Aspects of Treatment Quality in Modulated Radiation Therapy

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Author's Contribution

This thesis is based upon work published in the following articles:

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J Hofmaier, S Kantz, M Söhn, O S Dohm, S Bächle, M Alber, K Parodi, C Belka, and M Niyazi. "Hippocampal sparing radiotherapy for glioblastoma patients: a planning study using volumetric modulated arc therapy". In: *Radiation Oncology* 11:118 (2016)

A Troeller, S Garny, S Pachmann, S Kantz, S Gerum, F Manapov, U Ganswindt, C Belka, and M Söhn. "Stereotactic radiotherapy of intrapulmonary lesions: comparison of different dose calculation algorithms for Oncentra MasterPlan®". In: *Radiation Oncology* 10:51 (2015)

A Jahnke, L Jahnke, F Molina-Duran, M Ehmann, S Kantz, Volker Steil, Frederik Wenz, G Glatting, F Lohr, and M Polednik. "Arc therapy for total body irradiation - A robust novel treatment technique for standard treatment rooms." In: *Radiotherapy and Oncology* 110.3 (2014), pages 553–557

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Contents

Abbreviations

3DCRT 3D conformal radiation therapy

CT computed tomography

CTV clinical target volume

dMLC dynamic sliding window

DVH dose-volume-histogram

EPID electronic portal imaging device

EUD equivalent uniform dose

GTV gross tumor volume

IMRT intensity modulated radiation therapy

linac linear accelerator

MLC multi-leaf collimator

MU monitor units

NTCP normal tissue complication probability

OAR organ of risk

PTV planning target volume

QA quality assurance

sIMRT step-and-shoot or static IMRT

TCP tumor control probability

TPS treatment planning system

VMAT volumetric modulated arc therapy

Abstract

Improvements in computational power eventually led to intensity modulated radiation therapy (IMRT) and volumetric modulated arc therapy (VMAT) techniques. Since these techniques offer many degrees of freedom, the choice of the treatment technique, the planning system, the characteristics of the linear accelerator (linac) and the quality assurance (QA) of the dose delivery are still discussed extensively. This thesis contributes to resolving the main concerns of treatment technique, linac properties in terms of the MLC as well as the QA potentials of commercially available 2D arrays with respect to plan-individual QA and linac-oriented QA procedures.

First, a planning study, using constraint optimization and biologically oriented constraints, was designed such that the impact of the treatment delivery technique (static IMRT, dynamic IMRT, VMAT) as well as the impact of major MLC design characteristics (leaf width, interdigitation, leaf velocity) could be studied by means of dose to the tumor (i.e. planning target volume - PTV) and plan characteristics, especially delivery time. It is shown that the delivery technique has a larger impact on planning target volume (PTV) coverage and treatment time than MLC design features. However, an improved MLC design (especially smaller leaf width, higher leaf velocity and reduced transmission) contributes to better PTV homogeneity and mean dose as well as to faster treatments for all techniques.

Arrays of ion chambers or diodes are frequently used for the plan-individual QA. By example of a head and neck case, the ability of three commercially available 2D arrays and the subsequent evaluation with the widespread gamma method was investigated to determine the extent to which MLC or dose miscalibrations can be revealed, as second part of the thesis. Introduced errors of 1mm leaf miscalibration had already a large impact on the dose distribution inside the patient, but the widely used gamma-evaluation with the $3\%/3mm \leq 95\%$ criterion did not detect these changes in the dose distribution using either array for the measurement.

On the basis of these results, the complexity of IMRT and VMAT plans was decomposed into their single components with suitable tests. Each array revealed specific shortcomings with respect to small dose measurements and steep gradient resolution, which lead to a different suitability for different checks for the regular verification of the MLC calibration and complex plans with large number of small dose segments or low dose rate delivery. Additionally, linac delivery limitations were found during ramp up and while very low dose rate delivery. These results imply that plan-individual QA - at least based on the measurement with arrays - might be inadequate for some plans. On the other hand, the used arrays are suitable for constancy checks of the linac with respect to all important delivery parameters for IMRT and VMAT.

Zusammenfassung

Verbesserungen der Rechenleistung führten zur intensitätsmodulierten Strahlentherapie (IMRT) und volumetrischen modulierten Strahlentherapie (VMAT). Da diese Techniken viele Freiheitsgrade bieten, wird weitläufig noch über die beste Technik, das Planungssystem, die Eigenschaften des Beschleunigers und die Qualitätssicherung (QA) der Bestrahlung diskutiert. Die vorliegende Arbeit trägt zu diesen wesentlichen Punkten im Hinblick auf die verwendete Bestrahlungstechnik, den Viel-Lamllen-Kollimator (MLC - multi-leaf collimator) sowie das Potential von handelsüblichen 2D-Arrays für plan-individuelle QA und beschleunigerorientierte QA-Verfahren bei.

Zunächst wurde eine Planungsstudie mit Einschränkungsoptimierung (constrained optimization) und biologisch orientierten Optimierungsgrenzen so konzipiert, dass die Auswirkungen der Bestrahlungstechnik (statische IMRT, dynamische IMRT, VMAT) sowie die Auswirkungen von grundlegenden MLC-Konstruktionsmerkmalen (Lamellenbreitebreite, Interdigationsfähigkeit, Lamellen-Geschwindigkeit) anhand der Dosis im Tumor (d.h. im Planungszielvolumen - PTV) und den Planeigenschaften, wie insbesondere der Abstrahlzeit, evaluiert werden können. Es zeigt sich, dass die Bestrahlungstechnik einen größeren Einfluss auf die PTV-Abdeckung und die Bestrahlungszeit hat als MLC-Konstruktionsmerkmale. Dennoch trägt ein verbessertes MLC-Design (insbesondere kleinere Lamellenbreite, höhere Lamellengeschwindigkeit und reduzierte Transmission) zur besseren PTV-Homogenität und PTV-Dosis sowie zur schnelleren Bestrahlungszeit für alle Techniken bei.

Für die plan-individuelle QA werden häufig Arrays mit Ionisationskammern oder Dioden verwendet. Beispielhaft wurde in einem zweiten Projekt für einen HNO-Plan die Eignung von drei handelsüblichen 2D-Arrays untersucht, inwiefern MLC- oder Dosisfehlkalibrierungen messtechnisch festzustellen sind. Zur Auswertung wurde die weit verbreitete Gamma-Index-Methode verwendet. Eingeführte Fehler von 1mm Lamellen-Fehlkalibrierung haben bereits großen Einfluss auf die Dosisverteilung innerhalb des Patienten. Diese wurden jedoch von der Gamma-Auswertung mit dem oft verwendeten $3\%/3mm \leq 95\%$-Kriterium bei der Messung mit keinem der Arrays entdeckt.

