Implementation and Evaluation of Volumetric Modulated Arc Therapy at the Radiation Therapy Department at The University Hospital of Umeå

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Abstract
The recently developed Volumetric Modulated Arc Therapy (VMAT) is a rotational delivery technique in which the gantry moves continuously during irradiation of the patient. The main purpose of this thesis is to implement and evaluate the VMAT treatment method as well as perform quality assurance on plans before they are clinically approved and delivered.
This study included the replanning of 11 patients (5 prostate, 6 head and neck) previously treated with step-and-shoot IMRT (Intensity Modulated Radio Therapy) with VMAT and evaluation of the performance of the resulting VMAT plans. Also the different dose volume objectives- and VMAT specific parameters such as collimator angle setting and maximum treatment time were evaluated.
The dose planning benefits of VMAT over IMRT found in this study are mainly the better target coverage including high dose homogeneity, as well as better sparing of highly prioritized organs at risk such as rectum and medulla spinalis. Recommended parameters to achieve acceptable plans are a 15 – 45° collimator angle setting combined with the use of the surrounding dose fall of objective as well as some or all of the original IMRT objectives.
Notably no statistically significant difference in number of used Monitor Units were observed for the prostate cases for neither IMRT (574.4 ± 127) nor VMAT (571.8 ± 103.5). The head and neck cases yielded slightly less MUs in average when planned with IMRT(622.3 ± 105.4) compared to VMAT (708.7 ± 65.7) , however neither patient group showed a statistically significant difference for this parameter.
Treatment times were found to be significantly shorter for both patient groups with VMAT(2.96 ± 0.05 min) being faster compared to IMRT (8.8 ± 3.5 min) for the prostate plans , and VMAT (2.95 ± 0.04 min) was also faster than IMRT (8.2 ± 1.8 min) in the head and neck cases.
Quality assurance was made with the MatriXX 2D diode array and yielded a >98.6% passing rate for all deliverable plans with a bolus correcting for table attenuation, and a secondary point dose measurement method with an RK-ionization chamber further verified the dosimetric accuracy of the MatriXX array.
Abbreviations and acronyms

3DCRT – 3D Conformal Radio Therapy
CCW – Counter Clock Wise
CPU – Central Processing Unit
CT – Computer Tomography
CW – Clock Wise
DICOM - Digital Imaging and Communications in Medicine
DNA – Deoxyribonucleic Acid
DVH – Dose Volume Histogram
DVO – Dose Volume Objective
Dx – Dexter (eng. right)
Gy – Gray (unit for absorbed dose)
IMRT – Intensity Modulated Radio Therapy
IMAT – Intensity Modulated Arc Therapy
Lgll – Lymphatic glands
Medulla spinalis – Spinal cord
MLC – Multi Leaf Collimator
MRI – Magnetic Resonance Imaging
MU – Monitor Units
MV – Megavolt
NTCP – Normal Tissue Complication Probability
NUS – Norrlands Universitetssjukhus
OAR – Organ At Risk
PTV – Planning Target Volume
SIB – Simultaneously Integrated Boost
Sin – Sinister (eng. left)
VMAT – Volumetric Modulated Arc Therapy
QA – Quality Assurance
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1. Introduction

In external photon radiation therapy the patients are treated with ionizing radiation either produced with linear accelerators (i.e high energy X-rays) or with radioactive sources like Cobalt 60. In the latter case where the origin of radiation comes from within the nucleus it is called γ-radiation. When ionizing radiation such as X-rays and γ-rays are absorbed in human tissue, there is a certain probability that they will induce damage to the DNA within the cell nucleus and therefore may affect its ability to reproduce itself, which is the underlying cause for radiation therapy of cancer. The often high reproduction rate of the cancerous cells make them more responsive to ionizing radiation since the repairing mechanisms require sufficient time to repair radiation induced damage to the DNA before undergoing mitosis, which consequently leads to that damaged DNA will be used as a blueprint for the next generation of cancer cells (Hall 1994, Nias 1990).

The world’s first successful radiation treatment with ionizing radiation was performed in Sweden 1899 at Stenbergs Röntgeninstitut by the pioneer Thor Stenbeck, in which a woman with basal cell carcinoma located on her nose tip had fractionated treatment during a 9 month period with an ordinary X-ray tube.

Later on the radiation therapy methods developed further during the 20th century, especially with the invention of the linear accelerator and the first primitive computers during the fifties, only to increase further in popularity at the latter part of the century by the advent of inverse planning with the support of Computer Tomography (CT) Magnetic Resonance Imaging (MRI) and Positron Emission Tomography (PET) (Walstam 1995).

The further development of the linear accelerator, the Multi Leaf Collimator (MLC) and the computational capacity made it possible to develop a new treatment technique in the mid 1990ies; Intensity Modulated Radio Therapy (IMRT) that makes use of inverse planning instead of the previously used forward planning.

The IMRT-technique enhances the conformity of the dose coverage around the target volumes (tumours) and reduces the high dose volumes to organs at risk. In the case of e.g. head and neck cancer, this leads to increased sparing of the medulla spinalis and parotid glands, which in turn yields less probability of radiation induced complications.
Volumetric Modulated Arc Therapy (VMAT) is a newly developed method, which in similarity with IMRT make use of optimization algorithms to find the optimal solution, albeit more complex and resource demanding for VMAT than for IMRT since the algorithm have to account for many more variables and a number of machine specific limitations (Tsai et al 2010).

During VMAT treatment, the MLC, gantry angle and dose rate varies continuously instead of being changed in discrete steps as the case of step and shoot IMRT treatment. This increases the degrees of freedom regarding dose coverage and Normal Tissue Complication Probability (NTCP), which in many recent studies including Hardcastle et al (2010), Boylan et al (2010), Bertelsen et al (2010) and Popescu et al (2010), indicates improvements in dose homogeneity and decreased number of Monitor Units (i.e dose output).

Furthermore, these studies clearly shows that VMAT is a significantly faster treatment method, since it instead of using discrete beams from specific gantry angle stations as is the case of step and shoot IMRT, continuously treats the patient in one or two gantry rotations, something that however is demanding on the mechanical equipment and calculating capabilities of the dose planning stations.

Remark: It should be mentioned for clarification that even though parts of the Rapid Arc®-technology from Varian (Varian Medical systems, Palo Alto, CA) was used in this multi vendor study, the treatment technique is from now on referred to as (Varian) VMAT if not mentioned otherwise.

VMAT which is the generic term for the treatment technique, is also adopted as a trademark by Elekta (Elekta Ltd, Crawley, UK) for their own solution of the rotational treatment technique (Feygelman et al 2010).
1.1 Purpose

The main purpose with this thesis is to implement a multi vendor based VMAT at the Radiation Therapy Department at Norrlands University Hospital and clarify if VMAT is a significantly better treatment method than the current clinically used method IMRT, regarding dose coverage to the tumour, dose to organs at risk, elapsed treatment time, and number of monitor units expelled. The thesis also includes the implementations of methods for Quality Assurance (QA) of the VMAT-treatment and to verify that the flow of patient specific data runs smoothly through the different steps of the multi vendor treatment chain. Furthermore the thesis includes an investigation of the influence by various user-selectable pre optimization parameters such as number of arcs, maximum allowed treatment time and the control point spacing on the plan quality to find the best combination of plan optimization parameters for optimal combination of treatment time and plan quality.
2. Theory/Background

2.1 The linear accelerator

A linear accelerator such as the Varian Clinac iX (Varian Medical systems, Palo Alto, CA), seen in figure 1 below, accelerates electrons to a high velocity (i.e. energy) using radiofrequency waves. The operator can often choose between two or more accelerating energies. After being accelerated, the electrons are allowed to interact with a target consisting of a high atomic number element such as wolfram, producing high energy Bremsstrahlung X-rays and the wolfram target needs to be water-cooled to cope with the immense heat losses created in the ineffective X-ray generating process.

Before the high energy X-rays enter the patient, the X-ray profile is flattened, collimated (shaped) and passes through two dosimetric monitor chambers for verification (Cherry et al 2009).

Figure 1. Varian Clinac iX linear accelerator. 1. Gantry 2. Collimator head 3. Imaging X-ray detector 4. Imaging X-ray tube. 5. I’mRT MatriXX Diode array with Multicube measurement setup on the treatment couch.
The MLC on Varian Clinac iX shown below in figure 2, has two sets of leaves, one part with thinner leaves in the middle for better resolution and one thicker part at the edges.

Figure 2. Collimator head with Varian Millenium 120 MLC. 1. Field opening highlighted with the field light function activated. 2. Thinner part of the tungsten Multi Leaf Collimator. 3. Thicker parts of the tungsten Multi Leaf Collimator

The influence of the collimator angle setting on the plan quality is widely discussed in other studies. Boylan et al (2010) conducted a VMAT vs IMRT study with a recommended 10° collimator offset.

The VMAT brain radiotherapy study made by Hsu et al (2010) recommends setting the collimator at a 45° angle so that the leaves are differentially oriented with compared to the patient throughout the gantry rotation.

Bedford et al. (2008) proposes a fixed 5° collimator angle to minimize the effects of tongue-and-groove effect and interleaf leakage, which is explained in figure 3 below.

Figure 3. The Tongue and Groove effect gives rise to irradiation leakage between the slits of the adjacent leaves of the collimator, yielding an intensity plot with peaks where the most transmission occur.
2.2 Conventional treatment

Before the time of IMRT and VMAT, conventional high energy photon treatment consisted of fixed source Co-60 (1.25 MV) treatment units which was developed during the 1950s, and linear accelerators in the 1960s. The main advantage of using megavoltage x-rays in simple beam deliveries such as relatively uniform and parallel opposed entrance beams is that the absorbed dose to the skin is reduced.

The advent of the radio therapy ‘simulator’ in the 1970s and 1980s made it possible using diagnostic x-rays in treatment planning, by using an imaging x-ray system mounted on a “dummy” accelerator with the same size, geometry and degrees of freedom as a Co-60 treatment machine or linear accelerator. While bone structures with relatively high density was clearly visible on the x-ray images, the soft tissue including tumours were harder to distinguish imposing a major problem with that technique.

However, the invention of the Computer Tomograph (CT) in the 1980s and even the opportunity to use Magnetic Resonance Imaging in 1990s gave the radiologist a reliable three dimensional overview of the patient anatomy where the soft tissues and tumours clearly could be outlined. Thus the need to deliver more conformal treatment fields out of the Co-60 and linear accelerators became obvious and the old method to shape fields in conventional treatment machines included the use of low melting point metal alloys, which was manually moulded into different shapes depending on the desired field. This time consuming moulding processes and having too few degrees of freedom paved way for the Multi Leaf Collimators which dismantled the tedious sculpture/moulding processes as well as increased the degrees of freedom due to the ability to deliver multiple field shapes of complicated nature even in the same treatment session.

Another great technological improvement was the use of electronic portal imaging systems for patient positioning verification, which improved the dosimetric conformance between the dose plan and the actually delivered plan (ICRU83 2010).

2.3 IMRT

In Intensity Modulated Radiation Therapy a set of intensity modulated beams enters the patient from multiple directions, resulting in a dose homogeneity of the tumour area in the same magnitude as conventional radiotherapy, with the difference that IMRT yields better dose conformity most noticeable in complex targets such as concavely shaped tumours (e.g prostate with lymph nodes and tumours wrapped around the medulla spinalis).
The need for conformity is important due to the possibility to spare normal tissues surrounding the tumour, something that is better achieved with IMRT due to its higher degrees of freedom regarding the treatment equipment. IMRT also have the ability to produce non uniform absorbed dose distributions for treatment of a targeted volume located within another targeted volume as is the case with Simultaneous Integrated Boost (SIB) techniques.

