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¹²⁵I放射性粒子链腔道内近距离放疗的进展

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• 综述 •

^{125}I 放射性粒子链腔道内近距离放疗的进展

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Advances of ^{125}I Radioactive Particle Chain Intracavitary Brachytherapy

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Abstract: The radioactive particle chain is a linear array of ^{125}I particles and placed in a tubular conduit. The dose distribution of the particle chain is similar to the shape of a cylinder. It may be adapted to the tumors in the lumen and exerts the radiotherapy effect that may not be achieved by single particles. This article aims to review the history of ^{125}I radioactive particle chains, dose distribution, placement methods and clinical application.

Key words: ^{125}I radioactive particles; Radiation therapy; Brachytherapy; Malignant tumor

摘要: 放射性粒子链是将 ^{125}I 粒子按照线性排列并置于管状导管中,使其剂量分布接近于圆柱形,进而适应腔道内的肿瘤放疗,发挥出单粒子所达不到的治疗效果。本文旨在综述 ^{125}I 放射性粒子链的发展历史、剂量分布、置入方法以及临床应用。

关键词: ^{125}I 放射性粒子; 放射治疗; 内照射; 恶性肿瘤

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0 引言

Pierre Curie于1901年在国际上首次提出近距离治疗的基本概念及理论。1914年法国Pasteau和Degrais医生首次使用镭管经尿管尿道插植治疗前列腺癌,开启了肿瘤组织间近距离治疗的先河。但当时没有精确的影像导引和相关防护系统,近距离放疗进展缓慢。20世纪70年代后期,随着低能核素的研发及CT/MR/US等影像新技术的临床应用,组织间近距离治疗运用更多。在美国,放射性粒子植入治疗已经成为早期前列腺癌的首选治疗方案^[1]。对于人体腔道内病变,经皮穿刺粒子植入技术恐难取得满意的粒子分布。基于 ^{192}Ir 对人体腔道内近距离放疗的启发^[2],有学者开始尝试将放射性粒子置入导管内串成链条状结构植入人体的腔道进行近距离放疗并取得成功。

1 ^{125}I 粒子链的剂量分布特点

国内学者通过3D-TPS、蒙特卡罗模拟、玻璃剂量计及IP板等方法,探究揭示了 ^{125}I 粒子链的剂量

分布特点,为临床工作提供了参考,现综述如下:

焦德超等^[3]分别制作了单链、双链以及三链的粒子链,将其置入到人体等效体模中,CT扫描后将信息上传TPS系统中,验证剂量分布,发现其剂量场为柱体,径向累计剂量(dose, Gy)在距离中心1厘米以上,剂量值快速跌落,并得出累计剂量方程:单链 $\ln \text{dose}=43.3\text{activity}-24.2\text{distance}+48.4$;双链 $\ln \text{dose}=95.4\text{activity}-55.8\text{distance}+112.0$;三链 $\ln \text{dose}=138.0 \text{ activity}-79.8 \text{ distance}+160.5$ (activity=离子活度, mCi; distance=测量点距离中心的距离, cm),这些剂量方程为临床工作提供了剂量参考依据。

牛璐莹^[4]模拟了 ^{125}I 粒子链在医用PVC导管和金属治疗支架中的剂量场分布,得出医用PVC导管和金属治疗支架对剂量分布有一定程度的影响,尤其是金属治疗支架对粒子源的剂量分布的影响很大。杨敏捷等^[5]通过玻璃剂量计及IP板测量粒子链剂量立体分布并与计算软件结果比较,发现其相关性良好且粒子链剂量分布呈柱体,为腔道肿瘤的治疗提供了参考。王耀明等^[6]将纵向严密排列的粒子链以单枚剂量计算为模型,用“标量叠加”的方法从理论上推导粒子链的剂量分布模型。李说^[7]将10颗 ^{125}I 粒子纵向连续排列,并将其封装在4F透明导管内制成粒子链,应用SPECT/CT扫描观

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察连续排列的粒子链在等效体模内的辐射分布，发现SPECT/CT观察剂量分布的优势和便利。

在实际临床过程中，¹²⁵I粒子链的剂量分布往往受多种因素的干扰，尤其是介质对于粒子链的剂量分布有较大的影响，在肝脏、骨、前列腺等不同的部位都呈现不同的剂量分布差异^[8-10]。因此，在实际肿瘤临床治疗过程中，应该谨慎把握各组织的剂量分布特点。

