DOI:10.3969/j.issn.1005-202X.2017.07.015

医学放射物理

不同类型多叶准直器对左侧乳腺癌保乳术后容积旋转调强放疗技术剂量分布的影响

张富利，许卫东，蒋华勇，王雅棣，高军茂，刘清智，路娜，陈点点，姚波，侯俊，陈建平，何合良
解放军陆军总医院放疗科，北京 100700

【摘 要】目的： 探讨3种不同类型多叶准直器对乳腺癌保乳术后容积旋转调强放疗（VMAT）计划剂量分布的影响。**方法：** 选择11例早期乳腺癌保乳术后患者，分别基于配置MLCi2、Agility多叶准直器（A-MLC）和Beam Modulator多叶准直器（B-MLC）的医科达直线加速器在Monaco治疗计划系统（TPS, version 5.1, Elekta, Sweden）上进行VMAT放疗设计。依据剂量体积直方图分析两种计划在靶区均匀性指数（HI）、适形度指数（CI）和一系列危及器官（OAR）剂量体积参数。**结果：** 就靶区而言，A-MLC较之MLCi2的VMAT计划的HI和CI分别提高约26.3%和10.8%；B-MLC较之MLCi2的VMAT计划的HI和CI分别提高15.8%和9.2%。就OAR而言，除患侧肺V_5、V_{10}和心脏V_5、V_{20}外，其余的剂量体积参数差异均无显著性意义（P>0.05）。A-MLC的VMAT计划实施效率较之MLCi2和B-MLC的VMAT计划分别提高6.2%和30.4%。**结论：** 与基于MLCi2的VMAT计划相比，A-MLC和B-MLC的VMAT计划提高了靶区的HI和CI。A-MLC的VMAT计划靶区剂量分布最佳，OAR的受照体积也最低，而且实施效率最高。总之，VMAT技术在剂量学和治疗实施效率方面具有一定优势，但仍需临床试验和长期随访来评估其临床价值。

【关键词】 乳腺癌；保乳术；多叶准直器；危及器官；容积旋转调强放疗
【中图分类号】 R730.55 **【文献标志码】** A **【文章编号】** 1005-202X(2017)07-0726-05

Effect of different types of multilead collimators on the dose distribution in volumetric-modulated arc therapy following breast-conservative surgery for left breast cancer

ZHANG Fuli, XU Weidong, JIANG Huayong, WANG Yadi, GAO Junmao, LIU Qingzhi, LU Na, CHEN Diandian, YAO Bo, HOU Jun, CHEN Jianping, HE Heliang
Department of Radiation Oncology, General Hospital of Chinese People's Liberation Army, Beijing 100700, China

Abstract: Objective To compare the impacts of 3 types of multileaf collimators (MLC), namely MLCi2, Agility WLC (A-MLC) and Beam Modulator-MLC (B-MLC), on the dose distribution in the volumetric modulated arc therapy (VMAT) for postoperative patients receiving breast-conservative surgery for left breast cancer. **Methods** Based on the Monaco treatment planning system (version 5.1, Elekta, Sweden), VMAT plans using MLCi2, A-MLC and B-MLC were designed for 11 postoperative patients receiving breast-conservative surgery for early-stage breast cancer. The conformity index (CI) and homogeneity index (HI) of target areas and the dose-volume parameters of organs-at-risk (OAR) were compared using dose volume histogram. **Results** As compared with those in VMAT plan using MLCi2, the HI and CI of target areas in VMAT plan using A-MLC were improved by 26.3% and 10.8%, respectively, while those in VMAT plan using B-MLC were increased by 15.8% and 9.2%, respectively. Except for the V_5, V_{10} of ipsilateral lung and the V_5, V_{20} of heart, no significant differences were found in the dose-volume parameters of OAR (P>0.05). The VMAT plan using A-MLC had a higher delivery efficiency than VMAT plan using MLCi2 and B-MLC (increasing by 6.2% and 30.4%, respectively). **Conclusion** Compared with VMAT plan using MLCi2, VMAT plan using A-MLC or B-MLC improves the HI and CI of the target areas. Among the 3 plans, VMAT plan using A-MLC has the optimal target dose distribution, the lowest irradiated volume of OAR, and the highest delivery efficiency. Though VMAT technique has advantages in dosimetry and delivery efficiency, clinical trials and long-term follow-up are required to evaluate the clinical significance of VMAT technique.

