

直肠癌术前不同照射技术剂量学比较

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【摘要】目的:通过比较常规放疗(Con-RT)、三维适形放疗(3DCRT)和调强放疗(IMRT)3种放疗计划模式的剂量分布,探讨直肠癌术前放疗的理想计划模式。**方法:**选取10例直肠癌术前患者,采用三维治疗计划系统对每例患者分别行3野Con-RT、3野三维适形(3DCRT₃)、5野三维适形(3DCRT₅)、5野调强放疗(IMRT₅)和7野调强放疗(IMRT₇)计划设计,利用剂量体积直方图(DVH)评价5种照射技术下靶区和危及器官的体积剂量分布,处方剂量为50 Gy。**结果:**Con-RT计划中肿瘤靶区(GTV)的最小剂量为(4991.5±69.1) cGy,靶区内有冷点。计划靶区(PTV)的适形指数(CI):IMRT₇>IMRT₅>3DCRT>Con-RT;PTV的剂量不均匀指数(HI):Con-RT>3DCRT₃>3DCRT₅>IMRT₅>IMRT₇。相比3DCRT计划,IMRT计划减少了小肠、膀胱、股骨头的V₄₀、V₅₀体积($P<0.05$)。**结论:**直肠癌术前放疗中Con-RT计划的靶区剂量分布不均,适形度差;相比于3DCRT计划,IMRT计划剂量分布均匀,适形度优,危及器官高剂量照射体积明显减少;在剂量分布和适形度方面,IMRT₇计划优于IMRT₅计划。

【关键词】直肠癌;常规放疗;三维适形放疗;调强适形放疗;剂量体积直方图

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Dosimetric comparison of different preoperative radiotherapy techniques for rectal cancer

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Abstract: Objective To discuss on the best preoperative radiotherapy plan for rectal cancer by evaluating the dose distribution of conventional radiotherapy (Con-RT), three-dimensional conformal radiotherapy (3DCRT) and intensity-modulated radiotherapy (IMRT). **Methods** Ten preoperative patients with rectal cancer were selected. Five plans were respectively designed for each patient by using 3D treatment planning system, including 3-field Con-RT plan, 3-field 3DCRT (3DCRT₃) plan, 5-field 3DCRT (3DCRT₅) plan, 5-field IMRT (IMRT₅) plan and 7-field IMRT (IMRT₇) plan. The volume-dose distribution of target volumes and organs at risk in the five plans were evaluated by using dose-volume histogram. The prescription dose was 50 Gy. **Results** The minimum dose of gross tumor volume in the Con-RT plan was (4991.5±69.1) cGy, and some cold spots were found in the target volume. The comparative result of conformity index (CI) of planning target volume (PTV) was IMRT₇>IMRT₅>3DCRT>Con-RT; the comparative result of homogeneity index of PTV was Con-RT>3DCRT₃>3DCRT₅>IMRT₅>IMRT₇. Compared with 3DCRT plan, IMRT plan reduced the V₄₀, V₅₀ of small intestine, bladder and femoral head ($P<0.05$). **Conclusion** The dose distribution of target volume in preoperative Con-RT plan for rectal cancer has unsatisfactory dose distribution and conformity. Compared with 3DCRT plan, IMRT plan has a satisfactory dose distribution and a good conformity, obviously reducing the high dose radiation volume of organs at risk. And IMRT₇ plan is superior to IMRT₅ plan in dose distribution and conformity.