IMRT treatments often consists of 5-9 gantry angles, where at each gantry angle an optimal absorbed dose distribution is achieved by subdividing the incident beam into a few smaller segments and modulating each segment to achieve its wanted fluence contribution. The travelling speed, mechanical flexibility and thin width leafs in the MLC are therefore crucial for this modulation to be successful, especially in the case with Sliding Window IMRT where the MLC is continuously moving while the beam is on to achieve modulation. Another method is Step and Shoot IMRT, currently used at the Radiation Therapy Department at NUS where the MLC only is allowed to move in between the segments when the beam is off.

The method for calculating the required fluence from each beam segment in IMRT is done by inverse treatment planning with high performance computers using an iterative approach to calculate doses with algorithms, starting with the desired result and then working backwards to generate an optimal way to reach the final goal, i.e the desired doses to targets and dose limits to organs at risk are the initial values of the optimization problem. When the inverse planning process within the treatment planning system has determined the optimal solution, the consecutive gantry angles, beam shapes and fluence patterns can be exported via DICOM format to the record and verify system and treatment accelerator.

The world wide use of IMRT has grown steadily during the first years of the new millennia, particularly in the US, increasing from 1\3 IMRT usage in 2003 to 2\3 in 2005 based on numbers from ICRU83 (2010) and the main reason was not the increased sparing of the normal tissues or tumour dose escalation, but rather that the US clinics received more money on IMRT treatments than with conventional treatments. The site most frequently treated with IMRT are prostate- and head and neck cancers. However in Sweden, where IMRT treatment is mainly used for curative intent it is used to a lesser extent than conventional treatment.
2.4 VMAT

Arc- or rotational treatment therapy methods can be traced back to the midst of 20th century and conformal arc therapy involving dynamic field shaping by MLCs were first described in the mid 1960s, and developed further during the 1980s along with the three-dimensional conformal radiation therapy (3DCRT). Eventually, in 1995 Cedric Yu introduced the Intensity Modulated Arc Therapy, (IMAT) in which photon treatment was conducted in a rotational cone beam manner, where the modulation consists of different field shapes and varying dose weightings along the 360° rotation.

With the prior knowledge of IMAT and by varying the dose rate of the linear accelerator, Karl Otto developed a single-arc IMAT-algorithm in 2008 which he called Volumetric Modulated Arc Therapy (VMAT). The algorithm uses a progressive beam angle sampling to optimize a number of apertures, using direct aperture optimization, where the aperture shapes and their corresponding weights are initially optimized for a set number of coarsely placed gantry angles without taking the aperture connectivity in too much consideration. When the optimization algorithm has found an optimal solution, the previously left out gantry angles are inserted with their associated apertures being linearly interpolated from their neighbouring apertures to ensure a smooth transition of the MLC (Yu et al 2011).

Even though IMAT was proposed back in 1995 by Yu, and different rotational planning methods had been developed since, e.g the widely used Tomotherapy® in which the dose is delivered slice by slice, the implementation of other rotational solutions at clinics around the world did not start in larger scale until Varian™ in the year 2007, incorporated Otto’s VMAT algorithm under the trade name Rapid Arc™. Soon Elekta followed suit and adopted their own solutions. Elekta’s IMAT solution was marketed under the trade name VMAT™ (Yu et al 2011).

The difference in planning between IMRT and VMAT is small, however VMAT with immensely more degrees of freedom is more computationally demanding during optimization. Shown in figure 4 below are an example of the differences in number of control points between step and shoot IMRT and VMAT (Oncentra 4.0, Nucletron, Netherlands).
Figure 4. Axial CT-slice view of the abdomen with an outlined prostate in the middle showing a side by side comparison of incident VMAT and IMRT fields respectively. In the VMAT case there are 90 evenly distributed control points around the prostate patient where the modulation consists of different aperture shape and dose rate between two control points. Also the magnitude of the green bars represent the amount of monitor units used (i.e correlated to absorbed dose). In the IMRT case, the prostate patient receives five treatment fields from different gantry angles, all with fixed dose rate but multiple aperture settings.

In Oncentra 4.0 the Dose Volume Objectives (DVO) are available for the Step and Shoot-IMRT and VMAT optimization. A weighting factor, (i.e DVO priority) has to be assigned to every DVO. The weights of the DVOs and using different DVOs can affect plan quality, a straight forward method for comparing IMRT with VMAT would then be to have the same DVOs, but since the result of VMAT optimization however strongly depends on the strategy of the dose planner, the alteration of DVOs/VMAT-parameters should be allowed. The latter includes different machine specific plan parameters such as the gantry angle spacing, collimator angle setting, maximal delivery time or number of arcs (Alvarez-Moret et al 2010), (Wolff et al 2009).

2.5 Findings of earlier VMAT vs. IMRT studies

In a study made by Popescu et al (2010) they included five breast cancer patients previously treated with cIMRT (i.e nine coplanar modulated fields equally spaced in a 190° arc, 50Gy/25 fractions) which were replanned using VMAT to evaluate the possible benefits of the latter
technique regarding PTV coverage, sparing of OARs and reducing treatment time and the number of monitor units used. They concluded that the use of two arc VMAT had equivalent target coverage and improved the sparing of the OARs (including the heart) compared to cIMRT due to the smaller amount of induced high dose volumes used in VMAT. The mean number of monitor units used were 862/1254 and the associated mean treatment times where 3.9/8.8 minutes for VMAT and cIMRT respectively.

In another study comparing IMRT and VMAT dose plans, Hardcastle et al (2010) found that the perceived benefit of VMAT over IMRT is a reduction in delivery time. In the study, 10 prostate patients previously treated with IMRT plans where compared to VMAT with the same planning objectives. The dose volume histograms were compared, which indicated that the rectal doses for all 10 patients were reduced using VMAT while keeping the target coverage equivalent with the IMRT plans. The treatment time was reduced to as much as 69% compared with IMRT.

Tsai et al. (2010) investigated the possible treatment and dosimetric advantages of VMAT, step-and-shoot IMRT and Helical Tomotherapy (HT). The study included 12 prostate cancer patients and for each case, three different treatment planning methods were made (VMAT, step-and-shoot IMRT and HT) to allow for the comparison of target coverage, conformity index, dose to rectum/bladder, treatment time and monitor units. In the results Tsai et al. concluded that HT provides a superior conformity, significantly less rectal volume exposed to 65 Gy and 40 Gy and had better properties of sparing and complications regarding the rectum than compared with step-and-shoot IMRT, meanwhile VMAT had a slight dosimetric advantage over step-and-shoot IMRT.

The amount of used MUs was significantly lower for VMAT (309.7 +/- 35.4) and step-and-shoot IMRT (336.1 +/- 16.8) than for HT (3368 +/- 638.7) while the treatment time (minutes) was significantly shorter for VMAT (2.6 +/- 0.5) than step-and-shoot IMRT (3.8 +/- 0.3) and HT (3.8 +/- 0.6). Their dose verification of VMAT was done using point dose and film dosimetry which met the accepted criteria. VMAT and step-and-shoot IMRT have both comparable dosimetry, but the treatment efficiency is significantly higher for VMAT than for step-and-shoot IMRT and HT due to the shorter treatment time.
Boylan et al (2010) compared one arc VMAT with fixed beam IMRT for prostate cancer. The team developed their own VMAT method in which a static step-and-shoot IMRT plan was segmented into 60 equally spaced control points in a 360 degree arc. Their consecutive results showed that their VMAT planning method gives the possibility of multiple dose level target coverage comparable to that from an ordinary IMRT method as well as superior sparing of critical organs like the rectum and bladder. The associated delivery times are reduced with VMAT and the dosimetric verification, resilience and repeatability tests clearly implies that the solution is robust. Furthermore, rotational treatment techniques such as VMAT tend to give larger volumes of the body a low dose but yields a shorter mean treatment time of only 2.5 minutes for VMAT compared to 6 minutes for IMRT. The mean number of MUs used between the techniques were 521 for VMAT and 555 for IMRT. Boylan et al comments that a much larger differences in MU (up to 50%) have been reported when comparing sliding-windows IMRT plans with VMAT, albeit this is mostly a consequence of the sliding window delivery technique.

Using VMAT, Bertelsen et al (2010) replanned 25 head and neck cancer patients previously treated with step-and-shoot IMRT. The original IMRT objectives were used when replanning and only one VMAT revolution was allowed. For all the patients included in the study, it was possible to produce VMAT plans with dose distributions that would have been accepted for clinical treatments at their department. The target doses were in favour for VMAT with the most pronounced difference being the improved conformity index of the VMAT plans which was statistically significant for the planning target volume 50 Gy (PTV50). Among the organs at risk (OARs), the spinal cord showed no reduced dose with VMAT, but the sparing of submandibular-parotid glands were in favour of the VMAT technique. Also, the high dose volumes (i.e volumes receiving > 15 Gy) in healthy tissues were reduced with VMAT although the low dose volumes increased which is a consequence of these rotational techniques.

Concerning the number of used MUs, Bertelsen et al concluded only a small reduction when using VMAT, and that the differences rather depend on the differences in IMRT optimization algorithms and techniques (such as sliding window and step-and-shoot). The average time reductions with VMAT were found to be 2 minutes compared to IMRT.
2.6 VMAT Optimization Algorithm

The general VMAT optimization algorithm is designed so that it could support any linear accelerator being able to deliver dynamic arcs. In principle, a coarse set of segments, separated by 24°, are generated and applied around the patient and then the first intensity modulation optimization commences. The fluence maps created by this intensity modulation are transformed into small beam segments, which after filtering and redistribution are interpolated so that smooth leaf travel is assured during the treatment rotation. Pre optimization, the dose planner can choose between a 6, 4, 3 or 2° control point spacing, yielding e.g. 90 control points for one arc treatment with 4° control point spacing, where a final optimization is performed to give every control point its optimal aperture-, dose-rate setting and/or gantry speed to fulfil the dose volume objectives and machine delivery constraints (Feygelman et al 2010).

The following text gives a more thorough explanation of the optimization algorithm within Oncentra 4.0 for VMAT treatment, based on the description of Ericsson et al (2009).

1. A coarse set of initial control points with associated fluence maps are created at the starting angle (e.g. 178°) and stopping angle (e.g. 182°) and with 24° increments from the starting angle.

2. The first intensity modulation is initialized yielding fluence maps that are optimized for each initial angle.

3. The generated fluence maps are transformed to 2-4 control points each by using a leaf sweep style conversion.

4. As seen in figure 5, the algorithm filters out the smallest control points and leaves 2 control points per initial 24° angle increment. Then another algorithm sorts the control points accordingly to minimize the overall leaf travel during the whole treatment arc.

5. The control points previously left out are then added by interpolation between the already existing control points.
Figure 5. An illustration of the filtration- and redistribution process of the segments. In the above example, the fluences at the initial 24° and 48° directions are transformed into 3 control points each (Segment 1a – 2c), in which one of the control points is discarded (large X) and the other two are repositioned (marked by green X). The missing control points in between are generated by interpolating their neighbouring control points until the desired gantry spacing is achieved (red circles).

6. Before the optimization can commence, the control points are tested for compliance with the motion constraints either set by the planner or the actual limitations of the linear accelerator, that is maximum leaf travel speed, total delivery time, and valid dose rate.

7. After testing that the machine parameters are not out of bounds, machine parameter optimization is performed on every control point taking both the machine and user set constraints into consideration.

8. At last, collimator jaws and passive leaves are positioned. For the machines that have static collimator jaws, they are locked into position, conforming to the union of the segment shapes. Machines that have dynamic collimator jaws take the maximum jaw speed and other relevant machine specific constraints into account when conforming the collimator jaws to each and every segment shape.