Auf Grundlage dieser Ergebnisse wurde die Komplexität von IMRT- und VMAT-Plänen mittels geeigneter Tests in ihre Einzelkomponenten zerlegt. Jedes Array zeigte spezifische Mängel in Bezug auf die Messung kleiner Dosen und steiler Dosisgradienten, die zu einer unterschiedlichen Eignung der Arrays für die regelhafte Überprüfung der MLC-Kalibrierung und komplexer Pläne mit einer großen Anzahl an Segmenten mit kleinen Dosen oder einer niedrigen Dosisleistung führen. Darüber hinaus wurden Einschränkungen des Beschleunigers während des Einschaltprozesses und beim Strahlen mit sehr niedriger Dosisleistung gefunden. Diese Ergebnisse implizieren, dass plan-individuelle QA - zumindest bei Messung mit Arrays - für einige Pläne unzureichend sein könnte. Andererseits sind die verwendeten

Arrays für Konstanzprüfungen des Beschleunigers für alle wichtigen Bestrahlungsparameter bei IMRT und VMAT geeignet.

1 Introduction

Radiation therapy evolved quickly in the last 20 years due to large improvements of computational power, which made

- routine use of computed tomography (CT) for treatment planning,
- routine use of multi-leaf collimators (MLCs) in digital linacs to better conform the dose to the tumor,
- dose calculation based on CT, and increasing use of Monte Carlo methods and
- efficient (inverse) optimization algorithms for treatment planning systems (TPSs)

available.

Large improvements in treatment technique followed. While in former times, the treated volume was scarcely conformed to the tumor, conformance is not only very well today but also dose painting (different dose levels for different tumor areas) and almost online adaptive treatment planning (adapting dose to the actual geometry of the patient shortly before or during the daily treatment) are possible.

These advancements formed modern treatment techniques, which can be summarized as modulated radiation therapy techniques: these comprise IMRT in static (step-and-shoot or static IMRT - sIMRT) and dynamic (dynamic sliding window - dMLC) mode as well as VMAT (volumetric modulated arc therapy).

With these technical improvements, the requirements for the quality assurance (QA) of the treatment chain (fig. 1.1) from CT over TPS to dose delivery at the linac increased and the dose engines, which calculate the dose on the planning CT, got more sophisticated. Additionally, modulated radiation therapy techniques introduced dose delivery based on superimposed often small beams, which are formed by the MLC of the linac.

The presented thesis comprises studies with respect to treatment planning and the QA of the dose delivery by the linac. Especially the influence of the treatment technique and MLC (as part of the linac properties) as well as the measurement device and its potential impact on QA philosophy are regarded.

1.1 Modulated radiation therapy techniques

Within the group of modulated radiation therapy techniques, step-and-shoot or static IMRT (sIMRT) is the closest to the most often used technique of 3D conformal radiation therapy (3DCRT). In 3DCRT, tumor (gross tumor volume - GTV) and organs of risk

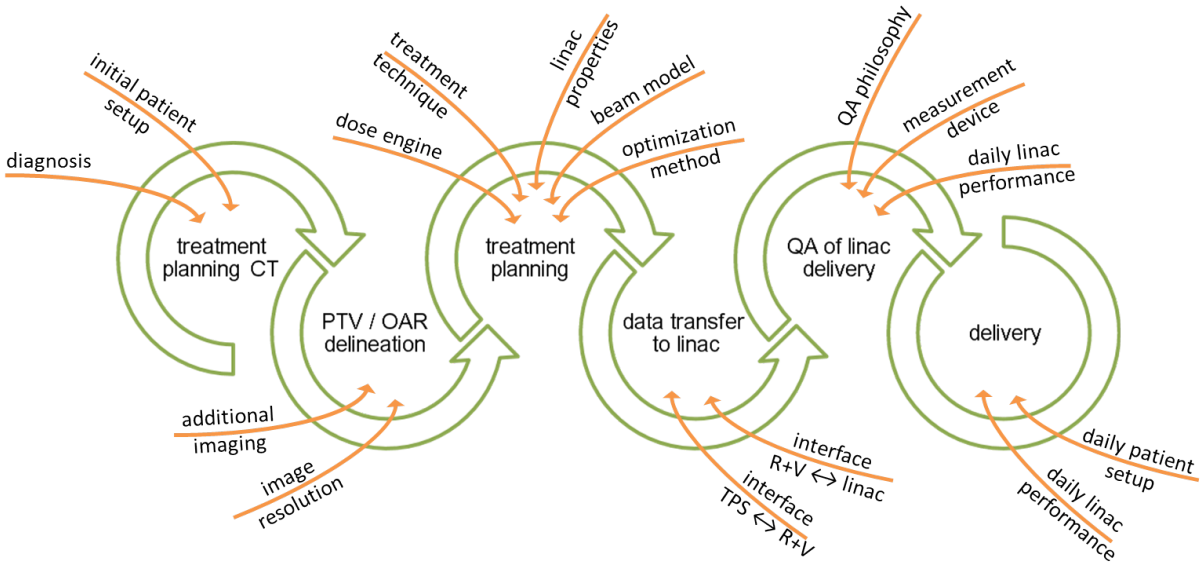

Figure 1.1: *Treatment chain from treatment planning to delivery (green), including main factors (orange) affecting treatment and plan quality.*

(OARs) are contoured on a 3D CT dataset of the patient. With margins for microscopic disease (clinical target volume - CTV), patient movement and setup inaccuracies a PTV is generated (fig. 1.2). The physician decides about the dose to the PTV and OARs. The physicist decides about entrance directions, shape and intensity of the beams (fields), such that the physician's intent is fulfilled. This results in simple to low complexity plans with one to about 10 to 15 single fields. The main delivery property in 3DCRT is that all parts of the treatment device (linac) are fixed while one field is being delivered (tab. 1.1).

Also in sIMRT, the beam is only switched on while all linac parts are fixed. In contrast to 3DCRT, the dose to the PTV can be better conformed in sIMRT, as optimization algorithms divide one field into several sub-fields (segments). Therefore, this so called "step and shoot" IMRT superimposes not only the fluence from several directions (3DCRT) but also the fluence of several differently shaped beams for one direction (tab. 1.1). Thereby, the fluence from one direction is no longer limited to the simple beam profile (flat or wedged), but can be modified using differently shaped beams with different intensity. As this approach enables better conformance to complex (especially concave) formed tumors, OARs can be spared more efficiently. This makes additional tight (daily) setup control of the patient necessary, which - by itself could also possibly result in the confidence that reduced PTV setup margin can be used and thereby an even more conformal treatment can be planned. Still, dose is only delivered while all parts of the linac are fixed which results in longer treatment times compared to 3DCRT.