Keywords: breast cancer; breast-conservative surgery; multileaf collimator; organs-at-risk; volumetric modulated arc therapy

【收稿日期】 2017-02-28
【基金项目】 陆军总医院院创新基金科研课题（2015-LC-18）
【作者简介】 张富利，主要从事肿瘤放射物理和保健物理相关技术研究，E-mail: wangyadi5588@163.com
【通信作者】 王雅棣，E-mail: wangyadi@hotmail.com

前 言

保乳手术联合术后辅助全乳腺放疗是早期乳腺癌的主要治疗手段之一,长期随机临床研究随访发现,其总生存率和无病生存率与乳腺癌根治手术相似[1-3]。有研究显示,容积旋转调强放射治疗(VMAT)技术能够提高乳腺剂量适形度和均匀度,降低周围正常组织受照剂量[4-7]。笔者通过评估3种不同类型多叶准直器(Multileaf Collimator, MLC)对乳腺癌保乳术后VMAT放疗技术剂量分布的影响,为临床应用和设备选择提供借鉴。

VMAT技术是在固定野调强放疗(IMRT)技术上伴随设备、计算机、医学图像技术的发展而产生的一种调强新技术。与常规三维适形放疗和IMRT技术相比,VMAT技术实施过程中机架转速、MLC叶片和剂量率同时变化以获得调制级更高的放疗计划。VMAT技术已广泛应用于各类肿瘤的放疗并获得了良好的临床效果[8-12]。

本文分别基于配置MLCi2、Agility多叶准直器(A-MLC)和Beam Modulator多叶准直器(B-MLC)的医科达直线加速器(Elekta AB, Stockholm, Sweden),设计乳腺癌保乳术后VMAT放疗计划,分析比较3种不同类型MLC对VMAT计划剂量分布的影响,为临床应用和设备购置提供一定参考。

1 材料与方法

1.1 临床资料选择

采用回顾性分析方法,随机选择2006年9月~2016年1月接受左侧乳腺癌保乳术后放疗的11例患者,年龄38~63岁,中位年龄55岁。

1.2 MLC类型

MLCi2由40对叶片构成,在等中心处投影宽度为10 mm,可形成的最大射野为40 cm×40 cm,叶片最大移动速度为2 cm/s。相对叶片之间间隙至少为5 mm。叶片下方为自动射野跟随的备份光阑,同侧MLC最大移动距离为32.5 cm,可过中心线12.5 cm,MLCi2能够形成孤岛野。

A-MLC由80对叶片构成,在等中心处投影宽度为5 mm,可形成最大射野为40 cm×40 cm,叶片最大移动速度为3.5 cm/s,或者联合DLG(Dynamic Leaf Guide)功能情况下达到6.5 cm/s,叶片可形成孤岛野[13]。

B-MLC由40对叶片构成,在等中心处投影宽度为4 mm,最大射野尺寸为21 cm×16 cm。叶片最大移动速度为3 cm/s。相对叶片间最小间隙为5 mm,叶片也可形成孤岛野。

将分别配置了上述3种不同类型MLC的加速器在Monaco治疗计划系统(version 5.1, Elekta AB, Stockholm, Sweden)中予以建模,并依据厂家技术手册中提供的测试包验证射束模型从而保证MLC建模的准确性[14]。

1.3 体位固定和CT扫描

患者放疗前需先行CT螺旋扫描,应用85 cm大孔径CT模拟定位机(Bigbore, Brilliance, Philips, Holland)。患者仰卧于乳腺托架(Medtec, USA)上,双侧上臂举过头顶握住特定支架。扫描范围上至锁骨上区,下达肾上腺区。

