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Original paper

Performance assessment of a new optimization system for robotic SBRT MLC-based plans

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ABSTRACT

Purpose: To assess the performance of a new optimization system, VOLO, for CyberKnife MLC-based SBRT plans in comparison with the existing Sequential optimizer.
Methods: MLC-plans were created for 25 SBRT cases (liver, prostate, pancreas and spine) using both VOLO and Sequential. Monitor units (MU), delivery time (DT), PTV coverage, conformity (nCI), dose gradient (R50%) and OAR doses were used for comparison and combined to obtain a mathematical score (MS) of plan quality for each solution. MS strength was validated by changing parameter weights and by a blinded clinical plan evaluation. The optimization times (OT) and the average segment areas (SA) were also compared.
Results: VOLO solutions offered significantly lower mean DT (−19%) and MU (−13%). OT were below 15 min for VOLO, whereas for Sequential, values spanned from 8 to 160 min. SAs were significantly larger for VOLO: on average 10 cm^2 versus 7 cm^2. VOLO optimized plans achieved a higher MS than Sequential for all tested parameter combinations. PTV coverage and OAR sparing were comparable for both groups of solutions. Although slight differences in R50% and nCI were found, the parameters most affecting MS were MU and DT. VOLO solutions were selected in 80% of cases by both physicians with 88% inter-observer agreement.
Conclusions: The good performance of the VOLO optimization system, together with the large reduction in OT, make it a useful tool to improve the efficiency of CK SBRT planning and delivery. The proposed methodology for comparing different planning solutions can be applied in other contexts.

1. Introduction

The CyberKnife (CK) (Accuray Inc., Sunnyvale, CA, USA) is a system for robotic radiosurgery/radiotherapy treatments. Radiation is delivered by a linac mounted on a robotic arm while tumor position is tracked with sub-millimeter accuracy using an X-ray image guidance system. Traditionally, circular (fixed cones) or pseudo circular (Iris collimator) collimating systems were used to create highly conformed dose distributions with sharp dose gradients, obtained through the sum of small circular radiation fields delivered at a large number of robot positions by several non-isocentric and non-coplanar beams [1]. For these reasons, CK is widely used for Stereotactic Body Radiation Therapy (SBRT) treatments of different anatomical sites. However, CK SBRT has poor delivery efficiency due to the large number of monitor units (MUs) and to the time required for the robot to move to different node positions [2–6]. The recent implementation of a multileaf collimator (MLC) (InCise™) gives the possibility to treat larger tumors and to reduce MUs and treatment times [7–10]; these characteristics make this collimator the preferred choice for treatment of large body lesions. However, the dose optimization with MLC becomes more memory intensive and time-consuming. A new and faster optimization system (VOLO) has been implemented in the new version of the CK dedicated Treatment Planning System (TPS), Precision, which also retains the original Sequential optimizer.

The main limitations of the Sequential optimizer for MLC-based plans are i) the use of predefined segment shapes based on geometric heuristics [3,11] which limits the modulation capability of the system and ii) the required long optimization time. The system optimizes, in sequence, several cost functions each assigned to different user defined dose objectives. Additional steps to improve delivery efficiency

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optimization may also be necessary [12]. As a result, complex treatment plans requiring many objectives and/or targeted to large lesions may necessitate extremely long optimization times which can extend up to four hours [12–15].

The VOLO optimization system was implemented to overcome the limitations of the Sequential algorithm. With the aim of reducing optimization time this system uses GPU memory to speed up calculation processes, and the optimization is carried out minimizing a single cost function. The cost function combines all DVH constraints and delivery efficiency parameters with user-defined weights, so that the optimized plan is already a deliverable plan. MLC plan optimization is achieved by fluence optimization and leaf sequencing [16] which should overcome the limitations of Sequential predefined shapes.

The aim of this study was to assess VOLO performance on robotic MLC-based plans for different SBRT treatment sites in comparison with Sequential solutions. VOLO performance has already been evaluated by Zeverino et al. [15] for Iris-based plans whereas for MLC-based plans the analysis is limited to brain lesions treatments. VOLO Iris optimization does not use a fluence-based approach. Considering VOLO MLC fluence-based optimization, the advantages offered by VOLO are expected to be more evident for MLC-plans, which find a larger application for SBRT planning [17]. This study is the first evaluation performed for VOLO CK MLC plans over a variety of SBRT treatment sites. Here, several dosimetric and efficiency parameters and metrics were used to compare quality of plans optimized with both algorithms. However, it is well known that different parameters/metrics may show conflicting results when comparing the two examined solutions. The use of a single quality index is, therefore, highly recommended to reduce variability in plan quality evaluation [18]. To this purpose, a mathematical score was defined in this work, through a combination of dosimetric and efficiency parameters following the suggestions in [17,19,20]. However, the choice of the parameters to be used in the score and their weights, although based on clinical practice, remains a critical issue. Thus, our analysis was strengthened by studying the dependence of the mathematical score on the weights assigned to the single metrics, adopting a new critical approach not reported in the existing literature, to the best of our knowledge. The mathematical plan quality evaluation was further strengthened by an independent clinical selection carried out by two radiation oncologists. Finally, since better plan quality does not always correspond to a better quality of delivered dose distributions, delivery quality assurance (DQA) results of VOLO plans were evaluated and compared to those obtained for Sequential plans using the same measurement and analysis methods.

2. Materials and methods

2.1. Case selection and planning protocols

Twenty-five SBRT cases relating to different anatomical sites (7 liver, 7 prostate, 5 pancreas and 6 spine) previously treated with CK at our center were selected. The cases were chosen to represent a realistic sample of cases covering a wide range of PTV sizes (Table 1) and complexities in terms of distance between target and OARs. For each patient, previously delivered treatment plans using the InCise™ MLC were fully re-optimized both with Sequential and VOLO optimizers maintaining clinical dose prescription, fractionation schemes and constraints to OARs protocols used for clinical plans (listed in Table 1). Plans to be re-optimized were distributed between two planners: 3 Liver, 2 Pancreas, 4 prostate and 3 Spinal cases were assigned to the first planner and the remaining cases to the second one. For each case, the same planner created both the Sequential and VOLO-optimized plans.

Liver cases consisted of 7 single and multiple metastases treatments. Different fractionation schemes (3–5 fractions) and different prescription doses (30 Gy–45 Gy) were used depending on PTV dimensions and location. Planning was carried out limiting doses to OARs according to constraints recommended by AAPM TG 101 [21], while maintaining the percentage of PTV receiving the prescription dose above 95%.

