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Doctoral Thesis Summary

Dynamic Wave Arc: implementing a theoretical concept to clinical routine

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Chapter I: General introduction

The art of cancer treatment is in finding the right balance between tumor cure and injury to normal tissues. One of the ways of increasing the radiotherapeutic success is by optimization the treatment delivery technique. In the last 20 years there has been a huge technological leap forward in the technical aspects of radiotherapy, as well as developments in treatment planning systems leading to improved dose distributions and conformity.

The Vero system consists of a 6 MV linear accelerator (linac) mounted on an O-ring gantry that rotates around the patient by ± 185° and, unlike C-arm gantries, Vero can also rotate around the vertical axis (± 60°). The latter allows noncoplanar delivery without couch rotations. The system incorporates several imaging modalities in the O-ring structure: EPID for MV portal imaging, and two orthogonal kV X-ray tubes in combination with two flat panel detectors allowing patient imaging and positioning at any gantry and ring angle. The X-ray system offers cone-beam computed tomography (CBCT) and fluoroscopy, allowing real-time imaging of moving targets.

The research presented in this book focused on the dynamic combination of leaf motion and synchronized gantry-ring rotations, representing a novel noncoplanar rotational delivery technique under the name “Dynamic Wave Arc (DWA)”. The theoretical concept was first introduced in 2013, and highlighted the potential benefits of a new technique that allows both the radiation head unit and the ring-shaped gantry to rotate simultaneously during arc irradiation. However, it wasn’t until 2015 that the novel technique was supported with a commercially available treatment planning system and the Vero machine was mechanically capable of combined gantry-ring rotations. Characterization and clinical implementation of the DWA technique were subject of the studies performed in the preparation of this thesis and will be explained further throughout the thesis.

The structure of the thesis

The manuscript provides a detailed overview of the scientific development and successful clinical implementation of Dynamic Wave Arc treatment delivery technique at the Radiotherapy Department of the University Hospital of the VUB Brussels. The translation process of DWA from a theoretical concept to routine practice is described. Each chapter represents a major checkpoint along the translation model, answering to a key question in the process. At first, we started with a characterization of the Vero SBRT system, emphasizing its distinguished features (i.e. O-ring shaped mechanical structure; C-band standing-wave LINAC; gimbals-supported X-ray head; integrated IGRT system) in contrast with the conventional C-arm systems **[Chapter 1].**

The initial question to be answered was the feasibility of using the Vero system for cranial radiosurgery *(Can the Vero system achieve dose distributions characteristic with a sharp dose falloff outside the target and tight conformity around the lesion?)* **[Chapter 2].** The high mechanical stability of the machine, the noncoplanar liberty offered by the O-ring design, and the on-board imaging capabilities made it suitable to be considered for intracranial stereotactic treatments. The Vero SBRT system was benchmarked in a planning study against the Novalis SRS system for quality of radiosurgery dose distributions to intracranial lesions, to evaluate whether or not the Vero can be applied for SRS, and to identify patients that might benefit from this approach.

Secondly, we continued to pursue the noncoplanar capabilities of O-ring gantry structure, to determine the feasibility of synchronized rather than sequential gantry-ring rotations. *(Is the Vero capable of following complex noncoplanar trajectories while preserving its high geometric accuracy?)* **[Chapter 3].** This stage involved examining safety and efficacy of a novel delivery technique defined by gantry-ring simultaneous movements: Dynamic Wave Arc. The geometric accuracy was determined applying an independent, in-house developed method based on on-board x-ray fluoroscopy rotating along with the DWA delivery, using a phantom with predefined 3D spherical marker geometry. The methodology provides a simple and efficient pre-treatment verification for Vero acceptance testing or clinical quality assurance procedures, independent of future developments in dose optimization or trajectory optimization.

