宫颈癌腹主动脉旁淋巴结转移静态调强放疗与容积旋转调强放疗的剂量学比较

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[摘 要] **目的**:比较静态调强放疗(intensity modulated radiotherapy,IMRT)与容积旋转调强放疗(volumetric modulated arc therapy,VMAT)在宫颈癌伴腹主动脉旁淋巴结(para-aortic lymph node,PALN)转移患者放疗中的剂量学参数,为局部晚期宫颈癌放疗方式的选择提供参考依据。**方法**:对20例病理学证实经PET-CT检查诊断为宫颈鳞癌PALN转移接受放疗的患者,对同一CT图像分别进行IMRT和VMAT计划设计,比较两种放疗计划的靶区剂量和危及器官(organ at risk,OAR)的剂量学差异、靶区适形性指数(conformity index,CI)、均匀性指数(homogeneity index,HI)、加速器跳数(number of monitor units,MU)和治疗时间。**结果**:IMRT和VMAT组计划的靶区剂量均能够满足剂量学要求,在靶区CI和HI上,VMAT计划优于IMRT计划。OAR保护方面,VMAT计划中两侧肾脏平均剂量低于IMRT计划,直肠V_{40}、直肠V_{50}、小肠V_{40}和膀胱V_{40}的剂量均低于IMRT计划($P<0.05$)。VMAT计划的MU(859.92 ± 248.47)低于IMRT计划(1 649.50±167.44,t=11.836,$P<0.001$)。VMAT计划的治疗时间[(304.30 ± 41.98)s]明显短于IMRT计划[(435.90 ± 37.52)s,t=12.750,$P<0.001$]。**结论**:宫颈癌伴PALN转移患者,采取IMRT和VMAT技术均可达到临床靶区剂量要求和OAR的剂量保护,而VMAT计划在靶区CI和HI上优于IMRT计划,同时VMAT具有降低OAR剂量的优势,MU明显降低,照射时间缩短,提高了患者放疗的耐受性,提升了宫颈癌放射治疗的效率。

[关键词] 宫颈癌;腹主动脉旁淋巴结转移;放射治疗;静态调强放疗;容积旋转调强放疗

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Dosimetric study of intensity modulated radiotherapy and volumetric-modulated arc radiotherapy for cervical cancer with para-aortic lymph node metastasis

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[**Abstract**] **Objective**: To compare dosimetric difference between the intensity modulated radiotherapy (IMRT) and volumetric modulated arc therapy (VMAT) of cervical cancer with para-aortic lymph node metastasis, and to provide the reference basis for selecting the reasonable radiotherapy approach of locally advanced cervical cancer patients. **Methods**: Twenty patients of cervical cancer with para-aortic lymph node (PALN) metastasis whom confirmed by PET-CT examination and diagnosis and received radiotherapy were selected, and the same CT image was designed by IMRT and VMAT respectively. Then, we compared the parameters of target, organ at risk (OAR), homogeneity index (HI), conformity index (CI), the number of monitor units (MU) and treatment times between two plans. **Results**: The target dose of IMRT plan and VMAT plan could meet the dosimetric requirement. The CI and HI of planning target volume (PTV) for VMAT plan were superior to IMRT plan ($P<0.05$). Compared with the IMRT plan, the mean dose of kidney for VMAT plan were lower ($P<0.05$). The V_{40} and V_{50} of the rectum, V_{40} of the small intestine and the bladder of VMAT plan were better than those of IMRT plan ($P<0.05$). The number of MU for VMAT plan (859.92 ± 248.47) were lower than IMRT plan (1 649.50 ± 167.44) (t=11.836, $P<0.001$). The treatment time for VMAT plan [(304.30 ± 41.98) s] were shorter than IMRT plan [(435.90 ± 37.52) s, t=12.750, $P<0.001$]. **Conclusion**: Both of the IMRT and VMAT plans can achieve the clinical dosimetric demands and protect the OARs of cervical cancer with PALN. VMAT has the best performance on CI and HI, and protect the OARs

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better. VMAT plans have fewer MU and significantly improve the treatment efficiency. Thus it will improve the patient´s radiotherapy tolerance, enhance the efficiency of radiotherapy.