Pancreas cases included locally advanced unresectable pancreatic tumours. The prescription dose was 30 Gy in 5 fractions to 70–75% isodose line. OAR doses were kept below constraints recommended by AAPM TG 101 and a 95% of PTV covered by prescription dose was ideally required; in one case coverage as low as 90% was accepted to satisfy OAR constraints.

Treatments for low-intermediate risk prostate cancer were planned following the PACE SBRT protocol. The PTV was obtained by anisotropic CTV expansion (5 mm in superior, inferior, and anterior and 3 mm in posterior direction); 36.25 Gy dose was prescribed to cover at least 95% of the PTV with 40 Gy isodose covering at least 95% of the CTV. Dose constraints to OARs were specified in a previous study [17].

Spinal metastases were treated prescribing 24–30 Gy in 3 fractions to the PTV, which was obtained by adding a margin of 1 mm to the CTV. A spinal cord Planning Risk Volume (cord PRV) was created by an expansion of the spinal cord (1 mm). PTV coverage was maintained as high as possible while limiting the dose to cord PRV according to dose constraints suggested by AAPM TG101 [21] for spinal cord. Two out of six spinal cases were re-irradiations, in these cases dose prescriptions and constraints for the spinal cord were decided by the radiation oncologist on a case-by-case basis using literature results [22].

2.2. Treatment plans optimization

In the Sequential MLC plan-optimization process, the system initially sets a large number of segments to point the target from fixed positions called nodes; their shapes are defined with geometric heuristics choosing among pre-defined shapes (conformal, conformal-avoidance, eroded, perimeter and random) [3,11]. The TPS then optimizes the MUs assigned to each segment. The plans selected for this study were created in conformal-avoidance modality using all the shapes permitted by the system. In Sequential optimizer the user defines a set of hard constraints, which limit the solution space, and several objectives; for each objective a cost function is defined, and the optimization process minimizes each cost function sequentially, giving higher priority to top objectives. The result of each optimization step adds a new hard constraint, so that the solution proceeds in a predictable way defined by the ordering of the steps and removing the need for weighting factors [12]. These optimization process for complex plans where several objectives are necessary, can require an extremely long time. Moreover the optimization of delivery efficiency may require two additional optional steps: time reduction and beam/

Table 1
Clinical data of treatment plans selected for the study.

Treatment site	Number of cases	PTV cm^3	Prescription dose Gy	Fractions	Protocol for OARs constraints
Liver	7	19–197	35–45	3–5	AAPM TG101
Pancreas	5	37–267	25–30	5	AAPM TG101
Prostate	7	61–143	36.25	5	PACE trial
Spine	6	7–15	21–30	3	AAPM TG101 and clinical evaluation*

*Spinal cases included re-treatments, for which constraints were discussed case by case with physicians.

node reduction [15]. If a high delivery efficiency is required, these processes can lead to a deterioration of target coverage. In this work Sequential treatment plan optimization was carried out following criteria derived both from literature and our experience [12–14,17].

Dose optimization with VOLO for MLC plans is carried out in three steps: fluence optimization, leaf sequencing and segment shape and weight adaptation. Initially the user sets the goals for target and OARs or help structures; the optimization process minimizes a single cost function that combines all user-defined requirements together with dose delivery efficiency parameters, using the relative weights set by the user. With this approach, VOLO was expected to overcome Sequential long optimizing time and limitations associated with the use of pre-defined segment shapes.

The Finite Size Pencil Beam (FSPB) algorithm [23] was used for dose calculation in most plans whereas Monte Carlo dose calculation algorithm was used for lesions in close proximity to air cavities (liver lesions near diaphragm and thoracic spinal lesions).

2.3. Sequential and VOLO plans: parameters for comparison

Plan Quality was evaluated using several parameters describing delivery efficiency (monitor units normalized to prescription dose, MU/PD, and delivery time, DT), doses to OARs, PTV coverage, dose to target conformity and dose gradient.

Dose to target conformity was evaluated in terms of the new conformity index (nCI), calculated by the CK TPS as [7,10]:

$$nCI = \frac{PTV \times PIV}{TIV^2} \tag{1}$$

where PIV is the prescription isodose volume and TIV is tumor volume covered by the prescription isodose; this index is the inverse of the Paddick conformity index [24].

Low doses spillage was evaluated through the R50% parameter, defined as:

$$R50\% = \frac{V_{50\%}}{PTV} \tag{2}$$

where $V_{50\%}$ is the volume receiving 50% of the dose prescribed to PTV.

PTV coverage (PTV%) was examined in terms of PTV volume receiving the prescription dose, mean dose (D_{mean}) and $D_{98\%}$. In prostate cases the $V_{40\ Gy}$ parameter for the CTV was used instead of the PTV D_{mean}.

Delivery time presented here does not include setup time for either Sequential and VOLO.

Doses to OARs were compared through parameters chosen depending on the treatment site listed in Table 2.

Two more variables were examined: the time required by the systems to run the final optimization scripts, excluding user's interaction, (OT) and the weighted average size of segments created (SA) for each plan [25]:

$$SA = \sum_i A_i \frac{MU_i}{MU_{tot}} \tag{3}$$

where i runs over the segments, A_i is the area of the i-th segment, MU_i are the MUs associated to the i-th segment and MU_{tot} are the total MUs of the plan.

Table 2
OAR DVH parameters used to compare VOLO and Sequential solutions for each anatomical site.

Anatomical site	OAR DVH parameters			
liver	Liver: healthy volume inside 15 Gy or 21 Gy isodose lines	Bowel $D_{0.03\ cc}$ D_{mean}	Stomach $D_{0.03\ cc}$ D_{mean}	Duodenum $D_{0.03\ cc}$ D_{mean}
pancreas	Bowel $D_{0.03\ cc}$ $V_{19.5\ Gy}$	Stomach $D_{0.03\ cc}$ $V_{18\ Gy}$	Duodenum $D_{0.03\ cc}$ $V_{18\ Gy}$	
prostate	Rectum $V_{36\ Gy}$ $V_{29\ Gy}$ $V_{18,1\ Gy}$		Bladder $V_{37\ Gy}$ $V_{18,1\ Gy}$	
spine	Cord PRV $D_{0.03\ cc}$ $D_{0.35\ cc}$		Cord $D_{0.03\ cc}$	

2.4. Plan quality scoring: mathematical score

For each plan a score was assigned to each parameter described in Section 2.3 (except for OT and SA) using a linear scale. The scale was defined by setting the score to 6 for the ideal value achievable for that parameter and to 0 for the threshold value defining clinical acceptability. The average scores ($score parameter_i$) of each parameter were combined in a weighted sum to obtain a mathematical score (MS) of quality for each plan, similarly to what was defined in a previous study [17]:

$$MS = \sum_i w_i \ score parameter_i \tag{4}$$

The ideal goal value and the value corresponding to score zero as well as the weights (w_i) of Eq. (4), were chosen together with radiation oncologists to reflect their clinical choices. w_i were normalized to obtain MS ranging in 0–6 interval. MS values can depend on the parameters selected for the computation as well as on the weights assigned to each parameter's score. To investigate the dependence of MS values on w_i, tests were performed by changing the weights as summarized in Table 3.

