Oncology and Translational Medicine
DOI 10.1007/s10330-018-0302-2

October 2018, Vol. 4, No. 5, P208–P214

ORIGINAL ARTICLE

Dosimetric evaluation of VMAT radiation therapy technique for breast cancer after conservative surgery based on three different types of multileaf collimators

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Abstract

Objective Radiotherapy combined with conservative surgery plays an important role in the treatment of early-stage breast cancer. Volumetric modulated arc therapy (VMAT) has been introduced into clinical practice. The purpose of this study was to investigate the dosimetric effects of different multileaf collimators (MLC) on VMAT radiotherapy plans for treating breast cancer.

Methods Fifteen breast cancer patients who were treated using a conventional technique in our department were selected to participate in this retrospective analysis. VMAT plans based on three types of Elekta MLCs [Beam Modulator (BM) with 4-mm leaf width, Agility with 5-mm leaf width and MLCi2 with 10-mm leaf width] were independently generated for each patient. Plan comparisons were performed based on dose-volume histogram (DVH) analysis including dosimetric parameters such as the homogeneity index (HI), conformity index (CI), Dmax, Dmin, and Dmean for the planning treatment volume (PTV), in addition to dose-volume parameters for the organs at risk (OARs). The delivery efficiency of the three types of MLCs was compared in terms of the beam delivery time and the monitor units (MUs) per fraction for each plan.

Results Both target uniformity and conformity were improved in plans for Agility and BM MLC compared with the plan using MLCi2. The mean HI decreased from 1.14 for MLCi2 to 1.13 for BM and 1.10 for Agility, while the mean CI increased from 0.68 for MLCi2 to 0.73 for BM and 0.75 for Agility. Furthermore, at both low and high dose levels, smaller volumes of ipsilateral lung, heart, contralateral lung, and breast were irradiated with Agility MLC than with the other two types of MLCs. The delivery time with Agility MLC was reduced by 10.8% and 32.1%, respectively, compared with that for MLCi2 and BM.

Conclusion Our results indicate that the Agility MLC exhibits a dosimetric advantage and a significant improvement in delivery efficiency for the treatment of breast cancer using VMAT.

Received: 17 September 2018
Revised: 29 September 2018
Accepted: 9 October 2018

Key words: multileaf collimator; leaf width; volumetric modulated arc therapy (VMAT); breast cancer; agility; MLCi2; beam modulator (BM)

Whole breast irradiation (WBI) combined with conservative surgery is a well-established treatment for early-stage breast cancer. Long-term follow-up of randomized trials have shown comparable overall survival and disease-free survival results for conservative surgery and WBI compared with mastectomy [1–3]. Conventionally, two tangential beams with paired wedges are employed to treat the breast and chest wall tissue. Additional megavoltage electron fields abutting photon fields are often used to treat the supraclavicular (SV), axillary, and internal mammary lymph nodes [4–5]. Treatment planning and delivery techniques have advanced significantly in the past two decades as external beam radiation therapy has evolved from conventional wedged tangential fields to three-dimensional conformal radiation therapy (3DCRT) and intensity-modulated radiation therapy (IMRT).

Volumetric modulated arc therapy (VMAT) is a rotational IMRT technique was introduced into clinical practice over six years ago. VMAT can achieve a high degree of intensity modulation by simultaneously varying the dose rate, gantry rotation speed, and MLC speed. A series of studies have shown that VMAT

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results in at least equivalent and possibly better target dose distributions with the same or better organs at risk (OARs) sparing compared to IMRT or 3DCRT. More importantly, this approach facilitates a remarkable improvement in delivery efficiency with a significant reduction in the number of monitor units (MUs) compared to conventional IMRT [6–16].

Several types of MLCs with different widths are available for different VMAT treatment plans. There is a body of literature based on the investigation of the impact of the MLC leaf width on VMAT treatment planning for several tumor sites including head and neck, rectum, and prostate, etc. [17–23]. However, to the best of our knowledge, no comparative studies on the dosimetric effects of the MLC leaf width on VMAT planning for breast cancer after conservative surgery has been conducted. This study investigated the impact of different MLCs on the treatment of breast cancer with VMAT by comparing the treatment plans for 15 patients using Elekta Agility, MLCi2, and Beam Modulator™ (BM) (Elekta AB, Sweden).