2.7 The Gamma evaluation method

The gamma evaluation method takes into consideration the difference in calculated and measured dose and the spatial displacement between the analyzed pixels representing a dose value, and returns a $\gamma$-index as a result of the comparison. It allows one to find localized hot-spots created either by faulty leaf motion, the Tongue-and-Groove effect (see figure 3) or that
the treatment planning system yields minor miscalculations of the dose. The gamma method is a reliable and effective instrument for e.g IMRT treatment verification, represented either by a gamma histogram, or a 2D gamma-map (Low et al 2003).
3. Materials and methods

3.1 Delivery chain components.

The specific multi-vendor delivery chain (figure 6) used in this study included the Oncentra 4.0 (Nucletron, Veenendal, The Netherlands) treatment planning system, Mosaiq Record and Verify system (IMPAC Medical Systems, Sunnydale, CA), Varian 4D treatment console and linear accelerator (Varian Medical systems, Palo Alto, CA).

![Delivery chain components included in this study.](image)

The plan optimization with the Oncentra 4.0.0.227 (Nucletron 2010) software was done on two separate computers one with Intel® Xeon™ CPU 3.20 GHz, 6 GB of RAM and Windows XP as operating system and one Intel® Xeon® CPU 5160 3.00 GHz 8GB of RAM and Windows 2003 as operating system.

3.2 Treatment planning

In the case of prostate cancer treatment at NUS, the whole treatment schedule consists of a total accumulated dose of 78 Gy divided by 39 treatment sessions, in which the first 14 of the total 39 treatment sessions are conventional “four field box treatments”, and the latter part is IMRT treatment from 28 to 78 Gy.

For the generic head and neck cancer, a total of 68 Gy is delivered during 34 sessions, either with conventional treatment accounting for 22 Gy, or no conventional treatment at all.

If conventional treatment is part of the patient prescription, the remaining 46 Gy are given with IMRT treatment, also with 2 Gy fractions/day.

A total of 11 patients previously planned and treated with linear accelerator based step-and-shoot IMRT underwent replanning with VMAT using the same normal structure and target
contours as defined after the CT scans. Both IMRT and VMAT were planned for two Varian Clinac iX linear accelerators (Millenium 120- and 160-leaf MLC).

6MV photon energy and a prescribed cumulative dose of 46/68 Gy were used for Head and Neck cases. For the prostate cases, 15MV photon energy and a prescribed cumulative dose of 50 Gy was used. The patient anatomy was obtained prior to IMRT treatment with a Computer Tomograph using an axial slice thickness of 2.5 mm coinciding with the Oncentra 4.0 dose grid resolution in Y-direction. For the optimization, the RaySearch® package included in Oncentra 4.0 was used while Oncentras own enhanced pencil beam algorithm accounted for the dose calculation.

The anatomic contours and tumours were delineated by the physicians at the department of radiotherapy prior to the IMRT-treatment, and included organs at risk (OAR) such as rectum, femoral heads and urinal bladder for the five prostate cases. In the six remaining head and neck cases, the OARs included the brain, medulla spinalis and glandula parotis dx\sin. The iso-centre (point of rotation) of all VMAT plans was placed identical to the iso-centre of the IMRT-plans.

At first, the original IMRT objectives in terms of target coverage and dose to OARs were used, as well as only one 356° (from 178° to 182° CCW) VMAT arc around the patient to thoroughly test the capability of the optimizer. All VMAT plans utilized a 4° control point spacing as this according to Feygelman et al (2010) was found to be a good compromise between calculation speed and accuracy, an opinion also supported by Alvarez-Moret et al (2010). Furthermore, a 150 seconds maximum treatment time was used for all VMAT plans as recommended by the conclusions of Alvarez-Moret et al, that maximum treatment time have no clear systematic influence of the plan quality, however they also stated that this might be vendor specific. To verify the latter statement, a maximum treatment time comparison for two prostate cases was made for 75, 100, and 150 seconds in this study. Also, a comparison between different collimator angles were performed on two prostate cases and two head and neck cases. The tested angles were 0°, 3°, 15°, 30° and 45°. If the resulting Dose Volume Histograms (DVHs) showed insufficient target coverage or unacceptable doses to OARs, alterations in the dose volume objectives
were made, such as the addition of a simulated ROI-margin of the planning target volume consisting of an isotropic 1-3 mm extension to increase target coverage. One arc VMAT was tested and if the plan proved inferior, two arc VMAT was tested.

Also a final alternative before commissioning VMAT on accelerator, is to choose between fixed or dynamic gantry speed. The Varian accelerator can handle dynamic gantry speed and that option was therefore used. For some patients a fixed gantry speed was also used.

In Oncentra 4.0 the optimizer needs to know the hardware constraints of the accelerator since wrong settings can result in undeliverable plans. For example, setting the leaf motion parameter larger than 0.469 cm/deg can yield plans that can not be handled by the accelerator.

According to facility protocol, it is recommended to start the optimization with hard constraints on doses to organs at risk, and if necessary slightly decrease them to achieve appropriate target dose coverage.

Table 1. Norrlands Universitetssjukhus Radiation Therapy Department 78 Gy prostate planning guidelines for IMRT, also applicable for VMAT.

<table>
<thead>
<tr>
<th>Structure</th>
<th>Clinical constraints used for plan evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTV</td>
<td>Target isodose coverage: Min 95%, Max 105%</td>
</tr>
<tr>
<td>Rectum</td>
<td>Less than 15% of the volume should receive doses greater than 90% of the PTV dose.</td>
</tr>
<tr>
<td>Bladder wall</td>
<td>Max 28 Gy</td>
</tr>
<tr>
<td>Femoral heads</td>
<td>Max 35 Gy</td>
</tr>
</tbody>
</table>

Table 2. Norrlands Universitetssjukhus Radiation Therapy Department 46/68 Gy head and neck planning guidelines for IMRT, also applicable for VMAT.

<table>
<thead>
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</tr>
<tr>
<td>Medulla spinalis</td>
<td>Max 44 Gy</td>
</tr>
<tr>
<td>Brain</td>
<td>Max 50 Gy</td>
</tr>
<tr>
<td>Parotid glands</td>
<td>Mean dose below 26 Gy</td>
</tr>
</tbody>
</table>
3.3 Dose Volume Objectives used

The standard dose volume objectives used for VMAT optimization in this study included in the Oncentra 4.0 package consists of:

*Min Dose / Max Dose* – The optimizer tries to give the region of interest the specified minimum or maximum dose. Inputs are desired dose level and weight (priority of the objective).

*Uniform Dose*

The optimizer tries to achieve a uniform dose level within the target. Inputs are uniform dose level and weight.

*Surrounding Dose Fall Off* – Can only be used on the External region.

The optimizer tries to contain the high dose region to the target only by creating an artificial ring around the circumference of the target in which the dose gradient supposedly falls off with respect to used selected values. Inputs are high dose region level, low dose region level, width of the artificial ring and weight.

*Max Average Dose* – The optimizer tries to keep the average dose to the specified region below the specified maximum average dose. Inputs are desired dose level and weight.
Figure 7. A schematic of the principle behind the Surrounding Dose Fall-off objective. The external volume (i.e. non specific area of the patient) is given the high and low dose levels, and the optimizer then tries to linearly fit this dose gradient between the inner and outer rings of the target, yielding a dose fall off phenomenon which yields greater dose conformity to the target and spares organs at risk.

The intent of the newly implemented surrounding dose fall off objective in Oncentra 4.0 is to minimize the need for many dose volume objectives for several organs at risk. Thus in theory only a target DVO and surrounding dose fall objective for the external volume is required, with a recommendation setting the “high dose level” similar to the lowest target dose, and the “low dose level” to about 50% of the high dose level. The low dose distance explained in figure 7 above, is recommended to be in the order of 1 – 3 cm, depending on the desired conformity and outcome of the optimization results. However, if undesired conformance is obtained, there might be a need for additional DVOs to sensitive organs at risk receiving too high doses.

The maximum average dose volume objective is intended for “parallel” OARs like liver and the lung which are organs characterised by the ability to maintain its vital functions by a percentage level relative to the absorbed dose. If the Maximum average dose is set to 35 Gy the optimizing algorithm receives a penalty when the dose goes above this value to the specified OAR.

All the DVOs used in the final plan optimizations are represented in Appendix 1.
3.4 User-selectable VMAT parameters in Oncentra

Prior to optimization, the initial arc parameters are set such as number of arcs, (i.e 1 or 2 arcs) collimator angle setting (0-90°), maximum treatment time (75-150 seconds), and initial control point spacing (2,3,4,6, 8°).

Also, settings such as maximum gantry speed, total arc delivery time, leaf travel speed and dose rate are determined.

Other alternatives include fluence matrix resolution, inhomogeneity correction and tumour overlap fraction. At last, stopping criterions such as optimality tolerance and maximum number of iterations can also be set to desired values.

Figure 8. VMAT specific parameters within the treatment planning system Oncentra 4.0

Figure 8 above shows the parameters and their associated values.

- VMAT conversion after n iterations: Was set either to 10 or 20.
- Optimality tolerance: Was always set to 0.01 (Stop the optimizing process when reaching 0.01 difference in the objective function).
- Max number of iterations: Was set to 50, 60 or 70 depending on how the optimizer managed the plan dependant CPU work load.
- Tumour overlap fraction: Was either set to 100% or switched off.
- Fluence matrix X res. (cm): Was either set to “high” (0.30 cm) or “medium” (0.50 cm) depending on how the optimizer managed the plan dependant CPU work load.
- The target margin parameter is set by the optimization engine regardless of the user selected value.
Figure 9. The specific VMAT beam settings tab shows additional selectable VMAT parameters such as gantry spacing, maximum delivery time, number of arcs and maximum leaf motion.

Figure 9 shows the Constrain Leaf Motion parameter that can be selected by the user. This setting is only user selectable if the dynamic gantry angle option is switched off. If a dynamic gantry angle is used the constrain leaf motion will be automatically computed and used behind the scenes.

All the final VMAT parameters of clinical interest that was used are represented in table 9 in Appendix 1.

3.5 Treatment optimization

The already optimized and clinically delivered IMRT plans were based on the Direct Step and Shoot-IMRT alternative and to minimize the collimator leaf dose leakage, all the IMRT plans had a collimator head rotation of 3°. In the Beam Modelling module of treatment planning system Oncentra 4.0, the Accelerator energy (6/15 MV) and collimator angle (0-180°) are defined by the user. For a single arc VMAT, one beam needs to be added from a specified gantry angle direction, and when opting for dual arc VMAT, an additional beam is required, but both beams must have the same beam setup. In order to improve plan results, it is also recommended to do a secondary run of the VMAT optimization according to Alvarez-Moret et al (2010).
3.6 Patient characteristics

The patient cases in this study were real patients from the patient data base at NUS consisting of 5 prostate cancer cases all with lymphatic glands included, and 6 head and neck cases of different diagnoses.

Patient 1-5: Located progressive prostate cancer with suspected proliferation to lymphatic glands. Prescribed cumulative IMRT dose of 50 Gy each, delivered with 2 Gy fractions to the PTV. Prior to the IMRT treatment, the patients also underwent 28 Gy with conventional radio therapy. (i.e opposed 2- and 4-field beams). Organs at risk are rectum, bladder and femoral heads. PTV sizes are 1164, 510, 370, 490 and 625 ccm. 7-14 IMRT fields are applied from 7 different angles (0°, 50°, 103°, 160°, 200°/210°, 257° and 310°)

Patient 6: A woman with carcinoma in one of the tonsils including proliferation to lgl (lymphoglandulae), were prescribed a cumulative IMRT dose of 46 Gy delivered during 23 sessions (2 Gy per fraction). Considered organs at risk are medulla spinalis, parotid glands and the brain. Volume of PTV is 446 ccm. 7 IMRT fields are applied (from 0°, 45°, 70°, 150°, 210°, 290° and 315°.)