The combination in test 1 is a clinically acceptable variation of the original one; in both cases the MS was calculated also not considering the delivery efficiency (without MU and DT). In test 2 MUs and DT were excluded from the plan quality evaluation, while assigning a higher weight (15% each) to nCI and R50%. In test 3 a lower weight to the PTV coverage and higher weights to PTV $D_{98\%}$ and D_{mean} (CTV V_{40Gy} for prostate cases) were considered to study the influence of PTV DVH shape in MS results. Plan solutions obtained by the two optimizing algorithms were also compared in terms of partial scores obtained considering each group of parameters: T&MU score, PTV score, nCI&R50% score, OARs score. Partial scores were calculated using the same weights used in the MS calculation. Better performances of VOLO or Sequential optimization algorithm were assessed upon differences normalized to the maximum score (6), calculated using the formula:

$$relative\ difference\,(\%) = \frac{MS(VOLO) - MS(sequential)}{6} \tag{5}$$

Normality of distributions of data was tested using the Shapiro-Wilk test (confidence level 0.05). Statistical significance of the observed differences between Sequential and VOLO was evaluated using paired two-sided Wilcoxon's signed-rank tests for not normally distributed parameters and a paired t-student test for normally distributed parameters with a significance level of 0.05 in both cases. All statistical analyses were performed using OriginPro (version 9.0.0, OriginLab Corporation, Northampton, MA).

2.5. Sequential and VOLO plans: clinical selection

Clinical evaluation was performed by two expert CyberKnife radiation oncologists who were asked to blindly select either Sequential or VOLO optimized treatment plan. As in clinical practice, the evaluation was based on target coverage, sparing of healthy tissues, dose conformity and low dose bath, and plan delivery efficiency.

Table 3
Relative weights used in each test for the calculation of the global score index.

Test	PTVgroup	OARgroup	nCI, R50%	MU and DT
	$w_{parameter}$			
Original combination	35% (PTV%, 17.5%; $D_{98\%}$, 8.75%; D_{mean}*, 8.75%)	35%	15%	15%
Original combination without MU and DT	44.5% (PTV%, 22.25%; $D_{98\%}$, 11.125%; D_{mean}*, 11.125%)	44.5%	11%	0%
Test1	40% (PTV%, 20%; $D_{98\%}$, 10%; D_{mean}*, 10%)	40%	10%	10%
Test1 without MU and DT	41.2% (PTV%, 20.6%; $D_{98\%}$, 10.3%; D_{mean}*, 10.3%)	41.2%	17.6%	0%
Test2	35% (PTV%, 17.5%; $D_{98\%}$, 8.75%; D_{mean}*, 8.75%)	35%	30%	0%
Test3	35% (PTV%, 5%; $D_{98\%}$, 15%; D_{mean}*, 15%)	35%	15%	15%

*In prostate cases the CTV $V_{40\ Gy}$ is used instead of the PTV D_{mean}.

2.6. Sequential and VOLO plans: delivery QA

Pre-treatment delivery quality assurance results were analysed respectively for 128 Sequential plans and for the first 95 VOLO-optimized plans, including the plans optimized by both algorithms for the 25 cases used in this study. Delivered dose distributions were measured by using a liquid filled ionization chamber array (Octavius-1000 SRS PTW, Germany) and comparison with planned distributions analysed in terms of local gamma index pass rates at 2% 2 mm. Correction for the dose per pulse dependence of the detector response was applied to measured data, whereas a correction for beam angle incidence was not necessary because only beams from a limited angular distribution were tested. Details of the DQA method had been published in a previous study and in two conference abstracts [26–28].

3. Results

3.1. Sequential and VOLO plans comparison: delivery and optimization efficiency

From the Shapiro-Wilk test results, MU/PD, DT, nodes, segments, OT, SA and all versions of MS followed a normal distribution, while PTV coverage, nCI and R50 data were not normally distributed.

Compared to Sequential, VOLO solutions offered significantly lower average DT (−15%) and MU/PD (−19%), reducing significantly nodes (−12%) and segments (−23%) as well, see Fig. 1 and Table 4. Results are also shown as percentage difference for each couple of plans in Fig. 2 (((#VOLO-#sequential)/#VOLO)*100). Apart from a few (2–3) exceptions VOLO plans had always higher delivery efficiency and a lower segment number than Sequential plans, reaching percentage differences up to 80–100%. This explains the high statistical significance observed for the comparison of these parameters.

OT remained below 15 min for VOLO, whereas for Sequential, spanned from 8 to 160 min.

SA results demonstrated that on average VOLO optimizer used segments with larger areas (10 ± 5 cm^2 vs 7 ± 3 cm^2 for Sequential plans) lying in a wider range (2–22 cm^2 VOLO vs 3–14 cm^2 Sequential).

3.2. Sequential and VOLO plans comparison: dosimetric parameters and metrics

Average PTV coverage was similar for both groups of solutions, but significantly higher for VOLO plans, since 19/25 VOLO plans obtained a higher PTV coverage. For liver, pancreas and prostate cases both Sequential and VOLO solutions achieved 97% average coverage. The differences in PTV coverage were much larger when spinal cases were considered separately: on average 94% VOLO vs 88% Sequential, making VOLO optimization clearly advantageous for this treatment site. 18/25 VOLO plans had better conformity index respect to Sequential plans, even if percentage differences remained within 10%. Lower nCI values were reached in liver, pancreas and prostate cases for both solutions (1.20 for Sequential and 1.16 for VOLO), whereas in spinal plans average nCi was higher than 1.5 for both Sequential and VOLO solutions. OARs sparing was ensured in all plans by both solutions and no significant difference was observed, although, on average, Sequential dose fall-off was slightly but significantly steeper (R50% = 3.4) than VOLO (R50% = 3.6), see Table 4.