[**Key words**] cervical cancer; para-aortic lymph node metastasis; radiotherapy; IMRT; VMAT

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宫颈癌是女性生殖系统最常见的恶性肿瘤，严重威胁女性生命健康，发病率和病死率呈逐年升高趋势，居女性恶性肿瘤死亡率第2位[1]，且约有85%的病例发生在发展中国家。淋巴结转移是宫颈癌主要的转移途径[2]，美国妇科肿瘤学组（Gynecologic Oncology Group，GOG）的研究显示，5%的Ⅰb期、16%的Ⅱ期、25%的Ⅲ期宫颈癌患者会发生腹主动脉旁淋巴结（para-aortic lymph node，PALN）转移[3]，且为宫颈癌重要的预后不良因素[4]。宫颈癌伴PALN转移患者的治疗以放射治疗为主，辅以化疗[5]。近年来，随着精确放疗技术的不断发展，放疗进入了精确化、个体化、综合化的治疗时代，其中涌现出精确调强放疗（intensity modulated radiotherapy，IMRT）、容积旋转调强放疗（volumetric modulated arc therapy，VMAT）、影像引导放射治疗（image guided radiation therapy，IGRT）等多项新技术，VMAT是在IMRT基础上发展的更为先进的放射治疗技术，在覆盖目标靶区以及对正常器官组织保护上较IMRT更有优势，精准度得到进一步提高[6-9]。而目前对于宫颈癌PALN转移患者精确放疗技术的选择尚无明确报道。本研究旨在比较IMRT/VMAT在宫颈癌PALN转移患者靶区和危及器官（organ at risk，OAR）剂量以及加速器跳数（number of monitor units，MU）在内的剂量学差异，探讨宫颈癌PALN转移患者的最佳放疗方案。

1 对象和方法

1.1 对象

选取2017年1月—2018年4月在江苏省肿瘤医院就诊的20例宫颈癌PALN转移患者，所有患者均经病理确诊，且经PET-CT证实为腹主动脉旁淋巴结转移（PET-CT检查显示标化摄取值≥2.5或淋巴结直径≥10 mm者被判定为腹主动脉旁淋巴结有转移），所有患者PET-CT检查均未显示盆腔淋巴结及腹主动脉旁淋巴结以外部位转移。治疗方法为腹主动脉旁延伸野放疗+盆腔野放疗，同步配合TP方案化疗。患者年龄34~58岁，中位年龄50岁，根据FIGO分期，其中8例为Ⅱb期，12例为Ⅲb期，病理类型均为鳞癌。各例患者腹主动脉旁淋巴结最大径线为12~34 mm，平均最大径线为19 mm，患者临床资料详见表1。

表1 20例宫颈癌PALN转移患者基本临床资料

Table 1 The clinical data of 20 cervical cancer patients with para-aortic lymph node metastases

因素	例数[n(%)]
年龄	
30~45岁	4(20)
46~60岁	16(80)
分期	
Ⅱ期	8(40)
Ⅲ期	12(60)
分化程度	
Ⅰ~Ⅱ级或Ⅱ级	13(65)
Ⅱ~Ⅲ级或Ⅲ级	7(35)
腹主动脉旁淋巴结直径	
<2 cm	11(55)
≥2 cm	9(45)
肿瘤直径	
<4 cm	8(40)
≥4 cm	12(60)

1.2 方法

1.2.1 CT模拟定位

定位前要求患者排空直肠，充盈膀胱（扫描1 h前排空膀胱）。患者仰卧位，平躺在真空垫上，双手交叉抱肘关节放至前额部，双腿自然平放。采用西门子螺旋CT模拟定位机扫描CT，扫描前2 h口服造影剂（碘海醇20 mL稀释于600 mL温水中，分2次口服，每小时1次），CT扫描范围自第10胸椎下缘到坐骨结节下缘3~5 cm，扫描层厚5 mm。

1.2.2 靶区及OAR勾画及定义

根据国际辐射单位与测量委员会（International Commission on Radiation Units and Measurements，ICRU）83号文件标准定义勾画靶区及OAR[10]。靶区包括：临床靶体积（clinical target volume，CTV）、计划靶体积（planning target volume，PTV）、OAR。其中CTV包括原瘤区、上段阴道、宫旁及髂总、髂内、髂外、骶前、闭孔和腹主动脉旁淋巴引流区。上界根