1.4 靶区、危及器官(OAR)界定及处方剂量要求

将获取的患者CT图像经由专用网络传输至Pinnacle³ 9.2 f(ADAC Inc. Philips, Holland)治疗计划工作站,由专业放射肿瘤医师依据ICRU 62、83号报告[15-16]依次勾画临床靶区(CTV)、计划靶区(PTV)和各OAR,包括左右肺、心脏、对侧乳腺、左冠状动脉(LAD)、右冠状动脉(RCA)。CTV包括皮肤下0.5 cm乳腺腺体和腺体下胸壁。而PTV由CTV外放得到,在头脚方向、乳腺内侧向胸骨方向、外侧向腋窝方向各自外放1 cm,胸壁内侧向肺部方向外放0.5 cm,皮肤方向不外放以抵消建成效应的影响。处方剂量50 Gy,采用常规分割模式,治疗25次。

1.5 计划设计

每位患者的3个VMAT计划在Monaco计划工作站上完成,选用6 MV X线。采用两个部分弧(partial-arc),起始角度为170°,终止角度为310°。由于B-MLC所能形成的最大射野为21 cm×16 cm,为了完全包绕靶区,故将小机头旋转90°[10],为了尽量保证计划比较时标准一致,设计计划时将S-MLC和A-MLC的小机头也旋转90°。OAR的剂量限定条件列于表1中,LAD和RCA未给予剂量体积限定条件,仅用于评估。

表1 OAR剂量体积限制条件

Tab.1 Dose-volume constraint for organs-at-riak (OAR)

OAR	Dose/Gy	Volume/%
Ipsilateral lung	30	<20
	20	<30
	10	<55
Contralateral breast	3	<15
Contralateral lung	3	<10
Heart	30	<8

1.6 计划比较

根据3种VMAT治疗计划在靶区最大剂量(D_{max})(2%的靶区体积对应的剂量)、最小剂量(D_{min})(98%的靶区体积对应的剂量)、平均剂量(D_{mean})、均匀性指数(HI)[16]、适形性指数(CI)[17],OAR的评估参数为受到特定剂量水平照射的OAR体积百分比。

1.7 统计学方法

统计学分析采用SPSS 18.0统计软件(IBM Inc. USA),统计学方法采用单因素方差分析(one-way analysis of variance),显著性水平α=0.05。

2 结 果

2.1 PTV剂量参数

3种VMAT放疗计划的靶区剂量分布如表2所示。ICRU83号报告[16]中将靶区的D_{max}定义为大于等于2%靶区体积接受的剂量,将靶区的D_{min}定义为大于等于98%靶区体积接受的剂量。本研究中3种VMAT放疗计划的D_{max}差异有显著性意义(P=0.048),D_{min}差异无显著性意义(P=0.128),而D_{mean}差异有显著性意义(P=0.047)。

表2 3种VMAT计划PTV剂量分布($\bar{x}\pm s$)

Tab.2 Dose distribution of PTV in VMAT plans using MLCi2, A-MLC and B-MLC (*Mean±SD*)

Paramete	MLCi2	A-MLC	B-MLC	*F* value	*P* value
D_{max}/Gy	57.88±2.45	55.59±1.87	56.43±1.92	3.364	0.048
D_{min}/Gy	47.43±1.01	48.29±0.89	47.94±0.99	2.199	0.128
D_{mean}/Gy	54.62±1.70	53.02±1.30	53.54±1.38	3.393	0.047
HI	0.19±0.05	0.14±0.05	0.16±0.05	3.058	0.062
CI	0.65±0.21	0.72±0.23	0.71±0.23	0.313	0.733

PTV: Planning target volume; VMAT: Volumetric modulated arc therapy; HI: Homogeneity index; CI: Conformity index