Key words: rectal cancer; conventional radiotherapy; three-dimensional conformal radiotherapy; intensity-modulated radiotherapy; dose-volume histogram

前言

结直肠癌是我国常见的恶性肿瘤之一,手术是大多数直肠癌患者的首选,但是对于Ⅱ~Ⅲ期直肠癌,局部复发率高仍然是一个棘手的问题。直肠癌

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术前放化疗不但能降低局部复发率和总复发率,还提高了直肠癌患者保留肛门的几率^[1]。相对于常规放射治疗(Con-RT),三维适形放疗(3DCRT)和调强放疗(IMRT)技术已经广泛用于各种肿瘤的放射治疗中,本研究旨在通过比较3种计划模式的优缺点,探索更加理想的临床放疗方式,用于指导临床实践。

1 材料与方法

1.1 临床资料

本研究收集2011年2月至2012年6月期间在本院放疗科行直肠癌术前放疗的患者10例,术前病理诊断明确。根据UICC临床分期标准,10例患者均处于II期和III期,其中II期7例,III期3例。

1.2 CT扫描定位及图像采集

CT激光定位扫描,所有患者全部采取俯卧位,采用有孔腹部定位器+体膜固定体位。CT模拟定位扫描前空腹3 h,前1 h叮嘱患者排空膀胱和直肠,然后口服20%泛影葡胺15 mL+800 mL水,1 h后行CT增强扫描,扫描前静脉注射100 mL欧乃派克造影剂,采用GE AcQsim CT模拟定位机扫描,扫描从第四腰椎上缘开始到肛门下缘,扫描层厚为0.5 cm,层间距为0.5 cm。通过院内局域网将CT图像传至VARIAN ECLIPSE10.0三维适形治疗计划系统,在放射治疗计划系统(TPS)上对图像进行三维重建,调整窗宽和窗位至统一标准,勾画靶区和危及器官。

1.3 靶区及危及器官的勾画

由两位资深的肿瘤放疗医生在TPS三维重建图像上勾画肿瘤靶区(GTV)和临床靶区(CTV)。GTV的勾画可根据CT增强后肠壁外缘的光滑程度和肠壁的厚度以及MRI图像来确定肿瘤的大小和外侵范围。根据ICRU 62号报告,CTV的上界通常为腰5骶1椎体之间,下界为肿瘤下缘下3 cm,外界为真骨盆外1 cm,具体包括肿瘤原发灶、部分乙状结肠、盆腔侧壁、坐骨直肠窝,还包括闭孔淋巴结、髂内及部分髂总和(或)髂外血管周围淋巴结,以及膀胱部分后壁;其中女性患者应包括部分阴道和子宫后壁,男性还应包括前列腺和精囊腺后壁。计划靶区(PTV)通过CTV外放1 cm。对于危及器官,为便于各计划小肠受量评价,将小肠统一勾画至第5腰椎上缘,根据CT定位扫描图像依次画出膀胱、左右股骨头及肛管。

1.4 制定放射治疗计划

对每例患者分别行Con-RT、3野三维适形(3DCRT₃)、5野三维适形(3DCRT₅)、5野调强放疗

(IMRT₅)和7野调强放疗(IMRT₇)计划设计。Con-RT计划其实是虚拟常规治疗计划,传统Con-RT计划是采用模拟机下定位,模拟机透视下确定病灶中心,采用1后野加两水平侧野三野等中心照射。Con-RT计划采用CT模拟定位,射野中心为TPS根据PTV自动生成的等中心点,采用常规计划的三野布局,两侧野均为30°楔形板。使用多叶光栅(MLC)对3个射野进行模拟挡铅,虚拟Con-RT计划也采用等中心点剂量归一。3DCRT₃计划采用1后野加两侧野三野等中心照射,两侧野入射角度可根据患者的靶区形状调节两侧照射野的角度,所采用的楔形板也根据剂量分布调换。3DCRT₅计划射野角度分别为0°、45°、95°、265°和315°,可根据剂量分布调节楔形板的度数以及照射野的权重。IMRT₅计划射野角度分别为0°、50°、100°、260°和310°。IMRT₇计划射野角度分别为0°、33°、66°、100°、260°、327°和294°。3DCRT和IMRT的处方剂量规定为95% PTV接受的照射剂量,IMRT的GTV 100%的体积接受处方剂量照射。