据腹主动脉旁淋巴结具体位置确定,下界根据阴道累及情况决定。PTV为CTV在各个方向外放0.7 cm。OAR包括:肾脏、直肠、膀胱、小肠、双侧股骨头。所有靶区的勾画均由同一医师完成,并由同一物理师协同设计。

1.2.3 治疗计划设计

对同一CT图像,采用Monaco计划设计系统分别设计9野IMRT和双弧VMAT两种放疗计划。根据靶体积剂量、OAR的限制剂量设置野数及权重。处方剂量50.4 Gy,分次剂量1.8 Gy/次,腹主动脉旁肿大淋巴结加量6.0~8.0 Gy,2.0 Gy/次,共3~4次。IMRT计划在患者盆腔周围360°方向共设计9野,相邻照射野间隔相同;VAMT为弧形照射,均设计2弧照射(分别为顺时针180°~179°,再逆时针到180°)。要求95%等剂量曲线覆盖PTV,靶区最大及最小剂量不超过处方剂量±10%。98%以上的PTV达到处方剂量,没有剂量冷点。所关注的OAR没有剂量热点。热点剂量不超过处方剂量的110%。

1.2.4 OAR受照剂量比较

OAR的受照剂量限制要求:肾脏平均受照剂量<12 Gy,直肠50.0 Gy的受照体积(V_{50})≤50%、膀胱50.0 Gy的受照体积(V_{50})≤30%、小肠50.0 Gy的受照体积(V_{50})≤10%、双侧股骨头50.0 Gy的受照体积(V_{50})≤5%。评估IMRT和VMAT两种治疗计划之间的OAR受照剂量差异。

1.2.5 靶区剂量学参数比较

ICRU 83号报告提出,通过靶区适形性指数(conformity index,CI)和均匀性指数(homogeneity index,HI)来评估放疗计划的质量。$D_{2\%}$(2%PTV体积受照的最大剂量)表示近似最大剂量,$D_{98\%}$表示近似最小剂量,$D_{50\%}$为中位剂量。CI值在0~1之间,CI值越大表明靶区适形度越高,HI值越低说明靶区剂量均匀性越好。TV_{RI}为处方剂量线所包裹的靶区体积,TV为靶体积,V_{RI}为处方剂量线所包裹的总体积。$CI=\frac{TV_{RI}}{TV}\times\frac{TV_{RI}}{V_{RI}}$;$HI=\frac{D_{2\%}-D_{98\%}}{D_{50\%}}$。

1.2.6 MU及治疗时间

统计分析IMRT和VMAT放疗技术的MU及治疗时间(治疗时间是指摆位完成及位置验证完成后,第1个照射野开始照射到治疗结束所用的时间)。

1.3 统计学方法

采用SPSS20.0统计软件进行分析,计量资料用均数±标准差($\bar{x}\pm s$)表示,组间比较采用t检验。$P\leq0.05$为差异有统计学意义。

2 结 果

2.1 靶区剂量的分布

IMRT和VMAT两种放疗计划的剂量分布均能够满足靶区处方剂量要求,与IMRT计划相比,VMAT计划除$D_{50\%}$外,$D_{2\%}$和$D_{98\%}$靶区剂量学参数比较差异均有统计学意义($P<0.05$)。VMAT计划靶区近似最大剂量($D_{2\%}$)低于IMRT计划(t=3.668,P=0.002),而靶区近似最小剂量($D_{98\%}$)高于IMRT计划(t=−2.402,P=0.027),且VMAT计划的CI值大、HI值小,两者相比差异有统计学意义(t=−2.432、2.395,$P<0.05$,表2)。

表2 宫颈癌PALN转移患者IMRT、VMAT治疗计划的靶体积剂量

Table 2 Target volumes of IMRT/VMAT treatment plans of cervical cancer patients with para-aortic lymph node metastases

指标	VMAT组	IMRT组	t值	P值
$D_{2\%}$(Gy)	49.97 ± 2.04	52.75 ± 2.98	3.668	0.002
$D_{50\%}$(Gy)	46.88 ± 0.65	46.70 ± 0.65	−1.123	0.275
$D_{98\%}$(Gy)	47.06 ± 1.66	46.18 ± 0.49	−2.402	0.027
HI	0.08 ± 0.04	0.11 ± 0.02	2.395	0.027
CI	0.83 ± 0.07	0.79 ± 0.05	−2.432	0.025