3.3. Sequential and VOLO plans comparison: plan quality scoring

In order to rule out that the large difference in PTV coverage observed for spinal cases between VOLO and Sequential did not bias the global MS results, MS average values for the two optimization algorithms were computed both including and excluding spinal cases. In Fig. 3 the average MS values for plans optimized with sequential (black) and VOLO (grey) algorithms are reported. Values are shown for each test including (tot) and excluding treatment plans for spinal cases (no Spinal). Asterisks indicate statistical significance. MS was always higher for VOLO plans. When MU and delivery time were not used in the computation and spinal cases were excluded, statistical significance was lost. When including treatment plans created for spinal cases, globally lower MS scores were observed for both solutions and the difference between Sequential and VOLO was higher and always statistically significant, principally due to increased VOLO PTV coverage.

Finally, even when analysing separately data related to each planner, VOLO higher MS values were confirmed by both users.

As we can observe in Fig. 4, for the “original combination” of Table 2, VOLO plans achieved a higher MS than Sequential in 21/25 cases and the average value was significantly higher for VOLO (average and standard deviation 3.6 ± 0.7 for VOLO vs 2.9 ± 1.2 for Sequential, $p < 0.01$). MS remained higher for VOLO in 17/25 plans even when delivery efficiency was not included. Most VOLO plans obtained a higher score for MU and delivery time (22/25), and for the metrics related to the PTV coverage (16/25). A similar behaviour was observed when considering together dose conformity and gradient (16/25). Practically no difference was observed for OARs.

The relative MS variation, defined as standard deviation divided by average MS value, was lower for VOLO, ranging in all test combinations, between 17.5% and 22.5% for VOLO and between 25% and 44.6% for Sequential.

3.4. Sequential and VOLO plans comparison: clinical selection

All plans were evaluated as clinically acceptable by both radiation

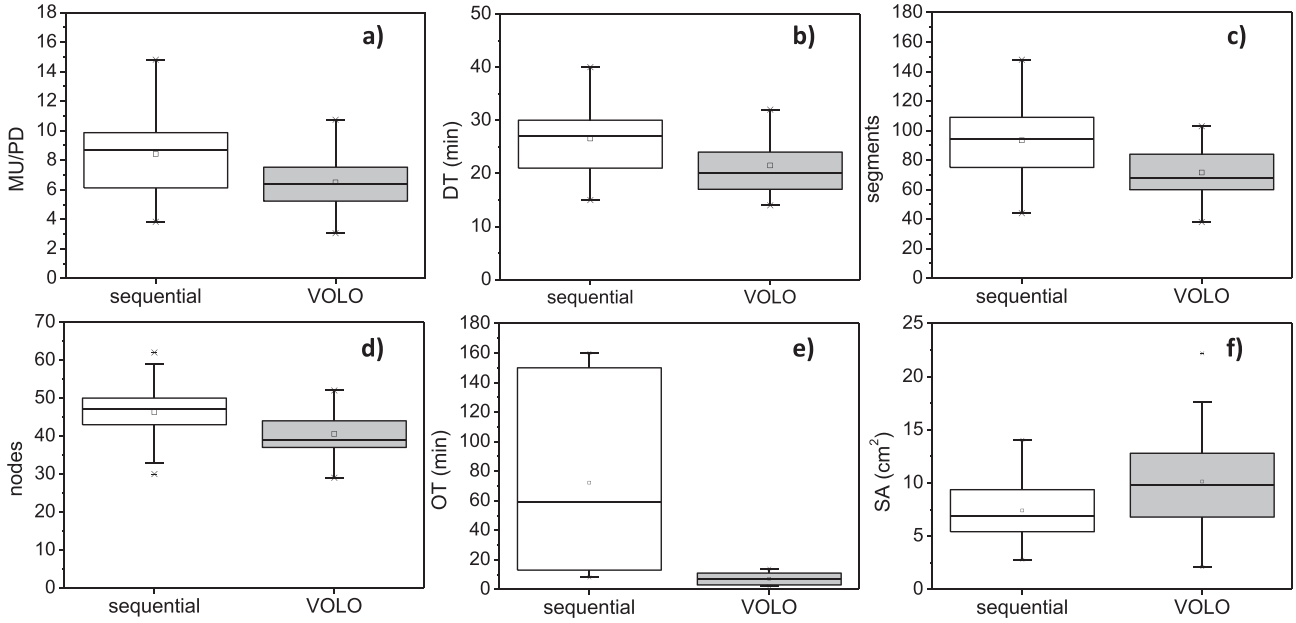

Fig. 1. Box charts of MU/PD (a), DT (b), segments (c) nodes (d), OT (e) and SA (f) distributions for all plans optimized with Sequential and VOLO (grey filling) optimizers.

Table 4
Average values and standard deviations of parameters used for comaprison with the associated p values.

Parameter	Sequential	VOLO	p
MU/PD (MU/cGy)	8 ± 3	6.5 ± 1.9	< 0.01
DT (min)	26 ± 6	22 ± 5	< 0.01
Nodes	46 ± 9	41 ± 6	< 0.01
Segments	90 ± 30	72 ± 16	< 0.01
OT (min)	70 ± 60	7 ± 4	< 0.01
SA (cm^2)	10 ± 5	7 ± 3	< 0.01
PTV (%)	95 ± 5	96 ± 2	< 0.01*
nCI	1.3 ± 0.2	1.2 ± 0.2	0.01*
R50%	3.4 ± 0.7	3.6 ± 0.7	< 0.01*

*Asterisks indicate not normally distributed data, for which a Wilcoxon test was carried out.

oncologists, who preferred VOLO solutions in 20/25 cases, basing their decision on target coverage, sparing of healthy tissues, dose conformity and low dose bath, and plan delivery efficiency. One observer preferred Sequential plans in 4/25 cases and expressed no preferences in 1 case, while the other observer selected the Sequential solution in 3/25 cases and had no preferences in 2/25 cases. The percentage of inter-observer agreement was 88%. For the 22 plans where the two physicians agreed, MS results and clinical decisions were in agreement in 21 cases.

3.5. Sequential and VOLO plans: delivery QA

Local gamma passing rates resulting from comparison between delivered and calculated dose distributions were 98% average, ranging within 90–100%, for VOLO and 95% average, ranging within 84–100%, for Sequential plans, using 2%, 2 mm criteria. A gamma passing rate below 90% was observed just in four Sequential plans. Reducing the analysis to the 25 cases used in this study, the average gamma passing rates obtained were 98% and 96% for VOLO and Sequential-optimized plans respectively.