Patient 7: A man with carcinoma in one of his tonsils, were prescribed a cumulative IMRT dose of 46 Gy delivered with 2 Gy per fraction. Organs at risk are medulla spinalis, parotid glands and the brain. Volume of PTV is 551 ccm. 14 IMRT fields are applied (from 0°, 45°, 70°, 150°, 210°, 290°, 315°)

Patient 8: A man with cancer in the epipharynx, was prescribed a cumulative IMRT dose of 46 Gy delivered with 2 Gy per fraction. Organs at risk include medulla spinalis, parotid glands and the brain. Volume of PTV is 386 ccm and 12 IMRT fields are given (0°,45°, 70°, 150°, 210°, 290°, 315°)

Patient 9: A man with gingival carcinoma with a prescribed dose of 46 Gy with IMRT divided amongst 23 occasions. The organs at risk are medulla spinalis, parotid glands and the brain. Volume of the PTV is 622 ccm and 14 IMRT fields are applied (from 0°, 45°, 70°, 150°, 210°, 290°, 315°)
Patient 10: A man with carcinoma in the hypopharynx. Was prescribed a dose of 46 Gy with IMRT, in 23 fractions with 2 Gy each. Delineated organs at risk are medulla spinalis, parotid glands, and the brain. Volume of PTV is 271 ccm and the 7 IMRT fields are incident from 0°, 45°, 74°, 150°, 210°, 286°, and 315°.

Patient 11: A man with cancer in radix linguæ (tongue base), a prescribed dose of 68 Gy delivered in 34 fractions with 2 Gy each. Was the only patient in the study that received 68 Gy IMRT without additional conventional treatment. Organs at risk are medulla spinalis and parotid glands. The volume of the PTV is 1293 ccm. The patient was given 14 IMRT-fields from the following gantry angles 0°, 45°, 70°, 150°, 210°, 290° and 315°.

3.7. Plan verification

The often fast moving MLC which is an essentiality to VMAT, is associated with the need for extensive Quality Assurance (QA) methods to assure that the intended dose is delivered for each patient. The dosimetric error induced by imprecision of the MLC includes over- and undershooting, but also inconsistencies in gantry motion and the dynamic dose rate are subjects to uncertainties. Routine quality assurance and verification of plans are common practice world wide in every radiation therapy clinic to ensure that the equipment actually delivers the calculated dose within tolerance levels. For this study, a primary and secondary plan verification method was performed, including a table correction using a 3D-rendered bolus as table substitute, as well as testing the integrity of the plans.

3.8 I’mRT MatriXX 2D-measurement device.

The I’mRT MatriXX (IBA, Schwarzenbruck Germany) is a two dimensional ionization chamber array that consists of 1024 parallel plate ionization chambers arranged in a 32 x 32 matrix, covering a square of 24 x 24 cm, which can be used to measure dosimetric intensity maps in two dimensions. Every chamber is distanced 0.762 cm (3/10”) from each other and has a height of 0.55 cm and a 0.4 cm diameter. This dimensions yield a sensitive volume of only 0.07 cm³. (Wagner et al 2011)
With its movie mode function, it can measure dynamic fields typical for VMAT with a sampling rate as fast as 20 ms. The optional water equivalent MultiCube® phantom was used to more accurately determine the plan dosimetry.

(OmniPro-I’mRT User’s Guide 2009)

3.9 Primary plan verification with MatriXX diode array

By using the I’mRT MatriXX and the associated evaluation software, OmniPro I’mRT (version 1.7, IBA Schwarzenbruck, Germany), one can assess the widely used gamma method to compare the TPS calculated dose plan, versus the real tested plan on the accelerator for dosimetric verification. The specific dose difference used in this paper is 3% and its specific displacement is 3mm. Also, reproducibility of the measurements should be checked for consistency.

All the dose planned cases were exported from the treatment planning system Oncentra 4.0®, to the record and verify system Mosaiq®. The MatriXX-diode array was set up at the treatment table along with the Multicube phantom and a gantry angle sensor was attached with velcro tape on the gantry. The MatriXX\Multicube was then aligned properly with the support of room-lasers (see figure 10 below).

Figure 10. Left: Laser positioned MatriXX inserted in Multicube phantom. Right: Gantry angle sensor.

A pre-irradiation with 300 MU and 20 x 20 cm field size was delivered to warm up the electronics of the measurement system. At last, before commencing measurements, a 10 x 10 cm reference field was irradiated on the MatriXX to allow the operator to nullify daily fluctuations by using the mid point reference field dose as a normalization value.
Various measurement parameters such as diode-array sampling time and maximum treatment dose rate of 300/600 MU/min was examined to verify if the parameters have impact on plan quality. A measurement in the low dose region where e.g. the medulla spinalis is localised was also conducted for two head and neck cases to assure consistency between calculated and given dose.

The MatriXX was set in “Movie-Mode” and a sampling time of 1 second was used to accurately account for the MatriXX angular dependence. Also a faster sampling rate of 0.5 second was used for patient 6 and 10, for further comparison.

When evaluating the plans in the Omnipro software, standard facility protocol was followed which included gantry angle correction, grid interpolation conversion to achieve the correct matrix sizes between the calculated and measured data, and normalization to account for daily fluctuations. For analysis, the Omnipro gamma evaluation function with 3% Delta dose / 3mm Delta distance setting was used to evaluate all pixel values, yielding a percentage figure representing how many pixels that are in the relative 0 – 1 dose range. This percentage can then be used to estimate a suitable passing rate for the VMAT plans.

Since calculated dose plans was needed for the comparison with the measurements, a CT scan of the MatriXX phantom was imported to Oncentra 4.0, and each plan had its dose distribution calculated and exported to the MatriXX I’mRT evaluation software.

3.10 Table correction for MatriXX-MultiCube phantom

Due to the inability for Oncentra 4.0 to correct for the attenuation in the treatment table for the calculated dose plans, a method where an applied artificial bolus with calculated thickness equivalent to the treatment table was used.

By knowing the attenuation factor of the table provided by the manufacturer at the pelvis, and head and neck-area respectively and using a computer modelled water phantom in Oncentra 4.0, a bolus thickness equivalent of the treatment table could be iteratively calculated.

Head and Neck: 1.02

Figure 11  The table top (viewed from the side) and its correction factors currently used by the Linear Accelerator for 6MV
Since all pelvis patients are treated with 15MV, and all Head and Neck patients are treated with 6MV, the attenuation factor from the above figures 11 and 12, is 1.02 in both cases.

The table equivalent bolus thickness was found to be 0.8 cm for 15 MV (Prostate cases) and 0.6 cm for 6 MV (Head and neck cases). The method to determine how large the virtual bolus applied to the MatriXX MultiCube should be, is showed in the following example of figure 13.
By setting up an artificial table in the treatment planning system beneath the 3d-rendered Multicube with the use of the ruler-tool, one could easily pin point the start and ending points on the side of the MultiCube, by drawing additional measurement lines (see figure 14). The method should be fairly accurate, considering the small central displacement of the MultiCube on the treatment table and the drawing of the lines from the known isocentre.

Figure 14. Screenshot taken from Oncentra 4.0 of an axial view of a prostate patient plan which was exported to the MultiCube. The 2D-rendered bolus(green) and its extent was calculated from the 53 cm artificial table, which creates an equilateral triangle with the blue/red edges, acting as an artificial table which attenuates a part of the high energy X-ray photons.

3.11 Secondary verification measurements with RK-chamber
To be able to compare the calculated point dose acquired from inverse planning, with the measured dose at a single dose point, a thimble RK-ionization chamber (IBA, Schwarzenbruck Germany) surrounded by a cylindrical PMMA phantom (figure 15) was used together with a Unidos (PTWFreiburg, Germany) electrometer to read out the collected charges. This is considered as a secondary dose verification measurement independent to the primary 2D-array measurements. By using 10 x 10 cm reference fields in both
calculation/measurement and comparing their ratios to the reference fields respectively, the
daily fluctuations caused by electronic drift, temperature and pressure are eliminated, thus
leaving only the accuracy of the dose calculation algorithm to be evaluated against the
measured dose point.

![Image of dose verification setup](image15.png)

Figure 15. The secondary dose verification setup emplaced on the treatment table, consisting of a cylindrical
PMMA (Poly-methyl methacrylate) phantom with an inserted RK-cylindrical ionization chamber.

The prostate and head and neck patients were exported to the Cylindrical-IMRT phantom in
Oncentra 4.0® and the isocentre were placed either in the centre of the ionization chamber at
the initial plane or at a slight offset depending on anatomical characteristics.

The calculated dose to reference field ratio was then compared with the measured dose to
reference field ratio. The dose calculation resolution was set to 0.1 cm and an artificial bolus
correcting for table attenuation was applied to the CT-rendered Cylinder-IMRT phantom in
the treatment planning system, in the same manner as for the primary plan verification with
MatriXX.

3.12 Time measurements of delivered plans.

For timing purposes, a stopwatch was used to measure the actual delivery time from beam on,
to beam off, including the time it takes the operator to change from first to second arc.
Timing estimates for the delivery of different IMRT plans which had already been given to
actual patients during the fall of 2010 was done by measuring average times of current
standard IMRT treatment fields at the clinic.
3.13 Statistical Analysis

To compare the dose volume histogram results between IMRT and VMAT, the Wilcoxon nonparametric signed rank test was applied, with a p-value ≤ 0.05 considered statistically significant, a statistical test used by many IMRT vs. VMAT articles including Wolff et al (2009) Verbakel et al (2009) and Shaffer (2009).

The reason for choosing this particular test is because the comparison is made for a small group of patients (n = 11), including only a large amount of non Gaussian parameters. However, it is statistically problematic to calculate such a large number of p-values as in this study, which are all slightly dependent on each other as well as based on such a small patient group (n_{Prostate} = 5, n_{Total} = 11).

The individual p-values should therefore not be seen as a direct statistical test of differences at a specific dose level but rather be used as a way to easily visualize where differences in the dose ranges exists between the mean DVHs of the two techniques. (Bertelsen et al 2010).

To be able to compare and perform statistical analysis of the DVHs of all the head and neck cases, the only case receiving 68 Gy was normalized to 46 Gy.

The analysis was performed using the Statistical Package for Social Sciences, version 10.0 (SPSS, Chicago, IL). Ordinary statistics (i.e mean and standard deviation values) for plan verification data were performed in Microsoft Excel 2003.
4. Results and discussion

All plans were successfully optimized, evaluated and exported to the Mosaiq® record and verify system. Every plan except the Epipharynx case were then transferred to the linear accelerator without problem, the Epipharynx plan could not be loaded into the accelerator because of wrong settings in Oncentra that exceeded VMAT hardware constraints. When delivering the plans on the accelerator one plan (Gingiva) encountered multiple MLC interlocks mid treatment, and consequently a reset of the treatment plan was needed. No reason for the sudden MLC interlocks was found.

The estimated time to complete the whole workflow for 2 arc VMAT, is normally in the 40 – 80 minutes interval for the whole process depending on plan complexity. The workload for the planner is almost identical for VMAT and IMRT, due to the same steps in planning procedure although the optimization/calculation time for IMRT is only a factor ½- ⅓ that of VMAT.