2.2 OAR的剂量参数

通过比较两种放疗计划OAR的剂量学参数发现,VMAT计划对直肠V_{40}和V_{50}较IMRT计划更有优势,差异有统计学意义(t=11.776、7.453,$P<0.001$),而对于V_{10}、V_{20}、V_{30}无明显优势作用($P>0.05$)。VMAT计划双侧肾脏的平均剂量均低于IMRT计划,二者相比差异有统计学意义(t=9.557、7.241,$P<0.001$)。VMAT计划的膀胱V_{40}、小肠V_{40}低于IMRT计划,差异有统计学意义(t=2.156、5.851,$P<0.05$)。2种放疗计划股骨头的组织剂量类似,差异没有统计学意义($P>0.05$,表3)。

2.3 IMRT、VMAT计划的MU和治疗时间

VMAT计划的MU值为859.92 ± 248.47,明显少于IMRT计划(1 649.50 ± 167.44),两组相比差异有统计学意义(t=11.836,$P<0.001$),治疗时间也较IMRT计划明显缩短[(304.30 ± 41.98)s *vs.*(435.90 ± 37.52)s,t=12.750,$P<0.001$]。

3 讨 论

宫颈癌的放射治疗最初为二维全盆腔照射,近

表3　宫颈癌PALN转移患者IMRT、VMAT治疗计划OAR的剂量参数

Table 3　Dosimetric comparison of OAR between IMRT/VMAT treatment plans of cervical cancer patients with para-aortic lymph node metastases

OAR	剂量参数	VMAT组	IMRT组	*t*值	*P*值
直肠	V_{10}(%)	97.97 ± 1.19	98.44 ± 1.37	−1.892	0.074
	V_{20}(%)	97.51 ± 0.82	97.76 ± 0.59	1.035	0.314
	V_{30}(%)	90.88 ± 1.42	91.19 ± 1.13	0.740	0.468
	V_{40}(%)	50.25 ± 2.92	62.43 ± 4.16	11.776	< 0.001
	V_{50}(%)	38.01 ± 1.39	42.10 ± 1.92	7.453	< 0.001
膀胱	V_{10}(%)	100.00 ± 0.0	100.0 ± 0.0	0.000	1.000
	V_{20}(%)	97.96 ± 0.64	98.14 ± 0.58	0.950	0.354
	V_{30}(%)	76.24 ± 2.79	76.65 ± 2.88	0.707	0.488
	V_{40}(%)	46.59 ± 3.89	48.03 ± 6.01	2.156	0.044
	V_{50}(%)	25.36 ± 2.42	25.40 ± 2.87	0.044	0.966
小肠	V_{10}(%)	81.39 ± 0.94	80.79 ± 1.18	−1.790	0.089
	V_{20}(%)	58.11 ± 5.76	57.75 ± 1.29	−0.192	0.850
	V_{30}(%)	36.71 ± 6.71	38.89 ± 7.67	1.012	0.324
	V_{40}(%)	17.49 ± 2.52	27.15 ± 6.97	5.851	< 0.001
	V_{50}(%)	6.45 ± 0.51	6.49 ± 0.52	0.707	0.488
股骨头	V_{10}(%)	92.04 ± 1.84	92.44 ± 1.47	1.042	0.311
	V_{20}(%)	81.36 ± 4.36	81.25 ± 5.11	−0.094	0.926
	V_{30}(%)	49.52 ± 4.82	48.58 ± 4.76	−1.111	0.281
	V_{40}(%)	30.59 ± 1.08	30.94 ± 0.88	0.975	0.342
	V_{50}(%)	3.28 ± 0.59	3.22 ± 0.53	−0.322	0.751
左侧肾脏	平均受照射剂量(Gy)	8.57 ± 1.11	10.68 ± 1.14	9.557	< 0.001
右侧肾脏	平均受照射剂量(Gy)	8.23 ± 1.07	10.45 ± 0.69	7.241	< 0.001