4. Discussion

A new GPU-based optimization system, VOLO, was introduced into clinical use at the end of 2018 for CyberKnife treatment planning. For CK SBRT plans, optimized with the existing Sequential algorithm, MLC had been demonstrated to offer advantages in terms of delivery efficiency when compared to Iris and became, in some centres, the first choice of collimating system for selected SBRT treatment sites [7,10,17]. However, the Sequential optimizer has several limitations when managing MLC-based plans due to the use of segments with limited predefined shapes [10], the large memory required for the optimization and the long optimization time. VOLO was implemented to overcome these limitations and it is expected to offer, especially for

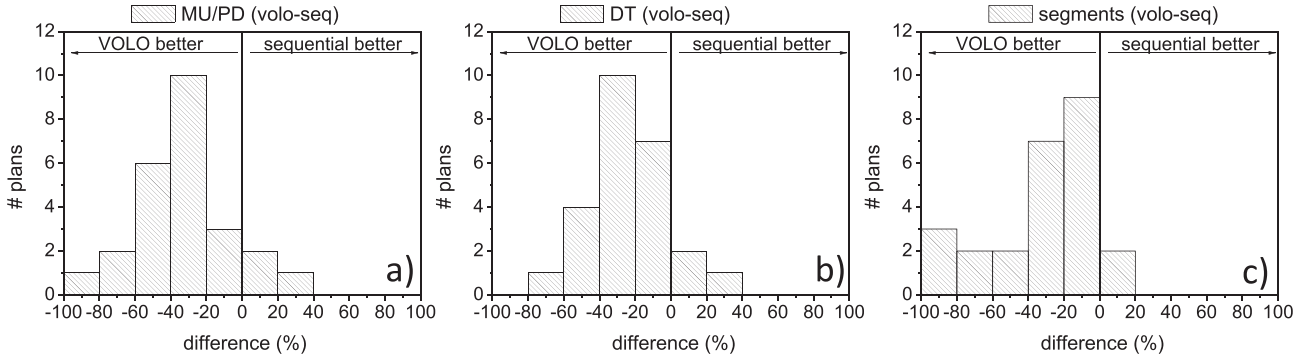

Fig. 2. Histograms of percentage difference between VOLO and Sequential efficiency parameters (MU/PD (a), DT (b)) and segment numbers (c). Positive differences indicate a better performance for Sequential solution and negative difference a better performance for VOLO solution.

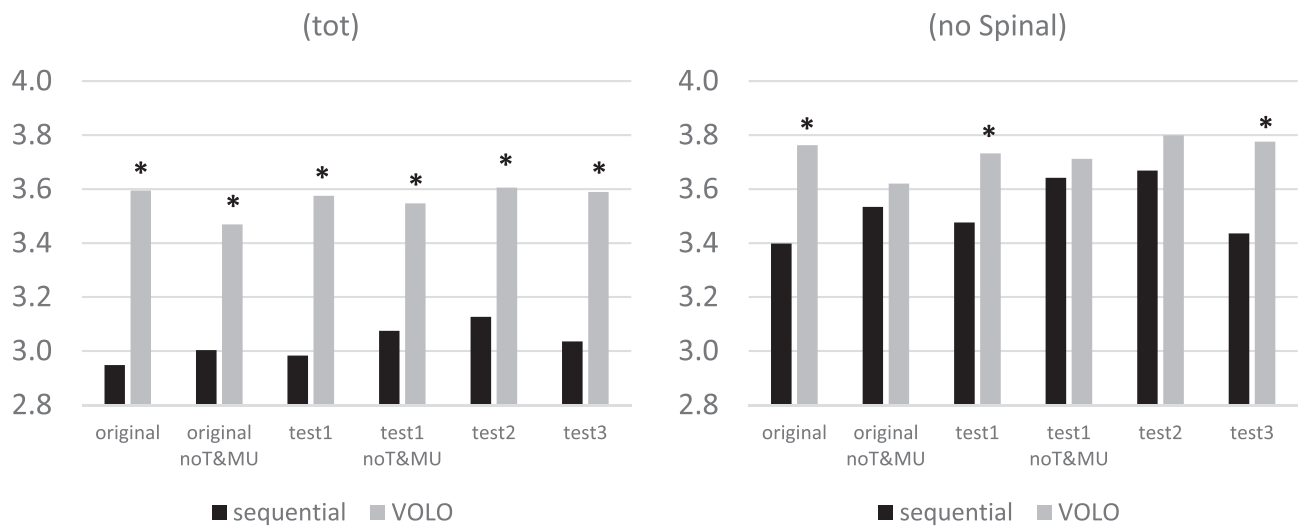

Fig. 3. Average MS values for plans optimized with sequential (black) and VOLO (grey) algorithms. Left: scores averaged over all plans (tot). Right: average scores excluding treatment plans for spinal cases (no Spinal). Asterisks indicate statistically significant differences.

MLC plans, much shorter optimization time, to improve delivery efficiency and possibly to achieve a better plan quality especially for complex SBRT treatments. An evaluation of VOLO over MLC-based SBRT plans is therefore required. In the present study, for the first time, VOLO performances were evaluated in SBRT cases for different treatment sites planned with MLC.

Performances of VOLO optimization algorithm for Cyberknife treatment planning has been recently investigated by Zeverino et al. [15]. That study is mainly dedicated to the assessment of VOLO performances for optimization of Iris collimator treatment plans. Fifty cases were investigated including brain, spine, prostate and lung treatments, all planned with the Iris collimator, and ten brain cases for which MLC was employed. Dosimetric results were comparable for both optimization solutions except for some statistically significant differences depending upon the anatomical site and collimator used. The authors obtained a significant reduction in treatment time with VOLO for Iris SBRT plans, while maintaining good target coverage and conformity, and concluded that this was likely due to the higher number of larger Iris collimator sizes employed by VOLO plans compared to those used in Sequential-based plans. The authors observed a conflicting result for brain treatments using MLC optimized with VOLO, which showed unexpectedly higher MU and delivery time, maintaining superior dosimetric parameters.

Our results arising from the comparison between VOLO and Sequential optimized plans highlighted a significant reduction of nodes, segments, total number of MU and treatment time in VOLO solutions.