4.1 Maximum treatment time comparison

Presented below in figure 16 and 17 are the dose volume histograms from the maximum treatment time comparison based on the two prostate plans 1 and 2, including the three evaluated maximum treatment times 75, 100, and 150 s. The original IMRT dose volume objectives were used and tumour overlap was set to 0% in prostate case 1, and 100% in prostate case 2.
Figure 16. Dose Volume histogram depicting the Maximum treatment time comparison for prostate 1 case and the amount of MU that each timing option required.

For prostate 1, the maximum treatment time alternatives 75 and 150 seconds yielded almost similar results regarding PTV coverage, sparing of the organ at risk (i.e rectum) and number of MUs dispelled. Although, the 150 second alternative have a slight dose overshoot in the high dose area of the rectum, indicating that the 75 second might be a better alternative for this particular case.

While the 100 second alternative used the least amount of monitor units, it somehow did not manage to achieve sufficient PTV coverage and conformity since the rectum sparing both shows a slight dose overshot compared to the 75 s case, and inferior low dose region performance.
For prostate 2, the 150 s and 100 s alternatives perform almost identical, yielding superior PTV coverage over the 75 s alternative, and similar OAR sparing capacities, with a minor advantage of the 150 s alternative performing slightly better in the rectal high dose area. As was the previous case with Prostate 1, the best considered alternative also had the highest number of MUs.

Since the specified physical constraints of the gantry limits the maximum treatment time to 75 seconds per arc (4.8 degrees/second), it could be argued that allotting only 75 seconds per arc for delivery may induce difficulties for the optimizer to achieve proper target coverage as in this specific case.

Due to the inferior performance of 100 second treatment time option in the previous prostate 1 case and the 75 second treatment time in case 2, drawing the conclusion that 150 second is the best choice out of these 2 plans based on only two cases is troublesome. However, as stated by Alvarez-Moret et al. (2010) the 4 degree gantry angle spacing and 150 second maximum
treatment time is supposed to be the best parameter set to achieve optimal combination of plan quality and treatment delivery time in the head and neck cancer cases, which is coherent with the prostate case findings of this study. However, since these results are implied to be vendor-specific, it should be emphasized that every clinic performs their own comparison studies to verify the most efficient treatment time options.

4.2 Collimator angle comparison

Represented below are the cases evaluated with the different collimator angle settings 0°, 3°, 15°, 30°, 45° for prostate 1, prostate 2 and the epipharynx case.

Also, a comparison for the tonsil 2 case with the 14°, 16°, 23°, 30° and 45° angles were performed to further investigate the intermediate angles in the interval 15° and 30°.

The prostate 1 case was optimized with the original IMRT objectives and the tumour Overlap set to 0%.

![Dose Volume histogram depicting the collimator angle comparison for prostate 1 case and the amount of MU that each collimator angle option required.](image)

<table>
<thead>
<tr>
<th>Collimator degree</th>
<th>0°</th>
<th>3°</th>
<th>15°</th>
<th>30°</th>
<th>45°</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monitor Units (MU)</td>
<td>505</td>
<td>512</td>
<td>532</td>
<td>527</td>
<td>514</td>
</tr>
</tbody>
</table>

Figure 18. Dose Volume histogram depicting the collimator angle comparison for prostate 1 case and the amount of MU that each collimator angle option required.
As shown in figure 18, both 15° and 30° gives better PTV coverage and spares the rectum well, however the 15° alternative spares the rectum slightly more in the high dose region which is of more importance to avoid irritated bowel side effects being uncomfortable for the patient, in agreement with the clinical doses protocol of priority.

The fact that 0° uses the least amount of MU is probably a consequence of the applied MLC modulation technique c), being unfavourable for this particular tumour shape, shown in the figure 19 below. Also noticeable is the slightly better sparing of rectum for 0°, however it has the tradeback of inferior PTV coverage and a slight overshoot at high dose levels and since it also gives rise to the troublesome tongue-and-groove effect, the 0° alternative should clearly be rejected.

Figure 19 . A schematic over different MLC modulation outcomes regarding 0° and 45° collimator rotation of an exemplified target shape.

a) No collimator rotation, the MLC is unable to align to this specific geometrical target and dose leakage to organs at risk might occur.

b) 45° collimator rotation, the MLC aligns to a greater extent than 0°, but may still leak doses to OARs.

c) The MLC closes the gap and maximum sparing of OARs is achieved, however PTV is largely neglected for this particular Beams Eye View (BEV).

d) The MLC successfully closes the gap, and both maximum sparing of OARs and target coverage is achieved.
The prostate 2 case was optimized with the original IMRT objectives and the tumour Overlap set to 100%.

![Prostate 2 dose distribution](image)

**Table 1: Monitor Units (MU)**

<table>
<thead>
<tr>
<th>Collimator degree</th>
<th>0°</th>
<th>3°</th>
<th>15°</th>
<th>30°</th>
<th>45°</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monitor Units (MU)</td>
<td>483</td>
<td>477</td>
<td>475</td>
<td>490</td>
<td>503</td>
</tr>
</tbody>
</table>

Figure 20. Dose Volume histogram depicting the collimator angle comparison for prostate 2 case and the amount of MU that each collimator angle option required.

The 30° collimator angle option yielded both better target coverage and better sparing of the rectum and once again the 0° angle alternative had difficulties with PTV coverage, but also overshoots the rectum dose.
The collimator comparison for the epipharynx case was optimized with single arc VMAT, original IMRT objectives and a tumour overlap of 0%. It should be noticed that this comparison was made with the 22 Gy treatment part, however this should not affect the MLC performance or the outcome of the results, which are shown in figure 21 below.

Collimator degree | 0° | 3° | 15° | 30° | 45° |
------------------|----|----|-----|-----|-----|
Monitor Units (MU)| 555| 522| 540 | 547 | 505 |

Figure 21. Dose Volume histogram depicting the collimator angle comparison for epipharynx case and the amount of MU that each collimator angle option required. Note that the abscissa is disrupted between the 28 and 52 dose percentages to be able to view medulla spinalis and PTV22 in the same graph.

For this particular patient case, the 30° collimator rotation was clearly the best choice with its better PTV coverage and improved sparing of the main organ at risk, medulla spinalis which is considered a serial organ and therefore the maximum dose is a concern.
To further investigate if other gantry angles than 0°, 3°, 15°, 30°, and 45° could prove usable, 14°, 16° and 23° was added to the notoriously achieving 30° and 45° options when optimizing the tonsil 2 case. Original IMRT objectives were used and tumour overlap was set to 0%. The results are shown in figure 22 below.

<table>
<thead>
<tr>
<th>Collimator degree</th>
<th>14°</th>
<th>16°</th>
<th>23°</th>
<th>30°</th>
<th>45°</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monitor Units (MU)</td>
<td>759</td>
<td>755</td>
<td>779</td>
<td>786</td>
<td>769</td>
</tr>
</tbody>
</table>

Figure 22. Dose Volume histogram depicting the collimator angle comparison for tonsil 2 case and the amount of MU that each collimator angle option required.

The 23° alternative yielded better PTV coverage and while not having the best OAR sparing performance, it kept within the allotted dose maximum of the organ at risk medulla spinalis, something that was done pre-eminently by the 45° option, however 45° somehow did not manage to achieve satisfying PTV coverage as well as a dose overshoot beyond 50 Gy (108.7%).

The reason for 23° being the best alternative other than being most suitable for the current patient case, was further examined by viewing the MLC field setup shown in figure 23 below.
Figure 23. Investigation of the initial gantry angle MLC patterns for the tonsil 2 case.

Consistency in the MLC pattern is obvious for the angles $14^\circ$, $16^\circ$ and $23^\circ$ but something distinct occurs in the MLC pattern between the $23^\circ$ and $30^\circ$ options, a point where the optimizer changes its fundamental starting MLC shape. Although this described occurrence is only shown for the first MLC pattern out of the 180 control points, it can be argued that based on the four patient cases evaluated in this collimator comparison, an arbitrary angle on either side of the collimator angle spectra (i.e. $23^\circ$ or $30^\circ$) should be tested during optimization, and evaluated before commissioning the final plan on the accelerator.
4.3 Prostate plan optimization results

The performance of the 2 arc VMAT and IMRT prostate plans are presented below in Table 3, where $D_{X\%}$ is the absorbed dose in Gy, delivered to $X\%$ of the particular volume and Homogeneity Index, i.e. $(D_{2\%} - D_{98\%})/D_{50\%}$ is represented as recommended by ICRU83 (2010).

Table 3 All prostate cases. All uncertainties are reported as one standard deviation.

<table>
<thead>
<tr>
<th>REGION</th>
<th>PARAMETER</th>
<th>IMRT</th>
<th>VMAT 2 ARC</th>
<th>p-value$^1$</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTV</td>
<td>$D_{98%}$</td>
<td>47.3 ± 0.3 Gy</td>
<td>47.8 ± 0.6 Gy</td>
<td>0.043</td>
</tr>
<tr>
<td></td>
<td>$D_{2%}$</td>
<td>52.2 ± 0.3 Gy</td>
<td>51.6 ± 0.6 Gy</td>
<td>0.068</td>
</tr>
<tr>
<td></td>
<td>$D_{50%}$</td>
<td>49.9 ± 0.05 Gy</td>
<td>49.9 ± 0.08 Gy</td>
<td>0.50</td>
</tr>
<tr>
<td></td>
<td>Homogeneity ICRU83</td>
<td>0.100 ± 0.009 Gy</td>
<td>0.07 ± 0.02 Gy</td>
<td>0.043</td>
</tr>
<tr>
<td></td>
<td>Standard Deviation</td>
<td>1.2 ± 0.2 Gy</td>
<td>0.9 ± 0.3 Gy</td>
<td>0.042</td>
</tr>
<tr>
<td>Rectum</td>
<td>$D_{50%}$</td>
<td>33.8 ± 7.8 Gy</td>
<td>28.0 ± 11.0 Gy</td>
<td>0.080</td>
</tr>
<tr>
<td></td>
<td>$D_{Average}$</td>
<td>33.7 ± 6.3 Gy</td>
<td>30.3 ± 8.6 Gy</td>
<td>0.080</td>
</tr>
<tr>
<td></td>
<td>$D_{2%}$</td>
<td>50.1 ± 0.7 Gy</td>
<td>50.3 ± 0.2 Gy</td>
<td>0.893</td>
</tr>
<tr>
<td>Bladder</td>
<td>$D_{50%}$</td>
<td>40.4 ± 6.1 Gy</td>
<td>38.7 ± 7.6 Gy</td>
<td>0.080</td>
</tr>
<tr>
<td></td>
<td>$D_{Average}$</td>
<td>39.5 ± 4.4 Gy</td>
<td>38.0 ± 4.8 Gy</td>
<td>0.043</td>
</tr>
<tr>
<td></td>
<td>$D_{2%}$</td>
<td>51.2 ± 0.4 Gy</td>
<td>50.8 ± 0.5 Gy</td>
<td>0.138</td>
</tr>
<tr>
<td>Femoral Head Dx</td>
<td>$D_{50%}$</td>
<td>20.3 ± 1.7 Gy</td>
<td>22.9 ± 2.3 Gy</td>
<td>0.043</td>
</tr>
<tr>
<td></td>
<td>$D_{Average}$</td>
<td>20.3 ± 1.5 Gy</td>
<td>23.3 ± 2.1 Gy</td>
<td>0.043</td>
</tr>
<tr>
<td>Femoral Head Sin</td>
<td>$D_{50%}$</td>
<td>20.1 ± 2.0 Gy</td>
<td>23.0 ± 2.6 Gy</td>
<td>0.138</td>
</tr>
<tr>
<td></td>
<td>$D_{Average}$</td>
<td>20.3 ± 1.8 Gy</td>
<td>23.4 ± 2.4 Gy</td>
<td>0.080</td>
</tr>
<tr>
<td>External</td>
<td>$D_{Average}$</td>
<td>10.6 ± 2.4 Gy</td>
<td>11.1 ± 2.3 Gy</td>
<td>0.043</td>
</tr>
<tr>
<td></td>
<td>Monitor Units</td>
<td>574.4 ± 127.8 MU</td>
<td>571.8 ± 103.5 MU</td>
<td>0.893</td>
</tr>
<tr>
<td></td>
<td>Treatment time (min)</td>
<td>Approx. 8.8 ± 3.5 min</td>
<td>2.96 ± 0.05 min</td>
<td>0.041</td>
</tr>
</tbody>
</table>

$^1$ P-value < 0.05

$^2$ Bold values indicate a significance difference in between the two delivery techniques.