As a preparatory step to introduce DWA in clinical practice, the VERO SBRT approach was integrated into a dedicated commercially available TPS. *(What is DWA treatment approach and which patients would benefit from it?)* **[Chapter 4].** The study included a descriptive characterization of DWA, followed by a benchmark against the current clinical approaches and coplanar VMAT for various anatomical tumor regions. Each plan was evaluated with regard to dose distribution, modulation complexity, monitor units and treatment time efficiency. Various tests were developed to determine if the LINAC performs within specifications during irradiation The delivery accuracy was evaluated using a 2D diode array able to cope with the multi-dimensionality of DWA during dose reconstruction.

Based on the experience accumulated in the previous studies, a clinical site-specific DWA template solution was developed and clinically implemented in our department. Once available, the validation steps started and continued with a first assessment of DWA workflow in clinical conditions. *(What does DWA implementation in routine practice require and what has to be further improved?)* **[Chapter 5]**. The first section gives and overview of beam commissioning, verification of the beam model, and measurements verifying that generated plans are deliverable with sufficient accuracy. Based on the data acquired during the preparations and delivery of the first 15 treatments, the second subchapter reports our preliminary clinical experience with DWA, and highlights several avenues for further improvements. A first assessment of DWA workflow in clinical conditions is presented, written with the aim of facilitating introduction of DWA to other clinical sites.

The last chapter **[Chapter 6]** contains a discussion on some interesting topics that have relevance in the current noncoplanar rotational VMAT evolution.

Chapter II: Feasibility of using the Vero SBRT system for intracranial SRS

The high mechanical stability of the machine, the noncoplanar liberty offered by the O-ring design, and the on-board imaging capabilities made it suitable to be considered for intracranial stereotactic treatments.

The Vero SBRT system was benchmarked in a planning study against the Novalis SRS system for quality of delivered dose distributions to intracranial lesions and assessing the Vero system's capacity for SRS.□ A total of 27 patients with one brain lesion treated on the Novalis system, with 3 mm leaf width MLC and C-arm gantry, were replanned for Vero, with a 5 mm leaf width MLC mounted on an O-ring gantry allowing rotations around both the horizontal and vertical axis. The Novalis dynamic conformal arc (DCA) planning included vertex arcs, using 90° couch rotation. These vertex arcs cannot be reproduced with Vero due to the mechanical limitations of the O-ring gantry. Alternative class solutions were investigated for the Vero (Figure 1). Additionally, to distinguish between the effect of MLC leaf width and different beam arrangements on dose distributions, the Vero class solutions were also applied for Novalis. In addition, the added value of noncoplanar IMRT was investigated in this study. Quality of the achieved dose distributions was expressed in the conformity index (CI) and gradient index (GI), and compared using a paired Student's t-test with statistical significance for p-values ≤ 0.05.