Materials and methods

Patient selection and simulation

Fifteen patients with T1N0 breast carcinoma (10 left-sided and 5 right-sided) who were initially treated using 3DCRT or fixed field IMRT in our clinic were selected for this retrospective analysis based on VMAT planning. The median age of the patients was 51 years (range: 39–63 years). The patients were simulated in the supine position with both arms raised above the head. The computed tomography (CT) imaging was performed using a Philips Brilliance BigBore simulator (Philips Medical Systems, Madison, WI) from the level of the larynx to the bottom of the lungs with a 5-mm slice thickness and slice spacing. The study was approved by the ethics committee of Chinese PLA Army General Hospital. All patients provided written consent for storage of their medical information in the hospital's database and for research use.

Contouring of target volumes and organs at risk

The delineation of the target and critical structures for all patients was performed by a single expert radiation oncologist in breast cancer treatment. For the 15 cases without regional lymph node involvement, the clinical target volume (CTV) consisted of the lumpectomy cavity with a margin of 15-mm, modified to stay within the glandular tissue identified using the CT scan. The planning target volume (PTV) was constructed by adding a 5-mm margin to the CTV and retracting the PTV to the tissue inside 3-mm of the skin, to account for dose build-up during dose calculation. The delineated organs at risk (OARs) consisted of the double lung, the heart, and the contralateral breast.

Collimator specification and modeling

The Agility MLC has 80 pairs of leaves of 5-mm width at the isocenter, and the maximum field size was 40 cm × 40 cm. The maximum leaf speed was 3.5 cm s^{-1}, or up to 6.5 cm s^{-1}, combined with a dynamic leaf guide [24] and the leaves can interdigitate.

The MLCi2 has 40 pairs of leaves with a 10-mm leaf width at the isocenter. The maximum field size was 40 cm × 40 cm. The maximum leaf speed was 2 cm s^{-1} and there was a minimum gap of 5 mm between opposite leaves. Under the leaves, there were auto tracking backup diaphragms that were movable during the treatment to minimize leakage. A set of perpendicular jaws were also movable during the treatment. The maximum distance between leaves on the same leaf guide was 32.5 cm, and a leaf can move over the central axis up to a distance of 12.5 cm. MLCi2 can also interdigitate.

The BM MLC has 80 leaves with a leaf width of 4-mm at the isocenter, and the maximum field size was 21 cm × 16 cm. The leaf can move at the maximum speed of 3 cm s^{-1}. The minimum gap between opposite leaves was 5 mm and the maximum distance between leaves on the same leaf guide was 21 cm (full field travel). The leaves have the ability to interdigitate.

Three accelerators equipped with three types of MLCs were modeled in the Monaco treatment planning system (version 5.00.02, Elekta AB, Sweden). The beam models were validated using 8 specific fields in a standard QA package called 'ExpressQAPlan'. This package was described in Elekta technical document [25] to ensure the accuracy of the MLC modeling.

VMAT planning and verification

All VMAT plans were generated on the Monaco system using 6 MV photon beams from am Elekta Axesse™ linac with Agility MLC, a Synergy™ linac with MLCi2, and a Synergy S™ linac with BM.

For each patient, three VMAT plans were created. The couch angle was set at 0° for all the plans and the collimator angle was set at 90°. Two partial arcs at 220°ranging from 50° to 190° for the right-sided tumors and from 170° to 310° for the left-sided tumors were used. These angles were chosen to avoid direct irradiation to the spinal cord, contralateral breast, and contralateral lung. The prescribed dose to the PTV was 50 Gy in 25 fractions. The plans were normalized to cover 95% of the PTV with 100% of the prescribed dose. The optimization objectives and constraints that were listed in Table 1 were the same for all plans. In order to ensure equitable dosimetric comparisons, identical objectives functions were utilized for all three machines. The dose calculation

Table 1 Dose-volume constraints for PTV and OARs

Structures	Volume (%)	Dose (Gy)
PTV	95	50
Heart	≤ 10	30
Contralateral breast	≤ 15	3
Contralateral lung	≤ 15	3
Ipsilateral lung	≤ 70	5
	≤ 50	10
	≤ 30	20
	≤ 20	30

was performed using a Monte Carlo algorithm with a grid size of $3 \times 3 \times 3$ mm^3.