2.2 OAR剂量、体积参数

患侧肺、心脏、LAD、对侧肺、对侧乳腺的剂量和受照体积参数参见表3。

表3 3种VMAT治疗计划危及器官剂量体积参数比较(%, $\bar{x}\pm s$)

Tab.3 Comparison of OAR dose-volume parameters among three VMAT plans (%, *Mean±SD*)

OAR	Parameter	MLCi2	A-MLC	B-MLC	*F* value	*P* value
Ipsilateral lung	V_5/%	75.05±9.68	65.29±7.74	82.46±5.57	13.268	0.000
	V_{10}/%	48.30±5.81	40.80±6.01	50.47±5.56	8.429	0.001
	V_{20}/%	29.48±4.78	25.18±4.71	27.89±4.25	2.473	0.101
	V_{30}/%	20.20±4.47	16.45±3.94	17.85±3.94	2.328	0.115
Contralateral breast	V_3/%	11.25±3.91	9.48±2.48	12.98±3.28	3.149	0.057
Contralateral lung	V_3/%	7.77±2.16	7.60±2.31	8.76±2.47	0.808	0.455
	V_5/%	1.67±0.94	2.13±1.21	1.86±1.12	0.503	0.609
Heart	V_5/%	65.01±7.91	64.70±6.83	74.15±7.59	5.706	0.008
	V_{10}/%	37.33±8.14	36.01±8.28	40.81±10.47	0.829	0.446
	V_{20}/%	15.68±2.60	12.22±2.87	12.34±3.40	4.778	0.016
	V_{30}/%	7.26±3.01	4.92±2.10	5.31±2.20	2.828	0.075
LAD	D_{mean}/Gy	24.73±5.59	22.57±6.63	24.63±7.17	0.386	0.683
RCA	D_{mean}/Gy	4.81±2.33	4.36±1.27	5.25±1.90	0.625	0.542

LAD: Left anterior descending (coronary artery); RCA: Right coronary artery

本研究中3种VMAT放疗计划患侧肺的V_5、V_{10}差异有显著性意义（P=0.000, P=0.001），而V_{20}、V_{30}差异无显著性意义（P=0.101, P=0.115）；对侧乳腺V_3差异无显著性意义（P=0.057）；对侧肺V_3、V_5差异均无显著性意义（P=0.455, P=0.609）；心脏V_5、V_{20}差异有显著性意义（P=0.008, P=0.016），而V_{10}、V_{30}差异无显著性意义（P=0.446, P=0.075）；LAD和RCA差异均无显著性意义（P=0.683, P=0.542）。

2.3 实施效率

3种治疗计划的实施效率见表4，3种VMAT放疗计划实施需要的MU数差异无显著性意义（P=0.842），实施时间差异有显著性意义（P=0.000）。

表4 3种治疗计划的MU和治疗时间（$\bar{x}\pm s$）

Tab.4 Comparison of monitor units and treatment delivery time among 3 plans (*Mean±SD*)

Parameter	MLCi2	A-MLC	B-MLC	*F* value	*P* value
Monitor units/MU	1 169.1±170.2	1 215.6±281.6	1 166.3±195.0	0.173	0.842
Treatment delivery time/min	2.91±0.19	2.73±0.50	3.92±0.21	41.195	0.000