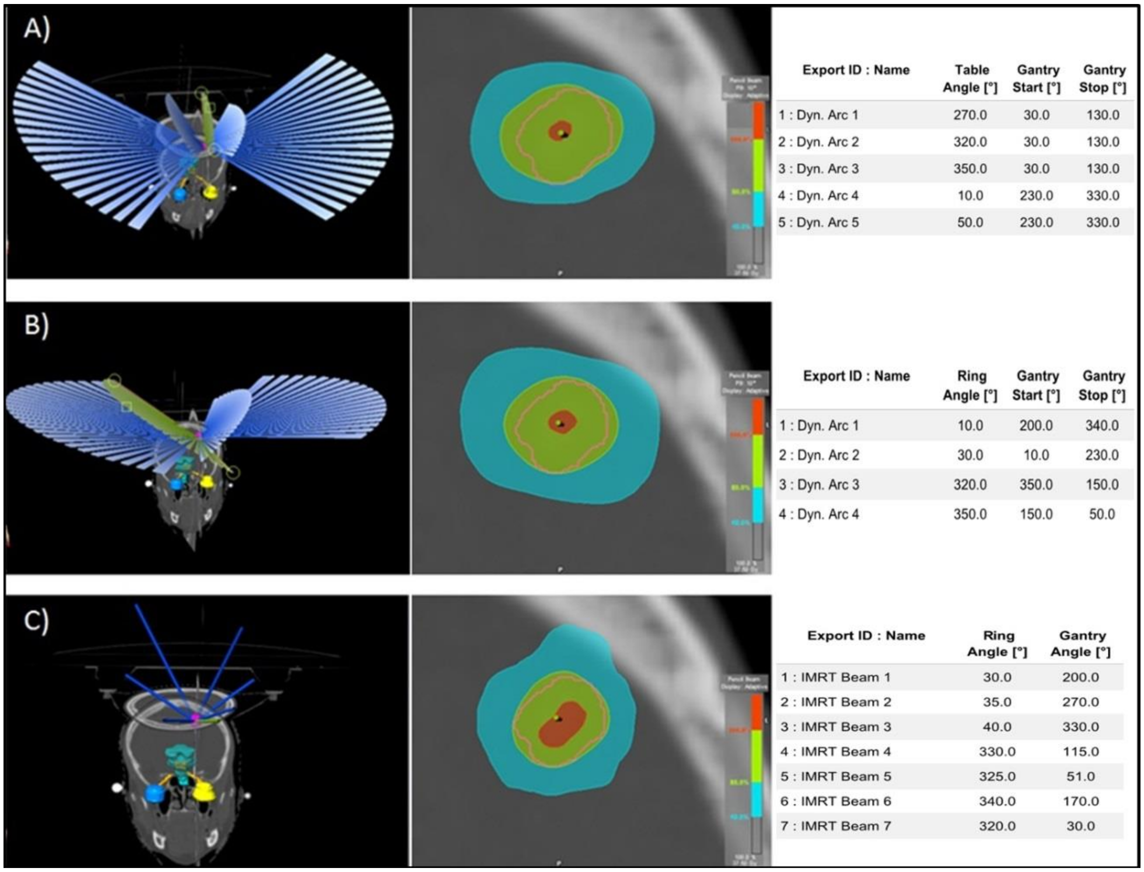

Figure 1. Illustration of the planning approaches, dose distribution and beam setup for the same patient: (a) Novalis template, (b) Vero "4 noncoplanar arcs approach", and (c) Vero IMRT template.

For lesions larger than 5 cm3, no statistical significant difference in conformity was observed between Vero and Novalis, but for smaller lesions, the dose distributions showed a significantly better conformity for the Novalis (ΔCI = 13.74%, p = 0.0002) mainly due to the smaller MLC leaf width. Using IMRT on Vero reduces this conformity difference to nonsignificant levels. The cutoff for achieving a GI around 3, characterizing a sharp dose falloff outside the target volume was 4 cm3 for Novalis and 7 cm3 for Vero using DCA technique. Using noncoplanar IMRT, this threshold was reduced to 3 cm3 for the Vero system. The smaller MLC and the presence of the vertex fields allow the Novalis system to better conform the dose around the lesion and to obtain steeper dose falloff outside the lesion. Comparable dosimetric characteristics can be achieved with Vero for lesions larger than 3 cm3 and using IMRT.

Chapter III: Geometric verification of Dynamic Wave Arc delivery using orthogonal X-ray fluoroscopic imaging

The purpose of the study was to define an independent verification method based on on-board orthogonal fluoroscopy to determine the geometric accuracy of synchronized gantry-ring rotations during dynamic wave arc delivery (DWA) available on the Vero system. A verification method for DWA was developed to calculate O-ring-gantry (G/R) positional information from ball-bearing positions retrieved from fluoroscopic images of a cubic phantom acquired during DWA delivery.

The fluoroscopy image acquisition was enabled before the beam delivery started. From the BB's detected positions the G/R angular information was determined through an iterative process: the BB's position was projected for a certain predicted G/R as starting point and a search space was extended around the predicted angulation with a step size of 0.1° within the interval G+3°, G-3°; R+3°, R-3°. The distance between detected and predicted positions was calculated for each marker, and the G/R angulation corresponding to a certain image was establish when the overall distance between detected and predicted positions became minimal (Figure 2).