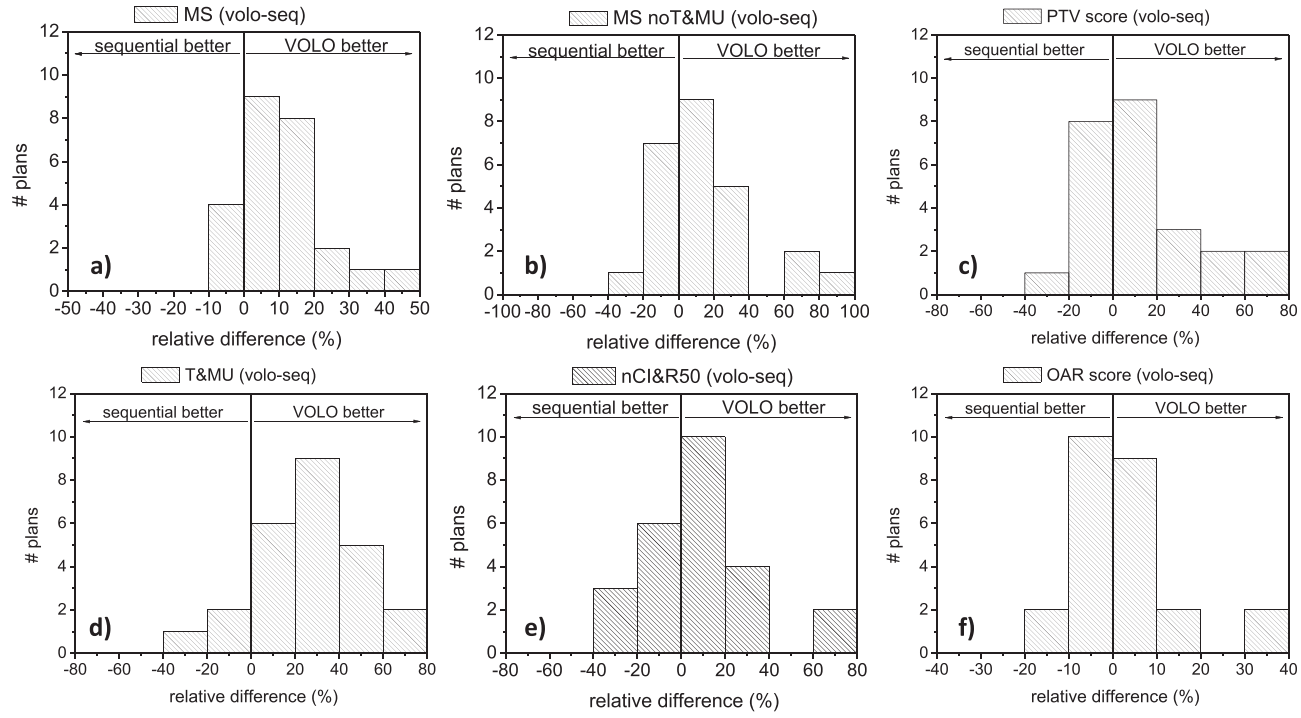

Fig. 4. Histograms of differences normalized to the maximum score (%) between VOLO and Sequential MS values. Global MS (a), MS without MU and DT (b) and partial scores obtained considering separately each group of parameters (PTV score (c), T&MU score (d), nCI&R50% score (e), OARs score (f)) are reported. Positive differences indicate a better performance for VOLO solution; whereas plans showing a negative difference are those where Sequential achieved better results.

Comparing our results with those obtained in [15] we can suppose that higher efficiency of MLC VOLO-optimized plans is achievable for body lesions which are generally more complex and larger than most brain tumors. In Zeverino et al. there is not a direct comparison between optimization times using the two algorithms, however they estimated a reduction of the optimization time up to ten times for SIB cases. In our study, VOLO expected capability to reduce optimization time, was evaluated and confirmed.

When considering average dosimetric parameters, VOLO and Sequential solutions showed comparable PTV coverage and OAR's sparing, except for spinal cases, where a significant and clinically relevant improvement in PTV coverage for plans optimized with VOLO was observed. This is a good example of VOLO's ability to achieve better results in complex treatment sites than possible with Sequential's limited and predefined segment shapes. Dose conformity to target is improved in VOLO-optimized plans whereas dose fall-off at 50% of prescription isodose is slightly steeper for Sequential-optimized plans. These differences, even if statistically significant, are too small to have clinical relevance, as confirmed by the clinical selection by two radiation oncologists.

Several parameters must be taken into account when plan quality is evaluated, and solutions obtained using different techniques can give conflicting results for different parameters. Thus, comparison of plan quality considering several distinct parameters is not easy. Mathematical scores that combine dosimetric parameters have been proposed following different strategies [17,19,20,29–34] and their use is highly recommended to objectively compare treatment plans [18]. In [33] a special index was defined to evaluate simultaneously plan modulation, PTV coverage and dose to heart for breast treatments; in [34] a quality index was defined combining PTV coverage, dose conformity, dose fall-off and the cord maximum dose for spinal cases. In the study by Akpati et al. [29] and Licon et al. [32] two indexes were defined measuring the deviations of the created plan with respect to an ideal plan. In the first study the index was based on PTV coverage, dose-to-target conformity, dose homogeneity and dose gradient; in the second one, the distance of the obtained DVH from QUANTEC objectives was taken into account. The scoring system described in [30] is based on DVH statistics from previous clinical plans. Alfonso et al. [31] created a mathematical score as a weighted sum of three components, which takes into account PTV-related parameters, doses to organs at risk and doses to remaining volume at risk. In our work we adopted a quality score (MS) defined as the weighted sum of scores assigned linearly to dosimetric parameters in a previous study performed at our institute [17] and computed similarly to the approach described in [19,20]. The ideal and threshold values used to set the linear scores were based on previous clinical experience by two expert radiation oncologists. On the whole, in all described scoring systems including the one adopted in this study, plan quality is assessed against reference parameters, which are generally based on previous clinical experience and/or previously clinically accepted plans depending, thus, on the quality of these plans. Generally, although mathematical scores of plan quality are necessary and useful tools of analysis, the users should be aware of some critical issues in their definition. Critical issues are, among others, the choice of parameters to be included in the score, the relative weights and when used, the linear scoring assigned to each parameter [18]. To the best of our knowledge, no previous work has evaluated the criticality of the choice of these parameters and weights. In our study, the variability of the results with different clinically-acceptable weight-parameter combinations were investigated, and the linear scoring of parameters was decided together with radiation oncologists. In the original combination, average MS scores obtained by the two groups of solutions is statistically different and is higher for VOLO plans; These results are maintained and confirmed even when:

- a different, clinically acceptable weights distribution among PTV, OAR, nCI&R50%, MU&DT groups is used (test1)
- zero weight is given to MU and DT for both combinations
- zero weight is given to MU&DT and more importance is attributed to nCI and R50% parameters (test2)
- more importance is given to the PTV DVH shape at the expenses of PTV coverage inside the PTV group of parameters (test3).