1.5 处方剂量

5种计划的处方剂量均为50 Gy, 50 Gy/25次。

1.6 数据统计及评价参数

(1)GTV采用最小剂量(D_{\min})、最大剂量(D_{\max})和平均剂量(D_{mean})评价;(2)靶区PTV采用适形度指数(CI)和不均匀指数(HI)评价,根据ICRU 62号报告定义, $CI = V_{47.5}/V_{\text{PTV}}$, $HI = D_{5\%}/D_{95\%}$ ^[2]; (3)危及器官的评价参数:小肠的 V_{20} 、 V_{30} 、 V_{40} 、 V_{50} ,即通过DVH图评价小肠受20、30、40和50 Gy等剂量曲线所包括的小肠体积,膀胱的 V_{30} 、 V_{40} 、 V_{50} ,股骨头的 V_{30} 、 V_{40} 、 V_{50} ,肛管的 V_{50} 、 V_{55} 。

1.7 统计学分析

采用SPSS17.0软件进行统计学分析,所测数据采用均数±标准差,检验标准 $\alpha=0.05$,治疗计划各指标之间的比较采用配对样本 t 检验。

2 结果

2.1 3DCRT₃计划与Con-RT、3DCRT₅、IMRT计划的GTV剂量分布比较

直肠癌术前放疗与直肠癌术后放疗相比最大差异就是有明确的GTV。Con-RT计划的GTV所受最小剂量与3DCRT计划相比有显著差异($P<0.01$),说明3DCRT显著改善了Con-RT剂量不足的缺陷,IMRT较3DCRT改善了剂量均匀性。结果见表1。

2.2 3DCRT₃计划与Con-RT、3DCRT₅、IMRT计划的

PTV 剂量分布比较

5种计划的CI和HI的比较, CI: $\text{IMRT}_7 > \text{IMRT}_5 > 3\text{DCRT} > \text{Con-RT}$; HI: $\text{Con-RT} > 3\text{DCRT}_3 > 3\text{DCRT}_5 > \text{IMRT}_5 > \text{IMRT}_7$ 。结果见表2。

2.3 3DCRT₃计划与Con-RT、3DCRT₅、IMRT计划的小肠剂量分布比较

与3DCRT₃计划比较, Con-RT计划和3DCRT₅计划中, 小肠的 V_{20} 、 V_{30} 、 V_{40} 、 V_{50} 4组数据均无统计学意义($P > 0.05$)。3DCRT₃计划与两种IMRT计划相比较, IMRT的小肠 V_{40} 、 V_{50} 显著降低($P < 0.05$), 表明IMRT计划可以减少高剂量照射区的小肠体积, 同时低剂量区小肠的体积未明显增加。两种IMRT计划未有明显差别。小肠受照体积比的具体数值见表3。

2.4 3DCRT₃计划与Con-RT、3DCRT₅、IMRT计划的膀胱、股骨头、肛管剂量分布比较

与3DCRT₃计划比较, Con-RT计划的膀胱 V_{30} 和 V_{40} 没有明显差异($P > 0.05$), 膀胱 V_{50} 明显低于3DCRT₃计划($P < 0.01$), 这是由于Con-RT靠近膀胱后壁处剂量不足造成的; Con-RT计划的股骨头 V_{30} 和肛

管的 V_{55} 高于3DCRT₃计划($P < 0.05$)。两种3DCRT₃计划中, 膀胱、股骨头和肛管的受照体积未有显著差异。相对于3DCRT₃计划, IMRT计划中膀胱的 V_{30} 差异不明显, 但 V_{40} 和 V_{50} 显著减少($P < 0.05$), 表明IMRT可以减少膀胱的高剂量照射体积; 3DCRT₃计划中股骨头的 V_{30} 、 V_{40} 和 V_{50} 均高于IMRT计划, 这表明IMRT可以显著降低股骨头的受照剂量; 3DCRT₃和IMRT放疗中肛管 V_{55} 均为零。两种IMRT计划相比较, 膀胱、股骨头和肛管的受照剂量未有明显差异。具体数值见表4~表6。