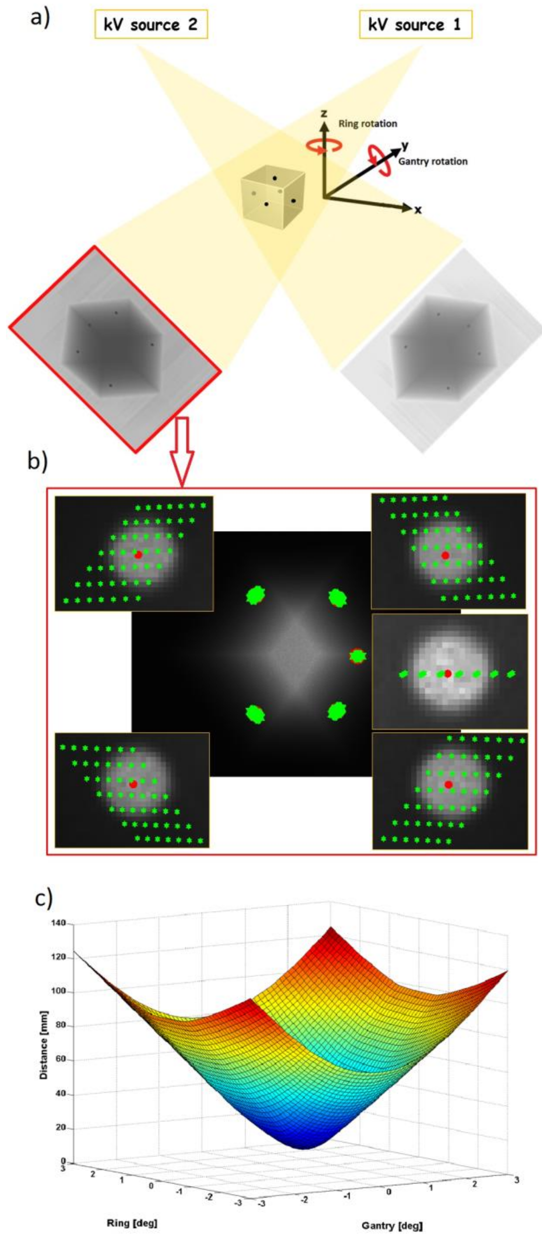

Figure 2. An illustration of the G/R detection process for G/R=0°/0°. a) Orthogonal kV images of the cubic phantom with BBs attached are acquired. b) The projected BBs positions are detected (red dots) and a set of predicted positions in the interval G±3°, R±3° is generated (green dots). c) In the search interval, the shortest distance between detected and predicted positions will provide the G/R angulation.

Different non-coplanar trajectories were generated in order to investigate the influence of path complexity on delivery accuracy. The G/R positions detected from the fluoroscopy images (DetPositions) were benchmarked against the G/R angulations retrieved from the control points (CP) of the DWA DICOM RT plan, and the DWA log files recorded by the treatment console during DWA delivery (LogActed). The G/R rotational accuracy was quantified as the mean absolute deviation +/- standard deviation. The maximum G/R absolute deviation was calculated as the maximum 3D distance between the CP and the closest DetPositions.

In the CP vs. DetPositions comparison, an overall mean G/R deviation of 0.13°/0.16° ± 0.16°/0.16° was obtained, with a maximum G/R deviation of 0.6°/0.2°. For the LogActed vs. DetPositions evaluation, the overall mean deviation was 0.08°/0.15° ± 0.10°/0.10° with a maximum G/R of 0.3°/0.4°. The largest decoupled deviations registered for gantry and ring were 0.6° and 0.4° respectively. No directional dependence was observed between clockwise and counter clockwise rotations. Doubling the dose resulted in a double number of detected points around each CP, and an angular deviation reduction in all cases.

An independent geometric QA approach has been developed for DWA delivery verification and was successfully applied on diverse trajectories. Results showed that the Vero system is capable of following complex G/R trajectories with maximum deviations during DWA below 0.6°. The methodology provides a simple and efficient pre-treatment verification for Vero acceptance testing or clinical quality assurance procedures, independent of future developments in dose optimization or trajectory optimization.