Dose verification was performed using a Delta^4 diode detector array (ScandiDos, Inc. Sweden). The passing criterion with the Gamma tests for verification of the VMAT plan was 90% (3% dose difference, 3mm distance to agreement) in our clinic.

Dosimetric parameters for plan evaluation

For the PTV, the parameters based on dose-volume histogram (DVH) data included the homogeneity index (HI), conformity index (CI), the maximum dose (Dmax), the minimum dose (Dmin), and Dmean. The HI was defined as D5/D95 (D5, D95 are the dose received by the high-end 5% and 95% of the PTV volume, respectively). Clearly, a lower HI value means better dose homogeneity. The CI used to evaluate the PTV coverage based on the prescription isodose was defined as $\mathrm{CI}=\frac{TV_{\mathrm{ref}}}{TV}\times\frac{TV_{\mathrm{ref}}}{V}$ (TV was the target volume, V was the volume covered by the prescription dose, and TV_{ref} was the volume of the target that was covered by the prescription dose). The CI value was less than one and the conformity was better as this value approaches one [26]. Dmax represents the dose received by the high-end 2% of the PTV volume. Dmin represents the lowest dose received by 98% of the PTV volume [27]. For the OARs, Vx denotes the percentage volume that receives a dose of x Gy. V5, V10, V20, V30 of the ipsilateral lung, V5 of the heart, V3 of the contralateral lung, and V3 of the contralateral breast were evaluated for each plan.

Statistical analysis

One-way analysis of variance (ANOVA) was used to compare multiple groups of means after the equal check of the variance, and the least significant difference (LSD) was used to implement the two-two comparisons between any two means. Statistical analyses were conducted using SPSS software (version 18.0, SPSS Inc, USA). The confidence interval was 95% and the statistical significance was assigned a P-value of < 0.05.

Results

Comparison of dosimetric metrics of PTV

Isodose lines and DVHs of the three plans for a typical patient are presented in Fig. 1 and Fig. 2, respectively. Target metrics including D_{max}, D_{min}, D_{mean}, HI, and CI are listed in Table 2. The one-way ANOVA test revealed a significant difference in the value of HI for the plans based on three types of MLC ($P = 0.015$), and further LSD test demonstrated that Agility yielded significantly better uniformity than MLCi2 and BM ($P = 0.005$, $P = 0.046$). The difference between the three MLCs was statistically significant in terms of CI ($P = 0.033$). The CI for the Agility and BM plans were better than that of MLCi2, but there was no significant difference between Agility and BM ($P = 0.425$). A statistically significant difference between the three plans for D_{max}, D_{min}, and D_{mean} (D_{max}: $P = 0.012$, D_{min}: $P = 0.041$, D_{mean}: $P = 0.014$) was also observed.

Comparison of dosimetric parameters of OARs

The dosimetric parameters of OARs as indicated in the preceding section were presented in Table 3. The DVHs of clinically important OARs of the three plans for a typical patient were illustrated in Fig. 2.

A one-way ANOVA analysis revealed significant differences between the dose of the contralateral breast and the ipsilateral lung, for the three plans (contralateral breast V3: $P = 0.020$; ipsilateral lung V5: $P = 0.000$, V10: $P = 0.000$, V20: $P = 0.001$, and V30: $P = 0.002$). In the LSD test, Agility and MLCi2 plans had significantly lower values than BM plan in V3 of the contralateral breast ($P = 0.007$, $P = 0.050$), as well as V5 and V10 of the ipsilateral lung (V5: $P = 0.000$, $P = 0.000$, V10: $P = 0.000$, $P = 0.029$). However, there were no significant differences between V3 of the contralateral lung and V30 of the heart (contralateral lung V3: $P = 0.351$; heart V30: $P = 0.528$). In addition, the volume of the ipsilateral lung irradiated in the Agility plan was significantly smaller than the volume in the MLCi2 and BM plans (V20: $P = 0.001$ and $P = 0.005$, V30: $P = 0.000$ and $P = 0.049$, respectively). No significant difference between the MLCi2 and BM plans was determined for V20 and V30 of the ipsilateral lung (P

Table 2 Comparison of target volume dosimetric metrics for three VMAT plans

Parameter	Agility	MLCi2	BM™	*P* value
D_{max}	55.22 ± 1.46	57.46 ± 2.32	56.77 ± 2.16	0.012
D_{min}	48.30 ± 0.82	47.41 ± 1.01	47.78 ± 0.95	0.041
D_{mean}	52.82 ± 1.06	54.41 ± 1.67	53.77 ± 1.48	0.014
HI	1.10 ± 0.03	1.14 ± 0.05	1.13 ± 0.04	0.015
CI	0.75 ± 0.07	0.68 ± 0.06	0.73 ± 0.08	0.033