In contrast to sIMRT, dose in dMLC mode is delivered while the radiation beam is switched on (from one fixed gantry position). This means that the beam is no longer paused to change the field size but the fluence is delivered by sweeping the beam limiting devices

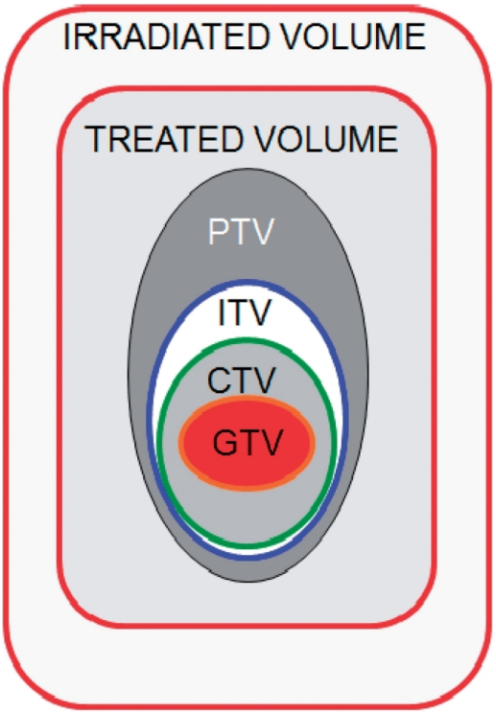

Figure 1.2: *Volume definition according to ICRU 62 [1].*
gross tumor volume (GTV) = gross tumor volume: macroscopic tumor
clinical target volume (CTV) = clinical target volume: GTV + margin accounting for microscopic tumor
ITV= internal target volume: CTV + margin accounting for tumor motion (especially used for stereotactic treatments of lung and liver)
PTV = planning target volume: ITV + margin accounting for patient motion, daily setup uncertainties and linac delivery uncertainties
treated volume = volume covered by dose, which is regarded appropriate to achieve the purpose of treatment (often 95% of the prescribed dose to the PTV)
irradiated volume = volume receiving dose that is considered significant for normal tissue

Table 1.1: *Differences between 3DCRT and modulated treatment techniques*

technique	fluence division into segments (subfields)	dose rate variation while beam-on	moving linac parts while beam-on
3DCRT	no	no	none
sIMRT	yes	no	none
dMLC	yes	yes	MLC
VMAT	yes	yes	MLC, gantry

(MLC and jaws) across the field and simultaneously controlling the dose rate between two control points (tab. 1.1). These control points can be regarded as start and end point of one segment. Therefore, dMLC adds the complexity of changing field size and variable dose rate, which fastens the treatment. The dynamic delivery also challenges the dose computation since instead of static, clearly defined beam outlines and MU, the dose has to be calculated from the partial leaf opening which depends on the actual leaf speed and dose rate between two control points. For two sweeping gaps of the same width to deliver the same dose across the field with different dose rates, the leaf speed has to be adapted accordingly. As the actually delivered dose rate may depend on daily and intra-treatment variation, the leaf speed has to be adapted from control point to control point during treatment and is controlled by the linac contol unit. Therefore, the fluence optimization as well as the dose computation have to challenge the estimation of the leaf movement and varying dose rate, that is only estimated by means of a sequence of control points. Furthermore, the linac control unit interprets the planned control point sequence and may merge several consecutive control points or may create new control points in between two control points initially created by the TPS. Consequently, the assumed constant leaf speed and constant dose rate between two planned control points may not be delivered as planned and thereby result in dose delivery different from the planned dose distribution.

Additionally to dMLC, the gantry is moving and changing its speed in VMAT mode, meaning that not only the beam shape and dose rate, but also the gantry position are controlled simultaneously (tab. 1.1). This makes treatments in VMAT technique potentially even faster than dMLC delivery. On the other hand, the moving gantry adds another degree of complexity to the delivery and optimization in the same manner as described above for dMLC delivery. Therefore, VMAT can be regarded as more complex than the introduction of changing field outline in dMLC (compared to sIMRT) alone, as both the leaf speed and the gantry speed have to be synchronized with the dose rate and its variations. This complexity in treatment technique has to be evenly adapted into a clinical QA routine procedure.

1.2 Design components of multi-leaf collimators

Multi-leaf collimators (MLCs) are used to define the field outline of the radiation beam. MLCs consist of two opposing leaf banks on which several small “leaf-like” absorbers, that can be moved almost independently, are mounted. Perpendicular to the leaf travel direction, one large jaw is mounted per side. Important for the plan generation are the leaf travel limits, width of the leaf, its transmission through leaf body, leaf tip, adjacent (tongue-and-grove) and opposing leaves (minimal leaf gap). Important for the treatment time is the leaf travel velocity. An overview of MLC components and design is shown in figure 1.3.

The leaf width is essential with respect to conformance and OAR sparing as larger leaves may not effectively block small structures. Too narrow leaves on the other hand will not effectively block radiation. Leaf travel limits have to balance weight and construction limits

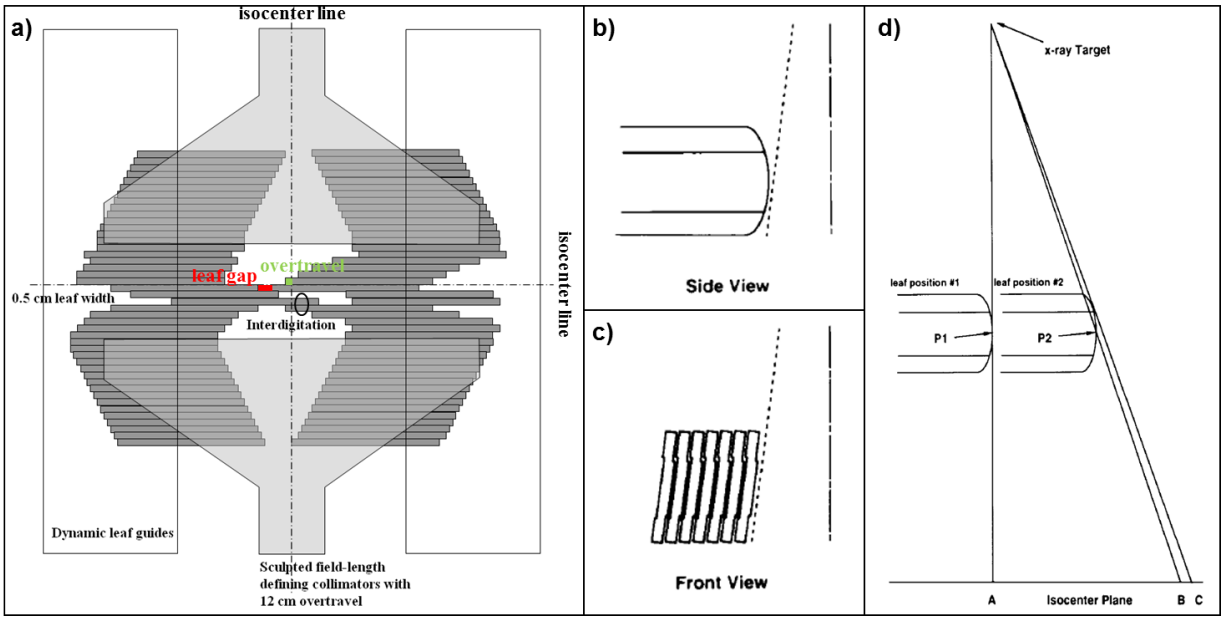

Figure 1.3: *MLC design and components.*
a) schematic beams eye view of the Elekta Agility MLC (drawing adapted from [2])
b, c, d) additional design components of a MLC influencing transmission (redrawn from [3])
b) schematic diagram of rounded leaf end shape
c) example of tongue-and-groove design between adjacent leaves
d) schematic drawing of the influence of the leaf position to the leaf and beam ray geometry