3 讨论

直肠癌术前放疗, 由于盆腔血运未破坏, 肿瘤氧供充足, 放射生物学效应明显, 因而肿瘤缩小降期成为可能。本研究数据表明Con-RT计划中有3例患者GTV剂量不足, 7例病人髂内血管旁剂量分布不足, 小肠受量偏高。3DCRT₃计划改善了靶区剂量分布, 但小肠受量未改善。IMRT靶区适形度和剂量均匀度均明显优于3DCRT₃, 且小肠、股骨头、膀胱及肛管

表1 3DCRT₃计划与Con-RT、3DCRT₅、IMRT计划的GTV剂量分布比较($\bar{x} \pm s$, cGy)

Tab.1 Dose comparison of GTV between 3DCRT₃ and Con-RT, 3DCRT₅, IMRT ($\text{Mean} \pm \text{SD}$, cGy)

Parameter	Con-RT	3DCRT ₃	3DCRT ₅	IMRT ₅	IMRT ₇
D_{\min}	4991.5±69.1	5083.5±49.7	5139.8±39.1	5039.6±19.7	5033.2±16.3
	$P=0.003\ 4$		$P=0.205\ 9$	$P=0.023\ 7$	$P=0.011\ 3$
D_{\max}	5374.5±161.5	5383.2±137.7	5454.8±128.3	5334.7±16.3	5293.1±15.5
	$P=0.898\ 3$		$P=0.602\ 0$	$P=0.296\ 6$	$P=0.069\ 1$
D_{mean}	5226.4±80.5	5232.5±74.1	5391.3±69.8	5159.7±20.3	5105.4±17.8
	$P=0.862\ 0$		$P=0.000\ 1$	$P=0.013\ 0$	$P=0.000\ 4$

P values are the results of paired-sample t test between each program and 3DCRT₃.

GTV: Gross tumor volume; Con-RT: Conventional radiotherapy; 3DCRT₃: Three-field three-dimensional conformal radiotherapy; 3DCRT₅: Five-field three-dimensional conformal radiotherapy; IMRT₅: Five-field intensity-modulated radiotherapy; IMRT₇: Seven-field intensity-modulated radiotherapy

表2 3DCRT₃计划与Con-RT、3DCRT₅、IMRT计划PTV剂量分布比较

Tab.2 Dose comparison of PTV between 3DCRT₃ and Con-RT, 3DCRT₅, IMRT

Item	Con-RT	3DCRT ₃	3DCRT ₅	IMRT ₅	IMRT ₇
CI	0.69±0.03	0.75±0.02	0.76±0.02	0.86±0.02	0.89±0.01 ^a
	$P=0.000\ 0$		$P=0.053\ 6$	$P=0.000\ 0$	$P=0.000\ 0$
HI	1.23±0.02	1.10±0.01	1.09±0.01	1.06±0.01	1.05±0.01 ^b
	$P=0.000\ 0$		$P=0.027\ 3$	$P=0.000\ 0$	$P=0.000\ 0$

P values are the results of paired-sample t test between each program and 3DCRT₃. Compared with

IMRT₅, P value of ^a is 0.000 0, and P value of ^b is 0.000 0.

PTV: Planning target volume; CI: Conformity index; HI: Homogeneity index

表3 3DCRT₃计划与Con-RT、3DCRT₅、IMRT计划的小肠的剂量分布比较($\bar{x} \pm s$, %)Tab.3 Dose comparison of small intestine between 3DCRT₃ and Con-RT, 3DCRT₅, IMRT ($Mean \pm SD$, %)