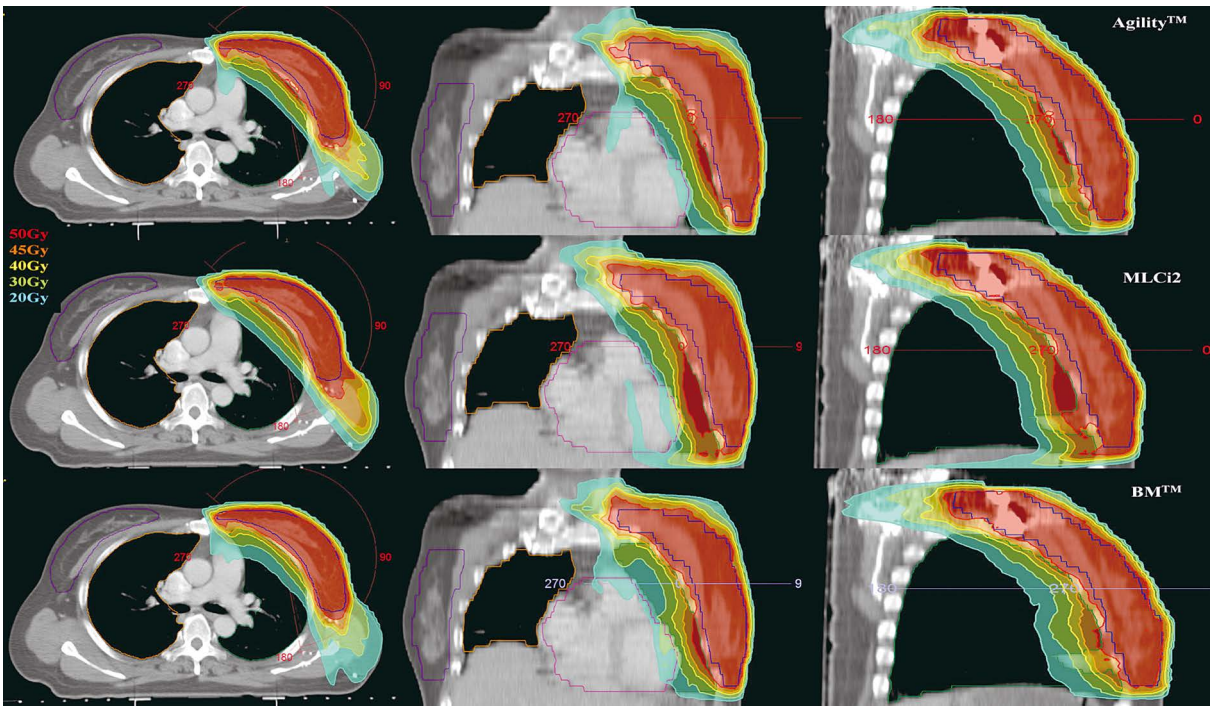

Fig. 1 Comparison of VMAT plans with different MLC widths. Transverse, coronal, and sagittal isodose distributions of the three modalities plans were shown for a typical patient