of the linac head with the MLCs functionality to deliver dose to several parts of the PTV, as often used in modulated radiation therapy. This means that a compact construction with capability to travel over the isocenter line and interdigitation is wanted, but with the least possible transmission. As transmission results in dose even to blocked regions, too large transmission will result in smaller modulation potential in the optimization and thus minor quality of the treatment plan. To prevent colliding opposing leaves - especially in dynamic mode - opposing leaves will not close beyond a minimal leaf gap. Dose through this minimal leaf gap may depend on the off-axis position and may also degrade plan quality, if large with respect to dose deposition. Therefore, backup jaws to hide the minimal leaf gap can be used instead of designing the leaves such that the dose deposition due to this gap is minimal in large off-axis positions.

2 Plan optimization of modulated radiation therapy techniques

2.1 Constrained optimization

The fluences, which should be delivered by the linac in the different techniques, are calculated based on CT data of the patient. Instead of predefining the beam shape and its fluence manually as it is done in 3DCRT, better results are obtained by inverse optimization algorithms.

Challenges of the optimization process in modulated radiation therapy are the translation of the physician's intent into optimization constraints using the given resources, which include the optimization algorithm as well as available delivery technique, linac and MLC. The physician's intent is normally given as dose (D) or volume (V) constraints ($D_{V=x\%}$, $V_{D=xGy}$), comprising minimal, maximal or mean dose as well as percentage of volume not to exceed a certain dose. These constraints can be either translated as one point in the dose to volume relation (dose-volume-histogram (DVH))[4] (fig. 2.1a) or as function of the whole DVH curve (fig. 2.1b+c). The latter is often related to biological models of radiation effects in tissue expressed as tumor control probability (TCP) and normal tissue complication probability (NTCP). To approximate the radiation effects, the inhomogeneous dose distributions - especially in OARs - are converted into equivalent uniform dose (EUD) [5–7]. This uniform dose is supposed to cause the same NTCP (or TCP) as the real inhomogeneous dose. Depending on the response of tissue to radiation, a tissue specific factor within the model is tuned. While single DVH point constraints might not be representative for the dose distribution of a single OAR and introduce local minima in the objective function, EUD based constraints are able to control the whole DVH and can be related to the biological effect of the delivered dose, even though more evidence for the dose-effect-relationship is necessary [8]. Further enhancement can be accomplished by constrained optimization. This method guarantees the given constraints while maximizing dose to the tumor under the given constraints. Using cost functions, which are able to control the DVH, instead of single point DVH constraints, the optimization is more efficient and the input parameters better relate to the physician's intent. [9]

Compared to 3DCRT, modulated delivery techniques have shown to improve either TCP or NTCP or both using diverse optimization algorithms and different MLCs [11–27]. On the one hand, this is possible due to improvements in treatment technique, as non-flat fluences better conform to the PTV and improve the homogeneity inside the PTV. On the other hand, delivery improvements with modern linacs result in more conformal

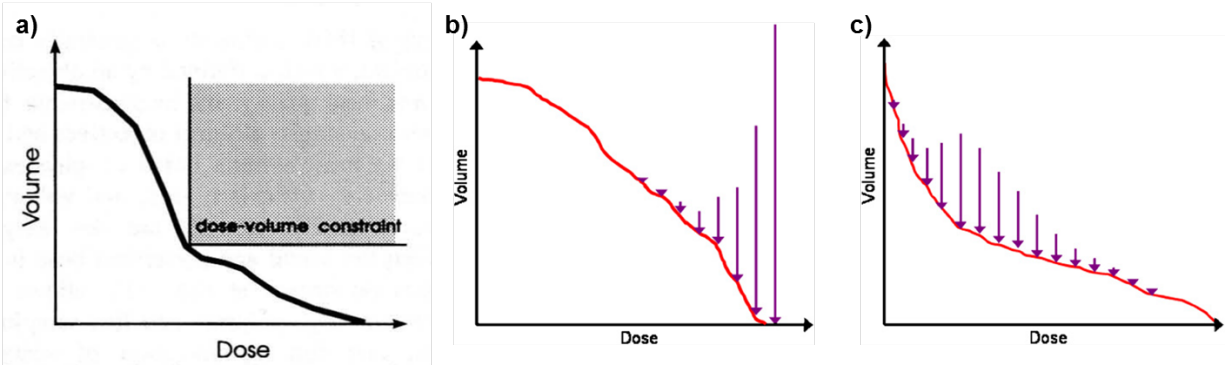

Figure 2.1: *Influence of different definitions of constraint functions to the DVH.*
a) simple dose-volume constraints impact on one single point of the DVH (redrawn from [4])
b) constraint reducing the maximal dose using a serial dose-effect-relationship and thereby controlling the high dose part of the DVH with increasing weight towards higher doses, as indicated by the arrows (redrawn from [10])
c) constraint reducing a given dose-volume-relation using a parallel dose-effect-relationship and thereby controlling large parts of the DVH, with an increasing weight towards the given dose-volume-relation, as indicated by the arrows (redrawn from [10])

treatments, because of smaller MLC leaf width, which better conforms to complex-formed PTVs and blocks OARs more effectively. Furthermore, the ability of the MLC and linac to deliver the treatment faster due to higher leaf speed and higher dose rate enables smaller safety margins, as the patient and its organs have less time to move. So far, studies have investigated either the impact of treatment technique or MLC to certain treatment sites. As studies were undertaken by several authors, the used techniques, resources (like TPS, beam model or optimization algorithm), linac-MLC-combinations and reported parameters were different. Therefore comparability as well as conclusions about the impact of the treatment technique and the MLC are limited.

2.2 Impact of technique and MLC

Isolating the impact of the treatment technique and advancements due to MLC improvements, plans should be generated using the same beam model and optimization regime. Therefore, a treatment planning study was conducted for medium to challenging prescriptions, to assess plan quality in terms of target coverage, dose to critical OAR and clinically important plan parameters. Depending on the used technique and used MLC, the optimization has different degrees of freedom. One aim of this thesis was to quantify the impact of delivery technique and MLC with respect to plan quality in terms of dose to the tumor, sparing of OARs and treatment time. Nine plans with all combinations of sIMRT, dMLC and VMAT with three different MLCs for five meningioma and five head-and-neck

patients were evaluated.