According to the Wilcoxon nonparametric signed rank test, 2 arc VMAT plans yielded better PTV performance as shown by the statistically significant higher $D_{98\%}$-values, lower standard deviation, and higher dose homogeneity-ICRU83. The $D_{2\%}$ parameter for PTV which is a direct indication of the amount of unwanted hot spots, shows a lower mean value, 51.6 Gy for VMAT compared to IMRT 52.2 Gy, however this was not considered statistical significant and both values are within the tolerated value 52.5 Gy.

Dose values for the rectum showed lower $D_{50\%}$ (i.e. median doses) and $D_{Average}$ with 2 arc VMAT, however this was not considered statistical significant. The maximum dose
parameter, $D_{2\%}$ showed no significant difference between the two methods and although 0.2 Gy higher in average for VMAT than with IMRT, this is a consequence of the significantly higher PTV $D_{98\%}$-parameter for VMAT, since a few percent of the rectal volume overlaps the tumour and tumour dose coverage should always be prioritized over the rectum in that specific region. Also, the standard deviation for rectum-$D_{2\%}$ is only 0.2 Gy for VMAT compared to 0.7 Gy for IMRT indicating that VMAT has a steeper dose gradient based on the above PTV/rectum reasoning.

The urinal bladder receives a significantly lower average dose with VMAT than with IMRT, and while not statistically significant, the median and top dose values indicates that VMAT spares the urinal bladder well.

Femoral head dx receives a significantly higher average/median dose with VMAT and femoral head sin receives higher average/median dose while not being considered statistically significant. The trend is clear for the femoral heads, which are the only organs at risk not positioned adjacent to the PTV and thus are only subject to lower doses, something that seems unfavourable to VMAT being a rotational treatment technique having higher integral doses as indicated by the significantly higher external $D_{\text{Average}}$ dose.

Significantly shorter treatment times are observed with VMAT compared to IMRT, with approximately a factor $\frac{1}{3}$ shorter treatment times in the average prostate case. This is a great benefit for patients spending less time being anxious in the treatment room and being less prone to dosimetric errors induced by movements due to tension and tremors building up over time while trying to lie still during treatment.

The shortened treatment times associated with VMAT is also a benefit for the clinic as well, since they have the option to treat more than twice the number of prostate patients previously treated with IMRT.

No significant decrease in the number of monitor units were observed in cohort with a similar VMAT vs step and shoot IMRT prostate study by Ost et al(2010), however they used single arc VMAT.

A more in depth analysis of select cases of the prostate plans are discussed in Appendix 2.
4.4 Head and neck plan optimization results

The performance of the 2 arc VMAT and IMRT head and neck plans are presented below in Table 4.

Table 4 All head and neck cases. All uncertainties are reported as one standard deviation.

<table>
<thead>
<tr>
<th>REGION</th>
<th>PARAMETER</th>
<th>IMRT</th>
<th>VMAT 2 ARC</th>
<th>p-value(^1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTV</td>
<td>( D_{98%} )</td>
<td>42.8 ± 0.5 Gy</td>
<td>43.4 ± 0.7 Gy</td>
<td>0.028</td>
</tr>
<tr>
<td></td>
<td>( D_{2%} )</td>
<td>48.0 ± 0.3 Gy</td>
<td>47.4 ± 0.5 Gy</td>
<td>0.028</td>
</tr>
<tr>
<td></td>
<td>( D_{50%} )</td>
<td>45.8 ± 0.2 Gy</td>
<td>45.6 ± 0.2 Gy</td>
<td>0.463</td>
</tr>
<tr>
<td></td>
<td>Homogeneity ICRU83</td>
<td>0.11 ± 0.02</td>
<td>0.088 ± 0.02</td>
<td>0.028</td>
</tr>
<tr>
<td></td>
<td>Standard Deviation</td>
<td>1.4 ± 0.2 Gy</td>
<td>1.1 ± 0.3 Gy</td>
<td>0.028</td>
</tr>
<tr>
<td>Medulla Spinalis</td>
<td>( D_{2%} )</td>
<td>30.2 ± 2.0</td>
<td>28.5 ± 1.0 Gy</td>
<td>0.028</td>
</tr>
<tr>
<td>Brain(^4)</td>
<td>( D_{50%} )</td>
<td>2.3 ± 1.5 Gy</td>
<td>3.4 ± 2.2 Gy</td>
<td>0.068</td>
</tr>
<tr>
<td></td>
<td>( D_{\text{Average}} )</td>
<td>4.2 ± 2.2 Gy</td>
<td>5.2 ± 2.9 Gy</td>
<td>0.068</td>
</tr>
<tr>
<td></td>
<td>( D_{2%} )</td>
<td>17.5 ± 11.6 Gy</td>
<td>17.9 ± 10.8 Gy</td>
<td>0.715</td>
</tr>
<tr>
<td>Parotis Dx</td>
<td>( D_{50%} )</td>
<td>18.4 ± 7.8 Gy</td>
<td>19.0 ± 6.5 Gy</td>
<td>0.60</td>
</tr>
<tr>
<td></td>
<td>( D_{\text{Average}} )</td>
<td>20.8 ± 5.1 Gy</td>
<td>21.8 ± 5.8 Gy</td>
<td>0.075</td>
</tr>
<tr>
<td>Parotis Sin</td>
<td>( D_{50%} )</td>
<td>22.5 ± 8.4 Gy</td>
<td>21.6 ± 8.0 Gy</td>
<td>0.249</td>
</tr>
<tr>
<td></td>
<td>( D_{\text{Average}} )</td>
<td>22.5 ± 6.9 Gy</td>
<td>23.9 ± 7.3 Gy</td>
<td>0.463</td>
</tr>
<tr>
<td>External</td>
<td>( D_{\text{Average}} )</td>
<td>11.9 ± 1.7 Gy</td>
<td>12.5 ± 3.5 Gy</td>
<td>0.028</td>
</tr>
<tr>
<td></td>
<td>Monitor Units</td>
<td>622.3 ± 105.4 MU</td>
<td>708.7 ± 65.7 MU</td>
<td>0.173</td>
</tr>
<tr>
<td></td>
<td>Treatment time (min)</td>
<td>Approx. 8.2 ± 1.8 min</td>
<td>2.95 ± 0.04 min</td>
<td>0.026</td>
</tr>
</tbody>
</table>

\(^1\) p-value < 0.05

\(^2\) Bold values indicate significance in difference between the two delivery techniques.

\(^3\) Note: Values for patient 11 are normalized to 46Gy from 68Gy initially.

\(^4\) Note: The tongue base case did not include the brain as organ at risk.

Similarly to the prostate cancer cases, the 2 arc VMAT yields statistically significant and improved PTV performance regarding \( D_{98\%} \), dose homogeneity (ICRU83) and standard deviation of the dose, but also the max dose indicator \( D_{2\%} \) was significantly better.

With 2 arc VMAT the medulla spinalis receives a statistically significant lower \( D_{2\%} \) dose. The remaining organs at risk; brain and parotis dx\sin shows no significant sparing with VMAT compared with IMRT. Since the brain is located distant from the tumour in all head and neck cases, it is subject to very low doses and due to the nature of the rotational technique of VMAT inducing a statistically significant increase in integral dose to the patient; external \( D_{\text{Average}} \), the brain consequently receives slightly higher doses with VMAT than with IMRT.
Regarding the treatment times, they were at average 2.8 times faster for VMAT compared with IMRT. The mean number of monitor units used was equal or larger compared to that of IMRT, which is similar to the findings of Alvarez-Moret et al (2010). They also implied that single arc used the least amount of MU per fraction dose, and that the number of expelled MU were dependent on the gantry spacing angle. The larger the gantry spacing angle, the lower the number of MU.

A more in depth analysis of select cases of the head & neck plans are discussed in Appendix 2

4.5 Primary plan verification results, dose rate and \( t_{\text{sample}} \)

No difference was found between the dose rates 300 and 600 MU/minute, neither did the sampling time of the Matrixx; \( t_{\text{sample}} \) of 1 and 0.5 s yield different results in the 2D-gamma 3%/3mm analysis. The latter result shows that the sampling time of 1 second is enough to get a fair compromise between acquired data points and resolution for the gantry angle corrections made within the MatriXX software before gamma-evaluating the case. This is to ensure that cases that would otherwise suffer from low sampling rate are evaluated in a correct manner.

An encountered problem while evaluating the plans in the Omnipro I’mRT gamma evaluation software was that some comparisons yielded large differences between calculated and measured dose. To examine if this could be due to the effect on erroneous displacement in z-direction, the measurement plane was shifted in steps of 1 mm to verify if the evaluation yielded better results.

In figure 24 is an example of a prostate 2 plan with large deviations in calculated and measured dose distribution along with shifts in measurement plane.
Figure 24. A comparison between gamma evaluations when shifting the measurement plane. The picture at the top shows the gamma evaluation with the original measurement plane, the middle picture when it is elevated +1 mm and the lower picture shows a +2 mm change of measurement plane.
The +1 and +2 mm shifts clearly reduce the large differences in doses and therefore indicate that either the physical MatriXX measurement device is slightly misplaced in its vertical position, or that the isocentre placed by the planner before optimization and calculation of the dose plan is off by as little as tenths of an mm. The latter contribution seems unlikely to be the source of error, since the certainty of the treatment table which the MatriXX diode array is placed upon is in the magnitude of mm compared to that of the smaller uncertainty in isocentre emplacement.
4.6 Primary prostate plan verification results and bolus correction

Presented below in figure 25 are the resulting 3 mm/3% 2D-gamma map evaluations between measured and calculated doses for each prostate case in ascending order (1 to 5), where the bolus correction has been applied to all cases to the right.

Figure 25. Gamma analysis 3% / 3mm between measured and calculated dose for the five prostate cases without(left) and with the table bolus correction(right).
Table 5. Obtained numerical pixel values from the 2D gamma map evaluation for the prostate cases. SD is the standard deviation of the pixel values and the 0-1-column represents the percentage of the differential pixel values being in the 0-1 range.