2 ¹²⁵I粒子链的临床应用

2.1 恶性胆管梗阻¹²⁵I放射性粒子腔道近距离治疗

金属支架置入是阻塞性黄疸的首选姑息治疗方法^[11]，但随着肿瘤进展和肉芽组织增生，支架会很快出现再狭窄，中位通畅时间约在150~255天^[12]。为治疗肿瘤，提高支架通畅率，国内学者提出放射性粒子链概念，并将之经皮肝穿刺胆道引流术（PTCD）或内镜逆行性胰胆管造影术（ERCP）途径置入胆管内进行腔道内近距离放疗。依据粒子链置入的方式分为四种：（1）将放射性粒子置入医用3-4F导管中，导管远端及近端封闭，使用5F鞘管将粒子链推入支架外，支架将粒子链条固定于支架与胆管壁之间；（2）将放射性粒子置入医用3-4F导管中，导管远端封闭，经过双导丝技术，先释放胆管支架，之后将粒子链直接置入胆管支架内，同时经另一根导丝植入8.5F内外引流管；（3）将放射性粒子链直接留置于胆道内外引流管内；（4）基于对引流导管的改进，设计一种可携带放射性粒子的胆道引流导管，该引流管三腔或双腔结构的导管，达到胆汁引流和胆道腔内放疗的双重效果。滕皋军等^[13]使用分体套叠式胆道内照射架，实现了支架与粒子

的完美结合。

刘素丽等^[14]在2006年首次报道了在经ERCP下逆行入胆管把¹²⁵I粒子放置于胆管内，初步证实了将¹²⁵I粒子放置于胆道，治疗恶性梗阻的安全性和有效性。2007年，常钢等^[15]采用在血管造影（digital subtraction angiography, DSA）引导下经PTCD途径植入支架联合粒子链的方案，首次证实了经PTCD途径置入放射性粒子链的安全性和可行性。在之后的十多年，¹²⁵I粒子链治疗腔道内近距离放疗蓬勃发展，近年来最新的研究文献见表1。

2.2 门静脉癌栓的¹²⁵I放射性粒子链腔道近距离治疗

门静脉癌栓（Portal vein tumor thrombus, PVTT）是肝细胞癌（Hepatocellular carcinoma, HCC）常见的病理改变，发生率高达30%~60.2%^[22]。PVTT的出现意味着HCC严重预后不良，其不仅堵塞门脉，加重门脉高压，严重影响肝脏正常功能，同时，也加速了癌细胞的转移，因此有学者采用置入门脉支架的办法疏通门脉，使门脉血流能够入肝，缓解了肝功能的恶化以及门脉高压的症状^[23]。但是，由于肿瘤的增生与迁徙，支架很容易堵塞，中位通常时间仅为2~3月。Zhang等^[24]首先报道了在CT引导下，门脉癌栓的粒子治疗，近期随访结果发现疗效确切。之后也有学者报道在CT或DSA引导下，经皮穿刺置入单体粒子的治疗手段，虽然有一定疗效，但是，由于门脉解剖结构的缘故，单体粒子不能很好地进行适形的内照射，会产生很多剂量冷区；同时，肝癌合并门脉癌栓的患者多数由于肝功能异常而造成凝血功能的异常，因此反复的经皮穿刺容易造成出血甚至于死亡^[25]。颜志平等首次将放射性粒子穿成链条，运用双导丝技术将放射性粒子链置入到门脉当中，实现了长时间的近距离照射，支架的通

表1 ¹²⁵I粒子链治疗恶性胆道梗阻近3年文献回顾

Table1 Literature review of ¹²⁵I particle chain therapy for malignant biliary obstruction in recent 3 years

Year	Author	Experiment design (sample size)	Treatment	Unobstructed situation (Experiment group vs. Control group)	Survival situation (Experiment group vs. Control group)
2017	Jiao D ^[16]	Retrospective Control Study (64)	Y-stent+particle chain	(368±42.4) days vs. (222.0±34.8) days	(355±71.5) days vs. (271.0±29.0) days
2018	Ma J ^[17]	Retrospective observational study (107)	Metal stent + particle chain	Median time 278 days	Median survival 394 days
2018	Zhou CG ^[18]	Retrospective Control Study (38)	Particle chain+ biliary metal stent	(192.94±28.59) days vs. (121.40±15.39) days	(201.83±27.50) days vs. (142.25±15.46) days
2019	Zhou WZ ^[19]	Retrospective Control Study (132)	Self-expanding metal stent+ particle chain	194days vs. 86days	Median survival 194 days vs. 96 days
2019	Zhang ZP ^[20]	Retrospective Control Study (120)	Particle chain biliary stent+ chemotherapy drug	(9.4±0.8) months vs. (4.3±0.4) months	14.6 months vs. 6.1 months
2019	Jiao DC ^[21]	Retrospective observational study (15)	New integrated biliary drainage tube with ¹²⁵ I particles	Median time 255 days, 6 months patency rate 64.5%	Median survival 368 days