The research treatment planning system (TPS) Hyperion (University of Tübingen, research tool to the commercially available TPS Monaco) was used, as constrained optimization guarantees the physician's intent, introduced as cost functions into the optimization. Besides fulfilling the constraints while maximizing dose to the PTV, this TPS offers biologically related cost functions. In the beginning of the optimization, the constraints were set such that the physicians intent was achieved. In the following optimization steps, the constraints were tightened where possible such that the PTV was just covered by the prescribed dose. This can be achieved by running the optimization with harder constraints compared to the physician's intent, such that each constraint can just be fulfilled instead of being loose and offering tolerance for the optimization. All constraints were found for the plan with the highest degrees of freedom, which was a VMAT plan using a MLC with 0.5 cm leaf width and with interdigitating capabilities.

The presented planning study (author's contribution A) provides the first study to distinguish the influence of the delivery technique and the MLC by largely eliminating the influence of the optimization and dose calculation algorithms. By using constraint optimization and tightly restricting the dose to organs at risk during the optimization, the effects of treatment delivery technique (sIMRT, dMLC, VMAT) and different MLC designs on tumor dose and treatment time were studied. It was found that the delivery of VMAT is fastest without sacrificing dose to the tumor or OAR constraints. In conjunction with small and fast driving leaves, the delivery is not only accelerated, but also improved with respect to PTV dose. As intended by the use of constraint optimization, dose to OARs was the same for all generated treatments plans for each patient, while mean dose and dose homogeneity as well as treatment time improved with more complex techniques (sIMRT<dMLC<VMAT). However, the influence of the MLC design is smaller than the influence of the delivery technique. While interdigitation does not add much to the plan quality in terms of the dose distribution, it may reduce treatment time for some (complex) cases and thereby enhances delivery efficiency. Smaller leaf width, on the other hand, improves dose homogeneity to the tumor as well as PTV mean dose, if small structures in the vicinity of the PTV have to be spared. Especially faster leaf speed accelerates the treatment time, which largely improves patient comfort and minimizes organ motion during treatment.

Author Contribution

For this planning study, the first author (=author of this thesis) is responsible for the the manuscript draft, the concept of the study, patient enrolment, plan generation, data collection and acquisition as well as literature revision with contributions of co-authors to each part as defined in the publication.

3 Quality Assurance of modulated treatment plans

3.1 Setup of treatment planning system

Since calculated dose distributions are virtual, the correct delivery by the linac has to be verified. Starting with the correct beam model in the TPS and the correct data transfer to the linac, the delivery by the linac itself as well as the suitability of the measurement device has to be guaranteed.

The beam model inside the TPS characterizes the linac and provides the base for the dose calculation engine, which calculates based on the CT data how dose is delivered to the patient (fig.3.1). To characterize the linac, measurements of square fields are collected in a large water phantom with single detectors. The measurements include depth dose profiles and profiles across the middle axes of the field in several depths. Mainly ion chambers and diode detectors are used. While ion chambers lack resolution in steep penumbra regions due to the volume averaging effect, shielded diodes may overestimate dose due to low energies in out-of-field-regions and large depths due to the density perturbation effect. Especially small fields should therefore be measured with more than one detector [28]. For all modulated techniques, but especially for dynamic techniques, MLC parameters concerning transmission through the leaf tip, the leaf body, adjacent leaves (tongue-and-grove) and small leaf gaps between opposing leaves (minimal leaf gap) as well as leaf scatter contributions have a large impact on the agreement of the calculation with the measurement of IMRT plans. [29]

The calculated plan is expressed in control points, with each one defining the position of the gantry, jaws, leaf positions and delivered dose in terms of monitor unitss (MUs). These control points are stored in a DICOM-RT plan file, which will be interpreted by the linac control unit. A linac log file stores surrogate values for each parameter (e.g. potentiometer values) while treatment. These surrogate values of the log file can be translated into a "delivered" DICOM-RT plan file, which can be compared to the original DICOM-RT plan file. Since this plan verification approach may suffer from timely uncertainties of the treatment log frequency and potential miscalibrations, measurements of the treatment plan are still the most often used plan verifications.

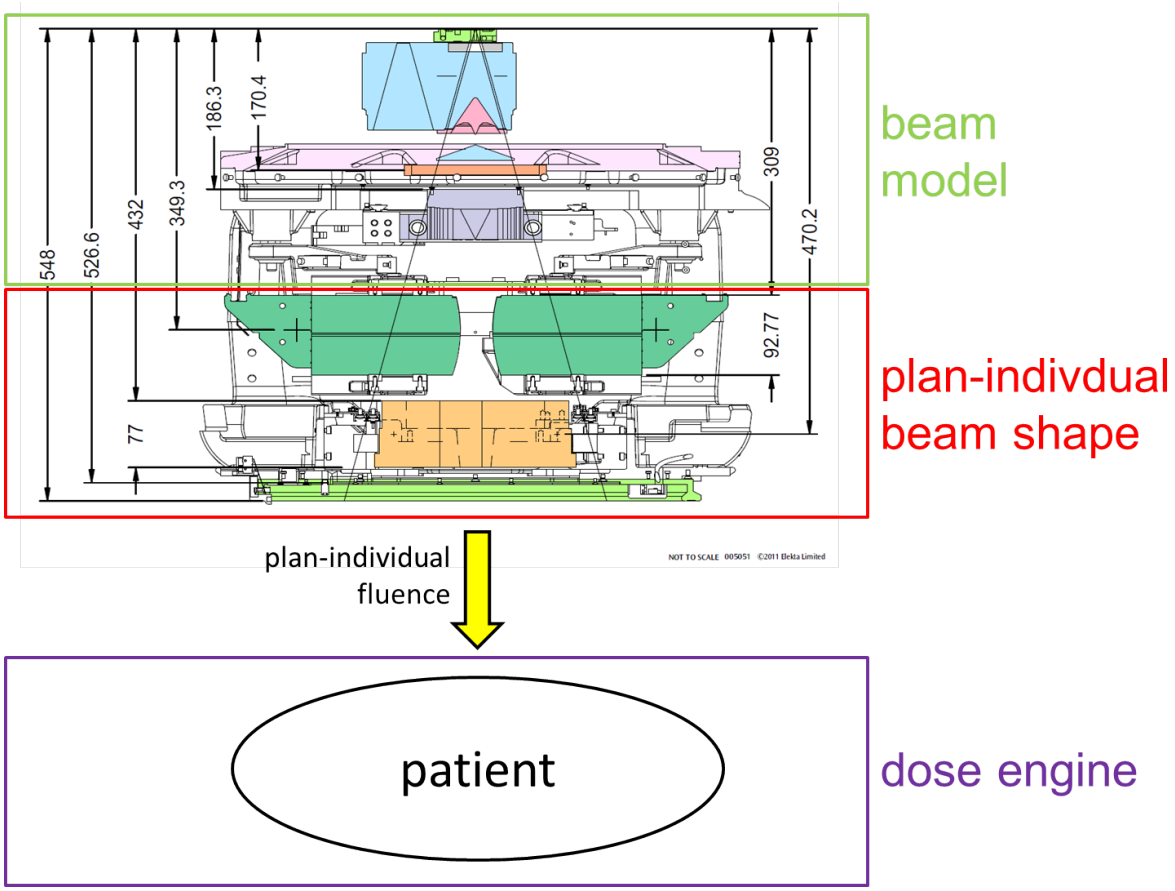

Figure 3.1: *schematic overview of the treatment delivery head and its simulation parts in the treatment planning system.*
The beam model handles the constant parts, e.g. energy; the plan-individual beam shape is optimized based on the MLC properties. This gives the plan-individual fluence, which is used by the dose engine to calculate the dose distribution on the patient based on the treatment planning CT (drawing adapted from [30]).