When MU and DT are not used in the computation and spinal cases are excluded, statistical significance is lost, but for all tests average MS score is still higher for VOLO solutions. On the whole, variations in the relative weights of parameters used for MS computation do not affect our main finding of VOLO showing a superior quality than sequential solutions. The reliability of the employed score was confirmed also by the good agreement between MS results and clinical decisions. This critical analysis of the results yielded by MS is new in the literature and can be adopted for other planning solutions comparisons.

It is worth noting that variation of MS scores obtained by VOLO-optimized plans is significantly lower than that obtained by Sequential plans, indicating that plan quality of VOLO solutions can be considered less dependent on planners, anatomical site and plan complexity.

The size of segments used by VOLO is on average higher, thus suggesting that the higher efficiency of VOLO plans could be due to the use of less complex MLC segment shapes compared to Sequential solutions. A detailed analysis of Plan complexity for CK plans, although highly interesting, would require a specific discussion given the peculiarity of these plans. Adoption for CK plans of already proposed complexity metrics for VMAT and IMRT is not straightforward due to CK large number of non-coplanar beams covering a wide solid angle and exhibiting a low number of segments per beam (typical range 1–3). This is why this kind of analysis has not been addressed up to now; a deeper insight into CK plans complexity is in progress and will be object of a future paper. For the same reason complexity and plan modulation were not included into the MS computation as proposed by Russo et al. [33].

It must be also considered, that since VOLO was introduced into clinical practice less than a year ago, in a limited number of centres, it is still probably too early for a multi-centre comparison. The first step is a single center analysis to assess if VOLO can substitute Sequential offering better delivery efficiency, shorter optimization time, without compromising plan quality and even increasing it, as demonstrated by our data and by dosimetric accuracy measurements.

5. Conclusion

For the first time, the performance of a new optimizing algorithm, VOLO, for CK MLC-based SBRT plans was evaluated. In this setting a critical analysis of a mathematical score of plan quality was adopted. Our analysis confirmed that VOLO plans are more efficiently deliverable than Sequential ones, moreover, the VOLO optimizer offered extremely lower optimization time giving the user more possibilities to explore possible trade-offs, which can potentially increase plan quality.

For the selected 25 MLC-based robotic SBRT cases plan quality was found to be higher for VOLO solutions using a mathematical evaluation and a clinical selection. The VOLO optimizer implementation into clinical use can thus improve efficiency of both treatment planning and treatment delivery. The proposed methodology can be adopted in other settings, for comparison of different planning solutions.