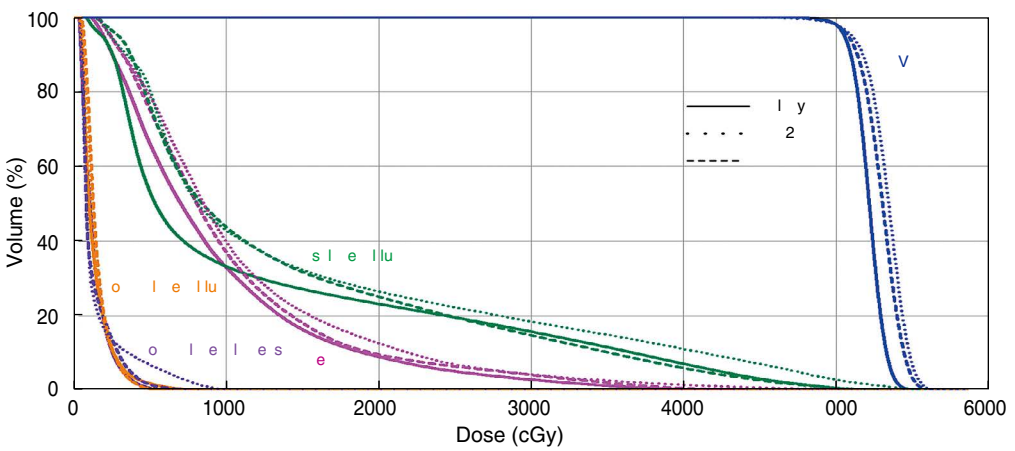

Fig. 2 Comparison of VMAT plans with different MLC widths. Dose-volume histograms of the three plans for a typical patient were shown for PTV, heart, contralateral breast, contralateral lung, and ipsilateral lung

Table 3 Comparison of OARs dosimetric parameters for three VMAT plans

OARs	Parameters	Agility	MLCi2	BM	*P* value
Contralateral lung	V3	6.78 ± 1.66	7.02 ± 1.77	7.85 ± 2.72	0.351
Contralateral Breast	V3	8.78 ± 3.21	9.99 ± 3.35	12.92 ± 5.10	0.020
Heart	V30	3.20 ± 2.46	4.52 ± 3.92	3.56 ± 3.28	0.528
Ipsilaterla lung	V5	64.82 ± 6.52	68.06 ± 5.06	80.10 ± 5.06	0.000
	V10	39.81 ± 5.24	46.90 ± 4.67	50.91 ± 4.61	0.000
	V20	24.35 ± 3.77	29.02 ± 3.19	28.05 ± 3.21	0.001
	V30	15.46 ± 2.75	19.68 ± 3.13	17.66 ± 3.04	0.002

Table 4 Number of MUs and delivery time with each type of MLC

Item	Agility	MLCi2	BM	*P* value
MUs	1164.9 ± 203.2	1092.5 ± 171.9	1144.8 ± 174.8	0.542
Delivery time (min)	2.56 ± 0.24	2.87 ± 0.29	3.77 ± 0.35	0.000

= 0.439, $P = 0.070$).

Delivery efficiency

Delivery efficiency was assessed by measuring the MUs per fraction and the beam delivery time for each plan. The results were listed in Table 4. There was no significant difference among the three plans in term of the MU required. However, the delivery time for VMAT not only depends on the number of MUs, but also depends on the dose rate, speed of MLC movement, as well as the gantry rotation. Therefore, the MU results of our current study do not reflect the actual delivery time. The actual delivery time with Agility was 10.8% and 32.1% less than those with MLCi2 and BM, respectively.

Discussion

MLC, as one of the key inventions for the modernization of radiation therapy [28], is crucial for generating the intensity-modulated beam in VMAT delivery. This is a sophisticated application of dynamic IMRT that involves simultaneous beam angle rotation. The leaf width of MLCs is important for both the target shaping resolution and fine intensity modulation. Numerous studies have investigated the effect of the MLC leaf width on VMAT planning at several tumor sites. Chae SM *et al.* [21] compared 2.5-mm and 5-mm MLC with VMAT techniques for spine lesion treatment and determined that the target volume coverage and the dose gradient index was better with the 2.5-mm MLC. However, there was no statistically significant difference in the CI. A similar result was also obtained in a study by Serna A *et al.*[23]. In a study on the impact of MLC width on VMAT for head and neck cancer (HNC), Hong CS *et al.* [18] found that replacing a 5-mm MLC with a 2.5-mm MLC yielded dosimetric benefits which included a noticeably improved CI and a lower spinal cord dose. However, the benefits were insignificant for large HNC tumors. Furthermore, the delivery efficiency was indifferent with the leaf width for either small or large tumors. Lafond C *et al.*[19] compared VMAT plans using 10-mm and 4-mm MLCs for 16 patients with HNC. The HI and CI for the target volume increased by 7.9% and 4.7% with 4-mm MLC, respectively. The indices for the OARs were as follows: Dmax of spinal cord and brain stem decreased by 1.2 Gy and 4.2 Gy, respectively and D50% (dose covering > 50% of OARs volume) of contralateral parotid decreased by 1.5 Gy with 4-mm MLC. The study by Blümer *et al.* [22] compared VMAT plans using 5-mm and 10-mm MLCs for anal cancer, HNC and prostate cancer. The results showed that the HI and CI of the target volume using 5-mm MLC were better than those obtained using 10-mm MLC. However, the average DVH for the OARs using different MLCs exhibited similar results for all three tumor sites using 10-mm MLC VMAT plans, except for a lower dose to the femoral head in anal and prostate cancer patients, and a lower dose to the spinal cord in HNC patients. The study of van Kesteren *et al.* [20] investigated the impact of MLC of 5-mm and 10-mm leaf width on VMAT in the case of prostate and rectum cancer and found increased OARs sparing for thinner MLCs for both tumor sites. In addition, the mean doses of the OARs decreased from 0.5 Gy to 2.5 Gy.