3.2 Measurement devices

In the beginning of IMRT, relative film measurements in one plane in combination with a one point ion chamber measurement to check the absolute dose were used. As film measurements are time and cost intensive and one point ion chamber measurements may lack accuracy in steep dose gradients, multi-detector 2D arrays were invented and used instead. For the QA of sIMRT and dMLC, these 2D arrays were mostly not irradiated from the originally planned gantry angle but from gantry angle 0°, as this was easy to accomplish by setting up the measurement device on the table top. With the advent of VMAT, QA methods including gantry movement became necessary, as gantry speed, dose rate and leaf speed influence each other. One possibility is to attach the used 2D array to the gantry. A second approach is to use the electronic portal imaging device (EPID) for dose measurement, which was originally introduced for the patient setup verification. Furthermore, so-called 3D arrays, which are different cylindrical measurement devices for the rotational needs of VMAT, were introduced with different detector arrangements (diode detectors beneath the surface, two crossed 2D diode arrays in the middle of the cylinder, rotating cylinder with one 2D ion chamber array in the middle).

EPIDs consist of amorphous silicon photodiodes behind a film transistor and scintillator material. Cumbersome calibrations are necessary to convert the measured signal to dose, as EPIDs are energy dependent. Therefore corrections for field size, off-axis, low dose as well as dose rate, ghosting and image lag have to be introduced. These characteristics may degrade the measurement, if not studied and implemented correctly. [31–34]

In contrast to EPIDs, 2D and 3D arrays may suffer from resolution due to the volume effect (if ion chambers are used) and the distance between single measurement points as well as their geometrical arrangement. Contrary, the measurement principles are well known and can be corrected much easier, if necessary.

3.3 Linac- and plan-individual quality assurance

For 3DCRT, QA procedures monitor the basic components of the treatment delivery system, such as dose, dose linearity, dose rate linearity, profile stability in different gantry angles and correct field size. The appropriate tests are established according to national (e.g. DIN) and international (e.g. AAPM reports) guidelines. As in 3DCRT open, clearly defined fields and beam arrangements are used, effects to the patient plan in case of miscalibrations of any delivery component can be anticipated quite easily. Therefore, a linac-oriented QA procedure is regarded as appropriate.

With overlaying several open fields of varying intensity, like in sIMRT, the effects of any miscalibrations to a patient plan may not be as clear as in 3DCRT. Therefore, linac-oriented QA as was used so far for 3DCRT is regarded as insufficient and plan-individual QA was introduced. Since measurements inside the patient are not possible, the plan is irradiated to a phantom and the resulting surrogate dose distribution is analyzed - either field by field or the entire plan. Starting with cumbersome film measurements, 2D and 3D

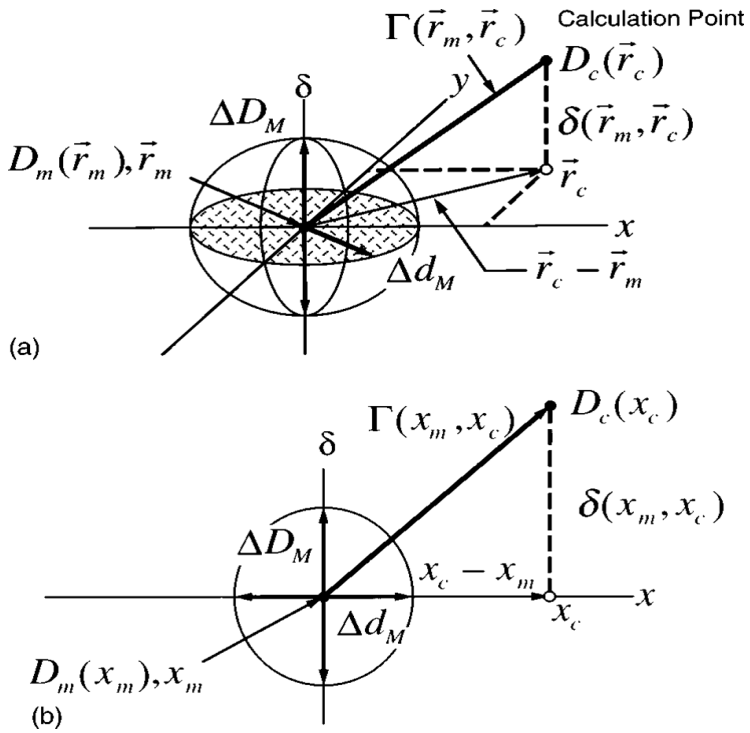

Figure 3.2: *Illustration of the* Γ*-value in a) 2D and b) 1D. (redrawn from [35])*

arrays as well as EPIDs made plan-individual QA much faster with the potential to review the whole delivered dose distribution. By measuring the delivered fluence with respect to the gantry angle, there will be no longer a limitation to a dose distribution inside a certain phantom. Instead, a "measured" dose distribution can be calculated on the planning CT and compared to the original plan calculation. As an alternative to measurements, linac-log files can be evaluated. Surrogate parameters of all linac parameters, e.g. MLC position, dose rate or gantry position, are logged, which can be used to calculate the delivered dose distribution on a CT dataset.

Regardless of the method used for plan-individual QA, the evaluation can mask shortcomings of the plan, because of the measurement itself or the dose comparison metrics.

Comparing dose distributions, the gamma-evaluation method [35] is most popular. This method combines a comparison in terms of predefined dose difference (ΔD, termed dose difference criterion) and distance (Δd, termed distance-to-agreement criterion or DTA criterion). For each dose point in the tested (e.g. measured) distribution r_m the distance $r(r_m, r_c)$ and the dose difference $\delta(r_m, r_c)$ to the reference (e.g. calculated) dose distribution within a certain radius are calculated. The geometric mean of both with respect to the predefined criteria is termed gamma value Γ (fig.3.2):

$$\Gamma = \sqrt{\frac{r^2(r_m, r_c)}{\Delta d^2} + \frac{\delta^2(r_m, r_c)}{\Delta D^2}}$$

with the geometric distance r between the measured r_m and calculated r_c dose point:

$$r(r_m, r_c) = |r_c - r_m|$$

and the dose difference δ between the measured r_m and calculated r_c dose point:

$$\delta(r_m, r) = D(r_c) - D(r_m)$$

The lowest gamma value found for one point is regarded as closest match to the reference distribution and used for further evaluation. As long as this gamma value is $\Gamma \leq 1$, the tested and reference dose point are within the predefined criteria. Subsequent to the evaluation of all single points, the percentage of all points of the distribution with $\Gamma \leq 1$ is termed as gamma pass rate γ. During the last years, the gamma pass rate calculated for $\Delta D \leq 3\%$ dose difference and $\Delta d \leq 3mm$ distance to agreement being larger than 95% of all evaluated points ($\gamma^{3\%/3mm} \geq 95\%$) got gradually established in clinical routine [36]. However, several studies show, that γ pass rates of different measurement devices are not comparable and, that tighter pass criteria (lower dose difference or smaller distance to agreement or larger pass rate or all) would be necessary to detect patient relevant delivery errors. [37–45] Furthermore, one could argue about treatment site or case specific pass criteria.