<table>
<thead>
<tr>
<th>Sample</th>
<th>Average</th>
<th>SD</th>
<th>0-1 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No Bolus</td>
<td>0.35</td>
<td>0.23</td>
<td>99.56</td>
</tr>
<tr>
<td>Bolus</td>
<td>0.29</td>
<td>0.2</td>
<td>99.94</td>
</tr>
<tr>
<td>Prostate 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No Bolus</td>
<td>0.28</td>
<td>0.21</td>
<td>99.72</td>
</tr>
<tr>
<td>Bolus</td>
<td>0.25</td>
<td>0.19</td>
<td>99.86</td>
</tr>
<tr>
<td>Prostate 3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No Bolus</td>
<td>0.26</td>
<td>0.23</td>
<td>99.52</td>
</tr>
<tr>
<td>Bolus</td>
<td>0.25</td>
<td>0.23</td>
<td>99.27</td>
</tr>
<tr>
<td>Prostate 4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No Bolus</td>
<td>0.24</td>
<td>0.18</td>
<td>99.76</td>
</tr>
<tr>
<td>Bolus</td>
<td>0.22</td>
<td>0.17</td>
<td>99.83</td>
</tr>
<tr>
<td>Prostate 5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No Bolus</td>
<td>0.26</td>
<td>0.19</td>
<td>99.66</td>
</tr>
<tr>
<td>Bolus</td>
<td>0.26</td>
<td>0.19</td>
<td>99.61</td>
</tr>
<tr>
<td>Mean (no bolus)</td>
<td>0.26 ± 0.04*</td>
<td>0.21</td>
<td>99.64</td>
</tr>
<tr>
<td>Mean (bolus)</td>
<td>0.25 ± 0.03*</td>
<td>0.20</td>
<td>99.70</td>
</tr>
</tbody>
</table>

*Standard deviation for the average value

All prostate cases showed >99% dose conformance between measured and calculated dose, where the cases 1, 2 and 4 showed small improvements in all gamma-parameters with the bolus correction. Cases 3 and 5 showed slight decreases in the differential dose pixel range 0-1 with bolus correction, but had similar or better average- and standard deviation values compared to the ones without bolus correction.

One explanation of the “red borderlines” seen in example Prostate III in figure 25 above, is according to Schreibmann et al (2009) a consequence of the relatively low spatial resolution of the MatriXX measurement system and very often occurs at high gradients such as the edges of the PTV. Another explanation may be the tongue and groove effect explained earlier in the Theory/Background (figure 3.)

To emphasize the benefit of the bolus correction, an example out of the first series of measurements are included in figure 26 for the prostate 2 case.

The gamma map and X-direction dose profiles shown to the left are without bolus correction, and the ones to the right are with bolus correction.
4.7 Primary head and neck plan verification results

Presented below are resulting 3 mm/3% 2D-gamma map evaluations between measured and calculated doses for every head and neck case except the undeliverable epipharynx case, where a bolus correction has been applied to all pictures to the right. Also included are the low dose regions where the medulla spinalis is located for the tonsil 1 and hypopharynx cases.
Tonsil 1 without(left) and with(right) bolus correction.

Tonsil 1 with bolus correction in the medulla spinalis low dose region.

Tonsil 2 without(left) and with(right) bolus correction.

Gingiva without(left) and with(right) bolus correction.
Hypopharynx without (left) and with (right) bolus correction.

Hypopharynx with bolus correction in the medulla spinalis low dose region.

Tongue base without (left) and with (right) bolus correction.

Figure 27. 2D gamma analyses of head and neck patient cases with and with bolus correction. Also included are 2 cases with the low dose region of medulla spinalis.
Table 6. Obtained numerical pixel values from the 2D gamma map evaluation for the head and neck cases. SD is the standard deviation of the pixel values and the 0-1-column represents the percentage of the differential pixel values being in the 0-1 range.

<table>
<thead>
<tr>
<th>Sample = 1 s</th>
<th>Average</th>
<th>SD</th>
<th>0-1 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tonsil 1</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No Bolus</td>
<td>0.29</td>
<td>0.24</td>
<td>98.87</td>
</tr>
<tr>
<td>Bolus</td>
<td>0.27</td>
<td>0.23</td>
<td>98.68</td>
</tr>
<tr>
<td>Bolus medulla</td>
<td>0.3</td>
<td>0.23</td>
<td>99.28</td>
</tr>
<tr>
<td><strong>Tonsil 2</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No Bolus</td>
<td>0.34</td>
<td>0.28</td>
<td>97.91</td>
</tr>
<tr>
<td>Bolus</td>
<td>0.30</td>
<td>0.24</td>
<td>98.81</td>
</tr>
<tr>
<td><strong>Gingiva</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No Bolus</td>
<td>0.31</td>
<td>0.22</td>
<td>99.14</td>
</tr>
<tr>
<td>Bolus</td>
<td>0.28</td>
<td>0.21</td>
<td>99.47</td>
</tr>
<tr>
<td><strong>Hypopharynx</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No bolus</td>
<td>0.28</td>
<td>0.24</td>
<td>99.34</td>
</tr>
<tr>
<td>Bolus</td>
<td>0.29</td>
<td>0.25</td>
<td>99.07</td>
</tr>
<tr>
<td>Bolus medulla</td>
<td>0.26</td>
<td>0.22</td>
<td>99.78</td>
</tr>
<tr>
<td><strong>Tongue Base</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No bolus</td>
<td>0.3</td>
<td>0.21</td>
<td>99.34</td>
</tr>
<tr>
<td>Bolus</td>
<td>0.27</td>
<td>0.21</td>
<td>99.45</td>
</tr>
<tr>
<td>Mean (no bolus)</td>
<td>0.30 ± 0.02*</td>
<td>0.24</td>
<td>98.92</td>
</tr>
<tr>
<td>Mean* (bolus)</td>
<td>0.28 ± 0.01*</td>
<td>0.23</td>
<td>99.10</td>
</tr>
</tbody>
</table>

* Standard deviation for the average value  
** Excludes the two bolus corrected medulla values.

As seen in table 6, all cases showed >97.9% dose conformance between measured and calculated dose, without bolus correction and >98.6% with bolus correction.

The tonsil 2, gingiva and tongue base cases all improved the gamma parameters with the bolus correction, tonsil case 1 improved the average- and standard deviation value, but not the differential dose pixel range 0-1. In the hypopharynx case, the bolus correction somehow decreased all gamma parameters slightly, the reason for this is occurrence is still unknown.

Shown in the figure 28 below is the low dose region of the medulla spinalis which was further examined and showed similar dose profiles for the measured and calculated doses, except at the edges of the Y-profile where the MatriXX diode array tend to overshoot the measurement due to its low spatial resolution as stated by Schreibmann et al (2009).
Figure 28. Low dose region of medulla spinalis in the tonsil 1 case where the measured (red) and calculated (green) profiles in the X-direction and measured 2D dose map are to the left. The measured(red) and calculated(green) profiles in the Y-direction and calculated 2D dose map are to the right.

Included below is another example of a more evident dose overshoot phenomenon, which however is not located at the edges of the PTV and therefore is not caused by the inferior spatial resolution of the MatriXX diode array. These “hot spots” that sometimes appear at random places in the middle of the PTV (see figure 29) can not be a consequence of faulty diodes in the array since they then would systematically appear at the same spot during each new evaluation. A more reasonable explanation is that by chance, small deviations in the MLC movement overlap each other and creates a superposition phenomenon of unwanted dose (Chandraraj et al 2011). Furthermore Chandraraj concludes that the more complex the PTV shape is, the faster and more frequent the MLC has to move to achieve satisfying modulation which tend to induce more “hot-spots” within the PTV.
Figure 29. Two types of hotspots that can occur during 2D- gamma evaluations: The “red borderline” at the upper PTV region in the gamma evaluation map, and the randomly occurring mid PTV “hotspots” shown in the middle region of the gamma evaluation map and also in the difference in X-direction dose profiles depicted in the upper right corner.

As a final conclusion of the primary plan verification measurements, an acceptance level was to be determined. Bedford et al (2009) and Korreman et al (2009) suggests that values above 95% conformance should be clinically acceptable while Wagner et al (2010) used 99.0% as a clinical acceptable passing rate together with gamma criterions 3% / 3 mm.

The proposed uncertainty budget of Wagner et al implied a combined uncertainty of 2.9% / 1.9 mm for the measurement equipment and 1% / 2 mm for the calculation equipment.

Based on the results of the primary plan verification results for prostate and head and neck cases in this study, and taken into account the above stated uncertainty figures, the reasonable conformance level percentage in which clinical VMAT plans are considered acceptable were said to be in between the recommended values of the other studies, i.e 97%.
4.8 Secondary dose verification results

All optimized prostate and head and neck plans are presented below in their respective tables. Both the measured and calculated Oncentra 4.0 doses have been normalized to a 10x10 cm\(^2\) field in the tables 7 and 8 below.

Table 7. Secondary verification of prostate cases with cylindrical phantom and RK ionization chamber where the point of measurement is located in the centre of PTV.

<table>
<thead>
<tr>
<th></th>
<th>Measured dose (Norm. against ref-field)</th>
<th>Oncentra 4.0 dose (Norm. against ref-field)</th>
<th>Measured/Oncentra 4.0</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prostate 1</strong></td>
<td>2,283</td>
<td>2,298</td>
<td>0.994</td>
</tr>
<tr>
<td><strong>Prostate 2</strong></td>
<td>2,332</td>
<td>2,340</td>
<td>0.996</td>
</tr>
<tr>
<td><strong>Prostate 3</strong></td>
<td>2,332</td>
<td>2,340</td>
<td>0.996</td>
</tr>
<tr>
<td><strong>Prostate 4</strong></td>
<td>2,303</td>
<td>2,321</td>
<td>0.992</td>
</tr>
<tr>
<td><strong>Prostate 5</strong></td>
<td>2,258</td>
<td>2,274</td>
<td>0.993</td>
</tr>
<tr>
<td><strong>Mean</strong></td>
<td></td>
<td></td>
<td><strong>0.997</strong> Mean</td>
</tr>
<tr>
<td><strong>Std</strong></td>
<td></td>
<td></td>
<td><strong>0.008</strong> Std</td>
</tr>
</tbody>
</table>

Table 8. Secondary verification of head and neck cases with cylindrical phantom and RK ionization chamber where the point of measurement is located in the centre of PTV.

<table>
<thead>
<tr>
<th></th>
<th>Measured dose (Norm. against ref-field)</th>
<th>Oncentra 4.0 dose (Norm. against ref-field)</th>
<th>Measured/Oncentra 4.0</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tonsil 1</strong></td>
<td>2,340</td>
<td>2,340</td>
<td>1.000</td>
</tr>
<tr>
<td><strong>Tonsil 2</strong></td>
<td>2,410</td>
<td>2,419</td>
<td>0.996</td>
</tr>
<tr>
<td><strong>Gingiva</strong></td>
<td>2,398</td>
<td>2,413</td>
<td>0.994</td>
</tr>
<tr>
<td><strong>Hypopharynx</strong></td>
<td>2,213</td>
<td>2,193</td>
<td>1.009</td>
</tr>
<tr>
<td><strong>Tounge base</strong></td>
<td>2,677</td>
<td>2,681</td>
<td>0.998</td>
</tr>
<tr>
<td><strong>Mean</strong></td>
<td></td>
<td></td>
<td><strong>1.000</strong> Mean</td>
</tr>
<tr>
<td><strong>Std</strong></td>
<td></td>
<td></td>
<td><strong>0.006</strong> Std</td>
</tr>
</tbody>
</table>

The calculated ratios of measured and calculated point doses from Oncentra 4.0 implied that the average deviation for the pencil beam calculated dose and the measured point dose in the prostate cases are 3‰, with a maximum deviation of 8‰, whereas the head and neck cases incidentally yielded no average deviation, but a maximum deviation of 9‰.
5. Conclusion

The dual arc VMAT plans created with Oncentra 4.0 achieves improved PTV dose performance and are in average delivered 2.8 - 3 times as fast compared to IMRT for head and neck and prostate cancer cases. Although being a faster delivery method than IMRT, VMAT has the drawback of requiring more time during the optimization step.

OAR sparing capabilities for highly prioritized organs such as rectum and medulla spinalis are better with dual arc VMAT and for OARs with lower priority receives similar or slightly higher doses compared to IMRT, while the external patient volume being subject to the lowest doses receives a significantly higher integral dose, although clearly within clinical limits. For the prostate cases the average amount of MUs used were similar to IMRT, but in the head and neck cases the average MUs used were slightly higher.