Chapter IV: Initial characterization, dosimetric benchmark and performance validation of Dynamic Wave Arc

DWA is a clinical approach designed to maximize the versatility of Vero SBRT system by synchronizing the gantry-ring noncoplanar movement with D-MLC optimization. The purpose of this study was to verify the delivery accuracy of DWA approach and to evaluate the potential dosimetric benefits.

DWA is an extended form of VMAT with a continuous varying ring position. The main difference in the optimization modules of VMAT and DWA is during the angular spacing, where the DWA algorithm does not consider the gantry spacing, but only the Euclidian norm of the ring and gantry angle. A preclinical version of RayStation v4.6 (RaySearch Laboratories, Sweden) was used to create patient specific wave arc trajectories for 31 patients with various anatomical tumor regions (prostate, oligometatstatic cases, centrally-located non- small cell lung cancer (NSCLC) and locally advanced pancreatic cancer-LAPC). DWA was benchmarked against the current clinical approaches and coplanar VMAT (Figure 3). Each plan was evaluated with regards to dose distribution, modulation complexity (MCS), monitor units and treatment time efficiency. The delivery accuracy was evaluated using a 2D diode array that takes in consideration the multi-dimensionality of DWA during dose reconstruction.

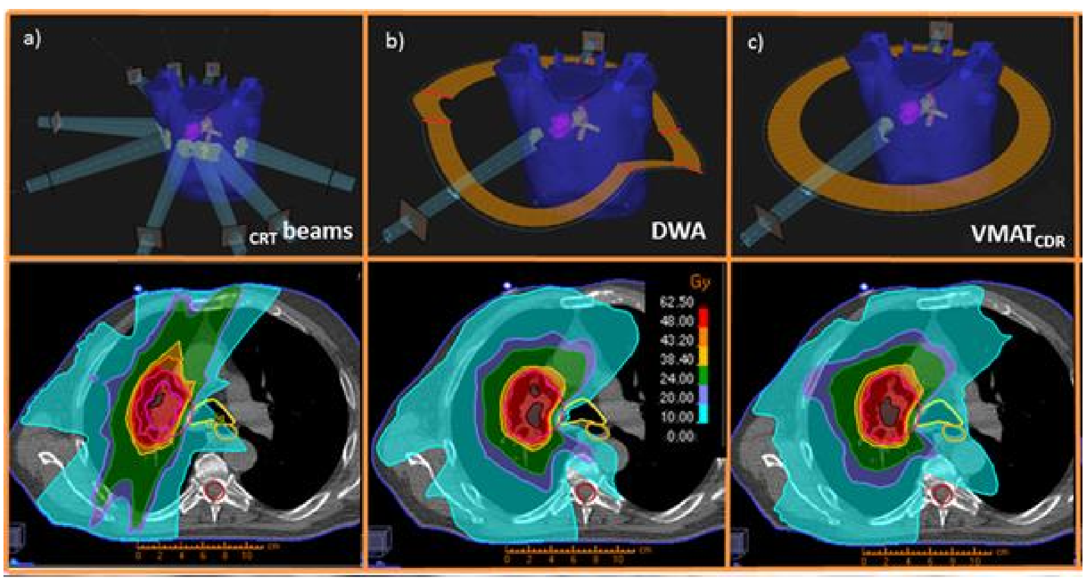

Figure 3. Treatment delivery scenarios investigated along with the dose distribution in the axial plane. a) coplanar/ noncoplanar static beams b) DWA noncoplanar trajectory defined by 7 MPs highlighted in red c) VMATCDR denotes a coplanar arc solution with MLC filed shape modulation, but constant gantry speed and constant dose rate

In centrally-located NSCLC cases, DWA improved the low dose spillage with 20 %, while the target coverage was increased with 17 % compared to 3D CRT. The structures that significantly benefited from using DWA were proximal bronchus and esophagus, with the maximal dose being reduced by 17 % and 24 %, respectively. For prostate and LAPC, neither technique seemed clearly superior to the other; however, DWA reduced with more than 65 % of the delivery time over IMRT. A steeper dose gradient outside the target was observed for all treatment sites ($p < 0.01$) with DWA. Except the oligometastatic cases, where the DWA-MCSs indicate a higher modulation, both DWA and VMATCDR modalities provide plans of similar complexity. The average ɣ (3 % / 3 mm) passing rate for DWA plans was 99.2 ± 1 % (range from 96.8 to 100 %).
DWA proven to be a fully functional treatment technique, allowing additional flexibility in dose shaping, while preserving dosimetrically robust delivery and treatment times comparable with coplanar VMAT.