In this study, we observed a clear dosimetric advantage with Agility and BM MLC over MLCi2 in both target uniformity and conformity in the treatment of breast cancer patients. The mean HI was 1.13 for BM and 1.10 for Agility, respectively, versus 1.14 for MLCi2. The mean CI was 0.73 for BM and 0.75 for Agility, versus 0.68 for MLCi2, which demonstrates that Agility MLC may improve the cosmetic effects of breast cancer patients. Another observation was that Agility and MLCi2 exposed smaller volumes of ipsilateral lung, contralateral lung, and contralateral breast at low dose levels compared with BM. In addition to the leaf width, the transmission and the maximum leaf speed can affect the quality of VMAT plans, and MLC transmission is crucial for regions outside of the target. The average transmission of Agility is about 0.3%. Although MLCi2 and BM MLC have nearly the same average transmission (0.60%–0.70%), the leakage dose in the patient was different because the MLCi2 has two pairs of jaws: a pair of major jaws and a pair of backup jaws that move perpendicular and parallel to the MLC leaves, respectively. These jaws can move automatically by tracking the open and most extended leaves. Our data revealed that the jaws that are movable during treatment delivery assisted in reducing the whole-body dose. For BM, the collimator angle was set at 90° to exploit the maximal dimension of the MLC (21 cm) in the craniocaudal direction. To ensure an equitable comparison, the collimator angle was also set at 90° for Agility and MLCi2 during the generation of the VMAT plans.

The faster leaf travel speed of the Agility MLC was shown to be very beneficial to treatment delivery efficiency. The most prominent result obtained is that VMAT can be delivered with high-efficient using Agility, and the delivery time was reduced for Agility by 10.8% and 32.1%, respectively, compared with MLCi2 and BM. This would likely improve patient comfort and reduce the intra-fraction motion of organs during radiation delivery.

The VMAT technique has an improved dosimetry and reduced treatment time compared to conventional IMRT for breast cancer patients [13]. However, the probability of radiation-induced secondary malignancies may increase when larger volumes of normal tissues are exposed to lower doses [29]. Many breast cancer patients survive for a long time after treatment. Therefore, one should be mindful about the increased risk of secondary malignancy due to low dose radiation when designing the treatment strategy or choosing the radiation technique, even though this risk may not be accurately quantified at this point. Until now, only the difference in skin toxicity based on several techniques has been reported. This difference is significant to the cosmetic effects [30]. Clinical trials and long-term follow-up may be required to evaluate the clinical significance of dosimetric characteristics with VMAT.

Another issue which demands consideration is inter- and intra-fraction motion. The auto flash margin function embedded in the Monaco planning system can assist in addressing this problem. In addition, the accuracy of the setup in VMAT can be further improved using a breathing control device and an appropriate image guidance technique. The impact of breathing motion on plan delivery is currently under investigation using four-dimensional computed tomography (4D-CT) in our department, and the results will be reported in the near future.

Conclusions

For breast cancer radiation therapy after conservative surgery, Agility VMAT plans are dosimetrically advantageous compared to the plans based on MLCi2 and BM. This approach yields better dose homogeneity and conformity of the target volume, as well as OARs sparing. Delivery of VMAT on Agility is significantly faster compared MLCi2 and BM.

Conflicts of interest

The authors indicated no potential conflicts of interest.

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DOI 10.1007/s10330-018-0302-2
Cite this article as: Zhang FL, Xu WD, Jia HY, *et al*. Dosimetric evaluation of VMAT radiation therapy technique for breast cancer after conservative surgery based on three different types of multileaf collimators. Oncol Transl Med, 2018, 4: 208–214.