远期不良反应严重，近年来随着放疗技术的不断更新和放疗机器的发展，三维适形放疗（3-dimensional conformal radiotherapy，3D-CRT）和固定野IMRT广泛应用于宫颈癌的放射治疗，IMRT较3D-CRT技术有明显优势，它实现了照射野内靶区剂量分布的有效调节，可减少OAR和正常组织的受照剂量，如肾脏、直肠、膀胱、小肠等，从而减轻其不良反应，提高宫颈恶性肿瘤的放射治疗疗效[11]。然而IMRT技术也存在着劣势，主要体现在治疗效率上，IMRT治疗时间较3D-CRT延长，增加了MU，患者接受低剂量射线的正常组织体积也增加，影响靶区的生物效应[12]。

VMAT作为一种新的放疗调强技术，自应用于临床以来，已在头颈部肿瘤、食管癌、宫颈癌及直肠癌等多种恶性肿瘤的放射治疗中均表现出一定的剂量学优势[13-17]，与IMRT相比的优点就是在不降低靶区剂量分布的同时，可减少治疗时间和MU。长时间的治疗过程会增加患者的不自主运动，引起摆位误差，因此减少治疗时间有效提高了治疗效率；而且由于MU减少，减少了机器散射，正常组织接受的散射量也相应减少。Huang等[18]评价了13例宫颈癌患者VMAT和7野IMRT两种放疗的剂量分布情况，结果显示VMAT计划较前7野IMRT在靶区剂量的均匀性和OAR保护方面均有明显优势。有研究发现与常规IMRT计划相比，VMAT可实现靶区高度适形的靶区剂量分布，更安全地保护正常组织[19]。

CT、MRI检查是常见的检测宫颈癌淋巴结转移的方法，通常用淋巴结大小作为鉴别淋巴结是否转移的标准，10 mm是正常淋巴结的最大直径。宫颈癌淋巴结直径≥10 mm时，93%的淋巴结被确诊为转移。近年来研究显示，PET-CT在检查宫颈癌PALN转移方面更有优势，PET-CT检查显示PALN转移的特异度为90%~97%[20]，准确性约85%[21]。因此，本研究20例患者全部采用PET-CT证实PALN转移。

对于宫颈癌伴PALN转移患者的治疗方式为腹主动脉旁延伸野放疗，既往有研究显示，在3D-CRT时代，对宫颈癌伴PALN转移患者行腹主动脉旁延伸野放疗，患者3级以上急性不良反应的发生率为

80%，而晚期不良反应发生率为40%[22]。随着调强放疗的成熟应用，与3D-CRT技术相比，IMRT放疗的膀胱、直肠和小肠受照面积明显下降，明显降低了周围正常组织的受量，更好地保护了正常组织[23]。但目前关于VMAT放疗在宫颈癌伴PALN转移患者中的应用研究尚未见报道，因此本研究主要对20例宫颈癌PALN转移患者分别设计IMRT、VMAT两种治疗计划，比较两种放疗计划剂量学参数以及两组患者OAR剂量学差异。本研究结果显示，两种治疗计划的靶区剂量均能满足剂量学要求，在靶区均匀性和适形度上，双弧VMAT计划优于9野IMRT计划，在肾脏、直肠、膀胱和小肠的保护上，两种计划均未超出正常组织的耐受剂量，VMAT在双侧肾脏，直肠V_{40}、V_{50}，小肠和膀胱V_{40}上较IMRT计划表现出优势，更好地保护了双侧肾脏，避免了肾损害的发生，也为局部晚期宫颈癌患者全身化疗的顺利实施提供了保障。VMAT计划的MU低于IMRT计划，治疗时间明显短于IMRT计划，因此VMAT计划明显减少了机器损耗，突出了其临床价值。然而在实际工作中，由于不同的计划系统，单、双弧射线能量的不同，优化算法的差异以及操作人员对计划质量的控制等因素的影响，研究结果可能会有所差异。因此，一个好的VMAT计划，在临床上需有效控制各种影响因素，减少不必要的误差，实现放疗计划的最优化。

总之，VMAT技术在宫颈癌PALN转移患者的放射治疗中，靶区适形性较IMRT更理想，更好地保护了肾脏、直肠、小肠等OAR，缩短了照射时间，减少患者在照射过程中的体位移动以及器官运动引起的误差。因此在宫颈癌PALN转移患者放疗中，VMAT技术是较IMRT更有优势的一种放疗技术。由于宫颈癌伴PALN转移患者病例数少，故本研究样本量较少，后期需要大样本进一步探索，且还需加强临床近远期疗效和不良反应的进一步评估。

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