Treatment plan	V ₂₀	V ₃₀	V ₄₀	V ₅₀
Con-RT	28.88±18.81	20.54±15.92	10.18±6.67	5.38±5.30
	<i>P</i> =0.719 9	<i>P</i> =0.378 3	<i>P</i> =0.247 4	<i>P</i> =0.527 8
3DCRT ₃	32.01±19.61	26.05±10.77	14.34±8.72	7.02±4.48
3DCRT ₅	29.94±18.33	24.45±10.08	15.67±8.56	7.44±4.90
	<i>P</i> =0.810 1	<i>P</i> =0.735 6	<i>P</i> =0.734 7	<i>P</i> =0.843 7
IMRT ₅	37.75±12.37	22.54±10.41	5.44±6.61	3.17±3.08
	<i>P</i> =0.445 7	<i>P</i> =0.468 2	<i>P</i> =0.019 9	<i>P</i> =0.039 7
IMRT ₇	37.35±12.16 ^b	20.46±9.92 ^b	4.18±3.35 ^b	2.27±2.09 ^b
	<i>P</i> =0.475 5	<i>P</i> =0.243 1	<i>P</i> =0.005 1	<i>P</i> =0.009 7

P values are the results of paired-sample *t* test between each program and 3DCRT₃.

Compared with IMRT₅, *P* values of ^b are respectively 0.9427, 0.6529, 0.5997, 0.4557.

表4 3DCRT₃计划与Con-RT、3DCRT₅、IMRT计划的膀胱剂量分布比较($\bar{x} \pm s$, %)Tab.4 Dose comparison of bladder between 3DCRT₃ and Con-RT, 3DCRT₅, IMRT ($Mean \pm SD$, %)

Treatment plan	V ₅₀	V ₄₀	V ₃₀
Con-RT	51.62±10.81	40.29±9.14	9.88±7.02
	<i>P</i> =0.295 9	<i>P</i> =0.783 7	<i>P</i> =0.000 4
3DCRT ₃	45.33±14.92	38.82±13.91	27.12±10.07
3DCRT ₅	45.14±14.45	35.49±13.58	23.96±9.93
	<i>P</i> =0.977 2	<i>P</i> =0.594 7	<i>P</i> =0.488 9
IMRT ₅	39.38±8.85	25.95±7.94	9.65±3.15
	<i>P</i> =0.295 6	<i>P</i> =0.023 2	<i>P</i> =0.000 3
IMRT ₇	36.54±8.02 ^b	22.91±8.04 ^b	7.75±2.77 ^b
	<i>P</i> =0.123 4	<i>P</i> =0.007 1	<i>P</i> =0.000 1

P values are the results of paired-sample *t* test between each program and 3DCRT₃. Compared with IMRT₅, *P* values of ^b are respectively 0.4619, 0.4061, 0.1695.

表5 3DCRT₃计划与Con-RT、3DCRT₅、IMRT计划的股骨头剂量分布比较($\bar{x} \pm s$, %)Tab.5 Dose comparison of femoral head between 3DCRT₃ and Con-RT, 3DCRT₅, IMRT ($Mean \pm SD$, %)

Treatment plan	V ₃₀	V ₄₀	V ₅₀
Con-RT	55.81±9.26	16.75±6.61	3.49±3.51
	<i>P</i> =0.015 6	<i>P</i> =0.743 4	<i>P</i> =0.541 1
3DCRT ₃	68.36±11.53	18.24±12.46	2.62±2.67
3DCRT ₅	67.53±10.83	17.97±12.18	2.45±1.98
	<i>P</i> =0.870 1	<i>P</i> =0.961 5	<i>P</i> =0.873 5
IMRT ₅	14.62±8.72	4.79±3.69	0.00±0.00
	<i>P</i> =0.000 0	<i>P</i> =0.007 8	<i>P</i> =0.012 7
IMRT ₇	14.93±6.44 ^b	4.66±2.81 ^b	0.00±0.00
	<i>P</i> =0.000 0	<i>P</i> =0.007 3	<i>P</i> =0.012 7

P values are the results of paired-sample *t* test between each program and 3DCRT₃. Compared with IMRT₅, *P* values of ^b are respectively 0.9290, 0.9304.