畅时间明显提高^[26]；因此，最佳的手段是将粒子封装到医用导管里做成粒子链，在支架置入之后将粒子链留置在支架与癌栓之间，这样既符合门脉的解剖结构，同时也能避免单独粒子插值治疗所发生的移位，门脉通畅率大大提高。

经过不断地改良与突破，对于门脉癌栓相关治疗组合手段大致分为两种：（1）¹²⁵I放射性粒子链+金属支架+经导管动脉化疗栓塞术（TACE）；（2）¹²⁵I放射性粒子链+金属支架+TACE+索拉菲尼。粒子链治疗门脉癌栓不仅是一种适形内放疗的探索，更是对肿瘤综合治疗的尝试，它的普适性、便利性和有效性逐渐被广大的介入科医师所接受。近年来最新研究进展的相关文献见表2。

3 其他肿瘤的¹²⁵I放射性粒子链腔道近距离治疗

有些研究人员试图将其延伸到其他类型腔道肿瘤：Zhang等^[32]首先将¹²⁵I放射性粒子链置入到下腔静脉癌栓的动物模型中证明该方案的安全性。Yang等^[33]采用TACE联合放疗支架（粒子链捆绑于Z型支架上）治疗肝癌合并下腔静脉癌栓，33例患者采用粒子链支架，28例患者采用裸支架，A组的中位生存期（203.0±28.135）天明显优于B组（93.0±24.341）天（ $P=0.006$ ）。Li等^[34]对52例肝癌合并下腔静脉的梗阻患者进行回顾性分析，18例接受¹²⁵I粒子链支架，患者有效率为94.4%，34例使用裸支架，有效率仅为35.3%。Gong等^[35]将其延伸到更广范围的肿瘤相关静脉阻塞（CAVO），他们将装载放射性粒子链的自膨式支架置入到1例CAVO患者静脉中，3月的影像学随访显示髂股静脉通畅良好没有严重并发症。焦德超等^[36]首次报

道了放射性粒子链治疗输尿管癌，患者的肿瘤2月回缩95%以上，该项技术对于高龄、孤立肾、不接受外科手术的患者，将会是一种很好的替代方案。以此为基础，焦德超等^[37]将10例输尿管癌患者采用肾造瘘+粒子链置入的治疗模式，结果显示完全缓解（CR）4例，部分缓解（PR）6例，局部控制率（CR+PR）100%，输尿管通畅率50%。焦德超等^[38]还首次使用双粒子链和三粒子链并将其捆绑到胃肠营养管对KPS评分50以下的患者进行治疗，局部控制率100%，未来可能在食管恶性梗阻合并体质虚弱的患者中发挥有益的作用。

4 小结

¹²⁵I放射性粒子链腔道近距离治疗优势如下：

- （1）对于腔道肿瘤，有独特的适形性；
- （2）粒子回收方便，不留异物；
- （3）粒子链可以配合导管、支架等器械，甚至制作创意性发明，起到一箭双雕的作用；
- （4）操作方便、技术简单，便于基层掌握。然而，粒子链也存在诸多缺陷：
 - （1）粒子衰减较快，不适用于增殖较快的肿瘤；
 - （2）国内技术较为混乱，没有统一的制作与置入标准；
 - （3）缺乏高质量的循证医学证据；
 - （4）缺乏粒子与支架或导管的一体化研究，期待出现更多的新技术和产品研发。

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表2 ¹²⁵I粒子链治疗门脉癌栓文献回顾

Table2 Literature review on portal vein carcinoma thrombus treated with ¹²⁵I particle chain

Year	Journal	Author	Experiment design	Sample size	Treatment	Unobstructed situation (Experiment group vs. Control group)	Median survival time (Experiment group vs. Control group)
2016	Hepatol Int	Luo J ^[27]	Retrospective controlled study	276	Particle Chain+Portal Vein stent+TACE vs. Portal Vein stent+TACE	9.2 months vs. 4.8 months	9.3 months vs. 4.9 months
2016	Natl Med J China	Li WH ^[28]	Retrospective controlled study	53	Particle Chain+Portal Vein stent+TACE vs. Particle Chain+Portal Vein stent+TACE+Solafenib	Unavailable	14.8 months vs. 12.1 months
2016	Biomed Res Int	Sun JH ^[29]	Retrospective observational study	34	Particle Chain+Portal Vein stent	One-year cumulative patency rate: 29.4% (10/34)	147 days
2017	Oncotarget	Yu TZ ^[30]	Retrospective controlled study	123	Particle Chain+Portal Vein stent vs. Portal Vein stent+External radiotherapy	10.3 months vs. 8.7 months	11.7 months vs. 9.5 months
2018	Chin J Inter Rad (Electronic Edition)	Miao TG ^[31]	Case report	1	Particle Chain+Portal Vein stent	More than 6 months	More than 6 months

Note: TACE: transcatheter arterial chemoembolization

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