能减低使得含有 ^{131}I 的胆汁淤积有关[11,20]。

2.2 囊肿

囊肿可以摄取 ^{131}I，如胸膜心包囊肿[21]、肝囊肿[26]、乳腺囊肿、支气管囊肿[29]、肾囊肿[30-31]、卵巢囊肿[32]、子宫颈纳氏囊肿[18,33]、上皮样囊肿[34]、骨囊肿[35]等。囊肿摄取 ^{131}I 的机制：^{131}I 通过被动扩散和部分主动运输进入囊肿，由于囊肿中的水和化学成分与周围细胞和(或)血管外环境之间的交换缓慢，因此滞留在囊肿中。如肾囊肿系 ^{131}I 经肾小管主动分泌或经肾窦淋巴系统弥散入囊肿所致[29,31]。

2.3 非来源于甲状腺的良性肿瘤

不同病理类型的良性肿瘤假阳性 ^{131}I 摄取时有报道，但其摄取机制不完全清楚，来源于唾液腺、乳腺、卵巢的良性肿瘤，其假阳性 ^{131}I 摄取机制可能是由于表达功能性 NIS 蛋白；某些血管瘤的假阳性 ^{131}I 摄取可能由于血管内血池和 ^{131}I 经毛细血管漏出。具体病理类型及摄取机制见表 1。

2.4 非来源于甲状腺的恶性肿瘤

非来源于甲状腺的恶性肿瘤假阳性 ^{131}I 摄取也有报道，包括原发性肿瘤和转移灶，主要涉及胸部、盆腹部和骨骼。非来源于甲状腺的恶性肿瘤假阳性 ^{131}I 摄取机制：某些肿瘤细胞表达 NIS 蛋白，具有摄碘功能；另一个可能原因是肿瘤继发炎症反应。具体病理类型见表 2。

2.5 创伤

一些创伤可以引起假阳性 ^{131}I 摄取，例如：硬膜下血肿[58]、气管切开处、腋窝淋巴结清扫后[2]、胸壁穿刺活检处[59]、皮肤表面结痂处[49]等。目前认为在创伤处出现假阳性 ^{131}I 摄取的机制有两种：一种观点认为来源于创伤后炎性反应，与血管舒张、血流增加及毛细血管渗透性增加有关；另一种观点认为白细胞能通过髓过氧化酶诱导 ^{131}I 的有机化，使得 ^{131}I 在白细胞中停留，血凝块因含有丰富的白细胞而产生假阳性[60]。

3 体内滞留

3.1 病理性渗出液或漏出液

由于体液内含有 ^{131}I，机体存在漏出或渗出液时，积液部位也会聚集 ^{131}I，例如：颞下颌关节积

表 1 非来源于甲状腺的良性肿瘤及其摄碘机制

Table 1 Radioiodine uptake in non-thyroidal benign neoplasms and the mechanisms

病理类型	摄碘机制	参考文献
头颈部		
脑膜瘤	脑水肿或血供丰富	[36]
海绵状血管瘤	机制不清，可能是因为血供丰富	[37]
腮腺嗜酸性腺瘤	血供增加、毛细血管通透性增加和 ^{131}I 的主动运输	[38]
沃辛瘤(Warthin′s tumor)	唾液腺的主动运输	[39]
胸部		
乳腺纤维腺瘤	表达功能性 NIS 蛋白	[26]
胸膜囊性间皮瘤	^{131}I 的主动扩散和滞留	[40]
盆腹部		
肝血管瘤	血管内血池和 ^{131}I 经毛细血管漏出及间质内滞留	[41]
脾血管瘤	机制不清，可能是因为血管内血池	[11]
腹部神经鞘瘤	机制不清	[11]
子宫肌瘤	机制不清	[33]
卵巢甲状腺瘤	表达功能性 NIS 蛋白	[42]
卵巢黏液性囊腺瘤	表达功能性 NIS 蛋白以及体液潴留	[43]
卵巢浆液性囊腺瘤	表达功能性 NIS 蛋白以及体液潴留	[44-45]
卵巢畸胎瘤	表达功能性 NIS 蛋白	[42]
骨骼		
鼻骨骨样骨瘤	机制不清，可能是因为血供丰富	[46]
颅骨血管瘤	血管内血池和 ^{131}I 经毛细血管漏出	[47]
椎体血管瘤	血管内血池和 ^{131}I 经毛细血管漏出及间质内滞留	[11]

注：表中，NIS：钠碘同向转运体。

表 2 非来源于甲状腺的恶性肿瘤

Table 2 Radioiodine uptake in non-thyroidal malignant neoplasms

病理类型	参考文献
头部	
腮腺黏液表皮样癌	[48]
胸部	
原发性肺癌	[11，49]
肺转移癌	[50]
宫颈癌	
卵巢甲状腺肿	[51]
乳腺癌	[11]
盆腹部	
胃腺癌	[11]
胆囊癌	[52]
卵巢甲状腺肿肝转移	[53]
卵巢甲状腺肿腹膜后转移	[54]
腹膜后恶性纤维组织细胞瘤	[55]
腹膜后平滑肌肉瘤	[56]
恶性卵巢甲状腺肿	[42]
骨骼	
肺腺癌骨转移	[49]
消化系统肿瘤骨转移	[57]

液[61]、腹水、心包积液、胸腔积液[2,11,62]等。

3.2 扩张的导管和腔隙内滞留

胃肠道异常，例如 Zenker's 憩室、膈上食管憩室、食管裂孔疝、贲门失弛缓症[5]、肠扭转[63]、腹股沟疝[2]等，可使 ^{131}I 滞留。胆道异常，如肝内胆管扩张[11]，可使 ^{131}I 在肝内滞留。尿道异常，例如憩室、瘘管、积水，使得 ^{131}I 排泄迟缓[64]。血管扩张使血流速度减慢从而使得血池显影，例如颈动脉扩张[5]、胸主动脉扩张[65]及大隐静脉曲张[24]。处女膜闭锁导致经血滞留在阴道内，可出现盆腔内 ^{131}I 异常浓聚[66]。

3.3 体内化学材料吸附

一些化学材料如金属(带正电子可与碘离子相互作用)、硅胶(具有亲水性)可以吸附 ^{131}I，当体内存在含有这些材料的物质时，就会使 ^{131}I 滞留而显影，如金属假牙[67]、颅骨术后金属缝线[68]、宫内节育器[49]及隆胸术后假体等[69]。宫内节育器的摄取原因不清，也可能与节育器长期刺激引起宫腔慢性炎症反应有关。

4 分泌物的体外污染

分泌物的污染也是假阳性 ^{131}I 摄取的原因之一，例如：唾液、鼻部分泌物、泪液、汗液等[5,24]。分泌物污染的原因往往与一些不良生活习惯有关，采集图像前的患者准备有助于减少此类假阳性 ^{131}I 摄取。污染大多是体表的，使用侧位和斜位可以帮助鉴别。

总之，^{131}I 全身显像假阳性的发生率虽较低，但情况多种多样，常给诊断带来困难。判读图像时需考虑到这些假阳性的情况，密切结合患者的临床症状、体征、血清 Tg 水平以及其他影像学检查结果，以排除假阳性结果，避免给患者造成不必要的或创伤性治疗[10]。^{131}I SPECT/CT 融合显像，借助CT的解剖图像，能克服 ^{131}I 全身显像的局限性，对 ^{131}I 摄取灶的定位乃至辅助定性诊断都有意义。对于 ^{131}I 全身显像诊断不明的患者行 SPECT/CT 融合显像可提高诊断正确率，对调整治疗方案有重要临床价值[70]。

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