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References

[1] Kilby W, Dooley JR, Kuduvalli G, Sayeh S, Maurer CR. The CyberKnife® robotic

radiosurgery system in 2010. Technol Cancer Res Treat 2010;9:433–52. https://doi.org/10.1177/153303461000900502.
[2] Zhang S, Yang R, Shi C, Li J, Zhuang H, Tian S, et al. Noncoplanar VMAT for brain metastases: a plan quality and delivery efficiency comparison with coplanar VMAT, IMRT, and CyberKnife. Technol Cancer Res Treat 2019;18. https://doi.org/10.1177/1533033819871621.
[3] Jang SY, Lalonde R, Ozhasoglu C, Burton S, Heron D, Huq MS. Dosimetric comparison between cone/Iris-based and InCise MLC-based CyberKnife plans for single and multiple brain metastases. J Appl Clin Med Phys 2016;17:184–99. https://doi.org/10.1120/jacmp.v17i5.6260.
[4] Jin L, Price RA, Wang L, Meyer J, Fan JJ, Charlie Ma CM. Dosimetric and delivery efficiency investigation for treating hepatic lesions with a MLC-equipped robotic radiosurgery-radiotherapy combined system. Med Phys 2016;43:727–33. https://doi.org/10.1118/1.4939259.
[5] Yang J, Ma L, Ph D, Wang X, Xu WX, Cong X, et al. Medical dosimetry dosimetric evaluation of 4 different treatment modalities for curative-intent stereotactic body radiation therapy for isolated thoracic spinal metastases. Med Dosim 2016:1–8. https://doi.org/10.1016/j.meddos.2015.10.003.
[6] Paik K, Kim MS, Choi CW, Jang WIl, Lee SH, Choi SH, et al. Dosimetric comparison of volumetric modulated arc therapy with robotic stereotactic radiation therapy in hepatocellular carcinoma. Radiat Oncol J 2015;33:233–41. https://doi.org/10.3857/roj.2015.33.3.233.
[7] Kathriarachchi V, Shang C, Evans G, Leventouri T, Kalantzis G. Dosimetric and radiobiological comparison of CyberKnife M6 TM InCise multileaf collimator over IRIS TM variable collimator in prostate stereotactic body radiation therapy. J Med Phys 2016;41:135. https://doi.org/10.1259/bjr.20170523.
[8] Kim N, Lee H, Kim JS, Baek JG, Lee CG, Chang SK, et al. Clinical outcomes of multileaf collimator-based CyberKnife for spine stereotactic body radiation therapy. Br J Radiol 2017;90:20170523. https://doi.org/10.1259/bjr.20170523.
[9] Murai T, Hattori Y, Sugie C, Iwata H, Iwabuchi M, Shibamoto Y. Comparison of multileaf collimator and conventional circular collimator systems in Cyberknife stereotactic radiotherapy. J Radiat Res 2017;58:693–700. https://doi.org/10.1093/jrr/rrw130.
[10] McGuinness CM, Gottschalk AR, Lessard E, Nakamura JL, Pinnaduwage D, Pouliot J, et al. Investigating the clinical advantages of a robotic linac equipped with a multileaf collimator in the treatment of brain and prostate cancer patients. J Appl Clin Med Phys 2015;16:284–95. https://doi.org/10.1120/jacmp.v16i5.5502.
[11] Schmitt D, El Shafie R, Klüter S, Arians N, Schubert K, Rieken S, et al. Treatment planning for MLC based robotic radiosurgery for brain metastases: plan comparison with circular fields and suggestions for planning strategies. Curr Dir Biomed Eng 2017;3:151–4. https://doi.org/10.1515/cdbme-2017-0032.
[12] Schlaefer A, Schweikard A. Stepwise multi-criteria optimization for robotic radiosurgery. Med Phys 2008;35:2094–103. https://doi.org/10.1118/1.2900716.
[13] Blanck O, Wang L, Baus W, Grimm J, Lacornerie T, Nilsson J, et al. Inverse treatment planning for spinal robotic radiosurgery: an international multi-institutional benchmark trial. J Appl Clin Med Phys 2016;17:313–30. https://doi.org/10.1120/jacmp.v17i3.6151.
[14] Ding C, Saw CB, Timmerman RD. Cyberknife stereotactic radiosurgery and radiation therapy treatment planning system. Med Dosim 2018;43:129–40. https://doi.org/10.1016/j.meddos.2018.02.006.
[15] Zeverino M, Marguet M, Zulliger C, Durham A, Jumeau R. Novel inverse planning optimization algorithm for robotic radiosurgery: first clinical implementation and dosimetric evaluation. Phys Medica 2019;64:230–7. https://doi.org/10.1016/j.ejmp.2019.07.020.
[16] Xia P, Verhey LJ. Multileaf collimator leaf sequencing algorithm for intensity modulated beams with multiple static segments. Med Phys 1998;25:1424–34. https://doi.org/10.1118/1.598315.
[17] Masi L, Zani M, Doro R, Calusi S, Di Cataldo V, Bonucci I, et al. CyberKnife MLC-based treatment planning for abdominal and pelvic SBRT: analysis of multiple dosimetric parameters, overall scoring index and clinical scoring. Phys Medica 2018;56:25–33. https://doi.org/10.1016/j.ejmp.2018.11.012.
[18] Giglioli FR, Garibaldi C, Blanck O, Villaggi E, Russo S, Esposito M, et al. dosimetric multicenter planning comparison studies for SBRT: methodology and future perspectives. Int J Radiat Oncol 2019. https://doi.org/10.1016/j.ijrobp.2019.10.041.
[19] Ventura T, Lopes Mdo C, Ferreira BC, Khouri L. SPIDERplan: a tool to support decision-making in radiation therapy treatment plan assessment. Rep Pract Oncol Radiother 2016;21:508–16. https://doi.org/10.1016/j.rpor.2016.07.002.
[20] Nelms BE, Robinson G, Markham J, Velasco K, Boyd S, Narayan S, et al. Variation in external beam treatment plan quality: an inter-institutional study of planners and planning systems. Pract Radiat Oncol 2012;2:296–305. https://doi.org/10.1016/j.prro.2011.11.012.
[21] Benedict SH, Yenice KM, Followill D, Galvin JM, Hinson W, Kavanagh B, et al. Stereotactic body radiation therapy: the report of AAPM Task Group 101. Med Phys 2010;37:4078–101. https://doi.org/10.1118/1.3438081.
[22] Sahgal A, Ma L, Weinberg V, Gibbs IC, Chao S, Chang U-K, et al. Reirradiation human spinal cord tolerance for stereotactic body radiotherapy. Int J Radiat Oncol 2012;82:107–16. https://doi.org/10.1016/j.ijrobp.2010.08.021.
[23] Jeleń U, Söhn M, Alber M. A finite size pencil beam for IMRT dose optimization. Phys Med Biol 2005;50:1747–66. https://doi.org/10.1088/0031-9155/50/8/009.
[24] Paddick I, Lippitz B. A simple dose gradient measurement tool to complement the conformity index. J Neurosurg 2006;105:194–201. https://doi.org/10.3171/sup.2006.105.7.194.
[25] Du W, Cho SH, Zhang X, Hoffman KE, Kudchadker RJ. Quantification of beam complexity in intensity-modulated radiation therapy treatment plans. Med Phys 2014;41:021716https://doi.org/10.1118/1.4861821.
[26] Blanck O, Masi L, Chan MKH, Adamczyk S, Albrecht C, Damme M-C, et al. High resolution ion chamber array delivery quality assurance for robotic radiosurgery: commissioning and validation. Phys Medica 2016;32:838–46. https://doi.org/10.1016/j.ejmp.2016.05.060.
[27] Zani M, Calusi S, Doro R, Bellosi N, Cassinelli M, Pazzaglini S, et al. Sensitivity of patient specific quality assurance to simulated delivery errors for CyberKnife MLC treatments and effects on DVH. Phys Medica 2018. https://doi.org/10.1016/j.ejmp.2018.04.021.
[28] Masi L, Doro R, Blanck O, Calusi S, Bonucci I, Cipressi S, et al. EP-1483: pre-treatment QA of MLC plans on a CyberKnife M6 using a liquid ion chamber array. Radiother Oncol 2017. https://doi.org/10.1016/s0167-8140(17)31918-7.
[29] Akpati H, Kim C, Kim B, Park T, Meek A. Unified dosimetry index (UDI): a figure of merit for ranking treatment plans. J Appl Clin Med Phys 2008;9:99–108. https://doi.org/10.1120/jacmp.v9i3.2803.
[30] Mayo CS, Yao J, Eisbruch A, Balter JM, Litzenberg DW, Matuszak MM, et al. Incorporating big data into treatment plan evaluation: development of statistical DVH metrics and visualization dashboards. Adv Radiat Oncol 2017;2:503–14. https://doi.org/10.1016/j.adro.2017.04.005.
[31] Alfonso JC, Herrero MA, Núñez L. A dose-volume histogram based decision-support system for dosimetric comparison of radiotherapy treatment plans. Radiat Oncol 2015;10:263. https://doi.org/10.1186/s13014-015-0569-3.
[32] Licon AL, Defoor D, Ford J, Crownover R, Li Y, Ha C, et al. A quantitative measure for radiation treatment plan quality. J BUON 2018;23:1460–6.
[33] Russo S, Esposito M, Hernandez V, Saez J, Rossi F, Paoletti L, et al. Does deep inspiration breath hold reduce plan complexity? Multicentric experience of left breast cancer radiotherapy with volumetric modulated arc therapy. Phys Medica 2019;59:79–85. https://doi.org/10.1016/j.ejmp.2019.02.018.
[34] Esposito M, Masi L, Zani M, Doro R, Fedele D, Garibaldi C, et al. SBRT planning for spinal metastasis : indications from a large multicentric study 2018. https://doi.org/10.1007/s00066-018-1383-2.