A small study with one nine field sIMRT and one nine field dMLC head-and-neck patient plan was conducted during this thesis, to show the impact of leaf and dose miscalibrations of 1 to $3mm$ and 1 to 3%, respectively, to the dose distribution inside the patient as well as to the gamma-evaluation, when measuring with three different 2D arrays. The dose distribution showed large differences, especially when altering the leaves. Leaf position manipulations of $1mm$ had larger impact on OARs than monitor units (MU) manipulations of 3%, while the difference between techniques was minimal. The change of OAR dose depends on target proximity and extent of sparing. The largest deviation was found for the spinal cord, which was surrounded by the PTV. Altering the leaves by $1mm$ already resulted in a change of the maximal dose of $3Gy$. Altering the leaves by $3mm$ changed the maximal dose of the spinal cord by $12Gy$. The mean dose in the PTV changed by at least $1.3Gy$ (sIMRT) and $2.2Gy$ (dMLC), when altering the leaves by $1mm$ (fig.3.3). Therefore, the evaluation of the measurement should reveal leaf miscalibrations of 1mm, as these can be patient relevant. The measurement with different 2D arrays and subsequent gamma-evaluation (mean of γ pass rate of the nine fields) showed different results for different arrays and that ion chamber arrays require a dose difference criterion of 2% and a distance-to-agreement criterion of $2mm$; the used diode arrays can be used with the widely used 3% and $3mm$ criterion, but with a pass rate of at least 98% for sIMRT and 96% for dMLC. Even though these results may be case specific, this study shows that the gamma-evaluation method, especially with the widely used $\gamma^{3\%/3mm} \geq 95\%$ criteria, can hide patient relevant miscalibrations. (fig.3.4)

In order to find reasons for this insensitivity of the measurements, the complexity of modulated treatment plans (sIMRT, dMLC and VMAT) was decomposed into its basic components, for which simple tests were composed. Using the same geometry for all three

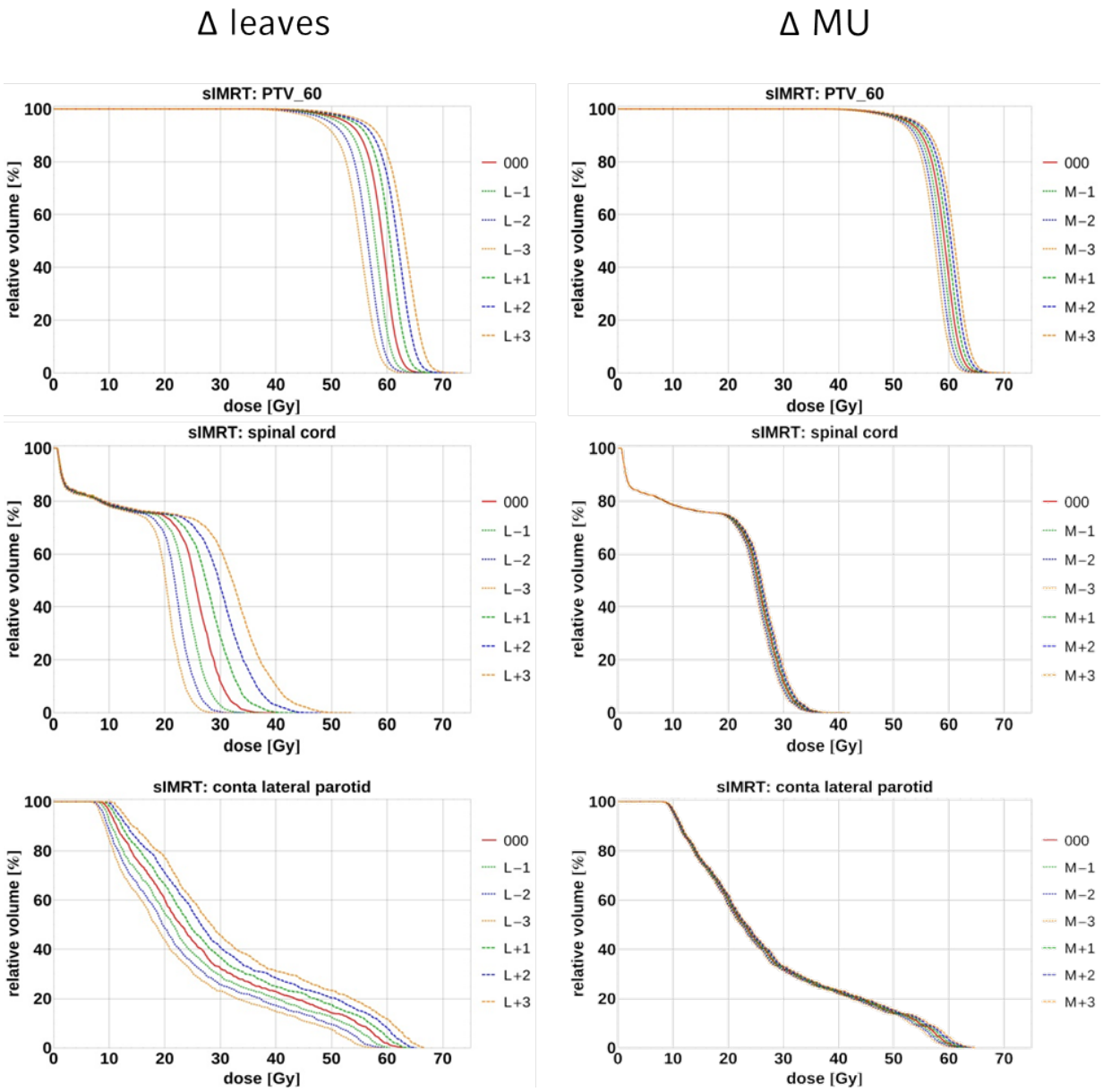

Figure 3.3: *Impact of leaf or dose miscalibration to the DVHs of the PTV, spinal cord and contra lateral parotid for on example sIMRT head-and-neck case.*
L refers to changed leaves, which were opened (+) or closed (-) by 1, 2 *or* 3*mm in each segment.*
M refers to changed dose in terms of MU, which were increased (+) or decreased (-) by 1, 2 *or* 3% *for each segment with respect to the total plan MU*