3 讨论

MLC是现代放疗技术发展中的一项重要发明，在VMAT实施过程中发挥着举足轻重的作用[18]。叶片宽度对于靶区剂量的雕刻和强度调制程度影响较大。许多研究探讨了MLC宽度对于不同部位肿瘤VMAT计划的影响。Chae等[19]比较了2.5和5.0 mm宽度MLC在椎体病变VMAT放疗技术中的差别，发现2.5 mm MLC的VMAT计划具有更好的靶区适形度和均匀度。在一项探讨MLC宽度对头颈部肿瘤VMAT计划影响的研究中，Hong等[20]发现2.5 mm宽度MLC较之5.0 mm宽度MLC提高了靶区适形度，同时降低脊髓的受照剂量。Lafond等[21]比较10和4 mm MLC在16例头颈部肿瘤VMAT计划中的差异，采用4 mm MLC设计的VMAT计划的HI和CI分别提高7.9%和4.7%。本研究中，基于MLCi2、A-MLC、B-MLC的VMAT计划的HI、CI差异均无显著性意义，进一步行最小显著性差异法分析发现，A-MLC较之MLCi2的VMAT计划的HI明显改善，提高约26.3%，而A-MLC较之MLCi2的VMAT计划的CI亦提高约10.8%；B-MLC较之MLCi2的VMAT计划的HI和CI分别提高15.8%和9.2%，与Lafond等研究结果一致。Blümer等[22]比较了分别采用5和10 mm MLC在肛管癌、头颈部肿瘤和前列腺癌VMAT计划中的差异，结果显示，5 mm MLC的VMAT计划靶区HI和CI均优于10 mm MLC的VMAT计划。然而，该研究中5和10 mm MLC的VMAT计划多数OAR的剂量体积参数差异并无显著性差异。本研究中，除患侧肺V_5、V_{10}和心脏V_5、V_{20}差异有显著性意义外，其余均无显著性差异。

与B-MLC相比较，MLCi2和A-MLC的VMAT计划中患侧肺、对侧肺、对侧乳腺的低剂量受照区域（患侧肺V_5和V_{10}、对侧乳腺V_3、对侧肺V_3、心脏V_5和V_{10}）均小于B-MLC的VMAT计划。原因可能在于A-MLC的平均透射率大约仅为0.3%，尽管MLCi2的平均透射率与B-MLC的大致相同，约为0.6%~0.7%，但因MLCi2下方有备份光阑，故而可在一定程度上进一步降低透射率。A-MLC叶片移动速度最快，因而计划实施效率大幅提升，本研究中，A-MLC的VMAT计划较之MLCi2和B-MLC分别提高6.2%和30.4%，有利于保证患者治疗过程中的舒适度和体位的重复性，并有助于降低分次内器官移动对治疗效果的影响。

对于接受放疗的乳腺癌患者而言，VMAT技术在剂量学和治疗实施效率方面具有一定优势，但仍需临床试验和长期随访来评估其临床价值[23]。

【参考文献】

[1] FISHER B, JEONG J H, ANDERSON S, et al. Twenty-five-year follow-up of a randomized trial comparing radical mastectomy, total mastectomy, and total mastectomy followed by irradiation[J]. N Engl J Med, 2002, 347(16): 567-575.

[2] VERONESI U, CASCINELLI N, MARIANI L, et al. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer[J]. N Engl J Med, 2002, 347(16): 1227-1232.

[3] RUSTHOVEN K E, CARTER D L, HOWELL K, et al. Accelerated partial-breast intensity-modulated radiotherapy results in improved dose distribution when compared with three-dimensional treatment-planning techniques[J]. Int J Radiat Oncol Biol Phys, 2008, 70(1): 296-302.

[4] PEREZ C A, PAJAK T F, RUBIN P. Long-term observations of the patterns of failure in patients with unresectable non-oat cell carcinoma of the lung treated with definitive radiotherapy: report of the radiation therapy oncology group[J]. Cancer, 1987, 59(11): 1874-1881.

[5] VANETTI E, CLIVIO A, NICOLINI G, et al. Volumetric modulated arc radiotherapy for carcinomas of the oropharynx, hypopharynx and larynx: a treatment planning comparison with fixed field IMRT[J]. Radiother Oncol, 2009, 92(1): 111-117.

[6] LU S H, CHENG C H, KUO S H, et al. Volumetric modulated arc therapy for nasopharyngeal carcinoma: a dosimetric comparison with tomotherapy and step-and-shoot IMRT[J]. Radiother Oncol, 2012, 104(3): 324-330.

[7] MCGRATH S D, MATUSZAK M M, YAN D, et al. Volumetric modulated arc therap for delivery of hypofractionated stereotactic lung radiotherapy: a dosimetric and treatment efficiency analysis[J]. Radiother Oncol, 2010, 95(2): 153-157.