Chapter V: Treating patients with Dynamic Wave Arc: first clinical experience

DWA was implemented in a multi-vendor environment, with three major components in the delivery chain. First, the DWA module, available in RayStation TPS (RaySearch Laboratories, Sweden). Second, the Record&Verify and Vero SBRT system (Mitsubishi Heavy Industries, Japan), able to automatically import and mechanically deliver DWA plans. Lastly, the ExacTrac Vero (BrainLAB AG, Germany) as the patient positioning system. With the Wave arc-planning module it is possible to plan DWA treatments where the gantry ring is allowed to turn at the same time as the gantry angle changes, allowing to design patient individualized treatments.
Proper beam commissioning and QA procedures are important for the implementation and use of a new treatment delivery technique. The purpose of this work was to perform a dosimetric commissioning assessment for the Vero

SBRT system modeled for the first time in Raystation TPS, and to validate the DWA delivery accuracy in comparison with VMAT and IMRT. The AAPM TG119 set consisting of four commissioning problems (test prostate, head-and-neck (H&N), C- shaped target, and Multi Target) was used to verify that each treatment type can be planned, prepared, and delivered with sufficient accuracy (Figure 4).

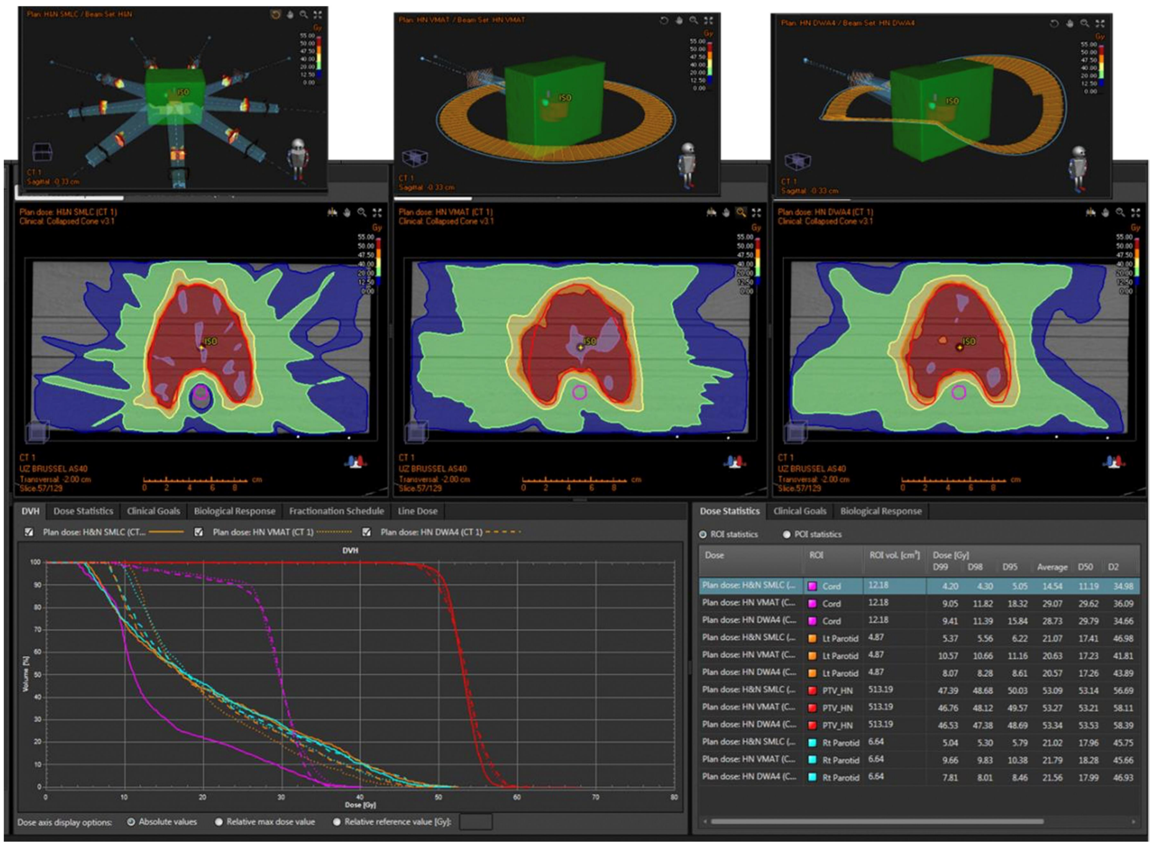

Figure 4: Dose distribution by technique for the TG119 H&N case (IMRT, VMAT and DWA). The first row presents the 3D geometry for each delivery technique, while the second row displays the afferent transversal dose distributions. The corresponding cumulative DVHs and statistics for both PTV and OARs are lastly presented.

Averaged over all four cases, isocentric point ratio were 98.5%, 101.1% and 101.4% for IMRT, VMAT and DWA plans respectively. Gamma analysis (3 mmL/3%) for the film measurements showed passing rates of 96.5%, 95.3%, 95.9% for the IMRT, VMAT and DWA plans, respectively.

Dynamic Wave Arc (DWA) is a system-specific noncoplanar arc technique that combines synchronized gantry-ring rotation with D-MLC optimization. This paper presents the clinical workflow, quality assurance program, and reports the geometric and dosimetric results of the first patient cohort treated with DWA.