Depending on which planning strategy being employed when optimizing the VMAT plans, i.e. DVO/VMAT parameters, the resulting plan quality can vary. It is therefore important to be aware of which settings to use in which particular case. However applying the original IMRT dose volume objectives on 2 arc VMAT in combination with the surrounding dose fall off objective and a fairly large collimator setting (i.e. 15° to 45°) and running the optimization procedure twice, often yields the best results.

All delivered plans had >98.6% conformance when using the table correction bolus between measured and calculated dose according to the gamma evaluation material obtained with the MatriXX 2D diode array. These results were verified by the secondary plan verification consisting of a single point dose measurement with a RK-ionization chamber in another type of phantom. By using the artificial bolus table correction, Oncentra 4.0 adequately accounts for photon attenuation in the table.

The primary plan verification chain is easy to implement into a clinical routine and the verification of the 2D dose distribution with the MatriXX diode array for VMAT treatment plans combined with the Omnipro I’mRT evaluation software. And since the secondary plan verification which used independent measurement equipment compared to the primary plan verification method, the user is ensured that the MatriXX-diode array setup indeed yields reliable results which were the case for both the prostate and head and neck cases.

These particular measurement setups gives the attending physicist easy, fast and reliable means for quality assurance of clinical plans before commencing the treatment of the patient.
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Appendix 1

Final DVO and VMAT optimization parameters.

Table 9. Summary of optimization/VMAT parameters. All plans used two arcs VMAT and 150 second maximum treatment time.

<table>
<thead>
<tr>
<th>Plan</th>
<th>ROI Margin:</th>
<th>Collimator:</th>
<th>Dynamic gantry speed:</th>
<th>Tumour overlap fraction:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate 1</td>
<td>No</td>
<td>15°</td>
<td>Yes</td>
<td>0%</td>
</tr>
<tr>
<td>Prostate 2</td>
<td>Yes, 3 mm</td>
<td>23°</td>
<td>Yes</td>
<td>100%</td>
</tr>
<tr>
<td>Prostate 3</td>
<td>No</td>
<td>23°</td>
<td>No</td>
<td>100%</td>
</tr>
<tr>
<td>Prostate 4</td>
<td>Yes, 1 mm</td>
<td>23°</td>
<td>Yes</td>
<td>0%</td>
</tr>
<tr>
<td>Prostate 5</td>
<td>Yes, 1 mm (-3mm of rectum)</td>
<td>30°</td>
<td>Yes</td>
<td>100%</td>
</tr>
<tr>
<td>Tonsil 1</td>
<td>Yes, 1 mm</td>
<td>23°</td>
<td>No</td>
<td>0%</td>
</tr>
<tr>
<td>Tonsil 2</td>
<td>No</td>
<td>15°</td>
<td>Yes</td>
<td>0%</td>
</tr>
<tr>
<td>Epipharynx</td>
<td>Yes, 1 mm</td>
<td>23°</td>
<td>No</td>
<td>0%</td>
</tr>
<tr>
<td>Gingiva</td>
<td>No</td>
<td>23°</td>
<td>No</td>
<td>0%</td>
</tr>
<tr>
<td>Hypopharynx</td>
<td>Yes, 1 mm</td>
<td>23°</td>
<td>Yes</td>
<td>100%</td>
</tr>
<tr>
<td>Tongue base</td>
<td>No</td>
<td>15°</td>
<td>No</td>
<td>0%</td>
</tr>
</tbody>
</table>

Abbreviation ROI = Region of Interest

Figure 30 through 40 below shows the Dose Volume Objectives for the final VMAT plans:
Figure 31 VMAT DVOs for Prostate 2

Figure 32 VMAT DVOs for Prostate 3
Figure 33  VMAT DVOs for Prostate 4

Figure 34  VMAT DVOs for Prostate 5
Figure 35 VMAT DVOs for Tonsil 1

Figure 36 VMAT DVOs for Tonsil 2
Figure 37 VMAT DVOs for Epipharynx

Figure 38 VMAT DVOs for Gingiva
Figure 39  VMAT DVOs for Hypopharynx

Figure 40  VMAT DVOs for Tongue Base
Appendix 2

Discussion regarding VMAT specific settings and DVOs.

To examine the impact of different VMAT specific optimization parameters such as collimator angle and tumour overlap, as well as dose volume objectives, the dose volume histograms and dose volume objectives of a few selected cases are shown below and discussed.

![Dose Volume Histogram](image)

Figure 41. Dose volume histogram for prostate cancer case 1, showing the performance of IMRT and 2 arc VMAT regarding PTV50 coverage and sparing of organs at risk.

The 2 arc VMAT plan for prostate 1 case was successfully optimized with the original IMRT dose volume objectives, 15° collimator angle and no tumour overlap fraction, yielding a better target coverage and similar OAR sparing capabilities compared to IMRT (figure 41), while only requiring 513 MU compared to 714 with IMRT. However, as observed by Hardcastle et
al (2010) an slightly increased dose in the femoral heads are expected since VMAT uses delivery angles that result in a delivery of target dose through the femoral heads, while the IMRT fields supposedly avoids them to a larger extent.

![Figure 42. Side by side isodose comparison for the prostate 1 case, with 2 arc VMAT (left) and IMRT (right). The largely central H-shaped contour are the lymphatic glands of the prostate and the round contours above/below are the bladder and rectum respectively. To the right and left side of the lymphatic glands are the circular contours of the femoral heads.](image)

The isodose comparison for prostate case 1 at this particular axial slice (figure 42), shows no significant difference between VMAT and IMRT, except small deviations in femoral head sin doses. This particular prostate case shows that it is possible to obtain a treatment plan from the optimizer that is clinically acceptable based on the original IMRT objectives with the addition of a second VMAT arc and e.g 15º collimator angle instead of 3º as is the case with IMRT.
However, the next case indicates that going beyond the original IMRT optimization parameters the optimizer may yield a better plan regarding both PTV coverage and sparing of organs at risk.

Neither the 1 nor 2 arc VMAT plans for the Hypopharynx case did achieve clinically acceptable results when optimized with the original IMRT dose volume objectives and different collimator angles. Thus the need for alteration of the original objectives as shown in figure 43 below.

![Figure 43. Associated dose volume objectives for VMAT (left) and IMRT (right) used in the Hypopharynx case. The VMAT plan had an addition of a 1mm PTV margin and a larger optimization weight on the medulla spinalis compared to the objectives of the IMRT plan.](image-url)
Using the DVOs shown above in figure 43, improved PTV46 coverage and sparing of the OARs resulted from setting the collimator to 23° and tumour overlap fraction to 100% (figure 44.) The only exception where IMRT performed better is the sparing of the brain in which VMAT induces a higher dose due to the nature of rotational delivery technique which irradiates the patient from all angles. This gives the low dose regions of the external volumes (i.e the brain) doses to a larger extent than IMRT, however the brain is considered very radio resistant compared to the medulla spinalis which can inflict paralysis if subject to fairly high doses, i.e >48 Gy (Priestman 2007). The rotational techniques are often accompanied with an increase in the number of monitor units, clarified by that 2 arc VMAT resulted in 633 and IMRT only 514 monitor units. It should be emphasized however, that since the brain is one of the most radio resistant organs in the body, and that the brain in this case received very low doses compared to other organs at risk, this yielded no clear clinical benefit for IMRT over VMAT regarding the brain dose.
The 2 arc VMAT have a better PTV dose homogeneity and conformity compared to that of the IMRT plan (figure 45). Regarding organs at risk, the comparison shows no significant difference in sparing of the medulla spinalis or parotid glands at this particular axial slice, however, the VMAT plan shows only a single dose bridge between the PTV, whereas IMRT with worse conformity, shows two dose bridges on each side of the medulla spinalis.
In the prostate 4 case, neither the 1 nor 2 arc VMAT plans did achieve clinically acceptable results when optimized with the original IMRT dose volume objectives and different collimator angles. However, the use of the *max average dose, and surrounding dose fall-off* objectives in combination with slightly changed original IMRT objectives shown below in figure 46, and a collimator setting of 23° yielded clear DVH improvements for 2 arc VMAT shown in figure 47.

![Figure 46. Associated dose volume objectives for VMAT (left) and IMRT (right) used in the Prostate 4 case. The VMAT plan had an addition of a 1mm PTV margin, max average dose defined to the rectum, surrounding dose fall off to the external volumes, and increased weights on the rectum and femoral heads compared to the objectives of the IMRT plan.](image-url)
Better PTV 50 coverage and a greatly reduced average rectum dose are the clear improvements of 2 arc VMAT, also an increased sparing of the urinal bladder is evident due to the better dose conformance of the PTV. The femoral heads however, are subject to a significantly higher mean dose with 2 arc VMAT, although having the same dose maxima as IMRT (ie 35 Gy). The femoral heads doses are consistent with the results of the prostate 1 case, and the observations by Hardcastle et al (2010), that a slightly increased dose in the femoral heads are expected since VMAT uses delivery angles that result in a delivery of target dose trough the femoral heads which had an optimization weight of only 30 compared to 100 of the rectum. The IMRT fields supposedly avoids the femoral heads to a larger extent but induces higher doses to the far more valuable organ at risk; rectum, due to its inferior PTV conformance, a noticeable disadvantage as the rectum in most cases is conjoined with the prostate tumour. Also the number of dispelled monitor units was slightly higher with IMRT, (575) than with VMAT (529).
Since the PTV in this axial CT slice (figure 48) is merged with the urinal bladder, the optimizer faces a very complex problem to be solved. Neither the 2 arc VMAT or IMRT manages to entirely modulate the complex inwards rifts on top of the tumour\urinal-bladder compound.

Along the rest of the PTV border, VMAT achieves better PTV conformity than IMRT, something that yields better sparing of the rectum and bladder. As seen before, at least one of the lower weighted OARs (i.e femoral heads) receives a larger dose with VMAT than with IMRT.

By analyzing the outskirts of the external volume of the patient, VMAT seems to give a slightly larger integral dose since the whole patient is covered with the 10th percent isodose level, compared to IMRT that has three smaller areas that are not covered in any isodose percentage.
The tonsil 2 case was optimized with Original IMRT objectives (figure 49) with the addition of the surrounding dose fall off objective, increased priority weight for Medulla spinalis and the use of the Uniform dose objective to the PTV instead of “traditional” max- and min dose objectives. Tumour overlap was set to off and a 15° collimator angle was found to be most effective.

Figure 49. Associated dose volume objectives for VMAT (left) and IMRT (right) used in the Tonsil 2 case. The VMAT plan included the use of the surrounding dose fall off objective to the external volumes, and the removal of the original IMRT Parotis Dx objective.
Better PTV coverage and sparing of the medulla spinalis was evident for 2 arc VMAT as shown in figure 50. The parotid glands were subject to slightly higher doses, especially Parotis Dx. The VMAT 2 arc used a total of 759 monitor units while IMRT used 597, which is consistent with the foundings of Alvarez-Moret et al (2010), that while single arc technique requires the lowest MU per fraction dose, the 2 arc VMAT results in higher or similar MU as IMRT.
Figure 51. Side by side isodose comparison for the tonsil 2 case, with 2 arc VMAT (left) and IMRT (right).
The patient CT is oriented feet to head. The central bean shaped contour is the PTV. The ring shaped contour below the PTV is the medulla spinalis and the smaller contours on each side of the PTV are the parotid glands.

The CT slice from figure 51 above indicates improved target coverage and homogeneity for 2 arc VMAT compared to IMRT. The sparing of the medulla spinalis in the VMAT case is done with very high precision boundaries with the 23 Gy isodose, while the IMRT 32.2 Gy isodose actually is found within the medulla spinalis region. Parotid glands appear equally spared by VMAT and IMRT judging from this axial CT slice.