受量均有改善。IMRT₇计划优于IMRT₅计划。姚波等^[3]和胡克等^[4]对直肠癌术前放疗患者的研究也表明IMRT较3DCRT能改善靶区均匀度。是否IMRT射野越多越好?李宝生等^[5]从理论上讲射野数越多,IMRT剂量分布越好,但当射野大于10个后,并不会明显提高剂量优化。

小肠属于对放射线反应敏感器官。在直肠癌放疗中小肠是最主要剂量限制器官,小肠照射剂量与小肠的早期和晚期毒性反应呈正相关性^[6-8]。且照射剂量在45 Gy以上的小肠体积与放射损伤的发生率

密切相关,减少小肠的照射剂量是避免放射性损伤的主要方法^[9]。Celia等^[10]用3DCRT代替常规三野方案显示改善了靶区剂量分布,而小肠及膀胱照射剂量未增加。Engels等^[11]用IMRT替代3DCRT,发现剂量分布与靶区高度吻合,高剂量区的小肠体积明显减少,从而减少了小肠的损伤几率。Urbano等^[12]研究也得出类似的结论。且由于直肠癌术前放疗小肠未降入盆腔,减少了照射野范围内的小肠受照体积;而且相对于直肠癌术后小肠容易粘连,术前放疗时小肠活动良好,因此术前放疗较术后放疗可以降低

表6 3DCRT₃计划与Con-RT、3DCRT₅、IMRT计划的肛管剂量分布比较($\bar{x} \pm s$, %)

Tab.6 Dose comparison of anal canal between 3DCRT₃ and Con-RT, 3DCRT₅, IMRT (Mean \pm SD, %)

Treatment plan	V ₅₀	V ₅₅
Con-RT	35.21 \pm 10.53	2.07 \pm 2.11
	P=0.435 4	P=0.012 7
3DCRT ₃	30.75 \pm 14.16	0.00 \pm 0.00
3DCRT ₅	29.64 \pm 17.13	0.00 \pm 0.00
	P=0.876 3	
IMRT ₅	31.34 \pm 7.86	0.00 \pm 0.00
	P=0.909 9	
IMRT ₇	30.26 \pm 8.12 ^b	0.00 \pm 0.00
	P=0.925 7	

P values are the results of paired-sample *t* test between each program and 3DCRT₃. Compared with IMRT₅, P value of ^b is 0.7660.

小肠放射性损伤。FFCD-9203 试验^[13]、German-CAO/ARO-94 试验^[14]和 NSABP R-03 随机试验^[15]都证实术前放化疗较术后放化疗降低了小肠的毒副作用。由于开展直肠癌术前 IMRT 临床研究时间较短,能否降低小肠远期毒副作用,还需要做更多的临床。

本研究中 3DCRT₃ 中膀胱 V₅₀ 体积百分比为 27.12%, 而 IMRT₅ 计划中为 9.65%, 两者相比有显著差异 ($P < 0.01$)。由于膀胱的毒副作用与照射体积和剂量有关, 因此理论上 IMRT 在直肠癌术前放疗中可降低膀胱的毒副作用发生率。股骨头的放疗损伤与 V₅₀ 的体积有关, 两种 IMRT 的 V₅₀ 均为零, 优势明显。因部分肛管包绕在 PTV 内, IMRT 与 3DCRT 相比较, 优势不明显, 3DCRT 计划和 IMRT 计划的肛管 V₅₅ 均为零, 而 Con-RT 为 2.07%, 这与 Con-RT 高剂量区明显靠近骶前区分布有关。

综上所述, Con-RT 不符合临床剂量学要求, 尽量避免使用。IMRT 在剂量分布和小肠等危及器官保护方面明显优于 3DCRT。IMRT₇ 计划在适形度和剂量均匀性方面优于 IMRT₅ 计划。

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