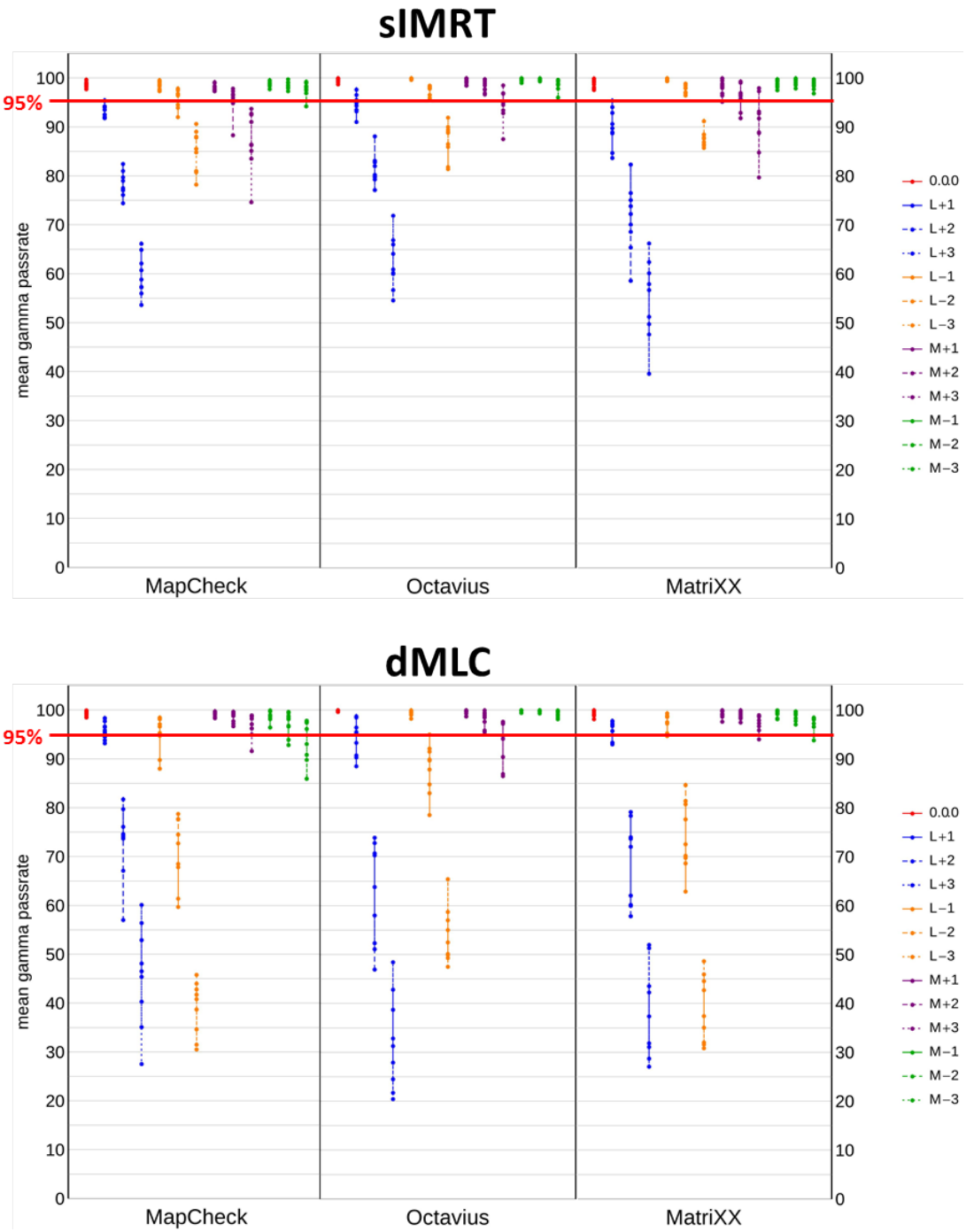

Figure 3.4: *Mean γ pass rate for the evaluated sIMRT and dMLC head-and-neck example case, when using $\Delta D = 3\%$ and $\Delta d = 3mm$ criterion. As indicated in red, 95% pass rate is not suitable to find the introduced patient relevant leaf and dose errors of $1mm$ and 2%, respectively.*

arrays that were used for the previous miscalibration study, these tests were delivered to the arrays using one single linac. Main results were verified on two matched linacs (author's contribution B).

The presented study of three of the most popular 2D arrays provides the first consistent measurements of these devices and shows influences of the device as well as linac delivery characteristics to QA results. This was achieved by decomposing the delivery complexity in modulated radiation therapy into its single components. It was found that linac instabilities exist during the ramp up phase and while delivering small dose rates. The measurement devices lack linear dose measurement for small doses and low dose rates to different extent. Especially in plan-individual QA, these aspects need to be considered as parameters that may degrade either the plan delivery in general, the measurement or the obtained results so that, eventually, the plan-individual QA procedure might be non-meaningful. Therefore, plan QA should already start while planning by considering linac delivery constraints during the optimization process. Furthermore, tight linac-oriented QA, that checks the limits used during plan generation, can provide enough confidence about the correct plan delivery without extensive and only partially meaningful plan-individual QA.

Author Contribution

For this study of measurement devices, the first author (=author of this thesis) is respnsible for the the manuscript draft, the concept of the study, measurement paradigms, data collection, aquisition and analysis as well as literature revision. Co-authors contributed to single sections and detailed question of each part. All co-authors read and approved the manuscript.

4 Conclusion

Two of the main quality concerns in planning of modulated treatment techniques were investigated: The impact of MLC properties and delivery technique and the potential of current measurement devices for effective quality assurance.

Treatment plan quality, only judged by the dose distribution calculated on CT, is affected to a higher degree by the use of more complex techniques like VMAT than by MLC design. Including patient comfort and organ motion during treatment into the evaluation of plan quality, MLC improvements like fast driving leaves are essential as well as this will shorten treatment time.

Furthermore, the correct delivery is a crucial criterion for plan quality as the dose distribution is assumed to be delivered as planned. Effective QA methods should thus include the characteristics of the measurement device in case of plan-individual QA. In contrast, evaluating shortcomings of the delivery in advance and including these findings into the treatment planning process offers the opportunity for improved plan delivery quality based on tight linac QA instead of time-consuming plan QA and re-planning in case of failing plan QA.

To date, neither efficient linac QA nor plan constraints that consider delivery and measurement shortcomings during the planning phase are implemented into routine QA procedures. While the discussed linac QA methods using 2D arrays have proven to be meaningful, these tests have to be implemented into clinical routine workflow additionally to known plan QA. To fully abandon plan QA and rely on the suggested extended linac QA, exact plan and plan QA inspection will be necessary to distinguish between non-optimal plan generation, degraded plan delivery, measurement or evaluation method. This can eventually lead to eliminating plans with poor delivery quality during the planning process and to increased confidence in linac QA.

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