[8] HAERTL P M, POHL F, WEIDNER K, et al. Treatment of left sided breast cancer for a patient with funnel chest: volumetric-modulated arc therapy *vs* 3D-CRT and intensity-modulated radiotherapy[J]. Med Dosim, 2013, 38(1): 1-4.

[9] WANG J, LI X, DENG Q, et al. Postoperative radiotherapy following mastectomy for patients with left-sided breast cancer: a comparative dosimetric study[J]. Med Dosim, 2015, 40(3): 190-194.

[10] QI X S, LIU T X, LIU A K, et al. Left-sided breast cancer irradiation using rotational and fixed-field radiotherapy[J]. Med Dosim, 2014, 39(3): 227-234.

[11] PASLER M, GEORG D, BARTELT S, et al. Node-positive left-sided breast cancer: does VMAT improve treatment plan quality with respect to IMRT?[J]. Strahlenther Onkol, 2013, 189(5): 380-386.

[12] SCORSETTI M, ALONGI F, FOGLIATA A, et al. Phase I-II study of hypofractionated simultaneous integrated boost using volumetric modulated arc therapy for adjuvant radiation therapy in breast cancer patients: a report of feasibility and early toxicity results in the first 50 treatments[J]. Radiat Oncol, 2012, 7(1): 145.

[13] NING Z H, MU J M, JIN J X, et al. Single arc volumetric-modulated arc therapy is sufficient for nasopharyngeal carcinoma: a dosimetric comparison with dual arc VMAT and dynamic MLC and step-and-shoot intensity-modulated radiotherapy[J]. Radiat Oncol, 2013, 8(1): 237.

[14] Elekta. Monaco training guide[R]. 2013.

[15] International Commission on Radiation Units and Measurements (ICRU). Report number 62. Prescribing, recording and reporting photon beam therapy[R]. Washington: ICRU, 1999.

[16] International Commission on Radiation Units and Measurements (ICRU). Report number 83. Prescribing, recording, and reporting photon-beam intensity-modulated radiation therapy (IMRT)[R]. Washington: ICRU, 2010.

[17] WEISS E, SIEBERS J V, KEALL P J. An analysis of 6-MV *versus* 18-MV photon energy plans for intensity-modulated radiation therapy (IMRT) of lung cancer[J]. Radiother Oncol, 2007, 82(1): 55-62.

[18] DEVITA V T, ROSENBERG S A. Two hundred years of cancer research[J]. N Engl J Med, 2012, 366(23): 2207-2214 .

[19] CHAE S M, LEE G W, SON S H. The effect of multileaf collimator leaf width on the radiosurgery planning for spine lesion treatment in terms of the modulated techniques and target complexity[J]. Radiat Oncol, 2014, 9(1): 72.

[20] HONG C S, JU S G, KIM M, et al. Dosimetric effects of multileaf collimator leaf width on intensity-modulated radiotherapy for head and neck cancer[J]. Med Phys, 2014, 41(2): 021712.

[21] LAFOND C, CHAJON E, DEVILLERS A, et al. Impact of MLC leaf width on volumetric-modulated arc therapy planning for head and neck cancers[J]. J Appl Clin Med Phys, 2013, 14(6): 4074.

[22] BLÜMER N, SCHERF C, KOHN J, et al. New possibilities for volumetric-modulated arc therapy using the Agility 160-leaf multileaf collimator[J]. Strahlenther Onkol, 2014, 190(1): 1066-1074.

[23] POPESCU C C, OLIVOTTO I A, BECKHAM W A, et al. Volumetric modulated arc therapy improves dosimetry and reduces treatment time compared to conventional intensity-modulated radiotherapy for locoregional radiotherapy of left-sided breast cancer and internal mammary nodes[J]. Int J Radiat Oncol Biol Phys, 2010, 76(1): 287-295.

(编辑:陈丽霞)