The RayStation TPS was clinically integrated on the Vero SBRT platform for DWA treatments. The first 15 patients treated with DWA represent a broad range of treatment sites: breast boost, prostate, lung SBRT and bone metastases, which allowed us to explore the potentials and assess the limitations of the current DWA site-specific template solution. For the DWA verification a variety of QA equipment was used, from 3D diode array to an anthropomorphic end-to-end phantom. The geometric accuracy of each arc was verified with an independent orthogonal fluoroscopy method.

Table1. Summary of patient diagnoses, dose prescription and DWA plan parameters

Patient Nr.	Indication		Fractionation	DWA template	Nr. of MPs	Nr. of CPs	Nr. kV images	Nr. MU	Delivery time (min)
1	Right breast boost		8 x 2Gy	B3	6	59	195	505	1,60
2	Prostate		39 x 2Gy	X1 X1ccw	9 9	89 89	146 160	239 220	2,37
3	Lung LLL centrally		8 x 7,5Gy	L5 X5	5 5	90 45	298 132	969 423	3,48
4	Prostate		39 x 2Gy	X2 X2ccw	6 6	89 89	129 130	168 233	2,07
5	Lung RML centrally		3 x 17Gy	L1 X3	7 5	90 45	523 571	1686 1840	8,82
6	Left Breast boost		4 x 2,5Gy	B2	6	51	185	435	1,43
7	Lung RUL peripherally		4 x 12Gy	B2 X1	6 9	51 89	335 556	1082 1823	7,28
8	Lung RUL centrally		8 x 7,5Gy	X2 B2	6 6	89 51	324 288	1057 842	4,92
9	Lung RUL paravertebral		4 x 12Gy	X2 X3	6 5	89 45	625 161	2062 522	6,48
10	Left Breast boost		4 x 2,5Gy	B2	6	51	175	427	1,42
11	Right Breast boost		8 x 2Gy	B1	6	51	195	521	1,60
12	Prostate		39 x 2Gy	X1 X1ccw	9 9	89 89	148 149	194 200	2,37
13	Left breast boost		8 x 2Gy	B2	6	51	188	472	1,50
14	Prostate		39 x 2Gy	X1 X1ccw	9 9	89 89	152 150	208 282	2,37
15	Bone metastases	Right 8th rib	5 x 4Gy	X5	5	45	155	487	1,22
		Left 3th rib	5 x 4Gy	B2	5	45	228	740	1,85
		Vertebra L5	5 x 4Gy	P2	5	90	213	697	1,73
		Right ilium	5 x 4Gy	E1	5	90	200	662	1,67

Abbreviations: LLL=left lower lobe; RML=right middle lobe, RUL=right upper lobe; MP= Manipulation Points i.e. gantry-ring angle positions where the direction of the ring rotation can change; CP= Control Points, i.e. gantry-ring angle positions spaced every 4° where the beam aperture shaped by the MLC can change; Nr. kV images=fluoroscopic images acquired during DWA QA delivery for the gantry-ring geometric verification; Delivery time=measured beam-on delivery time.

The average beam-on delivery time was 3 min, ranging from 1.22min to 8.82min. All patient QAs passed our institutional clinical criteria of gamma index. For both EBT3 film and Delta4 measurements, DWA planned versus delivered dose distributions presented an average agreement above 97%. An overall mean gantry-ring geometric deviation of -0.03° ± 0.46° and 0.18° ± 0.26° was obtained, respectively.

For the first time, DWA has been translated into the clinic and used to treat various treatment sides. DWA has been successfully added to the noncoplanar rotational IMRT techniques arsenal, allowing additional flexibility in dose shaping while preserving dosimetrically robust delivery.

Chapter VI: General discussion

While new technologies are ultimately aimed at improving treatment outcome, the immediate goal is to improve treatment quality. A new technology could be instrumental in reducing doses to critical tissues or may give a better dose distribution to the target volume. By using the benchmarking of DVHs, we could objectively determine the DWA dosimetric value in comparison with other established techniques. In centrally-located NSCLC cases, DWA improved the low dose spillage with 20 %, while the target coverage was increased with 17 % compared to 3D CRT. The structures that significantly benefited from using DWA were proximal bronchus and esophagus, with the maximal dose being reduced by 17 % and 24 %, respectively. A steeper dose gradient outside the target was observed for all treatment sites ($p < 0.01$) with DWA. In general, DWA presented a faster planning option, faster treatment delivery times, and more workload for the radiotherapist. Therefore, the progress introduced by DWA is based on its operational characteristics rather than its direct effect on treatment outcome.

DWA maximizes the noncoplanar versatility of Vero SBRT system by combining the gantry-ring synchronized rotation with D-MLC optimization. DWA opens the possibility to create patient-individualized treatment plans, allowing additional flexibility in organ at risk sparing while preserving dosimetrically robust delivery.

Noncoplanar rotational IMRT is a relatively new application of radiotherapy still in full evolution. DWA can play a role in the future development and optimization. Already being in clinical use, DWA will push forward and facilitate the exaptation of personalized radiotherapy treatments, as dynamic - couch VMAT is becoming available on most state-of-the-art LINAC systems

List of publications

1. Burghelea M, Verellen D, Gevaert T, Depuydt T, Poels K, Simon V, De Ridder M. Feasibility of using the Vero SBRT system for intracranial SRS. J Appl Clin Med Phys. 2014; 15(1): 4437

2. Burghelea M, Verellen D, Poels K, Gevaert T, Depuydt T, Tournel K, Hung C, Simon V, Hiraoka M, de Ridder M. Geometric Verification of Dynamic Wave Arc Delivery With the Vero System Using Orthogonal X-ray Fluoroscopic Imaging. Int J Radiat Oncol Biol Phys. 2015; 92(4): 754-61

3. Burghelea M, Verellen D, Poels K, Hung C, Nakamura M, Dhont J, Gevaert T, Van den Begin R, Collen C, Matsuo Y, Kishi T, Simon V, Hiraoka M, de Ridder M. Initial characterization, dosimetric benchmark and performance validation of Dynamic Wave Arc. Radiat Oncol. 2016; 11:63

4. Burghelea M, Verellen D, Dhont J, Hung C, Gevaert T, Van den Begin R, Collen C, Poels K, Tournel K, Boussaer M, Jaudet C, Reynders R, Simon V, de Ridder M. Treating patients with Dynamic Wave Arc: First clinical experience. Radiother Oncol. 2017;122(3):347-351